



Wie lässt sich das individuelle Risiko für Demenz reduzieren? Neue Erkenntnisse aus der Demenz-Präventionsforschung

Prof. Dr. Anja Leist, Universität Luxemburg

Konferenz „Demenzforschung & Preventioun“
association luxembourg alzheimer, 16. Juni 2023

Financial disclosures

I have received remuneration from Roche
for advisory and speaker activities.

Was ist Demenz?

Eine Bandbreite von Störungen, charakterisiert durch das Nachlassen des Gedächtnisses und anderer Denkfähigkeiten, die die Aktivitäten des täglichen Lebens beeinträchtigt

10 frühe Symptome

- Gedächtnisverlust, der das tägliche Leben beeinträchtigt
- Herausforderungen bei Planung und Lösung von Problemen
- Schwierigkeiten, gewohnte Aufgaben zu Hause, in der Arbeit oder in der Freizeit durchzuführen
- Verwirrung bei Zeit und Ort
- Probleme beim Verstehen von visuellen Eindrücken und räumlichen Zusammenhängen
- Neue Probleme beim Sprechen oder Schreiben von Wörtern
- Verlegen von Gegenständen und Verlust der Fähigkeit, Schritte nachzuvollziehen
- Vermindertes oder schlechtes Urteilsvermögen
- Rückzug von Arbeiten oder sozialen Aktivitäten
- Veränderungen der Stimmung und des Charakters

[https://www.alz.org/de/was-
ist-demenz.asp](https://www.alz.org/de/was-ist-demenz.asp)

Warum ist Demenz-Prävention wichtig?

Demenz geht mit großen Einschränkungen und hoher Belastung einher für Betroffene, deren Angehörige und Pflegende (Livingston et al., 2017)

Kognitive Beeinträchtigungen und Demenz sind eine der größten Herausforderungen alternder Gesellschaften: Schätzungen gehen von 14,3 Mio. Menschen mit Demenz aus im Jahr 2050 in Europa (Alzheimer Europe, 2019)

Es gibt keine Heilung von Demenz mittels medikamentöser Behandlung, auch wenn erste Medikamente kognitiven Abbau verlangsamen können (van Dyck et al., 2022)

Alzheimer Europe. (2019). Dementia in Europe Yearbook 2019: Estimating the prevalence of dementia in Europe. Alzheimer Europe.

van Dyck, C. H., Swanson, C. J., ... & Iwatsubo, T. (2022). Lecanemab in Early Alzheimer's Disease. New England Journal of Medicine, NEJMoa2212948. <https://doi.org/10.1056/NEJMoa2212948>

Was sind modifizierbare
Risikofaktoren für Demenz?

