Spring 4-2020

How Does the Social World Shape the Experience of a Rare Disease? Social Position and the Development, Progression, and Medical Care for People With Amyotrophic Lateral Sclerosis

Jennifer A. Andersen
University of Nebraska-Lincoln, jmilliman@huskers.unl.edu

HOW DOES THE SOCIAL WORLD SHAPE THE EXPERIENCE OF A RARE DISEASE? SOCIAL POSITION AND THE DEVELOPMENT, PROGRESSION, AND MEDICAL CARE FOR PEOPLE WITH AMYOTROPHIC LATERAL SCLEROSIS

by

Jennifer Audrey Andersen

A DISSERTATION

Presented to the Faculty of

The Graduate College at the University of Nebraska

In Partial Fulfillment of Requirements

For the Degree of Doctor of Philosophy

Major: Sociology

Under the Supervision of Professor Julia McQuillan

Lincoln, Nebraska

March, 2020

HOW DOES THE SOCIAL WORLD SHAPE THE EXPERIENCE OF A RARE DISEASE? SOCIAL POSITION AND THE DEVELOPMENT, PROGRESSION, AND MEDICAL CARE FOR PEOPLE WITH AMYOTROPHIC LATERAL SCLEROSIS

Jennifer Audrey Andersen, Ph.D.

University of Nebraska, 2020

Advisor: Julia McQuillan

This dissertation focuses on the implications of social position and life course on the experience of Amyotrophic Lateral Sclerosis (ALS). Using a sociology in medicine frame, I test three theoretical perspectives (fundamental cause theory, social determinants of health, and life course theory) to determine the influence of social conditions on the development and progression of, and medical care for, people with ALS (pALS). Further, I use ALS as an exemplar of the need for a sociology of disease.

Using the Amyotrophic Lateral Sclerosis National Registry, I first assess the association of social position with the reported onset location at the time of diagnosis of ALS. Second, I assess the influence of social position on the time between reported date of symptom development and diagnosis. The final study evaluates the odds of reporting several types of medical care dependent on the position in the life course.

Results indicate that social position (race/ethnicity, gender, and education) influence the experience of the onset of ALS. Further, position in the life course is associated with the reporting of onset location, with those at older ages being more likely

to report bulbar or global onset in contrast to limb onset. Position in the life course is also associated with symptoms of ALS, with older persons with ALS (pALS) experiencing symptoms earlier, often prior to diagnosis. Social position and position in the life course also influenced the adoption of life-extending medical care for pALS, with younger pALS adopting more of these interventions.

Overall, the results indicate that even in a rare disease with an unknown cause, fundamental cause theory, the social determinants of health, and life course theory provide a valuable framework for understanding the experience of ALS. These theories, however, need refinement when used in the sociology of disease. Additionally, the results are evidence of a need for a sociology of disease. Finally, the results highlight the need for more inclusive research designs, as well as additional qualitative and quantitative work in understanding how social position shapes the lived experience of ALS.

DEDICATION

"It's not going to be easy, but it's going to be awesome. Awesome Ain't Easy."

-Steve Gleason

I dedicate this dissertation in memory of my father, Timothy J. Milliman, Sr., and to all pALS and their caregivers.

AUTHOR'S ACKNOWLEDGEMENTS

Dissertations do not happen in a vacuum, and I have been blessed to have an amazing support system throughout the journey to a Ph.D. I know I can't possibly thank everyone who has played a part in my story, but this is a pretty good start.

First and foremost, I want to thank my amazing supervisor and dissertation chair, Julia McQuillan. You have been my biggest cheerleader through an often-difficult journey, and there will never be enough words to tell you how much that has meant over the past five years. I don't think I could have done it without having you in my corner. Kristen, thank you for having an open door more often than not—I've learned so much from you in those impromptu conversations. David, thank you for being open to discussing a multitude of potential research ideas with me, and for eliminating the word impact from all of my future papers. Dr. K-B, thank you for being an amazing example of what a mentor should be, even before I knew you personally. Angela, thank you for welcoming this sociologist into your health communications class and for embracing my story. I am grateful for all of the time and effort my committee has put into this dissertation and for their support along the way.

One of the best things about being a part of the sociology program at UNL has been the people I have been surrounded by over the years. To the faculty, thank you for everything, including the things I don't even know to thank you for. To my cohort, thank you for being the best cohort ever—I couldn't imagine a better group of people to take this journey with. To Shawn, thank you for being your amazingly wonderful self, and the other member of the 2015 bachelor's degree holdouts. Jess, I have been blessed to have you as an officemate and as a friend, thank you for all of the adventures and whiteboard

notes. I need to also thank Trenton, Jerry, Sela, Colleen, Zach, and Josey for listening to me, challenging me, and supporting me. I would not be nearly as on top of things if it wasn't for the amazing support staff in the department and in CAS. Lori, Deborah, Breana, and Tim, you all are amazing and keep everything running smoothly. I can't possibly thank you often enough in person, so I'll do it here.

I am so incredibly grateful to Eve Brank, Josh Haby, Lindsey Wylie, Lori Hoetger, Kate Hazen, and the entire Law and Policy Lab in the Dept. of Psychology at UNL for their support. I also need to thank the UNL McNair Scholars Program for the support and for keeping me around for so many years. To Kassie, my McNair bestie, thank you for being a bright light in my life. I promise to always protect your pens.

To Dan Fogell, thank you for telling me I was too smart for medicine. I still think you are wrong, but I have to admit I'm much happier as a medical sociologist. On that note, I need to thank Eve and Carol Boehler for suggesting that I might actually be sociologist. Obviously, you were right.

I am grateful and incredibly honored to have been able to use the National ALS Registry to complete my dissertation. Thank you to those living with ALS who took the time to contribute to the registry, as without your efforts, these findings and countless others would not be possible.

I need to thank the people who knew me before I pursued this adventure called academia. Thank you to my parents, Tim and Jeanne Milliman, for instilling in me the confidence and the tenacity to finish my degree(s). Dad— You know if I had just one wish, it'd be that you didn't have to miss this. To my brothers, Jeremy, David, and Timmy, thank you for keeping me grounded and reminding me to have fun. Jessi,

Heather, Stephanie, Brandi, and Becca, thank you for being my chosen family. To my bonus kids, Geoff, Dustin, Jarrett, and Jessi, my daughter-in-law Jessica, and my granddaughter Harper, thank you for bringing such joy and light to my life. I love you all.

Finally, thank you to my husband, Jasen. I am truly the luckiest girl in the world to be married to my best friend. I could not have accomplished this without your love, support, and general awesomeness. Thank you for being my companion on this rollercoaster ride called life.

Table of Contents

CHAPTER ONE: INTRODUCTION

Amyotrophic Lateral Sclerosis (ALS) is a progressive disease characterized by the degeneration of the motor neurons and resulting atrophy and paralysis of the muscles, leading to respiratory distress and eventually death two to five years after diagnosis. ALS is a rare diagnosis, affecting approximately five per 100,000 people in the United States (Mehta et al., 2016). Furthermore, the number of people diagnosed with ALS is expected to increase globally as the population ages, from 222,801 people with ALS in 2015 to a projected number of 376,674 in 2040 (Arthur et al., 2016).

A diagnosis of ALS is a process of elimination, and the cost of simply obtaining a diagnosis can be in the tens of thousands of dollars prior to insurance coverage, which may factor into the perception of a short survival time after diagnosis (Kiernan et al., 2011; Obermann & Lyon, 2015). Further complicating the detection of ALS is the presentation of the disease. The onset location of ALS symptoms, as well as the symptoms themselves, vary by case. *Limb onset* ALS often begins with weakness in the hand or foot, with the first symptoms presenting as drop foot or trouble grasping objects, *bulbar onset* begins as difficulty in speaking or swallowing, and *global onset* can be a combination of limb and bulbar and/or weakness in the chest and trunk muscles (Kiernan et al., 2011; Andersen, 2018). Further, atypical presentations can include weight loss, fasciculations, and frontal-temporal dementia, among others (Kiernan et al., 2011; Andersen, 2018).

The variability in onset location has been implicated in the failure of clinical trials for promising treatments for ALS, as well as the inconsistency in the effectiveness of currently approved treatments (Belsh and Schiffman, 1996; Srinivasan et al., 2006).

Additionally, the variability of the earliest symptoms can lead to incorrect diagnoses and unnecessary medical procedures, culminating in a substantially delayed diagnosis which prevents access to medications and enrollment in clinical trials before the disease has progressed into later stages (Mitchell et al., 2010; Rothstein, 2017; Jaiswal, 2019).

In the absence of a cure, understanding how social position might shape the experience of ALS is an important part of understanding the differences in onset location, symptoms, and medical care among pALS. A considerable amount of ALS research is biomedical. In the biomedical research, the emphasis is on how suspected risk factors[1] are associated with the development and progression of ALS (Del Agulia et al., 2003; Paillisse et al., 2005; Watanabe et al., 2014; Pupillo et al., 2014). Yet a sociological perspective highlights the potential importance of social position in the experience of ALS and may demonstrate that social position is more than just a control variable, but a signal of larger social processes which can lead to disparities in access to medical care, support, and altering the experience of ALS. The ability to understand ALS from a sociological perspective may provide insight on how social factors shape the experience of the disease and the health of the population effected by the disease (Link, 2008). Whether the biological aspects of ALS are so powerful as to supersede the effects of the social position remains unknown at this time, but as with other diseases (e.g. diabetes, cancer, Alzheimer's), there is the potential for a greater understanding of the biological disease process by incorporating attention to social position, as well as the how the social world shapes the experience of the disease by pALS (Cassileth et al., 1985; Lyman, 1989; Luftey & Freese, 2005; Timmermans and Haas, 2008).

[1] A risk factor is any attribute, characteristic or exposure of an individual that increases the likelihood of developing a disease or injury (WHO, 2017).

Overall, the goal of this dissertation is threefold. First, the work presented here contributes to the understanding of the both biological disease process of ALS and the illness experience of pALS by using a sociological lens to understand how social position shapes the experience of ALS. Additionally, the research presented here tests three of the prominent theories in medical sociology on a rare disease with unknown causes, a category of conditions often overlooked by social scientists. Finally, using ALS as an exemplar, I turn the attention of broader theories to a specific disease, in order to illustrate the need for a sociology of disease, a more targeted form of medical sociology. Moreover, this dissertation provides an opportunity to engage not only sociologists, but epidemiologists, biomedical researchers, and medical providers in a conversation across disciplines, opening doors to a new perspective in understanding ALS as a disease process and as a lived experience.

The Status of Current Research on the Onset of ALS

The onset of ALS is heterogeneous, and without a clear understanding of the underlying reasons for the differences. The unknown factors in ALS onset makes prevention efforts and diagnosis difficult. In addition, risk factors for the development of ALS are largely unknown, however, researchers have identified several potential candidates. Several genetic mutations, such as the mutation of the SOD1 gene, have been suspected in the development of familial ALS and may be a risk factor for sporadic ALS as well (Wang et al., 2016). Exposures to heavy metals (e.g. lead), organic chemicals (e.g. pesticides used in farming), and occupational exposures (e.g. electrical shock), are considered potential risk factors that have been studied extensively, although not in connection to each other (Sutedja et al., 2007; Fang et al., 2009; Yu et al., 2014; Wang et

al., 2017). Research on ALS in Guam, where rates historically have been high, has linked exposure to Beta-N-methylamino-L-alanin (BMAA) to a potential gene-by-environment trigger. Exposure to BMAA is high in Guam due to its presence in water sources and marine animals, and prior research links BMAA exposure to pockets of high ALS rates in areas of the Atlantic seaboard due to participation in the fishing industry (Caller et al., 2011; Stommel et al., 2013; Wang et al., 2017).

Military service has been linked to ALS development, as veterans are twice as likely as civilians to develop the disease, but the link is currently unclear (Weisskopf et al., 2015; Wang et al., 2017). For example, previous research has indicated physical trauma or injury, lower BMI, lower educational attainment, and the higher levels of physical activity found in higher rates among service members may be particular risk factors for the development of ALS (Weisskopf et al., 2015; Wang et al., 2017). Findings on the link between ALS and physical activity, however, are unclear (Longstreth et al., 1998; Wang et al., 2017). Previous research, for example, has suggested that professional sports players are more likely to develop ALS as a result of their occupation (e.g. American football, soccer) which includes both a high level of physical activity, but also the potential for head injuries both of which are linked to ALS development (Chiò et al., 2005; Wang et al., 2017).

Research suggests health conditions and health behaviors are potential risk factors for ALS development. For example, viral infections, through a mechanism of the immune response, may initiate the cascade of symptoms associated with ALS (Wang et al, 2017). In addition, researchers have posited that ALS may be an issue of energy consumption in the body, and metabolic conditions as a potential risk factor may be linked to the lower

BMI and high levels of physical activity seen in people with ALS (Ingre et al., 2015). In addition, individuals who smoke are at higher risk of developing ALS, however, this correlation has been debated as the association appears in some studies and not in others when other risk factors are included in the measures (Sutedija et al., 2007; Yu et al., 2014; Wang et al., 2017).

The Status of Current Research on the Symptoms and Progression of ALS

ALS progression is measured using the Amyotrophic Lateral Sclerosis Functional Rating Scale revised scale (Cedarbaum et al., 1999) which monitors the progression of impairment in people with ALS from the date of their diagnosis, including both limb and bulbar function as well as difficulty breathing and ventilator support. Understanding the variability in progression, however, is difficult given that many symptoms often develop long before a diagnosis is reached.

Much of the work in ALS progression has been biomedical, focusing on nutritional status (e.g. weight loss, vitamin D deficiencies), comorbidities (e.g. hyperlipidemia, diabetes), and genetics as factors in symptom development and the rate of progression (Dupuis et al., 2011; Wang et al., 2017). Social position, when included in research on the diagnosis and progression of ALS, is considered through a biomedical lens and are often limited to age and gender (Del Agulia et al., 2003; Paillisse et al., 2005; Watanabe et al., 2014; Pupillo et al., 2014). Socioeconomic status does, however, influence both health and the ability to access to care (Adler et al., 1994), leading to the potential for SES to be linked through these factors to a delayed diagnosis and a perception of a more rapid progression of ALS.

The Status of Current Research on Medical Care in the Treatment of ALS

Treatment of ALS is complex for all involved, including health professionals (Radunovic et al, 2007). Multidisciplinary ALS clinics (MDCs) and palliative home care are the most recommended options, with MDCs being the option of choice of ALS experts (Radunovic et al, 2007; Obermann & Lyon, 2015). Not all patients, however, choose to use or have access to multidisciplinary ALS clinics without a long journey (Stephens et al., 2015; Horton et al., 2018) and palliative care services and in-home respite care can be limited by financial constraints and availability (Radunovic et al, 2007; Obermann & Lyon, 2015). For those who are not referred by a medical provider to an MDC or Telemedicine program, other barriers including the lack of knowledge or lack of time to research and consider such treatment options may prevent access (Stephens et al., 2015). In addition, it can take approximately five months to receive Medicare coverage after a diagnosis of ALS. Without these resources, people with ALS may find that they have needs that they are not prepared for (e.g. mobility, nutrition, speech assistance) and/or have limited time to research and access assistance due to disease progression.

Additionally, there are concerns and confusion over what types of care are considered supportive (e.g. improving quality of life) versus life-sustaining (Shneerson, 2011). People with ALS may avoid care seen as life-extending due to fears of being a burden to family members, the cost of life-sustaining care, and the potential of being locked-in and unable to express wishes to end such care (Oliver and Turner, 2010). Moreover, life-sustaining care can be complex and highly technical, which may deter older and less technologically savvy patients from accessing such care.

Theoretical Perspectives

Sociology in Medicine and Social Position

Robert Straus outlined two distinct divisions in medical sociology—sociology *of* medicine and sociology *in* medicine. Sociology of medicine is interested in the structure, role relationships, rituals, and functions of medicine as a system of behavior, while sociology in medicine is primarily concerned with the disease process or factors influencing the response to illness (Strauss, 1957; Gevitz, 1986). The dissertation is framed within the ideas of sociology in medicine, with its primary goal to gain a better understanding of the disease process of ALS as well as pALS responses to the disease in the form of medical care.

In using sociology in medicine as a frame, one must carefully consider how to present the topic of social hierarchies and how they influence the disease process, as well as the response to illness. Doing so is important, as using the biomedical terminology (e.g. race, sex) can inadvertently give the impression that biology, rather than social experiences, are being described as variables of interest when discussing disease development and outcomes.

Social location is more commonly used to describe how people are situated in history and society, specifically positioning within the matrix of domination (Crenshaw, 1990; Collins, 1990). Social location encompasses race/ethnicity, gender, social class, age, ability, and other factors that can be used to describe people's location within social hierarchies. Social location often suggests intersectionality; someone who identifies as Black, queer, and a woman will have a vastly different social location within the matrix of domination than a White, cisgender, heterosexual man (Crenshaw, 1990).

Rather than risking the implication of an intersectional approach, I have opted to use social position to represent dichotomous distinctions (e.g. man/woman, White/Non-white) in the analysis presented in the dissertation. The decision to use social position is threefold: (1) ALS has long been described and represented as a disease predominantly affecting White, middle-aged men (e.g., Lou Gehrig disease) (2) the known population of people diagnosed with ALS is very small and often has a short time of survival after diagnosis, which limits data collection and restricts the ability to complete intersectional analysis within the confines of the dissertation, and (3) the limitations of the data used in the dissertation, including the admitted underrepresentation of racial/ethnic minority populations. The use of social position to describe a dichotomous distinction recognizes these limitations, while acknowledging that the ALS community represented here is more than a dichotomy of several different statuses.

Sociology of Disease

More recently, Timmermans and Haas (2008) noted the need for a 'sociology of disease', in which sociologists explore the connection between the social world and disease. Few sociologists make one disease, such as ALS, the focus of their work. Further, few have used clinical endpoints in their analysis, which is one way to determine how social processes affect disease outcomes (Timmermans and Haas, 2008). Overall, the goal of a sociology of disease is to take the themes and theories from the sociology of health and illness and focus attention on specific health outcomes. Although social epidemiology may seem like a more natural fit for this type of work, the goal is not to point out collective risk factors but to account for the multiple pathways in which the experience of the social world may influence disease directly (Pescosolido, 2006;

Timmermans and Haas, 2008). In fact, the success of epidemiology and biomedicine highlights the need to understand how the social affects the development and experience of disease (Pescosolido, 2006; Link, 2008; Timmermans and Haas, 2008). In this dissertation, I use ALS as an exemplar to illustrate the need for a sociology of disease, as well as testing the use of more general sociological theories—including fundamental cause theory, social determinants of health, and life course theory—in a specific disease which has already been diagnosed.

Fundamental Cause Theory and Social Determinants of Health

Many medical sociologists have posited that social position, such as socioeconomic status, race/ethnicity, and education, are fundamental causes of health disparities that can influence overall health, leading to differential outcomes in interventions and potentially altering outcomes of clinical trials (Link & Phelan, 1995; Williams & Collins, 2001; Phelan et al., 2004; Braveman et al., 2005; Pampel, 2009; Phelan et al., 2010; Freese & Luftey, 2011; Phelan & Link, 2013; Phelan & Link, 2015; Masters et al., 2015). Social factors, such as social position, are useful in understanding what factors differentially places people at 'risk of risks' of exposure to proximal risk factors (Link & Phelan, 1995).

Fundamental cause theory posits that decreased risk reflects metamechanisms, which include flexible resources (e.g. education, income). Flexible resources allow individuals, when they have access, to take purposive action to prevent disease or improve prognosis after an disease is diagnosed, the ability to avoid proximal risks (e.g. avoiding polluted neighborhoods, avoiding smoking), and unintentional exposure to health enhancing norms (Link & Phelan, 1995; Williams & Collins, 2001; Mirowsky and

Ross, 2010; Freese & Luftey, 2011; Diez Roux, 2012; Phelan & Link, 2013). Moreover, the unequal distribution of flexible resources affects multiple disease outcomes through multiple pathways that can change over time as people with more access to the resources develop strategies to avoid risk (Link & Phelan, 1995; Williams & Collins, 2001; Freese & Luftey, 2011; Diez Roux, 2012; Phelan & Link, 2013).

The influence of fundamental causes on the outcomes of disease are expected in medical sociology, however, they are too often disregarded or taken for granted in traditional epidemiological research (Link, 2008). Modern epidemiology, though beginning to consider social position as a potential contributor to health disparities, still largely focuses on proximal risk factors (e.g. diet, chemical exposure) (Link & Phelan, 1995). Additionally, social factors—over and above their contributory nature to health outcomes—can influence how scientific progress is communicated and how treatment and recommendations are understood and utilized by the larger population (Link, 2008).

The fundamental causes of health disparities, in particular socioeconomic status, are tied to the social determinants of health (Braveman, Egerter, and Williams, 2011). For example, people in a lower socioeconomic position may be exposed to higher levels of environmental toxins in their neighborhood, may have constrained choices and therefore be led to a career that increases the risk of injury or exposure to dangerous chemicals, and/or may have less access to healthcare resources, all of which have been implicated in the increased risk of developing ALS and the potential for a delayed diagnosis of the disease. The use of fundamental cause theory and the social determinants of health framework allows for a better grasp of both the upstream and downstream effects on

health (Link & Phelan, 1995; Glass & McAtee, 2006; Braveman, Egerter, and Williams, 2011).

Fundamental cause theory and the social determinants of health are often used to describe how inequities increase the risk of developing medical conditions in specific populations. I, however, have opted to use these theories in another way. In an attempt to understand how inequity might shape the biological disease course and the illness experience of a disease with an unknown cause, I use fundamental cause theory and the social determinants of health on a population already diagnosed with ALS. In other words, the fundamental causes of health disparities may not only make a difference between experiencing good health or disease, but also how the experience of disease is shaped by social position.

Given that those in more privileged positions are able to access more flexible resources, they could be more apt to notice ALS symptoms and pursue diagnosis earlier in the disease course, with the results being illustrated by differences in onset type. Further, those with more flexible resources may be more likely to opt into more time consuming and higher cost options for care, improving the quality of life for the pALS in these positions. Overall, the ability to understand a disease from fundamental cause/social determinants perspective prior to the discovery of an eventual cause could provide insight on how social factors shape the experience of the disease itself, the health and wellbeing of the population affected, and the ability to access future treatments or cures (Link, 2008).

Life Course Theory

Timing of life transitions within the life course can also affect health outcomes (Elder, 1998). For example, care decisions by and for those diagnosed with ALS can be different based on the when the diagnosis is given in the life course. The diagnosis of ALS and the likelihood of a fatal outcome within a few years would be considered an off-time transition—ALS often strikes in the years where people are in the prime of their careers, raising children, and caring for elderly parents (Elder & Rockwell, 1979). Research illustrates that people who are over the age of 70 when diagnosed with ALS tend to be more accepting of the disease course than those in early-to-mid adulthood (Foley et al., 2014). Further, it suggests the difference may be that people diagnosed with ALS in late adulthood are more likely to anticipate the end of their lives, and the diagnosis comes after important milestones such as raising children into adulthood and reaching other important life transitions (Foley et al., 2014). People with ALS who have a partner and adult children, more common in late adulthood, are likely less reliant on in-home nursing care or respite care and potentially make different decisions regarding mechanical ventilation and other invasive treatments, especially if the pALS feels as though these options puts undue burden on others (Foley et al., 2014). Further, the timing of ALS development in the life course potentially influences resources available to those diagnosed. For example, already qualifying for Medicare coverage could allow for shorter time to diagnosis, allowing more intervention to take place earlier in the disease course, thereby influencing the rate of progression. In addition, life course theory includes human agency, allowing for people diagnosed with ALS to construct their life course in a way best suited to their needs (Elder, 1994).

Using life course theory, in conjunction with fundamental cause theory and the social determinants framework, informs the considerations of how disadvantage and misfortune can accumulate over the life course, increasing the potential for ALS development in those who are susceptible (Ferraro et al., 2009; Ferraro et al., 2016). Life course theory illustrates that timing of diagnosis in the life course, the lives the pALS are linked to, and the experience of life transitions, should matter in the decisions to pursue medical treatments for ALS.

Summary

Amyotrophic Lateral Sclerosis (ALS) is a relatively rare disease, approximately 5,000 people in the US are diagnosed per year. At any given time, it is estimated that 16,000 people in the US are living with ALS. Ninety to ninety-five percent of cases of ALS are sporadic with no known cause, and the remaining 5-10% are familial (genetic). Moreover, the majority of people with ALS die within 2-to-5 years. Consequently, longitudinal studies with sufficient baseline data that allow for comprehensive research on determining who will develop ALS and who will not do not currently exist. Further, using matched cases (e.g. American Community Survey) is difficult, as ALS may strike anyone at any point in the life course and there is no known test to show otherwise. Among those who have been diagnosed, however, there are many questions about patterns of onset type, the patterns of symptom development and progression, and medical care utilization. Therefore, this dissertation focuses on a population of people who have already diagnosed with ALS.

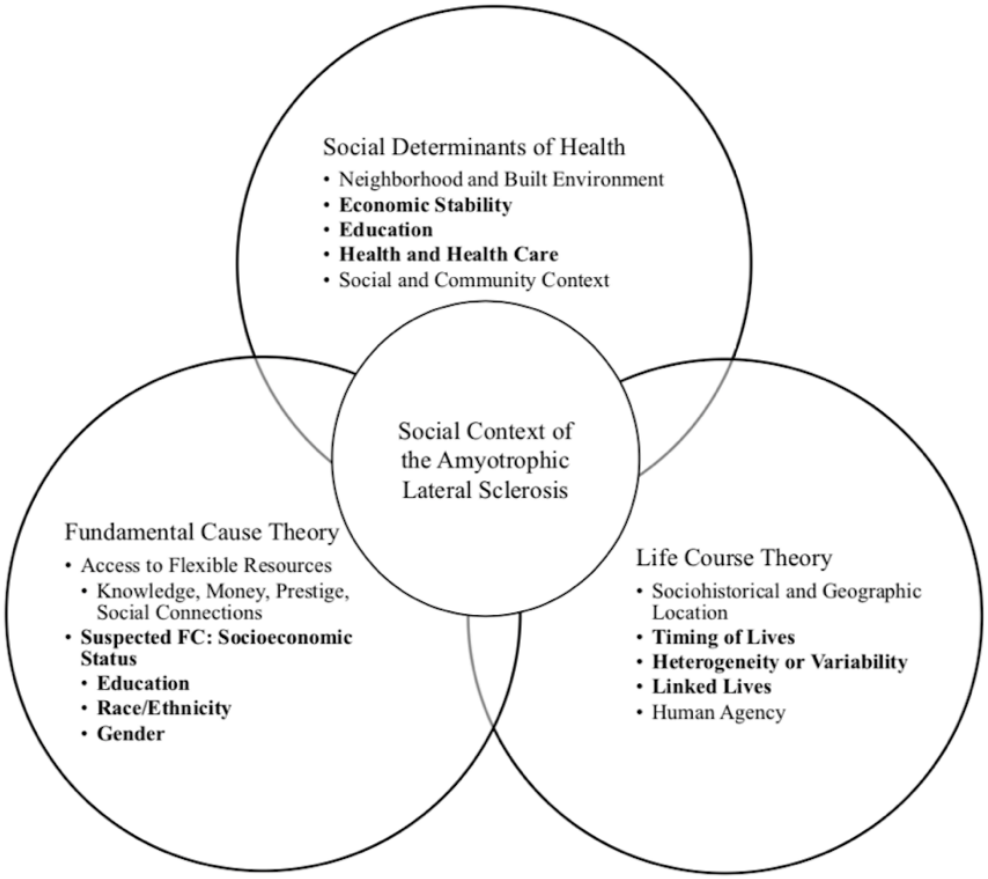
Using fundamental cause theory, the social determinants of health, and life course theory as a theoretical guide (Figure 1.1 and 1.2), I look at if, and how, social position

shapes the experience of ALS. Currently, ALS is not well understood by either the biological or the social sciences. While the biological research is underway, a next step for medical sociologists is to understand how these theories may apply in a little understood, relatively rare, and deadly disease in those who are already diagnosed in ALS. ALS is often thought of as solely a biological disease; however, a sociological perspective allows for the expansion of ideas to social position in order to develop a better understanding of the experience of the disease (Ingre et al., 2015; Brown and Al-Chalabi, 2017). Previous work in diseases such as diabetes (Lutfey & Freese, 2005), arthritis (Reisine et al., 1995), and cancer (Rubin et al., 2014) have highlighted how the social affects the biological, and the dissertation expands this line of research into understanding the experience of ALS. Further, using these theories, I turn the attention of theories used in the broader study of the sociology of health and illness to ALS, to illustrate the need for a sociology of disease.

To accomplish the goals of the dissertation, the second chapter explores how social position shapes the reported onset location at the time of an ALS diagnosis. The third chapter investigates how social position shapes the time between reported symptom development and diagnosis of ALS. Chapter four examines how position in the life course and social position shape medical care decisions reported by people with ALS. Understanding the way social position and life course position shape these experiences will potentially inform the fruitfulness of fundamental cause, social determinants, sociology of disease, and life course theory for better understanding the experience of a rare and incurable disease plus inform clinical trial formation, access to and the effectiveness of ALS treatments, and advances efforts to prevent health disparities, thus

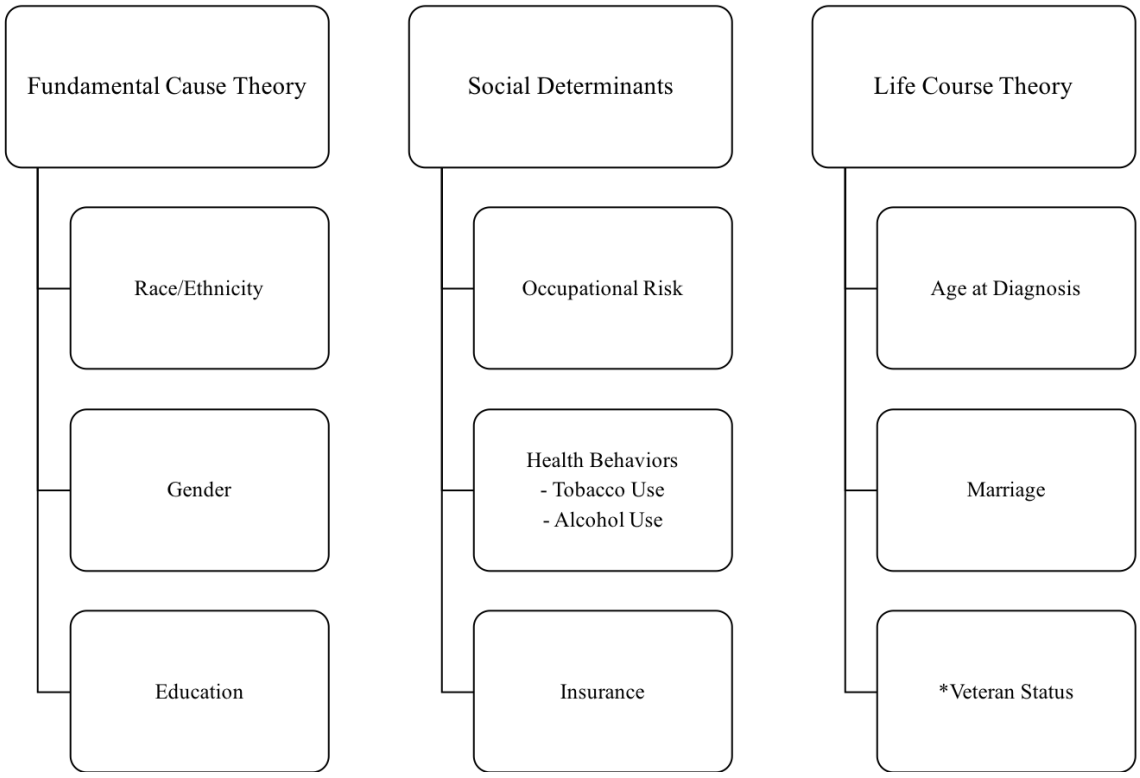
hopefully improving the quality of life for people with ALS. The concluding chapter of the dissertation discusses the contribution of the research presented in the preceding chapters, the limitations of the National ALS Registry, and directions for future research.

Figure 1.1 Using Sociological Theories to understand the Social Context of ALS[2]



[2] Bolded text indicates available variables in the National ALS Registry Dataset.

Figure 1.2 Outline of Variables connected to theories used in understanding the Social Context of ALS



* Veteran status may be considered a life transition, a social determinant of health, or as a potential indicator of flexible resources.

CHAPTER TWO: HOW DOES SOCIAL POSITION SHAPE ALS ONSET LOCATION?

Introduction

Amyotrophic Lateral Sclerosis (ALS) researchers often study social position in isolation as individual risk factors (e.g. race/ethnicity, gender, socioeconomic class) (Ingre et al., 2015). For example, previous epidemiological and biomedical studies have implicated exposures to toxic chemicals, smoking behavior, and physical activity levels as potential risk factors for the development of amyotrophic lateral sclerosis (ALS), including where symptoms first appear on the body (Swinnen and Robberecht, 2014; Wang et al., 2016). Without understanding these exposures and behaviors within their social context, however, Ingre et al. (2015) suggests that scientists are unable to determine if they are risk factors in and of themselves, or proxies for larger social processes interacting with biological factors (Ingre et al., 2015). I posit, based upon fundamental cause theory and the social determinants of health that social position shapes the onset location of ALS, and therefore shaping the earliest experiences of ALS (Link & Phelan, 1995; Glass & McAtee, 2006; Braveman, Egerter, and Williams, 2011). Further I evaluate how fundamental cause theory, social determinants of health, and life course theory (Elder & Rockwell, 1979; Elder, 1998) define the social dimensions of ALS, further indicating a need for a sociology of disease (Timmermans and Haas, 2008).

Diagnosis of ALS and Onset Location

A diagnosis of ALS is a process of elimination, and the cost of simply obtaining a diagnosis can be in the tens of thousands of dollars prior to insurance coverage (Kiernan et al., 2011; Obermann & Lyon, 2015). Common tests in the diagnostic pathway for ALS

include an electromyogram (EMG), MRIs of the brain, neck, and cervical spine, lumbar puncture (also known as a spinal tap), and biopsies of the muscle tissues in affected areas (Iwasaki, and Kinoshita, 2001). The EMG is essential for the confirmation of a diagnosis of ALS, and muscle biopsy is often the last step in the confirmation process (Iwasaki, and Kinoshita, 2001).

The diagnostic pathway is how a physician, most of a neurologist, determines diagnosis of ALS and the suspected onset location of ALS symptoms. The onset location of ALS is heterogeneous, however, and there is not a clear understanding of the underlying reasons for the differences in onset location. ALS onset is classified by the motor neurons affected, with the resulting damage being expressed by the different regions of the body (Kiernan et al., 2011; Andersen, 2018). Limb onset, the most common onset location, begins with asymmetric, painless weakness in a limb. The person with ALS often presents with atrophy and weakness of the muscles, fasciculations (twitching), and abnormal reflexes. Bulbar onset, which affects about 20% of patients, affects the bulbar (neck and jaw) muscles, leading to slurred speech and difficulty swallowing. Trunk or global onset affects 3-5% of people with ALS (pALS), and symptoms are first reported in the trunk, including the back or abdominal areas, breathing muscles, or total body weakness. All forms of ALS, limb, bulbar, and trunk/global, eventually progress, leaving the person who is affected unable to speak, move, or breathe on their own. ALS is universally fatal with an average life expectancy of 2-5 years, however, with medical intervention (e.g. tracheostomy, PEG tube) people with ALS may potentially live for much longer (Georgoulopoulou et al., 2013).

