UNSW SYDNEY | Australia's Global University

Centre for Healthy Brain Ageing (CHeBA)

COSMIC: Cohort Studies of Memory in an International Consortium

NEWSLETTER | April 2020

Dear COSMIC friends,

We hope that you, your colleagues and families are remaining safe during the COVID-19 pandemic. Now with your teams working from home we are even more grateful than usual for your continued support of COSMIC, by sending data or responding to questions from project workgroups. Some of you have indicated that there may be delays in providing data, which is perfectly understandable with the transition to different working conditions.

Below is an update about the current 24 COSMIC projects, which are at various stages of progress, from data being obtained to having manuscripts under review. Unlike last year at AAIC, this year we may not meet to present and discuss our projects, but are looking forward to the day when we can do so.

Regards,

Darren Lipnicki, Perminder Sachdev, and the Sydney team.

Scientia Professor Perminder Sachdev AM (Co-Director, CHeBA)

Dr Darren Lipnicki (Study Co-ordinator, COSMIC)

CHeBA Healthy Brains Positive Ageing

1. Relationship between body mass index and cognitive decline

Workgroup leader: Steve Makkar (CHeBA, UNSW)

Included studies: Bambui, CHAS, EAS, ESPRIT, HELIAD, Invece.Ab, KLOSCAD, MoVIES, PATH, SALSA, SGS, SLASI, Sydney MAS.

Aims: Examine the association between body mass index (BMI) and the rate of prospective decline on general cognition and memory. Investigate whether this association:

a. Differs between sexes.
b. Is moderated by (baseline) age.
c. Differs depending on carriage or non-carriage of the Apolipoprotein epsilon 4 (APOE*4).
d. Is influenced by vascular risk factors.
e. Differs between ethnicities, namely Whites and Asians

Findings: Specific to older-aged (i.e., 80-year old) elderly female adults, higher BMI was associated with attenuated decline of general cognition, and obese (i.e., BMI≥30 kg/m^2) participants displayed a significantly slower rate of general cognitive decline compared to lower-normal participants. Between-sex comparisons indicated that both effects were significantly larger in women than men. BMI was not associated with cognitive decline in men overall. The association between BMI and decline of either general cognition or memory did not differ between APOE*4 carriers and non-carriers. The analysis of vascular risk factors indicated that the relationship between higher BMI and slower MMSE decline observed in older women was significantly weakened by the presence of vascular risk factors. Also, in this group, vascular risk factors counteracted the reduction in memory decline at higher BMI cut-points. In terms of ethnoregional differences:

a. There was a stronger association between higher BMI and attenuation of memory decline, and a larger protective effect of obesity against MMSE decline in older Asian women versus White women.
b. Although BMI was unrelated to cognitive decline in men as a whole, we found different effects of upper-normal weight (i.e., 23≤BMI<25 kg/m^2) on MMSE decline in older Asian and White men. Namely, upper-normal weight was more strongly related to MMSE decline in Asians compared to Whites.
c. Overweight men (25≤BMI<30 kg/m^2) also displayed a significantly slower rate of MMSE decline than lower-normal weight men among Whites, but not Asians.

Status: Manuscript rejected by *Neurology, Journal of Gerontology: Medical Sciences.* Being revised for submission to a new journal.

2. Apolipoprotein E4 and cognitive decline: the moderating roles of sex, age, and ethnicity

Workgroup leader: Steve Makkar (CHeBA, UNSW)

Included studies: Bambui, CFAS, CHAS, EAS, ESPRIT, HELIAD, HK-MAPS, Invece.Ab, KLOSCAD, LEILA75+, MoVIES, PATH, SALSA, SLASI, Sydney MAS.

Aims:

1. Examine if carriage of the Apolipoprotein E ε4 (APOE*4) allele is associated with decline of general cognitive functions and memory in late adulthood, and if this effect is dose-dependent.
2. Investigate if the effect of APOE*4 on general cognitive and/or memory decline is moderated by:
    a. Age
    b. Sex
    c. Vascular risk factors
3. Examine if the effect of APOE*4 on general cognitive and/or memory decline differs between ethnicities, namely Asians and Whites.