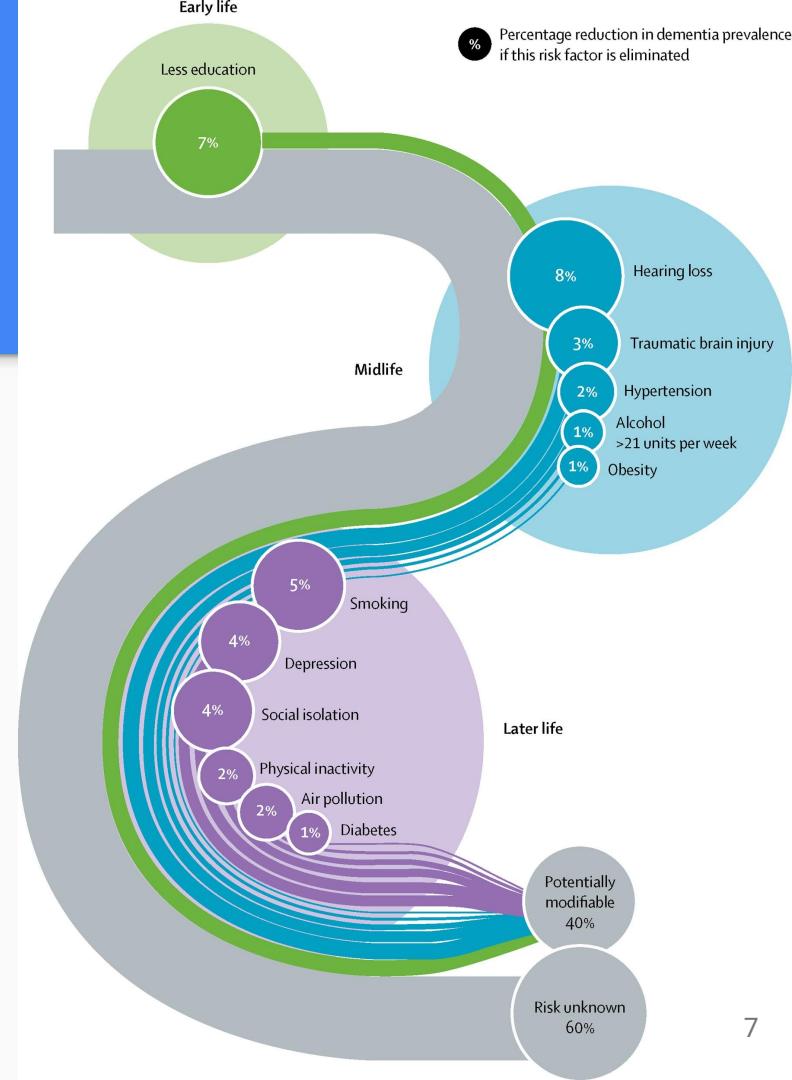
Modifizierbare Risikofaktoren

Potentiell modifizierbare Risikofaktoren tragen bis zu 40% zu Demenz bei.

Im Vergleich liegt der Beitrag genetischer Belastung bei $\approx 7\%$.

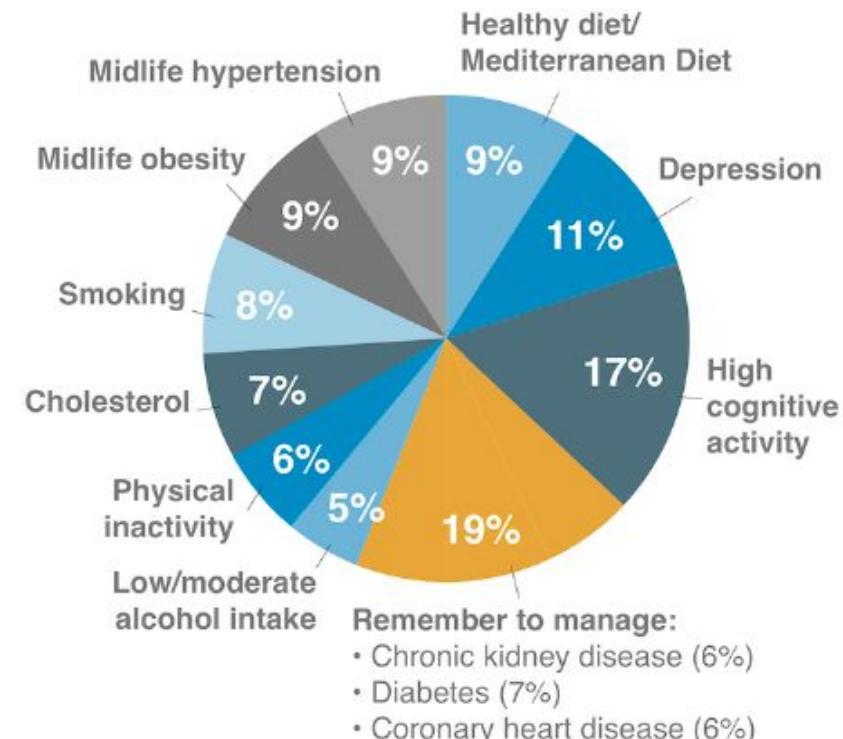
→ Großes Potential für Prävention.

Livingston, G., Huntley, J., Sommerlad, A., Ames, D., Ballard, C., Banerjee, S., ... & Mukadam, N. (2020). Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *The Lancet*, 396(10248), 413-446.



Lifestyle for Brain Health (LIBRA)

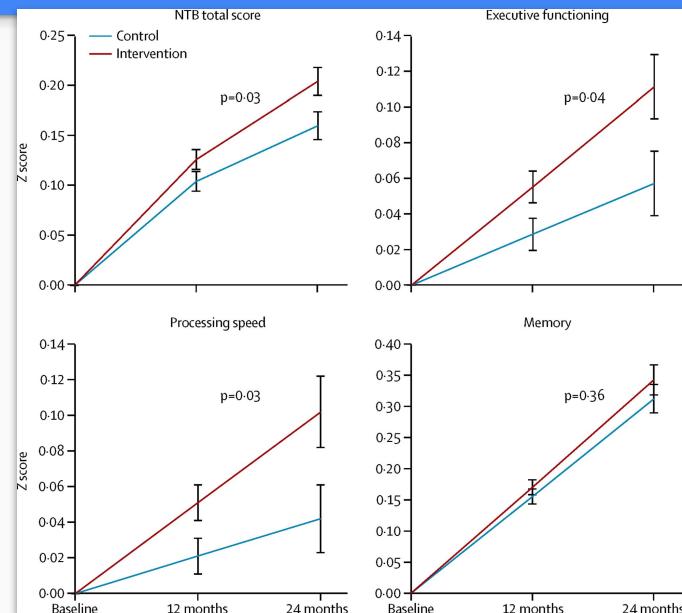
Schiepers, O. J., Köhler, S., Deckers, K., Irving, K., O'Donnell, C. A., van den Akker, M., ... & van Boxtel, M. P. (2018). Lifestyle for Brain Health (LIBRA): a new model for dementia prevention. *International journal of geriatric psychiatry*, 33(1), 167-175.