The heterogeneity of ALS onset and the relative rarity of the disease may lead to incorrect diagnoses or a delayed diagnosis of ALS (Belsh and Schiffman, 1996; Srinivasan et al., 2006; Kraemer, Buerger, and Berlit, 2010; Nzwalo et al, 2014). Moreover, the diagnosis of ALS may be delayed until further into its progression if symptoms are not recognized as significant by the patient, their family members, or their family physicians (O'Brien et al., 2011). A delayed diagnosis of ALS may mean that the disease has progressed further than the original onset site, leading to a distorted clinical picture of where onset truly began. Further, a delay in diagnosis may give the appearance of shorter survival times for the patient, which may be a source of distress (Household and Swash, 2000; O'Brien et al., 2011).

Proximate Risk Factors in ALS

Risk factors for the development of ALS are largely unclear; however, researchers have identified several potential candidates. These risk factors are often considered largely from a biomedical lens. Several genetic mutations, such as the mutation of the SOD1 gene, have been suspected in the development of familial ALS and may be a risk factor for sporadic ALS as well (Wang et al., 2016). Exposures to heavy metals (e.g. lead), organic chemicals (e.g. pesticides used in farming), and occupational exposures (e.g. electrical shock, chemical exposure), are considered potential risk factors that have been studied extensively, although not in connection to each other (Sutedija et al., 2007; Fang et al., 2009; Yu et al., 2014; Wang et al., 2016). Additionally, research suggests health behaviors are potential risk factors for ALS development. Individuals who smoke are at higher risk of developing ALS, however, this correlation has been debated as the association appears in some studies and not in others when other proximal risk factors are

included in the measures (Sutedija et al., 2007; Yu et al., 2014; Wang et al., 2016). Alcohol consumption has been reported as having a potential protective effect (de Jong et al, 2012) or no association with the development of ALS (Nelson et al., 2000).

Social Position and ALS Onset Location

Social position (e.g. indicated by gender, race/ethnicity, or social class), when it is included in ALS research, is often considered largely through a biomedical lens. The wide variation of potential proximate risk factors, however, indicates there may be more at work than simple environmental exposures. As Ingre et al. (2015) noted, different risk factors have been studied independently of each other, but little work has been done to study how they may interact and what factors may predispose a person to those circumstances. Further, the onset location of ALS may be, in part, due to the differences in the vulnerability of nerves to exposure to proximal risk factors linked to ALS development (Brown, Lockwood, and Sonawane, 2005; Aschbacher et al., 2013; D'Amico et al., 2013; Bozzo et al., 2017).

Exposures to risks, however, is often a function of experiences in the social world. Extant research has considered that social position—race/ethnicity, education, and socioeconomic status—operate as fundamental causes of health disparities (Link and Phelan, 1995; Williams and Collins, 2001; Lutfey and Freese; 2005; Mirowsky and Ross, 2010). Fundamental cause theory is useful in understanding what social factors may differentially place people at 'risk of risks,' including the proximate risk factors related to the development of ALS (Link & Phelan, 1995). Fewer studies explore how fundamental social structures shape the experience of those with a disease (Timmermans and Buchbinder, 2010; Umberson et al., 2016). Moreover, understanding the patterns of

social position in an illness may help to understand how ALS symptoms are expressed and experienced through differing exposures (Link & Phelan, 1995; Glass & McAtee, 2006; Braveman, Egerter, and Williams, 2011). For example, women and people of color are often at higher risk of poorer health due to exposure to socio-environmental stressors (e.g. discrimination and harassment). Social and environmental stressors may increase the level of cortisol, as well as increase oxidative stress within the cells (Fidler et al., 2011; Goosby and Heidbrink, 2013; Aschbacher et al., 2013). In the case of ALS, the weathering of the body from these constant insults may leave the central nervous system more vulnerable to damage, leading to differences in the expression of individual symptoms (Geronimus et al., 2001). Differences in stressors due to social position is one potential explanation for variations in the experience of ALS; yet there are other potential connections that I detail below.

Race and Ethnicity. ALS is often depicted as a disease that effects White men, however, this may be due to White men being overrepresented in many clinical and registry studies (Chiò et al., 2011; Mitsumoto et al., 2014; Kaye et al., 2018). Further, White men may be overrepresented in cases of ALS because they have fewer competing risks of death compared to Black men (Ferraro and Farmer, 1996; Howard et al; 2000). Currently, development of ALS is thought to be less frequent in minorities and is often hypothesized as perhaps a result of genetic differences (e.g., protective genes) (Gundogdu et al., 2014). Considering fundamental cause theory and the social determinants of health, it is more likely that racial/ethnic minority populations have differing access to resources, leading to this population remaining undiagnosed until the disease has advanced to later stages. Further, people of color have reported believing ALS is a ‘White disease’ leading

to the potential dismissal of symptoms or a delay of diagnostic tests, especially if the provider is under the same impression, due to the majority of ALS coverage in popular media portraying the disease as affecting only White men (Carter, 2019). In addition, later diagnosis of ALS may limit the ability of racial/ethnic minority populations to access specialty clinics and clinical trials, limiting information on this population. Based upon prior data and fundamental cause theory and the social determinants of health, I hypothesize that:

> **H1:** Given that racial/ethnic minorities face greater social and environmental risk factors which may cause widespread damage to the nervous system, as well as may face later diagnosis due to the perception of ALS as disease of White men, racial/ethnic minorities will have different patterns of onset, with minorities having higher odds of reporting global onset of ALS symptoms.

Gender. Although ALS has been presented as overwhelmingly affecting males, European studies have indicated the differences in rates of ALS diagnosis between men and women diminish in the fifth and sixth decade of life (Mehta et al., 2014; Manjaly et al., 2010). In addition, the onset location for women tends to be different than for men. For example, studies report women are much more likely to report bulbar onset of ALS symptoms, but posit the differences is potentially due to gonadal hormones or biological differences in the nervous system (McCombe and Henderson, 2010; Swinnen and Robberecht, 2014). Other potential behavioral and environmental factors, such as cigarette smoking and occupational risk exposure, have previously been shown to explain the increased rate of bulbar onset in women (McCombe and Henderson, 2010; Sutedja, 2010). The differences in ALS prevalence rates between men and women, as well as the

differences in onset location between the genders is not well understood. Previous studies, however, have not accounted for race/ethnicity or socioeconomic status, as well as proximate risk factors, when attempting to explain the differences in onset location between men and women. Therefore, I posit that:

> **H2:** Women will have different patterns of onset than men, with women having higher odds of reporting bulbar onset of ALS symptoms, which will not be explained by proximate risk factors when including social positions of race/ethnicity or socioeconomic status.

Socioeconomic Status and Education. Socioeconomic status and education are linked (Krieger, Williams, and Moss; 1996; Mirowsky and Ross, 2010). Further, education is both thought of as a fundamental cause of health disparities and as a proxy for socioeconomic status (Krieger, Williams, and Moss; 1996; Mirowsky and Ross, 2010). Exposure to hazards such as pesticides or environmental toxins are influenced by socioeconomic status and education—people of lower socioeconomic status and minorities may live in areas with a greater level of environmental pollution—and lower educational attainment may prohibit leaving an occupation or a home where proximate risks occur. In addition, those with lower education levels may have constrained choices and therefore be led to a career that increases the risk of injury, and/or may have less access to healthcare resources (Link & Phelan, 1995; Williams & Collins, 2001; Mirowsky and Ross, 2010; Freese & Luftey, 2011; Diez Roux, 2012; Phelan & Link, 2013). All these risks have been individually implicated in the increased risk of developing ALS; however, research has not connected these factors back to socioeconomic status or education level. Moreover, lower education may lead to a

difference in the type of work one engages in, as well as in how symptoms of ALS become salient (Krieger, Williams, and Moss; 1996; Mirowsky and Ross, 2010). For example, a job that requires more physical labor (e.g., mechanic) may lead to the belief that limb onset symptoms are due to overuse or injury rather than signs of ALS, whereas trouble with speech or swallowing may be more unusual and require attention. Considering these factors, I hypothesize:

> **H3:** pALS with different levels of education will have different patterns of onset, with those with a college degree or more having lower odds of reporting global or bulbar onset of ALS symptoms than those with an education of high school or less.

Military service has been linked to ALS development, as veterans are twice as likely as civilians to develop the disease, but the link is currently unclear (Weisskopf et al., 2015; Wang et al., 2016). For example, previous research has indicated physical trauma or injury, lower BMI, lower educational attainment, and the higher levels of physical activity found among service members may be particular risk factors for the development of ALS (Weisskopf et al., 2015; Wang et al., 2016). Although military service is often described as a proximate risk factor, it may also operate as an indicator of social position. For example, military enlistment is particularly attractive to young people with lower socioeconomic statuses, larger family sizes, and less-educated parents (Kleykamp, 2006). The development of ALS is twice as common among military veterans, which may be in part due to the exposures during military service but may also be influenced by the experiences of the veteran both pre- and post-enlistment. Given the

potential similarities between veterans and those with lower levels of education, I hypothesis that:

> **H4:** Civilians will be more likely to report bulbar and trunk/global onset of ALS symptoms than Veterans.

Life course and social resources. Position in the life course, including age and marital status, may influence when symptoms become salient for an individual. Having a partner or spouse in the home may act as another set of eyes, allowing for earlier detection of ALS symptoms and a clearer picture of where the symptoms started (Waite and Gallagher, 2001). Furthermore, younger adults who are more physically active may recognize limb onset symptoms as unusual for their daily activities (e.g. difficulty running), whereas an older adult may dismiss troubles with daily activities (e.g. dressing) as a sign of aging, consequently delaying diagnosis until there is greater involvement of the nerves. Therefore, it is reasonable to suspect that these social factors may influence the reported onset location of ALS via how the person affected by ALS may come to realize that something has changed within their body in the time leading up to diagnosis. I posit that:

> **H5:** Those who are not married (e.g. never married, divorced, or widowed) will have higher odds of reporting global onset of ALS symptoms, compared to their married counterparts.
>
> and
>
> **H6:** Those younger than 50 will be less likely to report bulbar or global onset, whereas those older than 59 will more likely to reporting bulbar or global onset, compared to those aged 50-59.

Data and Methods

Data

The National ALS Registry, created in October 2010, is a voluntary web-based registry for people who have been diagnosed with ALS. The registry collects data on demographic characteristics, risk factors, current and lifetime occupational and military history, family history of ALS, clinical data such as phenotype, and outcome data. In addition, the registry collects information from the Department of Veterans Affairs and Medicare for people diagnosed with ALS. The risk factor survey in the ALS Registry was created and validated by the Stanford University School of Medicine's ALS Consortium of Epidemiologic Studies and is constructed to eliminate the need for healthcare provider involvement in answering the survey questions (Bryan et al., 2016; Raymond et al., 2019). Due to the potential physical, mental, and emotional limitations of pALS, the risk factor survey utilizes smaller modules to facilitate completion (Bryan et al., 2016). The National ALS Registry collects data through a secure web portal from those who have self-identified as having ALS. In addition, each participant completes a separate questionnaire developed by the U.S. Department of Veterans Affairs ALS registry to confirm an accurate ALS diagnosis (Bryan et al., 2016). One potential drawback to the online survey is the potential for self-selection bias, with the data slanted toward an urban dwelling, younger, better educated patient.

The clinical symptoms survey module was created in partnership with the ALS Research Group to examine physical symptoms participants developed before and after a diagnosis of ALS (Raymond et al, 2019). The survey contains fifty-four questions on topics such as site of onset, time of initial symptom onset to diagnosis, and time of

diagnosis to hospice referral. The module launched in December 2013 to new enrollees and previous enrollees were prompted to return to the web portal to complete this survey. Therefore, this analysis covers from 19 October 2010 to 31 December 2016. In total, 9,789 respondents are included in this study with no exclusions.

Measures

Onset Location. The dependent variable is the part of the body where the patient first reported ALS-related weakness or symptoms. In order to create a categorical variable for analysis, the body was subdivided into 3 areas: 1) limb—symptoms first reported in the extremities, including the hand, arm, foot or leg, 2) bulbar— symptoms first reported in the oral and facial muscles, including issues with speech and/or swallowing, and 3) trunk/global—symptoms first reported in the trunk, including the neck, back or abdominal areas, breathing muscles, or total body weakness. Onset location was missing for .54% of the registry respondents.

Social Position. Potential factors in the development of ALS include the social position of the patient at the time they entered the registry. Race/ethnicity was constructed as a dichotomous variable due to the small number of racial/ethnic minority patients in the registry, with White (=0) and Minority (=1) as populations of interest. The gender of the patient is a dichotomous variable of men (=0) and women (=1). Education is a categorical variable of high school or less (=0), tech or trade school or some college education (=1) and a bachelor's degree or more (=2). Race/ethnicity, sex, and education did not have missing data.

Veteran's Status. I include veteran status as a dichotomous variable in the model, with veteran (=0) and civilian (=1). Military enlistment data was missing for .07% of the registry respondents.

Proximal Risk Factors. The National ALS Registry asks for respondent' longest occupation. In order to create categories which would include enough respondents, this variable is categorized as low risk (= 0) and high risk (= 1). Occupations were categorized using previous research as a guide; if exposure to risks would be considered low (e.g. secretarial work) or high (e.g. automotive technician) the occupation was included in the corresponding category. Occupational data was missing for 38.18% of the respondents. A dichotomous question of personal history of ever smoking (yes = 1) or ever drinking (yes = 1) was asked of the respondents. Smoking history was missing for .72% of the respondents, and drinking history was missing for .23% of the respondents.

Life Course and resources. In order to account for a potential social relationship which may influence recall of diagnosis or an earlier diagnosis, I include marital status. Marital status is a dichotomous variable of married or cohabitating (= 0) or never married, separated/divorced, or widowed (= 1), with missing data for .12% of the respondents. As age may play a role in what symptoms are noticed first, I included age as a categorical variable: 18-39 (= 0), 40-49, 50-59, 60-69, 70-79, and 80+ (= 5). Age was missing for .02% of the respondents.

Analysis

Multiple Imputation using Chained Equations was used to impute missing data with ten imputations completed (Bodner, 2008). Table 1.1 reports the pre- and post-imputation proportions in each category. The similar estimates for each variable, as well

as between the pre-and-post imputation bivariate analyses, demonstrate reliably imputed data. Bivariate tests of the association between onset location and each of the dependent variables were then performed. I use multinomial logistic regression to examine the relative risk ratio of reporting bulbar onset or global onset compared to limb onset. Model 1 includes the distal factors of social position (race/ethnicity, gender, education). Model 2 includes social position and veteran status. Model 3 includes social position, veteran status, and proximal risk factors, including occupational risk and smoking/drinking history. Finally, Model 4 includes the addition of marital status and age at diagnosis. Results for Model 4 are reported in this chapter; tables for Models 1-3 can be found in appendix A. All analyses were completed using STATA version 15.

Results

Demographics

As indicated by Table 1.1, just over 73% of the respondents reported limb onset, just over 20% reported bulbar onset, and nearly 6% reported trunk/global onset. The sample is almost exclusively White (97.18%), and nearly 60% of the sample is male. Over 60% of the respondents reported having at least a bachelor's degree. Veterans make up nearly 24% of the sample. Over 60% of the individuals in the registry records report working in a low risk occupation, while just over 45% report a history of smoking and 81% report a history of drinking alcohol. The majority of the sample is married or cohabitating (82%). Most of the respondents are between the ages of 50-59 and 60-69 (29.79% and 35.99 % respectively).

Bivariate Associations

Table 1.2 displays the F tests results used to determine if there were relationships between the dependent variable of onset location and the independent variables. Tests of the bivariate associations do not show associations between onset type and race/ethnicity, occupational risk category, marital status, or a history of smoking. The results show there is an association between onset location and (1) gender, with women being more likely to report bulbar onset than men, (2) education, with higher levels of education less likely to report global onset than lower levels of education, (3) alcohol consumption, with pALS who consume alcohol more likely to report limb onset than pALS who do not consume alcohol, (4) veteran status, with veterans more likely to report limb onset than civilians and, (5) age at diagnosis, with younger pALS more likely to report limb onset than older pALS ($p < .001$).

Multinomial Logistic Regression of Reporting of Onset Location

Table 1.3 presents the results of the multinomial logistic regression. In contrast to Hypothesis 1, racial/ethnic minorities are no more likely to report bulbar onset (RR = 1.29, 95% CI [.96, 1.73]) versus limb onset, or global onset (RR = .93, 95% CI [.54, 1.60]) versus limb onset, compared to whites. This finding is surprising, given the existing literature on racial/ethnic minority health disparities we would expect to see a potentially greater level of nerve involvement at diagnosis. Due to the small number of nonwhite participants in the registry, however, the lack of association may be an issue of power. Therefore, Hypothesis 1 is not supported.

The results show women, in comparison to men, are more likely to report bulbar onset compared to limb onset of ALS symptoms, supporting Hypothesis 2 and consistent

with existing research in onset location. The higher risk of bulbar onset among women is interesting, given that many clinical studies are populated by pALS with limb onset, and thus there are gaps in knowledge relevant to the disease for women. Compared to men, women are more likely to report bulbar onset compared to limb onset (RR = 1.43, 95% CI [1.28, 1.61]), and less likely to report global onset compared to limb onset (RR = .93, 95% CI [.33, .51]).

The results of education and onset location partially support Hypothesis 3, as results do show that those with the highest level of educational attainment are 28% less likely to report global onset (RR = .72, 95% CI [.57, .90]) compared to limb onset in contrast to pALS with a technical or trade degree or at least some college education. With the addition of age at diagnosis and marital status, pALS with a high school education or less compared to those with pALS with a technical or trade degree or at least some college education do not significantly differ in their risk of bulbar onset versus limb onset (RR = 1.09, 95% CI [.92, 1.30]). Education level may make a difference in the perception of onset, as those with higher levels of education (e.g. bachelor's degree of greater) could have fewer work-related explanations for symptoms in the limbs than those with less education.

In comparison to veterans, civilians are 25% more likely to report bulbar onset versus limb onset (RR = 1.25, 95% CI [1.09, 1.44]) and 119% more likely to report global onset versus limb onset (RR = 2.19, 95% CI [1.73, 2.79]). These results support Hypothesis 4, as civilian pALS have higher odds of reporting bulbar and trunk/global onset of ALS symptoms than those pALS who served in the military.

Concerning marital status, those pALS who are not married are no more likely to report bulbar onset versus limb onset (RR = 1.01, 95% CI [.89, 1.16), however, they are 47% more likely to report global onset versus limb onset (RR = 1.47, 95% CI [1.18, 1.84]) when compared to those who are married. These results support Hypothesis 5. For married pALS, it may be that a spouse notices symptom earlier in the disease course and wives may be more insistent on their spouse obtaining medical care. Further, in support of Hypothesis 5, the results show that pALS under the age of 50 are less likely to report bulbar or global onset of symptoms compared to limb onset, and those pALS over the age of 59 are more likely to report bulbar onset or global onset compared to limb onset, when compared to those between the ages of 50 and 59. One exception to this is pALS who are ages 40-49 are no more or less likely to report bulbar onset over limb onset than those ages 50-to-59. Overall, the results indicate a pattern of younger pALS being less likely to report bulbar or global onset compared to limb onset (see Table 1.3 for full results), which may be due to the perception of the initial onset of ALS being confused with the normal process of aging in older adults.

Discussion

In an attempt to better understand how social position may shape the reported onset location of ALS symptoms, I use fundamental cause theory, social determinants of health, and life course theory in analyzing the National ALS Registry data. The use of these theories in analyzing the registry data provides new insights into how social position may shape the onset location of ALS. Further, I use sociological theories to understand the social dimensions of a disease that is often conceptualized and studied as purely biological (Ingre et al., 2015; Brown and Al-Chalabi, 2017).

Social position and position in the life course does seem to shape onset location, which is a new finding in research on ALS. There are several potential explanations for these findings. Social position and position in the life course could influence the perception of symptoms of ALS and where they begin. Moreover, social position could be an influence on the exposures that trigger a gene by environment interaction which influences the biological development of symptoms are where they begin. Finally, social position has been shown in previous work to influence access to healthcare resources, allowing the symptoms to spread prior to diagnosis and changing the reported onset location.

Women and people of color are often at higher risk of poorer health due to exposure to socio-environmental stressors (e.g. discrimination, harassment) (Schultz et al., 2001; Williams and Jackson, 2005). In the case of ALS, the weathering of the body from socio-environmental stressors leave the central nervous system more vulnerable to damage, leading to differences in the expression of individual symptoms. pALS of color in the National ALS Registry, however, were no more likely to report bulbar or global onset versus limb onset in comparison to white pALS. Biomedical research has posited this is due to a potential difference in genetics, as it appears that minorities are less likely overall to develop ALS. Alternatively, there is a small sample of racial/ethnic minority pALS in the registry and issues overall with collecting data on ALS, potentially masking differences. Previous work has compared the registry to other sources of data and has noted that the registry underreports cases of ALS among non-whites (Kaye et al., 2018). In addition, health disparities research has illustrated the issues with access to and the quality of care/diagnosis for minorities in the US healthcare system (Phillips, Meyer, and

Adiar, 2000; Shi, Lebrun, and Tsai, 2010; Shi et al., 2014). Cases of ALS are difficult to diagnosis, taking a good deal of time and resources, which may limit the number of accurate diagnoses in racial/ethnic minority populations. Finally, the differences in life expectancy between Whites and minorities could affect the reported numbers of ALS diagnosis in racial/ethnic minority patients. For example, it may be that Black-Americans develop other serious health conditions and have other social exposures (e.g. violence) that increase the potential they do not live long enough to develop ALS, as the average age of diagnosis is in the late fifties and early sixties (Geronimus et al., 2001).

Women were more likely to report bulbar onset in comparison to limb onset when compared to men, consistent with previous research in this area. Previous work in gender differences in ALS onset have posited biomedical explanations for the increase in bulbar onset in women. For example, higher levels of bulbar onset reports in women may be due to differences in gonadal hormones (e.g. estrogen, progesterone, testosterone) or biological differences in the central nervous system (McCombe and Henderson, 2010; Swinnen and Robberecht, 2014). Other potential behavioral and environmental factors, such as cigarette smoking and occupational risk exposure, have previously been shown to explain the increased rate of bulbar onset in women (McCombe and Henderson, 2010; Sutedja, 2010), however, the inclusion of these proximal risk factors in these models does not explain away the higher likelihood of women reporting bulbar onset.

Women, given their position in the social hierarchy, face potential differences in the amount and type of chronic stressors in comparison to men. Higher levels of chronic stress for women leads to higher levels of oxidative stress via the repeated activation of the HPA axis, causing damage to the cells in the body, including the nervous system

(Aschbacher et al., 2013). Oxidative stress has been implicated as one potential trigger for ALS, and may influence the onset location (Bozzo et al., 2017). Gender, however, does not seem to affect survival rates between women and men, meaning the oxidative stress may only trigger ALS, but not influence mortality (McCombe and Henderson, 2010). Therefore, it is important to not disregard the potential of social position to shape ALS experience when including women in biomedical research of ALS, including the potential of exploring stress-related biomarkers in the development of ALS.

Education and socioeconomic status are often thought of as the fundamental causes of health disparities (Link & Phelan, 1995; Williams & Collins, 2001; Mirowsky and Ross, 2010; Freese & Luftey, 2011; Diez Roux, 2012; Phelan & Link, 2013). For the population of people with ALS in the National Registry, pALS with the highest-level of education were less likely to report global onset than limb onset, however, there was no difference in the likelihood of reporting bulbar onset compared to limb onset. pALS with higher levels of education (and by proxy potentially higher socioeconomic status) are more aware of the potential for symptoms to mean that something is going on with their body and are likely to seek medical care for symptoms earlier in the disease course, preventing the appearance of global symptoms (e.g. total body weakness). In addition, individuals with higher education levels may be less likely to be exposed to environmental and occupational hazards and have occupations that allow for less of the symptoms to be explained as related to activities on the job.

Civilians are more likely to report onset of ALS symptoms in the bulbar region or in the trunk/global region than limb onset, in comparison to their veteran peers. Prior research has hypothesized that differences in both the rate of development and onset

location may be due to differences between those who enlist in the military and those who do not, including higher rates of physical trauma or injury, lower BMI, lower educational attainment, and the higher levels of physical activity (Weisskopf et al., 2015; Wang et al., 2016). Considering prior research has shown that military enlistment is particularly attractive to young people with lower socioeconomic statuses, larger family sizes, and less-educated parents (Kleykamp, 2006), it is likely that onset location is influenced by the experiences of the veteran both pre-and-post enlistment, including higher rates of occupational and environmental exposures. It is important to future research to include early life experience and related exposures, in addition to military service, to begin to understand the differences in reported onset location between veterans and civilians. Additionally, veterans often have access to different healthcare systems (e.g. VA system) which are aware of the greater risk of ALS among veterans, allowing for the testing of suspicious symptoms earlier in disease development.

pALS who are not married are more likely to report global onset compared to limb onset, with no differences between bulbar and limb onset, compared to their married peers. Given that ALS eventually affects all areas of the body, having a partner in the home may help to catch the gradual onset of limb or bulbar symptoms before they begin to affect other areas of the body. Further, extant research has shown that marriage is beneficial to one's health, by lowering the impact of stress on both physical and psychological health (Slatcher, 2010; Carr et al., 2014). Therefore, it might be that marriage and its potential for reducing stress protects the central nervous system from damage, leading to ALS symptoms developing in one region of the body (e.g. bulbar or limb) rather than in a widespread manner.

It becomes apparent when considering age at diagnosis that position in the life course may influence the reported onset location of ALS. pALS diagnosed with ALS who are younger are less likely to report bulbar or global onset than limb onset compared to those who are diagnosed between the ages of 50-59, the average age at diagnosis. pALS older than 50-59 are more likely to report bulbar or global onset than limb onset. There are several potential reasons for these results. Previous research has postulated aging itself may cause damage to neurons, leading to an increase in global onset (Atsuta et al., 2009; Yokoi et al., 2016). People diagnosed with Familial ALS (FALS), which is due to genetic causes, tend to be younger with limb onset being most common among these patients (Gaudette et al., 2000). FALS only makes up 5-10% of ALS cases, however, which does not fully explain the differences in onset location. It may be that symptoms of ALS that develop in the limbs are more salient to those who are younger and are more physically active. Older adults may dismiss troubles with daily activities as a sign of aging, which may delay diagnosis until there is further involvement of the nerves. Finally, in line with many of the other patterns found in the data, it may be that the effects of stress accumulate over the life course, causing damage to the nervous system and affecting onset location (Geronimus. 1992; Geronimus et al., 2001; Ferraro et al., 2009; Ferraro et al., 2016).

Limitations

There are a number of limitations to consider with this study. The first is the nature of the National ALS Registry. The National ALS Registry has been designed for biomedical and epidemiological research, and therefore limits the work of the social scientist. The ALS Registry is reliant on patient self-reporting data and may be subject to

recall bias and bias due to self-identification. Further, the registry is a large non-random sample that is opt-in and is therefore not generalizable to the ALS population.

The registry is available in an online format only, which may limit access and cause the registry to reflect a younger, White, and educated patient sample. The registry sample provided by the CDC is less racially diverse than the overall registry which includes Medicare and Veteran's Association claims data. There are several potential reasons for this, including access to computers that are required for self-registration; reduced awareness of the registry; and reduced participation in areas with substantial nonwhite populations (Kaye et al., 2018). In addition, while the sample size overall is robust, smaller numbers of specific populations, such as non-white patients, makes it difficult to detect single axis disparities and limits the ability to do intersectional analysis to better understand the relationship of social position and ALS. Finally, the limited access to data due to reidentification risks limit the analysis to a small number of survey modules, which prevents a fuller picture of the experience of ALS. Even with these limitations, the National ALS Registry is the most comprehensive, geographically diverse sample of people diagnosed with ALS.

Conclusion and Implications

Fundamental cause theory, social determinants of health, and life course theory are valuable sociological theories in understanding health disparities and differences in disease development. These theories have helped to highlight differences in social position and reported onset location of ALS in patients who have registered with the National ALS Registry. Although fundamental cause theory, as well as the social determinants of health, do not fully and consistently explain the differences in onset

location among pALS, they do highlight areas where these theories may help clarify where differences are occurring in the disease course. Further, the use of these theories shows where potential refinements in the theories are needed to allow for their use at the micro-level in a rare disease with unknown causes. Additionally, the findings reinforce the need for a sociology of disease, in order to understand the disparities in trajectories and health outcomes in specific diseases rather than understanding disparities from a general overview (Timmermans and Haas, 2008). The goal of a sociology of disease in the case of ALS is to take the themes and theories from the sociology of health and illness and focus attention on specific health outcomes such as onset location. Although social epidemiology may seem like a more natural fit for this type of work, the goal here is not to point out collective risk factors but to account for the multiple pathways in which the experience of the social world may influence ALS onset directly (Pescosolido, 2006; Timmermans and Haas, 2008). In fact, the previous successes of epidemiology and biomedicine in understanding ALS highlights the need to understand how the social affects the development and experience of ALS (Pescosolido, 2006; Link, 2008; Timmermans and Haas, 2008).

Future research in ALS should consider the implications of social position and the position in the life course on the experience of ALS. These considerations are especially important as it relates to risk exposures, to not only suspected proximate risk factors, but to the experience of stress. Stress is known to affect health in a myriad of ways, both physically and psychologically. Previous research has examined the effects of stress in ALS through pathways related to hormones (e.g. cortisol) and damage to the nervous system (e.g. oxidative stress) (Fidler et al, 2011; Bozzo et al., 2017). The addition of a

module to the registry asking about life events and chronic stressors, in combination with biomarker data, could begin to clarify the connection between stress and ALS.

An additional implication of the work presented here is the need to rethink the way clinical trials are designed. The results presented illustrate concerns—reported onset location varies by social position—which is often not accounted for in clinical trials for ALS treatments. Prior research evaluating clinical trials implicated a lack of consideration of variations in the disease (e.g. onset location, speed of progression) in the widespread failure of promising trials, as the majority of trial participants are young, white and male, the majority of those with limb onset (Chiò et al., 2011; Mitsumoto et al., 2014). I argue that addition to ensuring variation in onset location in clinical trials, it is important to take into consideration the social position of the participant, as variations in onset location do appear to have connections to social forces. By beginning to understand how social position and position in the life course are related to the reported onset location of ALS, researchers and health professionals can begin to incorporate the social factors into research on the diagnosis, treatment, and biomedical research of ALS.

Table 2.1. Descriptive Statistics for Pre and Post Imputation Data (N = 9789)

	Pre-Imputation		Post-Imputation
			Percentage
Variable	Frequency	Percent	
Onset Location			
Limb (0)	7169	73.24	73.61
Speech/Swallowing (1)	2003	20.46	20.59
Trunk/Global (2)	564	5.76	5.80
Missing	53	.54	0
Race/Ethnicity			
White (0)	9513	97.18	97.18
Non-White (1)	276	2.82	2.82
Missing	0	0	0
Gender			
Men (0)	5861	59.87	59.87
Women (1)	3928	40.13	40.13
Missing	0	0	0
Education			
High School or Less (0)	1392	14.22	14.22
Tech/Trade/Some College (1)	2034	20.78	20.78
College Degree (2)	6363	62.00	62.00
Missing	0	0	0
Veteran Status			
Civilian or Other (0)	7473	76.34	76.41
Veteran (1)	2309	23.59	23.59
Missing	7	.07	0
Occupational Risk Category			
Low Risk (0)	3810	38.92	62.22
High Risk (1)	2242	22.90	37.78
Missing	3737	38.18	0
Ever Smoked Cigarettes			
No (0)	5288	54.02	54.40
Yes (1)	4431	45.27	45.60
Missing	70	.72	0
Ever Drank Alcohol			
No (0)	1815	18.54	18.61
Yes (0)	7951	81.22	81.39
Missing	23	.23	0
Marital Status			
Married or Cohabitating (0)	7998	81.70	81.80
Never Married, Separated, Divorced, Widowed (1)	1779	18.17	18.20
Missing	12	.12	0
Age at Diagnosis			
18-39 (0)	427	4.36	4.36
40-49 (1)	1382	14.12	14.12
50-59 (2)	2916	29.79	29.79
60-69 (3)	3522	35.99	35.99
70-79 (4)	1406	14.37	14.36
80+ (5)	134	1.37	1.37
Missing	2	.02	0

Table 2.2. Bivariate Associations by Reported Onset Location (N = 9789)

	Limb Onset	Bulbar Onset	Trunk/Global Onset	Chi-Square Test Pre-Imputation P Value	F-Test Post-Imputation P Value
Race/Ethnicity				p = .51	p = .51
White	.74	.20	.06		
Non-White	.71	.23	.05		
Gender				p < .001 ***	p < .001 ***
Men	.75	.18	.07		
Women	.71	.25	.04		
Education				p = .01 **	p = .01 **
High School or Less	.71	.22	.07		
Tech/Trade/Some College	.74	.19	.07		
College Degree or More	.74	.21	.05		
Veteran Status					
Civilian or Other	.73	.21	.06	p < .001 ***	p < .001 ***
Veteran	.77	.18	.05		
Occupational Risk Category				p = .05 *	p = .06
Low Risk	.73	.20	.06		
High Risk	.74	.21	.05		
Ever Smoked Cigarettes				p = .20	p = .20
No	.74	.20	.06		
Yes	.73	.21	.05		
Ever Drank Alcohol				p = .03 *	p = .04 *
No	.72	.23	.05		
Yes	.74	.20	.06		
Marital Status				p = .07	p = .08
Married or Cohabitating	.74	.20	.06		
Never Married, Separated, Divorced, Widowed	.72	.22	.07		
Age at Diagnosis				p < .001 ***	p < .001 ***
18-39	.95	.03	.01		
40-49	.79	.17	.04		
50-59	.78	.17	.05		
60-69	.69	.25	.06		
70-79	.66	.24	.10		
80+	.60	.34	.06		

*p < .05, **p < .01, ***p < .001

Table 2.3. Model 4: Multinomial Logistic Regression Predicting Reporting of Onset Location, Risk Factors, Social Position, Marital Status, and Age at Diagnosis, Relative Risk Ratios (N=9789)

Base Category: Limb

	Bulbar		**Global**	
	Relative Risk Ratio	Confidence Interval	Relative Risk Ratio	Confidence Interval
Racial/Ethnic Minority	1.29	(.96, 1.73)	.93	(.54, 1.60)
Women	1.43***	(1.28, 1.61)	.41***	(.33, .51)
Education (ref= Tech, Trade, or Some College)				
High School or Less	1.09	(.92, 1.30)	1.02	(.77, 1.37)
College or More	1.14	(1.00, 1.30)	.72**	(.57, .90)
Civilian	1.25***	(1.09, 1.44)	2.19***	(1.73, 2.79)
Low Occupational Risk	.93	(.79, 1.08)	1.46**	(1.10, 1.93)
Ever Smoked Cigarettes (ref=Never)	1.02	(.91, 1.13)	.78*	(.65, .95)
Ever Drank Alcohol (ref=Never)	.94	(.82, 1.08)	1.14	(.89, 1.50)
Single/Separated/Divorced	1.01	(.89, 1.16)	1.47***	(1.18, 1.84)
Age at Diagnosis (ref=50-59)				
18-39	.15***	(.09, .25)	.22***	(.10, .50)
40-49	.98	(.83, 1.18)	.71*	(.52, .97)
60-69	1.67***	(1.48, 1.91)	1.34**	(1.07, 1.67)
70-79	1.77***	(1.50, 2.09)	2.79***	(2.17, 3.59)
80+	2.72***	(1.84, 4.00)	1.87	(.88, 4.00)
Constant	.15***	(.11, .20)	.03***	(.02, .05)

*p < .05, **p < .01, ***p < .001

CHAPTER THREE: DO SOCIAL FACTORS SHAPE THE TIME FROM ALS SYMPTOMS TO DIAGNOSIS?

