



Modifiable risk factors for cognitive ageing and dementia

Prof. Dr. Anja Leist, University of Luxembourg

UniTalk, University of Luxembourg
29 March 2023



European Research Council
Established by the European Commission

Financial disclosures

I have received remuneration from Roche for advisory activities related to expanding health equity in AD (December 2021).

What is dementia?

Why focus on the modifiable determinants of cognitive ageing and dementia?

Cognitive impairment and dementia are among the great societal challenges in ageing societies: 14.3 million cases of dementia expected for 2050 in Europe (Alzheimer Europe, 2019)

No medical cure for dementia, even if cognitive decline can be delayed (van Dyck et al., 2022)

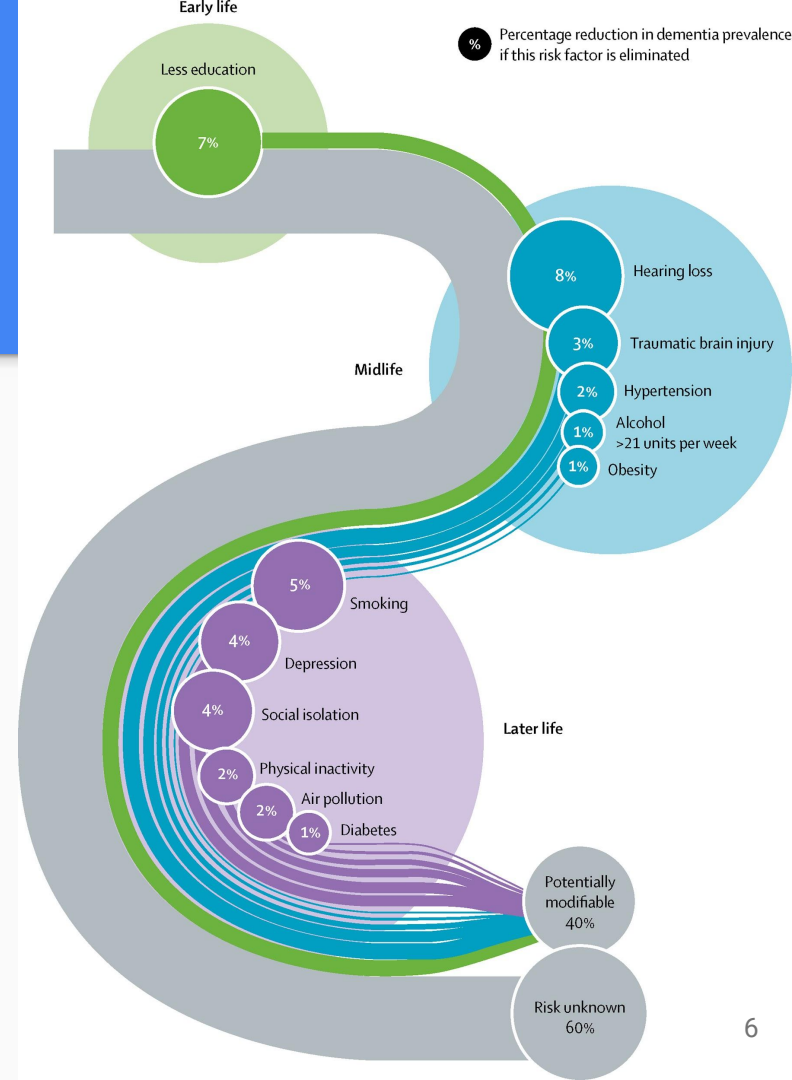
What are modifiable risk factors for cognitive ageing and dementia?

Modifiable dementia risk

Potentially modifiable risk factors account for up to 40% to all dementia cases.

