

Frailty and depression in later life

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Introduction

Frailty can be considered as a condition of increased risk of adverse health outcomes, such as falls, reduced mobility, reduced independence, hospitalization, disability and death. (1) The explanation of the increased health risks is sought in a reduction of the reserve capacity of various physiological systems. Frailty is prevalent when the reserve capacity has decreased to a critically low point, where even small disturbances can lead to a series of complications. This theoretical foundation is not yet supported by a clear underlying pathophysiological process. (2) Notwithstanding the limited knowledge of underlying processes, consensus has been reached about the clinical relevance of the concept of frailty. Research on this subject, however, has led to a variety of frailty definitions. (3) (4) (1) (5) (2) Most definitions are at a syndromal level, namely the presence of a subset of characteristics that have been identified as independent predictors of future adverse health outcomes in epidemiological research projects. When occurring simultaneously, these characteristics do have a stronger negative impact on the future health of the older adult than the sum of each of these characteristics individually. (1) An ongoing debate is whether frailty should be conceptualized as a purely physical condition, or as a broader phenotype including also psychological and psychosocial characteristics. (6) (7) Estimates in population studies, using various criteria for frailty, report prevalence rates ranging from 7% to 32%. Nonetheless, these studies report a consistently increased prevalence of frailty with higher age as well as higher prevalence rates in women. (1) (5) (8) (9)

Like frailty, depression is a highly prevalent condition among older adults (up to 15%), (10) (11) and an important predictor of mortality in older adults. (12) Depression decreases the quality of life significantly, (13) (14) just like frailty lowers life satisfaction. (15) Furthermore, analogue to the concept of frailty, depression is a syndromal diagnosis. Depending on the definition and operationalization of frailty both syndromes partially overlap, even if frailty is defined as a purely physical condition (table 1). For example, physical complaints such as fatigue, weight loss and poor endurance, may be related to depression, to frailty or to both. Despite similarities in several domains, there is a lack of research into the relationship between frailty and depression. In current geriatric mental health care it is possible for a depressed older person, who might in fact be frail with only mood disturbance, to be treated solely with anti-depressive medication. In somatic conditions it has already been shown that the optimal treatment can be very different for frail and for non-frail persons. (16) Despite scarce evidence on the appropriate treatment of frailty, it is most likely that a multidisciplinary approach is best applied for persons with frailty, and physical training programs are essential components of evidence-based interventions. (17) (18) It has been stated before that the emphasis should be on those health care professionals who can identify early stages of frailty, before it is too late. (19) Because nurses are professionals in dealing with

consequences of diseases and supporting patients in their daily activities, they are particularly well equipped for this job.

<table 1>

In order to examine the relationship between depression and frailty, it should be specified whether researchers define depression as a core component of frailty, (20) as a precipitant or risk factor (8) or a result of frailty. In this study the frailty criteria by Fried and colleagues (1) were applied. These criteria are widely used in geriatric research and encompass a purely physical phenotype of frailty. (21) (22) (8) (23)

Problem statement, aims and hypotheses

Insight into the (reciprocal) relationship between depression and frailty will guide the development of intervention strategies for frailty and add to the concept of late-life depression. Because the characteristics of frailty and depression partially overlap, the prevalence of depression might be (falsely) inflated in the case of frailty. If this is the case, classical correlates of depressive disorder might be less prevalent in persons suffering from both depression and frailty, as compared to depressed persons who are not frail. Furthermore, it may be hypothesized that among persons who are both depressed and frail, there is a higher prevalence of somatic comorbidity and late-onset type of depressive disorder compared to depressed elderly persons without frailty. In current health care there is a lack of information on this subject, while nurses and other health care professionals are confronted with decisions concerning the care for depressed (frail) elderly on a daily basis.

The objectives of the present study are 1) to determine the prevalence of frailty in depressed older adults and compare this to the prevalence of frailty in non-depressed older adults, and 2) to compare classical correlates of depressive disorder between depressed elderly with and without frailty, in order to enable health care professionals to differentiate between these two groups.

As part of the depressive symptoms in depressed elderly might be related to frailty processes, it is hypothesized that a higher number of somatic comorbid diseases will be found, there will be a late-onset type of depressive disorder (late-onset type is associated with underlying somatic diseases) more often, a lower severity of neuroticism, less often cognitive symptoms of depression like feelings of guilt and worthlessness, and finally less comorbidity with anxiety disorders in depressed elderly with frailty compared to their non-frail counterparts.

