

# Appearance of depression in later life

Hegeman, J.M.

## Citation

Hegeman, J. M. (2016, May 18). *Appearance of depression in later life*. Retrieved from https://hdl.handle.net/1887/39582

Version: Not Applicable (or Unknown)

License: License agreement concerning inclusion of doctoral thesis in the

Institutional Repository of the University of Leiden

Downloaded from: <a href="https://hdl.handle.net/1887/39582">https://hdl.handle.net/1887/39582</a>

**Note:** To cite this publication please use the final published version (if applicable).

## Cover Page



# Universiteit Leiden



The handle <a href="http://hdl.handle.net/1887/39582">http://hdl.handle.net/1887/39582</a> holds various files of this Leiden University dissertation

Author: Hegeman, Annette

**Title:** Appearance of depression in later life **Issue Date:** 2016-05-18

# Chapter 4

Depression in later life: a more somatic presentation?

J.M. Hegeman M.W.M. de Waal H.C. Comijs R.M. Kok R.C. van der Mast

Journal of Affective Disorders 2015; 170:196-202

## **Abstract**

#### **Background**

Depression later in life may have a more somatic presentation compared with depression earlier in life due to chronic somatic disease and increasing age. This study examines the influence of the presence of chronic somatic diseases and increasing age on symptom dimensions of late-life depression.

#### Methods

Baseline data of 429 depressed and non-depressed older persons (aged 60-93 years) in the Netherlands Study of Depression in Old Age were used, including symptom dimension scores as assessed with the mood, somatic and motivation subscales of the Inventory of Depressive Symptomatology-Self Report (IDS-SR). Linear regression was performed to investigate the effect of chronic somatic diseases and age on the IDS-SR subscale scores.

#### Results

In depressed older persons a higher somatic disease burden was associated with higher scores on the mood subscale (B=2.02, p=0.001), whereas higher age was associated with lower scores on the mood (B=-2.30, p<0.001) and motivation (B=-1.01, p=0.006) subscales. In depressed compared with non-depressed persons, a higher somatic disease burden showed no different association with higher scores on the somatic subscale (F(1,12)=9.2, p=0.003, partial P=0.022).

#### Limitations

Because the IDS-SR subscales are specific for old age, it was not feasible to include persons aged <60 years to investigate differences between earlier and later life.

#### Conclusions

It seems that neither higher somatic disease burden nor higher age contribute to more severe somatic symptoms in late-life depression. In older old persons aged ≥70 years, late-life depression may not be adequately recognized because they may show less mood and motivational symptoms compared with younger old persons.

## Introduction

Depression later in life may have a more somatic presentation compared with depression earlier in life,<sup>1</sup> thereby complicating the recognition of depression.<sup>2</sup> For instance, a recent meta-analysis found that depressed older persons showed more hypochondriasis and somatic symptoms of depression, whereas feelings of guilt and loss of sexual interest were more related to early-life depression.<sup>3</sup>

There are several explanations for a possibly more somatic presentation of depression in late-life. For example, the symptoms of (more frequent) somatic diseases in older age may be mistaken for somatic symptoms of depression. Also, several studies found an association between late-life depression and somatic comorbidity, whereas others found a weakening association between depression and somatic diseases with increasing age, despite an increase in the prevalence of somatic diseases.<sup>47</sup> Alternatively, with increasing age depression might be characterized by more somatic symptoms due to various underlying age-related biological pathways in late-life depression compared with depression earlier in life.<sup>8-13</sup>

Using the Inventory of Depressive Symptomatology Self Report (IDS-SR) among older people, we earlier identified a mood, motivation and somatic subscale reflecting three homogeneous symptom dimensions.<sup>14</sup> These IDS-SR symptom dimensions appeared to be specific for old age, as only two symptom dimensions including 'mood/cognition' and 'anxiety/arousal' were found at a younger age.<sup>15</sup>

The present study aims to investigate the effects of both somatic comorbidity and increasing age on the presentation of late-life depression according to the mood, motivation and somatic subscales of the IDS-SR. <sup>14,16</sup> To unravel the possible misattribution of symptoms of chronic somatic diseases and aging to depression, we examined the effects of chronic diseases and aging on IDS-SR symptom severity in depressed and non-depressed older people. We hypothesized that, with a higher number of chronic somatic diseases and higher age, there would be a more prominent somatic presentation of late-life depression as reflected in higher scores on the IDS-SR somatic subscale. However, we expected that a higher number of chronic somatic diseases and higher age would not affect the presentation of late-life depression with respect to mood and motivation symptoms according to the corresponding IDS-SR symptom subscales.

