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*Document Version*

Publisher's PDF, also known as Version of record

*Publication date:*

2019

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

Joustra, M. L. (2019). *Similar but different: Implications for the one versus many functional somatic syndromes discussion*. [Thesis fully internal (DIV), University of Groningen]. Rijksuniversiteit Groningen.

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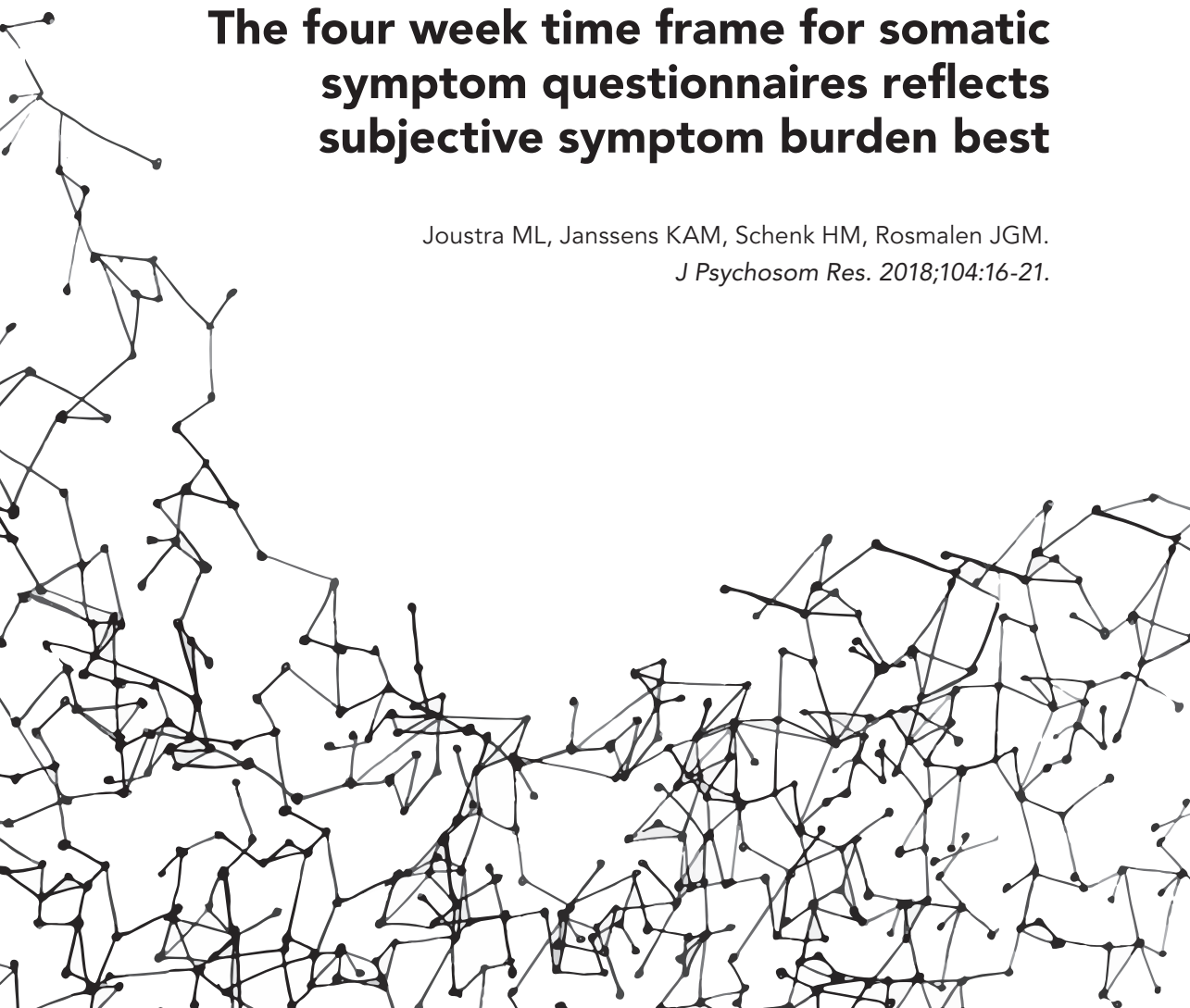
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## **The four week time frame for somatic symptom questionnaires reflects subjective symptom burden best**

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*J Psychosom Res.* 2018;104:16-21.



## ABSTRACT

**Objective:** Various questionnaires are available to assess somatic symptom burden, however their assessment time frames vary largely. The aim of this study was to investigate the most relevant assessment time frame for somatic symptoms by relating somatic symptom burden, with varying time frames, to quality of life (QoL) and health anxiety as indicators for clinical relevance of symptoms.