Sekundärprävention

Erste Evidenz dafür, dass kognitiver Abbau verlangsamt werden kann, indem vorhandene Risikofaktoren reduziert werden mittels “multi-domain” Lebensstil-Intervention.

Ngandu, T., Lehtisalo, J., Solomon, A., Levälahti, E., Ahtilo, 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

RISK REDUCTION OF COGNITIVE DECLINE AND DEMENTIA

WHO GUIDELINES



World Health
Organization

Preventing Cognitive Decline and Dementia: A Way Forward

PREVENTING COGNITIVE DECLINE AND DEMENTIA A WAY FORWARD

Committee on Preventing Dementia and Cognitive Impairment,
Alain I. Leshner, Story Landis, Clara Stroud, and Autumn Dowling,
Editors

Board on Health Sciences Policy
Health and Medicine Division

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

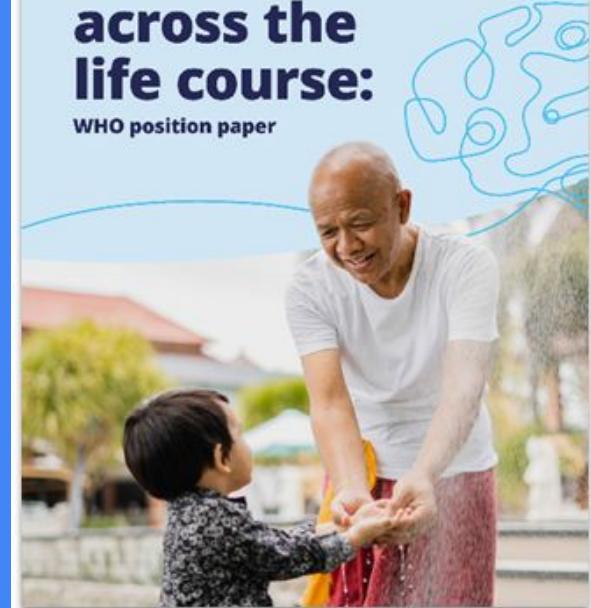
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Washington, DC
www.nap.edu

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Optimizing brain health across the life course:

WHO position paper





MEDITAGING Study: *Mindfulness training on aging: the effects of mindfulness based-stress reduction in older Portuguese-speaking migrants residing in Luxembourg (2021-23)*

Randomized controlled trial
8-week intervention



Mindfulness-Based Stress Reduction (N=45)



Health Promotion Program (N=45)

Cognition, emotional measures, mindfulness, sleep, cortisol and heart rate variability



Dr. Ana Carolina Teixeira Santos,
University of Luxembourg and Zitha

Wie interagieren 'soziale Determinanten von Gesundheit' mit modifizierbaren Risikofaktoren für Demenz?

Soziale Determinanten von Gesundheit

Soziale Determinanten können auf individueller Ebene, aber auch auf Nachbarschafts-, Regions-, Länderebene gemessen werden.

Sehr schwierig, die Einflüsse einzelner Ebenen auseinanderzuhalten

Lebenslaufeinflüsse beachten



© 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
- 1.15 mio. EUR

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



Wichtigste Erkenntnisse

1. Großer Einfluss von sozioökonomischem Status auf Demenz, unabhängig von genetischer Vorbelastung
2. Großer Einfluss des ‘westlichen Lebensstils’ auf Gesundheit und auch Demenz
3. Die Rolle des Lebensstils gleichermaßen wichtig bei Männern und Frauen, und bei sozioökonomisch günstigen und weniger günstigen Lebensbedingungen

Do neighbourhood socioeconomic conditions interact with genetic risk for dementia?

