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# Health-Related Quality of Life in Older Persons with Medically Unexplained Symptoms

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**Objective:** *Research on health-related quality of life (HRQoL) in older persons with medically unexplained symptoms (MUS) is scarce, and, in contrast with younger patients, interactions with chronic somatic diseases are more complex. Design:* *In the current study we compared HRQoL between older persons with MUS and older persons with medically explained symptoms (MES). Our study sample consisted of 118 older MUS-patients and 154 older MES-patients. Setting/Measurements:* *The diagnosis of MUS was ascertained by the general practitioner and confirmed by a geriatrician within a multidisciplinary diagnostic assessment. Additional characteristics, including the HRQoL (Short Form-36), were assessed during a home visit. MES-patients received two home visits to assess all measures. Multiple linear regression analyses, adjusted for age, sex, education, cognitive functioning, and psychiatric diagnoses, were performed to assess the relationship between group (MUS/MES) and HRQoL. Analyses were repeated with additional adjustments for somatization and hypochondriacal cognitions. Results:* *Older patients with MUS had a significantly lower level of HRQoL compared with older patients with MES. Even after adjustments, the presence of MUS was still associated with both a lower physical and mental HRQoL. These associations disappeared, however, after additional adjustments for somatization and hypochondriacal cognitions. Within the subgroup of MUS-patients, higher levels of hypochondriac anxiety and of somatization were significantly associated with both lower physical and mental HRQoL. Conclusions:* *Associations between HRQoL and late-life MUS disappear when corrected for somatization and hypochondriacal cognitions, which is in line with the DSM-5 classification of somatic symptom disorder. Appropriate psychological treatment seems needed to improve HRQoL in older MUS-patients. (Am J Geriatr Psychiatry 2016; 24:1117-1127)*

**Key Words:** aged, medically unexplained symptoms, quality of life, somatization

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The World Health Organization defines quality of life (QoL) as the “individuals’ perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.” Following this definition, QoL is a subjective, multidimensional concept in which physical, material, social, and emotional well-being, as well as activity and development, should be taken into account.<sup>1</sup> Over the years, much research in medicine has been performed on health-related quality of life (HRQoL) on the assumption that medical treatment should not only improve disease outcomes but also HRQoL.<sup>2,3</sup>

Knowledge of HRQoL in older adults with medically unexplained symptoms (MUS) is limited. MUS are physical symptoms that are present for more than several weeks and for which, even after adequate medical examination, no sufficient medical explanation has been found.<sup>4</sup> In the DSM-IV-TR,<sup>5</sup> MUS are classified under the section of somatoform disorders. This section has been replaced by the section on somatic symptom disorders in DSM-5,<sup>6</sup> in which the distinction between MUS and medically explained symptoms (MES) is abandoned and replaced by positive criteria like disproportionate thoughts (e.g., health anxiety) or behavior (e.g., somatization) associated with a physical symptom. MUS-patients are highly expensive for society because of their frequent use of health services,<sup>7</sup> although their needs are not adequately addressed by the medical system. Moreover, older MUS-patients have high levels of psychiatric comorbidity, especially depression and anxiety,<sup>8</sup> as well as multiple somatic diseases.<sup>9</sup> In addition to the severity of the MUS, HRQoL may thus be affected by these high psychiatric and somatic comorbidity rates.<sup>10</sup>

In younger age groups, the presence of MUS has consistently been associated with lower HRQoL scores,<sup>11–16</sup> which are persistent over time.<sup>17</sup> Depending on the severity of MUS, the strength of this association may somewhat differ for mental and physical HRQoL. For example, in a general primary care sample, early-stage MUS was most strongly related to the physical component of HRQoL,<sup>18</sup> whereas in patients with severe, persistent chronic fatigue, mental and physical components were equally affected.<sup>11</sup>

