



Balance and strength measures are associated with incident dementia in older men

Jack Paterson^{a,*}, Michelle Trevenen^b, Keith Hill^c, Osvaldo P. Almeida^d, Bu B. Yeap^e, Jonathan Golledge^f, Graeme J. Hankey^g, Leon Flicker^h

^a Medical School, University of Western Australia, Perth, Australia

^b Western Australian Centre for Health & Ageing, Medical School, University of Western Australia, WACHA, Level 6, Rear 50 Murray Street, Perth, WA 6000, Australia

^c Rehabilitation Ageing and Independent Living (RAIL) Research Centre, Monash University, School of Primary and Allied Health Care, Peninsula Campus, McMahon's Road, Frankston, Victoria, Australia 3199

^d Institute for Health Research, The University of Notre Dame Australia, 19 Mouat Street (PO Box 1225), Fremantle, WA 6959, Australia

^e Department of Endocrinology and Diabetes, Fiona Stanley Hospital, Perth, Australia

^f Queensland Research Centre for peripheral Vascular Disease, James Cook University, Department of Vascular and Endovascular Surgery, Townsville University Hospital, Townsville, Queensland, Australia 4814

^g Perron Institute for Neurological and Translational Science, Nedlands, Western Australia 6009, Australia

^h Western Australian Centre for Health & Ageing, Medical School, University of Western Australia, M577 University of Western Australia, Stirling Hwy, Crawley, Perth 6009, Australia

ARTICLE INFO

Keywords:

Physical performance
Dementia
Cognitive impairment
Balance
Strength

ABSTRACT

Background: As people age the risk of dementia increases. Balance and strength deteriorate with ageing, but their associations with dementia are not clear. We aimed to determine relationships of balance and strength performance with incident dementia in the Health in Men Study (HIMS) cohort.

Methods: We used wave 4 of the HIMS as baseline for analyses (2011–2013), following 1261 men until December 2017 via data linkage to determine incident dementia. Balance was measured using a modified Balance Outcome Measure for Elder Rehabilitation (mBOOMER) Score and strength with the knee extension test. Cox proportional hazards regression was used, adjusting for sociodemographic and health data. Strength and balance scores were analysed non-linearly using restricted cubic splines.

Results: 13.7% of men were diagnosed with dementia over a mean period of 4.7 (SD 1.5) years. Higher baseline mBOOMER scores were associated with a reduced risk of incident dementia, with greater changes in risk at higher mBOOMER scores (9 vs 8: HR 0.80, 95% CI 0.73–0.88; 12 vs 11: 0.49, 95% HR 0.36–0.68). Higher baseline lower limb strength was associated with a reduced risk of incident dementia, with greater changes occurring at lower scores, plateauing at around 25 kg (5 vs 4: HR 0.93, 95% CI 0.89–0.98; 25 vs 24: HR 0.99, 95% CI 0.95–1.03).

Conclusions: This study demonstrated a non-linear association of better performance in both strength and balance with reduced likelihood of incident dementia. These results raise the hypothesis that strategies to improve strength and balance could reduce the incidence of dementia in older men.

1. Introduction

Functional decline is common as people age, but the rate of individual decline varies [1]. Individuals who perform poorly in specific domains, or experience rapid decline in performance, are at higher risk of early morbidity and mortality [1–5]. One modifiable domain of interest is physical performance, which can be investigated with

objectively measured whole-body mobility tasks such as the timed up and go, with different tasks emphasising different physical areas such as strength or balance [6,7]. Additionally of interest are tests of muscle function, such as the strength-focused knee extension test, although these are viewed as precursors to physical performance as they do not incorporate the whole body nor are they mobility-related [8,9].

Studies evaluating physical performance mostly utilise composite

* Corresponding author.

E-mail address: jack.paterson.research@gmail.com (J. Paterson).

<https://doi.org/10.1016/j.ahr.2024.100199>

Received 22 November 2023; Received in revised form 24 July 2024; Accepted 25 July 2024

Available online 28 July 2024

2667-0321/© 2024 The Author(s). Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

measures of physical ability which blend multiple physical attributes such as strength, balance, and flexibility. The Short Physical Performance Battery, for example, blends strength and balance with no clear predominance. While this is useful in capturing the physical performance of participants from a holistic standpoint, it makes it difficult to identify the influence of different attributes [10]. Other studies only assess a single test, such as standing one-legged balance, hindering direct comparison of different physical attributes within the same population [11].

There are a number of studies examining the longitudinal association between physical performance and likelihood of incident dementia. In general, there is agreement that poorer performance on tests of grip strength, gait, and mobility is associated with a higher risk of incident dementia [4,12,13]. The mechanisms underlying this association are not well understood. However, it seems likely that there are common processes which drive declines in both physical and cognitive function [14]. Declining function in both physical and cognitive domains appears to be associated with increases in markers of inflammation, oxidative stress, and metabolic health; as well as a loss of protective factors such as those triggered during physical activity [14–16]. A major potential protective factor is brain-derived neurotrophic factor (BDNF), which likely inhibits hippocampal neurodegeneration and is associated with reduced disease severity in numerous animal models of neurodegenerative diseases [17]. Hippocampal BDNF is increased in response to numerous circulating factors produced during exercise, including: myokines (e.g. irisin), lactate, cathepsin B, and beta-hydroxybutyrate [17]. Physical activity/inactivity may also modulate neurodegeneration through effects on insulin-like growth factor-1, kynurenine, the gut microbiome and iron metabolism [17]. Interestingly, combined impairment in cognitive and physical function, known as the physio-cognitive decline syndrome (PCDS), has a stronger association with incident dementia than either impairment alone. This may reflect that the common processes driving declines in both domains are more active in those experiencing the PCDS than in those experiencing either impairment alone, and they are consequently more likely to develop dementia [18]. There is also evidence for a structural basis to the association between physical performance and incident dementia, with worse physical performance associated with increased brain atrophy [19].

