**Walking speed, cognitive function and dementia risk in the English Longitudinal Study of Ageing**

**Running title:** Walking speed, cognition & dementia risk

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**Abstract**

**Background:** Physical and cognitive function decline with age. Slow walking speed has been associated with negative health outcomes and dementia is often preceded by cognitive decline. This study investigated walking speed, cognitive function and the interaction between changes in these measures in relation to dementia risk.

**Method:** Walking speed and cognition were assessed in 3,932 individuals aged ≥60 years at wave 1 (2002-03) and 2 (2004-05) of the English Longitudinal Study of Ageing. New dementia cases were assessed from wave 3 (2006-07) to wave 7 (2014-15). The associations were modelled using Cox proportional hazards regression.

**Results:** Participants withfaster baseline walking speeds (HR 0.36; 95% CI 0.22 - 0.60) had a decreased risk of dementia. Those who had a greater decline in walking speed (waves 1 - 2 (HR 1.23; 95% CI 1.03 - 1.47) had an increased dementia risk. Participants with greater baseline cognition (HR 0.42; 95% CI 0.34 - 0.54) had a reduced dementia risk. Those who had a greater decline in cognition (waves 1-2) had a greater risk of dementia (HR 1.78; 95% CI 1.53 - 2.06). Change in walking speed and change in cognition did not interact significantly in relation to dementia risk (HR 1.01; 95% CI 0.88 – 1.17).

**Conclusions:** In this community-dwelling sample of English adults those with slower walking speeds and a greater decline in speed over time had an increased risk of developing dementia independent of changes in cognition. Further research is required to understand the mechanisms that may drive these associations.

**Keywords:** Gait speed, cognition, dementia

**Introduction**

In 2015, an estimated 46.8 million people worldwide had dementia 1. Dementia is a contributor to disability and life years lost among older individuals 2. There is currently no cure for dementia, so identifying potential risk factors may reveal opportunities for prevention. One area of interest is whether physical function is related to dementia onset, since declines in physical and cognitive functioning are indicators of ageing and gait disorders increase with age 3 and are associated with incident dementia 4.

Walking speed is easier to assess than other gait parameters. Slow walking speed is associated with negative outcomes in older individuals 5–7. Individuals with cognitive impairment and dementia walk more slowly than individuals without these conditions 8. Furthermore, meta-analytic evidence indicates that slow walking speed is a predictor of dementia 4,9. Change in walking speed has been less well researched in relation to dementia risk. But in 3,663 French adults, those with a steeper decline in walking speed had a greater risk of dementia than those with a slower decline 10. Similar findings have been reported in Swedish and Japanese samples 11,12.

Dementia develops slowly and be preceded by years of decline in cognitive functioning 13. Cognition and physical function influence one another in a complex manner 14. There is some evidence that the association between cognition and walking speed is bidirectional 15. However, most studies find that slow walking is a predictor of decline in cognition but not vice versa 16,17.

The relationship between changes in cognition and walking speed has been assessed in several studies, but the results are equivocal 18–20. Findings from a sample of 762 participants in the MacArthur Studies of Successful Aging suggest that cognition and walking speed decline in tandem over a 7 year period 18. A limited association was also detected in a Tasmanian sample, where a decline in executive function (but no other domains) was associated with a decrease in walking speed 19. Whereas, an analysis from the Women’s Health Initiative Memory Study failed to detect any association 20.

Overall, it appears that slow walking speed 9 is associated with increased dementia risk, with more limited evidence that a faster decline in walking speed is also relevant 10–12. The evidence is mixed whether changes in cognition are associated with changes in walking speed 18–20 and these associations have yet to be examined in relation to dementia risk. To address these issues, we evaluated whether walking speed and change in walking speed are predictive of dementia in a sample of 3,932 English adults. We also evaluated whether changes in cognition and walking speed interact in relation to dementia risk.

**Methods**

***Study Population***

Our data come from the English Longitudinal Study of Ageing (ELSA); a representative study of community-dwelling adults aged 50 and over in England 21. Data collection began in 2002-2003, with follow-ups every two years. We used data from wave 1 (2002-2003) to wave 7 (2014-2015). All participants gave informed consent. Ethical approval was obtained from the National Research Ethics Committee.

***Dementia***

The outcome was incident dementia from wave 3 (2006-2007) to wave 7 (2014-2015). We used two information sources to define dementia, as in previous work 22. The primary indicator was physician-diagnosed dementia. The second criterion was applied to participants who were not able to respond directly and was a carer’s assessment of functional performance compared with two years before. We used a 16-item adapted short-form version of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) 23, and defined those with an average score ≥3.5 as dementia cases, based on previous work 24. There were 289 incident cases of dementia between waves 3-7, of these 240 were based on physician-diagnosed dementia and 49 on IQCODE scores.

