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Depression and Wish to Die in a Multi-Center Cohort of ALS Patients

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Abstract

Objective—To determine prevalence of depressive disorders and wish to die at the baseline visit of a longitudinal multi-site study of patients with ALS.

Methods—Structured telephone interviews were conducted with patients diagnosed in past 18 months at 16 U.S. ALS centers. Demographic, medical, psychiatric and other psychological measures were administered.

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Results—Of 329 patients assessed, mean ALSFRS-R score was 36.6; 88% (289/329) had no depressive disorder, 7% (24/329) had minor depression, and 5% (16/329) had current major depressive disorder (DSM-IV criteria). Demographic, financial and employment factors were unrelated to depression, as were duration of ALS symptoms and respiratory status, although depressed patients had lower scores on the total ALSFRS-R ($p = .004$) and gross motor function ($p < .001$). Depressed patients reported less pleasure, greater suffering, weariness and anxiety, more stress, were less hopeful, felt less control over illness management, reported lower quality of life, more often had thoughts about ending their lives and hastening death (all $p < .001$). Of the 62 patients (19% of the sample) who expressed a wish to die, only 37% (23/62) were clinically depressed.

Conclusions—Depressive disorders are not only to be expected of ALS patients. Wish to die is not always expressed in the context of depression and does not necessarily represent psychopathology as such.

Keywords

ALS; depressive disorder; wish to die

INTRODUCTION

The link between clinical depressive disorders and wish to die or desire for hastened death among terminally ill patients or those with a fatal, untreatable disease has been debated but not resolved. While depression has long been associated with suicidal ideation in medically healthy people, it remains unclear whether this is also true of patients with a terminal disease. Inconsistent results have been reported, with Stutzki et al (1) finding that wish to hasten death among ALS patients was associated with depression, while Maessen and colleagues in two Dutch studies did not find an association between choice of euthanasia and depression (2,3). Further, in the context of ALS, prevalence rates of both clinical depression and wish to die also remain to be clarified.

When our group published our findings about prevalence of depressive disorders in a small sample of late-stage ALS patients 14 years ago, (4) we noted the paucity and inconsistency of evidence. Since then, despite additional studies, inconsistency prevails. Reported rates of "depression" in literature reviews range from 10% to 75% (5-8). Factors contributing to this variability include differences in definition, assessment methods, and inclusion of items from standardized depression scales likely to reflect symptoms of ALS (e.g. "moved so slowly others noticed"). Many scales include problems not in the diagnostic criteria, e.g. "I talked less than usual," or "I was bothered by things that usually don't bother me," as on the CES-D scale used by Lou, (9) who reported that 44% of 25 patients had depression. Other self-rating scales that correspond more closely to psychiatric diagnostic criteria have generated lower rates, such as the study by Gibbons et al. (10) using the Hospital Anxiety and Depression Scale with 147 ALS patients of whom 10.1% had scores indicating "case level" or clinical depression.

A minority of investigators have used structured psychiatric interviews and/or DSM-IV diagnostic criteria to diagnose depressive disorders among patients with ALS including

Ganzini N = 100 (11); Rabkin N = 56 (4); Rabkin 2005 N = 80 (12); Hammer N = 39 (13); McElhiney N = 223 (14); Huey N = 13 (6). The first five studies reported low rates of major depression (2% to 11%) and minor depression (7-10%), while the Huey study found 23% (3/13) for major depression and 15% (2/13) for minor depression. Relatively low rates also were noted by Averill et al (8) in their review of 28 studies conducted over the past 20 years, leading them to conclude that "clinically significant depression is neither as prevalent nor as severe as might be expected" (p. 243).

Overall, evidence for widespread depressive disorders among ALS patients is limited. Most investigators studied small samples, usually recruited from a single site. Related psychological domains such as perceived stress, quality of life, future orientation, and concurrent positive and negative affect were seldom included.

