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Associations Between Physical Function and Depression in Nursing Home Residents with Mild and Moderate Dementia: A cross-sectional study

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ABSTRACT

Objectives: The primary aim of this study is to describe depression and physical function in nursing home residents with dementia, as well as to examine the associations between depression and balance function, lower limb muscle strength, mobility and activities of daily living. The secondary aim is to examine differences in physical function between the groups classified as depressed and not depressed.

Design: The study has a cross-sectional design.

Setting: A convenience sample of eighteen nursing homes in, and around, Oslo, Norway participated.

Participants: We included 170 nursing home residents aged 60-100 years suffering from mild or moderate degree of dementia (defined by score of 1 or 2 on the Clinical Dementia Rating Scale).

Outcome Measures: Assessments used were Cornell Scale for Depression in Dementia (CSDD), Bergs Balance Scale (BBS), "the 6-meter walking test" (walking speed), 30 seconds Chair Stand Test (CST) and the Barthel Index.

Results: Nursing home residents with dementia are a heterogeneous group in terms of physical function and depression. By applying the recommended cutoff of ≥ 8 on CSDD, 23.5% of the participants were classified as being depressed. The results revealed significant associations between higher scores on the CSDD (indicating more symptoms of depression) and lower scores on BBS (95% CI: -0.12 to -0.02, p=0.006), 30 seconds CST (95% CI: -0.54 to -0.07, p=0.001) as well as maximum walking speed (95% CI: -4.56 to -0.20, p=0.003) (indicating lower level of physical function).

Conclusion: Better muscle strength, balance and higher walking speed were significantly associated with less depressive symptoms. These results suggest that interventions aiming to increase physical performance may influence depression in older people who live in nursing homes. Future research should explore this relationship through a person-centered approach.

Keywords: Nursing home, dementia, depression, physical function, balance, muscle strength, mobility, walking-speed, activities of daily living.

Strengths and limitations of this study

- This study reports important information about the associations between physical function and depression in nursing home residents with dementia.
- The study included a well-defined population of older nursing homes residents with mild and moderate dementia defined by score of 1 or 2 on the Clinical Dementia Rating Scale.
- Measuring instruments employed in this study are standardized and commonly used in clinical practice among frail elderly in nursing homes.
- The participants were enrolled in a physical exercise intervention trial (EXDEM), so they were likely to be fitter than the average nursing home population.
- Because of the cross-sectional design of the study we cannot draw conclusions about causality.

INTRODUCTION

Dementia impact has received increasing attention of governments and politicians across the world in recent years. Societies globally face an increasing proportion of older people who, by reason of age alone, are at increasing risk of dementia.(1) On an international level the prevalence of dementia among older adults in long-term care homes has a median of 58%,(2) but the underdiagnosis of dementia in nursing homes is commenly reported in literature worldwide.(3-5) Approximately 80% of people living in nursing homes in Norway suffer from dementia.(6) The prevalence of depressive disorders among nursing home residents is 10% while the prevalence of depressive symptoms is 29% on an international level.(2) Depression is frequently occurring in nursing home residents with dementia (43%),(7) and is associated with reduced quality of life,(8) poor medical health and more severe cognitive impairment.(9) The World Health Organization (WHO) defines depression as: ”a mental disorder, characterized by sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, feelings of tiredness and poor concentration”.(10) Reduced physical function and dependency in old age as well as somatic disorders are the main risk factors for developing depression.(9, 11) Loneliness and lack of social support are other risk factors.(12-13) Depression is a multifactorial concept and results from a complex interaction of social, psychological and biological factors.(14) According to WHO there are interrelationships between depression and physical health.(15)

Among elderly people in general, better physical function is associated with lower incidence of depressive symptoms.(16-17) It is also related to better mental health, quality of life and wellbeing.(18-19) Despite recommendations of regular physical activity, research shows that nursing home residents are spending most of their time seated or lying down, even when they are capable of independent or assisted activity.(20) It is alarming that residents who are capable of performing ADL activities independently or with assistance, often do not get the opportunity to participate actively, especially since physical function is a modifiable factor reliant on the continuous use of the musculoskeletal system.(21)

It is well known that physical function is modifiable through exercise. Even though the importance of physical activity for the preservation of function in elderly is well documented,(21-28) the relationship between physical function and depression in nursing home residents with dementia is unclear and results from studies are ambiguous. Some studies indicate that nursing home residents with good physical function are less depressed than those

with low level of physical function,(8, 29) while others do not find any significant associations between the two factors.(9)

Studies that have investigated the relationship between physical function and depression in persons with dementia in nursing homes have largely employed proxy-reported measures of physical function, and not performance-based tests. Performance-based tests are more sensitive than self- or proxy-reported measures of physical function and may be better to identify the true abilities of an individual.(30) The relationship between physical function, tested with performance-based tests, and depression in nursing home residents with dementia seem to constitute a provisional "gap" in knowledge. The topic is important because depression in nursing home residents with dementia is common,(31-32) and good alternatives to psychotropic drugs are called for.(32-34)

It is important to identify modifiable factors underlying or associated with depression in the growing population of nursing home residents with dementia. Therefore, the primary aim of this study was to describe physical function and depression in this population, as well as to examine the associations between depression and levels of balance, muscle strength, mobility and daily life activity. The secondary aim was to examine differences in physical function between the group classified as depressed and not depressed. Although the authors have an assumption about relationships, the study is explorative and thus no hypotheses are tested.

METHODS

Design

The study has a cross-sectional design. The data were collected from baseline measurements of a randomized controlled trial (EXDEM) that was carried out in Norway in 2012 and 2013.

Setting and Participants

A convenience sample of eighteen nursing homes in Oslo, as well as in the counties of Akershus, Oppegård and Buskerud participated. We included one hundred and seventy nursing-home residents. The inclusion criteria were the following: suffering from mild or moderate degree of dementia (defined by score of 1 or 2 on the Clinical Dementia Rating Scale),(35) age above 55 years, able to stand up independently or with help from one person, able to walk six meters with or without a walking aid, and able to give informed consent. The exclusion criteria were the following: residents suffering from psychosis or severe communication problems and residents who were medically unstable. The nursing-home

employees at participating nursing homes found suitable participants, between six and 12 persons at each nursing home. A total of 182 persons agreed to participate in the study, however eight changed their mind prior to first assessment and four participants were excluded because the inclusion criteria were not met.

Ethical and legal considerations

Verbal and written information about the study was given to the residents and their family members by their primary care giver. The participants themselves gave their written consent to participate in the study and were informed that they could refuse to participate at any stage. The RCT-study was approved by The Regional Committee for Medical Ethics in south east of Norway.

Measurements

Depression: Depression was measured with Cornell Scale for Depression in Dementia (CSDD), a proxy-rated scale.(36) The informants were caregivers who knew the resident well and had observed the residents for the last two weeks.(37) CSDD is valid among nursing home residents with and without dementia, and the reliability is good.(38) The questionnaire consists of 19 symptom items. Each item is rated from 0 (no symptom) to 2 (severe symptom), which gives a total range = 0-38 points. The scale allows the entry ”not possible to evaluate”.(36) A score of 8 or more on Cornell Depression Scale classified those with depression.(38)

Balance: To measure the residents´ balance we employed the Berg Balance Scale (BBS), a widely used performance-based measure of balance. The BBS consists of 14 observable tasks frequently encountered in everyday life. BBS assesses performance on a 5-level scale from 0 (cannot perform) to 4 (normal performance) on 14 different movement tasks involving functional balance control, including transfer, stepping and turning.(39) The test is simple and easy to administer and is safe for the elderly to perform.(40) The total score ranges from 0 to 56 and high score indicates good balance.(41) The scale has shown good intra-rater and inter-rater reliability when used with an elderly population in Norway.(42-43) In addition acceptable validity estimates have been reported.(44)

Muscle strength: Lower limb muscle strength was measured by the 30 seconds Chair Stand Test (CST), which equals the number of rises from the chair in 30 seconds with arms folded across the chest.(45) However, in this study the participants were allowed to use the support of armrest when necessary.(46) The test correlates well with other functional tests such as

walking speed, climbing stairs and balance.(40, 47) The 30 seconds Chair Stand Test is a valid measure of dynamic balance and functional mobility,(48) and good inter-rater reliability has been reported when used among nursing home residents with mild and moderate dementia.(43)

Mobility: Mobility/walking speed was measured by the six-meter walking test. We assessed both comfortable speed and maximum walking speed, with or without a walking aid, and the time in seconds was recorded and calculated as meters per second.(49) Good inter-rater reliability has been demonstrated when used among nursing home residents with mild and moderate dementia in Norway.(43) Walking speed is regarded as an important measure in geriatric evaluation.(50)

Activities of daily living: The Barthel Index (BI) was used to assess ability to perform the basic Activities of Daily Living (ADL), a widely used measure of ADL function.(51) The Barthel Index consists of 10 activities focusing on the residents' level of dependence, and the scores range from 0 (completely dependent) to 20 (independent).(52) The maximum score of 20 implies that the resident independently can attend to personal hygiene, eat, get dresssed, go to the bathroom, walk at least 50 m and use stairs.