## Methods

#### Study sample

Data were used from the baseline assessment of the Netherlands Study of Depression in Old Persons (NESDO), conducted among people aged ≥60 years. NESDO is a multi-site naturalistic cohort study examining the determinants, long-time course and consequences of depressive disorders at old age. The design of the NESDO is described in detail elsewhere. In short, between 2007 and 2010 participants were enrolled from mental healthcare and primary healthcare settings to create a sample reflecting all different stages of depression. Excluded were persons with a psychotic disorder, obsessive-compulsive disorder or severe addiction disorder, and insufficient command of the Dutch language. Also excluded were persons with a Mini-Mental State Examination score (MMSE) <18 or a primary diagnosis of dementia.

The baseline NESDO sample consists of 378 depressed (diagnosis within the last 6 months according to DSM-IV criteria) and 132 non-depressed persons aged 60-93 years (total sample n=510). The present study included 303 persons diagnosed with a depressive disorder according to the DSM-IV criteria within the last month before baseline assessment, and 132 non-depressed persons, all with complete data on the IDS-SR. Persons with missing total scores on all three subscales were excluded. For this reason, 3 persons from the 303 depressed group and 3 persons from the 132 non-depressed group were excluded, leaving 300 depressed and 129 non-depressed persons (total=429) for the present analysis. The persons with missing scores on all three subscales did not differ from the included persons with respect to gender (p=0.313) and number of years of education (p=0.057). Both depressed and non-depressed persons were included to examine differences in the presentation of depressive symptoms due to somatic diseases and higher age in their own right, and in relation to depression.

The study protocol was approved by the ethical review boards of all the participating centers and informed consent was signed by all participants.

#### Measures

#### Socio-demographics

Demographic information was collected with standard questions concerning age, gender and years of education. Age was used as a categorical variable with a cut-off age of 70 years, being close to both the median and mean age of the whole sample. Thus, the 'younger old' are defined as people aged <70 years and the 'older old' as people aged ≥70 years.

## Depressive symptoms and neuropsychiatric characteristics

The presence of a depressive disorder (major depression, dysthymia and minor depression) according to the DSM-IV criteria within the last month before the baseline assessment was measured with the Composite International Diagnostic Interview (CIDI; WHO version 2.1; lifetime version).<sup>18</sup> The Dutch translation of the IDS-SR<sup>16</sup> was used to compute total scores of the three old-age specific IDS-SR subscales.<sup>14</sup> The IDS-SR items of the mood, somatic and

Figure 1. Items of the IDS-SR subscales.

tem 5	Feeling sad
tem 6	Feeling irritable
Item 7	Feeling anxious or tense
Item 8	Reactivity of mood
Item 10	Quality of mood
Item 17	Future pessimism
Item 18	Suicidal thoughts
Item 27	Panic/phobic symptoms
Item 29	Interpersonal sensitivity
Somatic subscale	
Item 1	Initial insomnia
Item 2	Middle insomnia
Item 3	Early morning awakening
Item 11/12	Appetite disturbance
Item 13/14	Weight disturbance
Item 22	Interest in sex
Item 25	Aches and pains
Item 26	Sympathetic arousal
Motivation subscale	
Item 4	Sleeping too much
Item 16	Self criticism and blame
Item 19	Interest in people/activities
Item 20	Energy/fatiguability
Item 23	Psychomotor retardation

motivation subscales were scored on a four-point scale (range 0-3 points) (Figure 1). These age-specific subscales of the IDS-SR can be used in older persons with no or different stages of depression and have shown adequate properties across different age and gender groups in late-life.<sup>14</sup>

Global cognitive functioning was assessed with the MMSE.<sup>19</sup>

#### Clinical characteristics

A self-report questionnaire was used to assess the presence of chronic somatic diseases as follows: participants were asked whether they had chronic non-specific lung disease, cardiovascular diseases, diabetes mellitus, stroke, intestinal disorders, arthritis or arthrosis, cancer, thyroid gland diseases, or any other disease. Obtaining information on the presence of chronic somatic diseases using a self-report questionnaire has shown to be adequate compared with obtaining information from the general practitioner.<sup>20</sup> The total number of chronic somatic diseases was obtained by counting the number of self-reported chronic somatic diseases (count 0-8), excluding hypertension, and dichotomized into 0 or 1, and 2 or more chronic somatic diseases. The cut-off of 2 chronic somatic diseases is close to the mean number of chronic somatic diseases (1.9) in the whole sample, and distinguishes between no/lower somatic disease burden and a higher somatic disease burden.

The current smoking status was derived from the Fagerstrom test for Nicotine Dependence. Alcohol use was defined as the amount of glasses consumed per day and assessed with the Alcohol Use Disorders Identification Test; the results were categorized into 0, 1-2, and >2 glasses a day.<sup>21</sup>

### Statistical analyses

Data were analysed using SPSS version 20.0. First, differences in demographic, and neuropsychiatric and clinical characteristics, between depressed and non-depressed older persons were evaluated using a t-test for continuous variables, chi-square tests for categorical variables, and non-parametric tests for not normally distributed variables. All analyses were carried out two-sided with a significance level of p<0.05.

