



# Participation and mental well-being of mothers of home-living patients with spinal muscular atrophy

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## Abstract

Proximal spinal muscular atrophy (SMA) causes severe physical limitations but also has a major impact on the lives of parents. The aim of this study was to investigate participation and mental well-being (burden, emotional distress and satisfaction with participation) of parents of home-living patients with SMA. Caregiver burden was assessed with the Caregiver Strain Index, emotional distress with the Hospital Anxiety and Depression Scale and satisfaction with participation with the Utrecht Scale for Evaluation of Rehabilitation-Participation. Because the majority of parents were mothers of home-living SMA patients (76%), further analyses were restricted to mothers. Seventy-seven percent of mothers of patients with SMA had paid work. A substantial proportion of mothers (76%) perceived high caregiver burden. Burden, emotional distress and satisfaction with participation were comparable between mothers of children and mothers of adults with SMA. Caregivers' participation in leisure activities was significantly related to their perceived level of caregiver burden, emotional distress and satisfaction with participation. Mothers engaging in more social and leisure activities reported lower emotional distress and caregiver burden. Considering the high level of burden attention should be paid to mental well-being of primary caregivers of patients with SMA. Caregivers should be motivated to keep participating in social/leisure activities.

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## 1. Introduction

Proximal spinal muscular atrophy (SMA) is an autosomal recessive neuromuscular disease caused by homozygous loss of function of the survival motor neuron (*SMN*) 1 gene. SMA displays significant variability in severity, mainly due to copy number variation of the nearly homologous *SMN2* gene. The clinical classification that distinguishes SMA types (i.e., types 1, 2, 3, and 4), based on age at onset and motor

milestones achieved, captures the severity spectrum. Despite recent successes in the development of SMN augmenting therapies [1], SMA is in essence a disorder of developmental arrest followed by progressive weakness [2]. The majority of patients with SMA face serious complications such as scoliosis, feeding problems and insufficient coughing and breathing, caused by the typical pattern of axial, bulbar and proximal weakness. Disability negatively affects the quality of life of adults with SMA [3].

Having a child with SMA probably also has a significant impact on the lives of primary caregivers [4,5]. A qualitative study found high levels of burden experienced by individuals with SMA and their families [4]. In addition, parents of children with SMA experience higher levels of parenting

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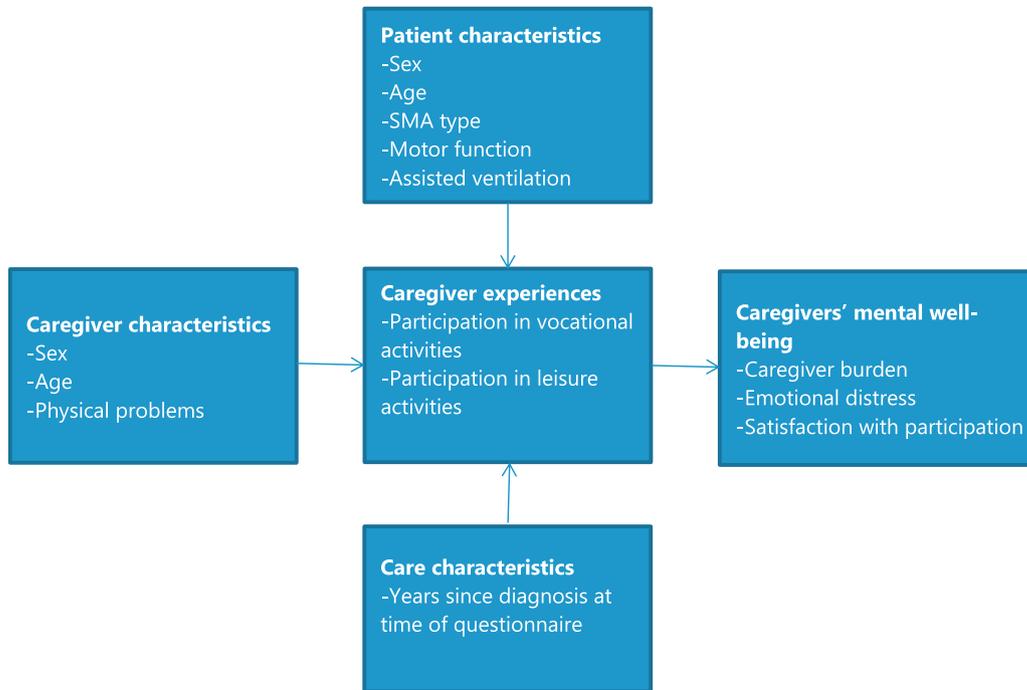


Fig. 1. Conceptual research model for studying caregivers' participation and the mental well-being of mothers of patients with SMA (figure is adapted from [7]).

stress than those of healthy children [5]. SMA severity, reduced social support, child behavior and family resources were found to be factors associated with high degrees of stress or reduced quality of life [5,6].