Cognition: Clinical Dementia Rating scale (CDR) was used to rate the severity of cognitive impairment. It is a six point scale used to characterize domains of cognitive and functional performance applicable to Alzheimer`s disease and related dementias.(35) Norwegian studies have shown that Clinical Dementia Rating scale is a valid substitute for a dementia assessment among nursing home residents to rate dementia and dementia severity.(53-54) The Norwegian version of Mini Mental State Examination, MMSE-NR, was used to assess global cognition. MMSE-NR consists of items concerning orientation, word registration and recall, attention, naming, reading, writing, following commends and figure copying. It can be scored between 0 and 30. High score indicates better performance.(55-56) CDR is thus a measure to rate dementia and dementia severity, while MMSE assess global cognition. As the dementia severity increases, the global cognition performance reduces.

Demographic factors

Participants' age and gender, length of stay in a nursing home (from date of admission), number of drugs, number of chronic disorders (musculoskeletal, neurological, cardiovascular and psychiatric diagnoses), use of walking aids and the residents' ability to rise from chair

independently were registrated. Demographic factors were extracted from the residents' journals.

Procedure

All assessments of physical function were performed by research physiotherapists. To ensure high inter-rater test reliability the testers took part in a training program on testing procedures before the study was initiated. The cognitive tests were administered by nursing home staff who had previous experience in using these tests. The proxy assessments, including CSDD and Barthel Index, were filled out by nursing home staff who knew the participants well. Primary caregivers extracted information from the resident records.

Statistics

All statistical analyses were conducted with SPSS, Statistical Package for the Social Science, version 22 for Windows. Data are presented with percentages and proportions for categorical values and means with standard deviation (SD) for interval data. The t-test was applied for interval data, and the Chi-square test for categorical data to access statistical differences between groups. Correlation analyses (Pearsons´s r) were conducted to examine the associations between the variables of physical function in order to discover multicollinearity.

Linear regression analyses were applied to explore bivariate and multivariate associations between Cornell Scale score and the independent variables. Each of the univariate regression models was examined separately to make sure the conditions for linear regression analysis existed. We analyzed linearity, homoscedasticity and the normal distribution of the residuals by inspecting Normal Probability Plots, different scatterplots and histograms.(57) Extreme values were examined in line with Outliers Labeling Tecnique.(58) We identified one extreme value based on the Cornell sumscore, two based on maximum walking speed and one based on comfortable walking speed. However, according to Pallant,(57) it is not necessary to correct for these as long as the numbers are few and the group is large enough. We considered the group to be large (N=170) and have therefore not adjusted for these in the further analyses.(57) From the unadjusted linear regression analyses we selected variables having the strongest association with the outcome ($p < 0.05$) and fitted multiple linear regression models in addition to the variables of age and gender. Three different multiple linear regression models were fitted because of high correlation (multicollinearity) between the variables of physical performance (see table 2). BBS was included in the first model, CST in the second model and maximum walking speed was included in the third model. This measure was taken to identify a model that explained the largest proportion of the variance in the Cornell scale.

To compare the strength of the associations between the various possible predictors and the main outcome (Cornell scale), we used the standardized betas from the regression models with their p-values and the adjusted coefficient of determination (R^2).

The CSDD is commonly used in nursing homes to distinguish between groups of depressed and not depressed. This is important in the detection and treatment of depression in persons with dementia. Because of this clinical relevance we found it necessary to perform logistic regression analysis to see if the results from logistic regression analysis differed significante from the results of linear regression analysis. The odds ratio (OR), based on logistic regression analysis, showed the strength of association between the groups with and without depression and physical function. A score of 8 or more on CSDD classified the participants with depression.(38) Two multiple logistic regression models were fitted because of multicollinearity (r = 0.7) between BBS and CST. In the first model BBS was included and in the second model we included CST, in addition to age and gender. The level of statistical significance was set at $p < 0.05$ in all analyses, and all tests were two-tailed.

RESULTS

Sample characteristics: Characteristics for whole sample, depressed and not depressed participants are shown in table 1. Of the 170 nursing home residents with dementia, 73.5% were woman with a mean age of 88.2 years. The mean duration of stay in nursing home for the whole sample was 2 years and 2 months, the depressed participants´ stay were approximately four months longer.

About 50% of the participants suffered from cardiovascular disease and almost one in four had a psychiatric diagnosis. Further approximately 40% was diagnosed with a musculoskeletal diagnosis and about one in three suffered from a neurological condition. The depressed participants had significantly more psychiatric diagnoses than the not depressed (p = 0.02). Approximately 10% of the nursing home residents with dementia used a wheelchair, and 50% used a zimmer frame.

Table 1: Characteristics for whole sample, depressed participants (Cornell Cutoff ≥ 8) and not depressed participants

	Number of registered (n)	Whole sample (N=170)	Range (min-max)	Depressed (n = 38)	Not depressed (n = 124)	*p*-value
Gender, women, n (%) #	170	125 (73.5)	**	29 (76.3)	90 (72.6)	0.65
Age in years, mean (SD)	169	86.9 (7.4)	60 – 100	86.1 (7.6)	86.7 (7.5)	0.85
Duration of stay in nursing home (months), mean (SD)	154	25.7 (24.5)	3 - 199	28.7 (23.9)	25 (25.3)	0.43
Number of chronic disorders, mean (SD)	142	3.4 (1.9)	0 - 11	3.9 (2.3)	3.3 (1.8)	0.09
Number of drugs, mean (SD)	142	6.4 (3.4)	0 - 21	7.3 (3.5)	6.1 (3.3)	0.09
Use of walking aid, n (%) #	170	118 (69.4)	**	29 (76.3)	83 (66.9)	0.27
Able to rise from chair independently, n (%) #	168	158 (92.9)	**	33 (86.8)	118 (95.2)	0.04*
Mini-Mental State Examination score in points, mean (SD)	147	15.6 (4.9)	2 - 28	15.6 (5.2)	15.7 (4.9)	0.86
Berg Balance Scale in points, mean (SD)	166	34.7 (14.0)	3 - 56	29.6 (15.7)	36 (13.3)	0.03*
Bergs Cutoff 45, number in risk of falling, n (%) # ¤	166	115 (67.6)	**	29 (76.3)	82 (66.1)	0.32
30 Seconds Chair Stand Test, number of rises from chair, mean (SD)	167	6.1 (3.0)	0 - 14	5.0 (3.0)	6.4 (3.0)	0.02*
Comfortable walking speed in m/s, mean (SD)	166	0.5 (0.2)	0.1 – 1.4	0.4 (0.2)	0.5 (0.2)	0.32
Maximum walking speed in m/s, mean (SD)	166	0.8 (0.3)	0.1 – 2.1	0.7 (0.3)	0.8 (0.3)	0.08
Barthel Index in points, mean (SD)	162	13.5 (3.5)	5 - 20	12.7 (3.3)	13.7 (3.6)	0.13
Cornell Scale for Depression in Dementia, mean (SD)	162	4.9 (4.6)	0 - 21	11.7 (3.6)	2.8 (2.1)	0.000*

Explanation of table: SD = Standard deviation, Min = minimum value, Max = maximum value, n = number of registered, N = whole sample, p = Significance level based on Independent–samples T-test between depressed and not depressed (# = Significance level based on Chi-Square-Test), * = $p < 0.05$, ** = range as a measure is not applicable since the variable represents categorical data, gender (1 = female and 2 = male), age expressed in years, length of nursing home stay in months, diagnoses and medications given in number, the use of walking aids (0 = no and 1 = yes), able to rise from chair independently (0 = no and 1 = yes), MMSE = Mini Mental State Examination: range 0-30; low score indicates poor cognitive function, Bergs Balance Test: range 0-56; high score indicates good balance, ¤ = number in risk of falling (0 = no, score ≥ 45 and 1 = yes, score < 45),(39) 30 seconds Chair Stand Test: number of rises from chair within 30 sec., comfortable and maximum walking speed in m/s; high score on the physical tests are positive (better physical function), Barthel ADL Index: range 0-20; high score indicates dependency, Cornell Scale for Depression in Dementia: range 0-38; high score indicates more depressive symptoms (0 = not depressed: Cornell score < 8, 1 = depressed: Cornell score ≥ 8)

Cognition: Regarding cognition the participants` scores on the Mini Mental State Examination ranged from 2 to 28 points. A total of 88.7% of the participants` MMSE scores fell within mild and moderate dementia (10-26 points),(59) 16 (10.9%) scored less than 10 points (indicating severe dementia) and 1.4% scored higher than 26 points. Only 60% (n=101) of the participants had a pre-existing dementia diagnosis; 25 were diagnosed with Alzheimer's disease, 22 with vascular dementia, one with subcortical dementia and one with frontotemporal dementia. A group of 52 participants did not have a specific diagnosis but were suffering from dementia according to medical records.