**Methods:** This study was performed in data derived from a convenience sample of 3,477 participants (age: 48.0 (SD 14.1), 66.4% female) of the Dutch research platform HowNutsAreTheDutch. Symptom burden was assessed using all items from the Patient Health Questionnaire-15 (PHQ-15) and 6 items of the Symptom Checklist-90 SOM (SCL-90 SOM). Five versions of the questionnaire were constructed, which evaluated symptom burden during the past 24 hours, 1 week, 2 weeks, 4 weeks, and 3 months.

**Results:** Symptom burden significantly increased with each step increase in time frame until 4 weeks, with no further increase when comparing 4 weeks and 3 months. The time frame of 4 weeks provided the strongest associations between somatic symptom burden and health anxiety ( $B=1.635$ ; 95%CI: 1.368 to 1.938;  $p \leq .001$ ). This was also true when analysing the association between QoL and the symptom groups of musculoskeletal ( $B=-1.54$ ; 95%CI: -1.93 to -1.16;  $p \leq .001$ ) and gastrointestinal symptoms ( $B=-0.71$ ; 95%CI: -0.96 to -0.47;  $p \leq .001$ ).

**Conclusion:** An assessment time frame of 4 weeks for somatic symptom questionnaires reflects clinically relevant somatic symptom burden in terms of QoL and health anxiety best, followed by the 3 months' time frame.

## INTRODUCTION

A considerable proportion of the consultations in both primary and secondary care is due to the experience of somatic symptoms (1,2). High levels of somatic symptoms are associated with a reduced quality of life (QoL), an increase of functional limitations (3), health care service use (4), prolonged sickness absence, and health-related job loss (5). Therefore, the assessment, recognition, and evaluation of somatic symptom burden are essential in both patient care and research. Physicians, researchers, and other healthcare professionals must rely on patients' reports for the recognition and evaluation of somatic symptom burden. Self-report questionnaires are useful tools to assess symptom burden. They provide a predictor of health care use and health status over and above the effects of general medical illnesses, anxiety and depression (6).

Self-report questionnaires have been used in research for a long time, and their use in clinical practice is increasing. This is partly due to requirements of health insurance companies that want to evaluate the quality of care delivered, especially in mental health care settings. It has also been argued that the use of systematic instruments might improve clinical care for somatic symptoms, comparable to the use of biomarkers to monitor clinical outcomes of recognized diseases (7). A systematic review indicated that there are many different self-reported questionnaires available for the assessment of somatic symptoms (8,9). The use of these symptom questionnaires differs, and the content of the questionnaires varies considerably. This applies not only to characteristics of the symptoms included, but also to their answering scales and time frames of assessment (8,9). Some validated questionnaires are based on life-time symptoms, while others address time frames of a week or less. For example, the Patient-Reported Outcomes Measurement Information System (PROMIS), an initiative that established a resource for efficient and precise measurement of patient-reported symptoms, functioning, and health-related quality of life, opted for the 7-day recall period (10). They argue that the 7-day recall period provides a sufficiently long interval to capture a clinically relevant window of time and experience with minimal bias.

Both short and long recall time frames for assessing somatic symptom burden have associated problems. On the one hand, recall of life-time somatic symptoms seems unreliable and inconsistent (11). Patients frequently have forgotten previously

reported somatic symptoms, and therefore underreport (12). Recall of somatic symptoms diminishes largely over time, up to 100% over a period of 11 years (11). However, retrospective assessment of somatic symptoms over shorter time frames may also overestimate somatic symptom burden (13). At the same time, detection of daily fluctuations in somatic symptom burden by making use of a shorter time frame may not be meaningful for the evaluation of the somatic symptom burden of patients, since short recall time frames only reflect a momentary period that might not be representative for symptom burden in general (14). The balance between the risk of unreliable recall of life-time somatic symptoms and the detection of meaningful fluctuations in somatic symptoms remains to be examined.

This balance might differ between types of somatic symptoms. Somatic symptoms that are episodic in nature, such as headaches or palpitations, might require a longer time frame than symptoms typically present more or less continuously, such as fatigue or musculoskeletal pain. Somatic symptoms can be clustered into cardiopulmonary, gastrointestinal, musculoskeletal, and general symptom clusters (15,16). The most suitable time frame for specific symptom clusters may thus differ in comparison with the overall somatic symptom burden.

The question arises what the most clinically relevant time frame of assessment would be for somatic symptom questionnaires. We define clinical relevance as the time frame that reflects subjective symptom burden in daily life, in terms of QoL and health anxiety, best among participants. This is different from the time frame that gives the most realistic estimate of symptom occurrence. Both QoL and health anxiety have been shown to be associated with symptom burden in patients (3,6,17,18). To the best of our knowledge, there are no studies that examine the clinical relevance of different time frames in one large cohort. Existing studies have used symptom questionnaires that differed in time frames, but these questionnaires also differed in other aspects such as the specific somatic symptoms included (8,9). This precludes any conclusions on the assessment time frame specifically.

