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Neuroticism in Four Non-Cancer Populations at the End-of-life

By

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Abstract

Statement of the Problem

Neuroticism is a significant predictor of adverse psychological outcomes in cancer. However, less is known about how this relationship manifests in those with non-cancer illness at the end-of-life. In assessing such patients, reliance on proxy-reports of patient symptoms and experiences are common. The purpose of this thesis was to examine two separate, yet related aspects of neuroticism at the end-of-life – neuroticism as moderator of physical symptoms and depression, and caregiver-patient congruence (i.e., the extent to which patients and caregivers rated patient neuroticism similarly) on ratings of patient neuroticism.

Methods

Secondary analysis of data was assessed using data collected in the *Dignity and Distress across End-of-Life Populations* study (Chochinov et al, 2016). The data included $N = 404$ patients with amyotrophic lateral sclerosis (ALS) ($N = 101$), chronic obstructive pulmonary disease (COPD) ($N = 100$), end-stage renal disease (ESRD) ($N = 101$), and frailty ($N = 102$) in the estimated last six months of life. $N = 216$ of these participants had an identified caregiver as a co-participant. Using ordinary least squares (OLS) regression, Study 1 explored neuroticism as a moderator between illness-related symptoms at Time 1 (~six-months prior to death) and depression at Time 2 (~three-months prior to death). Study 2 explored degree and predictors of incongruence between patient-participants and their caregivers on patients' neuroticism (NEO-FFI) using hierarchical linear modelling.

Results

Neuroticism significantly moderated the relationship between the following symptoms and depression three months later: drowsiness, fatigue, shortness of breath, wellbeing (ALS);

drowsiness, trouble sleeping, will to live, activity (COPD); constipation (ESRD); and weakness and will to live (Frailty). Degree of congruence between patients and caregivers on patient neuroticism varied significantly across dyads. Caregivers rated patients' average neuroticism significantly higher than patients. Patient depression, anxiety, illness group, and caregiver burden were positively associated with the dyad's mean level of patient neuroticism. Congruence increased when patients perceived themselves as more dependent, and when relatives other than adult children or spouses provided proxy ratings.

Conclusion

Neuroticism represents a vulnerability factor that either attenuates or amplifies the relationship of specific illness and depressive symptoms in these non-cancer illness groups at the EOL. As patients and caregivers may perceive neuroticism differently, care must be taken when using proxy assessment of this trait that has such important public health consequences.

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Dedication

This thesis is dedicated to my beloved father-in-law Mendel Schnitzer (z"l), who through his love of life, sense of humour, and perseverance in the face of relentless suffering, taught me the complexities of living and dying with chronic illness. Through our relationship I learned how to be a better clinician and researcher, and I feel his lasting impact each time I interact with patients. True to the nature of this dissertation and to Mendel, from one 'Madwoman in the Academy' to another, I also dedicate this work to the other half of the dynamic-dyad, Debbie, a source of ongoing support, inspiration, and love.

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Chapter One: General Introduction

Perhaps the most important part of providing good care to families and helping patients cope at the end of life is in understanding who the patient *is* as a person (Chochinov, 2004). Though it is now well known that dying patients experience feelings of hopelessness, being a burden, loneliness, loss of dignity, and existential/spiritual concerns (Breitbart et al., 2000; Chochinov et al., 2009; Chochinov, Wilson, Enns, & Lander, 1998; Wilson, Chochinov, McPherson, et al., 2007; Wilson, Chochinov, Skirko, et al., 2007), very little is known about who is most likely to experience such distress. Personality, the dynamic interplay of physical and psychological systems within the person that influence a pattern of actions, thoughts, and feelings (Allport, 1961), is one dimension that plays a role in the experience of distress at the end-of-life, though research in this area has been limited. Personality is a major factor in coping with life-threatening illness (Carver & Connor-Smith, 2010; Carver, 2005). Neuroticism has been identified as the personality trait with the strongest relationship to psychopathology (Barlow, Sauer-Zavala, Carl, Bullis, & Ellard, 2013; Kendler & Myers, 2010; Watson, 2001; Widiger & Seidlitz, 2002), and in particular has been identified as a significant predictor of depression, hopelessness, anxiety, worry, loss of dignity, concentration, and quality of life in cancer patients in palliative care (Chochinov et al., 2006). Yet, it is unknown how this relationship manifests in those with non-cancer illness at the end of life. Further, in assessing such patients, care must be taken to decrease burden with multiple or lengthy questionnaires, and as such, reliance on proxy-reports of patient symptoms and experiences is common in the palliative care literature (Janssen, Spruit, Wouters, & Schols, 2012; Jones et al., 2011; Kutner, Bryant, Beaty, & Fairclough, 2006; Sebring et al., 2018).

Researchers and clinicians increasingly recognize the need to expand research in palliative and end-of-life (EOL) care to non-cancer populations (Addington-Hall & Higginson, 2001; Moens, Higginson, & Harding, 2014). Illnesses such as chronic obstructive pulmonary disease (COPD) and end stage renal disease (ESRD) are among the top causes of death in Canada (Statistics Canada, 2009). Additionally, Canada's rapidly aging population (Employment and Social Development Canada, 2014) is resulting in an increasing number of individuals who are considered the frail elderly (FE), with multiple care needs at the end-of-life (Clegg, Young, Iliffe, Rikkert, & Rockwood, 2013). Amyotrophic lateral sclerosis (ALS), though less common, has a rapid deteriorating course associated with significant symptom distress and impaired quality of life (Aoun et al., 2013). ALS, COPD, ESRD, and frailty have less predictable courses than cancer and relatedly, suboptimal end of life or palliative care, though the need for adequate palliative care in these groups has been highlighted (Aoun et al., 2013; Gardiner et al., 2010; Hobson, Gomm, Murtagh, & Caress, 2011; Kristjanson, Aoun, & Oldham, 2006). Patients dying of non-cancer illnesses experience similar physical and psychological issues as those with cancer, including dyspnea, pain, depression, and anxiety (Stiel et al., 2014). Gaining additional information about neuroticism at the end of life in ALS, COPD, ESRD and frailty is important given its demonstrated link with various aspects of psychological distress in cancer populations and its significant public health implications (Aarstad, Beisland, & Aarstad, 2012; Aarstad, Beisland, Osthus, & Aarstad, 2011; Beisland, Aarstad, Osthus, & Aarstad, 2013; Cardenal, Cerezo, Martinez, Ortiz-Tallo, & Jose Blanca, 2012; Carter & Acton, 2006; Chochinov et al., 2006; Lahey, 2009; Rutskij et al., 2010).

The primary purpose of this thesis was to examine two separate, yet related aspects of neuroticism at the end-of-life – (1) its role in understanding the course of physical symptoms and

depression over time, and (2) whether caregivers and patients are concordant in their ratings of patient neuroticism. Essentially, this thesis addresses how and why neuroticism is important in understanding the relationship between physical and psychological distress at the end of life, and who can then provide information regarding this trait. The specific research objectives were:

1. To examine the role of neuroticism as a moderator of physical symptoms at Time 1 on depression at Time 2 in four non-cancer illnesses (ALS, COPD, ESRD and frailty) in the last six months of life (Study 1). I hypothesized that physical symptoms at baseline would be associated with increased depression (approximately) three months later more so for those high in neuroticism.

2. To examine the degree and predictors of congruence between patient and caregiver ratings of patient neuroticism in ALS, COPD, ESRD and frailty in the last six months of life (Study 2). I hypothesized that caregivers would rate patients significantly higher on neuroticism than patients would rate themselves. I hypothesized that the degree of incongruence between patient and caregiver ratings of patients' neuroticism would be associated with patients' illness group, perceived dependency, current quality of life, depression, anxiety, fatigue, cognitive status; and caregivers' burden, psychological distress, length and type of relationship to patient, age, gender, and education.

Overview of the illness groups

ALS is a progressive neurological disease that is characterized by the degeneration of motor neurons that control voluntary muscles involved in movement, speech, breathing, and swallowing (Aoun et al., 2013), for which there is no determinate cause and no cure (Rabkin et al., 2006). ALS's course includes progressive paralysis, with a median life expectancy of 2-4 years post-diagnosis, with the most common cause of death related to respiratory failure (Aoun

et al., 2013). After cancer, ALS and other neurodegenerative diseases are predicted to be the second leading cause of death in Canada by 2040, and there are currently estimated to be 2500 to 3000 Canadians living with ALS (ALS Canada, 2014). Over the course of the illness, chronic shortness of breath results in increased suffering for patients and decreased quality of life, and is also associated with caregiver burden (Kaub-Wittemer, Steinbüchel, Wasner, Laier-Groeneveld, & Borasio, 2003). Shortness of breath in ALS marks the terminal phase of the illness and is typically a signal that the patient will either die within six months or require invasive ventilation supports (Aoun et al., 2013; Mitsumoto & Rabkin, 2007).

COPD is caused by an inflammatory response to particles or gases in the lungs, which results in progressive airflow limitation (obstructive bronchitis and/or emphysema) (Maltais, Dennis, & Chan, 2013). It is responsible for 5% of deaths worldwide (WHO, 2014), and it is estimated that 13% of Canadians have lung function scores indicative of COPD (Statistics Canada, 2013). COPD is categorized into four stages, ranging from mild to severe, based on the ratio between one's forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) (GOLD, 2014). Patients with COPD face prognostic uncertainty and an illness trajectory characterized by periods of relative stability interspersed with acute exacerbations (Gysels & Higginson, 2009; Utens et al., 2014). As such, there is considerable variability in time to death even in the final stages of COPD (Weiss, 2019).

ESRD, also known as kidney or chronic renal failure, is the fifth and final stage of kidney disease in which kidney function is less than 15%. The kidneys play an essential role in regulation of water, waste removal, mineral balance, and hormone production in the body, and kidney failure is associated with uremia in which the kidneys cannot effectively remove waste from the body. This is associated with an array of symptoms that span multiple areas of

functioning, including, but not limited to, decreased appetite, nausea, impaired sleep and sex drive, swelling, pain, and weakness. The lifetime risk for ESRD in Canadians is 1/40 for men and 1/60 for women (The Kidney Foundation of Canada, 2014). Rates of ESRD have been steadily increasing for the last three decades, in large part due to increasing rates of diabetes (CIHI, 2017; Manns, Mendelssohn, & Taub, 2007). ESRD is a unique population due to various treatment options at the EOL, where transplant is not an option or not desired. These include dialysis, a life-sustaining yet demanding procedure, or conservative management (management of symptoms without dialysis) through a multidisciplinary team (Schell & Arnold, 2019). EOL for patients with ESRD is associated with high burden of symptoms and significant levels of physical and psychological distress (Murtagh et al., 2010).

As the Canadian population rapidly ages, with an estimated 25% of all adults projected to be over the age of 65 by 2051 (Employment and Social Development Canada, 2014), there is an increased need for understanding end-of-life care needs for frail older adults (Koller & Rockwood, 2013). Frailty is considered a medical condition (Clegg et al., 2013) and has been conceptualized based on cumulative functional deficits, including symptoms, lab abnormalities, diseases and disabilities (Mitnitski, Mogilner, & Rockwood, 2001) and phenotypic presentation which includes the presence of three or more of the following criteria: involuntary weight loss, exhaustion, slow gait speed, poor handgrip strength, and sedentary behaviour (Fried et al., 2001). Frailty is prevalent in approximately 10% of older adults, and this increases between the ages of 65-85 (Collard, Boter, Schoevers, & Oude Voshaar, 2012). Frailty has significant impacts on older adults' physical and mental health. It has been linked to decreased self-esteem (Guerrero-Escobedo, Tamez-Rivera, Amieva, & Avila-Funes, 2014), and poorer psychological well-being. Canadian research suggests that the effect of frailty is additive – as symptoms increase, aspects

of psychological well-being (personal growth, environmental mastery, positive relations, and self-acceptance) decreases irrespective of demographic factors, cognitive impairment, and mental health (Andrew, Fisk, & Rockwood, 2012).

The role of personality in illness and end-of-life

Across the life course, there is evidence of mean-change in personality, which varies as a function of trait and life stage. In particular, the largest period of mean-change is represented in ages 20-40 with increases in social dominance, conscientiousness, and emotional stability (low neuroticism). Social vitality and openness to experience decrease after age 60. There are aggregate mean-level decreases in emotional stability (i.e., increases in neuroticism) above age 70 (Roberts, Walton, & Viechtbauer, 2006). However, ongoing questions remain related to the stability of personality in the face of extreme stress and distress, which is nuanced in the context of aging, serious illness, and the EOL. There is ample evidence that personality changes over the lifespan (e.g., Leszko, Elleman, Bastarache, Graham, & Mroczek, 2016) and impacts and is impacted by a range of developmental experiences (Roberts & Mroczek, 2008; Roberts, et al., 2006; Srivastava, John, Gosling, & Potter, 2003). Personality change and in particular, decreases in conscientiousness and increases in neuroticism over time are associated with increased metabolic syndrome and poorer psychological health (Human et al., 2013). There is evidence that personality is influenced by cohort effects (Smits, Dolan, Vorst, Wicherts, & Timmerman, 2011) and environmental influences accounting for longitudinal personality change in twin studies (Kandler et al., 2010). However, intra-individual personality tends to be quite stable by adulthood and remains relatively unaffected by factors such as sex, education, ethnicity, and religiosity (Terracciano, McCrae, & Costa, 2010). More recently, researchers have posited the Behavioural Reaction Model (BRA), which suggests that personality does not imply entirely

consistent behaviour. Rather, these researchers suggest that personality traits can be stable or different between people across contexts, and plastic within people across contexts. As such, this theory highlights that individuals have a mean level of trait expression, but trait expression varies depending on the environment (Dingemanse, Kazem, Réale, & Wright, 2010). For example, a population-based study in Germany and Great Britain demonstrated negative associations between age and neuroticism in the British sample and the reverse in the German sample, which was not moderated by gender or education (Donnellan & Lucas, 2008).

Ferguson (2013) suggests that the BRA model is useful in extending long-standing findings by seminal researchers such as Walter Mischel, demonstrating "stable dynamic personality" that changes situationally but whose fundamental structure is constant (Ferguson, 2013, p. S49). Friedman suggests that using a lifespan approach in some ways bypasses the person-situation debate, because there is recognition that while personality is a predictor of health outcomes both by changing course and trajectory, "health behaviours, social relations, physiological changes, and health outcomes can feed back and affect personality" (Friedman et al., 2014, p. 1379).

Neuroticism. Longitudinal aging studies suggest that there is a trend of decreasing neuroticism over the lifespan, such that neuroticism decreases until young adulthood, with the largest decreases apparent between ages 20-40. It then stabilizes until approximately age 70, after which very slight increases are apparent (Roberts, et al., 2006; Srivastava et al, 2003; Steunenberg, Twisk, Beekman, Deeg, & Kerkhof, 2005). Such findings echo research on aging and mental health, suggesting improved mental health into old age with a slight levelling off or worsening in very old age (Charles, 2010). Several explanations for deteriorating mental health at end-of-life include terminal decline, greater vulnerability to stress response due to immune

suppression, and the increase in comorbidities that may all play a role in increasing or exacerbating negative affect/neuroticism (Charles, 2010; Mroczek et al., 2006), however research into this phenomenon is somewhat limited. The impact of neuroticism on illness may be bidirectional (Ferguson, 2013), particularly at the end of life. Cognitive and functional deteriorations related to terminal decline preceding death, though variable across individuals (Gerstorf et al., 2008; Muniz-terrera, Van Den Hout, Piccinin, Matthews, & Hofer, 2013), have been implicated in personality change at the very end of life (Mroczek, Spiro, & Griffin, 2006). Further research exploring the nature and utility of neuroticism at the EOL will be beneficial in understanding the role of this trait in this distinct life stage.

Proxy assessment. Reliance on proxy assessment in the palliative care setting is common. This is due to potential impacts of illness, including cognitive changes, delirium, and fatigue, on self-reported symptoms and traits, and the related burden of completing self-report measures when seriously ill. There is an assumption among clinicians that proxy assessment reflects an accurate or interchangeable description of symptoms or experiences of the patient. However, there is evidence that such ratings may be distorted or incongruent, particularly for internal experiences, as proxies must infer patient experience from observable behaviours (Asadi-Lari, Tamburini, & Gray, 2004; Infurna et al., 2014). In a cohort of prostate cancer survivors and their spouses, spouses rated the survivors' symptom severity significantly higher than did the survivors' themselves, especially when survivors were younger and when spouses reported greater caregiver strain (Winters-Stone, Lyons, Bennett, & Beer, 2014). Similarly, in patients with COPD, chronic heart failure, and ESRD, family caregivers reported greater patient fatigue, coughing, muscle weakness, loss of appetite, low mood, anxiety, panic attacks, edema, and chest pain, than did patients themselves. Overall agreement was moderate for the majority of

symptoms, though was higher for more observable symptoms such as dyspnea, loss of appetite, pain, and muscle cramps (Janssen et al., 2012). Proxy ratings are commonly used to assess functioning in dementia by caregivers, where there is incongruence in ratings of patient quality of life, with caregivers generally reporting poorer quality of life than patients (e.g., Hoe, Katona, Orrell, & Livingston, 2007).

Using the same dataset as the current dissertation, compared to patient self-reports, caregivers underreported patients' quality of life, satisfaction with quality of life, and desire for death, while they over-reported the majority of items related to loss of dignity and existential distress (Hack et al., 2018). As such, there is evidence both in prior research and in the present dataset that in patients with ALS, COPD, ESRD, and frailty, there is incongruence in self-other symptom reports, which will likely extend to neuroticism. Practically speaking, it will be helpful to know how caregivers reports of patients' neuroticism compare to self-reports, to enhance the validity of patient assessments that rely on proxy assessment (Hack et al., 2018).

Methodological issues. Several methodological concerns have been raised related to much of the literature assessing concordance in proxy reports. These concerns center around the use of methodology that is suited to independent data rather than dyadic reports, the use of difference scores as outcome measures, and use of correlational methods. When proxy concordance is assessed from correlations between components that encompass a difference score (e.g., proxy rating minus patient rating) are associated with decreased reliability, and increased variability in one component of the difference score will have a greater impact on the difference score (Furr, 2011), which can result in significantly different results and conclusions. Additionally, methods which divide scores based on high and low agreement, for example, assume the risks inherent in categorizing continuous measures, including lost statistical power

(Cano, Johansen, & Franz, 2005). Within the methodological literature, multilevel modelling approaches have been identified as ideal for examining congruence in dyadic, nonindependent data, as such approaches account "for the nonindependence of partners within a couple and can be used to estimate simultaneously couples' mean ratings and congruence, thus reducing Type I error" (Cano, 2005, p.372).

Depression in serious illness

The bidirectional nature of depression and chronic illness has been well established (e.g., Evans et al., 2005). Further, depression, chronic illness, and aspects of aging all share overlapping symptoms, which complicates clear delineation of directionality (Wilson-Genderson, Heid, & Pruchno, 2017). The presence of chronic illness and accompanying symptoms is a known risk factor for depression onset (Boockvar, 2014) and duration (Ohayon & Schatzberg, 2003), and individuals with chronic illness and comorbid depression or anxiety report more somatic symptoms (Katon, Lin, & Kroenke, 2007). As such, the cyclical nature of depression and physical illness has significant implications for quality of life related to both physical and mental health (Evans et al., 2005). Understanding the relationship between physical symptoms and depression is particularly relevant at the end-of-life, where time is limited and untreated or undertreated depression results in significant barriers to accomplishing the "work" of a "good death" (Chochinov, 2002). Depression is in fact one of the most common psychological problems faced by patients with terminal illness (Chochinov et al., 1998). Estimated rates of depression are most robust for cancer populations, where an estimated 22% of patients meet diagnostic criteria (Fitzgerald, Miller, Li, & Rodin, 2015). It is a similarly widespread problem in non-cancer populations, with criteria for depression met in 22% of patients with ESRD (Shirazian et al., 2017), 23% in COPD (Albrecht et al., 2016), 20.7% to

53.8% in frailty (Vaughan, Corbin, & Goveas, 2015), and 19% in ALS (Rabkin et al., 2005). In summary, across these illness groups, approximately 20% of patients meet criteria for depression.

Theoretical Background

Personality, illness and coping. There is a significant gap in the literature in understanding the role of personality at the very end of life (Mueller, Wagner, Wagner, Ram, & Gerstorf, 2019). However, what is known can be extrapolated from several theories examining coping and wellbeing in aging. The strength and vulnerability integration (SAVI) model suggests that as individuals age, they are generally able to employ attentional strategies, appraisals, and behaviours to regulate everyday emotional experiences and avoid negative situations (Charles, 2010, p.1068), and are motivated to do so as a function of their awareness of limited time left in life (Carstensen, 2006). Individuals who are less able to use such aforementioned strategies as they age experience reduced well-being and increased psychological morbidity. Those high in neuroticism experience consistently high levels of negative affect as they age, and do not benefit from reduced negative affect typically brought about in the aging process (Charles, Reynolds, & Gatz, 2001). Further, terminal illness likely reflects a situation of chronic uncontrollable stressors, in addition to neurological dysregulation, and at times, social isolation, each of which limit the ability to use attentional strategies, appraisals, and behaviours typically gleaned with increased age, and thus limit the ability for emotional regulation resulting in increased emotional distress, physiological arousal and decreased well-being (Charles, 2010; Charles & Luong, 2013).

Neuroticism at its core is a difficulty in emotional regulation, and those higher in neuroticism are “more reactive to threats and negative emotional stimuli” (Mueller et al., 2019,

p. 8). As such, within the context of declining resources, those higher in neuroticism may be less able to use resources to promote coping and emotional regulation, as these have not been strengths throughout their lives. SAVI further posits that sensitivity to "physiological perturbations" (Eysenck, 1963/1998 cf. Charles, 2010, p. 1084) in those high in neuroticism may limit their emotion regulation ability, which has applicability in the present research due to the many physical symptoms experienced towards the end of life in each illness group. In the same vein, low neuroticism may be protective, such that even in the context of a stressor such as illness, those low in neuroticism approaching the end of life may be able to utilize the skills gained throughout their lives including attentional, appraisal, and behavioural strategies to manage the various sources of distress at the end of life (Charles, 2010).

In contrast to theory suggesting that neuroticism is a vulnerability at end-of-life, an alternate perspective is that neuroticism may be protective, at least under some circumstances. Selective optimization with compensation theory (SOC; Baltes & Baltes, 1990), suggests that successful aging involves the selection of important goals, and a focus on optimizing resources and compensating for age-related losses. Within the context of terminal illness, threats to the self become increasingly salient, and personality, in particular neuroticism, may play an important role in increasing behavioural inhibition (fear or withdrawal from unfamiliar or risky situations) (Hirshfeld-Becker et al., 2008) and thus avoiding additional burden "in the face of severe resource constraints" (Mueller et al., 2019, p. 11). As such, higher levels of neuroticism may predispose individuals to poor coping and increased distress in the face of threat, but may also be protective against compounding losses (Mueller et al., 2019) and thus reduce distress. The aforementioned theories have not been explored within specific illness populations who are actually approaching death. The threats and stressors within various illnesses likely have both

overlapping and unique stressors, related to the commonality in the dying process (e.g., existential concerns, anticipatory grief, loss of control) but differences in course and symptoms that may be associated with distress. As such, understanding how neuroticism may moderate the impact of various symptoms (stressors/losses) - which may be differentially problematic across illness groups – on depression, adds to this theoretical literature.

Self-other agreement. SAVI is informative regarding how people evaluate themselves in the context of diminished time horizons (Charles, 2010). When assessing older adults regarding affective experiences, "...questions often demand that people weigh information about themselves against what they perceive about other people, or what them perceive about themselves at other points of time to form their basis of comparison...age-related changes result from an awareness of diminished temporal horizons and the self-knowledge and social expertise gained from time lived." (Charles, 2010, p. 1071). Caregivers may not have access to this self-reflective process, which may contribute to incongruent ratings. Interestingly, models of self-other agreement such as the self-other asymmetry model (SOKA; Vazire, 2010), propose and demonstrate experimentally that neuroticism is more difficult to judge that other personality traits such as extraversion because neuroticism is less observable. Yet, the aforementioned studies examining congruence in ratings of patients' personality in couples within illness populations show the opposite, with highest agreement for neuroticism (Haider et al., 2002; Schwartz et al., 2011). As such, there may be significant differences in examining personality agreement within the context of samples experiencing serious illness as compared to college and/or acquaintance-based samples that are commonly used within personality research. Use of multilevel modelling in assessing congruence is thus valuable because it can take into account

variables that influence the perceptions and characteristics of observers as well as those being observed.

The Present Research

This thesis is comprised of two studies in which I conducted secondary analysis of data collected in the study *Dignity and Distress across End-of-Life Populations* study, funded by the Canadian Institutes for Health Research (Chochinov et al., 2016; Chochinov et al., 2009-2012). Data was collected between February, 2009 and December, 2012 in Winnipeg, Manitoba and Edmonton, Alberta. Clinical staff in outpatient clinics, inpatient facilities and personal care homes identified potential participants for the study based on the following criteria. For ALS, participants 1) had a confirmed diagnosis of ALS, and 2) had symptoms or limitations in a domain that interfered with their social or occupation functioning: a) mobility, b) dysphasia, c) dyspnea, or d) speech, and were 18 years of age or older. For COPD, participants were 65-80 years of age with Stage 4 disease based on GOLD classification (FEV1/FVC < 70%, FEV1 post-bronchodilator < 30% predicted, or FEV1 post-bronchodilator < 50% predicted plus chronic respiratory failure) (GOLD, 2014). For ESRD, participants were on dialysis > 3 months and 65-80 years of age. For the frail elderly, participants 1) were > 80 years of age; 2) resided in a Personal Care Home (PCH); and 3) required assistance with two or more basic activities of daily living (bathing, dressing, toileting, grooming, feeding, ambulation); (Katz, Ford, Moskowitz, Jackson, & Jaffe, 1963).

Participants in all groups were required to be able to read and understand English and be competent to provide informed consent and engage in the protocol, determined by clinical consensus, or if there was uncertainty, a score of ≤15 on the short Blessed Orientation-Memory-Concentration (BOMC) test (Katzman et al., 1983). Participants could not meet entry criteria for

more than one group. A total of $N = 404$ patients participated in the study (ALS = 101; COPD = 100; ESRD = 101; Frail Elderly = 102). A total of $N = 216$ of these participants had an identified caregiver as a co-participant who completed the NEO-FFI inventory (Costa & McRae, 1992) as a proxy for the patient (in addition to other proxy measures discussed in (Hack et al., 2018)), and also completed measures of their own health and functioning. The broad nature of this sample in terms of illness group and measurements taken at two time points has allowed for a unique exploration into the intersection of neuroticism and distress longitudinally, and the assessment of neuroticism at the end of life.

Chapter Two explores neuroticism as a moderator between illness-related symptoms at Time 1 (approximately six months prior to death) on depression at Time 2 (approximately three months prior to death). Chapter Three explores congruence between patient-participants and their caregivers on patients' neuroticism, as measured by the NEO-FFI (Costa & McRae, 1992). While the first study examines the role of neuroticism in distress, the focus of the second study was to explore who is able to report on patient neuroticism. Given the severity of illness in the populations studied, reducing burden is important. In this study, I examined both degree and predictors of patient-caregiver congruence of patient neuroticism. Chapter Four presents a summary regarding neuroticism in the four illness groups, in addition to general commentary regarding theoretical and practical applications of the findings.

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Chapter Two: Neuroticism moderates the longitudinal relationship between illness-specific symptoms and depression in four non-cancer illnesses at the end of life

Introduction

Depression is one of the most common mental health problems faced by individuals with terminal illness, yet remains "misunderstood, underdiagnosed, and undertreated" (Breitbart & Dickerman, 2019; Wilson, 2009). Reasons for this include limited understanding by clinicians regarding normal emotional experience versus clinically significant symptoms in those approaching death, difficulty distinguishing physical symptoms from symptoms of depression, and uncertainty regarding use of psychotropic medications and psychotherapy in this medically complex population (Massie, 1989; Wilson, Lander, & Chochinov, 2009). Facilitating clinicians to be better equipped in recognizing and treating depression at the end-of-life has significant implications for patients' and families' quality of life (Breitbart & Dickerman, 2019). Further, undertreated depression can reduce treatment adherence and increase physical symptoms related to the patients' medical illness, and "...also impairs the patient's capacity for pleasure, meaning, connection, and doing the emotional work of separating and saying goodbye." (Breitbart & Dickerman, 2019).

Neuroticism is described as a tendency toward negative affect, which includes low emotional stability, anger, self-consciousness, anxiety, irritability, and depression (Widiger, 2009) and has been identified as the central biological and psychological vulnerability to experiencing emotional disorders (Barlow, 2008, p. 238). The broad trait of neuroticism is comprised of six facets; anxiety, angry hostility, depression, self-consciousness, impulsivity, and vulnerability to stress (Costa, 1992). Emerging research demonstrates that each facet is associated with unique genetic variants and biological pathways, associated with phenotypically-

related psychological disorders (Kim et al., 2017). According to the "triple vulnerability" model (Barlow, 2000), the trait of neuroticism develops and is expressed as a function of general biological (e.g., genetic and neurobiological reactivity in brain structures associated with emotion) and psychological vulnerabilities (e.g., sense of uncontrollability, perceived inability to cope), which together contribute to a dysregulated stress response. Neuroticism in turn predicts the development of emotional disorders, the specifics of which is moderated by specific psychological vulnerability (i.e., a learned focus of distress). Emotional disorders in turn loop back and impact general biological and psychological vulnerabilities to neuroticism (Barlow, Ellard, Sauer-Zavala, Bullis, & Carl, 2014).

