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Original Research

Poor Physical Performance Predicts Future Onset of Depression in Elderly People: Pro.V.A. Longitudinal Study

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ABSTRACT

Background: Reduced physical performance is predictive of deleterious outcomes in older adults. Data considering objective physical performance and incident depression is sparse.

Objective: We investigated whether objective physical performance can predict incident depression among non-depressed older adults during a 4-year study.

Design: longitudinal.

Methods: From 3,099 older individuals initially enrolled in the Progetto Veneto Anziani study, 970 participants without depression at baseline were included (mean age 72.5 years, 54.6 % females). Physical performance measures included the Short Physical Performance Battery (SPPB), 4m gait speed, five times sit-to-stand test, leg extension and flexion, handgrip strength, and 6-Minute Walking Test (6MWT), categorized in gender-specific tertiles. Depression was classified based on the Geriatric Depression Scale (GDS) and a diagnosis from a geriatric psychiatrist. Area under the curve (AUC) and logistic regression analyses were conducted.

Results: At baseline, participants developing depression during follow-up (n=207) scored significantly worse across all physical performance measures than those who did not develop depression. The AUC and predictive power for each physical performance test was similar for all the tests assessed. In logistic regression analysis, after adjusting for 14 potential confounders, worse physical performance across all tests increased the risk of depression. The lowest tertile of the SPPB were at notable odds of developing depression (OR=1.79; 95%CI: 1.18-2.71). The association between poor physical performance and depression was typically stronger in women than in men, except for 4m gait speed.

Limitations: no gold standard used for depression diagnosis; oxidative stress and inflammatory markers were not included; high rate of missing data at follow-up.

Conclusion: Low physical performance appears to be an independent predictor of depression over a 4.4-year follow-up in our sample of elderly people.

INTRODUCTION

Depression is a common and pervasive condition in the elderly. The prevalence of depression ranges from 0.9% to 9.4% in community dwelling people, but is higher in other settings like hospitals and nursing homes.[1] The presence of depression is significantly associated with disability, reduced quality of life, increased mortality and higher cardiovascular disease risk.[2–4] The prevention of depression is of critical importance and the development of objective predictors of future depression is essential in order to identify early those who may be at risk. To this end, numerous risk factors for depression in older age have been identified including physical comorbidities (in particular cardiovascular disease), insomnia, stressful life events, cognitive decline and genetic predisposition.[5]

Recent research has suggested a potential role of low physical activity (i.e. any bodily movement produced by skeletal muscles that results in energy expenditure)[6] is a risk factor for depression.[7] The relationship between physical performance capabilities and depression is less clear. Physical performance is a multidimensional concept, including several subdomains: muscle strength, mobility (lower extremity function), dexterity (upper extremity function), axial ability (neck and back function), and ability to carry out instrumental activities of daily living.[8] Some cross-sectional studies showed a significant relationship between low physical performance and depression.[9,10] However, there is a lack of clarity about these results, due to the cross sectional nature and the directionality of the association, since depression is characterized by fatigue and asthenia, which may themselves lead to a decrease in activity.[11] Other longitudinal studies have reported that low physical performance[11–13] is associated with a higher risk of depression in older people suggesting that low physical performance could play a role in the development of depression. Whilst helpful, physical performance data, captured via self-report questionnaires, have poor recall properties, reliability and validity in

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older adults and might introduce bias.[14] For instance, numerous studies have demonstrated that older adults self-report physical function is inconsistent and weakly associated with their actual physical performance when measured objectively.[15] Therefore, studies investigating self-report physical performance and depression are likely to be limited by poor reflection of older person's true functional abilities.[14]

Objective measures of physical performance, such as measuring gait speed, provide a more accurate measure of a person's physical capability. Objective physical performance tests have been demonstrated to be associated with various future outcomes in older age such as cognitive decline [14] and mortality.[16] To date, a paucity of research has considered if objective physical performance can predict future depression in the elderly. To the best of our knowledge, only two studies have investigated a single objective physical performance tests and future depression. One study [17] found that slow gait speed was associated with 2.0 times increased odds of having the worst depressive symptoms trajectory compared those without slow gait speed. Another study among older people aged over 85 years showed that low handgrip strength was associated with worse symptoms depression over time.[18] In addition to a paucity of data, there is an absence of studies comparing the prognostic ability of the different physical performance and muscle strength tests in predicting depression in older adults. Understanding such information is important and valuable for clinicians to identify those most at risks and previous research considering objective physical performance and future mortality[16] and poor cognitive status,[14] have demonstrated that not all tests have the same predictive power.[16]

Given the aforementioned limitations and gaps in the literature, the aim of the present study was thus to examine which objective physical performance measures provide an optimal

predictor of incident depression in a representative cohort of older subjects over 4 years of follow-up. We hypothesized that low physical performance would be a determinant of a higher depression risk after 4.4 years of follow-up.