The aim of the current paper was to identify the time frame of assessment for somatic symptom questionnaires that reflects clinically relevant subjective somatic symptom burden best. The following research questions were examined. First, how does somatic symptom burden vary over the different time frames

used to assess symptoms? It is hypothesized that somatic symptom burden increases with longer assessments windows, until the point that the increase in captured symptoms is counterbalanced by decreases in reported symptoms due to recall bias. Second, what is the clinically most relevant time frame, as indicated by the highest association between symptom burden and QoL and health anxiety of the participants? Third, does the clinically most relevant time frame vary between different symptom clusters? To study these questions, a somatic symptom questionnaire was composed, based on all symptoms included in the two questionnaires that are most widely used and recommended: the Patient Health Questionnaire-15 (PHQ-15) (19,20), and the 12-item Symptom Checklist-90 SOM (SCL-90 SOM) (21). Five versions of this somatic symptom questionnaire were constructed, which only differed in time frame of somatic symptom assessment. These five versions were sequentially added to an online survey, together with assessments of QoL and health anxiety.

## METHODS

### The sample/Participants

This study is part of the HowNutsAreTheDutch (Dutch: HoeGeklsNL) crowdsourcing study (22). HowNutsAreTheDutch (henceforth HND) is a national study in the Netherlands, examining multiple mental health dimensions in a sample from the general population. An open call was launched to residents of the Netherlands to join our research, and they were invited to visit the Dutch website [www.HoeGekls.nl](http://www.HoeGekls.nl) (also [www.HowNutsAreTheDutch.com](http://www.HowNutsAreTheDutch.com)). The open call was announced on both local and national radio broadcasts, television, in newspapers, in magazines, and during local podium discussions. The news about the HND project was picked up and further disseminated via online blogs, twitter, and other social media. To join the project, participants had to register online and create an account. HND collects self-report data on mental health by making use of an internet platform. On this internet platform participants can compare themselves to other participants via cross-sectional questionnaires. The primary aim of HND is to investigate the associations and dynamic interactions between mental strengths and vulnerabilities. HND is specifically designed to reduce mental health stigma and discrete categorization of mental health. Data were available of 3,477 participants, which were included during the period 13 December 2013 until 16 June 2015, with a mean age of 48.0 (SD 14.1) years and 66.4% female.

## Measures

### *Somatic symptoms*

The somatic symptom questionnaire was based on a combination of all the 15 PHQ-15 items and 6 items from the SCL-90 SOM. The PHQ-15 is a frequently used self-reported questionnaire to assess somatic symptom burden (19,20). This questionnaire assesses the symptom burden of 15 symptoms that account for more than 90% of the somatic complaints observed in primary care. The PHQ-15 is a well validated questionnaire for monitoring symptom burden in research and clinical practice (19,20). The 12-item somatization scale (SOM) of the SCL-90 was used to investigate the presence of common somatic symptoms not covered by the PHQ-15 (21): hot or cold spells, numbness or tingling in parts of your body, a lump in your throat, feeling weak in parts of your body, heavy feelings in your arms or legs, soreness of your muscles. Participants were asked to indicate how much they have been bothered by these 21 (15 PHQ and 6 SCL) somatic complaints. The PHQ-15 is originally rated on a three-point scale, while the SCL-90 SOM is rated on a five-point scale. In order to obtain consistent results, all somatic complaints were rated on a three-point scale in the current study, i.e. (0) "not bothered at all", (1) "bothered a little" or (2) "bothered a lot". The total symptom burden, calculated as the sum of all 21 answers, thus could theoretically range between 0 and 42 points.

Five versions of the questionnaire were assessed during different time periods. We initially aimed to obtain groups of about equal sizes, replacing the questionnaire by a new variant with a different time frame after a sufficient number of respondents had completed it. However, inclusion rates were highly variable, mainly related to media attention for the HND project. Therefore, length of the time periods during which the versions were administered was also highly variable: version 1 was administered during the period 21 January until 3 April 2014 and evaluated somatic complaints during the past 4 weeks, version 2 was administered during the period 4 April until 22 April 2014 and evaluated somatic complaints during the past 24 hours, version 3 was administered during the period 22 April until 12 May 2014 and evaluated somatic complaints during the past week, version 4 was administered during the period 13 May until 18 November 2014 and evaluated somatic complaints during the past 2 weeks, and version 5 was administered during the period 19 November 2014 until 16 June 2015 and evaluated somatic complaints during the past 3 months.