Findings: APOE*4 carriage was related to faster general cognitive decline in women and men, and faster memory decline in men. However, carriage of two versus one APOE*4 alleles was associated with faster general cognitive and memory decline in men only. Significant effects in men were specific to the older-aged (i.e., 80-year-old) participants. Furthermore, the negative effects of carrying two versus one APOE*4 allele on general cognitive decline worsened with age in men more than women. Increasing numbers of vascular risk factors worsened the effects of APOE*4 carriage on general cognitive decline in *younger-aged* participants, with the effect being significant in women. In contrast, increasing numbers of vascular risk factors decreased the effects of APOE*4 carriage on general cognitive decline in older-aged participants, with the effect being significant in men. Regarding ethnoregional differences, in older-aged participants, APOE*4 had a stronger effect on memory decline in Asians versus Whites. Also, increasing numbers of vascular risk factors attenuated the effects of *APOE*4* on MMSE decline in Asians, but not Whites.

Status: Manuscript accepted for publication by *Journal of Gerontology: Biological Sciences* (April 13).

3. Relationship between education, apolipoprotein epsilon 4 (APOE*4) and cognitive impairment

Workgroup leader: Steve Makkar (CHeBA, UNSW)

Included studies: Bambui, CFAS, CHAS, EAS, ESPRIT, HELIAD, HK-MAPS, Invece.Ab, KLOSCAD, LEILA75+, MoVIES, PATH, SALSA, SGS, SLASI, Sydney MAS, Tajiri, ZARADEMP.

Aims:

1. Examine whether years of education is associated with a reduced risk of cognitive impairment.
2. Further explore the nature of this relationship, namely:
    a. Whether the association between education and attenuated risk of cognitive impairment is nonlinear.
    b. By treating education as categorical, to identify the maximum level of educational attainment that provides protection against cognitive impairment.
3. Explore whether the protective effects of education against cognitive impairment are moderated by sex and age.
4. To clarify the nature of ethnoregional differences in the relationship between education and the risk of cognitive decline.
5. To determine whether education can reduce the risk of cognitive decline associated with carriage of the APOE*4 allele, and if these effects are moderated by sex, age, and ethnicity.

Findings: Education was associated with a reduced risk of cognitive impairment. This association, however, was non-linear, indicating that at very high levels of education, the reduction in the risk of cognitive impairment was less pronounced. Categorical analyses of education indicated that a middle level of education (i.e., about 8-11 years, typically signifying the completion of middle school or intermediate high school) significantly attenuated cognitive impairment risk relative to primary education (up to 5-7 years of education). These protective effects of middle education weakened with older age at baseline, and a trend for the effect to be larger in women than men. High school education did not provide significant additional protection against cognitive impairment risk relative to middle education. In terms of ethnoregional differences, compared to Whites, there was a larger protective effect of high school (versus primary) education in Asians, and a larger protective effect of middle (versus primary) education in Blacks. Middle education reduced the risk of cognitive impairment in non-APOE*4 carriers, but not among APOE*4 carriers, both overall, and in White participants specifically. In Asians, however, both high school and middle education reduced the risk of cognitive impairment in APOE*4 carriers, compared to primary education. In Blacks also, middle school reduced cognitive impairment risk among APOE*4 carriers.

Status: Manuscript being revised for re-submission to *Archives of Gerontology and Geriatrics.*

4. Parity and the risk of dementia across geographic regions: a COSMIC study

Workgroup leader: Jong Bin Bae (KLOSCAD, South Korea).

Included studies: CHAS, ESPRIT, GothenburgH70, HELIAD, KLOSCAD, Kurihara, LEILA75+, MAAS, SAS, SPAH, ZARADEMP.

Aim: To expand upon an earlier COSMIC project to determine the association between number of childbirths and risk of dementia for women across various geographic regions.

Findings: Across all cohorts, grand multiparous (5 or more childbirths) women had a 47% greater risk of dementia than primiparous (1 childbirth) women, while nulliparous (no childbirth) women and women with 2 to 4 childbirths showed a comparable risk of dementia to primiparous women. However, there were differences associated with geographic region and dementia subtype. Compared to women with 1 to 4 childbirths, grand multiparous women showed a higher risk of dementia in European and Latin America cohorts, while nulliparous women showed a higher risk of dementia in Asian cohorts. Grand multiparity was associated with 6.9-fold higher risk of vascular dementia in European cohorts, whereas nulliparity was associated with a higher risk of nonvascular dementia in Asian cohorts (1.9-fold risk of Alzheimer's disease and 3.5-fold risk of non-Alzheimer, non-vascular dementia).

