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Cooper, R , Kuh, D, Cooper, C, Gale, CR, Lawlor, DA, Matthews, F and Hardy, R (2010) Objective measures of physical capability and subsequent health: A systematic review. *Age and Ageing*, 40 (1). pp. 14-23. ISSN 0002-0729

DOI: <https://doi.org/10.1093/ageing/afq117>

Publisher: Oxford University Press (OUP)

Version: Published Version

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SYSTEMATIC REVIEWS

Objective measures of physical capability and subsequent health: a systematic review

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Abstract

Background: measures of physical capability may be predictive of subsequent health, but existing published studies have not been systematically reviewed. We hypothesised that weaker grip strength, slower walking speed and chair rising and shorter standing balance time, in community-dwelling populations, would be associated with higher subsequent risk of fracture, cognitive outcomes, cardiovascular disease, hospitalisation and institutionalisation.

Methods: studies were identified through systematic searches of the electronic databases MEDLINE and EMBASE (to May 2009). Reference lists of eligible papers were also manually searched.

Results: twenty-four papers had examined the associations between at least one physical capability measure and one of the outcomes. As the physical capability measures and outcomes had been assessed and categorised in different ways in different studies, and there were differences in the potential confounding factors taken into account, this made it impossible to pool results. There were more studies examining fractures than other outcomes, and grip strength and walking speed were the most commonly examined capability measures. Most studies found that weaker grip strength and slower walking speed were associated with increased risk of future fractures and cognitive decline, but residual confounding may explain results in some studies. Associations between physical capability levels and the other specified outcomes have not been tested widely.

Conclusions: there is some evidence to suggest that objective measures of physical capability may be predictors of subsequent health in older community-dwelling populations. Most hypothesised associations have not been studied sufficiently to draw definitive conclusions suggesting the need for further research.

Keywords: *grip strength, walking speed, chair rises, standing balance, fracture, cognitive outcomes, cardiovascular disease, systematic review*

Introduction

Physical capability, a concept also referred to as physical functioning, is a term used to describe an individual's capacity to undertake the physical tasks of everyday living. There is growing evidence that objective measures of physical performance such as grip strength, walking speed, chair rising and standing balance not only characterise physical capability but also act as markers of current and future health. For instance, a systematic review [1] has recently

demonstrated associations between each of these measures of physical capability and all-cause mortality in community-dwelling populations. If the underlying explanations of the associations found with mortality are to be elucidated, there is a need to establish whether associations are also found with important health outcomes which may subsequently lead to death or disablement. Some published evidence suggests that objective measures of physical capability levels may be predictive of subsequent health problems; however, few attempts have been made to review this

literature systematically. Existing published reviews [2, 3] focus only on one component of physical capability, grip strength, so conclusions about other measures of physical capability cannot be drawn. Furthermore, the number of outcomes, other than mortality, assessed in these reviews is limited. It is important to assess whether physical capability levels are consistently associated with subsequent health outcomes in populations who are free from the outcome of interest at the time of capability assessment. If associations can only be demonstrated in cross-sectional analyses, in populations in which the specified health outcome of interest is prevalent at the time of capability assessment, it is not possible to determine the direction of any associations given that poor health could influence physical capability levels.

We hypothesised that lower physical capability levels in community-dwelling populations would be associated with higher subsequent risk of poor health. The objective of this paper was to test this hypothesis by reviewing the published literature examining the associations between individual measures of physical capability and a range of pre-specified health outcomes including fracture, cognitive outcomes, cardiovascular disease, hospitalisation and institutionalisation.

Methods

Search strategy and selection criteria

A systematic review of the published literature was undertaken following the Meta-analysis of Observational Studies in Epidemiology guidelines [4]. As defined in a pre-specified protocol (available on request), eligible observational studies were those conducted at the individual level which examined the association of at least one of the specified measures of physical capability (grip strength, chair rises, balance and walking speed) with at least one of the specified outcomes, selected because of their relationships with risk of death and/or disablement: fracture; cognitive outcomes (including dementia, cognitive decline and Alzheimer's disease); cardiovascular disease (including stroke and diabetes); hospitalisation; institutionalisation. Eligible study populations were of any age, non-disabled and community-dwelling at the time of physical capability assessment. As it is possible that poor health could influence physical capability levels, eligible studies had to have measured physical capability levels at an earlier time point than the assessment of outcome and so cross-sectional studies were necessarily excluded. In addition, studies were excluded if individuals who presented with the health outcome of interest at the time of physical capability assessment were included in the study sample.

To identify eligible studies, searches of the electronic databases MEDLINE (1950 to May 2009) and EMBASE (1980 to May 2009) were performed using free text search terms (see Supplementary data available in *Age and Ageing* online for details of search strategy). These searches were not restricted by language of publication.