Methods

The present study was embedded within a larger, multisite research project: the Netherlands Study of Depression in Older people (NESDO). The aim of NESDO is to build a research infrastructure and a high quality database, allowing researchers to examine the role of the independent contribution and interaction of determinants of depressive disorders, and its course and consequences in a large cohort of older persons within an epidemiological approach. The ethical review boards of the participating institutes approved of this study.

In this prospective cohort study, 450 depressed persons, aged 60 years and older, will be followed-up for a period of four years, every two years. After oral and written information, participants signed informed consent.

Included were persons with current DSM-IV diagnosis of major depressive disorder, minor depression (research criteria) or dysthymia. The project aims to follow a cohort of older adults with depressive disorder in different stages of the disease and severity ranging from mild to severe depression, in order to cover the complete spectrum of depressive disorder. Therefore, depressed participants were recruited from mental health institutes (both in- and outpatients) and from primary care. Persons with a primary diagnosis of dementia, a Mini Mental State Examination-score (MMSE) under 19 or an organic or psychotic disorder were excluded, since the course of these persons will be largely determined by the primary disorder. Insufficient mastery of the Dutch language is also an exclusion criterion.

During a four-six hour baseline examination, including written questionnaires, interviews, a medical examination, cognitive tests and collection of blood and saliva samples, extensive information was gathered about key (mental) health outcomes and demographic, psychosocial and biological research paradigms.

Interviews and assessments will be done at the participating clinics by extensively trained and supervised research assistants. If the baseline examination is too much of a burden for the participants or if the available time is not sufficient, a second appointment will be made at the homes of the participants in order to complete the examination. The same procedures will be followed at the follow-up assessments. A non-depressed control group (n=150) will be recruited and followed up once every two years, for four years.

Baseline data is expected to be concluded in august 2010. On April 1st 2010, baseline data of 321 depressed older persons and 55 non-depressed older persons had been gathered. This sample was considered the population of interest for the present study, which can be considered a cross-sectional, observational study.

Below only the data of interest for the present manuscript will be reported in more detail.

Measures

Depression

The Composite International Diagnostic Interview (CIDI), version 2.1 was used in order to determine the presence of depression. (24) The CIDI is a fully structured interview that diagnoses psychiatric disorders in adults according to the criteria of Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) and the criteria of the International Classification of Diseases-10 (ICD-10). The World Health Organization (WHO) field trials found high inter-rater reliability (kappa: 0.97), (25) high test–retest reliability (kappa: 0.66) and high validity for depressive and anxiety disorders. (26) (25)

Frailty

Frailty was assessed according to the criteria of Fried et al. (1)

Unintentional weight loss was assessed by a CIDI question and body mass index (BMI). The presence of one of these two items led to a positive score on this frailty criterion. The CIDI question about unwanted weight loss was used to determine the loss of a minimum of one kilogram a week, during two or more consecutive weeks. BMI was defined as weight in kilograms divided by height in meters squared. With a BMI of $<18,5 \text{ kg/ m}^2$ this item was also considered to be present.

A handgrip dynamometer was used to assess weakness. Participants were asked to perform two squeezes with the dynamometer, using the dominant hand. The best performance, recorded as strength in kilograms, was used for analysis. Participants unable to perform the test, male participants with a grip strength of 21 kilograms or less and female participants squeezing 14 kilograms or less were considered weak. (22)

Poor endurance and energy (exhaustion) were determined by two questions from the Center for Epidemiologic Studies-Depression scale (CES-D), (27) similar to other studies (21) (1) (28) (22) (29): “I felt that everything I did was an effort” and “I could not get going.” The items asked “How often in the last week did you feel this way?” and subjects responded on a four-point scale: 0=rarely or never (<1 day), 1=some or a little of the time (1–2 days), 2=a moderate amount of the time (3–4 days), 3=most of the time (5–7 days). Participants answering 2 or 3 to either of these two items were categorized as positive for this criterion.

