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Individual and combined associations of physical activity and cognitive function with all-cause mortality in older men and women: a prospective analysis of the German National Cohort (NAKO)

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Abstract

Objectives Low physical activity (PA) and poor cognitive function are associated with higher mortality risks. However, little is known about their interaction, including whether PA may moderate cognition-related mortality risks. This study examines the combined associations of PA and cognition with all-cause mortality, with attention to sex differences.

Methods Using data from the German National Cohort and its mortality follow-up, we analyzed mortality risk based on: a) baseline low vs. sufficient PA (assessed via the global physical activity questionnaire using a threshold of < vs. ≥ 600 MET-minutes/week), b) baseline low vs. medium vs. high semantic memory (SM) and executive function/processing speed (EF/PS), assessed through factor analyses of a neurocognitive test battery, and c) their interaction on mortality in individuals aged 65 + up to 10 years of follow-up (N = 28,892). Cox models were estimated both in the total sample and stratified by sex, adjusting for relevant confounders and reporting both distinct and combined associations.

Results During follow-up, 1,605 individuals (5.6%) died: 1,097 men (7.5%) and 508 women (3.6%). Compared to individuals with low cognitive function, those with high SM (Hazard Ratio (HR) = 0.83 [95%CI: 0.67–1.02]), as well as high EF/PS (HR = 0.66 [0.53–0.83]) and medium EF/PS (HR = 0.68 [0.60–0.78]) had lower mortality risks. PA was associated with a 29% decreased mortality risk (HR = 0.71 [0.62–0.82]) compared to low PA. PA moderated the elevated risk from low cognition, with regard to EF/PS (low EF/PS*PA: HR = 0.65 [0.50–0.84] vs. low EF/PS*low PA: HR = 1 (ref.))

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and SM (low SM*PA: HR = 0.60 [0.46–0.77] vs. low SM*low PA: HR = 1 (ref.)). The associations did not differ between men and women.

Conclusion Maintaining cognitive function and PA in older age is relevant for reducing mortality risk in both men and women. PA may offset risks linked to low cognition in both sexes, though mechanisms require further study.

Trial registration Clinical trial number: not applicable.

Keywords Cognitive function, Physical activity, Sex differences, Healthy aging

Background

Mortality is a pivotal public health outcome influenced by myriad factors, including cognitive function, which affects long-term health [31]. Cognitive impairment has been recognized as a significant predictor of elevated mortality risk in numerous studies [2, 31, 34, 58]. This association is partly attributable to cognitive decline, impairing individuals' ability to manage their health and adhere to treatments, which can exacerbate chronic conditions [66]. Furthermore, cognitive impairment might be an early predictor of dementia [27], and has been associated with an increased risk of frailty and a broader systemic health deterioration [74], as well as an elevated risk of social isolation, depression, and a cessation of health-promoting activities [27, 49].

Growing evidence indicates that the strength of the association between cognitive function and mortality varies by cognitive domain [27, 29, 57, 58]. Across multiple cohort studies assessing different cognitive domains, verbal fluency (semantic retrieval) and processing speed/executive function consistently stand out as the strongest predictors of health trajectories and mortality, even when compared with episodic memory or general cognitive measures [12, 20, 22]. Executive function, which governs planning and executing goal-directed behaviors, reasoning, and judgment, demonstrates the strongest association with mortality risk, likely due to its critical role in maintaining independence and managing complex health behaviors [29]. Memory function, involving the encoding, storage, and retrieval of information, predicts mortality with more variable and by tendency weaker impact [21, 27]. Memory likely affects mortality through early neurodegeneration and the capacity to recall medical instructions and health-related cues [27]. These domain-specific patterns elucidate that not all cognitive aspects possess equal prognostic significance.

As cognitive decline typically commences in the mid-60s [70, 73] and life expectancy continues to rise, cognitive impairment is becoming increasingly prevalent in aging populations. The etiology of (unhealthy) cognitive decline is multifactorial, shaped by health behaviors, and comorbidities across the lifespan [11, 55]. Consequently, cognitive function serves as an independent predictor of mortality and may interact with lifestyle factors.

In recent decades, considerable shifts in environmental conditions, occupational demands, and patterns of leisure activities have contributed to significant changes in physical activity (PA) behaviors [52, 62]. Physical inactivity has emerged as a critical health concern, often referred to as a global pandemic [33]. Around one-third of the global adult population does not engage in sufficient PA [24, 52, 62]. Low PA contributes to increased mortality through mechanisms like impaired cardiometabolic regulation, increased inflammation, sarcopenia, and reduced neuroplasticity [35, 54], and is a major risk factor for non-communicable diseases, including cardiovascular diseases, diabetes, and cancers [14, 15, 38]. Furthermore, low PA has been linked to cognitive decline, possibly due to reduced cerebral blood flow, lower brain-derived neurotrophic factor levels, and less exposure to cognitively stimulating environments [3, 17]. Conversely, poor cognitive function may lead to lower PA levels through executive dysfunction, reduced motivation, or depressive symptoms [19]. Consequently, low PA and low cognitive performance not only emerge as independent determinants of mortality, potentially exerting reciprocal influences and interactively increasing mortality risk. Individuals who exhibit both low PA and impaired cognitive function experience the greatest mortality risk [18, 41].

Sex differences play a crucial role in the interplay between cognitive abilities, PA, and mortality. Women have longer lifespans but experience a higher morbidity in later life [50]. Cognitive aging also differs by sex,women tend to possess greater cognitive reserve but may face faster post-menopausal cognitive decline [40]. The association between cognition and mortality partly differs by sex [63], as do the magnitude and effects of PA [10, 13, 61]. Despite these differences, the combined impact and underlying mechanisms linking cognitive function, PA, and mortality – especially by sex – remain insufficiently understood.