***Walking speed***

Walking speed was assessed in participants aged 60 years and older. Participants were asked to walk a distance of 8ft (2.43m) at their usual pace and the time taken was recorded. The participants then repeated the timed walk and the average time taken was calculated. We used walking speed at wave 1 (2002-2003) as a predictor of dementia.

***Cognitive function***

We aggregated information from four cognitive tests to obtain a cognitive function score at waves 1 and 2. These were memory (immediate and delayed), time orientation, verbal fluency, and processing speed. To compute an overall score, we transformed each of the measures into z scores and derived average total scores in 2002/03 and 2004/05. More information about these tasks is provided elsewhere 25.

***Covariates***

We classified age into three categories (60-69, 60-79, 80+ years). Socioeconomic status was defined using deciles of non-pension wealth (1=low, 10=high). We divided education into three categories: no formal qualifications, intermediate (junior high and high school) and higher education (university). Mobility impairment at baseline was ascertained by asking participants whether they had difficulties with one or more common arm and leg functions (e.g. “Getting in or out of bed”). Impairment of activities of daily living (ADLs) was indexed by asking participants whether they had difficulties with 6 activities (e.g. “dressing, including putting on shoes and socks”). Physician diagnoses of coronary heart disease, stroke, diabetes, cancer and hypertension were entered as binary (yes/no) variables, since these conditions may impact dementia risk. As depression is associated with dementia onset, we included the 8-item Center for Epidemiologic Studies Depression scale (CES-D).

***Statistical analysis***

We compared participant characteristics at wave 1 in those who developed dementia and those who did not, using logistic regression and univariate ANOVAs. As age is an important factor in dementia risk, we controlled for age. To model the association between walking speed at wave 1 (2002-2003) and cumulative dementia from waves 3 (2006-2007) to wave 7 (2014-2015) we used Cox proportional hazards regression. Participants who had dementia at waves 1 and 2 were excluded. If the precise date of dementia diagnosis was unknown, we used the midpoint date between the waves of data collection. We censored individuals who dropped out of the study or who died. We used the last ELSA interview date as the censor date. We calculated change scores in walking speed and cognition by subtracting values in 2004/05 from values in 2002/2003.We then computed an interaction term between changes in walking speed and cognitive function. Preliminary analyses removing those who died did not change the pattern of results. We conducted three sensitivity analyses. First, we modelled the association between walking speed at wave 2 (2004-2005) and cumulative dementia risk (waves 3-7). Second, we used only physician diagnosed dementia as the outcome, and finally we conducting the analyses including new dementia cases from waves 4-7 (2008-2015) rather than wave 3. Results are presented as hazard ratios (HRs) and 95% confidence intervals (95% CI). All analyses were conducted using SPSS version 24.

**Results**

***Participant characteristics***

We compared the characteristics of those who developed dementia (n= 289) with those who remained dementia-free (n=3,643). As can be seen in Table 1 the future dementia group were significantly older on average than the comparison group. Those who developed dementia were less wealthy and had poorer cognition and mobility than the comparison group controlling for age. The dementia group had significantly slower walking speed and were more likely to have had a stroke or elevated depression symptoms

***Baseline walking speed as a predictor of dementia***

Walking speed at wave 1 was a predictor of new-onset dementia, with those with faster walker speeds being less likely to develop dementia (HR 0.36; 95% CI 0.22 - 0.60) in the follow-up period (Table 2). This association was robust to adjustment for covariates. Cognitive function at baseline was also an independent predictor of later dementia (HR 0.42; 95% 0.34 - 0.54), with those with higher cognitive function being less likely to develop dementia.

***Changes in walking speed and cognition as predictors of dementia***

Walking speed decreased on average from 0.86 to 0.85 m/s between wave 1 and wave 2. As can be seen in Table 3 change in walking speed was a significant predictor of dementia (HR 1.23; 95% CI 1.03 - 1.47), with those who had a greater decrease in walking speed from the wave 1 to the wave 2 assessment having a greater risk of developing dementia independent of covariates and walking speed in wave 1. Change in cognition was also a predictor since participants who had a more significant decline in cognitive function between waves 1 and 2 had a higher risk of developing dementia (HR 1.78; 95% CI 1.53 - 2.06). However, the interaction between walking speed and cognitive function was not a significant predictor of dementia (HR 1.01; 95% CI 0.88 – 1.17).