Slowness was measured by a six meter walking test. For men ≤ 173 centimeters (cm) tall the cut off time was 9 seconds, for men >173 cm the cut off time was 8 seconds. The cut off time on this criterion for women with a height of ≤ 159 cm was 9 seconds, for women >159 cm the cut off time was 8 seconds (extrapolated from the data of Fried and colleagues). (1)

Low physical activity level was defined as no daily activities such as walking and gardening, or the performance of sports less than once weekly. The last-seven-days long form of the self-administered version of the International physical Activities Questionnaire (IPAQ), (30)

consisting of eight items, was used to collect the physical activity data. Psychometric properties of the long and short version of the IPAQ are acceptable; criterion validity has a median rho of about 0.30. (30)

Other variables

Demographic data were collected during the interview (age, gender, living circumstances and educational level).

Somatic comorbidity was assessed by Statistics Netherlands (Centraal Bureau voor de Statistiek, www.CBS.nl) questionnaire: a questionnaire about the presence of diseases and health. The validity is adequate, with kappa's ranging from 0.31 to 0.85 accounted for each chronic disease separately. (31) The number of diseases was categorized in four categories (see table 2).

The symptom profile of depression was assessed by the 30-item self-rating Inventory of Depressive Symptomatology (IDS). (32) Each item consists of a series of four statements about the symptom, except items 11 and 12 about appetite and weight change. These items consist of seven statements. The psychometric properties of the IDS are acceptable, with Cronbach's alpha ranging from 0.76 to 0.82 for adults with current depression. (33)

Age of onset of the depression was determined by a CIDI question about the age of the participant at the time of the first depressive episode.

Trait neuroticism was assessed by the NEO-Five Factor Inventory (NEO-FFI), (34) a 60-item self-report questionnaire. Only the score on the neuroticism section was used and accounted as a continuous variable. The differential psychometric properties of NEO facet scales are robust, being generalizable across genders, ages and methods of measurement, (35) with Cronbach's alpha of 0.91 for trait neuroticism during a depressive episode. (36)

The CIDI anxiety diagnosis was used to determine the presence of an anxiety disorder in the past year.

The Beck Anxiety Inventory (BAI) was used to assess the presence of anxiety symptoms. (37) The internal consistency ($\alpha=0.92$) and test-retest reliability over one week ($r=0.75$) are high. (37) The score on the BAI was used as a continuous variable.

Statistical analyses

Demographics and clinical characteristics of the participants with and without depression were examined using independent samples t-tests for normally distributed, continuous variables, nonparametric Mann Whitney U tests for skewed continuous variables, and χ^2 tests for categorical variables. The difference in frailty prevalence between the depressed group and the non-depressed group, was subsequently assessed by multiple logistic

regression analysis corrected for age, gender, educational level, living circumstances and number of comorbid somatic diseases.

The second objective was evaluated within the depressed subgroup only. Multiple logistic regression analyses were used to compare all variables of interest (independent variables) between depressed elderly persons with and without frailty (dependent variable). First, all variables of interest (see hypotheses) were tested univariately. Subsequently, the regression analyses were corrected for the following covariates (potential confounders): age, gender, educational level, living circumstances and number of comorbid somatic diseases (model 1). As the severity of depressive symptoms was significantly different between depressed persons with and without frailty (see results), these final analyses were repeated while also controlling for the severity of depressive symptoms (model 2). Robustness of the results was checked by repeating these analyses with two different definitions of frailty, namely weakness and slowness as these definitions do not overlap with symptoms of depression. Subsequently, post-hoc analyses were performed in order to examine whether this difference in depressive symptoms could be related to specific depressive symptoms that might overlap with the criteria of frailty or to specific symptom clusters of depression based on IDS factor analysis. Varimax rotation was selected because it forces factors to be uncorrelated. Factor scores were calculated on the basis of unstandardized item factor loadings and transformed into standardized z-scores (using the Anderson-Rubin method) to increase their interpretability.

All p values were two-tailed. As the number of comparisons for the second objective was five, the level of statistical significance was set at $.05 / 5 = .01$ (bonferroni correction). Statistical analyses were carried out using Statistical Package for the Social Sciences (SPSS), version 17.0.

Results

The study sample included 321 participants in the depressed group, of which 21 had to be excluded due to missing data on frailty criteria. Participants with complete data and participants with missing data, however, did not differ with respect to age ($t=1.0$, degrees of freedom [df]=21590, $p= .35$) and gender ($\chi^2=0.0$, $df=1$, $p= .60$). Participants with missing data did report more depressive symptoms on the IDS than participants without missing data ($t=3.3$, $df=313$, $p= .001$).

