Physical frailty: vulnerability of patients suffering from late-life depression

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RESEARCH ARTICLE

Physical frailty: vulnerability of patients suffering from late-life depression

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Objectives: Frailty, a state of increased risk of negative health outcomes, is increasingly recognized as a relevant concept for identifying older persons in need of preventative geriatric interventions. Even though broader concepts of frailty include psychological characteristics, frailty is largely neglected in mental health care. The aim of the present study is to examine the prevalence of physical frailty in depressed older patients and its potential overlap with depression criteria.

Method: Cross-sectional observational study including 378 depressed and 132 non-depressed adults aged ≥60 years according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria. Physical frailty was defined as ≥3 out of 5 criteria (hand grip strength, weight loss, poor endurance, walking speed, low physical activity).

Results: Prevalence rates of physical frailty were 27.2% and 9.1% among depressed and non-depressed participants, respectively, which remained significant after controlling for relevant covariates (odds ratio [OR] = 2.66 [95% confidence interval [C.I.] = 1.36, 5.24], p = .004). Physical frailty in depression was associated with more severe depressive symptoms; this association remained significant in subsequent analyses with purely physical proxies for frailty (hand grip strength, walking speed) and different severity measures of depressive symptoms.

Conclusion: A quarter of depressed older patients is physically frail, especially the most depressed group. This cannot be explained by overlap in criteria and should be examined in future studies, primarily on its presumed clinical relevance.

Keywords: depression; frailty; elderly; Netherlands Study of Depression in Older persons (NESDO)

Introduction

Frailty is conceptualized as a state of increased risk of adverse health outcomes, such as falls, reduced mobility, reduced independence, hospitalization, disability and death (Fried et al., 2001). 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. As this theoretical foundation is not (yet) supported by a clear underlying pathophysiological process, research has led to various operationalizations of frailty and prevalence rates vary widely (Fried et al., 2001; Rockwood et al., 2004; Woods et al., 2005). Among community-dwelling older people, meta-analysis showed a prevalence rate of frailty of 9.9% for physical frailty and 13.6% for the broader operationalization of frailty (Collard, Boter, Schoevers, & Oude Voshaar, 2012). The latter also includes psychological and psychosocial characteristics.

Irrespective of the exact conceptualization of frailty, prospective studies have unequivocally demonstrated a worsening of prognosis of somatic conditions in the presence of frailty (Afifalou et al., 2012; Vaz Fragoso, Enright, McAvay, Van Ness, & Gill, 2012). Quite recently, the clinical relevance is further substantiated by several randomized controlled trials, showing that interventions targeted at frailty components, improve health outcomes of frail older persons (Chan et al., 2012; de Souto Barreto, 2010; Helbostad, Sletvold, & Moe-Nilssen, 2004; Langlois et al., 2012). For example, high-intensity progressive resistance training reduced mortality and nursing home admission after hip fracture surgery (Singh et al., 2012). In physically frail older persons, a home-based physical therapy targeted at underlying impairments in physical ability, significantly reduced functional decline (Gill et al., 2002). Finally, a home-based self-administered exercise program with protein supplementation led to significantly less decline in walking ability and instrumental activities of daily living (Bonafay et al., 2012).

Although hardly examined, frailty can be assumed to be of special relevance in older persons suffering from psychiatric diseases, especially depressive disorders that are also associated with increased mortality rates and negative health outcomes, such as somatic diseases and increased risk of suicide (Collard & Oude Voshaar, 2012; Pitchot, Scantamburlo, & Ansseau, 2012). However, the disparity between body and mind has probably led to the ignorance of physical frailty in psychiatric patients. Broader concepts of frailty include several psychiatric symptoms next to physical symptoms, thereby not discriminating anymore between them. Empirical data indeed show some overlap between frailty and late-life

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depression (Ni Mhaolain et al., 2012), but also underline that frailty and depression represent distinct syndromes rather than a single construct (Mezuk, Lohman, Dumenci, & Lapane, 2012). To improve treatment of older depressed persons it is important to further study frailty in this specific group.