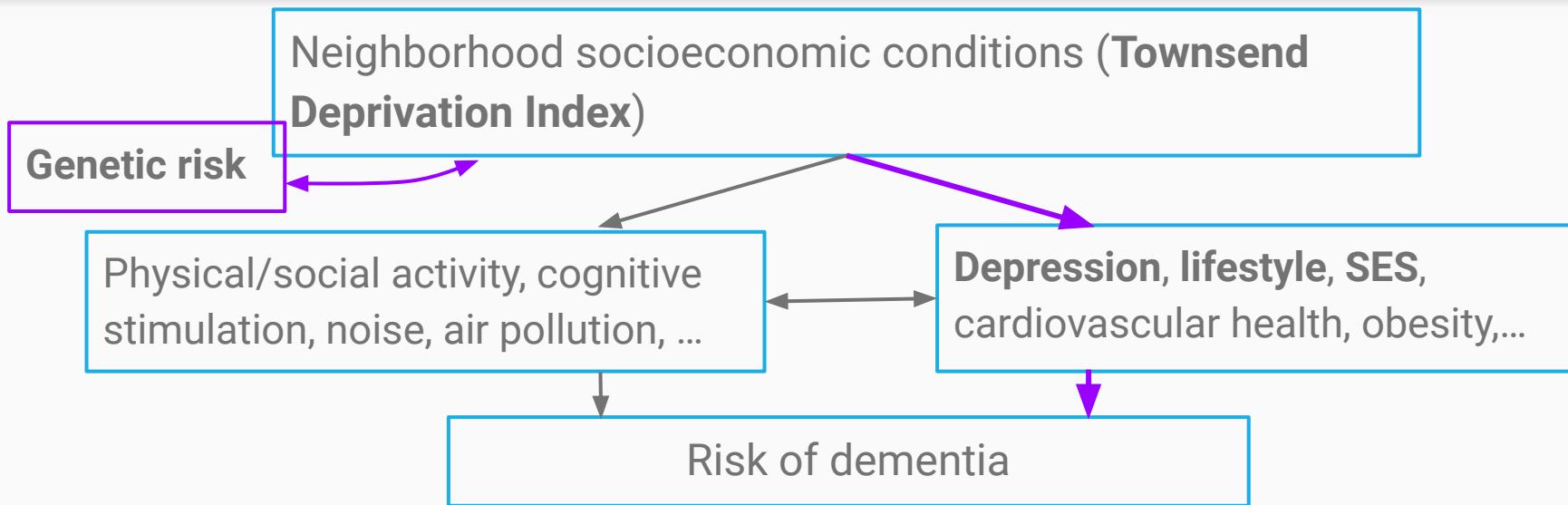


Klee, M., Leist, A.K., Veldsman, M., Ranson, J.M., Llewellyn, D.J. (2023). Socioeconomic deprivation, genetic risk, and incident dementia. *American Journal of Preventive Medicine*.

<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

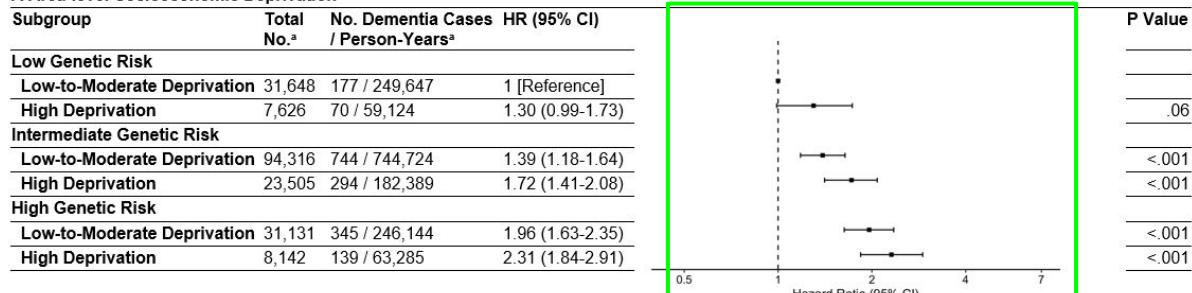
- UK Biobank: 196,368 participants 60+, European ancestry
- Time-to-event design: 2006-10 initial assessment, follow-up until 2016-17
- Dementia ascertained through hospital or death records
- Polygenic risk score for developing dementia: Quintiles 1 (low), 2-4 (moderate), 5 (high genetic risk)

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

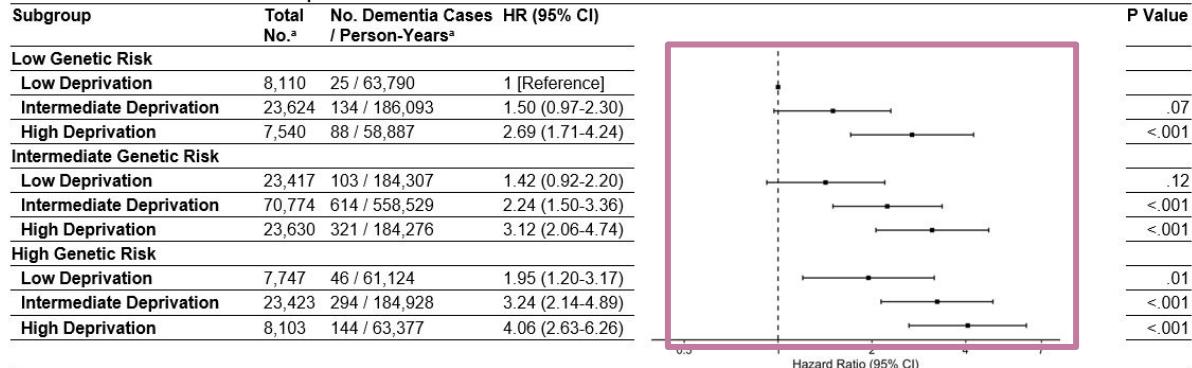
Neighbourhood deprivation x genetic risk

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

A Area-level Socioeconomic Deprivation



B Individual-level Socioeconomic Deprivation



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.