Wish to die among ALS patients approaching the end of life has been studied rarely, although one study in Oregon (11) found that most people with ALS favor physician-assisted suicide as an option. Our group followed 53 ALS patients with late stage ALS, of whom 19% (N=10) expressed a wish to die and 6% (N=3) acted on this wish (15). More generally, it is not clear how often such wishes occur, and whether people who wish or plan to hasten the end of their lives are necessarily depressed. It is also unclear whether such wishes necessarily reflect psychopathology warranting treatment, or whether they reflect despair and hopelessness independent of depression (16).

In this report, psychological scales were administered as part of a larger study designed to determine whether markers of oxidative stress (including depression) are associated with disease progression in the COSMOS study, a multi-center cohort of ALS patients with symptom onset within 18 months of study entry. We present baseline findings, and address the following questions: 1) What is the prevalence of depressive disorders and their socio-demographic, medical and psychological correlates? 2) How common is "wish to die," what are correlates, and is it reported in the absence of depression?

METHOD

Sample

Sixteen study sites across the United States enrolled patients between January 2010 and April 2013 with geographic distribution intended to reduce sampling bias. Eligibility criteria included a definite, probable or possible ALS diagnosis according to the EEC/Airlie House revision, widely used in clinical trials (17). Other inclusion/exclusion criteria are shown in **Table 1**. More detailed description of the study rationale, design, power calculations and measures are presented in Mitsumoto et al. (18). Based on clinic chart reviews, potentially eligible patients were approached during routine clinic visits to describe the study and invite their participation.

Standardized Assessments

Data reported here include the following measures: socio-demographic queries, ALS clinical measures (ALSFRRS-R (ALS Functional Rating Scale –Revised) and forced vital capacity (FVC)), and 7 psychiatric-psychosocial measures (19-26), shown in detail on **Table 2**:

number of items, contents, score range, and cut-offs (where applicable). Depression diagnosis was determined by the PHQ-9 (20) (Table 2).

Wish to die

We grouped patients by their response to the PHQ-9 item, "thoughts that you'd be better off dead/thoughts about ending your life " in terms of frequency in the past 2 weeks: not at all; several days, more than half the days; and nearly every day.

Procedures

Trained and supervised interviewers at the Columbia coordinating site conducted all interviews by telephone. The psychological scales were mailed in advance so that patients would be familiar with the queries. The protocol was approved by the coordinating site IRB (Columbia University, New York), and each of the local IRBs, and all participants gave informed consent.

Data Analysis

All data were managed by the Data Coordinating Center at Columbia. One way ANOVA was used to compare age and disease duration across the three diagnostic groups (absent, minor and major depression). ANCOVA was used to compare the ALSFRS-R, FVC%, modified PHQ Total, Beck Hopelessness Scale, Quality of Life Scale, and the GARS, covarying for age, sex, disease duration, education and race. MANCOVAs were used to compare the 4 Domains of the ALSFRS-R, PANAS Positive and Negative Scales, the Manne Positive and Negative Support Scales and the 12 Visual Analog Scales, also covarying for age, sex, disease duration, race and education. Post hoc pairwise comparisons are also presented.

The same procedures were applied to compare the patients grouped by the 4 response options to the PHQ queries about "wish to die". When we modified the original PHQ item, "thoughts that you would be better off dead or of hurting yourself in some way" by separating the component parts into passive thoughts ("better off dead") and active thoughts (revised to state, "thoughts about ending your life"), we had expected that patients who endorsed the latter would have higher rates of depression, but we found the rates were identical. We therefore included all patients who endorsed either one or both components, and in calculating severity, used the component with the higher score (greater frequency of thoughts). When comparing PHQ total scores for the four response options on the "wish to die" item, we used a modified total PHQ score excluding the "wish to die" item and prorating the total score. Because of the multiple analyses conducted, we use $p < .01$ to signify statistical significance.

