

Much is Known about Caregiver Burden in Dementia - What is Next? The Role of Comorbidities and Future Perspectives

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Abstract

Introduction and background: Care for family members suffering from neurological disorders is often demanding and increases with disease progression. Numerous patient- and caregiver-related factors underlying caregiver burden have been identified. Some potential factors need to be clarified. Little is known about the effects of comorbidities and dementia complications on the burden of care for persons living with dementia.

Objectives: We hypothesized that burdens of care for family members living with dementia increase with the number and severity of comorbidities and dementia complications.

Methods: Multi-center prospective registry study (PRODEM) on caregiver burden in family caregivers (median age 61, 66% female) of 556 persons living with mild to moderate dementia, mainly Alzheimer's disease (median age 77, 58% female).

Results: Caregiver burden (Zarit Burden Interview) did not correlate with arterial hypertension, diabetes, hypercholesterolemia, cardioembolic/thromboembolic diagnoses, heart failure, severe arrhythmia or heart valve disease, but was worse in care recipients with symptoms of anxiety, psychotic episodes, depression and emotional, psychotic, behavioral and somatic symptom clusters (Neuropsychiatric Inventory, Geriatric Depression Scale-15 items). Moreover, caregiver burden correlated with the number of drugs taken daily. MRI evidence of cerebrovascular pathology (total volume of white matter hyperintensities on axial T2w-FLAIR sequences related to intracranial volume, measured in 301 patients) did not correlate with caregiver burden.

Discussion and conclusions: Neuropsychiatric complications and the number of drugs taken daily, but not internal medicine diseases and cerebral white matter hyperintensities increased the burden of care for caregivers of family members suffering from dementia, which is in partial agreement with the literature. However, severe internal medicine comorbidities were rare in the study. Standardized and harmonized longitudinal assessment of the scope of care and caregiver burden is required including algorithms for age- and life situation-adjusted assessment of caregiver burden. Further studies on caregiver burden and stronger male involvement in family care are needed.

Keywords: Caregiver burden, Dementia, Comorbidities, Neuropsychiatric symptoms, Medication

Introduction and Background

Care for patients with chronic debilitating neurological diseases is often demanding and can result in a variety of negative consequences including mental and physical morbidity. Numerous studies have been published on the burden of care for persons caring for spouses, parents, siblings or children with chronic neurological disorders, particularly for those who live with the care recipient and are directly responsible for care. Most studies address the care for dementia and stroke patients, persons with epilepsy, Parkinson's disease and atypical parkinsonism, multiple sclerosis, motor neuron disease, Huntington's disease, brain tumours, chronic pain syndromes, traumatic central nervous system injury, ataxias, and muscular dystrophy [1]. Little is known about caregiver burden in advanced stages of myasthenia gravis, adult-onset myopathies, amyloidosis or other debilitating polyneuropathies or other rare neurological diseases. Most studies were performed in high- or middle-income countries. The literature from low-income countries on family care for persons with chronic neurological diseases including dementia is sparse [2-4]. Little is known about burdens for formal caregivers caring for persons in the clients' homes, in nursing homes or in palliative care [5-8].

Considerable differences have been found between countries concerning burdens and health-related quality of life of informal caregivers of family members living with dementia. The differences were explained by variable support, traditions and social norms, and occupational duties and other competing responsibilities [2-4]. A pattern was found with caregivers in eastern and southern European countries expressing more severe caregiver burdens than caregivers in central and western European countries. Differences in caregiver burden have been found between neurological diseases [1,9,10]. The risk of severe caregiver burden is high in persons caring for individuals with dementia [8-10].

Caregiver burden depends on objective, patient-related parameters, such as age, disease duration, disease severity, physical and mental morbidity including behavioural and neuropsychiatric impairments, daily hours and total duration of care, impairment of activities of daily living, dependency, and proximity between care recipients and caregiver. On the other hand, caregiver-related objective

parameters contribute to caregiver burden, such as age, health state, incompatibility of care and occupational and family responsibilities and lack of personal, psychological and financial support. Moreover, subjective factors influence caregiver burden, such as emotional relationship between the caregiver and the care recipient, personality traits, missing agreement between involved persons, strict social norms, high expectations of the care recipient and other family members, negative social reactions, lack of choice in taking on the caregiving role, feeling of insecurity, loneliness, lack of self-esteem, self-efficacy and resilience, and poor coping strategies [2,4,7,8,11,22-28].

