# Centre for Healthy Brain Ageing (CHeBA)
# COSMIC

## NEWSLETTER | March 2021

Dear COSMIC colleagues,

We hope you are all well and have traversed the unprecedented 2020 unfazed by social distancing, lockdowns and isolation. We also hope that your loved ones were untouched by the virus.

The work of COSMIC has continued unabated through this challenging year, thanks to all our dedicated collaborators. The COSMIC community has grown to 44 studies from 33 countries. A number of exciting developments are on the cards.  In partnership with Dementias Platform UK, we are developing Dementias Platform Australia (DPAU) to host COSMIC data in a secure environment.  We have started a partnership with the Institute of Health Metrics and Evaluation, Washington DC for use of COSMIC data for the Global Burden of Disease project. We have also just begun a conversation with the Davos Alzheimer Collaborative to help enhance some of the cohorts in countries that are not well-represented in dementia epidemiology as part of this new international venture to defeat dementia.

This newsletter will bring you up to date on the current activities within COSMIC. We hope you will share our excitement in the breadth and depth of the work being carried out.

On behalf of the Sydney team (Dr John Crawford, Dr Anbu Thalamuthu, Dr Ben Lam, Dr Nicole Kochan), we want to thank you profusely for your generous contribution of data and time to make COSMIC such a vibrant endeavour. We think we are building a global community in the epidemiology of ageing and dementia.

Our best wishes, with the hope that 2021 will bring a post-covid world with peace, shared prosperity, belief in science, and COSMIC collaboration.

*Scientia Professor Perminder Sachdev AM, CHeBA Co-Director*

*Dr Darren Lipnicki, COSMIC Study Co-ordinator*

**Professor Perminder Sachdev**

**Dr Darren Lipnicki**

# Active Projects

1. BMI and cognitive decline (Darren Lipnicki, CHeBA):
   - Steve Makkar no longer available to work on this so Darren has taken over;
   - Original manuscript rejected by Journal of Gerontology: Medical Sciences;
   - Reviewing recent literature that will guide a new analytical approach to be undertaken by John Crawford and Ben Lam at CHeBA:
     i. Possibly expand to studies not previously included.

2. Decline in verbal and visual memory in mild cognitive impairment: predictors of AD and associations with biomarkers (Javier Oltra Cucarella):
   - Javi sent a revised manuscript; only Sydney MAS data was able to be used (March 16).

3. Risk factor clustering (Ruth Peters, NeuRA):
   - Ruth not intending to take the project any further;
   - We could expand the scope of the project by adding cognitive domain scores to the outcomes, including more studies, and looking beyond a priori clusters.

4. The relationship between alcohol use trajectories and health, mortality and cognition in older adults (Louise Mewton, CHeBA):
   - Manuscript on Dementia ready early in 2021 (for submission to A&D or JAMA Neurology); second manuscript on Cognition later in 2021;
   - EAS Side-project.

5. Sleep, Mild Cognitive Impairment, and Dementia in Elderly Cohorts with Ethnoracial Diversity (Seung Wan Suh; KLOSCAD):
   - Data from Bambui, HELIAD, Invece.Ab, ESPRIT, ZARADEMP, SALSA, CLAS, Sydney MAS (and KLOSCAD);
   - Conducting a preliminary analysis with a mixed effect model; determining the best statistical approach.

6. Risk of MCI and dementia after cancer, and vice versa (Darren Lipnicki, CHeBA):
   - Need to write Sydney MAS paper and send request for COSMIC data.

7. Nutrition and cognitive health in the older population: emphasis on food groups consumption and dietary patterns (Costas Anastasiou, HELIAD; Henry Brodaty to be collaborator):
   - Data from Bambui, CLAS, EPIDEMCA, Gothenburg H70, Invece.Ab, ISA, LRGS-TUA, PATH, SLASII, Sydney MAS;
   - Sent Costas a harmonized risk factor dataset (used for PLoS Med 2019) and offered help to harmonise the cognitive data (December 15);
   - Asked for an update (March 5).