There are few studies directly comparing the associations of strength, particularly lower limb strength, and balance measures with likelihood of incident dementia within the same cohort [4,20]. The association of the PCDS with incident dementia would suggest a similar association between balance measures and incident dementia, as the PCDS includes a mobility impairment component [12]. Indeed, there is some suggestion that balance measures are more strongly associated with risk of incident dementia than measures of upper limb strength [20].

This study sought to characterise the individual relationships of balance and strength with incident dementia in a longitudinal cohort study of older Australian men. Specifically, we assessed both measurements of lower limb muscle function (strength) and balance-focused physical performance within the same cohort and analysed the association of each with dementia incidence, a relatively novel approach.

2. Methods

2.1. Study population

We analysed data from the Health in Men Study (HIMS), an Australian longitudinal cohort study (details published elsewhere) [21]. Eligible participants for the HIMS were men aged 65–79 years at recruitment (1996–99), who were residents of Perth, Western Australia, drawn from the electoral roll. Only those who were able to mobilise (with or without a walking aid) were included. The complete case analysis focused on physical performance and muscle function data collected during wave 4 (2011–2013; $n = 1335$; participants with missing data excluded (pre-exclusion $n = 1588$)), with this being the first

wave in which these physical performance measures were collected. Data for dementia diagnoses were obtained from the Western Australian Data Linkage System (WADLS). WADLS, through a unique patient identifier, links HIMS survey data to hospital admissions, non-admitted emergency and mental attendances and diagnoses, and mortality [21]. The quality and completeness of data obtained via the WADLS is high, as the WADLS codes disease state outcomes by using both an ICD-10 coded record generated from hospital admissions and other sources by the Australian Bureau of Statistics [22,23]. Dementia data were also partly drawn from the questionnaire data collected at each HIMS wave, as were data not relating to disease status.

2.2. Measures of physical performance

Balance was assessed with the modified Balance Outcome Measure for Elder Rehabilitation (mBOOMER) score, which was calculated from the timed up and go, step test, and functional reach test [24–27]. Balance is multidimensional, meaning that a comprehensive overview of balance performance is best achieved by combining performance across several tasks (as in the mBOOMER), rather than any single test [28]. Of the four tests used in the original BOOMER score, the three selected for the mBOOMER score are the dynamic balance and mobility tasks, considered to be more reflective of overall balance abilities than the remaining component of the original score, the timed static stance, which was not measured at wave 4 [29–31]. Scores can range from 0 to 12, 12 being the optimal balance score.

The timed up and go score was the time participants took to stand from a chair (height ~45 cm), walk three metres at their usual speed, turn around and return to a sitting position. Usual indoor walking aids were allowed and normal walking pace was used. The step test involved participants placing one foot on a 7.5 cm high step and then returning it to the ground, repeating this as many times as possible in 15 s, with the score derived from the average of right and left foot scores. The functional reach test involved participants standing with their preferred arm next to (but not leaning on) a wall, raised to shoulder height, and extended at the elbow. Participants then reached forward, and the distance reached without losing balance was recorded.

Lower limb strength was assessed using the knee extension test [8]. Participants were seated with their knee flexed at 90° and a spring dynamometer attached to their ankle. They were then asked to maximally extend their leg at the knee against the resistance of the dynamometer. Higher scores, measured in kilograms, indicate greater lower limb strength, particularly in the quadriceps [32].

2.3. Measurement of dementia

The outcome variable of incident dementia was identified using the linked datasets plus the HIMS wave questionnaires. Dementia was identified using ICD-9 codes 290, 290.0–290.4, 294.1–294.2, 331.0, 331.1, 331.82, and ICD-10 codes F00–F03, F05.1, G30, G31.0 from the WADLS hospital morbidity dataset, emergency department dataset and mental health dataset. Diagnoses of dementia were also identified from the national Aged Care Assessment Program (ACAP). Health conditions are recorded on ACAP as Mental and Behavioural diagnosis codes, the following of which were used to identify dementia: 500–530. Additionally, to maximise sensitivity, dementia was identified in HIMS waves 5–6 as an answer of ‘yes’ to a question asking participants if they had been told by a doctor that they had Alzheimer’s disease or dementia.

2.4. Other study measures

Sociodemographic variables included age, education (never attended school, completed primary, some secondary, completed secondary, completed tertiary), cohabitation (living alone, living with others), and socioeconomic status as inferred by the Socio-Economic Index for Area (SEIFA) Index of Disadvantage at wave 1 (not recorded at subsequent

waves). Health behaviours included alcohol use (standard drinks per week), smoking (non-smoker, ex-smoker, current smoker), diet, sleeping difficulties, and physical activity (metabolic equivalent hours per week). Sleep difficulties were scored with one point for each of: waking up in the early morning hours, lying awake for most of the night, delayed sleep onset, anxiety preventing sleep, sleeping badly at night, and excessive daytime sleepiness [33]. Health data included: systolic blood pressure (mmHg), body mass index (BMI) (kg/m^2), the presence of depressive symptoms scoring mild or higher on the PHQ-9 or a prior diagnosis of depression based on participant questionnaire answers, prior cardiovascular disease, prior cancer diagnoses, and a prior diagnosis of diabetes. Prevalent cardiovascular disease (ICD-10 codes I00-I99 and H34.1, ICD-9 codes 390–459 and 362.3; includes cerebrovascular mortality), cancer (ICD-10 codes C00-C97, ICD-9 codes 140.x-209.x), and diabetes (ICD-10 codes E10-E14, ICD-9 codes 249.0–250.9) were identified from both the WADLS dataset using relevant ICD-9/10 codes, as well as by participant report from the linked questionnaire dataset. The above covariates were selected from the available data because they are generally accepted as potential contributors to incident dementia risk in the existing literature [34–39].

