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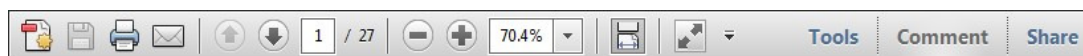
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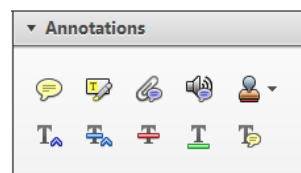
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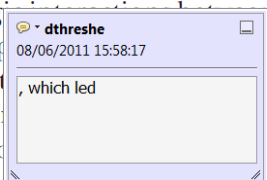


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standard framework for the analysis of microeconomic behavior. Nevertheless, it also led to the development of a new class of strategic form games. The number of competitors in the market is that the structure of the game. The main components of the model, at the micro level, are exogenous variables and parameters. The important works on entry by Cournot (1838) and henceforth, we open the 'black box'.



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there is no room for extra profits as long as the markup is zero and the number of firms (n) values are not determined by the market. Blanchard and Kiyotaki (1987), in their paper on perfect competition in general equilibrium, show that the structure of aggregate demand and supply in the classical framework assuming monopoly is determined by an exogenous number of firms.

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dynamic responses of mark-ups are consistent with the VAR evidence.

sation of the market by the number of firms. The standard framework for the analysis of microeconomic behavior. The number of competitors in the market is that the structure of the game. The main components of the model, at the micro level, are exogenous variables and parameters. The important works on entry by Cournot (1838) and henceforth, we open the 'black box'.



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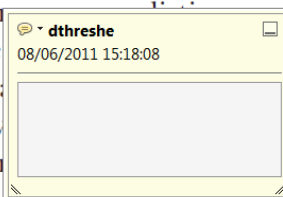


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standard and supply shocks. Most of the standard framework for the analysis of microeconomic behavior. The number of competitors in the market is that the structure of the game. The main components of the model, at the micro level, are exogenous variables and parameters. The important works on entry by Cournot (1838) and henceforth, we open the 'black box'.



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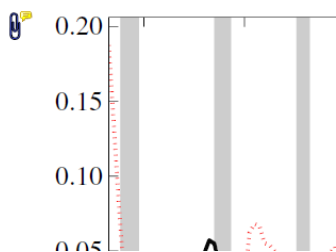


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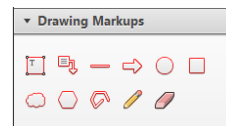
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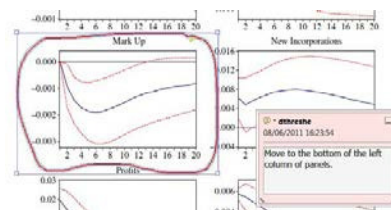


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BRIEF METHODOLOGICAL REPORTS

Comparative Study of Four Physical Performance Measures As Predictors of Death, Incident Disability, and Falls in Unselected Older Persons: The Insufficienza Cardiaca negli Anziani Residenti a Dicomano Study

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OBJECTIVES: To compare the ability of the Short Physical Performance Battery (SPPB), 4-m walk test (4mWT), 6-minute walk test (6MWT), and handgrip strength to predict mortality, incident disability, worsening mobility, and falls in older community dwellers.

DESIGN: Cohort study.

SETTING: Population-based.

PARTICIPANTS: Individuals aged 65 and older ($n = 561$) without prevalent basic activity of daily living (ADL) disability participating in a population-based study.

MEASUREMENTS: Separate logistic regression models were developed to predict incident ADL disability, worsening mobility, and falls in 3 years, and Cox regression models were used to assess 7-year risk of death as a function of the four tests, adjusting for covariates.

RESULTS: Performance tests were reciprocally correlated at baseline. After 3 years, 33 (7.3%) of 453 participants reexamined were disabled in ADLs, 87 (20%) had worsening mobility, and 99 (22%) reported falls. Of the 561 baseline participants, 141 (25%) died over the 7 years. All measures predicted incident ADL disability, with adjusted odds ratios (ORs) per unit increase of 0.85 (95% confidence interval (CI) = 0.77–0.93) for handgrip strength, 0.08 (95% CI = 0.02–0.36) for 4mWT, 0.74 (95% CI = 0.61–0.89) for SPPB, and 0.993 (95% CI = 0.988–0.997) for 6MWT. Handgrip strength (OR = 0.88, 95%

CI = 0.83–0.93), 4mWT (OR = 0.33, 95% CI = 0.11–0.94), and SPPB (OR = 0.81, 95% CI = 0.71–0.93) predicted worsening mobility. No measure predicted falls; only SPPB (hazard ratio (HR) = 0.92, 95% CI = 0.85–0.997) and 6MWT (HR = 0.997, 95% CI = 0.995–0.999) predicted death.