None of the participants in the control group ($n=55$) had missing data. Therefore, the final study sample consisted of 300 depressed older adults (mean age [standard deviation (SD)]=70.7 [7.4] years, 67% female gender) and 55 non-depressed elderly (mean age [SD]=71.1 [7.0] years, 55% female gender).

Table 2 presents the characteristics of both the depressed and non-depressed group. The two groups only differed significantly with respect to the number of chronic diseases ($U=6539$, $p= .013$) and the prevalence of frailty (21.3% versus 1.8%, [$\chi^2=11.9$, $df=1$, $p= .001$]). This latter difference remained significant after correcting for potential confounders, (age, gender and somatic comorbidity) using logistic regression analysis (odds ratio [OR] =0.08, 95% confidence interval [CI] = 0.01, 0.60, $p= .014$).

<Table 2>

Comparison of frail and non-frail depressed older adults

Frail depressed older persons ($n=64$) were significantly older compared to their non-frail counterparts ($n=235$) ($t=-2.7$, $df=297$, $p= .007$), more severely depressed ($t=-4.79$, $df=295$, $p < .001$), and had significantly more comorbid chronic diseases ($U=4580$, $p < .001$). Both groups, however, did not differ with respect to gender ($\chi^2=1.7$, $df=1$, $p= .19$), level of education ($\chi^2=3.5$, $df=1$, $p= .062$) or living circumstances ($\chi^2=0.2$, $df=1$, $p= .633$). Including all potential confounders in a multivariate model, only differences with respect to the number of chronic diseases (OR=1.20, 95% CI= 1.05, 1.37, $p= .007$) and severity of depression (OR=1.06, 95% CI= 1.03, 1.08, $p < .001$) remained statistically significant.

Table 3 presents the difference in classical correlates of depression separately and after controlling for potential confounders of the relationship between depression and frailty (model 1). After controlling for these covariates, neuroticism and anxiety symptoms were significantly correlated with frailty. As the frail depressed persons were more severely depressed, the analysis were subsequently adjusted for the severity of depression by including the IDS sum score as covariate (model 2). In this final model, none of the classical correlates remained significant.

<Table 3>

Deconstructing frailty

In order to disentangle the relationship between frailty and depression, the analyses were repeated with two unidimensional definitions of frailty: weakness (operationalized as grip strength) and slowness (operationalized as gait velocity). As both variables had a skewed distribution that could not be transformed to a normal distribution and outliers were considered informative (a very low grip strength certainly points to frailty and should not be excluded), analyses were performed on dichotomized scores of both dependent variables. These analyses yielded similar results to those performed on frailty defined according to the criteria of Fried and colleagues (1) (table 3).

Deconstructing depression

Since the severity of depressive symptoms was significantly higher among frail depressed elderly compared to their non-frail counterparts, and none of the hypothesized differences were significantly different between both groups after controlling for the severity of depression, post-hoc analyses were conducted to explore which depressive symptoms or dimensions contributed to these differences.

First, the IDS sum score was recalculated without all items that may overlap with the criteria of frailty. Items 11-14 (appetite and weight change), item 20 (energy level), item 23 (feeling slowed down) and item 28 (physical energy) were removed. Comparing frail and non-frail participants, there was still a significant difference in the IDS adapted sum score ($t=-4.87$, $df=251$, $p<.001$). This difference persisted after controlling for covariates (age, gender, educational level, living circumstances and number of somatic comorbidities) in a multivariate model ($OR=1.07$, 95% $CI= 1.04, 1.11$, $p<.001$).

Secondly, a principal components analysis (PCA) was conducted on the 30 individual IDS items to deconstruct the underlying dimensions of depression, while retaining the original item information. Although the first PCA yielded seven factors with an eigenvalue greater than one (Kaiser's criterion for selecting the optimal number of factors), based on the screeplot and the interpretability of the factors, a five-factor solution was considered the most optimal (KMO-measure of sampling adequacy: 0.92; Bartlett's test of sphericity: $\chi^2=3699$, $df=435$, $p<.001$). The five factors were labeled as 1) cognitive-affective dimension (explained variance 16.4%), 2) anxious-affective dimension (explained variance 13.9%), 3) somatic-affective dimension (explained variance 8.1%), 4) appetite and weight changes (explained variance 6.4%), and 5) sleep disturbances (explained variance 6.2%).