The Zarit Burden Interview (ZBI) is the most frequently applied inventory to estimate subjective caregiver burden [2,4,11]. Subjective caregiver burden has also been assessed in the literature using the Caregiver Strain Index (CSI) [12], the Burden Scale for Family Caregivers [13], the Multidimensional Index and the Modified Caregiver Strain Index [14,15], and other individually designed scales. The Caregiver Burden Scale [16] assesses both subjective and objective caregiver burden. In individual studies caregiver burden and caregiver strain are distinguished [14].

Different quality of life and health scales have been applied, such as the SF-36, EuroQL, Health Utility Index-3 [17-20]. Assessment tools for clinical characterisation of care recipients living with dementia depend on the type of dementia, disease severity and stage (early, advanced, late stage of dementia) and palliative care [1,2,4,6, 7,9,10,20-26].

Acknowledged, objective patient-related factors underlying caregiver burden reported in the literature are summarized in Table 1. Table 2 shows objective caregiver-related factors of caregiver burden [2,3,10,19,22-28]. However, the effect of a variety of parameters on caregiver burden is uncertain or considered controversial.

The influence of caregiver age on caregiver burden is complex. In several studies an inverse relationship was found between caregiver age and caregiver burden. Caregiving children reported more severe caregiver burden than caregiving spouses [2,10,24] because of difficulties integrating caregiving into busy daily routine that include work, family life, social activities, leisure, and sports. Spousal caregivers living with a sick family member,

Table 1: Objective patient-related predictors/factors of caregiver burden.

Severity of the disease
Impairments of activities of daily living, disabilities
Dependency
Duration of care
Motor impairments
Neurocognitive symptoms
Neuropsychiatric symptoms (depression, anxiety, hallucinations, delusions)
Autonomic nervous system disorders (constipation, diarrhea, incontinence, orthostatic hypotension and syncopes....)
Behavioral impairments (apathy, restlessness, irritability, aggressiveness, impulsivity, language and communication difficulties)
Body mass index
Pain
Insomnia
Fatigue
Quality of life
Comorbidities
Socioeconomic parameters
Acute versus subacute versus chronic need for care versus palliative care

Table 2: Caregiver-related objective factors of caregiver burden.

Younger age
Female caregiver
Cohabitation with care recipient
Lack of information and care instructions
Low level of education
Lack of planned and organized dismissal from hospital
Caregiving time per day and intensity of care
Duration of care
Lack of breaks
Mental health impairments (depression, anxiety, insomnia, mental exhaustion...)
Somatic health impairments (art. hypertension, heart diseases, oncological diagnoses, metabolic disorders,, somatic exhaustion)
Socio-economic (financial) distress
Difficulties of reconciling care, work and family life
Lack of choice
Lack of personal support
Lack of psychological and medical support
Lack of financial support
Cultural norms
Care environment (space, adaptive technical devices, equipment...)
Availability of medical, psychosocial and care interventions

however, may face greater challenges from care than adult children who mostly live in separate households. In old age caregiver burden worsens with the age of the patient and the caregiver. Thus, studies are needed to further disentangle the complex relationship between caregiver and patient age, family relationship, co-residency, and caregiver burden [10, 23, 24,26-28].

In dementia studies female caregivers reported more severe caregiver burden than did male family members [10,21,27,28]. Whether this observation is related to the predominance of male care recipients receiving care from their spouses, gender-specific differences in neuropsychiatric and behavioral symptoms of care recipients, fewer daily routine tasks (parental upbringing, housekeeping) for male than for female caregivers, gender-specific differences in support or psychological factors should be clarified.

Finally, most studies on the care for persons living with dementia are cross-sectional, but valid longitudinal data on the development of caregiver burden with disease progression is needed since dementia is a chronic disease [8-10].