Depression: The score on CSDD ranged from 0 (n = 20) to 21(n = 1) points. The mean value for the whole sample was 4.9 points, and no significant gender difference was observed regarding CSDD (p = 0.45). By applying the recommended cutoff of ≥ 8 on CSDD,(38) 23.5% (n=38) of the participants were classified as being depressed, and 29 (76.3%) of them were women. The participants classified as not depressed were significantly better to rise from chair independently (p=0.04). The number of chronic diseases ranged between 0 and 11, the mean number was 3.4 diagnoses (SD = 1.9), and the average number of medications was 6.4 (SD = 3.4). There was a statistical trend ($p < 0.10$) that participants classified as depressed had more diagnoses and used more medications than the participants in the group without depression.

Physical function: Regarding the physical performance assessments, the mean values of the tests and standard deviations are shown i table 1. The mean score on BBS was 34.7 for the whole sample, and the scores ranged from 3 to 56 points. On average, the participants were able to stand up 6 times in 30 seconds and mean maximum walking speed was 0.8 m/s. The participants classified as depressed had significantly lower score on Bergs Balance Scale (p=0.03) and 30 seconds Chair Stand Test (p=0.02), indicating poorer balance function and lower limb strength compared to those without depression (Table 1). The associations between the different variables of physical function are shown in table 2. The highest correlation was found between BBS, CST and maximum walking speed, which had consequences for the further analyses (see statistics).

Table 2: Correlations between the different physical function measures and CSDD

(The Pearsons Correlation Co-efficients)

	Bergs Balance Test (n=166)	Chair Stand Test (n=167)	Comfortable walking speed (n=166)	Maximum walking speed (n=166)	Barthel ADL Index (n=162)
Chair Stand Test (n= 167)	0.7 ($p < 0.01$)				
Comfortable walking speed (n=166)	0.6 ($p < 0.01$)	0.7 ($p < 0.01$)			
Maximum walking speed (n=166)	0.7 ($p < 0.01$)	0.7 ($p < 0.01$)	0.8 ($p < 0.01$)		
Barthel ADL Index (n=162)	0.7 ($p < 0.01$)	0.6 ($p < 0.01$)	0.5 ($p < 0.01$)	0.6 ($p < 0.01$)	
Cornell Scale for Depression (n=162)	-0.2 ($p < 0.01$)	-0.2 ($p = 0.01$)	-0.12 ($p = 0.12$)	-0.2 ($p = 0.03$)	-0.13 ($p = 0.12$)

Association between physical performance and level of depression:

The unadjusted and adjusted linear regression analyses showed a significant relationship between depressive symptoms (CSDD score) and physical function for the variables measuring balance (BBS), muscle strength (CST) and maximum walking speed. Higher scores on the CST, BBS and maximum walking speed were associated with less depressive symptoms (Table 3).

Furthermore, the unadjusted linear regression analyses provided a statistical trend ($p < 0.10$) for the association between greater severity of depressive symptoms (Cornell) and more chronic diseases (p=0.09) as well as less ability to rise from chair independently (p=0.07).

Table 3: Unadjusted and adjusted linear regression analyses of the associations between Cornell (dependent variable) and variables measuring demographic factors, cognitive and physical performance

Independent variables	Unadjusted analysis				Adjusted analysis Model 1 R^2 = .033			Adjusted analysis Model 2 R^2 = .025			Adjusted analysis Model 3 R^2 = .015		
	n	*β*	*B (95 % CI)*	*Sig.*	*β*	*B (95 % CI)*	*Sig.*	*β*	*B (95 % CI)*	*Sig.*	*β*	*B (95 % CI)*	*Sig.*
Age in years	170	-0.06	-0.61 (-2.21 – 0.99)	0.45	-	-	0.93	-	-	0.82	-	-	0.83
Gender (1=women and 2=men)	169	0.05	0.03 (-0.07 – 0.12)	0.56	-	-	0.65	-	-	0.87	-	-	0.82
Duration of stay in nursing home (months)	154	0.06	0.01 (-0.02 – 0.04)	0.50									
Number of diagnoses	142	0.15	0.35 (-0.05 – 0.76)	0.09									
Number of drugs	142	0.11	0.14 (-0.09 – 0.37)	0.23									
Use of walking aid (0=no and 1=yes)	170	0.10	0.97 (-0.56 – 2.5)	0.21									
Able to rise from chair independently (0=no and 1=yes)	168	0.14	2.68 (-0.25 – 5.60)	0.07									
Mine-Mental State Examination (MMSE) in Points	147	-0.01	-0.01 (-0.17 – 0.15)	0.90									
Bergs Balance Test (BBS) in Points	166	-0.22	-0.07 (-0.12 – -0.02)	0.005*	-0.22	-0.07 (-0.12 – -0.02)	0.006*						
30 Seconds Chair Stand Test (CST) in number	167	-0.20	-0.30 (-0.53 – -0.07)	0.01*				-0.20	-0.31 (-0.54 – -0.07)	0.01*			
Comfortable walking speed in m/s	166	-0.12	-3.01 (-6.81 – 0.80)	0.12									
Maximum walking speed in m/s	166	-0.18	-2.39 (-4.48 – -0.30)	0.03*							-0.18	-2.38 (-4.56 – -0.20)	0.03*
Barthel ADL Index in Points	162	-0.13	-0.16 (-0.36 – 0.04)	0.12									

Explanation of table: Model 1 is not including CST and maximum walking speed because of their high correlation with BBS (r=0.7). Modell 2 is not including BBS and maximum walking speed because of their high correlation with CST (r=0.7). Modell 3 is not including BBS and CST because of their high correlation with maximum walking speed (r=0.7), n = number of registered, R^2 = adjusted coefficient of determination, *B* = Unstandardised beta, *CI* = 95% confidence interval, β = standardised beta, *Sig.* = levels of significance (p-value), * = $p < 0.05$, MMSE: range 0-30; low score indicates poor cognitive function, BBS range 0-56; high score indicates good balance, 30 seconds CST: number of rises from chair within 30 sec., comfortable and maximum walking speed in m/s; high score on the physical tests are positive (better physical function), Barthel ADL Index: range 0-20; high score indicates dependency, Cornell Scale for Depression in Dementia: range 0-38; high score indicates more depressive symptoms

Associations between physical function and being depressed or not being depressed:

The unadjusted and adjusted logistic regression analyses revealed significant differences between the group classified as depressed (Cornell ≥ 8) and the group classified as not depressed in terms of the variables measuring balance (BBS) and muscle strength (CST). The group classified as not depressed revealed higher scores on The Berg Balance Test and 30 Seconds Chair Stand Test compared to the group classified as depressed (Table 4).

Table 4: Logistic unadjusted and adjusted regression analyses of the strength of associations between the groups with depression (Cornell ≥ 8) and without depression (Cornell < 8) and variables measuring demographic factors, cognitive and physical performance

Independent variables	**Unadjusted analysis**			**Adjusted analysis Model 1**			**Adjusted analysis Model 2**		
	B	*OR (95% CI)*	*Sig.*	*B*	*OR (95% CI)*	*Sig.*	*B*	*OR (95% CI)*	*Sig.*
Age in years	-0.20	0.822 (0.35 – 1.91)	0.65	-0.02	0.983 (0.93 – 1.04)	0.51	-0.01	0.988 (0.94 – 1.04)	0.65
Gender (1=women and 2=men)	-0.01	0.995 (0.95 – 1.05)	0.85	-0.27	0.765 (0.31 – 1.92)	0.57	-0.10	0.907 0.37 – 2.25)	0.83
Duration of stay in nursing home (months)	0.01	1.006 (0.99 – 1.02)	0.43						
Number of diagnoses	0.17	1.183 0.97 – 1.44)	0.09						
Number of drugs	0.10	1.104 (0.98 – 1.24)	0.09						
Use of walking aid (0=no and 1=yes)	0.47	1.592 (0.69 – 3.67)	0.28						
Able to rise from chair independently (0=no and 1=yes)	1.27	3.576 (0.98 – 13.10)	0.054						
Mini-Mental State Examination in Points	-0.01	0.993 (0.92 – 1.07)	0.86						
Bergs Balance Test in Points	-0.03	0.969 (0.95 – 0.99)	0.02*	-0.03	0.968 (0.94 – 0.99)	0.01*			
30 Seconds Chair Stand Test in number	-0.16	0.853 (0.75 – 0.97)	0.02*				-0.16	0.848 (0.74 – 0.97)	0.02*
Comfortable walking speed in m/s	-1.08	0.340 (0.04 – 2.77)	0.31						
Maximum walking speed in m/s	-1.07	0.342 (0.10 – 1.14)	0.08						
Barthel Index in Points	-0.08	0.924 (0.83 – 1.03)	0.14						

Explanation of table: Model 1is not including CST because of high correlation with BBS (r=0.7). Model 2 is not including BBS because of high correlation with CST (r=0.7), *B* = Unstandardised beta, *OR* = Odd ratio, *CI* = 95% confidence interval, *Sig*. = levels of significance (p-value), * = p < 0.05, MMSE: range 0-30; low score indicates poor cognitive function, BBS range 0-56; high score indicates good balance, 30 seconds CST: number of rises from chair within 30 sec., comfortable and maximum walking speed in m/s; high score on the physical tests are positive (better physical function), Barthel ADL Index: range 0-20; high score indicates dependency, CSDD: range 0-38: 0 = not depressed: Cornell score < 8, 1 = depressed: Cornell score ≥ 8

Furthermore the unadjusted logistic regression analysis provided a statistical trend, p < 0.10, were the group with depression have multiple diagnoses and use more medications (p = 0.09), have a lower maximum walking speed (p = 0.08) and are less able to rise from chair independently (p = 0.05), compared to the group without depression.