This study examines the relationship between executive and memory function and all-cause mortality, with a focus on whether these associations are modified by PA. The analysis places particular emphasis on the nature and strength of these relationships across cognitive domains and adopts a sex-sensitive perspective. The primary research questions guiding this study are as follows: (1)

How are executive and memory function associated with mortality risk in older adults? (2) Does PA moderate the mortality risk associated with poor cognition? (3) Do these associations differ by sex? It is hypothesized that executive dysfunction is more strongly associated with increased mortality than memory impairment, and that PA has a particularly beneficial effect on individuals with low cognitive levels. Moreover, it is anticipated that these effects will vary according to sex.

Methods

Data source

This study used data from the initial examinations of the German National Cohort (NAKO) carried out between 2014 and 2019, and the longitudinal Mortality Follow-Up (MoFU) of the NAKO. The NAKO is a multidisciplinary, population-based prospective cohort study that investigates widespread diseases, their risks and protective factors as well as prevention measures in the general population aged 19 to 74 years in Germany [53]. The NAKO examined over 200,000 men and women in 18 study centers in Germany. Examinations included face-to-face-interviews, self-administered touchscreen questionnaires and biomedical examinations [53]. In addition to life circumstances and disease biographies, PA measurements and a brief neurocognitive test battery have been implemented in the NAKO [32, 39].

Mortality

The NAKO MoFU collected and validated death certificates, cause(s) of death and dates of death via case-by-case tracking of deceased subjects. This process involved active and passive follow-up procedures, including a regular rolling vital status survey of all study participants via a health follow-up questionnaire and the utilization of secondary data sources, such as inquiries at the registry offices or health authorities, death certificates, or other pertinent documentation such as from cancer registries or health insurance companies [36]. All events (examination and death) were assigned to the middle of the month. The survival time was calculated as the interval between December 2023 or month and year of death and the month and year of the initial examination. For those who survived, the survival time ranged between 51.5 months to 117.5 months, and for those who died, it ranged from 0.5 to 112.5 months. Five deceased participants with missing information regarding the year of death were excluded from the analyses.

Measures of cognitive function

Cognitive function was assessed using a brief neurocognitive test battery. Our approach represents a modified version of the procedure described by Kleineidam et al. [32]. The present analyses incorporated six tests: two immediate word list recall trials, which assess the ability to recall words from a digitally recorded and presented list of 12 words,one delayed 12-word list recall trial; an animal name test, which requires enumerating as many animal names as possible within one minute; and two Stroop color-word tasks. To ensure conceptual consistency across indicators, the two Stroop color-word task variables – originally scaled such that higher values reflected lower cognitive function – were reverse-coded accordingly. Thus, higher scores indicate superior cognitive function across all measures. To identify latent cognitive domains, a principal component factor analysis was performed on the six cognitive test variables within the age group of 65 years and older, basically following the approach described by Kleineidam et al. [32]. Two distinct factors emerged: the first comprised the results of the three word recall trials, which reflect semantic memory (SM) (based on varimax rotated factors with scoring coefficients of 0.37–0.41). The second comprised the results of the animal names test and the two Stroop tasks, which reflect executive function and processing speed (EF/PS) (scoring coefficients of 0.34–0.52). All six test variables underwent z-standardization and age-standardization for the 65 + age group in our sample. The composite scores were determined by summing the standardized values for each indicator, creating age-specific measures that are comparable within this older population. In order to acknowledge the non-linear relationship between cognitive function and mortality [27], to include cases with missing data in the cognitive tests, and to include disparate categories with sufficiently high case numbers [59], cognition level categories were built. After conducting a thorough analysis of the domain-specific means and standard deviations (sd), the added scores were subsequently categorized as follows: low cognitive function (score ≤ mean - 1 sd), medium (mean – 1 sd ≤ score ≥ mean + 1 sd), and high (score ≥ mean + 1 sd). A missing category, including all cases with incomplete or unavailable data on the cognitive tests, was added.

Physical Activity (PA)

The five sub-domains of PA recorded in the Global Physical Activity Questionnaire (GPAQ) – comprising self-reported moderate and vigorous PA at work as well as during leisure time and recreation, and PA when travelling to and from places within one week – have been combined and processed by the NAKO in accordance with the World Health Organization guideline [39, 72]. PA is quantified in minutes and weighted by intensity (moderate to vigorous) to estimate the total energy expenditure, expressed in metabolic equivalent of task (MET) minutes. In accordance with WHO recommendations, individuals engaging in less than 600 MET-minutes of PA per week were classified as low PA, while those

reaching or exceeding 600 MET-minutes were classified as PA [72]. Additionally, a missing category was incorporated to encompass cases with partial or complete missing information on the GPAQ.

Model specification

Within our models, we adjusted for a set of covariates beyond the two central exposures, with the objective of reducing confounding and isolating the independent associations [65]. The inclusion of age and sex was driven by prevailing scientific consensus, which consistently identified these factors as predictors of all-cause mortality in elderly populations and moderate the nexus of cognitive function, PA, and all-cause mortality [23]. Socioeconomic factors were added given robust associations between lower socioeconomic status and elevated mortality, poorer health and health behaviours, and constrained access to healthcare services [67, 68]. The potential for measurement bias, regional differences, and clustering effects was mitigated by controlling for language proficiency and study site [56, 64]. Lifestyle factors (smoking, body mass index, alcohol consumption) were included as known behavioural predictors of mortality and as potential confounders for both physical activity and health outcomes [42, 67]. Finally, the Charlson Comorbidity Index (CCI) was employed to adjust for the individual comorbidity burden. The CCI is a validated, weighted summary measure of multimorbidity that was originally developed to predict one-year mortality risk in patients. However, it has been demonstrated to be a versatile and robust predictor of broad health outcomes, not limited to short-term outcomes or specific patient groups [8].