It is thus no surprise that neuroticism is one of the most robust and consistent predictors of depression (e.g., Brown & Naragon-Gainey, 2013; Enns & Cox, 1997), and in older adults, predicts first time major depressive episodes and longitudinal depression symptoms (Eldesouky, Thompson, Oltmanns, & English, 2018). The majority of literature on depression at the end-of-life focuses on patients with cancer, with prevalence rates reported between 13-26 percent (Breitbart & Dickerman, 2019). There is less literature on depression in non-cancer populations at the end of life, but what is available indicates similarly increased rates in comparison to the general population (e.g., Matte et al., 2016).

Coping with illness can be impacted by aspects of the illness itself, such as physiological symptoms (e.g., pain, dyspnea, nausea) that may interact with psychological symptoms (e.g., depression and anxiety). These illness-related factors have been studied extensively in relation to coping with illness and end-of-life (Breitbart, Gibson, & Chochinov, 2004; Chochinov, Hack, Hassard, et al., 2002; Chochinov, Hack, McClement, Kristjanson, & Harlos, 2002; Ganzini & Chochinov, 2004; Wilson et al., 2007). It is well known that physical suffering is associated with

depression and desire for death and the end of life (Wilson et al., 2007). Given the significant barriers to adequate assessment and treatment of depression in these populations, there is great clinical value in aiding identification of those at risk for depression.

Neuroticism also plays a key role in coping with chronic and terminal illness. Sensitivity to threat and emotional instability, characteristic of neuroticism, is associated with avoidant coping, aimed at circumventing the distress which these individuals so easily experience (Carver & Connor-Smith, 2010; Caspi, Roberts, & Shiner, 2005; Costa, 1987; McCrae & Costa, 2004b; McCrae, 2003). In patients with cancer, high neuroticism longitudinally predicts distress and poor health related quality of life (Aarstad, Beisland, & Aarstad, 2012). Sense of coherence, a coping orientation in which health stressors are seen as predictable and that there are resources available to meet the demands of the illness (Antonovsky, 1987), has been negatively associated with neuroticism (Gibson & Cook, 1996). In terms of day-to-day functioning with illness, in populations with cancer, daily stressors are associated with negative mood for those high in neuroticism, regardless of perceived control, whereas those lower in neuroticism only experienced the impact of daily stresses on low mood if they also had low perceived control (Diehl & Hay, 2013).

Researchers and clinicians increasingly recognize the need to expand research in palliative and end-of-life care to non-cancer populations (Addington-Hall & Higginson, 2001; Moens, Higginson, & Harding, 2014) and recognize that patients dying of non-cancer illnesses experience similar physical and psychological issues as those with cancer, including dyspnea, pain, depression, and anxiety (Stiel et al., 2014). Amyotrophic lateral sclerosis (ALS), chronic obstructive pulmonary disease (COPD), end-stage renal disease (ESRD) and frailty are four of these understudied illness populations. These populations vary in terms of what is known about

symptom distress, personality, and depression (as well as the interplay of the three) at the end-of-life, and have both unique and overlapping characteristics that are relevant to the end-of-life experience of patients, reviewed below.

ALS. There is a wealth of information regarding the psychological distress faced by patients with ALS, however, there is limited research exploring the role of personality in such distress. Newly diagnosed ALS patients have significantly lower levels of (caregiver rated) openness on the NEO compared to other newly diagnosed neurological conditions, suggesting possible common genetic predispositions for this personality profile and the development of ALS (Grossman, Levin, & Bradley, 2006). Prevalence of major depression in late-stage ALS patients has been reported at 9%, with 10% of patients experiencing minor depression and over 80% of patients experiencing no depression (Rabkin et al., 2005). The proportion of patients with no depression in ALS has been linked to low neuroticism and high extraversion, which also buffer anxiety and depression in the general population (Moore, Moore, & Shaw, 1998).

COPD. Psychiatric disorders are three times more common in patients with COPD compared to the general population (Yohannes, Baldwin, & Connolly, 2000), with clinical depression prevalence estimated between 10-42% and anxiety estimated between 10-19% (Kunik et al., 2005). There is evidence that men with COPD are more harm-avoidant and are less self-directed than healthy controls (Kahraman et al., 2013), suggesting increased levels of neuroticism and decreased conscientiousness, which can account for decreased treatment adherence and reduction of overall functioning (Felker et al., 2001)

ESRD. Patients with ESRD experience many comorbidities including respiratory distress, heart disease, pain, and sexual dysfunction (Brown & Johansson, 2011; Kop et al., 2011; Nicholl et al., 2012; Salman, 2011; Wang et al., 2013). Additionally, mental health problems are

common in patients with ESRD, who when on dialysis have increased risk of suicide, suicidal ideation, and self-harm, which are associated with increased depression and anxiety (Pompili et al., 2013). Pain in ESRD also increases the risk of depression and is associated with a desire to withdraw from dialysis (Davison & Jhangri, 2005).

There is a large burden on patients in terms of self-care in ESRD, with dietary modifications, fluid management, and depending on treatment type, self-administered dialysis. Patients with increased self-control and resourcefulness are better able to manage fluid intake, a key factor in managing ESRD and dialysis (Rosenbaum & Smira, 1986). Research also shows increased trait anxiety and decreased aggression in dialysis patients (Björvell & Hylander, 1989). It is thus clear that elements of personality play a significant role in the illness experience of patients with ESRD, however, there is a paucity of recent literature on this topic and no research specifically exploring neuroticism in relation to mental health in this illness group.

Frailty. In comparing frail to non-frail elders who are at risk for falls, those with frailty are significantly more likely to be clinically depressed, which in turn predicts anxiety (Ni Mhaolain et al., 2012). The dispositional tendency toward positive affect (characteristic of individuals high in traits of agreeableness and optimism, and low in neuroticism) is a protective factor in the development of frailty (Ostir, Ottenbacher, & Markides, 2004). Further, older adults who are harm-avoidant and prone to worry, which is characteristic of neuroticism, are significantly more likely to report functional disability, regardless of frailty status (Wilson et al., 2006). Taken together, these findings suggest a key role for personality in both the perception of distress and objective level of disability. However, the present research will significantly expand this knowledge by directly assessing the impact of personality on various markers of distress and functionality in an already frail cohort.

Clearly, there is significant impact of neuroticism in terms of mood and coping in how one experiences illness, which may vary across diseases and symptoms. As such, identifying neuroticism as early as possible in the disease process, and understanding how it interacts with physical symptoms may aid clinicians in identifying those who are vulnerable to depression early, thus providing timely and appropriate treatment towards the end-of-life.

Therefore, the purpose of the present study was to examine whether neuroticism moderates the longitudinal relationship between physical symptoms and later depression in ALS, COPD, ESRD and frailty. I hypothesized that physical symptoms at baseline would be associated with increased depression (approximately) three months later for those high in neuroticism. To examine this, we tested whether neuroticism moderated the relationship between Time 1 physical symptoms and Time 2 depression. I examined this model individually for each illness group and controlled for Time 1 depression, Time 2 symptom on the Edmonton Symptom Assessment Scale-Revised (ESAS-R), age, and gender.

Method

Sample

I analyzed data collected in the study *Dignity and Distress across End-of-Life Populations*, funded by the Canadian Institutes for Health Research (Chochinov et al., 2016). This project involved a prospective, longitudinal, multi-site approach to examine physical, psychological, existential, and spiritual issues of patients with ALS, COPD, ESRD, and the frail elderly. For additional information concerning the data collection protocol and inclusion criteria see (Chochinov et al., 2016).

A total of $N = 663$ eligible patient-participants were approached for the study, with $N = 249$ declining participation and $N = 10$ ineligible due to level of cognitive impairment, resulting

in a total sample of $N = 404$ patient-participants. Participants were assessed at baseline (approximately six months prior to expected death) and three months later, allowing for longitudinal analyses. Demographics of the participants included in the present analyses are presented in Table 1. Date of death was tracked until September 2013, by which time 45% of participants had died (between groups, time of participation to death ranged from 1.1 to 1.6 years). The study was approved by the University of Manitoba Health Research Ethics Board.

Measures

Measures are included in Appendix B. Participants provided information regarding their age, gender, marital status, religion, education, and income, as summarized in Table 1. To measure neuroticism, participants completed the 12-item neuroticism subscale from the NEO-FFI a short-form, self-report measure of neuroticism (Costa & McRae, 1992; McCrae & Costa, 2004). This robust measure of personality is one of the most commonly used assessments of non-pathological personality in the health and social sciences. Internal consistency of the subscale is reported at $\alpha = 0.82$-0.86 across thousands of participants (high school students to older adults), with significant positive correlations with self- and other reported adjective scales ($r = 0.33$-0.44) and the longer NEO-PI-R neuroticism scale ($r = 0.75$) (McCrae & Costa, 2004). Internal consistency in the current sample was $\alpha = 0.83$. Higher scores indicate greater neuroticism [scored 0 (strongly disagree) to 4 (strongly agree), with a possible range of 0-48].

Depression was measured using the seven depression items from the Hospital Anxiety and Depression Scale (HADS). This measure was chosen as it was developed specifically for medically ill populations and thus does not include somatic symptoms of depression which may represent or overlap with physical illness symptoms (Olver & Hopwood, 2013; Zigmond & Snaith, 1983). The HADS is rated on a 0 (not at all/seldom) to 3 (most of the time/definitely)

scale in which high scores indicate greater depression, ranging from 0 (normal/no depression) to 21 (severe depression). The internal consistency reported in the literature is $\alpha = 0.82$, and r = 0.49-0.83 for concurrent validity with other measures (Bjelland, Dahl, Haug, & Neckelmann, 2002; Zigmond & Snaith, 1983). Internal consistency for the current sample was $\alpha = 0.76$.

Physical symptoms (pain, nausea, drowsiness, shortness of breath, anxious, fatigue, trouble sleeping, constipation, diarrhea, weakness, dizziness, difficulty thinking, appetite), as well as non-physical experiences (will to live, wellbeing, activity level) were assessed using the Revised Edmonton Symptom Assessment Scale (ESAS-R), a 16-item measure intended to assess 16 individual symptoms rather than as a total score. These single items are scored 0 (low/poor/no) -10 (high/very/strong). For items 1-12 (pain, nausea, drowsiness, shortness of breath, anxiety, fatigue, constipation, diarrhea, insomnia, weakness, dizziness, difficulty thinking), a higher score is indicative of worse functioning. For items 13-16 (will to live, appetite, active, wellbeing) a higher score is indicative of better functioning (Bruera, Kuehn, Miller, Selmser, & Macmillan, 1991). Scores on ESAS-R items correlate highly with other symptom assessment measures, and same-day test-retest reliability is above 0.8. The measure has been validated in a range of illness groups and in several cultures, and is among the most widely used symptom assessment tools in palliative care (Richardson & Jones, 2009).

Statistical analyses

Descriptive and correlational analyses were performed using SPSS 25 (IBM, 2017). Moderation analyses were conducted using the PROCESS v.3 macro (Model 1) for SPSS 25, which includes computational tools for estimating and probing interactions (Hayes, 2018). We ran Model 1 individually for each illness group with each Time 1 ESAS-R item as predictor, neuroticism as the moderator, and Time 2 HADS depression symptoms as the outcome. All

presented regression coefficients are unstandardized as recommended by Hayes (2018). Neuroticism and ESAS-R symptom were mean-centered for ease of interpretation. ESAS-R symptom and neuroticism, together with their interaction term were entered into the linear regression model to predict depression. Age, gender, Time 1 depression and Time 2 ESAS-R symptom were included as covariates. All assumptions of OLS regression were met. Though the variables in the model had moderate positive skews, analysis of the residuals of the above models yielded normal distributions and, as a result, there was no need to transform them (e.g., Ernst & Albers, 2017; Habeck & Brickman, 2014; Hayes, 2018; Howell, 2007).

The difficulty of low power in moderation analyses is well known in the social sciences (Shieh, 2009), with small effect sizes for the interaction being common (Aguinis, Edwards, & Bradley, 2017). As the above analyses were underpowered given the sample size of each illness group (Cohen's *d* for range of interaction affects = 0.14 - 0.38), we relied on the Rsq-change effect sizes proposed by Green (1991) for moderated multiple regression, where change in R^2 after adding the interaction term of .008, .07, and 0.194 are considered small, medium, and large effects, respectively (Bodner, 2017).

Results

Descriptive statistics and correlations

Demographic information is presented in Table 1 and descriptive statistics for the ESAS-R symptoms, neuroticism, and depression, are presented by illness group in Table 2. Zero-order correlations of the predictors, covariates and outcome are presented by group in Table 3.

Table 1. *Demographics by illness group*

	ALS	COPD	ESRD	FE	p-value
N	99	99	97	99	394
		M (SD)			
Age (years)	63.87 (12.07)	72.34 (4.86)	72.25 (4.40)	88.11 (5.02)	<.001
		N (%)			
Gender					0.01
Male	66 (66.7)	39 (39.4)	56 (57.7)	41 (41.4)	
Marital Status					<.001
Married or common-law	67 (67.7)	50 (50.5)	49 (50.5)	13 (13.1)	
Other	32 (32.3)	49 (49.5)	48 (49.5)	86 (86.9)	
Religion					<.01
Roman Catholic	28 (28.6)	28 (28.3)	24 (25.0)	22 (22.2)	
Protestant	18 (18.4)	24 (24.2)	35 (36.5)	29 (29.3)	
Jewish	0	0	2 (2.1)	9 (9.1)	
Muslim	1 (1.0)	0	2 (2.1)	0	
Other	27 (27.6)	22 (22.2)	18 (18.8)	23 (23.2)	
Education					0.01
Some elementary	1 (1.0)	3 (3.0)	7 (7.2)	4 (4.0)	
Grade 8	3 (3.1)	8 (8.1)	10 (10.3)	6 (6.1)	
Some high school	19 (19.4)	35 (35.4)	26 (26.8)	35 (35.4)	
Grade 12	21 (21.4)	19 (19.2)	18 (18.6)	12 (12.1)	
Some university/college	21 (21.4)	17 (17.2)	12 (12.4)	14 (14.1)	
	25 (25.5)	14 (14.1)	22 (22.7)	16 (16.2)	
University/college complete					
Postgraduate	8 (8.2)	3 (3.0)	2 (2.1)	12 (12.1)	
Income					<.001
<60k/year	48 (48.4)	70 (70.7)	70 (72.2)	47 (47.5)	
>60k/year	24 (24.2)	8 (8.0)	15 (15.5)	6 (6.1)	
No answer	27 (27.3)	21 (21.2)	12 (12.4)	46 (46.5)	

Table 2. *Descriptive statistics of Time 1 and Time 2 ESAS symptoms, depression, and neuroticism by illness group*

	ALS		COPD		ESRD		FE		p-value	p-value
	Time 1	Time 2	Time 1	Time 2	Time 1	Time 2	Time 1	Time 2	Time 1 between groups	Time 2 between groups
	N									
	99	69	99	82	97	86	99	76	390	309
	M (SD) p-value Time 1 to Time 2 within group*									
Pain[a]	2.33 (2.64)	2.43 (2.56)	3.48 (3.60)	2.88 (2.98)	3.05 (3.18)	3.07 (3.11)	2.77 (3.09)	2.18 (2.61)	0.07	0.19
	0.47		0.20		1.00		0.06			
Nausea[a]	0.55 (1.40)	0.59 (1.26)	0.76 (1.80)	0.71 (1.62)	1.07 (2.09)	0.77 (1.96)	0.68 (1.63)	0.71 (1.73)	0.19	0.94
	0.71		0.32		0.27		0.54			
Drowsiness[a]	2.18 (2.70)	2.30 (2.73)	2.38 (2.86)	2.05 (2.66)	2.55 (2.84)	2.36 (2.76)	1.59 (2.36)	1.76 (2.49)	0.07	0.48
	0.50		0.89		0.28		0.26			
Shortness of breath[a]	2.88 (3.07)	3.51 (2.82)	6.03 (2.88)	5.50 (3.04)	1.52 (2.29)	1.45 (2.29)	1.12 (1.96)	1.08 (1.90)	<.001	<.001
	<.01		0.36		0.72		0.74			
Anxious[a]	2.41 (2.64)	2.25 (2.30)	3.36 (3.37)	3.20 (3.21)	1.69 (2.50)	1.45 (2.34)	1.43 (2.33)	1.58 (2.48)	<.001	<.001
	0.56		0.58		0.42		0.48			
Fatigued[a]	4.38 (2.83)	4.25 (2.72)	4.13 (3.17)	3.55 (3.11)	3.82 (3.14)	3.69 (3.0)	2.63 (2.78)	3.03 (2.98)	<.001	0.11
	0.44		0.58		0.37		0.69			
Constipation[a]	1.81 (2.72(	1.84 (2.82)	1.00 (2.30)	1.01 (2.82)	1.61 (2.73)	1.66 (2.83)	1.69 (2.84)	1.66 (2.59)	0.72	0.29
	0.79		0.91		0.94		0.50			
Diarrhea[a]	2.37 (1.47)	0.72 (1.88)	0.23 (1.21)	0.41 (1.63)	1.06 (2.05)	0.84 (2.11)	0.65 (2.03)	0.72 (1.95)	0.26	0.57
	0.15		0.35		0.47		0.74			
Trouble sleeping[a]	1.90 (2.51)	2.06 (2.72)	2.47 (3.45)	2.01 (2.90)	3.27 (3.31)	2.71 (2.87)	1.40 (2.50)	1.36 (2.40)	<.001	0.02
	0.57		0.17		**0.03**		0.86			

(continued)

(continued)

	ALS		COPD		ESRD		FE		p-value	p-value
	Time 1	Time 2	Time 1	Time 2	Time 1	Time 2	Time 1	Time 2	Time 1 between groups	Time 2 between groups
Weakness[a]	5.71 (3.22)	5.44 (3.07)	3.42 (3.15)	2.99 (3.09)	3.24 (2.98)	2.76 (3.05)	2.51 (2.87)	2.43 (2.79)	<.001	<.001
	0.53		0.65		0.10		0.28			
Dizziness[a]	0.67 (1.33)	0.57 (1.56)	1.47 (2.46)	1.24 (2.24)	0.92 (1.92)	1.03 (2.21)	0.85 (2.02)	0.67 (1.60)	0.03	0.12
	0.47		0.71		0.91		0.37			
Difficulty thinking[a]	0.70 (1.53)	1.0 (1.93)	0.91 (2.05)	0.52 (1.42)	1.00 (2.02)	0.83 (1.74)	1.29 (2.39)	1.16 (1.87)	0.23	0.13
	0.22		0.67		0.07		0.36			
Will to live[b]	8.39 (2.89)	8.22 (2.98)	9.30 (1.75)	9.00 (2.34)	9.00 (2.27)	8.95 (2.22)	8.15 (2.73)	8.38 (2.68)	0.05	0.10
	0.57		0.12		0.80		0.48			
Appetite[a]	6.75 (3.36)	6.36 (3.36)	7.49 (3.08)	7.27 (3.00)	8.11 (2.41)	8.12 (2.38)	7.43 (2.59)	7.49 (2.78)	0.003	0.01
	0.22		0.54		0.83		0.37			
Active[a]	3.97 (2.61)	3.70 (2.73(	4.86 (2.73)	4.42 (3.13)	5.91 (2.58)	5.93 (2.77)	4.31 (2.68)	4.09 (2.93)	<.001	<.001
	0.40		0.16		0.90		0.33			
Sense of wellbeing[c]	6.91 (3.03)	6.34 (2.84)	7.82 (2.19)	7.63 (2.88)	7.83 (2.12)	7.72 (2.56)	8.03 (2.64)	7.75 (2.58)	0.27	0.55
	0.89		0.42		0.79		0.06			
Depression[d]	5.63 (3.60)	6.13 (3.81)	5.43 (3.72)	5.23 (3.51)	3.92 (3.15)	3.85 (3.02)	4.72 (3.40)	5.07 (3.68)	0.002	0.001
	0.52		0.60		0.59		0.32			
Neuroticism[e1]	15.86 (6.87)		17.83 (7.93)		13.98 (7.25)		15.40 (7.04)		0.003	

[*]Paired sample t-test
[a]ESAS-R item; scored 0 (low) to 10 (high/very)
[b]ESAS-R item; scored 0 (no will to live) to 10 (strong will to live)
[c]ESAS-R item; scored 0 (poor sense of wellbeing) to 10 (very good sense of wellbeing)
[d]HADS (depression items only); Scored 0 (normal/no depression) to 21 (severe depression) (scores over 8 signal clinically relevant symptoms)
[e]NEO-FFI
[1]only collected at Time

Table 3a. *Correlations - ALS*

		Age	Gen	1	2	3	4	5	6	7	8	9	10
	Age in years	1.00											
	Gender	0.12	1.00										
1	Pain1	-.25*	0.17	1.00									
2	Pain2	-0.12	0.19	.50**	1.00								
3	Nausea1	-0.09	0.05	.36**	.38**	1.00							
4	Nausea2	-0.13	-0.10	0.08	0.23	.53**	1.00						
5	Drowsiness1	-0.08	0.00	0.17	0.17	.34**	.32**	1.00					
6	Drowsiness2	-0.03	0.08	.27*	.40**	0.17	.28*	.52**	1.00				
7	Shortness of breath1	-0.02	0.01	.22*	0.08	.31**	.28*	.43**	0.16	1.00			
8	Shortness of breath2	-0.06	0.02	.24*	0.10	.30*	.37**	.37**	0.21	.71**	1.00		
9	Anxious1	-0.18	0.00	.28**	0.19	0.14	-0.15	0.04	0.15	0.07	0.16	1.00	
10	Anxious2	-0.11	0.15	0.24	.38**	0.04	0.03	0.09	.35**	0.08	0.24	.40**	1.00
11	Fatigued1	-0.04	0.07	.33**	.35**	0.19	0.23	.46**	.39**	.41**	.32**	.29**	.37**
12	Fatigued2	-0.14	0.02	.32*	.31*	0.17	0.16	.41**	.46**	0.17	0.24	0.18	.40**
13	Trouble sleeping1	-.25*	0.08	0.18	0.19	0.13	0.03	0.15	0.05	0.19	0.21	.37**	0.04
14	Trouble sleeping2	-.45**	0.04	.42**	.30*	.37**	0.21	0.20	0.13	0.17	.28*	0.17	0.20
15	Weakness1	-0.12	-0.14	0.15	0.23	0.05	0.08	.32**	.25*	.25*	0.22	0.16	0.08
16	Weakness2	-0.08	-0.04	.44**	.31*	0.09	-0.05	.36**	0.22	.28*	.43**	.36**	0.22
17	Dizziness1	-0.04	-0.08	.32**	.36**	.50**	0.17	0.08	0.14	0.11	-0.01	.25*	0.18
18	Dizziness2	-0.01	0.04	0.16	0.18	0.20	0.01	0.07	.34**	-0.16	0.00	0.06	0.12
19	Difficulty thinking1	0.03	-0.04	0.13	0.14	.28**	0.04	0.05	0.18	0.01	-0.05	.28**	.28*
20	Difficulty thinking2	0.02	0.11	0.10	.31*	0.08	0.11	0.01	.28*	0.02	0.07	0.07	.50**
21	Neuroticism	0.16	0.08	0.01	0.01	0.07	-0.12	0.03	0.09	0.08	0.05	.48**	.28*
22	Depression1	0.11	0.04	0.10	0.18	0.02	-0.04	0.15	0.15	0.15	0.10	.30**	0.12
23	Depression2	0.08	-0.03	0.07	.28*	-0.09	-0.05	0.11	0.21	.26*	.33**	.36**	.30*

(continued)

(continued)

		11	12	13	14	15	16	17	18	19	20	21	22	23
	Age in years													
	Gender													
1	Pain1													
2	Pain2													
3	Nausea1													
4	Nausea2													
5	Drowsiness1													
6	Drowsiness2													
7	Shortness of breath1													
8	Shortness of breath2													
9	Anxious1													
10	Anxious2													
11	Fatigued1	1.00												
12	Fatigued2	.71**	1.00											
13	Trouble sleeping1	0.18	0.16	1.00										
14	Trouble sleeping2	0.16	0.24	.48**	1.00									
15	Weakness1	.39**	.31*	0.07	0.09	1.00								
16	Weakness2	.58**	.56**	0.22	.32**	.62**	1.00							
17	Dizziness1	.25*	0.15	0.12	0.23	0.13	0.13	1.00						
18	Dizziness2	0.01	0.12	0.14	0.11	0.06	0.12	0.18	1.00					
19	Difficulty thinking1	0.19	0.15	0.12	-0.09	-0.06	-0.11	.40**	0.08	1.00				
20	Difficulty thinking2	0.23	0.17	-0.16	-0.14	-0.03	-0.02	.30*	0.11	.50**	1.00			
21	Neuroticism	.23*	0.05	0.15	0.05	.22*	0.16	0.10	0.13	.23*	0.16	1.00		
22	Depression1	.36**	0.22	0.19	-0.08	.33**	.36**	0.06	0.20	0.09	0.12	.87**	1.00	
23	Depression2	.35**	0.19	0.16	0.04	.35**	.47**	0.10	0.16	-0.08	0.20	.37**	.68**	1.00

Table 3b. *Correlations – COPD*

		Age	Gen	1	2	3	4	5	6	7	8	9	10
	Age in years	1.00											
	Gender	-0.05	1.00										
1	Pain1	-0.05	0.13	1.00									
2	Pain2	-0.02	0.07	.73**	1.00								
3	Nausea1	-0.05	0.05	.37**	.31**	1.00							
4	Nausea2	-0.03	0.00	.27*	.27*	.48**	1.00						
5	Drowsiness1	-0.03	0.03	.26*	.23*	.48**	.42**	1.00					
6	Drowsiness2	.23*	-0.16	0.17	.29**	.28*	.41**	.60**	1.00				
7	Shortness of breath1	0.00	-.25*	0.18	.25*	0.12	0.16	.25*	.22*	1.00			
8	Shortness of breath2	-0.04	-.29**	-0.12	0.00	-0.04	0.00	0.12	0.12	.52**	1.00		
9	Anxious1	0.06	0.05	.44**	.35**	.32**	.27*	.23*	0.18	.48**	0.18	1.00	
10	Anxious2	-0.04	0.05	0.18	.35**	.27*	.41**	0.14	.32**	0.22	0.20	.47**	1.00
11	Fatigued1	0.00	-0.01	.45**	.46**	.36**	.28*	.49**	0.20	.36**	.33**	.51**	.29*
12	Fatigued2	0.01	-.22*	.28*	.40**	.29*	.24*	.40**	.44**	.26*	.48**	.24*	.34**
13	Trouble sleeping1	0.00	-0.03	.34**	.36**	.29**	0.22	.32**	.30**	.23*	0.02	.22*	0.18
14	Trouble sleeping2	0.20	0.01	.31**	.33**	0.18	.40**	.44**	.42**	0.17	0.14	0.14	.28*
15	Weakness1	0.02	-0.12	.28**	.25*	.40**	0.15	.40**	0.19	.47**	0.21	.46**	.25*
16	Weakness2	-0.01	-0.18	0.10	.28*	.27*	.33**	.42**	.33**	.37**	.52**	.27*	.30**
17	Dizziness1	0.03	-0.03	.41**	.41**	.48**	.33**	.56**	.47**	.20*	0.14	.30**	.27*
18	Dizziness2	0.13	-0.12	0.15	0.19	0.19	.45**	.35**	.36**	0.14	0.10	0.00	0.22
19	Difficulty thinking1	-0.07	0.10	.35**	0.18	.32**	0.12	.34**	0.06	.21*	0.20	.34**	0.13
20	Difficulty thinking2	-0.04	-0.16	0.15	0.11	.41**	.49**	.28*	.31**	0.15	0.13	0.11	.25*
21	Neuroticism	0.06	0.09	.38**	.47**	.33**	.28*	.33**	.30**	.49**	.23*	.58**	.41**
22	Depression1	-0.07	-0.11	.22*	.24*	.24*	.31**	.27**	0.13	.50**	.33**	.42**	0.20
23	Depression2	-0.13	-0.16	.29**	.36**	.27*	.26*	.26*	0.20	.47**	.48**	.41**	.32**