8. The relationship between blood pressure and risk of cognitive decline (Matthew Lennon, CHeBA; Ruth Peters to be collaborator):
   - Data from Bambui, CLAS, EAS, EPIDEMCA, ESPRIT, Gothenburg H70, Indianapolis-Ibadan, Invece.Ab, KLOSCAD, LEILA75+, MYHAT, PATH, SALSA, SAS, SGS, SLAS, Sydney MAS, Tajiri Project, SPAH, ZARADEMP;
   - Asked Indianapolis-Ibadan if they have individual test scores from the CERAD (May 25);
   - Matthew probably won't be able to resume the project until September 2021;
   - HELIAD hadn't sent data and will do so.

9. Development and validation of risk models for the prediction of dementia in Low- and Middle-Income Countries: A consortium of population-based cohort studies (Eduwin Pakpahan, Northumbria University):
   - Data from Bambui, CLAS, EPIDEMCA, ISA, MMAP, SPAH;
   - The project was delayed last year, but Eduwin is back to writing the paper and hopes to provide an update soon; planning for a very high impact journal (March 5).

10. The associations among education, occupational complexity, and late-life cognition (Jinshil Hyun, EAS):
    - Data from CLAS, EPIDEMCA, HELIAD, Invece.Ab, KLOSCAD, LEILA75+, MYHAT, PREHCO, Sydney MAS, Tajiri Project, ZARADEMP;
    - Analysis plan:
        i. Starting with 6 studies that have detailed occupational codes (paper 1);
        ii. Will later target studies with less detailed codes;
    - Abstract for AAIC 2021:
    - First draft complete and reviewed by Einstein Medicine group, working on some statistical issues and hoping to be done by the end of March (March 5).

11. Delta and incident dementia: Ben, John, Darren:
    - Data from Bambui, CLAS, EAS, EPIDEMCA, ESPRIT, Gothenburg H70, HELIAD, Invece.Ab, ISA, KLOSCAD, Leiden85+, LEILA75+, MMAP, MYHAT, PATH, SALSA, SGS, SLAS, Sydney MAS, ZARADEMP;
    - Maastricht data agreement completed, but awaiting clearance from their legal department to release the data;
    - Some data not usable (Bambui, ISA, EPIDEMCA, MMAP unless IADLs at baseline for more participants);
    - Asked HELIAD for missing ID variable for Wave B (December 20, and again February 8);
    - Ben wrote the Methods and Results sections:
        i. Some revisions being implemented after CHeBA comments.

12. The association between cardiovascular risk factor variability with dementia risk and cognitive impairment (Phillip Tully, University of Adelaide):
    - Data from Bambui, CLAS, EAS, EPIDEMCA, ESPRIT, Gothenburg H70, HELIAD, Invece.Ab, ISA, Leiden85+, LEILA75+, LRGS TUA, PATH, SALSA, SGS, Sydney MAS, ZARADEMP;
    - Data from non-COSMIC cohorts included;
    - Sydney MAS wave 5 and 6 data provided.

13. Maximizing dementia risk reduction: the impact of demographic/diversity factors on a modifiable dementia risk score (Kay Deckers, Maastricht University):
    - Data from Bambui, CLAS, EAS, ESPRIT, Gothenburg H70, HELIAD, Invece.Ab, ISA, KLOSCAD, Leiden85+, LEILA75+, LRGS TUA, MYHAT, SALSA, SLAS, Sydney MAS;
    - Project was slowed last year; continuing with harmonisation of 20 datasets (March 5).

14. Physical activity and cognitive impairment (Ding Ding, Shanghai Aging Study):
    - Data from CLAS, EAS, EPIDEMCA, ESPRIT, HELIAD, Invece.Ab, ISA, LRGS TUA, MYHAT, SALSA, SGS, SLAS, Sydney MAS;
    - Abstract for AAIC 2021;
    - Emailed HELIAD about MMSE versions and low education (February 8).

15. Sex differences in risk factors for dementia and cognitive decline (Jessica Gong, PhD student, The George Institute):
    - Data from Bambui, CLAS, EAS, EPIDEMCA, ESPRIT, Gothenburg H70, HELIAD, Invece.Ab, ISA, Leiden85+, LEILA75+, LRGS TUA, MAAS, SALSA, SAS, SGS, SLAS, SPAH, Sydney MAS;
    - Note request for within wave BP measures rather than just average – Jess is aware we need to watch for overlap with Phil's project;
    - Ingmar and Carol remain interested in collaboration – there has been some contact with Jess about forming a larger group;
    - Analysis complete end of March 2021; Manuscript ready for review end of May 2021:
        i. First paper will focus on Lancet commission risk factors with dementia and subtypes as outcomes;
        ii. Second paper on cognitive test data;
    - Gothenburg University and The George Institute continue to work on DTA (March 18).

