Cancer history and memory decline among middle-aged and older adults

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Introduction

- Decline in memory and other cognitive functions severe enough to reduce a person's ability to perform everyday activities → dementia
- Both cancer and dementia are common disorders in aging populations; shared risk factors
- Yamada et al. (1999): inverse association between cancer history and Alzheimer’s disease (AD), the most common type of dementia

Meta-Analysis > J Alzheimers Dis. 2022;89(1):367-380. doi: 10.3233/JAD-220436.

Risk of Dementia in Cancer Survivors: A Meta-Analysis of Population-Based Cohort Studies

Dan-Dan Zhang [1], Ya-Nan Ou [1], Yan Fu [1], Zhi-Bo Wang [1], Liang-Yu Huang [1], Lan Tan [1], Jin-Tai Yu [2]

Biological plausibility and sources of bias

- Same genes, proteins, and pathways are dysregulated in both cancer and neurodegenerative diseases — often in opposite directions (e.g. PIN1 enzyme) *(Drive et al. 2016)*

- Competing risk of death and selective survival, **diagnostic delay** ("chemo brain")

- Simulation studies:
  - Selective survival too small to explain the observed association *(Hayes-Larson 2020)*
  - When dementia diagnosis rates were at least 20% slower (i.e., delayed by at least 4.5 months) among people with cancer, incidence rate ratios were sufficiently biased. *(Hayes-Larson 2022)*

- An approach focused on long-term **cognitive decline**, which may inform the progression to dementia, might be **less biased by diagnostic delay.**

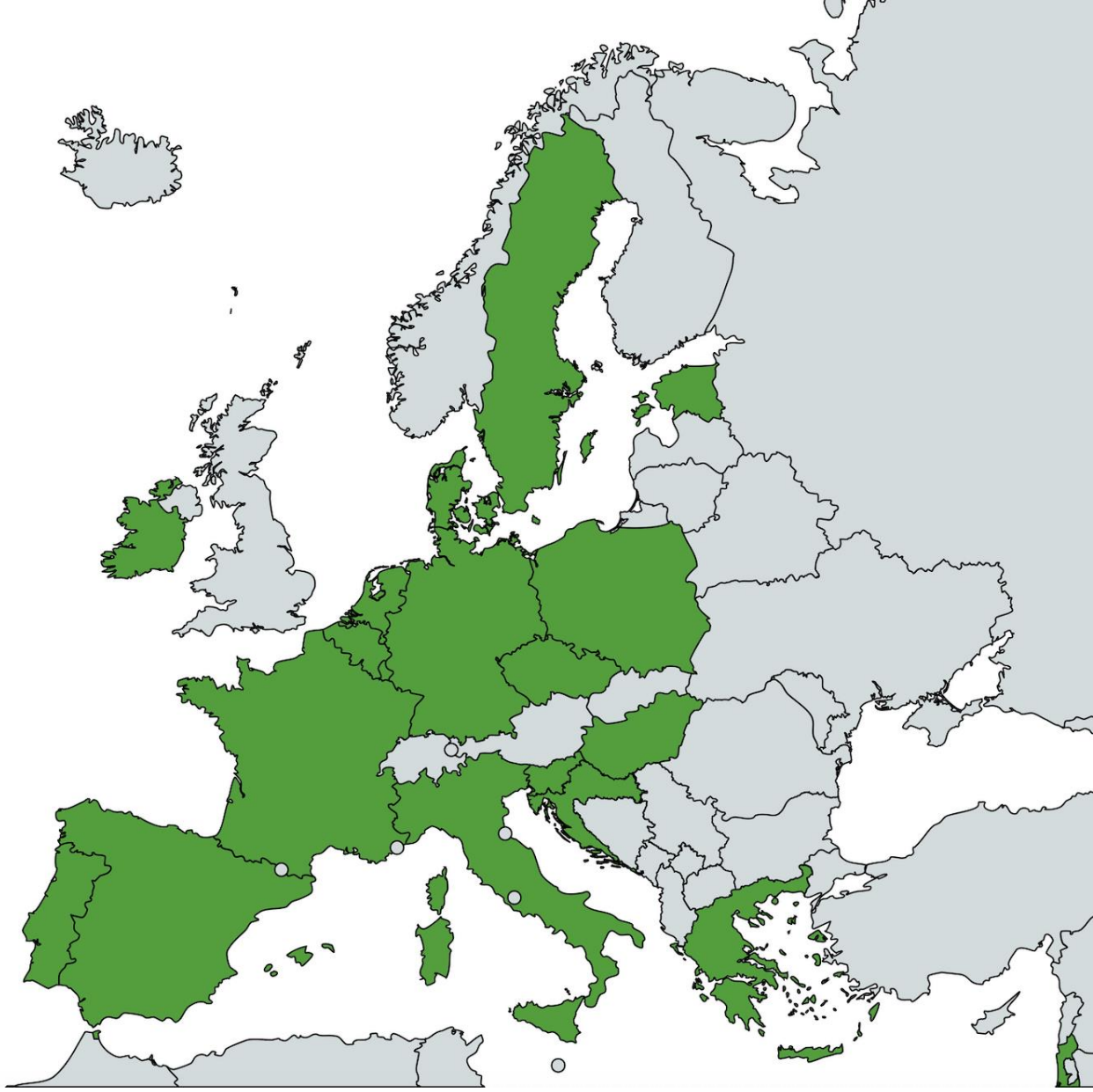
Objective

Primary: To examine the relationship between cancer history and decline in episodic memory, the most affected cognitive domain in AD, among middle-aged and older adults.

