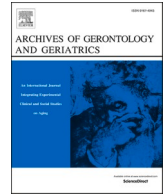


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Physical performance across the cognitive spectrum and between dementia subtypes in a population-based sample of older adults: The HUNT study

Karen Sverdrup^{a,b,c,*}, Geir Selbæk^{a,b,d}, Sverre Bergh^{a,e}, Bjørn Heine Strand^{a,b,f},
Pernille Thingstad^{g,h}, Håvard Kjesbu Skjellegrind^{i,j}, Kjerstin Næss Skjerve^{g,h},
Gro Gujord Tangen^{a,b}

^a Norwegian National Advisory Unit on Ageing and Health, Vestfold Hospital Trust, Norway

^b Department of Geriatric Medicine, Oslo University Hospital, Norway

^c Department of Interdisciplinary Health Sciences, Institute of Health and Society, Faculty of Medicine, University of Oslo, Norway

^d Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway

^e Research Centre for Age-related Functional Decline and Disease, Innlandet Hospital Trust, Ottestad, Norway

^f Department of Chronic Diseases and Ageing, Norwegian Institute of Public Health, Oslo, Norway

^g Department of Neuromedicine and Movement Science, Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology, Trondheim, Norway

^h Trondheim Municipality, Trondheim, Norway

ⁱ HUNT Research Centre, Department of Public Health and Nursing, Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology, Levanger, Norway

^j Levanger Hospital, Nord-Trøndelag Hospital Trust, Levanger, Norway

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ABSTRACT

Background: Literature on physical performance in older adults across the cognitive spectrum remains inconclusive, and knowledge on differences between dementia subtypes is lacking. We aim to identify distinct physical-performance deficits across the cognitive spectrum and between dementia subtypes.

Methods: 11,466 persons were included from the 70-year-and-older cohort in the fourth wave of the Trøndelag Health Study (HUNT4 70+). Physical performance was assessed with the Short Physical Performance Battery (SPPB), 4-meter gait speed, five-times-sit-to-stand (FTSS), grip strength and one-leg-standing (OLS). Clinical experts diagnosed dementia per DSM-5 criteria. Multiple linear and logistic regression were performed to analyze differences between groups. Age, sex, education, somatic comorbidity, physical activity and smoking status were used as covariates.

Results: Gait speed declined across the cognitive spectrum, beginning in people with subjective cognitive decline (SCD). Participants with mild cognitive impairment (MCI) additionally showed reduced lower-limb muscle strength, balance and grip strength. Those with dementia scored lowest on all physical-performance measures. Participants with Alzheimer's disease (AD) had a higher SPPB sum score and faster gait speed than participants with vascular dementia (VaD) and Lewy body dementia (LBD); participants with VaD and LBD had lower odds of being able to perform FTSS and OLS than participants with AD.

Conclusions: Physical performance declined across the spectrum from cognitively healthy to SCD to MCI and to dementia. Participants with AD performed better on all assessments except grip strength than participants with VaD and LBD. Stage of cognitive impairment and dementia subtype should guide exercise interventions to prevent mobility decline and dependency.

1. Introduction

In 2016, 43.8 million people worldwide lived with dementia, a 117% increase since 1990 (GBD 2016 Neurology Collaborators, 2019). Despite

growing awareness of dementia as a global public health crisis (World Health Organization, 2017), no cure exists. Accordingly, research interest has increased in identifying people at risk, such as those with subjective cognitive decline (SCD) (Jessen et al., 2020) and mild

* Corresponding author.

E-mail address: karen.sverdrup@aldringoghelse.no (K. Sverdrup).

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cognitive impairment (MCI) (DeCarli, 2003). Further, early detection of potentially modifiable characteristics, such as physical-performance deficits, has received growing attention.

Cognitive impairment and physical-performance limitations coexist, and deficits in multiple aspects of physical performance including gait, muscle strength and balance are concurrent with dementia (Annweiler et al., 2011; Bahureksa et al., 2017; Cohen & Verghese, 2019; Demnitz et al., 2016; Waite, Broe, Grayson & Creasey, 2000; Zammit et al., 2021). Yet few population-based studies have applied comprehensive cognitive and physical assessments across the cognitive spectrum and, additionally, included persons living in long-term care facilities (LTCF). Current evidence shows that gait and cognition are particularly closely related (Cohen & Verghese, 2019; Peel, Alapatt, Jones & Hubbard, 2019;

Valkanova & Ebmeier, 2017). Studies indicate that slow gait speed precedes and predicts MCI and dementia (Bahureksa et al., 2017; Grande et al., 2019) and that slow gait speed combined with SCD is a stronger predictor of future cognitive decline and dementia compared to cognitive impairment or slow gait speed alone (Semba, Tian, Carlson, Xue & Ferrucci, 2020). Accumulating evidence also indicates that people with MCI have reduced grip- (Kobayashi-Cuya et al., 2018; Vancampfort et al., 2019; Zammit et al., 2021) and lower-limb muscle strength (Annweiler et al., 2011; Doi et al., 2019) and balance deficits (Bahureksa et al., 2017; Goto et al., 2018), and that people with SCD show balance deficits (Tangen, Engedal, Bergland, Moger & Mengshoel, 2014; Yoon et al., 2020). However, studies of physical performance in people with SCD are few, and research on physical performance in people with

