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PURPOSE IN LIFE IN ALS PATIENT-CAREGIVER DYADS: A MULTILEVEL LONGITUDINAL ANALYSIS

Natasha E. Garcia
University of Kentucky, natasha.garcia@uky.edu

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Natasha E. Garcia, Student

Dr. Suzanne C. Segerstrom, Major Professor

Dr. Mark Fillmore, Director of Graduate Studies

PURPOSE IN LIFE IN ALS PATIENT-CAREGIVER DYADS: A MULTILEVEL LONGITUDINAL ANALYSIS

THESIS

A thesis submitted in partial fulfillment of the
requirements for the degree of Master of Science in the
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By

Natasha Elsa Garcia

Lexington, Kentucky

Director: Dr. Suzanne C. Segerstrom, Professor of Psychology

Lexington, Kentucky

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ABSTRACT OF THESIS

PURPOSE IN LIFE IN ALS PATIENT-CAREGIVER DYADS: A MULTILEVEL LONGITUDINAL ANALYSIS

Amyotrophic Lateral Sclerosis (ALS) is a progressive neurodegenerative disease. Despite the debilitating nature of this disease, some evidence suggests patients maintain their quality of life (QOL). Caregivers, on the other hand, experience decreased QOL. Evidence suggests existential aspects of well-being such as purpose in life (PIL) may be unique and stable sources of well-being for patients and caregivers. Furthermore, patients' and caregivers' well-being may impact one another. The present study examined the variance structure, trajectory, and dyadic relationship of PIL and QOL in patients with ALS and their caregivers (N = 110 dyads). Data from the Seattle ALS Patient Profile Project were utilized; PIL and QOL were assessed seven times, over eighteen months. PIL was more stable than QOL and therefore a psychological resource for patients and caregivers. PIL and QOL declined with time and disease severity. Individual differences in proximity to diagnosis and death moderated within-individual change. Decline was more rapid following diagnosis and approaching death, suggesting these are critical periods in which individuals need increased support. Well-being within the dyad was interrelated. Average QOL was similar across dyads. PIL within the dyad changed together over time. Dyadic relationships may reflect similar life conditions and a shared disease experience.

KEYWORDS: Amyotrophic Lateral Sclerosis, caregiving, purpose in life, quality of life, dyad

Natasha Garcia

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By

Natasha Elsa Garcia

Dr. Suzanne Segerstrom
Director of Thesis

Dr. Mark Fillmore
Director of Graduate Studies

6/1/2015

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Chapter One: Introduction

Terminal illness is accompanied by emotional distress, including depression and hopelessness, for some individuals. Other individuals are able to maintain their psychological well-being following a terminal diagnosis (Block, 2001). Existential aspects, including purpose in life (PIL), may be a source of resiliency in patients. Caregivers may also derive a sense of purpose in their role. Maintaining PIL potentially benefits patients' and caregivers' physical and psychological health. Patients with Amyotrophic Lateral Sclerosis (ALS) in particular have exhibited resiliency, including sustained quality of life, despite disease progression (Neudert, Wasner, & Borasio, 2004; Robbins, Simmons, Bremer, Walsh, & Fischer, 2001; Simmons, Bremer, Robbins, Walsh, & Fischer, 2000). In contrast, caregivers to these patients experience decline in their overall quality of life as the patient becomes progressively more ill (Roach, Averill, Segerstrom, & Kasarskis, 2009). Evidence suggests that patients' existential quality of life impacts aspects of psychological well-being in their caregivers (Pagnini et al., 2011). However, little is known about how PIL shifts within the dyad over the patient's disease course. The present study examined the variance structure, trajectory, and dyadic relationship of PIL in patients with ALS and their caregivers. The trajectory of quality of life (QOL) was also examined to replicate and extend previous research.

Amyotrophic Lateral Sclerosis

ALS is a progressive neurodegenerative disease with cardinal features including upper and lower motor neuron degeneration appearing in multiple regions of the body and leading to muscle weakness and wasting (Chaudhuri et al., 1995). Challenges

associated with ALS include a rapid progression rate with a median survival of 4 years (Ringel et al., 1993), an unknown disease cause, a single available treatment option, and no cure. The disease course is heterogeneous with differing sites of onset and progression rates among patients (Ringel et al., 1993).

Over time, patients with ALS require increased care as their disease progresses. Many of these care providers are family members. Caregivers of patients with ALS face multiple challenges, often including leaving the workforce, physical demands as the patients' illness progresses, and, for spousal caregivers, nearing widowhood. Ultimately, caregivers will take over responsibilities including managing the household, patient hygiene, and implementing the multidisciplinary care needs of the patient. The challenges associated with ALS patients' physical decline for caregivers may not only reflect an increasing caregiver load but also grieving the patients' loss of physical ability over time (Rhoades & McFarland, 1999).

Well-being Measures

Maintaining well-being is a salient goal in providing care to patients with ALS and their caregivers. Well-being can be characterized by a variety of constructs including QOL and PIL. QOL reflects multidimensional aspects of objective (e.g., measurable life conditions and circumstances) and subjective (e.g., personal satisfaction) well-being (Felce & Perry, 1995). Due to its multidimensional nature, consensus on the definition of QOL is unresolved. QOL generally involves a combination of life conditions, satisfaction with these conditions, and appraisal of the importance of such conditions in one's life (Felce & Perry, 1995). QOL is comprised of several domains, which may include physical, material, social, developmental, and/or emotional well-being. The emotional

well-being aspect of QOL may relate primarily to hedonic factors (e.g., positive affect and satisfaction) but may also include eudemonic factors (e.g., fulfillment and spiritual well-being). Notably, individuals may weigh the importance of QOL domains differently (e.g., one person highly valuing emotional well-being, and another highly valuing physical well-being). Individual perception is a critical aspect of QOL, though measures infrequently account for the subjective appraisal of domain importance.

PIL is a more concise construct focused on existential well-being and eudemonia independent of adversity (Ryff, Singer, & Love, 2004). Frankl's experience as a Holocaust concentration camp prisoner inspired his writings about finding meaning in life through extreme hardships, including the loss of his family and physical suffering (Frankl, 1963; Frankl, 1967). These writings have influenced the development of the psychological constructs PIL and meaning in life. Crumbaugh and Maholick (1964) defined PIL as "the ontological significance of life from the point of view of the experiencing individual" (p. 201). Reker and Wong (1988) defined meaning in life as "the cognizance of order, coherence, and purpose in one's existence, the pursuit and attainment of worthwhile goals, and an accompanying sense of fulfillment" (p. 221). Meaning in life has been proposed to have cognitive, motivational, emotional, relational, and personal components (Maddi, 1967; Reker & Wong, 1988; Wong, 1998). Several PIL and meaning in life measures exist. The Purpose in Life Test has demonstrated strong concurrent validity with other meaning in life measures including the Frankl Questionnaire, the Life Regard Index, the Sense of Coherence Scale, the Meaningful Life Measure, the Meaning in Life Questionnaire, and the Scales of Psychological Well-Being Purpose in Life subscale (Crumbaugh & Maholick, 1964; Crumbaugh & Maholick, 1969;

Debats, 1990; McDonald, Wong, & Gingras, 2012; Morgan & Farsides, 2009; Ryff 1989; Steger, Frazier, Oishi, & Kaler, 2006; Zika & Chamberlain, 1992). For clarity, "PIL" will be used henceforth to refer to the overlapping meaning in life and PIL constructs.

Purpose in Life Health Relevance

PIL measures associate with positive psychological indices (e.g., mood and happiness) as well as markers of better physical health spanning from biomarkers (e.g., cardiovascular and immune) to decreased risk of premature mortality (Boehm & Kubzansky, 2012; Boyle, Barnes, Buchman, & Bennett, 2009; Friedman, Hayney, Love, Singer, & Ryff, 2007; Matthews, Owens, Edmundowicz, Lee, & Kuller, 2006; Ryff, 1989; Ryff & Keyes, 1995; Ryff, Lee, Essex, & Schmutte, 1994; Ryff et al., 2004; Westerhof, Bohlmeijer, Beljouw, & Pot, 2010; Zika & Chamberlain, 1992). Positive psychological elements, including PIL, may also reduce the burden of illness in older adults (Boyle et al., 2009). The Rush Memory and Aging Project discovered that PIL attenuated the relationship between physical brain pathology and longitudinal measures of cognitive ability in patients with Alzheimer's disease (Boyle, Buchman, Wilson, Yu, Schneider, & Bennett, 2012). Psychological factors have also been associated with longer disease survival in ALS (Johnston et al., 1999; McDonald, Wiedenfeld, Hillel, Carpenter, & Walter, 1994).

Well-being in Patients with ALS and Caregivers

Despite physical impairments, patients with ALS have generally been shown to be psychologically resilient. Evidence suggests that rates of clinical depression in patients with ALS are low (Averill, Kasarskis, & Segerstrom, 2007; McDonald et al., 1994; McDonald, Hillel, & Wiedenfeld, 1996; Rabkin, Wagner, & Del Bene, 2000). In contrast,

other research has reported elevated distress including depression and anxiety levels similar to psychiatric outpatients (Felgoise et al., 2010). Existential themes among patients coping with ALS may give insight into psychological resiliency (Bello-Haas et al., 2000; Fegg et al., 2010; Ozanne, Graneheim, & Strang, 2013; Pagnini et al., 2011; Young & McNicoll, 1998). For example, individuals with ALS who were hand-picked in a qualitative study as exceptionally adapted to the disease "developed an enhanced philosophical perspective on life as a result of living with ALS" (p. 39; Young & McNicoll, 1998). In patients with ALS, spiritual well-being, specifically in religious context, positively relates to better psychological, social, and physical health status ratings on the Sickness Impact Profile (Bello-Haas et al., 2000).

For caregivers, research also suggests that despite losses and perceived burden, some individuals are able to find meaning in their role (Noonan & Tennstedt, 1997; Rabkin et al., 2000; Rhoades & McFarland, 1999). There is also evidence that individuals who experience lower levels of meaning in caregiving may be more likely to experience depressive symptoms (Noonan & Tennstedt, 1997).