The somatic symptoms assessed by the PHQ and SCL were, in line with previous studies (15,16), divided into the following symptom clusters: cardiopulmonary (chest pain; feeling your heart pound or race; shortness of breath; hot or cold spells), gastrointestinal (stomach pain; constipation, loose bowels, or diarrhoea; nausea, gas, or indigestion), musculoskeletal (back pain; pain in your arms, legs, or joints [knees, hips, etc.]); numbness or tingling in parts of your body; feeling weak in parts of your body; heavy feelings in your arms or legs; soreness of your muscles), and general symptoms (headache; dizziness; fainting spells; menstrual cramps or other problems with your periods; pain or problems during sexual intercourse; feeling tired or having low energy; trouble sleeping; a lump in your throat).

Principal component analyses of somatic symptom burden items were performed to investigate the dimensionality of the 21-item somatic symptom questionnaire for the different time frames. The analyses and corresponding scree plots for the different time frame groups revealed one main factor for all versions of the somatic symptom questionnaire (Eigenvalues: 4.92-5.93). The underlying main factor explained most variance in the 4 weeks' time frame group (28.2%) compared to the 24 hours (23.7%), 1 week (25.2%), 2 week (23.4%), and 3 months' (25.8%) time frame groups. The structure coefficient matrix shows that most items had a loading of  $>.4$ . Three items that had a loading of  $<.4$  in the different time frames were the general symptoms: (a) fainting spells, (b) menstrual cramps or other problems with periods, and (c) pain or problems during sexual intercourse.

### *Quality of Life*

QoL was assessed using the Manchester Short Assessment of Quality of Life (MANSA) (23). This study used the self-reported subscale of the MANSA. The self-reported subscale of the MANSA rates participants' satisfaction with 12 aspects of life without mentioning a specific time frame, namely life in general, employment, financial status, friendships, leisure activities, living conditions, personal safety, fellow residents, sex life, relationship with family, physical health, and mental health. Satisfaction was rated on a seven-point scale, ranging from (1) "could not be worse" to (7) "could not be better", with (4) as a neutral middle point. The underlying concept of the questionnaire is generic: all items allow comparison with the general population and are not specifically illness-related.



## Chapter 2

The summary score of the QoL is the mean of the self-reported 12 items with a range from 1 to 7 points, with a higher score reflecting better QoL.

### *Health anxiety*

The Whitely Index (WI) was used to assess health anxiety (24,25). The WI consists of 14 items that assess three different dimensions of health anxiety without mentioning a specific time frame, namely disease phobia, somatic symptoms, and disease conviction. The participants were asked to indicate if each statement describes their health worries, with a dichotomised response format of (0) "no" or (1) "yes". The total scale score, calculated as the sum of all "yes" answers, ranged between 0 and 14 points. Thus, a higher WI score indicates more illness concerns in the participants.

### *Covariates*

Information on age, sex, and educational level was obtained by questionnaire, since these variables are associated with both somatic symptoms (3,17), QoL, and health anxiety (3,17,18). Educational level was classified in low, middle, and high educational level. Low educational level was defined as lower secondary education or less, middle educational level was defined as higher secondary education, and high educational level was defined as tertiary education.

### **Statistical analyses**

All analyses across the different time frames were between subjects, and were performed using SPSS version 23. Chi-squared tests were used to examine the differences between the time frame groups in sex, and educational level. Analyses of covariance (ANCOVA) with Bonferroni correction were conducted to examine whether the time frame groups differed in age, symptom burden, QoL, and health anxiety. The reliability of the 21-item somatic symptom questionnaire for the different time frames was examined by calculating the internal consistency of the items (i.e. by calculating Cronbach's alpha). Statistical tests for the comparison between two or more alpha coefficients were performed using the R package 'cocron' (online available at <http://comparingcronbachalphas.org>). Furthermore, multiple linear regression analyses were performed to predict QoL and health anxiety based on somatic symptom burden, and to predict QoL and health anxiety based on somatic symptom burden in the different symptom clusters. The outcomes of the regression analyses were reanalysed while excluding the

three somatic items with low factor loading. Since somatic symptom burden was not normally distributed, post-hoc bootstraps were conducted for ANCOVA and regression analyses. ANCOVA and regression analyses were adjusted for age, sex, and educational level. Findings were considered statistically significant if  $p < 0.05$ .

## RESULTS

### Sample characteristics

The somatic symptom questionnaire was completed by 3,477 participants, with a mean age of 48.0 (SD 14.1) years, and 66.4% female. The numbers of participants for the different time frames, including the corresponding descriptives (sex, age, educational level, QoL, health anxiety) are shown in Table 1.

Participants who filled out the questionnaire referring to somatic symptoms in the last 24 hours and last week reported a slightly higher QoL than the participants who filled out the questionnaire referring to somatic symptoms in the last 2 weeks, 4 weeks, and 3 months. There were no significant differences in health anxiety between the participants who filled out the questionnaires with the different time frames.