The results of the electronic searches were combined and duplicate records removed. The abstracts of all 2,467 unique records were screened for eligibility independently by two authors. The full text of all 59 papers identified as potentially eligible were obtained to make a final decision about eligibility. Relevant data from the 18 eligible papers [5–22] were independently extracted by two authors using a standardised form. In addition to relevant published results, information was also extracted on the study population, their selection and baseline characteristics, study exclusion criteria, details of the methods of ascertainment of physical capability levels and outcomes and identification of potential confounders and methods of controlling for these. An assessment of each study's quality was made, based on a modified version of the Newcastle-Ottawa quality assessment scale [23]. The reference lists of all eligible papers were searched by hand and the abstracts of the 64 additional references identified were screened independently by two authors with data then extracted from the six additional eligible papers [24–29] identified. Any disagreements about study eligibility or differences between the two sets of information extracted were resolved through discussion. Through these processes, 24 papers were included in the review (Figure 1). Where more than one paper reported results using data from the same study population, this is reported. In summarising study findings, results from different papers testing the same association in the same study population are not reported more than once. In such situations, we chose to report the results based on the longest follow-up. It was decided that the outcomes across studies were too heterogeneous to carry out meta-analyses. Hence, no attempts were made to contact study authors for additional information.

Results

All 24 papers included in the review had a cohort design. Table 1 presents a summary of each of these papers.

Fracture

Twelve papers [5, 8, 11–14, 16, 18, 21, 22, 25, 26] using data from nine different study populations were identified, which reported on the association between at least one of the specified measures of physical capability and subsequent fracture risk (Table 1). The majority of these studies examined women only, with only two studies examining both sexes [18, 22] and one study examining men only [8].

The association of grip strength with subsequent fracture risk had been examined in all nine study populations identified. Seven studies reported an association between lower grip strength and higher subsequent risk of fracture, although three of these only presented unadjusted results. The two other studies reported null associations between grip strength and fracture risk. Some studies found an association only for specific types of fracture and one only

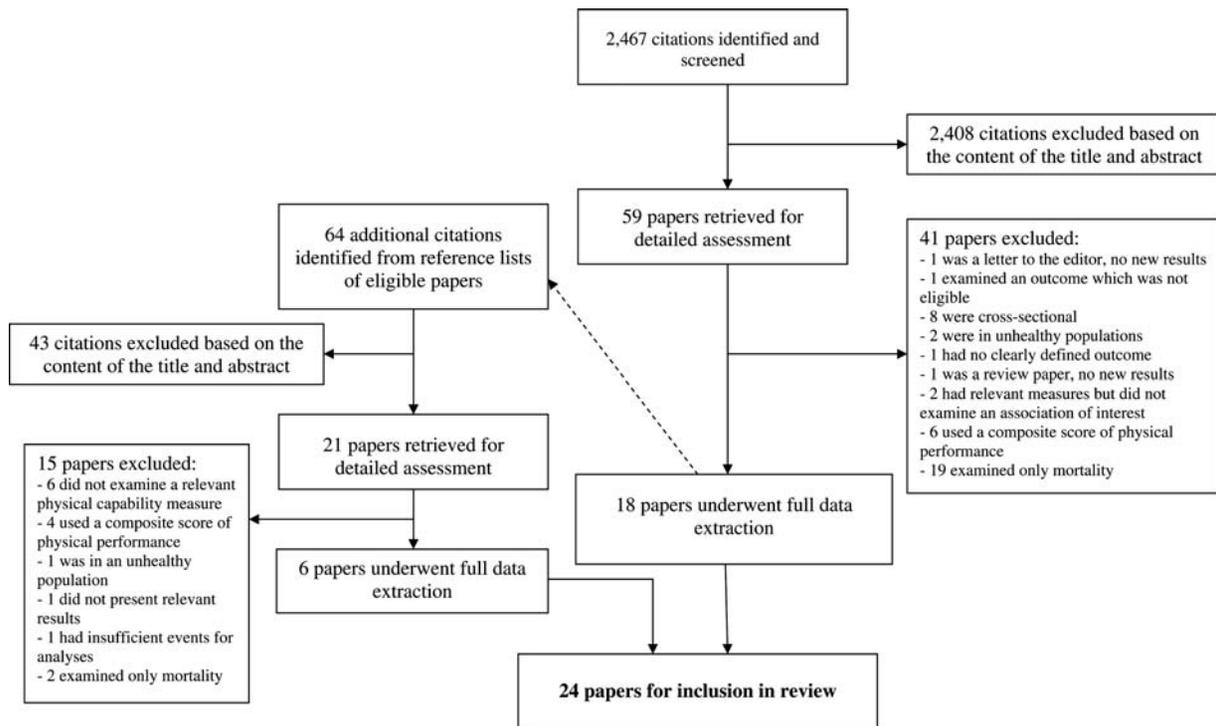


Figure 1. Flow diagram for identification of published studies.

observed an association in the subgroup of women with normal bone mineral density at baseline (see Table 2 and Supplementary data available in *Age and Ageing* online).

The association of walking speed with subsequent fracture risk was examined in five study populations with all but one study suggesting that slower walking speed was associated with higher subsequent risk of fracture, whatever the fracture site examined (Table 2 and Supplementary data available in *Age and Ageing* online).