DISCUSSION

Nursing home residents with dementia are a heterogeneous group in terms of physical function and depression. By applying the recommended cutoff of ≥ 8 on CSDD, 23.5% of the participants were classified as being depressed. Large differences in physical and mental health among institutional residents have also been underlined by other authors,(19, 40, 60) as well as the prevalence of depression in nursing home residents with dementia.(6, 9, 19, 61) A Swedish study among persons aged 85 and over showed a 27% prevalence of depression in general but a 42% prevalence among those living in institutions.(7) Studies have shown that depression among those in residential care is associated with decreased cognitive status, functional capacity, clinician-rated health,(62) and increased mortality.(63) The common comorbidity of depression and dementia further increases risks of functional disability and nursing home admissions.(64)

Our results revealed significant associations between higher scores on the CSDD, indicating more symptoms of depression, and lower scores on BBS (p=0.006), 30 seconds CST (p=0.001) as well as maximum walking speed (p=0.003), indicating lower level of physical function. This corresponds well with the notion that high level of physical activity is associated with preservation of physical function in daily life,(22, 27, 65-67) and a low prevalence of depressive symptoms.(16-17) Further, with the exception of walking speed, the differences in physical function remained significant between the groups classified as depressed (CSDD ≥ 8) and not depressed (CSDD < 8) in the logistic regression analyses. The findings confirmed our assumption that depression and depressive symptoms among nursing home residents with dementia are significantly associated with functional performance.

Our findings regarding age, gender and duration of stay in nursing home corresponded well with results from similar studies and reports among nursing home residents.(40, 68-71) Depression is a complex phenomenon in terms of causes and symptoms.(72) The adjusted determination coefficient (R^2) was low, and approximately the same, in all three models (Table 3) indicating that depression is a complex phenomenon. Overall our results underline the fact that depression has many explanatory mechanisms. Physical function alone cannot explain depression, although there are significant associations.(73)

We found no significant associations between ADL-function and depression, which is in line with the study of Barca and colleagues,(9) and in contrast to other studies.(8, 29) However,

the Barthel Index is a proxy-reported measurement, and may not be sensitive enough to identify the true abilities of an individual.(30) The readiness of the nursing home staff to assist as well as the institutionalization of the residents may influence the scores on Barthel Index. Our study showed no significant associations between depression and the degree of cognitive impairment. This is in line with another study that included participants with dementia,(74) but it is inconsistent with results from a study that included both cognitively intact and dementia sufferers.(9)

Several factors can influence physical function. Psychotropic medications, benzodiazapines or antipsychotic medications may affect balance and physical functioning. Inactivity, the precursor for reduced physical function, can be a direct result of depression as common symptoms are lack of interest in activities and loss of energy.(6,8,12) Unfortunately, there are no available data on the types of medications that the participating residents used. The category “chronic disorders” embraces musculoskeletal diagnoses, cardiovascular disorders, psychiatric diagnoses and co-morbid neurological conditions such as for example epilepsy, stroke, and Parkinson`s Disease. These are all disorders that can affect balance and physical function. However there were no significant differences between the group of depressed and not depressed regarding musculoskeletal, neurological or cardiovascular diagnoses. Depressed participants had significantly more psychiatric diagnoses than the not depressed ($p = 0,02$), which were expected considering depression was included in this category.

When more than one statistical test is conducted in analysing data from clinical studies, some demand that a more stringent criterion should be used for statistical significance than the conventional $p < 0,05$. However according to Perneger and coworkers adjustments for multiple tests (Bonferroni adjustments) creates more problems than it solves. They state that simply describing what tests of significance that have been performed, and why, is generally the best way of dealing with multiple comparisons.(75) Although we have conducted several tests, we have therefore not performed adjustments for statistical significance (the Bonferroni method), but recommend reflective and cautious interpretation of the results. There are some variables missing from the dataset. Regarding the physical tests, the main reason for this is the fact that the residents were not available in the testing moment the specific day. Some residents were not capable of performing the MMSE test because of hearing and vision impairment. The MMSE measurement is sensitive to factors like education level, age, sensory impairment, literacy problems, lack of motivation, impaired vision and hearing and depressive

disorders.(56) These factors may also explain the lack of correlation with depression in this study.

Strength and limitations of the study

The study included a well-defined population of older nursing homes residents with mild and moderate dementia defined by score of 1 or 2 on the Clinical Dementia Rating Scale.(35) The inclusion criteria made it possible to include participants with a broad range of mental and functional capacities. In addition, the study population seems to represent nursing home residents with respect to age and gender, which is a further strength.(40, 69) Measuring instruments employed in this study are standardized and commonly used in clinical practice among frail elderly in nursing homes.

The present study has several limitations. The participants were enrolled in a physical exercise intervention trail (EXDEM), so they were likely to be fitter and maybe more motivated than those who would not have agreed to be part of the intervention. In addition, due to safety and the importance of the participants receiving instruction during exercise, the residents with severe communication problems were excluded. Because of this, the associations revealed in this study may not be applicable to the overall population of nursing home residents with dementia. Many of the participants in our study did not have a prior dementia diagnosis. However, all the residents had been diagnosed using the CDR, a commonly used instrument in nursing homes. CDR score have been found to be in agreement with the golden standard of dementia diagnosis.(76) According to score on CDR all the residents were suffering from mild and moderate dementia. However, on MMSE 11% scored lower than 10 points, which may indicate severe dementia. This means that 16 participants may have been wrongly categorized as sufferers of mild/moderate dementia, which may have influenced the results. Drugs and diagnoses were to be reported in the case report. Regretfully, some of the designated health care workers failed to complete the case report. This resulted in lacking information about drugs and diagnoses in some cases, which could be of importance regarding the interpretation of the results. Because of the cross-sectional design of the study we cannot draw conclusions about causality.

Despite the limitations, the study represent important information about associations between depression and physical function in a population of elderly nursing home residents with mild to moderate dementia.

CONCLUSION

Our study has shown that nursing homes residents with good physical function (balance, muscle strength and walking speed) experienced less depressive symptoms. These results suggest that interventions aiming to increase physical performance may influence symptoms of depression in older people who live in nursing homes and that preventative strategies at latest should be implemented when nursing home residents shows decline in balance and muscle strength. Further studies should investigate possible methods how to motivate nursing home residents to participate in physical activity and how health workers in nursing home might contribute to improve physical functioning and thus to decrease depressive symptoms in nursing home residents. The potential interaction of dementia with poor physical function and depression indicates an area to explore in future epidemiological studies with a prospective design.

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			Page 4-5
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 5
Methods			Page 5-9
Study design	4	Present key elements of study design early in the paper	Page 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	Page 5-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 6-8
Bias	9	Describe any efforts to address potential sources of bias	Page 8 and 16-17
Study size	10	Explain how the study size was arrived at	Page 5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 8-9 and 16
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Page 8-9
		(*b*) Describe any methods used to examine subgroups and interactions	Page 8-9
		(*c*) Explain how missing data were addressed	Page 16-17
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	Page 8-9
		(*e*) Describe any sensitivity analyses	Page 8-9
Results			Page 9-14

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 5-6
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 9-10
		(b) Indicate number of participants with missing data for each variable of interest	Page 10
Outcome data	15*	Report numbers of outcome events or summary measures	Page 11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 12-13
		(*b*) Report category boundaries when continuous variables were categorized	Page 14
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Page 12
Discussion			Page 15-17
Key results	18	Summarise key results with reference to study objectives	Page 15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 16-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 15-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 17
Other information			Page 18
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Associations Between Physical Function and Depression in Nursing Home Residents with Mild and Moderate Dementia: A cross-sectional study

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ABSTRACT

Objectives: The primary aim of this study is to describe depression and physical function in nursing home residents with dementia, as well as to examine the associations between depression and balance function, lower limb muscle strength, mobility and activities of daily living. The secondary aim is to examine differences in physical function between the groups classified as depressed and not depressed.

Design: The study has a cross-sectional design.

