

## The long-term caregiver burden in World Health Organization grade I and II meningioma: It is not just the patient

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### Abstract

**Background.** Little is known about long-term caregiver burden in meningioma patients. We assessed meningioma caregiver burden, its association with informal caregiver's well-being and possible determinants.

**Methods.** In this multicenter cross-sectional study, informal caregivers completed the Caregiver Burden Scale (five domains and total score). Patients completed a disease-specific health-related quality of life (HRQoL) questionnaire focusing on symptoms (EORTC QLQ-BN20) and underwent neurocognitive assessment. Both groups completed a generic HRQoL questionnaire (SF-36) and the Hospital Anxiety, and Depression Scale. We assessed the association between caregiver burden and their HRQoL, anxiety and depression. Furthermore, we assessed determinants for the caregiver burden. Multivariable regression analysis was used to correct for confounders.

**Results.** One hundred and twenty-nine informal caregivers were included (median 10 years after patients' treatment). Caregivers reported burden in  $\geq 1$  domain (34%) or total burden score (15%). A one-point increase in total caregiver burden score was associated with a clinically relevant decrease in caregiver's HRQoL (SF-36) in 5/8 domains (score range:  $-10.4$  to  $-14.7$ ) and 2/2 component scores ( $-3.5$  to  $-5.9$ ), and with more anxiety (3.8) and depression (3.0). Patients' lower HRQoL, increased symptom burden, and increased anxiety and depression were determinants for higher caregiver burden, but not patients' or caregivers' sociodemographic characteristics, patients' neurocognitive functioning, or tumor- and treatment-related characteristics.

**Conclusions.** Ten years after initial treatment, up to 35% of informal caregivers reported a clinically relevant burden, which was linked with worse HRQoL, and more anxiety and depression in both patients and caregivers, emphasizing the strong interdependent relationship. Support for meningioma caregivers is therefore warranted.

### Key Points

- 34% of meningioma informal caregivers report a clinically relevant caregiver burden.
- Caregiver burden was associated with lower HRQoL and more anxiety and depression.
- Caregiver support could not only benefit caregivers themselves but also patients.

## Importance of the Study

Previous studies have described a significant caregiver burden in caregivers of patients with neurological and oncological conditions. However, no studies have been performed to evaluate the caregiver burden in meningioma. We describe that up to 35% of informal caregivers of meningioma patients reported a clinically relevant caregiver burden, in a sample assessed at least 5 years after diagnosis and treatment. This burden was associated with significantly lower levels of HRQoL and higher levels of anxiety and depression in caregivers. Interestingly, the caregiver burden was related

to the patient's HRQoL, but not determined by the patient's neurocognitive functioning, nor their sociodemographic, tumor- or treatment-related characteristics. Our results emphasize that the caregiver burden is inherently part of the chronic nature of meningioma and support for caregivers of meningioma patients is therefore needed. Further studies should be performed to identify resources to support informal caregivers. As our results show that caregiver and patient wellbeing are strongly interlinked, caregiver support could not only benefit caregivers themselves but also patients.

Meningioma comprises the majority of primary intracranial tumors (37%) and is classified as World Health Organization (WHO) grade I and II tumors in more than 95% of cases.<sup>1</sup> There has been a paucity of research on the possible long-term negative effects of tumor and treatment.<sup>2</sup> Recent studies, however, have reported a significant disease burden in terms of diminished health-related quality of life (HRQoL) and neurocognitive impairment after treatment.<sup>3,4</sup> Although no studies are published on the caregiver burden in the meningioma context, one might expect that patients' functioning and well-being may also have a noteworthy impact on informal caregivers.