In the following section we address the role of comorbidities and dementia complications on the burden of care for persons caring for a family member living with dementia.

Do comorbidities of dementia patients and dementia complications aggravate caregiver burden?

In the vast majority of studies on the burden of care for persons living with dementia caregiver burden was related to the main diagnosis, such as Alzheimer's disease (AD). Few studies have analyzed potential effects of comorbidities on caregiver burden. Comorbidities are common in dementia patients, can have debilitating effects, and may require complex therapies and medical care management [21,23]. The question arises whether age-related comorbidities of persons living with dementia and dementia complications play a significant role in the context of caregiver burden.

The PRODEM Registry-Study on caregiver burden-Part one

We present the data from a multicenter register study sponsored by the Austrian Alzheimer Society (Prospective Dementia Registry, PRODEM) on patients suffering from early to moderately advanced dementia. This study aimed at a longitudinal analysis of clinical, neuroradiological, and neuropsychological data, comorbidities, medication, activities of daily living, disabilities, dependency, occupational, psychosocial and family parameters, need

for care, and caregiver burden.

The project was approved by the ethics committees of the participating centers and was performed in compliance with the Declaration of Helsinki. Written informed consent of the patient and a person of trust, mostly a family caregiver, were mandatory for participation. Between 2009 and 2016 nine primary, secondary and tertiary, mainly academic centers for cognitive disorders recruited patients with dementia, mainly AD, and their caregivers.

The first study from the PRODEM registry on caregiving and the burden of care for mainly informal caregivers of family members living with dementia was published in 2018. For details see Ransmayr et al. 2018 [10]. Aims, methods and results of this study are briefly summarized:

The following parameters were assessed at baseline and during follow-up at six, 12 and 24 months after baseline: Age, sex, disease duration, clinical diagnosis, occupational categories and retirement, years of formal education, relationship of the patient to the caregiver, severity of cognitive decline (CERAD-Plus battery including Mini-Mental State Examination, MMSE [29,30], and the Clinical Dementia Rating, (CDR [31]), neuropsychiatric symptoms (Neuropsychiatric Inventory, NPI, severity times frequency total score) [32], disability (Disability Assessment for Dementia, DAD, percentage score [33]), dependency (Dependency Scales sum score [34]), comorbidities, medication and caregiver burden (ZBI sum score) [11].

Included were 585 patients (59% female) with mild to moderate dementia (571 with possible or probable AD [35]) and their caregivers (68% female; 95.7% spouses, children or other family members of the patients). At baseline, median patient age was 77, median symptom duration 24 months, median CERAD-plus z sum score -9.7, median MMSE z-sum score -3.3, median MMSE raw score 23, median caregiver age 61 and caregiver burden on average little to mild (ZBI sum score median 16). Caregiver burden worsened with disease duration (ZBI sum score median 22 after two years). A linear mixed model over time revealed that disease duration increased caregiver burden beyond what could be explained by cognitive decline, neuropsychiatric symptoms and dependency. Caregiver burden was more severe in female than in male care recipients and in younger than in older caregivers and was not related to patient age. Moreover, neuropsychiatric impairments, severity of neurocognitive decline, dependency, proximity of patient and caregiver (spouse versus other family member), and a high educational level of the care recipient had significant negative effects on caregiver burden (ordered logistic regression analysis).

The PRODEM Registry-Study on caregiver burden-Part two: Influence of comorbidities and dementia complications on caregiver burden

We hypothesized that in addition to the main diagnosis dementia, comorbidities and complications of dementia (AD) might have a significant negative effect on caregiver burden.

Patients and Methods

Demographic and clinical data, comorbidities, dementia complications, and caregiver burden

The so far unpublished, second study from the PRODEM registry on caregiver burden was conducted in 556 patient-caregiver dyads. Demographic and clinical data are shown in Table 3.

The following comorbidities needing medical treatment were registered at baseline:

Arterial hypertension, diabetes mellitus treated with oral antidiabetics (excluding insulin-dependency were incomplete, therefore insulin-dependent diabetes); further cardioembolic, arterio-arterial thromboembolic or coronary heart disease, hypercholesterolemia, depression, psychotic episodes, anxiety, nervousness or restlessness (Table 3). Of the 556 patients 12% received no medication, 17% one, 21% two, 24% three and the remainder (26%) four or more drugs per day.