Measurement of covariates

We adjusted for and stratified by self-administered sex (male/female). Furthermore, we adjusted for sociodemographic characteristics: age (both the metric and the square of the metric, each in deviation from the mean age of 71.2 years), educational level (the highest educational qualification, allocated according to the International Standard Classification of Education (ISCED) 1997, and categorized as follows: low (level 0–2; pre-school, primary school, secondary school), medium (3–4; secondary school and vocational training completed), high (5–6; university degree, doctorate), and missing/incomplete information), income (categorized into quartiles and a missing/incomplete information category), German language proficiency (derived from self-reported indication on mother tongue and interviewer's assessment, and categorized as follows: German as the mother tongue or (very) good German abilities; moderate or (very) weak German abilities; missing/incomplete information), and place of examination. Finally, the following two variables indicating the individual health status were included. The categorical covariate concerning major health-related lifestyle risks indicates the number of three unhealthy behaviors: current smoking, risky alcohol consumption (AUDIT-C score ≥ 4 in men or ≥ 3 in women), and obesity (body mass index > 30 kg/m^2). The summarized integration of these three indicators, as demonstrated to be effective in predicting mortality, cognition, and PA, was driven by statistical and substantial considerations, namely their high intercorrelation and their reinforcing effects [6, 44]. The variable ranges from 0 to 3 and includes one category with missing data and incomplete information. Additionally, an adjusted CCI was included, encompassing the following self-reported comorbid conditions: myocardial infarction (weight, if applicable: 1), cardiac insufficiency or heart failure (1), stroke (1), intermittent claudication or arterial occlusive disease (1), chronic bronchitis, COPD or asthma (1), liver cirrhosis (1), diabetes mellitus (1), limited kidney function or chronic renal insufficiency (2), leukemia (2), other tumor diseases (2), and HIV infection or AIDS disease (6). The CCI score ranged from 0 to 12, with a higher score indicating a greater illness burden. The score was categorized as follows: 0, 1–2, 3–4, 5 and above, missing/incomplete information. No cases with missing information were excluded due to the exposures or covariates.

Sample selection

Participants in the NAKO were randomly selected if they were 20–69 years old and lived in the study area; individuals unable to provide informed consent or participate in the examinations were excluded. Considering the age-related process of cognitive degeneration from the mid-60s onwards [70, 73] and the transition to retirement, the respondents included in this study are adults aged 65 and older ($N = 28{,}897$). Data on mortality was collected from the baseline visit date (between 2014 and 2019) until December 31, 2023 (follow-up period mean (SD): 46.4 months (28.0)). After excluding five subjects with missing data regarding the year of death, the final analyses encompassed 28,892 individuals, with 216,427 person-years (py) of observation.

Statistical analyses

We adjusted our models for covariates that affect differences in cognition, PA or mortality risk. Except for age, all covariates were considered time-constant and derived from the baseline examination. Missing values, if any, were included as an additional category in all variables.

For descriptive statistics, the proportions were calculated, and Kaplan–Meier curves were derived for PA and the two cognition domains. For bivariate analyses, chi-square tests were conducted to examine the association between the outcome of follow-up all-cause mortality

and the exposures, as well as the associations between the exposures. Cox proportional hazard regression models were employed to evaluate the association of multiple risk factors with the risk of mortality, with the resulting hazard ratios (HR), 95% confidence intervals (95%CI), and p-values being reported. Model 1 was adjusted for all variables. In order to examine interaction effects between cognitive function PA, interaction terms with categorical variables were included in models 2a and 2b. Interaction effects were interpreted by computing combined HR for each level of cognitive function, comparing low PA and sufficient PA, with statistical significance assessed using Wald tests. For easier interpretation of the association between PA and mortality across cognitive performance levels, within each cognitive level, the HR for low PA was set to 1, and the corresponding HR for sufficient PA was derived from the model estimates. Specifically, the HRs were obtained by combining the main effect of PA with the respective interaction term for each cognitive level from the model, i.e. $HR_{\text{cognition level, lowPA}} = 1$ (ref.), and $HR_{\text{cognition level, PA}} = \exp(\beta_{PA} + \beta_{\text{interaction(cognition level*PA)}})$. The effects (HRs and 95% CIs) were calculating using Stata's postestimation lincom command. All analyses were conducted both for the analytic sample and stratified by sex. To ascertain whether the association between PA and cognitive function varied by sex, we expanded the Cox model to encompass a three-way interaction term between one cognitive domain, PA, and sex. For each model, the proportional hazards assumption was checked and verified using Schoenfeld residuals with the estat phtest command in Stata.

Furthermore, sensitivity analyses were conducted. These include the interaction models with a reduced set of covariates (models S1a/b: excluding socio-economic covariates, models S2a/b: excluding health-related covariates), continuous measures of cognitive function and PA (MET time) (models S3a/b), excluding individuals with a history of stroke (models S4a/b) or diabetes (models S5a/b) and right censoring starting after December 31, 2021 (models S6a/b). All analyses were conducted using Stata version 19.