RESULTS

Sample

Of 355 patients enrolled in the ALS COSMOS study, 329 patients completed psychological measures; they were not administered to the first 26 participants. Another 887 patients were ineligible, most often because disease onset >18 months ago; lived too far away; ALS was

familial. Recruitment numbers ranged from <10 to over 100 per study site. Mean age was 61 years (SD=10.2) and 61% (N=200) were male. Eighty-nine percent were white (N=292), 5% (N=18) Black, 2% (N=6) Asian, and 4% (N=13), other. For analysis purposes race is recoded as white/non-white. Only 3% (N=10) did not graduate from high school; 29% (N=94) were high school graduates. Another 19% (N=64) had some college, and 49% (N=161) were college graduates or had higher degrees. Seventeen percent (N=56) had incomes under \$40,000, 66% (N=218) were in the \$40,000-\$99,000 range, and 33% (N=106) had incomes over \$100,000. At study entry, 34% (N=112) were working full-time or part-time. Most had either Medicare (31%, N= 102) or private insurance (64%, N = 209). Mean disease duration at study entry was 11.7 months; mean ALSFRS-R score was 36.6 (SD=6.14) and mean FVC % of expected was 80% (SD=22.3%).

Prevalence of Clinical Depression

Based on the PHQ-9, 3 groups were identified: 289 patients without depression (88%); 24 patients (7%) with minor depression, and 16 (5%) with major depression. Mean PHQ-9 severity scores were, respectively, 3.4 (SD=3.02), 10.7 (SD = 2.78) and 15.7 (SD = 4.11) for these groups. The three diagnostic groups did not differ on any demographic variables, site of symptom onset, disease duration or FVC. Total ALSFRS-R scale scores and the subscale scores of fine motor and gross motor differed overall ($F = 5.55$, $p = .004$). Total scores significantly differed between patients without depression, (mean = 37, SD = 6.14) and the patients with minor depression (mean score of 32.9, SD = 6.08). Patients with major depression (mean = 34.6 (SD = 4.29) did not differ from either, so the relationship was not entirely linear.

We conducted a further analysis of the relationship of disease level and depression by dividing the sample into quartiles based on baseline ALSFRS ratings (0-32, 33-37, 38-41, and 42-48). For nearly every measure in our study (8 of 10 VAS items, and all scales except the Manne Spousal support and GARS scales), there was an overall statistically significant inverse linear pattern across quartiles such that distress was highest in the lowest ALSFRS-R quartile and lowest for the highest quartile. For example, total PHQ-9 depression scores were respectively 6.1, 5.5, 4.1 and 2.8 from lowest to highest quartile. It should be noted that all of these mean scores fall within the "not depressed" range when evaluated categorically, but nevertheless, there is a gradient of distress that is seen on every measure.

Demographic, Medical and Psychological correlates of depression

Table 3 shows demographic and medical characteristics, as well as psychological measures for patients with no depression, minor depression and major depression based on the PHQ diagnostic classifications. Age, disease duration, FVC% and the Manne Support scales did not differ across the PHQ-9 diagnosis. No differences in rates of major depression, wish to die or wish to hasten death were found between subgroups of disease duration (< 6 months, 6-12 months, 13-18 months) (data not shown).

On psychological measures, patients without depression scored higher on positive affect, lower on the PHQ-9 numeric score, negative affect and hopelessness, and had higher scores reflecting better quality of life and lower stress. These relationships showed a consistent

gradient: lowest (or highest) for those without depression, mid-range for minor and the other extreme for those with major depression. This consistency across measures is noteworthy.

Scores across groups on 9 of the 12 Visual Analog Scales (VAS) similarly differentiated the groups in linear fashion. Using 1-10 scoring, patients without depression based on the PHQ scored lowest on depression, suffering, weariness, anxiety and interest in hastening death and those with major depression scored highest. Patients without depression scored highest on the VAS scales rating pleasure, hopefulness, sense of control over illness management, and overall quality of life and those with major depression scored lowest. The items concerning family support, support by the medical team, and importance of religion/spirituality did not differentiate between groups; high levels of support were reported in all groups.

Prevalence of Wish to Die

Patients were grouped by presence and frequency of responses regarding wish to die: "not at all," "several days", "more than half the days", and "nearly every day", and compared in terms of psychological, demographic and medical variables.