Further diagnoses considered as serious, such as heart failure, severe arrhythmia, and heart valve disease, were documented (N=56). Moreover, medical therapies for dementia (N=435 patients), the total number of drugs taken daily and body weight were included in the

Table 3: Study on the effects of co-morbidities on caregiver burden (PRODEM-registry).

Demographic and clinical data and caregiver burden		
	Patients N=556	Caregivers N=556
Age	76.6 ± 8.07 (77)	60.6 ± 14.1 (61)
Sex	M: 226; F: 330	M: 184; F: 372
Duration of symptoms (months)	28.8 ± 25.1 (24)	
Mini-Mental State Examination		
raw sum score	22.0 ± 4.2 (23)	
z sum score	-3.9 ± 2.6 (-3.5)	
CERAD-Plus z sum score	-10.1 ± 6.8 (-9)	
Neuropsychiatric Inventory total score	13.4 ± 17.2 (7)	
Geriatric Depression Scale 15-items		
sum score	2.6 ± 2.3 (2)	
WMH-volume mm ³ , normalized by intracranial volume	0.0106 ± 0.0123 (0.0062)	
Zarit Burden Interview sum score		19.3 ± 14.0 (16)
Arterial hypertension- antihypertensive drugs	N=342	
Diabetes mellitus-oral antidiabetics	N=60	
Cardioembolic, arterio-arterial thromboembolic or coronary heart disease-thrombocyte aggregation inhibitors and/or oral anticoagulants	N=282	
Hypercholesterolemia -lipid lowering substances	N=195	
Depression-antidepressants	N=278	
Psychotic episodes- antipsychotic medication	N=110	
Anxiety, restlessness-anxiolytics, sedatives	N=86	
Mean ± standard deviation (median)		
F: Female; M: Male; N: Number of persons; WMH: White Matter Hyperintensities		

analysis. Depressive symptoms were quantified using the Geriatric Depression Scale (GDS), 15-item version [36]. The frequency scores of the twelve neuropsychiatric/behavioral and somatic sub-domains of the NPI were multiplied by the respective frequency scores and the resulting twelve product scores summarized (NPI sum score). Moreover, the frequency times severity scores of symptom groups of the NPI were added, resulting in cluster scores according to Garre-Olmo et al., [37]: delusions, hallucinations - psychotic cluster; agitation/aggression, depression/dysphoria, anxiety, irritability - emotional cluster; elation/euphoria, apathy, disinhibition, aberrant motor behaviour - behavioural cluster; sleep and eating behaviour - additional somatic cluster) and correlated with the ZBI sum scores. Severity of caregiver burden was classified according to ranges of the ZBI sum scores: ZBI sum scores between zero and 20 were classified as no or little caregiver burden, 21-40, mild to moderate, 41-60, moderate to severe, ≥ 61 , severe caregiver burden (ZBI sum score groups).

Magnetic resonance imaging-white matter hyperintensities

In 301 patients MRI data were on record for volumetric studies. The total volume of white matter hyperintensities (WMH) on axial T2w-FLAIR sequence (TR = 10000 ms, TE = 69 ms, TI = 2500 ms, TI = 800/1100 ms (1.5/3 T), number of slices = 40, slice thickness = 3 mm, in-plane resolution = $0.9 \times 0.9 \text{ mm}^2$) was quantified at baseline and normalized by intracranial volume (ICV), as previously described [38]. The resulting normalized total WMH volume served as marker for white matter cerebrovascular ischemic pathology.

Statistics

For nominal data absolute frequencies are provided. Metric data are presented as mean \pm standard deviation (SD) and medians (in parenthesis). Level of significance was 0.05 and all tests were performed two-sided. Tests for normality were conducted using the Shapiro-Wilk test. Spearman rank correlation coefficients were calculated to test the association between ZBI sum scores (or the grouped ZBI sum scores) and WMH total volume related to intracranial volume, GDS short scale sum scores, number of drugs taken daily, and body weight. The Wilcoxon rank sum test was applied to investigate the difference in ZBI sum scores (and the grouped ZBI sum score) between dichotomic variables such as medication, gender, and dementia type. The analysis was performed using the statistics software R including the packages MASS, AER, regiro, and Deducer.