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 and Livingston.

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

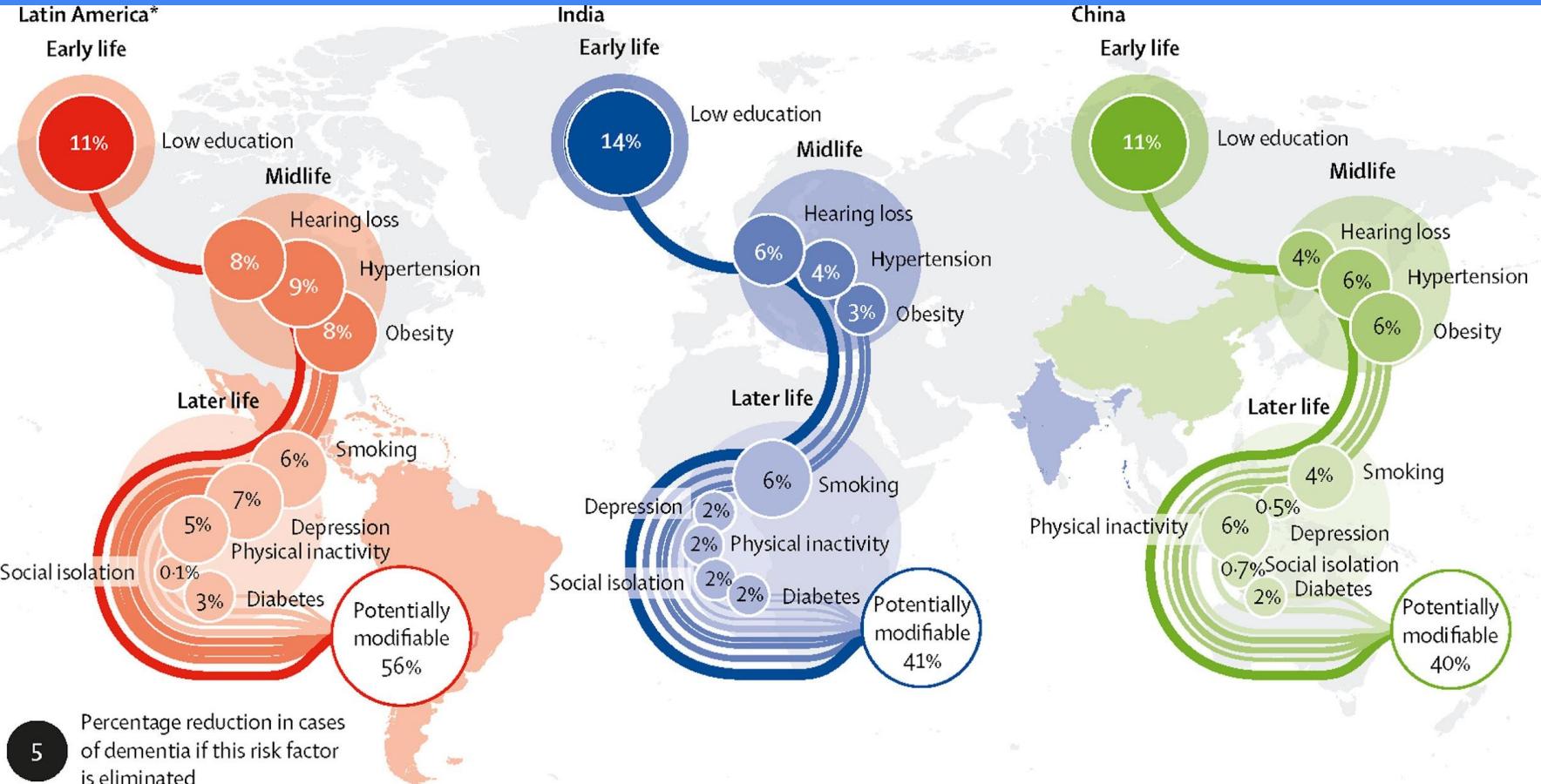
- Sex/gender differences in modifiable risk factors
 - Low cognitive activity was associated with a higher dementia risk for women [HR = 2.61 (1.89; 3.60)] compared to men [HR = 1.73 (1.20; 2.49)].
- No consistent socioeconomic differences in modifiable dementia risk factors.

→ Suggests that population-based approaches that tackle inequalities and modifiable risk factor burden directly will be successful.