Introduction

Sociologists are uniquely positioned to translate how social factors influence symptoms of disease progression and to inform biomedical researchers of the potential perils of taking social factors for granted in biomedical research. Further, there is a need for sociologists to understand how well existing theories, including fundamental cause theory, social determinants of health, and life course theory, describe the social factors involved in the experience of ALS. Finally, in response to Timmermans and Haas' (2008) call for a sociology of disease, sociologists need to understand how well existing theories in the sociology of health and illness fit the experience of disease, especially one as rare as ALS.

Therefore, this paper addresses the question: How does social position shape the time between early symptoms of ALS and diagnosis? I posit that differences in the time between symptoms and diagnosis for people with ALS may in part be due to differences in social position and position in the life course. Developing a better understanding of how social position can potentially reveal patterns in the time between reported symptom development and diagnosis may help to understand how social forces shape the variability of ALS symptoms among people with ALS.

Guided by fundamental cause theory, I expect that those in less advantaged social positions (e.g. minorities, women, lower levels of education) will report more time between the development of ALS symptoms than their more advantaged peers. Guided by life course theory, I expect that older adults will report less time between the

development of symptoms and diagnosis than younger adults. Overall, I expect that the development of most of the early symptoms of ALS will be reported as happening before diagnosis by participants in the ALS registry, indicating the disease must progress to later stages in order to be noticed and diagnosed.

Social Position and the Time Between ALS Symptoms and Diagnosis

The order of appearance of ALS symptoms and the rate of progression are highly variable (Havercamp et al., 1995; Voustianiouk et al., 2008). Given that many symptoms of ALS develop prior to diagnosis, a delay in diagnosis may give the appearance of shorter survival times, as well as limit access to medications during the time when they would be most beneficial (Househam and Swash, 2000).

In order to assess disease progression, ALS progression is typically measured using the Amyotrophic Lateral Sclerosis Functional Rating Scale Revised Scale (ALSFR-R) (Cedarbaum et al., 1999) or the Appel Rating Scale (Appel et al., 1987). Both scales monitor the progression of impairment in people with ALS from the time of diagnosis, including strength and function of the muscles, speech and swallowing function, as well as respiratory function and ventilator support. The ALSFR-R and Appel Rating Scale are used as predictors of progression to the terminal stage of ALS (Appel et al., 1987; Cedarbaum et al., 1999).

Given that many of the early symptoms of ALS develop long before diagnosis, progression estimates may be influenced by the mechanisms which drive variability in symptom development. The potential for ALSFR-R scores to be influenced by these unknown mechanisms is concerning—ALSFR-R scores are used extensively in as part of the qualification requirements for clinical trials testing new ALS treatments—and a poor

initial ALSFR-R score may preventing enrollment in clinical trials (Mitchell et al., 2010; Rothstein, 2017; Jaiswal, 2019).

The variability of the earliest symptoms can lead to incorrect diagnoses and unnecessary medical procedures, culminating in a delayed diagnosis and preventing access to medications when they are most effective (Belsh and Schiffman, 1996; Srinivasan et al., 2006). For example, two pharmaceutical drugs are thought to slow ALS progression - Riluzole and Edaravone; however, these medications slow progression only in certain subgroups of people in the initial stages of ALS (Rothstein, 2017; Jaiswal, 2019). Without a better understanding of symptom development and progression of ALS, many people with ALS (pALS) may miss the window where these medications are most effective.

Fundamental cause theory may be useful in understanding why there is variability in ALS symptom development and the timing of diagnosis. Fundamental cause theory posits that social factors, such as the stratification of people by social position, are underlying causes of health disparities leading to worse health outcomes in the form of disease development (Link & Phelan, 1995). ALS itself may be due in large part to biological factors interacting with the social, however, the discovery and treatment of the disease itself may be influenced by fundamental causes (e.g. the ability to react to the disease).

For example, race/ethnicity, as well as socioeconomic status (SES), have been shown to influence both health care access and utilization for those in less advantaged positions (Adler et al., 1994). pALS in lower SES positions may disregard symptoms as a consequence of their work and of getting older. Additionally, there are many potential

penalties for lower SES groups needing to attend to health needs (e.g. lost wages, employment termination) which may delay seeing a physician until the symptoms can no longer be ignored, leading to longer times between symptom development and diagnosis.

Similarly, veterans seem to have symptoms develop more quickly than civilians, yet this association may be spurious and simply reflect socioeconomic status or education levels related to military enlistment (Muddasir Qureshi et al., 2006; Kleykamp, 2006). Therefore, fundamental cause theory and the social determinants of health may help to explain the variability of time between symptom development and diagnosis.

Life Course Theory and the Time Between ALS Symptoms and Diagnosis

Position in the life course, including age and marital status, may influence when symptoms become salient for an individual as an indicator of a potential disease process. Having a partner or spouse in the home may act as another set of eyes, allowing for earlier detection of ALS symptoms (Waite and Gallagher, 2001). Furthermore, younger adults who are more physically active may react to some symptoms as unusual (e.g. difficulty running), whereas an older adult may dismiss these symptoms as a sign of aging. Therefore, it is reasonable to suspect that these social factors may influence the time between symptom onset and diagnosis via how the person perceives symptoms as they develop.

The Current Study

The role of fundamental causes (e.g. social stratification) in the progression of ALS symptoms is an area in need of further exploration. Existing research tests potential social factors such as gender and age with a biomedical lens, while disregarding the potential effects of racial and class (i.e. education) stratification (Del Agulia et al., 2003;

Paillisse et al., 2005; Watanabe et al., 2014; Pupillo et al., 2014). The emphasis on social inequality in fundamental cause theory and the lack of prior emphasis on social status in prior research on ALS leads me to ask: How does social position shape the length of time between awareness of ALS symptoms an ALS diagnosis? Using the framework provided by fundamental cause theory, I posit that social position will shape the time between symptom development and diagnosis. In addition, I ask: Do fundamental cause theory, social determinants, and life course theory fit in the case of a rare disease? These sociological theories suggest the importance of examining if social stratification (e.g. fundamental cause theory) and age (e.g. life course theory) are associated with the time between the development of the symptoms of ALS and diagnosis of ALS. At this time, it is unclear if people with more or less privilege will have a shorter period of time between the development of ALS symptoms and a diagnosis of ALS. Potentially, people with more privilege could have more knowledge of symptoms as an issue that can be addressed, as well as more resources to access medical care that can lead to diagnosis. The access to resources for people with more privilege suggests that the time between symptoms and diagnosis may be shorter. People with fewer resources, however, tend to have more physical jobs and the physical impairments that often signal ALS (e.g. weakness and cramping) may be more salient when the symptoms begin to affect their job performance. The result of a reduction in productivity may lead to people with less privilege to seek medical care more quickly after recognizing symptoms. Thus, fundamental cause theory highlights the importance of examining how social positions are likely to matter for time between symptom appearance and diagnosis. Finally, I posit that these broader theories will be useful in a sociology of disease framework to

understand how social position and life course position shape the experience ALS. To explore the potential connection between social position, position in the life course, and the development of symptoms, I use data from the National ALS Registry.

Data and Methods

Data

The National ALS Registry, created in October 2010, is a voluntary web-based registry for people who have been diagnosed with ALS. The registry collects data on demographic characteristics, risk factors, current and lifetime occupational and military history, family history of ALS, clinical data such as phenotype, and outcome data. Due to the potential physical, mental, and emotional limitations of pALS, the risk factor survey utilizes smaller modules to facilitate completion (Bryan et al., 2016). The clinical symptoms survey module was created in partnership with the ALS Research Group to examine physical symptoms participants developed before and after a diagnosis of ALS (Raymond et al., 2019). The survey contains fifty-four questions on topics including the time between symptom onset and diagnosis. The clinical symptom module launched in December 2013 to new enrollees and previous enrollees were prompted to return to the web portal to complete this survey. Therefore, this analysis covers from 19 October 2010 to 31 December 2016. The number of respondents who reported a symptom varies by category and are reported in Table 3.1.

Measures

Dependent variable: Time between symptom development and diagnosis.

Five symptoms, weakness, cramping, trouble swallowing, twitching (fasciculations), and trouble with bowels, were available in the dataset provided from the National ALS Registry. To calculate the time between symptom and diagnosis, only those who reported

developing the symptom were included in the analysis. Because the data is cross-sectional it is not possible to do time-to-event analysis. I measure the time between symptom development and diagnosis in years by subtracting the reported date of symptom development from the date the respondent was diagnosed with ALS. Negative values represent symptom development *before* diagnosis and positive values represent symptom development *after* diagnosis.

Independent variables. The independent variables include: (1) social position (race/ethnicity, gender, education), (2) age at diagnosis, (3) onset location, (4) veteran status, (5) proximal risk factors, and (6) social resource of marriage, which are detailed in chapter 2. In addition, the analysis includes insurance coverage and multidisciplinary clinic usage. Insurance coverage provides a measure for access to medical care, which may influence the ability to receive a diagnosis in a timely manner. In the case of the National ALS Registry, all participants reported some form of insurance, which is not unusual as ALS qualifies pALS for Medicare, Veterans Administration coverage, and/or Medicaid. Insurance is a count variable of one (reference), two (=1), or three (=2) types of insurance policies. Multidisciplinary ALS clinic (MDC) attendance is a resource for people with ALS in recognizing symptoms. I categorize MDC use as never attended (reference), attended but discontinued (=1), and currently attending (=2).

Analysis

Multiple Imputation using Chained Equations was used to impute missing data (Enders, 2003). Table 3.1 reports the post imputation means and proportions in each category. I then perform bivariate tests of association to explore potential bivariate patterns of the time between the development of a symptom and diagnosis and each of

the dependent variables. I use multivariable ordinary least squares regression to examine the time between the development of each symptom and diagnosis. Each regression is created in steps; (1) social position, (2) social position and age at diagnosis, (3) social position, age at diagnosis, onset location (to control for disease variability), veteran status, and proximate risk factors (to control for exposures and the potential relationship with social position), and (4) social position, age at diagnosis, onset location, veteran status, proximate risk factors, and social resources. Reference categories were chosen in order for the constant to represent the characteristics of those most commonly diagnosed with ALS; White males in between the ages of 50-59 with at least some college education, who are veterans and married, have healthy health behaviors, and report limb onset of ALS symptoms. The discussion of the results focuses primarily on the final models.

Results

Demographics

Table 3.1 reports the proportion of people with different characteristics overall, the proportion in each category with a symptom, and the mean time between each symptom and ALS diagnosis for each category of each variable. All 9,787 members of the registry reported weakness, with a mean time between symptom development and diagnosis of 1.29 years *before* diagnosis. Fewer (N = 5,675) respondents reported cramping, with a mean time between symptom development and diagnosis of 2.07 years *after* diagnosis. Trouble swallowing was reported 2,170 respondents, with a mean time between symptom development and diagnosis of .62 years *before* diagnosis. Twitching, also known as fasciculations, was reported by 5,410 members of the sample with a mean time between symptom and diagnosis of 1.32 years *before* diagnosis. The final symptom,

trouble with bowels, was reported by 1138 respondents, with a mean time between symptom and diagnosis of 2.11 years *before* diagnosis. Four symptoms, weakness, trouble swallowing, twitching, and trouble with bowels are, on average, reported as developing *before* diagnosis and cramping as developing *after* diagnosis. The results potentially indicate that ALS must progress further than the earliest symptom in order to be noticed and diagnosed.

The registry sample is mostly White (97%) and nearly 60% male. The sample is also more educated than the US population as a whole with over 60% of the respondents having at least a bachelor's degree. Veterans make up nearly 24% of the sample. Over 60% of the sample report working in a low risk occupation, while just over 45% report a history of smoking and 81% report a history of drinking alcohol. The majority of the sample is married or cohabitating (82%). Most of the respondents are between the ages of 50-59 and 60-69 (29.79% and 35.99 % respectively). The individual demographics for each symptom sample are described in Table 3.1 as not all pALS reported each symptom and the sample sizes vary.

Bivariate Analysis

In addition to the descriptive statistics described above, Table 3.1 also displays the F tests results used to determine if there were associations between the dependent variable of time between symptoms and diagnosis and the independent variables (Cohen et al., 2014). Results are reported for each symptom. Overall, there is evidence that the time between symptom development and diagnosis is shaped by social position and position in the life course, although the same patterns do not exist in the case of every

symptom, suggesting that a combination of fundamental cause and life course theory are fruitful for understanding social position patterns of the experience of ALS.

Weakness. The only social position indicator associated with the time between weakness and diagnosis is education. pALS with a high school or less education reported less time between weakness and diagnosis than those with at least a tech degree or some. pALS who were older at diagnosis report more time between weakness and diagnosis. pALS with bulbar onset report less time between recognizing weakness and diagnosis, as do civilians. pALS who are single report less time between developing weakness and their diagnosis date.

Cramping. Women report less time between cramping and the date of diagnosis. Civilians also report less time between the development of cramping and diagnosis. pALS who have a history of smoking report more time between the development of cramping and diagnosis, as do those who are single.

Trouble Swallowing. Differences in reporting trouble swallowing do seem to be related to more proximal risks and resources. pALS who are in the higher occupational risk category reported more time between trouble swallowing and diagnosis than those in the low occupational risk category, and those with a history of drinking reported less time between the development of swallowing issues and diagnosis. pALS with three types of insurance reported less time between trouble swallowing and diagnosis, and those who no longer attend an MDC reported trouble with swallowing, on average, after diagnosis, compared to reported developing trouble swallowing prior to diagnosis.

Twitching. pALS with higher education and those who are older have longer times between the development of twitching and diagnosis. pALS with bulbar onset

reported less time between twitching and diagnosis. Veterans, those in low risk occupations, as well as those who have a history of smoking or drinking reported developing twitching longer before diagnosis.

Trouble with Bowels. The time between reporting developing trouble with bowels and diagnosis is associated with the social position variables race/ethnicity, gender, and education. Racial/ethnic minority pALS report trouble with bowels longer before diagnosis, as do women. pALS with the highest levels of education report more time between trouble with bowels and diagnosis. In addition to social position indicators, several other characteristics and resources are associated with the difference between trouble with bowels and diagnosis. Those who are older, have limb onset, are civilians, have high occupational risk, and no history of smoking nor alcohol use have longer times between trouble with bowels and diagnosis. pALS who are currently attending an MDC also had more time between developing bowel trouble and diagnosis.

Multivariate OLS Regression of Time between Symptoms and the Date of Diagnosis

Time between weakness and diagnosis. Table 3.2 reports the results of the regression analysis for time between weakness and diagnosis. The constant for the regression models represent the characteristics of those with the value "zero" on all of the variables – coded so that the reference categories represent those most commonly diagnosed with ALS (i.e. exemplar pALS); White males in between the ages of 50-59 with at least some college education, who are veterans and married, have healthy health behaviors, and report limb onset of ALS symptoms. Measured by the constant, the average time between developing weakness and diagnosis is just over a year ($\beta = -1.13$, $p < .001$) for exemplar pALS. In what might appear to be contrary to fundamental cause

theory and the social determinants of health, those with a high school education or less report less time between the development of weakness and the diagnosis of ALS than those with at least a tech or trade degree or some college, meaning they may be more likely to think of weakness as related to a disease, rather than as a sign of aging or work-related ($\beta = .31$, $p < .001$; therefore for this group the time is -1.13 + .31 = -.82). It is also possible that due to limited resources, those with less education may be concerned about the costs of seeing a doctor (e.g. losing a physical job or taking time off of work) and therefore they may wait until the symptoms of ALS have advanced to a point they can no longer be ignored, thus resulting in a quicker time to diagnosis. There were no differences between pALS with a college education or more and those with a tech or trade degree or some college. Age at diagnosis further shapes when weakness is experienced, with pALS who are 60-69 ($\beta = -.46$, $p < .001$), 70-79 ($\beta = -.32$, $p < .001$), and 80+ ($\beta = -.96$, $p < .001$), report more time between developing weakness and diagnosis than those at younger ages, with results consistent with life course theory. pALS with bulbar onset report less time between the onset of weakness and diagnosis than other onset types, perhaps due to the nature of bulbar onset having more involvement of the muscles in the tongue, mouth, and neck ($\beta = .53$, $p < .001$). In contrast to the idea that resources should shorten the time between symptoms and diagnosis, those pALS who report having two types of insurance report more time between weakness and diagnosis than those with one type of insurance ($\beta = -.14$, $p = .05$), and consistent with the work of family sociologists (Waite and Gallagher, 2001) pALS who are unmarried also report more time between the onset of weakness and diagnosis than those who are married ($\beta = -.30$, $p < .001$). Both

marriage and insurance could be signs of social resources, allowing for another person or healthcare provider to notice weakness earlier than the pALS themselves.

Time between cramping and diagnosis. Gender shapes the experience of cramping as an ALS symptom. The constant value shows that the exemplar pALS report developing cramping about two years prior to diagnosis on average ($\beta = -2.29$, $p < .001$). Women report less time between developing cramping and diagnosis ($\beta = .33$ $p < .05$ or -2.29+.33 or -1.96), compared to men. The time between experiencing cramping and diagnosis may be due to the differences in onset type, as bulbar onset develops more often in women (Table 3.3). In addition, those with the lowest level of education report less time between the development of cramping and diagnosis than those with at least a tech or trade degree or some college, similar to the pattern for weakness ($\beta = .43$, $p < .05$). Further, there is less time between the development of cramping and diagnosis for pALS who are younger (the ages of 18 and 39 ($\beta = 1.19$, $p < .001$), and more time between cramping and diagnosis among those who are older (60-69 ($\beta = -.35$, $p < .01$)) and over 80 years old ($\beta = -6.32$, $p < .001$) compared to pALS who are between the ages of 50 and 59. pALS who report bulbar onset also report less time between the development of cramping and diagnosis. The findings for bulbar onset reflect the findings for women, the group who are most often diagnosed with bulbar onset ($\beta = .90$, $p < .001$). pALS who previously attended a multidisciplinary ALS clinic (MDC) but have discontinued attendance report more time between the onset of cramping symptoms and diagnosis ($\beta = -1.29$, $p < .001$). Finally, pALS who are unmarried have, on average, more time between the onset of cramping and diagnosis ($\beta = -.37$, $p < .01$).

Time between trouble swallowing and diagnosis. Table 3.4 reports the results of the regression analysis of the time between trouble swallowing and diagnosis. Exemplar pALS report developing trouble swallowing one year before diagnosis on average (β = -1,00 $p < .01$). In the final model, none of the social position variables are associated with the time between the trouble swallowing symptom onset and diagnosis, however, prior to the addition of onset location and proximate risk factors into the model (Model 2), women reported less time between developing trouble swallowing and diagnosis than men ($\beta = .27$, $p < .05$). Women are more likely to have bulbar onset of ALS, and those with bulbar onset report less time between the development of trouble swallowing and diagnosis ($\beta = .37$, $p < .05$), thus adding the indicator for bulbar onset may have explained the association between the onset of trouble swallowing and the diagnosis of ALS. Age shapes the time between the experience of trouble swallowing symptoms and diagnosis, with those who are between the ages of 40-49 (β = -.64, $p <$ .01), 60-69 (β = -1.23, $p < .001$), 70-79 (β = -1.09, $p < .001$), and over 80 (β = -1.61, $p <$ .01) reporting more time between swallowing symptoms and diagnosis than those who are ages 50-59. Civilians report less time between the development of trouble swallowing and diagnosis than veterans ($\beta = .37$, $p < .05$), consistent with the findings in chapter 2 that civilians are more likely to develop bulbar onset ALS.

Proximate risk factors are related to symptoms of trouble swallowing as well, with those who report lower occupational risk experiencing less time between swallowing symptoms and diagnosis than those with high occupational risk ($\beta = .67$, $p <$ .01), and those with a history of alcohol use (β = -56, $p < .01$) reporting more time between developing swallowing symptoms and diagnosis. pALS with two forms of health

insurance (β = .51, p < .01) and three forms of health insurance (β = 1.22, p < .001) report less time between developing trouble swallowing and diagnosis, and those with three forms of insurance reporting swallowing symptoms after diagnosis. Finally, resources in the form of MDC attendance, also shape the time when pALS notice trouble swallowing. pALS who do not attend an MDC clinic (β = .62, p < .001) and have attended but since discontinued MDC use (β = .96, p < .01) report less time between the development of trouble swallowing and diagnosis.

Time between twitching and diagnosis. Table 3.5 reports the results of the regression models for the time between twitching symptoms and diagnosis. The constant for this model shows the exemplar pALS report developing twitching at the same time as diagnosis (β = .31, p >.05). The only social position variable that is associated with the time between twitching and diagnosis is education, with those with a high school education or less reporting less time between developing twitching and diagnosis, following the patterns of weakness and cramping (β = .53, p < .01). pALS with bulbar onset of ALS report less time between twitching and diagnosis, following the patterns of other symptoms as well (β = .69, p < .001). For both woman and pALS with bulbar onset, twitching is reported as developing after diagnosis. Civilians report developing twitching earlier than veterans (β = -.28, p < .05). pALS who have a history of smoking report more time between developing twitching and diagnosis (β = -.26, p < .01). Resources, such as insurance coverage, MDC attendance, and marriage are also associated with the time between cramping and diagnosis. pALS with two forms of insurance (β = -.70 p < .001) and three types of insurance (β = -1.40, p < .001) report recognizing twitching longer before diagnosis than those with one form of insurance. pALS who do not attend an

MDC clinic (β = -.30, p < .01) and who are not married (β = -.25, p < .05) report more time between the development of twitching and diagnosis than those who do attend an MDC and who are married.

Time between trouble with bowels and diagnosis. For the constant value representing the exemplar pALS, trouble with bowels is reported as developing at the same time as diagnosis (β = .44, p >.05) on average. Similar to the time between swallowing and diagnosis, of the social position indicators, only gender (not race/ethnicity nor education) is associated with the time between trouble with bowels and diagnosis (Table 3.6). Women report more time between having trouble with bowels and diagnosis than men (β = -1.50, p < .001). This association could reflect that women are more willing to seek medical help, or the association could be spurious because women are also more likely to have bulbar onset, and bulbar onset has a strong association with trouble with bowels. Age does shape the experience of trouble with bowels, with those who are in between the ages of 40 and 49 reporting less time between developing trouble with bowels and diagnosis (β = 2.16, p < .001) with bowel symptoms reported as developed post diagnosis by 1.7 years. pALS who are 60-69 (β = -1.22, p < .01), 70-79 (β = -1.61, p < .01), and over the age of 80 (β = -3.18, p < .05) report more time between bowel issues and diagnosis, with bowel issues developing prior to diagnosis. Age may play a role here due to the salience of these symptoms for older adults but may often be disregarded as a potential consequence of aging.

Proximate risk factors also influence time to trouble with bowels. pALS who report low occupational risk (β = 1.39, p < .01) and who report a history of smoking (β = 1.95, p < .01) experience more time between bowel trouble and diagnosis, with bowl

trouble developing post diagnosis, while those who report alcohol use report more time between the development of bowel issues and diagnosis ($\beta = -2.23$, $p < .001$). Social resources also shape the experience of bowel issues. pALS who do not use an MDC report more time between bowel issues and diagnosis than those who do ($\beta = -1.22$, $p < .001$). Unmarried pALS report more time between the development of bowel trouble and diagnosis than married pALS, with trouble with being noticed post diagnosis ($\beta = 1.01$, $p < .01$; solving the equation indicates $-.44 + 1.01 = .59$), or about half a year after diagnosis.

Discussion

Four of the symptoms included in the analysis presented here—weakness, trouble swallowing, twitching, and trouble with bowels—are on average reported by pALS in the National ALS Registry as appearing prior to diagnosis. The appearance of faster progression for some pALS may be, in part, due to the length of time between when pALS notice and/or experience symptoms and the diagnosis of ALS. Therefore, understanding how social position shapes when symptoms first occur and are noticed is important to understanding the experience of progression of ALS. Time is of the essence when it comes to a diagnosis of ALS, as the median survival time from diagnosis is between 20 and 48 months (Chiò et al., 2009)

Whilst the analysis presented here includes proximate risk factors which are often the focus of ALS progression research, proximate risks are not the sole factor in the timing of the development of symptoms. Education, gender, and age all have a role over and above the proximate risks included in the models, either through their relationship

with the biological processes underlying ALS or through the perception and reporting of symptoms.

Education level shapes when symptoms occur, with pALS who have a high school or less education reporting the development of weakness, cramping, and twitching as developing closer to the date of diagnosis than those with higher levels of education. Weakness and twitching are often the very earliest signs of ALS, therefore the reporting by people with higher levels of education of these symptoms earlier than their peers with lower education is potentially a concern as pALS with lower levels of education may be missing earlier signs of weakness. Reporting of these symptoms closer to the date of diagnosis for those pALS with lower levels of education may be due to the speed of the biological development of the disease, however, it may be due to the type of work people with lower levels of education engage in, as well as access and utilization of healthcare services. As one example, people who work in highly physical jobs may think early weakness is due to aging, a higher than normal workload, or being overly tired. Earliest experiences of twitching may be disregarded as a consequence of overtired and overworked muscles. Therefore, these symptoms may be dismissed as normal consequences of daily activities, and the date reported to the registry may be when the symptoms became salient as something outside of the norm. In addition, fundamental cause theory often posits education (as well as its connection to socioeconomic status) as a cause of health disparities, with access to and utilization of health care being a part of these inequalities. pALS with lower education levels are more likely to not have been able to access medical care due to cost (e.g. copays, lost time at work) to ask questions about these symptoms until they become too hard to ignore, therefore delaying diagnosis.

Women report cramping and trouble swallowing later in the disease course and trouble with bowels earlier in the disease course, perhaps due to the higher prevalence of bulbar onset in this population. pALS often do not recognize bulbar dysfunction if the rate of progression is slow, therefore pALS unknowingly adapt to swallowing issues until the symptoms become hard to ignore (Onesti et al., 2017). The delay in recognizing swallowing difficulties may lead to a delay in diagnosis (Onesti et al., 2017). Moreover, the gradual adaptation to difficulty swallowing may result in changes in the diet, leading to constipation and other difficulties with the bowels. Therefore, as noted in chapter two, it is important to better understand why women disproportionately develop bulbar symptoms.

Age at diagnosis also has some bearing on when pALS report symptoms occurring. Older pALS report symptoms occurring earlier in the disease course than younger pALS. As noted in chapter two, one reason for this difference might be that ALS onset is influenced by the aging of the central nervous system, and extant research also implicates aging of the central nervous system in symptom development and the rate of disease progression. The timing of diagnosis in the life course, however, would also be related to the perception of symptoms as outside the norm. For pALS who are older, as well as their spouses, caregivers, and physicians, early symptoms of ALS may be considered as signs of aging and not as potential signs of a fatal disease.

Social and material resources, including marriage, insurance coverage, and MDC use, also shape the experience of symptoms of ALS. Compared to those who are married, unmarried pALS report earlier development of twitching and later development of weakness. Changes in strength or ability are something that is potentially noticed by a

partner or spouse as unusual, therefore may be recognized by married pALS earlier. Twitching, on the other hand, is often visible throughout the muscles, and for unmarried pALS may be one of the first signs that something is amiss that cannot be reasonably explained away. Moreover, pALS who are single may attempt to solve issues on their own for a longer period of time before realizing that symptoms are not due to a lack of self-care, whereas the inability to solve a health issue with self-care may be pointed out earlier by a partner or spouse leading to earlier help-seeking behavior.

Insurance and MDC use are difficult to parse out, however, as these may change after diagnosis. It may be that an increase in the number of insurances policies may mean that the pALS is further into disease progression, as Medicare coverage is not available until five months post diagnosis and the determination of permanent disability. Insurance coverage may also be an indicator of socioeconomic status. Reporting discontinuation of using an MDC may be due to progression of the disease, as many pALS find it is difficult to travel the distance to these providers once they are no longer able to move (Radunovic et al, 2007; Hodgen et al., 2012; Obermann & Lyon, 2015; Stephens et al., 2016; Horton et al., 2018). In addition, never using or discontinuing MDCs may be an indicator of socioeconomic status or geographical location, as many MDCs are located in highly populated cities rather than rural areas (Radunovic et al, 2007; Hodgen et al., 2012; Obermann & Lyon, 2015; Stephens et al., 2016; Horton et al., 2018).

There are several limitations to the research presented here. Designed for biomedical and epidemiological research, the National ALS Registry has limited measures of social status and social experiences. In addition, the registry limits access to survey data due to reidentification risks, therefore limiting the analysis. For example, it

would be ideal to have measures of parental status to assess if the demands of parenting make some symptoms more salient earlier in disease progression. Further, not all of the registry participants reported symptom development, either due to slowly progressing ALS, or perhaps due to not recognizing the symptom as described in the module. In addition, while the sample size overall is robust, smaller numbers of specific populations such as non-white patients, impedes intersectional analysis. Being able to assess the combined effects of gender, race/ethnicity and education is often important for understanding health (Warner and Brown, 2011) to better understand the relationship of social position and ALS. Doing intersectional analysis could help to parse out if social location (e.g. the intersection of several social positions) explains the association between social position and ALS symptoms.

The ALS Registry is reliant on patient self-reporting data and may be subject to recall bias and bias due to self-identification. In addition, patients can complete the registry survey only online, which may limit access and cause the registry to reflect a younger, mostly white, and more educated patient sample. The registry sample provided by the CDC is less racially diverse than the overall registry which includes Medicare and Veteran's Association claims data. There are several potential reasons for this, including access to computers that are required for self-registration; reduced awareness of the registry; and reduced participation in areas with substantial nonwhite populations (Kaye et al., 2018). Further, the registry is a large non-random sample that is opt-in and therefore results are not generalizable to the ALS population as a whole. Even with these limitations, the National ALS Registry is the most comprehensive, geographically diverse sample of people diagnosed with ALS.

Fundamental cause theory provides important guidance for exploring the social structural dimensions of ALS symptom development and diagnosis, yet the findings suggest limited support for the theory, as those with limited resources often have less time between symptom onset and diagnosis. In the case of ALS, however, it may be that a shorter time between symptoms and diagnosis is not evidence of greater resources, but of less opportunity to acknowledge symptoms as something out of the ordinary and less opportunity to seek medical care for what might seem to be a minor complaint. In addition, using fundamental cause theory in the design of the research presented here further suggests the need for a sociology of disease, as well as an adjustment in sociologists' conceptualization of existing sociological theories to use them within this framework. Future research on ALS should consider the implications of social position in the development of symptoms, especially in the early in the diagnostic process. For example, including education level in the design of future research projects would help to distinguish if education level is causally related to symptom development and progression, or if it influences the perception of symptoms.

Many of the earliest symptoms of ALS develop, on average, more than a year prior to diagnosis. Therefore, social position may influence ALSFR-R progression estimates. This is of particular concern, as ALSFR-R scores are used extensively as part of the evaluation process for participation in clinical trials. If trial administrators assume that time from symptom development to diagnosis reflects only the disease and not social position factors, then inclusion criteria will be inconsistently applied. There is the potential for symptoms to progress to a point prior to diagnosis that pALS are excluded from participating in these trials. As noted in chapter 2, trial participants are often young,

white, male, and mostly with limb onset (Chiò et al., 2011; Mitsumoto et al., 2014). Ensuring the inclusion of those who occupy different social positions, even with lower ALSFR-R scores, may help to bring more effective treatments that work for a broader spectrum of those experiencing ALS.

Symptom development and progression can influence the effectiveness of approved treatments. The medications Riluzole and Edaravone slow progression only in certain subgroups of people with initial stages of ALS (Rothstein, 2017; Jaiswal, 2019). Social position shapes when symptoms develop and are reported, which may delay diagnosis and prevent access to these medications when they are most effective. In addition, the results presented in chapter two and here indicate that social position should be included in future analysis of ALS subgroups in order to better understand who benefits from new treatments and technologies.

Similarly, it is important to understand how social position interacts with biological processes, as noted in the previous chapter. For example, women are more likely to develop bulbar onset ALS, which changes the nature of symptoms and the order in which they develop, as well as when symptoms become salient to the pALS. Being able to understand why women are more likely to develop bulbar onset ALS and the behaviors they engage in when symptoms begin to develop, may improve diagnosis and treatment for women with bulbar onset ALS. Moreover, these connections may help to clarify if there is a biological (e.g. hormones), a social exposure (e.g. stress), or a combination of the two implicated in the onset location and development of symptoms for women.

Conclusion

The analyses of the timing of symptoms relative to diagnosis contributes to the knowledge of both sociology of disease and research, specifically on ALS. First, for several symptoms, the timing of symptoms relative to diagnosis is shaped by social position, as suggested by fundamental cause theory and the social determinants of health. These theories guided the exploration of social position and disease experience, but the patterns for ALS are not all consistent with predictions by the theories. In the case of a specific disease, it may be that the ways in which sociologists understand fundamental cause theory and the social determinants of health need to be adjusted in order to be used in a sociology of disease (Pescosolido, 2006; Link, 2008; Timmermans and Haas, 2008). In the case of ALS, people with limited resources often have less time between symptom onset and diagnosis. Rather than an indicator of greater access to resources, a diagnosis closer to the reported appearance of symptoms may be a sign of having less opportunity to acknowledge the signs of a disease that may at first seem to be a minor complaint related to people's circumstances. The results from this work reaffirms the need for a sociology of disease, as dealing with a disease just prior to and after diagnosis is different from understanding how disease can be prevented altogether. Additionally, age, as an indicator of life course theory, shapes the experience of ALS symptoms. Future research should address if these differences are due to the perception and salience of symptom development, or if the differences may be due to the interaction of the biological and social aspects of ALS.