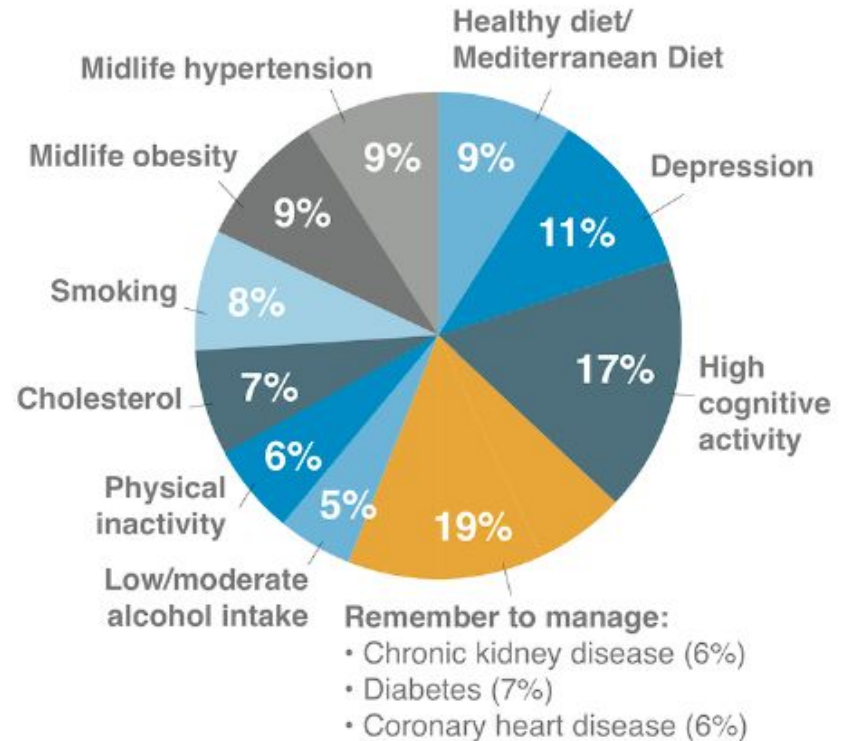
In comparison, genetic risk for dementia contributes to $\approx 7\%$ of all dementia cases.

➔ Great potential for prevention.



Lifestyle for Brain Health (LIBRA)

Schiepers, O. J., Köhler, S., Deckers, K., Irving, K., O'Donnell, C. A., van den Akker, M., ... & van Boxtel, M. P. (2018). Lifestyle for Brain Health (LIBRA): a new model for dementia prevention. *International journal of geriatric psychiatry*, 33(1), 167-175.

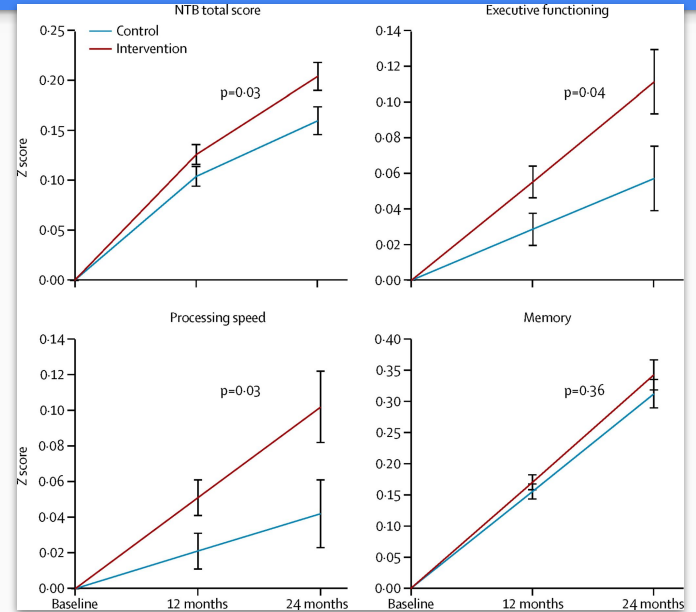


Secondary prevention

Some evidence for modifying risk factors to reduce cognitive impairment and dementia risk

Ngandu, T., Lehtisalo, J., Solomon, A., Levälähti, E., Ahtiluoto, S., Antikainen, R., ... & Kivipelto, M. (2015). A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial. *The Lancet*, 385(9984), 2255-2263.

Williamson, J. D., Pajewski, N. M., Auchus, A. P., Bryan, R. N., Chelune, G., Cheung, A. K., ... & SPRINT Mind Investigators for the SPRINT Research Group. (2019). Effect of intensive vs standard blood pressure control on probable dementia: a randomized clinical trial. *Jama*, 321(6), 553-561.