CONCLUSION: Performance measures are independent predictors of relevant health outcomes, with the exception of falls. Because SPPB is easily applied and is the only measure predicting incident ADL disability, worsening mobility, and death, it is preferable to the other tests.

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Key words: performance tests; cohort studies; predictive value

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Aging is characterized by a decline in physical performance, a complex phenomenon with multifactorial etiology. It represents a marker of frailty,¹ which stems from reduced homeostatic reserves, and increases the risk of adverse health outcomes.¹ Diminished physical performance, even without overt disability, predicts loss of independence, institutionalization, and death in older adults.^{2–9} Therefore, several tests have been proposed as components of comprehensive geriatric assessment to obtain objective, quantitative, sensitive, specific, responsive-to-change measures of physical performance.^{10–12}

Among others, handgrip strength,¹³ the 4-m walk test (4mWT), the Short Physical Performance Battery (SPPB),³ and the 6-minute walk test (6MWT)¹⁴ are of particular interest. Their independent prognostic value toward relevant outcomes has been documented in population studies^{2,3,9,13} and clinical settings,^{6,11} but these four tests differ in their burden of administration, which is minimal for handgrip

strength, intermediate for 4mWT and SPPB, and definitively greater for 6MWT. Thus, it was decided to verify whether the longer time and greater resources required for performance of some of these tests are better able to predict important outcomes, such as worsening functional status, falls, and mortality.

METHODS

Study Population and Protocol

Data were obtained from the Insufficienza Cardiaca negli Anziani Residenti a Dicomano (ICARe Dicomano) Study, a cohort study of heart failure in older persons conducted in Dicomano, a small rural town near Florence, Italy, whose methods have been published previously¹⁵ and are consistent with the principles of the Declaration of Helsinki. Briefly, in 1996, the entire unselected community-dwelling elderly (≥ 65) population recorded in the city registry office was enrolled in the parent study, with the only exclusion criterion being living in a nursing home. This cohort was reexamined in 1999, and the city registry office was consulted again in 2003 to define vital status. Individuals with prevalent activity of daily living (ADL) disability were excluded from the present study.

Data Collection

After obtaining informed consent, study physicians collected multidimensional geriatric assessment data at baseline, including complete clinical examination, laboratory studies, 12-lead electrocardiogram, echocardiography, carotid ultrasound, and bell spirometry. This information, assembled in prespecified diagnostic algorithms, enabled the diagnosis of 14 comorbidities and quantification of the burden of comorbidity as disease count.¹⁶

Cognitive impairment and depressive symptoms, frequent nonsomatic comorbidities of late life, were evaluated using the Mini-Mental State Examination (MMSE)¹⁷ and the 30-item Geriatric Depression Scale (GDS).¹⁸

Subjective assessment of functional status was obtained at baseline and in the follow-up from the number of tasks in which the participant reported complete inability or need for help, separately for the two domains of activities of daily living (ADLs) (washing hands and face, dressing and undressing self, toileting, transferring from bed to chair, maintaining continence, eating) and mobility (walking in the house, walking outdoors, walking for 400 m, climbing stairs, bathing or showering, cutting toe nails). Individuals with prevalent disability in one or more ADLs were excluded, so those reporting disability in one or more ADLs in 1999 represent incident cases. Worsening mobility disability was defined as an increase from baseline to follow-up in the number of mobility items in which the participant reported complete inability or need for help.