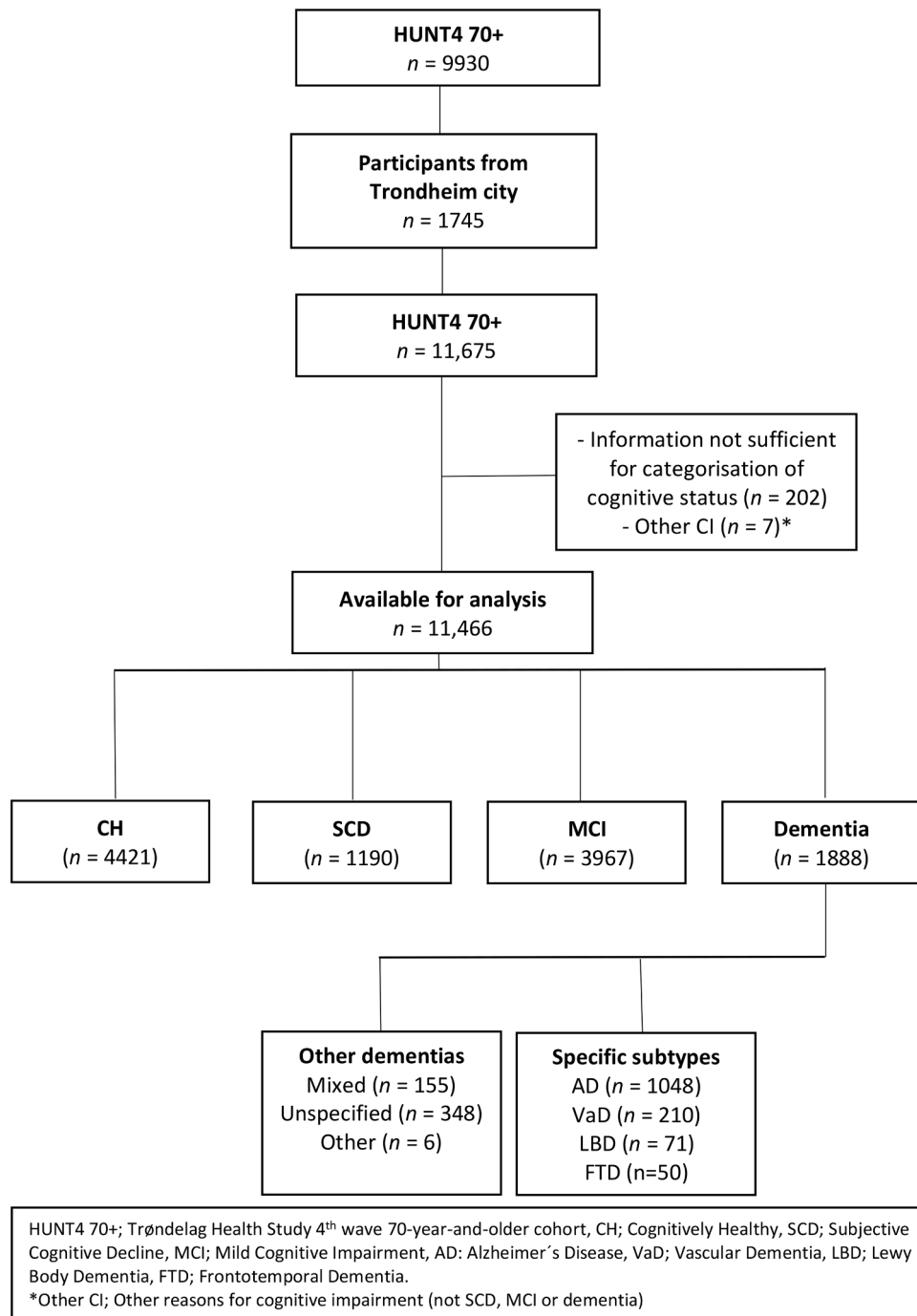


Fig. 1. Flow-chart of participants included in the study.

MCI remains inconclusive (Bahureksa et al., 2017; Demnitz et al., 2016).

Furthermore, studies have reported that gait differ across subtypes of dementia. These suggest that people with vascular dementia (VaD) (Allan, Ballard, Burn & Kenny, 2005; Thomas, Vandenberg & Potter, 2002), Lewy body dementias (LBD, dementia with Lewy bodies and Parkinson's disease dementia) (Fritz et al., 2016; Scharre et al., 2016), and frontotemporal dementia (FTD) (Allali et al., 2010) have greater deficits in gait compared to people with Alzheimer's disease (AD). In research including more than two dementia subtypes, physical performance is often contrasted by comparing AD and non-AD dementia, and studies comparing multiple subtypes are needed (McArdle et al., 2017). Still, existing papers suggest that people with AD have better overall physical performance and less gait deficits than people with non-AD dementias (Allan et al., 2005; McArdle et al., 2017; Tangen, Londos, Olsson & Minthon, 2012; Tolea, Morris & Galvin, 2016; Waite et al., 2000). To date, research on differences in physical performance between dementia subtypes has been limited to studies of gait and small samples, and a population-based study of multiple aspects of physical performance between dementia subtypes is warranted.

The coexistence of cognitive impairment and physical-performance deficits generates a high risk of mobility decline, dependency, nursing home admission and mortality (Grande et al., 2019; Payette et al., 2011; Snowden et al., 2017). In people with cognitive impairment and dementia, physical performance is potentially modifiable through exercise interventions (Lam et al., 2018). To enable targeted interventions, our aim was to describe and identify distinct physical-performance deficits across the cognitive spectrum and between dementia subtypes, in a large-scale, population-based sample of community-dwelling older adults as well as those in LTCF.

2. Methods

2.1. Study design, procedure, and participants

In this population-based, cross-sectional study, we included 11,466 people from the 70-year-and-older cohort in the fourth wave of the Trøndelag Health Study (HUNT4 70+). The HUNT4 70+ cohort was extended beyond the former HUNT catchment area to include 1745 Trondheim city inhabitants (Fig. 1). The study procedure, methods and participants vs. non-participants in HUNT and HUNT4 70+ have been described in detail previously (Gjøra et al., 2021; Krokstad et al., 2013). Briefly, participants completed a self-report questionnaire at home, and standardised interviews and clinical assessments were conducted at field stations, in participants' homes or at the institution where they lived (e. g. LTCF). If dementia was suspected, a structured interview with the participant's next of kin was conducted. Clinical assessment was performed by trained research assistants using standardised protocols. Data were collected between August 2017 and June 2019.