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		11	12	13	14	15	16	17	18	19	20	21	22	23
	Age in years													
	Gender													
1	Pain1													
2	Pain2													
3	Nausea1													
4	Nausea2													
5	Drowsiness1													
6	Drowsiness2													
7	Shortness of breath1													
8	Shortness of breath2													
9	Anxious1													
10	Anxious2													
11	Fatigued1	1.00												
12	Fatigued2	.68**	1.00											
13	Trouble sleeping1	.28**	.34**	1.00										
14	Trouble sleeping2	0.22	.35**	.549**	1.00									
15	Weakness1	.48**	.27*	.523**	0.19	1.00								
16	Weakness2	.45**	.58**	0.20	.26*	.43**	1.00							
17	Dizziness1	.43**	.40**	.336**	0.21	.42**	.40**	1.00						
18	Dizziness2	.26*	.33**	.338**	.39**	.34**	.40**	.45**	1.00					
19	Difficulty thinking1	.43**	.24*	0.16	0.02	.44**	0.21	.49**	0.18	1.00				
20	Difficulty thinking2	.34**	.32**	0.10	0.20	0.18	.25*	.31**	.48**	.50**	1.00			
21	Neuroticism	.47**	.33**	0.18	0.21	.28**	.23*	.29**	0.10	.35**	.27*	1.00		
22	Depression1	.33**	.26*	0.12	-0.08	.52**	.44**	.24*	0.21	.40**	.34**	.48**	1.00	
23	Depression2	.46**	.48**	0.13	0.11	.37**	.63**	.33**	0.16	.34**	.33**	.54**	.70**	1.00

Table 3c. *Correlations – ESRD*

		Age	Gen	1	2	3	4	5	6	7	8	9	10
	Age in years	1.00											
	Gender	0.04	1.00										
1	Pain1	0.05	.25*	1.00									
2	Pain2	0.15	.22*	.52**	1.00								
3	Nausea1	0.00	0.13	.29**	.22*	1.00							
4	Nausea2	0.12	0.17	0.06	.27*	.34**	1.00						
5	Drowsiness1	0.11	-0.08	.24*	0.20	.34**	0.17	1.00					
6	Drowsiness2	0.09	0.17	.26*	.47**	0.11	.41**	.41**	1.00				
7	Shortness of breath1	-0.14	-0.06	.20*	0.21	.38**	0.12	.33**	.21*	1.00			
8	Shortness of breath2	-0.17	0.00	0.10	.28*	.26*	0.18	.22*	.26*	.60**	1.00		
9	Anxious1	0.03	.26*	.28**	.34**	.34**	.41**	.27**	.36**	.27**	0.19	1.00	
10	Anxious2	0.07	0.16	.43**	.51**	.23*	.43**	.30**	.58**	.27*	.31**	.42**	1.00
11	Fatigued1	0.00	0.02	.33**	.24*	.29**	.23*	.52**	.25*	.33**	.22*	.50**	.25*
12	Fatigued2	0.03	0.13	.31**	.98**	.38**	.39**	.41**	.58**	.32**	.25*	.52**	.36**
13	Trouble sleeping1	0.16	0.16	.36**	.36**	0.02	0.05	.33**	.32**	0.11	0.01	.40**	.38**
14	Trouble sleeping2	0.00	0.10	.29**	.26*	0.10	0.15	.33**	.45**	.25*	.26*	.45**	.41**
15	Weakness1	0.05	-0.01	.32**	0.20	.24*	0.19	.34**	.25*	.36**	0.19	.33**	0.10
16	Weakness2	0.09	0.10	.37**	.46*	.33**	.36**	.40**	.41**	.37**	0.16	.50**	.39**
17	Dizziness1	-0.10	0.02	.27**	.30**	.42**	.31**	.29**	.29**	0.13	0.16	.32**	.30**
18	Dizziness2	-0.07	0.06	.37**	.40**	.28**	.30**	0.15	.35**	0.13	0.16	.49**	.23*
19	Difficulty thinking1	.22*	0.17	0.17	.26*	0.10	.40**	.44**	.37**	0.00	-0.02	.41**	.39**
20	Difficulty thinking2	0.21	0.18	0.17	.31**	0.06	.48**	.33**	.38**	-0.02	0.07	.25*	.56**
21	Neuroticism	-0.03	.20*	.34**	.39**	.210*	.39**	.24*	.39**	0.15	0.18	.45**	.52**
22	Depression1	0.01	0.04	.35**	.28**	0.17	0.13	.32**	.27*	0.14	0.06	.44**	.24*
23	Depression2	-0.07	0.02	0.19	0.18	0.09	0.16	.29**	.31**	0.18	0.07	.41**	.22*

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		11	12	13	14	15	16	17	18	19	20	21	22	23
	Age in years													
	Gender													
1	Pain1													
2	Pain2													
3	Nausea1													
4	Nausea2													
5	Drowsiness1													
6	Drowsiness2													
7	Shortness of breath1													
8	Shortness of breath2													
9	Anxious1													
10	Anxious2													
11	Fatigued1	1.00												
12	Fatigued2	.56**	1.00											
13	Trouble sleeping1	.34**	.26*	1.00										
14	Trouble sleeping2	.36**	.35**	.62**	1.00									
15	Weakness1	.62**	.45**	.25*	.33**	1.00								
16	Weakness2	.52**	.53**	.27*	.35**	.60**	1.00							
17	Dizziness1	.37**	.48**	0.10	0.11	.36**	.53**	1.00						
18	Dizziness2	.24*	.50**	0.14	.25*	.42**	.58**	.57**	1.00					
19	Difficulty thinking1	.28**	.35**	.28**	.32**	.31**	.35**	0.15	.33**	1.00				
20	Difficulty thinking2	0.14	.28*	.22*	.21*	.22*	.31**	.21*	.37**	.75**	1.00			
21	Neuroticism	.36**	.44**	.25*	.30**	.34**	.51**	.30**	.42**	.32**	.414**	1.00		
22	Depression1	.39**	.38**	.28**	.36**	.41**	.56**	.30**	.52**	.28**	0.16	.51**	1.00	.
23	Depression2	.32**	.37**	.26*	.27*	.26*	.40**	0.09	.34**	.30**	0.06	.41**	.76**	1.00

Table 3d. *Correlations – Frailty*

		Age	Gen	1	2	3	4	5	6	7	8	9	10
	Age in years	1.00											
	Gender	0.04	1.00										
1	Pain1	-0.01	0.12	1.00									
2	Pain2	0.03	0.08	.53**	1.00								
3	Nausea1	-0.04	.21*	0.19	0.17	1.00							
4	Nausea2	0.02	.28*	0.16	0.20	.34**	1.00						
5	Drowsiness1	0.02	-0.14	0.14	0.06	.33**	.24*	1.00					
6	Drowsiness2	-0.09	0.04	0.04	0.16	.27*	.36**	.59**	1.00				
7	Shortness of breath1	0.10	0.14	.28**	0.18	.29**	.37**	.35**	0.11	1.00			
8	Shortness of breath2	0.02	0.09	0.05	0.10	.37**	.32**	0.16	.28*	.45**	1.00		
9	Anxious1	-0.10	0.01	.31**	0.18	.30**	0.22	.27**	.29*	.25*	-0.02	1.00	
10	Anxious2	-0.10	0.06	0.15	0.23	.30**	.38**	.28*	.34**	0.02	0.09	.50**	1.00
11	Fatigued1	0.00	0.01	.27**	.30**	0.05	.26*	.42**	.49**	.26**	0.11	.47**	.42**
12	Fatigued2	0.08	0.09	.26*	.30**	0.18	.32**	.58**	.68**	.25*	.24*	0.18	.24*
13	Trouble sleeping1	-0.01	-0.09	0.13	0.13	-0.02	0.18	.28**	.50**	-0.01	0.11	0.18	.39**
14	Trouble sleeping2	-0.01	-0.12	0.15	0.16	.33**	.32**	.34**	.50**	0.15	0.18	.42**	.31**
15	Weakness1	-0.09	-0.12	.36**	0.14	0.11	0.20	.22*	.51**	.23*	0.13	.43**	0.22
16	Weakness2	0.04	0.11	0.07	0.20	0.07	.30**	0.19	.67**	0.15	.32**	0.10	0.12
17	Dizziness1	-0.03	0.03	0.06	0.04	.24*	.27*	.27**	.26*	.30**	0.20	.20*	0.12
18	Dizziness2	0.05	0.11	0.07	0.17	0.14	.43**	0.09	.40**	.31**	.51**	0.14	0.08
19	Difficulty thinking1	-0.03	-.23*	.26*	.23*	0.14	0.11	.41**	.31**	.30**	0.05	.33**	.27*
20	Difficulty thinking2	0.01	-0.16	0.13	.26*	0.20	0.15	.38**	.44**	.29*	0.17	.32**	.33**
21	Neuroticism	-0.05	0.01	0.09	0.12	-0.03	.26*	.28**	.36**	0.04	-0.04	.25*	.45**
22	Depression1	-0.07	-.20*	0.09	0.13	0.09	0.20	.26*	.39**	0.10	-0.09	.26**	.28*
23	Depression2	-0.14	-0.21	0.09	0.18	0.04	0.18	.33**	.44**	0.08	0.02	.35**	.40**

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		11	12	13	14	15	16	17	18	19	20	21	22	23
	Age in years													
	Gender													
1	Pain1													
2	Pain2													
3	Nausea1													
4	Nausea2													
5	Drowsiness1													
6	Drowsiness2													
7	Shortness of breath1													
8	Shortness of breath2													
9	Anxious1													
10	Anxious2													
11	Fatigued1	1.00												
12	Fatigued2	.68**	1.00											
13	Trouble sleeping1	.27**	.41**	1.00										
14	Trouble sleeping2	.26*	0.19	.47**	1.00									
15	Weakness1	.50**	.45**	.24*	.32**	1.00								
16	Weakness2	.34**	.60**	.31**	.26*	.63**	1.00							
17	Dizziness1	.33**	0.18	0.06	.29*	.39**	.24*	1.00						
18	Dizziness2	0.13	.29*	0.10	.29*	.36**	.48**	.44**	1.00					
19	Difficulty thinking1	.43**	.25*	.22*	.28*	.37**	0.18	.55**	0.16	1.00				
20	Difficulty thinking2	.55**	.36**	.39**	.33**	.47**	.29*	.35**	0.13	.70**	1.00			
21	Neuroticism	.50**	.34**	.31**	.34**	.36**	.35**	.36**	0.00	.38**	.52**	1.00		
22	Depression1	.38**	.37**	.25*	.28*	.37**	.24*	.24*	0.01	.29**	.43**	.50**	1.00	
23	Depression2	.61**	.40**	.35**	.29*	.50**	.34**	.29**	0.10	.40**	.52**	.66**	.78**	1.00

Moderation

I hypothesized that physical symptoms at baseline would be associated with increased depression (approximately) three months later for those high in neuroticism. The results of the moderation analyses are presented by group and summarized in Table 3. Conditional effects associated with the symptom by neuroticism interactions (the primary effects of interest) presented in Table 3 reflect values of the Time 1 symptom on Time 2 depression for individuals who are average on neuroticism (50^{th} percentile) as well as for those one standard deviation below and above the mean (16^{th} and 84^{th} percentiles, respectively) (Figures 1-4). In cases where the interaction was significant but these conditional effects were not, I further probed the interaction of neuroticism and different levels of the symptom (-1 *SD*, *M*, 1 *SD*) on depression. Due to the large number of variables assessed within and across illness groups, we only present the significant interactions in Table 3. Given the aforementioned issues with low power, and the increasing awareness of reliance on p-values alone in interpreting data (Cumming, 2014), we report on full results for interactions with a p-value of ≤ 0.1 *and* in which the corresponding confidence interval did not include zero (± 0.01) (Table 3). I thus did not find that neuroticism moderated the effect of pain, nausea, anxiety, diarrhea, dizziness, difficulty thinking, or appetite on Time 2 depression for any of the illness groups (Appendix Table 1).

Table 3. *Moderating effects of neuroticism on the relationship between ESAS-R symptoms and HADS depression*

Variables	ß	SE	95% CI		p-value	N	Rsq-change
			Lower bound	Upper Bound			
ALS						68	
Drowsy[a]	-0.17	0.16	-0.48	0.15	0.29		
Neuroticism	0.07	0.06	-0.05	0.20	0.26		
Interaction	0.05	0.03	0	0.10	**0.06**		0.0316
Conditional effects of drowsy at values of neuroticism (-1 SD, mean, 1 SD)							
-5.70	-0.45	0.24	-0.94	0.04	**0.07**		
0.42	-0.15	0.16	-0.46	0.16	0.34		
7.54	0.20	0.21	-0.22	0.62	0.34		
Age	0	0.03	-0.06	0.05	0.88		
Gender	-0.15	0.75	-1.65	1.35	0.84		
Time 1 Dep	0.66	0.11	0.44	0.89	<0.001		
Time 2 Drowsy	0.22	0.15	-0.09	0.54	0.16		
Fatigue[a]	0.23	0.18	-0.13	0.59	0.20	66	
Neuroticism	0.04	0.06	-0.08	0.16	0.49		
Interaction	0.04	0.02	0	0.08	**0.04**		0.0378
Conditional effects of fatigue at values of neuroticism (-1 SD, mean, 1 SD)							
-5.89	-0.01	0.21	-0.43	0.42	0.98		
0.39	0.25	0.18	-0.11	0.61	0.17		
7.67	0.54	0.23	0.08	1.00	**0.02**		
Age	0	0.03	-0.05	0.06	0.83		
Gender	0.15	0.74	-1.33	1.63	0.84		
Time 1 Dep	0.60	0.12	0.36	0.84	<.001		
Time 2 Fatigue	-0.08	0.18	-0.45	0.29	0.65		
Shortness of breath[a]	-0.09	0.16	-0.42	0.23	0.56		
Neuroticism	0.06	0.06	-0.06	0.18	0.34		
Interaction	0.03	0.02	-0.01	0.08	**0.11**	67	0.0195
Conditional effects of SOB at values of neuroticism (-1 SD, mean, 1 SD)							
-5.70	-0.29	0.22	-0.73	0.15	0.19		
0.30	-0.08	0.16	-0.41	0.24	0.60		
7.42	0.16	0.21	-0.25	0.57	0.44		
Age	0.01	0.71	-0.04	0.06	0.73		
Gender	0.10	0.71	0.89	-1.32	1.51		
Time 1 Dep	0.66	0.11	0.45	0.87	<.001		
Time 2 SOB	0.40	0.17	0.06	0.74	0.23		

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Variables	ß	SE	95% CI		p-value	N	Rsq-change
			Lower bound	Upper Bound			
Wellbeing[b]	-0.11	0.15	-0.41	0.20	0.49	67	
Neuroticism	0.05	0.06	-0.06	0.16	0.40		
Interaction	-0.04	0.02	-0.08	0	**0.03**		0.0316
Conditional effects of fatigue at values of neuroticism (-1 SD, mean, 1 SD)							
-5.57	0.12	0.20	-0.27	0.51	0.54		
0.55	-0.13	0.15	-0.44	0.17	0.40		
7.67	-0.42	0.20	-0.81	-0.03	**0.04**		
Age	-0.01	0.03	-0.06	0.04	0.77		
Gender	0.37	0.69	-1.01	1.76	0.60		
Time 1 Dep	0.51	0.11	0.29	0.73	>.001		
Time 2 Wellbeing	-0.35	0.16	-0.67	-0.03	0.03		
COPD						80	
Drowsy[a]	0.05	0.14	-0.23	0.34	0.70		
Neuroticism	0.09	0.04	0	0.18	**0.05**		
Interaction	0.03	0.01	0	0.06	**0.05**		0.0052
Conditional effects of drowsy at values of neuroticism (-1 SD, mean, 1 SD)							
-7.13	-0.15	0.19	-0.52	0.23	0.44		
-1.13	0.02	0.15	-0.27	0.31	0.87		
6.92	0.25	0.16	-0.07	0.56	0.12		
Age	-0.04	0.06	-0.17	0.08	0.47		
Gender	-0.18	0.56	-1.31	0.95	0.75		
Time 1 Dep	0.54	0.09	0.36	0.72	<.001		
Time 2 Drowsy	0.08	0.14	-0.20	0.36	0.57		
Trouble Sleeping[a]	-0.08	0.10	-0.27	0.12	0.44	79	
Neuroticism	0.17	0.05	0.07	0.26	<.001		
Interaction	-0.02	0.01	-0.04	0	**0.06**		0.0210
Conditional effects of trouble sleeping at values of neuroticism (-1 SD, mean, 1 SD)							
-7.13	0.05	0.13	-0.21	0.32	0.68		
-1.13	-0.06	0.10	-0.26	0.15	0.58		
7.07	-0.21	0.10	-0.42	0	**0.05**		
Age	-0.05	0.06	-0.17	0.06	0.37		
Gender	-0.49	0.55	-1.59	0.62	0.38		
Time 1 Dep	0.52	0.10	0.33	0.71	<.001		
Time 2 Trouble Sleeping	0.14	0.12	-0.10	0.37	0.25		

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Variables	ß	SE	95% CI		p-value	N	Rsq-change
			Lower bound	Upper Bound			
Will to live[c]	-0.40	0.29	-0.98	0.18	0.17	79	
Neuroticism	0.08	0.04	0	0.16	0.04		
Interaction	0.05	0.02	0	0.09	**0.02**		0.0288
Conditional effects of will to live at values of neuroticism (-1 SD, mean, 1 SD)							
-6.91	-0.75	0.39	-1.52	0.03	**0.06**		
-0.91	-0.45	0.30	-1.05	0.15	0.14		
6.29	-0.09	0.25	-0.58	0.41	0.73		
Age	-0.06	0.05	-.16	0.04	0.25		
Gender	-0.13	0.51	-1.16	0.89	0.80		
Time 1 Dep	0.49	0.09	0.32	0.67	<.001		
Time 2 Will to live	-0.57	0.15	-0.87	-0.27	<.001		
Active[a]	0.07	0.13	-0.20	0.32	0.62	75	
Neuroticism	0.11	0.04	0.02	0.19	0.01		
Interaction	-0.03	0.01	-0.05	0	**0.03**		0.0248
Conditional effects of activity at values of neuroticism (-1 SD, mean, 1 SD)							
-7.24	0.26	0.17	-0.08	0.60	0.13		
-1.24	-0.10	0.13	-0.17	0.37	0.46		
7.60	-0.14	0.15	-0.44	0.16	0.36		
Age	-0.08	0.06	-0.20	0.03	0.14		
Gender	-0.32	0.55	-1.42	0.77	0.55		
Time 1 Dep	0.41	0.10	0.20	0.62	<.001		
Time 2 Active	-0.39	0.11	-0.61	-0.16	<.01		
ESRD						90	
Constipation[a]	0.18	0.10	-0.02	0.39	0.08		
Neuroticism	0.04	0.04	-0.03	0.11	0.29		
Interaction	-0.02	0.01	-0.04	0.00	**0.10**		0.0128
Conditional effects of activity at values of neuroticism (-1 SD, mean, 1 SD)							
-9.07	0.34	0.16	0.01	0.66	**0.04**		
0.37	0.18	0.10	-0.02	0.38	**0.08**		
6.81	0.07	0.09	-0.12	0.26	0.48		
Age	-0.04	0.05	-0.14	0.06	0.41		
Gender	-0.11	0.45	-1.0	0.78	0.81		
Time 1 Dep	0.66	0.08	0.51	0.82	<.001		
Time 2 Constipation	-0.22	0.09	-0.40	-0.04	0.02		

(continued)

(continued)

Variables	ß	SE	95% CI		p-value	N	Rsq-change
			Lower bound	Upper Bound			
Frailty						76	
Weak[a]	-0.04	0.12	-0.27	0.20	0.77		
Neuroticism	0.15	0.04	0.07	0.22	<.001		
Interaction	0.02	0.01	0	0.04	**0.07**		
Conditional effects of weakness at values of neuroticism (-1 SD, mean, 1 SD)							
-5.64	-0.14	0.15	-0.43	0.15	0.33		
-1.64	-0.07	0.12	-0.31	0.18	0.59		
8.04	0.12	0.12	-0.13	0.37	0.35		
Age	-0.04	0.05	-0.13	0.05	0.37		
Gender	-0.83	0.50	-1.82	0.16	0.10		
Time 1 Dep	0.57	0.08	0.40	0.73	<.001		
Time 2 Weak	0.19	0.12	-0.05	0.42	0.12		
Will to live[c]	0.14	0.13	-0.12	0.39	0.28	74	
Neuroticism	0.16	0.04	0.08	0.24	0.16		
Interaction	0.02	0.01	0	0.04	**0.10**		
Conditional effects of will to live at values of neuroticism (-1 SD, mean, 1 SD)							
-5.77	0.04	0.15	-0.27	0.35	0.79		
-1.77	0.11	0.13	-0.16	0.37	0.42		
8.23	0.27	0.13	0.02	0.52	**0.04**		
Age	-0.09	0.04	-0.18	-0.01	**0.03**		
Gender	-0.36	0.48	-1.31	0.59	0.45		
Time 1 Dep	0.60	0.09	0.43	0.78	<.001		
Time 2 Will to live	-0.30	0.14	-0.58	-0.01	0.04		

Note: The interaction term was generated by multiplying the mean-centered values of ESAS-R symptom and neuroticism. The effects of age, gender, Time 1 depression and Time 2 symptom were controlled. Coefficients for symptom and neuroticism are simple effects and represent the effect of X on Y when W=0.

[a] scored 0 (no/not) to 10 (very)

[b] scored 0 (poor sense of wellbeing) to 10 (very good sense of wellbeing)

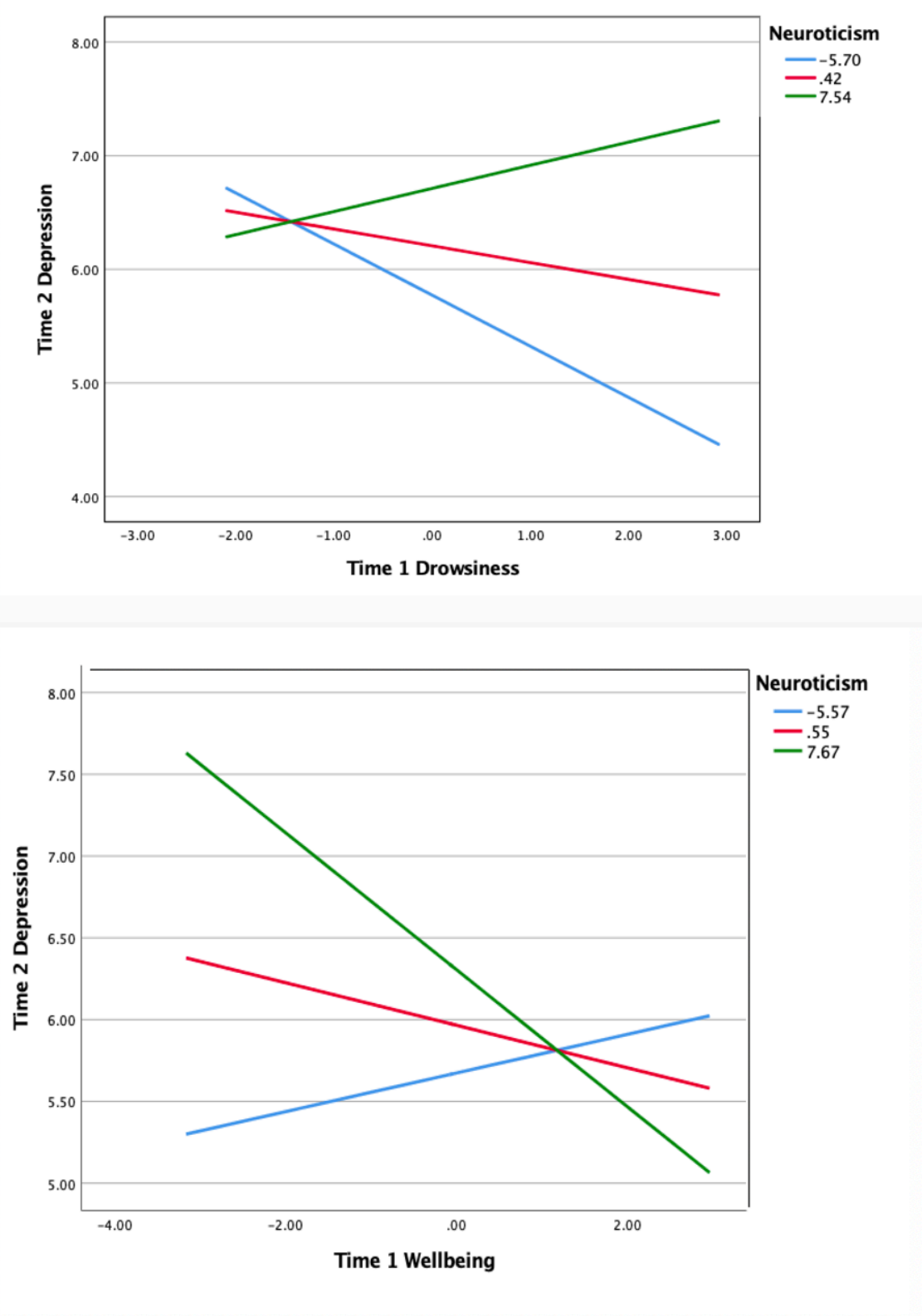
[c] scored 0 (no will to live) to 10 (strong will to live)

ALS. Neuroticism moderated the relationship between Time 1 drowsiness, fatigue, shortness of breath and wellbeing on Time 2 depression (Table 4). As shown in Figure 1, the interaction between Time 1 drowsiness and neuroticism was significantly related to Time 2 depression $\beta = 0.05$, $p = .06$, *95% CI* [0, 0.10], $\Delta R^2 = 0.03$), greater drowsiness was associated with greater depressive symptoms for those high in neuroticism, whereas greater drowsiness was associated with less depression at Time 2 for those low in neuroticism. The slope of the relationship between Time 1 drowsiness and Time 2 depression was positive but non-significant for those high in neuroticism. A similar pattern emerged in the interaction between Time 1 *fatigue* and *neuroticism* in its' relation to Time 2 depression ($\beta = 0.04$, $p = .04$, *95% CI* [0, 0.08], $\Delta R^2 = 0.04$). Consistent with our expectations, the slope of the relationship between Time 1 fatigue and Time 2 depression was strong and positive for those high in neuroticism, such that higher levels of fatigue at Time 1 was associated with greater levels of depression at Time 2. There was no significant relationship between fatigue and subsequent depression for those with levels of neuroticism at or one standard deviation below the mean. For those reporting high levels of fatigue, there is over a 2-point difference in depression score between those 1 *SD* above and 1 *SD* below on neuroticism, with the score of those high in neuroticism in the clinical range (> 8).

Neuroticism moderated the relationship between Time 1 shortness of breath and Time 2 depression ($\beta = 0.03$, $p = .11$, *95% CI* [-0.01, 0.08], $\Delta R^2 = 0.02$) (Figure 1). The effect of neuroticism on subsequent depression was strongest and positive at higher levels of shortness of breath ($\beta = 0.21$, $p = .10$, *95% CI* [-0.04, 0.46]). The interaction between Time 1 *wellbeing* and *neuroticism* was significantly related to Time 2 depression ($\beta = -0.04$, $p = .03$, *95% CI* [-0.08, 0], $\Delta R^2 = 0.03$), such that for those high on neuroticism, low wellbeing at Time 1 was associated

with greater depression at Time 2. There was no significant relationship between Time 1 wellbeing and Time 2 depression at lower levels of neuroticism (Figure 1).