Results

Caregivers reported significantly more severe caregiver

burden (significantly higher ZBI sum scores) in connection with care recipients with depression ($p=0.0153$, Wilcoxon rank sum), psychotic episodes ($p<0.0001$, Wilcoxon rank sum) and anxiety and nervousness/restlessness ($p=0.0481$, Wilcoxon rank sum) than with care recipients without these neuropsychiatric complications of dementia (Figure 1). ZBI sum scores were not statistically significantly different between caregivers of persons suffering from internal medicine diseases (arterial hypertension, diabetes, hypercholesterolemia, cardioembolic/thromboembolic disease ($p>0.05$, Wilcoxon rank sum) than persons without these diseases. A significant positive correlation was observed between the total number of drugs taken daily and the ZBI sum scores ($p=0.0094$, Spearman; Figure 1). There were significant differences in the ZBI sum scores between caregivers of care recipients with and without (presence vs. absence of) symptoms of the four symptom clusters of the NPI ($p<0.0001$ for all four Wilcoxon rank sum tests; Table 4).

ZBI sum score groups (no to little, mild to moderate, moderate to severe, severe caregiver burden) significantly differed between caregivers of care recipients with and care recipients without, psychotic episodes (Wilcoxon rank sum, $p<0.001$). The ZBI sum score groups did not statistically differ between persons with and without depression and anxiety-nervousness/restlessness (Table 4). They also did not differ between care recipients with and without other neuropsychiatric or internal medicine disorders (range of p values 0.0947 to 0.8551, Wilcoxon rank sum). A close to significant positive correlation was estimated between ZBI sum score groups and the number of drugs taken daily ($p=0.0562$, Spearman). ZBI sum score groups correlated significantly positively with the emotional, behavioral, psychotic, and somatic cluster scores of the NPI (range of ρ 0.2346 to 0.3214, $p<0.0001$, Spearman).

Neither ZBI sum scores nor ZBI sum score groups showed a significant correlation with the normalized WMH total volume ($p=0.8073$ and $p=0.7705$, Spearman).

For both ZBI sum scores and ZBI sum score groups significant positive correlation was observed with the GDS-15 sum scores ($p=0.0032$ and $p=0.0485$, Spearman).

ZBI sum scores did not statistically significantly differ in care recipients with and without comorbidities considered severe ($p=0.42$, Wilcoxon rank sum) and did not correlate with body weight ($p=0.35$, Spearman).

Discussion

Numerous studies have shown that neuropsychiatric symptoms and behavioral complications in dementia patients affect the level of caregiver burden [5,8,10,24,28]. In the caregiver burden follow-up study of the PRODEM registry all care recipients with neuropsychiatric