Of the four studies examining the association between chair rising and fracture risk, three (two of hip fracture and one of fragility fracture) found evidence of an association, whereas the fourth (of proximal humeral fracture) found a reduced risk in those who were unable to rise from a chair compared to those who could, but with wide confidence intervals that included the null (Table 2 and Supplementary data available in *Age and Ageing* online).

In five studies of the association between standing balance and fracture risk, four found increased risk of fractures associated with poorer balance performance, though one was imprecisely estimated with wide confidence intervals that included the null and one did not adjust for any potential confounding factors (Table 2 and Supplementary data available in *Age and Ageing* online).

Cognitive outcomes

Four papers [6, 7, 24, 28], each examining a unique study population, were identified which had investigated the associations between at least one of the specified measures of physical capability and subsequent cognitive outcomes in samples with normal cognitive function at the time of

physical capability assessment (Table 1 and Supplementary data available in *Age and Ageing* online).

Of the three studies which had examined grip strength [6, 7, 28], all found evidence that weaker grip strength was associated with higher subsequent risk of cognitive decline, development of Alzheimer's disease or other forms of dementia (Table 2 and Supplementary data available in *Age and Ageing* online).

The two studies [24, 28] which had examined walking speed found that those who were slower were at increased subsequent risk of incident cognitive impairment or Alzheimer's disease and dementia (Table 2 and Supplementary data available in *Age and Ageing* online).

The one study [28] which had reported on associations between chair rising and cognitive outcomes found that there was evidence of associations with Alzheimer's disease and dementia in models adjusted for age and sex but that these were not maintained after further adjustments (Table 2 and Supplementary data available in *Age and Ageing* online).

The two studies examining standing balance [24, 28] were not consistent, with one finding evidence that those people who performed less well in this test were at increased risk of dementia whereas the other reported no evidence of association. However, this latter study had only 85 participants, 18 of whom became cognitively impaired during follow-up (Table 2 and Supplementary data available in *Age and Ageing* online).

Cardiovascular disease

Four papers [15, 17, 20, 27], each examining a unique study population, were identified which had examined the

Table I. Characteristics of studies included in the review

Reference/outcome	Study name and country	Characteristics of study population, mean (sd) age (years) at baseline; range (where available) (% female)	Measures of physical capability examined	Ascertainment of outcome	Length of follow-up	QA score ^a
Fracture ^b						
Albrand <i>et al.</i> [5]	The OFELY study, France ^c	Not reported for whole sample; 31–89 (100%)	Grip strength, walking speed, standing balance, chair rises	Incident fragility fractures—assessed during annual visits and confirmed by radiologist	Average: 5.3 years	7
Cawthon <i>et al.</i> [8]	Osteoporotic Fractures in Men (MrOS) study, USA	Mean not reported; 65–100 (0, i.e. 100% male)	Grip strength, walking time, chair rises	Incident hip fractures—ascertained every 4 months via contact with study participants and confirmed by radiology reports	Average: 5.3 years	7
Cummings <i>et al.</i> [25]	Cohort study of older women (no name given), USA	72 (5); 65+ (100%)	Grip strength, walking speed, standing balance, chair rises	Incident hip fractures—reported by postcard or telephone every 4 months and confirmed by radiograph	Average: 4.1 years	6.5
Dargent-Molina <i>et al.</i> [11]	The EPIDOS (Epidemiologie de l'Osteoporose) study, France ^c	80.5 (3.8); 75+ (100%)	Grip strength, walking speed, standing balance, chair rises	Incident hip fractures—contact via mail or telephone every 4 months and confirmed by radiograph	1.94 years	7
Dargent-Molina <i>et al.</i> [12]	The EPIDOS study, France ^c	80.5 (3.8); 75+ (100%)	Walking speed	Incident hip fractures—contact via mail or telephone every 4 months and confirmed by radiograph	Average: 2.75 years	6.5
Finigan <i>et al.</i> [13]	Prospective population based study (no name given), UK	64.61 (9.1); 50–85 (100%)	Grip strength	Incident vertebral and non-vertebral fracture—vertebral from spinal radiographs obtained at regular time points and non-vertebral from GP medical notes	Up to 10 years	7.5
Karkkainen <i>et al.</i> [14]	Osteoporosis Risk Factor and Prevention Study (OSTPRE), Finland ^c	59.1 (2.9); 53–62 (100%)	Grip strength, standing balance	First fracture during follow-up (excluding those due to high energy trauma)—self-reported at follow-ups and validated using radiological reports	Up to 10 years (mean: 8.37 years)	7.5
Kelsey <i>et al.</i> [26]	The Study of Osteoporotic Fractures (SOF), USA	Mean age not reported; 65+ (100%)	Grip strength, walking speed, standing balance	Fractures of distal forearm and proximal humerus—self-reported at time of event or at contact every 4 months via mail or telephone, all confirmed by radiologist report	2.2 years	6.5
Lee <i>et al.</i> [16]	The EPIDOS study, France ^c	80.5 (3.7); 75+ (100%)	Grip strength, standing balance, chair rises	Proximal humeral fractures—contact via mail or telephone every 4 months and confirmed by radiograph or surgery report	Average: 3.6 years	6.5
Piirtola <i>et al.</i> [18]	The Lieto study, Finland	75; 65–97 (59.05%)	Grip strength	Incident fracture (excluding those with pathological backgrounds or caused by serious accident)—from medical records of health centres, Finnish hospital discharge register and Finnish cause of death statistics	Up to 12 years (mean: 8.5 years)	7