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



Dr. Fabiana Ribeiro, IRSEI, UL

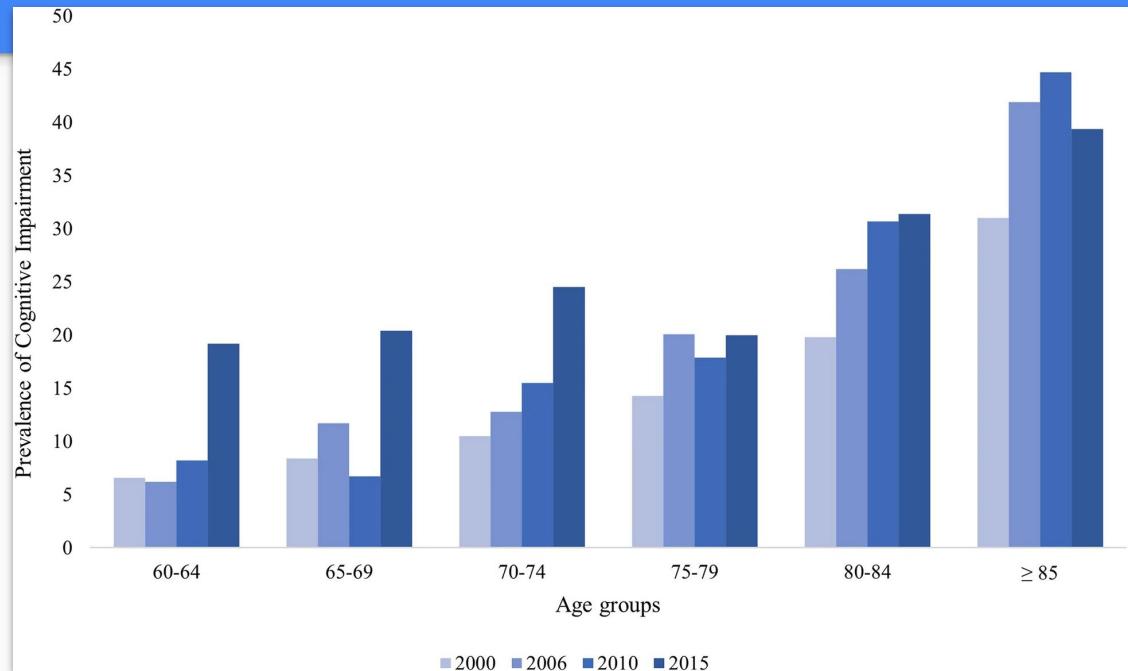


Mukadam, N., Sommerlad, A., Huntley, J., & Livingston, G. (2019). Population attributable fractions for risk factors for dementia in low-income and middle-income countries: an analysis using cross-sectional survey data. *The Lancet Global Health*, 7(5), e596-e603.

Motivation

- 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

Wie können wir das Demenzrisiko durch
einen gesunden Lebensstil verringern?

Wie entsteht das Demenzrisiko?

Mögliche Pfade:

- Kognitive Stimulation
- Chronischer Stress
- Entzündungen
- Soziale Stimulation/Unterstützung
- Mikrobiom?
- Umwelt(neuro)toxine
- Resilienz/Widerstandsfähigkeit gegenüber Stressoren
- ...

Wichtigste zu empfehlende Verhaltensweisen für Erwachsene mittleren Alters

- Körperliche Aktivität steigern, insbesondere Ausdauertraining
- Alkoholkonsum einschränken (v.a. weniger als 21 Einheiten/Woche)
- Überwachung des kardiovaskulären und Diabetes-Risikos, falls erforderlich: Behandlung
- Kalorienaufnahme angepasst an das Verhaltensprofil
- Mit dem Rauchen aufhören
- Schlafqualität verbessern, insb. Schlafdauer

Erwägungen zu Geschlechtsunterschieden

- Zeitverwendung zwischen den Geschlechtern (Fürsorgearbeit)
- Hormonelle/biologische Überlegungen bei der Ausübung von Sport, Kalorienaufnahme
- Unterschiede zwischen den Geschlechtern hinsichtlich der Schwellenwerte für Alkoholkonsum
- ...

Wichtigste zusätzliche Verhaltensweisen für ältere Erwachsene (60+ Jahre)

- Hinreichende Flüssigkeitsaufnahme
- Körperliche Aktivität steigern durch Kraft-/Widerstandstraining
- Wenn das Gehör beeinträchtigt ist, das Hörgerät regelmäßig tragen
- Kognitiv und sozial aktiv bleiben

Neue Gewohnheiten zu
etablieren ('habit formation')
ist kein triviales Vorhaben...