MATERIALS AND METHODS

Data source and subjects

The data included participants from the *Progetto Veneto Anziani* (Pro.V.A.), an observational cohort study among Italian older adults aged ≥65 years. The study population initially included 3,099 age- and sex-stratified Caucasian participants (1,854 women and 1,245 men) randomly selected between 1995 and 1997 using a multistage stratification method. Sampling procedures and data collection methods have been described elsewhere.[19] The follow-up visit was scheduled after 4 years from baseline and made after a mean of 4.4 years.

Clinical data

Participants were examined at city hospitals by trained physicians and nurses. Information was collected during a face-to-face interview. Regular physical activity was defined as ≥ 4 h/week in the previous month of at least moderate physical activity (brisk walking, cycling, gardening, dancing, or physical exercising), being 4 h/week the median value of the PRO.V.A. sample. Monthly income was categorized as ≥500 vs. <500 €, being 500 € the median value of the sample as whole. Smoking status was classified as "current" vs. "never"/ "previous" (for at least 1 year in the past). Educational level was categorized as >5 vs. ≤5 years of schooling (which corresponds to the years of compulsory education in Italy when our participants were of school age). Body weight and height were measured by trained physicians, and body mass index (BMI) (kg/m^2) was calculated. Functional status was assessed using the ADL (activities of daily living) score.[20] Cognitive status was assessed at

the baseline and follow-up by administering the 30-item mini-mental state examination (MMSE), adjusted for age and education.[21,22]

The presence of cardiovascular diseases (CVD), fractures, chronic obstructive pulmonary disease (COPD), hypertension, diabetes or cancer was ascertained by board-certified physicians involved in the study, who examined all of the clinical information collected for each participant. Additional information included disease history, symptoms self-reported using standardized questionnaires, medical and hospital records, blood tests, and a physical examination. [19]

Definition of exposure and outcome

a. Physical performance tests

Physical performance (i.e. tests more depending on aerobic capacity than muscle power) and muscle strength (i.e. tests more depending on muscle power than aerobic capacity) measures were assessed using standardized objective tests. Since the aim of our work was to investigate the predictive role of these tests on depression onset, we included only the participants with all these measures at baseline. Since a significant difference existed between genders for all the parameters investigated (p<0.0001), the tertiles for each test were calculated using gender-specific cut-offs.

➤ Short Physical Performance Battery (SPPB)[23] scores were derived from three objective physical function tests. Each test was scored from 0 (inability to complete the test) to 4 (highest level of performance). The scores for all three tests were pooled to obtain a composite score of 0 to 12, higher scores reflecting a better physical function. The cutoffs for dividing the sample into tertiles were 10 and 11 points in men, and 9 and 11 points in women.

- ✓ Tandem test: participants were asked to maintain their balance in side-by-side, semi-tandem, and full-tandem positions.

- ✓ 4 m walking speed: the best performance achieved in two walks at participants' usual pace along a 4-m corridor was recorded in meters per second. Participants were allowed to use canes or walkers.

- ✓ Five times sit-to-stand test: participants were asked to stand up and sit down 5 times as quickly as possible, with their hands folded across their chest. The time taken to complete the test, in seconds was recorded.

Since the 4 m walking speed and five times sit-to-stand test are independent predictors of several negative outcomes in older people[24,25], these parameters were also considered as separate items in this analysis. The cutoffs used for the 4 m gait speed were 0.83 and 0.98 m/s in males, and 0.72 and 0.85 m/s in females; for the five times sit-to-stand test, the corresponding cut-offs were 11.2 and 9.4 in males, and 10.2 and 12.6 s in females.

- ➢ Leg strength: knee extensor (quadriceps) and hip flexor (iliopsoas) muscle strength was ascertained using a Nicholas Manual dynamometer (BK-7454, Fred Sammons, Inc.). A "break" test was used. The reliability of this tool was already shown.[26] The highest value recorded between the two legs for quadriceps strength was used in this analysis.[27] The cutoffs for leg extension were 22.7 and 33.6 kg in men, and 16.4 and 23.5 kg in women; for leg flexion, they were 23.5 and 31.0 kg in men, and 15.2 and 21.4 kg in women.

- ➢ Handgrip strength: this was measured in kg using a JAMAR hand-held dynamometer (BK-7498, Fred Sammons, Inc.). A "make" test was used. The validity and reliability of this tool was already demonstrated in a large cohort of American older people.[28] The best result obtained at three attempts with each hand was used for our analyses in agreement with a large study showing that the best attempt is a good proxy for incident disability.[29] The cutoffs were 32.7 and 39.3 kg in men, and 20.7 and 26.0 kg in women.