2.5. Statistical analyses

Throughout all analyses, separate models were used for the mBOOMER score and the knee extension test. Relationships between incident dementia following wave 4 and balance or strength were analysed using Cox proportional hazards models. Age was used as the analysis time, as it compares risk at a given age rather than at time since baseline. Participants with dementia prior to or at wave 4 were excluded from the analyses. The proportional hazards assumption was assessed using Schoenfeld residuals. To allow for non-linear relationships, continuous mBOOMER and knee extension test scores were entered into the models using restricted cubic splines. Three knots were selected for spline analysis after iterative assessment of the Bayesian Information Criterion for the linear model and splines of knots 3–5. In order to describe the non-linear relationships, hazard ratios (HRs) and 95% confidence intervals (CIs) are provided for 1-unit change in mBOOMER score and 1 kg change in knee extension score over a range of scores.

For each event of interest, two models were examined to determine the impact of potential confounders. The unadjusted model assessed the crude relationship between balance or strength tests and incident dementia. The adjusted model accounted for the sociodemographic and health variables described above. Adjusted survival analysis data for both mBOOMER score and the knee extension test are presented graphically and in a representative tabular format to demonstrate non-linear relationships.

A sensitivity analysis was also performed, with those participants who died within two-years post-physical assessment being excluded. The aim of this was to assess if the relationships from the original analysis were maintained, even when eliminating the participants most likely to be unwell from the analysis.

3. Results

3.1. Baseline characteristics

Participant baseline characteristics are described in Table 1, stratified by incident dementia occurring within the analysis period. Of the 1335 participants who completed the physical assessment with complete covariate data, 74 (5.5%) had a diagnosis of dementia at the time of the assessment and were excluded from the analysis, with a total of 1261 participants subsequently analysed.

3.2. Incident dementia

Of the 1261 participants included in the analysis, 173 (13.7%) were

Table 1

Baseline characteristics of the HIMS cohort at baseline (wave 4) stratified by dementia status at the end of follow-up.

Characteristic	Total (n = 1261)	Dementia Status by 17 December 2017	
		Incident Dementia (n = 173)	No Dementia (n = 1088)
Mean (SD) Age at wave 4, years	84.5 (3.4)	85.1 (3.6)	84.4 (3.3)
Completed Highschool or Higher, n (%)	706 (56%)	101 (58.4%)	605 (55.6%)
Living with Someone, n (%)	952 (75.5%)	127 (73.4%)	825 (75.8%)
Mean (SD) Socioeconomic Advantage, SEIFA Index ^a	1052.8 (79.5)	1060.3 (75.8)	1051.6 (80)
Median (IQR, 25th percentile, 75th percentile) Alcohol Consumption, standard drinks per week	5 (10, 0, 10)	2 (8, 0, 8)	5 (10.5, 0, 10.5)
Never Smokers, n (%)	511 (40.5%)	69 (39.9%)	442 (40.6%)
Ex-Smokers, n (%)	720 (57.1%)	102 (59%)	618 (56.8%)
Median (IQR, 25th percentile, 75th percentile) Physical Activity, METhrs	15.75 (28.5, 3.5, 32)	9 (22.75, 0.5, 23.25)	17.5 (28.5, 4.5, 33)
Mean (SD) Sleep Score	1.3 (1.3)	1.3 (1.3)	1.4 (1.3)
Mean (SD) Dietary Prudence Score	1.7 (1)	1.9 (0.98)	1.7 (1)
Mean (SD) Systolic Blood Pressure, mmHg	145.7 (20.5)	143.2 (22.7)	146.1 (20.2)
Median (IQR, 25th percentile, 75th percentile) Systolic Blood Pressure, mmHg	145 (28.5, 131, 159.5)	143.5 (29.5, 127.5, 157)	145.5 (28, 132, 160)
Mean (SD) BMI, kg/m^2	26.7 (4)	25.7 (4.5)	26.8 (3.8)
Median (IQR, 25th percentile, 75th percentile) BMI, kg/m^2	26.4 (4.5, 24.2, 28.7)	25.3 (4.9, 22.8, 27.7)	26.6 (4.5, 24.5, 29)
Mean (SD) MMSE	28.1 (1.6)	27.2 (2)	28.3 (1.5)
Mean (SD) Modified BOOMER Score	8.9 (1.8)	8.2 (1.8)	9 (1.8)
Median (IQR) Modified BOOMER Score	9 (2)	8 (1)	9 (2)
Mean (SD) Knee Extension Test, kg	21.8 (6.4)	20 (6.4)	22.1 (6.4)
Median (IQR) Knee Extension Test, kg	21 (8)	19 (8)	22 (8)

Normally distributed data are reported as mean (SD) and non-normally distributed or categorical data are reported as median (IQR).

diagnosed with dementia within the follow-up study period. The median mBOOMER and knee extension scores at baseline were 8 (IQR 1) and 19 (IQR 8) for those who developed dementia, respectively, and 9 (IQR 2) and 22 (IQR 8) for those that did not develop dementia.

Higher (better) mBOOMER scores were associated with decreased risk of incident dementia, with greater changes in risk occurring at higher mBOOMER scores and negligible changes in risk at lower mBOOMER scores (Table 2, Fig. 1).

Higher (better) knee extension strength was associated with a decreased risk of incident dementia, with greater changes occurring at lower levels then plateauing at approximately 25 kgs (Table 2, Fig. 1).

3.3. Sensitivity analysis

Removing those who died within two years post-physical assessment left a cohort of 1218 for analysis, of which 130 (10.7%) were subsequently diagnosed with dementia within the study period. Higher mBOOMER scores remained associated with decreased risk of incident dementia, with larger reductions in risk occurring at higher mBOOMER scores. Similarly, higher knee extension scores remained associated with decreased risk of incident dementia at the lower levels (Table 2).

Table 2
Comparison of multiple physical measure score thresholds to illustrate the non-linearity of their relationships with incident dementia. Sensitivity analyses exclude those who died within two years post-physical assessment. All analyses are fully adjusted.^a.

