How to actively protect against dementia. Epidemiological data from Luxembourg

Anja Leist, University of Luxembourg

Mardis en Neurosciences, CHL, 5 February 2020

Dementia

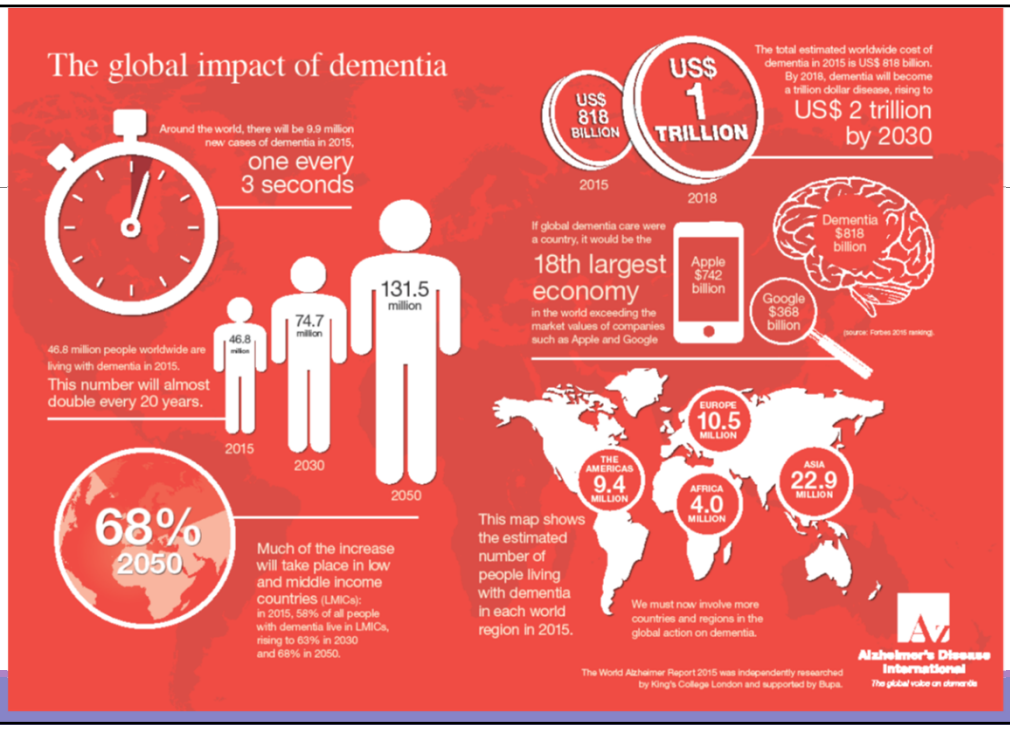
- Range of conditions characterized by memory impairment
- Alzheimer's Disease (40-60%), vascular dementia (up to 40 %), mixed, Lewy-Body, Parkinson's dementia etc.

Medical Treatment

- There is no medical treatment able to cure dementia
- In October 2019, Biogen requested FDA approval of aducanumab after re-analysis of data of 2 trials that were ended in March 2019. On 28 January 2020, FDA approved a re-dosing study to begin approx. in March 2020.

Risk Reduction and Prevention

- Onset and progression of dementia are highly variable
- Lifestyle changes can help delay onset and progression of the disease



Facts on dementia funding and progress

- Goal of finding a disease-modifying therapy by 2025 (G8 Summit 2013)
  - US Government increased funding for Alzheimer's and related research: $562 million in 2013; $2.6 billion in 2019
  - Dementia research still seriously underfunded and underresearched compared to other diseases[1]
- WHO Global Action Plan on Dementia, May 2017
  - To improve conditions for people living with dementia across countries, 15 national dementia plans per year need to be initiated
  - Update Oct. 2018: 3 national plans being prepared

Pickett et al., 2018; World Alzheimer Report, 2015
[1]Rate of publications on neurodegenerative diseases versus cancer is 1:12, World Dementia Council Report, 2018

Cognitive reserve and brain health

Cognitive reserve (CR)

Stern et al. (2018), p. 2: “The term CR refers to the adaptability (i.e., efficiency, capacity, flexibility … of cognitive processes that helps to explain **differential susceptibility** of cognitive abilities or day-to-day function to brain aging, pathology, or insult.”