Continued

Table I. Continued

Reference/outcome	Study name and country	Characteristics of study population, mean (sd) age (years) at baseline; range (where available) (% female)	Measures of physical capability examined	Ascertainment of outcome	Length of follow-up	QA score ^a
Sirola <i>et al.</i> [21]	Osteoporosis Risk Factor and Prevention Study (OSTPRE), Finland ^c	53.3 (2.9); 48–57 (100%)	Grip strength	Low trauma energy fractures—self-reported and validated using medical records or radiological reports	15 years	6
Stel <i>et al.</i> [22]	The Longitudinal Aging Study Amsterdam (LASA), The Netherlands	75.8 (6.6); 64.8–88.8 (51.60%)	Grip strength	Incident fracture (any reported)—prospective self-report, completion of calendar, contact via telephone with confirmation from GPs and radiographs	3 years	7
Cognitive outcomes ^a						
Alfaro-Acha <i>et al.</i> [6]	The Hispanic Established Population for the Epidemiological Study of the Elderly (H-EPESE), USA	71.9 (5.9); 65+ (57.50%)	Grip strength	Cognitive decline—as indicated by decrease in MMSE score over time (assessed at baseline, 2, 5 and 7-year follow-ups)	7 years	8
Buchman <i>et al.</i> [7]	The Religious Orders Study, USA	Developed disease 79.3 (6.5); did not develop disease 73.5 (6.6) (developed disease 72.7%; did not develop disease 68.7%)	Grip strength	Alzheimer's disease—ascertained during annual clinical evaluations and brain donation at time of death	Average: 5.7 years	7
Camicioli <i>et al.</i> [24]	The Oregon Brain Aging Study, USA	Became cognitively impaired 88.7 (6.5); did not 78.3 (7.6) (58.8%)	Standing balance, walking speed	Incident cognitive impairment—assessed at end of 3y follow-up as Clinical Dementia Rating Scale ≥ 0.5	3 years	5
Wang <i>et al.</i> [28]	Adult Changes in Thought (ACT) study, USA	Developed dementia 78.7 (6.1); did not 73.5 (6.1); range 65+ (60%)	Grip strength, walking speed, standing balance, chair rises	Dementia and Alzheimer's disease—assessed at biennial follow-ups based on results of Cognitive Ability Screening Instrument and clinical examination	Average 5.9 years	7.5
Cardiovascular disease						
Manolio <i>et al.</i> [27]	The Cardiovascular Health Study, USA	Had a stroke during follow-up 75.4; did not have a stroke 72.7; 65+ (not reported)	Walking time, chair rises	Incident stroke—identified during annual follow-ups and at interim 6-month phone calls, hospital records obtained	Up to 4 years (average 3.3 years)	6
McGinn <i>et al.</i> [17]	Women's Health Initiative, USA	65 (100%)	Grip strength, walking speed, chair rises	Incident ischemic stroke resulting in hospitalisation—self-report at regular contacts with medical records obtained for verification	Those who had a stroke, median 5.2 years; those who did not, median 9.4 years	7
Silventoinen <i>et al.</i> [20]	Swedish Military Service Conscription Register, Sweden	18; 16–25 (0, i.e. 100% male)	Grip strength	Any stroke or coronary heart disease event (non-fatal or fatal)—linkage to Swedish cause of death register, Swedish hospital discharge register and statistics Sweden's emigration register	Median: 24.4 years	7.5

Author	Study	Age (years)	Sex	Measure of physical capability	Outcome	Follow-up (years)
Lazarus <i>et al.</i> [15]	The Normative Aging Study, USA	41.5 (7.9)	21–80 (0, i.e. 100% male)	Grip strength	Fasting insulin—measured after overnight fasting at clinic visits	Average 22.9 years
Cesari <i>et al.</i> [9]	Hospitalisation/institutionalisation Health, Aging and Body Composition (ABC) study, USA ^c	74.2 (2.9)	(51.50%)	Walking speed	Hospitalisation (defined as any overnight hospitalisation in an acute care setting) self-reported and verified by hospital record	1 year
Cesari <i>et al.</i> [10]	Health, Aging and Body Composition (ABC) study, USA ^c	73.6 (2.9)	70–79 (51.60%)	Walking speed, chair rises, standing balance	Hospitalisation (defined as any overnight hospitalisation in an acute care setting) self-reported and verified by hospital record	1 year
Rothman <i>et al.</i> [19]	Precipitating Events Project (PEP), USA	78.4 (5.3)	70+ (64.60%)	Grip strength, walking time	Nursing home stay (which persisted for 4 or more months)—reported during monthly telephone interviews	Up to 7.5 years
Woo <i>et al.</i> [29]	Hong Kong Old-Old Study, Hong Kong	79.7 (7.13)	70–107 (50.80%)	Walking time	Institutionalisation	3 years

^aQuality assessment score (maximum score:8); average of two independent assessor's scores presented.