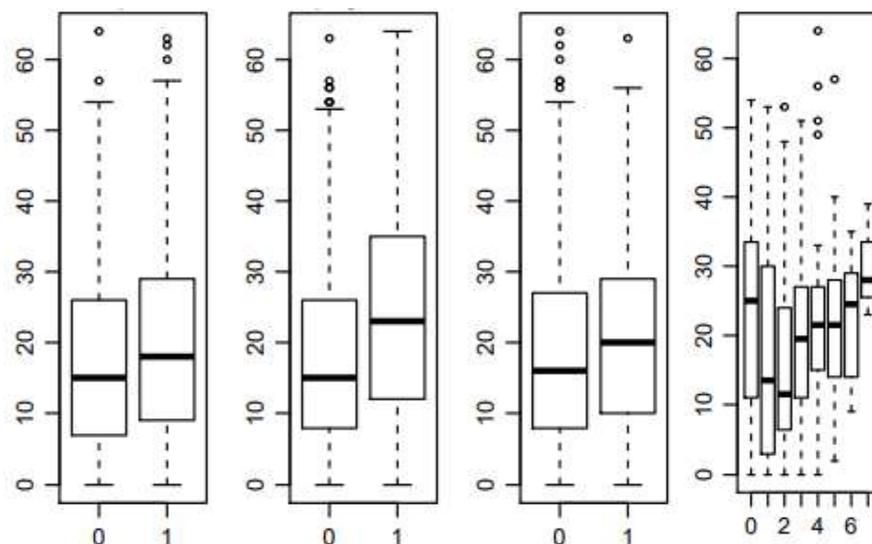


Figure 1: Zarit Burden Interview sum scores (Box plots, y-axis) in patients without (score 0, x-axis) and with (score 1, x-axis) medically treated neuropsychiatric/behavioral complications of dementia: Left to right: depression, psychotic episodes, anxiety-nervousness/restlessness. Zarit Burden Interview sum scores (y-axis) in patients with zero to seven or more drugs taken daily (x-axis) on the right side.

Statistics see Results section.

Table 4: Zarit Burden Interview scores in relation to neuropsychiatric/behavioral complications of dementia.

Zarit Burden Interview – Groups of severity		no-little	mild- moderate	moderate-severe	severe	p-value
<i>Range of sum scores</i>		0-20	21-40	41-60	≥ 61	
Depression*	Yes	55	33	11	0%	0.095
	No	60	32	7	0%	
Psychotic episodes*	Yes	41	41	15	3%	<.0001
	No	62	30	8	0%	
Anxiety, restlessness*	Yes	49	45	5	1%	0.219
	No	59	30	10	1%	

Zarit Burden Interview sum scores[§] in relation to absence (0)/presence (≥ 1) of neuropsychiatric cluster symptoms:

	0	1	
Psychotic cluster	29.7 ± 14.2 (27)	17.5 ± 13.1 (15)	<.0001
Emotional cluster	24.6 ± 14.2 (23)	14.8 ± 12.2 (12)	<.0001
Behavioural cluster	25.7 ± 13.8 (23)	17.2 ± 14.0 (14)	<.0001
Somatic cluster	22.4 ± 14.6 (21)	17.3 ± 13.2 (14)	<.0001

*Percentage of patients in the groups of severity of caregiver burden according to the indicated ranges of the Zarit Burden Interview sum scores

§mean ± standard deviation (median)

Statistics see text

complications received psychopharmacological treatment. Medical treatments did not lessen caregiver burden to the level of caregiver burden in patients without neuropsychiatric complications.

Notably, the results of our study apply for the mild to moderate dementia stages of Alzheimer's disease and not for those in more advanced stages. It is likely that in more advanced dementia stages than in our study neuropsychiatric complications become more severe and have a more profound effect on caregiver burden. This could also be the case for comorbid internal diseases since internal comorbidities usually increase with age and dementia duration.

A further limitation of our study is that internal medicine diseases were only partially updated at follow-up visits so that we could not perform a longitudinal study on their effects on caregiver burden. WMH were quantified cross-sectionally at baseline in 54% of our patients (N=301) because valid MRI data was available only in this proportion of included persons. Finally, we only analyzed neuropsychiatric complications and internal medicine comorbidities. Other relevant comorbid diseases were not registered and could therefore not be analyzed.

Very few studies have investigated the potential effects of somatic co-morbidities on caregiver burden in patients living with dementia [23]. In a Korean study diagnoses of diabetes and arterial hypertension in addition to AD had no negative effect on caregiver burden. However, heart disease aggravated caregiver burden in this study [21]. Complex or poor diabetes management may aggravate caregiver burden in dementia patients [39]. Because of a lack of data, we could not analyze how complex diabetes management including insulin treatment affected caregiver burden in our study. Most diabetic patients were on oral antidiabetics and had relatively stable glucose metabolism. Renal and lung diseases and cancer can aggravate caregiver burden in AD [21]. In our study population, severe kidney or lung disease or cancer was not diagnosed. We did not find an effect of advanced heart disease on the burden of care in our persons living with dementia. Apparently, this group was sufficiently medically stable so that these diseases had no negative effect on caregiver burden. Repeated admissions to emergency departments due to comorbidities or dementia complications may cause substantial caregiver burden. On the other hand, admission to a hospital can also be triggered by depression and exhaustion of a caregiver [40].