Figure 1. ALS – Significant Interactions of Neuroticism and ESAS-R Symptom on Subsequent Depression



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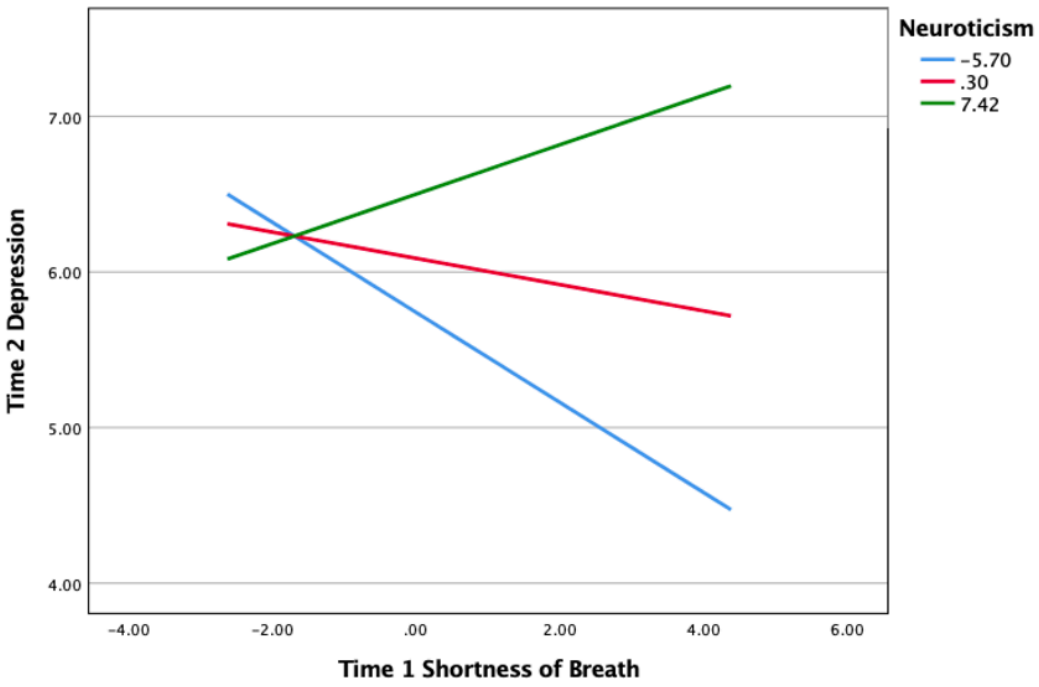
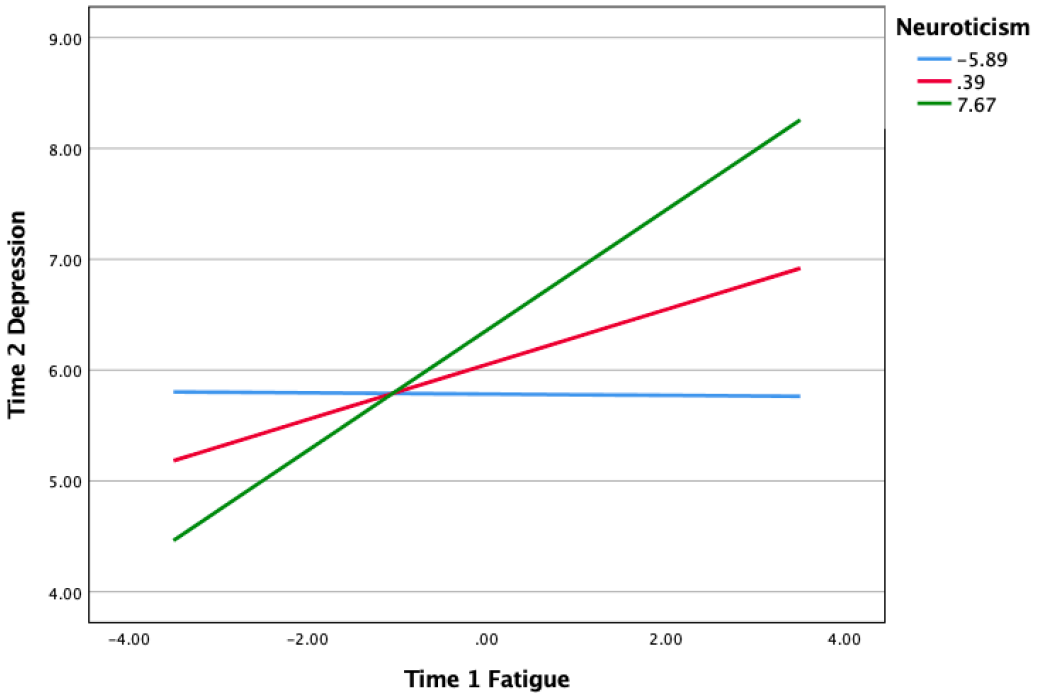
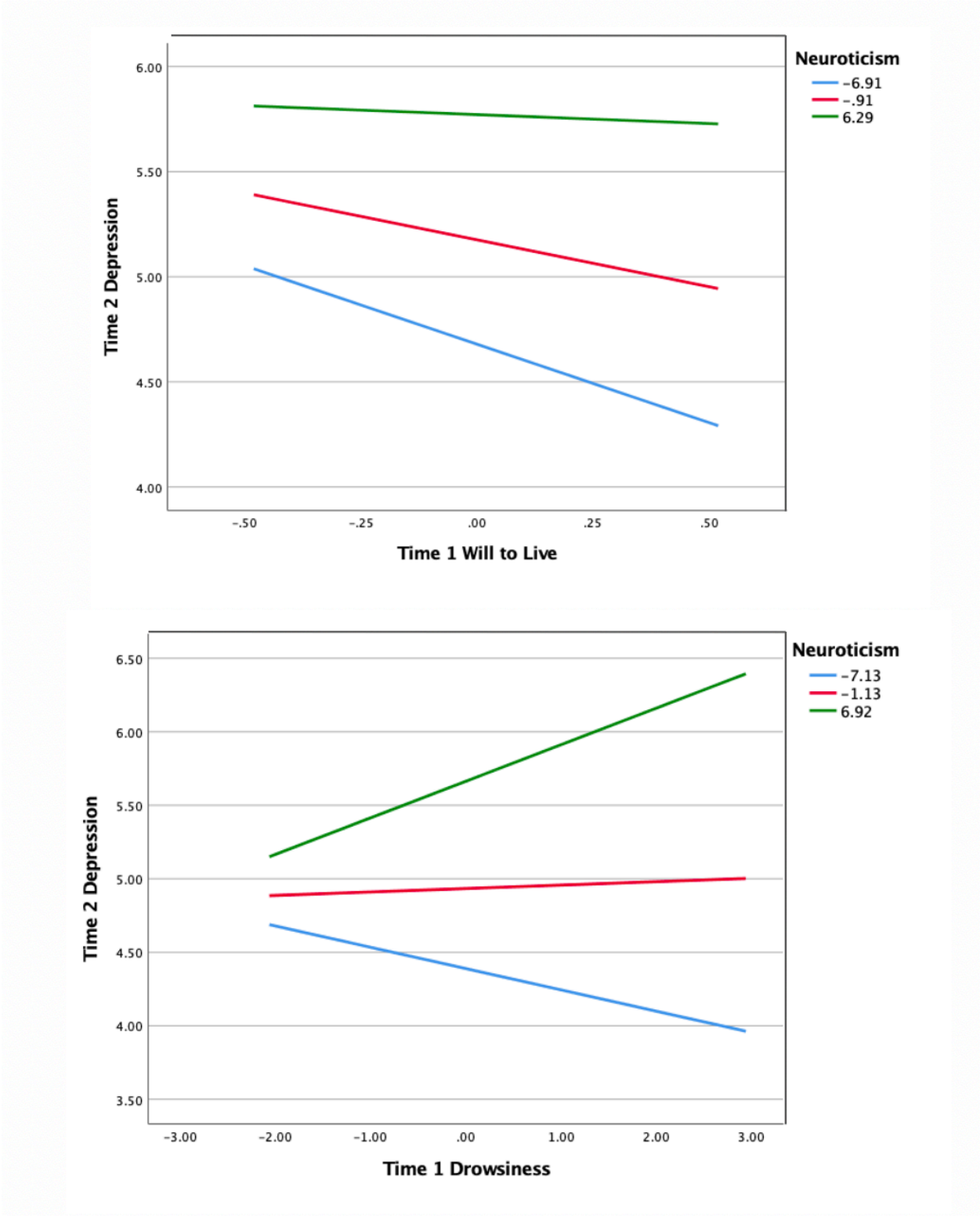

Neuroticism
-5.70
.30
7.42
Time 2 Depression
7.00
6.00
5.00
4.00
-4.00
-2.00
.00
2.00
4.00
6.00
Time 1 Shortness of Breath


Neuroticism
-5.89
.39
7.67
Time 2 Depression
9.00
8.00
7.00
6.00
5.00
4.00
-4.00
-2.00
.00
2.00
4.00
Time 1 Fatigue

COPD. We found that neuroticism significantly moderated the relationship between Time 1 drowsiness, trouble sleeping, will to live, and activity on Time 2 depression (Table 4). These interactions are shown in Figure 2. The interaction between Time 1 *drowsy* and *neuroticism* was significantly related to Time 2 depression ($\beta = 0.03$, $p = .05$, *95% CI* [0, 0.06], $\Delta R^2 = 0.02$), and the effect of neuroticism on depression was strongest and positive at higher levels of drowsiness ($\beta = 0.17$, $p < .01$, *95% CI* [0.07, 0.27], $\Delta R^2 = 0.02$). Further, the relationship between Time 1 trouble sleeping and time 2 depression was significantly moderated by neuroticism ($\beta = -0.02$, $p = .06$, *95% CI* [-0.04, 0], $\Delta R^2 = 0.02$), such that increased trouble sleeping at Time 1 was associated with less depression at Time 2 among those high in neuroticism, and that at low levels of trouble sleeping, those high in neuroticism had greater depression symptoms than those low in neuroticism.

The relationship between Time 1 *will to live* and Time 2 depression was significantly moderated by neuroticism ($\beta = 0.05$, $p = .02$, *95% CI* [0, 0.09], $\Delta R^2 = 0.03$), such that in those low in neuroticism, low will to live at time 1 is associated with greater depression at time 2. Interestingly, for those high in neuroticism, depression scores at time 2 were relatively invariant as a function of will to live at Time 1. Similarly, the interaction between Time 1 *active* and *neuroticism* and was significantly related to Time 2 depression ($\beta = -0.03$, $p = .03$, 95% CI [-0.05, 0], $\Delta R^2 = 0.02$). The effect of neuroticism on subsequent depression was strongest and positive at lower levels of activity ($\beta = 0.20$, $p = 0.001$, *95% CI* [0.08, 0.32]), weaker though still significant at moderate activity ($\beta = 0.10$, $p = 0.02$, *95% CI* [0.02, 0.18]), and not significant at high levels of activity.

Figure 2. COPD – Significant Interactions of Neuroticism and ESAS-R Symptom on Subsequent Depression



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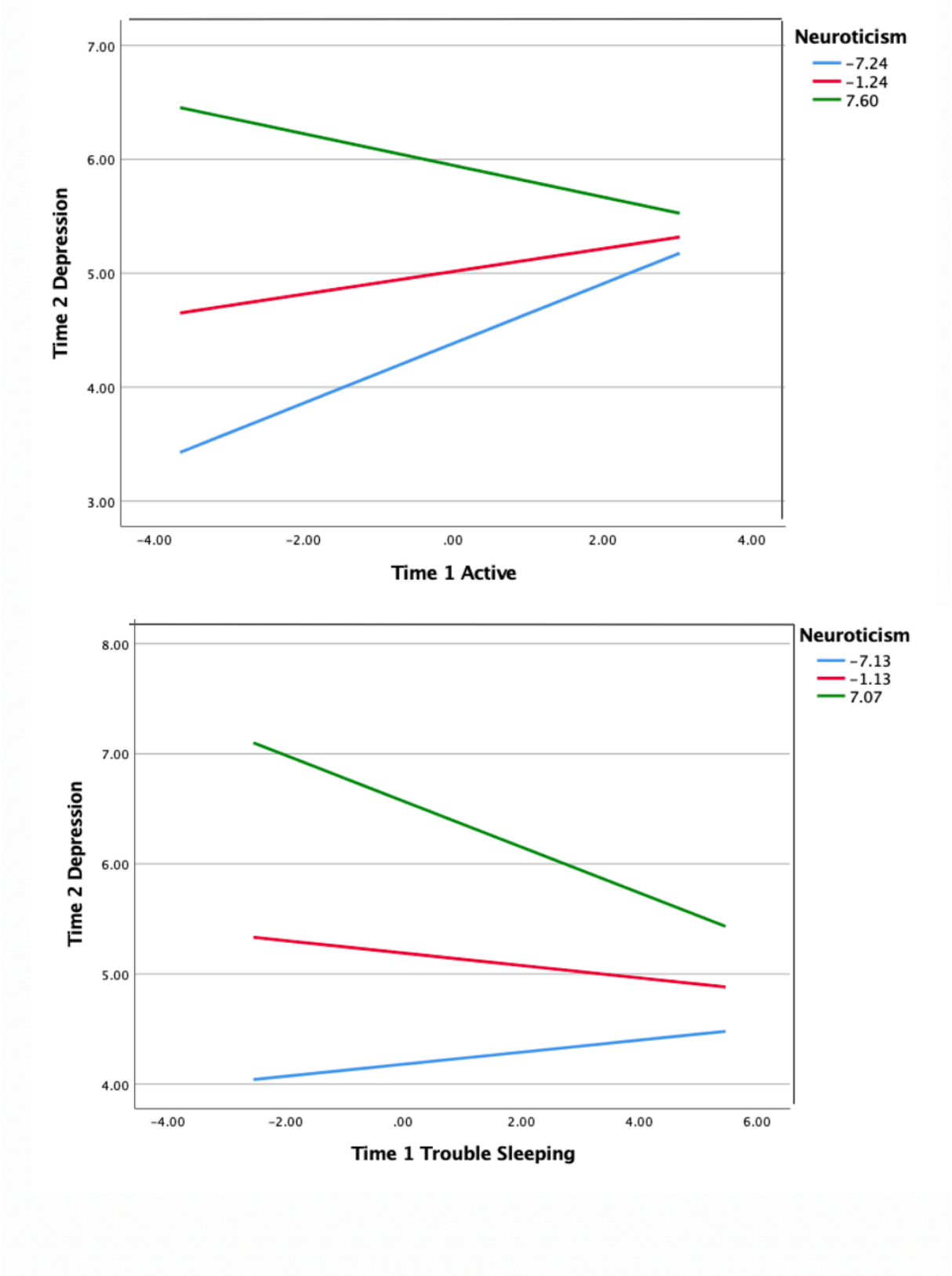
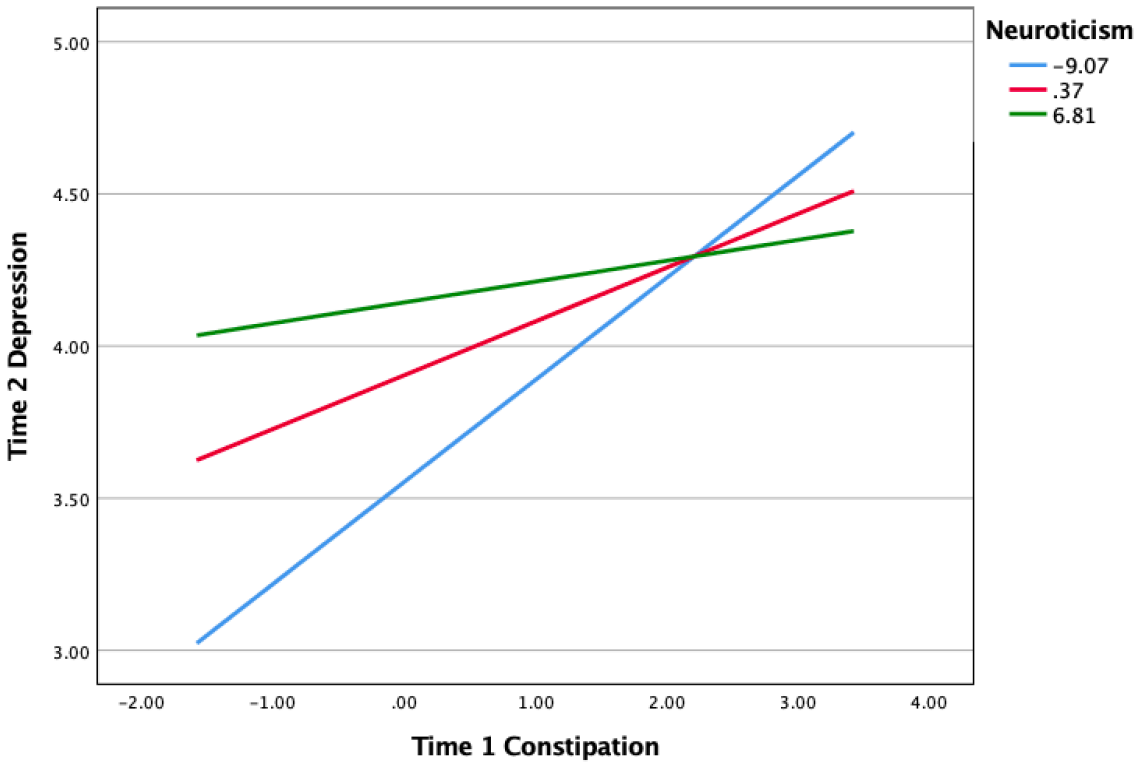

Neuroticism
-7.24
-1.24
7.60
Time 2 Depression
7.00
6.00
5.00
4.00
3.00
-4.00
-2.00
.00
2.00
4.00
Time 1 Active
Neuroticism
-7.13
-1.13
7.07
Time 2 Depression
8.00
7.00
6.00
5.00
4.00
-4.00
-2.00
.00
2.00
4.00
6.00
Time 1 Trouble Sleeping

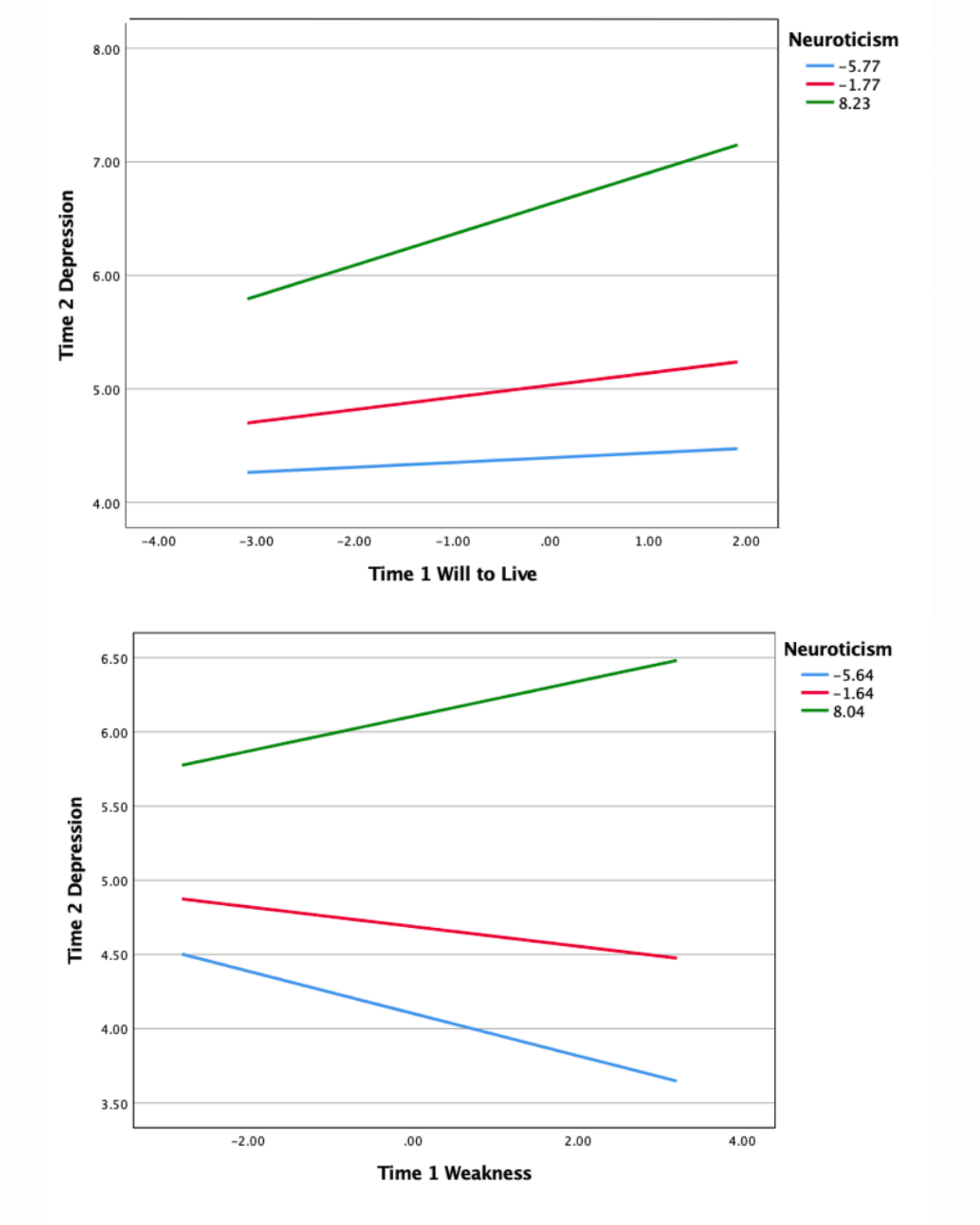
ESRD. The relationship between Time 1 constipation and Time 2 depression was moderated by neuroticism (β = -0.02, p = 0.1, *95% CI* [-0.04, 0], ΔR^2 = 0.01) (Table 4). As shown in Figure 3, the slope of the relationship between Time 1 constipation and Time 2 depression was strong and positive for those low in neuroticism, such that higher levels of constipation at Time 1 was associated with greater of depression at Time 2. A similar, though weaker pattern emerged for those with average level of neuroticism, while at high levels of neuroticism this relationship showed no statistical difference.

Figure 3. ESRD – Significant Interaction of Neuroticism and ESAS-R Symptom on Subsequent Depression



Frailty. The relationship between Time 1 weakness and Time 2 depression was moderated by neuroticism ($\beta = 0.02$, $p = .07$, *95% CI* [0, 0.04], $\Delta R^2 = 0.01$) (Table 4). As shown in Figure 4, at high levels of Time 1 weakness, those highest in neuroticism demonstrated a Time 2 depression score that is almost 3 points higher than those lowest in neuroticism. Probing the interaction revealed that the positive relationship between neuroticism and weakness on subsequent depression was strongest at high levels of weakness ($\beta = 0.20$, $p = <0.001$, *95% CI* [0.12, 0.29]), and weakest at low levels of weakness ($\beta = 0.09$, $p = <0.001$, *95% CI* [-0.02, 0.20]). Also in Figure 4, the interaction between Time 1 *will to live* and *neuroticism* and its relationship to Time 2 depression ($\beta = 0.02$, $p = .10$, *95% CI* [0, 0.04], $\Delta R^2 = 0.01$) shows a strong positive slope for those with high neuroticism demonstrating that for these individuals, greater will to live at Time 1 was associated with greater depression at Time 2.

Figure 4. Frailty – Significant Interactions of Neuroticism and ESAS-R Symptoms on Subsequent Depression



Discussion

To our knowledge, the present study is the first to examine neuroticism as a moderator between commonly assessed symptoms and later depression in non-cancer populations at the end-of-life. We found partial support for our hypothesis that the relationship between physical symptoms (as measured by the ESAS-R) and depressive symptoms three months later (as measured by the HADS) is dependent on neuroticism. Specifically, we found significant moderating effects of neuroticism in patients with ALS, COPD, ESRD, and frailty. Amongst each of these illness groups, there were both shared and unique ESAS-R symptoms that interacted with neuroticism to predict depression. Perhaps unsurprisingly, neuroticism tended to increase the likelihood of depressive symptoms for individuals reporting those physical symptoms most common or problematic to the specific illnesses.

In patients with ALS, both higher levels of fatigue, drowsiness, and shortness of breath, and lower levels of wellbeing at baseline, predicted increased symptoms of depression three months later only for those with above-average (relative to the sample) neuroticism. In fact, fatigue was associated with clinically significant levels of depression in those with high neuroticism. Fatigue is present in up to 83% of patients with ALS, and fatigue is a common "insidious" symptom for which patients present, related to respiratory insufficiency as a function of disease progression (Rudnicki, McVey, Jackson, Dimachkie, & Barohn, 2015). Though the relationship between fatigue and depression is likely bidirectional and complex in this population (as in others), given that fatigue is such a pervasive symptom in ALS, the ability to 'flag' patients who may be most at risk for later depression, as a function of neuroticism, is promising. It is interesting that for drowsiness, which seems highly related to fatigue, the slope of the relationship with neuroticism on later depressive symptoms was only significant for those low in

neuroticism. Importantly, the pattern of findings of the conditional effects for both fatigue and drowsiness follow the same pattern, as such, with sufficient power what may emerge is significant cross-level interactions for both symptoms, such that for those high in neuroticism, there is a significant positive relationship between fatigue/drowsiness and later depression, and for those low in neuroticism, there is a protective effect such that those experiencing these symptoms in fact have less symptoms of depression. It has been established in the literature that both neuroticism and depression/anxiety play a significant role genetic risk for fatigue symptoms, though these findings are not specific to ALS (e.g., Vassend, Røysamb, Nielsen, & Cjajkowski, 2018).

Excessive daytime sleepiness (drowsiness), in part related to insomnia secondary to nocturnal respiratory disturbances, is common in COPD (Enz et al., 2016). As such, the significant positive association between drowsiness and later depression in those high in neuroticism may present an area of clinical focus. Interesting effects emerged in COPD for those low in neuroticism, such that low will to live at baseline was associated with later depression symptom scores. It may thus be relevant for clinicians to assess for symptoms of depression in those with low will to live who are known to be generally emotionally stable. In those higher in neuroticism, depressive symptoms were elevated and relatively invariant as a function of reported will to live in those higher in neuroticism.

At low levels of trouble sleeping and activity, those higher in neuroticism had greater depressive symptoms, suggesting that within the same symptom presentation, level of neuroticism may play a key role in mood outcomes, as would be expected based on prior research demonstrating the strong role of neuroticism in the development of depressive symptoms (e.g., Enns & Cox, 1997). There is little clinical evidence, and no research evidence,

to contextualize the significant negative association in COPD between trouble sleeping and later depression in those high in neuroticism (M. Blouw, personal communication, February 2019). Further, difficulty sleeping is significantly positively correlated with other forms of distress in our sample, including drowsiness and fatigue. Regarding the finding that the relationship between neuroticism and subsequent depression is positive and strongest in the context of lower levels of activity can be contexualized within what is known about the effects of activity in COPD. As activity is known to exacerbate breathlessness (e.g., Ambrosino, Gherardi, & Carpene, 2009), less activity may reflect a decline in functioning and engagement, which is more challenging to cope with for those high in neuroticism. This is supported by the significant negative correlation in our sample between neuroticism and activity at both time points, and prior research demonstrating the significant positive relationship between neuroticism and harm avoidance in patients with COPD (Kahraman et al., 2013).

There has been a call for an understanding of moderators in the relationship between frailty and depression (Vaughan, Corbin, & Goveas, 2015). In our sample, there is preliminary evidence that a key defining feature of frailty, weakness, is associated differentially with later depression dependent on level of neuroticism, and that at similarly high levels of weakness, those high in neuroticism have higher depression symptom scores than those low in neuroticism. Further, in frail older adults in our sample who were also high in neuroticism, an increased will to live at baseline was associated with increased depression symptoms at follow-up, whereas for those with low to moderate neuroticism, depression symptoms were relatively invariant as a function of will to live. The frail sample was the oldest of our four illness groups, and with their advanced age, may have had more prognostic awareness of their impending death (Carstensen, 2006). As such, a strong will to live in this group may be viewed as incompatible with reality,

death acceptance, and making peace, and may represent a target population for whom intervention related to meaning making and acceptance would be beneficial in improving coping, and reducing existential distress and depression (Cicirelli, 2003).

Functional gastrointestinal symptoms are common in ESRD (Cano et al., 2007; Gok, Inc, Coban, Kutsal, & Kursat, 2017). Constipation affects approximately 1/3 of patients with ESRD, and is highly associated with depression in some samples (So Yeon et al., 2009). Our results suggest that while those high in neuroticism maintain relatively stable levels of depression over time, regardless of constipation severity, in those with moderate to low neuroticism, the distress of higher levels of constipation is associated with a significant increase in depression symptoms over three months. In previous work with this data, we reported that patients with ESRD had the highest symptom burden and comorbidities, yet reported the lowest number of dignity related concerns and level of dependency; and the highest level of hopefulness (Chochinov et al, 2016). In the current analysis, those with ESRD had the lowest levels of neuroticism and depression symptoms of the four groups. The literature that does exist examining personality's impact in ESRD primarily points to the impact of conscientiousness in management of physical symptoms (Christensen & Smith, 1995). As there is a significant amount of daily illness management in ESRD related to dialysis, personality may exert its effect 'at the front end' in terms of symptom management and severity, which in turn may impact depression. There is evidence in hemodialysis patients that symptoms of depression are relatively static over time, and trajectories of mental health problems such as depression and anxiety are not predictable using demographic or clinical variables, and therefore require regular screening (Ng, Tan, Mooppil, Newman, & Griva, 2015).

The findings that higher neuroticism was associated with greater depressive symptoms in the context of increased drowsiness, fatigue, and shortness of breath and decreased wellbeing (ALS); increased drowsiness and decreased activity (COPD); and increased weakness and will to live (frailty) can be contextualized within the SAVI theory (Charles, 2010). There is evidence that lower neuroticism is associated with lower negative affect when exposed to stressors (Leger, Charles, Turiano, Almeida, 2016). Higher neuroticism represents an emotional vulnerability characterized by lower emotion regulation abilities. In the context of vulnerabilities of increased illness-related symptoms and decreased physiological flexibility, that those higher in neuroticism have more longitudinal difficulties with mood is unsurprising. Those higher in neuroticism are dispositionally less inclined to utilize attentional strategies, appraisals, and behaviours to modulate their experience of exposure to stressors. SAVI would suggest that when individuals cannot use the aforementioned strategies to "avoid negative experiences, age-related benefits in wellbeing may be attenuated or disappear" (Charles, 2010, p. 1069). However, it appears that even in the context of significant unrelenting stressors and neurobiological dysregulation associated with terminal illness, low neuroticism may confer benefits in terms of improved mood outcomes.