To our knowledge, only three studies have been conducted on HRQoL in older MUS-patients. The first study showed that the severity of fibromyalgia was lower and HRQoL better in patients aged 60 years and

older compared with their younger counterparts—although HRQoL in older participants was still significantly lower than the norm scores across all age groups.<sup>19</sup> The second study<sup>20</sup> investigated HRQoL in a general population sample consisting of persons with functional syndromes, persons with MES, and healthy controls, including participants over 60 years old. That study showed that patients with functional syndromes report lower HRQoL scores when compared with healthy controls, but equal HRQoL scores when compared with MES-patients. Unfortunately, the authors did not differentiate between age groups. The third study did differentiate between age groups and found that the association between MUS and HRQoL declines with age. Furthermore, the association between late-life MUS and HRQoL had a similar strength as the association between late-life MES and HRQoL, when corrected for the presence of depressive and anxiety disorders.<sup>21</sup> Though these studies show that late-life MUS possibly affect HRQoL, the results of two of these studies are based on highly selective patient groups (patients with functional syndromes) and all three studies lack a physical examination to classify patients into study groups. Also, even though these studies did correct for the presence of psychiatric disorder, the role of somatization and hypochondriacal cognitions in the association between HRQoL and late-life MUS remains unknown. Consequently, extensive research is needed to clarify the link between HRQoL and late-life MUS. If there is a link between HRQoL and MUS in older patients, this should have consequences for the treatment of older MUS-patients in the light of the limited availability of evidence-based treatments for MUS.

Therefore, the aim of the present study was to compare the level of both physical and mental HRQoL between a well-characterized and representative cohort of older patients with MUS and older patients with MES. Subsequently, we explore whether indicators of the severity of MUS are associated with HRQoL in the subgroup of older MUS-patients.

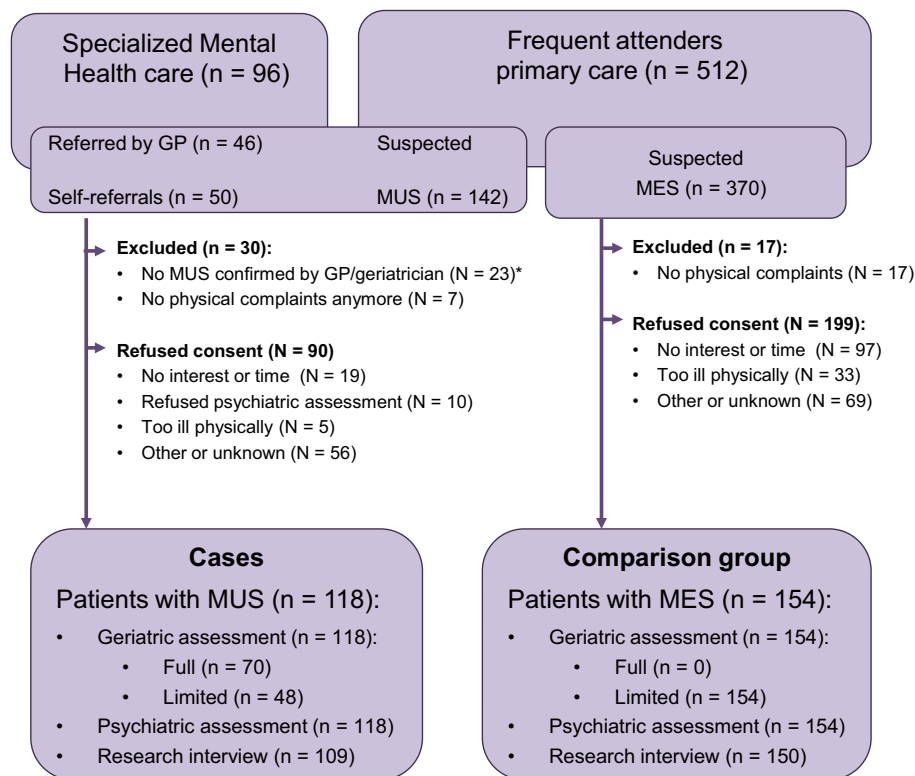
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## METHODS

### Study Design

The Older Persons with Medically Unexplained Symptoms (OPUS) project is a large observational study aiming to explore physical, psychological, and social

FIGURE 1. Recruitment of participants.



\* These 23 persons had responded to the community advertisement. They were only interested in receiving a full medical check-up, while not having any physical symptoms at all according to their GP /geriatrician

determinants of late-life MUS in order to develop suitable interventions for this patient group.