Further recent reviews by Cabeza et al., 2018; Nilsson & Lövden, 2018

Alzheimer's Research & Therapy

REVIEW Open Access

Naming is not explaining: future directions for the “cognitive reserve” and “brain maintenance” theories

Jonna Nilsson and Martin Lövdén

ARTICLE IN PRESS

Alzheimer's & Dementia

Review Article

Whitepaper: Defining and investigating cognitive reserve, brain reserve, and brain maintenance

Yaakov Stern, Eider M. Arenaza-Urquijo, David Bartrés-Faz, Sylvie Belleville, Marc Cantilon, Gael Chetelat, Michael Ewers, Nicolai Franzmeier, Gerd Kempermann, William S. Kremen, Ozioma Okonkwo, Nikolaos Scarmeas, Anja Soldan, Chinedu Udeh-Momoh, Michael Valenzuela, Prashanthi Vemuri, Eero Vuoksimaa, and the Reserve, Resilience and Protective Factors PIA Empirical Definitions and Conceptual Frameworks Workgroup

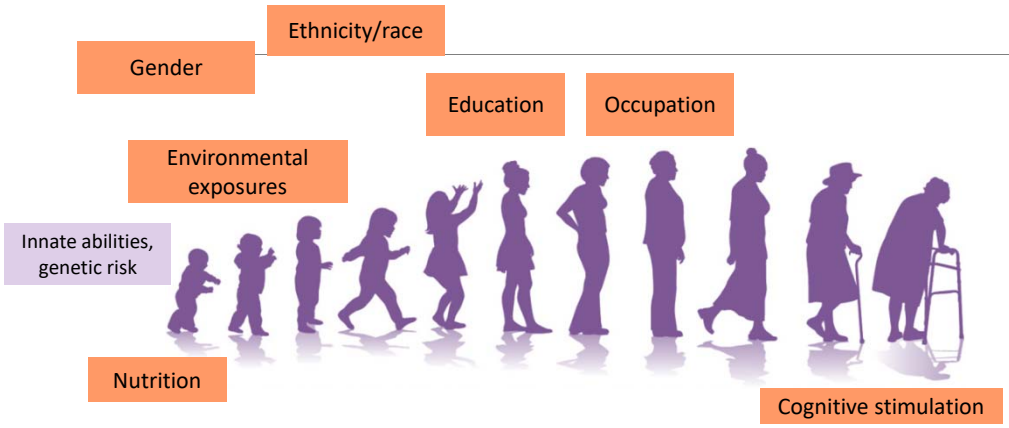
PERSPECTIVES

OPINION

Maintenance, reserve and compensation: the cognitive neuroscience of healthy ageing

Roberto Cabeza, Marilyn Albert, Sylvie Belleville, Fergus I. M. Craik, Audrey Duarte, Cheryl L. Grady, Ulman Lindenberger, Lars Nyberg, Denise C. Park, Patricia A. Reuter-Lorenz, Michael D. Rugg, Jason Steffener and M. Natasha Rajah

Life course influences on cognitive functioning



Leist, Novella, Olivera, 2018; Leist & Mackenbach, 2014; Leist et al., 2013

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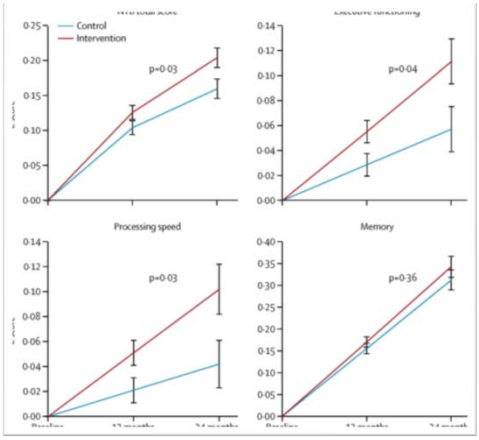
First evidence on reducing risk of dementia



Behavioral multidomain intervention over two years:
- Exercise
- Nutritional advice
- Management of vascular risk factors
- Cognitive training
- (Social support)

Ngandu, Kivipelto et al. (2015), Lancet

FINGER → WORLD WIDE FINGERS alzheimer's association

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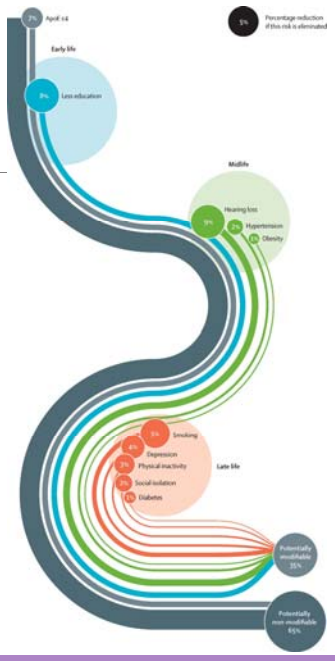
Prevention of /risk reduction in dementia