^bDetails of a specific outcome within a particular study reported in ascertainment of outcome column.

^cStudy population included in more than one published report.

Table 2. Summary of main findings from review of studies which examine the associations between objective measures of physical capability levels and subsequent specified health outcomes

Measure of physical capability	Outcome			
	Fracture	Cognitive decline	Cardiovascular disease	Hospitalisation and institutionalisation
Grip strength	++++eee--	+++	++-	e
Walking speed	++++-	++	++	++-
Chair rises	+++-	e	+-	e
Standing balance	+++e-	+-		+

Note: Each indicator shown in the table represents one study population. The plus sign indicates that there was evidence that poorer performance on the specified test was associated with increased risk of the specified outcome. e indicates an equivocal association, i.e. evidence of association was only weak or was attenuated after adjustments. The minus sign indicates that there was no evidence of association. See Supplementary data available in *Age and Ageing* online for a more detailed summary of each study's findings.

associations between at least one of the specified measures of physical capability and subsequent cardiovascular outcomes (including diabetes) (Table 1 and Supplementary data available in *Age and Ageing* online).

Of the three studies which had examined grip strength [15, 17, 20], one very large study found evidence that weaker grip strength in men, assessed in early adulthood, was associated with increased risk of incident coronary heart disease over approximately 24 years of follow-up, whereas the effect estimates for stroke had 95% confidence intervals including the null. Another study found no evidence of association with subsequent stroke risk in older women, although effect estimates were not presented to allow a full assessment of this. The third study found an association between weaker grip strength and higher levels of fasting insulin levels in men (Table 2 and Supplementary data available in *Age and Ageing* online).

Both studies that examined walking speed found evidence to suggest that those people who were slower had increased subsequent risk of stroke, even after adjustments for multiple confounding variables (Table 2 and Supplementary data available in *Age and Ageing* online).

One of the two studies to examine chair rising found those that were slower had increased risk of stroke but the other study reported finding no evidence of an association, although the estimate was not reported.

No study identified had examined the association between standing balance performance and cardiovascular outcomes.

Hospitalisation and institutionalisation

Four papers [9, 10, 19, 29], reporting on three study populations, were identified which had examined the associations between at least one of the specified measures of physical capability and subsequent hospitalisation or institutionalisation (Table 1 and Supplementary data available in *Age and Ageing* online).

In the one study examining grip strength, there was evidence that those who were weaker were at increased risk of subsequently reporting a long-term nursing home stay in models with basic adjustments, but this was not maintained after adjustment for other indicators of frailty which may mediate this association (Table 2 and Supplementary data available in *Age and Ageing* online).

The associations of walking speed were examined in all three study populations, and in two, there was evidence that those who were slower had increased risk of hospitalisation and long-term nursing home stay, whereas in the other study there was no clear evidence of association, although the effect estimates were in the same direction.

The one study of chair rising found an association with the risk of hospitalisation in unadjusted models but this was not maintained after adjustment. This same study found evidence to suggest that poorer performance in standing balance tests was associated with increased risk of hospitalisation even after adjustments (Table 2 and Supplementary data available in *Age and Ageing* online).

Discussion

There is some evidence in the published literature to suggest that objectively measured physical capability levels may be useful predictors of subsequent health outcomes, including fractures, cognitive outcomes, cardiovascular disease, hospitalisation and institutionalisation, in older community-dwelling populations.

Assessment of bias and justification for exclusions

Owing to variation between studies in the way in which each specified outcome had been defined and the lack of sufficient sets of results from analyses testing any one particular association, it was not possible to perform meta-analyses of results or formally test the heterogeneity (consistency) between studies. This also meant that we were unable to formally assess publication bias, and as we only examined published reports, this is a potential limitation of our review.

By systematically reviewing the literature in accordance with published guidelines [4], and following a strict protocol, we expect to have included all published results on the main associations of interest. However, as we limited the search to two electronic databases and did not include unpublished studies, we acknowledge that not all relevant studies may have been identified.

By excluding those studies in which the outcomes were present at the time of capability assessment and studies of populations which were not community-dwelling at baseline, the findings presented are unlikely to be due to reverse causality. Another strength of our review is that no exclusions were used which may bias our findings.

Study quality and characteristics

The majority of studies were considered to be of good quality with very few achieving a mean quality assessment score less than 6 [on a scale from 1 (poor) to 8 (excellent)] (Table 1). Despite these high scores, it can be seen from the tables in Supplementary data available in *Age and Ageing* online that the extent of adjustment for potential confounding factors varied markedly between studies, with some not taking account of any confounding factors.