The findings of this study must be viewed in the context of its strengths and limitations. In terms of strengths, the sample is unique and represents populations for whom data is difficult to obtain. Inclusion of diverse, non-cancer illnesses at the end of life, and the ability to examine the longitudinal course of the impact on symptom distress on depression as a function of neuroticism, provides an important contribution to the literature. Though such a sample is difficult to recruit and larger than many others in the literature, the power to detect moderation effects is nonetheless low. The challenge of low power in moderated multiple regression is

discussed extensively in the social sciences (e.g., Aguinis, 1995), and effect sizes related to the interaction terms were small to medium in the current study. That we found moderating effects for neuroticism despite being under-powered suggests the strong impact of this trait in the association between specific symptoms within the illness groups and later depressive symptoms, and future research with larger samples would help reinforce these findings. It is also important to consider that in running multiple tests with a more liberal *p*-value due to aforementioned issues with low power in moderation, the possibility of Type I error is inflated. As such, there is increased possibility that some of the significant results are due to chance. With these preliminary findings, there is early evidence to suggest that the relationship between a specific illness-related symptom and depression could vary and possibly be opposite between individuals who are low versus high in neuroticism. Additionally, the use of single item predictors in the ESAS-R is less ideal than comprehensive assessment tools for specific symptoms. However, given the common use of the ESAS-R across illnesses, both within our research sample and in clinical practice, it was appropriate for this preliminary investigation. Similarly, the HADS is not a diagnostic tool, though its strength is that it primarily avoids somatic symptoms of depression, which can confound accurate assessment in the medically ill.

To gain a deeper and more nuanced picture of the role of neuroticism in moderating the relationship between physical symptoms and later psychological distress in future research, the use of comprehensive measures of one symptom, within one illness, with illness-specific mental health measures would be appropriate. For example, replicating the current analysis using a validated measure of fatigue in ALS and a depression measure specific to patients with ALS (e.g., Hammer, Hacker, Hautzinger, Meyer, & Kubler, 2008; Krupp, LaRocca, Muir-Nash, & Steinberg, 1989). Relatedly, use of the full NEO-PI-R (Costa, 1992) includes sub-facets of

neuroticism (e.g., vulnerability to stress, depression, and anxiety) which may be particularly relevant to our research question and study populations. Additionally, inclusion of a measure that specifically assesses coping (e.g., Carver, 1997) would have allowed for direct rather than inferred assessment of coping, and also allow for assessment of coping as a mediator of the relationship between neuroticism and depression.

Clinically, the present research adds to the small body of literature examining the importance of neuroticism in end of life experience (Chochinov et al., 2006; Lattie et al., 2016). Our findings point to specific symptoms, within specific illness groups, for which neuroticism may be a particularly important variable to consider in terms of monitoring risk of depressive symptoms. With respect to treatment implications, our findings provide preliminary evidence for specific groups of patients who may be targeted for early intervention both in terms of physical and psychological symptoms.

Conclusions

Our findings support the notion that in the context of ALS, COPD, ESRD, and frailty, neuroticism represents a vulnerability factor that either attenuates or amplifies the relationship of specific symptom experiences and the development of depressive symptoms. This provides initial evidence that a psychological outcome or coping response occurs not just based on "merely the symptoms and concerns they are exposed to," but who they are as a person (Chochinov et al., 2006, p.339). This study thus provides preliminary evidence that neuroticism matters at the end of life, and provides important and novel information about who is at risk for depressive symptoms.

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Appendix A

Table 1. *Non-significant moderating effects of neuroticism on the relationship between ESAS-R symptoms and HADS depression*

Variables	ß	SE	95% CI		p-value	N	Rsq-change
			Lower bound	Upper Bound			
ALS						68	
Pain[a]	.002	0.17	-0.35	-0.35	0.99		
Neuroticism	0.04	0.06	0.46	-0.07	0.16		
Interaction	0.02	0.02	-0.02	0.06	0.37		0.0068
Nausea[a]	-0.01	0.34	-0.70	0.70	0.98		
Neuroticism	0.09	0.08	-0.07	0.25	0.24		
Interaction	0.15	0.12	-0.08	0.38	0.21		0.0139
Anxious[a]	0.29	0.20	-0.12	0.70	0.16		
Neuroticism	-0.07	0.07	-0.22	0.07	0.32		
Interaction	-0.04	0.03	-0.10	0.02	0.18		0.0145
Constipation[a]	0.12	0.15	-0.18	0.41	0.44		
Neuroticism	0.03	0.06	-0.08	0.15	0.59		
Interaction	0.01	0.02	-0.03	0.05	0.62		0.0019
Diarrhea[a]	0.09	0.35	-0.61	0.80	0.79		
Neuroticism	0.03	0.06	-0.09	0.15	0.63		
Interaction	0.03	0.04	-0.05	0.11	0.42		0.0056
Difficulty sleeping[a]	-0.01	0.20	-0.41	0.39	0.96		
Neuroticism	0.00	0.07	-0.13	0.13	0.99		
Interaction	-0.03	0.03	-0.09	0.04	0.38		0.0067
Weakness[a]	-0.09	0.14	-0.40	0.19	0.53		
Neuroticism	0.03	0.06	-0.08	0.14	0.59		
Interaction	0.00	0.01	-0.03	0.03	0.97		0.0000
Dizziness[a]	0.23	0.28	-0.33	0.80	0.41		
Neuroticism	0.03	0.06	-0.09	0.16	0.60		
Interaction	0.01	0.04	-0.07	0.10	0.75		0.0009
Difficulty Thinking[a]	-0.59	0.32	-1.24	0.06	0.07		
Neuroticism	0.05	0.06	-0.07	0.17	0.41		
Interaction	0.00	0.04	-0.09	0.08	0.92		0.001
Appetite[a]	-0.01	0.15	-0.32	0.29	0.93		
Neuroticism	0.07	0.06	-0.06	0.20	0.93		
Interaction	-0.02	0.02	-0.06	0.01	0.17		0.0161
Will to live[a]	-0.09	0.15	-0.40	0.22	0.57		
Neuroticism	0.05	0.06	-0.06	0.16	0.39		
Interaction	-0.02	0.02	-0.08	0.02	0.20		0.0123
Active[a]	0.10	0.18	-0.25	0.46	0.56		
Neuroticism	0.08	0.06	-0.05	0.20	0.22		
Interaction	-0.02	0.02	-0.06	0.03	0.44		0.0048

(continued)

(continued)

Variables	ß	SE	95% CI		p-value	N	Rsq-change
			Lower bound	Upper Bound			
COPD						80	
Pain[a]	0.04	0.11	-0.28	0.27	0.70		
Neuroticism	0.13	0.05	0.02	0.24	0.02		
Interaction	-0.01	0.01	-0.03	0.01	0.35		0.0052
Nausea[a]	-0.05	0.30	-0.65	0.55	0.88		
Neuroticism	0.16	0.05	0.07	0.26	<.001		
Interaction	-0.03	0.02	-0.07	0.02	0.24		0.0084
Shortness of breath[a]	-0.06	0.13	-0.33	0.20	0.63		
Neuroticism	0.11	0.04	0.02	0.19	0.01		
Interaction	0.02	0.01	-0.01	0.05	0.23		0.0078
Anxious[a]	0.03	0.12	-0.20	0.27	0.78		
Neuroticism	0.12	0.06	0	0.24	0.05		
Interaction	-0.01	0.01	-0.03	0.02	0.70		0.0009
Fatigue[a]	0.01	0.12	-0.23	0.25	0.94		
Neuroticism	0.12	0.05	0.03	0.22	0.01		
Interaction	0.03	0.01	-0.01	0.04	0.28		0.0058
Constipation[a]	0.10	0.17	-0.24	0.43	0.58		
Neuroticism	0.13	0.05	0.03	0.22	0.01		
Interaction	0	0.01	-0.02	0.03	0.88		0.0002
Diarrhea[a]	-0.17	0.28	-0.72	0.38	0.55		
Neuroticism	0.11	0.05	0.02	0.20	0.02		
Interaction	-0.08	0.09	-0.26	0.10	0.37		0.0051
Weakness[a]	-0.16	0.10	-0.36	0.04	0.12		
Neuroticism	0.13	0.04	0.06	0.21	0.001		
Interaction	0	0.01	-0.02	0.02	0.86		0.0001
Dizziness[a]	0.20	0.16	-0.11	0.52	0.20		
Neuroticism	0.12	0.05	0.02	0.21	0.02		
Interaction	0	0.01	-0.03	0.03	0.86		0.0002
Difficulty Thinking[a]	0.37	0.23	-0.10	0.83	0.12		
Neuroticism	0.12	0.04	0.05	0.22	<.01		
Interaction	-0.03	0.03	-0.08	0.03	0.31		0.0062
Appetite[a]	0.05	0.12	-0.20	0.29	0.71		
Neuroticism	0.13	0.04	0.05	0.20	<.01		
Interaction	0.01	0.01	-0.01	0.04	0.34		0.0049
Wellbeing[a]	0.05	0.17	-0.30	0.39	0.77		
Neuroticism	0.10	0.04	0.02	0.18	0.02		
Interaction	-0.01	0.01	-0.03	0.02	0.71		0.0008

(continued)

(continued)

Variables	ß	SE	95% CI		p-value	N	Rsq-change
			Lower bound	Upper Bound			
ESRD						90	
Pain[a]	-0.09	0.08	-0.25	0.07	0.25		
Neuroticism	0.02	0.04	-0.05	0.09	0.55		
Interaction	0.01	0.01	-0.01	0.03	0.41		0.0035
Nausea[a]	-0.11	0.13	-0.36	0.15	0.40		
Neuroticism	0.01	0.04	-0.07	0.08	0.81		
Interaction	0	0.02	-0.03	0.03	0.87		0.0001
Drowsy[a]	0	0.09	-0.17	0.17	0.96		
Neuroticism	0.01	0.04	-0.06	0.08	0.76		
Interaction	0	0.01	-0.02	0.03	0.70		0.0007
Shortness of breath[a]	0.08	0.13	-0.17	0.33	0.51		
Neuroticism	0.02	0.04	-0.05	0.09	0.59		
Interaction	0.01	0.02	-0.03	0.04	0.70		0.0008
Anxious[a]	0.02	0.12	-0.21	0.25	0.84		
Neuroticism	0.01	0.04	-0.07	0.08	0.87		
Interaction	0.01	0.01	-0.01	0.03	0.29		0.0056
Fatigue[a]	-0.07	0.08	-0.24	0.10	0.40		
Neuroticism	0	0.04	-0.07	0.08	0.90		
Interaction	0.01	0.01	-0.01	0.03	0.17		0.0093
Diarrhea[a]	-0.13	0.11	-0.36	0.09	0.23		
Neuroticism	0.01	0.03	-0.06	0.08	0.70		
Interaction	0.01	0.01	-0.01	0.04	0.26		0.0062
Difficulty sleeping[a]	-0.01	0.09	-0.18	0.16	0.90		
Neuroticism	0.02	0.04	-0.06	0.09	0.66		
Interaction	0.01	0.01	-0.01	0.03	0.22		0.0076
Weakness[a]	-0.01	0.10	-0.19	0.17	0.91		
Neuroticism	0.02	0.04	-0.05	0.09	0.57		
Interaction	0	0.01	-0.02	0.01	0.62		0.0012
Dizziness[a]	-0.30	0.14	-0.58	-0.02	0.04		
Neuroticism	0.04	0.03	-0.03	0.10	0.31		
Interaction	0	0.01	-0.03	0.02	0.88		0.0001
Difficulty Thinking[a]	0.47	0.16	0.14	0.80	0.01		
Neuroticism	0.04	0.04	-0.04	0.11	0.32		
Interaction	-0.01	0.01	-0.03	0.02	0.61		0.0012
Appetite[a]	-0.01	0.11	-0.23	0.20	0.91		
Neuroticism	0.02	0.04	-0.05	0.09	0.64		
Interaction	-0.01	0.01	-0.04	0.01	0.40		0.0039
Will to live[a]	0.33	0.17	-0.01	0.67	0.06		
Neuroticism	0.03	0.04	-0.04	0.10	0.40		
Interaction	-0.03	0.02	-0.07	0.01	0.17		0.0095

(continued)

(continued)

Variables	ß	SE	95% CI		p-value	N	Rsq-change
			Lower bound	Upper Bound			
ESRD						90	
Active[a]	0.08	0.10	-0.12	0.28	0.43		
Neuroticism	0.02	0.03	-0.05	0.09	0.65		
Interaction	0	0.01	-0.02	0.02	0.94		0.0000
Wellbeing[a]	0.16	0.14	-0.12	0.43	0.26		
Neuroticism	0.01	0.02	-0.06	0.07	0.88		
Interaction	0	0.01	-0.03	0.02	0.80		0.0003
Frailty						77	
Pain[a]	-0.14	0.09	-0.32	0.04	0.13		
Neuroticism	0.18	0.04	0.11	0.26	<.001		
Interaction	0	0.01	-0.02	0.02	0.98		0.000
Nausea[a]	-0.03	0.17	-0.38	0.31	0.85		
Neuroticism	0.18	0.04	0.10	0.26	<.001		
Interaction	0.01	0.03	-0.04	0.06	0.74		0.0005
Drowsy[a]	0	0.12	-0.24	0.24	0.99		
Neuroticism	0.17	0.04	0.10	0.25	<.001		
Interaction	0	0.01	-0.02	0.03	0.74		0.0005
Shortness of breath[a]	-0.04	0.14	-0.32	0.24	0.77		
Neuroticism	0.18	0.04	0.11	0.26	<.001		
Interaction	0.01	0.02	-0.02	0.04	0.66		0.0008
Anxious[a]	-0.07	0.12	-0.32	0.17	0.55		
Neuroticism	0.16	0.04	0.08	0.24	<.01		
Interaction	0.01	0.01	-0.02	0.03	0.65		0.0008
Fatigue[a]	0.26	0.13	0	0.53	0.05		
Neuroticism	0.14	0.04	0.06	0.22	<.01		
Interaction	0	0.01	-0.02	0.02	0.74		0.0004
Constipation[a]	0.01	0.09	-0.16	0.19	0.90		
Neuroticism	0.17	0.04	0.09	0.24	<.001		
Interaction	0.01	0.01	-0.01	0.03	0.21		0.0065
Diarrhea[a]	-0.27	0.16	-0.59	0.05	0.09		
Neuroticism	0.19	0.04	0.11	0.27	<.001		
Interaction	-0.01	0.01	-0.04	0.01	0.27		0.0048
Difficulty sleeping[a]	0.05	0.13	-0.21	0.32	0.68		
Neuroticism	0.18	0.04	0.10	0.26	<.001		
Interaction	0	0.01	-0.03	0.02	0.89		0.0001
Dizziness[a]	-0.03	0.21	-0.69	0.17	0.23		
Neuroticism	0.18	0.04	0.11	0.26	<.001		
Interaction	0.03	0.02	0.44	0.75	0.19		0.0068

(continued)

(continued)

Variables	ß	SE	95% CI		p-value	N	Rsq-change
			Lower bound	Upper Bound			
Frailty						77	
Difficulty Thinking[a]	-0.05	0.14	-0.33	0.22	0.71		
Neuroticism	0.15	0.04	0.07	0.23	<.01		
Interaction	0.01	0.01	-0.01	0.03	0.25		0.0050
Appetite[a]	0.12	0.11	-0.10	0.35	0.28		
Neuroticism	0.18	0.04	0.11	0.25	<.001		
Interaction	0	0.01	-0.02	0.03	0.69		0.0006
Active[a]	-0.14	0.11	-0.36	0.08	0.21		
Neuroticism	0.18	0.04	0.11	0.25	<.001		
Interaction	-0.01	0.01	-0.01	0.01	0.42		0.0026
Wellbeing[a]	0.07	0.18	-0.29	0.43	0.68		
Neuroticism	0.15	0.04	0.07	0.24	<.01		
Interaction	-0.01	0.01	-0.03	0.01	0.53		0.0016

Preface to Chapter Three

Chapter Two demonstrated preliminary evidence of the moderating role of neuroticsm in the relationship between specific illness-related symptoms in ALS, COPD, ESRD, and Frailty and subsequent symptoms of depression. When this moderation effect was significant, in the presence of illness symptoms, higher levels of neuroticism was generally associated with a longitudinal increase in symptoms of depression. However, this was not uniform across symptoms or illness groups. I used patients' self-reported neuroticism as the moderating variable in the above study, in line with both the symptom assessment (ESAS-R) and depression screen (HADS) being self-reported. Though several explanations for the mixed findings in Chapter Two were discussed, an important factor to consider is who may be best equipped to report on neuroticism, which is arguably a fairly stable trait, in the context of life-limiting illess.

Caregivers are often called upon in EOL research to provide proxy assessment of patient's symptoms, functioning, and preferences. This is routinely done to reduce burden on patients. In the context of neuroticism, while reducing burden is an important factor, examining how caregivers and patients differ on their reports of patients neuroticism may provide important information regarding how personality is viewed from these differing perspectives and what drives these differences. This has practical implications for understanding the nature and predictors of congruence in proxy assessment, as it is questionable whether caregiver reports can be true proxies for patient self-reports. Further, this study contributes to the sparse theoretical and empirical literature on ratings of neuroticism by self and close others at the very end of life. Chapter Three seeks to address these issues through an assessment of level and predictors of patient-caregiver congruence in patient neuroticism in ALS, ESRD, COPD, and frailty in the last six months of life.

Chapter Three: Patient-caregiver incongruence on ratings of patient neuroticism in four non-cancer populations at the end-of-life

Introduction

The experience of illness is inherently individual, often involving the journey of a person and their loved ones from relative health to a state of illness, and ultimately, death (Ferguson, 2013). Personality, the dynamic interplay of physical and psychological systems within the person that influence a pattern of actions, thoughts, and feelings (Allport, 1961), has been a major area of attention in the study of the psychology of health and illness (e.g., Roberts, Kuncel, Shiner, Caspi, & Goldberg, 2007). Individual differences in response to illness encompass psychological, physical, and behavioural domains and thus impact diagnosis, treatment, prognosis, and mortality (Ferguson, 2013). Neuroticism is described as "the ease and frequency with which a person becomes upset or distressed" (Carver & Connor-Smith, 2010, p. 683), and this tendency to negative affect includes low emotional stability, anger, self-consciousness, anxiety, irritability, and depression (Widiger, 2009). Neuroticism is identified as a primary predictor of psychopathology in general (e.g., Sauer-Zavala, Wilner, & Barlow, 2017) and is associated with challenges in coping with chronic and terminal illness (e.g., Carver & Connor-Smith, 2010; Chochinov et al, 2006)

Neuroticism at the EOL

There is a substantial body of research linking neuroticism to coping with cancer in particular (e.g., Aarstad, Beisland, & Aarstad, 2012; Aarstad, Beisland, Osthus, & Aarstad, 2011; Carver & Connor-Smith, 2010; Carver, 2005; Carver et al., 1993). In palliative cancer populations, personality is significantly correlated with a wide range of psychological, existential, physical, and social concerns (Chochinov et al, 2006). Neuroticism in particular is

significantly positively correlated ($r = \pm .40$) with anxiety, loss of sense of dignity, hopelessness, negative outlook, and depression; and negatively correlated with quality of life satisfaction in this population. Further, neuroticism (controlling for all other distress variables) has been found to significantly predict depression, hopelessness, anxiety, loss of dignity, concentration, quality of life, and life satisfaction (Chochinov et al., 2006). Higher levels of neuroticism, openness, and agreeableness in older adults are associated with a greater awareness of one's future care needs (Sörensen, Duberstein, Chapman, Lyness, & Pinquart, 2008). In a cohort of men with prostate cancer at the EOL, those high in neuroticism reported less inclination towards any EOL care and were categorized as "service reluctant" (Lattie et al., 2016), which may be related to perceiving health care providers as untrustworthy thus avoiding collaborative EOL conversations (Ha & Pai, 2012). Clearly, such avoidance may affect the quality of care these patients receive, and indicates a population for whom additional intervention or information may be required to ensure optimal EOL care. Additionally, neuroticism increases vulnerability to and is at the core of many mental disorders, including anxiety and depressive disorders (Sauer-Zavala, Wilner, & Barlow, 2017). Such disorders are often unrecognized or undertreated at the EOL, as symptoms are often confounded with the various complex physical and existential aspects of advanced disease, and such delays can prevent timely and/or efficacious treatment (Chochinov & Breitbart, 2009). As such, knowledge regarding patients' neuroticism may be clinically useful in anticipating who is more at risk of developing psychological distress and mental disorders as their disease progresses and thus expediting diagnosis and treatment.

Illnesses such as amyotrophic lateral sclerosis (ALS) are well known to produce personality changes in relation to cognitive decline and frontotemporal dysfunction, often resulting in irritability, obsessive behaviour, and deficits in social functioning (Phukan, Pender,

& Hardiman, 2007). Further, elements of personality, in particular neuroticism, are related to a range of physiological systems. The stress response associated with negative affectivity and anxiety can negatively impact immune system functioning (Thomsen et al., 2004), increased proinflammatory cytokines that initiate and maintain inflammatory responses (Kemeny, 2003) and increase cortisol levels (McEwen, 2003). Given the unique physiological and psychological processes in various illnesses, it is likely that neuroticism interacts differently dependent on diagnosis and stage of illness (Mueller, Wagner, Wagner, Ram, & Gerstorf, 2019).

Further, the relationship between personality and illness is bidirectional, with aspects of illness and old age influencing personality change (Wagner, Ram, Smith, & Gerstorf, 2015). Longitudinal aging studies suggest that there is a linear decrease in neuroticism across the lifespan, such that neuroticism with significant reductions between ages 20-40, with ongoing decreases until approximately age 70, after which slight increases are apparent (Roberts, Walton, & Viechtbauer, 2006; Steunenberg, Twisk, Beekman, Deeg, & Kerkhof, 2005; Terracciano et al., 2005), with steep increases close to death. Additionally, those who perceive their life is controlled by others display higher levels of neuroticism (Wagner et al., 2015).

Such findings echo research on aging and mental health, suggesting improved mental health into old age with a slight levelling off or worsening in very old age (Charles, 2010). This worsening is thought to be associated with "terminal decline," which occurs due to greater vulnerability to stress response due to immune suppression and an increase in comorbidities towards the EOL, which in turn contribute to increases in negative affect/neuroticism (Charles, 2010; Mroczek et al., 2006). Counter-intuitively, recent research suggests that those with low neuroticism experience a steeper terminal decline in the last year of life (Mueller et al., 2019), perhaps related to the concept of "compressed morbidity" (Fries, 2005), in which "lifetime

illness burden may be compressed into a shorter period of time nearer to the age of death" as a function of postponing the age of onset of illness (Swartz, 2008, p.1163). High neuroticism may in fact be adaptive at the very EOL, as the behavioural inhibition/avoidance and increased vigilance to threat can be self-protective in the context of significant limitations and vulnerabilities (Mueller et al., 2019). As such, aspects of illness and aging itself are likely associated with neuroticism, with significant implications for the EOL experience. Although it is useful to understand patient neuroticism at the EOL, it is not yet clear how best to measure it.

Proxy assessment of neuroticism in illness

Proxy assessment is a common method of collecting information regarding symptoms and experiences of patients with illness, particularly in populations for whom ability to self-report may be compromised due to illness characteristics or burden. Specifically, caregivers of patients at the end-of-life may be called upon as proxy-assessors of patients' pain, mood, quality of life, and treatment preferences. However, incongruence between patients and their caregivers on various measures of symptoms, functioning, and experience varies widely, and is dependent on a variety of factors (e.g., Jones et al., 2011; McPherson & Addington-Hall, 2003; McPherson, Wilson, Lobchuk, & Brajtman, 2008).

There is evidence of incongruence between caregiver and patient ratings of personality. In a cohort of lower-extremity trauma patients, spouses rated patients as more neurotic, more extraverted, less open to new experiences, and less conscientious than patients' self-reports, though these differences were small. Intraclass correlation coefficients between patients and spouses ranged from 0.44 to .51, with the highest agreement for neuroticism. Agreement was not associated with sociodemographics, patient characteristics, or aspects of the relationship (Haider et al., 2002). In a cohort of patients with multiple sclerosis and their caregivers, a similar pattern

emerged. Pearson correlations between self and other reports of the Big Five personality factors ranged from 0.33 to 0.46, with the highest correlation for neuroticism (Schwartz et al., 2011).

The accuracy and predictive value of other-rated personality may be particularly relevant when assessing personality and illness, as caregivers' proxy assessment can have significant implications for patients' health and care. Clinician awareness of possible incongruence in patient-caregiver reports is essential in accurately treating symptoms and mitigating physical and psychological distress in terminal illness. It also offers insight into varying perceptions of patients versus family members, which is important given that both are the focus of palliative care (WHO, 2012). For example, spouse's ratings of patient neuroticism have been found to be significantly positively associated with coronary artery calcification (a risk factor for coronary artery disease), whereas self-reports were not (Smith et al., 2008). Neuroticism has much to offer in terms of a 'flag' for who may be most at risk of psychological problems (Barlow, 2008; Sauer-Zavala et al., 2017). Early detection of such problems is essential in patients with terminal illness, as accurate diagnosis and treatment of mental disorders that develop in this context are complex, often neglected, or left too long to provide meaningful intervention (Chochinov & Breitbart, 2009). Therefore, assessing neuroticism as early in the illness trajectory as possible may provide clinicians with a sense of those most at risk for more significant depression, anxiety, and adjustment issues as their illness progresses. Further, assessing neuroticism may provide insight into who the patient is at the very core of their personhood, a central tenet of palliative care and a key factor in preserving and enhancing dignity at the EOL (Chochinov, 2007). In doing so, clinicians avail themselves of a wealth of information, which can improve their communication and therapeutic effectiveness with patients and families, and potentially

avoid or mitigate interpersonal issues within the healthcare setting that may arise for patients who are less emotionally stable (e.g., mistrust of healthcare providers).

Theoretical models of self-other personality judgement

The literature on accurate personality judgement provides important context regarding the reasons for the aforementioned observed differences in self-other neuroticism ratings in ill versus healthy populations. The Realistic Accuracy Model (RAM; Funder, 1995) provides a framework for understanding how personality judgement occurs, which include that the person being judged must behave in ways relevant to the trait, that this behaviour must be available and detectable to the judge, and then this information must be utilized correctly to make an accurate judgement. Importantly, there are several moderators of accurate personality judgement, which include elements of the individual being judged, the trait being judged, the type of information available, and the quality of the judge. Visible traits are easier to judge; however, not all traits are better judged by others. Vazire's (2010) self-other knowledge asymmetry model (SOKA) suggests that less visible traits are better judged by the self, and more visible traits are better judged by others. It has thus been proposed that neuroticism may be more difficult to judge than other traits that contain more dimensions of observable behavior, such as extraversion and social vitality (Funder, 2012).

Additionally, there is a wealth of research demonstrating that both quantity and quality of information about another's personality aids in judgement. As such, individuals are more accurate at rating the personality of people they have known for a long time. Further, the ability to view another's behaviour in a range of settings also positively impacts congruence and provides context and cues, such as facial expression and environmental interaction, that increases accuracy (see Funder, 2012, for a review). In addition to the relationship to the individual whose

personality is being judged, characteristics of the assessor play a role in accuracy. Those who are more agreeable and less anxious tend to be better judges of another's personality, and women may be better than men at such judgements due to their increased ability to consider the range of 'normal' behaviour based on interpersonal skill and affective awareness (Funder, 2012).

Proxy assessment at the EOL

The research in proxy assessment in serious illness is consistent with what the SOKA and RAM models predict in terms of visibility of the characteristic being judged and the quality and quantity of information available to the rater. Caregivers of ill patients are more concordant in rating observable symptoms (e.g., vomiting, dyspnea) compared to more internal experiences (e.g., depression, pain) (Lobchuk & Degner, 2002; McPherson & Addington-Hall, 2003; McPherson et al., 2008). Research suggests that proxy assessors tend to overestimate patient experiences of 'negative' states (e.g., pain) and underestimate 'positive' states (e.g., quality of life) – that is, they often report that patients are worse off than the patients' self-reports would suggest. This bias is typically small to moderate, and most likely to occur when judging emotional distress and fatigue (McPherson & Addington-Hall, 2003; Sneeuw et al, 1997a, 1997b, 1998). Additionally, various aspects of patients, caregivers, and the dyad have been associated with increase incongruence, including the proxy's own distress and burden at the EOL (McPherson & Addington-Hall, 2003); patient fatigue, disturbed mood, and low quality of life (Miaskowski et al, 1997); and the relationship between the patient and proxy, with spouses tending to be more congruent than other proxies, which may be a function of increased availability and detectability of various traits (Funder, 2012) or symptoms vis a vis interpersonal closeness or increased time spent together (McPherson & Addington-Hall, 2003).

In a cohort of prostate cancer survivors and their spouses, spouses rated the survivors' symptom severity significantly higher than did the survivors themselves; younger survivor age and greater caregiver strain were positively associated with this incongruence (Winters-Stone, Lyons, Bennett, & Beer, 2014). In patients with chronic obstructive pulmonary disease (COPD), chronic heart failure, or chronic renal failure, family caregivers reported a significantly higher number of symptoms and increased severity of fatigue, coughing, muscle weakness, loss of appetite, low mood, anxiety, panic attacks, edema, and chest pain than did patients themselves. Overall agreement was moderate for the majority of symptoms, and higher for more observable symptoms such as dyspnea, loss of appetite, pain, and muscle cramps (Janssen, Spruit, Wouters, & Schols, 2012). In a previous publication by our research group using the present dataset comprised of patients with ALS, COPD, ESRD, and frailty, caregivers overestimated patient distress and underestimated quality of life, dignity, and life satisfaction (Hack et al., 2018).