Objectives

The objective of the present study is to determine the prevalence of physical frailty in depressed older and non-depressed older adults, adjusted for potential confounders. For this purpose, frailty should be defined in purely physical terms. Therefore, a definition was chosen that did not contain depression as a characteristic of frailty. The definition of Fried and colleagues (Fried et al., 2001) is widely used in geriatric research and encompasses a physical phenotype of frailty (Avila-Funes et al., 2008; Fried et al., 2001; Santos-Eggimann, Cuenod, Spagnoli, & Junod, 2009; Woods et al., 2005). Nevertheless, as included physical symptoms such as exhaustion, weight loss and slowness may also be related to depression, we further explored whether the hypothesized association between depression and physical frailty can be explained by shared characteristics.

Methods

Ethics statement

The study was approved by the Ethical Review Board of the VU University Medical Center in Amsterdam. Since this was a multi-center study, the ethical review boards of the other participating institutes approved of the local feasibility of the study, of which the details are described elsewhere (Comijs et al., 2011). Participants received written and oral information about the study. They had the opportunity to ask questions and it was checked by the research nurses whether the participants understood the consequences of the study. All participants were competent to consent to participation. Written informed consent was obtained from all participants.

The present study was embedded within a prospective cohort study: The Netherlands Study of Depression in Older persons (NESDO)(Comijs et al., 2011). The aims for NESDO are to examine the (determinants of the) course and consequences of depressive disorders in older persons, and to compare the course and determinants of late-life depression with that of early-life depression.

The NESDO sample consists of 378 depressed subjects with a current Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) diagnosis of major depressive disorder (95%), minor depression (5.6%) or dysthymia (26.5%), of which 26.5% have two depressive disorders. The comparison group consists of 132 non-depressed subjects, aged 60 through 93 years. Persons with a primary diagnosis of dementia, a Mini Mental State Examination-score (MMSE) under 18 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 (Comijs et al., 2011).

Of the depressed participants, 86.2% were recruited from mental health institutes (both in- and outpatients) and 13.8% from primary care. The non-depressed comparison group was recruited from 14 primary care practices and screened for absence of depression. All participants underwent a baseline examination at one of the research locations or at the homes of the participants. A questionnaire including several of the written measurement instruments was sent to the home of the participants prior to the baseline examination and when necessary, the assessment was spread over two appointments.

Measures

Depression

The Composite International Diagnostic Interview (CIDI), version 2.1, life time version was used in order to determine depression classification according to the criteria of DSM-IV and the criteria of the International Classification of Diseases-10 (ICD-10) (World Health, 1997). The CIDI has high validity for depressive disorders (Wittchen et al., 1991). To determine the research DSM-IV diagnosis of current minor depression, questions were added to the CIDI, as in The Netherlands Study of Depression and Anxiety (NESDA) (Penninx et al., 2008).

Severity of depression was measured by the 30-item self-rating Inventory of Depressive Symptomatology (IDS), which has acceptable psychometric properties (Rush et al., 1986; Rush, Gullion, Basco, Jarrett, & Trivedi, 1996). IDS sum score (range 0–84) was used as a continuous variable. The clinical interpretation of the IDS sum score is as follows: 0–13 = normal, 14–25 = mild depression, 26–38 = moderate depression, 39–48 = severe depression and 49–84 = very severe depression (Rush, First, & Burns, 2008). Principal component analysis and confirmatory factor analysis of the IDS-SR indicated a three-factor model of which two factors could be optimized with Rasch analyses to function as homogenous measures of depressive symptoms dimensions: the mood/cognition factor and the anxiety/arousal factor (age range 18–65) (Wardenaar et al., 2010).

Frailty

Frailty was assessed according to the criteria of Fried et al. (Fried et al., 2001), which are weight loss, weakness, poor endurance and energy, slowness and low physical activity level. A person is classified as frail when ≥3 criteria are present, classified as pre-frail when 1 or 2 criteria are present and classified as robust when none of the criteria are present.

Unintentional weight loss was defined as a positive response on the CIDI question about unwanted weight loss of a minimum of one kilogram a week, during two or more consecutive weeks or a body mass index (BMI) of less than 18.5 kg/m².
A handgrip dynamometer was used to assess weakness. Participants were asked to perform two squeezes with the dynamometer, using their dominant hand. The best performance, recorded as strength in kilograms, was used for analysis. Cut-off scores were stratified by gender and BMI quartiles according to Fried et al. (Fried et al., 2001). Participants unable to perform the test were also considered weak.

Poor endurance and energy (exhaustion) were determined by two questions from the Center for Epidemiologic Studies-Depression scale (CES-D), (Radloff, 1997) similar to other studies (Avila-Funes et al., 2008; Fried et al., 2001): ‘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 item.