➢ 6-minute walking test (6MWT): participants were asked to walk at their usual pace for 6 minutes, and the distance they covered was recording in meters.[30] The cutoffs were 376 and 444 m in men, and 320 and 385 m in women.

b. Depression

The presence of depressive symptoms was assessed at the baseline and at the follow-up with the geriatric depression scale (GDS), a 30-item validated tool for use in the elderly.[31] In line with previous research, a cut off score for depressive symptoms of more than 10 over 30 points was used. [31] After this, a geriatric psychiatrist used a standardized questionnaire that includes additional relevant information such as signs and symptoms, medical records, and medication use to confirm the presence or absence of "depression".[32,33] We did not make a diagnosis of major depressive disorder (MDD) or depressive disorder which are ascertained using ICD/ DSM criteria. Henceforth, in this article we refer to depression, based on a validated symptom tool and medical diagnosis and are not referring to MDD or a depressive disorder.

Statistical analyses

For the continuous variables, normal distributions were tested using the Shapiro-Wilk test. Participants' characteristics by presence or not of depression at follow-up were summarized using means (± standard deviations) for continuous variables, and counts and percentages for categorical variables. Age- and gender-adjusted p values were calculated as follows: the differences between the means of the covariates were analyzed for continuous variables using a general linear model (GLM); logistic regression was used for categorical variables.

The proportional hazards assumption was checked by plotting the Schoenfeld residuals versus time. Since the p-values for all physical tests were <0.05, logistic regression was used instead of Cox's regression. Factors known to be associated with physical performance and/or muscle strength, and/or depression were considered for inclusion in the analysis. The predictors included in the final model were all the variables significantly different across tertiles of physical performance/muscle strength tests (for at least two tests) and/or the variables significantly different by the presence of depression at the follow-up (p<0.05).

Collinearity among covariates was estimated with the variance inflation factor (VIF). A VIF≥2 was considered an exclusion criterion, although no variables were excluded based on a violation of VIF. Odds ratios (ORs) and 95% confidence intervals (CIs) were used to compare depression rates across tertiles of physical performance and muscle strength tests, taking those in the third tertile (best scores) for reference. Since a significant difference existed for both exposure and outcome parameters, the analyses were also conducted by gender.

The estimated mean changes in the GDS score recorded at the follow-up, modeled as a continuous variable, was obtained for each tertile and compared using a GLM. The Bonferroni's correction was consequently used in this analysis, since a comparison across tertiles was made.

Finally, receiver operator characteristic (ROC) curves were analyzed to compare the sensitivity and specificity of the different physical performance/muscle strength parameters as a risk factor for the onset of depression, measuring the relative area under the curve (AUC).

All analyses were performed using the SPSS 21.0 for Windows (SPSS Inc., Chicago, Illinois). All statistical tests were two-tailed and statistical significance was assumed for a p-value <0.05.

RESULTS

Study flow of participants

At baseline, from 3,099 potentially eligible older adults, 990 participants were excluded because they had missing information on one or more physical performance tests and 794 people were already depressed. After excluding a further 153 with missing follow-up data regarding depression and 192 who died during the follow-up period, the final sample consisted of 970 participants (see Figure 1 for study flow).

At baseline, excluded participants were more likely to be male (58.1% vs. 45.4%; p<0.0001), and older (81.4±8.0 vs. 72.5±6.0; p<0.0001) than those with no depression and included in our study. The dropouts and the individuals who died had significantly higher GDS scores at

baseline (13.4±2.8 vs. 6.6±2.1 points; p<0.0001) than those included in the study, and they also had worse scores in all the physical performance and muscle strength measures investigated (p<0.0001 for all tests). Compared to those included in our analysis, depressed people at baseline showed worse physical performance results in all the tests considered (p<0.0001 for all tests).

Sociodemographic and medical factors according to depression at follow up

The final sample consisted of 970 community-dwelling elderly subjects without depression at the baseline. The mean age of the sample was 72.5±6.0 years [range: 65-96], 54.6% were females. The mean GDS score was 6.6±2.1.

Table 1 shows the participants' baseline characteristics by the onset of depression during the follow-up. The group of 207 participants diagnosed with depression during the follow-up was significantly older (p=0.004) and had a higher proportion of females (p=0.04) than those with no depression (n=763). After adjusting for age and gender, depressed people showed significantly worse cognitive status as indicated by lower MMSE (25.2±4.1 vs. 26.0±3.2 points, p=0.006) and higher GDS score (7.3±2.2 vs. 6.4±2.0, p<0.0001) than those with no depression.

No significant differences emerged between depressed and no depressed at follow-up in terms of current smoking, education, monthly income, self-reported physical activity level, BMI, and co-morbidities presence or ADL score (Table 1).

Differences in baseline physical performance and depression at follow up

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Participants developing depression at the follow-up scored significantly worse than those with no depression in all the physical performance tests assessed (SPPB, 4 m walking speed, five times sit-to-stand test, leg strength, handgrip strength, and 6MWT) (Table 1).