Handgrip strength, 4mWT, SPPB, and 6MWT were performed at baseline. Handgrip strength was evaluated as the best of three measures taken 1 minute apart using the dominant hand using a handheld dynamometer. The 4mWT, performed as part of the SPPB, was assessed as the fastest speed (m/s) in two attempts. The SPPB assesses balance, time needed to complete a short-distance (4 m)

walk, and ability to stand up from a chair without using the arms five times consecutively as quickly as possible. The results are transformed into a score based on test results in a reference older population, and a summary score (ranging from 0 (worst performance) to 12 (best performance)) is calculated as the sum of individual test scores.² Sustainable walking capacity was assessed using the 6MWT, which measures the distance an individual is able to walk in 6 minutes at their preferred speed. In individuals with lung disease or heart failure, the 6MWT reflects cardiovascular and respiratory fitness,¹⁹ whereas in older persons, the test is a measure of overall mobility and physical functioning.²⁰

The 1999 follow-up visit was conducted to identify cases of incident ADL disability and worsening mobility disability, as previously defined, and falls in the 12 months preceding the assessment. These three conditions and death by 2003 were separate final endpoints of the study.

Statistical Analysis

Statistical analysis was performed using SPSS for Windows 18 (SPSS, Inc., Chicago, IL). Continuous variables are reported as mean and standard errors of the mean. Relative frequencies were compared using the chi-square test. Correlation between continuous variables was analyzed using Pearson correlation coefficients.

The risk of incident ADL disability, worsening mobility disability, and falling as a function of the individual performance measures was expressed as odds ratios (ORs) and 95% confidence intervals (CIs) from separate logistic regression models, adjusting for age, sex, height, weight, disease count, and MMSE and GDS scores, with backward deletion of redundant variables (P out $>.10$). The Hosmer-Lemeshow test was used to check for goodness of fit of the models. The risk of death associated with the individual performance measures was predicted as hazard ratios (HRs) with 95% CIs from Cox proportional hazards models, with the same covariates reported above added in a second step and backward deleted when redundant (P out $>.10$). The method proposed by May and Lemeshow was used to verify the goodness of fit of the models. Areas under the receiver operating characteristic (ROC) curves (AUCs) and their 95% CIs were calculated to test the predictive accuracy of the individual performance measures for each outcome.

$P < .05$ was considered statistically significant.

RESULTS

Baseline Assessment

Of 697 participants assessed in the parent ICARe Dicomano Study, 56 were excluded from this report because of prevalent ADL disability and 80 because of missing data, leaving 561 available for the present study. Included participants were younger (72.9 ± 0.3 vs 79.3 ± 0.6 , $P < .001$), had a similar proportion of men (42.4% vs 36.8%, $P = .23$), and less frequently reported mobility disability (13.7% vs 71.3%, $P < .001$) than the 136 excluded. One hundred forty-nine participants (26.6%) were aged 75 to 84, and 28 (5.0%) were aged 85 and older.

As shown in Table 1, participants were on average slightly overweight and had a mild burden of comorbidity; their cognitive status was preserved, whereas physical performance, albeit in the absence of ADL disability according to the inclusion criteria, was suboptimal, as low SPPB scores and slow 4mWT speed indicated. All performance tests were reciprocally highly correlated, with Pearson r values between 0.292 (handgrip strength vs 4mWT) and 0.639 (SPPBV vs 4mWT) (all $P < .001$).

Follow-up Assessment

In 1999, 453 participants (81% of those seen at baseline) were reexamined; 33 (7.3%) had developed ADL disability, 87 (19.7%) had worsening mobility disability, and 99 (21.9%) reported at least one fall in the prior 12 months. All 561 participants assessed at baseline could be traced for vital status; 141 (25.1%) had died by 2003.

Table 1. General Characteristics of Baseline Participants (N = 561)

Characteristic	Value
Age, mean (SEM)	72.9 (0.3)
Male, n (%)	238 (42.4)
Weight, kg, mean (SEM)	67.4 (0.5)
Height, cm, mean (SEM)	157.8 (0.4)
Body mass index, kg/m^2 , mean (SEM)	27.0 (0.2)
Mobility disability, number of items lost, mean (SEM)	0.24 (0.03)
Disease count, mean (SEM)	3.8 (0.7)
Mini-Mental State Examination score, mean (SEM)	26.0 (0.1)
Geriatric Depression Scale score, mean (SEM)	8.2 (0.3)
Handgrip strength, kg, mean (SEM)	25.4 (0.4)
4-m walk speed, m/s, mean (SEM)	0.82 (0.01)
Short Physical Performance Battery score, mean (SEM)	9.3 (0.1)
6-minute walk test, m, mean (SEM)	315 (4.1)

SEM = Standard error of the mean.