Previous research utilizing QOL as a measure of well-being in patients with ALS has found similar results indicative of patient resiliency. In one sample, patient general QOL did not significantly decline across a 6-month period and no relationship was found with disease severity (Robbins et al., 2001). In another sample, patient QOL did not significantly decrease over a 5-month period, though a significant relationship was found with disease severity (Rabkin et al., 2000). Additionally, patients with ALS followed up to 5 years were able to maintain their QOL as their disease progressed (Roach et al., 2009). Conversely, it appears caregivers' psychological well-being may be more

impacted by patient disease severity; caregivers' total QOL declined significantly over this 5-year period (Roach et al., 2009). Notably, caregiver ratings on the QOL Existential subscale were more stable than their total or single-item QOL score (Roach et al., 2009), suggesting existential QOL is distinct from overall and self-assessed QOL in caregivers.

Dyadic Relationships

A reciprocal relationship between patient and caregiver distress has been reported (Rabkin et al., 2000). In patients with ALS, existential QOL was positively associated with their caregiver's self-assessed QOL and existential QOL and negatively associated with their caregiver's ratings of depression, anxiety, and caregiver burden (Pagnini et al., 2011). Similarly, in patients with cancer and their caregivers, spiritual well-being was positively associated with the dyad partner's physical health component of QOL (Kim, Carver, Spillers, Crammer, & Zhou, 2011). Therefore, it is plausible that although caregivers may face declines in QOL, some caregivers may be able to adapt by developing PIL over time, which may in turn be influenced by the patient's perceptions of his or her own PIL.

Stability and Variability in Purpose in Life

It is unclear whether PIL is a stable trait. Some have suggested that PIL is fairly stable (Reker, Peacock, & Wong, 1987), yet others have suggested changes in PIL occur through various life stages (Lazarus & DeLongis,1983; Pinquart, 2002; Yalom, 1980). Moreover, an individual may derive a sense of purpose from a variety of sources including religion or spirituality, career or volunteer experiences, education, personal roles, values, feelings of usefulness, competency, interpersonal relationships, lifetime achievements, and life experiences (Pinquart, 2002; Reker et al., 1987) which may

change over both short periods of time and longer developmental periods (e.g., over the lifespan; Yalom, 1980). Therefore, one's source of purpose may result from past experiences as well as current activities. Loss of sources an individual previously relied on for PIL has been suggested to account for age-related changes found in PIL (Pinquart, 2002).

Diagnosis and death are two critical yet distinct points in the lives of both patients and caregivers. Receiving a fatal diagnosis may alter the life course, provoking individuals to reframe their life, its quality, and their sources of purpose. This event may also change the caregivers' life course, as caregivers often leave the workforce once patients' illness becomes severe. Additionally, as the patient approaches death, existential distress or acceptance may cause variance in well-being. Both patients and caregivers may experience a sense of loss, including autonomy and the eventual death of the patient. Caregiver responsibilities also increase as the patient becomes paralyzed. Therefore, variance in PIL and QOL may be explained by time since patient diagnosis or time to death.

Psychological well-being can be characterized both by its mean across time and its variability, which may have distinct consequences. Variance structure provides insight into differences between people or changes within an individual. Within-individual change over time is also termed intraindividual variability (IIV). Time-structured and net IIV are two kinds of within-individual change: time-structured IIV is variance that is systematically structured in relation to time, and net IIV is variance that is unstructured in relation to time (Ram & Gerstorf, 2009). Examining variance characteristics allows for better understanding of psychological phenomena in regard to context including dynamic

characteristics and processes (Ram & Gerstorf, 2009). Mean levels and IIV can both predict later health (Boehm, Winning, Segerstrom, & Kubzansky, in press).

Variance structure can provide insight to changes in well-being in the context of progressive diseases including ALS. Previous research in patients with ALS and their caregivers reported greater within-person variability in overall QOL than existential QOL. Patient within-individual change reflected net IIV, in which overall QOL was unstructured with regard to time. Caregiver within-individual change reflected time-structured IIV, in which overall QOL decreased systematically with the passage of time (Roach et al., 2009). Applying IIV methods to the measure of PIL may aid in clarification of the nature of the stability of the construct as well as the sources of variance in patients and caregivers.

The Current Study

PIL may provide insight into resiliency in both patients and their caregivers, despite potential declines in caregiver QOL. The current study examined the variance structure, trajectory, and dyadic relationship of PIL in patients with ALS and their caregivers. Additionally, this study evaluated the trajectory of PIL in comparison to QOL in these two samples. These analyses give insight to well-being patterns in patients with ALS and their caregivers as well as provide clarity regarding PIL stability, a clinically relevant measure of psychological health. The current study aims were threefold:

Aim1: Examine the variance structure and trajectory of PIL in patients with ALS and their caregivers.

Hypothesis 1a: A greater portion of patient and caregiver variability in PIL will be due to differences between individuals than variability within the individual, reflecting greater within-person stability.

Hypothesis 1b: Neither patient nor caregiver PIL will be significantly systematically related to time since diagnosis.

Aim 2: Examine the variance structure and trajectory of QOL in patients with ALS and their caregivers

Hypothesis 2a: QOL will exhibit greater within-person variability than PIL, as indicated by the intraclass correlation coefficients, and consistent with previous research examining existential QOL (Roach et al., 2009).

Hypothesis 2b: Patient QOL will not be significantly systematically related to time since diagnosis.

Hypothesis 2c: Caregiver QOL will systematically decrease over time since patient diagnosis, replicating previous research (Roach et al., 2009).

Aim 3: Examine the relationship between patient and caregiver mean and intraindividual variability of PIL and QOL.

Hypothesis 3a: Patient-caregiver mean PIL will significantly covary within dyads.

Hypothesis 3b: Patient and caregiver PIL IIV will fluctuate together over time.

Hypothesis 3c: Patient-caregiver mean QOL will significantly covary within dyads.

Hypothesis 3d: Patient and caregiver QOL IIV will not fluctuate together over time.

Chapter Two: Methods

Participants

An archival sample of 130 patients with ALS (86 men, 44 women) and 110 caregivers (31 men, 79 women) was utilized in the current study (see Table 1 for demographics, disease characteristics, and baseline scores). Participants were recruited through the Seattle ALS Patient Profile Project. The patient sample consisted of adults aged 18 years or older who met inclusion criteria (i.e., a confirmed ALS diagnosis by a neurologist, and absence of dementia or alcoholism). The average age of the patient sample was 61 years at study entry (*SD* = 11 years) with a range of 33-82. Self-reported race of the patient sample was 94.6% white, 3.6% African American, 0.8% Hispanic, and 0.8% Native American. The average patient age at diagnosis was 57 years (*SD* = 12 years). The majority of patients' disease onset was in the limbs, 82.3% (*n* = 107). A wide range of patient physical function was included in the sample: 16 subjects (12.3%) were on a respirator, and 13 patients (10%) had a feeding tube at baseline. Of those using respirators at baseline, 18.75% (*n* = 3) used a respirator less than 8 hours per day, 6.25% (*n* = 1) used a respirator 8-15 hours per day, and 75% (*n* = 12) used a respirator 20-24 hours per day. The average ALS Severity Scale score was 24.32 (*SD* = 8.55) at study enrollment, reflecting moderate disease severity.

The average age of the caregiver sample at study entry was 57 years (*SD* = 14 years.) with a range of 19-79. Self-reported race of the caregiver sample was 93.6% white, 4.5% African American, 0.9% Asian, and 0.9% Native American. The majority of caregivers were spouses or significant others of the patient, 85.5% (*n* = 94); however, other relatives, 14.5% (*n* = 16), were also included in the sample.

The current study involved several model comparisons. Inequality in number of observations across models prevents direct comparison of fit statistics. Therefore, data from 10 dyads were excluded for missing diagnosis or date of death values. One additional caregiver was excluded from the sample for having a non-relative relationship to the patient (e.g., paid caregiver or friend), qualitatively different from relative caregivers. Three patient-caregiver dyads were also excluded as outliers due to enrollment greater than 20 years from diagnosis.

Design and Procedures

Data were collected by the Seattle ALS Patient Profile Project. This project commenced in 1986, and the last study visit occurred in 1989. Subjects were recruited from the ALS and Neuromuscular Research Foundation of San Francisco, the ALS Health Support Services of Seattle, and the ALS Clinic of Hahnemann University Philadelphia. The study was IRB approved at all three institutions, and all participants signed informed consent at their respective institution. Participants were interviewed at their residences by trained staff. Interviews occurred in 7 waves, repeated approximately every 3 months, over the course of 18 months for each subject. At baseline, participants completed forms including demographic information, medical history, patient disease severity, and a questionnaire battery including psychosocial measures. Psychosocial and disease severity measures were repeated at each successive wave. See McDonald and colleagues (1994) for further methodological details.

Measures

Purpose in Life Test. The Purpose in Life Test is a 20-item scale that assesses the degree to which an individual has found meaning and purpose in his or her life (e.g., “My

personal existence is very purposeful and meaningful" and "If I should die today, I would feel that my life has been worthwhile") (Crumbaugh & Maholick, 1969). Items are rated on a 7-point scale. The measure provides a single score ranging from 20-140 in which scores greater than 112 reflect definite purpose, scores of 92-112 reflect an indecisive level, and scores below 92 reflect a lack of clear meaning and purpose. The Spearman-Brown split-half reliability of PIL was .87 among a sample of University students (Crumbaugh & Maholick, 1964) and .92 among a sample of Protestant parishioners (Crumbaugh, 1968). Additionally, test-retest reliability over six weeks was .79 among the student sample (Crumbaugh & Maholick, 1964).

Discriminant validity of PIL has been examined with regard to other measures of psychological well-being and depression (Zika & Chamberlain, 1992; Boyle et al., 2009; Ryff et al., 2004). The Purpose in Life Test has been found to have a moderate negative correlation with the MMPI Depression scale (Crumbaugh & Maholick, 1964). Evidence for discriminant validity comes from a higher correlation between PIL and religiosity than between psychological well-being and religiosity (Chamberlain & Zika, 1992), and a significant relationship between PIL and reduced risk of premature mortality in older adults after controlling for depressive symptoms (Boyle et al., 2009).

Life Rating Scale. The Life Rating Scale (LRS) is a single item measure in which an individual is asked to rate QOL on a 5-point scale. This measure reflects individuals' self-assessed QOL. A rating of 1 is "uncomfortable" and reflects the lowest QOL, a rating of 2 is "dissatisfied", a rating of 3 is "content", a rating of 4 is "happy", and a rating of 5 is "joyous" and reflects the highest QOL (unpublished scale, ALS Patient Profile Project).