Subsequently, logistic regression analysis (corrected for age, gender, educational level, living circumstances and number of somatic comorbidities) showed that factor one and four were significantly associated with the presence of frailty, whereas factor two, three and five were not. When the analyses were repeated using weakness and slowness as dependent variables, none of the factors were associated with weakness, and factor one and three were associated with slowness (table 4).

<Table 4>

Discussion

With an overall prevalence of 21.3%, the prevalence of frailty was significantly higher among depressed elderly compared to non-depressed elderly persons. Age and somatic comorbidity were associated with frailty in depressed older adults. It is known that somatic comorbidity is a risk factor for both depressive disorder (38) and frailty. (39) (8) Nevertheless, when corrected for differences in somatic comorbidity, the severity of depressive symptoms, even when frailty-related IDS-items were removed, was still correlated with all measures of frailty. Except for the higher frequency of comorbid somatic diseases, none of the hypotheses of the second objective were confirmed. All differences identified, could be explained by differences in depressive symptom severity between frail and non-frail depressed older adults. A priori, a similar level of depressive symptoms was expected (as all persons met the diagnostic threshold for depressive disorder, confirmed by a structured psychiatric interview). This raises the question whether depressed frail persons might have inflated depressive symptom scores (due to the overlap of both syndromes). Therefore, the construct of depression was decomposed and different measures of frailty were used (weakness and slowness). These analyses, however, still revealed a significant association between depressive symptom severity and frailty.

Two out of five factors within the IDS symptom profile were independently associated with an increased risk of frailty: cognitive-affective dimension and appetite and weight changes. Anxious-affective dimension, somatic-affective dimension and sleep disturbances were not associated with frailty. Moreover, the cognitive-affective dimension was also independently associated with slowness, although not with weakness. These results imply that the somatic-affective dimension doesn't increase the risk of frailty, as was expected. Higher scores on cognitive-affective dimension, on the other hand, were associated with frailty, independent of the number comorbid somatic diseases. This suggests that frail older persons do experience themselves as less healthy or vital, thereby increasing the odds of negative feelings about themselves as reflected by the cognitive-affective symptoms of depression.

These results show that, with respect to the cognitive-affective dimension, both concepts are correlated, independent of overlap in their definitions, whereas the correlation between appetite-weight dimension and frailty is probably based on overlap in their definitions. However, whether a positive correlation is partly due to overlap of items related to somatic-affective symptoms of depression and the "exhaustion" item of frailty remains unclear, as the results were not unequivocal for all frailty measures. A recent study showed that only 14% of frail elderly persons who report exhaustion also met criteria for major depressive disorder. (29) All in all these results may suggest that in clinical practice it seems possible to differentiate between exhaustion as a symptom of depression and exhaustion as a symptom of frailty.

As this was a cross-sectional study, no information is given on the direction of the associations. It may be hypothesized that depressed elderly are more prone to developing frailty by both life-style factors associated with depression (inactivity and non-compliance of medication in case of somatic comorbidity), as well as physiological disturbances associated with depression (for example hypo- and hypercortisolemia affecting the endothelium or autonomic nervous system disturbances (40)).

On the other hand, frailty may result in depression by functional limitations. However, as the regression models were corrected for differences in somatic comorbidity, this explanation seems less likely. A more obvious explanation might be a process called low-graded inflammation, which is considered one of the underlying mechanisms of frailty (4) and is also related to depression. (41) (42)

Since the emergence of frailty is a multifactorial process, etiological factors can be divided into four categories: genetic factors, diseases and accidents, lifestyle and old age. (39) Although genetic factors play a role in the development of frailty, lifestyle is the greatest contributor to the onset of frailty according to Bortz. (39) Findings of Woods et al. (8) show that frailty is associated with health behavioral factors, such as smoking, alcohol consumption, overweight and underweight. This makes frailty susceptible to intervention. Considering the high prevalence of frailty among depressed elderly, screening on frailty should be part of the current mental health care. Markle-Reid et al. (43) show that nursing health promotion, proactively provided to frail older adults, increases their quality of life, reduces depressive symptoms, while not increasing the overall healthcare costs.

The benefits of integrated, multidisciplinary geriatric care have been determined in several studies. (44) (45) (46) Frailty highlights the need to individualize and integrate guidelines for treatment, and to prevent adverse outcomes by choosing health care interventions fit for such frail elderly. (47) By differentiating between frail and non-frail elderly, it will be easier to treat frail older adults with the appropriate, multidisciplinary interventions.