Results

Descriptives and bivariate associations

Additional file 1 presents the descriptive statistics for the analytic sample ($N = 28{,}892$), men ($N = 14{,}665$), and women ($N = 14{,}227$). Overall, 5.6% of the total sample ($N = 1{,}605$) died within the follow-up period, 7.5% of the men ($N = 1{,}097$), and 3.6% of the women ($N = 508$).

The mean age at baseline was 67.4 years, with an almost balanced sex ratio (50.8% male, 49.2% female; Additional file 1). As anticipated, the majority demonstrated medium levels of cognitive function (EF/PS: 68.6%; SM: 65.6%). The proportion of high cognitive levels was greater in SM (14.9%) than in EF/PS (11.6%). Low PA was evident in 10.9%. Both the cognitive domains and PA as well as most of the covariates (with the exception of German language proficiency) were correlated with mortality (Additional file 1). Moreover, a bivariate association was observed between PA and the domains of cognitive function (each $p < 0.001$). A negative correlation was identified between low PA and an elevated frequency of low levels of cognition.

Kaplan–Meier estimation

In Fig. 1 survival probabilities according to SM, EF/PS, and PA are depicted. The lowest survival probabilities were associated with low cognitive function. At the end of the observation period, that is, after a maximum of ten years, the survival probabilities were as follows: 88.7% (95%CI: [86.1; 90.8]) in individuals with low SM, 93.4% [92.9; 93.9] in individuals with medium SM, and 96.0% [95.2; 96.7] in individuals with high SM. For EF/PS the probabilities were 87.9% [86.5; 89.2], 93.4% [92.5; 94.2], and 94.8% [93.4; 95.8], respectively. The 10-year survival probability of physically active individuals was 93.5% [92.6; 94.3] compared to 88.6% [87.1; 89.9] observed in low PA individuals.

Cox proportional hazard models for the association between cognition, PA and mortality

Table 1 presents the findings of Cox proportional hazard models that investigated the association between cognition, PA and mortality for the analytic sample.

In comparison with low levels of SM, both medium (HR = 0.92 [0.81; 1.04]) and high levels (HR = 0.83 [95%CI: 0.67; 1.02]) of SM by tendency exhibited a slight decrease in mortality risk. Both medium (HR = 0.68 [0.60; 0.78]) and high levels (HR = 0.66 [053; 0.83]) of EF/PS were associated with a lower mortality risk compared to the low group (HR = 1). PA demonstrated a 29% decreased mortality risk (HR = 0.71 [0.62; 0.82]) compared to low PA (HR = 1). The results of the full model are presented in Additional file 2.

As illustrated in Fig. 2, the disparities in the mortality risk by PA were evident across the levels of SM (top panel, model 2a) and EF/PS (bottom panel, model 2b). The main effects and interaction effects utilized in the calculations are shown in Additional file 3.

Across both cognitive domains, PA generally exhibited lower mortality risks compared to low PA, most pronounced in the low cognitive function groups. For individuals with low SM or EF/PS, the HRs for PA were below 1 (low SM*PA: HR = 0.60 [0.46; 0.77]; low EF/PS*PA: HR = 0.65 [0.50; 0.84]), suggesting a potential association between PA and a lower risk of mortality in these subgroups. In medium cognitive function groups the differences based on PA levels were less pronounced, and in