Status: Manuscript rejected by *NEJM, Lancet, World Psychiatry, BMJ, Nature Communications, Annals of Neurology, Neurology, Journal of Neurology, Neurosurgery, and Psychiatry*. Submitted to *BMC Medicine* (March 14).

5. The prevalence of subjective cognitive decline in and across different geographical and ethno-cultural regions

Workgroup leader: Susanne Roehr (LEILA75+, Germany).

Included studies: ActiveAging, CFAS, EAS, EPIDEMCA, ESPRIT, Invece.Ab, KLOSCAD, LEILA75+, LRGS-TUA, MAAS, MoVIES, PATH, SGS, SLASII, Sydney MAS, ZARADEMP.

Aim: Establish the prevalence of subjective cognitive decline (SCD) in and across different geographical and ethno-cultural regions.

Findings: Data were analysed for 44,228 dementia-free individuals at least 60 years of age (mean = 73.3) and with a female proportion of 58.1 %. While the heterogeneity of SCD assessments was high, qualitative and quantitative measures showed comparable estimates, robustly suggesting an age- and sex-standardized SCD prevalence of one third in the population above 60 years of age. Regional income and education may be associated with differences in SCD prevalence.

Status: Manuscript rejected by *Alzheimer's & Dementia*, *Lancet Global Health*. Submitted to *Neurology* (April 3).

6. A Cross-National Study of Depression in Pre-clinical Alzheimer's Disease: a COSMIC Collaboration Study

Workgroup leaders: Simone Reppermund (UNSW); Karen Ritchie (INSERM, France).

Included studies: ESPRIT, Invece.Ab, KLOSCAD, LEILA75+, MYHAT, SALSA, Sydney MAS, ZARADEMP.

Aim: (1) Characterise the trajectory of depressive symptoms within the pre-clinical period leading up to the diagnosis of AD, and determine its clinical correlates (notably cardiovascular disease, diabetes, hypertension, head trauma); (2) Assess the longitudinal association between depressive symptoms and cognitive decline taking into account findings from the first aim.

Findings: Depression incidence varied across the 8 included studies, from 3.5 to 15.5 cases per 100 person years. Taking into account methodological differences between studies, an increase in the incidence of depression was observed as the time to dementia diagnosis decreased despite cross-national variability in depression rates. The results support the hypothesis that depression occurring in the pre-clinical phases of dementia is more likely to be attributable to brain changes than environmental risk factors or reverse causality.

Status: Manuscript being revised for re-submission to *Alzheimer's and Dementia*.

7. Decline in verbal and visual memory in mild cognitive impairment: predictors of AD and associations with biomarkers

Workgroup leader: Javier Oltra Cucarella (University of Alicante, Spain).

Included studies: Sydney MAS.

Aim: This study will expand upon an earlier COSMIC project to use a Reliable Change Index to quantify cognitive decline separately for verbal memory and visual memory. The risk of AD for individuals with amnestic mild cognitive impairment (aMCI) who are visual memory decliners will be compared against those who are verbal memory decliners. Whether decline on visual or verbal memory tests outperforms biomarkers (APOE status and grey matter volumes) for predicting risk of AD will also be investigated. A secondary aspect of the study will use MRI data to investigate any differences in brain connectivity between individuals with aMCI who decline in verbal memory tests, visual memory tests, or both (in collaboration with researchers at the IBERBASKE Research Institute).

Status: Manuscript being prepared.

8. Risk factor clustering and incident cognitive decline

Workgroup leader: Ruth Peters (NeuRA, UNSW)

Included studies: Bambui, CHAS, EAS, ESPRIT, HELIAD, Invece.Ab, KLOSCAD, PATH, SALSA, Sydney MAS.

Aim: (1) To assess the presence of risk factor clusters (baseline risk factors for dementia and cognitive decline) in the COSMIC data sets (specific risk factors to include where available are smoking, low physical activity, sedentary lifestyle, poor diet, excess alcohol consumption, midlife obesity, high blood pressure, midlife high cholesterol and diabetes and depression); (2) If clusters are present, to evaluate the association of such clusters with incident dementia/cognitive decline/ change in cognitive functioning over follow up. Two additional aims, if feasible, are (1) to look at whether possession of one or more APOE E4 alleles changes the prevalence or pattern of clustering and their relationship with cognitive outcome, and (2) evaluate the impact of clustering and patterns of clusters on imaging measures.