Overlap between PHQ-9 diagnosis of depression based on all items, and wish to die (one of the PHQ-9 items) is substantial but not complete. Of those without depression, 13% (39/289) thought about ending their lives at least several days in the past two weeks, compared to 42% (N=10/24) of patients with minor depression and 81% (13/16) with major depression

Among the 62 patients who thought they would be better off dead and/or thought about ending their lives "several days" in the past 2 weeks, 28% (13/46) had a depression diagnosis (major or minor). Of those who thought about this "more than half the days", 67% (4/6) had a diagnosis, and of those who had such thoughts "nearly every day," 60% (6/10) had a diagnosis. Overall, of the 62 patients, 37% (23/62) were clinically depressed.

Demographic, Medical and Psychological Correlates of Wish to Die

As seen when patients were classified by PHQ depression diagnosis, age, disease duration, FVC% and the Manne Positive Support Scale did not differ across the PHQ-9 "wish to die" query. Those who did not report a wish to die had higher scores on total ALSFRS-R (37.3 [SD= 6]) and those who wished to die nearly every day had the lowest total (31.6 [SD = 6.84]), with a similar pattern on the domain ratings of gross motor and respiratory function, both of which reached statistical significance.

Table 4 also shows results of group comparisons (PHQ-9 "wish to die" item) for each of the VAS scales, and other measures of well-being and distress. The overall MANCOVA was highly significant, and 8 of 12 VAS scales exhibited significance ($p < .001$). Those who had no wish to die rated themselves lower on depression, suffering, weariness, anxiety and interest in hastening death. Their scores were higher on VAS scales assessing capacity for pleasure, hope, and overall quality of life.

In terms of positive and negative affect (PANAS), patients who did not express a wish to die had higher scores on positive mood and lower scores on negative mood. Their scores were lower on the Beck Hopelessness Scale and the Global Assessment of Recent Stress (GARS) and they rated their overall quality of life higher (QOL).

Overall, the consistency and magnitude of differences among the patients who did or did not endorse a wish to die supports this classification.

Current Psychiatric Treatment

Patients were asked whether they were currently seeing a mental health professional, and if so, whether they received counseling, medication or both. Data are available for 265 patients (81% of the total sample). Of those without a depression diagnosis, 8% (19/213) were in treatment, compared to 20% (4/16) of patients with minor depression and 5% (2/11) of those with major depression. The frequencies are too small to identify group differences in type of treatment. Current use of antidepressants (prescribed for depression) was reported by 97 patients (35% of patients with current depression and 29% of patients without depression who presumably were benefiting from the medication, $p = \text{NS}$), and 33 patients were taking anxiolytic medication (18% with current depression, 9% without current depression, $p = \text{NS}$).

DISCUSSION

Our finding of 12% of patients with any depressive disorder, including 5% with major depression, is in line with prior studies of ALS patients using DSM-IV criteria with structured interviews. It is somewhat higher than the prevalence rate of 6% for adults age 65+ in the general population, among whom only 18% met criteria for major depressive disorder (27). The observed rate of 12% is, however, lower than that reported for patients with a variety of other medical and neurological conditions such as multiple sclerosis, coronary artery disease and diabetes (28-30).

Comparing patients with no depression, minor depression and major depression, associations were consistently found with standard rating scales assessing positive or negative affect, hope for the future, stress level, and quality of life. There was also a consistent relationship between ALSFRS-R scores and rates of distress/depression, even though this cohort had, on average, only moderate functional impairment.

Specific questions about wish to die (thoughts of being better off dead or of ending one's life) were endorsed by 19% of the sample, also reported by Albert et al. (15), while 14% expressed a current wish to die in the Stutzki study of 66 patients (1). As observed with the analyses of depression, those who endorsed such wishes reported more distress on the other psychological scales. However, it is important to note that there is considerable variation among those who endorse thoughts about ending their lives. We did not distinguish, as is done in the suicide literature, between ideation, intent or plan and if the latter, whether the patient has access to means. We also did not ask whether such thoughts were transient or persistent, and whether they refer to the immediate present or some future time should symptoms become intolerable.