Related to the observability of symptoms, there is evidence that patients may conceal their symptoms to avoid feeling like a burden to caregivers (Dar, Beach, Barden, & Cleeland, 1992), which also may result in a discrepancy between caregiver and patient ratings, with caregiver ratings being higher due to 'underestimation' by patients. Indeed, perceived dependency and perceived burden to others are significant sources of distress in many patients with terminal illness (Chochinov et al., 2007; Filiberti et al., 2001; McPherson, Wilson, & Murray, 2007; Tang et al., 2014; Wilson, Curran, & McPherson, 2005), and thus may impact congruence between patient-caregiver ratings. Further, there is mixed evidence on the role of sociodemographic factors in incongruence, with limited evidence showing female proxies are more concordant than male proxies, and that higher education in proxies is associated with less incongruence (McPherson & Addington-Hall, 2003).

Prior research in proxy assessment at the EOL has primarily focused on patients with cancer and has often relied on correlational methods, difference scores as outcome measures, intraclass correlation coefficients which assess the magnitude but not direction of agreement, and repeated measures ANOVA (e.g., Maguire, 1999). However, these approaches have limitations. Difference scores cannot simultaneously model predictors of mean response, incongruence, and their relationship. They also do not generalize beyond paired data. Correlation coefficients are merely descriptive. Further, ratings by caregivers and patients on the same trait reflect non-independent data that are not suited to methods commonly used in the social sciences that assume independence of observations (Kenny, Kashy, & Cook, 2006), which calls into question the conclusions of prior research in proxy assessment at the EOL using such methods.

Hierarchical linear modelling (HLM; multilevel models) (Raudenbush, 2002) overcomes the methodological limitations associated with dyadic data by allowing for the simultaneous estimation of both individual- and dyad-level effects. This makes it possible to discover individual characteristics which affect neuroticism, separate dyad characteristics which predict incongruence, and their interactions. The use of random effects in HLM allows for the modeling of not only conditional means, as with ordinary linear regression, but also variances, which captures between-dyad heterogeneity and incorporates the statistical dependence within dyads into hypothesis tests. By examining the variance components it is also possible to quantify the inter-rater agreement via the intraclass correlation coefficient, expressed as the ratio of between-dyad variance in neuroticism scores to the total variance. HLM is a superior method for assessing mean ratings and incongruence within dyads and the direction of difference (e.g., Cano, Johansen, & Franz, 2005; Maguire, 1999; Sayer & Klute, 2005). In examining incongruence within the current dataset, Hack and colleagues (2018) note that studies should move beyond

simply examining agreement to determine predictors of incongruence, which can provide information about the dyad, enhancing clinical care for both patient and caregiver. HLM can accomplish this task quantitatively, by taking into account perspectives of both patients and caregivers in level and predictors of incongruence.

Interestingly, past research suggests that when self-other agreement in personality is studied within couples in which one partner is ill (e.g., Haider et al., 2002), agreement is greater for neuroticism than for other personality traits. This is counter to what SOKA and RAM suggest in terms of 'internal' traits like neuroticism being more difficult to judge, resulting in greater discrepancy of self-other ratings. This poses an interesting question regarding the unique impact of illness on self-other agreement of neuroticism within caregiving relationships, which may differ significantly from self-other agreement literature in the general population and using college/acquaintance samples. Such differences may be a function of various patient, caregiver, and relationship-level factors.

Therefore, the purpose of the present study was to examine the following objectives: 1) level of patient and caregiver rated patient neuroticism, and 2) predictors of patient-caregiver incongruence of patient neuroticism, which to our knowledge has not been explored in an EOL population. Our objectives and hypotheses are based on a synthesis of the literature related to the SOKA and RAM models of self-other agreement in personality and factors affecting proxy assessment at the EOL. With regards to Objective 1, I hypothesize that consistent with prior literature on proxy assessment at the EOL, caregivers will rate patients significantly higher on neuroticism than patients would rate themselves. With regards to Objective 2, I hypothesize that the degree of incongruence between patient and caregiver ratings of patients' neuroticism will be associated with patients' illness group, perceived dependency, current quality of life, depression,

anxiety, fatigue, cognitive status; and caregivers' burden, psychological distress, length and type of relationship to patient, age, gender, and education.

Method

Sample and Procedure

The current study employed data collected in the study *Dignity and Distress across End-of-Life Populations*, funded by the Canadian Institutes for Health Research (Chochinov et al., 2016). This project involved a prospective, longitudinal, multi-site approach to examine physical, psychological, existential, and spiritual issues of patients with ALS, COPD, ESRD, and the frail elderly (institutionalized and alert). For additional information concerning the data collection protocol and inclusion criteria see (Chochinov et al., 2016).

Eligible patient-participants were approached for the study, with $N = 249$ declining participation and $N = 10$ deemed ineligible due to level of cognitive impairment, resulting in a total sample of $N = 404$ patient-participants, of which $N = 216$ had an identified caregiver co-participant who completed measures of their own health and functioning as well as proxy assessment of several patient measures (Appendix B), including the NEO. It is these 216 dyads that are included in the present study. Detailed demographic information of the study patient-population can be found elsewhere (Chochinov et al., 2016), while demographics of the dyads in the present study are presented in Table 1. Date of death was tracked until September 2013, by which time 45% of participants had died (between groups, time of participation to death ranged from 1.1 to 1.6 years).

Measures

Sociodemographic variables. Patients and their caregiver co-participants both provided information concerning their age, gender, marital status, education, and income (see Table 1).

Table 1. *Demographics*

	ALS		COPD		ESRD		FE		Total			
	N											
	73		51		42		73		217			
	Patient	Caregiver	Patient	Caregiver	Patient	Caregiver	Patient	Caregiver	Patient	Caregiver		
	M (SD) [CI95]											
Age	64.82 (11.15) [62.20, 67.44]	60.22 (12.25) [57.31, 63.15]	72.27 (4.85) [70.87, 73.66]	64.49 (13.96) [60.14, 68.85]	72.17 (4.58) [70.72, 73.62]	61.31 (15.53) [56.34, 66.28]	87.98 (5.31) [86.47, 89.49]	60.54 (16.45) [55.81, 65.26]	73.49 (11.59) [71.93, 75.06]	61.42 (14.35) [59.42, 63.42]		
	N (%)										*p* patient	*p* caregiver
Marital Status											<.001	0.04
Married or common-law	57 (78.1)	67 (91.7)	31 (60.8)	38 (76)	21 (50)	26 (61.9)	8 (15.7)	40 (78.4)	117 (53.9)	171 (79.1)		
Other	16 (21.9)	8 (8.3)	20 (39.2)	16 (24)	21 (50)	18 (38.1)	43 (84.3)	13 (21.6)	100 (46.1)	45 (20.9)		
Gender (female)	21 (28.8)	60 (82.2)	30 (58.8)	31 (60.8)	19 (45.2)	35 (83.3)	31 (60.8)	37 (72.5)	101 (46.5)	163 (75.1)	.001	0.03
Religion											.001	<.001
Roman Catholic	20 (27.8)	24 (32.9)	15 (29.4)	17 (34)	8 (19.5)	6 (14.3)	11 (21.6)	9 (17.6)	54 (25.1)	56 (25.9)		
Protestant	13 (18.1)	14 (19.2)	14 (27.5)	12 (24)	18 (43.9)	17 (40.5)	17 (33.3)	9 (17.6)	62 (28.8)	52 (24.1)		
Jewish	0	0	0	0	0	0	6 (11.8)	6 (11.8)	6 (2.8)	6 (2.8)		
Muslim	1 (1.4)	0	0	0	0	0	0	0	1 (0.5)	0		
Other	23 (31.9)	23 (31.5)	9 (17.6)	8 (16)	6 (14.6)	10 (23.8)	13 (25.5)	13 (25.5)	51 (23.7)	54 (25)		
None	15 (20.8)	12 (16.4)	13 (25.5)	13 (26)	9 (22)	9 (21.4)	4 (7.8)	14 (27.5)	41 (19.1)	48 (22.2)		

(continued)

(continued)

	N (%)										*p* patient	*p* caregiver
Education complete											0.30	0.08
< High School	20 (27.8)	13 (17.8)	27 (52.9)	17 (34.7)	22 (52.4)	7 (16.7)	24 (47.1)	5 (9.8)	93 (43.1)	42 (19.5)		
High School complete	12 (16.7)	16 (21.9)	8 (15.7)	15 (30.6)	8 (19)	9 (21.4)	6 (11.8)	5 (9.8)	34 (15.7)	45 (20.9)		
Some University	16 (22.2)	19 (26)	7 (13.7)	9 (18.4)	5 (11.9)	10 (23.8)	6 (11.8)	16 (31.4)	34 (15.7)	54 (25.1)		
University/postgraduate complete	24 (33.3)	25 (34.2)	9 (17.6)	8 (16.3)	7 (16.7)	16 (38.1)	15 (29.4)	25 (49)	55 (25.5)	74 (34.4)		
Annual income (net last 12 months)											.002	0.07
≤60k	36 (49.4)	30 (48.8)	34 (66.7)	30 (81.6)	32 (76.2)	25 (71.4)	23 (45.1)	21 (51.2)	125 (57.5)	107 (64.8)		0.02
>60k	19 (26)	21 (41.2)	7 (13.8)	7 (18.4)	8 (30.9)	10 (28.6)	6 (11.8)	20 (48.8)	40 (18.4)	58 (35.2)		0.02

Neuroticism. Patients completed the 12-item neuroticism subscale from the NEO-FFI, with higher scores indicating greater neuroticism [scored 0 (strongly disagree) to 4 (strongly agree)] (Costa & McCrae, 1992; McCrae & Costa, 2004). Internal consistency in the current patient sample was $\alpha = 0.86$.

Caregivers also completed this measure on behalf of the patient. Caregivers were prompted to consider the patients' personality *in general* rather than with regards to changes that may have occurred with illness onset or aging. Questions were changed from beginning with "I am..." to "S/he is..." Internal consistency in the current caregiver sample was $\alpha = 0.84$.

Predictors of incongruence. Based on prior literature describing individual and dyadic variables that are associated with patient-caregiver incongruence in assessing both symptoms at the end-of-life (e.g., McPherson & Addington-Hall, 2003; McPherson et al., 2008) and self-other agreement in personality (e.g., Funder, 2012; Vazire, 2010), we assessed the following variables:

Patient-level. *Dependency* was assessed using the 3-item subscale (not being able to perform tasks of daily living, not able to attend to bodily functions, reduced privacy) from the 25-item Patient Dignity Inventory (PDI) [scored 1 (not at all a problem) to 5 (a major problem). Internal consistency was $\alpha = 0.73$.

Cognitive function was assessed using the Blessed Orientation-Memory-Concentration (BOMC) test (Katzman et al., 1983). This is a 6-item measure of cognition and memory functioning, scored from 0-29 (weighted points assigned for errors), in which a higher score reflects more cognitive impairment. Participants were eligible for the study if they scored ≤ 15.

Quality of life was assessed using the quality of life rating item from the 2-item Quality of Life Scale, in which participants rated their current quality of life on a scale of 0-10 in which low sores indicate poorer quality of life (Graham & Longman, 1987).

Depression was measured using the seven depression items from the Hospital Anxiety and Depression Scale (HADS), in which high scores indicate greater depression (scored 0 (normal/no depression) to 21 (severe depression). Internal consistency for the current sample was $\alpha = 0.78$. This measure was chosen specifically as the item content does not focus on somatic manifestations of depression and anxiety.

Fatigue and *anxiety* were assessed using items from the Revised Edmonton Symptom Assessment Scale (ESAS-R), a 16-item measure in which each item is scored to assess each individual symptom, 0 (no problem) to 10 (very significant problem) and 0 (low/poor) to 10 (high/good) (Bruera, Kuehn, Miller, Selmser, & Macmillan, 1991). Scores on ESAS-R items correlate highly with other symptom assessment measures, and same-day test-retest reliability is above 0.8. The measure has been validated in a range of illness groups and in several cultures, and is amongst the most widely used symptom assessment tools in palliative care (Richardson & Jones, 2009).

Caregiver-level. *Caregiver burden*, specific to EOL care, was assessed with the Caregiver Burden Scale in EOL Care (CBS-EOLC; Dumont, Fillion, Gagnon, & Bernier, 2008) a 16-item measure in which high scores denote higher perceived burden. Internal consistency for the current sample was $\alpha = 0.90$.

Psychological distress of the caregiver, related to the patients' needs and how patient distress affects the caregiver was assessed using the Psychological Distress Index, a 14-item measure in which high scores indicate increased distress (Boyer, Préville, Légaré, & Valois, 1993). Internal consistency for the current sample was $\alpha = 0.85$.

Length of relationship to patient. Caregivers reported the number of years they had known the patient.

Hours spent caregiving. Caregivers reported "how many hours of care do you provide for the patient every week?" (0, 1-4, 4-8, 8-12, >12).

Statistical Analysis

I used mixed-effects HLM models to estimate predictors of mean neuroticism and patient-caregiver incongruence. PROC MIXED of SAS version 9.3 (SAS Institute, Cary NC) was used with restricted maximum likelihood model (REML). I combined illness groups to yield a larger sample size, and included illness group as a predictor in the model.

Level 1 model. In order to address Objective 1 (level of incongruence), I first modeled an unconditional means model of neuroticism, with no predictors, to determine how much total variance in neuroticism is due to between-dyad differences, expressed as an intraclass correlation coefficient.

Next, I expanded this model to include a rater effect, with a random slope that is allowed to vary between dyads. As such, the indicator (predictor) is a variable coded -0.5 for the patient and 0.5 for the caregiver. The slope ($ß_{1j}$) represents the incongruence between the patient and caregiver. The goal of this model was to test for heterogeneity in rater incongruence, which if significant would permit modeling predictors of incongruence. The intercept and slope, unique for each dyad, totally explains the two observations, with no variance left over for the subject-level residual. Therefore, to prevent, I set the lower-bound for the subject-level residual to be a small value (0.0001). The random intercept and slope, our main interests, were estimated freely. I fit the following model to the neuroticism data for all subjects i and dyads j:

$$\text{Neuroticism}_{ij} = ß_{0j} + ß_{1j} (\text{RATER}_{ij}) + r_{ij}$$

Level 2 model. Following this, in addressing Objective 2 (predictors of incongruence), given the significant variation in intercept and slope between dyads, I created univariate models

for each dyad-level predictor of interest regressed upon the mean neuroticism score (intercept) and rater incongruence (slope). That is, the intercept and slope themselves became the dependent variables in the Level 2 model. Mean-centered variables were used where possible. These models were formulated as follows:

$$Neuroticism_{ij} = ß_0 + ß_1*rater + ß_2*covariate + ß_3*(rater*covariate) + U_{0j} + U_{1j}*rater + R_{ij}$$

Where U_{0j} and U_{ij} are the random intercept and slope terms, respectively, and Rij is the person-level residual. A significant main effect for the covariate indicates that it is predictive of the average neuroticism rating for dyads. A significant interaction with "rater" indicates a cross-level interaction [i.e., predictive of rating incongruence (slope)].

Next, I entered all significant univariate predictors as simultaneous predictors of dyad-level average neuroticism rating (random intercept). I then used backwards elimination to arrive at a parsimonious list of variables that were multivariately significant. I then added predictors to generate a multivariate model to explain differences in the average neuroticism rating (random intercept) and incongruence in neuroticism rating (random slope) across dyads as follows:

$$ß_{0j} = y_{00}+y_{01}CGBurden+y_{02}PtGroup+y_{03}PtDependency+y_{04}PtDepression+y_{05}PtFatigue+y_{06}PtAnxiety+y_{07}CGRelationship+U_{0j}$$

$$ß_{1j} = y_{10}+y_{11}CGBurden+y_{12}PtGroup+y_{13}PtDependency+y_{14}PtDepression+y_{15}PtFatigue+Y_{16}PtAnxiety+y_{17}CGRelationship+U_{1j}$$

Results

Objective 1

Caregivers rated patients' average neuroticism significantly higher (M = 19.20, SD = 7.56) (T=48; average range, 45th percentile) than did patients' themselves (M = 15.73, SD = 7.94) (T=42, low range, 21st percentile) (McCrae & Costa, 2010); (t = -6.51, df = 215, p < .0001;

Cohen's $d = 0.44$). Descriptive statistics for neuroticism and predictors are presented in Table 2. Zero-order correlations between patient and caregiver rated patient neuroticism and the predictors (patient perceived dependency, current quality of life rating, depression, anxiety, fatigue; caregiver burden and psychological distress, length of relationship to patient, age, and gender) are presented in Table 3.

Table 2. *Descriptive Statistics*

		ALS	COPD	ESRD	FE	Total	p-value
				N			
		73	51	42	51	217	
Patient	Neuroticism	15.54 (7.23) [13.84, 17.24]	17.53 (8.49) [15.14, 19.92]	13.14 (8.0) [10.65, 15.64]	16.31 (7.93) [14.08, 18.54]	15.73 (7.94) [14.66, 16.79]	0.06
	Dependency	6.10 (2.88) [5.42, 6.77]	5.35 (2.42) [4.58, 5.93]	3.93 (1.20) [3.56, 4.30]	5.47 (2.53) [4.76, 6.18]	5.33 (2.54) [4.99, 5.67]	<.001
	Cognitive functioning	1.76 (2.52) [1.14, 2.38]	2.20 (2.86) [1.39, 3.01]	2.05 (1.97) [1.43, 2.67]	3.88 (3.45) [2.91, 4.85]	2.44 (2.88) [2.05, 2.84]	<.001
	QoL rating	6.51 (2.35) [5.96, 7.07]	6.56 (2.49) [5.85, 7.27]	6.95 (2.24) [6.25, 7.65]	6.49 (2.44) [5.79, 7.19]	6.61 (2.37) [6.28, 6.93]	0.77
	Depression	5.22 (3.50) [4.40, 6.05]	5.35 (3.48) [4.38, 6.33]	4.07 (3.70) [2.92, 5.23]	4.51 (3.31) [3.58, 5.44]	4.86 (3.50) [4.39, 5.33]	0.22
	Anxiety	2.28 (2.46) [1.70, 2.86]	2.92 (3.27) [1.98, 3.86]	1.88 (2.68) [1.05, 2.72]	1.78 (2.44) [1.08, 2.47]	2.23 (2.72) [1.86, 2.60]	0.16
	Fatigue	4.21 (2.95) [3.52, 4.90]	4.16 (3.17) [3.25, 5.07]	3.76 (3.55) [2.65, 4.87]	3.20 (2.65) [2.45, 3.94]	3.87 (3.07) [3.46, 4.28]	0.28
Caregiver	Caregiver burden	24.28 (6.35) [22.74, 25.83]	23.12 (6.14) [21.34, 24.89]	23.42 (6.27) [21.30, 25.54]	23.76 (6.37) [21.93, 25.58]	23.72 (6.26) [22.85, 24.59]	0.79
	Patient Neuroticism	17.21 (7.20) [15.53, 18.88]	21.94 (7.82) [19.74, 24.14]	18.19 (6.70) [16.10, 20.28]	20.02 (7.65) [17.87, 22.17]	19.17 (7.55) [18.16, 20.18]	0.004
	Psych Distress	25.29 (6.50) [23.77, 26.80]	24.71 (4.83) [23.35, 26.07]	24.43 (6.23) [22.49, 26.37]	22.82 (4.10) [21.67, 23.98]	24.41 (5.62) [23.65, 25.16]	0.11
	Length of relationship (years)	38.49 (15.75) [34.82, 42.17]	44.27 (14.51) [40.10, 48.43]	44.50 (13.68) [40.24, 48.76]	58.43 (10.0) [55.62, 61.24]	45.71 (15.72) [43.61, 47.82]	<.001

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	ALS	COPD	ESRD	FE	Total	p-value
			N			
	73	51	42	51	217	
Relationship to patient						<.001
Spouse/partner	54 (74)	32 (64)	19 (45.2)	4 (8)	109 (50.7)	
Adult child	9 (12.3)	11 (22)	16 (38.1)	34 (68)	70 (32.6)	
Other relative	5 (6.8)	4 (8)	1 (2.4)	11 (22)	21 (9.8)	
Friend or other	5 (6.8)	3 (6)	6 (14.3)	1 (2)	15 (7)	
Hours spent caregiving/week						.001
>12	42 (58.3)	22 (44)	14 (33)	14 (28)	92 (43)	
8-12	8 (11.1)	3 (6)	2 (4.8)	5 (10)	18 (8.4)	
4-8	3 (4.2)	4 (8)	7 (16.7)	14 (28)	28 (13.1)	
1-4	13 (18.1)	16 (32)	17 (40.5)	16 (32)	62 (29)	
0	6 (8.3)	5 (10)	2 (4.8)	1 (2)	14 (6.5)	

Table 3. *Zero-order correlations among independent variables and neuroticism (as reported by both patient and caregiver)*

		1	2	3	4	5	6	7	8	9	10	11	12
	Pt Rated Neuroticism (0.49**)	.32**	.41**	0.09	.55**	-.37**	.45**	0.03	0.03	-0.09	.24**	0.06	0.07
	CG Rated Neuroticism	0.12	.23**	0.08	.35**	-.30**	.34**	0.03	0.05	-0.05	.26**	.17*	0.03
1	Dependency	1.00											
2	Fatigue	.27**	1.00										
3	Cognition	-0.04	0.06	1.00									
4	Anxiety	.33**	.50**	0.03	1.00								
5	QoL	-.29**	-.39**	-0.04	-.32**	1.00							
6	Depression	.31**	.37**	0.03	.39**	-.64**	1.00						
7	Years known	-0.13	-0.05	.22**	-0.10	-0.03	-0.02	1.00					
8	CG Gender	-0.10	0.01	-0.05	-0.04	0.08	-0.11	0.11	1.00				
9	CG Age	-.21**	0.01	0.12	-.18*	-0.03	0.01	.31**	.19**	1.00			
10	CG Burden	.31**	0.12	-0.01	.17*	-.24**	.25**	-0.10	-.22**	-.14*	1.00		
11	CG Psych Distress	.14*	0.00	-.14*	0.04	-.18**	.24**	-.20**	-.14*	-0.09	.49**	1.00	
12	>12 hrs care/wk	.17*	0.06	-0.12	.15*	-.21**	.24**	-0.10	0.07	0.06	.25**	.19**	1.00

		13	14	15	16	17	18	19	20	21	22	23	24	25	26
	Pt Rated Neuroticism	-0.07	0.00	0.02	-0.10	-0.10	0.01	0.03	0.11	0.05	0.01	-0.08	0.02	-0.06	0.06
	CG Rated Neuroticism	-.13*	-0.02	0.01	0.09	-0.12	.15*	0.01	-0.04	0.04	0.05	-0.06	-0.03	-0.12	0.12
13	8-12 hrs care/wk	1.00													
14	4-8 hrs care/wk	-0.12	1.00												
15	1-4 hrs care/wk	-.19**	-.25**	1.00											
16	0 hrs care/wk	-0.08	-0.10	-.17*	1.00										
17	CG spouse	0.03	-.25**	-.20**	0.07	1.00									

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		13	14	15	16	17	18	19	20	21	22	23	24	25	26
18	CG adult child	-0.07	.34**	0.06	-0.06	-.71**	1.00								
19	CG Other	0.06	-0.05	0.04	0.01	-.28**	-.19**	1.00							
20	CG other relative	0.01	-0.08	.20**	-0.03	-.33**	-.23**	-0.09	1.00						
21	CG edu <HS	-0.11	-0.05	0.05	-0.04	.24**	-.19**	-0.03	-0.08	1.00					
22	CG edu HS	-0.03	-0.10	0.00	-0.04	0.02	-0.01	-0.09	0.06	-.25**	1.00				
23	CG edu some uni	0.13	0.13	0.01	0.02	-0.11	0.04	0.07	0.07	-.29**	-.30**	1.00			
24	CG edu uni	0.00	0.02	-0.04	0.05	-0.12	0.13	0.05	-0.04	-.36**	-.37**	-.42**	1.00		
25	CG income >60k	0.13	-0.03	0.03	-0.04	-0.13	.163*	-.159*	0.09	-.26**	-0.08	-0.05	.32**	1.00	-
26	CG income <60k	-0.13	0.03	-0.03	0.04	0.13	-.16*	.159*	-0.09	.26**	0.08	0.05	-.32**	-1.00**	1.00

*p<.05 (two-tailed), **p<.01 (two-tailed)

Level 1 model: Patient-caregiver neuroticism incongruence. I estimated the proportion of variance between dyads using the intraclass correlation coefficient $\rho = \tau_{00}/ (\tau_{00} + \sigma^2)$, which for neuroticism is 42%, where τ is the proportion of variance due to between dyad differences ($\tau = 26.28$) and σ^2 is the individual variance ($\sigma^2 = 36.58$). I did not find a significant correlation between the random intercept and slope ($p = 0.40$), indicating that incongruence did not vary based on mean neuroticism scores, and vice versa.

Table 4 shows the mean score for dyads' rating of caregiver neuroticism was 17.44 (T = 45 for combined gender, 32nd percentile) (McCrae & Costa, 2010) (CI_{95} = 16.55, 18.34; p <.0001), which falls in the average range. The average incongruence score for neuroticism was 3.46 (CI_{95} = 2.41, 4.51; p <.0001). The positive direction of incongruence indicates that, on average, caregivers rated patients significantly higher in neuroticism than patients rated themselves. Both the mean neuroticism rating and incongruence significantly varied between dyads. As such, I added level-2 predictors to explain the variance in dyad mean and incongruence.

Table 4. *Random intercepts and slopes model: Dyad mean and incongruence of neuroticism*

		Neuroticism		
Parameter	Coefficient	SE	p-value	95% CI
Fixed effects				
Dyad mean (intercept)	17.42	0.45	<.0001	16.55, 18.36
Incongruence (slope)	3.46	0.53	<.0001	2.41, 4.51
Random effects				
Dyad mean (intercept)	44.61	4.30	<.0001	
Incongruence (slope)	61.42	5.92	<.0001	

Objective 2

Level 2 model: Predictors of patient-caregiver neuroticism incongruence. In Table 5, I present the results of modelling both the univariate and multivariate relationships between the dyad-level predictors of interest and the mean neuroticism score (intercept) and rater discrepancy (slope). These predictors included patients' dependency, cognition, quality of life, fatigue, depression, anxiety, and illness group; and caregivers' psychological distress, caregiver burden, age, education, relationship to patient, and hours spent caregiving. Additionally, dyad length of relationship was included. When each independent variable was added univariately in its own model, the following were significant predictors of mean neuroticism: patient dependency, quality of life, depression, anxiety, fatigue, and illness group; and caregiver psychological distress and burden. Patient dependency, depression, anxiety, and fatigue were significant predictors of mean incongruence in the univariate models. Positive parameter estimates reflect an increase in mean neuroticism or incongruence (i.e., less agreement), whereas negative parameter estimates reflect a decrease in mean neuroticism or incongruence (i.e., more agreement); when the predictor increases beyond its average value. For example, Table 5 shows that when explored univariately, average neuroticism increases 0.88 per unit increase in patient depression, and incongruence decreases as depression increases beyond its average value, which can be interpreted by multiplying the parameter estimate (-0.30) by the predictor unit value above the mean (which is zero as variables were mean-centered), and comparing it to the average incongruence rating of 3.44 (e.g., a patient with a HADS depression score of 6 will have an incongruence rating of 1.64 [3.44 – 0.3*6] indicating that caregivers rate neuroticism 1.64 points higher than patients).