Die Psychologie der Verhaltensänderung

- Formulieren Sie ein Ziel
- Visualisieren Sie sich selbst in der Zukunft, wenn Sie Ihr Ziel erreicht haben
- Verantwortlichkeit (Rechenschaft) erhöhen
- Umstrukturierung negativer Erlebnisse bei den neuen Verhaltensweisen

Die Psychologie der Verhaltensänderung

Erkenntnisse über die Bildung und Aufrechterhaltung von Gewohnheiten nutzen:

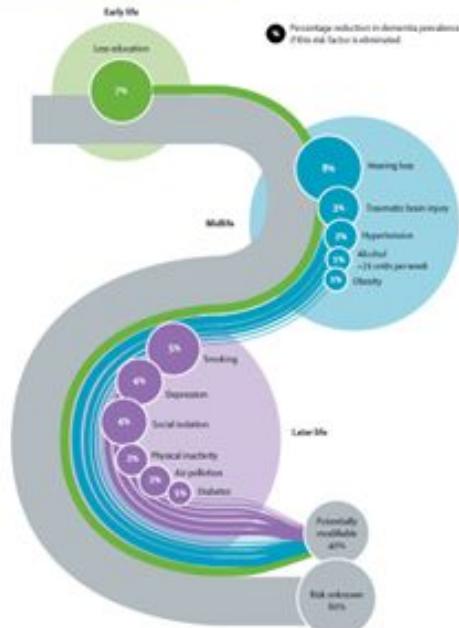
- Eine neue Gewohnheit nach der anderen
- Klein anfangen
- Verbinden Sie neue mit bestehenden Gewohnheiten
- Wenn die neue Gewohnheit bedeutet, mit etwas "aufzuhören", diese durch eine (harmlose) angenehme Alternative ersetzen

Selbsthilfegruppen, Wettbewerbe, Coaching nutzen...

Integrierte Versorgung bei milder kognitiver Beeinträchtigung

Programme for Dementia Prevention (pdp)

Concept



Risk factors for dementia

- Hypertension
- Cardiovascular diseases
- Hypercholesterolemia
- Physical inactivity
- Cognitive inactivity
- Diabetes
- Obesity
- Non-mediterranean diet
- Excessive alcohol consumption
- Smoking
- Depression
- Social isolation
- Kidney dysfunction
- Hearing loss
- Traumatic brain injury
- Air pollution

Livingston et al., The Lancet Commission, 2020

www.pdp.lu / info@pdp.lu

Bitte mitmachen!
Ein neues Forschungsprojekt in
Luxemburg:



THE MICHAEL J. FOX FOUNDATION
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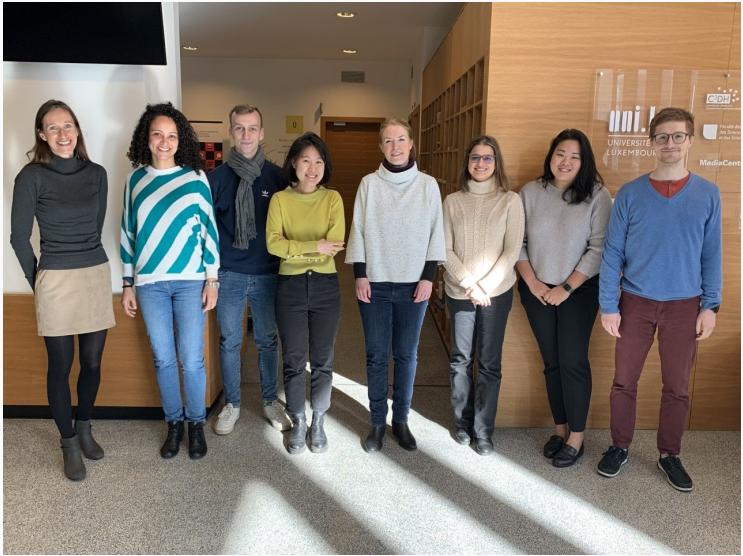
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INSTITUTE
OF HEALTH



**Schléisst lech eiser Fuerschung un,
fir Gehierkrankheeten ze vermeiden.**

www.heba.lu





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Matthias Klee
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INSTITUTE FOR ADVANCED STUDIES (IAS)