**Table 1.** General characteristics of the study groups.

	N	Female (%)	Age (years) mean (SD)	Education (%) Low – Middle -High	MANSA (1-7) Mean (SD) <sup>1</sup>	WI (0-14) Mean (SD) <sup>1</sup>
<b>All</b>	3477	66.4	48.0 (14.1)	1.0 – 17.8 – 81.2	5.2 (0.7)	3.1 (2.4)
Timeframe						
<b>24 hours</b>	1595	64.0 <sup>a,b</sup>	51.2 (13.1) <sup>a,c,e,f</sup>	0.5 – 13.7 – 85.8 <sup>a,c,e</sup>	5.3 (0.7) <sup>b,g</sup>	3.1 (2.5)
<b>1 week</b>	797	60.9 <sup>a,c,d</sup>	46.2 (14.0) <sup>a</sup>	1.4 – 21.8 – 76.8	5.2 (0.7) <sup>b,g</sup>	3.1 (2.4)
<b>2 weeks</b>	623	76.6	45.2 (14.5) <sup>b</sup>	1.3 – 20.4 – 78.3	5.1 (0.7)	3.2 (2.4)
<b>4 weeks</b>	295	71.5	42.4 (14.5)	2.0 – 23.1 – 74.9	5.1 (0.7)	3.3 (2.5)
<b>3 months</b>	167	69.5	45.7 (14.2)	1.2 – 18.6 – 80.2	5.1 (0.7)	3.0 (2.3)

<sup>1</sup>ANCOVA adjusted for age, sex, and educational level.

<sup>a</sup>  $p \leq .001$  versus 2 weeks, <sup>b</sup>  $p \leq .05$  versus 4 weeks, <sup>c</sup>  $p \leq .001$  versus 4 weeks, <sup>d</sup>  $p \leq .05$  versus 3 months, <sup>e</sup>  $p \leq .001$  versus 1 week, <sup>f</sup>  $p \leq .001$  versus 3 months, <sup>g</sup>  $p \leq .05$  versus 2 weeks.

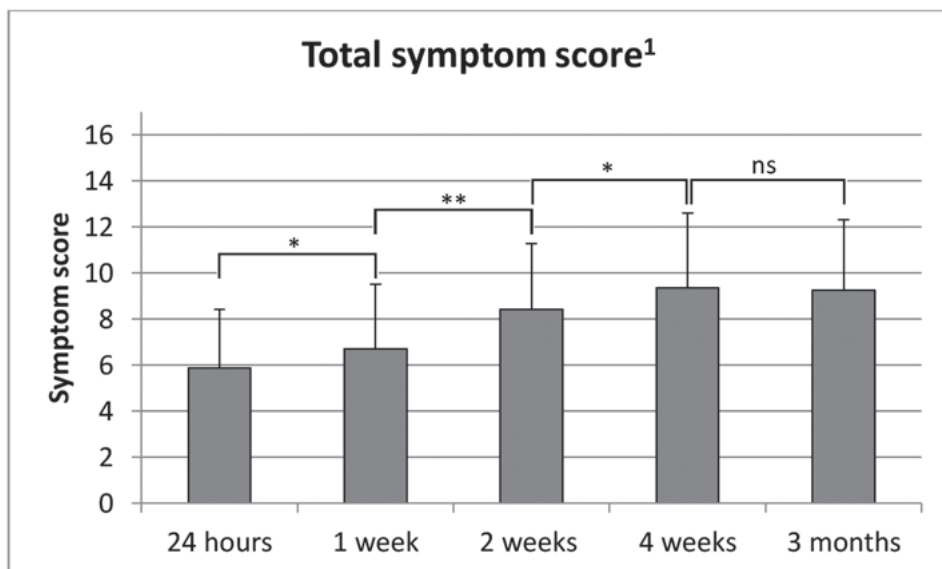
### **Reliability**

Cronbach's alpha was significantly higher in the 4 weeks' time frame (0.87, CI: 0.848-0.891) compared to the 24 hours (0.83, CI 0.818-0.842,  $p=0.006$ ), the 1 week (0.84, CI: 0.824-0.856,  $p=0.043$ ), and the 2 week (0.83, CI: 0.810-0.849,  $p=0.012$ ) time frame. There was no significant difference in Cronbach's alpha between the 4 week and 3 months' time frame (0.84, CI:0.803-0.873,  $p=0.146$ ), while the Cronbach's alpha of the 3 months' time frame did not significantly differ from the 24 hours, 1 week and 2 weeks' time frame.

### **Somatic symptom burden as assessed by the various time frames**

The somatic symptom burden significantly increased with each step increase in the symptom assessment time frame, as shown in Figure 1. This increase was not found any more when the participants who filled out the questionnaire referring to somatic symptoms in the last 4 weeks and 3 months were compared (9.4 (SD 6.5) vs. 9.3 (SD 6.2);  $p=.898$ ).