Participants who developed ADL disability, had increasing severity of mobility disability, or reported falling in the previous year had worse baseline performance than those who did not reach these endpoints, as indicated by lower handgrip strength, 4mWT, SPPB, and 6MWT scores. Similar findings were found when comparing 4mWT, SPPB, and 6MWT of long-term survivors and non-survivors, whereas the difference was nonsignificant for handgrip strength (Table 2).

The results of multivariable logistic regression models predicting functional outcomes and falls in 3 years and of Cox proportional hazards models predicting death in 7 years are shown in Table 3. All models were based on a single performance measure and included sex, age, height, weight, disease count, and MMSE and GDS scores in a subsequent step, with backward deletion of redundant variables to obtain a parsimonious model. Handgrip strength was an excellent independent predictor of incident ADL disability and worsening mobility but not of falls or death. Similar results were obtained using the 4mWT, which predicted incident ADL disability and worsening mobility but not falls or mortality. The SPPB predicted incident ADL disability, worsening mobility, and death but not falls. Finally, the 6MWT predicted incident ADL disability and was the strongest predictor of death. Age always contributed significantly to the prediction of all outcomes, whereas the contribution of the other covariates to the various outcomes was inconstant (Table 3). GDS score always predicted falls. The fitting of the models tested was always at least satisfactory.

ROC curve analysis was conducted for the performance measures that, in the models reported in Table 3, were significant predictors of the individual outcomes considered. Handgrip strength and the 4mWT obtained AUCs of 0.68 and 0.73 for incident ADL disability and 0.70 and 0.68 for worsening mobility, respectively. With the SPPB, AUCs were 0.71 for incident ADL disability, 0.68 for worsening mobility, and 0.63 for death, whereas the

Table 2. Bivariate Comparisons of Performance Tests Between Participants Who Did and Did Not Experience Clinical Outcomes

Outcome	Handgrip Strength, kg		4-m Walk Speed, m/s		Short Physical Performance Battery		6-Minute Walk Test, m	
	Mean (SEM)	P-Value	Mean (SEM)	P-Value	Mean (SEM)	P-Value	Mean (SEM)	P-Value
Incident activity of daily living disability ^a								
No ($n = 420$)	25.8 (0.41)	.002	0.84 (0.01)	<.001	9.6 (0.09)	<.001	325 (4.4)	<.001
Yes ($n = 33$)	21.0 (1.47)		0.62 (0.04)		7.6 (0.49)		242 (16.5)	
Worsening mobility ^a								
No ($n = 341$)	26.8 (0.46)	<.001	0.87 (0.02)	<.001	9.9 (0.09)	<.001	336 (4.7)	<.001
Yes ($n = 112$)	21.3 (0.73)		0.70 (0.03)		8.2 (0.23)		268 (9.1)	
Fall in previous year ^a								
No ($n = 354$)	26.2 (0.46)	<.001	0.84 (0.02)	.02	9.6 (0.10)	<.001	325 (4.8)	.02
Yes ($n = 99$)	22.8 (0.80)		0.76 (0.02)		8.7 (0.22)		299 (10.3)	
Death ^b								
No ($n = 420$)	25.7 (0.42)	.12	0.84 (0.01)	.003	9.6 (0.09)	<.001	327 (4.4)	<.001
Yes ($n = 141$)	24.4 (0.73)		0.76 (0.02)		8.5 (0.21)		276 (9.1)	

^a Based on 1999 in-person examination.

^b Based on 2003 city registry office consultation.

SEM = Standard error of the mean.

Table 3. Multivariable Prediction of Incident Activity of Daily Living (ADL) Disability, Worsening Mobility, Falls in Previous Year, and Death