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) (Fried et al., 2001).

Low physical activity level was defined as no daily activities such as walking and gardening, or sports activity less than once weekly. The last-seven-day short form of the self-administered version of the International physical Activities Questionnaire (IPAQ) (Craig et al., 2003), consisting of seven items, was used to collect the physical activity data. Psychometric properties of the short and long version of the IPAQ are acceptable (Craig et al., 2003).

In addition to the syndromal definition of frailty based on the Fried criteria, we also included two unidimensional proxies for frailty based on previous research into physical frailty, i.e. muscle weakness (Syddall, Cooper, Martin, Briggs, & Aihie Sayer, 2003) and gait velocity (Cesari et al., 2005). Muscle weakness was defined as the hand-grip strength, as described above. Gait velocity was based on the six-meter walking test, as described above.

**Covariates**

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

Somatic comorbidity was assessed using a self-report questionnaire about the presence of somatic diseases (lung disease, cardiovascular disease, diabetes, arthritis, rheumatism, cancer, ulcer, intestinal disorder, liver disease, epilepsy, allergy, thyroid gland disease and (head) injury), as originally developed by Statistics Netherlands (Centraal Bureau voor de Statistiek, www.cbs.nl). This questionnaire has high accuracy for chronic somatic disease as previously reported (Kriegsman, Penninx, van Eijk, Boeke, & Deeg, 1996).

Global cognitive functioning was assessed by the MMSE (Folstein, Folstein, & McHugh, 1975). MMSE score (range 0–30) will be measured as a continuous variable, with higher scores indicating better cognitive functioning. Interrater reliability and test-retest reliability are good (Cockrell & Folstein, 1988; Mackin, Ayalon, Feliciano, & Arean, 2010).

**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 χ² tests for categorical variables. The association between physical frailty and depression diagnoses (yes/no) as the dependent variable was subsequently assessed by multiple logistic regression analysis corrected for age, gender, educational level, living circumstances, number of comorbid somatic diseases and MMSE score.

Multicollinearity was tested by calculating the bivariate correlation coefficient of all pairs of independent variables. These tests showed no multicollinearity problems.

The second objective was evaluated within the depressed subgroup only. Multiple logistic regression analyses were used to investigate the association between severity of depression (independent variable) and physical frailty (dependent variable). First, the variable was tested univariately. Subsequently, the regression analyses were corrected for the following potential confounders: age, gender, educational level, living circumstances, number of comorbid somatic diseases and MMSE score (model 1).

To examine whether overlap in criteria may explain some of the associations, analyses were repeated with different definitions of frailty and depressive symptoms. Frailty was operationalized with two unidimensional proxies for frailty, namely weakness (Syddall et al., 2003) and slowness (Cesari et al., 2005), as these definitions do not overlap with symptoms of depression. Severity of depression was included in the model in different ways.

First by calculating the IDS sum score excluding all items that overlap with physical frailty (i.e. items 11–14 [appetite and weight change], item 20 [energy level], item 23 [feeling slowed down] and item 28 [physical energy]). Secondly, the two IDS subscale scores as identified by Wardenaar and colleagues (Wardenaar et al., 2010).

All p values were two-tailed, and the level of statistical significance was set at p < 0.05. Statistical analyses were carried out using Statistical Package for the Social Sciences (SPSS), version 16.0.

**Results**

**Comparison depressed patients and non-depressed comparison group**

The mean age [standard deviation (SD)] of the 510 participants was 70.6 [7.3] years, and 64.9% was female.
Table 1 presents the characteristics of both the depressed and non-depressed groups.

Four participants had missing data on one physical frailty criterion (weakness). However, frailty status could be computed based on the four remaining criteria. In order to be classified as frail, three or more out of five criteria had to be present. Two of the participants with missing data were considered frail (because of 3 out of 4 positive criteria) and two participants were classified non-frail (because of 0 or 1 positive criteria, respectively).

The prevalence of physical frailty was significantly higher in the depressed group compared to the non-depressed comparison group (27.2% versus 9.1%; $\chi^2 = 18.5$, df = 1, $p < 0.001$). Logistic regression analysis, adjusted for age, gender, and all baseline characteristics that differed between both groups (number of somatic diseases, educational level, MMSE score and living status), showed an increased odds ratio of frailty for depression (odds ratio [OR] = 2.66, 95% confidence interval [CI] = 1.36, 5.24, $p = 0.004$).