A better understanding of factors associated with caregivers' mental well-being is necessary for the development of effective interventions to support them. A conceptual model, developed by Nijboer et al., regards family members' caregiving experiences as a central contributing factor to their mental well-being [7]. This caregiving experience is thought to be linked to characteristics of the caregiver and patient, as well as caregiving details (See Fig. 1 for our conceptual research model). Support for this model has been provided in several studies among caregivers of patients with different neuromuscular diseases, in which patient factors (e.g., level of disability, disease duration and use of ventilation at home), caregiver factors (e.g., age and employment) and caregiving details (e.g., time spent daily on caregiving) were found to be associated with caregiver burden [8–11].

The objective of the present study was to increase our understanding of the participation and mental well-being, including burden, emotional distress and satisfaction with participation, of parents of patients with SMA. In addition, we investigated variables associated with caregivers' mental well-being, and whether participation and mental well-being differed between parents of children and parents of adults with SMA. The rationale for comparing these two subgroups was the fact that professional care for children with SMA and adults with SMA is organized differently.

## 2. Patients and methods

### 2.1. Design

Participants were recruited through the Dutch national SMA database ([www.treat-nmd.eu/resources/patient-registries/SMA-national-registries/](http://www.treat-nmd.eu/resources/patient-registries/SMA-national-registries/)). All patients in this database have genetically confirmed SMA. The database contains detailed information on medical history, severity and current motor abilities, as outlined previously [2]. None of the SMA patients were treated with a SMN modifying drug. We enrolled parents of children and parents of adults with SMA (i.e. younger and older than 18 years) in two separate studies. Both studies were approved by the Medical Ethics Review Committee of the University Medical Center Utrecht (UMCU). These studies were performed to investigate participation and mental well-being in caregivers of patients with SMA. One study investigated caregivers of adults with SMA, while the second study investigated caregivers of children with SMA. In this study we selected only the parents of the patients and no other types of caregivers.

Parents of adults with SMA were recruited as part of a cross-sectional study of patients with SMA who visited the UMCU between September 2010 and December 2012.

Parents of children with SMA were enrolled as part of a cross-sectional study between December 2014 and October 2015.

Informed consent was obtained from all study participants. The only exclusion criterion was inability to read Dutch.

All caregivers received a digital or paper questionnaire with a prepaid return envelope.

## 2.2. Questionnaire content

### 2.2.1. Caregiver characteristics, patient characteristics and care characteristics

We used questionnaires to document caregivers' sex, age and presence of physical problems, as well as patients' sex, age and disease duration.

### 2.2.2. Caregiver experiences

We used the Utrecht Scale for Evaluation of Rehabilitation-Participation (USER-P) to assess caregivers' participation in vocational and leisure activities [12]. The USER-P is a questionnaire designed for patients with chronic disabilities and assesses participation in daily life. Although the USER-P was designed for patients, the questionnaire can also be used to determine participation and satisfaction in healthy caregivers [13]. The USER-P assesses three domains of participation, namely frequency of participation, restrictions in participation and satisfaction with participation (<https://www.kcrutrecht.nl/wp-content/uploads/2018/09/USER-Participation-English.pdf>). Since our study investigated parents of SMA patients, the USER-P Restriction was not applicable because it assesses illness related restrictions. The USER-P Frequency is divided into two components: the USER-P Frequency A evaluates the number of hours per week spent on work, study and household chores; the USER-P Frequency B documents the frequency of social and leisure activities in the last four weeks, such as visiting friends and outdoor activities. Respondents' answers were combined and transformed into one score per component. Each component has a score range of 0–100, with higher scores reflecting better participation (i.e. higher frequency of activities).

### 2.2.3. Caregivers' mental well-being

To investigate the burden perceived by parents of SMA patients, we used the Caregiver Strain Index (CSI) [14]. This questionnaire consists of 13 items about physical burden, time investment, emotional health and financial pressure, which can only be answered as 'present' or 'absent'. The sum-score consists of the number of items scored as 'present' (range: 0–13). Scores  $\geq 7$  reflect a high burden. CSI is a tool intended for both practical caregiving and research among caregivers, and has been used for other neuromuscular disorders, including Duchenne muscular dystrophy and amyotrophic lateral sclerosis (ALS) [15,16].

Emotional distress was assessed with the Hospital Anxiety and Depression Scale (HADS) [17]. The HADS consists of two subscales with seven items that capture the degree of anxiety and depression. Both the depression and the anxiety scales range from 0 to 21. Higher scores indicate more symptoms and a score of 8 or more indicates elevated symptoms of anxiety or depression. A total HADS score of 11 or more was considered abnormal.

Satisfaction with the level of participation was assessed using the USER-P Satisfaction. This component of the USER-P also has a score range of 0–100, with a higher score reflecting greater satisfaction.

## 2.3. Clinical data: SMA severity and motor function

We used the following patient characteristics from the national SMA database: SMA type, need for nocturnal or daytime assisted ventilation and Hammersmith Functional Motor Scale-Expanded (HFMSE) scores. Age at onset and acquired motor milestones were used to define SMA type [2]. The HFMSE is a validated test for motor function in SMA consisting of 33 items [18,19]. HFMSE item scores range between 0 and 2, and the maximum score is 66 points. Higher scores indicate better motor skills.