2.2. Dementia diagnosis and cognitive impairment

The dementia diagnosis process in HUNT4 70+ has been described in detail elsewhere (Gjøra et al., 2021). Summarised, two scientific and clinical experts made independent diagnoses of dementia (major neurocognitive disorder) and MCI (minor neurocognitive disorder) for each participant according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (American Psychiatric Association, 2013) using all available information. If the two did not reach consensus, a third expert was consulted. The DSM-5 was also applied for specific dementia subtypes including AD, VaD, Lewy body dementia (LBD) (dementia with Lewy bodies and Parkinson's disease dementia) and FTD.

If the participant expressed a subjective cognitive complaint by answering yes to one of three questions, i.e. "Has your memory declined significantly during the last five years? Have other functions (such as spatial orientation, attention, or language) declined during the last five years? Are these functions poorer than in your peers?" but was not

classified as having MCI or dementia, the participant was categorised with SCD.

2.3. Physical performance

Overall physical performance was assessed with the Short Physical Performance Battery (SPPB) (Guralnik et al., 1994), which comprises a hierarchical balance test, 4-meter (m) walking test and five-times-sit-to-stand test. For the balance test participants were asked to stand with feet in side-by-side position for 10 seconds (s), progressing to feet in semi-tandem position for 10 s, and subsequently to tandem position. A 4-m walk at the participants habitual speed was timed, and the time of the faster of two walks were used for scoring. Lastly, participants were asked to fold their arms across their chest and to rise from a chair, if they succeeded, they were asked to stand up and sit down as fast as possible five times. Each component is scored 0–4, generating a total score (SPPB sum) 0–12; higher scores indicate better performance. Additionally, continuous gait speed (m/s) and timed five-times-sit-to-stand (FTSS, s) were derived from the SPPB. Grip strength was measured using the Jamar Plus+ Digital Hand Dynamometer (Patterson Medical, Sammons Preston) following the procedures from the Southampton protocol (Roberts et al., 2011). The dynamometer was fit to the hand size of the participant before they completed a practice trial. Participants reported their hand dominance before testing and starting with their nondominant hand participants squeezed the dynamometer with maximal effort. Three measures were completed at each hand, and the single highest recorded value from either hand was used. Balance was assessed with the one-leg-standing test (OLS) (Michikawa, Nishiwaki, Takebayashi & Toyama, 2009) as the longest time, up to a maximum of 30 s, the participant could maintain a one-legged stance with eyes open. The participant chose on which lower limb they wanted to complete the test, was instructed to stand with the non-balancing leg lifted back and could freely move their arms during the test. Evidence shows that all performance tests are valid and reliable (Bohannon, 2011; Michikawa et al., 2009; Olsen & Bergland, 2017; Roberts et al., 2011; Rydwick, Bergland, Forsén & Frändin, 2012).

2.4. Covariates

Selection of covariates in this study was done according to availability of data in HUNT4 70+, clinical reasoning and characteristics known to the literature associated with cognition and/ or physical performance. Final covariates included in the study and in the analytical models included age, sex, education, somatic comorbidity, physical activity (PA) and smoking status, and were determined using statistical modeling with directed acyclic graphs (Textor, van der Zander, Gilthorpe, Liskiewicz & Ellison, 2016). Age and sex were collected at assessment, and the remaining covariates were collected through self-reported questionnaires. Education was categorised as primary, secondary, tertiary. Somatic comorbidity was categorised as yes (two or more self-reported somatic diseases) or no (0–1 self-reported somatic diseases). PA was categorised as minimal (once weekly or less) or 2–3 times or more weekly. Finally, smoking status was categorised as never, previous, or current smoker.

2.5. Statistical analysis

Characteristics of participants were described as means with standard deviations (SD) or frequencies and percentages. Ability to perform the gait-speed test, FTSS and OLS were reported (able, unable), and means (SD) were reported for participants able to perform the tests. Between-group differences were analysed using Chi-Square Test or one-way between-groups analysis of variance.

Hierarchical linear and logistic regression models were conducted to explore differences across the cognitive spectrum when adjusted for

predefined covariates. Physical-performance outcome was set as the dependent variable and cognition as the independent variable, with cognitively healthy (CH) as the reference. Age and sex were added to the minimally adjusted model, and education, somatic comorbidity, physical activity and smoking status were added to the fully adjusted model. Post-hoc comparisons were performed between SCD and MCI, and between MCI and dementia. Due to missing data ($n = 1542$) on self-reported covariates, we did the minimally adjusted analyses for the full sample and the reduced sample with non-missing for all covariates, and results were comparable.

Of participants with a specific dementia subtype ($n = 1379$), 40.4% ($n = 557$) had missing on self-reported covariates. We did not consider these as missing at random and did not wish to exclude these participants from the analyses. Therefor only minimally adjusted linear or logistic regression models were conducted to explore differences between dementia subtypes. Physical-performance outcome was set as the dependent variable and specific dementia subtype as the independent variable, with AD as the reference and age and sex as covariates. Post-hoc comparisons were added for VaD and LBD, VaD and FTD, and LBD and FTD.

If one of the three component scores on the SPPB was missing, the total score was calculated as the sum of the two non-missing components plus the average of the two non-missing components (Ostir, Volpato, Fried, Chaves & Guralnik, 2002). Significance was set at $p < 0.05$. Bonferroni adjustments were applied for post-hoc comparisons with 5 and 6 group comparisons and significance was set at $p < 0.01$ and $p < 0.008$, respectively. IBM SPSS Statistics Version 26 and STATA Statistical Software: Release 16 were used for the analyses.