Physical Performance Score	Incident Dementia (n = 1261)	Sensitivity Analyses (n = 1218)
Adjusted Hazard Ratio (95% Confidence Interval)		
Modified BOOMER Score		
3 vs 2	0.98 (0.86–1.11)	1.18 (0.98–1.41)
6 vs 5	0.98 (0.86–1.11)	1.18 (0.98–1.41)
9 vs 8	0.80 (0.73–0.88)	0.91 (0.81–1.03)
12 vs 11	0.49 (0.36–0.68)	0.49 (0.34–0.70)
Knee Extension Test		
5 vs 4	0.93 (0.89–0.98)	0.95 (0.89–1.00)
15 vs 14	0.93 (0.89–0.98)	0.95 (0.89–1.00)
25 vs 24	0.99 (0.95–1.03)	1.00 (0.95–1.04)
35 vs 34	1.00 (0.95–1.06)	1.01 (0.95–1.08)

^a Adjusting for education, participants living alone, socioeconomic advantage, alcohol consumption, smoking status, physical activity, sleep habits, dietary habits, systolic blood pressure at wave 4, BMI at wave 4, presence of depressive symptoms at wave 4 or a prior diagnosis of depression, prior diagnoses of cancer, prior diagnoses of diabetes, and prior diagnoses of cardiovascular disease.

4. Discussion

The results of this study showed that higher scores on objective lower limb strength (knee extension test) and balance (mBOOMER score) tests are associated with reduced hazards of incident dementia, even after adjustment for demographic information, health behaviours and health

data.

These results contribute to the growing body of literature focusing on physical function and incident dementia. There are relatively few studies in this area, at least as compared to the research base focusing on physical function and prevalent dementia [4,40]. The measures of physical performance most commonly studied in association with incident dementia are grip strength and measures of gait or mobility [4,13,20,41]. There are few studies examining lower limb strength and incident dementia, although cross-sectional data suggests that there is an association with prevalent dementia [42]. Our results build on this existing literature, assessing the outcome of incident dementia. Interestingly, there is conflicting data around the association of grip strength with incident dementia, with our results indicating that lower limb strength may be a fruitful area of alternative study [4,13]. There are comparatively more studies examining the association between balance-related tests and incident dementia [12,20,41]. Research examining gait speed, mobility, and standing balance all suggests that better performance on these measures is associated with reduced hazards of incident dementia [12,20,41]. Our research is in keeping with existing data regarding balance performance, and expands on it through the novel inclusion of a lower limb strength measure within the same cohort for qualitative comparison.

Another novel component of the present study was the use of restricted cubic splines to demonstrate the non-linear relationships between incident dementia and strength or balance tests. Higher mBOOMER scores were associated with a reduction in risk of incident dementia at scores higher than 8, with minimal difference in risk prior to this point. This threshold effect has multiple potential explanations. First, it is possible that those participants with a pathophysiologic