We performed three-way independent analyses of covariance (ANCOVA) to obtain adjusted mean scores for each IDS-SR subscale in eight distinctive groups defined by the presence of depression, the number of chronic somatic diseases, and age, as follows: depressed persons aged <70 years with 0 or 1 chronic somatic diseases, depressed persons aged  $\geq$ 70 years with 0 or 1 chronic somatic diseases and with  $\geq$ 2 chronic somatic diseases, non-depressed persons aged  $\leq$ 70 years with 0 or 1 chronic somatic diseases, non-depressed persons aged  $\leq$ 70 years with  $\leq$ 2 chronic somatic diseases, non-depressed persons aged  $\leq$ 70 years with 0

or 1 chronic somatic diseases and with  $\geq$ 2 chronic somatic diseases. The dependent variable was the score on the IDS-SR subscale and the three independent variables were depression, chronic somatic diseases, and age. Potential confounding variables including gender, years of education, alcohol use, smoking status, and MMSE were added as covariates. We did not adjust for overall depression severity because age-related or chronic somatic disease-related differences in the scores of the IDS-SR subscales are also part of the total severity score. Controlling for the severity of depression therefore involves circularity, which could result in overadjustment. A full factorial design was used in which the significance (p<0.10) of the two-way interaction terms of depression and chronic somatic diseases, depression and age, and chronic somatic diseases and age, and a three-way interaction term involving depression, chronic somatic diseases and age, were examined in the whole sample. Eta squared ( $\eta^2 > 0.01 \sim$  small effect size,  $\eta^2 > 0.06 \sim$  medium effect size, and  $\eta^2 > 0.14 \sim$  large effect size) and F ratios were used as a measure of effect size.

In case of significant interaction, the sample was stratified and multiple linear regression analyses were performed for each IDS-SR subscale in order to examine the influence of chronic somatic diseases and age, respectively, on the presentation of depressive symptoms. Potentially confounding variables including gender, years of education, alcohol use, smoking status, and MMSE were added to the regression model.

## Results

Table 1 presents the demographic, neuropsychiatric and clinical characteristics of the depressed and non-depressed persons. Depressed persons had fewer years of education, a lower median MMSE score, a higher number of chronic somatic diseases, were more often smokers and used less alcohol, compared with non-depressed persons. Some of the depressed persons had more than one depressive disorder within the last month before baseline assessment. Figure 2 presents the adjusted mean scores of the three IDS-SR subscales for subgroups defined by depression, the number of chronic somatic diseases and age (see also Table S1 Supplementary material).

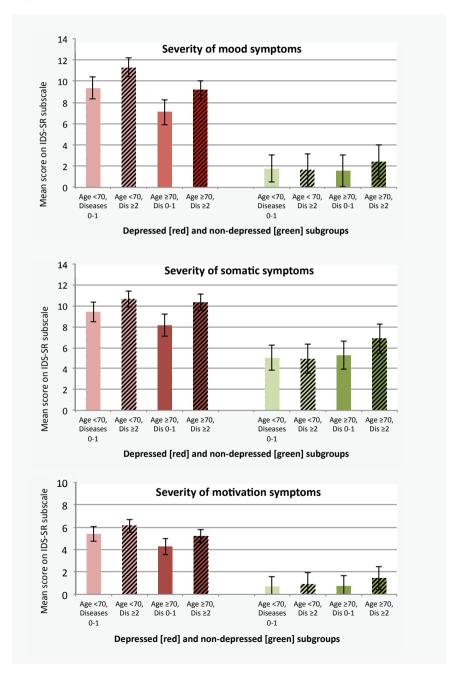
A significant interaction was found between depression and the number of chronic somatic diseases for the mood subscale (F(1,12)=3.47, p=0.063, partial  $\eta^2$ =0.008); this indicates that, in depressed compared with non-depressed persons, a higher somatic disease burden had a different association with scores on the IDS-SR mood subscale. However, no significant interaction was found between depression and the number of chronic somatic diseases for the somatic (F(1,12)=1.49, p=0.223, partial  $\eta^2$ =0.004) and motivation (F(1,12)=0.43, p=0.512, partial  $\eta^2$ =0.001) subscales. This indicates a similar association in depressed and non-

**Table 1.** Comparison of demographic, neuropsychiatric and clinical characteristics between depressed and non-depressed persons.