RISK REDUCTION OF COGNITIVE DECLINE AND DEMENTIA

WHO GUIDELINES



Preventing Cognitive Decline and Dementia: A Way Forward

PREVENTING COGNITIVE DECLINE AND DEMENTIA A WAY FORWARD

Committee on Preventing Dementia and Cognitive Impairment,
Alan I. Leshner, Story Landis, Clare Stroud, and Autumn Downey,
Editors

Board on Health Sciences Policy
Health and Medicine Division

A Consensus Study Report of
The National Academies of
SCIENCES • ENGINEERING • MEDICINE

THE NATIONAL ACADEMIES PRESS
Washington, DC
www.nap.edu

Copyright National Academy of Sciences. All rights reserved.



Optimizing brain health across the life course:

WHO position paper



How do social determinants of health interact with modifiable risk factors?

Social determinants of health

Our foci: Individual-level SES, neighborhood (area-)level SES, societal-level inequalities wrt gender, educational opportunity

Notoriously difficult to disentangle the different levels and determinants - clustering, interactions, life-course accumulation of (dis)advantage



© Institute for Future Studies, Stockholm

CRISP: Cognitive Aging: From Educational Opportunities to Individual Risk Profiles

- Panel *Social Sciences and Humanities* SH3: The Social World, Diversity, Population
- Analysis of panel datasets from large-scale cohort and ageing studies, specifically the family of *Health and Retirement Studies* (HRS, SHARE, ELSA, KLoSA, SABE), UK Biobank, and others

European Research Council grant
agreement no. 803239
<https://cognitiveageing.uni.lu>



Main take-home messages

1. Strong role of socioeconomic conditions regardless of genetic risk
2. Strong role of a 'Western' lifestyle
3. Role of lifestyle does not differ between men and women, or more or less favorable SES

Do neighbourhood socioeconomic conditions interact with genetic risk for dementia?

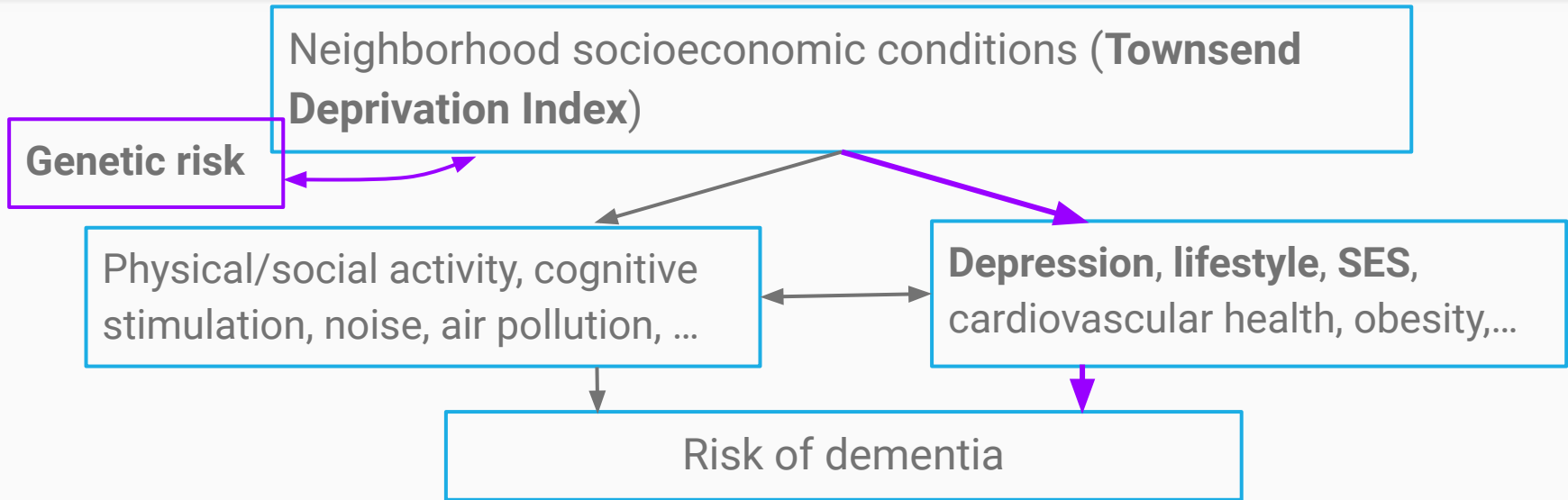


Klee, M., Leist, A.K., Veldsman, M., Ranson, J.M., Llewellyn, D.J. (2023). Socioeconomic deprivation, genetic risk, and incident dementia. *American Journal of Preventive Medicine*.