Table 5. *Estimated parameters of multilevel regression predicting neuroticism incongruence*

		Dyad-level covariates added univariately				Multivariate model[a]			
Parameter		Coefficient	SE	p-value	95% CI	Coefficient	SE	p-value	95% CI
Dyad mean (intercept) ($ß_0$)		17.44	0.45	<.0001	16.55, 18.36	17.22	1.17	<.0001	14.90, 19.53
Patient									
	Dependency[1]	0.68	0.17	0.0001	0.33, 1.02	0.03	0.18	0.89	-0.32, 0.38
	Quality of Life[2]	-1.10	0.18	<.0001	-1.45, -0.75				
	Cognition[3]	0.23	0.16	0.16	-0.09, 0.55	0.54	0.12	<.0001	0.31, 0.78
	Depression[4]	0.88	0.12	<.0001	0.65, 1.11	0.37	0.13	0.00	0.12, 0.62
	Fatigue[5]	0.81	0.14	<.0001	0.54, 1.07	0.29	0.13	0.03	0.02, 0.55
	Anxiety[6]	1.28	0.14	<.0001	0.99, 1.56	0.91	0.16	<.0001	0.60, 1.23
	Illness[b,c]								
	ALS	-1.81	1.20	0.13	-4.16, -0.55	-1.49	1.24	0.23	-3.94, 0.97
	COPD	1.57	1.30	0.22	-0.99, 4.12	1.12	1.25	0.37	-1.34, 3.58
	ESRD	-2.50	1.36	0.07	-5.18, 0.19	-1.51	1.27	0.23	-4.01, 0.99
Caregiver	Age	-0.04	0.03	0.26	-0.10, 0.03				
	Gender[d]								
	Female	-0.66	1.05	0.53	-2.75, 1.41				

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	Dyad-level covariates added univariately				Multivariate model[a]			
Parameter	Coefficient	SE	p-value	95% CI	Coefficient	SE	p-value	95% CI
Education[e]								
< High school	0.74	1.28	0.56	-1.78, 3.27				
High School	0.51	1.25	0.69	-1.96, 2.98				
Some college/university	-0.86	1.19	0.47	-3.20, 1.48				
Burden	0.28	0.07	<.0001	0.15, 0.40	0.18	0.07	0.008	0.05, 0.32
Psychological Distress	0.16	0.08	0.05	0.00, 0.32				
Time known patient	0.02	0.03	0.60	-0.04, 0.07				
Relationship to patient[f]								
Adult child	1.64	1.03	0.11	-0.39, 3.66	1.30	1.03	0.21	-0.73, 3.33
Other relative	1.68	1.60	0.29	-1.47, 4.82	1.52	1.46	0.30	-1.37, 4.41
Other	1.37	1.84	0.46	-2.27, 5.00	2.63	1.55	0.09	-0.42, 5.68
Hours spent caregiving[g]								
0	-0.62	1.90	0.74	-4.37, 3.12				
1-4	-0.22	1.09	0.84	-2.36, 1.93				

(continued)

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		Dyad-level covariates added univariately				Multivariate model[a]			
Parameter		Coefficient	SE	p-value	95% CI	Coefficient	SE	p-value	95% CI
	Hours spent caregiving[g]								
	4-8	-0.59	1.43	0.68	-3.41, 2.23				
	8-12	-2.98	1.71	0.08	-6.34, 0.39				
	Is primary caregiver[h]								
	No	1.26	1.34	0.35	-1.38, 3.90				
Incongruence ($ß_1$) (slope)		3.46	0.53	<.0001	2.41, 4.51	3.61	0.75	<.0001	2.13, 5.09
Patient									
	Dependency	-0.66	0.21	0.002	-1.07, -0.25	-0.71	0.21	0.001	-1.12, -0.29
	Cognition	-0.05	0.19	0.81	-0.42, 0.33				
	Quality of Life rating	0.27	0.23	0.23	-0.18, 0.72				
	Depression	-0.30	0.15	0.05	-0.59, 0.00				
	Fatigue	-0.48	0.17	0.005	-0.82, -0.14				
	Anxiety	-0.64	0.19	0.001	-1.02, -0.26				
Caregiver	Age	0.02	0.04	0.58	-0.06, 0.10				
	Gender[d]								
	Female	-0.30	1.23	0.81	-2.74, 2.13				

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	Dyad-level covariates added univariately				Multivariate model[a]			
Parameter	Coefficient	SE	p-value	95% CI	Coefficient	SE	p-value	95% CI
Education[e]								
< High school	0.39	1.53	0.80	-2.63, 3.41				
High School	1.07	1.50	0.48	-1.88, 4.02				
Some college/university	0.81	1.42	0.57	-1.99, 3.60				
Burden	0.02	0.08	0.85	-0.14, 0.17				
Psychological Distress	0.14	0.09	0.13	-0.04, 0.33				
Time known patient	-0.00	0.03	0.99	-0.07, 0.07				
Relationship to patient[f]								
Adult child	1.60	1.20	0.18	-0.75, 3.96	1.90	1.19	0.11	-0.44, 4.24
Other relative	-3.48	1.86	0.06	-7.14, 0.18	-5.07	1.89	0.008	-8.81, -1.34
Other	-0.67	2.14	0.75	-4.90, 3.55	-2.23	2.12	0.29	-6.41, 1.96
Hours spent caregiving[g]								
0	6.01	2.24	0.008	1.60, 10.43				
1-4	0.21	1.28	0.87	-2.32, 2.74				

(continued)

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	Dyad-level covariates added univariately				Multivariate model[a]			
Parameter	Coefficient	SE	p-value	95% CI	Coefficient	SE	p-value	95% CI
Hours spent caregiving[g]								
4-8	0.09	1.69	0.96	-3.24, 3.41				
8-12	-1.18	2.01	0.56	-5.15, 2.79				
Is primary caregiver[h]								
No	1.24	1.60	0.44	-1.91, 4.38				

[a] includes all variables that were simultaneously univariately significant predictors of incongruence
[b] Frail Elderly as reference group
[c] omnibus test for illness group is significant ($p<.01$) for dyad mean neuroticism
[d] Male as reference group
[e] University or postgraduate degree complete as reference group
[f] Spouse/partner as reference group
[g] >12 hours per week as reference group
[h] 'Yes' as reference group

I then entered all the significant predictors of mean neuroticism (above) simultaneously, which resulted in patient dependency, fatigue, and caregiver psychological distress no longer significantly predicting mean neuroticism, and then further used backwards elimination to arrive at a more parsimonious list of predictors for the multilevel model, which also included predictors of incongruence. Consequently, Table 5 also shows the multivariate model in which patient depression, anxiety, illness group, and caregiver burden all significantly predict mean neuroticism, controlling for other variables in the model. Specifically, each unit increase in patient depression, anxiety, and caregiver burden is associated with an increase (value of the parameter estimate) in mean neuroticism (17.22).

Additionally, patient dependency and the type of relationship of caregiver to patient significantly predict incongruence. I found the incongruence between raters to be dependent on (moderated by) the relationship between patient and caregiver, and the level of patients' self-reported dependency, per significant cross-level interaction effects. 'Spouses and partner' caregivers rated patient neuroticism to be 3.61 units higher than patients on average. However, caregivers who were 'other relatives' rated patient neuroticism to be [3.61 – 5.07 =] 1.46 units lower than patients, an effect in the opposite direction ($p = 0.0036$). 'Adult children' and 'other' types of caregivers did not significantly differ from spouses and partners with respect to incongruence. Additionally, incongruence is also moderated by patient dependency, such that incongruence decreases by 0.71 per unit increase in patients' self-reported dependency beyond its average value ($p = 0.008$). Therefore, when dependency is at the mean of zero, caregivers rated patients [3.61 – 0*0.71 =] 3.61 units higher on neuroticism than patients rated themselves. When dependency is 1, caregivers were less incongruent, rating neuroticism [3.61 – 1*0.71 =]

2.9 units higher than patients. When dependency reaches a score of 5.08, patients and caregivers have no incongruence in ratings of neuroticism [3.61 – 5.08*0.71 = 0].

Discussion

In this study, I first examined the level of incongruence of patient and caregiver ratings of patient neuroticism in four non-cancer populations at the EOL. Our descriptive findings indicate that in ALS, COPD, ESRD, and frailty, patients reported their level of neuroticism to be at the 21st percentile (average across groups), which is nearly one standard deviation below caregivers' average ratings of patient neuroticism at the 48th percentile. Though the NEO-FFI is not a measure of psychopathology, given the strong positive relationship between neuroticism and psychopathology (e.g., Barlow, Ellard, Sauer-Zavala, Bullis, & Carl, 2014), the magnitude of difference in scores between patients and caregivers would likely be associated with clinically observable differences in personality and affect. That caregivers rated neuroticism as significantly higher than did patients themselves is consistent with prior literature in proxy assessment at the EOL, indicating that caregivers tend to provide higher (i.e., more negative) ratings than patients across a range of symptoms, and are more incongruent on traits reflecting internal or emotional states (e.g., McPherson et al., 2008).

Those who volunteer for research studies tend to be lower in neuroticism (Jan-Erik et al., 2007), and this may be particularly true at the EOL, which can be a time of increased vulnerability, particularly for those more prone to emotional distress (Casarett, 1999). There is also evidence that self-reported neuroticism tends to decrease with age, while informant-reported neuroticism increases (Cooper et al., 2014). Our findings may provide evidence for patient concealment, potentially related to fears of being a burden to others (Wilson et al., 2005). Another possibility is that proximity to death does in fact lower patients' self-perceived level of

neuroticism. Within the existential-humanistic literature, personality change, including decreases in neuroticism, is a key component of fulfillment and wellbeing (Osafo Hounkpatin, Wood, Boyce, & Dunn, 2015). Such change may be relevant in our sample, who generally reported low levels of psychological and dignity-related distress (Chochinov et al., 2016), both of which are essential components of existential distress at the EOL (Chochinov et al., 2006)

In addressing our second objective, understanding the predictors of incongruence, I first examined predictors of dyad mean neuroticism (average of patient-caregiver rating). In our multivariate model, patient depression, fatigue, anxiety, poor cognition; and caregiver burden all positively increased dyad-level mean neuroticism ratings, though these ratings remained in the average range. Within the context of the RAM (Funder, 1995), it appears in our sample that participants who behave in ways that align with neuroticism (e.g., depressed, fatigued, tense, avoidant) indeed have higher mean neuroticism scores, perhaps by providing more information and opportunities for caregivers to observe behavior related to the trait being judged, which could raise caregiver reported scores. Alternatively (or concurrently), patients who are more depressed, anxious, fatigued, or cognitively compromised endorse higher neuroticism, which may reflect that neuroticism in this population is more reflective of state rather than trait variance (Chmielewski & Watson, 2009; Ormel et al., 2013; Watson, 2004). Further, caregiver burden seems to impact the 'quality of the judge', and could be reflective of caregivers' stress, leading them to perceive and rate patients as more neurotic, which would increase the dyad mean score of neuroticism. Relatedly, patients higher in neuroticism may have more stressed caregivers, or caregiver burden may increase the mean neuroticism score due to patients feeling that they are a burden and experiencing related emotional distress, which is reflected in their self-reported neuroticism (Chochinov, 2006).

Next, I examined predictors of incongruence. The existing literature suggests that in patients with advanced cancer, greater caregiver burden and caregiver low mood are related to incongruence in proxy ratings of a range of patients' physical and psychological symptoms, with a bias for caregivers to overestimate distress (McPherson et al., 2008). Similar findings have been found within the dementia caregiving literature (e.g., Boyer, Novella, Marrone, Jolly, & Blanchard, 2004; Thompson & Chochinov, 2006). Our study did not fully support these findings with regard to neuroticism. That is, in examining predictors of incongruence, level of caregiver burden and caregiver psychological distress were not significant univariate or multivariate predictors of incongruence in patient-caregiver neuroticism ratings. It is possible that while predictors of incongruence found in prior literature predict patient-proxy incongruence on ratings of physical symptoms or psychological states, they do not predict incongruence for neuroticism. However, a strength of the present study is the use of HLM, which avoids problems with difference scores used in studies demonstrating the effect of caregiver burden and distress in overestimation of symptoms and experiences (e.g., Lopez,et al.,2019; Miaskowski et al, 1997). As such, based on the current study, it cannot be assumed that caregiver burden or psychological distress has any significant impact on disparities in patient-caregiver neuroticism ratings. Further, there was no evidence for demographic effects such as caregiver age, education, or gender on incongruence.

Patient dependency and caregiver being an 'other relative' (compared to spouse) did significantly increase congruence on neuroticism ratings. That patient dependency increased congruence is interesting in the context of literature on aging, perceived control, and neuroticism. In the present study, dependency was comprised of not being able to perform tasks of daily living, not able to attend to bodily functions, and reduced privacy (Patient Dignity Inventory

(PDI); Chochinov et al., 2008). There is evidence that increased functional dependency is associated with decreased perceived control (which in turn lowers morale), in older adults in long term care (Ryden, 1984), and that higher neuroticism in late life is associated with decreased perceived control (Kandler, Kornadt, Hagemeyer, & Neyer, 2015). Further, there is a substantial body of literature in the area of palliative care and serious illness demonstrating that perceived burden to others is significantly associated with psychological distress, loss of dignity, poor quality of life, and loss of control (Beattie, Lebel, Labelle et al., 2016; Beattie, Lebel, Petricone-Westwood et al., 2016; Cohen & Leis, 2002; Wilson et al., 2005). Perceived burden is also common in those requesting assisted suicide (Ganzini, Silveira, & Johnston, 2002; Morita, Sakaguchi, Hirai, Tsuneto, & Shima, 2004), and is experienced as a threat to personhood (Chochinov, 2006). Predictors in the current study, such as caregiver burden and time spent caregiving, cannot account for the increased congruence as a function of increased dependency, as they did not emerge as significant within the multivariate model. Therefore, it is possible that those high in dependency experience lowered perceived control and relatedly, higher neuroticism, which may increase their neuroticism rating to come closer to that of the caregiver. However, this is speculative, as within our multilevel model, it is not possible to ascertain whose ratings 'move' to contribute to increased congruence. As such, it is also possible that caregivers' ratings of patient neuroticism decrease, or a combination of the two, which result in a score that is closer to the dyad mean. Use of more advanced statistical methodologies, such as latent class mixture modelling, could extend the findings by exploring dyads based on direction of incongruence within the dyad (patient higher than caregiver or caregiver higher than patient), and risk/protective factors within each of these groups (Lyons & Lee, 2018).

The finding that incongruence was predicted by relationship type, with other relatives (parents, siblings, and other) rating neuroticism significantly lower than patients (compared to spouses/partners, who rated neuroticism significantly higher than patients), may be contextualized within the person perception literature. The SOKA model posits that low acquaintance reduces accuracy for traits such as neuroticism, which are considered "low observability traits" (Vazire, 2010, p. 293). It is difficult to argue that "other relatives" could be categorized as having low acquaintance to patients in the current study, as they had known patients as long, if not longer, in most cases, than spousal caregivers. However, it is possible that spouses have more access to patients' internal, emotional experiences, and thus rate neuroticism as higher because they are able to see more traits and behaviours that align with that trait, and relatedly, other relatives may underestimate neuroticism due to unavailability of neuroticism-related behaviours. This is consistent with research showing that providing raters with information about a target's personal behavior is associated with higher positive correlation of self-other neuroticism ratings (Slatcher & Vazire, 2009). However, there is a recognized need for additional research on the role of emotional investment in incongruence between self-other ratings of personality (Vazire, 2010).

From a motivated social cognition perspective, just as there is motivation to view the self in a positive light, there is a motivation to do the same for those with whom we are in close social relationships (Hughes & Beer, 2012). As such, one might expect caregivers' reports of neuroticism are not inflated. Though neuroticism is considered a 'low evaluative trait' (Vazire, 2010), it seems likely that caregivers wishing to paint their loved one in a positive light would not over report dimensions of negative affectivity such as neuroticism. Importantly, the research in self-other knowledge asymmetries and personality agreement has not assessed those who are

seriously ill and/or at the EOL. Such circumstances clearly impact the emotional experience of the patient and caregiver in unique and overlapping ways, and also are associated with possible cognitive and physiologic changes that impact self-perception and social cognition (Gerstorf & Ram, 2013).

In integrating the above discussion within a theoretical context, the literature on dyadic illness management and perspective taking within caregiving relationships is helpful. The recent Theory of Dyadic Illness Management (Lyons & Lee, 2018) calls for the dyad as the unit of care, and that in the context of illness, the perspectives and appraisals of both members of the dyad hold equal weight. Specifically, the theory posits that "the way dyads appraise illness as a unit influences the ways in which they engage in behaviours to manage illness together in a recursive fashion that influences dyadic health" (p. 8). Within this context, the focus of our findings may shift from what drives incongruence to what incongruence means how the couple copes with challenges. As reviewed by Lyons and Lee (2018), incongruence in appraisals across a range of symptoms and illness groups yields poorer quality of life in patients, caregivers, or both (e.g., Lyons, Miller, & McCarthy, 2016; Merz et al., 2011; Moon, Townsend, Whitlatch, & Dilworth-Anderson, 2017).

With regard to perspective taking, caregivers who are prompted to imagine how the patient would respond (rather than imagining how they themselves would feel or viewing the patient from their own perspective) produce ratings that are more congruent with patient reports, likely as a function of this perspective-taking prompt re-orienting the caregiver away from the self and towards the patient (Lobchuk & Vorauer, 2003). As such, instructing caregivers to imagine the patients' perspective leads to increasing congruence with patient reports. It is likely that patient, caregiver, and dyad each contribute unique perspectives that provide different, yet

related, information that has to be weighed in caring for each individual patient, dyad, and family.

Relatedly, an important contextual factor in the present study is that the instructions provided on the NEO-FFI to caregivers did not encourage them to take the perspective of the patient, but rather was their own perspective of the patient in general. While this likely reflects 'real life' situations in which clinicians are asking caregivers for collateral information, it is likely to result in more incongruent reports. As such, inviting caregivers to answer as the patient would, or experimentally comparing perspective taking prompts to caregivers in assessing patients' neuroticism, would provide rich information in extending the current findings. Additionally, the present study uses cross-sectional data, and so changes in reported neuroticism as a function of disease progression cannot be determined. Ideally, future research would have baseline personality data from either prior to an illness diagnosis, or early in the disease trajectory, such that follow-up assessment(s) could determine change related to the illness itself. Additionally, the use of measures assessing anxiety and depression were self-report rather than diagnostic tools. Utilizing a more comprehensive assessment for depression and anxiety, in addition to measures assessing patient perceived control, coping, caregivers' own personality profile, and dyad relationship factors (e.g., warmth, emotional connection) would be advantageous in understanding predictors of neuroticism and incongruence between patients and caregivers. Qualitative interviews with patients and caregivers would also provide rich additional information in probing incongruence.

The study has several strengths. To our knowledge, it is the first to explore both level and predictors of neuroticism in non-cancer populations at the EOL. Having information regarding both self- and caregiver-reported neuroticism in ALS, COPD, ESRD and frailty provides an

important benchmark for future research, and also provides clinicians in these areas with information regarding assessment of (potentially) more 'high risk' groups in terms of mental health issues, such as depression and anxiety. Our findings confirm that patient and caregiver ratings are not interchangeable, but may each have their merits through providing insight into aspects of the dyad. This study enhances both the self-other agreement literature and the literature in proxy assessment at the EOL by utilizing rigorous statistical methods to assess predictors of incongruence between patient and caregiver reports of patient symptoms. The paper extends knowledge about self-other ratings to samples that are not often researched in this area, but for whom the implications of neuroticism are significant in terms of EOL experience. In reaching the goal of quality palliative care, clinicians consider the patient and family as a unit of care, which can be enhanced through increased awareness of something as fundamental to patient personhood as personality. Clinician understanding that proxy measures of patients' neuroticism are likely to be higher than EOL patients' self-reports, and this incongruence is reduced among patients with increased dependency or by having non-spouse relatives as raters, is one important way clinicians can contextualize and interpret proxy ratings to further the goal of considering the patient and family as the unit of care.

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Chapter Four: General Discussion

This thesis addresses the complex role of neuroticism in non-cancer illness at the end of life. Specifically, the goal for study 1 was to determine whether neuroticism moderated the relationship between (primarily) physical or illness-specific symptoms at baseline and depression three months later, within the context of the approximate last six months of life. This study demonstrated that neuroticism is indeed an important variable in understanding the relationship between illness-specific symptoms and depressive symptoms. As neuroticism plays an important role in end of life experience, it is important to determine how neuroticism can be assessed at the end of life, given the complexities in the patient sample. Specifically, given the high burden on patients in completing measures given the severity of illness, and the thought that their illness may in some ways alter their self-reports of neuroticism (Leventhal & Crouch, 1997), there are likely times when caregivers will be asked to provide proxy reports. However, practical issues emerged in terms of congruence with patient reports and thus how to contextualize proxy assessments of patient traits. Study 2 addressed these issues by examining the level of patient and caregiver reported patient neuroticism, and examining predictors of congruence in these ratings. This study demonstrated that caregivers rate patient neuroticism significantly higher than patients' self-reported neuroticism. Increased congruence in ratings was predicted by the caregiver being a relative other than the spouse, and increased patient dependency. If the goal of proxy ratings is to truly be a proxy for patient response, through awareness of these predictors, clinicians and researchers can be better equipped to identify when ratings are representative of the patient.

Contextualizing neuroticism in our sample

That patients across the four populations rated their neuroticism nearly one standard deviation below the mean (21st percentile) is inconsistent with the prior, though limited, research suggesting an uptick of neuroticism at the very end of life (e.g., Charles, 2010; Wagner, Ram, Smith, & Gerstorf, 2015). Though our personality data were cross-sectional and we do not know these patients' neuroticism scores prior to their illness onset, it seems unlikely that the current reported scores are an increase from baseline, as this would require baseline scores to be below the 21st percentile. As such, there are several potential explanations for the relatively low levels of self-reported neuroticism in our sample. In looking to the literature on mental disorders at the end of life, there is evidence that rates of mental disorders do not increase in populations with terminal illness as disease progresses. For example, in patients with terminal cancer, closeness to death was not associated with a significant increase in major depressive disorder, generalized anxiety disorder, panic disorder, or posttraumatic stress disorder (Lichtenthal et al., 2009). In another cohort of terminally ill cancer patients, anxiety was generally low and did not vary by illness severity (Kolva, Rosenfeld, Pessin, Breitbart, & Brescia, 2011). There is a clear link between neuroticism and depression and anxiety in the general population (Jylha & Isometsa, 2006). It thus seems plausible that in our study sample, the aforementioned pattern of stable mood and anxiety symptoms at the EOL would also apply to neuroticism.

That closeness to death is not associated with an increase in mental disorders is counter to what is generally reported in the gerontological literature regarding increased rates of mental disorders in the oldest old (e.g., Gerstorf et al., 2010; Reynolds, Pietrzak, El-Gabalawy, Mackenzie, & Sareen, 2015). As such, there is discordance between mental disorders reported for those who are 'actively' dying compared to those who are in the last years of life, and these experiences may reflect unique psychological processes as well as divergent EOL experiences.

This is supported by recent work demonstrating that neuroticism impacts wellbeing as a function of mortality proximity rather than age alone (Mueller, Wagner, Wagner, Ram, & Gerstorf, 2018). Further, our cohort may reflect the recent finding that low neuroticism is associated with a steeper terminal decline in the last year of life (Mueller et al., 2018).

Given the limited research that is specific to palliative or end of life populations explicitly, contextualizing my findings within the research on personality and aging is helpful. Mueller and colleagues summarize and integrate two theoretical perspectives regarding the impact of personality on aging and health outcomes (Mueller, Wagner, Smith, Voelkle, & Gerstorf, 2018). One theory suggests that personality loses relevance in old age in the face of physiological decline, while the other suggests that the effects of personality are amplified in old age due to functional vulnerabilities. That personality decreases in relevance is supported by the Selection Optimization and Compensation (SOC) theory, which suggests that successful aging is related to optimizing capacities and goal pursuits while compensating for declines (Baltes, 1997). Within this framework, as physical limitations become increasingly salient they may outweigh psychosocial factors such as personality (Baltes & Smith, 2003). Alternatively, another framework suggests that personality may more strongly impact health in the context of functional limitations (i.e., is protective or a risk factor) (Duberstein et al., 2003). Mueller and colleagues (2018) hypothesize that both of the above theories may be applicable dependent on age (young-old versus old-old) and provide evidence for bidirectional associations between personality and functional health, separating effects for the young-old and the oldest-old. Of particular relevance to our findings concerning the level of neuroticism in our sample, they found that “health decrements precede and predict change in neuroticism in the oldest-old more strongly as compared with the young old” and in particular, in the oldest-old, decreases in vision

and physical functioning predicted longitudinal increases in neuroticism, providing evidence that neuroticism is not stable in the context of declining health. Importantly, these findings have not been found in self-assessed health, suggesting that methodological issues may be at play when determining these relationships (Mueller et al., 2018, p.1127).

Individuals are notoriously poor at predicting how they will cope with suffering associated with physical illness, and often are more tolerant to a variety of symptoms than they thought they would be (Wilson et al., 2007). It is thus also plausible that in our study, the fact that patients had a diagnosis and were identified as in the probable last six months of life engaged in self-reflective processes, and perhaps sensed that they were doing better than they would have expected, proactively appraised and engaged in problem solving (Davis & Asliturk, 2010), or focused on the positive as a buffer to impending mortality (Davis & McKearney, 2003) which could improve coping and lower self-reported neuroticism. Caregivers, on the other hand, would not have access to these internal processes, leading them to see patients' neuroticism as it had always been. While both caregivers and patients were instructed to rate themselves on neuroticism 'in general', it is possible that caregivers were more able to do this than patients, whose illness states possibly altered their self-perceptions. Though I expected caregiver burden and caregiver psychological distress may also be a factor in over-reporting patient neuroticism, such a finding was not supported by the multilevel model.

In further contextualizing the incongruence between caregiver and patient ratings of patients' neuroticism, the Theory of Dyadic Illness Management (Lyons & Lee, 2018) suggests that rather than focus on proxy 'accuracy', the dyadic incongruence itself should be the major focus of research. That is, how congruent patients and their caregivers are speaks to how the dyad is functioning with regard to managing illness and the overall health of the dyad. This

provides important context within the EOL care literature. Though palliative care inherently involves the family as the unit of care, there does seem to be ongoing focus on proxy assessment as a way to assess and manage the patient, rather than on examining how incongruence impacts the health of the dyad.

It is possible that the rates of neuroticism in our sample reflected a self-selection bias. There is evidence that those who volunteer for research studies have lower levels of neuroticism (Jan-Erik et al., 2007), and one can surmise that if this occurs in the general population, it may be particularly relevant at the EOL. As such, it is plausible that our sample does not reflect the most distressed patients who are highest in neuroticism. Further, each of our patient samples was likely receiving quality care, as they were recruited via contact with clinics/personal care homes associated with their respective illnesses, within the context of a publicly-funded health care system. Each of these explanations are supported by the relatively low self-reported distress across illness groups in our patient sample (outlined in more detail in Chochinov et al, 2016).

The above suggestions imply that low neuroticism is protective, and this notion is certainly supported by a wealth of research indicating the risk factors in physical and psychological health for those high in neuroticism (e.g., Barlow, Ellard, Sauer-Zavala, Bullis, & Carl, 2014; Barlow, Sauer-Zavala, Carl, Bullis, & Ellard, 2013; Roberts, Kuncel, Shiner, Caspi, & Goldberg, 2007; Roberts, Walton, & Viechtbauer, 2006). However, recent research demonstrates that those low in neuroticism experience a steeper terminal decline in the last years of life for those who died after age 50 but before age 80, possibly because, “the high threat sensitivity and behavioural inhibition tendencies in individuals high in neuroticism might become increasingly adaptive and thus outweigh the emotional costs of worrying.” (Mueller et al., 2018, p. 26). Further, there is evidence that high neuroticism coupled with high

conscientiousness ("healthy neuroticism") is associated with lower levels of inflammatory biomarker interleukin-6 (underlying a range of immune-mediated disorders and identified as a target for intervention) (Nishimoto, 2010; Turiano, Mroczek, Moynihan, & Chapman, 2013). Additionally, there is research showing that higher neuroticism is associated with a significant decrease in all-cause mortality, and this relationship is mediated by those with either fair or poor self-rated health or those who have higher scores on neuroticism facets specific to worry and vulnerability (Gale et al., 2017). As such, low neuroticism may not be universally positive in the context of aging and illness. An example in the current findings is the positive relationship between low neuroticism and subsequent depression symptoms in the context of increased constipation in ESRD.

The aforementioned finding that those who died between ages 50-80 experience steeper terminal decline has specific applicability to the present sample, in which the patients in the non-frailty groups were relatively young (ALS M_{years} = 63.87, COPD M_{years} = 72.34, and ESRD M_{years} = 72.25) and experiencing aggressive illness. As such, the fact that COPD has the highest level of neuroticism in our sample makes sense if one thinks of the disease specific symptoms these patients experience (primarily breathlessness), so, "being more attentive to potential threats (i.e., more neurotic) could thus foster their ability to proactively avoid situations or activities that place a high burden on their already scarce resources." (Mueller et al, 2018, p. 26). Interestingly, a primary psychological intervention in COPD involves treatment of panic and avoidance through cognitive-behavioural, exposure-based activities for which individuals have avoided to attempt to reduce dyspneic episodes (Kunik et al., 2008; Yohannes, Junkes-Cunha, Smith, & Vestbo, 2017).

In sum, higher neuroticism may be adaptive at the end of life, but also has the potential to significantly impair quality of life from a social and experiential perspective. Age, health status, coping, and other personality traits are all factors that interact with neuroticism, with potential implications for the EOL experience. Further, incongruence in dyads' ratings of patient neuroticism has potential implications for the functioning of the dyad as a whole. Theoretical models of aging and illness are helpful in understanding the nuanced picture of neuroticism at the EOL.

Conceptualizing findings using theoretical models of adaptation to aging and illness

Several related, yet distinct theoretical models are helpful in contextualizing the findings of this thesis. It seems that in our sample, there is evidence that neuroticism has an impact on some symptoms within some illnesses, but not for others. There were no influences of neuroticism on the associations between pain, nausea, anxiety, difficulty thinking, or appetite on depression in any of our four illness groups. In our sample of patients with ESRD, the generally protective psychological resource of low neuroticism in fact strengthened the longitudinal relationship between increased constipation and greater depression. Essentially, for those with average to high neuroticism, constipation symptoms were not associated with depression (depression was relatively invariant in this group, regardless of constipation). However, increases in constipation were associated with increased depression in those low in neuroticism. As such, there is some evidence that physical constraints may overpower psychological resources, however, this pattern does not occur across our whole sample. As such, varying levels of neuroticism can reduce (resource) or enhance (risk factor) depressive symptoms dependent on illness-specific symptom (stressor). With regard to our other findings in Chapter Two, that higher neuroticism was associated with greater depression in the context of increased

drowsiness, fatigue, and shortness of breath and decreased wellbeing (ALS); increased drowsiness and decreased activity and will to live (COPD); and increased weakness and will to live (Frailty), the Strength and Vulnerability Integration Model (SAVI) (Charles, 2010) has much to offer.