Informal caregivers are often relatives or friends of patients, who deliver a substantial amount of emotional, physical, and/or psychological support. While this role can be rewarding, it often also results in caregiver burden.<sup>5</sup> Compared with other cancer groups (eg, lung, breast, and prostate), caregivers of patients with brain tumors—particularly glioblastoma—report more severe caregiver burden and poorer HRQoL.<sup>6,7</sup> Previously a conceptual model of caregiver burden in primary malignant brain tumor patients, and an updated version for oncology caregiving, has been described by Sherwood et al.<sup>5,8</sup> According to this model the patient disease characteristics (including tumor, treatment, functional, cognitive and neuropsychiatric status) alongside caregiver personal characteristics (eg, personal or social attributes) impact on caregiver psychological and behavioral responses, including caregiver burden. These may trigger biologic responses and affect caregivers' overall health and wellbeing (eg, HRQoL).<sup>5,8</sup>

A multitude of determinants of caregiver burden has been reported, which vary considerably between different patient groups (eg, malignant brain tumors, stroke), but comprise both patient and informal caregiver characteristics, including age, sex, and comorbidities.<sup>7,9</sup> However, the severity of the caregiver burden as well as the determinants of burden may be different in caregivers of meningioma patients, who generally have a better life-expectancy and fewer neurological deficits compared with patients with malignant brain tumors (eg, glioblastoma) or stroke. In addition, treatment regimens differ significantly

between groups, and therefore not only the disease but also the long-term effects of its treatment might differently affect caregivers.<sup>1,10</sup>

The primary aim of this study was to assess the long-term caregiver burden of informal caregivers. Furthermore, we investigated the association between caregiver burden and caregivers' HRQoL, and levels of anxiety and depression. We also assessed determinants for caregiver burden in terms of caregiver's and patients' sociodemographic characteristics, patients' clinical characteristics, tumor- and treatment-related characteristics, HRQoL, anxiety and depression scores, and level of neurocognitive functioning. Better knowledge of caregiver burden and its determinants can be used in clinical practice to guide caregivers, to relieve their burden, and to support them in caring for the patient, which might improve outcomes of not only informal caregivers, but also patients.

## Methods

### Participants

Patients and caregivers were invited to participate in a multicenter quantitative cross-sectional study on the long-term disease burden of meningioma patients and caregiver burden of their informal caregivers.<sup>11</sup> Patients and informal caregivers who were 18 years or older with sufficient mastery of Dutch were recruited between July 2016 and April 2019. Patients were recruited at least 5 years after their last anti-tumor treatment, or in case of a wait-and-scan follow-up at least 5 years after meningioma diagnosis. Patients were excluded if diagnosed with neurodegenerative disease, neurofibromatosis type II, or who had a history of whole brain radiotherapy. Informal caregivers were eligible for participation if they were a spouse, family member, or close friend to the patient, and provided the majority of physical, emotional, and/or social support to the patient. Detailed study procedures are described in the main report.<sup>11</sup>

## Procedures

### Questionnaires

On the same day, neurocognitive tests were administered in person by a research assistant, structured interviews conducted, and questionnaires were completed on paper. Informal caregivers completed the Caregiver Burden Scale (CBS), which is a 22-item questionnaire measuring caregiver burden in five domains: stress, social isolation, feeling of disappointment, emotional problems, and problems due to environmental factors.<sup>12,13</sup> Each of the 22 items is scored on a 4-point Likert scale (ranging from 1 = never to 4 = nearly always) and items within a domain are averaged to obtain the domain score. The average of the domain scores reflects the total caregiver burden score.<sup>12,13</sup> For dichotomous analysis, CBS domain, and total scores were classified into low burden (scores: 1–1.9) and medium/high burden (scores  $\geq 2$ ). Both patients and informal caregivers completed a generic HRQoL instrument, the Short-Form Health Survey (SF-36), ranging from 0 to 100 with higher scores indicating better HRQoL.<sup>14,15</sup> The SF-36 is the most frequently used HRQoL instrument in meningioma patients.<sup>2</sup> Patients additionally completed the European Organisation for Research and Treatment of Cancer quality of life questionnaire, brain neoplasm (EORTC QLO-BN20) module to specifically measures brain tumor-specific symptoms as part of HRQoL measurement, ranging from 0 to 100 with higher scores indicating worse HRQoL.<sup>16,17</sup> Both groups also completed the Hospital Anxiety and Depression Scale (HADS), for which clinically relevant cut-offs exist for individual patients: mild (0–7), moderate (8–10), and severe (11–21) anxiety or depression.<sup>18,19</sup> All questionnaires are validated in Dutch and further details, including references, are presented in [Supplemental Table 1](#).