Using logistic regression analysis, adjusted for 14 potential baseline confounders and taking participants with the best performance level as the reference (i.e. T3), those having worse physical performance at SPPB (T1: OR=2.71; 95%CI: 1.57-4.68, $p<0.0001$; T2: OR=1.88; 95%CI: 1.12-3.18, $p=0.02$), 4m gait speed (T1: OR=1.79; 95%CI: 1.18-2.71, $p=0.0006$), five times sit-to-stand test (T1: OR=2.05; 95%CI: 1.36-3.07, $p=0.001$), leg extension (T1: OR=1.68; 95%CI: 1.12-2.52, $p=0.01$), leg flexion (T1: OR=1.83; 95%CI: 1.23-2.72, $p=0.003$), handgrip strength (T1: OR=1.75; 95%CI: 1.14-2.68, $p=0.01$), and 6MWT (T1: OR=1.89; 95%CI: 1.23-2.91, $p=0.004$) had an increased risk of having depression during the follow-up.

As shown by Table 2, the association between poor physical performance at the baseline and depression was significant in women for all the tests investigated (except for 4 m gait speed), whilst in men only poor scores of the SPPB and 4m gait speed was associated with a higher risk of becoming depressed at the follow-up.

Figure 2 shows the changes in GDS between follow-up and baseline by tertiles of physical performance tests. Those with worse physical performance at baseline (T1) had a significant increase in GDS score ($p<0.0001$) when compared to those scored better (T3), independently from the physical test assessed.

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The power of predicting depression at the follow-up for each test is showed in Figure 3. ROC analyses demonstrated that all the tests significantly predicted the onset of depression at the follow-up with a similar estimate, although the highest AUC was for SPPB (AUC=0.629; 95%CI: 0.586-0.671, p<0.0001) and the lowest for handgrip strength (AUC=0.587; 95%CI: 0.542-0.631, p<0.0001).

DISCUSSION

Our population-based cohort study considering a comprehensive battery of objective physical performance measures, demonstrated that reduced physical performance is significantly associated with depression over a follow-up of 4.4 years in older adults. The ability of the different physical performance tests seems to be comparable, although perhaps the SPPB is the most optimal measures, with those scoring lowest in this measure at 2.7 times increased odds of developing depression. The ROC curves confirmed these findings since the area under the curve for SPPB was the highest among all the tests considered. The association between poor physical performance and depression was stronger in women than in men for almost all the outcomes investigated.

Regarding SPPB and its outcomes, after adjusting for potential confounders, poor SPPB was a significant predictor of depression in both men and women, whilst slow gait speed was associated with a higher risk of depression in men and poor five times sit-to-stand test in women. The clinical importance of the SPPB, gait speed and five times sit-to-stand test is widely known.[34] However, no study investigating the SPPB and five times sit-to-stand test and depression as an outcome is available, with only one study previous to our knowledge that has assessed the impact of slow gait speed on depression onset. The authors demonstrated that slow gait speed may represent important risk factor for worsening depressive symptoms over time in 3,939 people with or at high risk of knee osteoarthritis.[17] In agreement with the literature regarding this topic, we could hypothesize that people with low SPPB, gait speed and five times sit-to-stand test are at higher risk of depression, mainly due to a higher risk of functional limitation and consequently of disability and isolation that are significant risk factors for depressive mood in the elderly.[35] Why slow gait speed is a

predictor of depression in men and five times sit-to-stand test in women merits further and specific research.

On the contrary, as reported in a systematic review investigating the application of handgrip strength in the elderly[36], only one study assessed the impact of low handgrip strength on depression and found no significant association[18], which is in contrast to our results. This could be explained by a lack of power of this previous study (only 482 participants followed-up for 4 years), or by the fact that the population included in this study was over 85 years (thus limiting the incidence of depression to the advantage of other conditions, such as dementia) and by the different tools used for the assessment of depression (GDS at 15 questions in their study vs. 30 in our). Conversely, data considering lower limbs muscle strength and 6MWT and depression appears to be absent and our research is to the best of our knowledge the first to assess the importance of these tests in predicting depression. As shown by our analyses, the power of lower limb muscle strength and the 6MWT in predicting depression is similar to the other tests that are probably more simple to use in clinical settings (e.g. 4m gait speed, SPPB). Since these tests do not add any advantage compared to the others, we suggest clinicians may use SPPB and its items and/or handgrip for identifying people at higher risk of depression. However, when considering the ROC curve for handgrip strength, the data suggested this is not strongly associated with depression, reinforcing the concept that SPPB is probably the best test in predicting depression at the follow-up. When one considers that SPPB also appears to be useful in predicting cognitive decline[14] and mortality[16], routine screening of physical performance in clinical practice is warranted.