Table 3.1 Descriptive Statistics and Bivariate Association Results for Time between the development of Symptoms and Diagnosis

	Weakness n = 9787		Cramping n = 5675		Swallowing n = 2170		Twitching n = 5140		Bowels n = 1138	
	Sample Proportion	P Value Mean (SD)	Proportion Yes	P Value Mean (SD)	Proportion Yes	P Value Mean (SD)	Proportion Yes	P Value Mean (SD)	Proportion Yes	P Value Mean (SD)
Race/Ethnicity										*
White (0)	.97	-1.29 (.03)	.58	-2.07 (.06)	.22	-.62 (.25)	.76	-1.33 (.05)	.12	-.63 (.50)
Racial/Ethnic Minority (1)	.03	-1.39 (.12)	.76	-1.99 (.23)	.28	-.62 (.07)	.55	-1.13 (.19)	.21	-2.19 (.14)
Gender				**						***
Male (0)	.60	1.27 (.04)	.60	-2.20 (.08)	.20	-.73 (.07)	.59	-1.36 (.07)	.09	-1.22 (.17)
Female (1)	.40	1.32 (.04)	.55	-1.85 (.07)	.26	-.50 (.11)	.50	-1.25 (.05)	.16	-2.82 (.22)
Education		***						***		***
High School or Less (0)	.14	-1.04 (.11)	.64	-1.95 (.21)	.29	-.73 (.16)	.61	-.72 (.19)	.16	-1.57 (.30)
Tech/Trade/Some College (1)	.21	-1.31 (.04)	.62	-2.13 (.11)	.21	-.64 (.10)	.53	-1.30 (.09)	.14	-1.13 (.25)
College Degree or More (2)	.65	-1.34 (.03)	.56	-2.08 (.06)	.21	-.59 (.09)	.55	-1.47 (.05)	.10	-2.73 (.21)
Age at Diagnosis		***						***		***
18-39 (0)	.04	-1.18 (.07)	.66	-.92 (.15)	.11	.85 (.35)	.67	-1.05 (.14)	.06	.38 (.48)
40-49 (1)	.14	-1.19 (.07)	.62	-1.65 (.13)	.20	-.73 (.23)	.62	-1.27 (.11)	.07	.26 (.33)
50-59 (2)	.30	-1.04 (.07)	.62	-1.92 (.11)	.20	-.07 (.18)	.59	-1.14 (.11)	.19	-2.14 (.28)
60-69 (3)	.36	-1.50 (.04)	.57	-2.30 (.09)	.25	-.96 (.06)	.50	-1.50 (.07)	.12	-2.58 (.26)
70-79 (4)	.14	-1.37 (.06)	.50	-2.37 (.16)	.24	-.73 (.14)	.52	-1.48 (.13)	.17	-2.22 (.31)
80+ (5)	.01	-1.93 (.22)	.36	-8.29 (.96)	.44	-1.15 (.39)	.26	-1.30 (.64)	.18	-4.02 (1.37)
Onset Location		**						**		*
Limb	.74	-1.38 (.03)	.62	-2.17 (.06)	.13	-.74 (.09)	.58	-1.42 (.06)	.13	-2.24 (.18)
Bulbar	.21	-.92 (.07)	.40	-1.42 (.21)	.53	-.58 (.10)	.44	-.77 (.10)	.09	-1.85 (.30)
Trunk/Global	.05	-1.53 (.11)	.69	-2.35 (.21)	.32	-.26 (.20)	.62	-1.49 (.18	.06	.20 (.93)
Veteran Status		**		***				**		*
Civilian or Other (0)	.76	-1.25 (.03)	.57	-1.93 (.07)	.22	-.56 (.08)	.54	-1.25 (.05)	.11	-2.32 (.19)
Veteran (1)	.24	-1.43 (.04)	.61	-2.51 (.12)	.25	-.79 (.08)	.59	-1.53 (.10)	.14	-1.58 (.20)
Occupational Risk Category						***		**		**
Low Risk (0)	.62	-1.31 (.03)	.57	-2.16 (.09)	.22	-.34 (.09)	.53	-1.45 (.05)	.11	-1.45 (.21)
High Risk (1)	.38	-1.26 (.06)	.60	-1.93 (.15)	.23	-1.08 (.13)	.60	-1.13 (.10)	.13	-3.05 (.38)
Ever Smoked Cigarettes				***				**		***
No	.54	-1.27 (.04)	.56	-1.88 (.08)	.22	-.54 (.11)	.54	-1.21 (.07)	.10	-3.04 (.25)
Yes	.46	1.32 (.03)	.60	-2.28 (.08)	.23	-.71 (.07)	.57	-1.44 (.06)	.14	-1.30 (.15)
Ever Drank Alcohol						***		*		*
No	.19	-1.23 (.07)	.55	-2.14 (.14)	.28	-.57 (.17)	.52	-1.07 (.10)	.13	-1.40 (.32)
Yes	.81	-1.31 (.03)	.59	-2.06 (.06)	.21	-.18 (.15)	.56	-1.37 (.05)	.12	-2.29 (.16)
Insurance		***		***				***		
One	.49	-1.16 (.04)	.59	-1.79 (.10)	.21	-.75 (.08)	.54	-.92 (.08)	.12	-2.62 (.34)
Two	.44	-1.42 (.04)	.57	-2.32 (.09)	.23	-.54 (.12)	.56	-1.62 (.06)	.12	-1.59 (.40)
Three	.07	-1.43 (.11)	.62	-2.49 (.25)	.25	-.35 (.20)	.61	-2.15	.11	-1.51 (.65)
Marital Status		***		*		***				
Married or Cohabitating (0)	.82	-1.24 (.03)	.58	-2.00 (.07)	.21	-.62 (.08)	.55	-1.29 (.06)	.10	-2.28 (.18)
Divorced, Single, Widowed	.18	-1.52 (.05)	.60	-2.39 (.13)	.28	-.62 (.09)	.57	-1.46 (.08)	.19	-1.71 (.22)
Attend Multidisciplinary Clinic		*				***				***
Yes	.25	-1.20 (.06)	.60	-2.03 (.10)	.26	-.34 (.16)	.57	-1.43 (.09)	.13	-3.34 (.27)
Yes, but no longer attend	.05	-1.18 (.14)	.67	-3.49 (.37)	.28	.19 (.24)	.52	-.97 (.18)	.13	-.62 (.64)
No	.70	-1.33 (.03)	.57	-1.98 (.08)	.20	-.83 (.07)	.55	-1.30 (.06)	.11	-1.73 (.18)

Table 3.1 reports the proportion of people with different characteristics overall, the proportion in each category with a symptom, and the mean time between each symptom and ALS diagnosis for each category of each variable

Table 3.2 Multivariate Regression of Time between the development of Weakness and Diagnosis by Social Position, Age, Onset Location, Proximal Risk Factors, and Resources (n = 9787)

	Model 1: Distal Factors			Model 2: Distal Factors, Age, and Onset Location			Model 3: Distal Factors, Age, Onset Location, and Proximal Risk Factors			Model 4: Distal Factors, Age, Onset Location, Proximal Risk Factors, and Resources		
Dependent Variable	β		SE β	β		SE β	β		SE β	β		SE β
Racial/Ethnic Minority	-.14		.16	-.21		.16	-.22		.16	-.20		.16
Female	-.06		.05	-.09		.05	-.14	*	.06	-.10		.06
Education (ref = Tech/Trade/Some College)												
High School or Less	.27	**	.09	.31	***	.09	.30	***	.09	.31	***	.09
College or More	-.03		.07	-.04		.07	-.05		.07	-.04		.07
Age at Diagnosis (ref=50-59)												
18-39				-.03		.14	-.06		.14	-.04		.14
40-49				-.14		.09	-.15		.09	-.14		.09
60-69				-.50	***	.07	-.49	***	.07	-.46	***	.07
70-79				-.38	***	.08	-.35	***	.09	-.32	***	.09
80+				-1.06	***	.26	-1.02	***	.26	-.96	***	.27
Onset Location (ref = Limb)												
Bulbar							.53	***	.07	.53	***	.07
Trunk/Global							-.15		.12	-.13		.12
Civilian							.12		.06	.10		.08
Low Occupational Risk							.01		.07	.01		.08
History of Smoking							-.02		.06	-.01		.06
History of Drinking							-.06		.08	-.04		.08
Insurance (ref = 1 type)												
Two Types										-.14	*	.07
Three Types										-.03		.16
Multidisciplinary Clinic Use (ref = Currently Attend)												
Do not Attend										.12		.07
Previously Attended but Discontinued										.19		.15
Never Married, Separated, Divorced, Widowed										-.30	***	.07
Constant	-1.28	***	.06	-1.10	***	.08	-1.12	***	.12	-1.13	***	.13

+ p < .10, *p < .05, **p < .01, ***p < .001

Table 3.3 Multivariate Regression of Time between the development Cramping and Diagnosis by Social Position, Age, Onset Location, Proximal Risk Factors, and Resources (n = 5675)

	Model 1: Distal Factors			Model 2: Distal Factors, Age, and Onset Location			Model 3: Distal Factors, Age, Onset Location, and Proximal Risk Factors			Model 4: Distal Factors, Age, Onset Location, Proximal Risk Factors, and Resources		
Dependent Variable	*β*		SE *β*	*β*		SE *β*	*β*		SE *β*	*β*		SE *β*
Racial/Ethnic Minority	.11		.29	-.04		.29	-.04		.29	.005		.29
Female	.36	**	.13	.34	**	.12	.31	*	.13	.33	*	.14
Education (ref = Tech/Trade/Some College)												
High School or Less	.16		.18	.41	*	.18	.42	*	.18	.43	*	.18
College or More	.08		.14	.01		.14	-.01		.15	.03		.15
Age at Diagnosis (ref=50-59)												
18-39				1.09	***	.27	1.16	***	.27	1.19	***	.27
40-49				.25		.17	.23		.18	.23		.18
60-69				-.47	***	.13	-.38	**	.13	-.35	**	.13
70-79				-.48	**	.19	.29		.20	-.27		.21
80+				-6.84	***	.87	-6.66	***	.89	-6.32	***	.91
Onset Location (ref = Limb)												
Bulbar				.87	***	.22	.85	***	.22	.90	***	.22
Trunk/Global				-.08		.24	-.16		.24	-.15		.24
Civilian							.28		.17	.25		.20
Low Occupational Risk							-.20		.21	-.17		.20
History of Smoking							-.29	*	.12	-.21		.12
History of Drinking							.38	*	.17	.31		.18
Insurance (ref = 1 type)												
Two Types										-.19		.18
Three Types										-.03		.35
Multidisciplinary Clinic Use (ref = Currently Attend)												
Do not Attend										-.06		.15
Previously Attended but Discontinued										-1.29	***	.29
Never Married, Separated, Divorced, Widowed										-.37	**	.17
Constant	-2.28	***	.14	-2.20	***	.15	-2.49	***	.27	-2.29	***	.31

+ p < .10, *p < .05, **p < .01, ***p < .001

Table 3.4 Multivariate Regression of Time between the development of Trouble Swallowing and Diagnosis by Social Position, Age, Onset Location, Proximal Risk Factors, and Resources (n = 2170)

	Model 1: Distal Factors			Model 2: Distal Factors, Age, and Onset Location			Model 3: Distal Factors, Age, Onset Location, and Proximal Risk Factors			Model 4: Distal Factors, Age, Onset Location, Proximal Risk Factors, and Resources		
Dependent Variable	β		SE β	β		SE β	β		SE β	β		SE β
Racial/Ethnic Minority	-.02		.36	.06		.36	-.05		.36	-.49		.38
Female	.26	*	.13	.27	*	.13	.15		.14	.23		.15
Education (ref = Tech/Trade/Some College)												
High School or Less	-.09		.22	-.03		.23	-.14		.23	-.15		.23
College or More	.10		.18	.20		.17	.07		.18	.08		.18
Age at Diagnosis (ref=50-59)												
18-39				1.00	*	.48	.73		.48	.61		.47
40-49				-.63	**	.24	-.49	*	.24	-.64	**	.24
60-69				-.95	***	.16	-1.00	***	.16	-1.23	***	.16
70-79				-.65	***	.20	-.82	***	.21	-1.09	***	.22
80+				-1.09	*	.50	-1.14	*	.49	-1.61	**	.53
Onset Location (ref = Limb)												
Bulbar				.29		.15	.30	*	.15	.37	*	.15
Trunk/Global				.62	*	.25	.67	**	.25	.68	**	.25
Civilian							-.06		.17	.23		.18
Low Occupational Risk							.74	***	.17	.67	***	.18
History of Smoking							.15		.14	.06		.14
History of Drinking							-.60	***	.18	-.56	**	.18
Insurance (ref = 1 type)												
Two Types										.51	**	.17
Three Types										1.22	***	.33
Multidisciplinary Clinic Use (ref = Currently Attend)												
Do not Attend										.62	***	.15
Previously Attended but Discontinued										.96	**	.32
Never Married, Separated, Divorced, Widowed										.15		.17
Constant	-.79	***	.17	-.49	*	.21	-.32		.32	-1.00	**	.32

+ p < .10, *p < .05, **p < .01, ***p < .001

Table 3.5 Multivariate Regression of Time between the development of Twitching and Diagnosis by Social Position, Age, Onset Location, Proximal Risk Factors, and Resources (n = 5410)

	Model 1: Distal Factors			Model 2: Distal Factors, Age, and Onset Location			Model 3: Distal Factors, Age, Onset Location, and Proximal Risk Factors			Model 4: Distal Factors, Age, Onset Location, Proximal Risk Factors, and Resources		
Dependent Variable	β		SE β	β		SE β	β		SE β	β		SE β
Racial/Ethnic Minority	.08		.24	.06		.24	.07		.24	.16		.24
Female	.06		.10	.03		.10	.006		.11	.02		.11
Education (ref = Tech/Trade/Some College)												
High School or Less	.58	***	.17	.61	***	.17	.54	**	.17	.53	**	.17
College or More	-.17		.12	-.17		.12	-.20		.12	-.19		.13
Age at Diagnosis (ref=50-59)												
18-39				.23		.21	.16		.22	.22		.22
40-49				-.14		.14	-.19		.14	-.17		.14
60-69				-.45	***	.12	-.43		.12	-.23		.12
70-79				-.43	**	.17	-.38	***	.17	.03		.19
80+				-.67		.71	-.59	*	.72	.07		.71
Onset Location (ref = Limb)												
Bulbar				.70	***	.13	.70	***	.13	.69	***	.13
Trunk/Global				-.07		.19	-.05		.19	.01		.19
Civilian							.07		.12	-.28	*	.13
Low Occupational Risk							-.24	*	.12	-.19		.12
History of Smoking							-.26	**	.10	-.26	**	.10
History of Drinking							-.17		.15	-.06		.15
Insurance (ref = 1 type)												
Two Types										-.70	***	.12
Three Types										-1.40	***	.23
Multidisciplinary Clinic Use (ref = Currently Attend)												
Do not Attend										-.30	**	.12
Previously Attended but Discontinued										.48		.27
Never Married, Separated, Divorced, Widowed										-.25	*	.13
Constant	-1.33	***	.12	-1.22	***	.14	-.82	***	.23	-.31		.24

+ p < .10, *p < .05, **p < .01, ***p < .001

Table 3.6 Multivariate Regression of Time between the development of Trouble with Bowels and Diagnosis by Social Position, Age, Onset Location, Proximal Risk Factors, and Resources (n = 1138)

	Model 1: Distal Factors			Model 2: Distal Factors, Age, and Onset Location			Model 3: Distal Factors, Age, Onset Location, and Proximal Risk Factors			Model 4: Distal Factors, Age, Onset Location, Proximal Risk Factors, and Resources		
Dependent Variable	β		SE β	β		SE β	β		SE β	β		SE β
Racial/Ethnic Minority	.78		.73	.43		.73	.49		.71	.12		.38
Female	-1.54	***	.30	-1.86	***	.30	-.78	***	.30	-1.50	***	.30
Education (ref = Tech/Trade/Some College)												
High School or Less	-.32		.48	.13		.48	-.05		.49	.01		.47
College or More	-1.49	***	.37	-1.32	***	.34	-.67		.34	-.66		.35
Age at Diagnosis (ref=50-59)												
18-39				3.09	***	.91	1.45		.87	1.16		.86
40-49				2.18	***	.55	2.24	***	.53	2.16	***	.51
60-69				-.70		.40	-1.05	**	.39	-1.22	**	.46
70-79				-.74		.41	-1.38	***	.40	-1.61	**	.57
80+				-2.31		1.23	-2.98	*	1.14	-3.18	*	1.31
Onset Location (ref = Limb)												
Bulbar				.63		.38	.38		.38	.38		.39
Trunk/Global				1.83		1.08	1.89		1.03	1.65		1.00
Civilian							-.55		.35	-.30		.50
Low Occupational Risk							1.53	**	.35	1.39	**	.48
History of Smoking							2.13	***	.31	1.95	***	.35
History of Drinking							-2.16	***	.44	-2.23	***	.44
Insurance (ref = 1 type)												
Two Types										.93		.84
Three Types										.52		1.32
Multidisciplinary Clinic Use (ref = Currently Attend)												
Do not Attend										-1.22	***	.28
Previously Attended but Discontinued										.10		.80
Never Married, Separated, Divorced, Widowed										1.01	**	.32
Constant	-.39		.31	-.31		.43	-.26		.73	-.44		.72

+ p < .10, *p < .05, **p < .01, ***p < .001

CHAPTER FOUR: DOES POSITION IN THE LIFE COURSE SHAPE MEDICAL CARE FOR PEOPLE WITH ALS?

Introduction

Research has made clear the need to address gaps and shortcomings in treatment and care provision for ALS (Goutman & Simmons, 2018). Although calls for additional research are more general in nature, sociologists are well positioned to understand the disparities in care for people diagnosed with ALS. Therefore, this paper asks the question: Does position in the life course and social position shape medical and supportive care reported by people with ALS? Guided by life course theory and fundamental cause theory, I posit the timing in the life course of an ALS diagnosis and social position (e.g. race/ethnicity, gender, education level) shapes medical and supportive care accessed by people who are diagnosed with ALS.

Medical Care and ALS

Treatment of ALS is complex for all involved (Radunovic et al, 2007). Multidisciplinary ALS clinics (MDCs) are the option of choice of ALS experts (Radunovic et al, 2007; Obermann and Lyon, 2015). MDCs have teams of ALS specialists, allowing for care and needed devices and supplies to be coordinated from one center (Mitsumoto and Del Bene, 2000). Not all patients, however, choose to use or have access to multidisciplinary ALS clinics without facing a long journey or needing to overcome the financial constraints of travel (Radunovic et al, 2007; Hodgen et al., 2012; Obermann & Lyon, 2015; Stephens et al., 2016; Horton et al., 2018).

For pALS who are not referred by a medical provider or are otherwise unable to attend an MDC (e.g. cost, distance), other barriers to adequate care include a lack of pre-

existing knowledge of ALS (Stephens et al., 2015). Moreover, pALS often face lack of time to research ALS and to consider potential treatment options (Stephens et al., 2015). Each stage of ALS comes with new levels of care, which require difficult conversations and decisions. Medications, such as Riluzole, are often prescribed at diagnosis even before attending an MDC (if one is available) (Dorst et al., 2018). As patients lose the ability to walk, wheelchairs and scooters become necessary. As difficulties with speaking and swallowing become more frequent, people with ALS may need an assistive communication device in order to communicate with caregivers, a percutaneous gastrostomy (PEG) tube for nutrition, and may need to decide on non-invasive ventilation support (e.g. C-PAP or Bi-PAP) (Dorst et al., 2018). As the disease progresses and breathing becomes more difficult, people with ALS need to make the decision to accept or decline invasive mechanical ventilation (e.g. tracheotomy), which is accompanied by the need to complete advanced directives (Dorst et al., 2018). When ALS enters into the final stages, people are faced with making decisions about entering in-home or facility-based hospice care and ending treatments. Many care decisions have to be made quickly, depending on the rate of progression, in order to ensure the timing of care meets the needs of the person with ALS (Radunovic et al, 2007; Obermann and Lyon, 2015; Stephens et al., 2016; Horton et al., 2018; Dorst et al., 2018; Andersen, 2018).

Timing in the Life Course and Medical Care Decision Making

pALS make care decisions within the context of their lives. The diagnosis of ALS and the likelihood of death within a few years is an off-time transition, given ALS often strikes in the years where people are in the prime of their careers, raising children, and caring for elderly parents (Elder & Rockwell, 1979). Research illustrates that people who

are over the age of 70 when diagnosed with ALS tend to be more accepting of the natural course of the disease than those in early-to-mid adulthood (Foley et al., 2014). Older adults with a diagnosis of ALS have completed many important milestones (e.g. raising children into adulthood) (Foley et al., 2014). Further, pALS who perceive that the end of life is near often adjust their choices regarding interventions, placing more value on the social relationships and the remaining time they have left, rather than the potential extension of a life with limited means of communication and more burdensome care (Kotter-Grühn et al., 2010; Foley et al., 2014). In addition, those people with ALS who have a partner and adult children, more common in late adulthood, may be less reliant on hiring in-home nursing or respite care, and in that context make different decisions regarding mechanical ventilation and other invasive treatments (Foley et al., 2014). Given these factors, I hypothesize:

> **H1:** People who are diagnosed later in the life course will be less likely to report accessing each type of care due to their acceptance of the natural disease course, with the exception of advanced directives and hospice care which reflect preparing for the end of life.
>
> **H2:** Marital status will shape the medical and supportive care received, with those who are married being more likely to report accessing each type of care because they have caregivers and a support system in place prior to decision-making.

Fundamental Cause Theory and Disparities in Medical Care for ALS

Although many argue that healthcare is a right, the reality is that in the United States, healthcare is a commodity favoring those who can afford it (Pereira, 2003). Social

position, including race/ethnicity, gender, and socioeconomic status/education, have been considered social determinants of health and potentially fundamental causes of health disparities (Link & Phelan, 1995). Fundamental cause theory may be useful in understanding why there are variations in the medical and supportive care people with ALS access.

Race/ethnicity, gender and socioeconomic status, are indicators of structural inequalities, and are associated with both health care access and utilization. Lower socioeconomic status can prevent access to healthcare in multiple ways, including by limiting affordable options, limiting the time available to explore and gain knowledge of potential treatment options, and the decision to postpone needed care due to cost (Pereiria, 2004). Structures of inequality, as indicated by gender and race/ethnicity, may also play a role in access due to bias in the healthcare system, as demonstrated in the case of cardiac care (McMurray et al., 1991; Menezes et al., 2014; Gay, 2018). Further, education is important to overall health; Mirowsky and Ross (2010) find that education affects the evaluation and use of health information plus the ability to enact health knowledge.

Barriers due to social position may limit medical and supportive care used to improve quality of life for pALS. Therefore, fundamental cause theories suggests the following hypothesis:

> **H3:** Compared to those in more privileged positions, people who are racial/ethnic Minorities, women, and those with lower education will have lower odds of higher cost medical and supportive care for ALS (e.g. wheelchair or scooter use, invasive ventilation, assisted communication

devices, Riluzole, and MDC usage), due to potential bias in the medical system, cost, and level of knowledge and information provided.

Fundamental cause theory also suggests that race/ethnicity and gender are likely to play a role in the level of trust placed in genetic testing or in research studies. Historical evidence of research mistreatment and omissions of racial minorities and women shapes trust in research and providers. Clinical trials have illustrated that a lack of information on and access to clinical trials may influence the rate of racial/ethnic minority groups and women participating in clinical trials (Roberson, 1994; Shavers et al., 2001; Murthy et al., 2004; Suther and Kiros, 2012; Coakley et al., 2012). Results of clinical trials that have not included women have led to consequences for women and their children (e.g. thalidomide disaster, tetracycline in pregnancy), which may dissuade women from participating in clinical trials (Ridings, 2013; Vennila et al., 2014). Further, a history of abuse of Black-Americans in the name of research (e.g. Tuskegee Syphilis Study, the case of Henrietta Lacks) has created fear and distrust of the medical community in this population (Harris et al., 1996; Murthy et al., 2004). Therefore, I hypothesize:

H3a: Women and minorities will be less likely to report genetic testing and participating in clinical trials.

Although prior research has not studied the use of hospice by racial and ethnic minorities diagnosed with ALS, studies regarding cancer mortality have shown race/ethnicity shapes the use of hospice care in the United States with minorities entering hospice less often than Whites (Virnig et al., 2002; Connor et al., 2008; Turkman et al., 2019). Several factors seem to contribute to the underuse of hospice services by members

of the Black-American community in particular. For Black-Americans, personal or cultural values often conflict with hospice philosophy, which requires giving up lifesaving or life-extending measures for comfort care alone (Washington et al., 2008). In addition, Black-Americans often cite a lack of awareness of hospice services, as well as concerns of burdening family in terms of emotional burden and time/economic burden (Washington et al., 2008). Similar to research on clinical trials, there is a mistrust of the health care system which may limit the acceptance of hospice care (Washington et al., 2008). Finally, for racial and ethnic minorities, there is a fear that there will be little diversity among hospice workers, which may limit understanding of cultural and personal preferences (Washington et al., 2008).

Therefore, I postulate:

H3b: Minorities will be less likely to report being enrolled in hospice.

Data and Methods

Data

The National ALS Registry, created in October 2010, is a voluntary web-based registry for people who have been diagnosed with ALS. The registry collects data on demographic characteristics, clinical data such as phenotype, and outcome data. Due to the potential physical, mental, and emotional limitations of pALS, the risk factor survey utilizes smaller modules to facilitate completion (Bryan et al., 2016). The analysis covers from 19 October 2010 to 31 December 2016 and includes 9789 people diagnosed with ALS.

Measures

Dependent Variable: Medical Services and Supportive Care. The National ALS Registry gathers data on ten medical or supportive care options, including (1) wheelchair or scooter use, (2) non-invasive ventilation, (3) invasive ventilation (tracheostomy), (4) assisted communicative device, (5) research study participation, (6) genetic testing, (7) advanced directives, (8) hospice care, (9) Riluzole use, and (10) multidisciplinary clinic use (MDC). Riluzole and MDC usage are each a categorical variable with values of currently use (ref), used but discontinued (=1), and never used (=2). All other variables are dichotomous, with the categories of have not used (=0) and have used (=1).

Independent Variables. The independent variables include: (1) age at diagnosis, (2) onset location as an indicator of the disease process, (3) social position, with education as a dichotomous variable of less than or more than a bachelor's degree (4) veteran status, and (5) social resources, including insurance coverage and marital status. The independent variables, with the exception of the recoding of education, have been detailed in chapter 2 and chapter 3. I was unable to include proximal risk factors into the analysis due to the inability of the imputation model to converge. The large amount of missing data for some variables (e.g. health insurance), as well as the small number of pALS who reported accessing some types of medical and supportive care (e.g. invasive ventilation), required the omission of these variables used in chapters 2 and 3.

Analysis

Multiple Imputation using Chained Equations was used to impute missing data (Enders, 2006). I use logistic regression with odds ratios to examine odds of reporting

each dependent variable, with the exception of Riluzole and MDC use, which use multinomial logistic regression with relative risk ratios. Each model is created in steps; (1) age at diagnosis, (2) age at diagnosis and onset location, (3) age at diagnosis, onset location, and social position (4) age at diagnosis, onset location, social position, and social resources. Models are built to reflect the timing of the ALS diagnosis in the life course as the variable of interest, include the control for the disease process (e.g. global onset indicates a quicker timeline to deciding on invasive ventilation), social position, and finally the addition of social resources to determine if these factors change the relationship between life course and medical and supportive care decisions. Results are reported for the full models, and statistical significance was determined at the $p < .05$ level.

Results

Demographics

As indicated by Table 4.1, the sample is a majority White (97.18%), and nearly 60% male. Over 60% of the respondents reported having at least a bachelor's degree. Veterans make up nearly 24% of the sample. The majority of the sample is married or cohabitating (82%). Most of the respondents are between the ages of 50-59 and 60-69 (29.79% and 35.99 % respectively). Although all of the respondents reported health insurance coverage, the majority of the respondents reported either one type of insurance coverage (50.17%) or two types of insurance coverage (43.72%).

Most pALS use some kind of medical and/or supportive care. The most common kind is wheelchair or scooter use (72%), followed by non-invasive ventilation (29%). Fewer pALS use invasive ventilation (tracheotomy) (2%). Nearly 13% of respondents

reported assistive communication device use. About a fifth of respondents reported participating in a research study or having genetic testing done (22% and 20% respectively). Over two-thirds (68.89%) of respondents report having advanced directives in place, however, only 4% have reported enrolling in hospice care. Fifty percent report using Riluzole currently, and nearly 70% report currently attending an MDC.

Regression Models of Medical and Supportive Care

Life course and medical or supportive care. Age at diagnosis is associated with reported medical and/or supportive care for pALS, with many categories of care less likely to be reported by older pALS. There is, however, an exception with the reporting of non-invasive ventilation, with groups who have less privileged having higher odds of accessing non-invasive ventilation. In addition, end of life care, including advanced directives and hospice enrollment, were more likely to be reported by pALS diagnosed at younger ages. Therefore, Hypothesis 1 is partially supported.

In Table 4.2, the results show that pALS who are diagnosed between the ages of 60-69 (OR = .74, CI [.65, .83]), 70-79 (OR = .45, CI [.38, .53]), and who are diagnosed at 80+ (OR = .56, CI [.36, .86]) are less likely to report using a wheelchair or scooter than pALS who are between the ages of 50-59. The predicted probability of wheelchair or scooter use decreases as pALS age (Figure 4.1).

The association of age with non-invasive ventilation, reported in Table 4.3, was contrary to hypothesis one. pALS who are diagnosed between the age of 18 and 49 are 42% less likely to use non-invasive ventilation (OR = .58, CI [.44, .78]), whereas those who are diagnosed between the ages of 60 and 69 are 18% more likely to use non-invasive ventilation (OR = 1.18, CI [1.00, 1.38]) than those who are between the ages of

50 and 59. Age at diagnosis does not appear to shape the use of non-invasive ventilation, however, non-invasive ventilation is a standard of care for pALS who are having shortness of breath or other difficulties breathing which may mean all pALS are more likely to be accepting of this type of care.

Age is associated with invasive ventilator use (Table 4.4). pALS who are diagnosed between the ages of 40 and 49 are 114% more likely to report the use of invasive ventilator use compared to those who are diagnosed between the ages of 50-59 (OR = 2.14, CI [1.44, 3.16]). pALS who were diagnosed between the ages of 60 and 69 were 48% less likely (OR = .52, CI [.33, .82]) and 70 and 79 were 92% less likely (OR = .08, [.02, .27]) to report invasive ventilator use. For invasive ventilation, 4% of pALS between 40-49, 2% of pALS between 18-39 and between 50-59, and 1% of pALS between 60-69 are predicted to opt into invasive ventilation (Figure 4.2).

Age is also associated with the use of assistive communication devices among pALS (see Table 4.5). pALS who are diagnosed between the ages of 60 and 69 (OR = .52, CI [.43, .62]), 70 and 79 (OR = .39, CI [.31, .50]), or 80 and older (OR = .57, CI [.33, .98]) they are less likely to report the use of an assistive communication device than those who are diagnosed between the ages of 50 and 59. There is no statistically significant difference for assistive communication device use for pALS who are diagnosed between the ages of 18-49 and 40-49 when compared to pALS who are diagnosed between the ages of 50-59. The predicted probability of opting into assistive communication device use decreases for those who are diagnosed after age 50 (Figure 4.3).

Age at diagnosis also shapes participation in research studies, as well as genetic testing (Table 4.6 and 4.7). pALS who are younger at the time of an ALS diagnosis are

more likely to report participating in a research study, and pALS who are older at diagnosis are less likely to have participated (see Table 4.6 for full results). The probability of reporting participation in a research study decreases with older age, from 40% of pALS diagnosed between ages 18-19, to 2% diagnosed at ages 80 and older (Figure 4.4). For genetic testing, pALS who are diagnosed between the ages of 18-39 are 117% more likely (OR = 2.17, CI [1.71, 2.74]) and those diagnosed between 40 and 49 are 49% more likely (OR = 1.49, CI [1.26, 1.76]) to report using genetic testing performed than those who are between the ages of 50-59. pALS who were diagnosed between the ages of 70-79 were 47% less likely to report having genetic testing done than pALS between diagnosed between 50-59 (OR = .53, CI [.43, 1.19]). The predicted probability of reporting having genetic testing done were lowest (12%) for pALS diagnosed between ages 70-79, and highest (36%) between the ages for pALS diagnosed between 18-39 (Figure 4.5). For genetic testing, some of the differences in age may be due to familial (genetically linked) ALS developing earlier in the life course, leading to a higher likelihood of testing, although it is offered to all patients. The lower levels of reporting genetic testing in older pALS does support hypothesis one.

Table 4.10 reports the results of the multinomial logistic regression for Riluzole use. Riluzole is one of two medication options for pALS and is thought to extend survival by two to three months (Dorst et al., 2018). pALS who are over the age of 80 are 141% more likely to report never having used Riluzole (RR = 2.41, CI [1.62, 3.58] than pALS who are between the ages of 50 and 59. pALS between the ages of 60 and 69 are 40% less likely to report having discontinued the use of Riluzole (RR = .60, CI [.51, .86]), and pALS between the ages of 70 and 79 are 32% less likely to report discontinued the use of

Riluzole (RR = .68, CI [.54, .86]) than pALS between the ages of 50 and 59. The fact that older adults are less likely to report discontinuing Riluzole use may be due to these pALS never starting Riluzole, supporting hypothesis one.

Finally, age at the time of diagnosis also shapes who has never used a Multidisciplinary ALS clinic. When compared to attending an MDC, pALS who are in the older age groups (between the ages of 60 and 69 (RR = 1.15, CI [1.02, 1.32]), 70 and 79 (RR = 1.51, CI [1.28, 1.78]), and who are over 80 years of age (RR = 2.12, CI [1.38, 3.25]) are more likely to report never attending an MDC compared to pALS between the ages of 50 and 59. Age is not associated with discontinued MDC use compared to currently attending an MDC (Table 4.11). Again, this may be because older adults do not access MDCs in the first place.

Planning for end of life care, as well as accepting that the end of life is near, is also shaped by the pALS age at diagnosis in expected ways. Consistent with the idea that a diagnosis of ALS and the likelihood that death will happen in the future, which may be an on-time or off-time transition depending on the position in the life course, pALS who are between the ages of 18 and 39 at diagnosis are 57% less likely (OR = .43, CI [.34, .54]) and those who are diagnosed between the ages of 40 and 49 are 36% less likely (OR = .64, CI [.56, .73]) to have reported being having advanced directives in place than those diagnosed between the ages of 50 and 59 (Table 4.8). pALS who are 60 and older at diagnosis are more likely to report having advanced directives in place. The predicted probabilities of reporting having completed advanced directives increase with age, from 45% for pALS diagnosed between the ages of 18-49, to 99% for pALS diagnosed at ages 80 and older (Figure 4.6).

Further, as hypothesized, those who are older at diagnosis are more likely to report being enrolled in hospice care (Table 4.9). pALS diagnosed between the ages of 60 and 69 are 188% more likely to report being enrolled in hospice (OR = 2.88, CI [2.10, 3.96]), and those who are diagnosed between the ages of 70 and 79 are 183% more likely to report hospice enrollment (OR = 2.83, CI [1.86, 4.30]) than those who are diagnosed between the ages of 50 and 59. pALS diagnosed over the age of 80 are more likely report enrollment in hospice care as well (OR = 7.21, CI [3.35, 15.51]).

Marital status and medical or supportive care. Hypothesis 2 states that pALS who are unmarried compared to those who are married will be less likely to report all types of medical or supportive care except for advanced directives and enrollment in hospice care. Given the results, Hypothesis 2 is partially supported. Tables 4.6 and 4.7 illustrate that pALS who are unmarried are 26% less likely to report participating in a research study (OR = .74, CI [.64, .86]), and 27% less likely to report genetic testing (OR = .73, [.63, .85]).

In regard to Riluzole use, which may extend survival by a few months (Dorst et al., 2018), unmarried pALS were 38% more likely than married pALS to report never taking Riluzole compared to currently taking Riluzole (RR = 1.38, CI [1.24, 1.55]) (Table 4.10). Unmarried pALS are 135% more likely to report having discontinued attending an MDC versus currently attending compared to married pALS (RR = 2.35, CI [1.88, 2.93]) (Table 4.11).

Several types of medical care or supportive care were just as likely to be reported by unmarried and married pALS. There was no difference in wheelchair or scooter use (OR = .98, CI [.87, 1.10]), non-invasive ventilator use (OR = .98, CI [.87, 1.11]), or

assistive communication device (OR = 1.04, CI [.88, 1.23]) by marital status (Tables 4.2, 4.3, and 4.5). In addition, unmarried pALS are no more or less likely to report never attending an MDC versus currently attending when compared to their married peers (RR = .99, CI [.67, .99]) (Table 4.11). Surprisingly, Table 4.8 demonstrates that unmarried pALS are no more or less likely to report having advanced directives in place than their married peers, as there is a greater need for advanced directives in the case of unmarried pALS who are unable to communicate and do not have a spouse or next of kin to do so for them (OR = 1.10, CI [.97, 1.25]).

Finally, pALS who are single are 122% more likely to report invasive ventilator use (OR = 2.22, CI [1.53, 3.20]) (Table 4.4). The predicted probability of unmarried pALS to report invasive ventilator use is 2.9%, whereas the predicted probability for married pALS is 1.4% (Figure 4.7). The increased odds of invasive ventilation use being reported by unmarried pALS is unexpected, given the high-level of care required with a tracheostomy and mechanical ventilation and the need for in-home care cannot be met by a spouse or partner. pALS who are unmarried are 141% more likely to report having enrolled in hospice care in comparison to their married peers (OR = 2.41, CI [1.92, 3.02]) (Table 4.9). The probability of unmarried pALS reporting hospice enrollment is 7%, compared to 3% for married pALS (Figure 4.8).