3. Results

3.1. Physical performance across the cognitive spectrum

In total, 11,466 participants were included in this study: 4421 were CH, 1190 had SCD, 3967 had MCI and 1888 had dementia (Fig. 1). Those with dementia were the oldest ($M = 83.9$ years, $SD = 7.5$); a higher proportion were women (60.8%); and a higher proportion were assessed at a LTCF (62.9%) compared to the other groups. All physical-performance measures declined across the spectrum from CH to SCD to MCI and to dementia ($P < 0.001$) (Table 1). In the final models, adjusted for age, sex, education, somatic comorbidity, physical activity and smoking status, gait speed declined across the cognitive spectrum (CH to SCD -0.03 m/s, CH to MCI -0.06 m/s, CH to dementia -0.18 m/s, SCD to MCI -0.03 m/s and MCI to dementia -0.12 m/s, all $P < 0.001$). SPPB sum decreased, timed FTSS increased, and odds of being able to perform OLS decreased from CH to MCI ($-0.45p$, 0.57 s and $OR = 0.60$), CH to dementia ($-3.0p$, 2.45 s and $OR = 0.17$), SCD to MCI ($-0.46p$, 0.44 s and $OR = 0.65$), and MCI to dementia ($-2.56p$, 1.89 s and $OR = 0.37$), respectively (all $P < 0.003$). Grip strength decreased from CH to MCI (-0.96 kg), CH to dementia (-4.38 kg) and MCI to dementia (-3.42 kg) (all $P < 0.001$) (Table 2).

3.2. Physical performance according to specific dementia subtype

Of the 1888 participants with dementia, 1379 received a specific dementia subtype diagnosis (AD $n = 1048$, VaD $n = 210$, LBD $n = 71$, FTD $n = 50$) (Fig. 1). All physical-performance measures except grip strength differed between groups (SPPB $P < 0.001$, gait speed $P = 0.003$, FTSS $P = 0.015$, OLS $P = 0.002$) (Table 3). Point estimates indicated a decrease from AD to FTD to VaD to LBD. In age- and sex-adjusted models, participants with AD had a higher SPPB sum score and gait speed than participants with VaD (SPPB $-1.43p$, gait speed -0.06 m/s) and LBD (SPPB $-2.11p$, gait speed -0.13 m/s) (all $P < 0.008$). Furthermore, participants with VaD and LBD had lower odds of being able to perform FTSS (VaD; $OR = 0.57$, 95% CI 0.41–0.80 and LBD; $OR = 0.40$, 95% CI 0.23–0.70) and OLS (VaD; $OR = 0.53$, 95% CI 0.36–0.77

Table 1

Descriptive characteristics and physical performance across the cognitive spectrum ($n = 11,466$).

Characteristic	CH ($n = 4421$)	SCD ($n = 1190$)	MCI ($n = 3967$)	Dementia ($n = 1888$)
Assessment location				
Field Station, n (%)	4311 (97.5)	1122 (94.3)	3564 (89.9)	700 (37.1)
Home, n (%)	95 (2.1)	67 (5.6)	314 (7.9)	428 (22.7)
LTCF, n (%)	15 (0.3)	1 (0.1)	89 (2.2)	760 (40.2)
Age, mean (SD)	76.0 (5.0)	77.9 (5.6)	77.6 (6.2)	83.9 (7.5)
Sex, females, n (%)	2449 (55.4)	644 (54.1)	2053 (51.8)	1148 (60.8)
Education, (n missing)	(95)	(31)	(237)	(646)
Primary, n (%)	904 (20.9)	289 (24.9)	1079 (28.9)	565 (45.5)
Secondary, n (%)	1923 (44.5)	496 (42.8)	1706 (45.7)	497 (40.0)
Tertiary, n (%)	1499 (34.7)	374 (32.3)	945 (25.3)	180 (14.5)
Somatic comorbidity, (n missing)	(100)	(37)	(230)	(609)
No, n (%)	2760 (63.9)	678 (58.8)	2154 (57.6)	670 (52.4)
Yes, n (%)	1561 (36.1)	475 (41.2)	1583 (42.4)	609 (47.6)
Physical activity, (n missing)	(177)	(60)	(331)	(691)
Once weekly or less (minimal), n (%)	1143 (26.9)	316 (28.0)	1142 (31.4)	660 (55.1)
2–3 times or more weekly, n (%)	3101 (73.1)	814 (72.0)	2494 (68.6)	537 (44.9)
Smoking, (n missing)	(107)	(28)	(239)	(615)
Never, n (%)	1762 (40.8)	454 (39.1)	1344 (36.1)	507 (39.8)
Previous, n (%)	2283 (52.9)	646 (55.6)	2128 (57.1)	683 (53.7)
Current, n (%)	269 (6.2)	62 (5.3)	256 (6.9)	83 (6.5)
Physical performance				
SPPB sum, mean (SD), (n missing)	10.5 (2.2) (48)	10.1 (2.5) (18)	9.5 (3.0) (75)	4.6 (4.1) (117)
Gait, (n missing)	(54)	(21)	(88)	(128)
Not Able, n (%)	53 (1.2)	16 (1.4)	101 (2.6)	395 (22.4)
Able, n (%)	4314 (98.8)	1153 (98.6)	3778 (97.4)	1365 (77.6)
Gait speed (m/s), mean (SD)	1.04 (0.2)	0.98 (0.2)	0.94 (0.3)	0.66 (0.3)
FTSS, (n missing)	(60)	(22)	(85)	(110)
Not able, n (%)	241 (5.5)	86 (7.4)	432 (11.1)	947 (53.3)
Able, n (%)	4120 (94.5)	1082 (92.6)	3450 (88.9)	831 (46.7)
FTSS (s), mean (SD)	11.1 (3.4)	11.6 (4.1)	12.1 (4.5)	16.1 (8.9)
Grip strength (kg), mean (SD), (n missing)	35.8 (11.0) (164)	34.4 (11.2) (41)	34.3 (11.2) (154)	25.5 (11.4) (237)
OLS, (n missing)	(119)	(41)	(170)	(189)
Not able, n (%)	433 (10.1)	175 (15.2)	782 (20.6)	1189 (70.0)
Able, n (%)	3869 (89.9)	974 (84.8)	3015 (79.4)	510 (30.0)
OLS (s), mean (SD)	18.1 (10.6)	16.5 (10.7)	15.5 (10.5)	11.1 (9.6)

Between-group differences were analysed using one-way between groups analysis of variance for continuous variables and Chi-Square Test for categorical variables. For all characteristics across the spectrum $p < 0.001$.