<https://doi.org/10.1016/j.amepre.2023.01.012>

Top decile, *Public Health, Environmental and Occupational Health* (Scopus)

Neighbourhood deprivation x genetic dementia risk?



Neighbourhood deprivation x genetic risk

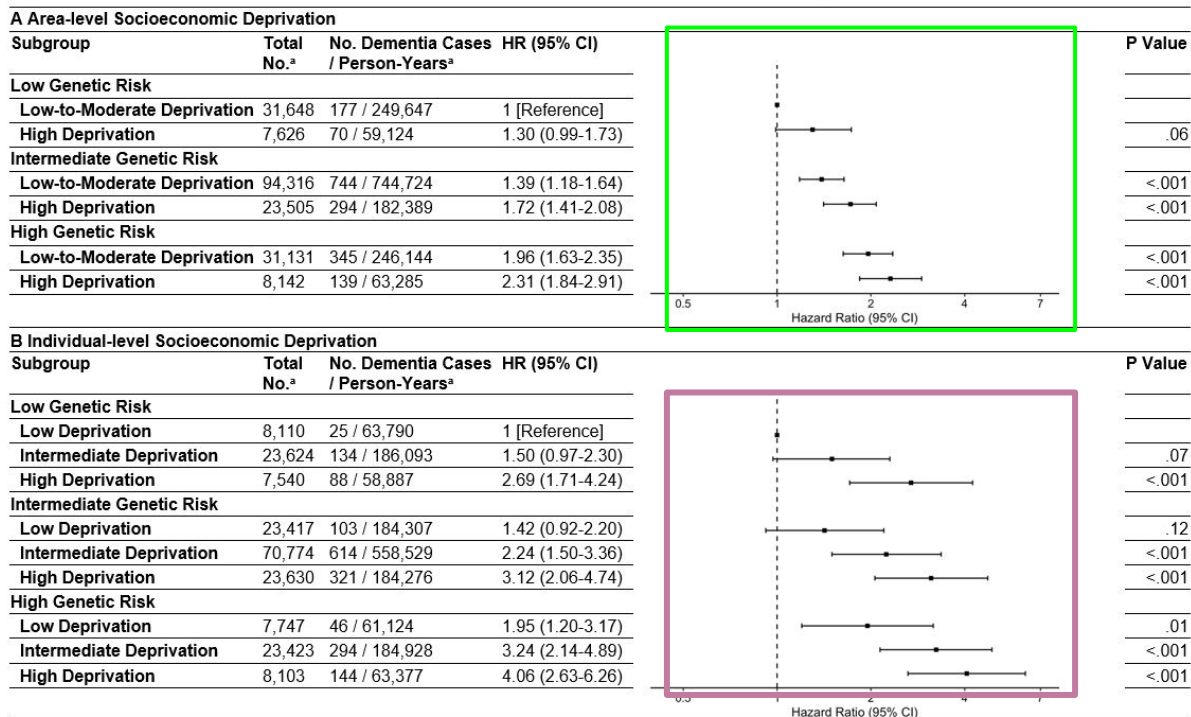
- UK Biobank: 196,368 participants 60+, European ancestry
- Time-to-event design: 2006-10 initial assessment, follow-up until 2016-17
- Dementia ascertained through hospital or death records
- Polygenic risk score for developing dementia: Quintiles 1 (low), 2-4 (moderate), 5 (high genetic risk)

Townsend Deprivation Index: Quintiles 1-4 (low) vs. quintile 5 (high deprivation)
Individual-level socioeconomic deprivation (income, home, car)

Klee, M., Leist, A.K., Veldsman, M., Ranson, J.M., Llewellyn, D.J. (in press). Socioeconomic deprivation, genetic risk, and incident dementia. *American Journal of Preventive Medicine*. <https://doi.org/10.1016/j.amepre.2023.01.012>