Setting: A convenience sample of eighteen nursing homes in, and around, Oslo, Norway participated.

Participants: We included 170 nursing home residents aged 60-100 years suffering from mild or moderate degree of dementia defined by score of 1 or 2 on the Clinical Dementia Rating Scale (CDR).

Outcome Measures: Assessments used were Cornell Scale for Depression in Dementia (CSDD), Bergs Balance Scale (BBS), "the 6-meter walking test" (walking speed), 30 seconds Chair Stand Test (CST) and the Barthel Index.

Results: Nursing home residents with dementia are a heterogeneous group in terms of physical function and depression. By applying the recommended cutoff of ≥ 8 on CSDD, 23.5% of the participants were classified as being depressed. The results revealed significant associations between higher scores on the CSDD (indicating more symptoms of depression) and lower scores on BBS (95% CI: -0.12 to -0.02, p=0.006), 30 seconds CST (95% CI: -0.54 to -0.07, p=0.001) as well as maximum walking speed (95% CI: -4.56 to -0.20, p=0.003) (indicating lower level of physical function).

Conclusion: Better muscle strength, balance and higher walking speed were significantly associated with less depressive symptoms. The potential interaction of dementia with poor physical function and depression indicates an area to explore in future epidemiological studies with a prospective design.

Keywords: Nursing home, dementia, depression, physical function, balance, muscle strength, mobility, walking-speed, activities of daily living.

Strengths and limitations of this study

- This study reports important information about the associations between physical function, assessed by performance-based tests, and depression in nursing home residents with dementia.
- The study included a well-defined population of older nursing homes residents with mild and moderate dementia defined by score of 1 or 2 on the Clinical Dementia Rating Scale.
- Measuring instruments employed in this study are standardized and commonly used in clinical practice among frail elderly in nursing homes.
- The participants were enrolled in a physical exercise intervention trial (EXDEM), so they were likely to be fitter than the average nursing home population.
- Because of the cross-sectional design of the study we cannot draw conclusions about causality.

INTRODUCTION

Dementia impact has received increasing attention of governments and politicians across the world in recent years. Societies globally face an increasing proportion of older people who, by reason of age alone, are at increasing risk of dementia.(1) On an international level the prevalence of dementia among older adults in long-term care homes has a median of 58%,(2) but the underdiagnosis of dementia in nursing homes is commenly reported in literature worldwide.(3-5) Approximately 80% of people living in nursing homes in Norway suffer from dementia.(6) The prevalence of depressive disorders among nursing home residents is 10% while the prevalence of depressive symptoms is 29% on an international level.(2) Depression is frequently occurring in nursing home residents with dementia (43%),(7) and is associated with reduced quality of life,(8) poor medical health and more severe cognitive impairment.(9) The World Health Organization (WHO) defines depression as: ”a mental disorder, characterized by sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, feelings of tiredness and poor concentration”.(10) Reduced physical function and dependency in old age as well as somatic disorders are the main risk factors for developing depression.(9, 11) Loneliness and lack of social support are other risk factors.(12-13) Depression is a multifactorial concept and results from a complex interaction of social, psychological and biological factors.(14) According to WHO there are interrelationships between depression and physical health.(15)

Among elderly people in general, better physical function is associated with lower incidence of depressive symptoms.(16-17) It is also related to better mental health, quality of life and wellbeing.(18-19) Despite recommendations of regular physical activity, research shows that nursing home residents are spending most of their time seated or lying down, even when they are capable of independent or assisted activity.(20) It is alarming that residents who are capable of performing ADL activities independently or with assistance, often do not get the opportunity to participate actively, especially since physical function is a modifiable factor reliant on the continuous use of the musculoskeletal system.(21)

It is well known that physical function is modifiable through exercise. Even though the importance of physical activity for the preservation of function in elderly is well documented,(21-28) the relationship between physical function and depression in nursing home residents with dementia is unclear and results from studies are ambiguous. Some studies indicate that nursing home residents with good physical function are less depressed than those

with low level of physical function,(8, 29) while others do not find any significant associations between the two factors.(9)

Studies that have investigated the relationship between physical function and depression in persons with dementia in nursing homes have largely employed proxy-reported measures of physical function, and not performance-based tests. Performance-based tests are more sensitive than self- or proxy-reported measures of physical function and may be better to identify the true abilities of an individual.(30) The relationship between physical function, tested with performance-based tests, and depression in nursing home residents with dementia seem to constitute a provisional "gap" in knowledge. The topic is important because depression in nursing home residents with dementia is common,(31-32) and good alternatives to psychotropic drugs are called for.(32-34)

It is important to identify modifiable factors underlying or associated with depression in the growing population of nursing home residents with dementia. Therefore, the primary aim of this study was to describe physical function and depression in this population, as well as to examine the associations between depression and levels of balance, muscle strength, mobility and daily life activity. The secondary aim was to examine differences in physical function between the group classified as depressed and not depressed. Although the authors have an assumption that there is a negative relationship between depression and physical function, the study is explorative and thus no hypotheses are tested.

METHODS

Design

The study has a cross-sectional design. The data were collected from baseline measurements of a randomized controlled trial (EXDEM) that was carried out in Norway in 2012 and 2013.

Setting and Participants

A convenience sample of eighteen nursing homes in Oslo, as well as in the counties of Akershus, Oppegård and Buskerud participated. We included one hundred and seventy nursing-home residents. The inclusion criteria were the following: mild or moderate degree of dementia (defined by score of 1 or 2 on the Clinical Dementia Rating Scale),(35) age above 55 years, able to stand up independently or with help from one person, able to walk six meters with or without a walking aid, and able to give informed consent. The exclusion criteria were the following: residents suffering from psychosis or severe communication problems and

residents who were medically unstable. The nursing-home employees at participating nursing homes found suitable participants, between six and 12 persons at each nursing home. A total of 182 persons agreed to participate in the study, however eight changed their mind prior to first assessment and four participants were excluded because the inclusion criteria were not met.

Ethical and legal considerations

Verbal and written information about the study was given to the residents and their family members by their primary care giver. The participants themselves gave their written consent to participate in the study and were informed that they could refuse to participate at any stage. The Regional Committee for Medical Ethics in south east of Norway approved the RCT-study.

Measurements

Depression: Depression was measured with Cornell Scale for Depression in Dementia (CSDD), a proxy-rated scale.(36) The informants were caregivers who knew the resident well and had observed the residents for the last two weeks.(37) CSDD is valid among nursing home residents with and without dementia, and the reliability is good (Cronbach`s α values were 0.81 and 0.95).(38) The questionnaire consists of 19 symptom items. Each item is rated from 0 (no symptom) to 2 (severe symptom), which gives a total range = 0-38 points. The scale allows the entry ”not possible to evaluate”.(36) A score of 8 or more on Cornell Depression Scale classified those with depression.(38)

Balance: To measure the residents´ balance we employed the Berg Balance Scale (BBS), a widely used performance-based measure of balance. The BBS consists of 14 observable tasks frequently encountered in everyday life. BBS assesses performance on a 5-level scale from 0 (cannot perform) to 4 (normal performance) on 14 different movement tasks involving functional balance control, including transfer, stepping and turning.(39) The test is simple and easy to administer and is safe for the elderly to perform.(40) The total score ranges from 0 to 56 and high score indicates good balance.(41) The scale has shown good intra-rater and inter-rater reliability when used with an elderly population in Norway (Cronbach`s α values were 0.87 and 0.9).(42-43) In addition acceptable validity estimates have been reported.(44)

Muscle strength: Lower limb muscle strength was measured by the 30 seconds Chair Stand Test (CST), which equals the number of rises from the chair in 30 seconds with arms folded across the chest.(45) However, in this study the participants were allowed to use the support

of armrest when necessary.(46) The test correlates well with other functional tests such as walking speed, climbing stairs and balance.(40, 47) The 30 seconds Chair Stand Test is a valid measure of dynamic balance and functional mobility,(48) and good inter-rater reliability has been reported when used among nursing home residents with mild and moderate dementia (the intraclass correlation coefficient, ICC, was 1).(43)

Mobility: Mobility/walking speed was measured by the six-meter walking test. We assessed both comfortable speed and maximum walking speed, with or without a walking aid, and the time in seconds was recorded and calculated as meters per second.(49) Good inter-rater reliability has been demonstrated when used among nursing home residents with mild and moderate dementia in Norway (ICC=0.97).(43) Walking speed is regarded as an important measure in geriatric evaluation.(50)

Activities of daily living: The Barthel Index (BI) was used to assess ability to perform the basic Activities of Daily Living (ADL), a widely used measure of ADL function.(51) The Barthel Index consists of 10 activities focusing on the residents' level of dependence, and the scores range from 0 (completely dependent) to 20 (independent).(52) The maximum score of 20 implies that the resident independently can attend to personal hygiene, eat, get dresssed, go to the bathroom, walk at least 50 m and use stairs.