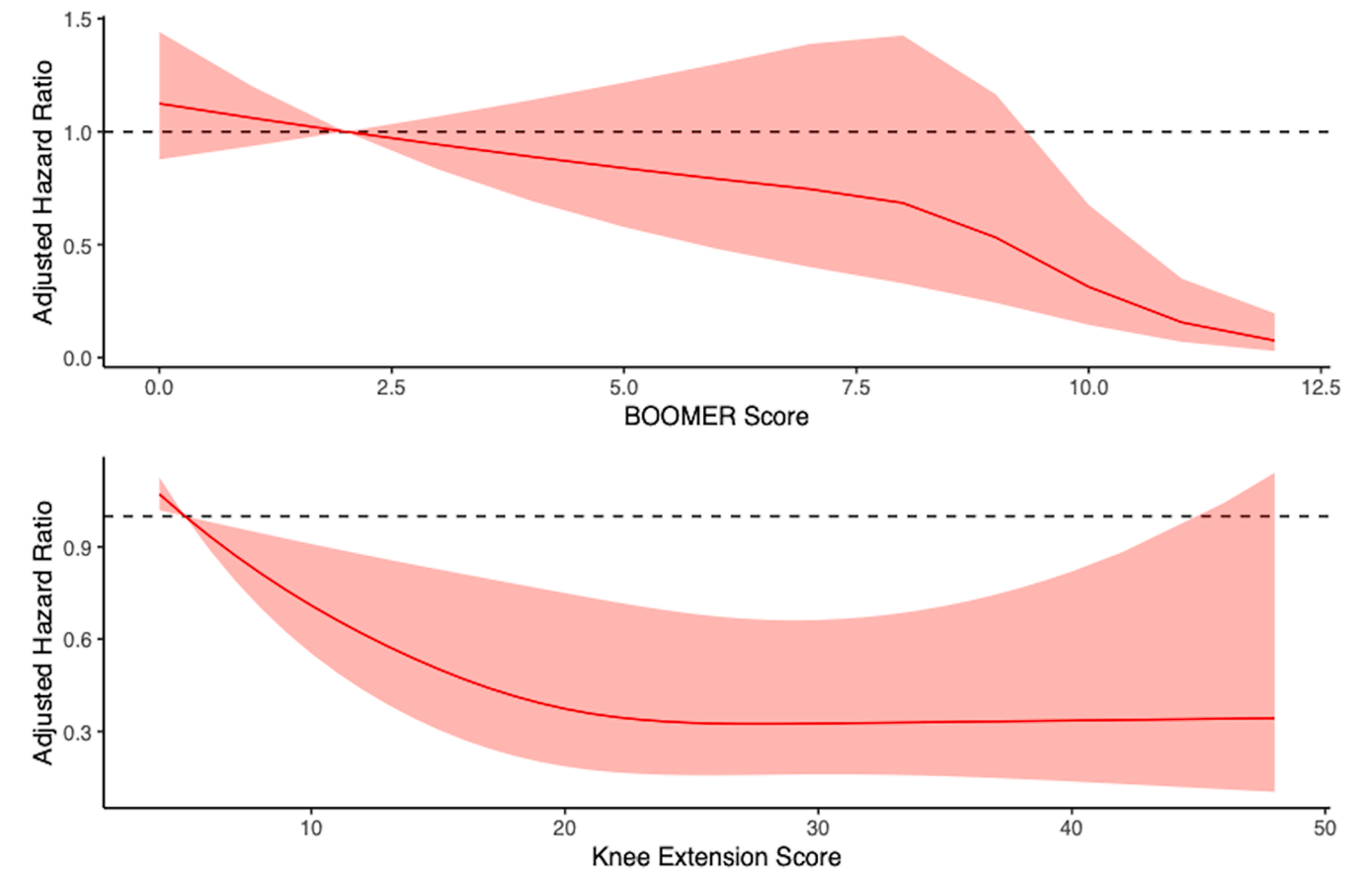


Fig. 1. Adjusted hazard ratios with 95% confidence intervals for the relationship between mBOOMER scores or Knee Extension scores (kg) and incident dementia. Hazard ratios are presented for a reference level of 2 for mBOOMER and 5 for knee extension (representative of the worst performers in each test) with the solid red line as the reference level, and the shaded red area representing the 95% confidence interval; the dashed black line represents a hazard ratio equal to 1.

substrate predisposing them to future dementia also have sufficient co-existing damage to the complex neuromuscular systems coordinating balance, possibly through shared pathological mechanisms, that they are much less likely to be able to perform in the highest range of mBOOMER scores. Second, if we view balance as a modifiable risk factor for future dementia, this relationship could be interpreted as indicating that it is necessary for participants to improve their balance to a relatively high level of performance in order to see a reduction in future dementia risk.

Similarly, higher knee extension scores were typically associated with a lower risk of incident dementia. However, this relationship plateaued at a knee extension score of approximately 25 kg. Again, this relationship can be interpreted in multiple ways. First, if we take the view of weakness and dementia potentially sharing pathophysiologic mechanisms, our data suggests that only once these mechanisms reach the threshold required to cause knee extension strength to reduce below 25 kg do they also begin to increase dementia risk. Second, if we take the view of muscle strength as a modifiable protective factor (e.g. through protective mediators released from muscle tissue during activity), then our data suggests that improvements in lower limb strength in the weakest individuals may reduce risk of future dementia, however there are diminishing returns above a certain threshold.

To compare the nature of these two relationships, it appears that incident dementia risk roughly starts to reduce as balance scores increase above the cohort median, whereas risk reduction slows with lower limb strength scores higher than the median (Table 1). First, taking the perspective of shared pathophysiological mechanisms driving changes in physical performance and dementia risk, this could indicate that the degree of dementia-inducing substrate required to increase dementia risk also induces a lower than median strength, with a correlation between risk and worsening strength after this point. Conversely, the amount of shared substrate required to increase dementia risk causes an initial reduction in balance performance as dementia risk increases, with a plateau at a median level of balance beyond which dementia risk does not keep increasing as balance continues to deteriorate. Second, from the view of these measures as modifiable risk factors, these results could suggest that a median level of strength provides protection from incident dementia, whereas higher than median balance is required to see benefit. Rather than only one of the above explanations being at play, the relationship between physical performance and dementia pathophysiology is likely to be complex and bidirectional, with prospective studies assessing the effects of balance and strength training on incident dementia required to support a causal relationship [43,44].

The results of the present study also help expand on previous studies of physical performance and muscle function tests in different populations. A study of physical performance predictors and incident dementia in older Japanese adults found that higher lower body performance measures (sit-to-stand, timed up-and-go) were associated with lower risk of incident dementia [4]. These results concur with our own, as the mBOOMER composite utilises lower body balance performance measures. However, this study did not find a significant association between upper body strength (grip strength) and incident dementia, whereas our study does demonstrate a relationship between lower body strength and this outcome. Whether this reflects the fact that lower body strength is more strongly associated with incident dementia than upper body strength, or instead reflects the limited sensitivity of the available data, is difficult to determine. Indeed, in the initial crude analyses, the Japanese study did suggest a plateau-effect of increasing grip strength on future dementia risk, similar to that observed in our study [4]. Additionally, a later meta-analysis suggests that grip strength does have an association with incident dementia across a large enough cohort [13]. To clarify the nature of these relationships, future research might compare the association of incident dementia and upper or lower body strength measures, with attention paid to the potential insights provided by modelling non-linear relationships.

The clinical implications of these results are as follows. First, both

strength and balance measures were associated with future dementia, although the causal relationship is not clear given the relatively short duration of follow-up. Simultaneous assessment of both strength tests and balance test suites as relates to incident dementia has not been explored in detail previously, with this study supporting clinical use of both tests for risk-stratification in general populations. The clinical utility of these findings should be considered in the context of the limitations of the observational data used. These data may indicate that thresholds exist for increased dementia risk amongst strength and balance measures, but these performance measure thresholds require further study and validation prior to considering their use in clinical practice. Second, these results suggest that the future study of the impact of both strength and balance training interventions on incident dementia would be of interest. At present, the research into these interventions has been limited, with no randomised controlled trials assessing their impact on incident dementia; although some studies have assessed the impact of exercise interventions on complications of prevalent dementia [45]. As such, randomised prospective research investigating whether there is a preventative effect of either strength training or balance training on incident dementia may be of benefit.

This study has several strengths. We studied a large cohort of older men who were originally sampled from the general population. As there are few men in this age group who migrate outside Western Australia, the WADLS provides nearly complete outcome data [21]. We also had data available for many potentially confounding factors. Additionally, the present study analysed dementia incidence amongst participants in relation to both strength and balance attributes, a neglected area of study in the existing literature.