ALS Severity Scale. The ALS Severity Scale (ALSS) is used to rate functional impairment in patients with ALS (Hillel et al., 1989). The patient's functionality is rated on four domains including the ability to speak or swallow and the movement of upper extremities and lower extremities (i.e., patient disease severity). A total score is calculated by adding the score on the four domains. Total severity ratings range from 2, indicating complete loss of function, to 40, indicating completely intact function. Total severity scores of 2-16 reflect severe ALS severity, scores of 17-28 reflect moderate severity, and scores of 29-39 reflect mild ALS severity at the time of assessment. Inter-rater reliability is estimated at .95 (Hillel et. al, 1989). Within growth models, ALSS was linearly transformed (40-score) so higher scores reflect greater disease severity.

Data Analysis

Multilevel modeling (MLM) using PROC MIXED with maximum likelihood estimation in SAS 9.4 was utilized to evaluate the hypothesized trajectories and relationships. Separate analyses were run for patients and caregivers, except for dyadic analyses. MLM can accommodate repeated measures and nested data, including dyadic relationships, and allows for the use of all data points available (Singer & Willett, 2003). This made MLM well suited for this data set in which the number of and time between assessments varied by participant.

The first set of hypotheses (i.e., 1a and 2a) involved the variance structure of PIL and QOL without regard to time. To examine whether variance in PIL and QOL was due to differences between individuals or changes within individuals, unconditional means models were applied. This type of model evaluates total variation of a measure without predictors, producing intraclass correlation coefficients (ICC). Unconditional means

models also provide an indication of whether a significant amount of within-individual change exists. When within-individual variance was non-zero, linear growth models were applied to explain contributing factors of within-individual change.

The following equation represents an unconditional means model. PIL_{ij} corresponds to PIL at wave *i* for person *j*. An individual's average PIL score corresponds to β_{0j}, and e_{ij} is the residual associated with wave *i*. The individual's average score, β_{0j}, can be expressed in terms of the prototypic intercept or grand mean of the sample, γ_{00}, and the individual β_{0j}'s residual or deviation from the grand mean, ζ_{0j}. The random term, $\zeta_{0}j$, in Level 2 of this model allowed individuals' average PIL to differ from the sample mean.

Unconditional means model:

Level 1 $\quad PIL_{ij} = \beta_{0j} + e_{ij}$

Level 2 $\quad \beta_{0j} = \gamma_{00} + \zeta_{0j}$

The second set of hypotheses (i.e., 1b, 2b, and 2c) tested the relationship between time and well-being (i.e., PIL and QOL). To examine whether time explained variance in PIL and QOL, linear growth models were applied. These models predict well-being from time. The goal of these analyses was to shed light on whether change in well-being was structured with time and how much of the variance was explained by the passage of time.

Time since patient diagnosis was hypothesized as the best functional form for time; however, additional centering options were examined for best model fit. Three systematic ways of modeling the change in PIL and QOL over time were explored. The first two methods involved centering time at date of patient diagnosis and date of death. Data collected over the course of the study varied in the length of time the patient had

lived with the disease, their proximity to death, and disease stage. Therefore, to better interpret how these measures of well-being change around critical points of the disease, time was centered allowing for these trajectory comparisons.

The following equation represents a linear growth model. Level 1 of these models introduces time (centered at patient diagnosis date or death date) as a predictor of change in the outcome (PIL or QOL). PIL_{ij} corresponds to PIL for wave *i,* for person *j*. β_{0j} corresponds to an individual's PIL at the centered date (i.e., diagnosis date or death date). β_{1j} is the coefficient for the time since patient diagnosis ($T_{diagnosis}$) or time to death (T_{death}) and e_{ij} is the residual. Random effects were tested for the slope, which evaluated significant individual differences in change over time (β_{1j}). These analyses shed light on whether the passage of time since patient diagnosis affects change in well-being differently for different people.

Linear growth model:

Level 1 $PIL_{ij} = \beta_{0j} + \beta_{1j} (T_{diagnosis}) + e_{ij}$

Level 2 $\beta_{0j} = \gamma_{00} + e_{ij}$

$\beta_{1j} = \gamma_{10} + [\zeta_{0j}]$

The third model accounted for both when individuals entered the study (i.e., nearness to diagnosis or death) and how individuals changed across time in the study. These models separated out individuals' characteristics at baseline and their change over time within the study. To examine between-individual differences, an interaction term was also included that allowed individual trajectories to differ based on patient baseline characteristics (i.e., time from patient diagnosis at initial visit and time to death at initial

visit). Therefore, these "between-within" models evaluated both between-individual and within-individual differences in PIL and QOL.

The following equation represents a between-within model predicting PIL change over time within the study from time since patient diagnosis at initial study visit. The passage of time in the study (T_W), within people is at Level 1 and time since patient diagnosis at initial study visit ($T_{Bdiagnosis}$), between people is at Level 2. An interaction was tested between these effects ($T_{W*Bdiagnosis}$). At Level 1, β_{1j} is the coefficient for time in the study, or the passage of time during study participation. β_{0j} represents the intercept centered at patient diagnosis date (or death). γ_{11} represents the coefficient for the cross-level interaction; passage of time in the study moderated by time since diagnosis at baseline.

Between-within model:

Level 1 $\quad PIL_{ij} = \beta_{0j} + \beta_{1j} \ (T_W) + e_{ij}$

Level 2 $\quad \beta_{0j} = \gamma_{00} + \gamma_{01} \ (T_{Bdiagnosis}) + e_{ij}$

$\beta_{1j} = \gamma_{10} + \gamma_{11} \ (T_{W*Bdiagnosis}) + [\zeta_{1j}]$

ALS is a progressive disease; therefore it is possible that time acts as a proxy for disease progression. However, unlike time, functional rating scales for disease severity in patients with ALS are not necessarily linear. Some evidence suggests that disease progression in ALS is curvilinear (Gordon et al., 2010). In addition, as patients receive multidisciplinary care and adaptive equipment, disease progression may slow for a period of time. It is possible that the pattern of variability in disease severity may capture change that is not adequately captured by linear time. Therefore, disease severity was examined in its relationship to time predictors and an alternative growth model including disease

severity was explored. First, a model was constructed predicting ALSS scores from time to evaluate convergence of time with disease severity. Next, models predicting PIL and QOL from disease severity were examined. Third, disease severity was added to linear growth models of time to examine whether disease severity explained variance in well-being (PIL and QOL) above and beyond change due to time. This information was used to determine if the pattern of disease progression was similar to time, whether disease severity predicts well-being, and if disease severity accounts for variability in well-being that time does not.

Criteria for evaluating the best model among the aforementioned methods included both fit statistics and explained variance. First, models were compared in terms of lowest -2 log likelihood (-2LL) and Akaike's information criterion (AIC); lower numbers indicate better quality of model fit. Second, the Level 1 pseudo-R^2 was examined for the amount of within-individual variance each model explained for patients and caregivers. The model most convergent on these criteria for patients and caregivers was selected for further analysis.

Lastly, the third set of hypotheses (i.e., 3a and 3b) involved whether a relationship exists in PIL or QOL within the dyad (i.e., patients and their respective caregivers). The basic structure of these models was the unconditional means model and the linear growth model described above. In addition, these models utilized dummy coding for dyad members and a covariance matrix to evaluate patient and caregiver intercepts and slopes for interrelation within and across dyads.

Table 1
Sample Demographics, Disease Characteristics, and Baseline Scores

	Patients	Caregivers
Demographics		
Age at enrollment in years	61 (11)	57 (14)
Male	66.2%	28.2%
Female	33.8%	71.8%
White	94.6%	93.6%
African American	3.6%	4.5%
Hispanic	0.8%	---
Asian	---	0.9%
Native American	0.8%	0.9%
Spouse to patient	---	85.5%
Family member to patient	---	14.5%
Disease characteristics		
Age at diagnosis in years	57 (12)	---
Disease duration years (diagnosis to death)	7 (8)	---
Limb onset	82.3%	---
Bulbar onset	16.1%	---
Other onset	1.6%	---
Respirator use at enrollment	12.3%	---
Feeding tube at enrollment	10%	---
Years since diagnosis at enrollment	4.02 (4.07)	---
Years to death at enrollment	3.88 (5.00)	---
Baseline scores		
Baseline PIL	106.02 (16.88)	111.09 (15.97)
Baseline QOL	2.68 (1.03)	2.70 (.98)
Baseline ALSS	24.32 (8.55)	---

Chapter Three: Results

Preliminary Analyses

Preliminary analyses were conducted to examine the data distribution and inspect the independent and dependent variables in respect to normality and adherence to statistical assumptions of MLM. Tests for normality revealed that time to patient death (expressed in yearly quarters) had moderate skewness of -1.29 (*SE* = .099). The other independent and dependent variables exhibited normal distribution characteristics. This study aimed to better understand the trajectory of PIL and QOL over the course of the disease. Enrollment was widely inclusive to patients at different disease stages. Therefore, observed data varied across a range of time from critical points (diagnosis and death). Wide variation was expected among these time points. For this reason artificially transforming this variability was avoided and no correctional action was taken for time to patient death.

Furthermore, the sample included patients using respirators and feeding tubes at baseline. The decision to use a respirator long-term may accompany a process of adaptation and coping prior to patient death. Two respirator status covariates were applied separately within each model to ensure that respirator status did not impact the pattern of results. The first covariate included was dichotomously coded for any respirator use at each time point within the study. The second covariate included was dichotomously coded for respirator dependence (i.e., 20-24 hour use per day) at each time point within the study. Neither covariate resulted in substantive effects on the models. Therefore, the models presented below did not include respirator status covariates.

Correlations among dependent variables and sample descriptives are illustrated in Table 2. A strong correlation was observed for average PIL and QOL collapsed across all subjects and time points ($r = .60$, $p < .01$). However, within-person correlations revealed a small to medium relationship between PIL and QOL for patients ($r = .20$, $p < .01$) and caregivers ($r = .35$, $p < .01$), suggestive of discriminant validity for PIL and QOL despite some overlap between these variables.