Abbreviations. CH = cognitively healthy; SCD = subjective cognitive decline; MCI = mild cognitive impairment; LTCF = long-term care facility; SPPB = Short Physical Performance Battery, score ranges 0–12; FTSS = five-times-sit-to-stand; OLS = one-leg-standing.

and LBD; $OR = 0.21$, 95% CI 0.09–0.48) than participants with AD (Table 4).

4. Discussion

In this large-scale, population-based, cross-sectional study of older

Table 2

Physical performance across the cognitive spectrum, in unadjusted and adjusted analyses. Linear regression was applied for SPPB, gait speed, grip strength and FTSS, and logistic regression for OLS.

Cognition	Unadjusted SPPB sum (n = 9750)			Minimally adjusted			Fully adjusted		
	β	95% CI	P value	β	95% CI	P value	β	95% CI	P value
(ref.: CH)									
SCD	-0.39	-0.57, -0.21	<0.001	-0.00	-0.16, 0.16	0.99	0.01	-0.14, 0.17	0.87
MCI	-0.80	-0.92, -0.68	<0.001	-0.55	-0.66, -0.44	<0.001	-0.45	-0.55, -0.34	<0.001
Dementia	-4.72	-4.90, -4.54	<0.001	-3.34	-3.52, -3.17	<0.001	-3.00	-3.16, -2.82	<0.001
<i>Post hoc</i>									
(ref.: SCD) MCI	-0.41	-0.59, -0.23	<0.001	-0.55	-0.71, -0.38	<0.001	-0.46	-0.62, -0.31	<0.001
(ref.: MCI) Dementia	-3.92	-4.10, -3.73	<0.001	-2.80	-2.97, -2.63	<0.001	-2.56	-2.73, -2.40	<0.001
	Gait speed (m/s) (n = 9434)			Minimally adjusted			Fully adjusted		
	β	95% CI	P value	B	95% CI	P value	β	95% CI	P value
(ref.: CH)									
SCD	-0.06	-0.08, -0.05	<0.001	-0.03	-0.05, 0.02	<0.001	-0.03	-0.04, -0.01	<0.001
MCI	-0.09	-0.10, -0.08	<0.001	-0.07	-0.08, -0.06	<0.001	-0.06	-0.07, -0.05	<0.001
Dementia	-0.32	-0.34, -0.31	<0.001	-0.22	-0.24, -0.20	<0.001	-0.18	-0.20, -0.17	<0.001
<i>Post hoc</i>									
(ref.: SCD) MCI	-0.03	-0.05, -0.01	0.001	-0.04	-0.06, -0.03	<0.001	-0.03	-0.05, -0.02	<0.001
(ref.: MCI) Dementia	-0.23	-0.25, -0.21	<0.001	-0.14	-0.16, -0.13	<0.001	-0.12	-0.14, -0.10	<0.001
	FTSS (s) (n = 8730)			Minimally adjusted			Fully adjusted		
	β	95% CI	P value	B	95% CI	P value	β	95% CI	P value
(ref.: CH)									
SCD	0.55	0.27, 0.84	<0.001	0.17	-0.10, 0.44	0.22	0.13	-0.14, 0.40	0.35
MCI	0.89	0.69, 1.08	<0.001	0.72	0.54, 0.91	<0.001	0.57	0.38, 0.75	<0.001
Dementia	3.89	3.53, 4.23	<0.001	2.85	2.50, 3.19	<0.001	2.45	2.11, 2.79	<0.001
<i>Post hoc</i>									
(ref.: SCD) MCI	0.34	0.05, 0.63	0.02	0.55	0.27, 0.83	<0.001	0.44	0.16, 0.71	0.002
(ref.: MCI) Dementia	3.00	2.63, 3.35	<0.001	2.12	1.78, 2.47	<0.001	1.89	1.54, 2.22	<0.001
	Grip strength (kg) (n = 9497)			Minimally adjusted			Fully adjusted		
	β	95% CI	P value	β	95% CI	P value	β	95% CI	P value
(ref.: CH)									
SCD	-1.21	-1.97, -0.47	0.001	-0.52	-0.99, -0.05	0.03	-0.50	-0.97, -0.03	0.04
MCI	-1.01	-1.52, -0.50	<0.001	-1.04	-1.35, -0.72	<0.001	-0.96	-1.30, -0.64	<0.001
Dementia	-8.04	-8.81, -7.27	<0.001	-4.58	-5.09, -4.08	<0.001	-4.38	-4.89, -3.88	<0.001
<i>Post hoc</i>									
(ref.: SCD) MCI	0.21	-0.55, 0.97	0.59	-0.52	-0.99, -0.04	0.03	-0.46	-0.93, -0.01	0.06
(ref.: MCI) Dementia	-7.03	-7.81, -6.25	<0.001	-3.55	-4.05, -3.04	<0.001	-3.42	-3.92, -2.92	<0.001
	OLS (0=Unable, 1=Able) (n = 9545)			Minimally adjusted			Fully adjusted		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
(ref.: CH)									
SCD	0.68	0.55, 0.84	<0.001	0.94	0.76, 1.18	0.60	0.93	0.75, 1.17	0.56
MCI	0.48	0.42, 0.55	<0.001	0.57	0.49, 0.67	<0.001	0.60	0.52, 0.70	<0.001
Dementia	0.07	0.06, 0.09	<0.001	0.14	0.12, 0.17	<0.001	0.17	0.14, 0.20	<0.001
<i>Post hoc</i>									
(ref.: SCD) MCI	0.70	0.57, 0.86	0.001	0.61	0.50, 0.75	<0.001	0.65	0.52, 0.81	<0.001
(ref.: MCI) Dementia	0.15	0.13, 0.18	<0.001	0.25	0.21, 0.29	<0.001	0.27	0.23, 0.33	<0.001

Abbreviations. CH = cognitively healthy; SCD = subjective cognitive decline; MCI = mild cognitive impairment; SPPB = Short Physical Performance Battery; FTSS = five-times-sit-to-stand; OLS = one-leg-standing.