Cognition: Clinical Dementia Rating scale (CDR) was used to rate the severity of cognitive impairment. It is a six point scale used to characterize domains of cognitive and functional performance applicable to Alzheimer`s disease and related dementias.(35) Norwegian studies have shown that Clinical Dementia Rating scale is a valid substitute for a dementia assessment among nursing home residents to rate dementia and dementia severity.(53-54) The Norwegian version of Mini Mental State Examination, MMSE-NR, was used to assess global cognition. MMSE-NR consists of items concerning orientation, word registration and recall, attention, naming, reading, writing, following commends and figure copying. It can be scored between 0 and 30. High score indicates better performance.(55-56) CDR is thus a measure to rate dementia and dementia severity, while MMSE assess global cognition. As the dementia severity increases, the global cognition performance reduces.

Demographic factors

Participants' age and gender, length of stay in a nursing home (from date of admission), number of drugs, number of chronic disorders (musculoskeletal, neurological, cardiovascular and psychiatric diagnoses), use of walking aids and the residents' ability to rise from chair

independently were registered. Demographic factors were extracted from the residents' journals.

Procedure

A nurse, and often the departmental nurse, who knew the participants well and was in regular contact with him/her, performed the CDR and filled in the Case Record Form. Mostly nursing staff was familiar with the questionnaires. However, they were encouraged to contact the project leader with any questions. A specially trained-nurse or an occupational therapist performed the MMSE. Research physiotherapists performed all assessments of physical function. To ensure high inter-rater test reliability the testers took part in a training program on testing procedures before the study was initiated. Nursing home staff that knew the participants well filled out the proxy assessments, including CSDD and Barthel Index. Primary caregivers extracted information from the resident records.

Statistics

All statistical analyses were conducted with SPSS, Statistical Package for the Social Science, version 22 for Windows. Data are presented with percentages and proportions for categorical values and means with standard deviation (SD) for interval data. The t-test was applied for interval data, and the Chi-square test for categorical data to access statistical differences between groups. Correlation analyses (Pearsons´s r) were conducted to examine the associations between the variables of physical function in order to discover multicollinearity.

Linear regression analyses were applied to explore bivariate and multivariate associations between Cornell Scale score and the independent variables. Each of the univariate regression models was examined separately to make sure the conditions for linear regression analysis existed. We analyzed linearity, homoscedasticity and the normal distribution of the residuals by inspecting Normal Probability Plots, different scatterplots and histograms.(57) Extreme values were examined in line with Outliers Labeling Tecnique.(58) We identified one extreme value based on the Cornell sumscore, two based on maximum walking speed and one based on comfortable walking speed. However, according to Pallant,(57) it is not necessary to correct for these as long as the numbers are few and the group is large enough. We considered the group to be large (N=170) and have therefore not adjusted for these in the further analyses.(57) From the unadjusted linear regression analyses we selected variables having the strongest association with the outcome ($p < 0.05$) and fitted multiple linear regression models in addition to the variables of age and gender. Three different multiple linear regression models were fitted because of high correlation (multicollinearity) between the variables of

physical performance (see table 2). BBS was included in the first model, CST in the second model and maximum walking speed was included in the third model. This measure was taken to identify a model that explained the largest proportion of the variance in the Cornell scale. To compare the strength of the associations between the various possible predictors and the main outcome (Cornell scale), we used the standardized betas from the regression models with their p-values and the adjusted coefficient of determination (R^2).

The CSDD is commonly used in nursing homes to distinguish between groups of depressed and not depressed. This is important in the detection and treatment of depression in persons with dementia. Because of this clinical relevance we found it necessary to perform logistic regression analysis to see if the results from logistic regression analysis differed significante from the results of linear regression analysis. The odds ratio (OR), based on logistic regression analysis, showed the strength of association between the groups with and without depression and physical function. A score of 8 or more on CSDD classified the participants with depression.(38) Two multiple logistic regression models were fitted because of multicollinearity (r = 0.7) between BBS and CST. In the first model BBS was included and in the second model we included CST, in addition to age and gender. The level of statistical significance was set at $p < 0.05$ in all analyses, and all tests were two-tailed.

RESULTS

Sample characteristics: Characteristics for whole sample, depressed and not depressed participants are shown in table 1. Of the 170 nursing home residents with dementia, 73.5% were woman with a mean age of 88.2 years. The mean duration of stay in nursing home for the whole sample was 2 years and 2 months, the depressed participants´ stay were approximately four months longer.

About 50% of the participants suffered from cardiovascular disease and one in five (n=34) had a psychiatric diagnosis (anxiety, depression, bipolar disorder) where the most common were anxiety and depression. Further approximately 40% was diagnosed with a musculoskeletal diagnosis and almost one in four suffered from a neurological condition. The depressed participants had significantly more psychiatric diagnoses than the not depressed (p=0.02). Approximately 10% of the nursing home residents with dementia used a wheelchair, and 50% used a zimmer frame.

Table 1: Characteristics for whole sample, depressed participants (Cornell Cutoff ≥ 8) and not depressed participants

	Number of registered (n)	Whole sample (N=170)	Range (min-max)	Depressed (n = 38)	Not depressed (n = 124)	*p*-value
Gender, women, n (%) #	170	125 (73.5)	**	29 (76.3)	90 (72.6)	0.65
Age in years, mean (SD)	169	86.9 (7.4)	60 – 100	86.1 (7.6)	86.7 (7.5)	0.85
Duration of stay in nursing home (months), mean (SD)	154	25.7 (24.5)	3 – 199	28.7 (23.9)	25 (25.3)	0.43
Number of chronic disorders, mean (SD)	142	3.4 (1.9)	0 –11	3.9 (2.3)	3.3 (1.8)	0.09
Number of drugs, mean (SD)	142	6.4 (3.4)	0 – 21	7.3 (3.5)	6.1 (3.3)	0.09
Use of walking aid, n (%) #	170	118 (69.4)	**	29 (76.3)	83 (66.9)	0.27
Able to rise from chair independently, n (%) #	168	158 (92.9)	**	33 (86.8)	118 (95.2)	0.04*
Mini-Mental State Examination score in points, mean (SD)	147	15.6 (4.9)	2 – 28	15.6 (5.2)	15.7 (4.9)	0.86
Berg Balance Scale in points, mean (SD)	166	34.7 (14.0)	3 – 56	29.6 (15.7)	36 (13.3)	0.03*
Bergs Cutoff 45, number in risk of falling, n (%) # ¤	166	115 (67.6)	**	29 (76.3)	82 (66.1)	0.32
30 Seconds Chair Stand Test, number of rises from chair, mean (SD)	167	6.1 (3.0)	0 –14	5.0 (3.0)	6.4 (3.0)	0.02*
Comfortable walking speed in m/s, mean (SD)	166	0.5 (0.2)	0.1 – 1.4	0.4 (0.2)	0.5 (0.2)	0.32
Maximum walking speed in m/s, mean (SD)	166	0.8 (0.3)	0.1 – 2.1	0.7 (0.3)	0.8 (0.3)	0.08
Barthel Index in points, mean (SD)	162	13.5 (3.5)	5 –20	12.7 (3.3)	13.7 (3.6)	0.13
Cornell Scale for Depression in Dementia, mean (SD)	162	4.9 (4.6)	0 – 21	11.7 (3.6)	2.8 (2.1)	0.000*

Explanation of table: SD = Standard deviation, Min = minimum value, Max = maximum value, n = number of registered, N = whole sample, p = Significance level based on Independent–samples T-test between depressed and not depressed (# = Significance level based on Chi-Square-Test), * = $p < 0.05$, ** = range as a measure is not applicable since the variable represents categorical data, gender (1 = female and 2 = male), age expressed in years, length of nursing home stay in months, diagnoses and medications given in number, the use of walking aids (0 = no and 1 = yes), able to rise from chair independently (0 = no and 1 = yes), MMSE = Mini Mental State Examination: range 0-30; low score indicates poor cognitive function, Bergs Balance Test: range 0-56; high score indicates good balance, ¤ = number in risk of falling (0 = no, score ≥ 45 and 1 = yes, score < 45),(39) 30 seconds Chair Stand Test: number of rises from chair within 30 sec., comfortable and maximum walking speed in m/s; high score on the physical tests are positive (better physical function), Barthel ADL Index: range 0-20; high score indicates dependency, Cornell Scale for Depression in Dementia: range 0-38; high score indicates more depressive symptoms (0 = not depressed: Cornell score < 8, 1 = depressed: Cornell score ≥ 8)

Cognition: Regarding cognition the participants` scores on the Mini Mental State Examination ranged from 2 to 28 points. A total of 88.7% of the participants` MMSE scores fell within mild and moderate dementia (10-26 points),(59) 16 (10.9%) scored less than 10 points (indicating severe dementia) and 1.4% scored higher than 26 points. Only 56% (n=95) of the participants had a pre-existing dementia diagnosis; 23 were diagnosed with Alzheimer's disease, 18 with vascular dementia, one with subcortical dementia and one with frontotemporal dementia. A group of 52 participants did not have a specific diagnosis but were suffering from dementia according to medical records.