16. The prevalence of poor mobility in older adults (Caterina Rosana, Briana Sprague, UPitt):
    - Data from EAS, EPIDEMCA, IDEA, ISA, HELIAD, KLOSCAD, Leiden85+, LEILA75+, LRGS-TUA, MYHAT, PATH, SGS, SPAH, SLASII, Sydney MAS;
    - Potential for an interest group within COSMIC to be established in Teams;
    - Gothenburg University DPA and RCA being worked on.

17. Social Health and Reserve in the Dementia patient journey project (JPND SHARED; Suraj Samtani and Henry Brodaty, CHeBA):
    - Data from Bambui, CLAS, EAS, EPIDEMCA, Gothenburg H70, HELIAD, KLOSCAD, LEILA75+, MYHAT, SLASI, Sydney MAS;
    - Possible sub-project involving one or two COSMIC studies;
    - Asked CLAS about marital status data;
    - First draft written; being revised after CHeBA comments.

18. Differential effect of family history on the risk for dementia by sex (Jong Bin Bae, KLOSCAD):
    - Data from EAS, Gothenburg H70, HELIAD, Invece.Ab, LEILA75+, MMAP, MYHAT, PATH, Sydney MAS, ZARADEMP;
    - PATH approved use of data; need an agreement.

19. The Global burden of dementia (Louise Mewton, CHeBA).
    - Data received or compiled for Active Aging, Bambui, CHAS, CLAS, EAS, EPIDEMCA, ESPRIT, Faroe Islands, Gothenburg, HELIAD, IDEA, Indianapolis Ibadan, Invece.Ab, ISA, KLOSCAD, Leiden85+, LEILA75+, LRGS TUA, MAAS, MMAP, MYHAT, MYNAH, PATH, PREHCO, SAS, SALSA, SGS, SLAS, SPAH, Sydney MAS, Tajiri, ZARADEMP;
    - SPAH: Marcia sent additional follow-up and mortality data; contacted Louise about being more involved in the project;
    - Gothenburg data agreements for this and 5 other projects approved by UNSW for signing (February 9);
    - PATH mortality data needs ethics approval by AIHW: Kaarin checking on the form naming Louise and myself we provided August 20, 2019;
    - Contacted CFAS to say IPD needed (IHME only have limited information);
    - Ugandan study – Vincent will send data (February 8);
    - Hisayama will provide tabular data of the presence of dementia – Louise will prepare an Excel sheet for them to complete;
    - TILDA need a data sharing agreement;
    - IHME data request:
        i. The original proposal is being amended to indicate how data will be used, who will have access, how long will the data be held etc;
        ii. Asked studies about sharing data:
            1. Yes from 17;
            2. 1 undecided (want more information first);
            3. No from 2 (though OK for Louise to send results for 1 of these);
            4. 7 studies want a data sharing agreement – will be contacted by IHME.

20. White matter lesions and their neuropsychological correspondence using data from COSMIC (Jiyang):
    • Data received from ALBION, Gothenburg H70, Indonesian study, KLOSCAD;
    • SLAS can contribute data – asked for details to send a link to their folder;
    • SALSA data not suitable.

## Potential projects

21. Darren is developing shared/unique risk factors for neurodegenerative diseases (AD, PD, PDD, LBD, vascular dementia).

22. Ageing factor project: John, Louise and Ben.

23. ZARADEMP group were going to prepare a proposal to investigate associations between anxiety and dementia (latest update July 2).

24. Look into statins and metformin as potential projects.

## Potential new members

25. Invited:
    • Polish PURE MIND sub-study agreed to join – Dorota needs to talk with study co-ordinators;
    • Population Study of Chinese Elderly in Chicago Study (PINE Study); interested, sent a follow-up email January 5;
    • Victoria Longitudinal Study (VLS); interested, sent additional information January 4;
    • Boston Puerto Rican Health Study; interested, sent a follow-up email January 6;
    • Shunyi study; interested, sent some more info February 18;
    • Birjand Longitudinal Aging Study (BLAS): Iran, invited January 8;
    • Tianjin Elderly Nutrition and Cognition Cohort Study, invited January 8;

26. Requested information on cognitive measures from Oulu35 and Oulu45, Northern Finland.

27. Maracaibo study (Venezuela) – invited 2 years ago when Gladys was interested at the time; Nick Scarmeas offered to help contact Gladys.