Most studies identified had been undertaken in older populations, the majority with an average age at capability assessment greater than 65 years (Table 1). Only two studies [15, 20] had measured physical capability levels in populations with an average age less than 50 years and both of these studies examined men only and tested the associations of grip strength with cardiovascular outcomes.

In the majority of studies, follow-up was usually for less than 10 years (Table 1). Most studies have been undertaken in the United States but studies have also been conducted in northern Europe and Hong Kong. A range of different instruments have been employed to measure grip strength, with either the maximum value recorded or the average achieved over a fixed number of trials used in analyses. Walking speed has been measured over distances of 4, 6 and 10 m and 8 and 16 feet. Of the studies of chair rises, all had asked participants to perform five. Standing balance has also been measured in a number of different ways in different studies.

Interpretation of findings

The fact that some studies provide evidence of association whereas others do not could be explained by methodological differences between them. For example, there are differences between studies in the definitions of the health outcomes employed, in statistical power due to variations in sample size and in the covariates adjusted for.

Where associations have been demonstrated, it is necessary to consider why this may be. There are a number of reasons to expect to find associations between objectively measured physical capability levels and subsequent health outcomes in community-dwelling populations. One possibility is that physical capability levels directly affect risk of some health outcomes. For example, those people with poor balance, who walk more slowly or who are weaker have been shown to be at higher risk of falling [30] which increases the risk of fracture.

It is also possible that the objectively measured physical capability levels are markers of subclinical disease and general health status. While only studies of community-dwelling populations free from the specified outcomes at the time of physical capability assessment were eligible for inclusion, it is possible that some people within these populations had undetected subclinical levels of the outcomes of interest which were affecting their performance and were soon to be manifested. A related possibility is that

underlying ageing processes lead to poorer performance and a higher probability of chronic disease and co-morbidities.

Physical capability levels in later life could also be acting as markers of exposure to risk factors across life, with those people with lower capability levels expected to have been exposed to more adverse risk factors across life and so at increased risk of poor health later in life.

Guidelines for future research

The aim of this review was to examine the associations of variation in levels of objective measures of physical capability at one point in time with subsequent health outcomes. However, it is possible that changes in capability levels over time, which occur with age, are stronger and hence more useful predictors than capability levels at one particular point in time and so this should be investigated in future work. Further, we chose to examine the relationship of each individual physical capability measure to see whether associations with health outcomes were similar for each measurement. The rationale behind this is that there are a variety of composite scores [31, 32] that are derived using these measurements in combination, but it is unclear whether results with such scores are driven by one measure in particular or whether they each have similar additive contributions. As levels of these physical capability measures are highly correlated with each other, more studies [10] are required which consider the value of each additional test, once the findings for one test are known. The next stage would then be to investigate whether a derived composite score representing overall lower or upper body function, such as the short physical performance battery score [31] or one of the frailty indices, may be a stronger predictor of subsequent health problems than any of the individual measures are by themselves.

The variation between studies in the way in which each specified outcome had been defined and the lack of sufficient sets of results from analyses testing any one particular association highlights the need to undertake more studies of the associations between physical capability levels and subsequent health problems using clearly defined, standardised outcome definitions. It is also important to adjust for all relevant potential confounding factors from across life in order to determine the extent to which variation in physical capability levels is causally related to health outcomes as opposed to it being a proxy for lifetime adverse exposures. Examining associations in populations covering a wider range of ages and which have longer follow-up would also be informative.

Conclusions

This systematic review suggests that objective measures of physical capability may be useful predictors of subsequent health outcomes in community-dwelling populations.

Further investigation is required following the guidelines suggested above.

Key points

- Associations between objective measures of physical capability (i.e. grip strength, walking speed, chair rise time and standing balance performance) and all-cause mortality in community-dwelling populations have been demonstrated.
- If the underlying explanations of these associations are to be elucidated, there is a need to establish whether associations are also found with important health outcomes which may subsequently lead to death or disablement.
- This systematic review identified 24 papers which had examined the association between at least one of the specified measures of physical capability and subsequent risk of one of the specified health outcomes (i.e. fracture, cognitive outcomes, cardiovascular disease, hospitalisation or institutionalisation).
- Most studies found some evidence to suggest that lower levels of physical capability were associated with higher risk of subsequent health problems, with weaker grip strength and slower walking speed found to be associated with increased risk of future fractures and cognitive decline in the majority of studies. However, associations between physical capability measures and other specified outcomes have not been tested widely.
- There is evidence to suggest that levels of objective measures of physical capability may predict subsequent health problems in older community-dwelling populations; but as most associations have not been studied sufficiently often to draw definitive conclusions, this suggests the need for further research.

Author contributions

Study concept and design: Rachel Cooper, Rebecca Hardy, Diana Kuh. *Literature review and data extraction:* Rachel Cooper, Rebecca Hardy. *Drafting of the manuscript:* Rachel Cooper. *Critical revision and approval of the manuscript:* all named authors.