Adjusted for age and sex.

Adjusted for age, sex, education, somatic comorbidity, physical activity and smoking status

$^{\dagger}p < 0.01$. Post-hoc Bonferroni adjustment, 5 group comparisons: $p = 0.05/5 = 0.01$. Statistically significant values are in bold.

adults, we observed a decline in gait speed across the cognitive spectrum, beginning in people with SCD. Participants with MCI showed reduced lower-limb muscle strength, balance and grip strength compared to CH participants. Participants with dementia exhibited substantially lower scores on all physical-performance measures. Still, physical performance differed between dementia subtypes, as participants with AD performed better on all assessments except grip strength than participants with VaD and LBD.

The negative association between gait speed and degree of cognitive impairment in our study corroborates previous findings (Peel et al., 2019; Valkanova & Ebmeier, 2017). Gait is a complex task requiring coordination and integration of multiple systems including motor, cognitive and perceptual processes, and cognition and gait share cortical regions in the brain Cohen and Verghese (2019). The integration of these systems and processing through shared mechanisms produce a high

cognitive load, which may explain the association between cognition and decline in gait speed across cognitive stages, even in SCD. In contrast to previous studies (Tangen et al., 2014; Yoon et al., 2020), participants with SCD did not exhibit deficits in balance compared to CH participants. However, the SCD participants in these studies were younger and recruited at memory clinics. Another novel finding of our study is that participants with SCD did not differ from CH on lower-limb muscle strength or SPPB sum. These functional-performance tests also require the integration of processes from multiple systems but assess different domains of physical performance compared to gait. People with SCD are characterised with unimpaired cognition on objective cognitive tests (Jessen et al., 2020), and physical tests not requiring ambulation might not generate a high enough combined cognitive and physical load to reveal deficits at this stage.

Although people with MCI, by definition, have preserved function in

Table 3
Descriptive characteristics and physical performance according to specific dementia subtype (n = 1379).

Characteristic	AD (n = 1048)	VaD (n = 210)	LBD (n = 71)	FTD (n = 50)	P value
Assessment location					<0.001
Field Station, n (%)	427 (40.7)	81 (38.6)	12 (16.9)	11 (22.0)	
Home, n (%)	213 (20.3)	48 (22.8)	13 (18.3)	10 (20.0)	
LTFC, n (%)	408 (39.0)	81 (38.6)	46 (64.8)	29 (58.0)	
Age, mean (SD)	84.2 (7.4)	81.7 (6.9)	84.0 (6.0)	82.4 (8.1)	<0.001
Sex, females, n (%)	653 (62.3)	108 (51.4)	37 (52.1)	33 (66.0)	0.01
Education, (n missing)	343	53	30	24	0.18
Primary, n (%)	335 (47.5)	59 (37.6)	18 (43.9)	11 (42.3)	
Secondary, n (%)	278 (39.4)	68 (43.3)	20 (48.8)	11 (42.3)	
Tertiary, n (%)	92 (13.1)	30 (19.1)	3 (7.3)	4 (15.4)	
Somatic comorbidity, (n missing)	322	47	32	23	<0.001
No, n (%)	434 (59.8)	46 (28.2)	19 (48.7)	12 (44.4)	
Yes, n (%)	292 (40.2)	117 (71.8)	20 (51.3)	15 (55.6)	
Physical performance					
SPPB sum, mean (SD), (n missing)	5.0 (4.1) (62)	4.2 (4.1) (13)	3.0 (3.4) (6)	4.6 (4.5) (6)	<0.001
Gait, (n missing)	67	13	7	6	<0.001
Able, n (%)	790 (80.5)	143 (72.6)	41 (64.1)	28 (63.6)	
Not Able, n (%)	191 (19.5)	54 (27.4)	23 (35.9)	16 (36.4)	
Gait speed (m/s), mean (SD)	0.67 (0.3)	0.65 (0.3)	0.53 (0.2)	0.76 (0.3)	0.003
FTSS, (n missing)	54	12	7	6	0.02
Able, n (%)	499 (50.2)	87 (43.9)	20 (31.3)	22 (50.0)	
Not able, n (%)	495 (49.8)	111 (56.1)	44 (68.8)	22 (50.0)	
FTSS (s), mean (SD)	15.9 (8.7)	16.7 (9.4)	20.2 (13.5)	13.9 (6.4)	0.10
Grip strength (kg), mean (SD) (n missing)	25.9 (11.5) (119)	26.9 (11.8) (28)	24.1 (12.4) (13)	24.8 (13.6) (12)	0.40
OLS, (n missing)	105	22	8	7	0.002
Able, n (%)	314 (33.3)	53 (28.2)	7 (11.1)	14 (32.6)	
Not able, n (%)	629 (66.7)	135 (71.8)	56 (88.9)	29 (67.4)	
OLS(s), mean (SD)	11.2 (9.5)	11.3 (10.1)	10.4 (6.8)	12.9 (11.8)	0.93

Abbreviations. AD = Alzheimer's disease; VaD = vascular dementia; LBD = Lewy body dementias; FTD = frontotemporal dementia; SPPB = Short Physical Performance Battery, score ranges 0–12; FTSS = five-times-sit-to-stand; OLS = one-leg-standing.

