Burden and health-related quality of life among caregivers of MND patients

# Introduction

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease that impacts not only patients but also their informal caregivers. Several studies on ALS in Australia (Lillo et al., 2012), USA (Qutub et al., 2014; Burke et al., 2015; Roach et al., 2019), Turkey (Tülek et al., 2023), Ireland (Galvin et al., 2016), Germany (Schischlevskij et al., 2021), and China (Geng et al., 2017) have investigated the factors contributing to caregiver burden in ALS and the associated impact of caregiving on the quality of life of these individuals. The Zarit Burden Interview was found to be the common tool used to measure caregivers' burden. However, while many studies statistically derive and report ≥ 24 as high burden on the 22-item tool, with scores ranging from 0-88, where 0-21 indicates little or no burden, 21-40 indicates mild to moderate burden, 42-60 indicates moderate to severe burden, and 61-88 indicates severe burden, in the study by Lillo et al. (2012), a score of ≥ 17 indicates high burden using a revised ZBI tool with a maximum score of 48. Depression and anxiety were measured using The Depression, Anxiety, Stress Scale (DASS 21) (Lillo et al., 2012), Hospital Anxiety and Depression Scale (Schischlevskij et al., 2021; Galvin et al., 2016; Tülek et al., 2023; Burke et al., 2015), and Beck Depression Inventory (Qutub et al., 2014). Caregivers' quality of life was assessed using the EuroQol Five Dimension Scale (Tülek et al., 2023; Schischlevskij et al., 2021), World Health Organization Quality of Life-BREF (Geng et al., 2017), and McGill Quality of Life Single Item Scale (Qutub et al., 2014; Roach et al., 2019). From the papers assessed, the proportion of female caregivers was found to be higher than male caregivers, with the age distribution of caregivers ranging from 18 years to 88 years. The majority of the caregivers recruited in the studies were informal caregivers, i.e., they had a personal relationship with the patient and were not being paid as caregivers.

In their study to determine if caregivers' burden was influenced by patients' change in behavior or deterioration in physical ability, Lillo et al. (2012) found that patients' abnormal behavior and caregiver stress were the strongest predictors of high caregiver burden, while physical disability was not significantly associated. This corresponds to Burke et al., (2015) cross-sectional study of 33 patient-caregiver pairs, which showed that high caregiver burden was associated with greater patient apathy, disinhibition, and executive dysfunction, as well as caregiver distress. Qutub et al., (2014) study also found that patients' functional status did not affect caregivers' burden. However, Schischlevskij et al., (2021) results showed that caregiver burden increased with patients' decline in functional status - patients' wheelchair use and need for supervision were the strongest predictors of burden.

Strong associations were found between caregivers' distress or depression and anxiety and caregiver burden. In Qutub et al., (2014) cross-sectional study of 50 caregivers, younger age, female gender, higher financial burden, other Christian religious denominations, and more daily caregiving hours were identified as risk factors for caregiver depression. While Tülek et al., (2023) study corroborates sex as having a significant relationship to caregivers' burden, Geng et al. (2017) found an association between caregiver burden and older caregiver age.

Other factors related to caregivers' burden are difficulties in managing ALS, the emotional or psychosocial impact of caregiving, limitations or restrictions, and the effects on relationships that caregiving has on the caregivers (Galvin et al., 2016).

There was an observed association between decreased patient quality of life and caregivers' burden. In their study, Roach et al. (2009) reported a significant decrease in caregivers' quality of life in relation to patients' functional status, i.e., physical ability, as increased tasks impacted their energy levels, leading to a high report of decreased quality of life. However, the impact of caregiver burden did not significantly influence patients' survival.

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# Method

## Data and variable

A cross-sectional study of caregivers of XXX was carried out in WHERE in WHEN. Caregivers were included if BRIEF INCLUSION CRITERIA [cite trial]. Data were collected using a questionnaire completed during an in-person interview.

The first set of variables were caregiver sociodemographic characteristics.[[1]](#footnote-1) such as sex (DEFINE), age (DEFINE), level of education (DEFINE), employment status (DEFINE). We also asked respondents if they had any medical conditions.