### Neuropsychological assessment of meningioma patients

A frequently used comprehensive battery of neuropsychological tests was administered to patients by trained research assistants and consisted of the Concept Shifting Test, Auditory Verbal Learning Test, Categorical Word Fluency

Test, Memory Comparison Test, Digit-Symbol Substitution Test, and the Stroop Colour-Word Test.<sup>20</sup> Based on these tests, scores for the following neurocognitive domains, which are relevant for meningioma patients, were calculated: verbal memory, executive functioning, psychomotor functioning, working memory, information processing speed, and attention ([Supplemental Table 1](#)).<sup>21</sup>

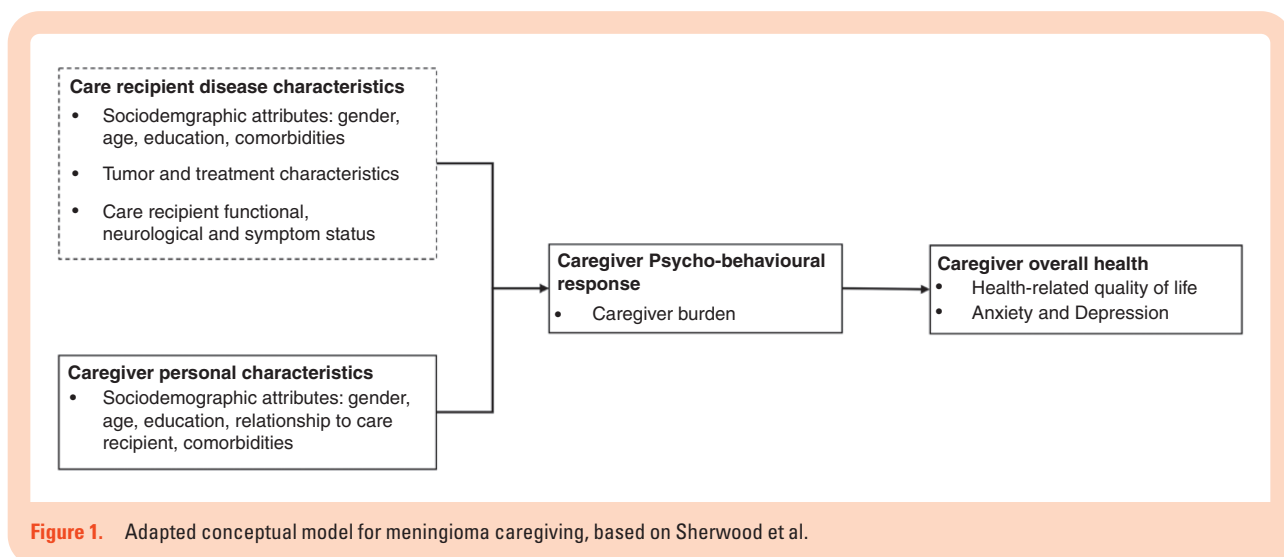
### Clinically relevant cut-offs

We used clinically relevant cut-offs, based on established minimal clinically important differences (MCID) as reported in the literature. For the CBS this was set on 1 point, based on the previously published cut-offs (low burden: 1–1.9, medium burden 2–2.9, high burden: 3.0–4.0).<sup>13</sup> Cut-off for the SF-36 domains was set at 10 points, as the majority of published studies reported MCID's for the different domains lower than 10 points.<sup>22</sup> For the SF-36 mental and physical component scored, cut-offs were set at 4.6 points and 3.0 points, respectively.<sup>23</sup> The cut-off for the HADS anxiety and depression scale were set at 2.0 points, as most studies report MCIDs lower than 2.0.<sup>24,25</sup> For calculation of Z-scores of patient's neurocognitive domains, means and standard deviations from a reference sample from the Dutch Maastricht Aging Study (MAAS) were used, matched on group-level for age, sex, and educational level.<sup>26</sup> Per domain, differences in z-scores greater than  $-1.5$  were considered clinically relevant.<sup>27</sup> MAAS is a large longitudinal study among the general Dutch population on the psychological and biological determinants of cognitive aging with reference data for all used tests.