Sample (n=429)	Depressed (n=300)	Non-depressed (n=129)	p-value
Demographic characteristics			
Mean age in years (SD)	70.5 (7.3)	70.0 (7.3)	
Age range in years	60-90	60-93	
Age 70, n (%)	146 (48.7)	56 (43.4)	
Women, n (%)	193 (64.3)	79 (61.2)	
Mean years of education (SD)	10.4 (3.5)	12.5 (3.5)	
Neuropsychiatric characteristics			
Depressive disorders in past month, n (%)			
Minor depression	20 (6.7)	-	
Dysthymia	94 (31.3)	-	
Major depression	272 (90.7)	-	
IDS-SR, mean total score (SD)	32.2 (12.4)	7.8 (6.4)	< 0.001
Mood subscale, mean total score	9.8 (5.0)	1.2 (2.0)	< 0.001
Somatic subscale, mean total score	10.1 (4.2)	4.9 (3.1)	< 0.001
Motivation subscale, mean total score	5.4 (3.1)	0.7 (1.2)	< 0.001
MMSE, median score (IQR)	28.0 (2)	29.0 (2)	<0.001
Clinical characteristics			
Mean number of chronic somatic diseases (SD)	2.1 (1.5)	1.5 (1.1)	< 0.001
Number of chronic somatic diseases present, n (%)			< 0.001
0-1	116 (38.7)	74 (57.4)	
≥2	184 (61.3)	55 (42.6)	
Chronic somatic disease present, n (%)			
Diabetes mellitus	36 (12.0)	18 (14.0)	0.576
Chronic Non Specific Lung Disease	48 (16.0)	9 (7.0)	0.012
Thyroid disease	32 (10.7)	7 (5.4)	0.083
Cardiovascular diseases	66 (22.0)	27 (20.9)	0.805
Stroke	35 (11.7)	3 (2.3)	0.002
Arthritis or arthrosis	146 (48.7)	59 (45.7)	0.577
Oncological diseases	57 (19.0)	24 (18.6)	0.924
Intestinal disorders	71 (23.7)	11 (8.5)	< 0.001
Current smoker, n (%)	82 (27.5)	10 (7.8)	< 0.001
Alcohol use, glasses/day, n (%)			< 0.001
0	122 (40.9)	17 (13.3)	
1-2	152 (51.0)	84 (65.6)	
>2	24 (8.1)	27 (21.1)	

Abbreviations: SD, standard deviation; IQR, interquartile range; MMSE, Mini-Mental State Examination; IDS-SR, Inventory of Depressive Symptomatology-Self Report; Means (standard deviations) and overall p-values with independent t-tests for normally distributed continuous variables; medians (interquartile range) and overall p-values with nonparametric Mann-Whitney tests for skewed distributed continuous variables; number of persons (percentages) and overall p-values with x2 tests for categorical variables.

**Figure 2.** Adjusted mean scores of the three IDS-SR subscales for subgroups defined by depression, age and the number of chronic somatic diseases. Whiskers represent 95% confidence intervals of sample mean.



depressed persons between chronic somatic diseases and symptom severity of the somatic subscale (F(1,12)=9.20, p=0.003, partial  $\eta^2$ =0.022), with a small effect size. The same applies to the association between somatic disease burden and symptom severity of the motivation subscale (F(1,12)=4.94, p=0.027, partial  $\eta^2$ =0.012). Furthermore, a significant interaction was found for depression and age for the mood (F(1,12)=7.57, p=0.006, partial  $\eta^2$ =0.018), somatic (F(1,12)=5.42, p=0.020, partial  $\eta^2$ =0.013), and motivation (F(1,12)=5.16, p=0.024, partial  $\eta^2$ =0.013) subscales demonstrating that, in depressed compared with non-depressed persons, age had a different association with symptom severity of all three subscales. The ANCOVAs for all three IDS-SR subscales, including all interaction terms, are shown in the supplementary material (Tables S1 and S2).

**Table 2.** Multivariate regression of age and chronic diseases on scores of IDS-SR subscales in depressed and non-depressed persons.

			Depress	ed		Non-	-depress	ed
Predictors	В	SE	β	<i>p</i> -value	В	SE	β	<i>p</i> -value
Severity of symptoms of mood subscale								
Diseases	2.02	0.58	0.197	0.001	0.64	0.37	0.162	0.082
Age	-2.30	0.56	-0.231	<0.001	0.48	0.36	0.120	0.189
Severity of symptoms of somatic subscale								
Diseases	1.61	0.49	0.185	0.001	1.01	0.54	0.164	0.065
Age	-0.70	0.48	-0.082	0.145	1.28	0.53	0.208	0.018
Severity of symptoms of motivation subscale								
Diseases	0.85	0.38	0.101	0.025	0.44	0.22	0.180	0.047
Age	-1.01	0.37	-0.163	0.006	0.17	0.21	0.069	0.435