Nutritional deficits and frailty may aggravate caregiver burden in dementia patients [41]. In the present study population significant nutritional deficits were sparse (data not shown) and caregiver burden did not correlate with body weight.

In the present study the number of drugs taken daily, a potential surrogate marker for the overall health status, correlated with caregiver burden, which could indicate that the totality of mild to moderately advanced comorbidities may have a negative effect on caregiver burden. A recent study has shown that WMH may have a negative effect on neuropsychiatric symptoms and, thus, on caregiver burden in patients with mild cognitive impairment and AD [42]. In our study concomitant chronic cerebrovascular white matter pathology had no effect on caregiver burden. However, our MRI volumetric study could have been underpowered and should therefore be repeated in a larger collective.

Future perspectives in the area of caregiver burden for people living with dementia

Standardized comprehensive international assessment of care and caregiver burden and gender aspects

Standardized, validated, internationally harmonized assessment of need for care, caregiver burden and patient- and caregiver-related objective factors of caregiver burden is needed. International experts from medicine, nursing professions, psychology, physiotherapy, speech therapy, occupational therapy, patient representatives, self-help organizations, health insurance, health economists, social workers, and technological experts should contribute to consensus statements. Patients and caregivers may live in different countries and have different citizenships. There is political interest in international standards. Health insurance operates internationally. Differences between dementia subtypes and disease stages, cultures, traditions, resources including care facilities, care management and socio-economic aspects have to be taken into account [9]. Comorbidities need to be systematically included in future studies since our knowledge about their influence on caregiver burden is limited. Whether new scales should be added to established inventories should be a topic of discussion. Whether or not subjective aspects of caregiver burden are recognized by authorities has thus far not been clarified. The economic value of care work of informal caregivers, in particular savings for the public health service, benefits for families of the patients, and the global value of family care need to be evaluated and determined. More studies on caregiving and caregiver burden are needed in low-income countries, where knowledge about chronic neurologic diseases and public support for caregivers is limited [43].

In all societies mainly women care for neurological patients. It seems as if this tradition is preserved in most societies. There is an urgent need for stronger male involvement in family care.

Interventions to mitigate or avoid caregiver burden

Caregivers for people living with dementia have special features, but also commonalities with caregivers of patients with other serious illnesses. Caregivers often provide long-term care in their roles as spouse, partner and child. Caregiver burden must be understood and taken seriously by professionals so that the best support can be given.

Psychological and medical (pharmacological) interventions can be helpful. Therapeutic counselling and interventions by support groups may mitigate caregiver burden. Education, information and personal and financial support are of the utmost importance. Caregivers should be able to take breaks. Supportive networks of competent caregivers are very important. Technology can reduce the dependence of a care recipient. Psycho-educative measures combined with new technologies are hopeful developments [44]. Nevertheless, further studies are needed to evaluate feasible and affordable support measures for caregivers.

Conflicts of Interests

The authors have no conflicts of interests to declare.

Authors' Roles

Gerhard Ransmayr: Study conception, inclusion of patients, data analysis, draft of the manuscript.

Michaela Defrancesco: Study conception, methods, inclusion of patients, data analysis, review of the manuscript.

Anna Damulina: Study conception, inclusion of patients, MRI studies including volumetries, review of the manuscript.

Philipp Hermann, Andreas Futschik: Methods, data analysis and statistics, review of the manuscript.

Thomas Benke: Study conception, inclusion of patients, data analysis, review of the manuscript.

Josef Marksteiner: Study conception, inclusion of patients, data analysis, review of the manuscript.

Peter Dal-Bianco: Study conception, inclusion of patients, data analysis, review of the manuscript.

Alexandra Fuchs: Neurocognitive testing, review of the manuscript.

Franz Fellner: Neuroradiological diagnosis, review of the manuscript.

Reinhold Schmidt: Overall concept of the project,

inclusion of patients, data analysis, review of the manuscript.

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