## Statistical Analysis

### Conceptual model

Based on our previous focus groups with meningioma patients and caregivers, we adapted Sherwood's conceptual model of caregiver burden in primary malignant brain tumors and used it to guide the evaluated associations ([Figure 1](#))<sup>5,8</sup>. Although originally developed for patients



**Figure 1.** Adapted conceptual model for meningioma caregiving, based on Sherwood et al.

with malignant brain tumors, this conceptual model is with small adaptations an excellent fit for the meningioma patient-caregiver population.<sup>5</sup>

### *Association between the caregiver burden and caregiver well-being*

Separate multivariable regression analyses were performed to assess the association between total Caregiver Burden Scale score (independent variable) and informal caregiver's HRQoL (SF-36), and levels of anxiety and depression as measured with the HADS (dependent variables). For these analyses, clinically relevant cut-offs as described above were used to interpret the impact of the total caregiver burden score on the outcomes (ie, SF-36 and HADS).

### *Associations between determinants and the caregiver burden*

Next, separate multivariable regression analyses were performed to assess the association between each potential patient determinant (independent variables) and the total Caregiver Burden Scale score (dependent variable). Based on the literature and Sherwood's conceptual model for caregiver burden in neuro-oncology, we hypothesized the following variables to be possible determinants: caregiver demographic characteristics (sex, age, Charlson Comorbidity Index, education level, relationship) patient demographic and clinical characteristics (sex, age, Charlson Comorbidity Index, education level, Karnofsky Performance Status [KPS]), tumor and treatment characteristics (tumor location (convexity/skull base), tumor size before intervention (largest diameter), baseline tumor size (largest diameter), surgery (yes/no), surgical complications (yes/no), Simpson grade (I-V), WHO Grade (I-II),

radiotherapy (yes/no)), time since diagnosis in years, patients' HRQoL as expressed with the mental and physical component scores (SF-36), level of anxiety and depression (HADS), neurocognitive impairment (clinically relevant impairment in any of the 6 domains), and the number of experienced brain-tumor related HRQoL symptoms (scales dichotomized: not at all vs. a little, quite a bit, or very much problems) as measured with the EORTC QLQ-BN20.<sup>5,9,28,29</sup>

To assess how the independent variables contribute to the total caregiver burden score, the explained variance ( $R^2$ ) from univariable analysis was used, describing the percentage that each variable explains the total caregiver burden score. For analysis modeling multiple variables simultaneously, the adjusted  $R^2$  was used, correcting for overprediction due to the presence of multiple variables within the same analysis.

### *Correction for confounding*

All multivariable analyses were corrected for confounders, which means that in addition to the independent variable, we included in each model variables defined as confounders specific for the assessed association to approximate the causal association between the dependent and independent variable.<sup>30-32</sup> Confounders were identified using the Directed Acyclic Graph representation (see [Supplementary Figure 1](#) for examples), defined as being associated with both the determinant and the outcome, but not in the causal path of the association, based on prior clinical knowledge.<sup>30-32</sup>

### *Ethics Committee Approval*

This cross-sectional study was approved by the medical ethical committees of all participating centers

**Table 1.** Sociodemographic and Clinical Characteristics of Informal Caregivers and Meningioma Patients

	Informal Caregivers (n = 129)	Meningioma Patients (n = 129)
Age, years	62.7 (SD 11.7)	61.3 (SD 13.5)
Female	47 (36.4%)	98 (76%)
Relationship with the patient		
Partner	105 (81%)	
Child	11 (9%)	
Friend	6 (5%)	
Sibling	5 (4%)	
Parent	2 (2%)	
Education level		
Primary/secondary	14 (11%)	25 (19%)
Tertiary: technical/vocational	55 (43%)	60 (47%)
Academic	54 (42%)	40 (31%)
Missing	6 (5%)	4 (3%)
Charlson comorbidity index		
1 $\geq$	36 (28%)	44 (34%)

N, number; SD, standard deviation.

(NL54866.029.15), and participants provided informed consent before study procedures.