As part of this research project, we performed a case-control study in which we compared 118 older (>60 years) patients with chronic MUS (cases) to 154 older persons suffering from MES (comparison group). To compose a diverse research group regarding the severity of MUS, possible participants with MUS and MES were recruited in the community by advertisements in local newspapers (self-referral), in primary care (specifically by General Practitioners [GPs]), and in secondary health care (including both an outpatient mental health clinic for old age psychiatry and the Department of Geriatrics of the Radboud University Medical Center, Nijmegen, the Netherlands). To assist GPs with selecting possible participants, the top 20% of older frequently attending patients in their own practice were extracted from the GP Information System. Subsequently, the GP manually selected

possible participants using the definition of MUS and MES and the following exclusion criteria: 1) presence of a primary psychotic disorder; 2) presence of cognitive impairment, defined as a Mini-Mental State Examination (MMSE)<sup>22</sup> total score below 19 or an established diagnosis of dementia; 3) suffering from terminal illness; 4) not sufficiently mastering the Dutch language; and 5) severe auditory and/or visual limitations hindering reliable data collection. This selection method was chosen based on previous research projects on MUS and other high-utilizing patient groups in primary care (e.g., Katon et al.,<sup>23</sup> Smits et al.<sup>24</sup>). A detailed illustration of our patient recruitment can be found in Figure 1.

If MUS-patients decided to participate in our study, they visited a multidisciplinary clinic specialized in late-life MUS for an extensive diagnostic process. First, a geriatrician performed a comprehensive physical examination in which the severity and location(s) of the

complaints, somatic comorbidity, and medication use were assessed, among others (“full geriatric assessment”). An old-age psychiatrist assessed the presence of a somatoform disorder according to DSM-IV criteria and checked for possible psychiatric comorbidity. Also, a psychologist explored illness cognitions, consequences of the physical complaints, and QoL of the older MUS-patients. Last, a researcher visited the older MUS-patients to assess additional measures, such as social and cognitive functioning. In case MUS-patients refused to participate or were physically unable to visit the clinic (N = 45), but nevertheless agreed to participate in the OPUS study, a well-trained researcher visited the participants twice. During the additional home visit all instruments used by the multidisciplinary team, with the exception of some geriatric measures (CIRS-G), for which training was deemed insufficient to ensure reliable data-collection, were assessed. In that case, the geriatric assessment was limited to the severity and location(s) of the complaints, somatic comorbidity, gait speed, handgrip strength, weight loss, and medication use (“limited geriatric assessment”). This procedure was similar to the procedure of participants in the comparison group that also did not receive the multidisciplinary screening, and also were visited twice by the researcher. All measurements were performed between September 2011 and March 2014.

All participants gave written informed consent after receiving oral and written information. The local medical ethics committee approved the study protocol.

### Cases and Comparison Group

MUS-patients were included if they met the definition of MUS of the Dutch General Practitioners Guideline,<sup>4</sup> meaning they had physical symptoms for which, after extensive physical examination, no sufficient medical explanation had been found. Also, patients were included if a so-called functional syndrome was present (i.e., fibromyalgia or chronic fatigue syndrome<sup>25</sup>). The unexplained symptoms needed to be present for at least three months. Furthermore, the older person’s GP and/or the multidisciplinary team needed to confirm the presence of MUS. Patients were included even when explained physical symptoms were present as well, as it is known that late-life MUS often presents as a combination of unexplained and explained physical symptoms.<sup>9</sup>

MES-patients were selected if they were frequently attending visitors of their GPs with one or more evident physical complaints that were present for three months or longer, that could be fully explained by the presence of at least one chronic somatic disease, (e.g., rheumatoid arthritis or asthma). The patient’s GP needed to reconfirm the explained nature of the complaints.

Exclusion criteria for both MUS-patients and MES-patients are described in the previous section.

### Measures

#### *Health-Related Quality of Life*

HRQoL was assessed with a Dutch version of the Medical Outcome Study Short Form Health Survey (SF-36<sup>26,27</sup>). The SF-36 consists of eight subscales: physical functioning (10 items), role limitations due to physical problem (4 items), bodily pain (2 items), general health (5 items)—these were combined into the physical HRQoL component score; and vitality (4 items), social functioning (2 items), role limitations due to emotional problem (3 items) and mental health (5 items)—these were combined into the mental HRQoL component score.

We scored the questionnaire in accordance with the official Dutch guidelines.<sup>27</sup> Subscale scores ranged from 0 to 100, zero meaning very low HRQoL. A higher component score indicates higher levels of physical or mental HRQoL. The SF-36 subscale scores and component scores were our primary variables of interest.

#### *Characteristics of Medically Unexplained Symptoms*

Several measures were included to characterize MUS in more detail. These additional measures are in fact severity measures of specific aspects of MUS:

The *severity of the primary physical complaint* was assessed with a visual analogue scale (VAS) ranging from 0 (not severe at all) to 100 (very severe). Higher scores on this scale indicate a more severe perceived intensity of the physical complaint.