Secondary: to investigate sex differences in this relationship.

Source of data

- Survey of Health, Ageing and Retirement in Europe (SHARE)
- Longitudinal population-based study
- 50+ adults from 18 European countries and Israel, cognition assessed biennially, 8 waves
- Sample restricted to those who had:
  - no history of dementia or Parkinson's disease at baseline
  - stable cancer status during follow-up
  - cognitive assessments in at least 2 time points
  - complete data on covariates
- N = 78,274



Methods

- Exposure: **self-reported cancer history at baseline**
  - Danish validation study of SHARE data *(Jens Mose et al. 2023)*
  - Self-reported cancer diagnoses in the HRS have reasonable validity *(Mullins et al. 2022)*

- Outcomes: decline in episodic memory measured by **immediate and delayed recall**
  - Read a list of 10 words + recall them immediately and after 5 minutes
  - Scores ranging between 0 and 10

- Linear mixed-effects model:
  - **Model 1**: baseline age, sex, education
  - **Model 2**: + number of chronic diseases, body mass index, limitations in instrumental activities of daily living, and physical inactivity

Cohort characteristics

- A total of 4,593 (**5.9%**) had cancer history at enrollment
- Median follow-up **6 years** (interquartile range 3.5-8.5), up to 16 years

	No cancer (N=73,681)	Cancer history (N=4,593)	Overall (N=78,274)
Female	40,210 (54.6%)	2,809 (61.2%)	4,3019 (55.0%)
Baseline Age, mean (SD)	63.3 (9.41)	66.5 (9.38)	63.4 (9.43)
Education			
Primary or less	17,166 (23.3%)	923 (20.1%)	18,089 (23.1%)
Lower secondary	13,041 (17.7%)	840 (18.3%)	13,881 (17.7%)
Upper secondary or post-secondary	27,661 (37.5%)	1,726 (37.6%)	29,387 (37.5%)
Tertiary	15,813 (21.5%)	1,104 (24.0%)	16,917 (21.6%)

Primary analysis

	Immediate recall B (95% CI)		**Delayed Recall B (95% CI)**	
	Model 1	Model 2	Model 1	Model 2
Intercept	4.319 (4.298; 4.340)	4.494 (4.440; 4.548)	2.846 (2.820; 2.872)	3.221 (3.154; 3.288)
Time	-0.026 (-0.028; -0.025)	-0.027 (-0.029; -0.026)	-0.021 (-0.023; -0.02)	-0.022 (-0.024; -0.02)
Cancer	0.114 (0.073; 0.156)	0.162 (0.121; 0.204)	0.092 (0.041; 0.142)	0.155 (0.105; 0.206)
Time × cancer	**-0.010** (-0.017; -0.004)	**-0.011** (-0.017; -0.004)	**-0.009** (-0.017; -0.001)	**-0.009** (-0.017; -0.001)

* Model 1: age, sex and education
Model 2: + number of chronic diseases, body mass index, limitations in instrumental activities of daily living and physical inactivity

Secondary analysis

	Immediate recall B (95% CI)		**Delayed Recall B (95% CI)**	
	Female	Male	Female	Male
Intercept	4.560 (4.536; 4.585)	4.429 (4.400; 4.458)	3.168 (3.138; 3.199)	2.982 (2.947; 3.017)
Time	-0.026 (-0.028; -0.024)	-0.027 (-0.029; -0.025)	-0.022 (-0.025; -0.020)	-0.021 (-0.023; -0.018)
Cancer	0.100 (0.047; 0.153)	0.131 (0.065; 0.197)	0.112 (0.047; 0.177)	0.045 (-0.034; 0.124)
Time × cancer	**-0.008** (-0.017; 0.000)	**-0.014** (-0.025; -0.003)	-0.009 (-0.019; 0.002)	-0.009 (-0.022; 0.004)

* Models adjusted for age and education

Conclusion

- Cancer history was associated with a **faster rate of decline in memory** and better baseline cognition

- Limitations:
  - Selection – individuals with higher cognition might have better survival
  - Not able to account for the risk of death during follow-up
  - Self-reported cancer history - people with worse memory might underreport cancer diagnosis

- Future plans: missing data, cancer sites and timing of diagnosis

Thank you for your attention.

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