## Results

A total of 190 meningioma patients were recruited to the original study, of whom 61 indicated to not have an informal caregiver willing to participate in the study. Therefore 129 informal caregivers with a mean age of 61.3 years (SD 13.5), and 129 meningioma patients with a mean age 62.7 (SD 11.7) were included in the described analyses. Median follow-up length since patient diagnosis was 10 years (interquartile range: 8–12) (Table 1 and Supplementary Table 2). Most informal caregivers were male ( $n = 82$ , 63%), while most patients were female ( $n = 98$ , 76%). The majority of informal caregivers were patients' partners ( $n = 105$ , 81%). Most patients were operated for their meningioma ( $n = 113$ , 87%) of whom 104 (92%) patients were diagnosed with a WHO grade I meningioma. Primary radiotherapy was limited to 6 (5%) patients and 18 (14%) received adjuvant radiotherapy (Supplementary Table 2).

### Caregiver Burden

Informal caregivers reported medium/high caregiver burden in at least one domain of the Caregiver Burden Scale in 44 (34%) cases, and on the total score in 19 (15%) cases. More specifically, 26 (20%) caregivers suffered from stress, 16 (12%) from social isolation, 17 (13%) from feelings of disappointment, 25 (19%) from emotional

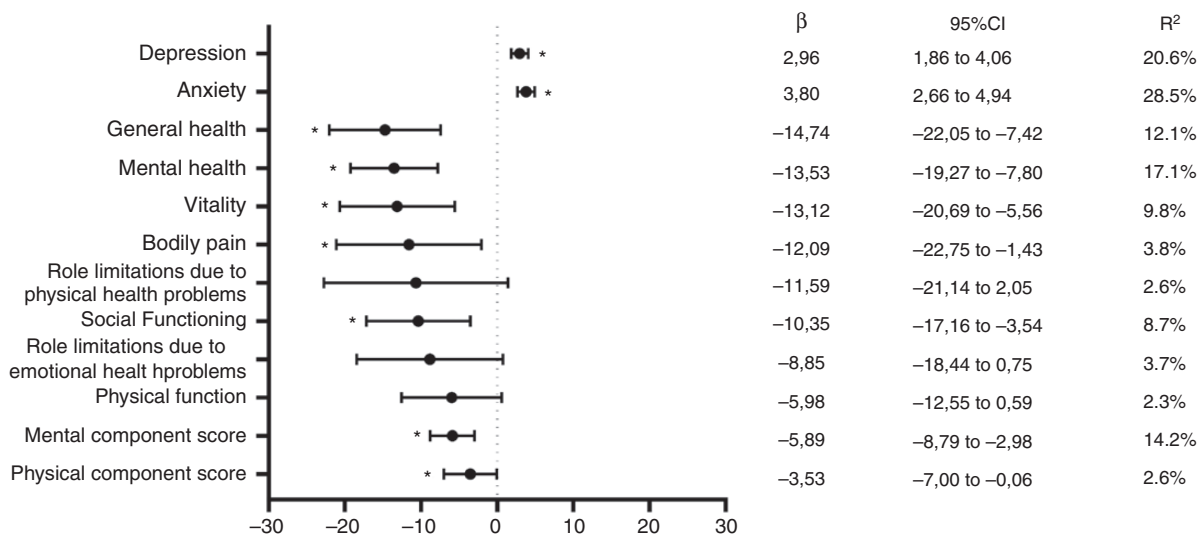
problems, and 16 (12%) from environmental factors complicating the care for the patient. Caregiver Burden Scale scores were similar comparing partners (mean 1.5, SD 0.4) with other relatives (1.4, SD 0.4; ( $p = 0.274$ ), and different types of caregivers were therefore combined in all further analyses. Uncorrected and untransformed outcome measures are presented in Supplementary Tables 3 and 4.

### Association Between Caregiver Burden and Caregiver HRQoL, Anxiety, and Depression

A one point increase in the total caregiver burden score (range 1–4) was significantly associated with clinically relevant worse HRQoL (SF-36) on 5/8 scales and 2/2 component scores, Figure 2: bodily pain ( $\beta = -12.1$ , 95%CI: -22.8 to -1.4), social function ( $\beta = -10.4$ , 95%CI: -17.2 to -3.5), mental health ( $\beta = -13.5$ , 95%CI: -19.3 to -7.8), vitality ( $\beta = -13.1$ , 95%CI: -20.7 to -5.6), general health ( $\beta = -14.7$ , 95%CI: -22.1 to -7.4), physical component score ( $\beta = -3.5$ , 95%CI: -7.0 to -0.1), and mental component score ( $\beta = -5.9$ , 95%CI: -8.8 to -3.0). Furthermore, a one-point increase in the total caregiver burden score was significantly associated with clinically relevant higher anxiety ( $\beta = 3.8$ , 95%CI: 2.7 to 4.9) and depression levels ( $\beta = 3.0$ , 95%CI: 1.9 to 4.1), as measured with the HADS.