The second set of variables were psychosocial, including coping strategies, social support, self-esteem, anxiety, and depression.

The third set of variables were caregiving context, including relationship with care recipient (DEFINE), whether living with patient (DEFINE), the type of support provided or care demands (DEFINE), intensity of caregiving activities (DEFINE), and how long has been looking after (DEFINE).

We also collected information on characteristics of care recipient. These were sex of care recipient (DEFINE), age of care recipient (DEFINE), severity of the disease (DEFINE), and disease duration (DEFINE).

The Zarit Burden Interview (ZBI) is the most widely-used instrument for measuring caregiver subjective burden [15], and we used the validated xxx version [16]. The ZBI contains 22 five-point Likert-style questions with reply options ranging from 0 “never” to 4, “nearly always”. The total score ranges from 0 to 88, with a higher score indicating a greater perceived care burden. The cut-off points are: 0 to 20 points = little or no burden; 21 to 40 = mild to moderate burden; 41 to 60 = moderate to severe burden; 61 to 88 = severe burden.

## Statistical analysis

Descriptive statistics including means, standard deviations, frequencies, and percentages were used to analyse the data.

Normality of the primary outcome was tested using the Kolmogorov-Smirnov test, and normal distribution of data was not confirmed.

Univariate linear regression was used to examine the direction and size of the relationships between caregiver burden and the variables examined, i.e., caregiver characteristics, caregiver resources (internal and external), caregiver-care recipient relationship, intensity of care, and care recipient characteristics.

To test the extent to which the variables explained caregiver burden, we will conduct a hierarchical (block-wise) multiple regression analysis, with XX blocks of variables. The variables that will compose the blocks used in the regression model will be selected by adopting a critical level of significance (p ≤ 0.10|0.05) in the univariate analysis. The first block will include caregiver characteristics as the predictors. We will add caregiving activities, caregiver resources, and care recipient characteristics as predictors in blocks two to four, respectively. Results are presented as coefficients (change in ZBI) and standard errors. The regression models included the following indicators: F-statistic and the corresponding p-value, adjusted R2, change in adjusted R2, and deviance statistics (AIC/BIC).

Regression diagnostics

Multicollinearity: Drop a variable was dropped if the variance inflation factor (VIF) is 10.

All analysis will be conducted using Stata version 18.0 (StataCorp, College Station, Texas, USA).

# Results

## Caregiver characteristics and caregiving context

## Patient characteristics and disease severity

Table 1. Characteristics of patients with motor neuron disease, their caregivers, and caregiving context at baseline from the COMMEND trial.

|  |  |
| --- | --- |
|  | Mean (SD) or n (%) |
| **Caregivers, N=85** |  |
| Age in years | 60.0 (12.2) |
| Female sex | 59 (69.4%) |
| Marital status | 81 (95.3%) |
| In paid employment | 41 (48.2%) |
| Relationship with patient |  |
| Spouse/partner | 70 (82.4%) |
| Child | 9 (10.6%) |
| Other family/friend | 6 (7.1%) |
| Years as primary caregiver | 1.7 (2.6) |
| Hours per week in caregiving | 53.7 (64.3) |
| **Patients, N=85** |  |
| Age in years | 62.5 (10.9) |
| Female sex | 35 (41.2%) |
| Marital status | 76 (89.4%) |
| In paid employment | 25 (29.4%) |
| Patient with comorbidity | 36 (42.4%) |
| Number of comorbidities | 0.6 (0.7) |
| Years since diagnosis | 1.6 (2.9) |
| King's stage at baseline |  |
| 1 | 18 (21.2%) |
| 2 | 27 (31.8%) |
| 3 | 35 (41.2%) |
| 4 | 5 (5.9%) |

Data are based on participants with non-missing baseline caregiver burden and quality of life data.

n, number; SD, standard deviation.