Variance Structure of PIL and QOL in Patients with ALS and their Caregivers

There were significant differences in PIL and QOL both between and within individuals (Model 1, Tables 3 & 4; both $p < .001$). The intercepts within Model 1 represent the sample average PIL scores, 103.61 for patients and 109.52 for caregivers. These scores fell within an "indecisive" level of PIL (scores 92-112). The proportion of total variance in PIL attributed to stable individual differences was 74% for patients and 76% for caregivers. The majority of the variance in PIL was due to differences between individuals, reflecting substantial stability over time. The QOL intercepts revealed that the sample average scores, 2.62 for patients and 2.65 for caregivers, fell between "content" and "dissatisfied" ratings. Variance in QOL attributed to stable individual differences was lower than that for PIL: 60% for patients and 55% for caregivers. Therefore, self-assessed QOL exhibited greater within-person variability than PIL, consistent with previous research examining existential QOL (Roach et al., 2009). Although the majority of the variance in PIL was due to stable between-individual differences, this model also suggested the existence of a significant amount of within-individual change in PIL. Therefore a linear growth model was warranted to assess the predictors of within-individual change for PIL and QOL.

Patient and Caregiver PIL and QOL Trajectories from Diagnosis Date

Analyses examining time from diagnosis and time to death as predictors of PIL and QOL revealed poor model fit. Although unconditional means models indicated a significant amount of within-individual variance to be explained, when time from diagnosis and time to death were added, residual variance increased rather than decreased. However, the third model for time, including an interaction accounting for individual differences in nearness to diagnosis and death at study enrollment and the passage of time in the study, produced good model fit. Therefore, individual differences in point of study entry from diagnosis and to death within the observed data impeded the fit of the first two models. Due to poor model fit and in the interest of parsimony, only the between-within models of time are presented.

Separate between-within models for patients and caregivers indicated length of time since diagnosis at study enrollment did not have a significant effect on differences in PIL among patients or among caregivers. Patient and caregiver PIL decreased significantly and systematically with the passage of time in the study. However, the between-within interaction term revealed that length of time from diagnosis at study enrollment moderated change in PIL for patients and caregivers, such that study enrollment closer to patient diagnosis date was associated with a faster decrease in PIL (Model 2a, Table 3). Those who enrolled in the study further from patient diagnosis date experienced a slower rate of decline, and in some cases stability (Figures 1 & 2). Model 2a accounted for similar amounts of variance in PIL among patients (within-person: 7%, between-person: 1%) and caregivers (within-person: 6%, between-person: 2%).

QOL in patients and caregivers exhibited different patterns. Length of time since diagnosis at study enrollment did not have a significant effect on differences in QOL among patients. However, caregivers who enrolled in the study closer to the patient diagnosis date had significantly lower QOL. With time centered at diagnosis, only patient QOL decreased significantly and systematically with the passage of time in the study; caregiver QOL did not. Caregiver QOL trajectory was significantly moderated by length of time from patient diagnosis at study enrollment (Model 2a, Table 4). Though not statistically significant, patients who enrolled in the study closer to their diagnosis date also appear to have a somewhat faster decrease in QOL (Figures 3 & 4). Model 2a accounted for more variance in QOL among patients (within-person: 2%, between-person: 6%) than caregivers (within-person: 1%, between-person: 1%). Therefore, time since diagnosis and the passage of time impacted within-individual change in PIL to a greater degree than QOL.

Patient and Caregiver PIL and QOL Trajectories Approaching Patient Death

Parallel growth models centered at date of death revealed a trend in which patients who enrolled in the study closer to their date of death had significantly lower PIL. For caregivers, nearness to patient death at study enrollment did not have a significant effect on differences in PIL. Patient and caregiver PIL decreased significantly and systematically with the passage of time in the study. Nearness to patient death at study enrollment moderated change in PIL for patients and caregivers, such that study enrollment closer to patient death was associated with a faster decrease in PIL. (Model 2b, Table 3, Figures 5 & 6). Model 2b accounted for similar amounts of variance in PIL among patients (within-person: 6%, between-person: 5%) and caregivers (within-person:

6%, between-person: 3%). Models centered at diagnosis and death (i.e. 2a & 2b) accounted for similar portions of within-individual change for PIL.

Patient and caregiver QOL trajectories centered at patient death were less congruent. Patients who enrolled in the study closer to their date of death had significantly lower QOL. For caregivers, nearness to patient death at study enrollment did not have a significant effect on differences in QOL. Patient and caregiver QOL decreased significantly and systematically with the passage of time in the study. The between-within interaction term revealed a tendency towards a faster decrease in QOL for patients who enrolled in the study closer to their date of death, although statistical significance was not reached. For caregivers, nearness to patient death at study enrollment moderated change in QOL, such that study enrollment closer to patient death was associated with a faster decrease in QOL (Model 2b, Table 4, Figure 8). Model 2b accounted for similar portions of variance in QOL among patients (within-person: 1%, between-person: 7%) and caregivers (within-person: 2%, between-person: 6%). Time to death explained greater between-individual differences than within-individual change in QOL.

The Impact of Disease Severity on Patient and Caregiver PIL and QOL Trajectories

Patient disease severity was also evaluated as a predictor of QOL. Preliminary models examined convergence between time and disease progression. Time since diagnosis at enrollment and the passage of time in the study explained 63% of the within-individual variance in disease progression (pseudo-R^2 = .63). No additional between-individual variance was accounted for. Within this model, time since diagnosis at study enrollment did not have a significant relationship to overall patient disease severity (p = .11). However, time within the study significantly predicted increases in disease severity

($p < .001$). Additionally, the interaction of time from patient diagnosis with the passage of time in the study also significantly predicted disease severity, such that patients who enrolled in the study closer to their diagnosis date had a faster rate of disease progression over time, ($p < .001$).

The model with time centered at date of death revealed that time to death at study enrollment and the passage of time explained 54% of the within-individual variance in disease progression (pseudo-$R^2 = .54$). No additional between-individual variance was accounted for. Time to patient death at study enrollment significantly predicted overall patient disease severity. Patients who enrolled in the study closer to their date of death had significantly greater disease severity ($p = .01$). Time within the study again significantly predicted increases in disease severity ($p < .001$). Additionally, the interaction of time to patient death with time in the study significantly predicted disease severity ($p < .001$). Patients who enrolled in the study closer to their date of death had a slower rate of disease progression across time within the study.

Most temporal variables were significantly related to disease severity. These models of time explained over half of the variance in disease severity. However, both of these models indicated a significant amount of residual variance in disease severity not explained by time (both $p < .001$). Therefore, an additional model predicting PIL and QOL from decreases in functional ratings on the ALSS scale (i.e., disease severity) was applied.

Growth models indicated that increases in patient disease severity significantly predicted decreases in both patient and caregiver PIL (both $p < 0.01$). There were significant individual differences in the effect of disease severity on PIL (i.e., a random

effect) among patients but not caregivers (Model 3, Table 3). Figure 9 illustrates the trajectory of change in PIL with disease severity. Model 3 accounted for more within-individual variance in PIL in patients (within-person: 15%) and caregivers (within-person: 8%) than the previously tested time models. No additional between-person variance in PIL was explained by disease severity beyond the unconditional models.

Patient disease severity also significantly predicted decreases in patient and caregiver QOL (both $p < 0.01$). However, there were individual differences in the effect of disease severity on QOL for caregivers but not patients, opposite to that of PIL (Model 3, Table 4). Figure 10 illustrates the trajectory of change in QOL with disease severity. Model 3 also accounted for more within-individual variance in QOL in patients (within-person: 3%, between-person: 1%) and caregivers (within-person: 9%, between-person: 4%) than prior models. Results indicated that for patients and caregivers, the greatest amount of within-individual variance in QOL was explained by patient disease severity, although to a greater extent for caregivers.

Next, disease severity was added to between-within models of time. In patients and caregivers with time centered at diagnosis, results revealed that disease severity accounted for 2% additional within-person and between-person variance in PIL, above and beyond change due to time. For patients with time centered at death, 2% additional within-person variance in PIL was accounted for by disease severity. No additional between-person variance in QOL was accounted for in patients. For caregivers, 2% additional within-person variance and 0.9% additional between-person variance in PIL were accounted for by disease severity.

Disease severity also explained additional variance in QOL beyond between-within models of time. In patients with time centered at diagnosis, disease severity accounted for 1% additional within-person variance and 2% additional between-person variance in QOL, above and beyond time. In caregivers with time centered at patient diagnosis, disease severity accounted for 1% additional within-person variance and 6% additional between-person variance in QOL. In patients with time centered at death, disease severity accounted for an additional 2% of within-person variance in QOL. No additional between-person variance was accounted for by disease severity in patients. In caregivers, disease severity accounted for 1% additional within-person variance and 3% additional between-person variance in QOL above and beyond time. Therefore time and disease severity both predicted decreases in PIL and QOL, but disease severity accounted for slightly more within-individual variance above and beyond time.

Growth Model Comparison

In order to select the best model for dyadic analyses, several comparisons were made. First, fit statistics for Models 1-4 were compared. The models predicting PIL and QOL from disease severity resulted in the smallest 2-log likelihood and AIC for both patients and caregivers, reflecting best model fit. However, for caregiver PIL and QOL, Model 2b evaluating time to death and time within the study produced comparable decreases in the -2LL. For patient PIL, Model 2a evaluating time since diagnosis and time within the study also produced a decrease in the -2LL similar to Model 3.

Next, these models were compared in regard to the amount of within-individual explained variance. Model 3 including disease severity as a predictor of PIL explained the greatest amount of within-person variance in both patients (15%) and caregivers

(8%). The same was found for QOL; Model 3 explained the greatest amount of within-person variance for patients (3%) and caregivers (9%). These criteria consistently favored disease severity as the best predictor of change in PIL and QOL, and therefore Model 3 was selected as the best model for the dyadic analyses.

The Dyadic Relationship between Patient and Caregiver Mean and Intraindividual Variability of PIL and QOL

Dyadic models revealed that patient and caregiver dyad mean PIL did not significantly covary (between-dyad covariance = 21.97, *SE* = 25.02, $p = .38$, $r = .10$). However, PIL did significantly fluctuate together within the dyad; a small within-dyad correlation was observed (within-dyad covariance = 14.97, *SE* = 4.39, $p < .001$, $r = .19$).

In contrast, patient and caregiver mean QOL significantly covaried; a moderate between-dyad correlation was observed (between-dyad covariance = .18, *SE* = .07, $p = .01$, $r = .31$). This reflects that the average QOL of the dyad was similar, whereas average PIL was not. QOL did not change together over time within the dyad (within-dyad covariance = .02, *SE* = .02, $p = .32$, $r = .05$).