Comparison of frail and non-frail depressed older persons

Compared to non-frail depressed older persons ($n = 275$), frail depressed elderly ($n = 103$) were significantly older, had fewer years of education, lower cognitive functioning, more comorbid somatic diseases, and were more severely depressed (see Table 2). Including all characteristics in a multivariate logistic regression model with physical frailty (yes/no) as the dependent variable, age (OR = 1.10, 95% CI = 1.06, 1.14, $p < 0.001$) and severity of depression (OR = 1.07, 95% CI = 1.05, 1.10, $p < 0.001$) were significantly associated with physical frailty in the depressed group.

The proportion of women was equal in both the frail and the non-frail groups ($\chi^2 = 0.49$, df = 1, $p = 0.482$) (Figure 1). Frailty did increase with age in the depressed group ($\chi^2 = 25$, df = 5, $p < 0.001$) (Figure 2). Frailty prevalence between health care setting did not differ significantly ($\chi^2 = 2$, df = 2, $p = 0.407$) (Figure 3).

Table 1. Demographics, clinical characteristics and frailty criteria.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Depressed group ($N = 378$)</th>
<th>Comparison group ($N = 132$)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>70.7 (7.4)</td>
<td>70.1 (7.2)</td>
<td>0.371</td>
</tr>
<tr>
<td>Age, range</td>
<td>60 – 90</td>
<td>60 – 93</td>
<td></td>
</tr>
<tr>
<td>Gender, % female</td>
<td>66.1</td>
<td>61.4</td>
<td>0.322</td>
</tr>
<tr>
<td>Living alone, %</td>
<td>54.0</td>
<td>34.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Education, % low education</td>
<td>79.1</td>
<td>60.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MMSE score, mean (SD)</td>
<td>27.6 (2.5)</td>
<td>28.3 (1.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chronic diseases, mean (SD), no</td>
<td>1.54 (1.21)</td>
<td>1.14 (0.99)</td>
<td>0.001</td>
</tr>
<tr>
<td>Frailty, %</td>
<td>27.2</td>
<td>9.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight loss, %</td>
<td>35.4</td>
<td>3.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weakness, %</td>
<td>25.1</td>
<td>19.7</td>
<td>0.205</td>
</tr>
<tr>
<td>Exhaustion, %</td>
<td>45.8</td>
<td>3.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Slowness, %</td>
<td>26.5</td>
<td>18.9</td>
<td>0.084</td>
</tr>
<tr>
<td>Low activity level, %</td>
<td>42.3</td>
<td>34.8</td>
<td>0.132</td>
</tr>
<tr>
<td>Number of frailty criteria:</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>% 0</td>
<td>15.6</td>
<td>48.1</td>
<td></td>
</tr>
<tr>
<td>% 1</td>
<td>30.8</td>
<td>32.8</td>
<td></td>
</tr>
<tr>
<td>% 2</td>
<td>26.3</td>
<td>9.9</td>
<td></td>
</tr>
<tr>
<td>% 3</td>
<td>18.8</td>
<td>7.6</td>
<td></td>
</tr>
<tr>
<td>% 4</td>
<td>6.6</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>% 5</td>
<td>1.6</td>
<td>0.0</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: SD, standard deviation; MMSE, Mini Mental State Examination.

*Comparison using analyses of variance (continuous variables), $\chi^2$ statistics (categorical variables) and U tests (continuous, skewed variables).

Table 2. Characteristics of frail and non-frail depressed participants.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Frail group ($N = 103$)</th>
<th>Non-frail group ($N = 275$)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>73.8 (8.0)</td>
<td>69.6 (6.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female gender</td>
<td>68.9</td>
<td>65.1</td>
<td>0.482</td>
</tr>
<tr>
<td>Living alone</td>
<td>57.3</td>
<td>52.7</td>
<td>0.429</td>
</tr>
<tr>
<td>Education, mean (SD), y</td>
<td>9.7 (3.2)</td>
<td>10.7 (3.5)</td>
<td>0.008</td>
</tr>
<tr>
<td>Cognition (MMSE score), mean (SD)</td>
<td>27.1 (2.5)</td>
<td>27.8 (2.5)</td>
<td>0.008</td>
</tr>
<tr>
<td>Chronic diseases, mean (SD), no</td>
<td>2.1 (1.5)</td>
<td>1.5 (1.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>IDS score, mean (SD)</td>
<td>37.2 (12.4)</td>
<td>27.5 (12.3)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Abbreviations: MMSE, Mini Mental State Examination; IDS, Inventory of Depressive Symptomatology.