***Sensitivity analyses***

Three sensitivity analyses were conducted. Firstly, we tested whether walking speed at wave 2 (2004-2005) was a predictor of later dementia. Participants with faster walking speeds were less likely to develop dementia (HR 0.25) between waves 3 and 7 (2006-2015) (Supplementary Table 1).

Secondly, we only considered new events in waves 4-7, omitting any that occurred within 2 years of wave 2. This reduced the number of cases from 289 to 225 (Supplementary Table 2), but walking speed at wave 1 remained a predictor of dementia (HR 0.33). Similarly, those with poorer cognition at wave 1 and those who had a greater decline in cognitive function between waves 1 and 2 remained more likely to develop dementia (HR 0.29 and HR 1.69 respectively). The effect size for changes in walking speed was similar to that in the full analysis, but the association was no longer significant because of the reduced number of cases.

For the final sensitivity analysis, we excluded cases who were diagnosed using the IQCODE and limited the analysis to those with physician diagnoses. This reduced the number of cases from 289 to 240 (Supplementary Table 3). Walking speed remained a predictor of dementia (HR 0.36). The findings for cognition also remained for baseline cognition (HR 0.26) and change in cognitive function (HR 1.83). However, similarly to the other sensitivity analysis change in walking speed no longer predicted new-onset dementia.

**Discussion**

In this sample of 3,932 older adults, we found that those with a slower walking speed had a greater risk of developing dementia. Individuals who experienced a greater decline in walking speed were also at increased risk. Participants with poorer cognition at baseline and those who experienced a greater decline in cognition were also more likely to be diagnosed with dementia. However, change in walking speed and change in cognition did not interact in relation to later dementia risk.

Our finding that slower walking speed is a predictor of subsequent dementia is in line with previous research 4,9. In a meta-analysis of 10 prospective studies in this area, 9 were conducted in the United States, and one was carried out in Sweden 9. Our study adds to this literature by demonstrating an association between walking speed and dementia in an English sample. To the best of our knowledge, this is also the largest sample to have addressed this question to date. The association remained significant in our sensitivity analyses, demonstrating the robustness of this finding.

Less research has investigated the association between change in walking speed and dementia risk. In the current study, those with a greater decline in walking speed over two measurement periods were more likely to develop dementia. This finding is in agreement with research from Swedish, French and Japanese cohorts 10–12. The relationship between change in walking speed and dementia remained after controlling for numerous covariates including baseline walking speed. This suggests that regardless of initial walking speed, a marked decrease over a relatively short period (2 years) may be an indicator of increased dementia risk.

We were interested in how cognition and walking speed might influence one another in relation to dementia risk. First, we found that individuals who had poorer baseline cognition were more likely to develop dementia. Secondly, those with a greater decline in cognitive function between waves 1 and 2 had a higher risk of dementia over the follow-up period. Finally, we investigated whether the changes in cognition and walking speed interacted in relation to future dementia onset. However, we found no evidence to support this hypothesis.

 It is well established that initial cognitive function and a decline in cognitive ability are associated with increased risk of subsequent dementia 13. However, understanding of the interplay between changes in walking speed and cognition is limited. Previous research attempting to ascertain whether these functions decline in parallel has been inconsistent, with one study suggesting these functions decline in tandem 18, another finding an association but only for one component of cognition (executive function) 19 and another finding no association at all 20.

The present study extends this research by investigating whether changes in cognition and changes in walking speed interact to predict future dementia. Our findings suggest that declining walking speed and declining cognitive function are independent predictors of dementia, and that these factors do not work synergistically. Cross-sectional evidence suggests that gait speed maps onto the stage of cognitive impairment; with the fastest speeds reported in those with mild cognitive impairment and the slowest psychomotor speed found in advanced dementia 26. It may be that this interplay between cognition and walking speed only emerges at the stage of clinically significant impairment rather than when individuals are still cognitively healthy.

 This observational study provides information on the chronological, but not the casual relationship between walking speed and dementia. Furthermore, reverse causality might be an issue. There is weak evidence from some 15,16 but not all studies 17 that cognitive function may predict walking speed, as well as walking influencing later cognitive states. In our sensitivity analysis excluding cases that occurred in the first 6 years after the walking speed assessment, the association between walking speed and subsequent dementia remained. This addresses the notion that undetected dementia cases impacted walking speed and adds weight to the temporal sequence that gait issues precede dementia onset.

 With regards to the mechanisms linking walking speed with future dementia, several possibilities could help explain our findings. It is thought that walking and cognition rely on similar brain regions, predominately in the prefrontal cortex 27,28. Gait is a complex process in which the locomotor systems receive input from the basal ganglia, motor cortex and the cerebellum 28. While this process is largely automatic, walking relies on sensory feedback and higher order cognitive control 27,28.