Some strengths and limitations of this study should be mentioned. A major strength of this study is the use of different measures of frailty. In addition to a multicomponent measure of frailty (1), weakness and slowness were also used as unidimensional frailty measures. Furthermore, the decomposing of the concept of depression gives more insight into the mechanisms between frailty and depression. Whereas other studies use questionnaires as a substitute for a depression diagnosis, this study used a formal diagnosis of depression according to DSM-IV criteria. Since participants were recruited from primary care as well as in- and outpatient secondary care clinics, this sample covers the whole spectrum of depressive disorders, varying from mildly depressed, independent living older adults to severely depressed inpatients. This enhances the generalizability of the results.

The main limitation was the cross-sectional design of the study, making it impossible to differentiate whether frailty preceded depression or the reverse. Although this study provides the opportunity of adequate control of potential confounders, it cannot be ruled out that the association between frailty and depression is caused by some unknown confounders (taking the scarcity of literature on this topic into account). Furthermore, the control group was relatively small. Yet the low prevalence rate of frailty that was found among non-depressed controls was in line with a previous study with voluntary participants, (29) although volunteers may not be representative of the true population.

Conclusion

The high prevalence of frailty among depressed elderly persons argues for the need of screening of this particularly vulnerable group of people. As frail depressed elderly were more severely depressed compared to non-frail depressed elderly, it may be expected that especially the frail subgroup be treated in secondary mental health care in which integrative geriatric care is not routinely available. Nevertheless, screening for frailty can easily be conducted by nurses, because of their holistic view of patients, from the viewpoint of cost-effectiveness, and finally, because especially nurse-led multidisciplinary interventions focused on life-styles and behavioral activation seems most promising in reducing the negative impact of frailty.

The complex relationship between frailty and depression should be further explored in prospective study designs. If replicated, future research should evaluate the effectiveness of nurse-led screening and treatment interventions.

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Tables

Table 1 Criteria for depression and frailty

Depression (DSM-IV)(48)	Frailty according to Fried et al. (1)*
<i>Core symptoms:</i>	
Depressed mood	
Loss of interest or pleasure	
<i>Remaining symptoms:</i>	
Weight loss	
Insomnia or hypersomnia	
Psychomotor agitation or retardation	
Fatigue or loss of energy	Weight loss
Feelings of worthlessness or excessive or inappropriate guilt	Slowness
Concentration problems or indecisiveness	Poor endurance and energy (exhaustion)
Suicidal ideations	Weakness**
	Low physical activity level**

* Positive for frailty when three or more criteria occur.

** Depressed persons often experience low physical activity level and as a result weakness. These are not included as criteria for depression.

Table 2 Demographics, clinical characteristics and frailty criteria

	Depressed group (N=300)	Control group (N=55)
Characteristic		
Age, mean (SD)	70.7 (7.4)	71.1 (7.0)
Age, range	60 – 88	60 – 93
Gender, % female : % male	66.7 : 33.3	54.5 : 45.5
Living alone, %	55.3	49.1
Education, % low education	77.3	61.8
Number of chronic diseases,		
% 0	12.0	16.4
% 1	18.3	23.6
% 2	26.0	34.5
% ≥ 3	43.7	25.5
Frailty, %	21.3	1.9
Exhaustion, %	47.3	1.8
Weight loss, %	37.7	1.8
Weakness, %	11.0	5.5
Slowness, %	28.0	21.8
Low activity level, %	38.3	30.9
Number of frailty criteria:		
% 0	18.5	55.6
% 1	30.0	27.8
% 2	30.3	14.8
% 3	14.8	1.9
% 4	4.7	0.0
% 5	1.7	0.0

Table 3 Association between classical correlates of depression and frailty, weakness and slowness in depressed persons aged 60 years and older