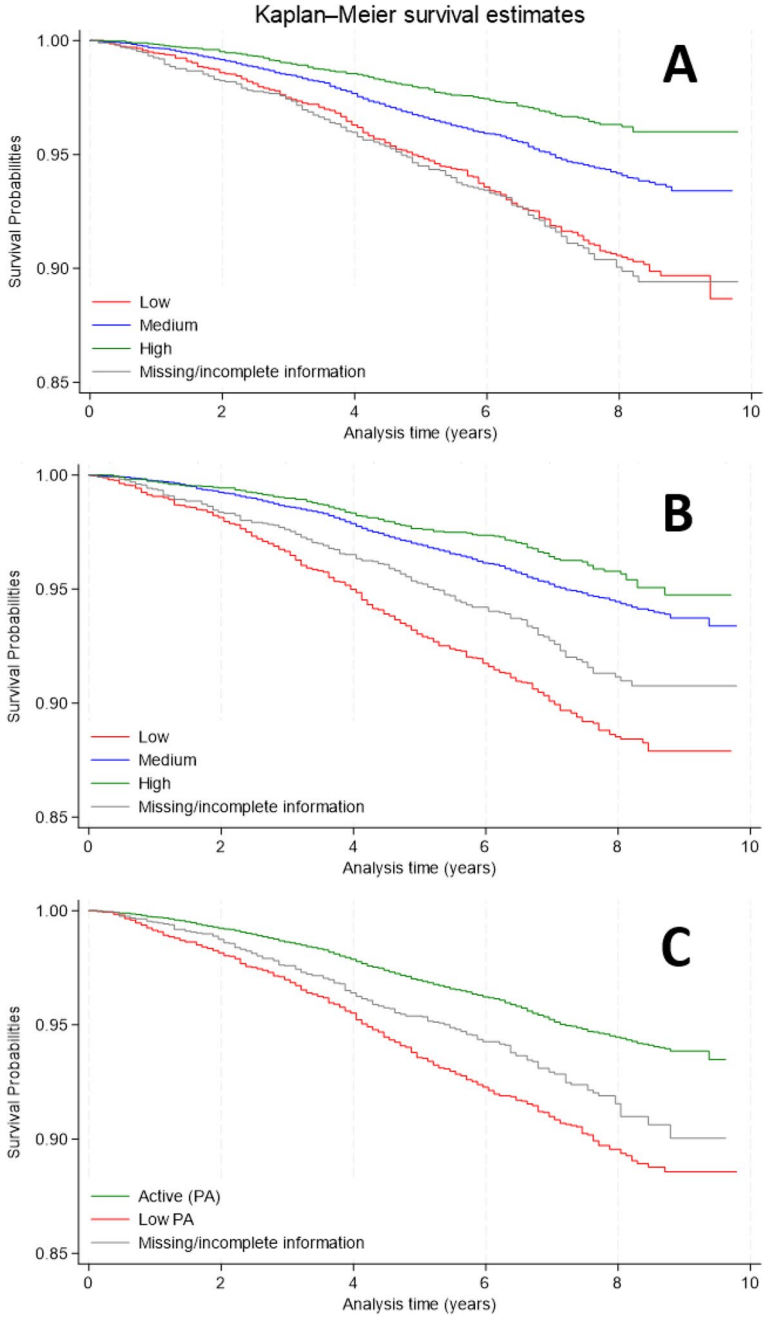

Fig. 1 Kaplan–Meier plots of survival
Note: **A** Semantic Memory (SM), **B** Executive Function/Processing Speed (EF/PS), **C** Physical activity (PA). Source: NAKO baseline and mortality follow-up ($N = 28{,}892$; py = 216,427) (own calculations)

high cognitive function groups they were insignificant. These findings may indicate that the association between PA and mortality varies by cognitive function level, with potentially stronger associations observed among individuals with lower cognitive function.

Sex-differences in the association between cognition, physical activity and mortality

In our general model, women exhibited a significantly lower mortality risk compared to men (HR = 0.50 [0.45; 0.56], Additional file 2). However, our sex-stratified Cox models indicated that this discrepancy remained largely unexplained by cognitive status and PA, either individually or in combination. Table 2 presents the primary

Table 1 Results of Cox proportional hazard model – distinct effects of cognition and PA (HR, p-values, 95%CI)

Variables		M1—Distinct effects			
		HR	p	lower 95%CI	upper 95%CI
Semantic Memory (SM)	Low (ref.)	1			
	Medium	0.92	0.184	0.81	1.04
	High	0.83	0.078	0.67	1.02
	Missing/incomplete	1.18	0.177	0.93	1.49
Executive function/ processing speed (EF/PS)	Low (ref.)	1			
	Medium	0.68	< 0.001	0.60	0.78
	High	0.66	< 0.001	0.53	0.83
	Missing/incomplete	0.74	0.010	0.58	0.93
Physical Activity (PA)	Active (PA)	0.71	< 0.001	0.62	0.82
	Low PA (ref.)	1			
	Missing/incomplete	1.19	0.037	1.01	1.40
Subjects		28,892			
Failures (Deaths)		1,605			
Observations (py)		216,427			
Time at risk		201,534			
LR chi^2		1,126			

HR hazard ratio, *95%CI* 95% confidence interval, *py* person-years, model adjusted for age, age^2, sex, education, income, Charlson Comorbidity Index score, lifestyle risk index, German language proficiency, and place of examination. Source: NAKO baseline and mortality follow-up (*N* = 28,892; py = 216,427) (own calculations)

results for both men and women. The complete model results are presented in Additional file 4.

In the sex-stratified models (model 1, Table 2), elevated levels of EF/PS and PA were consistently associated with diminished mortality risk in both men and women. For instance, high EF/PS levels were associated with a HR of 0.70 [0.54; 0.92] in men and 0.59 [0.40; 0.86] in women. PA exerted a protective effect in both sexes (men: HR = 0.72 [0.61; 0.84]; women: HR = 0.66 [0.50; 0.86]). SM demonstrated a weaker and less consistent association, reaching significance only among women at the high level (HR = 0.68 [0.48; 0.97]).

In the interaction models (M2a and M2b, Table 2), combinations of high cognitive function and PA were generally associated with the lowest mortality risks, but the interactions of cognitive function and PA were largely insignificant, and the patterns were broadly similar for men and women. While the effect estimates for women were numerically lower in several instances, indicating stronger protective effects, the three-way interaction term revealed that there were not statistically significant sex-differences ($p > 0.05$).

Sensitivity analyses

The results of our sensitivity analyses demonstrated the robustness of the primary findings. The models with a reduced set of covariates exhibited stronger associations between the cognitive domains, PA and mortality. In general, socio-economic characteristics partly explained the associations of the cognitive domains (models S1a/b), while health-related covariates partially explained the mortality disadvantage of those with low PA (models S2a/b). Subsequent to the adjustment of socio-economic covariates, the association between medium levels of SM and mortality became insignificant. The role of socio-economic characteristics was particularly pronounced among men, for whom no notable effect of SM was discernible following the adjustment for education and income. The analyses revealed that health-related characteristics accounted for approximately 50% of the observed mortality differences associated with PA, although the associations remained statistically significant. In women, the magnitude of the observed associations appeared to be less contingent on the specific modeling approach employed. Continuous measures of cognitive function and amount of PA (measured in MET) indicated significant associations (SM: HR = 0.96 [0.93; 0.99]; EF/PS: HR = 0.91 [0.88; 0.94]; PA-MET: HR = 1.00; models S3a/b). The results remained robust when individuals with a history of stroke (models S4a/b) or diabetes (models S5a/b) were excluded. The alteration of the censoring date (from December 31, 2021 onwards) led to a decline in the number of deaths, resulting in a lower statistical power but otherwise comparable outcomes. All results are demonstrated in Additional File 5.

Discussion

This study examined the relationship between cognitive function, physical activity and all-cause mortality in the population of Germany aged 65 and older, with a particular focus on how physical activity modifies cognition-related mortality differences.