Depression: The score on CSDD ranged from 0 (n=20) to 21(n=1) points. The mean value for the whole sample was 4.9 points, and no significant gender difference was observed regarding CSDD ($p = 0.45$). By applying the recommended cutoff of ≥ 8 on CSDD,(38) 23.5% (n=38) of the participants were classified as being depressed, and 29 (76.3%) of them were women. Only 13 participants in the depressed group had a pre-existing clinical diagnosis of mood disorder compared to 20 participants in the non-depressed group. The participants classified as not depressed were significantly better to rise from chair independently (p=0.04). The number of chronic diseases ranged between 0 and 11, the mean number was 3.4 diagnoses (SD=1.9), and the average number of medications was 6.4 (SD=3.4). There was a statistical trend ($p < 0.10$) that participants classified as depressed had more diagnoses and used more medications than the participants in the group without depression.

Physical function: Regarding the physical performance assessments, the mean values of the tests and standard deviations are shown i table 1. The mean score on BBS was 34.7 for the whole sample, and the scores ranged from 3 to 56 points. On average, the participants were able to stand up 6 times in 30 seconds and mean maximum walking speed was 0.8 m/s. The participants classified as depressed had significantly lower score on Bergs Balance Scale (p=0.03) and 30 seconds Chair Stand Test (p=0.02), indicating poorer balance function and lower limb strength compared to those without depression (Table 1). The associations between the different variables of physical function are shown in table 2. The highest correlation was found between BBS, CST and maximum walking speed, which had consequences for the further analyses (see statistics).

Table 2: Correlations between the different physical function measures and CSDD (The Pearsons Correlation Co-efficients)

	Bergs Balance Test (n=166)	Chair Stand Test (n=167)	Comfortable walking speed (n=166)	Maximum walking speed (n=166)	Barthel ADL Index (n=162)
Chair Stand Test (n= 167)	0.7 ($p < 0.01$)				
Comfortable walking speed (n=166)	0.6 ($p < 0.01$)	0.7 ($p < 0.01$)			
Maximum walking speed (n=166)	0.7 ($p < 0.01$)	0.7 ($p < 0.01$)	0.8 ($p < 0.01$)		
Barthel ADL Index (n=162)	0.7 ($p < 0.01$)	0.6 ($p < 0.01$)	0.5 ($p < 0.01$)	0.6 ($p < 0.01$)	
Cornell Scale for Depression (n=162)	-0.2 ($p < 0.01$)	-0.2 ($p = 0.01$)	-0.12 ($p = 0.12$)	-0.2 ($p = 0.03$)	-0.13 ($p = 0.12$)

Association between physical performance and level of depression:

The unadjusted and adjusted linear regression analyses showed a significant relationship between depressive symptoms (CSDD score) and physical function for the variables measuring balance (BBS), muscle strength (CST) and maximum walking speed. Higher scores on the CST, BBS and maximum walking speed were associated with less depressive symptoms (Table 3).

Furthermore, the unadjusted linear regression analyses provided a statistical trend ($p < 0.10$) for the association between greater severity of depressive symptoms (Cornell) and more chronic diseases ($p=0.09$) as well as less ability to rise from chair independently ($p=0.07$).

Table 3: Unadjusted and adjusted linear regression analyses of the associations between Cornell (dependent variable) and variables measuring demographic factors, cognitive and physical performance

Independent variables	Unadjusted analysis				Adjusted analysis Model 1 R^2 = .033			Adjusted analysis Model 2 R^2 = .025			Adjusted analysis Model 3 R^2 = .015		
	n	*β*	*B (95 % CI)*	*Sig.*	*β*	*B (95 % CI)*	*Sig.*	*β*	*B (95 % CI)*	*Sig.*	*β*	*B (95 % CI)*	*Sig.*
Age in years	170	-0.06	-0.61 (-2.21 – 0.99)	0.45	-	-	0.93	-	-	0.82	-	-	0.83
Gender (1=women and 2=men)	169	0.05	0.03 (-0.07 – 0.12)	0.56	-	-	0.65	-	-	0.87	-	-	0.82
Duration of stay in nursing home (months)	154	0.06	0.01 (-0.02 – 0.04)	0.50									
Number of diagnoses	142	0.15	0.35 (-0.05 – 0.76)	0.09									
Number of drugs	142	0.11	0.14 (-0.09 – 0.37)	0.23									
Use of walking aid (0=no and 1=yes)	170	0.10	0.97 (-0.56 – 2.5)	0.21									
Able to rise from chair independently (0=no and 1=yes)	168	0.14	2.68 (-0.25 – 5.60)	0.07									
Mine-Mental State Examination (MMSE) in Points	147	-0.01	-0.01 (-0.17 – 0.15)	0.90									
Bergs Balance Test (BBS) in Points	166	-0.22	-0.07 (-0.12 – -0.02)	0.005*	-0.22	-0.07 (-0.12 – -0.02)	0.006*						
30 Seconds Chair Stand Test (CST) in number	167	-0.20	-0.30 (-0.53 – -0.07)	0.01*				-0.20	-0.31 (-0.54 – -0.07)	0.01*			
Comfortable walking speed in m/s	166	-0.12	-3.01 (-6.81 – 0.80)	0.12									
Maximum walking speed in m/s	166	-0.18	-2.39 (-4.48 – -0.30)	0.03*							-0.18	-2.38 (-4.56 – -0.20)	0.03*
Barthel ADL Index in Points	162	-0.13	-0.16 (-0.36 – 0.04)	0.12									

Explanation of table: Model 1 is not including CST and maximum walking speed because of their high correlation with BBS (r=0.7). Modell 2 is not including BBS and maximum walking speed because of their high correlation with CST (r=0.7). Modell 3 is not including BBS and CST because of their high correlation with maximum walking speed (r=0.7), n = number of registered, R^2 = adjusted coefficient of determination, *B* = Unstandardised beta, *CI* = 95% confidence interval, *β* = standardised beta, *Sig.* = levels of significance (p-value), * = $p < 0.05$, MMSE: range 0-30; low score indicates poor cognitive function, BBS range 0-56; high score indicates good balance, 30 seconds CST: number of rises from chair within 30 sec., comfortable and maximum walking speed in m/s; high score on the physical tests are positive (better physical function), Barthel ADL Index: range 0-20; high score indicates dependency, Cornell Scale for Depression in Dementia: range 0-38; high score indicates more depressive symptoms

Associations between physical function and being depressed or not being depressed:

The unadjusted and adjusted logistic regression analyses revealed significant differences between the groups classified as depressed (Cornell ≥ 8) and not depressed in terms of the variables measuring balance (BBS) and muscle strength (CST). High scores on the physical tests reduced the likelihood of being depressed. One-unit increase in sumscore on BBS decreased the odds ratio (OR) by 3.2% and one increase in number of rises on CST decreased the OR by 15.2% for being classified as depressed adjusted for gender and age (Table 4).

Table 4: Logistic unadjusted and adjusted regression analyses of the strength of associations between the groups with depression (Cornell ≥ 8) and without depression (Cornell < 8) and variables measuring demographic factors, cognitive and physical performance

Independent variables	Unadjusted analysis			Adjusted analysis Model 1			Adjusted analysis Model 2		
	B	*OR (95% CI)*	*Sig.*	*B*	*OR (95% CI)*	*Sig.*	*B*	*OR (95% CI)*	*Sig.*
Age in years	-0.20	0.822 (0.35 – 1.91)	0.65	-0.02	0.983 (0.93 – 1.04)	0.51	-0.01	0.988 (0.94 – 1.04)	0.65
Gender (1=women and 2=men)	-0.01	0.995 (0.95 – 1.05)	0.85	-0.27	0.765 (0.31 – 1.92)	0.57	-0.10	0.907 0.37 – 2.25)	0.83
Duration of stay in nursing home (months)	0.01	1.006 (0.99 – 1.02)	0.43						
Number of diagnoses	0.17	1.183 0.97 – 1.44)	0.09						
Number of drugs	0.10	1.104 (0.98 – 1.24)	0.09						
Use of walking aid (0=no and 1=yes)	0.47	1.592 (0.69 – 3.67)	0.28						
Able to rise from chair independently (0=no and 1=yes)	1.27	3.576 (0.98 – 13.10)	0.054						
Mini-Mental State Examination in Points	-0.01	0.993 (0.92 – 1.07)	0.86						
Bergs Balance Test in Points	-0.03	0.969 (0.95 – 0.99)	0.02*	-0.03	0.968 (0.94 – 0.99)	0.01*			
30 Seconds Chair Stand Test in number	-0.16	0.853 (0.75 – 0.97)	0.02*				-0.16	0.848 (0.74 – 0.97)	0.02*
Comfortable walking speed in m/s	-1.08	0.340 (0.04 – 2.77)	0.31						
Maximum walking speed in m/s	-1.07	0.342 (0.10 – 1.14)	0.08						
Barthel Index in Points	-0.08	0.924 (0.83 – 1.03)	0.14						

Explanation of table: Model 1is not including CST because of high correlation with BBS (r=0.7). Model 2 is not including BBS because of high correlation with CST (r=0.7), *B* = Unstandardised beta, *OR* = Odd ratio, *CI* = 95% confidence interval, *Sig.* = levels of significance (p-value), * = p < 0.05, MMSE: range 0-30; low score indicates poor cognitive function, BBS range 0-56; high score indicates good balance, 30 seconds CST: number of rises from chair within 30 sec., comfortable and maximum walking speed in m/s; high score on the physical tests are positive (better physical function), Barthel ADL Index: range 0-20; high score indicates dependency, CSDD: range 0-38: 0 = not depressed: Cornell score < 8, 1 = depressed: Cornell score ≥ 8

Furthermore the unadjusted logistic regression analysis provided a statistical trend, p < 0.10, were the group with depression had multiple diagnoses and used more medications (p = 0.09),

had a lower maximum walking speed (p = 0.08) and were less able to rise from chair independently (p = 0.05), compared to the group without depression.