Social position and medical or supportive care. Social position is associated with some of the medical and supportive care reported by pALS. Table 4.2 reports the results for wheelchair or scooter use. Women are 22% more likely than men to report wheelchair or scooter use (OR = 1.22, CI [1.10, 1.35]). This finding is surprising, as women are more likely to develop bulbar onset ALS, and pALS with bulbar onset are less

likely to report wheelchair or scooter use (OR = .45, CI [.39, .51]). The finding may be due to women socialized to being more dependent on others for their needs, in this case, movement. Alternatively, men may feel that using assistive devices, such as a wheelchair, may be a threat to their masculinity and do not want to be seen as impaired. pALS with a college degree or higher are 18% more likely to report wheelchair or scooter use than those without a college degree (OR = 1.18, CI [1.04, 1.35]). There is no difference in wheelchair or scooter use by race/ethnicity (OR = .85, [.64, 1.14]) or by marital status (OR = .98, CI [.87, 1.10]).

Social position was associated with reported non-invasive ventilation, although in unexpected ways (Table 4.3). Racial/ethnic minorities are 76% more likely to report non-invasive ventilator use compared to Whites (OR = 1.76, CI [1.36, 2.27]). Women were 20% less likely to use non-invasive ventilation compared to men with ALS (OR = .80, CI = .72, .89]). Those with a college education or more were 13% more likely to report non-invasive ventilator use (OR = 1.13, CI [1.02, 1.24]). Social position, again, seems to shape invasive ventilation in unexpected ways (Table 4.4). Minorities were 509% more likely to report invasive ventilator use than Whites (OR = 6.09, CI [3.76, 9.84]), which is unexpected due to the previous literature on health disparities that suggests minorities would be less likely to access this type of care. The population of racial/ethnic minorities in the National ALS Registry is small and logistic regression does not handle small cell counts well. Therefore, to substantiate the results of the logistic regression I performed a sensitivity analysis using a complementary log-log regression which returned a similar odds ratio and confidence interval to the logistic regression (OR = 5.55, CI [3.56, 8.63]).

The predicted probability for reporting invasive ventilation for racial/ethnic minorities is 7.5%, compared to the predicted probability for whites of 1.5% (Figure 4.9).

Women were 51% less likely to report invasive ventilator use than men (OR = .49, CI [.33, .73]). The findings for both non-invasive and invasive ventilation use means that the associations for social position are perhaps more about personal and cultural expectations and less about social power at the time of the decision-making.

As expected, racial/ethnic minorities are 45% less likely than Whites to report the use of an assistive communication device (OR = .55, [.35, .87]), however, women were 99% more likely to report using an assistive communication device than men (OR = 1.99, CI [1.72, 2.31]) (Table 4.5). pALS with a college education or more were more likely to report the use of an assistive communication device (OR = 1.18, CI [1.03, 1.36]).

pALS with higher education also have a higher likelihood of reporting participation in a research study or genetic testing. pALS with a higher level of education were 69% more likely to report participating in a research study (OR = 1.69, CI [1.51, 1.90]) and 13% more likely to report having genetic testing done (OR = 1.13, [1.00, 1.27]) (Table 4.6 and 4.7). As previously described in chapters 1 and 2, this may mean that clinical trials suffer from issues of representation, which may lead to promising treatments failing when introduced into the larger population.

Women are 25% less likely than men to report having advanced directives in place than men (OR = .75, CI [.68, .83]). This finding is interesting, as women are often socialized to worry about their family, and advanced directives are often thought to lessen the burden on the family members at the end of life. pALS with higher levels of education are 57% more likely than those with lower levels of education to report having

advanced directives in place (OR = 1.57, CI [1.42, 1.73]) (Table 4.8). Women are 30% less likely than men to report enrollment in hospice care (OR = .70, CI [.55, .89]) (Table 4.9). pALS with higher levels of education are just as likely to report being enrolled in hospice as pALS with lower education levels (OR = 1.17, CI [.94, 1.45]). This finding may illustrate that hospice care, as it is often free and/or covered by Medicare, may not reflect the same disparities by education level.

The use of Riluzole varies by social position (Table 4.10). There are three categories of Riluzole use in the ALS Registry; currently using, discontinued using, and have never used. Racial/ethnic minorities are 49% less likely to report never taking Riluzole than Whites (RR = .51, CI [.38, .68]), however, are no more or less likely to report having discontinued its use (RR = 1.05, CI [.73, 1.52]). Women are more likely than men to report having never taken Riluzole (RR = 1.28, CI [1.16, 1.41]) and to have discontinued the use of Riluzole (OR = 1.33, CI [1.15, 1.54]) versus reporting the current use of Riluzole. pALS with higher levels of education are 21% less likely to report having never taken Riluzole than pALS with lower levels of education (RR = .79, CI = [.72, .86]), and are 29% more likely to report having discontinued the use of Riluzole (RR = 1.29, CI = [1.11, 1.50]). There is debate over the actual effectiveness of Riluzole, and those who choose not to take it may find it cost prohibitive, or potentially have reasoned it is not effective enough in slowing their symptoms to justify the continued cost.

Social position further shapes who attends an MDC (Table 4.11). Minorities are 81% more likely to report having never attending an MDC compared to currently attending an MDC, in contrast to their White peers (RR = 1.81, CI [1.38, 2.37]). Women,

when compared to men, are 24% more likely to report never attending an MDC clinic versus currently attending (RR = 1.24, CI [1.11, 1.39]), and are 21% less likely to report discontinued attendance at an MDC compared to currently attending (RR = .79, [.63, .99]. pALS with higher levels of education, in contrast to pALS with lower levels of education, are 35% less likely to report never attending an MDC (RR = .65, CI [.50, .66]), however, they are no more or less likely to report having discontinued attendance at an MDC (RR = .93, CI [.75, 1.14]), when compared to pALS currently attending an MDC. The results indicate that social position is associated with accessing what physicians regard as the 'gold standard' of care and may be indicative of barriers to attendance such as cost or travel distance.

Participation in research studies and genetic testing by gender and race/ethnicity. Social position is associated with the report of participation in a research study yet is not associated with genetic testing (Tables 4.6 and 4.7). Racial/ethnic minorities are 39% less likely to have participated in a research study than Whites (OR = .61, CI [.44, .86]), with the predicted probability of participating in a research study of 15% for racial/ethnic minorities compared to 22% for whites (Figure 4.10). There was no association with race/ethnicity and genetic testing. Women were 21% less likely to report participating in a research study (OR = .79, CI [.70, .88]) and 34% less likely to report having genetic testing done (OR = .66, CI [.58, .74]) than men. The predicted probability for participating in a research study is 20%, and the predicted probability of genetic testing is 16% for women, compared to 24% and 23% respectively for men (Figures 4.11 and 4.12).

Race/ethnicity and hospice care. Contrary to Hypothesis 3a, racial/ethnic minority status is not associated with enrollment in hospice. Racial/Ethnic minorities are no more or less likely to report being enrolled in hospice than Whites (OR = 1.26, CI [.71, 2.26]).

Discussion

Life Course Theory and the Shaping of Medical and Supportive Care

Addressing the gaps in care provision for ALS is an important part of improving the quality of life for people with ALS (Goutman & Simmons, 2018). As part of understanding the gaps in care for those with ALS it is important to determine where, as well as why, gaps in care exist. Using life course theory and fundamental cause theory as a framework for model creation, I explored how the timing of an ALS diagnosis, as well as social position, shapes the medical care reported by people diagnosed with ALS in the National ALS Registry. Although it is difficult to fully grasp why gaps in care exist and if these gaps are problematic in every case, the results do show where there are differences by both position in the life course and social position.

The timing of an ALS diagnosis in the life course does shape the types of care people with ALS chose to obtain. pALS who are older than 59 are less likely to report engaging in most types of medical and supportive care. These findings are expected when viewed through a life course lens. Qualitative research has demonstrated that people who are age 70 or over when diagnosed with ALS tend to be more accepting of the natural course of the disease than those in early-to-mid adulthood (Foley et al., 2014). Death, in the form of the diagnosis of a disease such as ALS, in later adulthood and old age may be more expected as part of the life course after reaching many previous life transition

milestones (Elder & Rockwell, 1979; Foley et al., 2014). When death is already expected in the short(er) term, the addition of an ALS diagnosis may cause people to adjust their goals for care, placing a higher value on spending time with family and limiting interventions to prevent the inevitable outcome (Kotter-Grühn et al., 2010; Foley et al., 2014). Therefore, it was not surprising that older adults were more likely to report enrollment in hospice care as well as having advanced directives in place, as these are often acknowledgements of an anticipated death.

The diagnosis of ALS and the likelihood of a fatal outcome within a few years, however, would be considered an off-time transition in young adulthood or middle ages, as they are often in the prime of their careers, raising young children, and potentially caring for elderly parents (Elder & Rockwell, 1979). The prospect of death leaves young people feeling cheated of a full life and robbed of their remaining years, and leaves those in middle age anxious regarding unfinished plans and responsibilities (Kalish, 1985). Just as older adults who expect death and thus make decisions to not forestall death, those earlier in the life course opt to do everything and anything to prevent death. Therefore, the higher likelihood of pALS in the early part of the life course to pursue every type of medical or supportive care is expected. In contrast, care for older adults is often conceptualized as dependent on the value placed on their lives and a differential in the availability of resources, however, these findings illustrate it may be more dependent the sense of the on-time versus off-time nature of a diagnosis. Therefore, what appears to be gaps in care for older pALS may be more of an intentional decision-making process among older pALS.

The one exception to the expected findings was for non-invasive ventilation. Age at diagnosis is not associated overall with non-invasive ventilation (e.g. Bi-PAP or C-PAP machine). Only pALS diagnosed between the ages of 18 and 49 showed a lower use of non-invasive ventilation, and those who were between the ages of 60 and 69 were more likely to report the use of non-invasive ventilation. One reason for this may be that non-invasive ventilation is the standard of care for pALS who are beginning to have difficulty breathing. In addition, the use of a Bi-PAP or C-PAP machine has been normalized as a supportive therapy for those with sleep apnea, which may suggest to pALS that non-invasive ventilation is perhaps within the realm of normal behavior rather than supportive care and is a potential area for future research. The widespread, non-age dependent, use of non-invasive ventilation is an important finding, as those who use non-invasive ventilation have longer survival times than those who do not (Lechtzin et al., 2007).

Marital status is associated with use of medical and supportive care. Unmarried pALS are less likely to report participating in a research study and genetic testing and are more likely to report discontinuing Riluzole use and having never attended an MDC. Several explanations for this exist. Unmarried pALS do not have a supportive partner to ensure they are able to be transported to clinical trial visits or MDC appointments, meaning unmarried pALS do not opt into research studies as often, as well as discontinue their MDC attendance once they are no longer able to drive or travel unassisted (Spataro et al., 2017). In addition, without a partner encouraging the continued use of Riluzole for its perceived benefits of extending life, unmarried pALS might be more apt to stop its use (Spataro et al., 2017). Finally, genetic testing is often seen as a tool to warn children of a

potentially genetic disease, and if unmarried pALS do not have children or are not close with their children, they may forgo such testing (Crook et al., 2017; van Es et al., 2017).

From the perspective of life course theory, it is surprising that unmarried pALS are much more likely to report invasive ventilation than their married peers. Invasive ventilation is less often adopted overall by pALS in the United States, which is reflected in the National ALS Registry, because of the prohibitive cost of round-the-clock care. In addition, many pALS are concerned over the potential burden placed on informal caregivers, both in providing an extraordinarily complex level of care and the financial cost that must be assumed. For unmarried pALS, it may be that when the costs can be managed and professional care can be brought into the home, then the perception of burden is lessened, and invasive ventilation is viewed as a reasonable choice. A second explanation also exists, as many pALS are placed on invasive ventilation as a result of complications of ALS, including pneumonia and other infections. Without having a partner as the next of kin to verbalize pALS wishes or to ensure advanced directives and DNR orders are communicated, unmarried pALS may be more likely to be placed on invasive ventilation. For some pALS, invasive ventilation can be discontinued once the crisis has passed, however, at least some remain on invasive ventilation indefinitely (Cazzolli and Oppenheimer, 1996; Benditt, 2002). To fully understand the patterns from the survey data, adding a qualitative study would be ideal.

Social Position and the Shaping of Medical and Supportive Care

Social position does shape some of the medical and supportive care reported by pALS, although not always in ways that are consistent with the research on health disparities using a fundamental cause and the social determinants of health framework.

Women, in comparison to men, are less likely to report using non-invasive and invasive ventilation, completing advanced directives or enrolling in hospice care, and are more likely to report never using or discontinuing the use of Riluzole. Women are also more likely to report never attending an MDC. Women, however, are more likely to report the use of a wheelchair or scooter and are less likely to report discontinuing attendance at an MDC. These differences may be in part due to differences in the disease course for men and women, which I attempt to control for with the inclusion of onset location; however, there are several other potential explanations. For example, previous research in gender differences in medical decision-making about stroke care demonstrates men and women do not differ in preference for interventions, although women were more dissatisfied with the provision of information on interventions (Crawford et al., 2000; Kapral et al., 2006; Saposnik et al., 2009). Women may need additional information from their providers to understand the risks and benefits of interventions with ALS and may avoid the intervention if their questions go unanswered. Further, many studies have shown that women are neglected in medical research and treated differently by the healthcare system. For example, cardiac care has been researched as a disease of men, men's symptoms are taken more seriously, and men are treated more aggressively than women (McMurray et al., 1991; Gay, 2018). As ALS is viewed as a disease of men, it may be that women are subject to the same types of biases from researchers and providers as are found in cardiac care and suggests a need for additional qualitative research with women diagnosed with ALS and their healthcare providers. Overall, the differences in care are concerning, especially within the context of bias.

Differences in education, which may be thought of as a proxy of socioeconomic status, also shaped the care reported by pALS. pALS with higher levels of education were more likely to report wheelchair or scooter use, the use of a non-invasive ventilator, using an assistive communication device, and of having advanced directives in place. Education also influenced the use of Riluzole, with fewer pALS with higher levels of education reporting having never taken Riluzole, and more stating that they have discontinued its use. pALS with higher levels of education are less likely to report having never attended an MDC than their peers with lower levels of education. Moreover, pALS with higher levels of education were more likely to participate in research studies and to have had genetic testing performed. The potential reason for the differences in care reported by education level are threefold. The first is that ALS onset is different for those with lower levels of education, as noted in chapter one and two, therefore care needs are different and are not completely captured in the registry data. Second, education acts as a proxy of socioeconomic status, and those with higher levels of education are more able to afford and access medical and supportive care. Finally, it may be that higher levels of education allow pALS to acquire, evaluate, and use information regarding their diagnosis in a way that informs their choices in care differently and allows pALS with higher levels of education to advocate for the care they need (Mirowsky and Ross, 2010). In any case, it is important to consider education in the development of interventions and the provision of care for pALS as this appears to be one source of the gaps in care.

The pALS identified as belonging to a racial/ethnic minority group in the National ALS Registry are less likely to report using an assistive communication device and are more likely to report having never attended an MDC clinic, both of which can be

expensive and difficult to access. There were no differences by race/ethnicity for the use of a wheelchair or scooter, however, this may be affected by other findings including the use of non-invasive and invasive ventilation.

pALS identified as racial/minorities in the sample were much more likely to report non-invasive and invasive ventilation. Given the potential for care disparities to exist in ALS, the two forms of ventilation are areas one would expect to see disparities given the issues of cost and/or access. Smaller clinic-based studies have also noted an increase in use of both types of ventilation for Black American pALS, with invasive ventilation being up to eight times more likely compared to White-American pALS (Quadri et al., 2019; Gungogdu et al., 2013). Although other studies have found comparable results, few studies have attempted to understand these differences. One reason for the difference could be that racial and ethnic minority populations present with far more advanced ALS or progress to later stages of the disease more quickly, or for complications for ALS to arise more often, leading to a higher than expected number of racial and ethnic minorities using invasive ventilation (Ceriana et al., 2017; Rodriguez et al., 2018).

Previous work in understanding why pALS choose to use invasive ventilation has focused on the idea that invasive ventilation is 'life-saving', meaning pALS who opt to pursue invasive ventilation believe they will live significantly longer with it than without and allowing them to live when they might otherwise die (Lemoignan and Ells, 2010). Given the difference in life expectancy for racial minorities in the United States, Black Americans are more likely to experience the death of a parent, a child, a sibling, or other loved ones (Umberson et al., 2017). In light of the higher numbers of deaths witnessed,

Black Americans may be more likely to opt into invasive ventilation to stay alive—preventing the loss of another family member—not only for their own desire to live but in order to protect their families. Developing an understanding of how the differences in the adoption of invasive ventilation may be rooted in a deeper history of racism in the United States is a critical area for future research.

Gender and race/ethnicity in research participation and genetic testing. Social position, in the form of gender and race/ethnicity, is associated with participation in a research study, but is not associated with genetic testing. Women were less likely to report participating in research studies and in genetic testing, yet minorities were less likely to participate in research studies. As discussed in both chapters one and two, clinical trials for ALS treatments suffer from widespread failure (e.g. treatments are ineffective), and the majority of trial participants are young, white, and male, with limb onset (Chiò et al., 2011; Mitsumoto et al., 2014). As discussed in the section of differences between the types of care reported by men and women, it is important to include women and racial/ethnic minority groups in clinical trials to ensure the trials and resulting treatments are not solely geared to white men, over and above increasing the potential for successful clinical trials.

Race/ethnicity and hospice care. Race and ethnicity are not associated with enrollment in hospice. Minorities are no more or less likely to report being enrolled in hospice than whites. Although studies examining the use of hospice for cancer diagnosis have previously shown minorities enter hospice less often than whites which may be due to barriers such as access to and knowledge of hospice care and cultural concerns (Virnig et al., 2002; Connor et al., 2008; Turkman et al., 2019), ALS diagnosis does not reflect

the same disparities. ALS is a fatal diagnosis and has no cure and little in the way of treatment, however, whereas cancer diagnoses are less certain and may present more options for a potential cure and the option to attempt to extend life. Additionally, the lack of association between race/ethnicity and hospice care may be due to the increase in use of invasive ventilation in racial/ethnic minority groups.

Limitations

There are a number of limitations to consider with this study. The first is the nature of the National ALS Registry. The National ALS Registry has been designed for biomedical and epidemiological research, and therefore limits the work of the social scientist, however, many of the needed components to understand where disparities in care exist are available. The ALS Registry is reliant on patient self-reporting data and may be subject to recall bias and bias due to self-identification. Further, the registry is a large non-random sample that is opt-in and is therefore not generalizable to the ALS population.

Another limitation is the issue of missing data. Unlike previous studies in the dissertation, I was unable to include proximal risk factors into the analysis of medical and supportive care due to the inability of the imputation model to converge. The large amount of missing data for some variables (e.g. health insurance), as well as the small number of pALS who reported accessing some types of medical and supportive care (e.g. invasive ventilation), required the omission of these variables. Future studies should attempt to account for proximal risk factors to better understand how they may influence the decision to access certain types of medical and supportive care.

In addition, the registry is available in an online format only, which may limit access and cause the registry to reflect a younger, white, and a more educated patient sample. The registry sample provided by the CDC is less racially diverse than the overall registry which includes Medicare and Veteran's Association claims data. There are several potential reasons for this, including access to computers that are required for self-registration; reduced awareness of the registry; and reduced participation in areas with substantial nonwhite populations (Kaye et al., 2018). In addition, while the sample size overall is robust, smaller numbers of specific populations, such as non-white patients, limits the ability to do intersectional analysis to better understand the relationship of social position and ALS. Finally, the limited access to data due to reidentification risks limit the analysis to a small number of survey modules, which prevents a fuller picture of the experience of ALS. Even with these limitations, the National ALS Registry is the most comprehensive, geographically diverse sample of people diagnosed with ALS.

Conclusion

The analyses of disparities in medical care contributes to the knowledge of both sociology and ALS. Position in the life course also shapes the experience care reported by pALS, although not always in ways theory would posit. There are many potential reasons for these findings, including a sense of burden, access and knowledge, and a fear or acceptance of death.

Medical care is shaped by social position, as suggested by fundamental cause theory. These theories do highlight the differences in medical and supportive care, however, some of the findings actually run counter to the theories' predictions. Therefore, although fundamental cause theory works fairly well in the case of a specific

disease, sociological theories created for the more general social experiences (e.g. who will get a disease and who will not) may need to be adjusted to reflect the differences in experiencing specific diseases. Further, adjustment of current theories in the sociology of health and illness allow for their use in exploring the connection between the social world and the experience and care for those diagnosed with the specific disease in question (Pescosolido, 2006; Link, 2008; Timmermans and Haas, 2008). In addition, the results from this work again reaffirm the need for a sociology of disease, as dealing with the care needs for a specific disease, such as ALS, is different from many other diseases. Future research should address the potential reasons why life course theory and fundamental cause theory drive findings that are different among people already diagnosed with ALS compared to the bigger picture of general illness, in order to better adjust the theories in a sociology of disease framework.

Table 4.1 Descriptive Statistics for Medical and Supportive Care (N = 9789)

Variable		Pre-Imputation Frequency	Pre-Imputation Percent	Post-Imputation Percentage
Powerchair/Scooter				
	No	6961	71.11	72.12
	Yes	2680	27.38	27.88
	Missing	148	1.51	0
	Total	9789	100.00	100.00
Non-Invasive Ventilation				
	No	6837	69.84	71.31
	Yes	2760	28.19	28.69
	Missing	192	1.96	0
	Total	9789	100.00	100.00
Invasive Ventilation				
	No	9402	96.05	98.34
	Yes	160	1.63	1.66
	Missing	227	2.32	0
	Total	100.00	100.00	100.00
Assistive Communication Device				
	No	8381	85.62	87.31
	Yes	1221	12.47	12.69
	Missing	187	1.91	0
	Total	9789	100.00	100.00
Genetic Testing Done				
	No	7115	72.68	79.76
	Yes	1774	18.12	20.24
	Missing	900	9.19	0
	Total	9789	100.00	100.00
Participate in Research Study				
	No	7460	76.21	77.86
	Yes	2123	21.72	22.14
	Missing	203	2.07	0
	Total	9789	100.00	100.00
Advanced Directives in Place				
	No	2985	30.49	31.11
	Yes	6604	67.46	68.89
	Missing	200	2.04	0
	Total	9789	100.00	100.00
Hospice				
	No	9232	94.31	95.77
	Yes	407	4.16	4.23
	Missing	150	1.53	0
	Total	9789	100.00	100.00
Riluzole Use				
	Never Used	3656	37.35	37.88
	Used to Take	1110	11.34	11.48
	Currently Use	4894	49.99	50.64
	Missing	129	1.32	0
	Total	9789	100.00	100.00
Multidisciplinary Clinic				
	Never Attended	2342	23.92	24.61
	Previously Attended but No Longer	430	4.39	4..49
	Currently Attend	6790	69.36	70.90
	Missing	227	2.32	0
	Total	9789	100.00	100.00
Age at Diagnosis				
	18-39 (0)	427	4.36	4.36
	40-49 (1)	1382	14.12	14.12
	50-59 (2)	2916	29.79	29.79
	60-69 (3)	3522	35.99	35.99
	70-79 (4)	1406	14.37	14.36
	80+ (5)	134	1.37	1.37
	Missing	2	.02	0
	Total	9789	100.00	100.00
Onset Location				
	Limb (0)	7169	73.24	73.61
	Speech/Swallowing (1)	2003	20.46	20.59
	Trunk/Global (2)	564	5.76	5.80
	Missing	53	.54	0
	Total	9789	100.00	100.00
Race/Ethnicity				
	White (0)	9513	97.18	97.18
	Racial/Ethnic Minority (1)	276	2.82	2.82
	Missing	0	0	0
	Total	9789	100.00	100.00
Gender				
	Male (0)	5861	59.87	59.87
	Female (1)	3928	40.13	40.13
	Missing	0	0	0
	Total	9789	100.00	100.00
Education				
	Less than a College Degree (0)	3426	35.00	35.00
	College Degree or More (1)	6363	65.00	65.00
	Missing	0	0	0
	Total	9789	100.00	100.00
Veteran Status				
	Civilian or Other (0)	7473	76.34	76.40
	Veteran (1)	2309	23.59	23.60
	Missing	7	.07	0
Insurance				
	One	1976	20.19	50.17
	Two	1823	18.62	43.72
	Three	259	2.65	6.11
	Missing	5731	58.55	0
	Total	9789	100.00	100.00
Marital Status				
	Married or Cohabitating (0)	7998	81.70	81.80
Never Married, Separated, Divorced, Widowed (1)		1779	18.17	18.20
	Missing	12	.12	0
	Total	9789	100.00	100.00

Table 4.2 Logistic Regression Predicting Odds of Reporting Wheelchair or Power Scooter Use (N=9789)

	Model 1: Age Only		Model 2: Age and Onset Location		Model 3: Age, Onset Location, and Social Position		Model 4: Age, Onset Location, Social Position, and Veteran Status		Model 5: Age, Onset Location, Social Position, Veteran Status, and Resources	
Dependent Variable	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval
Age at Diagnosis (ref= 50-59)										
18-39	1.36 **	1.09, 1.69	1.25 *	1.00, 1.55	1.22	.98, 1.53	1.23	.99, 1.53	1.20	(.96, 1.50)
40-49	1.11	.97, 1.27	1.11	.97, 1.28	1.12	.97, 1.29	1.12	.98, 1.29	1.13	(.98, 1.30)
60-69	.86 **	.77, .95	.90	.81, 1.01	.90	.81, 1.00	.89 *	.80, 1.00	.74 ***	(.65, .83)
70-79	.57 ***	.49, .67	.60 ***	.51, .70	.61 ***	.52, .71	.60 ***	.51, .70	.45 ***	(.38, .53)
80+	.79	.53, 1.17	.88	.59, 1.32	.90	.60, 1.36	.88	.59, 1.33	.56 **	(.36, .86)
Onset Location (ref=Limb)										
Bulbar			.47 ***	.42, .54	.47 ***	.41, .53	.47 ***	.41, .53	.45 ***	(.39, .51)
Trunk/Global			1.05	.87, 1.28	1.07	.89, 1.30	1.08	.90, 1.31	1.01	(.83, 1.23)
Racial/Ethnic Minority					.90	.68, 1.19	.90 **	.68, 1.19	.85	(.64, 1.14)
Female					1.12 *	1.02, 1.23	1.15 **	1.04, 1.27	1.22 ***	(1.10, 1.35)
College Degree or More					1.18 ***	1.07, 1.29	1.17 ***	1.06, 1.29	1.11 *	(1.01, 1.23)
Civilian							.93	.83, 1.05	1.18 **	(1.04, 1.35)
Number of Types of Insurance (ref= One type)										
Two Types									1.92 ***	(1.63, 2.26)
Three Types									2.90 ***	(2.21, 3.80)
Never Married, Separated, Divorced									.98	(.87, 1.10)
Constant	.43 ***	.39, .46			.41 ***	.37, .46	.43 ***	.37, .50	.29 ***	(.24, .34)

+ p < .10, *p < .05, **p < .01, ***p < .001

Table 4.3 Logistic Regression Predicting Odds of Reporting Non-Invasive Ventilation (N=9789)

	Model 1: Age Only		Model 2: Age and Onset Location		Model 3: Age, Onset Location, and Social Position		Model 4: Age, Onset Location, Social Position and Veteran Status		Model 5: Age, Onset Location, Social Position, Veteran Status, and Resources	
Dependent Variable	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval
Age at Diagnosis (ref= 50-59)										
18-39	.52 ***	(.39, .69)	.58 ***	(.44, .78)	.60 ***	(.45, .79)	.60 ***	(.45, .80)	.58 ***	(.44, .78)
40-49	1.13	(.98, 1.30)	1.15	(1.00, 1.33)	1.12	(.97, 1.30)	1.12	(.97, 1.30)	1.12	(.97, 1.30)
60-69	1.15 *	(1.03, 1.28)	1.11	(.99, 1.24)	1.12 *	(1.00, 1.26)	1.12	(1.00, 1.25)	1.01	(.89, 1.13)
70-79	1.50 ***	(1.31, 1.72)	1.37 ***	(1.19, 1.58)	1.39 ***	(.53, 1.31)	1.37 ***	(1.19, 1.59)	1.18 *	(1.00, 1.38)
80+	.87	(.56, 1.34)	.80	(.51, 1.24)	.83		.82	(.52, 1.28)	.64	(.41, 1.03)
Onset Location (ref=Limb)										
Bulbar			1.51 ***	(1.35, 1.68)	1.55 ***	(1.39, 1.73)	1.56 ***	(1.40, 2.31)	1.54 ***	(1.38, 1.72)
Trunk/Global			3.93 ***	(3.29, 4.70)	3.87 ***	(3.23, 4.63)	3.90 ***	(3.26, 4.67)	3.78 ***	(3.15, 4.54)
Racial/Ethnic Minority					1.80 ***	(1.40, 2.31)	1.80 ***	(1.40, 2.31)	1.76 ***	(1.36, 2.27)
Female					.76 ***	(.69, .83)	.77 ***	(.70, .85)	.80 ***	(.72, .89)
College Degree or More					1.17 **	(1.06, 1.29)	1.17 **	(1.06, 1.28)	1.13 *	(1.02, 1.24)
Veteran							.95	(.84, 1.06)	1.09	(.93, 1.23)
Number of Types of Insurance (ref= One type)										
Two Types									1.49 ***	(1.27, 1.74)
Three Types									1.70 **	(1.19, 2.44)
Never Married, Separated, Divorced									.98	(.87, 1.11)
Constant	.36 ***	(.33, .39)	.31 ***	(.28, .34)	.30 ***	(.27, .34)	.31 ***	(.27, .36)	.25 ***	(.21, .30)

+ p < .10, *p < .05, **p < .01, ***p < .001

Table 4.4 Logistic Regression Predicting Odds of Reporting Invasive Ventilation (N=9789)

	Model 1: Age Only		Model 2: Age and Onset Location		Model 3: Age, Onset Location, and Social Position		Model 4: Age, Onset Location, Social Position, and Veteran Status		Model 5: Age, Onset Location, Social Position, Veteran Status, and Resources	
Dependent Variable	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval
Age at Diagnosis (ref= 50-59)										
18-39	.85	(.38, 1.88)	1.14	(.51, 2.53)	1.23	(.55, 2.75)	1.29	(.58, 2.88)	1.31	(.58, 2.95)
40-49	2.00 ***	(1.37, 2.92)	2.14 ***	(1.46, 3.14)	2.05 ***	(1.39, 3.01)	2.10 ***	(1.43, 3.09)	2.14 ***	(1.44, 3.16)
60-69	.53 **	(.35, .81)	.50 ***	(.33, .76)	.51 **	(.34, .78)	.45 ***	(.30, .70)	.52 **	(.33, .82)
70-79	.10 ***	(.03, .33)	.08 ***	(.03, .26)	.08 ***	(.03, .27)	.07 ***	(.02, .22)	.08 ***	(.02, .27)
80+	.42	(.06, 3.03)	.37	(.05, 2.65)	.39	(.05, 2.83)	.28	(.04, 2.09)	.43	(.05, 3.49)
Onset Location (ref=Limb)										
Bulbar			1.97 ***	(1.33, 2.90)	2.01 ***	(1.36, 2.98)	2.03 ***	(1.37, 3.01)	2.19 ***	(1.47, 3.26)
Trunk/Global			7.56 ***	(4.99, 11.44)	7.59 ***	(4.96, 11.61)	8.34 ***	(5.41, 12.85)	8.46 ***	(5.44, 13.14)
Racial/Ethnic Minority					5.84 ***	(3.67, 9.30)	5.90 ***	(3.70, 9.40)	6.09 ***	(3.76, 9.84)
Female					.53 ***	(.37, .76)	.60 **	(.41, .88)	.49 ***	(.33, .73)
College Degree or More					.95	(.68, 1.34)	.92	(.65, 1.29)	.97	(.68, 1.37)
Civilian							.54 **	(.36, .79)	.45 ***	(.29, .70)
Number of Types of Insurance (ref= One type)										
Two Types									.82	(.49, 1.39)
Three Types									.28	(.06, 1.32)
Never Married, Separated, Divorced									2.22 ***	(1.53, 3.20)
Constant	.02 ***	(.02, .03)	.01 ***	(.01, .02)	.02 ***	(.01, .02)	.02 ***	(.02, .04)	.02 ***	(.01, .04)

+ p < .10, *p < .05, **p < .01, ***p < .001

Table 4.5 Logistic Regression Predicting Odds of Reporting using an Assistive Communication Device (N=9789)

	Model 1: Age Only		Model 2: Age and Onset Location		Model 3: Age, Onset Location, and Social Position		Model 4: Age, Onset Location, Social Position, and Veteran Status		Model 5: Age, Onset Location, Social Position, Veteran Status, and Resources	
Dependent Variable	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval
Age at Diagnosis (ref 50-59)										
18-39	.54 ***	(.37, .78)	.78	(.84, 1.16)	.74	(.50, 1.08)	.76	(.52, 1.11)	.71	(.48, 1.06)
40-49	1.09	(.91, 1.31)	1.10	(.91, 1.34)	1.14	(.94, 1.38)	1.16	(.95, 1.41)	1.17	(.96, 1.42)
60-69	.82 **	(.71, .95)	.65 ***	(.56, .76)	.62 ***	(.53, .73)	.61 ***	(.51, .71)	.52 ***	(.43, .62)
70-79	.69 ***	(.56, .85)	.55 ***	(.44, .68)	.53 ***	(.43, .66)	.51 ***	(.41, .63)	.39 ***	(.31, .50)
80+	1.28	(.80, 2.02)	.87	(.53, 1.42)	.87	(.53, 1.43)	.81	(.49, 1.33)	.57 *	(.33, .98)
Onset Location (ref=Limb)										
Bulbar			6.33 ***	(5.54, 7.23)	6.20 ***	(5.42, 7.09)	6.28 ***	(5.48, 7.18)	6.30 ***	(5.50, 7.23)
Trunk/Global			1.36 *	(1.01, 1.85)	1.49 *	(1.07, 1.98)	1.51 **	(1.11, 2.05)	1.46 *	(1.07, 1.99)
Racial/Ethnic Minority					.56 **	(.36, .88)	.56 **	(.36, .87)	.55 **	(.35, .87)
Female					1.70 ***	(1.50, 1.94)	1.87 ***	(1.62, 2.15)	1.99 ***	(1.72, 2.31)
College Degree or More					1.26 ***	(1.10, 1.44)	1.25 **	(1.09, 1.43)	1.18 *	(1.03, 1.36)
Civilian							.74 ***	(.62, .87)	.86	(.71, 1.04)
Number of Types of Insurance (ref= One type)										
Two Types									2.07 ***	(1.64, 2.63)
Three Types									1.81 *	(1.05, 3.11)
Never Married, Separated, Divorced									1.04	(.88, 1.23)
Constant	.16 ***	(.15, .18)	.10 ***	(.09, .11)	.07 ***	(.06, .08)	.08 ***	(.07, .10)	.06 ***	(.04, .07)

+ p < .10, *p < .05, **p < .01, ***p < .001

Table 4.6 Logistic Regression Predicting Odds of Reporting Participating in a Research Study (N=9789)