Several hypotheses may offer explanations between low physical performance and the higher onset of depression in the elderly. First, low physical performance might be an early marker

of a deterioration in the nervous system. It is known that, for example, an impaired balance, reduced activity levels and an increased fear of falling could contribute to depression and the latter is associated with reductions in regional grey matter volumes in older adults which may affect mood.[37] Second, low physical performance and depression share some risk and pathogenic factors (particularly increased rate of oxidative stress[38] and inflammation[39], and decreased sex hormone levels[40]) that may influence the onset of depression.[14,41,42] Third, it may be that individuals with low physical performance level were socially more isolated, and so at higher risk of depression, with an increasing evidence base suggesting that social isolation is associated with depression.[43] Fourth, older adults with reduced physical performance are likely to have reduced functional mobility, be at increased risk of falls and therefore avoid more activities due to a fear of falling.[44] Thus a vicious cycle of impaired balance, inactivity, escalating fear of falling and social isolation develops, potentially increasing the risk of depression. Clearly, future longitudinal research is required to disentangle such relationships.

Of interest is that the association between low physical performance and muscle strength and incident depression is stronger in women than in men. Although the exact reasons of these findings are not completely known, a number of potential hypotheses could account for this finding. First, there were more women than men in our study. Thus, it is possible that there was a lack of power to detect a difference in our results among males. Second, previous literature has found that slower gait speed is associated with an increased risk of dressing dependence among women, but not in men[45], indicating that the low physical performance and muscle strength have more deleterious effects in women than in men. In agreement with our findings, sarcopenic obesity was associated with the onset of depression in women and

not in men in a large study involving older English people.[46] However, future studies are needed to better explore this topic.

Whilst our study is the first cohort study investigating the comparative prognostic usefulness of physical performance and depression in older people to date, some limitations should be considered. The main limitation lies in that, even though we used a reliable method for diagnosis of depression, we did not use the gold standard method, i.e. structured clinical interview combined with a clinical interview by an experienced mental health professional. Future research should consider if physical performance can predict major depressive disorder. Second, whilst we adjusted for 14 pertinent confounders, we cannot investigate the role of other possible conditions like depression, which may also affect physical performance. A third limitation concerns the fact that we did not estimate body composition parameters, which could be important because some studies have suggested that high fat mass levels could also have a role in older subjects' depressive status.[47] Fourth, as stated previously, oxidative stress and inflammatory markers could play an important part in mediating the association between physical performance and depression, but were not assessed in our research. Fifth, due to missing data and excluding participants who were already depressed, the current data also represent some selection and survival bias. Finally, the use of hand-held dynamometry for strong muscle groups (like the quadriceps) is problematic, particularly in the elderly. Future studies using more modern techniques are so needed to confirm/ refute our findings.

In conclusion, poor objective physical performance appears to be an independent predictor of depression over a 4.4-year follow-up in our sample of elderly people. The predictive power of the tests examined seems to be similar, although those scoring particularly poorly in the SPPB

appear at particular risk of depression.   Future studies with a larger sample size are however needed to confirm our finding and to better understand potentially gender differences.

Ethics Approval

The ethical committees of the University of Padova, Padova, Italy, and the Local Health Units (USSL) n. 15 and n. 18 of the Veneto Region approved the study protocol. Participants provided written informed consent.

Disclosures and Presentations

The authors declare no potential conflicts of interest. Dr Sergi is a paid consultant to Servier Research and a lecturer for Pfizer.