We used the Brief Symptom Inventory (BSI-53)<sup>28</sup> somatization subscale to assess the *level of somatization*. This seven-item subscale with answering categories from 1 (not present at all) through 5 (present all the time) assesses the presence of physical complaints



typical for functional disorders. A higher subscale score indicates increased levels of somatization.

We used the Whitely Index (WI<sup>29</sup>) to assess the *presence of hypochondriac cognitions*. This questionnaire consists of 14 statements that have to be answered with yes or no; higher scores indicate more hypochondriac cognitions.

The *presence of psychiatric disorders* according to DSM-IV-TR criteria was assessed with the Mini International Neuropsychiatric Interview (MINI, version 5.0<sup>30</sup>), a semi-structured psychiatric interview. Psychiatric disorders were subsequently classified in the following categories because of low numbers for some individual disorders: the presence of a somatoform disorder (somatization disorder/hypochondria/pain disorder/undifferentiated somatoform disorder/somatoform disorder NOS), a mood disorder (major depressive disorder/dysthymia), an anxiety disorder (panic disorder/agoraphobia/social phobia/obsessive-compulsive disorder/posttraumatic stress disorder/general anxiety disorder), and finally a substance use disorder (alcohol and substance dependence and abuse).

### Covariates

We assessed *age* (in years) at the moment of inclusion, *sex* and *education* (low, average, high) as sociodemographic variables. Global cognitive functioning was assessed with the MMSE.<sup>22</sup>

### Statistical Analyses

First, we compared differences between older MUS-patients and older MES-patients regarding patient characteristics and HRQoL by t tests for independent samples in case of continuous, normally distributed variables, Mann Whitney U tests for continuous variables that are not normally distributed, and  $\chi^2$  tests for categorical variables. Subsequently, we performed multiple linear regression analyses with the SF-36 subscales and component scores as outcomes, adjusted for sociodemographic variables (age, sex, education), the presence of mood disorder (yes/no), anxiety disorder (yes/no), and substance use disorder (yes/no), and a global score of cognitive functioning (MMSE total score<sup>22</sup>), to explore the associations with the presence of late-life MUS (versus MES).

Finally, we explored the extent to which characteristics of late-life MUS (somatization, hypochondriac cognition, somatoform disorder according to DSM-IV, any other psychiatric diagnosis according to DSM-IV and severity of primary physical complaint) were associated with HRQoL scores in older MUS-patients. Multiple linear regression analyses were performed for the mental and physical HRQoL component scores, adjusted for sociodemographic variables and a global score of cognitive functioning. We detected no multicollinearity problems after inspecting the correlation matrix and the variance inflation factors (range: 1.044–1.874). All characteristics significant at the p less than 0.05 level were entered into the final models; final models were adjusted for sociodemographic variables and global cognitive functioning score.

For all linear regression analyses B-scores (B), Standard Errors (SE), standardized B-values (Beta values), t values, df values, and p values are reported. Furthermore, R<sup>2</sup> values are reported to express how much of the variability of HRQoL is explained by the tested model. Differences are considered statistically significant if p is less than 0.05. All statistical analyses were performed using IBM SPSS version 20.

## RESULTS

### Sample Characteristics

Table 1 shows the patient characteristics and levels of HRQoL for older adults with MUS and MES separately. MUS-patients were significantly younger and more often female than MES-patients. Furthermore, older MUS-patients scored approximately 10 points lower on all SF-36 subscales compared with older MES-patients, except for the General Health subscale and Social Functioning subscale. In line with this, MUS-patients reported lower mental and physical HRQoL component scores than MES-patients (Table 1).

### Associations Between Group (Late-Life MUS/MES) and HRQoL

Linear regression analysis (Table 2) showed that MUS were negatively associated with both mental and physical HRQoL component scores. Specifically, late-life MUS (versus MES as independent variable) were significantly and negatively associated with all but two

**TABLE 1. Patient Characteristics of the Study Sample (N = 272), Specified for Older Persons with chronic Medically Unexplained Symptoms (MUS) and Older Persons with Medically Explained Symptoms (MES)**