Acknowledgements

In addition to the named authors, the FALCon study team includes Avan Aihie Sayer, Eleni Bakra, Michaela Benzeval, Graciela Muniz Terrera and Andrew Wills and the HALCyon study team includes Yoav Ben-Shlomo, Leone Craig, Ian Day, Richard Martin, Kate Tilling, Tamuno Alfred, Mike Gardner, John Gallacher, Ian Deary, John Starr, Paul Shiels, Thomas von Zglinicki, Humphrey Southall, Paula Aucott, Jane Elliott, Chris Power, Geraldine McNeill, Avan Aihie Sayer, Alison Lennox, Marcus Richards, Gita Mishra, Zeinab Mulla and James Goodwin. We also thank Hugh McGuire (National Collaborating

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Centre for Women's and Children's Health) who provided advice on systematic reviews and performing literature searches and Jack Guralnik who commented on an early draft of the review protocol.

Conflicts of interest

None to declare.

Funding

This work was supported by a UK Medical Research Council Population Health Sciences Research Network (PHSRN) grant and a New Dynamics of Ageing collaborative research programme grant (RES-353-25-0001). R.C. originally received support from the PHSRN grant but is now receiving support from the HALCYon programme funded by the New Dynamics of Ageing (RES-353-25-0001). D.K., R.H., C.C., C.R.G. and F.M. are supported by the UK Medical Research Council. D.A.L. also works in a centre that is supported by the UK Medical Research Council. The funders had no role in study design, preparation of the manuscript or decision to publish.

Supplementary data

Supplementary data mentioned in the text is available to subscribers in *Age and Ageing* online.

References

1. Cooper R, Kuh D, Hardy R *et al* Objectively measured physical capability levels and mortality: a systematic review and meta-analysis. *Br Med J*. In press.
2. Rantanen T. Muscle strength, disability and mortality. *Scand J Med Sci Sports* 2003; 13: 3–8.
3. Bohannon RW. Hand-grip dynamometry predicts future outcomes in aging adults. *J Geriatr Phys Ther* 2008; 31: 3–10.
4. Stroup DF, Berlin JA, Morton SC *et al* Meta-analysis of observational studies in epidemiology—a proposal for reporting. *JAMA* 2000; 283: 2008–12.
5. Albrand G, Munoz F, Sornay-Rendu E *et al* Independent predictors of all osteoporosis-related fractures in healthy postmenopausal women: the OFELY study. *Bone* 2003; 32: 78–85.
6. Alfaro-Acha A, Al Snih S, Raji MA, Kuo YF, Markides KS, Ottenbacher KJ. Handgrip strength and cognitive decline in older Mexican Americans. *J Gerontol A Biol Sci Med Sci* 2006; 61: 859–65.
7. Buchman AS, Wilson RS, Boyle PA, Bienias JL, Bennett DA. Grip strength and the risk of incident Alzheimer's disease. *Neuroepidemiology* 2007; 29: 66–73.
8. Cawthon PM, Fullman RL, Marshall L *et al* Physical performance and risk of hip fractures in older men. *J Bone Miner Res* 2008; 23: 1037–44.
9. Cesari M, Kritchevsky SB, Penninx BW *et al* Prognostic value of usual gait speed in well-functioning older people—results from the Health, Aging and Body Composition Study. *J Am Geriatr Soc* 2005; 53: 1675–80.
10. Cesari M, Kritchevsky SB, Newman AB *et al* Added value of physical performance measures in predicting adverse health-related events: results from the Health, Aging and Body Composition Study. *J Am Geriatr Soc* 2009; 57: 251–9.
11. Dargent-Molina P, Favier F, Grandjean H *et al* Fall-related factors and risk of hip fracture: the EPIDOS prospective study. *Lancet* 1996; 348: 145–9.
12. Dargent-Molina P, Schott AM, Hans D *et al* Separate and combined value of bone mass and gait speed measurements in screening for hip fracture risk: results from the EPIDOS study. *Epidemiologie de l'Osteoporose. Osteoporos Int* 1999; 9: 188–92.
13. Finigan J, Greenfield DM, Blumsohn A *et al* Risk factors for vertebral and nonvertebral fracture over 10 years: a population-based study in women. *J Bone Miner Res* 2008; 23: 75–85.
14. Karkkainen M, Rikkonen T, Kroger H *et al* Association between functional capacity tests and fractures: an eight-year prospective population-based cohort study. *Osteoporos Int* 2008; 19: 1203–10.
15. Lazarus R, Sparrow D, Weiss ST. Handgrip strength and insulin levels: cross-sectional and prospective associations in the Normative Aging Study. *Metab Clin Exp* 1997; 46: 1266–9.
16. Lee SH, Dargent MP, Breart G. Risk factors for fractures of the proximal humerus: results from the EPIDOS prospective study. *J Bone Min Res* 2002; 17: 817–25.
17. McGinn AP, Kaplan RC, Verghese J *et al* Walking speed and risk of incident ischemic stroke among postmenopausal women. *Stroke* 2008; 39: 1233–9.
18. Piirtola M, Vahlberg T, Isoaho R, Aarnio P, Kivela SL. Predictors of fractures among the aged: a population-based study with 12-year follow-up in a Finnish municipality. *Aging Clin Exp Res* 2008; 20: 242–52.
19. Rothman MD, Leo-Summers L, Gill TM. Prognostic significance of potential frailty criteria. *J Am Geriatr Soc* 2008; 56: 2211–6.
20. Silventoinen K, Magnusson PK, Tynelius P, Batty GD, Rasmussen F. Association of body size and muscle strength with incidence of coronary heart disease and cerebrovascular diseases: a population-based cohort study of one million Swedish men. *Int J Epidemiol* 2009; 38: 110–8.
21. Sirola J, Rikkonen T, Tuppurainen M, Jurvelin JS, Alhava E, Kroger H. Grip strength may facilitate fracture prediction in perimenopausal women with normal BMD: a 15-year population-based study. *Calcif Tissue Int* 2008; 83: 93–100.
22. Stel VS, Pluijm SM, Deeg DJ, Smit JH, Bouter LM, Lips P. Functional limitations and poor physical performance as independent risk factors for self-reported fractures in older persons. *Osteoporos Int* 2004; 15: 742–50.
23. The Newcastle-Ottawa Quality Assessment Scale. http://www.ohri.ca/programs/clinical_epidemiology/nosgen.pdf (2009).
24. Camicioli R, Howieson D, Oken B, Sexton G, Kaye J. Motor slowing precedes cognitive impairment in the oldest old. *Neurology* 1998; 50: 1496–8.
25. Cummings SR, Nevitt MC, Browner WS. Risk-factors for hip fracture in white women. *N Engl J Med* 1995; 332: 767–73.