## 2.4. Analyses

We used t-tests to evaluate differences in burden, emotional distress and satisfaction with participation between parents of SMA children and parents of adult SMA patients. Next, we used correlation coefficients and multiple regression analyses to analyze associations between caregiver, patient and care characteristics, caregivers' participation and caregivers' mental well-being (burden, emotional distress and satisfaction with participation). Pearson correlations were calculated in case of normally distributed data, while Spearman correlation was used in case data did not have a normal distribution. Since SMA type was a categorical variable, three separate one-way ANOVAs were performed to investigate whether there were significant differences between the different types of SMA as regards CSI, total HADS and USER-P Satisfaction scores. For the multivariate regression analyses, variables that showed a significant univariate relation with the outcome ( $p \leq 0.10$ ) were entered into a linear regression model. This liberal significance level increased the power for the selection of true predictors. The candidate determinants were checked for multicollinearity. For all other calculations a  $p$ -value of  $< 0.05$  was considered statistically significant.

## 3. Results

### 3.1. Caregiver characteristics, patient characteristics and care characteristics

Sixty-three parents filled in the questionnaire. Since only 9 fathers (1 parent did not answer the question about gender) completed the questionnaire, and 5 patients were not living at home, only mothers of home-living patients with SMA ( $n = 48$ ) were retained for analyses. Characteristics of the mothers and their children, as well as care characteristics, are summarized in Table 1. Thirty-three out of the total of 48 patients (69%) had SMA type 2. Thirty-eight mothers (79%) in this sample were caring for a child with SMA (younger than 18 years of age). Six mothers of patients with SMA (13%) reported physical problems, including 3 mothers with

Table 1  
Caregiver and patient characteristics and care characteristics.

	Mothers of home-living patients with SMA (n = 48)	Mothers of home-living children with SMA (n = 38)	Mothers of home-living adults with SMA (n = 10)	Test value (mothers of children compared to adults)	p-value
<b>Caregiver characteristics</b>					
Age (mean, SD)	42.7 (9.0)	39.7 (6.7)	54.1 (7.4)	5.92 <sup>a</sup>	<0.001
Caregivers with physical problems (n, %)	6 (12.5%)	3 (7.9%)	3 (30.0%)	3.54 <sup>b</sup>	0.06
<b>Patient characteristics</b>					
Age (mean, SD)	12.2 (8.6)	8.9 (5.1)	24.6 (8.0)	7.65 <sup>a</sup>	<0.001
Male gender (n, %)	25 (52.1%)	21 (55.3%)	4 (40.0%)	0.74 <sup>b</sup>	0.39
<b>SMA type</b>					
1	5 (10.4%)	4 (10.5%)	1 (10.0%)	0.65 <sup>b</sup>	0.72
2	33 (68.8%)	27 (71.1%)	6 (60.0%)		
3	10 (20.8%)	7 (18.4%)	3 (30.0%)		
HFMSE (mean, range)	17.7 (0–66) <sup>c</sup>	19.7 (0–64) <sup>c</sup>	12.5 (0–66)	95.50 <sup>d</sup>	0.18
<b>Assisted ventilation (n, %)</b>					
No	41 (85.4%)	33 (86.8%)	8 (80.0%)	0.30 <sup>b</sup>	0.59
Nocturnal	6 (12.5%)	4 (10.5%)	2 (20.0%)		
Daytime + nocturnal	1 (2.1%)	1 (2.6%)	0 (0.0%)		
<b>Care characteristics</b>					
Years since diagnosis at time of questionnaire (mean, SD)	10.3 (8.0) <sup>e</sup>	7.5 (5.1) <sup>e</sup>	20.2 (8.5)	5.92 <sup>a</sup>	<0.001

<sup>a</sup> T-test.

<sup>b</sup> Chi-square test.

<sup>c</sup> 11 missing.

<sup>d</sup> Mann–Whitney U test.

<sup>e</sup> 3 missing.

reduced exercise capacity, 2 mothers with backache and 1 mother with muscle weakness in arms and legs.

As expected, mothers' age, children's age and years since diagnosis differed significantly between mothers of SMA children and mothers of adult SMA patients. There were no other significant differences between mothers of SMA children and mothers of adult SMA patients.

### 3.2. Caregiver experiences

Participation data are presented in Table 2. Seventy-seven percent of the mothers of patients with SMA had paid work, while 42% performed unpaid work (38% of mothers had both paid and unpaid work). In addition, 56% of the mothers of patients with SMA spent 25 or more hours a week on household chores. The scores on the different items concerning work-related activities (USER-P Frequency A) were very similar between mothers of children and adults. The scores on different items concerning leisure activities (USER-P Frequency B) were also highly comparable between the two subgroups. However, the mothers of adults with SMA enjoyed day trips and other outdoor activities more frequently, whereas mothers of children with SMA received more visits from family and friends. There was no significant difference in total score for USER-P Frequency A between mothers of children with SMA (mean 33.2, SD 9.9) and mothers of adults with SMA (mean 33.0, SD 12.7). In addition, there also was no significant difference in total score for USER-P Frequency B between mothers of children with SMA (mean 38.2, SD 14.5) and mothers of adults with SMA (mean 35.7, SD 15.0).