Characteristics			Values Comparison Group		t / U / $\chi^2$ (df)	p value
			Values Cases Older Persons with MUS <sup>a</sup> (N = 118)	Older Persons with MES <sup>b</sup> (N = 154)		
Patient characteristics	Age	Mean (SD)	70.54 (6.72)	73.42 (7.74)	-3.23 (270)	0.001 <sup>c</sup>
	Female	% (N)	64.4 (76)	43.5 (67)	11.70 (1)	0.001 <sup>c</sup>
	Education					
	lower	% (N)	26.9 (29)	17.8 (27)		
	average	% (N)	45.4 (49)	52.6 (80)		
Differential characteristics MUS/MES	higher	% (N)	27.8 (30)	29.6 (45)	3.17 (2)	0.205 <sup>e</sup>
	Somatization (BSI-53)	Mean (SD)	.81 (.65)	.52 (.50)	3.97 (241)	<0.001 <sup>c</sup>
	Hypochondriacal cognitions (WI)	Mean (SD)	4.31 (2.95)	2.18 (2.43)	4490	<0.001 <sup>d</sup>
	Somatoform Disorder according to DSM-IV criteria	% (N)	58.5 (69)	0 (0)	120.03 (1)	<0.001 <sup>c</sup>
	Mood Disorder according to DSM-IV criteria	% (N)	26.3 (31)	20.9 (32)	1.07 (1)	0.301 <sup>c</sup>
	Anxiety Disorder according to DSM-IV criteria	% (N)	18.6 (22)	8.5 (13)	6.10 (1)	0.014 <sup>e</sup>
	Substance Use Disorder according to DSM-IV criteria	% (N)	5.1 (6)	2.0 (3)	2.02 (1)	0.156 <sup>c</sup>
	Severity of primary physical complaint (VAS-scale)	Mean (SD)	48.79 (18.09)	46.24 (25.70)	0.86 (238)	0.393 <sup>c</sup>
Health-related quality of life	SF-36 subscales:					
	Physical functioning	Mean (SD)	63.05 (28.83)	72.29 (24.93)	-2.74 (256)	0.007 <sup>c</sup>
	Role limitations physical problem	Mean (SD)	45.71 (39.45)	66.50 (37.95)	-4.25 (256)	<0.001 <sup>c</sup>
	Bodily pain	Mean (SD)	55.87 (27.19)	70.81 (23.81)	-4.68 (257)	<0.001 <sup>c</sup>
	General health	Mean (SD)	53.94 (15.59)	57.75 (16.64)	-1.84 (255)	0.066 <sup>c</sup>
	Vitality	Mean (SD)	54.29 (23.33)	67.29 (20.14)	-4.77 (256)	<0.001 <sup>c</sup>
	Social functioning	Mean (SD)	45.79 (10.25)	47.55 (11.83)	-1.23 (255)	0.219 <sup>c</sup>
	Role limitations emotional problem	Mean (SD)	75.16 (36.82)	90.63 (25.21)	-4.02 (257)	<0.001 <sup>c</sup>
	Mental health	Mean (SD)	70.44 (22.30)	83.50 (16.60)	-5.39 (256)	<0.001 <sup>c</sup>
	Mental Health-Related Quality of Life Component Score (SF-36)	Mean (SD)	61.56 (18.64)	72.24 (13.52)	-5.33 (255)	<0.001 <sup>c</sup>
Physical Health-Related Quality of Life Component Score (SF-36)	Mean (SD)	55.46 (21.80)	66.84 (19.87)	-4.31 (253)	<0.001 <sup>c</sup>	

Notes: <sup>a</sup>Medically unexplained symptoms.  
<sup>b</sup>Medically explained symptoms.  
<sup>c</sup>Significance values derived from independent samples t tests.  
<sup>d</sup>Significance values derived from Mann-Whitney U tests.  
<sup>e</sup>Significance values derived from  $\chi^2$  tests.

**TABLE 2. Associations Between Group (Medically Unexplained Symptoms- MUS/Medically Explained Symptoms-MES) and Health-Related Quality of Life scores, Derived from Short Form-36 (SF-36) Scores**