N=300 Classical correlates of depression	Frailty					
	Unadjusted		Adjusted ¹		Adjusted ²	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Neuroticism (NEO-FFI)	1.06 (1.02, 1.11)	.004**	1.07 (1.03, 1.12)	.002**	1.03 (0.98, 1.05)	.300
Anxiety severity (BAI)	1.06 (1.03, 1.09)	<.001***	1.04 (1.02, 1.07)	.001***	1.01 (0.94, 1.05)	.365
Comorbid anxiety diagnosis	0.59 (0.34, 1.04)	.066	0.55 (0.30, 1.00)	.049*	0.63 (0.34, 1.18)	.149
Late onset depression	0.96 (0.54, 1.71)	.879	1.19 (0.625, 2.26)	.600	0.98 (0.50, 1.95)	.957
Feelings of guilt/ worthlessness	0.58 (0.28, 1.20)	.142	0.57 (0.26, 1.24)	.157	0.77 (0.34, 1.72)	.515
	Weakness					
Neuroticism (NEO-FFI)	1.05 (1.00, 1.11)	.065	1.06 (1.00, 1.12)	.058	1.04 (0.97, 1.11)	.275
Anxiety severity (BAI)	1.04 (1.01, 1.07)	.018*	1.03 (1.00, 1.07)	.072	1.02 (0.98, 1.06)	.359
Comorbid anxiety diagnosis	0.63 (0.31, 1.31)	.217	0.60 (0.28, 1.28)	.184	0.69 (0.32, 1.49)	.343
Late onset depression	0.97 (0.46, 2.05)	.932	1.19 (0.53, 2.64)	.677	1.12 (0.49, 2.55)	.782
Feelings of guilt/ worthlessness	0.59 (0.22, 1.58)	.290	0.66 (0.24, 1.82)	.424	0.77 (0.28, 2.17)	.627
	Slowness					
Neuroticism (NEO-FFI)	1.02 (0.98, 1.06)	.335	1.04 (1.00, 1.09)	.053	1.00 (0.95, 1.05)	.901
Anxiety severity (BAI)	1.05 (1.03, 1.08)	<.001***	1.04 (1.02, 1.07)	.002**	1.02 (0.99, 1.05)	.297
Comorbid anxiety diagnosis	0.76 (0.46, 1.27)	.297	0.60 (0.33, 1.09)	.093	0.72 (0.38, 1.34)	.295
Late onset depression	0.84 (0.50, 1.41)	.504	1.45 (0.77, 2.72)	.246	1.24 (0.64, 2.41)	.522
Feelings of guilt/ worthlessness	0.56 (0.29, 1.09)	.086	0.52 (0.25, 1.10)	.086	0.63 (0.29, 1.37)	.242

Notes: OR, odds ratio; 95% CI, 95% confidence interval; NEO-FFI, NEO-Five Factor Inventory; BAI, Beck Anxiety Inventory.

¹ Adjusted for age, gender, living circumstances, level of education and number of somatic comorbidities.

² Additionally adjusted for severity of depressive symptoms (IDS).

* P ≤ .05, ** p ≤ .01, *** p ≤ .001.

Table 4 Association between five factors and frailty, weakness and slowness in depressed persons aged 60 years and older (adjusted for age, gender, living circumstances, level of education and number of somatic comorbidities)

Factor number	Frailty		Weakness		Slowness	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
1. Cognitive-affective dimension	1.70 (1.19, 2.41)	.003**	1.38 (0.91, 2.11)	.134	1.57 (1.12, 2.22)	.009**
2. Anxious-affective dimension	1.35 (0.97, 1.87)	.071	1.16 (0.77, 1.76)	.480	1.16 (0.84, 1.60)	.371
3. Somatic-affective dimension	1.28 (0.93, 1.78)	.129	1.15 (0.75, 1.76)	.516	0.48 (1.26, 2.54)	.001***
4. Appetite and weight changes	1.52 (1.09, 2.13)	.013*	1.10 (0.74, 1.63)	.638	1.14 (0.84, 1.55)	.402
5. Sleep disturbances	1.17 (0.84, 1.62)	.353	1.12 (0.74, 1.69)	.609	1.12 (0.81, 1.54)	.509

Notes: OR, odds ratio; 95% CI, 95% confidence interval.

* $P \leq .05$, ** $p \leq .01$, *** $p \leq .001$.

Dutch abstract

Achtergrond: Hoewel criteria voor frailty (kwetsbaarheid) en depressie deels overlappen en beide geassocieerd zijn met het optreden van negatieve gezondheidsuitkomsten, is er nauwelijks onderzoek gedaan naar hun onderlinge relatie. Door symptoomoverlap kunnen kwetsbare ouderen onterecht een diagnose depressie krijgen, wat kan betekenen dat in deze groep de klassieke correlaten van depressie minder voorkomen.