### 3.3. Caregivers' mental well-being

#### 3.3.1. Burden

The majority of mothers (76%) perceived a high level of caregiver burden (73% for mothers of children and 88% for mothers of adults;  $p=0.09$ ). Mean total CSI score for mothers of patients with SMA was 8.1 (Table 3). There was no significant difference in total CSI score between mothers of children (mean 8.2, SD 2.7) and adults (mean 7.8, SD 2.7). Mothers often reported that they suffered from disturbed sleep and that caring for a patient with SMA was both physically demanding and time consuming. Although psychological and financial consequences were reported less often, this still was mentioned by one out of three mothers (Table 4).

#### 3.3.2. Emotional distress

HADS scores for mothers of patients with SMA are shown in Table 3. Twenty-five mothers (52%) had a total HADS score  $\geq 11$ . In addition, 17 mothers (35%) had a HADS depression score  $\geq 8$  and 20 (42%) had a HADS anxiety score  $\geq 8$ . Although mothers of children with SMA generally had higher HADS scores than mothers of adults with SMA, there were no significant differences.

#### 3.3.3. Satisfaction

Data on satisfaction with participation are presented in Table 5. Generally, mothers of patients with SMA were satisfied or very satisfied about their activities. Mothers were even more satisfied about their relationship and contacts with partner, family and friends compared to their participation

Table 2  
USER-P Frequency (subscales A and B) scores of mothers of home-living patients with SMA.

	Mothers of patients with SMA living at home (n = 48)			Mothers of children with SMA (n = 38)			Mothers of adults with SMA (n = 10)		
<b>Subscale A: Hours per week spent on vocational activities</b>									
	Not at all	1–24 h	≥25 h	Not at all	1–24 h	≥25 h	Not at all	1–24 h	≥25 h
Paid work	11 (23%)	22 (46%)	15 (31%)	8 (21%)	19 (50%)	11 (29%)	3 (30%)	3 (30%)	4 (40%)
Unpaid work	28 (58%)	20 (42%)	0 (0%)	22 (58%)	16 (42%)	0 (0%)	6 (60%)	4 (40%)	0 (0%)
Education	41 (85%)	7 (15%)	0 (0%)	32 (84%)	6 (16%)	0 (0%)	9 (90%)	1 (10%)	0 (0%)
Household chores	0 (0%)	21 (44%)	27 (56%)	0 (0%)	17 (45%)	21 (55%)	0 (0%)	4 (40%)	6 (60%)
<b>Subscale B: Frequency of leisure activities during the last 4 weeks</b>									
	Not at all	1–2 times	≥3 times	Not at all	1–2 times	≥3 times	Not at all	1–2 times	≥3 times
Sports/exercise	8 (17%)	12 (25%)	28 (58%)	6 (16%)	11 (29%)	21 (55%)	2 (20%)	1 (10%)	7 (70%)
Going out	14 (29%)	21 (44%)	13 (27%)	10 (26%)	17 (45%)	11 (29%)	4 (40%)	4 (40%)	2 (20%)
Day trips	13 (27%)	23 (48%)	12 (25%)	12 (32%)	16 (42%)	10 (26%)	1 (10%)	7 (70%)	2 (20%)
Leisure at home	8 (17%)	10 (21%)	30 (63%)	7 (18%)	7 (18%)	24 (63%)	1 (10%)	3 (30%)	6 (60%)
Visiting family/friends	4 (8%)	17 (35%)	27 (56%)	3 (8%)	13 (34%)	22 (58%)	1 (10%)	4 (40%)	5 (50%)
Visits from family/friends	3 (6%)	19 (40%)	26 (54%)	2 (5%)	13 (34%)	23 (61%)	1 (10%)	6 (60%)	3 (30%)
Contacts with others by phone or computer	2 (4%)	5 (10%)	41 (85%)	1 (3%)	4 (11%)	33 (87%)	1 (10%)	1 (10%)	8 (80%)

Table 3  
Outcome measures (measures of mental well-being) for mothers of home-living patients with SMA.

	Total group (n = 48)		Mothers of home-living children with SMA (n = 38)		Mothers of home-living adults with SMA (n = 10)		t-value	p-value
	Mean (SD)	% high symptoms	Mean (SD)	% high symptoms	Mean (SD)	% high symptoms		
Caregiver burden (CSI)	8.1 (2.6)	76%	8.2 (2.7) <sup>a</sup>	73% <sup>a</sup>	7.8 (2.7) <sup>b</sup>	88% <sup>b</sup>	−0.40	0.69
Distress (HADS)								
Total score	12.5 (7.9)	52%	13.1 (8.1)	53%	10.2 (7.0)	50%	−1.03	0.31
Depression	5.7 (4.6)	35%	6.0 (5.0)	37%	4.7 (3.1)	30%	−0.75	0.46
Anxiety	6.8 (3.9)	42%	7.2 (3.8)	42%	5.5 (4.3)	40%	−1.19	0.24
Satisfaction with participation (USER-P)	68.5 (14.9)	NA	68.5 (16.2)	NA	68.6 (8.9)	NA	0.01	0.99

Notes: Cut-off points for CSI ≥ 7, for total HADS score ≥ 11, for depressive symptoms ≥ 8; for anxiety symptoms ≥ 8.