*Determined using one-way between groups analysis of variance for continuous variables and Chi-Square Test for categorical variables. Statistically significant values are in bold.

everyday activities in MCI (DeCarli, 2003), we did observe changes in lower-limb muscle strength and balance compared to CH participants and those with SCD. While there was limited evidence to support their conclusion, this finding aligns with a recent systematic review (Bahureksa et al., 2017) suggesting that balance is affected in MCI, and our results support the notion that strength, too, is affected in MCI (Annweiler et al., 2011). Visuospatial skills, executive functions and processing speed may be important components of the ability to perform

Table 4
Physical performance for specific dementia subtypes, estimated in regression models. Linear regression was applied for SPPB and gait speed, and logistic regression for OLS and FTSS.

Dementia subtype	Unadjusted SPPB sum (n = 1292)			Minimally adjusted		
	β	95% CI	P value	β	95% CI	P value
(ref.: AD)						
VaD	-0.76	-1.39, -0.13	0.02	-1.43	-1.99, -0.86	<0.001
LBD	-2.00	-3.05, -0.97	<0.001	-2.11	-3.03, -1.19	<0.001
FTD	-0.42	-1.65, 0.84	0.52	-0.88	-1.99, 0.22	0.12
<i>Post hoc</i>						
(ref.: VaD)	-1.25	-2.40, -0.09	0.03	-0.68	-1.71, 0.35	0.19
(ref.: VaD)	0.35	-0.99, 1.70	0.60	-0.54	-0.66, 1.74	0.37
(ref.: LBD)	1.60	0.02, 3.13	0.05	1.22	-0.18, 2.62	0.09
	Gait speed (m/s) (n = 1002)					
	β	95% CI	P value	β	95% CI	P value
(ref.: AD)						
VaD	-0.03	-0.08, 0.02	0.27	-0.06	-0.11, -0.02	0.005
LBD	-0.14	-0.23, -0.05	0.002	-0.13	-0.21, -0.05	0.001
FTD	0.08	-0.02, 0.19	0.11	0.03	-0.06, 0.12	0.55
<i>Post hoc</i>						
(ref.: VaD)	-0.11	-0.21, -0.02	0.02	0.07	-0.15, 0.02	0.13
(ref.: VaD)	0.11	-0.0007, 0.23	0.05	0.09	-0.009, 0.19	0.07
(ref.: LBD)	0.23	0.09, 0.36	0.001	0.16	0.04, 0.28	0.01
	FTSS (0=Unable, 1=Able) (n = 1300)					
	OR	95% CI	P value	OR	95% CI	P value
(ref.: AD)						
VaD	0.78	0.57, 1.06	0.11	0.57	0.41, 0.80	0.001
LBD	0.45	0.26, 0.78	0.004	0.40	0.23, 0.70	0.002
FTD	0.99	0.54, 1.81	0.98	0.81	0.42, 1.56	0.52
<i>Post hoc</i>						
(ref.: VaD)	0.58	0.32, 1.06	0.07	0.69	0.37, 1.30	0.25
(ref.: VaD) FTD	1.27	0.66, 2.45	0.46	1.41	0.69, 2.86	0.34
(ref.: LBD) FTD	2.20	0.99, 4.86	0.05	2.03	0.87, 4.74	0.10
	OLS (0=Unable, 1=Able) (n = 1237)					
	OR	95% CI	P value	OR	95% CI	P value
(ref.: AD)						
VaD	0.79	0.56, 1.11	0.17	0.53	0.36, 0.77	0.001
LBD	0.25	0.11, 0.56	0.001	0.21	0.09, 0.48	<0.001
FTD	0.97	0.50, 1.86	0.92	0.66	0.31, 1.38	0.27
<i>Post hoc</i>						
(ref.: VaD) LBD	0.32	0.14, 0.74	0.008	0.40	0.16, 0.97	0.04
(ref.: VaD) FTD	1.23	0.60, 2.51	0.57	1.25	0.56, 2.79	0.58
(ref.: LBD) FTD	3.86	1.40, 10.62	0.009	3.15	1.05, 9.43	0.04

Abbreviations. AD = Alzheimer's disease; VaD = vascular dementia; LBD = Lewy body dementias; FTD = frontotemporal dementia; SPPB = Short Physical Performance Battery, score ranges 0–12; FTSS = five-times-sit-to-stand; OLS = one-leg-standing.

Adjusted for age and sex

^p<0.008. Post-hoc Bonferroni adjustment, 6 group comparisons: p = 0.05/6 = 0.008. Statistically significant values are in bold.

balance and lower-limb muscle-performance tests (Annweiler et al., 2011; Bahureksa et al., 2017; Demnitz et al., 2016; Doi et al., 2019; Waite et al., 2000). Impairments in these cognitive domains are often found in MCI (DeCarli, 2003) and can explain why these participants perform worse on such tests compared to CH participants and those with

SCD. Aligned with these findings, it was not surprising that SPPB sum also declined between these groups. The differences between CH and MCI ($-0.45p$) and SCD and MCI ($-0.46p$) are considered clinically meaningful (Perera, Mody, Woodman & Studenski, 2006).

Grip strength has been proposed as a biomarker for health in older adults and is associated with cognition and cognitive decline (Kobayashi-Cuya et al., 2018; Vancampfort et al., 2019; Zammit et al., 2021). We did not detect a difference in grip strength between CH and SCD or between SCD and MCI, but in line with previous studies, our results show reduced grip strength between CH and dementia (-4.4 kg) and between MCI and dementia (-3.4 kg) (Kobayashi-Cuya et al., 2018; Vancampfort et al., 2019; Zammit et al., 2021). Still, the differences observed were below a clinically meaningful difference of 5 kg (Roberts et al., 2011). Motor skill and motor output of grip strength might share interconnected mechanisms with cognition in brain regions, but associations appear to be undetectable in the early stages of cognitive disorder. The biological origin of the association between grip strength and cognition remains unclear and warrants further research.