### Determinants for Caregiver Burden

Patients' HRQoL (SF-36) was significantly associated with the total caregiver burden scale score for both the physical component score ( $\beta: -0.015$ , 95%CI -0.025 to -0.005,



**Figure 2.** The relation between caregiver burden and caregiver's level of depression, anxiety, and health-related quality of life. A higher caregiver burden was related to more depression and anxiety (represented with positive values) and lower health-related quality of life (represented with negative values). For each outcome a separate multivariable regression analysis was performed to estimate a regression coefficient corrected for confounders (age, sex, education level, and comorbidities) and presented with the 95% confidence intervals. Associations are significant when not crossing the dotted line, and are depicted with \*.  $R^2$  represent the explained variance regarding the total burden by each variable in univariable analysis.

$R^2 = 9.1\%$ ) and mental component score ( $\beta: -0.017$ , 95%CI  $-0.090$  to  $0.000$ ,  $R^2 = 20.4\%$ ). The number of symptoms (EORTC QLQ-BN20) patients experience was also significantly associated with the total caregiver burden scale score ( $\beta: 0.081$ , 95%CI  $0.014$  to  $0.149$ ,  $R^2 = 7.3\%$ ). The symptom most often reported by patients was future uncertainty (71% of patients, [Supplementary Table 4](#)). Furthermore, both patient anxiety ( $\beta: 0.042$ , 95%CI  $0.020$  to  $0.065$ ) and depression (HADS,  $\beta: 0.051$ , 95%CI  $0.031$  to  $0.072$ ) were significantly associated with and contributed greatly to the total caregiver burden score, respectively 27.8% and 14.3%. Patients' neurocognitive function, sociodemographic or clinical characteristics, and tumor and treatment characteristics were not associated with caregiver burden ([Supplementary Table 5](#)). Indeed, patient's sociodemographic and clinical characteristics (age, sex, KPS, education level, and Charlson Comorbidity Index) only contributed between 0.3% and 6.0% to the caregiver burden score, and tumor and treatment characteristics (ie, tumor location, length of follow-up, received anti-tumor treatment, tumor size, WHO grade, and Simpson grade in case of surgery) between 0.1% and 2.2% to the total caregiver burden score ([Supplementary Table 5](#)). Aspects as measured with the self-report questionnaires (SF-36, EORTC QLQ-BN20, HADS) contributed 43.8% of caregiver burden, which raised to 65.4% with the addition of patient's sociodemographic and clinical characteristics, and tumor and treatment characteristics ([Table 2](#)).

**Table 2.** Explained Variance of the Total Caregiver Burden Scale Score by Patient Variables

Variable(s)	$R^2$ Adjusted (Explained Variance)
Patient sociodemographic characteristics	3.8%
Caregiver sociodemographic characteristics	2.3%
Tumor and treatment characteristics	1.1%
Neurocognitive functioning	3.3%
Anxiety and depression (HADS)	28.0%
General HRQoL (SF-36)	34.5%
Brain tumor specific symptoms (EORTC QLQ-BN20)	27.7%
Anxiety and depression + general HRQoL + brain tumor-specific symptoms	43.8%
Neurocognitive functioning + anxiety and depression + General HRQoL + Brain tumor-specific symptoms	47.4%
Patient characteristics + neurocognitive functioning + anxiety and depression + general HRQoL + brain tumor-specific symptoms	50.7%
Tumor and treatment characteristics + neurocognitive functioning + anxiety and depression + general HRQoL + brain tumor-specific symptoms	53.8%
Patient characteristics + tumor and treatment characteristics + neurocognitive functioning + anxiety and depression + general HRQoL + brain tumor-specific symptoms	65.4%

Caregiver sociodemographic characteristics were poorly associated with the caregiver burden.