Doelen: 1) het vaststellen van de prevalentie van frailty onder depressieve ouderen, en deze vergelijken met de prevalentie van frailty onder niet-depressieve ouderen, en 2) een vergelijking maken van de klassieke correlaten van depressie (neuroticisme, angst, schuldgevoelens en gevoelens van waardeloosheid, leeftijd eerste depressie en somatische comorbiditeit) tussen depressieve ouderen met en zonder frailty.

Methode: Deze cross-sectionele, observationele studie vond plaats binnen een groter, multi-center onderzoeksproject; de Nederlandse Studie naar Depressie bij Ouderen. De steekproef bestond uit 300 depressieve ouderen (≥ 60 jaar) en 55 niet-depressieve ouderen. Depressie werd vastgesteld met het Composite International Diagnostic Interview. De ernst van de depressie werd beoordeeld met de Inventory of Depressive Symptomatology (IDS). Frailty werd bepaald volgens de definitie van Fried en collega's, te weten minimaal drie van de volgende vijf criteria: gewichtsverlies, traagheid, verminderd uithoudingsvermogen en energie, zwakheid en een laag activiteitsniveau.

Resultaten: Frailty kwam significant meer voor bij depressieve ouderen, dan bij niet-depressieve ouderen (21.3% versus 1.8%). Na correctie voor covariaten (leeftijd, geslacht, woonomstandigheden, opleidingsniveau, somatische comorbiditeit en ernst van de depressie), was er geen verschil in de frequentie van correlaten van depressie tussen depressieve ouderen met frailty en depressieve ouderen zonder frailty, behalve in het aantal comorbide chronische ziektes. Post-hoc analyses met zowel unidimensionele definities van frailty (traagheid, zwakheid), alsmede verschillende depressieve symptoom profielen (factoranalyse IDS, IDS-score zonder somatische items) bevestigden deze resultaten.

Conclusie: De prevalentie van frailty onder depressieve ouderen is hoog en kan niet (volledig) verklaard worden door symptoom overlap. Dit pleit zowel voor screening op frailty als een multidisciplinaire benadering, bij voorkeur uitgevoerd en gecoördineerd door verpleegkundigen gezien hun holistische werkwijze en praktische interventie mogelijkheden.

Trefwoorden: depressie, frailty, ouderen.

English abstract

Background: Although criteria for frailty and depression partially overlap and both syndromes are associated with adverse health outcomes, there is a lack of research into their (reciprocal) relationship. Due to symptom overlap, frail elderly may be misdiagnosed as depressed. If true, the classical correlates of depression would be less prevalent in this group.

Objectives: 1) to compare the prevalence of frailty in depressed older adults with the prevalence of frailty in non-depressed older adults, and 2) to compare classical correlates of depression (neuroticism, anxiety, feeling of guilt and worthlessness, age of onset, and somatic comorbidity) between depressed elderly with and those without frailty.

Methods: The reported cross-sectional observational study was embedded within a larger, multisite research project; the Netherlands Study of Depression in Older people. Participants were 300 older adults (aged ≥ 60 years) with depression and 55 non-depressed elderly. Depression was assessed with the Composite International Diagnostic Interview. Severity of depression was measured with Inventory of Depressive Symptomatology (IDS). Frailty was defined according to the criteria of Fried and colleagues. In this definition three or more of the following criteria must be present: weight loss, slowness, poor endurance and energy, weakness and low physical activity level.

Results: The prevalence of frailty was significantly higher in the depressed group than in the non-depressed group (21.3% versus 1.8%). After controlling for covariates (age, gender, living circumstances, educational level, somatic comorbidity and severity of depression), there was no difference in correlates of depression between frail depressed elderly and non-frail depressed elderly, except for the frequency of comorbid somatic diseases. Post-hoc analyses with both unidimensional definitions of frailty (weakness, slowness) and different symptom profiles of depression (IDS factor analysis, adjusted IDS-score without somatic items) confirmed these results.

Conclusion: The prevalence of frailty among depressed older adults is high, and cannot be explained fully by symptom overlap. This argues for the need of frailty screening, as well as multidisciplinary care. Given their holistic view and expertise with practical methods of intervention, this approach is preferably to be conducted and coordinated by nurses.

Keywords: Depression, frailty, elderly.