 Neurodegeneration is a possible underlying mechanism linking declines in physical and cognitive function, as changes in subcortical white matter 29 and cortical gray matter volumes 29 are associated with slower gait speeds. Vascular risk factors may also contribute to the link between gait decline and dementia through a similar pathway, as micro damage to the vessels of the prefrontal cortex and lesions (due to stroke for example) are associated with white matter changes 30. Our analyses, however, were robust to adjustment for vascular risk factors and history of cardiometabolic disease.

 Another potential mechanism is low-grade systemic inflammation. Heightened concentrations of inflammatory markers are predictive of new-onset dementia 31 and have also been implicated in mobility impairment 32. Neuroinflammation is thought to lead to impaired neuroplasticity in the brain areas controlling motor and cognitive function 28. Furthermore, walking speed relies on muscle strength 33 and muscle loss has been linked with deleterious inflammatory processes 34.

These findings may have implications for efforts to delay dementia onset. The impact of exercise interventions on cognitive function and dementia is disputed 35,36. Nonetheless, a meta-analysis of 42 studies examining the effects of three different exercise interventions on walking speed 37 suggested that all exercise types can lead to increases in walking speed of up to 9.3%. Exercise may also improve cognitive function. A 2017 meta-analysis of 36 randomised control trials found that various types of exercise had a beneficial effect on cognition, regardless of baseline cognitive status 38.

In the present study, we analysed data from a large representative sample of English adults using an objective test of walking speed. We were able to confirm associations between walking speed and dementia risk after adjusting for multiple confounders such as mobility impairment and cardiometabolic disease. However, dementia was primarily identified by physician diagnoses, which resulted in fewer cases than would be expected based on population estimates 39. When this was supplemented this by including diagnosis based on the IQCODE, the incidence of dementia was in line with UK estimates 39. Although it is possible that we missed cases, given the consistency of our findings with earlier studies 4,9–12, misclassification bias is unlikely to account for our results.

Overall, this study suggests that individuals with slower walking speeds and those who experience a greater decline in walking speed over time are at increased risk of dementia. However, changes in walking speed and cognition did not interact in relation to later dementia risk, implying that they operate through independent pathways. Further research is required to understand the causal mechanisms underlying these associations and to determine whether improvements in walking speed translate into reduced dementia risk.

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**Table legends**

Table 1: Participants’ characteristics (2002-04) by dementia (2006-15)

Table 2: Dementia incidence (2006-2015) on walking speed (2002-2003)

Table 3: Dementia incidence (2006-2015) on change in walking speed and cognition (2002-2003)

Supplementary Table 1: Cox proportional hazards regression of the incidence of dementia from waves 3-7 (2006-2015) on walking speed at wave 2 (2004-2005)

Supplementary Table 2: Cox proportional hazards regression of the incidence of dementia from waves 4-7 (2008-2015) on walking speed & cognitive function between waves 1 and 2 (2002-2005)

Supplementary Table 3: Cox proportional hazards regression of the incidence of doctor diagnosed dementia from waves 3-7 (2006-2015) on change in walking speed & cognitive function between waves 1 and 2 (2002-2005)

**Table 1: Participants’ characteristics (2002-04) by dementia (2006-15)**

Data are means (SD)/numbers (%)

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Dementia cases****(n= 289)** | **Non-cases****(n= 3643)** | **p value** |
| **Age (years)**  |  |  | < 0.001 |
|  60-69  | 63 (21.8%) | 2,016 (55.3%) |  |
|  70-79  | 135 (46.7%) | 1,248 (34.3%) |  |
|  80+ | 91 (31.5%) | 379 (10.4%) |  |
| **Sex (% men)** |  |  | = 0.064 |
| **Wealth (deciles)** | 5.34 ± 0.17 | 5.85 ± 0.05 | = 0.004 |
| **Education (% yes)** |  |  | = 0.700 |
|  No qualifications | 125 (43.2%) | 1,512 (41.5%) |  |
|  Intermediate | 99 (34.3%) |  1,293 (35.5%) |  |
|  Higher | 65 (22.5%) | 838 (23%) |  |
| **Walking speed (m/s)** | 0.78 ± 0.02 | 0.87 ± 0.01  | < 0.001 |
| **Cognition** | -0.32 ± 0.04  | -0.06 ± 0.01  | < 0.001 |
| **Mobility impairment**  | 2.44 ± 0.14  | 1.95 ± 0.04 | = 0.001 |
| **ADL**  | 0.41 ± 0.04  | 0.32 ± 0.01  | = 0.054 |
| **CHD (% yes)** | 50 (17.4%) | 532 (14.6%) | = 0.162 |
| **Stroke (% yes)** | 22 (7.5%) | 149 (4.1%) | = 0.018 |
| **Diabetes (% yes)** | 25 (8.8%) | 270 (7.4%) | = 0.256 |
| **Hypertension (% yes)** | 132 (45.6%) | 1,537 (42.2%) | = 0.158 |
| **Cancer (% yes)** | 16 (5.6%) |  189 (5.2%) | = 0.669 |
| **CES-D**  | 1.83 ± 0.11  | 1.38 ± 0.03  | < 0.001 |