 $Adjusted \ for \ gender, years \ of \ education, \ MMSE, \ current \ smoker \ and \ alcohol \ use. \ Abbreviations: \ IDS-SR, \ Inventory \ of \ Depressive \ Symptomatology-Self \ Report.$ 

Because significant interactions were found, the subsequent analyses were stratified according to depression status (Table 2). In Table 2, the *B* coefficient for chronic somatic diseases reflects the difference in mean subscale scores of persons with higher somatic disease burden compared with persons with lower somatic disease burden. Similarly, the *B* coefficient for age equals the difference in mean subscale scores found in 'older old' persons compared with 'younger old' persons. Table 2 shows that, with respect to the mood

subscale, depressed persons with higher somatic disease burden presented more severe mood symptoms compared with depressed persons with lower somatic disease burden, whereas older old depressed persons showed less severe mood symptoms compared with younger old depressed persons. In non-depressed persons, the presence of chronic somatic diseases and age were not associated with the severity of mood symptoms. With respect to the somatic subscale, the presence of chronic somatic diseases was associated with symptom severity of the somatic subscale in depressed but not in non-depressed persons. Age was not associated with symptom severity of the somatic subscale in depressed persons. However, in non-depressed persons, higher age was associated with higher somatic symptom severity. According to the motivation subscale, higher somatic disease burden was associated with more severe motivational symptoms in both depressed and in non-depressed persons. At the same time, older old depressed persons showed less severe symptoms on the motivation subscale compared with younger old depressed persons, whereas age was not associated with the severity of motivational symptoms in non-depressed persons.

## Discussion

This study examined the influence of somatic comorbidity and age on the presentation of late-life depression. Remarkably, our results demonstrate a reverse effect of the presence of chronic somatic diseases compared with the effect of higher age on the presentation of late-life depression on all three subscales. That is, for all three subscales late-life depression was characterized by higher symptom severity when a higher burden of somatic diseases was present, and by less symptom severity with higher age. However, the association between age and symptom severity of the somatic subscale did not reach significance. Thus, late-life depression was not only characterized by more somatic symptoms but also by more severe mood and motivational symptoms in the presence of higher somatic disease burden, whereas the expected more prominent somatic presentation of late-life depression in the older old compared with younger old depressed persons was not found.

In the non-depressed group, no such association in the opposite direction of chronic somatic diseases compared with age was consistently found for the three subscales. Non-depressed persons showed no clinically relevant symptom severity on the mood and motivation subscale, whereas chronic somatic diseases and age were positively associated with symptom severity of the somatic subscale. This finding that non-depressed persons showed more somatic symptoms with more somatic disease burden or higher age might be interpreted as somatic symptoms that appear with the occurrence of chronic somatic

diseases and aging. However, as no significant difference was found between depressed and non-depressed persons in symptom severity of the somatic subscale related to the presence of chronic somatic diseases, the more prominent somatic presentation of latelife depression found in the presence of higher somatic disease burden might be the consequence of misattribution of symptoms of chronic somatic diseases to depression. This latter finding concurs with our previous study showing a relatively low internal consistency of the somatic subscale compared with the other subscales and that internal consistency of the somatic subscale was decreased in the age group >70 years; this indicates a less homogeneous content of the somatic subscale due to overlap of somatic symptoms of depression and chronic diseases. Herthermore, the slightly higher symptom severity of the motivation subscale, found in the presence of higher somatic disease burden in depressed and non-depressed persons, might represent sickness behavior, even though the effect on symptom severity on the mood scale for non-depressed persons did not reach significance.

Our results are partly in line with others investigating the relation between somatic diseases, age and the phenomenology of depression as measured with a single item level of the Inventory of Depressive Symptomatology Clinician Rating (IDS- $C_{30}$ ) in depressed persons aged 18-72 years. <sup>22,23</sup> Although the age range of the studies of Hussain *et al.* and Yates *et al.* only partly reflected our age range and did not include the older old, some results were consistent with our study, i.e. in the presence of somatic comorbidity more symptoms of the somatic subscale (e.g. sympathetic arousal, and aches and pains) were found and, with increasing age, less symptoms of the mood subscale (e.g. irritability and negative cognitions) were found. <sup>22,23</sup>

In our study, the lower score found on the motivation subscale in the older old compared with the younger old depressed persons is in contrast to the generally found increase of apathy in older depressed persons.<sup>24</sup> However, besides the motivational symptoms resembling apathy, the motivational subscale also includes the item 'sleeping too much' as well as a depressive cognitive item. Therefore, it can be questioned whether scores on the motivational subscale adequately represent apathy severity. Furthermore, in an earlier meta-analysis on age-related differences in the phenomenology of depression, it was found that older depressed persons compared with younger depressed persons showed less feelings of guilt,<sup>3</sup> which is in line with our current finding. Alternatively, perhaps the increase of apathy generally found in older depressed persons is particularly associated with cognitive dysfunctioning rather than with higher age.

