Using Cohort Data to Emulate Lifestyle Interventions: Long-Term Beneficial Effects of Initiating Physical Activity on Cognitive Decline and Dementia

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Background: Intervention studies have shown beneficial short-term effects of physical activity on cognitive decline and reduced risk of dementia. However, randomized controlled trial data of lifestyle interventions over long time spans are not available due to lack of resources, feasibility or ethical reasons. Drawing from the principles of emulating a 'target trial', which apply design principles of randomized trials to the analysis of observational data, cohort data of a large European survey were analyzed to understand the long-term effects of physical activity changes.

Method: Biennial assessments of the economic, social, and health situation of respondents aged 50 and older came from the Survey of Health, Ageing and Retirement in Europe (2004-2017). Cognitive functioning (immediate recall, delayed recall, and verbal fluency) and self-reported diagnosis of dementia were assessed at each follow-up. The target trial included sedentary respondents at t1 who, at follow-up (t2), stayed sedentary ("control group") or newly reported vigorous physical activity more often than once a week (initiators, "treatment group"). Inclusion and exclusion criteria were implemented as close as possible to those of the FINGER trial. Inverse-probability weighting accounted for the probability of initiating physical activity with a large set of predictor variables.

Selecting respondents aged 50-85 years old who met the target trial inclusion and exclusion criteria, assessments of cognitive functioning and self-reported diagnosis of dementia were available for 8,781 respondents at t3 (on average 3.02 years later), 3,858 respondents at t4 (5.84 years), and 2,304 respondents at t5 (7.72 years). A total of 304 respondents reported a diagnosis of dementia.

Result: Initiators of vigorous physical activity had higher cognitive functioning at two follow-ups compared to non-initiators (t3: "average treatment effect on the treated", ATET=0.059, CI: 0.028, 0.090), which remained significant after implementing inclusion and exclusion criteria. Initiators had lower risk of dementia compared to non-initiators at all three follow-ups (t3: ATET=-0.009, CI: -0.015, -0.005, relative risk decrease -46.7%), remaining significant after implementing inclusion and exclusion criteria.

Conclusion: Emulating a target trial showed long-term benefits of initiating physical activity for cognitive functioning and dementia risk. Multidomain interventions related to nutrition, social, cognitive activities etc. can be similarly emulated.

Table 1. Long-Term Effects of Initiating Physical Activity on Cognitive Functioning and Risk of Dementia in a Sedentary Sample of Respondents of the Survey of Health, Ageing and Retirement in Europe at Three Follow-up Assessments.

		Time between assessments in years, M (SD)	N	Cognitive functioning	Dementia	
				ATET	ATET	Relative Risk Change of Initiators
Follow-up t3		3.02 (1.48)				
	Age 50-85, Adjusting for probability of initiating physical activity		11,841	0.059*** (0.028, 0.090)	-0.009** (-0.015, -0.005)	-46.7%
	+ Implementing trial inclusion criteria		8,781	0.045** (0.011, 0.079)	-0.008** (-0.013, -0.003)	-49.0%
Follow-up t4		5.84 (1.56)				
	Age 50-85, Adjusting for probability of initiating physical activity		6,364	0.083** (0.035, 0.132)	-0.012** (-0.020, -0.003)	-69.5%
	+ Implementing trial inclusion criteria		3,858	0.062* (0.010, 0.114)	-0.016*** (-0.024, -0.009)	-79.6%
Follow-up t5		7.76 (1.30)				
	Age 50-85, Adjusting for probability of initiating physical activity		2,916	0.043 n.s. (-0.019, 0.090)	-0.021*** (-0.033, -0.010)	-60.0%
	+ Implementing trial inclusion criteria		2,304	0.022 n.s. (-0.046, 0.090)	-0.021*** (-0.032, -0.010)	-70.0%

Note. N – sample size. ATET – Average treatment effect on the treated. Adjusted for time between initiating physical activity and assessment of cognitive functioning (immediate and delayed recall, executive functioning) and self-reported dementia or memory impairment. Each follow-up assessment has a delay of on average two years.

Defining the target trial: Sedentary respondents at t1 responded to an item assessing frequency of vigorous physical activity with 'hardly ever, or never'; respondents who responded similarly at t2 made up the "control group". Initiators of physical activity ("treatment group") responded to an item assessing frequency of vigorous physical activity with 'more than once a week' at t2.

Predictor variables for "treatment": Inverse-probability weights adjusted probability to initiate physical activity ("treatment") with cognitive functioning at baseline, age, sex, country of residence, education (primary up to lower secondary, upper secondary, post-secondary and tertiary, other), cohabitation status (living alone, living with partner), number of chronic conditions, depression (five or more symptoms on the EURO-D scale), been to the doctor in the last 12 months, presence of limitations). Cognitive functioning and diagnosis of dementia were predicted using "treatment" and time.

Inclusion criteria: Participating in at least three interview (non-SHARELIFE) waves of the SHARE survey, providing at least two measurements of physical activity and two cognitive assessments two waves apart.

Exclusion criteria: older than 85 years old, any ADL limitations, a recent heart attack or hip fracture, cancer, stroke, answering less than 1 of 4 orientation items, difficulty walking across a room.