Neighbourhood deprivation x genetic risk

Figure 1. Risk of Incident Dementia for A Area-level and B Individual-level Socioeconomic Deprivation with Genetic Risk

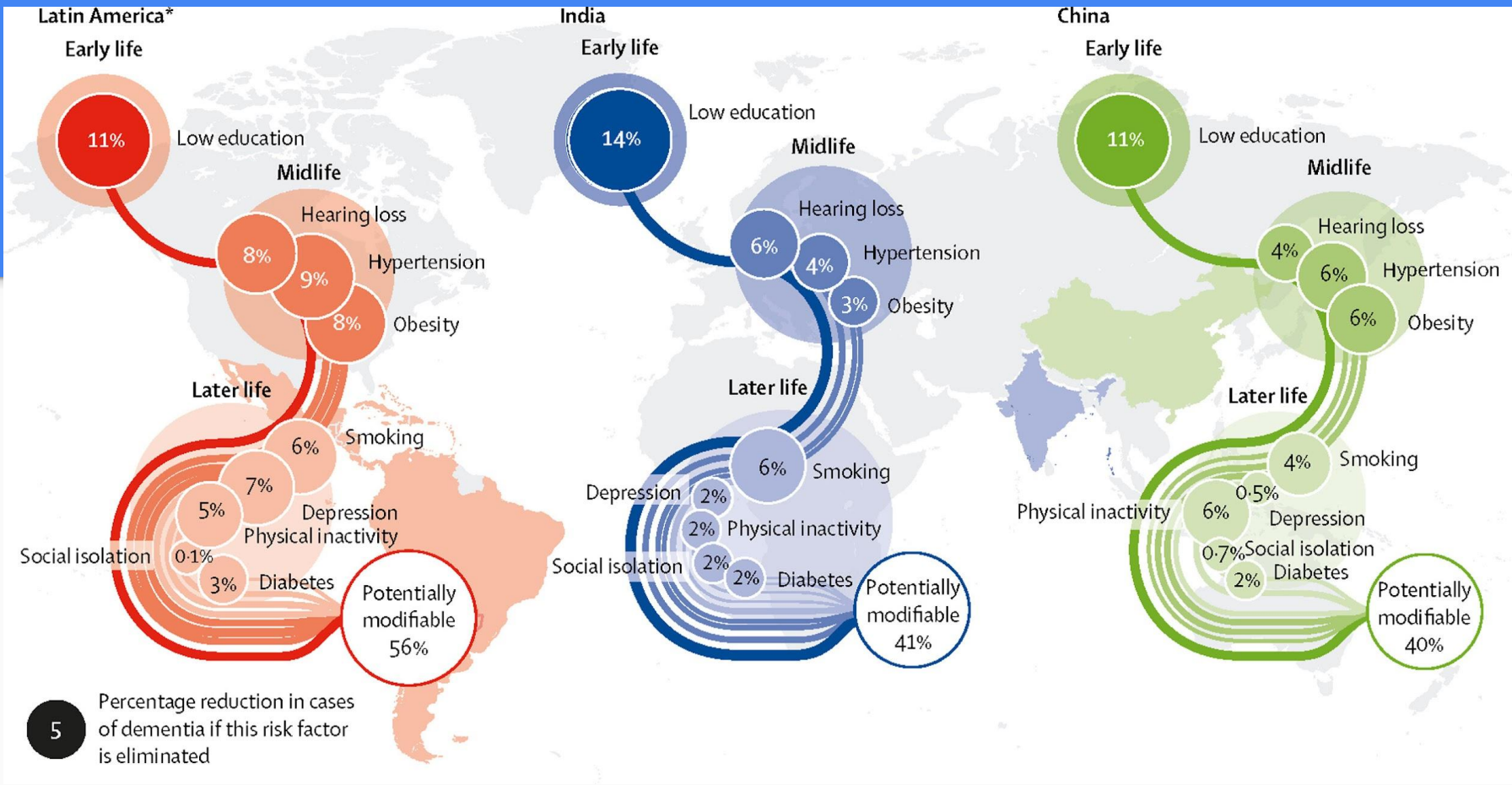


All Cox proportional-hazards regressions were adjusted for covariates relevant in polygenic risk analyses, age, sex, education, marital status, healthy lifestyle and depressive symptoms in last two weeks. Additionally, adjustments for individual-level (A) and area-level socioeconomic deprivation (B) were included.