Findings: There were 11,928 eligible individuals drawn from 10 cohorts across the Americas, Europe, Asia and Australia. Mean age 70 years (SD=6.7, range:54-100), 54% female, mean follow-up 2.5 years (SD=1.4, range:0.5-15). Mean baseline MMSE was 28.1 (SD=1.7) and 8% (965) had incident cognitive decline. There were 651 (5.5%) participants identified with high lifestyle and cardiovascular risk, 38% with high cardiovascular risk only, 5% with high lifestyle risk only, 51% were low risk. Only the cardiovascular group was associated with greater rates of decline in MMSE scores (B=-0.13,95%CI=-0.24:-0.02) (fig 2). Neither the lifestyle (OR=1.03(95%CI=0.77:1.38)), nor the cardiovascular (OR=1.07(95%CI=0.93:1.24)) group was associated with an increased risk of incident cognitive decline compared to the low risk group. Having both lifestyle and cardiovascular risk resulted in an OR=1.10 (95%CI=0.83:1.46). The impact of risk factor clusters varied by outcome, region, study, and key socio-demographic groups (age, sex). In conclusion, there were no robust relationships between a priori defined modifiable risk factor clusters and cognitive decline.

Status: We aim to expand the scope of the project by adding cognitive domain scores to the outcomes and including more studies in the analyses.

9. The relationship between alcohol use trajectories and health, mortality and cognition in older adults

Workgroup leader: Louise Mewton (CHeBA)

Aim: To examine inter-individual variation in the relationship between drinking trajectories and a range of variables related to health, mortality and cognition in adults aged 60+ years.

Status: Data received from EAS, EPIDEMCA, ESPRIT, Gothenburg H70, HELIAD, KLOSCAD, LEILA75+, MAAS, MYHAT, PATH, SALSA, SPAH, Sydney MAS, ZARADEMP, and analyses underway.

10. Sleep, Mild Cognitive Impairment, and Dementia in Elderly Cohorts with Ethnoracial Diversity

Workgroup leader: Seung Wan Suh (KLOSCAD)

Aim: (1) To identify subjective sleep parameters at baseline which have significant associations with cognitive decline at follow-up. (2) To investigate the association between a specific pattern of changes of sleep parameters over follow-up period and cognitive decline.

Status: Data received from Bambui, CLAS, ESPRIT, HELIAD, Invece.Ab, SALSA, Sydney MAS, ZARADEMP, and analyses underway.

11. Risk of MCI and dementia after skin cancer, and vice versa

Workgroup leader: Darren Lipnicki (CHeBA).

Aim: (1) Determine if individuals with a history of cancer are at greater risk of developing MCI; (2) Determine if individuals with MCI are at greater risk of developing cancer; (3) Contrast associations from 1 and 2 against those found using incident dementia rather than MCI; (4) Investigate if reportedly similar risk factors for cancer and dementia do indeed uniquely predict both outcomes (and MCI) in the same cohort(s): Smoking, physical inactivity, obesity, chronic inflammation (e.g., CRP), vitamin D levels, hyperhomocysteinemia, depression, as well as alcohol consumption; (5) Investigate ethno-regional differences in all of the above (very little relevant work in Asian samples); (6) Consider to the extent possible MCI and dementia subtypes, type of cancer, and cancer treatment.

Status: Data request is yet to be sent, but a preliminary study using Sydney MAS data was undertaken for an AAIC abstract.

Preliminary study aim: To investigate how skin cancer, including non-melanoma skin cancer, is associated with cognition, and with the development of dementia and Alzheimer's disease within six years of follow-up.

Preliminary study findings: History of any cancer was reported by 33% of participants, with 12% reporting NMSC. After adjusting for age, sex, education and APOE*4, any cancer was associated with better memory, and NMSC was associated with better memory and global cognition. Across all participants, dementia developed in 15%, and AD in 6%. Cancer other than NMSC was associated with lower odds of dementia or AD within 6 years. Basal cell carcinoma was associated with better global cognition and memory, and melanoma was associated with better global cognition and language scores. Gastrointestinal cancer was associated with better memory. No particular cancer type was statistically associated with dementia or AD, but there were no AD cases among those reporting gastrointestinal cancer. Cancer other than NMSC and melanoma were both associated with greater chances of mortality after 6 years.