We observed an association between disease progression (ALSFRS-R score) and measures of distress, with greater distress reported by patients with lower ALSFRS-R scores. However, even in late stage illness, some ALS patients continue to find meaning in life and hope for the future. Even ALS patients with locked-in syndrome may experience a satisfactory quality of life (31).

Overlap between wish to die and clinical depression was not complete: 13% (39/289) of patients who were not depressed expressed some degree of "wish to die." Conversely, of those who thought about being better off dead or ending their lives, 63% (39/62) were not clinically depressed. Thinking about end of life issues and even interest in death may not always reflect psychopathology in patients with an inevitably rapidly progressing, untreatable and incurable neurodegenerative disease with a median 30-month survival after diagnosis (32).

Study limitations include reliance on a brief screen for depressive disorders which, although widely recommended (e.g. by the NYC Department of Health for all primary care physicians), is not the same as a structured psychiatric interview. As such, these are approximate diagnoses. Similarly, there was no opportunity to conduct clinical interviews regarding expressed wishes to die. Participants were all enrolled in major ALS centers and did not include patients seen only in other settings, nor were all regions of the country covered. Even patients with depression reported that they perceived satisfactory support from their families and medical teams, which may not be true for patients seen in other settings.

In conclusion, our data indicate that depressive disorders are not necessarily to be expected in the context of an invariably progressive, untreatable and fatal illness, and that most patients are able to find enjoyment in the present and maintain some hope for the future. Expressions of wishes to die are not always manifested in the context of a depressive disorder, and do not necessarily represent psychopathology as such. In this large multi-site sample, we replicated rates of clinical depression reported by other investigators using structured diagnostic measures, demonstrated a strong association between clinical depression and functional impairment on the ALSFRS-R, and for the first time found consistent correlations with a broad range of psychological measures. It will be important to determine whether the large majority of these patients are able to maintain their positive mood in the presence of illness progression as they are observed over the next two years in this longitudinal cohort. In addition, supplementary sources of information from a truly representative national U.S. sample of patients will provide important confirmatory or contradictory information about the relations between mood and disease.

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Table 1

Inclusion/Exclusion Criteria for the COSMOS Study

<u>Inclusion Criteria</u>	
<ul style="list-style-type: none">• Disease duration <19 months after symptom onset• Age 20+• A reliable family caregiver who gives independent informed consent for providing information from structured interview.• English fluency• Capacity to consent• Willingness to return to the site for follow-up examinations	
<u>Exclusion Criteria</u>	
<ul style="list-style-type: none">• Familial ALS• Already participating in clinical trials prior to enrollment• Major active neurological diseases other than ALS or a history of neurological diseases• Major unstable medical diseases that require active medical treatment (e.g. active cancer, dialysis) in the past 6 months	

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Table 2

Study measures: Items, content, score range, and cut-offs (if applicable)

Scale	Number of Items	Content	Score Range*	Cut-offs
Patient Health Questionnaire (PHQ-9) (20)	9	Consists of the 9 criteria for diagnosis of major depression and minor depression (DSM-IV and 5); provides a provisional diagnosis and also a symptom severity. Two modifications were made: 1) we excluded 3 items if ALS-related: difficulty sleeping, difficulty eating, and moving or speaking so slowly others noticed and pro-rated the total score accordingly; 2) The original PHQ item, "thoughts that you would be better off dead or of hurting yourself in some way" was split in 2 parts: "thoughts that you'd be better off dead," and "thoughts of ending your life." Only the item with the higher score is included in total score. Time frame: past 2 weeks.	0 - 27	>10 = absent/mild 10 - 14 = moderate 15 - 19 = moderately severe 20+ = severe
Beck Hopelessness Scale (BHS) (23)	10	10 items from 20-item scale regarding future orientation; scores doubled to compare to norms. True/false response format	0 - 20	>8 = absent/mild 9 - 14 = moderate 15+ = severe
Positive and Negative Affect Scales (PANAS) (24)	20	Each subscale has 10 adjectives, scored 1 = "not at all" to 5 = "extremely." Scale scores are sum of items.	1 - 50	
Global Assessment of Recent Stress (GARS) (25)	7	Each of 7 domains is rated on a 10-point scale	7 - 70	
Endicott Quality of Life Enjoyment and Satisfaction Questionnaire (26)	11	Items are about specific areas of everyday living with a 5-point response scale.	11 - 55	
Manne Positive and Negative Partner Support (27)	15	8 negative support items and 7 positive items assessing both instrumental and emotional support or lack of it. 4-point response options scored 1-4.	8 - 32 7 - 28	
Visual Analog Scales (12)	11	Each scale represents one of the domains covered by the other scales, so that patients with diminished communication can still respond. Each is scores 1-10 with anchors Examples: depression, pleasure, suffering, hope for the future.	1 - 10	