Nine modifiable risk factors could explain 35 % of the risk of dementia

- Education to a maximum of age 11-12 years (8%)
- Midlife hypertension
- Midlife obesity
- Hearing loss
- Late-life depression
- Diabetes
- Physical inactivity
- Smoking
- Social isolation

… in comparison: eliminating ApoE ε4 allele would reduce 7 % of dementia incidence

Livingston et al., 2017; Norton et al., 2014

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Newer approaches: Lifestyle for Brain Health (LIBRA)

- Low/moderate alcohol consumption
- *Coronary heart disease*
- Physical inactivity
- *Renal dysfunction*
- Diabetes
- High cholesterol
- Smoking
- Obesity
- Hypertension
- Healthy diet (Mediterranean diet, low unsaturated fat intake)
- Depression
- High cognitive activity

Schiepers et al. (2018); Deckers, …, & Köhler (2019)

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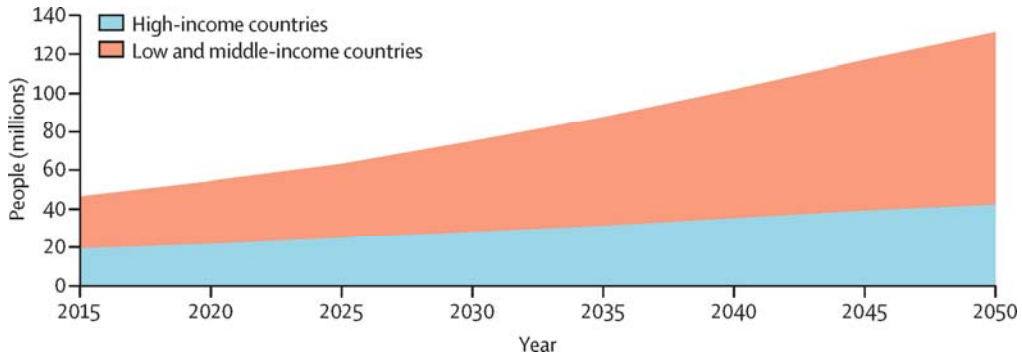
Increases in dementia cases



Livingston et al. (2017)

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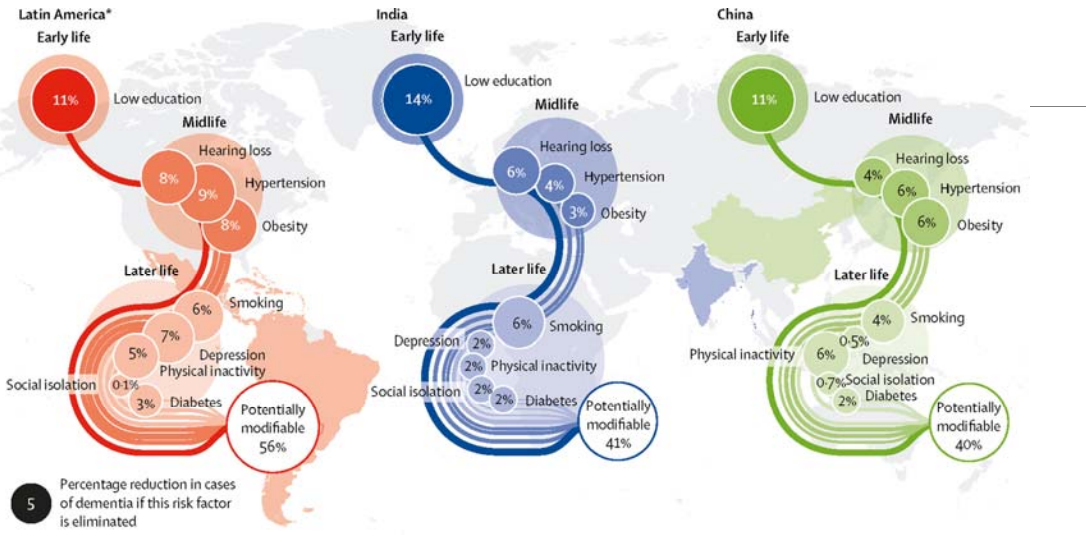

Mukadam et al. (2019)