12. Nutrition and cognitive health in the older population: emphasis on food groups consumption and dietary patterns

Workgroup leader: Costas A. Anastasiou (Harokopio University, Greece).

Aim: To examine the association between consumption of food groups, in isolation or in their combination into specific dietary patterns, and cognitive function in the older population (>60 years).

Status: Data received from CLAS, EPIDEMCA, Invece.Ab, ISA, LRGS-TUA, SLASII, Sydney MAS, and waiting for more studies to respond.

13. The relationship between blood pressure and risk of cognitive decline

Workgroup leader: Matthew Lennon (PhD candidate, CHeBA).

Aim: To examine the effect of BP and antihypertensives on cognitive function in late life. Specifically: (1) The relationship of hypertension (including systolic and diastolic) with cognitive decline and all cause dementia; (2) The relationship of hypotension with cognitive decline and all cause dementia and Alzheimer's disease; (3) Differences in late life BP trajectories among those who maintain normal cognition or develop MCI/dementia; (4) If antihypertensive treatment and type are related to risk of cognitive decline, including within BP groups; (5) Ethno-regional differences in hypertension as a risk for cognitive decline and dementia; (6) If the genetic determinants of hypertension are correlated with the genetic determinants of cognitive decline (if possible); (7) Investigate associations between BP and small vessel disease using MRI data (if possible).

Status: Data received from CLAS, EAS, EPIDEMCA, ESPRIT, Indianapolis-Ibadan, Invece.Ab, KLOSCAD, LEILA75+, MYHAT, SALSA, SAS, SGS, Sydney MAS, Tajiri Project, SPAH, ZARADEMP, and waiting for more studies to respond.

14. Development and validation of risk models for the prediction of dementia in Low- and Middle-Income Countries: A consortium of population-based cohort studies

Workgroup leader: Eduwin Pakpahan (Newcastle University Institute of Aging).

Aim: Within the field of dementia there is an urgent need for data pooling, particularly for undertaking risk stratification analysis, in order to have a sufficient number of outcome events and a sample large enough to undertake model development and validation. The aim of this project is to undertake a detailed program of research into dementia risk prediction modelling from harmonized data across low- and middle-income countries. We will start with the simple risk factors, such as demographic and socioeconomic status, then extend the analysis by including health and cognitive functions, includes lifestyle, medical history, genetics, etc. This project will address the research gap where usually health and its related predictors are limited.

Status: Data received from Bambui, CLAS, EPIDEMCA, ISA, SPAH, and waiting for other studies to respond.

15. The associations among education, occupational complexity, and late-life cognition

Workgroup leader: Jinshil Hyun (Albert Einstein College of Medicine).

Aim: Our overall aim is to examine the unique and interactive effects of occupational complexity and education on late-life cognition (cognitive impairment and normal cognitive aging, including levels and rates of change). Our specific aims are to examine:

1. Whether occupational complexity is associated with late-life cognition over and above the effect of education. H1.1. High occupational complexity is associated with lower likelihood of developing cognitive impairment. H1.2. High occupational complexity is associated with higher levels of cognition and slower rates of cognitive decline at earlier stages of cognitive aging.
2. Whether occupational complexity is the mechanism though which early-life education is associated with late-life cognition. H2.1. The association between education and cognitive impairment is mediated by occupational complexity. H2.2. The association between education and cognitive aging (i.e., levels, rates of change) is mediated by occupational complexity.
3. How education and occupational complexity interact. H3.1. There is an incremental effect of these factors on cognitive impairment. Being low in either education or occupation conveys greater risk for cognitive impairment than being high on both; being low in both conveys the greatest incidence risk. H3.2. There is an incremental effect of education and occupation on levels and rates of change in cognition.

We will also examine whether these effects are over and above the effects of late-life cognitive activities and whether they vary by APOE e4 status, gender, and race/ethnicity.

Status: Data received from CLAS, EPIDEMCA, HELIAD, Invece.Ab, KLOSCAD, LEILA75+, MYHAT, PREHCO, Sydney MAS, Tajiri Project, ZARADEMP, and analyses underway.