What is the prevalence of cognitive impairment in Latin America and the Caribbean, and what are the secular trends?



Dr. Fabiana Ribeiro, IRSEI, UL

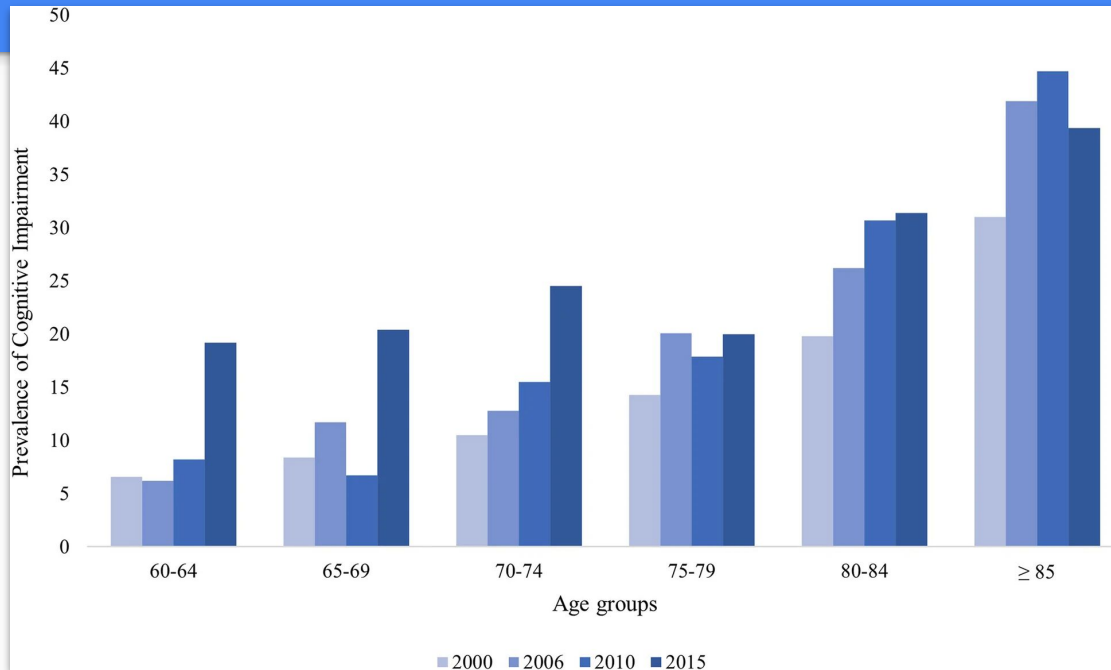


Mukadam, N., Sommerlad, A., Huntley, J., & Livingston, G. (2019). Population attributable fractions for risk factors for dementia in low-income and middle-income countries: an analysis using cross-sectional survey data. *The Lancet Global Health*, 7(5), e596-e603.

Background

- Estimate dementia prevalence in lower-resource settings
- Investigate secular trends in prevalence of cognitive impairment in lower-resource settings
- Investigate secular trends in risk factor burden

Prevalence of cognitive impairment by age group, São Paulo, 2000-2015



Increases in prevalence of cognitive impairment, specifically 60-79 years, 2000-2015

Increases in formal education and income, 2000-2015

Increases in prevalence of diabetes, hypertension, overweight/obesity, 2000-2015

Sex/gender and socioeconomic differences in modifiable risk factors for dementia



Dr. Anouk Geraets, IRSEI, UL

Sex/gender and socioeconomic differences in modifiable risk factors for dementia

Sex/gender and socioeconomic differences in dementia and modifiable risk factors for dementia

Different risk factor prevalence or different exposure-outcome relationships?

English Longitudinal Study of Ageing (2008/2009 to 2018/2019)

N = 8,941 individuals, mean age, 66.1 ± 9.8 years; n = 4,935 (55.2%) women

Modifiable risk factors according to the LIBRA score.