Interpretation of our results is subject to several limitations. Firstly, we only studied men, so these findings may not apply to women. We also only studied men who responded at wave 4, who were generally healthier than non-responders and those who had not survived prior waves, thus excluding the frailest members of the population and introducing both selection and survivorship bias [46]. Exacerbating this bias is the floor effect from some performance measures, such as those involved in calculating the mBOOMER Score, which limits discriminative power amongst the men who were unable to perform the tasks at all. As such, these results may not generalise to the frailest or least healthy members of the population. Additionally, in the interpretation of these results, it should be noted that while the mBOOMER score is a measure of dynamic balance, the attribute of 'dynamic balance' in and of itself is affected to a degree by participant muscle power. As such, a severe impairment of participant strength would lead to impairment in both of the physical measures studied herein. However, muscle strength is only necessary but not sufficient for dynamic balance, and the influence of relevant non-strength attributes (vestibular, visual, somatosensory and nervous) may be what drives the differing patterns of association seen with incident dementia risk. The mBOOMER score can thus be viewed as predominantly a measure of dynamic balance, with the caveat that it is not perfectly isolated from other physical attributes. The diagnosis of dementia also relied on accurate ICD coding, and although we attempted to reduce the potential for falsely negative misclassification by incorporating multiple datasets and the HIMS wave questionnaires, it is still possible that some falsely positive misclassification occurred. The diagnosis of dementia may also be more likely to be recorded in those attending hospitals for mobility-related reasons such as a fall, which could be a source of bias in our data, although we have attempted to mitigate this hospital-related bias by utilising national aged care assessment and HIMS questionnaire data. In addition to these limitations, there were a relatively small number of cases of incident dementia, partly related to death due to other causes but also to the limited duration of study follow-up. Evaluation of future WADLS data within this cohort may provide more incident cases and expand on the relationships demonstrated in the present study. Prior cross-sectional analyses have shown that different dementia subtypes are associated with differing degrees and types of physical impairment, but we did not have

a sufficient number of specific sub-types of incident dementia cases on which to perform subgroup analyses [40]. Additionally, physical testing was only performed at a single time-point and thus the rate of physical deterioration was unknown. We also did not have access to covariates which have been identified as contributing to dementia incidence; notably hearing impairment, low social contact, traumatic brain injury and air pollution. Finally, we did not have access to data regarding covariates which may have influenced participant balance, such as medications or vestibulocochlear function.

5. Conclusion

This study demonstrates independent, significant non-linear associations between poorer scores on both strength and balance tests, and future dementia in older men. The nature of the associations with incident dementia differ, with a plateau effect seen in the association between strength (below 25 kg) and dementia. These results should stimulate further research into whether balance or strength training programs may modify the frequency and severity of incident dementia.

Funding/Support statement

The work described in this paper has been supported by project grants from the National Health and Medical Research Council of Australia (1128083, 1045710). The funder had no role in the design, collection, analysis, and interpretation of the data; nor did it have a role in the writing of the report or in the decision to submit the article for publication. LF is supported by Medical Research Future Fund Clinical Practitioner Fellowship (1155669). Jack Paterson was supported by a Davis Scholarly Plus Award in Dementia and Ageing Research (F19/2327 M).

CRediT authorship contribution statement

Jack Paterson: Writing – review & editing, Writing – original draft, Formal analysis, Conceptualization. **Michelle Trevenen:** Writing – review & editing, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Keith Hill:** Writing – review & editing, Methodology, Conceptualization. **Osvaldo P. Almeida:** Writing – review & editing, Project administration, Investigation, Funding acquisition, Conceptualization. **Bu B. Yeap:** Writing – review & editing, Project administration, Methodology, Funding acquisition. **Jonathan Gollidge:** Writing – review & editing, Methodology, Investigation. **Graeme J. Hankey:** Writing – review & editing, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization. **Leon Flicker:** Writing – review & editing, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

Author Contributions

Jack Paterson: writing and revising the manuscript, collaborated on the initial planning of analyses, and adjusting the analyses for additional covariates.

Michelle Trevenen: performing the restricted spline modelling of incident dementia and advising on the content of the statistical methods and results sections.

Leon Flicker: involved in the initial planning and revision of the analyses and manuscript, corresponding author. Involved in the design

and continuation of the Health in Men Study.

Keith Hill: involved in the initial selection of physical performance measures for the Health in Men Study. Revised the manuscript, particularly relating to the descriptions of physical performance measures.

Osvaldo P. Almeida: Assisted in revising the manuscript and provided advice on the initial planning of manuscript and analyses. Involved in the design and continuation of the Health in Men Study.

Bu B. Yeap: Assisted in revising the manuscript. Involved in the design and continuation of the Health in Men Study.

Jonathan Gollidge: Assisted in revising the manuscript. Involved in the design and continuation of the Health in Men Study.

Graeme J Hankey: Assisted in revising the manuscript. Involved in the design and continuation of the Health in Men Study.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.ahr.2024.100199](https://doi.org/10.1016/j.ahr.2024.100199).