The findings indicated that low executive function/processing speed and low physical activity were associated with increased mortality by each around 30%. A protective effect was observed for high semantic memory, albeit to a lesser extent. Furthermore, the combination of low cognitive function (in both domains) and low activity yielded the highest mortality risk. However, the effect of physical activity was most pronounced among individuals with low cognition. In these groups, physical activity has been demonstrated to attenuate the risk of mortality by approximately 40% (semantic memory) and 35% (executive function/processing speed). The effect sizes did not differ significantly between men and women. The effect sizes did not differ significantly between men and women.

In men, semantic memory did not predict mortality. However, higher executive function/processing speed and physical activity were associated with reduced mortality. In women, high semantic memory, medium and

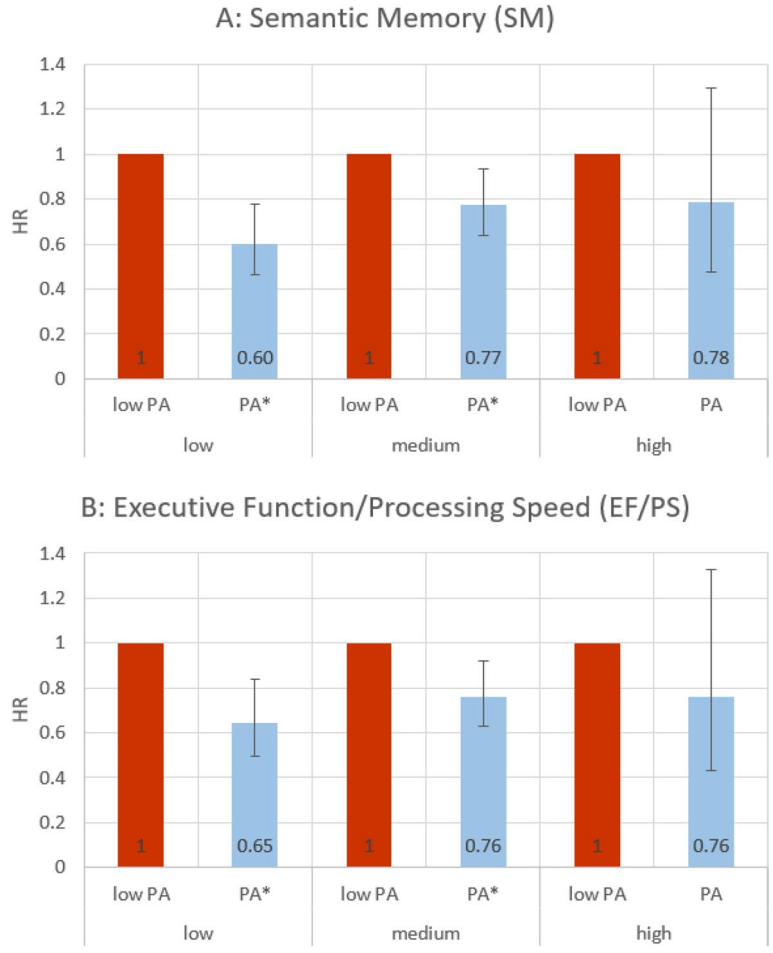

Fig. 2 Results of Cox proportional hazard models with interaction term (combined HR and 95%CI)
Note: The graphs show the HR and 95%CI for levels of PA across levels of cognitive function; PA = Physical Activity; HR = Hazard Ratio; asterisks (*) indicate significant differences between low PA and PA ($p < 0.05$); models adjusted for age, age.^{2}, sex, education, income, Charlson Comorbidity Index score, lifestyle risk index, German language proficiency, and place of examination. Results for missing categories ("missing/incomplete information") not shown. Source: NAKO baseline and mortality follow-up ($N = 28{,}892$; py = 216,427) (own calculations)

high executive function/processing speed, and physical activity were associated with lower mortality. Mortality differences by cognitive function and physical activity were slightly more pronounced among women. The interaction analyses demonstrated that in men, physical activity was associated with a lower mortality risk at low and medium semantic memory levels, as well as low executive function/processing speed. In women, this protective effect was observed at low levels of semantic memory and medium levels of executive function/processing speed.

These findings underscore the significance of preserving cognitive function and maintaining physical activity in older adults to foster healthy aging and curtail (premature) mortality. They further suggest that physical activity may moderate the increased mortality risk observed in individuals with low cognitive function in both sexes.

Our study confirms the mortality disadvantages associated with pathological cognitive impairments, such as those observed in dementia [31, 34]. Consistent with prior research, our findings demonstrate that even individuals in the early or preliminary stages of cognitive impairment, below-average cognitive performance or cognitive decline [1, 46] face elevated mortality risks. Our analyses account for mild degrees of cognitive impairment and differentiate two cognitive domains. The negligible correlation between semantic memory and executive function/processing speed indicates that cognitive function is broad and that these domains assess different abilities. Consequently, they contribute differently to mortality differentials. Our domain-dependent approach underscores this and indicates that executive function/processing speed is more predictive for mortality than semantic memory [21, 27]. Specifically, our study confirms the strong association between executive function and mortality reported by others [60], which persists even after adjusting for physical activity and covariates.