	Model 1: Age Only		Model 2: Age and Onset Location		Model 3: Age, Onset Location, and Social Position		Model 4: Age, Onset Location, Social Position, and Veteran Status		Model 5: Age, Onset Location, Social Position, Veteran Status, and Resources	
Dependent Variable	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval
Age at Diagnosis (ref 50-59)										
18-39	1.85 ***	(1.49, 2.30)	1.83 ***	(1.47, 2.28)	1.88 ***	(1.51, 2.35)	1.87 ***	(1.50, 2.34)	1.85 ***	(1.47, 2.33)
40-49	1.37 ***	(1.19, 1.58)	1.36 ***	(1.18, 1.57)	1.34 ***	(1.16, 1.55)	1.34 ***	(1.15, 1.54)	1.35 ***	(1.17, 1.57)
60-69	.77 ***	(.68, .86)	.76 ***	(.67, .85)	.75 ***	(.67, .85)	.76 ***	(.67, .86)	.63 ***	(.55, .72)
70-79	.37 ***	(.31, .45)	.38 ***	(.32, .46)	.40 ***	(.33, .48)	.41 ***	(.33, .49)	.30 ***	(.25, .37)
80+	.13 ***	(.05, .33)	.13 ***	(.05, .32)	.14 ***	(.06, .34)	.15 ***	(.06, .36)	.09 ***	(.04, .23)
Onset Location (ref=Limb)										
Bulbar			1.15 *	(1.02, 1.30)	1.19 **	(1.05, 1.35)	1.19 **	(1.05, 1.35)	1.16 *	(1.02, 1.32)
Trunk/Global			.31 ***	(.23, .43)	.31 ***	(.23, .43)	.31 ***	(.22, .42)	.28 ***	(.20, .39)
Racial/Ethnic Minority					.65 **	(.47, .91)	.65 **	(.47, .91)	.61 **	(.44, .86)
Female					.74 ***	(.67, .82)	.72 ***	(.65, .81)	.79 ***	(.70, .88)
College Degree or More					1.79 ***	(1.60, 2.01)	1.80 ***	(1.61, 2.01)	1.69 ***	(1.51, 1.90)
Civilian							1.11	(.97, 1.26)	1.41 ***	(1.22, 1.63)
Number of Types of Insurance (ref= One type)										
Two Types									1.88 ***	(1.59, 2.23)
Three Types									3.02 ***	(2.13, 4.28)
Never Married, Separated, Divorced									.74 ***	(.64, .86)
Constant	.33 ***	(.30, .36)	.33 ***	(.30, .36)	.25 ***	(.22, .28)	.23 ***	(.20, .27)	.16 ***	(.13, .19)

+ p < .10, *p < .05, **p < .01, ***p < .001

Table 4.7 Logistic Regression Predicting Odds of Reporting Genetic Testing (N=9789)

	Model 1: Age Only		Model 2: Age and Onset Location		Model 3: Age, Onset Location, and Social Position		Model 4: Age, Onset Location, Social Position, and Veteran Status		Model 5: Age, Onset Location, Social Position, Veteran Status, and Resources	
Dependent Variable	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval
Age at Diagnosis (ref 50-59)										
18-39	2.05 ***	(1.63, 2.58)	1.99 ***	(1.58, 2.51)	2.12 ***	(1.67, 2.67)	2.12 ***	(1.68, 2.68)	2.17 ***	(1.71, 2.74)
40-49	1.47 ***	(1.25, 1.72)	1.47 ***	(1.25, 1.72)	1.45 ***	(1.24, 1.71)	1.46 ***	(1.24, 1.72)	1.49 ***	(1.26, 1.76)
60-69	.85 **	(.74, .97)	.86 *	(.75, 1.72)	.87 *	(.78, .99)	.86 *	(.75, .99)	.89	(.77, 1.03)
70-79	.50 ***	(.41, .61)	.51 ***	(.42, .62)	.51 ***	(.42, .62)	.51 ***	(.42, .62)	.53 ***	(.43, .66)
80+	.50 **	(.28, .87)	.51 *	(.29, .90)	.53 *	(.30, .94)	.53 *	(.30, .93)	.64	(.34, 1.19)
Onset Location (ref=Limb)										
Bulbar			.85 *	(.75, .98)	.89	(.78, 1.02)	.89	(.78, 1.02)	.90	(.78, 1.03)
Trunk/Global			.79	(.60, 1.02)	.76 *	(.58, .99)	.77 *	(.59, 1.00)	.79	(.60, 1.04)
Racial/Ethnic Minority					.67 *	(.46, .97)	.67 *	(.46, .97)	.71	(.49, 1.01)
Female					.63 ***	(.56, .70)	.63 **	(.56, .71)	.66 ***	(.58, .74)
College Degree or More					1.15 **	(1.03, 1.29)	1.15 *	(1.03, 1.29)	1.13 *	(1.00, 1.27)
Civilian							.96	(.84, 1.10)	.88	(.75, 1.03)
Number of Types of Insurance (ref= One type)										
Two Types									.98	(.79, 1.22)
Three Types									.57 *	(.34, .97)
										(.63, .85)
Never Married, Separated, Divorced									.73 ***	
Constant	.27 ***	(.24, .29)	.28 ***	(.26, .31)	.30 ***	(.26, .34)	.31 ***	(.26, .36)	.35 ***	(.29, .43)

+ p < .10, *p < .05, **p < .01, ***p < .001

Table 4.8 Logistic Regression Predicting Odds of Reporting Having Advanced Directives (N=9789)

	Model 1: Age Only		Model 2: Age and Onset Location		Model 3: Age, Onset Location, and Social Position		Model 4: Age, Onset Location, Social Position, and Veteran Status		Model 5: Age, Onset Location, Social Position, Veteran Status, and Resources	
Dependent Variable	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval
Age at Diagnosis (ref 50-59)										
18-39	.42 ***	(.34, .53)	.44 ***	(.36, .55)	.45 ***	(.36, .55)	.45 ***	(.36, .56)	.43 ***	(.34, .54)
40-49	.65 ***	(.57, .74)	.66 ***	(.58, .75)	.65 ***	(.57, .74)	.65 ***	(.57, .75)	.64 ***	(.56, .74)
60-69	2.15 ***	(1.93, 2.40)	2.13 ***	(1.91, 2.38)	2.18 ***	(1.95, 2.43)	2.14 ***	(1.91, 2.39)	1.83 ***	(1.61, 2.08)
70-79	4.05 ***	(3.41, 4.81)	3.92 ***	(3.30, 4.66)	4.25 ***	(3.58, 4.07)	4.09 ***	(3.43, 4.89)	3.25 ***	(2.68, 3.94)
80+	83.53***	(11.66, 598.25)	82.41***	(11.50, 590.3)	97.56***	(13.60, 699.84)	93.97 ***	(13.10, 674, 40)	61.18 ***	(8.43, 444.05)
Onset Location (ref=Limb)										
Bulbar			1.11	(.99, 1.25)	1.16 **	(1.03, 1.30)	1.17 **	(1.04, 1.31)	1.14 *	(1.01, 1.29)
Trunk/Global			2.15 ***	(1.70, 2.72)	2.20 ***	(1.73, 2.81)	2.25 ***	(1.77, 2.87)	2.13 *	(1.68, 2.73)
Racial/Ethnic Minority					.41 ***	(.31, .53)	.41 ***	(.31, .53)	.37 ***	(.29, .49)
Female					.69 ***	(.63, .76)	.73 ***	(.66, .80)	.75 ***	(.68, .83)
College Degree or More					1.64 ***	(1.49, 1.80)	1.62 ***	(1.48, 1.79)	1.57 ***	(1.42, 1.73)
Civilian							.83 **	(.73, .95)	1.04	(.91, 1.20)
Number of Types of Insurance (ref= One type)										
Two Types									1.83 ***	(1.52, 2.22)
Three Types									2.73 ***	(1.62, 4.60)
Never Married, Separated, Divorced									1.10	(.97, 1.25)
Constant	1.60 ***	(1.48, 1.72)	1.51 ***	(1.39, 1.63)	1.64 ***		1.48 ***	(1.28, 1.71)	1.01	(.84, 1.22)

+ p < .10, *p < .05, **p < .01, ***p < .001

Table 4.9 Logistic Regression Predicting Odds of Reporting Hospice Care (N=9789)

	Model 1: Age Only		Model 2: Age and Onset Location		Model 3: Age, Onset Location, and Social Position		Model 4: Age, Onset Location, Social Position, and Veteran Status		Model 5: Age, Onset Location, Social Position, Veteran Status, and Resources	
Dependent Variable	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval	Odds Ratio	Confidence Interval
Age at Diagnosis (ref= 50-59)										
18-39	1.42	(.79, 2.54)	1.51	(.84, 2.72)	1.51	(.84, 2.72)	1.47	(.82, 2.65)	1.47	(.81, 2.66)
40-49	1.07	(.71, 1.62)	1.08	(.72, 1.63)	1.07	(.71, 1.62)	1.05	(.69, 1.59)	1.02	(.67, 1.55)
60-69	2.55***	(1.93, 3.38)	2.49***	(1.89, 3.30)	2.50***	(1.89, 3.31)	2.63***	(1.98, 3.48)	2.88***	(2.10, 3.96)
70-79	2.82***	(1.63, 3.19)	2.17***	(1.55, 3.05)	2.19***	(1.56, 3.07)	2.40***	(1.70, 3.38)	2.83***	(1.86, 4.30)
80+	5.34***	(2.97, 9.61)	5.09***	(2.82, 9.17)	5.18***	(2.87, 9.35)	5.92***	(3.26, 10.77)	7.21***	(3.35, 15.51)
Onset Location (ref=Limb)										
Bulbar			1.32 *	(1.04, 1.66)	1.31 *	(1.04, 1.66)	1.29 *	(1.02, 1.64)	1.29 *	(1.02, 1.64)
Trunk/Global			1.70 **	(1.18, 2.44)	1.71 **	(1.19, 2.45)	1.62 **	(1.13, 2.34)	1.65 **	(1.13, 2.40)
Racial/Ethnic Minority					1.30	(.73, 2.30)	1.32	(.75, 2.34)	1.26	(.71, 2.26)
Female					1.01	(.82, 1.24)	.87	(.69, 1.09)	.70 **	(.55, .89)
College Degree or More					1.07	(.86, 1.32)	1.08	(.87, 1.33)	1.17	(.94, 1.45)
Civilian							1.53***	(1.16, 2.01)	1.33	(.94, 1.87)
Number of Types of Insurance (ref= One type)										
Two Types									.75	(.40, 1.43)
Three Types									.38	(.10, 1.38)
Never Married, Separated, Divorced									2.41***	(1.92, 3.02)
Constant	.02***	(.02, .03)			.02***	(.02, .03)	.02***	.01, .02	.02***	(.01, .03)

+ p < .10, *p < .05, **p < .01, ***p < .001

Table 4.10 Multinomial Logistic Regression Predicting Odds of Riluzole Use (n = 9789)

Base Outcome = Currently Use Riluzole

	Model 1: Age Only				Model 2: Age and Onset Location				Model 3: Age, Onset Location, and Social Position				Model 4: Age, Onset Location, Social Position, and Veteran Status				Model 5: Age, Onset Location, Social Position, Veteran Status, and Resources			
	Never Used		Discontinued		Never Used		Discontinued		Never Used		Discontinued		Never Used		Discontinued		Never Used		Discontinued	
Age at Diagnosis (ref 50-59)	OR	CI	OR	CI	OR	CI	OR	CI	OR	CI	OR	CI	OR	CI	OR	CI	OR	CI	OR	CI
18-39	.83	(.66, 1.05)	1.01	(.75, 1.36)	.88	(.69, 1.10)	.98	(.73, 1.32)	.83	(.65, 1.05)	.94	(.70, 1.27)	.81	(.64, 1.03)	.93	(.69, 1.25)	.81	(.64, 1.02)	.93	(.69, 1.26)
40-49	.99	(.86, 1.14)	.85	(.69, 1.03)	1.00	(.87, 1.15)	.85	(.69, 1.03)	1.03	(.90, 1.19)	.86	(.70, 1.05)	1.02	(.88, 1.17)	.85	(.70, 1.04)	1.00	(.87, 1.16)	.86	(.70, 1.05)
60-69	1.06	(.95, 1.18)	.87 ***	(.49, .67)	1.05	(.94, 1.17)	.89 ***	(.50, .69)	1.03	(.93, 1.15)	.58 ***	(.50, .69)	1.07	(.96, 1.19)	.60 ***	(.51, .70)	1.09	(.97, 1.22)	.60 ***	(.51, .72)
70-79	1.05	(.91, 1.21)	.62 ***	(.50, .77)	1.01	(.88, 1.16)	.62 ***	(.50, .77)	.99	(.86, 1.14)	.64 ***	(.51, .79)	1.06	(.92, 1.22)	.68 ***	(.54, .83)	1.10	(.93, 1.30)	.68 ***	(.54, .86)
80+	2.20 ***	(1.53, 3.18)	.34 *	(.13, .85)	2.17 ***	(1.50, 3.12)	.36 *	(1.62, 2.36)	2.01 ***	(1.39, 2.92)	.37 *	(.15, .95)	2.23 ***	(1.54, 3.25)	.40 *	(.16, 1.01)	2.41 ***	(1.62, 3.58)	.44	(.17, 1.12)
Onset Location (ref=Limb)																				
Bulbar					1.10	(.99, 1.23)	.64 ***	(.53, .78)	1.06	(.96, 1.18)	.62	(.52, .75)	1.05	(.94, 1.17)	.62 ***	(.51. .75)	1.06	(.95, 1.18)	.62 ***	(.51, .75)
Trunk/Global					1.96 ***	(1.62, 2.36)	1.80 ***	(1.37, 2.35)	2.05 ***	(1.69, 2.48)	1.88 ***	(1.44, 2.47)	1.97 ***	(1.63, 2.39)	1.84 ***	(1.40, 2.41)	1.98 ***	(1.63, 2.40)	1.89 ***	(1.43, 2.48)
Racial/Ethnic Minority									.52 ***	(.39, .69)	1.02	(.71, 1.47)	.52 ***	(.39, .69)	1.02	(.71, 1.47)	.51 ***	(.38, .68)	1.05	(.73, 1.52)
Female									1.51 ***	(1.38, 1.65)	1.40 ***	(1.22, 1.61)	1.36 ***	(1.23, 1.50)	1.32 ***	(1.14, 1.52)	1.28 ***	(1.16, 1.41)	1.33 ***	(1.15, 1.54)
College Degree or More									.76 ***	(.70, .84)	1.30 ***	(1.12, 1.51)	.77 ***	(.71, .85)	1.31 ***	(1.13, 1.52)	.79 ***	(.72, .86)	1.29 ***	(1.11, 1.50)
Civilian													1.39 ***	(1.24, 1.56)	1.22 *	(1.02, 1.45)	1.33 ***	(1.16, 1.52)	1.16	(.96, 1.41)
Number of Types of Insurance (ref= One type)																				
Two Types																	1.00	(.85, 1.19)	1.01	(.80, 1.29)
Three Types																	.71	(.50, 1.01)	.76	(.48, 1.19)
Never Married, Separated, Divorced																	1.38 ***	(1.24, 1.55)	.87	(.72, 1.05)
Constant	.72 ***	(.68, .78)	.30 ***	(.27, .33)	.67 ***	(.63, .75)	.31 ***	(.28, .35)	.71 ***	(.64, .79)	.23 ***	(.19, .27)	.56 ***	(.49, .65)	.20 ***	(.16, .24)	.56 ***	(.47, .66)	.21 ***	(.16, .27)

+ p < .10, *p < .05, **p < .01, ***p < .001

Table 4.11 Multinomial Logistic Regression Predicting Odds of Attending a Multidisciplinary Clinic (n = 9789)

Base Outcome = Currently Attend a Multidisciplinary Clinic

	Model 1: Age Only				Model 2: Age and Onset Location				Model 3: Age, Onset Location, and Social Position				Model 4: Age, Onset Location, Social Position, and Veteran Status				Model 5: Age, Onset Location, Social Position, Veteran Status, and Resources			
	Never Attended		Discontinued		Never Attended		Discontinued		Never Attended		Discontinued		Never Attended		Discontinued		Never Attended		Discontinued	
	OR	CI	OR	CI	OR	CI	OR	CI	OR	CI	OR	CI	OR	CI	OR	CI	OR	CI	OR	CI
Age at Diagnosis (ref 50-59)																				
18-39	.95	(.74, 1.22)	1.48	(.95, 2.30)	.94	(.73, 1.21)	1.46	(.94, 2.28)	.93	(.72, 1.20)	1.48	(.95, 2.30)	.95	(.73, 1.22)	1.47	(.94, 2.29)	.99	(.77, 1.28)	1.44	(.92, 2.26)
40-49	1.00	(.86, 1.16)	.81	(.58, 1.14)	1.00	(.86, 1.16)	.81	(.57, 1.13)	1.00	(.85, 1.16)	.80	(.57, 1.13)	1.01	(.87, 1.18)	.80	(.57, 1.12)	1.01	(.87, 1.18)	.77	(.54, 1.08)
60-69	.96	(.86, 1.08)	1.05	(.83, 1.34)	.97	(.86, 1.09)	1.05	(.83, 1.34)	.97	(.86, 1.09)	1.06	(.83, 1.34)	.94	(.84, 1.06)	1.06	(.83, 1.36)	1.15 *	(1.02, 1.32)	.99	(.76, 1.28)
70-79	1.21 **	(1.04, 1.40)	1.02	(.74, 1.40)	1.21 **	(1.04, 1.40)	1.03	(.74, 1.42)	1.16	(1.00, 1.34)	1.02	(.74, 1.41)	1.09	(.94, 1.27)	1.04	(.75, 1.44)	1.51 ***	(1.28, 1.78)	.97	(.68, 1.39)
80+	1.42	(.96, 2.09)	2.11 *	(1.07, 4.13)	1.44	(.98, 2.13)	2.11 *	(1.07, 4.14)	1.31	(.89, 1.94)	2.08 *	(1.05, 4.08)	1.21	(.82, 1.79)	2.12 *	(1.07, 4.20)	2.12 ***	(1.38, 3.25)	1.79	(.87, 3.68)
Onset Location (ref=Limb)																				
Bulbar					.90	(.80, 1.02)	1.01	(.80, 1.29)	.88 *	(.78, 1.00)	1.02	(.80, 1.29)	.89	(.79, 1.01)	1.01	(.80, 1.29)	.91	(.81, 1.03)	1.01	(.79, 1.29)
Trunk/Global					1.13	(.93, 1.38)	.65	(.39, 1.08)	1.13	(.94, 1.39)	.64	(.38, 1.07)	1.18	(.96, 1.43)	.63	(.38, 1.06)	1.29 *	(1.06, 1.60)	.59 *	(.35, 1.00)
Racial/Ethnic Minority									1.66 ***	(1.28, 2.17)	1.15	(.62, 2.12)	1.67 ***	(1.28, 2.17)	1.15	(.62, 2.12)	1.81 ***	(1.38, 2.37)	1.06	(.57, 1.96)
Female									1.20 ***	(1.09, 1.33)	.95	(.77, 1.17)	1.32 ***	(1.19, 1.47)	.93	(.75, 1.16)	1.24 ***	(1.11, 1.39)	.79 *	(.63, .99)
College Degree or More									.63 ***	(.57, .69)	.90	(.73, 1.10)	.62 ***	(.56, .68)	.90	(.73, 1.11)	.65 ***	(.50, .66)	.93	(.75, 1.14)
Civilian													.78 ***	(.67, .86)	1.08	(.83, 1.39)	.57 ***	(.38, .56)	1.12	(.83, 1.52)
Number of Types of Insurance (ref= One type)																				
Two Types																	.46 ***	(.38, .56)	1.55 *	(1.07, 2.23)
Three Types																	.30 ***	(.22, .40)	.80	(.32, 1.98)
Never Married, Separated, Divorced																	.99	(.67, .97)	2.35 ***	(1.88, 2.93)
Constant	.34 ***	(.31, .37)	.06 ***	(.05, .07)	.34 ***	(.31, .38)	.06 ***	(.05, .08)	.43 ***	(.57, .69)	.07 ***	(.05, .09)	.51 ***	(.45, .60)	.06 ***	(.05, .09)	.81 *	(.67, .97)	.05 ***	.03, .07

+ p < .10, *p < .05, **p < .01, ***p < .001

Figure 4.1 Predicted Probability of Wheelchair/Scooter Use by Age at Diagnosis

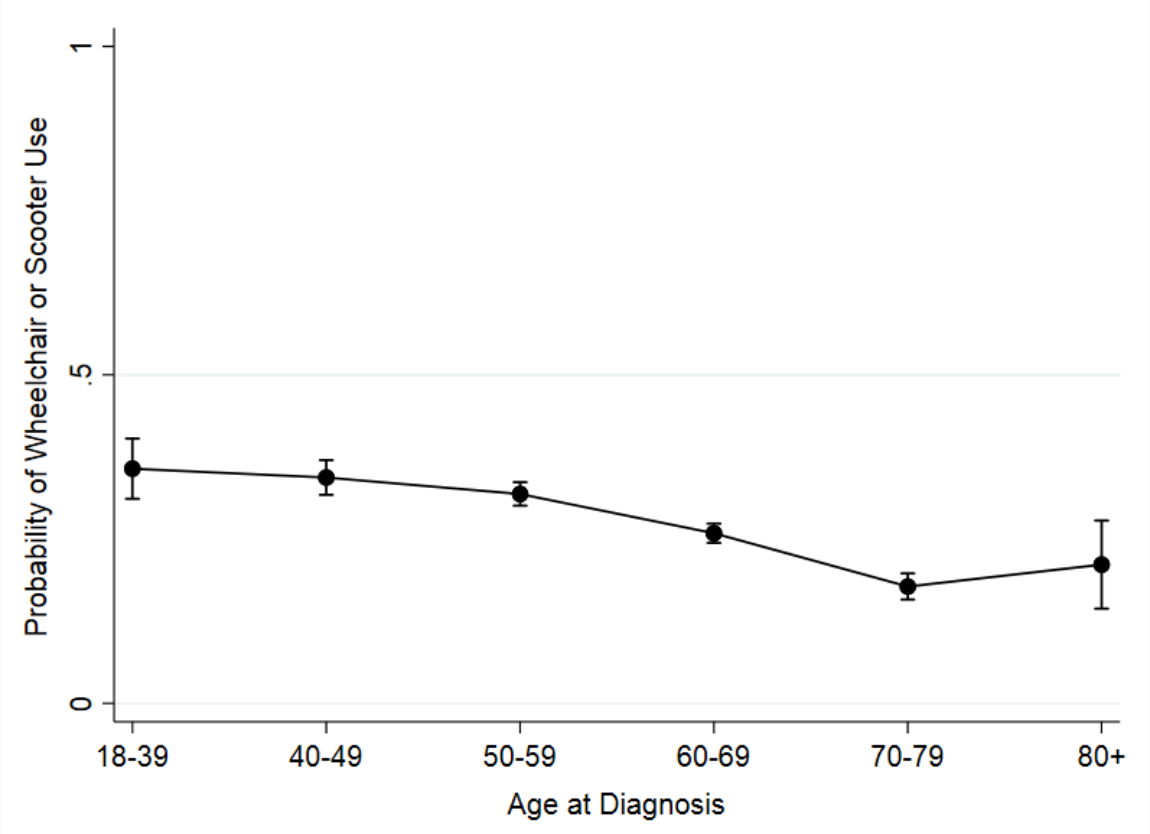


Figure 4.2 Predicted Probability of Invasive Ventilation by Age at Diagnosis

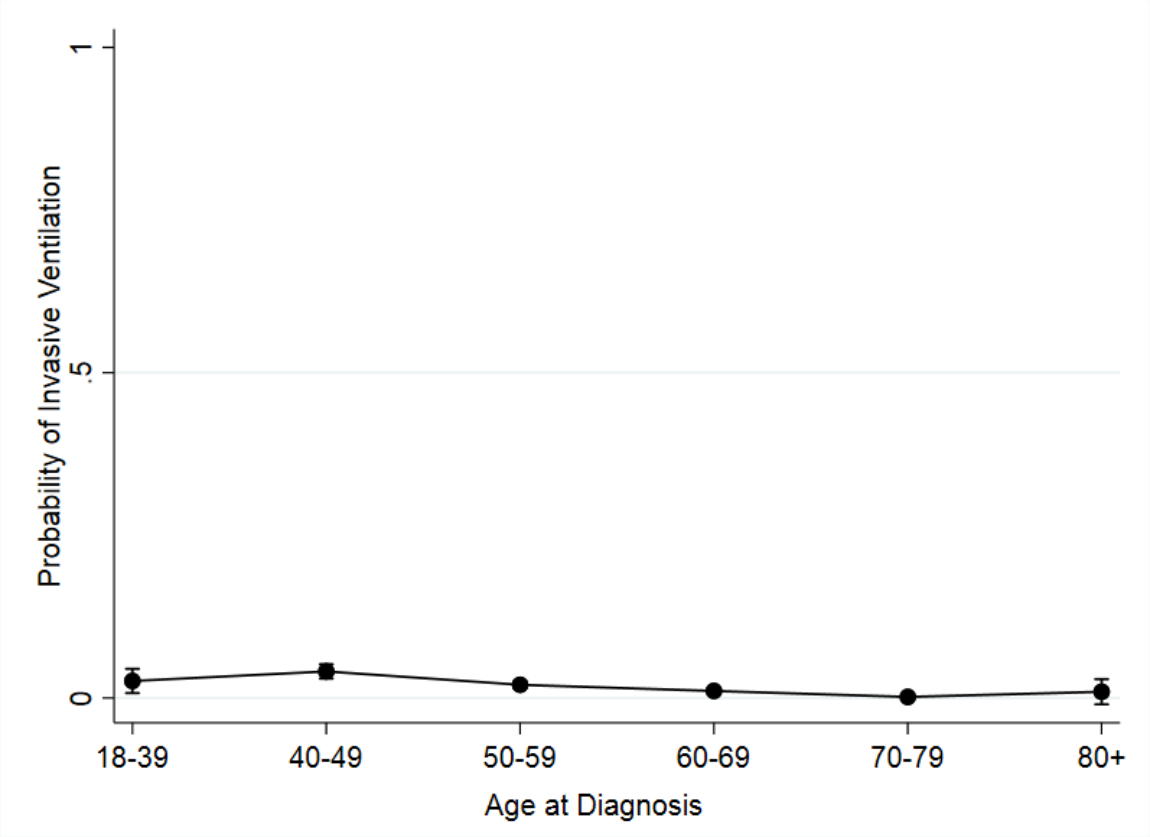


Figure 4.3 Predicted Probability of Assistive Communication Device Use by Age at Diagnosis

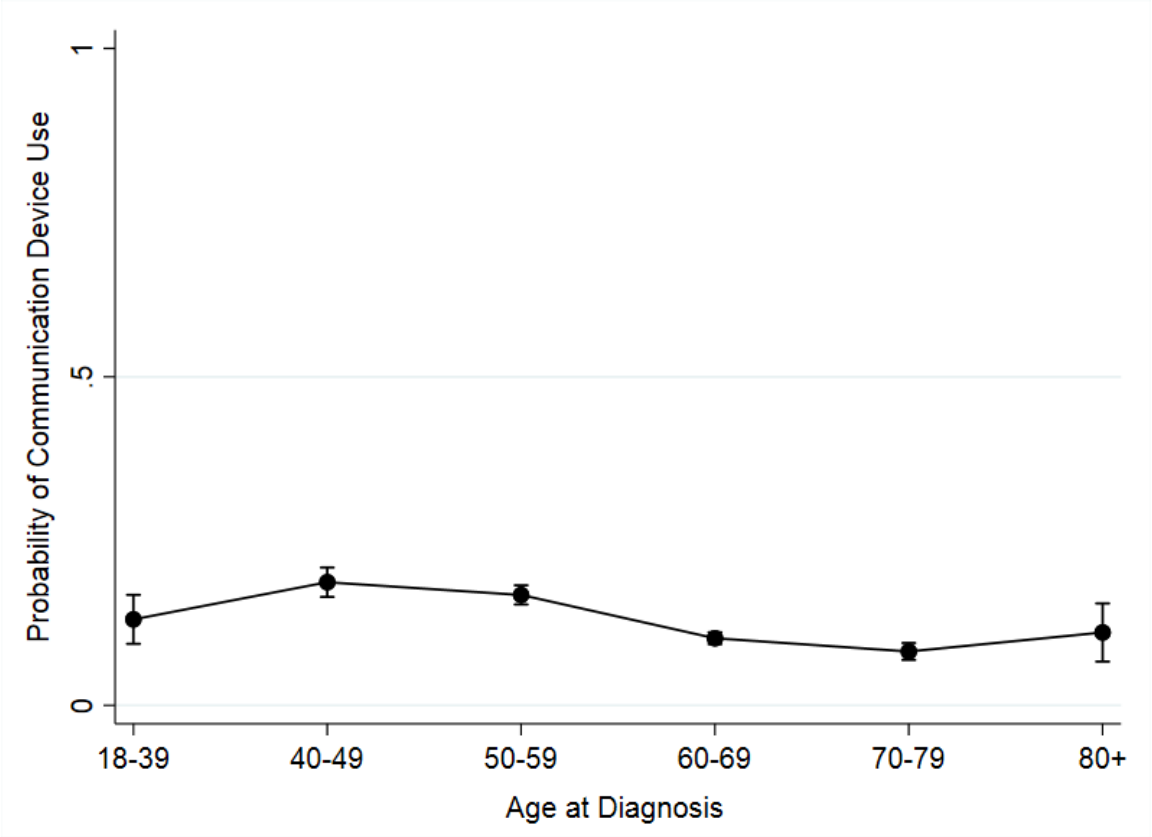


Figure 4.4 Predicted Probability of Participating in a Research Study by Age at Diagnosis

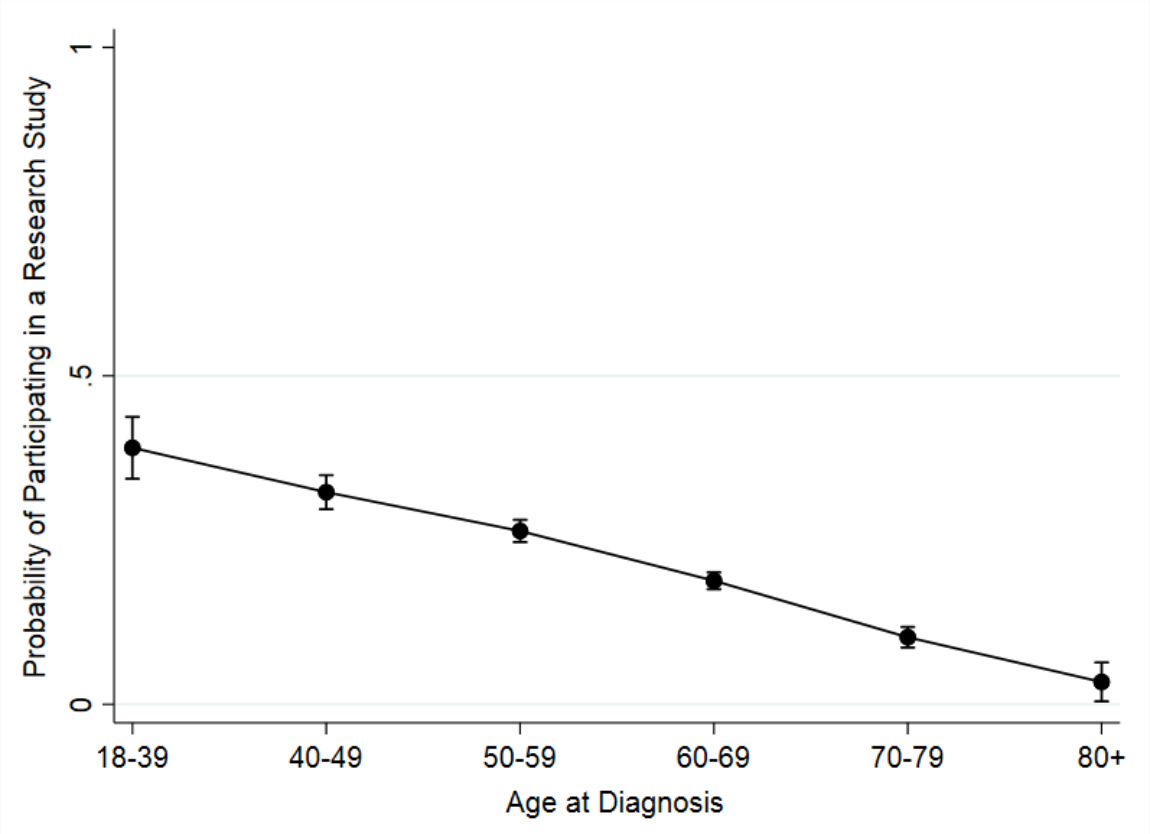


Figure 4.5 Predicted Probability of Genetic Testing by Age at Diagnosis

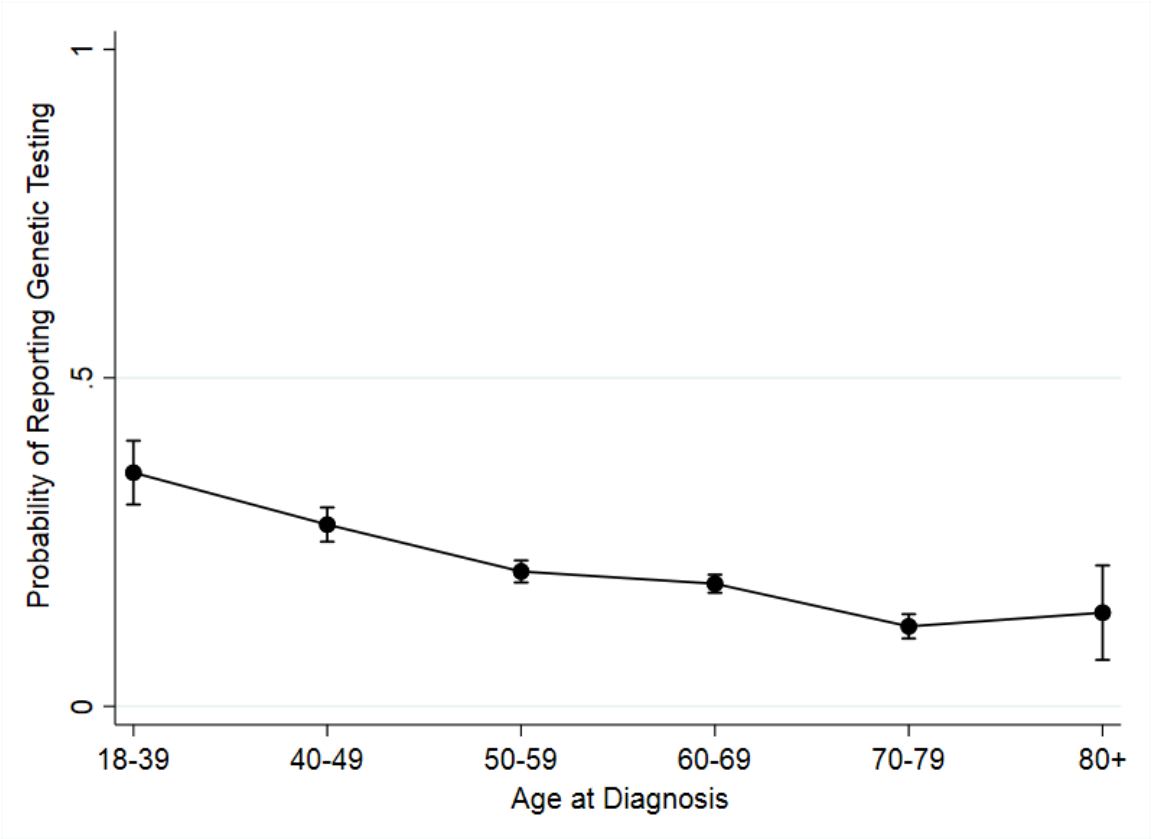


Figure 4.6 Predicted Probability of Completing Advanced Directives by Age at Diagnosis