16. Rates of progression to dementia in diverse ageing populations, using different dementia harmonisation methods including delta

Workgroup leader: Ben Lam (CHeBA)

Aim: A previous COSMIC paper examined longitudinal decline in continuous measures of cognition, as well as the effects of demographic characteristics and APOE e4 carrier status. This project will complement that work by examining rates of conversion to dementia in such populations and how they vary with the same characteristics examined earlier.

A challenge will be to harmonise dementia diagnoses across COSMIC cohorts. For studies with cognition and function (IADL) data, uniform algorithmic procedures that identify individuals impaired on both will be used. Impairment will be defined via comparisons with consensus diagnoses by expert panels, using the subset of studies with these data. For studies without suitable cognition and/or IADL data, scores on screening tests (MMSE, CDR etc) with appropriate cut-points, can tentatively be used.

Recently, continuous measures considered to be “homologues” or “proxies” for dementia have been developed. Royal et al. used structural equation modelling to define a latent variable (delta) representing the dementia-relevant shared variance between cognitive and functional measures. Similarly, Jutten et al. formed a novel cognitive-functional composite (CFC) subsequently shown to improve the detection of early stages of dementia.

The current project will explore the use of continuous proxies for dementia like delta and CFC to form harmonised dementia classifications across COSMIC cohorts. Dementia will be classified from the continuous measures by applying appropriate cut-points. Levels of agreement between such dementia classifications and those derived from consensus diagnoses and algorithmic approaches will be examined. We will also examine how measures like delta and CFC vary with demographic characteristics and APOE e4 carrier status.

Status: Data received from Bambui, CLAS, EPIDEMCA, HELIAD, ISA, Leiden85+, LEILA75+, Marikina, MYHAT, SGS Sydney MAS, and preliminary analyses being conducted while waiting for more studies to respond.

17. Parity and the risk of incident dementia: a COSMIC collaboration cohort study

Workgroup leader: Jong Bin Bae (KLOSCAD).

Included studies: Gothenburg H70, HELIAD, KLOSCAD, LEILA75+, SAS, ZARADEMP.

Aim: To investigate the association between parity and risk of incident dementia.

Findings: Of 9,756 women dementia-free at baseline, 7,010 completed one or more follow-up assessments. The number of parities was associated with the risk of incident dementia (Hazard ratio [HR] = 1.07, 95% CI = 1.02 – 1.13). Grand multiparity increased the risk of dementia by 30% compared to 1 – 4 parities (HR = 1.30, 95% CI = 1.02 – 1.67).

Status: Manuscript rejected by *Neurology*, and the *British Journal of Psychology.* Submitted to *Epidemiology and Psychiatric Sciences* (March 8).

18. The association between cardiovascular risk factor variability with dementia risk and cognitive impairment: an IPD meta-analysis from the COSMIC collaboration

Workgroup leader: Phillip J. Tully (University of Adelaide, Australia).

Aim: To examine whether variability in cardiovascular risk factors is independently associated with dementia and cognitive impairment. We hypothesise that higher intra-individual variability in cardiovascular risk factors will be associated with incident dementia and cognitive impairment, over and above mean levels of risk factors. Specifically, this study will assess visit-to-visit variability in systolic and diastolic blood pressure, HbA1c, fasting glucose, total cholesterol, LDL-cholesterol, HDL-cholesterol, and trigylcerides. Because these factors are known risk factors for cardiovascular diseases (and dementia), it is important to record the presence of cardiovascular diseases and their treatments at baseline and follow-up in order to adjust for potential protopathic and indication biases.

Status: Data received from CLAS, HELIAD, ISA, Leiden85+, LEILA75+, Sydney MAS, and waiting for more studies to respond.

19. Maximizing dementia risk reduction: the impact of demographic/diversity factors on a modifiable dementia risk score

Workgroup leader: Kay Deckers (Maastricht University, The Netherlands).

Aim: To investigate whether there are differences in dementia risk factor profiles (LIBRA scores) based on important demographic/diversity factors such as sex, educational level, ethnicity/race and socioeconomic status. Cox proportional hazard regression models will be used to test the predictive validity of these stratified LIBRA profiles for cognitive impairment, MCI and/or dementia.