References

- [1] Cohen-Mansfield J, Skornick-Bouchbinder M, Brill S. Trajectories of End of Life: A Systematic Review. *J Gerontol B Psychol Sci Soc Sci* 2018;73(4):564–72. <https://doi.org/10.1093/geronb/gbx093>.
- [2] Landré B, Fayosse A, Hassen CB, et al. Terminal decline in objective and self-reported measures of motor function before death: 10 year follow-up of Whitehall II cohort study. *BMJ* 2021;374:n1743. <https://doi.org/10.1136/bmj.n1743>.
- [3] Sabia S, Guéguen A, Marmot MG, Shipley MJ, Ankri J, Singh-Manoux A. Does cognition predict mortality in midlife? Results from the Whitehall II cohort study. *Neurobiol Aging* 2010;31(4):688–95. <https://doi.org/10.1016/j.neurobiolaging.2008.05.007>.
- [4] Doi T, Tsutsumimoto K, Nakakubo S, et al. Physical Performance Predictors for Incident Dementia Among Japanese Community-Dwelling Older Adults. *Phys Ther* 2019;99(9):1132–40. <https://doi.org/10.1093/ptj/pzz077>.
- [5] Paterson J, Trevenen M, Hill K, et al. Balance and Strength Measures are Associated With Mortality in Older Men. *J Am Med Dir Assoc* 2023. <https://doi.org/10.1016/j.jamda.2023.03.038>. Published online May 12.
- [6] Eng JJ, Tang PF. Gait training strategies to optimize walking ability in people with stroke: A synthesis of the evidence. *Expert Rev Neurother* 2007;7(10):1417–36. <https://doi.org/10.1586/14737175.7.10.1417>.
- [7] Portegijs E, Karavirta L, Saajanaho M, Rantalainen T, Rantanen T. Assessing physical performance and physical activity in large population-based aging studies: home-based assessments or visits to the research center? *BMC Public Health* 2019;19(1):1570. <https://doi.org/10.1186/s12889-019-7869-8>.
- [8] Lord SR, Menz HB, Tiedemann A. A Physiological Profile Approach to Falls Risk Assessment and Prevention. *Phys Ther* 2003;83(3):237–52. <https://doi.org/10.1093/ptj/83.3.237>.
- [9] Beaudart C, Rolland Y, Cruz-Jentoft AJ, et al. Assessment of Muscle Function and Physical Performance in Daily Clinical Practice: A position paper endorsed by the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO). *Calcif Tissue Int* 2019;105(1):1–14. <https://doi.org/10.1007/s00223-019-00545-w>.
- [10] Pavaresi R, Guralnik J, Brown JC, et al. Short Physical Performance Battery and all-cause mortality: systematic review and meta-analysis. *BMC Med* 2016;14(1):215. <https://doi.org/10.1186/s12916-016-0763-7>.
- [11] Araujo CG, de Silva CG, de S, Laukkanen JA, et al. Successful 10-second one-legged stance performance predicts survival in middle-aged and older individuals. *Br J Sports Med* 2022. <https://doi.org/10.1136/bjsports-2021-105360>. Published online May 15.
- [12] Lee WJ, Peng LN, Lin MH, et al. Six-year transition of physio-cognitive decline syndrome: Results from I-Lan Longitudinal Aging Study. *Arch Gerontol Geriatr* 2022;102:104743. <https://doi.org/10.1016/j.archger.2022.104743>.
- [13] Cui M, Zhang S, Liu Y, Gang X, Wang G. Grip Strength and the Risk of Cognitive Decline and Dementia: A Systematic Review and Meta-Analysis of Longitudinal Cohort Studies. *Front Aging Neurosci* 2021;13:625551. <https://doi.org/10.3389/fnagi.2021.625551>.
- [14] Sargent L, Nalls M, Starkweather A, et al. Shared biological pathways for frailty and cognitive impairment: A systematic review. *Ageing Res Rev* 2018;47:149–58. <https://doi.org/10.1016/j.arr.2018.08.001>.
- [15] Franceschi C, Garagnani P, Parini P, Giuliani C, Santoro A. Inflammaging: a new immune-metabolic viewpoint for age-related diseases. *Nat Rev Endocrinol* 2018;14(10):576–90. <https://doi.org/10.1038/s41574-018-0059-4>.
- [16] Chung YH, Wei CY, Tzeng RC, Chiu PY. Minimal amount of exercise prevents incident dementia in cognitively normal older adults with osteoarthritis: a retrospective longitudinal follow-up study. *Sci Rep* 2023;13:16568. <https://doi.org/10.1038/s41598-023-42737-3>.
- [17] Nay K, Smiles WJ, Kaiser J, et al. Molecular Mechanisms Underlying the Beneficial Effects of Exercise on Brain Function and Neurological Disorders. *Int J Mol Sci* 2021;22(8):4052. <https://doi.org/10.3390/ijms22084052>.