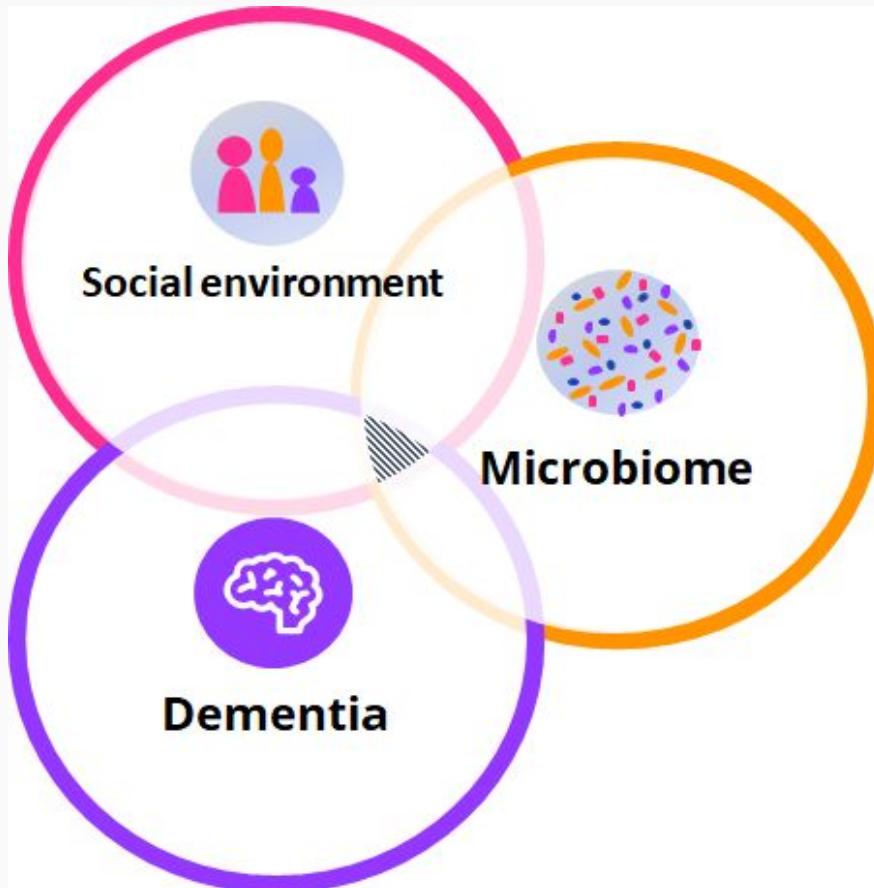


Luxembourg National
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<https://cognitiveageing.uni.lu>

Extra slides



MCI-BIOME

Relationship between socioeconomic status and the gut microbiome as a risk of dementia

co-PIs: Profs. Anja Leist, Paul Wilmes, Rejko Krüger

2019-23

Current status: Analysis of n=256 healthy controls with and without MCI of the NCER Parkinson cohort.

Submitted to the Alzheimer Association International Conference (AAIC), Amsterdam, July 2023

Presented at the Precision Medicine congress, Luxembourg, January 2023

Research Article

Partnership and Cognitive Aging in Europe: Mediating Factors and Social Stratification

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¹Department of University of Luxembourg

²Address correspondence to Universitätstrasse 7, 52072 Aachen, Germany

Received: August 2019

Decision Editor: D. J. C. Smith

Abstract

Objectives: Living in partnership may have an impact on cognitive health. Methods: Data panel for the partners' sample includes individuals who have stayed recall on variation in partner's cognitive functioning. Results: Partnership is associated with lower cognitive decline and higher cognitive functioning. Conclusions: Partnership may contribute to cognitive aging.

INTRODUCTION

Compared to many traditional studies, studies on aging and dementia are considerably more advanced as advances in prediction of detecting nonlinear exposures and confounds. However, uptake of machine learning (ML) approaches in clinical epidemiology remains fragmented due to a lack of communication of domain-specific ML approaches fitting the needs of clinical epidemiology. The aims of this paper are to introduce the toolbox of ML approaches in research designs in the methodology section and to elaborate on the potential of ML for research questions in the results section. As research units and reported variables, in addition to using ML, we present how it is that models are not only able to handle finite datasets from cross-sectional studies but also longitudinal studies.

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²Centre for Dementia Prevention, University, Aachen, OHU US

³Corresponding author: Erna Leist, PhD, erna.leist@uni.lu

Leist et al., *Soc Adv Psychol* 2021; 1(1).

SCIENCE ADVANCES | REVIEW

RESEARCH METHODS

Mapping of machine learning approaches for description, prediction, and causal inference in social and health sciences

Anja K. Leist^{1*}, Matthias Klef², Jung Hyun Kim¹, David H. Rehkopf², Stéphane P. A. Bordas³, Graciela Muniz-Terrera^{4,5}, Sara Wade⁶

Machine learning (ML) purposes of description, prediction, and causal inference. ML requirements to support description, prediction, and causal inference. ML estimating prevalence factors or causes of all fully exploit the potential of ML and hopefully contribute to social and health sciences

INTRODUCTION

Changes in neighborhood-level socioeconomic disadvantage and older Americans' cognitive functioning

Jason Settels¹, Anja K. Leist

¹University of Luxembourg, Department of Social Sciences, Institute for Research on Socio-Economic Inequality, 11, Porte des Sciences, Luxembourg

ARTICLE INFO

Keywords

Cognitive decline
Neighborhood
Socioeconomic disadvantage
Depression
Close social networks
Physical activity

Background

While associations of neighborhood conditions established, few studies have investigated with a dynamic perspective how older residents' cognitive declines, and a model of neighborhood-level socioeconomic disadvantage Project (NSHAP) survey (n = 18,871), ordinary least squares

adjusting for multiple confounders and testing eight potential mechanisms linking neighborhood socioeconomic circumstances to depressive symptoms, still close of social network relationships.

Discussion: While 18.10% of the total effect occurred through contextual- and individual-level variables not ass

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