Table 2 Results of sex-stratified Cox proportional hazard models with and without interaction term (HR, 95%CI)

Variables		Men				Women			
		M1—Distinct effects[a]							
		HR	p	lower 95% CI	upper 95% CI	HR	p	lower 95% CI	upper 95% CI
Semantic Memory (SM)	Low (ref.)	1				1			
	Medium	0.93	0.308	0.80	1.07	0.84	0.193	0.65	1.09
	High	0.93	0.588	0.70	1.22	0.68	0.033	0.48	0.97
	Missing/incomplete	1.17	0.235	0.90	1.52	1.29	0.329	0.77	2.17
Executive Function/Proc. Speed (EF/PS)	Low (ref.)	1				1			
	Medium	0.71	< 0.001	0.61	0.84	0.62	< 0.001	0.49	0.79
	High	0.70	0.011	0.54	0.92	0.59	0.006	0.40	0.86
	Missing/incomplete	0.83	0.159	0.64	1.08	0.47	0.007	0.27	0.81
Physical Activity (PA)	Active (PA)	0.72	< 0.001	0.61	0.86	0.66	0.002	0.50	0.86
	Low PA (ref.)	1				1			
	Missing/incomplete	0.84	0.131	0.67	1.05	0.85	0.306	0.61	1.17
		M2a: Interaction SM*PA							
Semantic Memory (SM) Main effects	Low (ref.)	1.00				1			
	Medium	0.80	0.172	0.58	1.10	0.57	0.035	0.34	0.96
	High	0.64	0.244	0.31	1.35	0.57	0.143	0.26	1.21
	Missing/incomplete	1.13	0.563	0.75	1.72	0.82	0.622	0.38	1.79
Physical Activity (PA) Main effects	Active (PA)	0.67	0.007	0.50	0.90	0.36	< 0.001	0.21	0.64
	Low PA (ref.)	1				1			
	Missing/incomplete	0.59	0.016	0.39	0.91	0.90	0.739	0.49	1.67
Semantic Memory*PA Interaction effects	Medium*Active	1.14	0.476	0.80	1.63	2.04	0.026	1.09	3.80
	Medium*Missing/Incomplete	1.59	0.088	0.93	2.71	0.86	0.709	0.40	1.85
	High*Active	1.43	0.373	0.65	1.63	1.73	0.215	0.73	4.12
	High*Missing/Incomplete	2.51	0.102	0.83	7.58	0.14	0.071	0.02	1.18
	Missing/Incomplete*Active	0.93	0.766	0.57	1.51	1.88	0.159	0.78	4.53
	Miss.*Miss.	1.57	0.175	0.82	3.01	1.58	0.352	0.60	4.16
		M2b: Interaction EF/PS*PA							
Executive Function/Proc. Speed (EF/PS) Main effects	Low (ref.)	1.00				1			
	Medium	0.56	< 0.001	0.41	0.77	0.70	0.159	0.43	1.15
	High	0.69	0.285	0.35	1.36	0.42	0.111	0.14	1.22
	Missing/incomplete	0.88	0.556	0.57	1.35	0.42	0.043	0.18	0.97
Physical Activity (PA) Main effects	Active (PA)	0.63	0.003	0.47	0.86	0.66	0.117	0.40	1.11
	Low PA (ref.)	1.00				1			
	Missing/incomplete	0.66	0.049	0.43	1.00	0.98	0.933	0.55	1.74
Executive Function/Proc. Speed*PA Interaction effects	Medium*Active	1.32	0.144	0.91	1.90	0.91	0.760	0.52	1.62
	Medium*Missing/Incomplete	1.48	0.142	0.88	2.50	0.64	0.240	0.31	1.34
	High*Active	1.04	0.915	0.50	2.15	1.48	0.506	0.47	4.65
	High*Missing/Incomplete	0.77	0.681	0.22	2.65	1.64	0.518	0.37	7.39
	Missing/Incomplete*Active	0.82	0.439	0.50	1.35	1.02	0.974	0.40	2.55
	Miss.*Miss.	1.47	0.253	0.76	2.82	1.48	0.456	0.53	4.20
Subjects		14,665				14,227			
Failures (Deaths)		1,097				508			
Observations (py)		108,914				107,513			
Time at risk		101,184				100,350			
LR chi^2		648/654/656				310/328/315			

PA Physical Activity, *HR* Hazard Ratio, *95%CI* 95% Confidence Interval

[a]Effects of the main model without interaction terms; models adjusted for age, age^2, sex, education, income, Charlson Comorbidity Index score, lifestyle risk factors, German language proficiency, and place of examination. The distinct effects and interaction effects were estimated in separate models

Source: NAKO baseline and mortality follow-up (men: $N = 14,665$; py = 108,914; women: $N = 14,227$; py = 107,513) (own calculations)

Notably, in older individuals, objective cognition levels may not accurately reflect (perceived) limitations or decline [25, 26]. In line with Hayat et al. [27], this suggests that our measures may serve as proxies for future cognitive and health-related changes rather than as direct reflections of current impairments.

The mortality gradients for physical activity exhibited greater robustness compared to those observed for cognition. Low physical activity often accompanies sedentary behavior – prolonged lying, sitting, or reclining – although their direct correlation remains debated [45, 51]. Physical inactivity may also involve reduced social contacts, social control and environmental influences, and stimulation, all linked to higher mortality risks [3, 16, 17, 28]. Furthermore, social isolation and prolonged periods spent at home may worsen unmet health needs [7]. However, when interpreting the physical activity effect estimate, it is important to recognize that the 600 MET minutes/week threshold involves heterogeneous comparison groups. Comparing inactive individuals with highly active ones would likely reveal even larger mortality differences [48].

Study strengths

Primary strengths of this study are the substantial sample size of the NAKO cohort and its linkage with the MoFU. This combination enabled the execution of differentiated analyses, including sex-stratified models, and facilitated the attainment of a longitudinal perspective that is seldom available in comparable population-based research.