* Note: Higher scores represent a greater endorsement of the construct being measured.

Table 3

Demographic, Medical and Psychological measures compared across Depression Status. †

	0	1	2			
	No Depression	Minor Depression	Major Depression	ANOVA F	p	Pairwise Comparisons
Demographics	n = 289	n = 24	n = 16			
Age in Years, mean (SD)	60.7 (10.1)	64.2 (10.6)	60.4 (10.3)	1.27	.282	
Disease Duration in Years, mean (SD)	0.97 (0.37)	1.11 (0.38)	1.02 (0.33)	1.70	.184	
Medical	n = 266-268	n = 22-23	n = 14-16			
Forced Vital Capacity, %, mean (SD)	81.0 (22.0)	70.8 (24.9)	77.9 (22.7)	1.50	.225	
ALSFRS-R Total Score, mean (SD)	37.0 (6.1)	32.9 (6.1)	34.6 (4.3)	5.55	.004*	0 > 1
ALSFRS-R Domains		MANCOVA Wilks' Lambda		1.66	.105	
Bulbar, mean (SD)	9.7 (2.3)	9.9 (2.7)	9.1 (2.9)	0.40	.674	
Fine motor, mean (SD)	8.7 (2.4)	7.2 (2.5)	8.1 (3.2)	4.43	.013*	0 > 1
Gross Motor, mean (SD)	8.1 (2.8)	6.3 (2.8)	7.1 (2.7)	4.67	.010*	0 > 1
Respiratory, mean (SD)	10.5 (2.4)	9.6 (3.0)	10.3 (3.0)	0.69	.256	
Psychological Measures	n = 238-289	n = 20-23	n = 13-16			
Modified PHQ Total, mean (SD)	3.3 (3.0)	10.7 (2.7)	15.8 (4.1)	175.2	<.001*	All
PANAS		MANCOVA Wilks' Lambda		28.14	<.001*	
PANAS: Positive Mood, mean (SD)	33.4 (7.5)	25.5 (7.4)	23.1 (8.4)	24.31	<.001*	0 > 1, 2
PANAS: Negative Mood, mean (SD)	16.5 (5.6)	22.7 (7.3)	30.8 (8.3)	51.97	<.001*	All
Beck Hopelessness Scale, mean (SD)	2.6 (2.7)	4.5 (3.6)	7.7 (2.7)	22.93	<.001*	All
Quality of Life Scale, mean (SD)	40.0 (6.8)	31.8 (5.8)	27.3 (6.4)	38.01	<.001*	0 > 1, 2
GARS: Stress, mean (SD)	19.1 (8.8)	27.2 (10.0)	28.3 (10.0)	15.19	<.001*	0 > 1, 2
Manne		MANCOVA Wilks' Lambda		1.19	.316	
Manne: Positive partner support, mean (SD)	21.6 (2.9)	22.2 (2.1)	21.5 (1.9)	0.12	.665	
Manne: Negative partner support, mean (SD)	9.6 (3.5)	10.1 (3.6)	11.4 (3.0)	1.85	.159	
Visual Analog Scales		MANCOVA Wilks' Lambda		7.87	<.001*	
Depressed, mean (SD)	2.6 (1.8)	4.7 (2.6)	6.8 (2.1)	37.27	<.001*	All
Pleasure, mean (SD)	6.8 (2.2)	5.1 (2.2)	3.8 (1.5)	13.62	<.001*	0 > 1
Suffering, mean (SD)	3.2 (2.2)	5.2 (2.6)	6.0 (2.3)	17.24	<.001*	0 > 1, 2
Weary, mean (SD)	4.4 (2.4)	7.0 (2.2)	7.8 (2.7)	19.57	<.001*	0 > 1, 2
Nervous/Anxious, mean (SD)	3.0 (2.1)	5.8 (2.4)	6.8 (2.8)	33.46	<.001*	0 > 1, 2
Hopeful, mean (SD)	6.4 (2.5)	4.4 (2.9)	2.4 (1.7)	20.37	<.001*	0 > 1, 2
Feels in Control of ALS, mean (SD)	5.2 (2.9)	4.5 (2.4)	2.5 (1.9)	5.26	.006*	0 > 2
Supported by Family, mean (SD)	9.3 (1.5)	9.7 (.70)	8.9 (2.0)	1.60	.203	