*Comparison using analyses of variance (continuous variables), $\chi^2$ statistics (categorical variables) and U tests (continuous, skewed variables).
Deconstructing frailty

In order to disentangle the relationship between physical frailty and depression, the analyses were repeated with two unidimensional proxies for 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 cut-off points of both dependent variables. These analyses yielded similar results compared to the analyses using the Fried Frailty Index as indicator for frailty (see Table 3).

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Deconstructing depression

Since the severity of depressive symptoms was significantly higher among frail depressed elderly compared to their non-frail counterparts, finally all analyses were repeated using the adapted IDS sum score (without overlapping frailty items) as well as the total scores on two IDS subscales. As shown in Table 4, all measures of depressive symptoms were significantly associated with frailty in depressed patients, irrespective of the used definition of frailty.

Discussion

With an overall prevalence of 27.0%, the prevalence of physical frailty was significantly higher among depressed compared to non-depressed older persons. Higher age and severity of depression were independently associated with physical frailty in depressed older adults.

This raises the question whether depressed frail persons might have inflated depressive symptom scores (due to the shared characteristics of both syndromes). Therefore, the construct of depression was decomposed (using the IDS sum score without items that might overlap with physical frailty, as well as using IDS subscale scores) and different measures of frailty were used (weakness and slowness). These analyses, however, still revealed a significant association between all measures of depressive symptom severity and all measures of frailty. It is thus unlikely that the higher severity of depressive symptoms in frail compared to non-frail depressed older persons can be explained by shared characteristics.

A review on the relationship of depression and frailty in later life suggests that depression and frailty might be bi-directionally related (Mezuk, Edwards, Lohman, Choi, & Lapane, 2011). Included studies, however, neither measured depression according to state-of-the-art diagnostic criteria nor considered the use of antidepressants (Mezuk et al., 2011). Another recent study found that depressive symptoms as well as antidepressant drug use were indeed associated with frailty after three years of follow-up (Lakey et al., 2012). Indirect evidence points to several explanations for the association between physical frailty and the severity of depressive symptoms in late-life depression. First, it may be hypothesized that most severely depressed patients 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 (Bremmer et al., 2007)). Secondly, frailty may result in a more severe depressed state due to its association with chronic somatic diseases and functional limitations. At population level, depression is more strongly associated with consequences of chronic disease than with the disease (Beekman et al., 1997). We a priori chose to include only somatic comorbidity as a confounder, because of the risk of over correcting. Nevertheless, additional adjustment for functional limitations (as assessed with the WHO-Disability Assessment Schedule; Chwastiak & Von Korff, 2003) yielded similar results to the analyses with somatic comorbidity only (data available on request). A third explanation may be common underlying processes, related to both frailty and depression. Low-grade inflammation, for example, is generally considered to be one of the underlying mechanisms of both frailty (Leng, Xue, Tian, Walston, & Fried, 2007) and late-life depression (Bremmer et al., 2008; Milaneschi et al., 2009).

Implications

Irrespective of the mechanisms by which frailty and late-life depression are related, late-life depression with

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Table 3. Association between severity of depression (IDS) and frailty, weakness and slowness in depressed persons aged 60 years and older.

<table>
<thead>
<tr>
<th>Severity of depression</th>
<th>Frailty</th>
<th>Weakness</th>
<th>Slowness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted 1.07 (1.05, 1.09)</td>
<td>&lt;0.001</td>
<td>1.02 (1.01, 1.04)</td>
<td>0.001</td>
</tr>
<tr>
<td>Adjusted1 1.07 (1.05, 1.10)</td>
<td>&lt;0.001</td>
<td>1.02 (1.00, 1.04)</td>
<td>0.025</td>
</tr>
</tbody>
</table>

Abbreviation: IDS, Inventory of Depressive Symptomatology.

1Adjusted for age, gender, living circumstances, level of education, number of somatic comorbidities and Mini Mental State Examination (MMSE) score.