26. Kelsey JL, Browner WS, Seeley DG, Nevitt MC, Cummings SR. Risk-factors for fractures of the distal forearm and proximal humerus. *Am J Epidemiol* 1992; 135: 477–89.
27. Manolio TA, Kronmal RA, Burke GL, O'leary DH, Price TR. Short-term predictors of incident stroke in older adults—The Cardiovascular Health Study. *Stroke* 1996; 27: 1479–86.
28. Wang L, Larson EB, Bowen JD, van Belle G. Performance-based physical function and future dementia in older people. *Arch Intern Med* 2006; 166: 1115–20.
29. Woo J, Ho SC, Yu ALM. Walking speed and stride length predicts 36 months dependency, mortality, and institutionalization in Chinese aged 70 and older. *J Am Geriatr Soc* 1999; 47: 1257–60.
30. Moreland JD, Richardson JA, Goldsmith CH, Clase CM. Muscle weakness and falls in older adults: a systematic review and meta-analysis. *J Am Geriatr Soc* 2004; 52: 1121–9.
31. Guralnik JM, Simonsick EM, Ferrucci L *et al* A short physical performance battery assessing lower-extremity function—association with self-reported disability and prediction of mortality and nursing-home admission. *J Gerontol* 1994; 49: M85–94.
32. Fried LP, Tangen CM, Walston J *et al* Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001; 56: M146–56.

Received 25 January 2010; accepted in revised form 5 May 2010

Age and Ageing 2011; **40**: 23–29
doi: 10.1093/ageing/afq140
Published electronically 9 November 2010

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Which medications to avoid in people at risk of delirium: a systematic review

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Abstract

Background: delirium is a common clinical problem and is associated with adverse health outcomes. Many medications have been associated with the development of delirium, but the strength of the associations is uncertain and it is unclear which medications should be avoided in people at risk of delirium.

Methods: we conducted a systematic review to identify prospective studies that investigated the association between medications and risk of delirium. A sensitivity analysis was performed to construct an evidence hierarchy for the risk of delirium with individual agents.

Results: a total of 18,767 studies were identified by the search strategy. Fourteen studies met the inclusion criteria. Delirium risk appears to be increased with opioids (odds ratio [OR] 2.5, 95% CI 1.2–5.2), benzodiazepines (3.0, 1.3–6.8), dihydropyridines (2.4, 1.0–5.8) and possibly antihistamines (1.8, 0.7–4.5). There appears to be no increased risk with neuroleptics (0.9, 0.6–1.3) or digoxin (0.5, 0.3–0.9). There is uncertainty regarding H₂ antagonists, tricyclic antidepressants, anti-parkinson medications, steroids, non-steroidal anti-inflammatory drugs and antimuscarinics.

Conclusion: for people at risk of delirium, avoid new prescriptions of benzodiazepines or consider reducing or stopping these medications where possible. Opioids should be prescribed with caution in people at risk of delirium, but this should be tempered by the observation that untreated severe pain can itself trigger delirium. Caution is also required when prescribing dihydropyridines and antihistamine H₁ antagonists for people at risk of delirium and considered individual patient assessment is advocated.

Keywords: delirium, drug toxicity, elderly, medication, prescriptions, systematic review