As suggested previously, late-life depression often remains unnoticed;² this is an important issue that may be further clarified by our results. The present finding that the older old compared with younger old depressed persons show less symptoms on the IDS-SR mood and motivational subscale implies that, particularly in older old persons aged ≥70 years, late-

life depression may not be recognized properly. A possible explanation for this is a cohort effect of the current older generation not being accustomed to expressing psychological symptoms.<sup>25</sup> Furthermore, inconsistent results are reported on the topic of specific agerelated pathophysiological pathways in late-life depression, such as the inflammatory and vascular depression hypothesis.<sup>26-28</sup> Age-specific pathophysiological pathways might explain differences in the phenomenology of depression at old age. However, until now, this issue has rarely been examined except for executive and cognitive dysfunction in relation to (cerebral) vascular diseases and vascular risk factors. For example, in an older old depressed population, thoughts of death, sleep and appetite-related symptoms of depression were found to be related to inflammatory factors, whereas motivation symptoms were related to vascular and degenerative risk factors.<sup>29</sup> Moreover, our result of fewer mood symptoms in older old depressed persons is unlikely to be the consequence of a wrongly diagnosed depression instead of apathy as a syndrome of its own, as no increase was found in symptoms on the motivation subscale, including items resembling apathy.

Diagnosing late-life depression may also be complicated by incorrect attribution of somatic symptoms of somatic diseases to depression. Suggested solutions are an inclusive or exclusive approach that includes or excludes all somatic symptoms of depression when diagnosing late-life depression. 30-32 These latter solutions are limited to somatic symptoms only, whereas the present study shows that somatic diseases are also related to more severe mood and motivational symptoms. In contrast to the somatic and motivational subscale, a significant difference was found in the association between severity of mood symptoms and a higher somatic disease burden in depressed compared with non-depressed persons. Accordingly, the higher symptom severity of the mood subscale found in depressed persons with higher somatic diseases burden, might reflect a strengthening of the symptoms of the depression itself and not only of mood symptoms that co-exist with somatic diseases. Therefore, an exclusive approach specifically related to all somatic symptoms seems an appropriate solution to examine the severity of late-life depression. Indeed, it may be difficult to establish whether a symptom is a result of a physical illness, sickness behavior, the aging process, or depression. Therefore, an etiological or substitutive approach, excluding or replacing only somatic symptoms specifically caused by a somatic disease, respectively, does not seem practical.<sup>33-38</sup> Thus, our results imply that severity of depression may be overestimated in the presence of somatic comorbidity, but only with respect to the somatic and motivational symptom domain.

This study has some limitations. The IDS-SR subscales used are specific for old age and differ from the previous IDS-SR subscales used in younger age.<sup>15</sup> Therefore, we could not include persons aged <60 years in this study to compare them with older adults regarding the associations of somatic diseases and IDS-SR symptom dimensions. Similarly, we could

not investigate the effect of younger age compared with older age on the presentation of depressive symptoms according to the symptom dimensions of the IDS-SR. A major strength of this study is the large study sample consisting of depressed and non-depressed persons. Therefore, differences in the effects of chronic somatic diseases and age on depressive symptomatology between depressed and non-depressed could be examined to distinguish between symptoms wrongly attributed to depression and symptoms of the depression itself. Moreover, in this study a depressive disorder was diagnosed using the CIDI and not by applying a cut-off score on a symptom severity scale. Therefore, incorrectly diagnosed depression due to misattribution of somatic symptoms of chronic somatic diseases to depression, was less likely to occur. Furthermore, the study sample reflects different stages of depression and healthcare settings, thereby increasing the generalizability of the results.

In conclusion, it appears that neither higher somatic disease burden nor higher age contribute to more severe somatic symptoms of late-life depression. Our results imply that severity of late-life depression may be overestimated in the presence of somatic comorbidity, but only with respect to the somatic and motivational symptom domain due to misattribution of symptoms of somatic diseases and sickness behavior. In fact, higher somatic disease burden does contribute to higher severity of mood symptoms of late-life depression. Finally, particularly in the older old aged ≥70 years, late-life depression may not be recognized properly as this group tend to show less mood and motivational symptoms.