Sex/gender and socioeconomic differences in modifiable risk factors for dementia

- No overall sex/gender difference in dementia risk
- Dementia risk was higher among those with
 - Childhood deprivation [hazard ratio (HR) = 1.51 (1.17; 1.96)];
 - Lower occupational attainment [HR low versus high = 1.60 (1.23; 2.09) and HR medium versus high = 1.53 (1.15; 2.06)];
 - Low wealth [HR low versus high = 1.63 (1.26; 2.12)].

Sex/gender and socioeconomic differences in modifiable risk factors for dementia

- Sex/gender differences in modifiable risk factors
 - Low cognitive activity was associated with a higher dementia risk for women [HR = 2.61 (1.89; 3.60)] compared to men [HR = 1.73 (1.20; 2.49)].
- No consistent socioeconomic differences in modifiable dementia risk factors.

➡ Preference for population-based approach that tackles inequalities and modifiable risk factor burden directly, compared to individual approaches in dementia prevention.

How can we reduce risk of dementia by adopting healthy lifestyle behaviours?

What are the pathways to dementia risk?

- Resilience/resistance to stressors
- Cognitive stimulation
- Chronic stress
- Inflammation
- Social stimulation/support
- Microbiome?
- Environmental (neuro)toxins
- ...

Most relevant health behaviours to recommend for mid-aged adults

- Increase physical activity, particularly cardio
- Stop heavy alcohol consumption (more than 21 units/week)
- Monitor cardiovascular and diabetes risk and, if necessary, treat
- Stop smoking
- Improve sleep quality

Sex/gender considerations

- Time use between the genders
- Hormonal/biological considerations when exercising
- Sex/gender differences in thresholds for alcohol uptake
- ...

Most relevant health behaviours *additionally* to recommend for older-aged adults

- Stay hydrated
- Increase physical activity with strength/resistance training
- If hearing is impaired, wear the hearing aid
- Stay cognitively and socially active

Habit formation:
not trivial...

The psychology of behaviour change

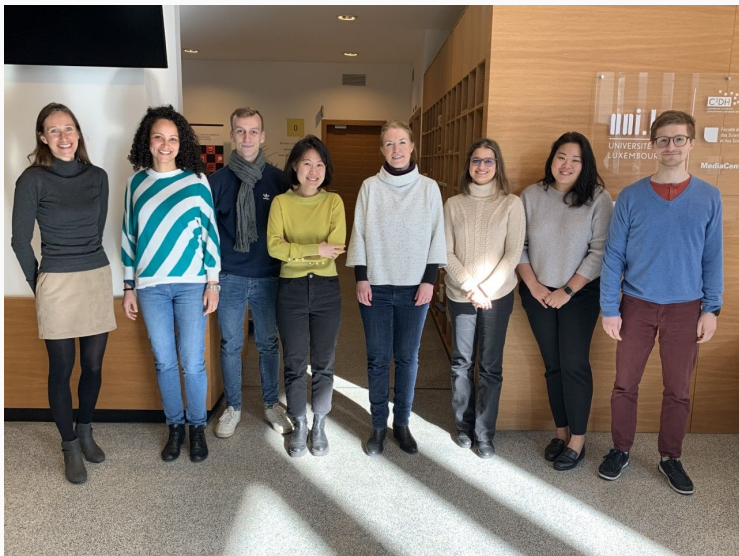
- Formulate a goal
- Visualise yourself at the time you achieved your goal
- Increase accountability
- Reframing

The psychology of behaviour change

Use insights on habit formation and maintenance:

- One new habit at a time
- Start small
- Link new to existing habits
- If the new habit involves 'stopping' something, replace it with a (harmless) enjoyable alternative

Use support groups, competitions, coaching...



Acknowledgements

Katherine Ford
Ivana Paccoud
Fabiana Ribeiro
Anouk Geraets
Ana Carolina Teixeira Santos
Jung Hyun Kim
Melissa Chan
Matthias Klee
Collaborators at UL and beyond
All study participants

Funding



European Research Council
Established by the European Commission

This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No. 803239).



INSTITUTE FOR ADVANCED STUDIES (IAS)



anja.leist@uni.lu
@AnjaLeist
<https://cognitiveageing.uni.lu>



Luxembourg National
Research Fund