Emotional regulation is a key component of emotional wellbeing, and is an area in which those higher in neuroticism by nature struggle (Charles, 2010). Within the context of shortened time horizon (Carstensen, 2006) of the last six months of life in ALS, COPD, ESRD, and frailty, increasing symptoms that are highly prevalent and perhaps most distressing within each illness were associated with later levels of depression, and in most cases, this relationship was amplified by neuroticism. As such, in the context of such symptoms, higher neuroticism represents a vulnerability in which patients experience limited ability to pursue developmentally healthy goals at the end of life, affecting emotional wellbeing. This is supported by SAVI (Charles, 2010), which posits that not only is wellbeing associated with perceived time left to live, but active use of emotion regulation strategies across the lifespan. However, the ability to utilize these emotion regulation strategies is compromised in the face of unrelenting stressors, sustained physiological arousal, and loss of social belonging (Charles, 2010). Importantly, the end of life typically encompasses all three of these areas, with chronic and continuing decline in functioning, decreased flexibility in physiological systems, and anticipatory grief regarding the end of relationships. As such, one can extrapolate findings based on SAVI related to aging to the final stage of life. Within our sample, it thus makes sense that as symptom severity increases (unrelenting stressor/neurobiological dysregulation), those with higher levels of neuroticism (emotional dysregulation) are more vulnerable to greater depressive symptoms (decreased wellbeing).

Research Directions

Neuroticism as characterized by sensitivity to threat has demonstrated predictive value in the development of both mental and physical disorders across the lifespan (e.g., Lahey, 2009; Widiger & Oltmanns, 2017; Zinbarg et al., 2016). There is increasing recognition that neuroticism is of "profound public health significance" and that "achieving a full understanding of the nature and origins of neuroticism, and the mechanisms through which neuroticism is linked to mental and physical disorders, should be a top priority for research." (Lahey, 2009, p. 241). That neuroticism moderates the relationship between some illness symptoms and depressive symptoms suggests that this trait has the potential to provide unique information beyond longitudinal assessment of depression. However, there was no moderating effect of neuroticism on the relationship between the majority of illness-related symptoms and subsequent depressive symptoms. There are several reasons this might be the case. First, these symptoms may be less relevant within the specific illness group and therefore have little implication for mood (e.g., nausea in frailty), or conversely have more direct impacts on mood (e.g., shortness of breath in COPD), leaving little room for additional impacts of neuroticism. Second, neuroticism may be so strongly tied to mood that illness-related symptoms have no impact on subsequent depressive symptoms. Some may argue that because depression at Time 1 is a robust predictor of depression at Time 2, there is little additional value in assessing neuroticism considering that most of the moderation interactions represented small-medium effect sizes. Statistical issues of low power discussed in Chapter Two aside (and further discussed in the limitations section below), some may question why neuroticism is truly important to assess at the EOL.

First, there is robust evidence that neuroticism is a significant longitudinal predictor of mental disorders and comorbidity when controlling for depression (e.g., Barlow et al., 2014).

Second, there has been increasing recognition of the importance of discovering and treating core processes in psychopathology, rather than symptom-specific treatments (e.g., Barlow et al., 2014; Insel et al., 2010). Given the aforementioned research suggesting that health decrements are associated with changes in neuroticism over time, but only for objective rather than self-reported health (Mueller et al., 2018), it will be important in future research to use objective measures of illness severity when assessing the influence of neuroticism. Furthermore, in the current dataset, neuroticism was measured only at baseline. The measurement of neuroticism at multiple time points throughout an illness trajectory will provide important information regarding the stability of this trait within various illness groups at the end of life.

Clinical Applications

Neuroticism plays a key role in patients' self-reported health. Clinicians should be aware that individuals high in neuroticism report higher subjective symptom severity and disability than what is captured in objective tests (Jang, Mortimer, Haley, & Graves, 2002). Neuroticism moderates the relationship between self-rated health and physician visits (Hajek, Bock, & Konig, 2017). Further, neuroticism has an impact on healthcare utilization, with those higher in neuroticism visiting physicians more frequently (Hajek et al., 2017), and increasing the probability of emergency department, nursing home, and skilled nursing facility use (Friedman, Veazie, Chapman, Manning, & Duberstein, 2013). Neuroticism also has important implications for the relationship between healthcare providers and patients. High level of neuroticism is identified as a factor in patient anger, such that in men with prostate cancer, anger-proneness in the context of high neuroticism is associated with patients' disagreement with their oncologists' prognosis and more pessimism regarding prognosis (Gerhart et al., 2017). As such, awareness of how personality may impact patients' coping and interactions with their physicians has important

implications for patient care and allows clinicians the opportunity to proactively address potential conflict.

Palliative care

Discussion of personhood, recognized as a central aspect in palliative care (e.g., Chochinov et al., 2015), does not often include the role of patient personality. However, there is evidence that in communication within palliative care settings, physicians maintain personhood in ways highly relevant to neuroticism. Through empathic responding to difficult emotions and reactions to challenging advice, physicians can respond in ways that facilitate trust and treat the patient and dying process as individual in nature (Ford, 2018). In identifying those at risk for adverse psychosocial outcomes, there is a call for increased distress screening in cancer (Jacobsen et al., 2005; Pal, 2018). There is evidence that screening for distress has beneficial outcomes for patients and healthcare providers (Tamagawa et al., 2016). Though this has been undertaken through the use of 'distress thermometers' and measures such as the ESAS, gaining further information regarding one of the most robust predictors of distress – neuroticism – has the potential to provide a wealth of information regarding potential distress. Due to its robust effects on a range of important outcomes, it has been recommended that neuroticism is screened for in routine medical visits (Widiger & Oltmanns, 2017). Use of briefer, two-item neuroticism measures, such as those embedded in the BFI-10 (Rammstedt & John, 2007) or the TIPI (Gosling, Rentfrow, & Swann, 2003) can be completed in under a minute and thus may be more suitable to medical and health research settings.

An emerging literature has suggested that level of neuroticism has implications for acceptance of medical assistance in dying (MAID). Using national surveys in the United States, Gerhart and colleagues demonstrated that in states with assisted death legislation, the general

population had lower average neuroticism and higher average openness (Gerhart, Chen, O'Mahony, Burns, & Hoerger, 2018). This is potentially consistent with higher neuroticism being linked to avoidance of EOL related issues (Ha & Pai, 2012). When individuals high in neuroticism are asked about EOL care preferences, those high in neuroticism reject both life support and palliative care approaches, suggesting that those "...high on neuroticism are likely to report reluctance toward all forms of end-of-life care and may benefit from in-depth information about the process and likely outcomes of receiving life support and palliative care services." (Lattie et al., 2016, p. 52).

Though the current study examined neuroticism as a moderator of physical symptoms on depression, there is evidence that neuroticism impacts physical symptoms, such as fatigue, beyond the effects of depression (e.g., Lau et al., 2017). As such, neuroticism can provide clinically relevant information regarding both who may experience more severe illness symptoms, as well as who may have difficulty coping with such symptoms.

Clinical and health psychology

There is emerging interest in neuroticism as a treatment target, as well as ample evidence that neuroticism changes as a function of psychological treatment targeting disorder-specific symptoms. In a large representative sample, Cuijpers and colleagues demonstrated that "the economic costs of neuroticism are enormous and exceed those of common mental disorders" (Cuijpers et al., 2010, p. 1086), and call for increased focus on treating the underlying cause rather than various outcomes (specific mental disorders). As neuroticism represents a "shared vulnerability" to the development and maintenance of psychological disorders, targeting neuroticism clinically "may represent a more efficient and cost-effective approach to psychological treatment" (Sauer-Zavala, Wilner, & Barlow, 2017, p. 191). Mindfulness-based

cognitive therapy (MBCT) interventions have demonstrated efficacy in reducing neuroticism, with reduction predicted by enhanced mindfulness skills, in addition to benefits in the primary treatment target (depression) (Spinhoven, Huijbers, Ormel, & Speckens, 2017). When MBCT is adapted to specifically target neuroticism, similar benefits emerge (Armstrong & Rimes, 2016). There is also some evidence that Acceptance and Commitment Therapy can reduce neuroticism in a non-medical population (Wang, Zhou, Yu, Ran, Liu, & Chen, 2017). Symptom catastrophizing is one mechanism through which neuroticism impacts poor health and is a target of cognitive behavioral treatment across illness groups including those with functional somatic syndromes (Frolund Pedersen, Frostholm, Sondergaard Jensen, Ornbol, & Schroder, 2016). Such findings may be relevant to EOL samples, for whom there is emerging evidence that mindfulness-based interventions can be beneficial for perceived stress (Latorraca, Martimbianco, Pachito, Pacheco, & Riera, 2017).

Strengths and Limitations

This dissertation research integrates several areas relevant to coping with terminal illness, and provides an important first step in understanding the relevance of neuroticism in this stage of life. First, there is limited research on neuroticism at the EOL in general, and this dissertation is the first to show both patient and caregiver reported levels of patient neuroticism in ALS, COPD, ESRD and the frail elderly. This has important implications for the theoretical literature on personality at the EOL, to provide a starting point from which to contextualize neuroticism scores across illnesses, as there is little to no literature examining level of neuroticism in these populations. Further, this research provides a methodological framework through which proxy assessment should be undertaken, as the proxy assessment literature in palliative care has suffered from use of inappropriate or outdated methodologies from which it is difficult to draw

definitive conclusions (Evans et al., 2013). The ability to explore the relationship between illness-related symptoms and depression across four understudied illness groups, and how these relationships are both similar and divergent provides novel clinical and theoretical information about illness-related distress.

Across studies, use of the brief NEO-FFI measure rather than the longer NEO-PI-R (Costa & McRae, 1992), which includes multiple facets of neuroticism, limits possible interpretations of results. There is evidence that specific facets of neuroticism, including vulnerability, anxiety, and depression, captured by the longer measure, are more predictive of distress within illness (Uliaszek et al., 2009; Zinbarg et al., 2016). Given the promising evidence in the present study for the role of neuroticism in illness experience, inclusion of this more comprehensive measure in the future would be beneficial.

It is unfortunate that neuroticism was not measured at both baseline and three-month follow-up. Repeated measurement of neuroticism would contribute significantly to the literature regarding the stability of neuroticism in old age and at the end of life. Considering the conflicting evidence within the personality and aging literatures regarding the stability and course of neuroticism at the end of life, providing such information would allow for further discernment of how neuroticism changes within and between illness groups in patients who are in the final stages of illness, and would further allow for more nuanced understanding of incongruence ratings. For example, *if* patient ratings changed but caregivers did not, this would provide insight into a potential mechanism of discrepancy (i.e., impact of approaching death alters self-perceived neuroticism but this is outside the purview of caregivers).

Caregiver personality impacts aspects of both patient and caregiver coping (Carter & Acton, 2006; Hajek & Konig, 2018; Nordtug, Krokstad, & Holen, 2011). As caregiver

personality was not assessed in the present data, future studies may benefit from the inclusion of such assessment to explore how caregiver personality impacts both congruence on ratings of patient personality, and patient distress measures. Because health of the dyad recursively impacts how dyads appraise and manage illness, future research could examine incongruence as a predictor of distress rather than outcome to get a complete picture of the cycle of contributors to and outcomes of dyadic appraisal (Lyons & Lee, 2018). By using dyad-appropriate methodology (HLM) in Chapter Three to assess predictors of incongruence that include both patient and caregiver variables, the research makes an important contribution to understanding predictors of dyadic appraisal at the EOL (Lyons & Lee, 2018). Further, altering the caregiver instructions in providing patient personality ratings to include a perspective taking prompt (e.g., 'answer the following as if you are the patient') will be important in future work, as this is one possible reason for incongruence in the ratings (Lobchuk & Vorauer, 2003).

Methodologically, caution is required when interpreting moderation results in study 1 due to limitations regarding sample size. Further, the ESAS-R is comprised of single-item measures, which can result in low sensitivity and reliability. While this measure was appropriate for this initial study, future work will likely benefit from use of illness-specific symptom measures (such as KD-QOL for ESRD, SGRQ for COPD (Hays, Kallich, Mapes, Coons, & Carter, 1994; Jones, Quirk, Baveystock, & Littlejohns, 1992) as well as depression measures validated in each illness group. A future study, replicating the moderation analysis using larger sample within one illness group, using a comprehensive illness-specific symptom measure, the NEO-PI-R (Costa & McRae, 1992) neuroticism measure, and an illness-normed depression measure would extend this work. Challenges associated with assessing neuroticism in this sample, including a lack of normative data and incongruence in proxy assessment, requires additional research. A challenge

in the novelty of this research is integrating the findings within the broader research and clinical context, in which each of the aforementioned areas are explored within silos making it difficult to extrapolate or generalize findings (e.g., personality psychologists do not routinely conduct research with patients currently experiencing illness, and conversely, palliative care researchers do not routinely assess neuroticism). A first step may be routine gathering of neuroticism data from both patients and caregivers within a palliative care program and replicating the present analyses. With increasing recognition of the importance of neuroticism in predicting and coping with physical and psychological illness, and the utility in targeting underlying neuroticism as a primary distress variable, the door is open for clinicians and researchers to assess this trait within the end of life context.

Conclusion

More than a decade ago, Chochinov and colleagues stated, that "exploring the relationship between various facets of personality and end-of-life distress, and mapping this information against optimal therapeutic responses, remains the challenge for future research broaching this intriguing and largely ignored area of palliative care." (Chochinov et al., 2006, p. 332). The present research is among the first to explicitly address this call for further exploration of the role of personality in EOL distress. In many ways, this dissertation intersects several areas of under-researched phenomena. First, and at a most basic level, both studies provide additional research in non-cancer illness at the EOL. Second, the dissertation provides novel information regarding how the symptoms experienced in ALS, COPD, ESRD, and frailty interact with neuroticism to predict subsequent depressive symptoms. These findings demonstrated preliminary evidence that for some symptoms, level of neuroticism is an important moderator in the relationship between symptom distress and later depressive symptoms, and these

relationships are unique in each illness group. Third, the dissertation used a methodologically sound approach to measure patient-caregiver congruence in assessing patients' neuroticism, providing novel information regarding individual and dyadic factors in proxy assessment of this trait at the EOL. Given the increasing interest and recognition in the importance of neuroticism for both physical and psychological outcomes across the lifespan, this dissertation provides important first steps in understanding critical issues in measurement and utility of neuroticism in understudied populations.

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Appendix B - Measures

Family Member/Friend - Psychological Distress Index (Preville et al., 1995)

The following questions are about various aspects of your health. How you felt last week could be different from how you felt during the past year. Please choose how often, DURING THE PAST WEEK, did you:

1. Feel hopeless about the future?

- ☐ 1. Never
- ☐ 2. Once in a while
- ☐ 3. Fairly often
- ☐ 4. Very Often

2. Feel lonely?

- ☐ 1. Never
- ☐ 2. Once in a while
- ☐ 3. Fairly often
- ☐ 4. Very Often

3. Have your mind go blank?

- ☐ 1. Never
- ☐ 2. Once in a while
- ☐ 3. Fairly often
- ☐ 4. Very Often

4. Feel downhearted or blue?

- ☐ 1. Never
- ☐ 2. Once in a while
- ☐ 3. Fairly often
- ☐ 4. Very Often

5. Feel tense or under pressure?

- ☐ 1. Never
- ☐ 2. Once in a while
- ☐ 3. Fairly often
- ☐ 4. Very Often

6. Lose your temper?

- ☐ 1. Never
- ☐ 2. Once in a while
- ☐ 3. Fairly often
- ☐ 4. Very Often

7. Feel bored or have little interest in things?

- ☐ 1. Never
- ☐ 2. Once in a while
- ☐ 3. Fairly often
- ☐ 4. Very Often

8. Feel fearful or afraid?

- ☐ 1. Never
- ☐ 2. Once in a while
- ☐ 3. Fairly often
- ☐ 4. Very Often

9. Have trouble remembering things?

- ☐ 1. Never
- ☐ 2. Once in a while
- ☐ 3. Fairly often
- ☐ 4. Very Often

10. Cry easily or feel like crying?

- ☐ 1. Never
- ☐ 2. Once in a while
- ☐ 3. Fairly often
- ☐ 4. Very Often

11. Feel nervous or shaky inside?

- ☐ 1. Never
- ☐ 2. Once in a while
- ☐ 3. Fairly often
- ☐ 4. Very Often

12. Feel critical of others?

- ☐ 1. Never
- ☐ 2. Once in a while
- ☐ 3. Fairly often
- ☐ 4. Very Often

13. Feel easily annoyed or irritated?

- ☐ 1. Never
- ☐ 2. Once in a while
- ☐ 3. Fairly often
- ☐ 4. Very Often

14. Get angry over things that are not too important?

- ☐ 1. Never

- ☐ 2. Once in a while
- ☐ 3. Fairly often
- ☐ 4. Very Often

Family Member/Friend - Caregiver Burden Scale (Dumont et al., 2008)

Please indicate which of the following descriptions most closely reflects the situation of the person to whom you provide care:

1. He/She can go out and run errands alone and without assistance

- ☐ 1. Yes
- ☐ 2. No

2. He/She can manage daily activities without help (washing, eating dressing, etc.)

- ☐ 1. Yes
- ☐ 2. No

3. He/She requires assistance to move around inside at home

- ☐ 1. Yes
- ☐ 2. No

4. He/She spends more than half of the day in bed or in a chair

- ☐ 1. Yes
- ☐ 2. No

5. He/She is practically completely confined to bed or chair

- ☐ 1. Yes
- ☐ 2. No

Currently, how often do you experience this feeling in your role as caregiver?

1. Do you ever find that the tasks required in caring for your family member are too demanding?

- ☐ 1. Never
- ☐ 2. From time to time
- ☐ 3. Fairly often
- ☐ 4. Very often

2. Do you ever feel emotionally exhausted?

- ☐ 1. Never
- ☐ 2. From time to time
- ☐ 3. Fairly often
- ☐ 4. Very often

3. Do you ever feel that you no longer have the strength to care for your family member?

- ☐ 1. Never
- ☐ 2. From time to time
- ☐ 3. Fairly often
- ☐ 4. Very often

4. Do you ever feel unable to go on?

- ☐ 1. Never
- ☐ 2. From time to time
- ☐ 3. Fairly often
- ☐ 4. Very often

5. Do you feel overwhelmed by everything that has happened to you?

- ☐ 1. Never
- ☐ 2. From time to time
- ☐ 3. Fairly often
- ☐ 4. Very often

6. Do you feel that you are up to dealing with this situation?

- ☐ 1. Never
- ☐ 2. From time to time
- ☐ 3. Fairly often
- ☐ 4. Very often

7. Do you have the impression that your role as caregiver is making you physically ill?

- ☐ 1. Never
- ☐ 2. From time to time
- ☐ 3. Fairly often
- ☐ 4. Very often

8. Do you ever feel emotionally drained?

- ☐ 1. Never
- ☐ 2. From time to time
- ☐ 3. Fairly often
- ☐ 4. Very often

9. Do you ever feel that you are no longer capable of caring for your family member?

- ☐ 1. Never
- ☐ 2. From time to time
- ☐ 3. Fairly often
- ☐ 4. Very often

10. Do you ever feel physically exhausted?

- ☐ 1. Never
- ☐ 2. From time to time
- ☐ 3. Fairly often

☐ 4. Very often

11. Do you have the impression that you are in control of the situation?

☐ 1. Never

☐ 2. From time to time

☐ 3. Fairly often

☐ 4. Very often

12. Are you ever afraid that you won't be able to hold out much longer?

☐ 1. Never

☐ 2. From time to time

☐ 3. Fairly often

☐ 4. Very often

13. Do you feel like you are at the end of your rope?

☐ 1. Never

☐ 2. From time to time

☐ 3. Fairly often

☐ 4. Very often

14. Are you uncomfortable with the type of care you must provide your family member with?

☐ 1. Never

☐ 2. From time to time

☐ 3. Fairly often

☐ 4. Very often

15. Do you ever feel discouraged by all the tasks you have to accomplish?

☐ 1. Never

☐ 2. From time to time

☐ 3. Fairly often

☐ 4. Very often

16. Do you ever think that caregiving is too demanding an experience for you?

☐ 1. Never

☐ 2. From time to time

☐ 3. Fairly often

☐ 4. Very often

17. Do you ever have the impression that you have lost control over your life?

☐ 1. Never

- ☐ 2. From time to time
- ☐ 3. Fairly often
- ☐ 4. Very often

18. Do you ever have the impression that you carry too heavy a burden?

- ☐ 1. Never
- ☐ 2. From time to time
- ☐ 3. Fairly often
- ☐ 4. Very often

Patient/Resident - Index of Independence in Activities Of Daily Living (Katz et al., 1963)

BATHING (Sponge, Shower, or Tub)

☐ 0. Dependent - assistance in bathing more than one part of the body or needs assistance getting in or out of the tub or does not bathe self

☐ 1. Independent - assistance only in bathing a single part of the body or bathes self completely

DRESSING

☐ 0. Dependent - does not dress self or remains partly undressed (tying shoes excluded)

☐ 1. Independent - gets clothes from closets and drawers; puts on clothes, outer garments, braces; manages fasteners

GOING TO TOILET

☐ 0. Dependent - uses bedpan or commode or receives assistance in getting to and using toilet

☐ 1. Independent - gets to toilet; gets on and off toilet; arranges clothes; cleans organs of excretion (may manage own bedpan used at night only and may or may not be using mechanical supports)

TRANSFER

☐ 0. Dependent - assistance in moving in or out of bed and/or chair; does not perform one or more transfers

☐ 1. Independent - moves in and out of bed and chair independently (may or may not be using mechanical supports)

CONTINENCE

☐ 0. Dependent - partial or total incontinence in urination or defecation, partial or total control by enemas, catheters, or regulated use of urinals and/or bedpans

☐ 1. Independent - urination and defecation entirely self-controlled

FEEDING

☐ 0. Dependent - assistance in act of feeding, does not eat all or parenteral feeding

☐ 1. Independent - gets food from plate or its equivalent into mouth (pre-cutting of meat and preparation of food, such as buttering bread, are excluded from evaluation)

Dependency Scoring (check 1 score): **Comments:**

☐ 0. - Independent in all six functions _____

☐ 1. - Independent in five functions _____

☐ 2. - Independent in four functions _____

☐ 3. - Independent in three functions _____

☐ 4. - Independent in two functions _____

☐ 5. - Independent in one function _____

☐ 6. - Dependent in all six functions _____

Patient/Resident - Rating Quality of Life Scale (Graham et al., 1987)

Please answer the following two questions. Choose the number that best matches your feelings.

1. How would you rate your current quality of life?

Poor	1	2	3	4	5	6	7	8	9	10	Excellent

2. How satisfied are you with your current quality of life?

Not satisfied at all	1	2	3	4	5	6	7	8	9	10	Very satisfied

Patient/Resident – HADS (Zigmond & Snaith, 1983)

Instructions: Read each item and check the box which comes closest to how you have been feeling in the past week. Don't take too long over your replies: your immediate reaction to each item will probably be more accurate than a long thought or response.

1. I still enjoy the things I used to enjoy.
- □ 1. Definitely as much
- □ 2. Not quite as much
- □ 3. Only a little
- □ 4. Hardly at all

2. I can laugh and see the funny side of things.
- □ 1. As much as I always could
- □ 2. Not quite so much now
- □ 3. Definitely not so much now
- □ 4. Not at all

3. I feel cheerful.
- □ 1. Not at all
- □ 2. Not often
- □ 3. Sometimes
- □ 4. Most of the time

4. I feel as if I am slowed down.
- □ 1. Nearly all the time
- □ 2. Very often
- □ 3. Sometimes
- □ 4. Not at all

5. I have lost interest in my appearance.
- □ 1. Definitely
- □ 2. I don't take so much care as I should
- □ 3. I may not take quite as much care
- □ 4. I take just as much care as ever

6. I look forward with enjoyment to things.
- □ 1. As much as I ever did
- □ 2. Rather less than I used to
- □ 3. Definitely less than I used to
- □ 4. Hardly at all

7. I can enjoy a good book or radio or TV program.
- □ 1. Often
- □ 2. Sometimes
- □ 3. Not often
- □ 4. Very seldom

Patient/Resident - The Blessed Orientation – Memory and Concentration test (BOMC) Katzman, et al., 1983

Questions	Maximal Error		Score		Weight
1. What year is it now?	1	x	4	=	_____
2. What month is it now?	1	x	3	=	_____
3. Memory phrase: Repeat this phrase after me: John Brown 42 Market Street, Toronto					
4. About what time is it? (Within 1 hour)	1	x	3	=	_____
5. Count backwards 20 – 1	1 or 2 (maximum errors counted = 2)	x	2	=	_____
6. Say the months in reverse order	1 or 2 (maximum errors counted = 2)	x	2	=	_____
7. **Repeat the memory phrase** ___ John ___ Brown ___ 42 ___ Market Street ___ Toronto	1, 2, 3, 4 or 5 (Add the number of incorrect answers, then multiply by 2)	x	2	=	_____
			TOTAL	=	_____

Participant must score ≤15 to participate in the study

NEO-FFI (Costa & McCrae, 1992) – example items only as measure is a protected test:

I often feel inferior to others.

- ☐ 1. Strongly disagree
- ☐ 2. Disagree
- ☐ 3. Neutral
- ☐ 4. Agree
- ☐ 5. Strongly agree

When I'm under a great deal of stress, sometimes I feel like I'm going to pieces.

- ☐ 1. Strongly disagree
- ☐ 2. Disagree
- ☐ 3. Neutral
- ☐ 4. Agree
- ☐ 5. Strongly agree

I often feel tense and jittery.

- ☐ 1. Strongly disagree
- ☐ 2. Disagree
- ☐ 3. Neutral
- ☐ 4. Agree
- ☐ 5. Strongly agree

Sometimes I feel completely worthless.

- ☐ 1. Strongly disagree
- ☐ 2. Disagree
- ☐ 3. Neutral
- ☐ 4. Agree
- ☐ 5. Strongly agree

REVISED EDMONTON ASSESSMENT SCALE (Bruera et al, 1991)

Please circle the number that best describes your symptoms or feelings over the past week:

Please circle the number that best describes your symptoms or feelings over the past week:

1. No pain	0 1 2 3 4 5 6 7 8 9 10	Worst pain
2. Not nauseated	0 1 2 3 4 5 6 7 8 9 10	Very nauseated
3. Not drowsy	0 1 2 3 4 5 6 7 8 9 10	Very drowsy
4. Not short of breath	0 1 2 3 4 5 6 7 8 9 10	Very short breath
5. Not anxious	0 1 2 3 4 5 6 7 8 9 10	Very anxious
6. Not fatigued (tired all time)	0 1 2 3 4 5 6 7 8 9 10	Very fatigued
7. No constipation	0 1 2 3 4 5 6 7 8 9 10	Very constipated
8. No diarrhoea	0 1 2 3 4 5 6 7 8 9 10	Very bad diarrhoea
9. No trouble sleeping(insomnia)	0 1 2 3 4 5 6 7 8 9 10	Lots of trouble sleeping
10. No weakness	0 1 2 3 4 5 6 7 8 9 10	Very weak
11. No dizziness	0 1 2 3 4 5 6 7 8 9 10	Very dizzy
12. No difficulty thinking	0 1 2 3 4 5 6 7 8 9 10	Very difficult to think
13. No will to live	0 1 2 3 4 5 6 7 8 9 10	Strong will to live
14. No appetite	0 1 2 3 4 5 6 7 8 9 10	Very good appetite
15. Not active	0 1 2 3 4 5 6 7 8 9 10	Very active
16. Poor sense of well-being	0 1 2 3 4 5 6 7 8 9 10	Very good sense of well-being

Patient/Resident - The Patient Dignity Inventory (Chochinov et al., 2008)

For each item, please indicate how much of a problem or concern these have been for you within the last few days.

1.Not being able to carry out tasks associated with daily living (e.g. washing, getting dressed).

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

2.Not being able to attend to bodily functions independently (eg. needing assistance with toileting-related activities)

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

3.Experiencing physically distressing symptoms (such as pain, shortness of breath, nausea).

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

4.Feeling that how I look to others has changed significantly.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

5.Feeling depressed.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

6.Feeling anxious.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

7.Feeling uncertain about my health.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

8.Worrying about my future.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

9.Not being able to think clearly.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

10.Not being able to continue with my usual routines.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

11.Feeling like I am no longer who I was.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

12.Not feeling worthwhile or valued.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

13. Not being able to carry out important roles (e.g. spouse, parent).

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

14. Feeling that life no longer has meaning or purpose.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

15.Feeling that I am not making a meaningful and/or lasting contribution in my life.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

16.Feeling I have 'unfinished business' (e.g. things that I have yet to say or do, or that feel incomplete)

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

17.Concern that my spiritual life is not meaningful.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

18.Feeling that I am a burden to others.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

19.Feeling that I don't have control over my life.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

20.Feeling that care needs have reduced my privacy.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

21. Not feeling supported by my community of friends and family.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

22.Not feeling supported by my health care providers.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

23.Feeling like I am no longer able to mentally cope with challenges to my health.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

24.Not being able to accept the way things are.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem

25.Not being treated with respect or understanding by others.

1	2	3	4	5
Not a Problem	A slight problem	A problem	A major problem	An overwhelming problem