## References

- Wilkowska-Chmielewska J, Szelenberger W, Wojnar M. Age-dependent symptomatology of depression in hospitalized patients and its implications for DSM-5. J Affect Disord 2013; 150:142-145.
- Mitchell AJ, Rao S, Vaze A. Do primary care physicians have particular difficulty identifying late-life depression? A meta-analysis stratified by age. Psychother. Psychosom 2010; 79:285-294.
- Hegeman JM, Kok RM, van der Mast RC, Giltay EJ. Phenomenology of depression in older compared with younger adults: meta-analysis. Br J Psychiatry 2012: 200: 275-281.
- Braam, AW, Prince MJ, Beekman AT et al. Physical health and depressive symptoms in older Europeans. Results from EURODEP. Br J Psychiatry 2005: 187:35-42.
- Kessler RC, Birnbaum HG, Shahly V et al. Age differences in the prevalence and co-morbidity of DSM-IV major depressive episodes: results from the WHO World Mental Health Survey Initiative. Depress Anxiety 2010; 27:351-364.
- Lyness JM, Niculescu A, Tu X, Reynolds CF, Caine ED. The relationship of medical comorbidity and depression in older, primary care patients. Psychosomatics 2006; 47:435-439.
- Scott KM, von Korff M, Alonso J et al. Age patterns in the prevalence of DSM-IV depressive/anxiety disorders with and without physical co-morbidity. Psychol Med 2008; 38:1659-1669.
- Alexopoulos GS, Buckwalter K, Olin J et al. Comorbidity of late life depression: an opportunity for research on mechanisms and treatment. Biol Psychiatry 2002; 52:543-558.
- Belvederi MM, Pariante C, Mondelli V et al. HPA axis and aging in depression: Systematic review and meta-analysis. Psychoneuroendocrinology 2014; 41C:46-62.

- Kapfhammer HP. Somatic symptoms in depression. Dialogues Clin Neurosci 2006; 8:227-239
- Krishnan KR, Delong M, Kraemer H et al. Comorbidity of depression with other medical diseases in the elderly. Biol Psychiatry 2002; 52:559-588.
- McKinney BC, Sibille E. The age-by-disease interaction hypothesis of late-life depression. Am J Geriatr Psychiatry 2013; 21:418-432.
- Naismith SL, Norrie LM, Mowszowski L, Hickie IB. The neurobiology of depression in later-life: clinical, neuropsychological, neuroimaging and pathophysiological features. Prog Neurobiol 2012; 98:99-143.
- Hegeman JM, Wardenaar KJ, Comijs HC et al. The subscale structure of the Inventory of Depressive Symptomatology Self Report (IDS-SR) in older persons. J Psychiatr Res 2012; 46:1383-1388.
- Wardenaar KJ, van Veen T, Giltay EJ et al. The structure and dimensionality of the Inventory of Depressive Symptomatology Self Report (IDS-SR) in patients with depressive disorders and healthy controls. J Affect Disord 2010; 125:146-154.
- Rush AJ, Gullion CM, Basco MR et al. The Inventory of Depressive Symptomatology (IDS): psychometric properties. Psychol Med 1996; 26:477-486.
- Comijs HC, van Marwijk HW, van der Mast RC et al. The Netherlands study of depression in older persons (NESDO); a prospective cohort study. BMC Res Notes 2011; 4:524.
- Wittchen HU, Robins LN, Cottler LB et al. Cross-cultural feasibility, reliability and sources of variance of the Composite International Diagnostic Interview (CIDI). The Multicentre WHO/ADAMHA Field Trials. Br J Psychiatry 1991; 159:645-653, 658.

- Folstein MF, Folstein SE, McHugh PR. "Minimental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975; 12:189-198.
- Kriegsman DM, Penninx BW, van Eijk JT et al. Selfreports and general practitioner information on the presence of chronic diseases in community dwelling elderly. A study on the accuracy of patients'self-reports and on determinants of inaccuracy. J Clin Epidemiol 1996; 49:407-1417.
- Babor TF, Kranzler HR, Lauerman RJ. 1989. Early detection of harmful alcohol consumption: comparison of clinical, laboratory, and self-report screening procedures. Addict Behav 1989; 14:139-157.
- Husain MM, Rush AJ, Sackeim HA et al. Agerelated characteristics of depression: a preliminary STAR\*D report. Am J Geriatr Psychiatry 2005; 13:852-860.
- Yates WR, Mitchell J, Rush AJ et al. Clinical features of depressed outpatients with and without cooccurring general medical conditions in STAR\*D. Gen Hosp Psychiatry 2004; 26:421-429.
- Groeneweg-Koolhoven I, Comijs HC, Naarding P et al. Presence and correlates of apathy in depressed and non-depressed older persons. Eur J Psychiatry 2015; 29:41-51.
- Lyness JM, Cox C, Curry J et al. Older age and the underreporting of depressive symptoms. J Am Geriatr Soc 1995; 43:216-221.
- Alexopoulos GS, Morimoto SS. The inflammation hypothesis in geriatric depression. Int J Geriatr Psychiatry 2011; 26:1109-1118.
- Jellinger KA. Organic bases of late-life depression: a critical update. J Neural Transm 2013; 120:1109-1125.
- Taylor WD, Aizenstein HJ, Alexopoulos GS. The vascular depression hypothesis: mechanisms linking vascular disease with depression. Mol Psychiatry 2013; 18:963-974.