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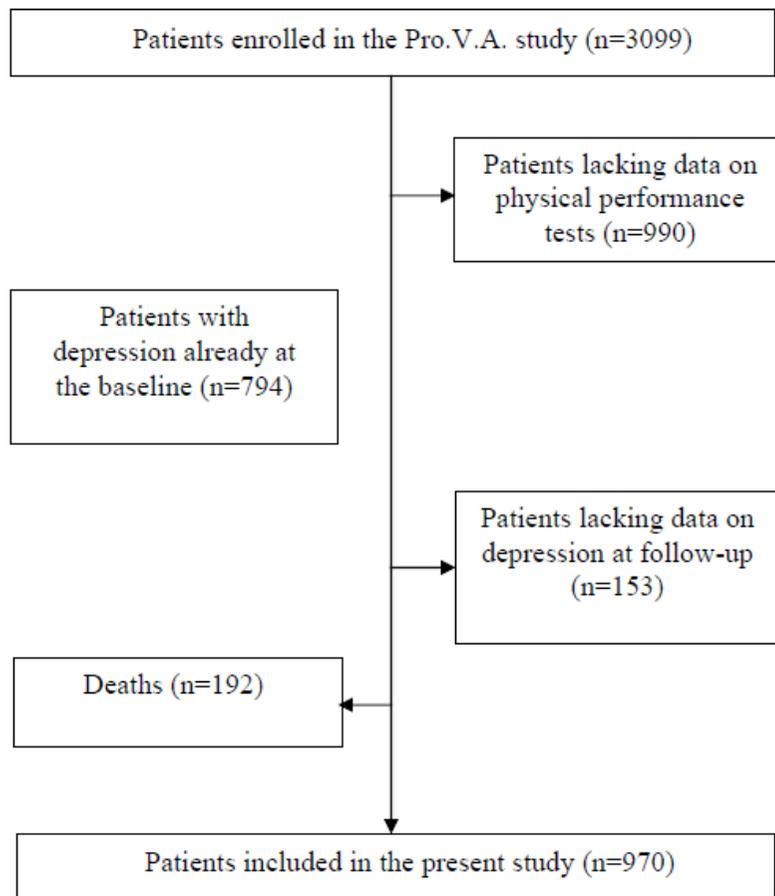
Figure 1. Flow-chart
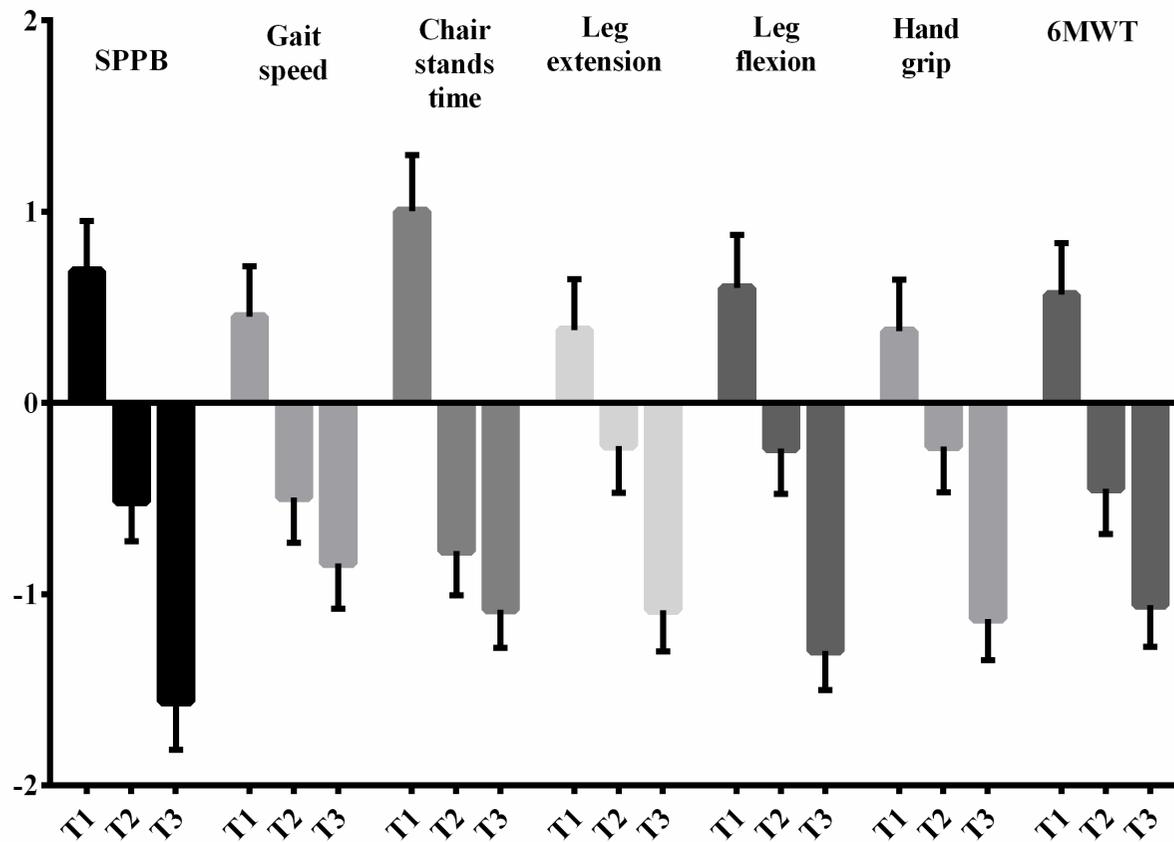
Figure 2. Changes in geriatric depression scale (calculated as follow-up vs. baseline values) by physical performance tests.

Notes: Data are presented as mean changes in geriatric depression scale (follow-up vs. baseline) and standard errors of the means. P values were calculated using the Analysis of Variance for all the comparisons. When comparing T1 vs. T3, T2 vs. T3 and T1 vs. T2, all p-values were less than 0.0001, after applying the Bonferroni's correction.