Next, the best-fit growth model, disease severity, was applied as a predictor of dyad covariance. Linear dyadic models revealed that within-dyad PIL covariance was significantly predicted by patient disease severity. Disease severity accounted for 44% of the PIL within-dyad covariance (pseudo-$R^2 = .44$). For QOL, disease severity did not significantly predict between-dyad QOL mean covariance (pseudo-$R^2 = .006$).

Table 2
Correlations among Dependent Variables and Descriptives

Variable	1	2	3	4	5
1. Caregiver status		-.39**	-.17**	.15*	.03
2. Male Gender			.07	.03	-.005
3. Age at enrollment				-.07	-.08
4. Average PIL					.60**
5. Average QOL					
a. Patient Within-person PIL with QOL					.20**
b. Patient Between-person PIL with QOL					.77**
c. Caregiver Within-person PIL with QOL					.35**
d. Caregiver Between-person PIL with QOL					.66**

Note: Correlations 1-5 are Pearson product-moment correlation coefficients. Correlations a-d were obtained through MLM estimates.
*$p < 0.05$; **$p < 0.01$

Table 3

Effects of Time and Disease Progression on PIL

Parameter	Patients				Caregivers			
	Model 1	Model 2a	Model 2b	Model 3	Model 1	Model 2a	Model 2b	Model 3
Fixed effects								
Intercept	103.62 (1.55)	104.84 (2.21)	103.42 (2.00)	114.14 (2.76)	109.52 (1.40)	109.37 (1.98)	109.38 (1.81)	120.00 (2.35)
$T_{Bdiagnosis}$		.05 (.10)				.10 (.09)		
T_{Bdeath}			-.14 (.08)				-.11 (.07)	
T_{W}		-1.95** (.34)	-1.75** (.35)			-1.48** (.32)	-1.60** (.33)	
Disease progression				-.62** (.14)				-.59** (.11)
Interactions								
$T_{W*Bdiagnosis}$		.05** (.01)				.04** (.01)		
$T_{W*Bdeath}$			-.03* (.01)				-.03** (.009)	
Random effects								
Intercept variance (between-person)	278.42 (38.33)	274.84 (37.68)	264.83 (36.53)	350.41 (101.01)	188.41 (28.14)	184.48 (27.54)	182.18 (27.20)	189.91 (28.26)
Disease progression slope variance				.59 (.28)				
Intercept slope covariance				-7.70 (4.96)				
Residual variance (within-people)	94.22 (6.18)	87.96 (5.77)	88.95 (5.83)	80.50 (5.59)	59.13 (4.43)	55.59 (4.17)	55.30 (4.14)	54.44 (4.08)
ICC	.74				.76			
Variance components								
-2 log likelihood	4710.7	4676.4**	4677.4**	4662.4**	3458.6	3434.1**	3430.9**	3429.2**
AIC	4716.7	4688.4	4689.4	4674.4	3464.6	3446.1	3442.9	3437.3
Level 1 pseudo-R^2 (within-person)		.07	.06	.15		.06	.06	.08
Level 2 pseudo-R^2 (between-person)		.01	.05	--		.02	.03	--

Note: ICC, intraclass correlation coefficient, AIC, Akaike's information criterion. *$p < 0.05$; **$p < 0.01$

Table 4

Effects of Time and Disease Progression on QOL

Parameter	Patients				Caregivers			
	Model 1	Model 2a	Model 2b	Model 3	Model 1	Model 2a	Model 2b	Model 3
Fixed effects								
Intercept	2.62 (.08)	2.54 (.12)	2.54 (.11)	3.12 (.15)	2.65 (.08)	2.50 (.11)	2.57 (.11)	3.11 (.18)
$T_{Bdiagnosis}$		.008 (.005)				.01* (.005)		
T_{Bdeath}			-.008* (.004)				-.007 (.004)	
T_{W}		-.08** (.02)	-.06** (.02)			-.05 (.03)	-.06* (.03)	
Disease progression				-.03** (.007)				-.02** (.009)
Interactions								
$T_{W*Bdiagnosis}$		.002** (.0009)				.002 (.001)		
$T_{W*Bdeath}$			-.001 (.0007)				-.002* (.0008)	
Random effects								
Intercept variance (between-person)	.68 (.10)	.64 (.10)	.63 (.10)	.67 (.10)	.52 (.09)	.47 (.08)	.49 (.09)	1.09 (.42)
Disease progression slope variance								.003 (.001)
Intercept slope covariance								-.04 (.02)
Residual variance (within-people)	.45 (.03)	.44 (.03)	.44 (.03)	.43 (.03)	.42 (.03)	.41 (.03)	.41 (.03)	.38 (.03)
ICC	.60				.55			
Variance components								
-2 log likelihood	1467.9	1451.6**	1453.8**	1451.5**	1093.6	1080.9*	1079.8**	1075.7**
AIC	1473.9	1463.6	1465.8	1459.5	1099.6	1092.9	1091.8	1087.7
Level 1 pseudo-R^2 (within-person)		.02	.01	.03		.01	.02	.09
Level 2 pseudo-R^2 (between-person)		.06	.07	.01		.01	.06	.04

Note: ICC, intraclass correlation coefficient, AIC, Akaike's information criterion. *$p < 0.05$; **$p < 0.01$

Figure 1
Model 2a: Effects of Time from Diagnosis and Time within the study on Patient PIL

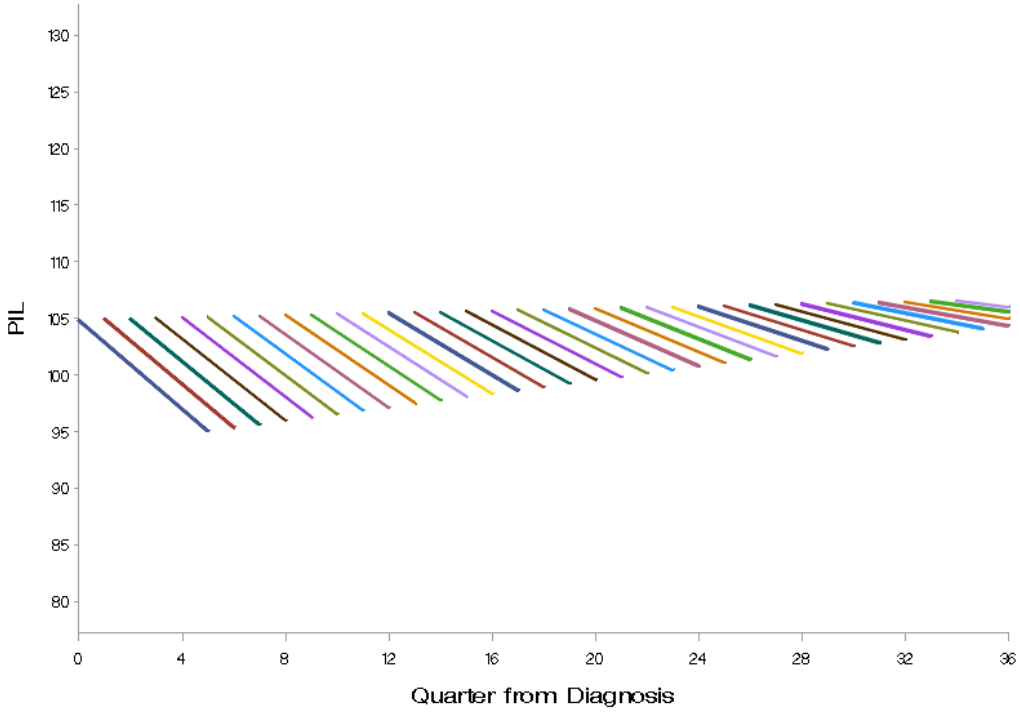


Figure 2
Model 2a: Effects of Time from Diagnosis and Time within the study on Caregiver PIL

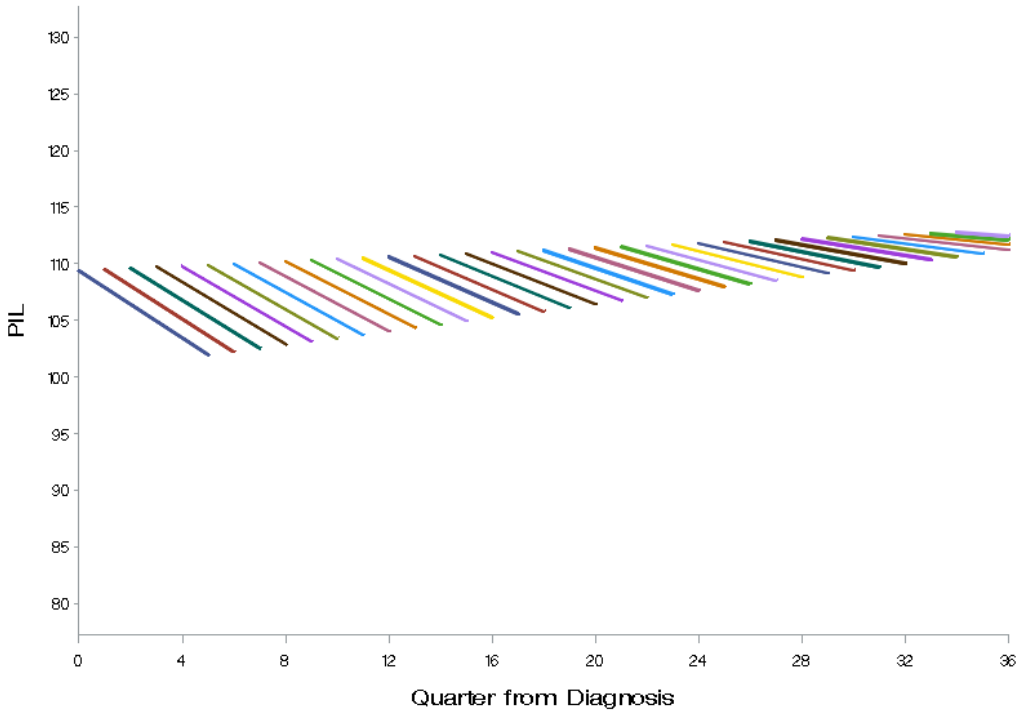


Figure 3

Model 2a: Effects of Time from Diagnosis and Time within the study on Patient QOL