## Discussion

This is the first, and therefore explorative study to assess caregiver burden specifically in meningioma, a population of patients and caregivers in a chronic setting who often have to deal with permanent sequelae and impairments.<sup>11</sup> A median of 10 years after the last meningioma intervention, up to 35% of caregivers reported caregiver burden in any domain and 15% reported overall caregiver burden. Higher caregiver burden was associated with lower HRQoL, and higher levels of anxiety and depression in informal caregivers. Determinants for caregiver burden were patients' generic HRQoL and disease-specific HRQoL focusing on brain tumor symptoms, and levels of anxiety and depression, but not patients' or caregivers' sociodemographic characteristics, patients' level of neurocognitive functioning, or tumor- and treatment-related characteristics.

### Clinical Implications: Caregiver Burden

Compared with other patient groups ([Table 3](#)), the average total meningioma Caregiver Burden Scale score at a median of 10 years postdiagnosis tends to be higher than caregiver burden in patients with traumatic brain injury, epilepsy, Parkinson's disease, multiple sclerosis, and lung cancer, but lower than the caregiver burden in stroke, dementia, and dialysis, most likely related to the severity of the disease of the patient.<sup>12,13,33-39</sup> Although some of these scores were fairly similar and therefore differences between scores not always clinically relevant. Higher caregiver burden was found to be strongly associated with a lower HRQoL and more anxiety and depression in meningioma informal caregivers. In contrast to studies in glioma patients and patients with stroke, we did not find that sociodemographic characteristics of patients were related to caregiver burden.<sup>7,9</sup> Also surprisingly, tumor- and treatment-related characteristics, such as the need for additional radiotherapy and reoperation, were not related to caregiver burden in this study. The differences between our results and the reported results in the literature in other patient groups might be explained by the fact that meningioma patients tend to have fewer complications of disease and treatment.<sup>2</sup> Furthermore, differences in follow-up length might affect both the disease burden of patients as well as the associated caregiver burden.<sup>11</sup> In the short-term, patients primarily suffer from physical impairments, while in the long-term role limitations become more prominent.<sup>2,3,11</sup> Informal caregivers might also adapt to their role as caregiver or might face new challenges in taking care of their loved ones, as shown in a study with informal caregivers of stroke patients 5 years after stroke.<sup>40</sup> Our results suggest that the current well-being of the patient is most strongly related to caregiver burden, emphasizing the strong interdependent relationship between caregiver and patient wellbeing. Similar relationships were previously

**Table 3.** Caregiver Burden in Meningioma and Other Diseases

Author Year	Patient Group	Caregiver Burden, Mean	Follow-Up Length, Mean or Median
<i>This study</i>	<i>Meningioma</i>	1.4	10 years
Elmståhl (1996) <sup>12</sup>	Stroke	1.7–2.0	3 years
Belasco (2006) <sup>35</sup>	Dialysis	2.1	2–4 years
Andrén (2007) <sup>13</sup>	Dementia	2.1	Not reported
Martinez-Martin (2007) <sup>36</sup>	Parkinson's disease	1.2*	Not reported
Rivera-Navarro (2009) <sup>37</sup>	Multiple sclerosis	1.0*	9 years
Pagnini (2010) <sup>38</sup>	Amyotrophic lateral sclerosis	0.9*	2 years
Manskow (2015) <sup>33</sup>	Traumatic brain injury	1.0	1 year
Karakis (2014) <sup>39</sup>	Epilepsy	0.9 <sup>a</sup>	16 years
Tan (2018) <sup>34</sup>	Lung cancer	1.1	Not reported

<sup>a</sup>Original values as reported by the authors were transformed to the scale used in this study, as different versions and scales exist of the Caregiver Burden Scale.

demonstrated in high-grade glioma patient-caregiver dyads and described in Sherwood's conceptual model of caregiver burden in primary malignant brain tumors and the updated version for oncology caregiving.<sup>7,8</sup> Furthermore, other studies suggest that worse neurocognitive status of glioma patients or elderly is related to higher caregiver burden.<sup>41,42</sup>