Abbreviations: 6MWT: 6-minute walking test; SPPB: short physical performance battery.
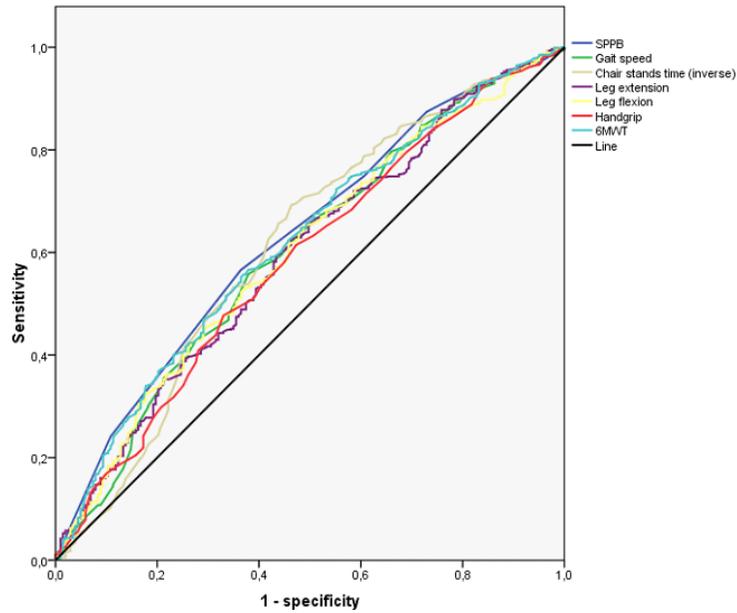
Physical performance test	Area	95% confidence interval		p-value
		Lower	Higher	
SPPB (points)	0.629	0.586	0.671	<0.0001
4 m walking speed (m/s)	0.602	0.558	0.647	<0.0001
Chair stands time (s)*	0.613	0.567	0.659	<0.0001
Leg extension (kg)	0.596	0.552	0.640	<0.0001
Leg flexion (kg)	0.602	0.558	0.645	<0.0001
Handgrip (kg)	0.587	0.542	0.631	<0.0001
6MWT (m)	0.619	0.576	0.662	<0.0001

Figure 3. Receiver operating characteristic curves and their areas the for physical performance tests as a predictor of depression onset during the

4.4-year follow-up.

* Since higher stands time corresponds to lower physical performance, differently from the other physical performance tests, the inverse of this item was used in the figure.

Abbreviations: 6MWT: 6-minute walking test; SPPB: short physical performance battery.

Table 1. Baseline characteristics of the study sample by depression presence during the follow-up.

Participants' characteristics	Depression (n=203)	No depression (n=763)	p-value*
Age (years)	73.6 (6.4)	72.3 (6.9)	0.004[†]
Female sex (%)	61.1	52.8	0.04[†]
General and anthropometric characteristics			
Current smokers (%)	13.3	9.6	0.10
Formal education > 5 years (%)	16.2	19.0	0.41
Monthly income ≥500 € (%)	41.3	41.2	1.00
Physical activity≥4 h/week (%)	27.6	33.2	0.15
ADL score	5.6 (0.7)	5.7 (0.6)	0.05
BMI (kg/m^2)	28.0 (4.6)	27.9 (4.3)	0.84
GDS (score)	7.3 (2.2)	6.4 (2.0)	<0.0001
MMSE (score)	25.2 (4.1)	26.0 (3.2)	0.006
Medical conditions			
Hypertension (%)	70.4	69.9	0.93
Diabetes (%)	13.3	13.8	0.91
CVD (%)	13.8	12.1	0.55
Fractures (%)	5.9	8.4	0.30
COPD (%)	5.4	5.9	0.87
Cancer (%)	7.4	4.5	0.10
Physical performance tests			
Short physical performance battery (points)	9.6 (1.8)	10.3 (1.6)	<0.0001
4 m gait speed (m/s)	0.80 (0.17)	0.86 (0.17)	<0.0001
Chair stands time (s)	13.4 (2.7)	11.1 (2.9)	<0.0001
Knee extension (kg)	21.7 (9.6)	25.4 (13.0)	<0.0001
Hip flexion (kg)	20.7 (9.1)	24.2 (12.5)	<0.0001
Handgrip (kg)	27.0 (8.9)	29.6 (9.0)	<0.0001

	6-minute walking test (m)	349.8 (88.5)	384.6 (83.0)	<0.0001

*Unless otherwise specified, *p* values were adjusted for age and gender using a general linear model or logistic regression, as appropriate. [†] Not adjusted for age or gender, respectively.

<u>Abbreviations</u>: ADL: activities of daily living; IADL: instrumental activities of daily living; BMI: body mass index; GDS: Geriatric Depression Scale; MMSE: Mini Mental State Examination; CVD: cardiovascular disease; COPD: chronic obstructive pulmonary disease.

Table 2. Association between physical performance tests at the baseline and depression at the follow-up