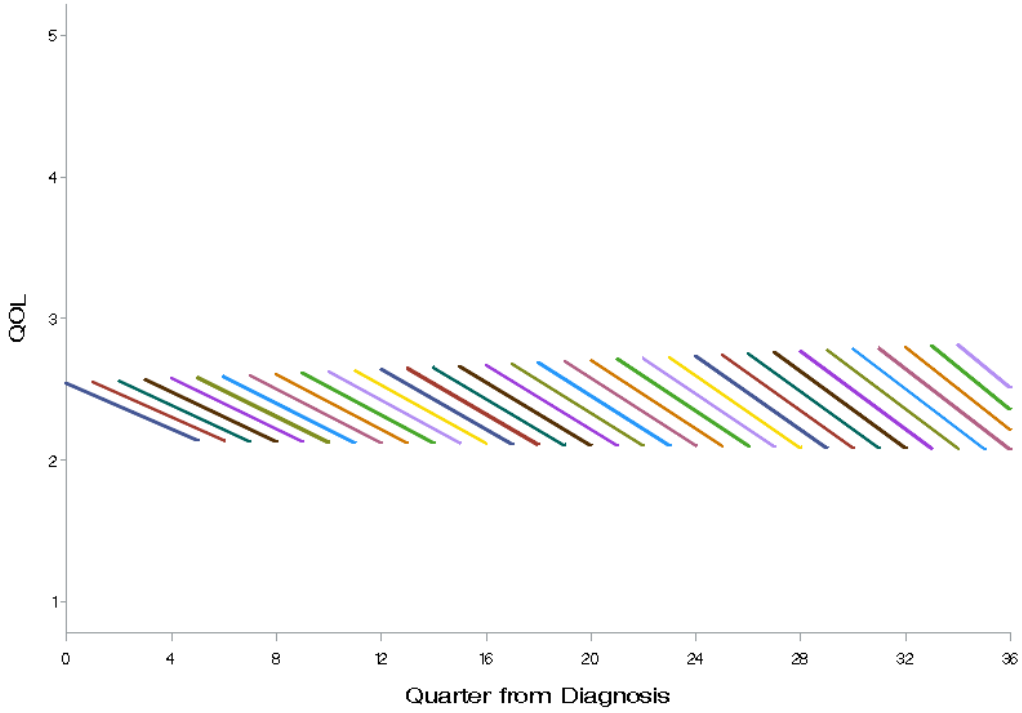


Figure 4

Model 2a: Effects of Time from Diagnosis and Time within the study on Caregiver QOL

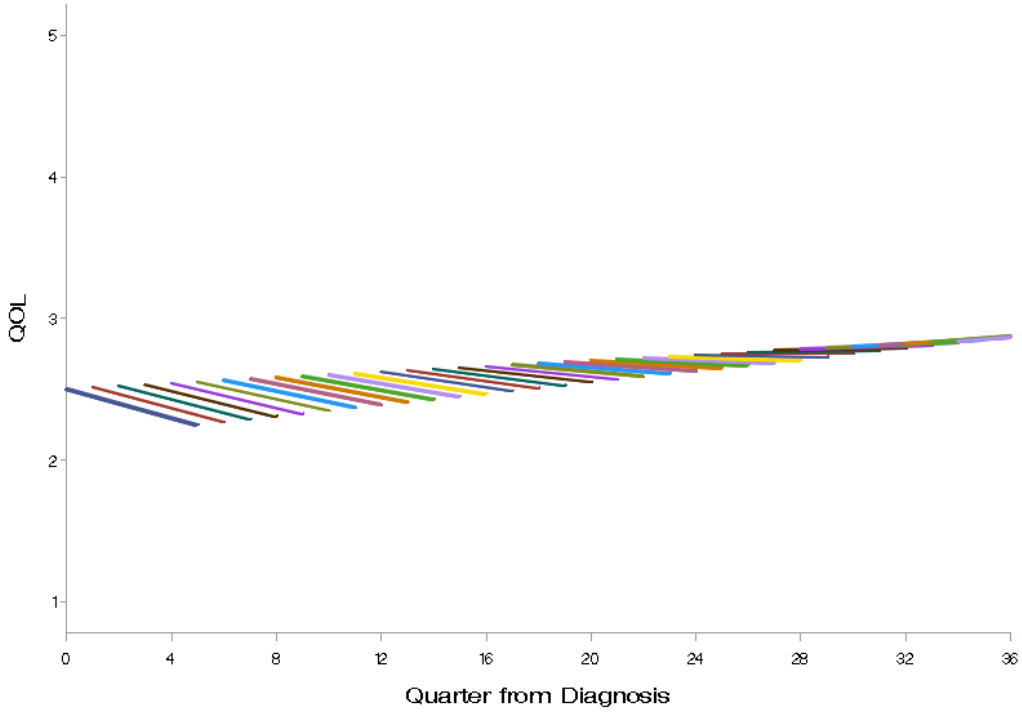


Figure 5
Model 2b: Effects of Time to Death and Time within the study on Patient PIL

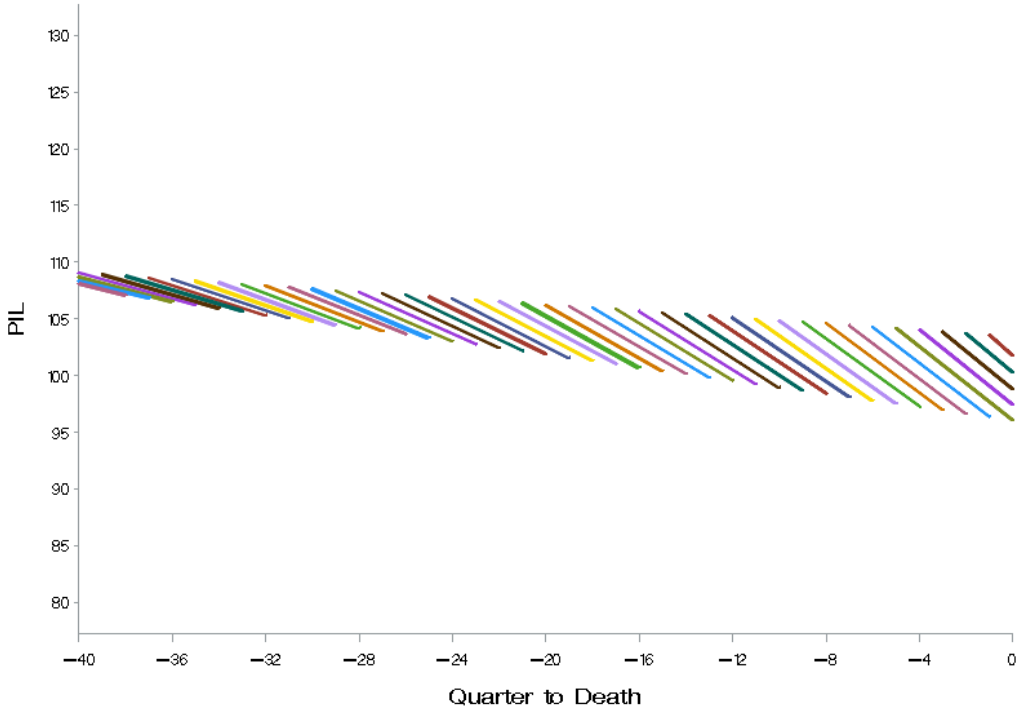


Figure 6
Model 2b: Effects of Time to Death and Time within the study on Caregiver PIL

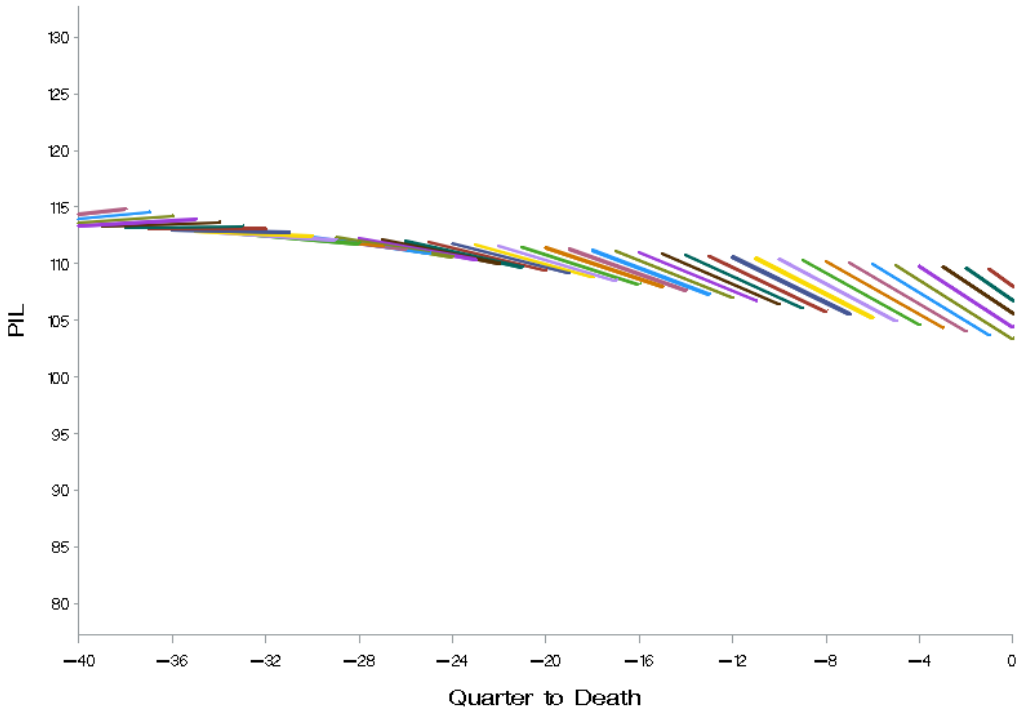


Figure 7
Model 2b: Effects of Time to Death and Time within the study on Patient QOL