Figure 1. EQ-5D-5L utility scores, domain scores and scores by King’s stage

Table 2. Pooled carer ZBI, EQ-VAS, and EQ-5D utility and domain scores by King’s stage1

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Stage 1  N=36 | Stage 2  N=59 | Stage 3  N=92 | Stage 4  N=35 | p-value2 |
| ZBI3 | 18.11 | 25.68 | 23.04 | 27.95 | 0.013 |
| EQ-5D5 | 0.89 | 0.85 | 0.81 | 0.77 | 0.001 |
| EQ-VAS4 | 80.94 | 80.39 | 80.44 | 79.79 | 0.999 |
|  |  |  |  |  |  |
| *EQ-5D domains6* |  |  |  |  |  |
| Mobility | 1.17 | 1.19 | 1.31 | 1.36 | 0.494 |
| Self-care | 1.03 | 1.00 | 1.02 | 1.09 | 0.304 |
| Usual activity | 1.14 | 1.28 | 1.36 | 1.55 | 0.011 |
| Pain/Discomfort | 1.34 | 1.44 | 1.63 | 1.97 | 0.003 |
| Anxiety/Depression | 1.31 | 1.61 | 1.83 | 1.73 | 0.010 |

1 Data from all caregivers at all timepoints (baseline, 6 months, and 9 months) have been pooled.

2 Comparisons of outcomes between King’s stages using analysis of variance (ANOVA)

3 ZBI total score range = 0–88, higher scores indicate greater burden

4 EQ-5D score range = 0 to 1.0, higher scores indicate better health-related quality of life.

5 EQ-VAS score range = 0–100, higher scores indicate better health-related quality of life.

6 EQ-5D domain scores range = 0-3, higher scores indicate greater restriction by domain

Table 3. Means (standard deviation) of caregiver ZBI, EQ-VAS, and EQ-5D scores and results of t-tests comparing changes over time.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Component | Baseline, N=85 | 6 months, N=68 | 9 months, N=66 | Baseline vs  6 months1 | 6 months vs  9 months1 | Baseline vs  9 months1 |
| ZBI score | 21.1 (12.2) | 25.8 (14.4) | 25.9 (15.8) | -6.18  p<0.001 | -1.01  p=0.363 | -6.39  p<0.001 |
| EQ-VAS score | 80.0 (18.0) | 81.6 (10.5) | 80.1 (16.5) | -1.77  p=0.355 | 0.56  p=0.769 | -0.84  p=0.743 |
| EQ-5D score | 0.81 (0.19) | 0.84 (0.14) | 0.81 (0.14) | <-0.01  p=0.703 | 0.02  p=0.068 | 0.02  p=0.17 |

EQ-5D, EuroQol 5-dimension questionnaire; VAS, visual analog scale; ZBI, Zarit Burden Interview

1 t-tests using complete data (N=68 for baseline vs 6 months, 62 for 6 months vs 9 months (61 for ZBI), and 66 for baseline vs 9 months (65 for ZBI))

Table 4. Spearman correlation coefficients between caregiver burden and quality of life scores at baseline, at 9 months, and change in scores between baseline and 9 months.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | ZBI vs EQ-5D | | ZBI vs EQ-VAS | | EQ-5D vs EQ-VAS | |
|  | Coefficient | P-value | Coefficient | P-value | Coefficient | P-value |
| Baseline score vs baseline score | -0.198 | 0.069 | -0.210 | 0.054 | 0.191 | 0.080 |
| 9 months score vs 9 months score | -0.382 | 0.002 | -0.273 | 0.028 | 0.527 | 0.000 |
| Change in score vs change in score | -0.296 | 0.017 | -0.082 | 0.519 | 0.386 | 0.001 |

EQ-5D, EuroQol 5-dimension; EQ-VAS, EuroQol visual analog scale; ZBI, Zarit Burden Interview.

1. Ponzio, M., Tacchino, A., Verri, A. et al. Profile and burden of the family caregiver: the caring experience in multiple sclerosis. An observational study. BMC Psychol 12, 173 (2024). https://doi.org/10.1186/s40359-024-01678-w [↑](#footnote-ref-1)