<sup>a</sup> 1 missing.

<sup>b</sup> 2 missing.

in physical or leisure activities. There was no significant difference in total score for USER-P Satisfaction between mothers of children and adults (Table 3).

Mothers of children were more likely to be satisfied about going out than mothers of adults, while the mothers of adults were more likely to be satisfied about going on day trips and other outdoor activities and leisure activities at home.

### 3.4. Correlates of caregivers' mental well-being

#### 3.4.1. Burden

Data on univariate and multivariate analyses are presented in Table 6. Univariate analyses showed caregiver burden to be associated with the presence of assisted ventilation and

caregivers' frequency of social/leisure activities. Multivariate analysis only identified frequency of participation in social/leisure activities as a significant predictor of caregiver burden. The model explained 19% of the variance in CSI scores.

#### 3.4.2. Emotional distress

Univariate analyses showed the total HADS score to be significantly correlated with caregivers' age, patients' age, years since diagnosis and caregivers' frequency of participation in social/leisure activities (Table 6). Years since diagnosis showed high multicollinearity with the mothers' and children's age, and this variable was therefore excluded from the multivariate analysis. Multivariate analysis identified

Table 4  
Caregiver burden among mothers of home-living patients with SMA ( $n=48$ ).

CSI item	Mothers of home-living patients with SMA ( $n=48$ )	Mothers of home-living children with SMA ( $n=38$ ) <sup>a</sup>	Mothers of home-living adults with SMA ( $n=10$ ) <sup>b</sup>
a. Sleep is disturbed	40 (83%)	32 (84%)	8 (80%)
b. It is inconvenient	43 (90%)	36 (95%)	7 (70%)
c. It is a physical strain	36 (75%)	29 (76%)	7 (70%)
d. It is confining	32 (68%)	26 (68%)	6 (67%)
e. There have been family adjustments	38 (81%)	31 (82%)	7 (78%)
f. There have been changes in personal plans	38 (81%)	31 (82%)	7 (78%)
g. Demands on time	43 (91%)	35 (92%)	8 (89%)
h. There have been emotional adjustments	13 (28%)	11 (29%)	2 (22%)
i. Some behavior is upsetting	19 (40%)	16 (42%)	3 (33%)
j. It is upsetting to find that he/she has changed so much from his/her former self	14 (30%)	13 (34%)	1 (13%)
k. There have been adjustments at work	31 (66%)	27 (71%)	4 (44%)
l. Feeling completely overwhelmed	21 (46%)	16 (42%)	5 (63%)
m. It is a financial strain	13 (29%)	10 (27%)	3 (38%)

<sup>a</sup> 1 missing for question m.

<sup>b</sup> 1 missing for question d, e, f, g, h, i, k and 2 missings for question j, l, m.

Table 5  
USER-P Satisfaction for mothers of home-living patients with SMA ( $n=48$ ). Satisfaction about current daily life.

	Mothers of home-living patients with SMA ( $n=48$ ) (Very) satisfied	Mothers of children with SMA ( $n=38$ ) (Very) satisfied	Mothers of adults with SMA ( $n=10$ ) (Very) satisfied
Paid/unpaid work/education	30 (75%)	24 (73%) <sup>a</sup>	6 (86%) <sup>b</sup>
Household chores	27 (56%)	20 (53%)	7 (70%)
Moving about outdoors	37 (77%)	28 (74%)	9 (90%)
Sports or other exercise	25 (52%)	21 (55%)	4 (40%)
Going out	22 (47%)	19 (50%)	3 (33%) <sup>c</sup>
Day trips	28 (58%)	21 (55%)	7 (70%)
Leisure at home	29 (60%)	21 (55%)	8 (80%)
Relationship with partner	38 (93%)	32 (94%) <sup>d</sup>	6 (86%) <sup>b</sup>
Relationship with family	44 (92%)	34 (89%)	10 (100%)
Contacts with friends and acquaintances	40 (83%)	31 (82%)	9 (90%)

<sup>a</sup> 5 patients with 'not applicable'.

<sup>b</sup> 3 patients with 'not applicable'.

<sup>c</sup> 1 patient with 'not applicable'.

<sup>d</sup> 4 patients with 'not applicable'. All patients with 'not applicable' were omitted from the calculations.

frequency of participation in social/leisure activities as the only variable that was significantly associated with caregivers' emotional distress. The model explained 51% of the variance in HADS scores.

### 3.4.3. Satisfaction

Univariate analyses showed that satisfaction with caregivers' level of participation (USER-P Satisfaction) was associated with patients' gender and caregivers' frequency of participation in social/leisure activities (Table 6). Satisfaction with participation was higher in mothers of male patients compared to mothers of female patients. Caregivers' frequency of participation in vocational activities was not associated with satisfaction. Multivariate analysis identified

only frequency of participation in social/leisure activities as a significant predictor of satisfaction. The model explained 36% of the variance in satisfaction with participation.