- [18] Chung CP, Lee WJ, Peng LN, et al. Physio-Cognitive Decline Syndrome as the Phenotype and Treatment Target of Unhealthy Aging. *J Nutr Health Aging* 2021;25(10):1179–89. <https://doi.org/10.1007/s12603-021-1693-4>.
- [19] Rosano C, Sigurdsson S, Siggeirsdottir K, et al. Magnetization transfer imaging, white matter hyperintensities, brain atrophy and slower gait in older men and women. *Neurobiol Aging* 2010;31(7):1197–204. <https://doi.org/10.1016/j.neurobiolaging.2008.08.004>.
- [20] Bullain SS, Corrada MM, Perry SM, Kawas CH. Sound Body Sound Mind? Physical Performance and the Risk of Dementia in the Oldest-Old: The 90+ Study. *J Am Geriatr Soc* 2016;64(7):1408–15. <https://doi.org/10.1111/jgs.14224>.
- [21] Norman PE, Flicker L, Almeida OP, Hankey GJ, Hyde Z, Jamrozik K. Cohort Profile: The Health In Men Study (HIMS). *Int J Epidemiol* 2009;38(1):48–52. <https://doi.org/10.1093/ije/dyn041>.
- [22] Holman CDJ, Bass AJ, Rouse IL, Hobbs MST. Population-based linkage of health records in Western Australia: development of a health services research linked database. *Aust N Z J Public Health* 1999;23(5):453–9. <https://doi.org/10.1111/j.1467-842X.1999.tb01297.x>.
- [23] Brook EL, Rosman DL, Holman CDJ. Public good through data linkage: measuring research outputs from the Western Australian Data Linkage System. *Aust N Z J Public Health* 2008;32(1):19–23. <https://doi.org/10.1111/j.1753-6405.2008.00160.x>.
- [24] Duncan PW, Weiner DK, Chandler J, Studenski S. Functional reach: a new clinical measure of balance. *J Gerontol* 1990;45(6):M192–7. <https://doi.org/10.1093/geronj/45.6.m192>.
- [25] Haines T, Kuys SS, Morrison G, Clarke J, Bew P, McPhail S. Development and validation of the balance outcome measure for elder rehabilitation. *Arch Phys Med Rehabil* 2007;88(12):1614–21. <https://doi.org/10.1016/j.apmr.2007.09.012>.
- [26] Barry E, Galvin R, Keogh C, Horgan F, Fahey T. Is the Timed Up and Go test a useful predictor of risk of falls in community dwelling older adults: a systematic review and meta-analysis. *BMC Geriatr* 2014;14(1):14. <https://doi.org/10.1186/1471-2318-14-14>.
- [27] Hill KD, Bernhardt J, McGann AM, Maltese D, Berkovits D. A New Test of Dynamic Standing Balance for Stroke Patients: Reliability, Validity and Comparison with Healthy Elderly. *Physiother Can* 1996;48(4):257–62. <https://doi.org/10.3138/ptc.48.4.257>.
- [28] Pardasane PK, Slavin MD, Wagenaar RC, Latham NK, Ni P, Jette AM. Conceptual Limitations of Balance Measures for Community-Dwelling Older Adults. *Phys Ther* 2013;93(10):1351–68. <https://doi.org/10.2522/ptj.20130028>.
- [29] Shirai N, Yamamoto S, Osawa Y, Tsubaki A, Morishita S, Narita I. Dysfunction in dynamic, but not static balance is associated with risk of accidental falls in hemodialysis patients: a prospective cohort study. *BMC Nephrol* 2022;23(1):237. <https://doi.org/10.1186/s12882-022-02877-6>.
- [30] Bower K, Thilarajah S, Pua YH, et al. Dynamic balance and instrumented gait variables are independent predictors of falls following stroke. *J Neuroengineering Rehabil* 2019;16(1):3. <https://doi.org/10.1186/s12984-018-0478-4>.
- [31] Bani Hassan E, Phu S, Vogrin S, Duque G. Appendicular and mid-thigh lean mass are associated with muscle strength, physical performance, and dynamic balance in older persons at high risk of falls. *Gait Posture* 2022;93:90–5. <https://doi.org/10.1016/j.gaitpost.2022.01.022>.
- [32] Kim WK, Kim DK, Seo KM, Kang SH. Reliability and Validity of Isometric Knee Extensor Strength Test With Hand-Held Dynamometer Depending on Its Fixation: A Pilot Study. *Ann Rehabil Med* 2014;38(1):84–93. <https://doi.org/10.5535/arm.2014.38.1.84>.
- [33] Hill Almeida LM, Flicker L, Hankey GJ, Golledge J, Yeap BB, Almeida OP. Disrupted sleep and risk of depression in later life: A prospective cohort study with extended follow up and a systematic review and meta-analysis. *J Affect Disord* 2022;309:314–23. <https://doi.org/10.1016/j.jad.2022.04.133>.
- [34] Kao YS, Yeh CC, Chen YF. The Relationship between Cancer and Dementia: An Updated Review. *Cancers* 2023;15(3):640. <https://doi.org/10.3390/cancers15030640>.
- [35] White IR, Carlin JB. Bias and efficiency of multiple imputation compared with complete-case analysis for missing covariate values. *Stat Med* 2010;29(28):2920–31. <https://doi.org/10.1002/sim.3944>.
- [36] Livingston G, Huntley J, Sommerlad A, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *Lancet Lond Engl* 2020;396(10248):413–46. [https://doi.org/10.1016/S0140-6736\(20\)30367-6](https://doi.org/10.1016/S0140-6736(20)30367-6).
- [37] Lai KY, Webster C, Kumari S, Gallacher JEJ, Sarkar C. The associations of socioeconomic status with incident dementia and Alzheimer's disease are modified by leucocyte telomere length: a population-based cohort study. *Sci Rep* 2023;13(1):6163. <https://doi.org/10.1038/s41598-023-32974-x>.
- [38] Ellouze I, Sheffer J, Nagpal R, Arjmandi B. Dietary Patterns and Alzheimer's Disease: An Updated Review Linking Nutrition to Neuroscience. *Nutrients* 2023;15(14):3204. <https://doi.org/10.3390/nu15143204>.
- [39] Farnsworth von Cederwald B, Josefsson M, Wåhlin A, Nyberg L, Karalija N. Association of Cardiovascular Risk Trajectory With Cognitive Decline and Incident Dementia. *Neurology* 2022;98(20):e2013–22. <https://doi.org/10.1212/WNL.000000000000200255>.
- [40] Sverdrup K, Selbæk G, Bergh S, et al. Physical performance across the cognitive spectrum and between dementia subtypes in a population-based sample of older adults: The HUNT study. *Arch Gerontol Geriatr* 2021;95:104400. <https://doi.org/10.1016/j.archger.2021.104400>.
- [41] Kueper JK, Speechley M, Lingum NR, Montero-Odasso M. Motor function and incident dementia: a systematic review and meta-analysis. *Age Ageing* 2017;46(5):729–38. <https://doi.org/10.1093/ageing/afx084>.
- [42] Chen WL, Peng TC, Sun YS, et al. Examining the Association Between Quadriceps Strength and Cognitive Performance in the Elderly. *Medicine (Baltimore)* 2015;94(32). <https://doi.org/10.1097/MD.0000000000001335>.
- [43] Mielke MM, Roberts RO, Savica R, et al. Assessing the Temporal Relationship Between Cognition and Gait: Slow Gait Predicts Cognitive Decline in the Mayo Clinic Study of Aging. *J Gerontol Ser - Biol Sci Med Sci* 2013;68(8):929–37. <https://doi.org/10.1093/gerona/gls256>.
- [44] Atkinson HH, Rosano C, Simonsick EM, et al. Cognitive function, gait speed decline, and comorbidities: the health, aging and body composition study. *J Gerontol A Biol Sci Med Sci* 2007;62(8):844–50. <https://doi.org/10.1093/gerona/62.8.844>.
- [45] Suttanon P, Hill K, Said C, Dodd K. Can balance exercise programmes improve balance and related physical performance measures in people with dementia? A systematic review. *Eur Rev Aging Phys Act* 2010;7(1):13–25. <https://doi.org/10.1007/s11556-010-0055-8>.
- [46] McCaul KA, Almeida OP, Norman PE, et al. How many older people are frail? Using multiple imputation to investigate frailty in the population. *J Am Med Dir Assoc* 2015;16(5):439.e1–7. <https://doi.org/10.1016/j.jamda.2015.02.003>.