Model	Incident ADL Disability (<i>n</i> = 453)			Worsening Mobility (<i>n</i> = 453)			Falls (<i>n</i> = 453)			Death (<i>n</i> = 561)		
	OR (95% CI)	P-Value		OR (95% CI)	P-Value		OR (95% CI)	P-Value		Hazard Ratio (95% CI)	P-Value	
Handgrip-based models												
Handgrip, kg	0.85 (0.77–0.93)	<.001		0.88 (0.83–0.93)	<.001		0.99 (0.96–1.02)	.446		0.99 (0.96–1.02)	.41	
Sex (1 = M, 2 = F)	0.14 (0.04–0.48)	.002		0.38 (0.16–0.93)	.03		–	–		0.42 (0.27–0.67)	<.001	
Age	1.09 (1.02–1.17)	.01		1.11 (1.06–1.17)	<.001		1.08 (1.04–1.13)	<.001		1.17 (1.08–1.15)	<.001	
Height, cm	–	–		–	–		–	–		–	–	
Weight, kg	1.04 (1.01–1.07)	.02		1.04 (1.01–1.07)	<.001		–	–		–	–	
Disease count	1.62 (1.27–2.06)	<.001		1.19 (1.01–1.40)	.04		–	–		1.17 (1.06–1.28)	.001	
MMSE score	–	–		–	–		–	–		0.96 (0.92–0.996)	.03	
GDS score	–	–		1.03 (0.99–1.08)	.10		1.08 (1.04–1.12)	<.001		–	–	
4mWT-based models												
4mWT speed, m/s	0.08 (0.02–0.36)	.001		0.33 (0.11–0.94)	.04		0.94 (0.38–2.35)	.90		0.83 (0.43–1.63)	.59	
Sex (1 = M, 2 = F)	–	–		–	–		–	–		0.47 (0.34–0.67)	<.001	
Age	1.12 (1.05–1.20)	<.001		1.13 (1.07–1.19)	<.001		1.09 (1.04–1.13)	<.001		1.12 (1.09–1.15)	<.001	
Height, cm	–	–		0.95 (0.92–0.99)	.01		–	–		–	–	
Weight, kg	1.03 (1.002–1.06)	.04		1.04 (1.02–1.07)	.001		–	–		–	–	
Disease count	1.55 (1.23–1.94)	<.001		1.20 (1.03–1.40)	.02		–	–		1.17 (1.07–1.29)	.001	
MMSE score	–	–		–	–		–	–		0.96 (0.92–0.998)	.04	
GDS score	–	–		–	–		1.08 (1.05–1.12)	<.001		–	–	
SPPB-based models												
SPPB	0.74 (0.61–0.89)	.001		0.81 (0.71–0.93)	.003		0.95 (0.84–1.08)	.44		0.92 (0.85–0.997)	.041	
Sex (1 = M, 2 = F)	0.45 (0.19–1.04)	.06		–	–		–	–		0.44 (0.31–0.62)	<.001	
Age	1.09 (1.02–1.17)	.008		1.12 (1.07–1.18)	<.001		1.06 (1.01–1.11)	.01		1.11 (1.08–1.15)	<.001	
Height, cm	–	–		0.96 (0.93–0.998)	.04		0.96 (0.92–0.997)	.03		–	–	
Weight, kg	–	–		1.04 (1.01–1.06)	.004		–	–		–	–	
Disease count	1.54 (1.23–1.93)	<.001		1.19 (1.01–1.39)	.03		–	–		1.16 (1.06–1.27)	.001	
MMSE score	–	–		–	–		–	–		0.96 (0.92–1.00)	.06	
GDS score	–	–		–	–		1.08 (1.04–1.12)	.001		–	–	
6MWT-based models												
6MWT	0.993 (0.988–0.997)	.001		0.997 (0.994–1.00)	.09		1.00 (0.998–1.004)	.55		0.997 (0.995–0.999)	.002	
Sex (1 = M, 2 = F)	0.39 (0.17–0.92)	.03		–	–		–	–		0.39 (0.27–0.56)	<.001	
Age	1.10 (1.03–1.17)	.003		1.13 (1.08–1.18)	<.001		1.08 (1.03–1.13)	.001		1.11 (1.07–1.14)	<.001	
Height, cm	–	–		0.97 (0.93–1.00)	.06		0.98 (0.95–1.01)	.10		–	–	
Weight, kg	–	–		1.04 (1.01–1.06)	.005		–	–		–	–	
Disease count	1.49 (1.19–1.87)	<.001		1.17 (0.996–1.37)	.05		–	–		1.15 (1.05–1.26)	.003	
MMSE score	–	–		–	–		–	–		0.96 (0.92–0.996)	.03	
GDS score	–	–		1.03 (0.996–1.08)	.08		1.08 (1.04–1.12)	<.001		–	–	

Parsimonious logistic regression models, each based on a separate performance measure and on covariates, which were backward deleted when redundant (dash), with $P_{out} > .1$.