Moreover, a significant strength of this study is the utilization of validated measures for physical activity via GPAQ [72], which is accompanied by a standardized recording and threshold of physical activity. This methodological approach ensures transferability, transparency, and comparability. However, to attain more detailed results, subsequent studies could differentiate between the activity subdomains [69]. Alternative metrics like Life's Essential 8 (LE8) could provide a broader perspective on lifestyle dimensions and prevention [43]. However, we focused on physical activity as the primary exposure, while carefully accounting for other health- and lifestyle-related factors, allowing a more precise assessment of its independent association with all-cause mortality.

The assessment of cognitive function across two distinct domains has been shown to be more efficient than the evaluation of a single global indicator. This approach facilitated the demonstration of domain-specific associations, both in terms of mortality differentials and the underlying mechanisms. In accordance with the findings of preceding studies [27, 29, 57, 58], the present study demonstrates a robust correlation between executive function/processing speed and mortality.

Another strength of this study is the broad set of covariates, which serve to clarify mortality differentials and the associations of physical activity and cognitive function. However, certain potential factors, such as comprehensive CCI information, living environment, biographical details, and subjective health indicators, were not included. Future studies should integrate these dimensions to enhance robustness.

Finally, the incorporation of sex stratification facilitates a more profound comprehension of sex-specific and global associations.

Study limitations

A limitation of this study is the cross-sectional design of the NAKO baseline examination, which prevents temporal differentiation between cognitive function and physical activity and precludes formal mediation analyses. Prior research suggests reciprocal associations [9, 19], with findings indicating physical activity can predict cognition [3, 17], and vice versa [19]. While this study provides important insights into the associations between cognitive function, physical activity, and mortality, subsequent longitudinal analyses are needed to establish causal pathways and formally examine potential mediation. However, by linking baseline and the NAKO MoFu, we could identify mortality trajectories prospectively. Consequently, these trajectories can be interpreted as subsequent in time and hence as potential consequences of physical activity and cognition, although they may also reflect proximity to death, and hence indicate reverse causality [30, 47, 71]. It is also plausible that third factors were in play, exerting influence on physical activity, cognition, and mortality. Despite our efforts to adjust for potential confounders, the possibility of residual confounding remains a concern.

Regarding mortality, only few deaths were observed soon after the baseline, and our cohort mortality rate was lower than in the population in Germany, potentially reflecting a "healthy volunteer bias" [4]. Timing of death cases may also reflect a reporting lag,right-censoring was applied from December 31, 2023. A more rigorous censoring approach, as implemented in our sensitivity analysis censoring from December 31, 2021, yielded comparable results and does not indicate selective bias. However, future NAKO data will enhance mortality ascertainment and bias evaluation.

Furthermore, the sample's health profile suggests a healthy volunteer bias [4] or a social desirability bias [37], which may also have affected the measurement of physical activity via GPAQ [5, 39]. Time-lagged effects of cognition, physical activity, and covariates on mortality cannot yet be assessed given the age range (65–75 years at baseline) and limited follow-up, potentially underestimating long-term associations.

Finally, a critical aspect of this study lies in the handling of missing data for the primary exposures of physical activity and cognition. We cautiously treated missing values as a separate category. This expanded approach of available case analysis appears appropriate, as the nature of missingness cannot be assessed and the affected variables are included as either outcomes or exposures in the regression models [36]. To address potential residual bias, we adjusted for relevant characteristics in our models.

Conclusions

This study provides novel insights into the sex-specific effects of physical activity and cognitive function on mortality among older adults in Germany. Individuals exhibiting low physical activity and low levels of executive function and processing speed have elevated mortality risks. The tendency of lower mortality risks in individuals with higher levels of semantic memory observed in the whole sample is only evident in the female subsample. However, no significant sex differences were observed with regard to the interaction of cognitive function and physical activity. The associations are not explained by socio-economic characteristics and health characteristics. The findings indicate a potential compensatory effect of physical activity in both sexes, as weaker and largely insignificant mortality differences were observed in the physically active groups. Future research and longitudinal analyses are necessary to elucidate the underlying pathways.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12877-026-07357-2.

Additional file 1. Descriptive statistics and bivariate associations for the analytic sample, men, and women.

Additional file 2. Results of Cox proportional hazard model for mortality – full model.

Additional file 3. Results of Cox proportional hazard models with interaction term (main effects and interaction effects; HR, 95%CI).

Additional file 4. Results of Cox proportional hazard models for mortality with distinct effects for men and women.

Additional file 5. Sensitivity Analyses - Results of Cox proportional hazard models with interaction term (main effects and interaction effects; HR, 95%CI).

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Authors' contributions

DG, ER, and GD developed the research question and study concept. DG and ER prepared the data and conducted the data analysis. All authors except DG, ER, and GD contributed to the data collection of the NAKO. DG, ER, and GD interpreted the data. DG drafted and revised the manuscript, including preparation of tables and figures. All authors commented on previous versions of the manuscript. GD supervised the project. All authors have read and approved the final manuscript.

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Data availability

The datasets analyzed during our study are not publicly available due to privacy concerns and strict data protection regulations. Data are available upon reasonable request via https://transfer.nako.de.

Declarations

Ethics approval and consent to participate

Initial ethics approval was obtained from the ethical committee of the Bavarian Medical Association (Nr. 13023) and all local ethical committees followed the initial approval. All individual participants were consulted, clarified, and accepted participation in the study by signing an Informed Consent Form. All data were anonymized prior to the author receiving the data. Special ethics approval was not required due to the processing of anonymized data for this paper. The German National Cohort (NAKO) is in accordance with national law and with the Declaration of Helsinki of 1975 (in the current, revised version).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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