No significant differences in CSI, total HADS or USER-P Satisfaction were found between the different SMA types.

## 4. Discussion

In this study we examined participation and mental well-being of mothers of patients with spinal muscular atrophy living at home. The majority of mothers of both children and adults with SMA perceived high caregiver burden. Furthermore, 50 percent of the mothers had signs of elevated

Table 6

Univariate and multivariate associations between caregiver, patient and care variables, caregivers' participation and caregiver burden, emotional distress and satisfaction with participation.

	Caregiver burden (CSI)		Caregiver emotional distress (HADS)		Satisfaction with participation (USER-P)	
	Zero-order correlation coefficients ( <i>p</i> -value)	Regression coefficients, Std Beta ( <i>p</i> -value)	Zero-order correlation coefficients ( <i>p</i> -value)	Regression coefficients, Std Beta ( <i>p</i> -value)	Zero-order correlation coefficients ( <i>p</i> -value)	Regression coefficients, Std Beta ( <i>p</i> -value)
<b>Caregiver characteristics</b>						
Age	−0.16 (0.30)	–	−0.25 (0.09)	−0.13 (0.53)	−0.04 (0.77)	–
Presence of physical problems	0.18 (0.24)	–	0.17 (0.26)	–	−0.05 (0.73)	–
<b>Patient characteristics</b>						
Sex	0.22 (0.15)	–	−0.14 (0.35)	–	0.27 (0.07)	0.21 (0.09)
Age	−0.17 (0.26)	–	−0.33 (0.03)	−0.08 (0.68)	0.06 (0.69)	–
Assisted ventilation	0.27 (0.08)	0.23 (0.11)	0.03 (0.83)	–	−0.04 (0.81)	–
Motor function	−0.15 (0.41) <sup>a</sup>	–	0.12 (0.47) <sup>a</sup>	–	0.00 (0.98) <sup>a</sup>	–
<b>Care characteristics</b>						
Years since diagnosis	−0.07 (0.68)	–	−0.25 (0.10)	Excluded <sup>b</sup>	−0.02 (0.91)	–
<b>Caregivers' participation</b>						
Freq. vocational activities	0.09 (0.55)	–	−0.05 (0.77)	–	−0.14 (0.35)	–
Freq. social/leisure activities	−0.38 (0.01)	−0.35 (0.02)	−0.69 (<0.001)	−0.66 (<0.001)	0.57 (<0.001)	0.54 (<0.001)
<b>Explained variance (R<sup>2</sup>)</b>		19.3% (adj. R <sup>2</sup> 15.4%)*		51.3% (adj. R <sup>2</sup> 47.9%)**		36.2% (adj. R <sup>2</sup> 33.3%***)

\* Model F (2, 42) = 5.01, *p* = 0.01.

\*\* Model F (3, 43) = 15.11, *p* < 0.001.

\*\*\* Model F (2, 44) = 12.51, *p* < 0.001.

<sup>a</sup> Spearman correlation coefficient.

<sup>b</sup> Excluded from regression analysis because of multicollinearity with age variables.

emotional distress, which was comparable between mothers of children with SMA and mothers of adults with SMA. Mothers' satisfaction with their participation varied between 47 and 93%, depending on the domain of participation, with social interaction and relationships receiving higher satisfaction scores than physical and outdoor activities. Caregivers' frequency of participation in leisure activities was negatively related to their perceived level of burden and emotional distress and positively related to satisfaction with level of participation.

Two other studies have examined levels of burden and mental well-being in caregivers of patients with SMA. One qualitative study using focus group sessions and interviews with patients with SMA and their caregivers reported high levels of burden of both patients with SMA and their families [4]. This study suggested a direct relation between the all-consuming nature of the demands of caring for a child with substantial physical needs on the one hand, and the emotional and social effects on their entire families on the other. This is consistent with the findings of the present study, which demonstrated a relation between participation in social and leisure activities and caregivers' mental well-being.

Another study among parents of children and adolescents with SMA concluded that their families showed high degrees of mental stress compared with matched controls [5]. The authors reported higher levels of stress in families with SMA type 1 or 2 compared to families with SMA type 3. We did not find differences in mental well-being between the different SMA types, but the small number of mothers of patients with SMA type 3 and the resulting lack of power may explain the discrepancy.

Our study found a higher mean caregiver burden among mothers of patients with SMA than studies of caregivers of patients with other neuromuscular diseases [15,16]. However, since these other studies among caregivers of patients with neuromuscular disorders also included fathers [15,16] and partners instead of parents [15], results are difficult to compare with the present investigation. In addition, the degree of disability might be different for each diagnostic group, leading to a different degree of burden.

To our knowledge, no studies have previously investigated the emotional distress of caregivers of patients with SMA using the HADS. However, HADS scores found among caregivers of adult Duchenne patients and ALS patients were

comparable to the HADS results we found among mothers of patient with SMA [15,16].