	Whole sample				Males				Females			
	Unadjusted odds ratio (95%CI)	*p – value*	*Fully-adjusted odds ratio (95%CI)*	*p – value*	*Unadjusted odds ratio (95%CI)*	*p – value*	*Fully-adjusted odds ratio (95%CI)*	*p – value*	*Unadjusted odds ratio (95%CI)*	*p – value*	*Fully-adjusted odds ratio (95%CI)*	*p – value*
	Short physical performance battery											
T3	1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]	
T2	3.38 (2.05-5.57)	<0.0001	**1.88 (1.12-3.18)**	**0.02**	1.31 (0.65-2.62)	0.45	1.37 (0.66-2.83)	0.40	2.80 (1.21-6.43)	0.02	**2.59 (1.11-6.03)**	**0.03**
T1	2.07 (1.25-3.42)	<0.0001	**2.71 (1.57-4.68)**	**<0.0001**	3.48 (1.82-6.67)	<0.0001	**2.92 (1.37-6.22)**	**<0.0001**	3.48 (1.51-8.04)	0.004	**3.04 (1.27-7.27)**	**0.01**
	4 m gait speed											
T3	1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]	
T2	1.10 (0.73-1.66)	0.65	1.02 (0.67-1.56)	0.92	1.20 (0.2-2.33)	0.58	1.15 (0.58-2.30)	0.69	0.99 (0.58-1.68)	0.97	0.92 (0.53-1.58)	0.75
T1	2.25 (1.54-3.31)	<0.0001	**1.79 (1.18-2.71)**	**0.006**	2.85 (1.56-5.20)	0.001	**2.22 (1.16-4.28)**	**0.02**	1.85 (1.12-3.05)	0.02	1.55 (0.90-2.68)	0.12
	Chair stands time											
T3	1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]	
T2	1.15 (0.76-1.74)	0.51	0.98 (0.64-1.50)	0.92	0.75 (0.38-1.47)	0.40	0.57 (0.28-1.16)	0.12	1.49 (0.88-2.53)	0.14	1.34 (0.78-2.31)	0.28
T1	2.37 (1.61-3.47)	<0.0001	**2.05 (1.36-3.07)**	**0.001**	2.20 (1.24-3.93)	0.007	1.80 (0.9-3.47)	0.08	2.50 (1.50-4.16)	<0.0001	**2.29 (1.35-3.89)**	**0.002**
	Leg extension											
T3	1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]	
T2	1.54 (1.03-2.28)	0.03	1.49 (0.99-2.24)	0.05	1.20 (0.64-2.25)	0.56	1.02 (0.53-1.99)	0.92	1.69 (1.00-2.83)	0.05	**1.78 (1.04-3.02)**	**0.03**
T1	1.64 (1.11-2.25)	0.01	**1.68 (1.12-2.52)**	**0.01**	1.58 (0.87-2.88)	0.13	1.46 (0.77-2.79)	0.25	1.80 (1.08-3.01)	0.03	**1.81 (1.07-3.04)**	**0.03**
	Leg flexion											
T3	1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]	
T2	1.17 (0.78-1.76)	0.44	1.18 (0.78-1.7)	0.45	1.40 (0.72-2.71)	0.32	1.30 (0.65-2.61)	0.45	1.05 (0.63-1.76)	0.86	1.08 (0.64-1.83)	0.77
T1	1.93 (1.32-2.83)	0.001	**1.83 (1.23-2.72)**	**0.003**	2.35 (1.31-4.52)	0.005	1.94 (0.99-3.81)	0.05	1.67 (1.02-2.72)	0.04	**1.69 (1.03-2.79)**	**0.04**
	Handgrip											
T3	1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]	
T2	1.41 (0.94-2.12)	0.10	1.33 (0.87-2.02)	0.19	1.43 (0.76-2.71)	0.27	1.32 (0.65-2.66)	0.44	1.36 (0.80-2.33)	0.26	1.31 (0.76-2.28)	0.33
T1	1.96 (1.32-2.91)	0.001	**1.75 (1.14-2.68)**	**0.01**	1.85 (1.01-3.41)	0.05	1.51 (0.77-2.70)	0.23	2.01 (1.20-3.37)	0.008	**2.02 (1.17-3.49)**	**0.01**
	6-minute walking test											
T3	1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]		1 [ref.]	

T2	1.37 (0.91-2.08)	0.14	1.32 (0.87-2.03)	0.20	1.38 (0.70-2.72)	0.35	1.29 (0.64-2.61)	0.48	1.37 (0.81-2.33)	0.24	1.35 (0.79-2.32)	0.27
T1	2.28 (1.54-3.36)	<0.0001	**1.89 (1.23-2.91)**	**0.004**	2.81 (1.51-5.24)	0.001	1.85 (0.92-3.71)	0.08	1.98 (1.20-3.26)	0.008	**1.85 (1.07-3.21)**	**0.03**

Notes:

Unless otherwise specified, data are presented as odds ratios and 95% confidence intervals.

Significant results (p<0.05), after fully adjustment, are highlighted in bold.

T3 indicates those with the best, T1 those with the worst scores in the physical performance tests.

The **fully-adjusted model** included: age, body mass index, preserved activities of daily living, baseline scores in the Mini Mental State Examination and Geriatric Depression Scale (all as continuous variables); presence at the baseline of: cardiovascular diseases, hypertension, fractures, chronic obstructive pulmonary disease, cancer (all "yes" vs. "no"); physical activity (≥ 4 vs. <4 h/week); smoking habits (current vs. never/former); monthly income (≥ 500 € vs. <500).

Gender was input as a covariate for the analyses on the sample as a whole.