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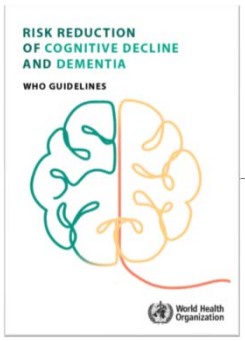
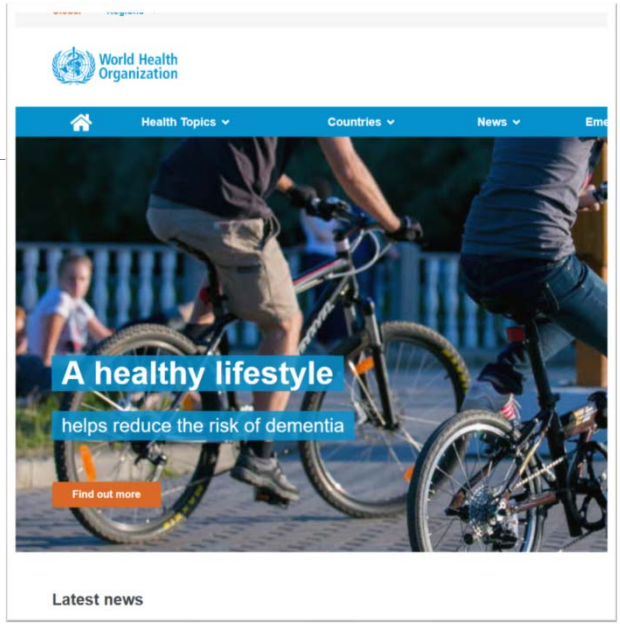
How much do we really know about the value of behavior changes to reduce risk of cognitive aging and dementia?

ERC StG CRISP (2019-2023, grant agreement no. 803239)



New World Health Organization Guidelines

Published 14 May 2019
In the Framework of the WHO Global Action Plan on the Public Health Response to Dementia (2017-2025)



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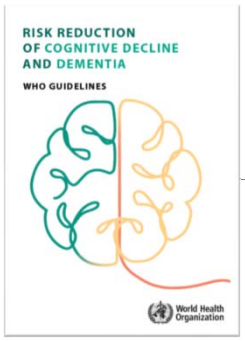

Interventions for **tobacco cessation** should be offered to adults who use tobacco since they may reduce the risk of cognitive decline and dementia in addition to other health benefits. *Quality of evidence: low; strength of the recommendation: strong*

The **Mediterranean-like diet** may be recommended to adults with normal cognition and mild cognitive impairment to reduce the risk of cognitive decline and/or dementia. *Quality of evidence: moderate; strength of the recommendation: conditional*

Interventions aimed at **reducing or ceasing hazardous and harmful drinking** should be offered to adults with normal cognition and mild cognitive impairment to reduce the risk of cognitive decline and/or dementia in addition to other health benefits. *Quality of evidence: moderate (for observational evidence); strength of the recommendation: conditional*

There is insufficient evidence to recommend either **social activity**, **use of antidepressant medicines**, or **use of hearing aids** to reduce of risk of cognitive decline/dementia.

There is low quality of evidence to recommend **cognitive interventions**, **weight management**, (**hypertension**), **management of diabetes mellitus, management of dyslipidaemia** to reduce risk of dementia.

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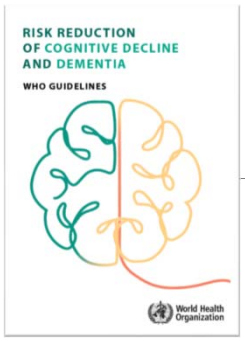
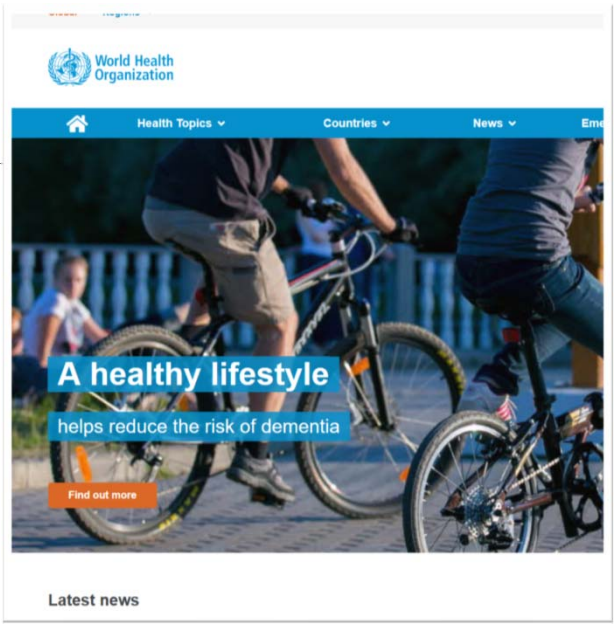