Outcomes	B (SE)	Beta	t (df)	p value	R <sup>2</sup>
Component score					
Physical Health-Related Quality of Life (SF-36)					
Group (MUS/MES) <sup>a</sup>	-11.10 (2.72)	-0.258	-4.09 (230)	<0.001	0.186
Corresponding SF-36 subscales					
Physical functioning					
Group (MUS/MES) <sup>a</sup>	-10.88 (3.40)	-0.201	-3.20 (231)	0.002	0.196
Role limitations physical problem					
Group (MUS/MES) <sup>a</sup>	-20.12 (5.18)	-0.251	-3.89 (232)	<0.001	0.142
Bodily pain					
Group (MUS/MES) <sup>a</sup>	-12.49 (3.35)	-0.236	-3.73 (232)	<0.001	0.174
General health					
Group (MUS/MES) <sup>a</sup>	-3.84 (2.22)	-0.117	-1.73 (231)	0.085	0.064
Component score					
Mental Health-Related Quality of Life (SF-36)					
Group (MUS/MES) <sup>a</sup>	-9.03 (1.97)	-0.270	-4.59 (232)	<0.001	0.286
Corresponding SF-36 subscales					
Vitality					
Group (MUS/MES) <sup>a</sup>	-11.74 (2.84)	-0.254	-4.04 (232)	<0.001	0.181
Social functioning					
Group (MUS/MES) <sup>a</sup>	-2.11 (1.55)	-0.093	-1.36 (232)	0.174	0.036
Role limitations emotional problem					
Group (MUS/MES) <sup>a</sup>	-13.02 (3.91)	-0.206	-3.33 (232)	0.001	0.211
Mental health					
Group (MUS/MES) <sup>b</sup>	-10.16 (2.34)	-0.250	-4.34 (232)	<0.001	0.315

<sup>a</sup>Associations examined using linear regression analyses.

<sup>b</sup>Adjusted for socio-demographic variables (age, gender, education), the presence of mood disorder (yes/no), of anxiety disorder (yes/no), and of substance use disorder (yes/no), and global score cognitive functioning (MMSE total score).

**TABLE 3. Associations Between Characteristics of Medically Unexplained Symptoms (MUS) and Health-Related Quality of Life (HRQoL) in Older Persons Suffering from MUS**

Characteristic of MUS	Mental HRQoL					Physical HRQoL				
	B (SE)	Beta	t (df)	p value	R <sup>2</sup>	B (SE)	Beta	t (df)	p-value	R <sup>2</sup>
Somatization <sup>a</sup>	-15.12 (2.83)	-0.526	-5.35 (76)	<0.001	0.340	-15.59 (3.12)	-0.464	-4.99 (76)	<0.001	0.411
Hypochondriacal cognitions <sup>a</sup>	-3.18 (.56)	-0.503	-5.63 (87)	<0.001	0.334	-3.03 (0.64)	-0.410	-4.71 (85)	<0.001	0.380
Somatoform disorder according to DSM-IV <sup>a</sup>	-14.88 (3.55)	-0.395	-4.19 (87)	<0.001	0.244	-11.52 (4.09)	-0.261	-2.82 (85)	0.006	0.285
Psychiatric disorder other than somatoform disorder (any) <sup>a</sup>	-10.51 (3.79)	-0.280	-2.78 (87)	0.007	0.165	-2.52 (4.33)	-0.057	-.58 (85)	0.563	0.221
Severity of primary physical complaint <sup>a</sup>	0.15 (0.11)	0.145	1.31 (82)	0.196	0.110	-0.06 (0.13)	-0.051	-.49 (82)	0.622	0.220

Notes: <sup>a</sup> Adjusted for sociodemographic variables (age, sex, education), and global score cognitive functioning (MMSE total score).

SF-36 subscales (as dependent variables), namely, General Health and Social Functioning (Table 2).

#### Associations Between HRQoL and Severity Measures Of Late-Life MUS

Because of the significant association between late-life MUS and HRQoL scores, more detailed analyses

on HRQoL in older MUS-patients were performed. Table 3 shows the results of our multiple linear regression analyses, adjusted for sociodemographic variables and cognitive functioning.

The final model ( $R^2 = 0.512$ ) showed significant, negative associations between mental HRQoL and hypochondriac cognitions (Beta = -0.299;  $t_{(73)} = -3.17$ ;  $p = 0.002$ ), somatization (Beta = -0.301;  $t_{(73)} = -2.99$ ;



**TABLE 4. Associations Between Group (Medically Unexplained Symptoms- MUS/Medically Explained Symptoms-MES) and Health-Related Quality of Life Scores, Additionally Adjusted for Levels of Somatization and Hypochondriacal Cognitions**