Our conceptual model for understanding caregivers' mental well-being was based on a model that was originally developed for caregivers of patients with cancer [7]. This model proposed that caregivers' experiences are predictive of their mental well-being. Longitudinal analyses has lent support to this hypothesis. In particular, a disrupted activity schedule appeared to be one of the most salient predictors of depressive symptoms among caregivers [7]. Our study also confirms the association between caregiver's participation and their mental well-being, but additionally illustrates that some areas of participation, namely the frequency of participation in social and leisure activities, may have a greater impact on mental well-being than others. Together, these studies suggest that it is important for care providers to be attentive to disruptions of social and leisure activities reported by caregivers of patients with SMA. This is in line with the findings of a study among caregivers of patients with traumatic brain injury, which found that one of the most common complaints of the caregivers was a lack of involvement in leisure activities [20].

Another hypothesis is that satisfaction with participation rather than frequency of participation is more associated to caregiver burden and emotional distress. However, in our study we found stronger correlations for frequency of participation with CSI and HADS compared with the correlations between satisfaction with participation and CSI and HADS.

In the study of Nijboer et al. the conceptual model was used to investigate caregiver's mental health in partners of patients with colorectal carcinoma [7]. Our study aimed to investigate mental health in parents of patients with SMA. In our study we used the model of Nijboer et al. as a conceptual framework that classifies different types of possible predictors. However, a comparison between both studies is complicated since the type of caregiver as well as the type of disease are completely different in both studies. As a result, the variables that were classified within the separate blocks were very different.

In our study there were no significant differences in burden and depression and anxiety scores between mothers of children or adults with SMA. And like other studies, we did not find a relation between caregivers' age and their mental well-being [7,21,22].

Our study found a very high satisfaction of mothers of SMA patients about their relationship with partner and family. No other studies have investigated satisfaction about the relationship with their partner in caregivers of patients with SMA or other neuromuscular disorders. Since in other patient categories the vast majority of caregivers are partners of the patients (instead of parents), this comparison would not be justified.

This study has limitations. First, given the modest sample size of this study, the statistical power of our analyses is limited. Second, generalizability of our findings to other caregivers of patients with SMA is limited because of the

modest sample size, and the exclusion of fathers and patients not living at home. Third, in some analyses there were a few missing data. Finally, since all variables in our study were assessed at one single time point, we are unable to draw conclusions on causality. However, a longitudinal study of the influence of caregivers' experiences on their mental well-being has been valuable since it showed that a disruption of planning and daily routine at 3 months after baseline was associated with caregivers' depression six months after baseline [7].

In spite of these limitations, our study indicates a very high level of caregiver burden, depression and anxiety among mothers of patients with SMA who live at home. This burden does not decrease with advancing age. We therefore feel that it is important to actively involve mothers of patients with SMA in the consultations and to assess and monitor their burden and emotional distress, in order to identify those mothers who are at risk of high caregiver burden or emotional distress. It is also important for the patient with SMA, as well as for the other children in the family, that mothers remain healthy. Therefore it seems relevant for healthcare professionals to facilitate mothers of patients with SMA in their participation in social and leisure activities, in order to preserve or improve their well-being, and to enable them to continue to take care of their child for as long and as effectively as possible.

As regards further research, we recommend conducting a longitudinal study to investigate changes in caregiver mental well-being over time and to investigate determinants explaining the variance in mental well-being. Moreover, future studies should try to increase the sample size by also including fathers and patients not living with their parents, allowing for better generalizability of results. Furthermore, patients' mental well-being and caregivers' mental well-being at baseline might be important determinants to include in future studies, as other studies have found important associations between patients' mental well-being, caregivers' mental well-being at baseline and caregivers' mental well-being over time [22–24]. Given the current development in treatment for SMA it might be interesting to investigate burden in mothers of patients with SMA again in the future.

In conclusion, we found a high level of caregiver burden among mothers of patients with SMA living at home. Burden, emotional distress and satisfaction with participation did not differ between mothers of children and mothers of adults with SMA. Importantly, participation in social and leisure activities was found to be strongly related to caregivers' mental well-being. Mothers who engaged in more leisure activities reported less emotional distress and lower caregiver burden. Therefore healthcare professionals should pro-actively assess the burden in caregivers and ask them what is needed to preserve or improve their well-being.

### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.nmd.2019.02.011](https://doi.org/10.1016/j.nmd.2019.02.011).