The pattern of somatic symptom burden increase with a longer time frame, was also seen when different somatic symptom clusters were studied, although this did not reach statistical significance in all instances (Figure 2). Comparable outcomes were found, when reanalysing the data while excluding the three somatic items with low factor loadings.



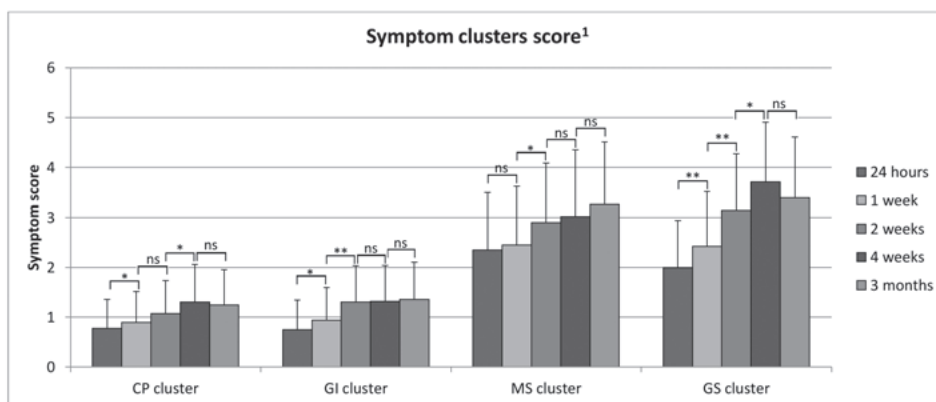
**Figure 1.** Total symptom score among the different time frames.

<sup>1</sup>ANCOVA adjusted for age, sex, and educational level.

Data are presented as mean and standard deviation.

Only comparisons between adjacent time frames are presented.

\*  $p \leq .05$ , \*\*  $p \leq .001$ , ns= non-significant.



**Figure 2.** Symptom clusters score among the different time frames.

CP = cardiopulmonary, GI = gastrointestinal, MS = musculoskeletal, GS = general symptom.

<sup>1</sup>ANCOVA adjusted for age, sex, and educational level.

Data are presented as mean and standard deviation.

Only comparisons between adjacent time frames are presented.

\*  $p \leq .05$ , \*\*  $p \leq .001$ , ns= non-significant.

### Somatic symptom burden associated with quality of life or health anxiety

Multiple linear regression analyses were conducted to predict QoL and health anxiety based on somatic symptom burden as assessed by the questionnaires using different time frames. Somatic symptom burden was significantly associated with both QoL and health anxiety in all time frame groups ( $p \leq .001$ ), see Table 2.

The strongest association between somatic symptom burden and QoL was found in the participants who filled out the questionnaire referring to somatic symptoms in the past 3 months, followed by participants referring to somatic symptoms in the past 4 weeks. The association between health anxiety and somatic symptom burden was strongest among the participants in the time frame of 4 weeks, followed by the 1 week and 24 hour time frame.

Results of multiple linear regression analyses to predict QoL and health anxiety in the different symptom clusters are shown in Table 3. The time frame of 4 weeks resulted in the strongest associations with QoL for musculoskeletal and gastrointestinal symptoms, whereas the 3 months' time frame showed the strongest association with QoL for cardiopulmonary and general symptoms. The time frame of 4 weeks showed the strongest association between somatic symptoms and health anxiety for all different symptom clusters. Comparable outcomes were found, when reanalysing the data while excluding the three somatic items with low factor loadings.

**Table 2.** Regression analyses of somatic symptom score as a predictor of quality of life (MANSA) and health anxiety (WI).

	MANSA <sup>1</sup>			WI <sup>1</sup>		
	$\beta$	B	95% CI	$\beta$	B	95% CI
<b>24 hours</b>	-0.50	-3.73	-4.09, -3.35	0.51	1.07	0.96, 1.17
<b>1 week</b>	-0.45	-3.73	-4.33, -3.11	0.51	1.19	1.01, 1.36
<b>2 weeks</b>	-0.43	-3.45	-4.10, -2.78	0.45	1.08	0.90, 1.28
<b>4 weeks</b>	-0.52	-4.61	-5.47, -3.75	0.62	1.63	1.34, 1.92
<b>3 months</b>	-0.56	-4.83	-6.02, -3.71	0.50	1.33	0.92, 1.78

<sup>1</sup> Regression analysis adjusted for age, sex, and educational level.  
All analyses  $p \leq .001$ .

**Table 3.** Regression analyses of somatic symptom clusters as a predictor of quality of life (MANSA) and health anxiety (WI).