Outcomes	B (SE)	Beta	t (df)	p value	R <sup>2</sup>
Component score					
Physical Health-Related Quality of Life (SF-36)					
Group (MUS/MES) <sup>a</sup>	-2.66 (2.45)	-0.062	-1.08 (219)	0.280	0.447
Corresponding SF-36 subscales					
Physical functioning					
Group (MUS/MES) <sup>a</sup>	-4.65 (3.47)	-0.086	-1.34 (219)	0.182	0.303
Role limitations physical problem					
Group (MUS/MES) <sup>a</sup>	-7.12 (5.09)	-0.089	-1.40 (219)	0.163	0.315
Bodily pain					
Group (MUS/MES) <sup>a</sup>	-4.01 (3.25)	-0.075	-1.23 (219)	0.220	0.358
General health					
Group (MUS/MES) <sup>a</sup>	1.82 (2.18)	0.055	0.83 (219)	0.406	0.249
Component score					
Mental Health-Related Quality of Life (SF-36)					
Group (MUS/MES) <sup>a</sup>	-3.10 (1.84)	-0.093	-1.68 (219)	0.094	0.483
Vitality					
Group (MUS/MES) <sup>a</sup>	-3.60 (2.72)	-0.080	-1.32 (219)	0.187	0.382
Social functioning					
Group (MUS/MES) <sup>a</sup>	-1.51 (1.69)	-0.067	-0.89 (219)	0.375	0.045
Role limitations emotional problem					
Group (MUS/MES) <sup>a</sup>	-4.33 (3.97)	-0.068	-1.09 (219)	0.277	0.330
Mental health					
Group (MUS/MES) <sup>a</sup>	-3.92 (2.27)	-0.097	-1.73 (219)	0.085	0.469

Notes: <sup>a</sup>Adjusted for sociodemographic variables (age, sex, education), the presence of mood disorder (yes/no), of anxiety disorder (yes/no), and of substance use disorder (yes/no), global score cognitive functioning (MMSE total score), levels of somatization (BSI-53), and hypochondriacal cognitions (WI).

p = 0.004), and the presence of a somatoform disorder (Beta = -0.263; t<sub>(73)</sub> = -3.07; p = 0.003) in older adults with MUS. The final model for physical HRQoL (R<sup>2</sup> = 0.486) showed negative associations with hypochondriac cognitions (Beta = -0.236; t<sub>(74)</sub> = -2.45; p = 0.017) and somatization (Beta = -0.327; t<sub>(74)</sub> = -3.32; p = 0.001).

Following these results, the linear regression analyses presented in Table 2 were additionally adjusted for levels of somatization and hypochondriacally cognitions. These analyses show that the group (MUS/MES) and HRQoL association was no longer statistically significant for both the SF-36 component scores and all SF-36 subscales (Table 4).

persons with medically explained symptoms. Interestingly, these associations disappeared when additionally corrected for somatization and hypochondriacal cognitions.

Within the subgroup of older persons with MUS, levels of somatization, hypochondriacal cognitions, and the presence of a primary somatoform disorder according to DSM-IV criteria explained most variance of mental HRQoL. Levels of somatization and hypochondriacal cognitions explained most variance of physical HRQoL in older MUS-patients. The perceived severity of the physical complaint was not associated with HRQoL.

### Comparison with Literature

Although previous research found that late-life MUS are associated with higher HRQoL scores compared with older MES-patients,<sup>21</sup> the current study indicates that MUS-patients report lower HRQoL compared with persons who received a clear diagnosis for their physical complaints. How can these contrasting

## CONCLUSIONS

### Main Findings

Older persons with medically unexplained symptoms reported decreased levels of mental and physical health-related quality of life when compared with older

findings be explained? Contrary to the study by Hilderink et al.,<sup>21</sup> in the current study all patients were classified as either MUS or MES by their own GPs, in most cases with confirmation by a geriatrician after a comprehensive geriatric assessment. This extensive physical examination and chart review possibly contributed to a more accurate diagnosis of late-life MUS and MES<sup>9</sup> than assessment of physical symptoms and classification as either MUS or MES with the CIDI. This being said, when statistical analyses were additionally adjusted for levels of somatization and hypochondriacal cognitions, group status (MUS/MES) and HRQoL were no longer statistically significantly associated, which is in line with the DSM-5 criteria for somatic symptom disorder.<sup>6,31</sup>

The current findings indicate that older MUS-patients score approximately 10 points lower on both physical and mental HRQoL scores than older MES-patients, which indicates a statistical significant difference. It is questionable whether or not these differences are clinically meaningful as well. We can assume that whether or not differences in HRQoL scores are clinically meaningful is eventually in the hands of doctors and the patients themselves.<sup>32</sup> As previous studies have shown the meaningfulness of decreased HRQoL scores in older persons with MES (e.g., Dominick et al.<sup>33</sup>), and as we know doctors report severe troubles with managing MUS,<sup>34</sup> we assume that the demonstrated differences between older MUS-patients and MES-patients are clinically relevant.