Physical activity should be recommended to adults with normal cognition to reduce the risk of cognitive decline

Quality of the evidence: moderate

Strength of the recommendation: strong



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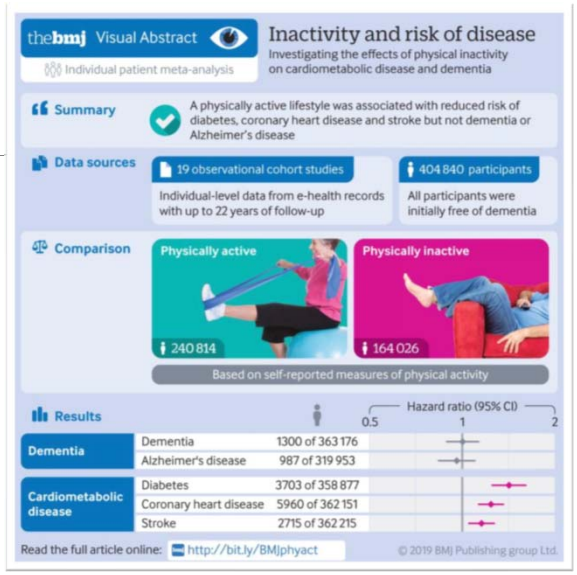
RESEARCH

Physical inactivity, cardiometabolic disease, and risk of dementia: an individual-participant meta-analysis

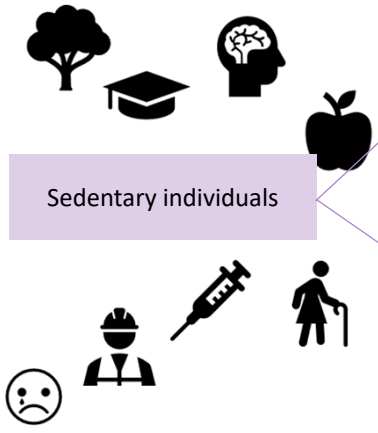
Mika Kivimäki,[1,2,3] Archana Singh-Manoux,[1,4] Jaana Pentti,[2,5] Séverine Sabia,[1,4] Solja T Nyberg,[2] Lars Alfredsson,[6] Marcel Goldberg,[7] Anders Knutsson,[8] Markku Koskenvuo,[2] Aki Koskinen,[9] Anne Kouvonen,[10,11,12] Maria Nordin,[13,14] Tuula Oksanen,[9] Timo Strandberg,[2,15,16] Sakari B Suominen,[5,17] Töres Theorell,[13] Jussi Vahtera,[5,18] Ari Väänänen,[9] Marianna Virtanen,[19] Peter Westerholm,[20] Hugo Westerlund,[13] Marie Zins,[7] Sudha Seshadri,[21,22] G David Batty,[1] Pyry N Sipilä,[23] Martin J Shipley,[1] Joni V Lindbohm,[2] Jane E Ferrie,[1,23] Markus Jokela,[24] on behalf of the IPD-Work consortium

published 17 April 2019 in BMJ:

In analyses that addressed bias due to reverse causation, physical inactivity was not associated with all-cause dementia or Alzheimer's disease



Should doctors prescribe physical activity?



Design inspired by the recommendations on target trials by Miguel Hernan & Jamie Robins

Have a look!

THE BOOK OF WHY

The New Science of Cause and Effect

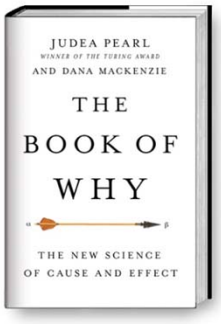
Coming May 15, 2018 from Basic Books

Friends,

We are thrilled to introduce our forthcoming book, ***The Book of Why: The New Science of Cause and Effect***.

"Correlation is not causation." This mantra, chanted by scientists for more than a century, has led to a virtual prohibition on causal talk. Today, that taboo is dead.

The causal revolution has cut through a century of confusion and established causality–the study of cause and effect–on a firm scientific basis.