## References

- [1] Mercuri E, Darras BT, Chiribogo CA, Day JW, Campbell C, Connolly AM, et al. Nusinersen versus sham control in later-onset spinal muscular atrophy. *N Eng J Med* 2018;378:625–35.
- [2] Wadman RI, Wijngaarde CA, Stam M, Bartels B, Otto LAM, Lemmink HH, et al. Muscle strength and motor function throughout life in a cross-sectional cohort of 180 patients with spinal muscular atrophy types 1c-4. *Eur J Neurol* 2018;25:512–18.
- [3] Kruitwagen-Van Reenen ET, Wadman RI, Visser-Meily JM, van den Berg LH, Schröder C, van der Pol WL. Correlates of health related quality of life in adult patients with spinal muscular atrophy. *Muscle Nerve* 2016;54:850–5.
- [4] Qian Y, McGraw S, Henne J, Jarecki J, Hobby K, Yeh WS. Understanding the experiences and needs of individuals with spinal muscular atrophy and their parents: a qualitative study. *BMC Neurol* 2015;15:217.
- [5] Von Gontard A, Rudnik-Schöneborn S, Zerres K. Stress and coping in parents of children and adolescents with spinal muscular atrophy. *Klin Padiatr* 2012;224:247–51.
- [6] Kocova H, Dvorackova O, Vondracek P, Haberlova J. Health-related quality of life in children and adolescents with spinal muscular atrophy in the Czech Republic. *Pediatr Neurol* 2014;50:591–4.
- [7] Nijboer C, Triemstra M, Tempelaar R, Sanderman R, van den Bos GA. Determinants of caregiving experiences and mental health of partners of cancer patients. *Cancer* 1999;86:577–88.
- [8] Evans R, Catapano MA, Brooks D, Goldstein RS, Avendano M. Family caregiver perspectives on caring for ventilator-assisted individuals at home. *Can Respir J* 2012;19:373–9.
- [9] Chiò A, Gauthier A, Calvo A, Ghiglione P, Mutani R. Caregiver burden and patients' perception of being a burden in ALS. *Neurology* 2005;64:1780–2.
- [10] Qutub K, Lacomis D, Albert SM, Feingold E. Life factors affecting depression and burden in amyotrophic lateral sclerosis caregivers. *Amyotroph Lateral Scler Frontotemporal Degener* 2014;15:292–7.
- [11] Mah JK, Thannhauser JE, McNeil DA, Dewey D. Being the lifeline: the parent experience of caring for a child with neuromuscular disease on home mechanical ventilation. *Neuromuscul Disord* 2008;18:983–8.
- [12] Van der Zee CH, Priesterbach AR, van der Dussen L, Kap A, Schepers VP, Visser-Meily JM, et al. Reproducibility of three self-report participation measures: the ICF measure of participation and activities screener, the participation scale, and the Utrecht scale for evaluation of rehabilitation-participation. *J Rehabil Med* 2010;42:752–7.
- [13] Tielemans NS, Visser-Meily JM, Schepers VP, Passier PE, Port IG, Vloothuis JD, et al. Effectiveness of the Restore4Stroke self-management intervention “Plan ahead!”: a randomized controlled trial in stroke patients and partners. *J Rehabil Med* 2015;47:901–9.
- [14] Robinson BC. Validation of a caregiver strain index. *J Gerontol* 1983;38:344–8.
- [15] Creemers H, de Morée S, Veldink JH, Nollet F, van den Berg LH, Beelen A. Factors related to caregiver strain in ALS: a longitudinal study. *J Neurol Neurosurg Psychiatry* 2016;87:775–81.
- [16] Pangalila RF, van den Bos GA, Stam HJ, van Exel NJ, Brouwer WB, Roebroek ME. Subjective caregiver burden of parents of adults with Duchenne muscular dystrophy. *Disabil Rehabil* 2012;34:988–96.
- [17] Snaith RP, Zigmond AS. The hospital anxiety and depression scale. *Br Med J (Clin Res Ed)* 1986;292:344.
- [18] O'Hagen JM, Glanzman AM, McDermott MP, Ryan PA, Flickinger J, Quigley J, et al. An expanded version of the Hammersmith functional motor scale for SMA II and III patients. *Neuromuscul Disord* 2007;17:693–7.
- [19] Glanzman AM, O'Hagen JM, McDermott MP, Martens WB, Flickinger J, Riley S, et al. Validation of the expanded Hammersmith functional motor scale in spinal muscular atrophy type II and III. *J Child Neurol* 2011;26:1499–507.
- [20] Hall KM, Karzmark P, Stevens M, Englander J, O'Hare P, Wright J. Family stressors in traumatic brain injury: a two-year follow-up. *Arch Phys Med Rehabil* 1994;75:876–84.
- [21] Sulkers E, Tissing WJ, Brinksma A, Roodbol PF, Kamps WA, Stewart RE, et al. Providing care to a child with cancer: a longitudinal study on the course, predictors, and impact of caregiving stress during the first year after diagnosis. *Psychooncology* 2015;24:318–24.
- [22] Cramm JM, Nieboer AP. Psychological well-being of caregivers of children with intellectual disabilities: using parental stress as a mediating factor. *J Intellect Disabil* 2011;15:101–13.
- [23] Kruithof WJ, Post MW, van Mierlo ML, van den Bos GA, de Man-van Ginkel JM, Visser-Meily JM. Caregiver burden and emotional problems in partners of stroke patients at two months and one year post-stroke: determinants and prediction. *Patient Educ Couns* 2016;99:1632–40.
- [24] Nijboer C, Tempelaar R, Triemstra M, van den Bos GA, Sanderman R. The role of social and psychological resources in caregiving of cancer patients. *Cancer* 2001;91:1029–39.