- Naarding P, Schoevers RA, Janzing JG et al. A study on symptom profiles of late-life depression: the influence of vascular, degenerative and inflammatory risk-indicators. J Affect Disord 2005; 88:155-162.
- Cohen-Cole SA, Stoudemire A. Major depression and physical illness. Special considerations in diagnosis and biologic treatment. Psychiatr Clin North Am 1987: 10:1-17.
- Drayer RA, Mulsant BH, Lenze EJ et al. Somatic symptoms of depression in elderly patients with medical comorbidities. Int J Geriatr Psychiatry 2005; 20:973-982.
- Zisook S, Downs NS. Diagnosis and treatment of depression in late life. J Clin Psychiatry 1998; 59(4):80-91.
- Clark DC, vonAmmon CS, Gibbons RD. The core symptoms of depression in medical and psychiatric patients. J Nerv Ment Dis 1983; 171:705-713.
- 34. Endicott J. Measurement of depression in patients with cancer. Cancer 1984; 53:2243-2249.
- Kathol RG, Mutgi A, Williams J et al. Diagnosis of major depression in cancer patients according to four sets of criteria. Am J Psychiatry 1990; 147:1021-1024.
- Koenig HG, George LK, Peterson BL, Pieper CF.
   Depression in medically ill hospitalized older adults: prevalence, characteristics, and course of symptoms according to six diagnostic schemes.

  Am J Psychiatry 1997; 154:1376-1383.
- Rapp SR, Vrana S. Substituting nonsomatic for somatic symptoms in the diagnosis of depression in elderly male medical patients. Am J Psychiatry 1989; 146:1197-1200.
- Robinson RG, Kubos KL, Starr LB et al. Mood disorders in stroke patients. Importance of location of lesion. Brain 1984; 107:81-93.

## Supplementary Material

Table S1. Mean scores (SE) of IDS-SR subscales (Figure 1).

Depressed			Non-depressed				
<7	0	≥7	70	<70		≥70	
0-1	≥2	0-1	≥2	0-1	≥2	0-1	≥2
Diseases	Diseases	Diseases	Diseases	Diseases	Diseases	Diseases	Disease
Mean score	(SE) mood sub	scale of the IL	DS-SR				
9.36	11.28	7.08	9.19	1.76	1.63	1.57	2.40
(0.52)	(0.45)	(0.60)	(0.44)	(0.65)	(0.80)	(0.76)	(0.82)
Mean score	(SE) somatic su	ubscale of the	IDS-SR				
9.40	10.64	8.13	10.34	5.03	4.91	5.26	6.87
(0.47)	(0.40)	(0.54)	(0.39)	(0.60)	(0.71)	(0.68)	(0.73)
Mean score	(SE) motivatio	n subscale of	the IDS-SR				
5.40	6.13	4.26	5.20	0.70	0.93	0.75	1.44
(0.33)	(0.29)	(0.38)	(0.28)	(0.43)	(0.51)	(0.49)	0.54)

Adjusted for gender, years of education, MMSE, current smoker and alcohol use.

**Table S2.** Associations between scores of IDS-SR subscales and number of somatic diseases, age and depression.

	F (df)	p-value	partial η²
Mood subscale			
Depression	228.5 (1,12)	< 0.001	0.358
Age	4.4 (1,12)	0.037	0.011
Diseases	6.8 (1,12)	0.010	0.016
Depression*age	7.6 (1,12)	0.006	0.018
Depression*diseases	3.5 (1,12)	0.063	0.008
Age*diseases	0.4 (1,12)	0.522	0.001
Depression*age*diseases	0.2 (1,12)	0.663	<0.001
Somatic subscale			
Depression	87.9 (1,12)	< 0.001	0.177
Age	0.2 (1,12)	0.700	<0.001
Diseases	9.2 (1,12)	0.003	0.022
Depression*age	5.4 (1,12)	0.020	0.013
Depression*diseases	1.5 (1,12)	0.223	0.004
Age*diseases	2.8 (1,12)	0.096	0.007
Depression*age*diseases	0.2 (1,12)	0.632	0.001
Motivation subscale			
Depression	185.2 (1,12)	< 0.001	0.316
Age	1.6 (1,12)	0.202	0.004
Diseases	4.9 (1,12)	0.027	0.012
Depression*age	5.2 (1,12)	0.024	0.013
Depression*diseases	0.4 (1,12)	0.512	0.001
Age*diseases	0.3 (1,12)	0.569	0.001
Depression*age*diseases	0.04 (1,12)	0.834	<0.001

 $\label{lem:mass} \mbox{Adjusted for gender, years of education, MMSE, current smoker and alcohol use.}$