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Cognitive functioning and dementia in the Survey of Health, Ageing and Retirement in Europe (SHARE)

Self-reported diagnosis of dementia

- "Doctor told you had" Alzheimer's disease, dementia, organic brain syndrome, senility or any other serious memory impairment
- Not population-representative: underdiagnosis, bias due to self-report, selective attrition/non-participation

Cognitive functioning

- Orientation (4 items): assessed at entry wave
- Numeracy (4 arithmetic tasks): assessed at entry wave
- Verbal fluency (number of animals named in 1 min)
- Immediate and delayed recall (remembering ten-word list immediately and after standardized delay)

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Prevalence of dementia in Luxembourg

Cognitive impairment no dementia (CIND)

- 11% of participants of the MemoVie study aged 65+ (Perquin, …, & Diederich (2013)
- Would translate to **9,716 cases of CIND** in Luxembourg* (Perquin et al. 2013)
- 65-74 years: 1.5%; 75-84 years: 5.4% in SHARE (0-1 points on a 4-point orientation scale)

Dementia

- 3.8% of people aged 65+ in a population-representative sample (Perquin, Diederich et al. 2015)
- Would translate to **3,356 cases of dementia in Luxembourg*** (prevalence from Perquin et al. 2015)
- 2.4% in 65+ year-olds in SHARE (65-74 years: 1.5%; 75-84 years: 4.3%; self-reported diagnosis of doctor)

*A total of 88,328 persons aged 65+ living Luxembourg on 1 January 2019 (Statec 2020)

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Prevention potential in Luxembourg?

- 7 risk factors: Diabetes, midlife hypertension, midlife obesity, physical inactivity, smoking, depression and educational attainment (Norton et al. 2014)

+ hearing loss (9%) and social isolation (2%) (Livingston et al. 2017)

+ Alcohol consumption + high cholesterol (Deckers et al. 2019; Lourida, … & Llewellyn, 2019)

→ *Total of 11 risk factors*

22

Prevalence of risk factors in Luxembourg

Later mid-life (50-64 years); early old age (65-74 years); old age (75-84 years)

- **Up to primary education**: 34.3% total, up to 48.5% of 75-84 year-olds; *gender differences*: 60.4% females vs. 34.5% of males in old age
- **High blood pressure**: 33.5% in total, up to 41.1% of 75-84 year-olds; *gender differences*: 40.2% of males vs 34.1% of females in early old age
- **Obesity**: 24.9% in total, up to 29.2% of 65-74 year-olds; *gender differences*: 32.7% in males vs 25.2% in females in early old age
- **High cholesterol**: 33.9% in total, up to 39.2% of 65-74 year-olds; *gender differences*: early old: 42.0% in males vs 36.1% in females
- **Depression**: 28.3% in total, up to 31.4% of 65-74 year-olds; *gender differences*: 33.7% in females vs 21.9% in males

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Prevalence of risk factors in Luxembourg

- **Diabetes**: 11.6% in total, up to 19.8% in 75-84 year-olds; *gender differences*: 19.9% in males vs 12.8% in females in early old age; 24.4% male vs. 15.8% female in old age
- **Hearing impairment**: 2.1% in total, up to 3.5% in 75-84 year-olds; *no gender differences*
- **Physical inactivity** (absence of vigorous physical activity): 37.8% in total, up to 57.4% in 75-84 year-olds; *gender differences*: 43.8% in females vs 36.7% in males in early old age
- **Smoking**: 16.4%, up to 20.8% of 50-64 year-olds; *gender differences*: later midlife highest prevalence: 22.4% in males vs. 19.4% in females
- **Alcohol consumption** daily: 16.0% in total, up to 21.2% of 65-74 year-olds; *gender differences*: 28.8% in males vs 12.8% in females in early old age: 30.3% in males and 12.2% in females in old age
- **Social isolation**: 3.6% in total, up to 3.9% of 65-74 year-olds; *no gender differences*

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Contribution of modifiable risk factors

Outcome: cognitive impairment/dementia (low orientation ***and/or*** diagnosis of dementia; age 65-84 years: 4.01%)

Risk score: sum of 11 risk factors

25% of the SHARE respondents have three or more risk factors (*M* = 2.40, *SD* = 1.62)

After adjusting for sex and age, each 1-point increase in the risk score was associated with a 39% increase in likelihood of having cognitive impairment (OR 1.39, CI 1.17-1.65; 1,971 respondents aged 50-84).

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Inequalities in Dementia

Risk of Dementia

Dementia Care

Dementia Research

Dementia Treatment

Leist, JAGS letter to editor, 2017

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Thank you!

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