28. Others to consider:
    • LASI-DAD; data can be applied for online: https://lasi-dad.org/;
    • Finland: CAIDE;
    • Malaysia: MELOR; has MoCA – can convert to MMSE (Falkowski, 2015);
    • DPUK studies to contact:
        i. The English Longitudinal Study of Ageing;
        ii. Lothian Birth Cohort;
        iii. Whitehall II from wave 5;
    • Healthy Aging and Body Composition Study (USA) – data publicly available healthabc.nia.nih.gov/;
    • HUNT Study (Nord-Trøndelag Health Study) MocA and word list, 4 waves https://www.ntnu.edu/hunt;
    • HABLE, a study of aging in Latino and non-Latino elders at the University of North Texas Health Sciences Center;
    • AGES – Reykjavik Study;
    • PsyCoLaus – Switzerland;
    • Mr/Mrs O Study – Hong Kong;
    • Chicago Health and Aging Project.

29. Dementias Platform Australia (DPAU):
   - Rory Chen is the DPAU data manager at CHeBA;
   - By June 2021, we aim to:
      i. Submit Ethics Amendment;
      ii. Sign a DPAU Data Deposit Agreement with studies;
      iii. Provide study metadata on the DPAU Data Portal website, including a descriptive summary and availability of different variable types, for a subgroup of studies;
      iv. Upload data for the subgroup of studies;
      v. Have DPAU projects led by CHeBA researchers hosted on the platform;
   - Rory has contacted most studies about providing data and checking their metadata:
      i. 13 have said yes to depositing data on DPAU;
      ii. 6 are in negotiation;
      iii. 4 have declined to deposit data but are OK with being listed on DPAU;
      iv. 18 have not replied yet (March 18);
   - Carol Brayne suggested mirroring data already on DPUK, including CFAS:
      i. Note that CFAS II is on DPUK but COSMIC member is CFAS I.

30. Davos Alzheimer's Collaborative (DAC):
   - https://www.davosalzheimerscollaborative.org/;
   - DAC are interested in data from under-represented regions, and in providing resources so cohorts from these regions can enhance their data collection;
   - Contacted all COSMIC studies from Africa and the Middle East, Asia, South and Latin America (and SALSA):
      ii. What resources are needed to obtain GWAS data?
      iii. An excel sheet asking for cohort information and data types available;
      iv. As of March 18 have received 2 data sheets and 4 replies about GWAS.

## Other Matters

31. Blog for ADI website.

32. Website: need to update publications and projects pages.

33. Look at Google Forms for gathering author information for manuscripts.

34. Webinars for 2021 (2 for different time-zones again).

35. Guidelines for analysing COSMIC data to include in research proposals, website etc:
   - Cite PLOS paper as an example;
   - Input from John Crawford:
      i. Types of longitudinal analyses that are generally accepted as "good enough" for reducing the problem of non-random attrition bias, such as using mixed models, multiple imputation, etc;
      ii. Ways of combining data - ie not simply pooling to form one big sample, but using IPD meta-analysis with study as a random effect. One-step or two-step meta-analyses?
      iii. For IPD meta-analysis, reviewers commonly want not only the pooled effects, but also some consideration of the pattern of variation between effects from individual studies, as displayed in forest plots. And not just the reporting of I-squareds, or other heterogeneity measures, but consideration in more detail of the possible reasons for variation between studies;
      iv. For groups seeking advice we could suggest specific ways that neuropsych test measures be handled, ie what tests should be allocated to particular domains and a common approach to how measures of cognition are standardised. Some groups might want to use other approaches that are quite acceptable and which they are familiar with, such as ones based on factor analysis or SEM;
   - Ben Lam has added some references and Jessica Lo will have input.

# COSMIC papers
**Published**

1. Sachdev et al. COSMIC (Cohort Studies of Memory in an International Consortium): an international consortium to identify risk and protective factors and biomarkers of cognitive ageing and dementia in diverse ethnic and sociocultural groups. BMC Neurol. 2013;13:165.