CI = confidence interval; OR = odds ratio; 4mWT = 4-m walk test; MMSE = Mini-Mental State Examination; GDS = Geriatric Depression Scale; SPPB = Short Physical Performance Battery; 6MWT = 6-minute walk test.

6MWT obtained AUCs of 0.74 for incident ADL disability and 0.63 for death. When different performance measures were compared against the same endpoint, the 95% CI of the AUCs always overlapped.

DISCUSSION

Four simple performance measures (handgrip strength, 4mWT, SPPB, and 6MWT), applied in older persons living in the community free from ADL disability, although well correlated cross-sectionally, differed in their ability to predict a variety of clinically relevant long-term outcomes. None of the measures predicted falls, whereas handgrip strength was an excellent predictor and 4mW speed a moderate to good predictor of incident ADL disability and worsening mobility. SPPB was the only measure able to predict independently three of four outcomes, although it was less able than the 6MWT to predict mortality.

Observational studies have reported that performance-based measures are good predictors of functional decline,^{2,3,16,21} mortality,^{3,8,16,22} and hospital-related outcomes;^{3,23} they have also been recently applied as outcome measures in randomized clinical trials,²⁴ but only a few studies compared these measures in the same population and on an array of outcomes.

In a clinic-based sample of 110 subjects (70% women) aged 67 to 98,⁷ the predictive value of the SPPB, 4mWT, Berg Balance Scale, Timed Up-and-Go Test, and handgrip strength was compared against onset of difficulty in ADLs at 6, 12, and 18 months, adjusting for comorbidity. The Berg Balance Scale was the most-consistent predictor at all three times, although the SPPB was slightly superior at 12 months. Using data collected in two large population-based epidemiological studies, the ability of a performance battery similar to the SPPB to predict incident disability in the domain of mobility only or also in the domain of ADLs was compared with that of 8-foot (2.44 m) distance gait speed alone.²¹ The risk of disability, adjusted for demographic characteristics and comorbidity, was lower with better performance, more for mobility than for ADL disability. In agreement with the findings of the current study, gait speed alone had the same predictive ability as the complete battery for onset of ADL disability in 4 years. Isometric muscle strength is easy, rapid, and inexpensive to assess and has been shown to be a good predictor of future decline in physical performance, loss of independence,¹³ and clinical outcomes,²³ possibly because it is a marker of age-related sarcopenia,²⁵ but the findings of the current study show that its predictive value for these outcomes is lower than that of the SPPB and 6MWT, which were also able to predict mortality. Finally, despite its widespread use in respiratory and cardiovascular medicine, no previous study has ever assessed the ability of the 6MWT to predict incident ADL disability and death in unselected older persons living in the community, although its application in very old subjects is difficult.²⁶

In contrast with previous findings that lower handgrip strength was longitudinally associated with falls,²⁷ none of the performance measures was a multivariable predictor of falls in the previous year. This is somewhat surprising, because the risk of falling in elderly adults depends, in addition to environmental conditions, on a variety of

intrinsic risk factors that might affect physical performance measures; in particular, the SPPB, which includes a test for balance, would be expected to be a predictor of falling risk. It is possible that the approach of the current study to detecting falls, based upon self-report over a long period, underestimated the true occurrence of this event, but depressive symptoms, expressed in the GDS score, predicted falls, an association consistent with previous studies,²⁸ thus suggesting that data collection on falls for the current study was adequate.

Study limitations cannot be ignored. In particular, in a secondary analysis of an epidemiological study whose original purpose was different,¹⁵ the quality of the data collected might be suboptimal for the intended purposes. This relates also to the fairly large proportion of participants with missing data. Nevertheless, most previous studies have been conducted with a similar approach and had even larger proportions of missing data.²¹

In conclusion, these findings offer a valid contribution to the ongoing debate on strengths and weaknesses of physical performance measures as prognostic tools in older persons. When the global predictive ability of the four tests considered in this study is weighted against their ease of application, the SPPB appears to offer the best compromise between these two different, potentially conflicting characteristics and should therefore be preferred in most clinical and epidemiological applications.

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