DISCUSSION

Nursing home residents with dementia are a heterogeneous group in terms of physical function and depression. By applying the recommended cutoff of ≥ 8 on CSDD, 23.5% of the participants were classified as being depressed. Large differences in physical and mental health among institutional residents have also been underlined by other authors,(19, 40, 60) as well as the prevalence of depression in nursing home residents with dementia.(6, 9, 19, 61) A Swedish study among persons aged 85 and over showed a 27% prevalence of depression in general but a 42% prevalence among those living in institutions.(7) Studies have shown that depression among those in residential care is associated with decreased cognitive status, functional capacity, clinician-rated health,(62) and increased mortality.(63) The common comorbidity of depression and dementia further increases risks of functional disability and nursing home admissions.(64)

Our results revealed significant associations between higher scores on the CSDD, indicating more symptoms of depression, and lower scores on BBS (p=0.006), 30 seconds CST (p=0.001) as well as maximum walking speed (p=0.003), indicating lower level of physical function. This corresponds well with the notion that high level of physical activity is associated with preservation of physical function in daily life,(22, 27, 65-67) and a low prevalence of depressive symptoms.(16-17) Further, with the exception of walking speed, the differences in physical function remained significant between the groups classified as depressed (CSDD ≥ 8) and not depressed (CSDD < 8) in the logistic regression analyses. The findings confirmed our assumption that depression and depressive symptoms among nursing home residents with dementia are significantly associated with functional performance.

Our findings regarding age, gender and duration of stay in nursing home corresponded well with results from similar studies and reports among nursing home residents.(40, 68-71) Depression is a complex phenomenon in terms of causes and symptoms.(72) The adjusted determination coefficient (R^2) was low, and approximately the same, in all three models (Table 3) indicating that depression is a complex phenomenon. Overall our results underline the fact that depression has many explanatory mechanisms. Physical function alone cannot explain depression, although there are significant associations.(73)

We found no significant associations between ADL-function and depression, which is in line with the study of Barca and colleagues,(9) and in contrast to other studies.(8, 29) However, the Barthel Index is a proxy-reported measurement, and may not be sensitive enough to identify the true abilities of an individual.(30) The readiness of the nursing home staff to assist as well as the institutionalization of the residents may influence the scores on Barthel Index. Our study showed no significant associations between depression and the degree of cognitive impairment. This is in line with another study that included participants with dementia,(74) but it is inconsistent with results from a study that included both cognitively intact and dementia sufferers.(9)

Several factors can influence physical function. Psychotropic medications, benzodiazapines or antipsychotic medications may affect balance and physical functioning. Inactivity, the precursor for reduced physical function, can be a direct result of depression as common symptoms are lack of interest in activities and loss of energy.(6,8,12) Unfortunately, there are no available data on the types of medications that the participating residents used. The category "chronic disorders" embraces musculoskeletal diagnoses, cardiovascular disorders, psychiatric diagnoses and co-morbid neurological conditions such as for example epilepsy, stroke, and Parkinson`s Disease. These are all disorders that can affect balance and physical function. However there were no significant differences between the group of depressed and not depressed regarding musculoskeletal, neurological or cardiovascular diagnoses. Depressed participants had significantly more psychiatric diagnoses than the not depressed ($p = 0.02$), which were expected considering depression was included in this category.

When more than one statistical test is conducted in analysing data from clinical studies, some demand that a more stringent criterion should be used for statistical significance than the conventional $p < 0.05$. However according to Perneger and coworkers adjustments for multiple tests (Bonferroni adjustments) creates more problems than it solves. They state that simply describing what tests of significance that have been performed, and why, is generally the best way of dealing with multiple comparisons.(75) Although we have conducted several tests, we have therefore not performed adjustments for statistical significance (the Bonferroni method), but recommend reflective and cautious interpretation of the results. There are some variables missing from the dataset. Regarding the physical tests, the main reason for this is the fact that the residents were not available in the testing moment the specific day. Some residents were not capable of performing the MMSE test because of hearing and vision

impairment. The MMSE measurement is sensitive to factors like education level, age, sensory impairment, literacy problems, lack of motivation, impaired vision and hearing and depressive disorders.(56) These factors may also explain the lack of correlation with depression in this study.

Strength and limitations of the study

The study included a well-defined population of older nursing homes residents with mild and moderate dementia defined by score of 1 or 2 on the Clinical Dementia Rating Scale.(35) The inclusion criteria made it possible to include participants with a broad range of mental and functional capacities. In addition, the study population seems to represent nursing home residents with respect to age and gender, which is a further strength.(40, 69) Measuring instruments employed in this study are standardized and commonly used in clinical practice among frail elderly in nursing homes.

The present study has several limitations. The participants were enrolled in a physical exercise intervention trail (EXDEM), so they were likely to be fitter and maybe more motivated than those who would not have agreed to be part of the intervention. In addition, due to safety and the importance of the participants receiving instruction during exercise, the residents with severe communication problems were excluded. Because of this, the associations revealed in this study may not be applicable to the overall population of nursing home residents with dementia. Many of the participants in our study did not have a prior dementia diagnosis. All the residents had been assessed by CDR, a commonly used instrument in nursing homes. It is important to underline that one single instrument is not as accurate as a clinical diagnosis, which implies the possibility that some participants may have been wrongly diagnosed with dementia.(76) However, the CDR score have been found to be in agreement with the golden standard of dementia diagnosis.(77) According to score on CDR all the residents were suffering from mild and moderate dementia. However, on MMSE 11% scored lower than 10 points, which may indicate severe dementia. This means that 16 participants may have been wrongly categorized as sufferers of mild/moderate dementia, which may have influenced the results. Drugs and diagnoses were to be reported in the case report. Regretfully, some of the designated health care workers failed to complete the case report. This resulted in lacking information about drugs and diagnoses in some cases, which could be of importance regarding the interpretation of the results. Because of the cross-sectional design of the study we cannot draw conclusions about causality.

Despite the limitations, the study represent important information about associations between depression and physical function in a population of elderly nursing home residents with mild to moderate dementia.

CONCLUSION

Our study has shown that nursing home residents with good physical function (balance, muscle strength and walking speed) experienced less depressive symptoms. Depression is complex and a multi-causal disorder. However, the implications of this study emphasize that physical activity is important for maintaining physical function for this vulnerable group and should at least be part of an intervention to improve depressive symptoms. Further studies should investigate possible methods how to motivate nursing home residents to participate in physical activity and how health workers in nursing home might contribute to improve physical functioning and hence possibly decrease depressive symptoms in nursing home residents. The potential interaction of dementia with poor physical function and depression indicates an area to explore in future epidemiological studies with a prospective design.

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			Page 4-5
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 5
Methods			Page 5-9
Study design	4	Present key elements of study design early in the paper	Page 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	Page 5-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 6-8
Bias	9	Describe any efforts to address potential sources of bias	Page 8 and 16-17
Study size	10	Explain how the study size was arrived at	Page 5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 8-9 and 16
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Page 8-9
		(*b*) Describe any methods used to examine subgroups and interactions	Page 8-9
		(*c*) Explain how missing data were addressed	Page 16-17
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	Page 8-9
		(*e*) Describe any sensitivity analyses	Page 8-9
Results			Page 9-15

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 5-6
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 9-10
		(b) Indicate number of participants with missing data for each variable of interest	Page 10
Outcome data	15*	Report numbers of outcome events or summary measures	Page 11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 12-13
		(*b*) Report category boundaries when continuous variables were categorized	Page 14
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Page 12
Discussion			Page 15-18
Key results	18	Summarise key results with reference to study objectives	Page 15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 16-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 15-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 17
Other information			Page 18-19
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.