	0	1	2			
	No Depression	Minor Depression	Major Depression	ANOVA F	p	Pairwise Comparisons
Supported by Medical team, mean (SD)	8.8 (1.9)	8.9 (1.6)	8.1 (1.6)	0.64	.526	
Wish to Hasten death, mean (SD)	1.4 (1.1)	3.6 (2.9)	6.3 (3.4)	77.13	<.001*	All
Importance of Religion, mean (SD)	6.9 (3.3)	6.8 (3.4)	6.2 (3.4)	0.35	.707	
Overall Quality of Life, mean (SD)	7.5 (2.0)	5.7 (1.4)	3.9 (1.9)	24.95	<.001	0 > 1, 2

Covariates are age, sex, duration of symptoms, education and race.

*
p < .05

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Table 4

Demographic, Medical and Psychological measures compared across the response to PHQ Item: Thoughts of better off dead or ending your life. [†]

	0	1	2	3			
	Not at all	Several days	More than half the days	Nearly every day	ANOVA F	p	Pairwise Comparisons
Demographics	n = 246-267	n = 41-46	n = 6	n = 9-10			
Age in Years, mean (SD)	60.8 (10.0)	61.4 (11.5)	59.6 (7.6)	66.4 (9.7)	1.05	.369	
Disease Duration in Years, mean (SD)	1.00 (0.37)	0.94 (0.40)	0.94 (0.46)	0.98 (0.32)	0.29	.831	
Medical	n = 246-249	n = 41-42	n = 6	n = 9			
Forced Vital Capacity, %, mean (SD)	81.7 (21.4)	73.2 (25.8)	72.7 (26.0)	71.7 (24.0)	2.65	.049	
ALSFRS-R Total Score, mean (SD)	37.3 (6.0)	33.7 (5.9)	35.5 (6.0)	31.6 (6.8)	7.78	<.001*	0>1, 3
ALSFRS-R Domains			MANCOVA Wilks' Lambda		2.52	.003*	
Bulbar, mean (SD)	9.8 (2.3)	8.9 (2.7)	9.5 (2.3)	9.4 (1.8)	2.72	.045*	
Fine motor, mean (SD)	8.7 (2.4)	8.2 (2.7)	7.3 (4.8)	7.3 (2.9)	1.98	.118	
Gross Motor, mean (SD)	8.2 (2.8)	7.0 (2.8)	7.3 (4.1)	6.2 (2.3)	3.97	.009*	
Respiratory, mean (SD)	10.6 (2.3)	9.6 (2.9)	11.3 (1.0)	10.4 (2.5)	3.86	.010*	
Psychological Measures	n = 219-267	n = 39-46	n = 5-6	n = 8-10			
Modified PHQ Total, mean (SD)	3.5 (3.4)	8.2 (4.5)	10.1 (4.6)	12.7 (8.0)	41.28	<.001*	0<1, 2, 3;1<3
PANAS			MANCOVA Wilks' Lambda		14.26	<.001*	
PANAS: Positive Mood, mean (SD)	33.6 (7.8)	27.3 (7.7)	29.1 (8.3)	21.4 (7.4)	13.40	<.001*	0<1, 3