### Clinical Implications: Providing Support for Informal Caregivers

Apart from supportive care for patients, which may help to decrease caregiver burden, informal caregivers' needs should also be addressed by healthcare providers, as it enables them to provide the needed care for their loved ones.<sup>43</sup> A recent Cochrane systematic review summarizing eight intervention studies (eg, support based on cognitive behavioral therapy; psychoeducation; cognitive rehabilitation) aimed at improving caregiver wellbeing in those taking care of a patient with a brain or spinal cord tumor, showed some evidence for positive effects of caregiver support on caregiver distress, mastery, and HRQoL, but no effect on caregiver burden.<sup>44</sup> However, in other patient groups psychoeducation programs have proven to decrease caregiver burden and depression, and improve caregiver general well-being.<sup>45,46</sup> Importantly, none of the trials included were focused on caregivers of meningioma patients, highlighting that much work is still needed in this area. This was confirmed in recent focus group studies by our groups and another group with meningioma patients and their informal caregivers, which, showed that current care trajectories have minimal focus on the needs of caregivers and most caregivers received no caregiver support.<sup>47,48</sup>

### Limitations

A limitation of this study is the cross-sectional study design, hampering assessment of causal relationships and the direct, possibly transient effects, of tumor and treatment on the outcomes. Similarly, we cannot exclude that

the reported results might be affected by reverse causation, however, most published studies in the literature as well as Sherwood's conceptual framework report the impact of the caregiver burden on their well-being and HRQoL, and not vice versa.<sup>7,39</sup> Another limitation of this study might be some degree of selection bias, in that informal caregivers with a high burden might be too distressed to participate in these studies or might actually participate in these studies as they have a strong relationship with the patient. Furthermore, our sample size could be considered relatively small, especially regarding certain statistical analyses, such as on determinants for the caregiver burden. Also, by using an existing instrument, it is possible that we have failed to measure aspects of caregiver burden that may be relevant in the meningioma setting, which is not covered by this instrument. Similarly, the SF-36 and EORTC QLQ-BN20 are not developed for meningioma patients, and hence might miss items relevant for this patient group. Nevertheless, we chose these instruments as they are often used in meningioma research to measure generic and disease-specific HRQoL.<sup>2,49</sup> Finally, there is no clear consensus on the exact MCIDs used for some of the used PROMs. A MCID can be estimated through different distribution and anchor-based methods, which might result in different MCIDs.<sup>50</sup> For this study we preferred the use of clinically relevant cut-offs based on MCIDs calculated using anchor based methods, as these MCIDs ensure clinical relevance.<sup>50</sup> Furthermore, if multiple MCIDs were reported in the literature, preference was given to more conservative cut-offs to prevent reporting of marginally clinically relevant outcomes.

### Conclusions

Even 5 years after the last intervention, one out of three informal caregivers still experienced a caregiver burden that also decreased their own HRQoL and increased their feelings of anxiety and depression, emphasizing that

caregiver burden is inherently a part of the chronic nature of meningioma. Findings of this study warrant especially attention for those caregivers who take care of patients who experience a lower HRQoL, and more anxiety and depression. Further high-quality studies should be performed to identify supportive care resources for patients and caregivers and the impact of these resources on patient and caregiver HRQoL, as well as caregiver burden. Ideally, these studies involve both patients and their informal caregivers, as we showed that the disease burden is strongly interlinked with the caregiver burden in the chronic care setting. Information on the effectiveness of supportive care resources helps to increase structural funding for these resources and is even needed in some countries for reimbursement by health care insurances. Indeed, previous qualitative studies showed a large unmet need regarding supportive care in the chronic care setting.<sup>47,48</sup>

## Supplementary Material

Supplementary material is available at *Neuro-Oncology Advances* online.

## Keywords

anxiety | caregiver burden | depression | health-related quality of life | meningioma

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**Authorship Statement.** L.D., F.W.B., and S.M.P. designed the study. Data collection was performed by A.H.Z.N. and P.Bvd.M. A.H.Z.N. performed data analysis with input from L.D. A.H.Z.N. wrote the first and successive versions of the manuscript. All authors contributed to the interpretation of the results, intellectual content, critical revisions to the drafts of the paper, and approved the final version. A.H.Z.N. had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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