2. Sachdev et al. The prevalence of mild cognitive impairment in diverse geographical and ethnocultural regions: The COSMIC collaboration. PLOS One. 2015;10:e0142388.

3. Lipnicki et al. Age-related cognitive decline and associations with sex, education and apolipoprotein E genotype across ethnocultural groups and geographic regions: a collaborative cohort study. PLoS Med. 2017;14(3):e1002261.

4. Jang et al. Differential effects of completed and incomplete pregnancies on the risk of Alzheimer disease. Neurology. 2018;91(7):e643-e651.

5. Oltra-Cucarella et al. Visual memory tests enhance the identification of amnestic MCI cases at greater risk of Alzheimer's disease. Int Psychogeriatr. 2018 Oct 25:1-10.

6. Lipnicki et al. Determinants of cognitive performance and decline in 20 diverse ethno-regional groups: A COSMIC collaboration cohort study. PLoS Med. 2019;16:e1002853.

7. Maasakkers et al. The association of sedentary behaviour and cognitive function in people without dementia: A coordinated analysis across five cohort studies. Sports Med. 2020 Feb;50(2):403-413.

8. Turana et al. Factors associated with odour identification in older Indonesian and white Australian adults. Aging Clin Exp Res. 2020 Feb;32(2):215-221.

9. Makkar et al. APOE ε4 and the Influence of Sex, Age, Vascular Risk Factors, and Ethnicity on Cognitive Decline. J Gerontol A Biol Sci Med Sci. 2020 May 12;glaa116.

10. Makkar et al. Education and the moderating roles of age, sex, ethnicity and apolipoprotein epsilon 4 on the risk of cognitive impairment. Arch Gerontol Geriatr. 2020 Jul 13;91:104112.

11. Bae et al. Does parity matter in women's risk of dementia?: a COSMIC collaboration cohort study. BMC Med. 2020 Aug 5;18(1):210. doi: 10.1186/s12916-020-01671-1.

12. Carles et al. A Cross-National Study of Depression in Pre-clinical Alzheimer's Disease: a COSMIC Collaboration Study. Alzheimers Dement. 2020 Sep 3. doi: 10.1002/alz.12149.



13. Bae et al. Parity and the risk of incident dementia: a COSMIC collaboration cohort study. Epidemiol Psychiatr Sci. 2020 Oct 20;29:e176.

14. Roehr et al. Estimating prevalence of subjective cognitive decline across international cohort studies of ageing: A COSMIC study. Alzheimers Res Ther. 2020;12(1):167.

**In Preparation**

1. Lipnicki et al. Body mass index and cognitive decline in diverse ethno-regional groups: The COSMIC Collaboration.

2. Oltra-Cucarella et al. Decline in verbal and visual memory in mild cognitive impairment: predictors of AD and associations with biomarkers.

3. Mewton et al. The relationship between alcohol use trajectories and health, mortality and cognition in older adults.

4. Suh et al. Sleep, Mild Cognitive Impairment, and Dementia in Elderly Cohorts with Ethnoracial Diversity.

5.  Lipnicki et al. Risk of MCI and dementia after cancer, and vice versa.

6.  Anastasiou et al. Nutrition and cognitive health in the older population: emphasis on food groups consumption and dietary patterns.

7.  Lennon et al. The relationship between blood pressure and risk of cognitive decline.

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

9.  Hyun et al. The associations among education, occupational complexity, and late-life cognition.

10. Lam et al. Rates of progression to dementia in diverse ageing populations, using different dementia harmonisation methods including delta.

11. Tuffy et al. The association between cardiovascular risk factor variability with dementia risk and cognitive impairment.

12. Deckers et al. Maximizing dementia risk reduction: the impact of demographic/diversity factors on a modifiable dementia risk score.

13. Ding et al. Physical activity and cognitive decline in older adults.

14. Gong et al. Sex differences in risk factors for dementia and cognitive decline.

15. Rosana et al. The prevalence of poor mobility in older adults: A coordinated analysis from the COSMIC collaboration

16. Samtani et al. Social Health and Reserve in the Dementia patient journey project.

17. Bae et al. Differential effect of family history on the risk for dementia by sex.

18. Mewton et al. The Global burden of dementia.

19. Jiang et al. White matter lesions and their neuropsychological correspondence.

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