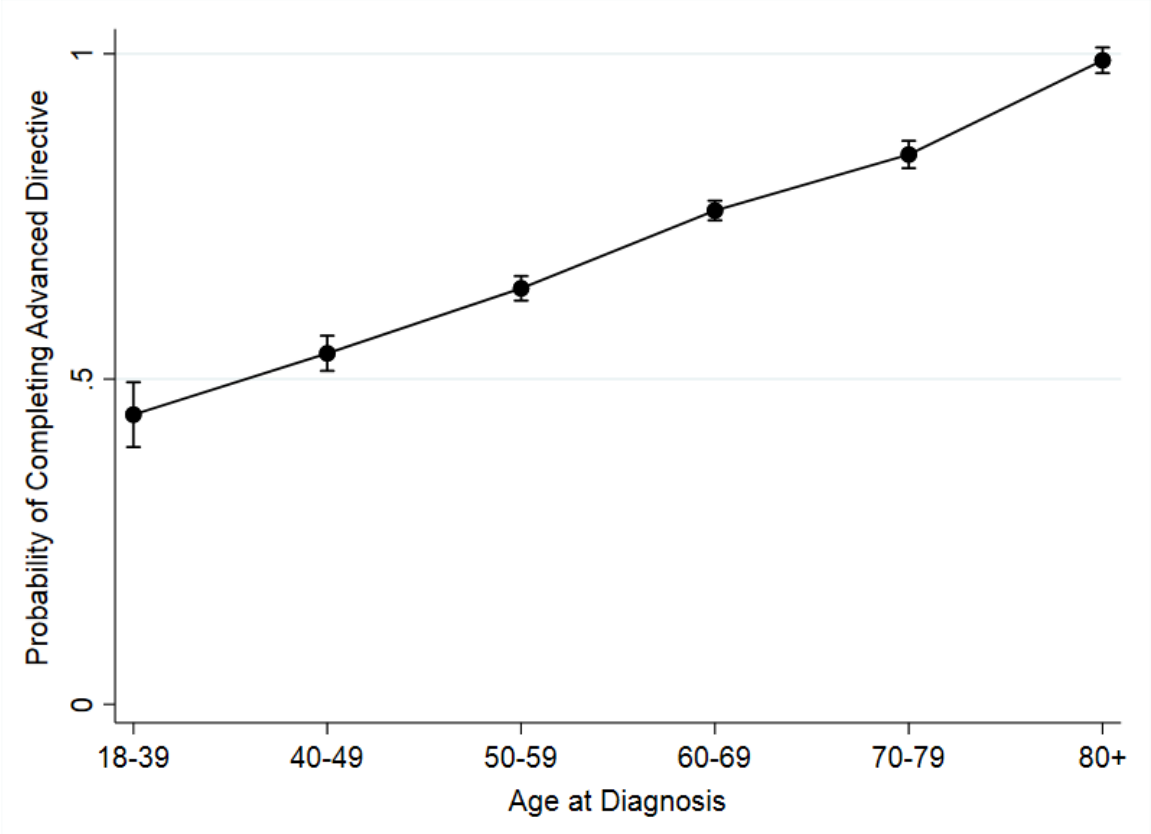


Figure 4.7 Predicted Probability of Invasive Ventilation by Marital Status

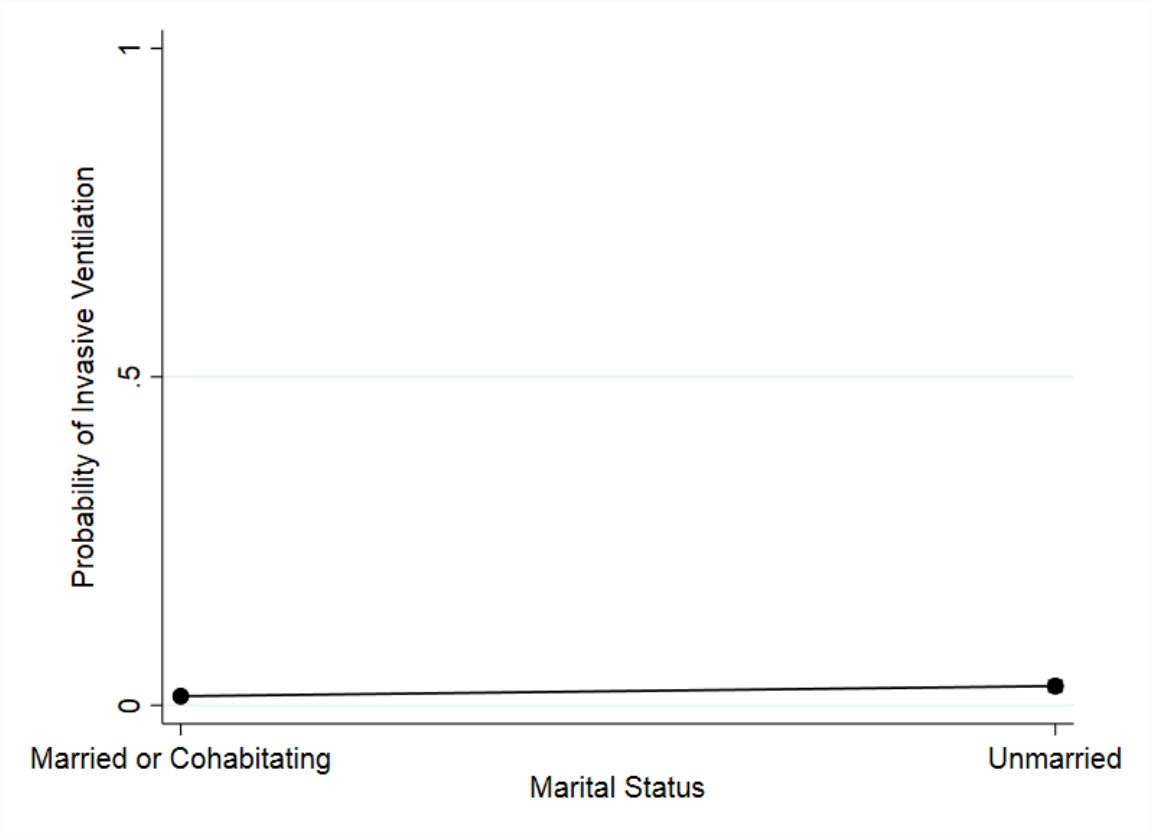


Figure 4.8 Predicted Probability of Enrolling in Hospice by Marital Status

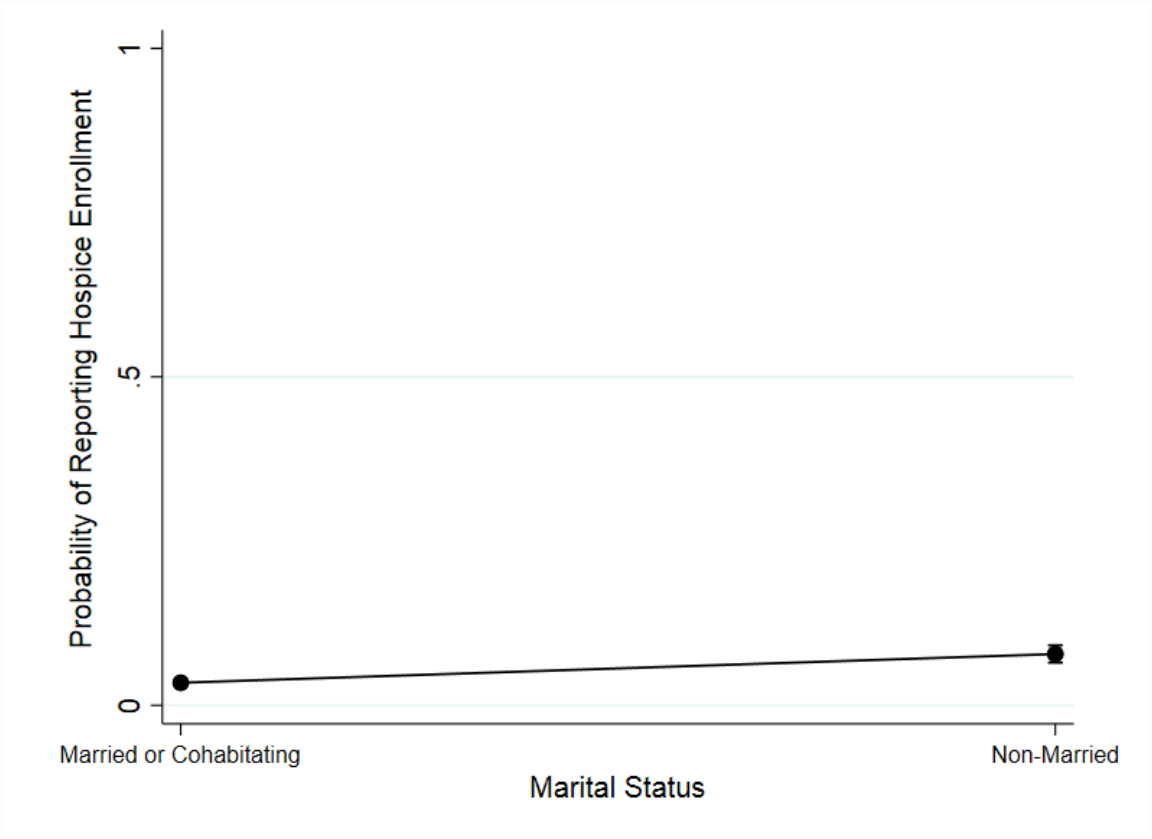


Figure 4.9 Predicted Probability of Invasive Ventilation by Race/Ethnicity

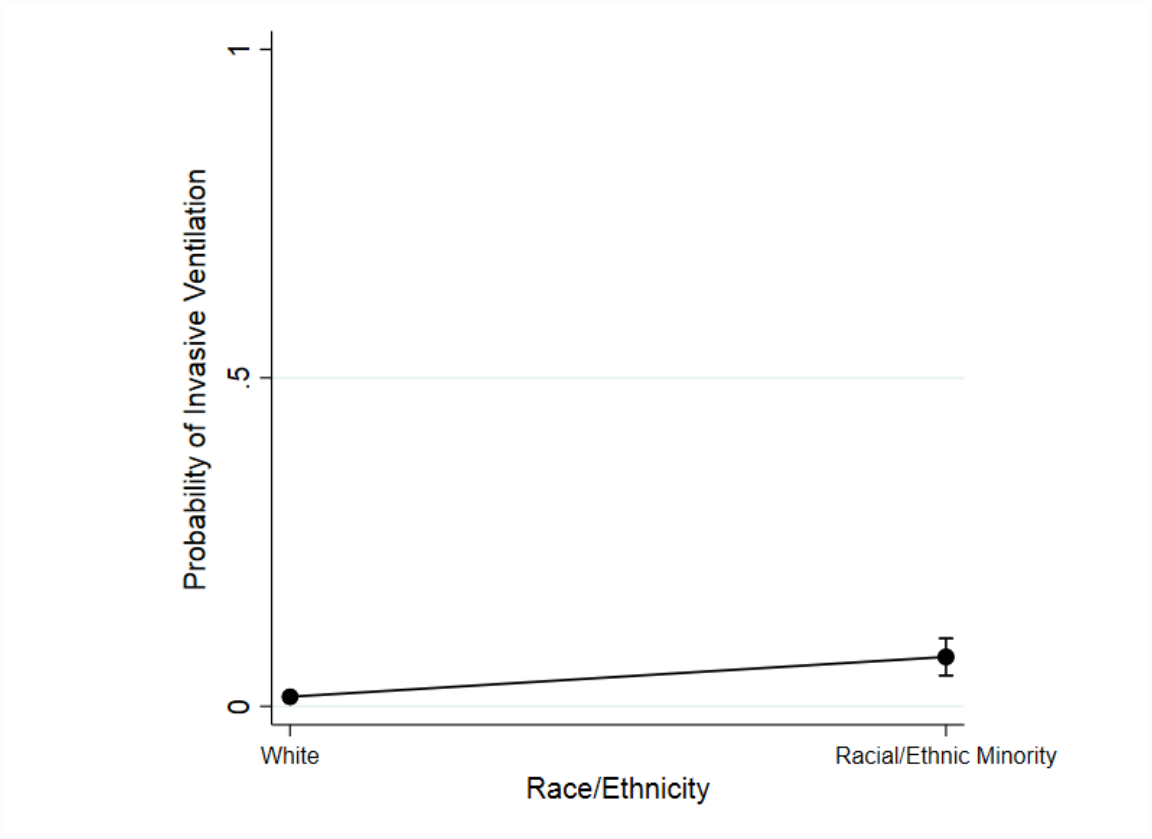


Figure 4.10 Predicted Probability of Participating in a Research Study by Race/Ethnicity

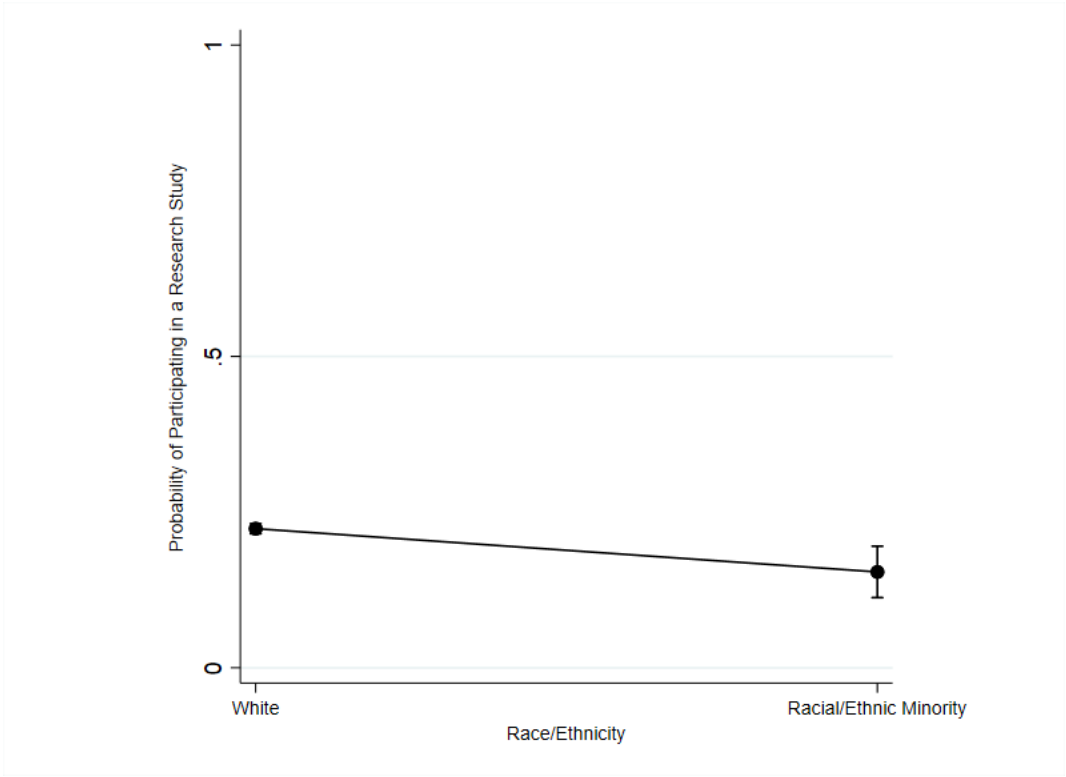


Figure 4.11 Predicted Probability of Participating in a Research Study by Gender

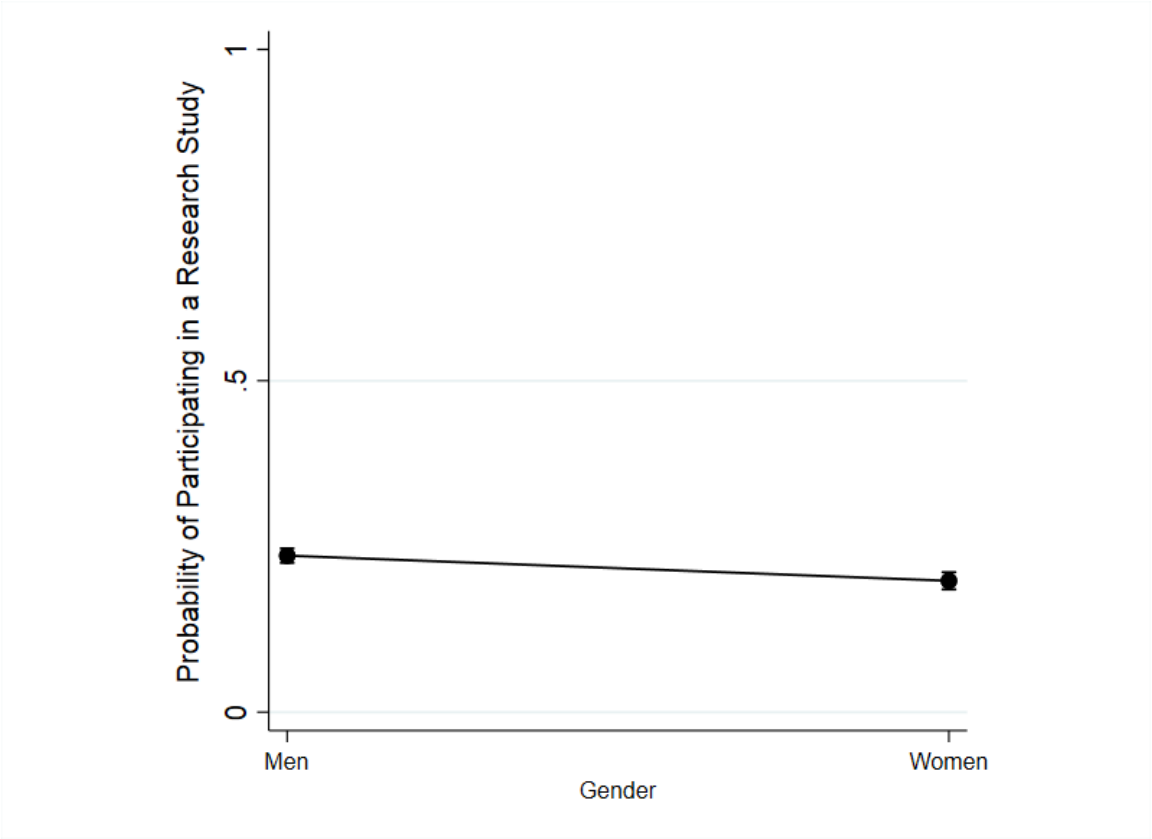
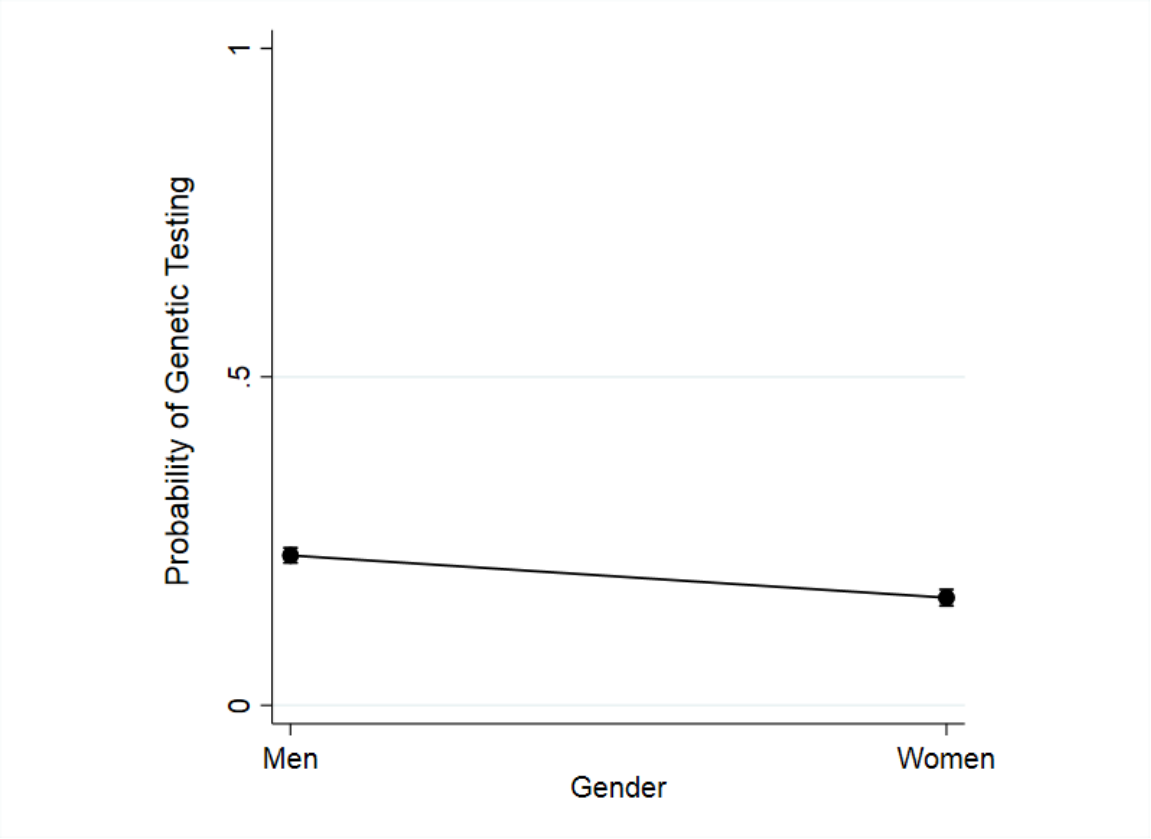


Figure 4.12 Predicted Probability of Genetic Testing by Gender



CHAPTER FIVE: SUMMARY OF RESULTS, CONCLUSION, AND FUTURE WORK

Summary of Results and Conclusion

For the dissertation, I looked at how social position and position in the life course shapes the experience of ALS. Currently, ALS is not well understood by either the biological or the social sciences. Although research to understand the biological basis of ALS is well underway, less social science research has focused on the experience of ALS. There is a need, however, to explore how sociological perspectives can advance knowledge even of diseases that are little understood, rare, and deadly. In the case of ALS, the results of the dissertation show how a sociological perspective and sociological theories (e.g. fundamental cause, life course) help develop a better understanding of the disease process and experience of the disease by pALS, albeit with some adjustment. Further, the findings presented here illustrate the need for a sociology of disease, in order to better understand how the social world affects the experience of a particular disease, rather than the general overview provided by the sociology of health and illness.

Overall, the dissertation shows that social position and position in the life course are relevant to both the disease process and the lived experiences of pALS. The results are useful to rethink the enrollment process for potential clinical trials and to understand a potential reason why trials fail, and to begin improving access and communication of ALS treatments to prevent health disparities among pALS. The dissertation further contributes to the efforts to improve the quality of life for people with ALS. Finally, the results from these studies supplies a potential opening for sociologists, epidemiologists, biomedical researchers, and medical providers to engage in conversation across

disciplines in developing new ways to understand ALS as a disease process and as a lived experience.

The second chapter of the dissertation explored how social position shaped the reported onset location at the time of an ALS diagnosis. Although there are still many unanswered questions regarding who will eventually develop ALS, I use sociological theories to understand the social dimensions of a disease that is often conceptualized as purely biological. The results show that social position does shape the onset location of ALS symptoms and that the mechanisms behind the onset of ALS are more complicated than just accounting for exposures to proximate risk factors and biological differences. Several potential explanations exist for these findings. Social position and position in the life course could influence the perception of symptoms of ALS and where they begin. Moreover, social position could be the trigger for a gene by environment interaction which influences the biological development of symptoms and where they begin. Finally, social position has been shown in previous work to influence access to healthcare resources, allowing the symptoms to spread throughout the body before a diagnosis can be made.

The goal of a sociology of disease in the case of ALS is to take the themes and theories from the sociology of health and illness and focus attention on specific health outcomes such as onset location. The goal of chapter two is not to point out collective risk factors but to account for the multiple pathways in which the experience of the social world may influence ALS onset location directly (Pescosolido, 2006; Timmermans and Haas, 2008). For example, the onset location of ALS is determined through diagnostic testing to determine the involvement of the nerves. The unrelenting progression that is

characteristic of ALS, however, may mean that pALS who go through diagnostic testing later in the disease course (e.g. due to the dismissal of symptoms as a sign of aging or of a hard life) appear to have greater involvement of the nerves, leading to a distorted clinical picture. A sociology of disease allows sociologists to think about how clinical endpoints may appear to differ due to social stratification, such as race/ethnicity, gender, and social class.

The third chapter examined how social position shapes the experience of symptoms of ALS. Overall, the results show the importance of social position in understanding symptom development and progression of ALS. Even though proximate risks are often the sole factor considered in biomedical research on ALS symptom development and disease progression, the results show education, gender, and age all have a role over and above the proximate risks included in the models. As sociologists have documented in earlier studies, many diseases consist of more than just exposure to proximate risks, and ALS has many of the same tendencies. Moreover, the use of fundamental cause theory, life course theory, and the social determinants of health help to highlight where differences occur, although refinements are needed to use theories in the sociology of health and illness in a disease to understand disparities. For example, guided by fundamental cause theory, one would expect that those in less advantaged social positions (e.g. minorities, women, lower levels of education) will report more time between the development of ALS symptoms than their more advantaged peers. Results indicate, however, that pALS with limited resources often have less time between symptom onset and diagnosis than their more advantaged peers. Rather than an indicator of greater access to resources, a diagnosis closer to the reported appearance of symptoms

may be a sign of having less opportunity and resources to acknowledge the signs of a disease that may at first seem to be a minor complaint. In the case of ALS, it may not be that fundamental cause theory is not supported, but that sociologists need to adjust the way they think about applying the theory. The results from this work reaffirms the need for a sociology of disease, as dealing with a disease just prior to and after diagnosis is different from understanding how disease can be prevented altogether.

Chapter four tested how position in the life course and social position has shaped medical care decisions reported by people with ALS. Disparities in medical and supportive care for pALS are clear in the National ALS Registry data, both by the timing in the life course of diagnosis and by social position. Although the disparities by age at diagnosis may be explained by the acceptance or refusal of death as the next stage of life, disparities by social position are much more difficult to explain.

Medical care is shaped by social position, as suggested by fundamental cause theory. Fundamental cause theory does highlight the differences in medical and supportive care, however, some of the findings actually run counter to the theories' predictions. Therefore, although fundamental cause theory works fairly well in the case of a specific disease, sociological theories created for the more general social experiences (e.g. who will get a disease and who will not) may need to be adjusted to reflect the differences in experiencing specific diseases. Further, adjustment of current theories in the sociology of health and illness allow for their use in exploring the connection between the social world and the experience and care for those diagnosed with the specific disease in question (Pescosolido, 2006; Link, 2008; Timmermans and Haas, 2008). Moreover, the

results from this work again reaffirm the need for a sociology of disease, as dealing with the care needs for a specific disease, such as ALS, is different from many other diseases.

Theories such as fundamental cause are often focused on the final outcomes of disease (e.g. mortality) and the influence of social factors (e.g. socioeconomic status) on those outcomes (Phelen et al., 2004). The focus on potential outcomes, such as the development of disease or the risk of death from a disease, is a weakness of the sociology of health and illness. Given the focus on the larger picture of outcomes, it is understandable why sociologists often do not focus on diseases such as ALS with no known cause or cure. Although ALS is universally fatal for those who are diagnosed, the results presented in the dissertation demonstrate the lived experience of ALS (and perhaps the disease itself) is influenced by the social position.

Given these findings, approaching ALS from a sociology of health and illness perspective misses important connections between social position and the experience of the disease itself. Therefore, the findings of the dissertation allow me to strongly echo Timmermans and Haas' (2008) call for a 'sociology of disease,' in which sociologists explore the connection between the social world and disease. As a medical sociologist who often focuses on one disease (e.g. ALS) and on clinical endpoints (e.g. onset location, symptom development, medical and supportive care), the further development of a sociology of disease allows for a better understanding of multiple pathways in which the experience of the social world may influence disease directly (Pescosolido, 2006; Timmermans and Haas, 2008). Moreover, testing the themes and theories from the sociology of health and illness and focusing on the clinical endpoints for a specific disease, such as I have done here with ALS, allows sociologists to understand when and

how general overarching theories may need to be adjusted or conceptualized differently to understand micro-level disease specific populations.

Although the current conceptualization of the theories may have their limitations in the research and in the interpretation of the results, a larger limitation was the data itself. Without the quest to understand the social context of ALS, as well a testing the need for a sociology of disease, many of the limitations of the National ALS Registry may not have been discovered. The limitations of the National ALS Registry reaffirm the need to understand the specific social context of a disease, rather than a general overview of illness on the macro-level.

The Limitations and Promise of the National ALS Registry

Limitations of the National ALS Registry

The National ALS Registry is one of several ALS registries in the United States, including the Veterans Administration National Registry, the Argeo Paul Cellucci ALS Registry of Massachusetts, and the Northeast ALS Consortium (NEALS) Upper Motor Neuron Disease (UMND) Registry (Allen et al., 2008; Murphy et al., 2014; Abille and Fraser, 2017). The National ALS Registry, however, is the most geographically diverse ALS registry in the United States. In addition, the National ALS Registry is attached to the national biobank repository, which allows individual data from the registry to be matched with data from the biobank, allowing for detailed biomedical research into the biological causes of ALS.

It is difficult, however, to define the ALS population in the United States. Coming to a final diagnosis of ALS is a process of elimination, the cost of which can be in the tens of thousands of dollars prior to insurance. (Kiernan et al., 2011; Obermann & Lyon,

2015). The variability of the earliest symptoms can lead to incorrect diagnoses and unnecessary medical procedures, culminating in a delayed diagnosis (Belsh and Schiffman, 1996; Srinivasan et al., 2006). Further, the understanding of ALS as a disease has changed to include frontotemporal dementia as a type of onset. Therefore, there is the potential that pALS are missed due to misdiagnosis or diagnosis prior to new findings. Moreover, if pALS are further into the progression of the disease, they may not take part in the registry due to physical and psychological limitations or pALS may die before completing the registration process. These limitations mean the National ALS Registry is the best-case scenario and where researchers should see the fewest disparities, however, disparities have been found across the three studies presented here.

With several potential registries to join, and limited time to do so given the nature of ALS, and the potential for misdiagnosis or uncertainty of the diagnosis, not every case may be counted in the National ALS Registry. For example, the latest CDC report estimates there were 16,583 cases of definite ALS in the United States in 2015 and (Mehta et al., 2018), however, the ALS Association estimates that up to 30,000 people may be affected by ALS each year (ALSA, 2020), meaning that the National ALS Registry may be missing up to 45% of the population of pALS. The incongruence of the estimates from the CDC and ALSA highlights the difficulties in defining the true population of pALS in the United States.

The National ALS Registry is available in an online format only, which may limit access and cause the registry to reflect a younger, white, and educated patient sample. The registry sample provided by the CDC is less racially diverse than the overall registry which includes Medicare and Veteran's Association claims data (Kaye et al., 2018).

There are several potential reasons for this, including access to computers that are needed for self-registration, reduced awareness of the registry, and reduced participation in areas with substantial nonwhite populations.

The nature of the design of the National ALS Registry, with individual modules the participant can complete at home on a schedule that works for their situation and their physical and psychological limitations, is one that makes sense for a disease like ALS. Although convenient and easier to use for the pALS, it does lead to issues with missing data. With the exception of the first module about demographic information (e.g. race/ethnicity, gender, education level), many of the questions in the dataset had at least some missing data. The highest amounts of missing data were in the insurance module and the clinical data module, which were added to the registry at a later date. At that time, pALS were notified of a new module to complete via email. Given the short survival time after a diagnosis of ALS, however, pALS may have been deceased at the time of the notification. pALS may choose to do some modules with the intent of returning to finish the others (e.g. with a caregiver or after retrieving information needed), but have their health deteriorate to a point where they are unable to do so. Further, pALS may find the modules to be too complex given their health situation and may forgo completing all the individual modules.

An important feature of the National ALS Registry is that it was designed with biomedical and epidemiological research in mind. Therefore, the registry is not ideal for research from a social science perspective. For example, chapter one of the dissertation supports earlier studies that show women are more likely to develop bulbar onset of ALS even when accounting for proximate risk factors. Without more information on other

types of exposures, including stress exposure and adverse childhood events, it is difficult to parse out the full picture of why there is a statistically significant difference in the onset location for women compare to men. Differences in onset location may be due to both biological and social factors, and without access to both types of information in registry data, both fields will suffer from incomplete analysis of the factors involved in ALS development and progression.

Concerns about deductive identification severely limited the amount of information available for the analyses. As ALS is rare, and participation in the registry is voluntary, reidentification is a serious concern. Therefore, the CDC limits access to a small number of survey modules. Although not ideal, the issue of reidentification does limit the work that can be done with registry data. For example, the analysis presented in chapter four may have benefited from more information on whether the pALS had children or not. To access the information on the number of children, however, I would have needed to relinquish access to other data important to answering the research questions in the dissertation. Further, although the sample size overall is robust, smaller numbers of specific populations, such as non-white patients, limits the ability to do intersectional analysis. The inclusion of an intersectional approach may have further clarified how social position shapes the onset location and symptom development for pALS. Additionally, the non-random sample opt-in nature of the survey means the results may not be generalizable to the ALS population as a whole.

The Potential Promise of the National ALS Registry

Although the National ALS Registry does pose some difficulties for researchers, it is one of the few sources of information existing on pALS in the United States. The

promise of the National ALS Registry in discovering treatments and cures for ALS is clear, although with improvements it could be even more promising for social science research. I present some possibilities for overcoming current barriers in the sections below. Although only a brief outline of potential suggestions to enhance social science research such as that done for the dissertation, the overall goal is to begin a conversation on potential improvements to the registry.

Implementing mandatory reporting. Only Massachusetts requires the mandatory reporting of ALS cases, which are then included in the Argeo Paul Cellucci ALS Registry of Massachusetts. To fully define the ALS population in the United States, the National ALS Registry needs to ensure every case is counted, which would require mandatory reporting. Further, mandatory reporting would allow physicians and other healthcare personnel to report protected health information including onset location, ALSFR-R scores, symptom development, and clinical data to the registry, potentially allowing for pALS to answer additional modules related to social and environmental risk factors and reducing some respondent burden. Creating a mandatory reporting system would help the registry increase its reach to pALS who are unable to access the current registry, as well as ensuring more complete and accurate information for research. Moreover, turning to a mandatory reporting system could increase sample sizes enough to allow for intersectional analysis of social position.

Increase awareness of and aid for registry completion among pALS. One of the flaws of the ALS Registry is the limited population from which data is collected. In addition to a lack of access to the internet, caregivers and patients have limited time to carry out an optional task such as a registry module due to the pressures of everyday

medical care needs. One potential solution is to offer access to completing the survey in clinics, as well as through organizations such as the ALS Association, Paralyzed Veterans of America, and the Muscular Dystrophy Association, all of which are involved in supporting the ALS community. Improving access, along with having a knowledgeable person available to help navigate the registry and answer questions, would increase the number of people taking part in the registry.

Including social factors in data collection. The results of the dissertation show that social position shapes both the disease process and the lived experiences of ALS. The inclusion of social factors, such as childhood adverse event scales, early life socioeconomic status, and reporting of life event and chronic stressors in adulthood, would provide additional valuable information on the potential interaction of the social world and biological processes over the course of pALS lives. Further, including social factors may help to determine where and why pALS may be facing disparities in healthcare.