Further, path analysis will be used to investigate potential mediation or effect modification between demographic/diversity factors, LIBRA and cognitive impairment, MCI and/or dementia.

Status: Data received from CLAS, HELIAD, KLOSCAD, Leiden85+, LEILA75+, Sydney MAS, and beginning to be harmonised while waiting for more studies to respond.

20. Physical activity and cognitive decline in older adults

Workgroup leader: Ding Ding (SAS).

Aim: To examine the effect of physical activity on cognitive functioning among elderly with different characteristics in diverse ethnic groups. Specifically:

1. Whether physical activity (incl. daily life activity, leisure time activity, occupational activity) is associated with a decreased risk of dementia onset or cognitive decline.
2. The association of type, amount and intensity of physical activity with late-life cognition, taking age, ethnicity, and health conditions into consideration.
3. The interaction/mediation with physical activity and/or additive effect to cognitive decline from sex, life-style, cognitive reserve, and APOE genotype.

Status: Data received from CLAS, HELIAD, ISA, SGS, Sydney MAS.

21. Sex differences in risk factors for dementia and cognitive decline

Workgroup leader: Jessica Gong (PhD candidate, The George Institute for Global Health, UNSW).

Aim: To provide a complete, systematic and comprehensive analysis of sex differences in risk factors for dementia using standardised methods, as opposed to examining a single risk factor and its association with dementia at a time. Also, sex will be our primary exposure and effect modifier, rather than of ancillary interest. We aim to look at all major and potentially modifiable risk factors for dementia, and the interactions between these risk factors given the multifactorial aetiology of dementia.

Status: Data received from CLAS, HELIAD, ISA, Leiden85+, LEILA75+, SGS, SPAH, Sydney MAS, and waiting for more studies to respond.

22. The prevalence of poor mobility in older adults: A coordinated analysis from the COSMIC collaboration

Workgroup leaders: Briana N. Sprague and Caterina Rosana (University of Pittsburg).

Aim: To implement a uniform gait speed threshold to more reliably estimate the worldwide prevalence of slow gait speed. Additionally, we aim to identify common modifiable predictors of poor mobility across different ethnocultural and geographic regions. The specific research questions are: (1) Is the prevalence of poor mobility (via objective measure of gait speed and self-reported measures of physical disability such as ADL/IADLs) similar across countries, and (2) What are the most common predictors of poor mobility across countries?

Status: Data received from ISA, HELIAD, KLOSCAD, Leiden85+, LEILA75+.

23. Social Health and Reserve in the Dementia patient journey (SHARED)

Workgroup leader: Suraj Samtani (CHeBA).

Aim: (1) Examine the variance in cognitive function explained by social health (marital status; social network size; frequency of interactions; social support received and provided; independence in daily functioning; loneliness; quality of relationships), beyond that explained by APOE*4, demographic variables, baseline cognitive function, and physical health; (2) Study the trajectory of social health as individuals progress from MCI to dementia (latent growth class analysis); (3) Investigate the pathways that mediate the relationship between social and cognitive health (brain reserve as indicated through MRI, health behaviours, physiological factors, psychological factors) using structural equation modelling; (4) Examine the variance in social health explained by cognitive function, physical health, and APOE*4.

Status: This project is funded by a European Union Joint Programme - Neurodegenerative Disease Research grant. Data received from Bambui, CLAS, HELIAD, ISA, KLOSCAD, LEILA75+, and waiting for more studies to respond.

24. Does the association between family history of dementia and dementia risk differ by sex?

Workgroup leader: Jong Bin Bae (KLOSCAD).

Aim: Family history of dementia is a known risk factor for dementia. The prevalence and incidence of dementia differ by sex, and the clinical course of dementia is also different between men and women. These differences might be due to different neuroendocrinal factors, life-styles and environmental factors between men and women, and they might affect the association between familial history of dementia and dementia risk. Therefore, we hypothesize that the association between familial history of dementia and dementia risk may differ by sex. Our primary goal is to investigate this hypothesis, which does not appear to have been previously studied. We also aim to investigate whether the association between a familial history of dementia and dementia risk is different for a history of dementia in the father or brothers compared to a history of dementia in the mother or sisters.

Status: Data received from HELIAD, LEILA75+, MMAP, and waiting for more studies to respond.

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