PANAS: Negative Mood, mean (SD)	16.5 (5.6)	22.2 (6.9)	29.5 (11.4)	26.3 (12.2)	24.45	<.001*	0<1, 2, 3;1<2
Beck Hopelessness Scale, mean (SD)	2.4 (2.5)	5.7 (2.7)	8.6 (0.9)	8.5 (1.7)	38.96	<.001*	0<1, 2, 3;1<3
Quality of Life Scale, mean (SD)	40.0 (7.0)	33.9 (7.2)	31.3 (4.0)	30.8 (10.7)	16.08	<.001*	0<1, 2, 3
GARS: Stress, mean (SD)	19.7 (9.5)	22.8 (8.7)	29.3 (6.1)	20.6 (9.1)	3.52	.015*	
Manne			MANCOVA Wilks' Lambda		2.03	.060	
Manne: Positive partner support, mean (SD)	21.9 (2.7)	21.2 (3.3)	21.8 (1.5)	21.3 (1.0)	0.74	.526	
Manne: Negative partner support, mean (SD)	9.3 (3.3)	11.2 (4.1)	11.0 (2.9)	9.9 (2.6)	3.96	.009*	0<1
Visual Analog Scales			MANCOVA Wilks' Lambda		7.19	<.001*	
Depressed, mean (SD)	2.5 (1.8)	4.3 (2.1)	7.2 (2.8)	7.3 (1.6)	33.48	<.001*	0<1, 2, 3;1<3

	0	1	2	3			
	Not at all	Several days	More than half the days	Nearly every day	ANOVA F	p	Pairwise Comparisons
Pleasure, mean (SD)	6.8 (2.3)	5.3 (2.0)	4.0 (1.4)	3.8 (1.4)	10.80	<.001*	0<1,2, 3
Suffering, mean (SD)	3.1 (2.2)	4.3 (2.2)	7.4 (2.4)	5.9 (2.6)	13.38	<.001*	0<1,2,3;1<2
Weary, mean (SD)	4.2 (2.3)	6.3 (2.7)	9.0 (1.4)	8.8 (1.8)	22.63	<.001*	0<1,2, 3
Nervous/Anxious, mean (SD)	2.9 (2.0)	5.2 (2.3)	7.2 (3.1)	6.4 (3.2)	22.80	<.001*	0<1,2,3
Hopeful, mean (SD)	6.6 (2.5)	4.5 (2.7)	2.2 (0.8)	1.8 (1.8)	18.40	<.001*	0<1,2, 3
Feels in Control of ALS, mean (SD)	5.1 (2.9)	4.3 (2.8)	3.8 (2.7)	3.3 (3.9)	1.51	.212	
Supported by Family, mean (SD)	9.4 (1.3)	8.8 (1.8)	9.8 (0.5)	9.9 (0.4)	2.76	.043*	
Supported by Medical team, mean (SD)	8.9 (1.8)	8.5 (2.1)	8.0 (1.9)	8.5 (1.9)	0.96	.414	
Wish to Hasten death, mean (SD)	1.4 (1.2)	2.8 (1.9)	5.2 (3.5)	8.1 (3.0)	67.04	<.001*	All
Importance of Religion, mean (SD)	7.0 (3.3)	6.5 (3.3)	4.2 (2.8)	6.0 (3.3)	1.21	.308	
Overall Quality of Life, mean (SD)	7.7 (1.9)	5.3 (1.9)	4.8 (1.1)	4.4 (2.6)	23.06	<.001*	0<1, 2, 3

[†] Covariates are age, sex, duration of symptoms, education and race.

* p<.05