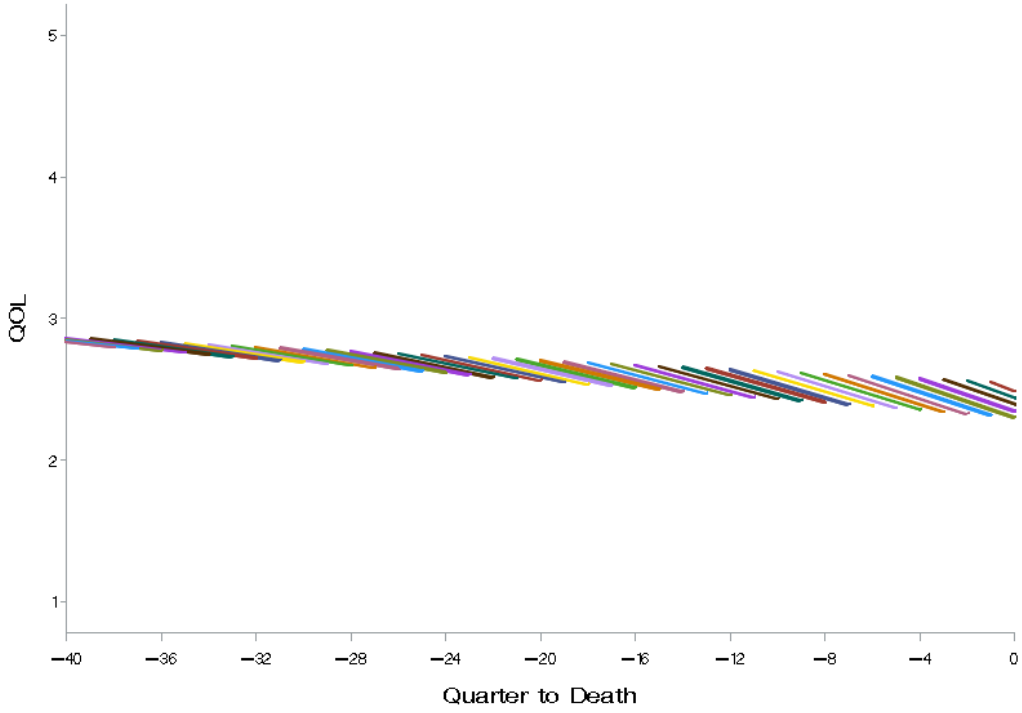


Figure 8
Model 2b: Effects of Time to Death and Time within the study on Caregiver QOL

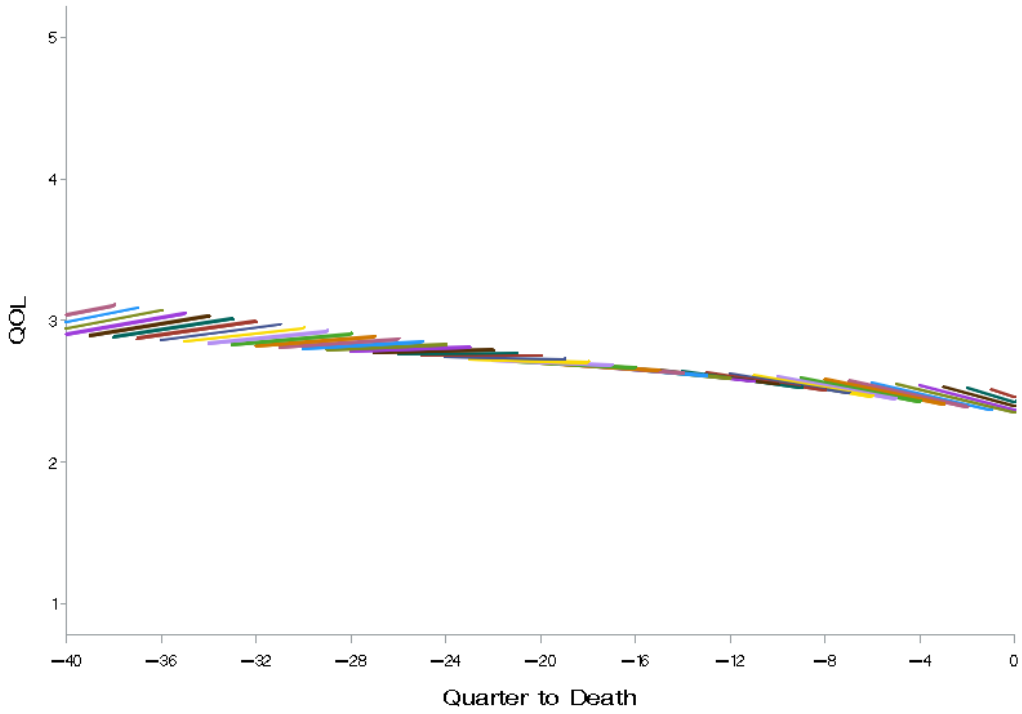


Figure 9
Model 3: Effects of Disease Progression on PIL

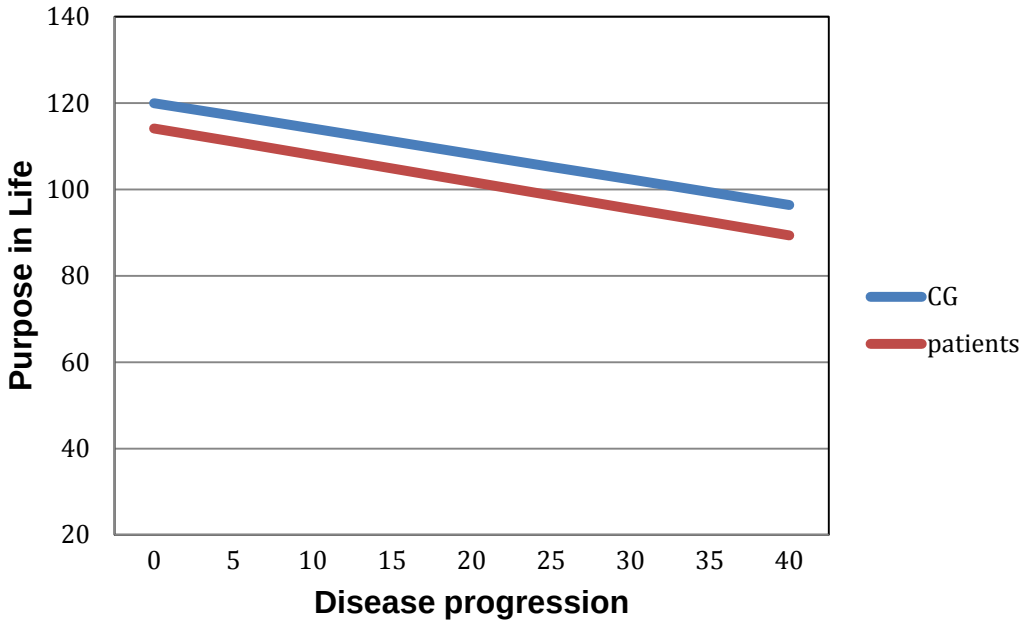
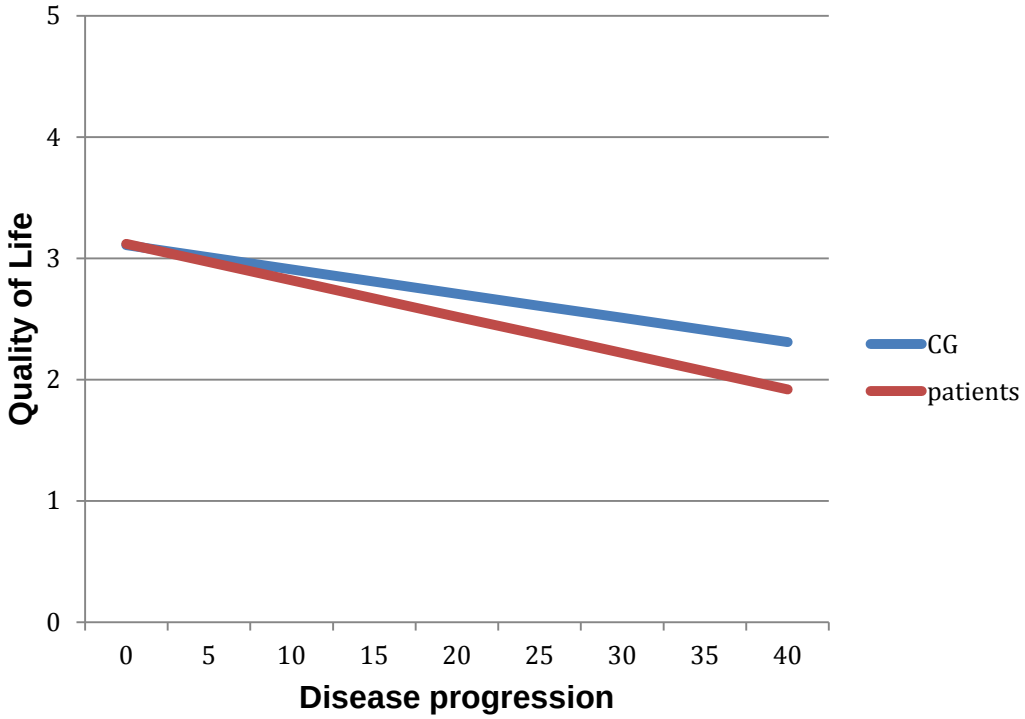


Figure 10
Model 3: Effects of Disease Progression on QOL



Chapter Four: Discussion

The aims of the current research were to evaluate the variance structure, trajectory, and dyadic coupling of PIL and QOL in patients with ALS and their caregivers. The present study revealed that PIL was generally stable, whereas QOL fluctuated more widely within patients with ALS and their caregivers. Additionally, PIL within the dyad changed together over time, suggesting that change in PIL for patients was reflected in their caregivers and vice versa. This work provides evidence to suggest that, in patients with ALS and their caregivers, PIL may be an especially valuable psychological resource. However, critical periods exist for PIL and QOL trajectories in patients and caregivers.

Variance Structure of PIL and QOL

In line with hypotheses, PIL exhibited a variance structure primarily consisting of stable between-individual differences opposed to within-individual fluctuations. Similar to previous research, the variance structure of QOL exhibited greater within-person fluctuation than existential well-being (i.e., PIL) in both patients with ALS and caregivers (Roach et al., 2009). In contrast, the variance structure of the single-item QOL measure in the current study more closely resembled the variance structure of the total QOL measure in the previous study rather than the single-item component. In the current study, patients and caregivers exhibited similar proportions of stability and variance among the PIL and QOL measures, suggesting that the nature of well-being was similar for patients and caregivers. PIL was more stable than QOL and therefore may represent a potential psychological resource for both patients and caregivers across the course of ALS.