Our current findings are in line with previous studies showing that HRQoL is associated with psychological factors, such as the level of somatization, in younger patients with a functional syndrome<sup>35</sup> and in older persons.<sup>36</sup> The current study shows somatization—measured by counting the number of physical symptoms using the BSI-53<sup>28</sup>—was associated with HRQoL, which is in line with the idea that the number of physical complaints is associated with health status in MUS-patients.<sup>37</sup> Furthermore, the severity of the physical complaints was not significantly associated with HRQoL. Given these findings and the additional finding that in our final models the presence of a somatoform disorder according to DSM-IV criteria was not or only weakly associated with HRQoL component scores in older MUS-patients, the DSM-5 diagnoses of somatic symptom and related disorders<sup>6</sup> seem to be more appropriate for older MUS-patients. These DSM-5 diagnoses are independent of a physical origin as well

as the severity of the MUS, but rather rely on positive psychiatric criteria accompanying a physical symptom, such as the presence of hypochondriacal cognitions or somatization.

### Strengths and Limitations of the Current Study

The current study has several methodological strengths. First of all, by comparing late-life MUS to late-life MES, we were able to investigate how unexplained physical symptoms are different from explained physical symptoms in older adults. The extensive multidisciplinary screening and the clinical judgment of each participant's GP contributed to a valid classification of MUS and MES. Furthermore, our comparison group consisted of MES-patients that were selected using the frequent-attenders method, meaning only patients with severe MES were included in our study sample. Taking this into account, even larger effects are expected in studies using a population-based comparison group. Another strength refers to the use of the SF-36 for measuring HRQoL, as the SF-36 is a well-validated<sup>38</sup> scale that shows good reliability rates<sup>39</sup> for older adults.

Nevertheless, the current study has methodological limitations as well. By recruiting patients across different settings (population/primary care/specialized health care), we succeeded in composing a sample of MUS-patients in various developmental and severity stages. Nonetheless, within these settings we still recruited convenience samples and our study was not designed to be epidemiologically representative of an underlying population. Second, a geriatrician examined some participants extensively, but other MUS-patients refused this examination (40.7% of the total MUS-sample), because of mobility problems or resistance against visiting the multidisciplinary clinic. The latter group of MUS-patients was only screened by their GP, herewith increasing the risk of unjust classification of MUS. However, excluding this latter group could be harmful, as this group of patients may vary with respect to the severity of physical complaints or the quality of the patient–doctor relationship when compared with those patients accepting the screening. Another limitation of the current study concerns the use of the BSI-53<sup>28</sup> for assessing somatization. Because the BSI somatization subscale actually assesses the presence of physical complaints that often remain medically unexplained (e.g., upset stomach), this might lead to

an overestimation of somatization levels in an older study sample. Consequently, our finding that somatization and physical HRQoL are associated should be interpreted cautiously. Lastly, longitudinal studies are needed to determine temporal relationships between medically unexplained symptoms and characteristics that are associated with HRQoL.

### Implications for Research and Clinical Practice

Even though the concept of MUS is abandoned in the DSM-5 criteria for somatic symptom disorder,<sup>6</sup> in clinical practice, MUS-patients are often considered difficult<sup>35</sup> and challenging patients.<sup>36</sup> GPs and medical specialists should keep in mind that, in the absence of disease, physical symptoms reduce HRQoL more than when disease is present, according to our findings. That being said, our study findings are in line with DSM-5 criteria, which allow MES to be influenced by somatization and hypochondriacal cognitions. Also, previous research in younger MUS-patients has shown that other factors, such as levels of anxiety, depression, and social

factors,<sup>11,40</sup> might affect HRQoL as well. During consultation it is important for doctors to explore the level of somatization and hypochondriacal cognitions in older patients with physical complaints, as these factors contribute negatively to the perceived HRQoL. When, for instance, the MUS are accompanied by hypochondriacal cognitions, general practitioners could refer these older patients to psychological treatment, in addition to possible somatic treatment. Because cognitive behavioral therapy<sup>41</sup> has proven to be an evidence-based treatment for MUS and somatization in general in younger patients, this treatment will most likely be effective in older adults too. Specific studies on the effectiveness of psychological or multidisciplinary treatment programs for late-life MUS are currently lacking, however.

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