		MANSA <sup>1</sup>			WI <sup>1</sup>		
		$\beta$	B <sup>2</sup>	95% CI <sup>2</sup>	$\beta$	B <sup>2</sup>	95% CI <sup>2</sup>
<b>24 hours</b>	CP	-0.31	-0.53	-0.63, -0.43	0.39	0.18	0.15, 0.21
	GI	-0.27	-0.48	-0.58, -0.38	0.35	0.17	0.14, 0.20
	MS	-0.42	-1.41	-1.58, -1.24	0.45	0.42	0.37, 0.471
	GS	-0.47	-1.31	-1.44, -1.18	0.39	0.30	0.26, 0.33
<b>1 week</b>	CP	-0.31	-0.57	-0.70, -0.43	0.43	0.22	0.18, 0.27
	GI	-0.23	-0.45	-0.60, -0.31	0.32	0.17	0.13, 0.22
	MS	-0.38	-1.34	-1.54, -1.10	0.44	0.43	0.35, 0.50
	GS	-0.42	-1.38	-1.60, -1.14	0.40	0.36	0.29, 0.44
<b>2 weeks</b>	CP	-0.31	-0.57	-0.72, -0.41	0.29	0.16	0.11, 0.21
	GI	-0.24	-0.48	-0.67, -0.31	0.23	0.20	0.14, 0.25
	MS	-0.34	-1.13	-1.40, -0.88	0.39	0.39	0.32, 0.47
	GS	-0.40	-1.26	-1.59, -0.98	0.34	0.33	0.25, 0.41
<b>4 weeks</b>	CP	-0.37	-0.77	-0.99, -0.56	0.48	0.29	0.23, 0.37
	GI	-0.37	-0.71	-0.96, -0.47	0.42	0.25	0.18, 0.32
	MS	-0.43	-1.54	-1.93, -1.16	0.55	0.59	0.46, 0.76
	GS	-0.50	-1.63	-1.93, -1.32	0.52	0.51	0.41, 0.60
<b>3 months</b>	CP	-0.40	-0.80	-1.13, -0.51	0.42	0.26	0.17, 0.34
	GI	-0.29	-0.61	-0.90, -0.31	0.37	0.24	0.15, 0.35
	MS	-0.42	-1.49	-2.08, -0.85	0.46	0.50	0.31, 0.71
	GS	-0.56	-1.93	-2.44, -1.50	0.32	0.34	0.17, 0.52

CP = cardiopulmonary, MS = musculoskeletal, GI = gastrointestinal, GS = general symptoms.

<sup>1</sup> Regression analysis adjusted for age, sex, and educational level, <sup>2</sup> Based on bootstrapped analyses. All analyses  $p \leq .001$ .

## DISCUSSION

Our study suggests the time frame of 4 weeks to be the most suitable for the assessment of somatic symptom burden, since it reflects clinically relevant somatic symptom burden in terms of QoL and health anxiety best. Somatic symptom burden significantly increased with a longer time frame up to and including the time frame of 4 weeks, with no additional increase when the assessment time frame was extended to 3 months. Assessments based on the time frame of 4 weeks also showed the strongest associations with both QoL for the musculoskeletal and gastrointestinal symptoms and health anxiety for all symptom clusters, indicating clinical relevance. The burden of cardiopulmonary and general symptoms had the strongest association with assessments based on the 3 months' time frame.

Furthermore, somatic symptom questionnaires using the 4 weeks' time frame had the best psychometric properties, in terms of internal reliability.

This study has several strengths. Firstly, the assessed somatic symptoms covered all symptoms in the two most widely used somatic symptom questionnaires, which provided a comprehensive estimate of the somatic symptom burden of the participants. Secondly, QoL and health anxiety were assessed using questionnaires not referring to a specific time frame, which made it possible to investigate the association with somatic symptom burden in general.

In addition to strengths, there are also some limitations in the present study. Self-selection bias is the main limitation of this study that was performed in a convenience sample. Self-selection likely leads to a sample with a specific motivation to participate, which might be reflected in the overrepresentation of highly educated participants, women and participants above age 65. Self-selection bias might attenuate the generalizability of the results. To estimate the role of self-selection bias in our convenience sample, the characteristics of the HND participants were compared with the general Dutch population (22). Scores of HND participants on several psychological characteristics, mainly those associated with differences in education, deviated somewhat from population averages. This is also evident from the WI scores in our study, which were slightly higher compared to the general Dutch population, but comparable to general practice patients (26). Thus, the convenience sample might attenuate the generalizability of the results to the general population. Secondly, because participants of the HND study could register themselves online, inclusion rates fluctuated depending on several external factors such as media attention. The five versions of the questionnaire were assessed during different time periods (varying from several days to months) and contained severely unbalanced numbers of participants for each time period. Although the assessment periods for reporting symptoms with longer time periods (4 weeks, 3 months) were relatively long, the numbers of participants reporting on these time periods were substantially lower than for the shorter time periods. This raises the possibility of differential selection bias among study periods and confounding by time of administration. Furthermore, the unbalanced sample sizes may influence the results since they affect statistical power. Nevertheless, the 4 weeks and 3 months' time frame contained the least participants, but had the strongest associations between QoL and health anxiety.