Note: All analyses are age-adjusted.

ADL= Activities of daily living; CES-D= Centre for Epidemiological Studies Depression Scale; CHD= Coronary Heart Disease

**Table 2: Dementia incidence (2006-2015) on walking speed (2002-2003)**

|  |  |  |
| --- | --- | --- |
|  | **Adjusted HR****(95% C.I.)** | **p value** |
| Walking speed (m/s) | 0.36 (0.22 – 0.60) | < 0.001 |
| Cognition | 0.42 (0.33 – 0.52) | < 0.001 |
| Sex1 | 1.09 (0.84 – 1.42) | = 0.484 |
| Age 60-69 years 70-79 ≥80 | 12.91 (2.14 – 3.94)6.68 (4.70 – 9.49) | < 0.001< 0.001 |
| Wealth (decile) | 0.96 (0.92 – 1.01) | = 0.086 |
| Education: Lower Intermediate Higher | 11.01 (0.76 – 1.33)1.24 (0.87 – 1.77) | = 0.960= 0.242 |
| Mobility impairmentsADL | 0.98 (0.92 – 1.05)1.03 (0.87 – 1.21) | = 0.596= 0.762 |
|  |  |  |
| CHD2 | 1.12 (0.83 – 1.52) | = 0.446 |
| Stroke2 | 1.26 (0.82 – 1.93) | = 0.295 |
| Diabetes2 | 1.11 (0.74 – 1.65) | = 0.614 |
| Hypertension2 | 1.06 (0.84 – 1.34) | = 0.626 |
| Cancer2 | 1.03 (0.63 – 1.70) | = 0.894 |
| Depression | 1.06 (0.99 – 1.13) | = 0.087 |
|  |  |  |

Note: 1 Male is the reference group; 2 No illness is the reference group

ADL= Activities of daily living; CHD= Coronary Heart Disease; HR= Hazard Ratio

**Table 3: Dementia incidence (2006-2015) on change in walking speed and cognition (2002-2003)**

|  |  |  |
| --- | --- | --- |
|  | **Adjusted HR****(95% C.I.)** | **p value** |
| Change in walking speed (m/s) | 1.23 (1.03 – 1.47) | = 0.020 |
| Change in cognition (z score) | 1.78 (1.53 – 2.06)  | < 0.001 |
| Walking\*Cognition | 1.01 (0.88 – 1.17) | = 0.876 |
| Baseline walking speed (m/s) | 0.28 (0.14 – 0.57) | < 0.001 |
| Baseline cognition | 0.27 (0.21 – 0.35) | < 0.001 |
|  |  |  |
| Sex1 | 1.19 (0.89 – 1.56) | = 0.232 |
| Age 60-69 years 70-79 ≥80 | 13.03 (2.17 – 4.22)6.59 (4.49 – 9.68) | < 0.001< 0.001 |
| Wealth (decile) | 0.97 (0.92 – 1.02) | = 0.276 |
| Education: Lower Intermediate Higher | 10.96 (0.71 – 1.31)1.44 (0.97 – 2.13) | = 0.805= 0.070 |
| Mobility impairmentsADL | 0.99 (0.92 – 1.06)0.99 (0.82 – 1.20) | = 0.684= 0.902 |
|  |  |  |
| CHD2 | 1.21 (0.87 – 1.67) | = 0.259 |
| Stroke2 | 1.04 (0.63 – 1.70) | = 0.881 |
| Diabetes2 | 1.18 (0.77 – 1.81) | = 0.447 |
| Hypertension2 | 0.96 (0.75 – 1.24) | = 0.767 |
| Cancer2 | 1.08 (0.62 – 1.90) | = 0.786 |
| Depression | 1.03 (0.96 – 1.10) | = 0.478 |
|  |  |  |

Note: 1 Male is the reference; 2 No illness is the reference

ADL= Activities of daily living; CHD= Coronary Heart Disease; HR= Hazard Ratio