Trajectory of PIL and QOL

Contrary to hypotheses, results revealed that both patient and caregiver PIL and QOL significantly decreased with disease severity and time. However, PIL and QOL trajectories differed based on proximity to critical points in the disease, diagnosis and death. Over the 18-month study period, individuals who enrolled closest to diagnosis and closest to death both showed the fastest decrease in PIL, whereas individuals enrolled in the middle phase of the disease, furthest from diagnosis and death, showed less decline in PIL. For QOL, the same moderation pattern emerged, though some results were not statistically significant. These findings highlight the complexity of modeling change in PIL and QOL in patients with ALS and their caregivers. It appears that phases of adjustment and adaptation occur for well-being in patients with ALS and their caregivers at different stages of the disease. At the middle stage of the disease, patients and caregivers may adapt, and PIL and QOL stabilize. It has been suggested that changes in one's expectations and response shift may contribute to stability in QOL (Cupp et al., 2011; Zamietra, 2012). However, the current results also suggest that PIL and QOL are not stable at all stages of the disease. Patients and caregivers appear to be vulnerable to losses in PIL and QOL during critical periods, following diagnosis and approaching end of life. These findings suggest patients with ALS and their caregivers need increased support especially at diagnosis, when approaching death, and in periods of rapid physical decline.

Few previous studies have examined meaning and purpose in patients with ALS in relation to time or disease severity. Current results are consistent with cross-sectional research reporting that disease severity is associated with lower patient satisfaction with

meaning in life (Fegg et al., 2010). QOL has received greater attention in the literature, though results have been mixed. A number of studies have reported that general and self-assessed QOL do not have significant relationships to time or disease severity in patients with ALS (Neudert, Wasner, & Borasio, 2004; Roach et al., 2009; Robbins et al., 2001; Simmons et al., 2000). Other studies have reported a significant relationship between patient general QOL and disease severity but not time (Rabkin et al., 2000), or an increase in general QOL over time (Gauthier et al., 2007). For caregivers, decreased general QOL over time has been reported (Roach et al., 2009). However, other research found no relationship between caregiver general QOL and patient disease severity (Gauthier et al., 2007). The current results indicate patient and caregiver self-assessed QOL decreased with disease severity and over time within the study.

As mentioned, the extant literature on QOL trajectories in regard to disease severity and time is mixed, and somewhat discrepant from the reported findings. Several factors within the present study may underlie these differences, including the assessment period, data collection proximity to death, QOL measure utilized, and statistical method. The current study assessed QOL and PIL over an 18-month period, whereas the majority of previous research evaluated change in QOL over shorter periods of time. The current sample also included patients spanning different stages of the disease. Data collection took place in the patients' homes, allowing individuals with more advanced illness to participate. Due to the challenges of studying ALS populations, the majority of previous research has been conducted in conjunction with multidisciplinary clinic visits. Patients at end-stage disease may be indirectly excluded due to the inability to travel. Multidisciplinary care has been shown to improve QOL (Van den Berg et al., 2005). Data

utilized in the current study was also collected prior to the Food and Drug Administration's approval of modern selective serotonin re-uptake inhibitor antidepressants and Riluzole, the only pharmacological treatment for ALS. Therefore, the current sample represents a natural history of well-being in ALS.

Differences in reports of stability in QOL in patients with ALS may also reflect the type of QOL measure utilized. A variety of QOL measures exist, including those assessing general QOL, health-related QOL, and self-assessed QOL. Health-related QOL produces different patterns over time and disease progression than other QOL indices (Neudert, Wasner, & Borasio, 2004; Robbins et al., 2001; Simmons et al., 2000). Yet, some research suggests general QOL and self-assessed QOL are highly correlated (Simmons et al., 2000). The discordance among different types of QOL measures in patients with ALS has been recognized as an important issue influenced by individual differences in patients' perceptions (Hardiman, Hickey, & O'Donerty, 2004). The current study utilized a self-assessed single item measure of QOL. Findings therefore reflect individuals' perceived QOL. Self-assessed QOL is focused on individual appraisal of the importance of one's life conditions; an aspect infrequently included in general and health-related QOL measures.

The statistical method is another strength of the current research. MLM allows for the assessment of between-individual and within-individual variance, changes in trajectories over time, and individual differences in trajectories based on personal characteristics. Our research suggests change in PIL and QOL are dynamic processes impacted by disease stage at the time of assessment. Trajectories may appear stable if averaged, masking individual differences.

Dyadic Relationships of PIL and QOL

Results of the current study suggest that patient and caregiver psychological health is intertwined. Relationships between PIL and QOL were evaluated at the level of the dyad (i.e., patients and their respective caregivers). In accordance with hypotheses, results indicate that average QOL between dyad members was significantly related. However, variance in QOL did not exhibit dyadic coupling over time in patients with ALS and their respective caregivers. Previous research supports the existence of a relationship between QOL in patients with ALS and caregivers. Relationships between self-assessed QOL (Trail, Nelson, Van, Appel, & Lai, 2003), general QOL (Gauthier et al., 2007; Rabkin et al., 2000), health-related QOL (Jenkinson et al., 2000), and existential QOL (Pagnini et al., 2011) have been reported among patient and caregiver groups. Contrary to the hypothesis, average PIL between dyad members was not significantly related. However, the current study provides novel evidence of dyadic coupling in PIL variance in patients with ALS and their caregivers. Dyadic relationships may reflect similar life conditions and a shared experience throughout the disease. These results provide support for conceptualizing ALS as a family disease, meaning that the patient and their family reciprocally impact one another through the disease experience (Gauthier et al., 2007).

Limitations

The present study has certain limitations. First, QOL was assessed with a single item patient-assessed measure that has not been previously validated. However, self-assessed QOL has been recognized as an important aspect of well-being in patients with ALS (Hardiman, Hickey, & O'Donerty, 2004). Additionally, the study sample included

some individuals with exceptionally slow rates of disease progression. The average survival time (i.e., date of diagnosis to patient death) was longer than what is generally reported in the literature (Ringel et al., 1993). However, because the sample included individuals both near and far from critical periods (i.e., diagnosis and death), accounting for individual differences revealed important trajectory patterns. Finally, health care for patients with ALS has evolved since the study took place. Adaptive equipment has improved, which may impact patient autonomy and caregiver burden.

Clinical and Research Implications

The current results have implications for informing both intervention and research design. PIL was a stable psychological resource, though critical periods exist in which intervention may be needed most. Applying psychological interventions early on, following patient diagnosis, may mitigate future decline in well-being. PIL may be a source of resiliency that clinicians could explore to provide support to patients and caregivers. A number of therapies exist aimed to foster meaning and purpose in the terminally ill (see LeMay & Wilson, 2008 for a review). However, research examining the efficacy of such therapies is limited.

Additional research is needed to examine how QOL and PIL affect end-of-life despair in patients with ALS as well as protective factors for PIL and QOL. Factors that impact PIL and QOL beyond time and disease progression should also be explored in patients with ALS and their caregivers. Coping styles may provide insight into individual differences in maintenance of well-being. Additionally, the extent to which patients and caregivers feel informed about the disease and empowered to make personal choices (e.g., treatment decision making and advance directives) may provide a sense of control,

which may impact well-being. Future research should also examine the factors that impact the disease experience in families of patients with ALS and to explore the direction of the relationship in well-being among patients and their respective caregivers.

By nature, the ALS patient population is heterogeneous. Accordingly, challenges in statistical design and interpretation exist in studying well-being in patients with ALS. The current study provides evidence that individual baseline characteristics (i.e., time since diagnosis and time to death) impact the trajectory of PIL and self-assessed QOL in patients with ALS and their caregivers. Observational research and clinical trials using QOL as an outcome measure should consider taking into account individual differences such as disease severity, time since diagnosis, and time to death. Results also suggest that time and disease progression are not synonymous when it comes to changes in well-being. Time and disease severity predicted well-being measures differently, although both had a negative impact. Therefore, examining well-being over time or in relation to disease severity in patients with ALS may produce different results.

Conclusions

The present study provides important new insight into the stability, variance structure, and dyadic coupling of PIL and self-assessed QOL in patients with ALS and their caregivers. PIL was markedly stable, yet QOL fluctuated more within individuals over the disease course, suggesting PIL is a potential psychological resource for patients and caregivers. However, periods of decline and stabilization were observed in PIL and QOL. Critical points in the disease (i.e., following diagnosis and approaching death) represent periods of decline in well-being trajectories. Disease severity was the strongest predictor of decreases in PIL and QOL, yet there were individual differences in the effect

of disease severity on PIL among patients and QOL among caregivers. Time and disease severity were more deleterious to PIL than to QOL. Factors other than disease severity likely play a larger role in QOL variability, such as coping styles or disease education. Finally, PIL and QOL in patients with ALS and their caregivers were interrelated. These findings build on the previous literature and highlight the dynamic and interwoven nature of well-being in patients with ALS and their caregivers, and provide avenues for future work investigating PIL as a resilience factor for individuals facing terminal illness and their caregivers.

Appendix: Abbreviations

ALS- Amyotrophic Lateral Sclerosis

ALSS- ALS Severity Scale

ICC- Intraclass Correlation Coefficients

IIV- Intraindividual Variability

MLM- Multilevel Modeling

PIL- Purpose in Life

QOL- Quality of Life

-2LL- -2 Log Likelihood

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Vita

Natasha Elsa Garcia

Degrees Awarded:

University of South Florida, B.A. 2009

Professional Positions:

Graduate Research Assistant July 2013 - Present
University of Kentucky, Department of Psychology

Clinical Trainee May 2014 - May 2015
Home Based Primary Care
Veterans Affairs Medical Center, Leestown Division

Clinical Research Coordinator Aug 2011 - June 2013
University of Miami, Department of Neurology

Research Coordinator May 2009 - July 2011
Tobacco Research and Intervention Program
University of South Florida, Moffitt Cancer Center

Undergraduate Research Intern Feb 2008 - April 2009
Tobacco Research and Intervention Program
University of South Florida, Moffitt Cancer Center

Scholastic Honors:

American Psychosomatic Society, Minority travel award 2015
Lyman T. Johnson Academic Fellowship 2013
Moffitt Cancer Center Scientific Retreat, Outstanding poster award 2011
Moffitt Cancer Center Scientific Retreat, Outstanding poster award 2010
USF Undergraduate Research Symposium, 1st place Behavioral Sciences 2009
Psi Chi International Honor Society in Psychology 2009
University of South Florida College of Arts and Sciences Honor Society 2009

Natasha Elsa Garcia
Signature