Table 4. IDS adapted sum score without overlapping frailty items and two IDS subscales yielded by factor analysis (Wardenaar et al., 2010): Association with frailty, weakness and slowness (adjusted for age, gender, living circumstances, level of education, number of somatic comorbidities and MMSE score).

<table>
<thead>
<tr>
<th>N = 373</th>
<th>Frailty</th>
<th>Weakness</th>
<th>Slowness</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDS adapted sum score 1.08 (1.06, 1.11)</td>
<td>&lt;0.001</td>
<td>1.04 (1.01, 1.06)</td>
<td>0.005</td>
</tr>
<tr>
<td>IDS subscales 1. Mood/cognition 1.13 (1.08, 1.19)</td>
<td>&lt;0.001</td>
<td>1.05 (1.01, 1.10)</td>
<td>0.022</td>
</tr>
<tr>
<td>2. Anxiety/ arousal 1.21 (1.13, 1.29)</td>
<td>&lt;0.001</td>
<td>1.07 (1.01, 1.14)</td>
<td>0.028</td>
</tr>
</tbody>
</table>

Abbreviations: IDS, Inventory of Depressive Symptomatology; MMSE, Mini Mental State Examination.
comorbid frailty is challenging in clinical practice. First, an older person with frailty can easily be misclassified as suffering from a depressive disorder during a period of (physiological) low mood. Such a person may inappropriately receive antidepressant drugs and may be withheld appropriate strategies to prevent negative health outcomes, associated with frailty. Secondly, although not examined yet, it is possible that treatment of depression among frail older persons benefits from adapted treatment strategies. In somatic conditions it has already been shown among frail older persons benefits from adapted treatment examined yet, it is possible that treatment of depression comes, associated with frailty. Secondly, although not lately receive antidepressant drugs and may be withheld (physiological) low mood. Such a person may inappropriately suffering from a depressive disorder during a period of an older person with frailty can easily be misclassified as

comorbid frailty as lifestyle is supposed to be the greatest contribu-
tional activation to reduce the negative impact of frailty

ciplinary interventions focused on life-style and behaviou-
aral activation to reduce the negative impact of frailty

future research should examine underlying mechanisms and consequences of frailty in late-life depression, as well as effectiveness of screening for frailty. Multidis-
ciplinary interventions focused on lifestyle behavior (Payne, Hybels, Bales, & Steffens, 2006; van Gool et al., 2003).

Methodological considerations

Some strengths and limitations of this study should be mentioned. A major strength of this study is the use of two proxies for physical frailty (weakness and slowness) in addition to a multi-component measure of frailty (Fried et al., 2001). Furthermore, where other studies use questionnaires as a substitute for depression diagnosis, this study used a formal diagnosis of depression according to DSM-IV criteria. Decomposing of the severity of depressive symptoms makes it unlikely that the higher severity of depression can be explained by overlapping concepts. Finally, since participants were recruited from primary care as well as in- and outpatient secondary care clinics, our 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, specifically the second aim of the study. Interestingly, frailty prevalence did not differ across the different echelons of our health care system (data not shown). Another limitation of the study was the small size of the 85+ group. Therefore, specific conclusions about this generally frail subgroup cannot be drawn. Furthermore, the comparison group was recruited among non-depressed general practice visitors, which can be assumed to have more illnesses and medical complaints than community-dwelling elderly. The difference between depressed and non-depressed persons in our study should thus be considered conservative. On the other hand, the found prevalence rates of frailty in our comparison group resembled those found in a recent meta-analysis on the prevalence of frailty in community-dwelling elderly (Collard et al., 2012) suggesting no or only limited selection bias.

Finally, this study provides the opportunity of adequate control of potential confounders, but it cannot be ruled out that the association between physical frailty and depression is confounded by unknown variables. Moreover, the cross-sectional nature of our study precludes causal interpretation of the association demonstrated.

Future perspective

The high prevalence of physical frailty among depressed elderly persons and potential benefits of targeting frailty argues for the need of screening of this particularly vulnerable group of people. As frail depressed older patients were more severely depressed than non-frail depressed patients, it may be required that especially the frail subgroup should be treated in secondary mental health care in which integrative geriatric care is more likely to be available. Future research should examine underlying mechanisms and consequences of frailty in late-life depression, as well as effectiveness of screening for frailty. Multidisciplinary interventions focused on life-style and behavior activation to reduce the negative impact of frailty within this particularly vulnerable group of patients should also be examined.

References

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