Participants with dementia exhibited deficits on all physical-performance measures compared to all other groups. SPPB sum declined by 3 points and gait speed decreased by 0.18 m/s compared to CH participants, both considered substantial clinical differences (Perera et al., 2006). Dementia is characterised by reduced ability to function in everyday activities (American Psychiatric Association, 2013), and our results support existing literature findings that multiple aspects of physical performance including gait, muscle strength and balance are affected in dementia (Annweiler et al., 2011; Bahureksa et al., 2017; Cohen & Verghese, 2019; Demnitz et al., 2016; Waite et al., 2000; Zammit et al., 2021). Still, we observed considerable variation in physical performance also within the dementia group.

To the best of the authors' knowledge, this is the first study to describe differences in physical performance between multiple dementia subtypes in a large population-based sample of older adults. Previous studies of physical performance across dementia subtypes have been limited by small sample sizes, restricted to memory-clinic patients, and were often limited to comparing AD with non-AD participants (Allan et al., 2005; McArdle et al., 2017; Tangen et al., 2012; Tolea et al., 2016; Waite et al., 2000). In our study, participants with VaD and LBD had lower SPPB sum scores and slower gait speed compared to people with AD. The differences between AD and VaD ($-1.4p$, -0.06 m/s) and AD and LBD ($-2.1p$, -0.9 m/s) are considered clinically meaningful (Perera et al., 2006). Further, the odds of being able to perform FTSS and OLS were higher for participants with AD compared to VaD, and for AD compared to LBD. These results expand the previous reported difference between AD vs VaD or LBD in gait (Allan et al., 2005; Fritz et al., 2016; McArdle et al., 2017; Thomas et al., 2002) to include balance and lower-limb muscle deficits in a large population-based study of older adults.

A key cognitive change in early AD is memory impairment, while attention and executive function, associated with physical performance, are affected early in VaD and LBD (O'Brien & Thomas, 2015; Scheltens et al., 2016; Walker, Possin, Boeve & Aarsland, 2015). Furthermore, LBD is characterised by neurodegeneration in the substantia nigra, which produces disturbances in motor control (Walker et al., 2015). VaD is heterogeneous in nature but characterised by subcortical infarcts and white-matter ischemia (O'Brien & Thomas, 2015). These underlying neuropathological changes in VaD and LBD and shared neural correlates with physical performance may explain the observed differences compared to AD. However, much remains to be understood about these mechanisms.

Disturbance in motor behavior is not considered a prominent clinical feature of FTD (Bang, Spina & Miller, 2015), and we could not detect significant differences between participants with FTD and other dementia subtypes. Allali et al. (2010) described greater gait variability in people with FTD compared to those with AD. Aligned with our findings, no differences in gait speed were observed. People with FTD had more

involuntary trunk movements compared to AD (Pijnenburg, Gillissen, Jonker & Scheltens, 2004), which could disturb postural control but might not hamper gait speed alone. Studies investigating physical performance in persons with FTD are lacking, and our results should be interpreted with caution.

Our study has several limitations. Our cross-sectional design does not allow us to draw conclusions about trajectories of decline across the cognitive spectrum or any causal inference. The covariates were based on self-report, inherently known for recall and social-desirability bias. Having information about distinct medical comorbidities would be particularly valuable as these might affect physical performance. Further, the self-report covariates were prone to missing values. Minimally adjusted analyses for the full and reduced sample across the cognitive spectrum was conducted and results were comparable. However, analyses between specific dementia subtypes are limited by the lack of adjusting for covariates beyond age and sex. Finally, the numbers of participants with LBD and FTD were small compared to the other groups, and the lack of statistically significant differences in physical performance between FTD and the other subtypes could result from lack of power. Several strengths of this research must be highlighted. This large-scale, population-based study includes participants with all levels of cognitive impairment. A comprehensive assessment battery was used to evaluate cognition, and all available information about each participant was thoroughly evaluated by two scientific and clinical experts. However, biomarkers were not assessed, and the study is based on clinical diagnosis. Finally, all physical-performance tests used are standardised and were conducted according to protocol by trained assessors.

5. Conclusions

In this large-scale, population-based, cross-sectional study of older adults, we observed a decline in gait speed across the cognitive spectrum, beginning in people with SCD. Participants with MCI additionally showed reduced lower-limb muscle strength, balance and grip strength. Participants with dementia exhibited substantially lower scores on all physical-performance measures. Participants with AD performed better on all assessments except grip strength compared to participants with VaD and LBD. This knowledge has implications for the development of preventive and follow-up strategies for older adults with cognitive impairment and dementia.

Author contributions

KS designed the study, prepared, analysed and interpreted the data, and drafted the manuscript. GS, SB, GGT and BHS contributed to study design, and GGT and BHS contributed to data analysis. GS, PT and HSK supervised the data collection, and KNS participated in data collection. All authors critically appraised the manuscript for important intellectual content and read and approved the final version of the manuscript.

Participant consent and ethics committee approval

Participation was based on informed consent by the participant or the participant's closest proxy. The participant's ability to consent was based on the judgement of health personnel in nursing homes and assessors. The study is approved by the Regional Committees for Medical and Health Research Ethics in Norway [id. 323333].

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Availability of data and materials

The original de-identified data used in this manuscript was obtained from the HUNT Databank. The dataset is not publicly available. However, data for research may be obtained upon application to the HUNT Data Access Committee. Further information can be found at <https://www.ntnu.edu/hunt>.

Declaration of Competing Interest

KS, SB, BHS, PT, HKS, KNS and GGT declare that they have no conflicts of interest. GS received honoraria for participating in one meeting of the Norwegian advisory board for Biogen regarding the aducanumab trials.

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