How to actively protect against dementia. Epidemiological data from Luxembourg

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**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

\(^1\)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
Life course influences on cognitive functioning

- Gender
- Ethnicity/race
- Education
- Occupation
- Environmental exposures
- Innate abilities, genetic risk
- Nutrition
- Cognitive stimulation

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

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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

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)
Increases in dementia cases

Livingston et al. (2017)

Mukadam et al. (2019)
How much do we really know about the value of behavior changes to reduce risk of cognitive aging and dementia?
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 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*
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?

Sedentary individuals

Physically active at follow-up

Cognitive decline

Physically inactive at follow-up

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

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
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

- **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*
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).
Inequalities in Dementia

Risk of Dementia

Dementia Care

Dementia Research

Dementia Treatment

Thank you!

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