Thirdly, because the different versions of the somatic symptom questionnaire were assessed during different time periods, somatic symptom burden may have been influenced by seasonal effects. Visual inspection revealed no indications for such seasonal effects. Fourthly, due to the study design, it was not possible to administer different versions of the questionnaire in one participant. Therefore, it was not possible to compare the association between somatic symptom score and the clinical parameters in the different time frames within a single participant. Lastly, the psychometric properties differ per time frame, which also can influence the association per time frame between somatic symptom score and the clinically relevant parameters.

This study found that somatic symptom burden significantly increased with a longer time frame until 4 weeks, with no further increase when comparing 4 weeks and 3 months. A possible explanation for this finding is that the short time frame questionnaire may not have included peaks in somatic symptom burden resulting in lower mean values. Extension of the assessment time frame simply increases the chance of having experienced somatic symptoms. Remarkably, somatic symptom burden did not further increase when prolonging the assessment frame from 4 weeks to 3 months, probably because of an increased influence of recall problems with the use of a longer time frame (14). Previous research indicated that participants frequently have forgotten previously reported somatic symptoms (12), and recall of somatic symptoms diminishes up to 100% over time (11). Furthermore, longer time frames might increasingly capture general beliefs based on personal experience with somatic symptoms (e.g. never experiencing or chronically suffering from symptoms), as opposed to the actual burden of symptoms experienced during the assessed time frame (27). The pattern of somatic symptom burden increasing with a longer time frame was not different when different types of somatic symptom clusters were studied. Based on these results, the assessment time frame of 4 weeks appears to provide the best balance between the increasing chance of capturing episodic symptoms and the increasing influence of recall problems of somatic symptoms with increasing time frames.

Our results indicate that the time frame of 4 weeks also provides the measure of subjective somatic symptom burden that is clinically most relevant. Somatic symptom burden of the different time frames were significant associated with QoL and health anxiety. However, the strongest associations were most commonly found



with the use of the assessment time frame of 4 weeks, except for the association between the burden of cardiopulmonary and general symptoms where the 3 months' time frame had the strongest association. As found in previous research (28,29), the impact of specific symptom clusters on patients' QoL and health anxiety varied. Nevertheless, the 4 weeks' time frame provided the strongest associations between the burden of musculoskeletal and gastrointestinal symptoms and QoL or health anxiety among all symptom clusters.

Currently, there are 46 different self-reported questionnaires available for the assessment of somatic symptoms, with varying time frames of assessment (8,9). This study used the PHQ-15 (19,20), with an original time frame referring to the past month, and the SCL-90 SOM (21), with an original time frame referring to the past week. Results of a previously conducted systematic review indicated that the PHQ-15 and the SCL-90 seem the most fit for purpose for use in large-scale studies (8,9). We now can add to these conclusions that the 4 weeks' time frame, which corresponds approximately to the time frame used in the PHQ-15, reflects clinically relevant somatic symptom burden best. Based on these results, other suitable questionnaires for the assessment of somatic symptoms are the 30-item Bodily Distress Syndrome Checklist (BDS checklist), that measures four symptom clusters: the cardiopulmonary/autonomic (arousal), gastrointestinal, musculoskeletal, and general symptoms (30), and the 29-item Subjective Health Complaints Inventory (SHC) (31).

In summary, our study suggests that the assessment time frame of 4 weeks is most suitable for somatic symptom questionnaires, since it reflects clinically relevant subjective somatic symptom burden in this sample. Further studies are necessary to gain more insight into the association between somatic symptom burden and external criteria that reflect clinical relevance, such as health care utilisation and work participation. Also other somatic symptom questionnaire characteristics could be studied. Remaining questions include the optimal number of response categories (e.g., binary, 3-points, 4-points, 5-points, or 7-points scale) which currently vary widely among somatic symptom questionnaires, as well as the most appropriate scoring algorithm (8,9). Furthermore, future studies may investigate whether the 4 weeks' time frame is also clinically relevant for measures of other health and mental health domains. Lastly, our recommendation is based on the quantification of symptom burden in a convenience sample from the general

population. The optimal time frame for somatic symptom questionnaires in clinical settings, in which the focus might be on recent symptoms or on quantification of treatment effects, remains unknown. Similar studies could be performed in different clinical settings (e.g. primary care, secondary care, tertiary care with patients suffering from somatoform disorders). Future studies could also investigate whether there is a difference in the optimal time frame between somatic symptoms that are episodic in nature, and symptoms that typically present more or less continuously.

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