Future Work

The dissertation has posed new questions about the role of social position in the disease course and lived experience of ALS. There are several potential avenues of inquiry. The first, from a quantitative perspective, is the inclusion of early life experiences, childhood exposure to proximate risk factors, and the experience of stress in future research on ALS. Previous research has examined the effects of stress in ALS through pathways related to hormones (e.g. cortisol) and damage to the nervous system (e.g. oxidative stress) (Fidler et al, 2011; Bozzo et al., 2017), and stress exposure can vary by social position and early life experiences. To study stress effects would require

recruiting pALS to complete a survey asking comparable questions to the registry's clinical questions, demographic information, as well as measures such as the childhood adverse events scale, childhood environmental exposures, and life events and chronic stressors across the life course. Collecting data of this nature could help to further clarify the interaction between the social and the biological in the development of ALS. Further, researchers might consider an analysis of ALS subgroups using data from the National ALS Registry. Exploring the potential subgroups using clinical data and data on social position may help to clarify why some pALS respond to new treatments and adopt the latest technologies, while others do not. In addition, gaining a better understanding of the potential variation in experiences and responses among subgroups of pALS may be one way to better understand what exposures and experiences may influence ALS development and progression.

There is a need for qualitative research to understand the association between social position and perceptions of ALS onset and symptom development. The meaning and salience of biological symptoms are likely to differ for people with more or less physically demanding jobs, regular medical care, and expectations for aging. For example, many of the social position results, such as those for education, could be due to a difference in exposures to proximate risks. The findings that social position matters over and above proximate risk exposure, however, may be due to when symptoms are perceived and become salient. People with lower levels of education usually have different types of work demands than people with higher education. Jobs requiring more physical labor could lead to pALS attributing symptoms to work-related exhaustion or as the consequence of a hard life, whereas people with more education might find the

symptoms harder to explain away. pALS with lower education could also attribute symptoms to the expected effects of getting older or might not have access to affordable medical care and thus ignore symptoms as long as possible in contrast to higher educated people who are more likely to have insurance and regular medical visits. To better understand how pALS make sense of symptoms prior to diagnosis, it will be valuable to conduct interviews with pALS about how they understood the changes in their bodies associated with ALS.

There is an important gap in the knowledge about how patient social position affects medical decision making for people with ALS. A few of the most interesting findings in chapter five are opposite of the hypothesized direction. One specific example is the higher number of unmarried pALS and pALS who are racial or ethnic minorities reporting adoption of invasive ventilation. Much of the research on health disparities runs counter to these findings and poses an interesting question of why these pALS are choosing this extremely expensive and care intensive treatment option. Qualitative work, including interviews with pALS and their caregivers, would provide valuable information to best interpret these results. Further, work to determine if the differences in the adoption of invasive ventilation among racial and ethnic minorities are potentially rooted in a deeper history of racism and its consequences is a critical area for future consideration.

Finally, the results of the studies presented in the dissertation support the need for a sociology of disease. Future work should include adapting existing theories used in the sociology of health and illness to better understand experiences of populations of people who have developed a specific disease. As the results presented here show, the experience of a disease like ALS differs from other diseases like cancer, and to

understand differences in outcomes for patients requires a new and different perspective, one offered by a sociology of disease.

REFERENCES

Adler, N. E., Boyce, T., Chesney, M. A., Cohen, S., Folkman, S., Kahn, R. L., & Syme, S. L. (1994). Socioeconomic status and health: the challenge of the gradient. *American Psychologist*, *49*(1), 15.

Abille, V., Fraser, A., & Knorr, R. (2017). ALS Surveillance in Massachusetts: A one-of-a-kind registry for tracking an elusive disease.

Al-Chalabi, A., Hardiman, O., Kiernan, M. C., Chiò, A., Rix-Brooks, B., & van den Berg, L. H. (2016). Amyotrophic lateral sclerosis: Moving towards a new classification system. *The Lancet Neurology*, *15*(11), 1182–1194. https://doi.org/10.1016/S1474-4422(16)30199-5

Allen, K. D., Kasarskis, E. J., Bedlack, R. S., Rozear, M. P., Morgenlander, J. C., Sabet, A., ... & Oddone, E. Z. (2008). The National Registry of Veterans with amyotrophic lateral sclerosis. *Neuroepidemiology*, *30*(3), 180-190.

Andersen, J. A. (2018). Amyotrophic Lateral Sclerosis and a" Death With Dignity". *Omega*, 30222818788254.

Appel, V., Stewart, S. S., Smith, G., & Appel, S. H. (1987). A rating scale for amyotrophic lateral sclerosis: description and preliminary experience. *Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society*, *22*(3), 328-333.

Arthur, K. C., Calvo, A., Price, T. R., Geiger, J. T., Chiò, A., & Traynor, B. J. (2016). Projected increase in amyotrophic lateral sclerosis from 2015 to 2040. *Nature Communications*, *7*, 12408.

Aschbacher, K., O'Donovan, A., Wolkowitz, O. M., Dhabhar, F. S., Su, Y., & Epel, E. (2013). Good stress, bad stress and oxidative stress: insights from anticipatory cortisol reactivity. *Psychoneuroendocrinology*, *38*(9), 1698-1708.

Atsuta, N., Watanabe, H., Ito, M., Tanaka, F., Tamakoshi, A., Nakano, I., Aoki, M., Tsuji, S., Yuasa, T., Takano, H., Hayashi, H., Kuzuhara, S., & Sobue, G. (2009). Age at onset influences on wide-ranged clinical features of sporadic amyotrophic lateral sclerosis. *Journal of the Neurological Sciences*, *276*(1), 163–169. https://doi.org/10.1016/j.jns.2008.09.024

Belsh, J. M., & Schiffman, P. L. (1996). The amyotrophic lateral sclerosis (ALS) patient perspective on misdiagnosis and its repercussions. *Journal of the Neurological Sciences*, *139*, 110-116.

Benditt, J. O. (2002). Respiratory complications of amyotrophic lateral sclerosis. In *Seminars in respiratory and critical care medicine* (Vol. 23, No. 03, pp. 239-247). Copyright© 2002 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA.

Bodner, T. E. (2008). What improves with increased missing data imputations?. *Structural Equation Modeling: A Multidisciplinary Journal*, *15*(4), 651-675.

Bozzo, F., Mirra, A., & Carrì, M. T. (2017). Oxidative stress and mitochondrial damage in the pathogenesis of ALS: New perspectives. *Neuroscience Letters*, *636*, 3–8. https://doi.org/10.1016/j.neulet.2016.04.065

Braveman, P. A., Cubbin, C., Egerter, S., Chideya, S., Marchi, K. S., Metzler, M., & Posner, S. (2005). Socioeconomic status in health research: one size does not fit all. *JAMA,* 294(22), 2879-2888.

Braveman, P., Egerter, S., & Williams, D. R. (2011). The social determinants of health: coming of age. *Annual Review of Public Health*, *32*, 381-398.

Brown, R. C., Lockwood, A. H., & Sonawane, B. R. (2005). Neurodegenerative diseases: an overview of environmental risk factors. *Environmental Health Perspectives*, *113*(9), 1250-1256.

Brown, R. H., & Al-Chalabi, A. (2017). Amyotrophic lateral sclerosis. *New England Journal of Medicine*, *377*(2), 162-172.

Bryan, L., Kaye, W., Antao, V., Mehta, P., Muravov, O., & Horton, D. K. (2016). Preliminary Results of National Amyotrophic Lateral Sclerosis (ALS) Registry Risk Factor Survey Data. *PLoS ONE*, *11*(4). https://doi.org/10.1371/journal.pone.0153683

Caller, T. A., Field, N. C., Chipman, J. W., Shi, X., Harris, B. T., & Stommel, E. W. (2012). Spatial clustering of amyotrophic lateral sclerosis and the potential role of BMAA. *Amyotrophic Lateral Sclerosis*, *13*(1), 25-32.

Caller, T., Henegan, P., & Stommel, E. (2018). The Potential Role of BMAA in Neurodegeneration. *Neurotoxicity Research*, *33*(1), 222–226. https://doi.org/10.1007/s12640-017-9752-7

Carr, D., Freedman, V. A., Cornman, J. C., & Schwarz, N. (2014). Happy Marriage, Happy Life? Marital Quality and Subjective Well-being in Later Life. *Journal of Marriage and Family*, *76*(5), 930–948. https://doi.org/10.1111/jomf.12133

Carter, Chelsey. 2019."'It's a White Disease!'" *Anthropology News* website, February 11, 2019. DOI: 10.1111/AN.1091

Cassileth, B. R., Lusk, E. J., Miller, D. S., Brown, L. L., & Miller, C. (1985). Psychosocial correlates of survival in advanced malignant disease?. *New England Journal of Medicine*, *312*(24), 1551-1555.

Cazzolli, P. A., & Oppenheimer, E. A. (1996). Home mechanical ventilation for amyotrophic lateral sclerosis: nasal compared to tracheostomy-intermittent positive pressure ventilation. *Journal of the Neurological Sciences*, *139*, 123-128.

Cedarbaum, J. M., Stambler, N., Malta, E., Fuller, C., Hilt, D., Thurmond, B., & Nakanishi, A. (1999). The ALSFRS-R: a revised ALS functional rating scale that incorporates assessments of respiratory function. *Journal of the Neurological Sciences*, 169(1), 13–21. https://doi.org/10.1016/S0022-510X(99)00210-5

Ceriana, P., Surbone, S., Segagni, D., Schreiber, A., & Carlucci, A. (2017). Decision-making for tracheostomy in amyotrophic lateral sclerosis (ALS): a retrospective study. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, *18*(7-8), 492-497.

Chiò, A., Benzi, G., Dossena, M., Mutani, R., & Mora, G. (2005). Severely increased risk of amyotrophic lateral sclerosis among Italian professional football players. *Brain*, 128(3), 472–476. https://doi.org/10.1093/brain/awh373

Chiò, A., Logroscino, G., Hardiman, O., Swingler, R., Mitchell, D., Beghi, E., ... & Eurals Consortium. (2009). Prognostic factors in ALS: a critical review. *Amyotrophic Lateral Sclerosis*, *10*(5-6), 310-323.

Chiò, A., Canosa, A., Gallo, S., Cammarosano, S., Moglia, C., Fuda, G., ... & Gabriele, M. (2011). ALS clinical trials: do enrolled patients accurately represent the ALS population?. *Neurology*, *77*(15), 1432-1437.

Coakley, M., Fadiran, E. O., Parrish, L. J., Griffith, R. A., Weiss, E., & Carter, C. (2012). Dialogues on diversifying clinical trials: successful strategies for engaging women and minorities in clinical trials. *Journal of Women's Health*, *21*(7), 713-716.

Cohen, P., West, S. G., & Aiken, L. S. (2014). *Applied Multiple Regression/Correlation Analysis for the Behavioral Sciences*. Psychology Press.

Collins, P. H. (1990). Black feminist thought in the matrix of domination. *Black Feminist Thought: Knowledge, Consciousness, and the Politics of Empowerment*, *138*, 221-238.

Connor, S. R. (2008). Development of hospice and palliative care in the United States. *OMEGA-Journal of Death and Dying*, *56*(1), 89-99.

Crawford, B. M., Meana, M., Stewart, D., & Cheung, A. M. (2000). Treatment decision making in mature adults: gender differences. *Health Care for Women International*, *21*(2), 91-104.

Crook, A., Williams, K., Adams, L., Blair, I., & Rowe, D. B. (2017). Predictive genetic testing for amyotrophic lateral sclerosis and frontotemporal dementia: genetic counselling considerations. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, *18*(7-8), 475-485.

de Jong, S. W., Huisman, M. H. B., Sutedja, N. A., van der Kooi, A. J., de Visser, M., Schelhaas, H. J., Fischer, K., Veldink, J. H., & van den Berg, L. H. (2012). Smoking, Alcohol Consumption, and the Risk of Amyotrophic Lateral Sclerosis: A Population-based Study. *American Journal of Epidemiology*, *176*(3), 233–239. https://doi.org/10.1093/aje/kws015

Del Aguila, M. A., Longstreth, W. T., McGuire, V., Koepsell, T. D., & Van Belle, G. (2003). Prognosis in amyotrophic lateral sclerosis: a population-based study. *Neurology*, *60*(5), 813-819.

D'Amico, E., Factor-Litvak, P., Santella, R. M., & Mitsumoto, H. (2013). Clinical perspective on oxidative stress in sporadic amyotrophic lateral sclerosis. *Free Radical Biology and Medicine*, *65*, 509-527.

Diez Roux, A. V. (2012). Conceptual approaches to the study of health disparities. *Annual Review of Public Health*, *33*, 41-58.

Dorst, J., Ludolph, A. C., & Huebers, A. (2018). Disease-modifying and symptomatic treatment of amyotrophic lateral sclerosis. *Therapeutic Advances in Neurological Disorders*, *11*, 1756285617734734.

Dupuis, L., Pradat, P.-F., Ludolph, A. C., & Loeffler, J.-P. (2011). Energy metabolism in amyotrophic lateral sclerosis. *The Lancet Neurology*, 10(1), 75–82. https://doi.org/10.1016/S1474-4422(10)70224-6

Elder Jr, G. H. (1994). Time, human agency, and social change: Perspectives on the life course. *Social Psychology Quarterly*, 4-15.

Elder Jr, G. H., & Rockwell, R. C. (1979). The life-course and human development: An ecological perspective. *International Journal of Behavioral Development*, *2*(1), 1-21.

Elder, G. H. (1998). The Life Course as Developmental Theory. *Child Development*, 69(1), 1–12. https://doi.org/10.1111/j.1467-8624.1998.tb06128.x

Enders, C. K. (2006). A primer on the use of modern missing-data methods in psychosomatic medicine research. *Psychosomatic Medicine*, *68*(3), 427-436.

Fang, F., Quinlan, P., Ye, W., Barber, M. K., Umbach, D. M., Sandler, D. P., & Kamel, F. (2009). Workplace exposures and the risk of amyotrophic lateral sclerosis. *Environmental Health Perspectives*, *117*(9), 1387-1392.

Ferraro, K. F., & Farmer, M. M. (1996). Double jeopardy, aging as leveler, or persistent health inequality? A longitudinal analysis of white and black Americans. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *51*(6), S319-S328.

Ferraro, K. F., Shippee, T. P., & Schafer, M. H. (2009). Cumulative inequality theory for research on aging and the life course.

Ferraro, K. F., Schafer, M. H., & Wilkinson, L. R. (2016). Childhood disadvantage and health problems in middle and later life: Early imprints on physical health?. *American Sociological Review*, *81*(1), 107-133.

Fidler, J. A., Treleaven, C. M., Frakes, A., Tamsett, T. J., McCrate, M., Cheng, S. H., Shihabuddin, L. S., Kaspar, B. K., & Dodge, J. C. (2011). Disease progression in a mouse

model of amyotrophic lateral sclerosis: The influence of chronic stress and corticosterone. *The FASEB Journal*, *25*(12), 4369–4377. https://doi.org/10.1096/fj.11-190819

Foley, G., Timonen, V., & Hardiman, O. (2014). Acceptance and Decision Making in Amyotrophic Lateral Sclerosis From a Life-Course Perspective. *Qualitative Health Research*, 24(1), 67–77. https://doi.org/10.1177/1049732313516545

Freese, J., & Lutfey, K. (2011). Fundamental Causality: Challenges of an Animating Concept for Medical Sociology. In B. A. Pescosolido, J. K. Martin, J. D. McLeod, & A. Rogers (Eds.), *Handbook of the Sociology of Health, Illness, and Healing: A Blueprint for the 21st Century* (pp. 67–81). Springer. https://doi.org/10.1007/978-1-4419-7261-3_4

Gay, J. (2018). *The Health of Women: A Global Perspective*. Routledge.

Georgoulopoulou, E., Fini, N., Vinceti, M., Monelli, M., Vacondio, P., Bianconi, G., ... & Mandrioli, J. (2013). The impact of clinical factors, riluzole and therapeutic interventions on ALS survival: a population based study in Modena, Italy. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, *14*(5-6), 338-345.

Geronimus, A. T. (1992). The weathering hypothesis and the health of African-American women and infants: evidence and speculations. *Ethnicity & Disease*, 2(3), 207-221.

Geronimus, A. T., Bound, J., Waidmann, T. A., Colen, C. G., & Steffick, D. (2001). Inequality in life expectancy, functional status, and active life expectancy across selected black and white populations in the United States. *Demography*, 38(2), 227-251.

Gevitz, N. (1986). Sociology in Medicine. *JAMA*, *256*(19), 2742-2742.

Glass, T. A., & Mcatee, M. J. (2005). *Extending Horizons, Envisioning The Future*.

Glass, T. A., & McAtee, M. J. (2006). Behavioral science at the crossroads in public health: extending horizons, envisioning the future. *Social science & medicine*, *62*(7), 1650-1671.

Goosby, B. J., & Heidbrink, C. (2013). The transgenerational consequences of discrimination on African-American health outcomes. *Sociology Compass*, *7*(8), 630-643.

Goutman, S. A., & Simmons, Z. (2018). Symptom management in ALS: we can do better. *Muscle & Nerve*, 57(1), 1.

Gundogdu, B., Al-Lahham, T., Kadlubar, F., Spencer, H., & Rudnicki, S. A. (2014). Racial differences in motor neuron disease. *Amyotrophic Lateral Sclerosis & Frontotemporal Degeneration*, *15*(0), 114–118. https://doi.org/10.3109/21678421.2013.837930

Harris, Y., Gorelick, P. B., Samuels, P., & Bempong, I. (1996). Why African Americans may not be participating in clinical trials. *Journal of the National Medical Association*, *88*(10), 630.

Haverkamp, L. J., Appel, V., & Appel, S. H. (1995). Natural history of amyotrophic lateral sclerosis in a database population Validation of a scoring system and a model for survival prediction. *Brain*, *118*(3), 707-719.

Horton, D. K., Graham, S., Punjani, R., Wilt, G., Kaye, W., Maginnis, K., … Mehta, P. (2018). A spatial analysis of amyotrophic lateral sclerosis (ALS) cases in the United States and their proximity to multidisciplinary ALS clinics, 2013. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, 19(1–2), 126–133. https://doi.org/10.1080/21678421.2017.1406953

Househam, E., & Swash, M. (2000). Diagnostic delay in amyotrophic lateral sclerosis: what scope for improvement?. *Journal of the Neurological Sciences*, *180*(1-2), 76-81.

Howard, G., Anderson, R. T., Russell, G., Howard, V. J., & Burke, G. L. (2000). Race, socioeconomic status, and cause-specific mortality. *Annals of epidemiology*, *10*(4), 214-223.

Ingre, C., Roos, P. M., Piehl, F., Kamel, F., & Fang, F. (2015). Risk factors for amyotrophic lateral sclerosis. *Clinical Epidemiology*, 7, 181–193. https://doi.org/10.2147/CLEP.S37505

Iwasaki, Y., Ikeda, K., & Kinoshita, M. (2001). The diagnostic pathway in amyotrophic lateral sclerosis. *Amyotrophic Lateral Sclerosis and Other Motor Neuron Disorders*, *2*(3), 123-126.

Jaiswal, M. K. (2019). Riluzole and edaravone: A tale of two amyotrophic lateral sclerosis drugs. *Medicinal Research Reviews*, *39*(2), 733-748.

Kalish, R. (1985). Coping with death. *The Final Transition*, *5*, 11.

Kapral, M. K., Devon, J., Winter, A. L., Wang, J., Peters, A., & Bondy, S. J. (2006). Gender differences in stroke care decision-making. *Medical Care*, 70-80.

Kaye, W. E., Wagner, L., Wu, R., & Mehta, P. (2018). Evaluating the completeness of the national ALS registry, United States. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, *19*(1–2), 112–117. https://doi.org/10.1080/21678421.2017.1384021

Kiernan, M. C., Vucic, S., Cheah, B. C., Turner, M. R., Eisen, A., Hardiman, O., ... & Zoing, M. C. (2011). Amyotrophic lateral sclerosis. *Lancet (London, England)*, *377*(9769), 942.

Kleykamp, M. A. (2006). College, jobs, or the military? Enlistment during a time of war. *Social Science Quarterly*, 87(2), 272-290.

Kotter-Grühn, D., Grühn, D., & Smith, J. (2010). Predicting one's own death: the relationship between subjective and objective nearness to death in very old age. *European Journal of Ageing*, *7*(4), 293-300.

Kraemer, M., Buerger, M., & Berlit, P. (2010). Diagnostic problems and delay of diagnosis in amyotrophic lateral sclerosis. *Clinical Neurology and Neurosurgery*, *112*(2), 103-105.

Lechtzin, N., Scott, Y., Busse, A. M., Clawson, L. L., Kimball, R., & Wiener, C. M. (2007). Early use of non-invasive ventilation prolongs survival in subjects with ALS. *Amyotrophic Lateral Sclerosis*, *8*(3), 185-188.

Lemoignan, J., & Ells, C. (2010). Amyotrophic lateral sclerosis and assisted ventilation: how patients decide. *Palliative & Supportive Care*, *8*(2), 207-213.

Levine, S. (1987). The changing terrains in medical sociology: emergent concern with quality of life. *Journal of Health and Social Behavior*, 1-6.

Link, B. G. (2008). Epidemiological sociology and the social shaping of population health. *Journal of Health and Social Behavior*, *49*(4), 367-384.

Link, B. G., & Phelan, J. (1995). Social conditions as fundamental causes of disease. *Journal of Health and Social Behavior*, 80-94.

Longstreth, W. T., McGuire, V., Koepsell, T. D., Wang, Y., & Belle, G. van. (1998). Risk of Amyotrophic Lateral Sclerosis and History of Physical Activity: A Population-Based Case-Control Study. *Archives of Neurology*, *55*(2), 201–206. https://doi.org/10.1001/archneur.55.2.201

Louwerse, E. S., Visser, C. E., Bossuyt, P. M. M., & Weverling, G. J. (1997). Amyotrophic lateral sclerosis: mortality risk during the course of the disease and prognostic factors. *Journal of the Neurological Sciences*, 152, s10–s17. https://doi.org/10.1016/S0022-510X(97)00238-4

Lutfey, K., & Freese, J. (2005). Toward some fundamentals of fundamental causality: Socioeconomic status and health in the routine clinic visit for diabetes. *American Journal of Sociology*, *110*(5), 1326-1372.

Lyman, K. A. (1989). Bringing the social back in: A critique of the biomedicalization of dementia. *The Gerontologist*, *29*(5), 597-605.

Magnus, T., Beck, M., Giess, R., Puls, I., Naumann, M., & Toyka, K. V. (2002). Disease progression in amyotrophic lateral sclerosis: Predictors of survival. *Muscle & Nerve*, 25(5), 709–714. https://doi.org/10.1002/mus.10090

Manjaly, Z. R., Scott, K. M., Abhinav, K., Wijesekera, L., Ganesalingam, J., Goldstein, L. H., ... & Turner, M. R. (2010). The sex ratio in amyotrophic lateral sclerosis: a population based study. *Amyotrophic Lateral Sclerosis*, *11*(5), 439-442.

Mara Gaudette, T. S., Makito Hirano. (2000). Current status of SOD1 mutations in familial amyotrophic lateral sclerosis. *Amyotrophic Lateral Sclerosis and Other Motor Neuron Disorders*, *1*(2), 83–89. https://doi.org/10.1080/14660820050515377

Masters, R. K., Link, B. G., & Phelan, J. C. (2015). Trends in education gradients of 'preventable' mortality: a test of fundamental cause theory. *Social Science & Medicine*, *127*, 19-28.

McCombe, P. A., & Henderson, R. D. (2010). Effects of gender in amyotrophic lateral sclerosis. *Gender Medicine*, *7*(6), 557–570. https://doi.org/10.1016/j.genm.2010.11.010

McMurray, R. J., Clarke, O. W., Barrasso, J. A., Clohan, D. B., Epps, C. H., Glasson, J., ... & Halkola, K. A. (1991). Gender disparities in clinical decision making. *JAMA*, *266*(4), 559-562.

Mehta, P., Kaye, W., Bryan, L., Larson, T., Copeland, T., Wu, J., ... & Horton, K. (2016). Prevalence of amyotrophic lateral sclerosis—United States, 2012–2013. *Morbidity and Mortality Weekly Report: Surveillance Summaries*, *65*(8), 1-12.

Mehta, P., Kaye, W., Raymond, J., Wu, R., Larson, T., Punjani, R., ... & Horton, K. (2018). Prevalence of amyotrophic lateral sclerosis—United States, 2014. *Morbidity and Mortality Weekly Report*, *67*(7), 216.

Menezes, A. R., Lavie, C. J., DeSchutter, A., & Milani, R. V. (2014). Gender, race and cardiac rehabilitation in the United States: is there a difference in care?. *The American Journal of the Medical Sciences*, *348*(2), 146-152.

Ross, C. E., & Mirowsky, J. (2010). Why education is the key to socioeconomic differentials in health. *Handbook of Medical Sociology*, *6*, 33-51.

Mitchell, John Douglas, Pauline Callagher, Joyce Gardham, Catriona Mitchell, Mandy Dixon, Robert Addison-Jones, Wendy Bennett, and Mary R. O'Brien. "Timelines in the diagnostic evaluation of people with suspected amyotrophic lateral sclerosis (ALS)/motor neuron disease (MND)–a 20-year review: can we do better?." *Amyotrophic Lateral Sclerosis* 11, no. 6 (2010): 537-541.

Mitsumoto, H., & Bene, M. D. (2000). Improving the quality of life for people with ALS: the challenge ahead. *Amyotrophic Lateral Sclerosis and Other Motor Neuron Disorders*, *1*(5), 329-336.

Mitsumoto, H., Brooks, B. R., & Silani, V. (2014). Clinical trials in amyotrophic lateral sclerosis: Why so many negative trials and how can trials be improved? *The Lancet Neurology*, *13*(11), 1127–1138. https://doi.org/10.1016/S1474-4422(14)70129-2

Muddasir Qureshi, M., Hayden, D., Urbinelli, L., Ferrante, K., Newhall, K., Myers, D., ... & Cudkowicz, M. E. (2006). Analysis of factors that modify susceptibility and rate of progression in amyotrophic lateral sclerosis (ALS). *Amyotrophic Lateral Sclerosis*, *7*(3), 173-182.

Murphy, A., Loci, L., Mitsumoto, H., Lomen-Hoerth, C., Kisanuki, Y., Andrews, J., ... & Atassi, N. (2014). The Northeast ALS Consortium (NEALS) Upper Motor Neuron Disease (UMND) Registry (P5. 076).

Murthy, V. H., Krumholz, H. M., & Gross, C. P. (2004). Participation in cancer clinical trials: race-, sex-, and age-based disparities. *JAMA*, *291*(22), 2720-2726.

Nelson, L. M., McGuire, V., Longstreth, W. T., & Matkin, C. (2000). Population-Based Case-Control Study of Amyotrophic Lateral Sclerosis in Western Washington State. I. Cigarette Smoking and Alcohol Consumption. *American Journal of Epidemiology*, *151*(2), 156–163. https://doi.org/10.1093/oxfordjournals.aje.a010183

Nzwalo, H., de Abreu, D., Swash, M., Pinto, S., & de Carvalho, M. (2014). Delayed diagnosis in ALS: the problem continues. *Journal of the Neurological Sciences*, *343*(1-2), 173-175.

Obermann, M., & Lyon, M. (2015). Financial cost of amyotrophic lateral sclerosis: a case study. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, *16*(1-2), 54-57.

O'Brien, M. R., Whitehead, B., Jack, B. A., & Mitchell, J. D. (2011). From symptom onset to a diagnosis of amyotrophic lateral sclerosis/motor neuron disease (ALS/MND): experiences of people with ALS/MND and family carers–a qualitative study. *Amyotrophic Lateral Sclerosis*, *12*(2), 97-104.

Oliver, D. J., & Turner, M. R. (2010). Some difficult decisions in ALS/MND. *Amyotrophic Lateral Sclerosis*, *11*(4), 339-343.

Onesti, E., Schettino, I., Gori, M. C., Frasca, V., Ceccanti, M., Cambieri, C., ... & Inghilleri, M. (2017). Dysphagia in amyotrophic lateral sclerosis: impact on patient behavior, diet adaptation, and riluzole management. *Frontiers in Neurology*, *8*, 94.

Paillisse, C., Lacomblez, L., Dib, M., Bensimon, G., Garcia-Acosta, S., & Meininger, V. (2005). Prognostic factors for survival in amyotrophic lateral sclerosis patients treated with riluzole. *Amyotrophic Lateral Sclerosis*, 6(1), 37–44. https://doi.org/10.1080/14660820510027035

Pampel, F. C. (2009). The persistence of educational disparities in smoking. *Social Problems*, *56*(3), 526-542.

Pereira, A. (2003). "Live and Let Live: Healthcare Is a Fundamental Human Right." *Connecticut Public Interest Law Journal* 3:481.

Pescosolido, B. A. (2006). Of pride and prejudice: the role of sociology and social networks in integrating the health sciences. *Journal of Health and Social Behavior*, *47*(3), 189-208.

Phelan, J. C., & Link, B. G. (2013). Fundamental cause theory. In *Medical Sociology on the Move* (pp. 105-125). Springer, Dordrecht.

Phelan, J. C., & Link, B. G. (2015). Is racism a fundamental cause of inequalities in health?. *Annual Review of Sociology*, *41*, 311-330.

Phelan, J. C., Link, B. G., & Tehranifar, P. (2010). Social conditions as fundamental causes of health inequalities: theory, evidence, and policy implications. *Journal of Health and Social Behavior*, *51*(1_suppl), S28-S40.

Phelan, J. C., Link, B. G., Diez-Roux, A., Kawachi, I., & Levin, B. (2004). "Fundamental causes" of social inequalities in mortality: a test of the theory. *Journal of Health and Social Behavior 45*(3), 265-285.

Phillips, K. A., Mayer, M. L., & Aday, L. A. (2000). Barriers To Care Among Racial/Ethnic Groups Under Managed Care: Ethnic minorities continue to encounter barriers to care in the current managed care–dominated US health care system. *Health Affairs*, *19*(4), 65-75.

Pulley, M. T., Brittain, R., Hodges, W., Frazier, C., Miller, L., Matyjasik-Liggett, M., ... & Berger, A. R. (2019). Multidisciplinary amyotrophic lateral sclerosis telemedicine care: the store and forward method. *Muscle & Nerve*, *59*(1), 34-39.

Pupillo, E., Messina, P., Giussani, G., Logroscino, G., Zoccolella, S., Chiò, A., … Beghi, E. (2014). Physical activity and amyotrophic lateral sclerosis: A European population-based case–control study. *Annals of Neurology*, 75(5), 708–716. https://doi.org/10.1002/ana.24150

Quick Facts About ALS & The ALS Association. (2020). Retrieved from http://www.alsa.org/news/media/quick-facts.html

Radunović, A., Mitsumoto, H., & Leigh, P. N. (2007). Clinical care of patients with amyotrophic lateral sclerosis. *The Lancet Neurology*, *6*(10), 913-925.

Raymond, J., Oskarsson, B., Mehta, P., & Horton, K. (2019). Clinical characteristics of a large cohort of US participants enrolled in the National Amyotrophic Lateral Sclerosis (ALS) Registry, 2010–2015. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, 20(5-6), 413-420.

Reisine, S., Mcquillan, J., & Fifield, J. (1995). Predictors of work disability in rheumatoid arthritis patients. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology*, *38*(11), 1630-1637.

Ridings, J. E. (2013). The thalidomide disaster, lessons from the past. In *Teratogenicity Testing* (pp. 575-586). Humana Press, Totowa, NJ.

Rodriguez, J., Chopade, P., & Chen, I. H. A. (2018). Characterization of Amyotrophic Lateral Sclerosis (ALS) Seen in the Medical University of South Carolina ALS Multidisciplinary Clinic (P1. 342).Roberson, N. L. (1994). Clinical trial participation: viewpoints from racial/ethnic groups. *Cancer*, *74*(S9), 2687-2691.

Rothstein, J. D. (2017). Edaravone: a new drug approved for ALS. *Cell*, *171*(4), 725.

Rubin, M. S., Clouston, S., & Link, B. G. (2014). A fundamental cause approach to the study of disparities in lung cancer and pancreatic cancer mortality in the United States. *Social Science & Medicine*, *100*, 54-61.

Saposnik, G., & Kapral, M. K. (2009). Understanding stroke in women: similar care, worse outcomes?.

Schulz, A., Parker, E., Israel, B., & Fisher, T. (2001). Social context, stressors, and disparities in women's health. *Journal-American Medical Womens Association*, 56(4), 143-150.

Shavers, V. L., Lynch, C. F., & Burmeister, L. F. (2001). Factors that influence African-Americans' willingness to participate in medical research studies. *Cancer: Interdisciplinary International Journal of the American Cancer Society*, *91*(S1), 233-236.

Shi, L., Lebrun, L. A., & Tsai, J. (2010). Access to medical care, dental care, and prescription drugs: the roles of race/ethnicity, health insurance, and income. *Southern Medical Journal*, *103*(6), 509.

Shi, L., Chen, C. C., Nie, X., Zhu, J., & Hu, R. (2014). Racial and socioeconomic disparities in access to primary care among people with chronic conditions. *The Journal of the American Board of Family Medicine*, *27*(2), 189-198.

Shneerson, J. M. (2011). Who will benefit from tracheostomy ventilation in motor neuron disease?.

Slatcher, R. B. (2010). Marital Functioning and Physical Health: Implications for Social and Personality Psychology. *Social and Personality Psychology Compass*, *4*(7), 455–469. https://doi.org/10.1111/j.1751-9004.2010.00273.x

Spataro, R., Volanti, P., Lo Coco, D., & La Bella, V. (2017). Marital status is a prognostic factor in amyotrophic lateral sclerosis. *Acta Neurologica Scandinavica*, *136*(6), 624-630.

Srinivasan, J., Scala, S., Jones, H. R., Saleh, F., & Russell, J. A. (2006). Inappropriate surgeries resulting from misdiagnosis of early amyotrophic lateral sclerosis. *Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic Medicine*, *34*(3), 359-360.

Stephens, H. E., Felgoise, S., Young, J., & Simmons, Z. (2015). Multidisciplinary ALS clinics in the USA: A comparison of those who attend and those who do not. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, *16*(3-4), 196-201.

Stephens, H. E., Young, J., Felgoise, S. H., & Simmons, Z. (2016). A qualitative study of multidisciplinary ALS clinic use in the United States. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, *17*(1-2), 55-61.

Stommel, E. W., Field, N. C., & Caller, T. A. (2013). Aerosolization of cyanobacteria as a risk factor for amyotrophic lateral sclerosis. *Medical Hypotheses*, 80(2), 142–145. https://doi.org/10.1016/j.mehy.2012.11.012

Straus, R. (1957). The nature and status of medical sociology. *American sociological review*, *22*(2), 200-204.

Sutedja, N. (2007). *Risk Factors for Motor Neuron Diseases*. 202.

Sutedja, N. A., Veldink, J. H., Fischer, K., Kromhout, H., Wokke, J. H. J., Huisman, M. H. B., ... & Van den Berg, L. H. (2007). Lifetime occupation, education, smoking, and risk of ALS. *Neurology*, *69*(15), 1508-1514.

Suther, S., & Kiros, G. E. (2009). Barriers to the use of genetic testing: a study of racial and ethnic disparities. *Genetics in Medicine*, *11*(9), 655-662.

Swinnen, B., & Robberecht, W. (2014). The phenotypic variability of amyotrophic lateral sclerosis. *Nature Reviews Neurology*, 10(11), 661–670. https://doi.org/10.1038/nrneurol.2014.184

Timmermans, S., & Haas, S. (2008). Towards a sociology of disease. *Sociology of Health & Illness*, *30*(5), 659-676.

Timmermans, S., & Buchbinder, M. (2010). Patients-in-waiting: living between sickness and health in the genomics era. *Journal of Health and Social Behavior, 51*(4), 408-423.

Turkman, Y. E., Williams, C. P., Jackson, B. E., Dionne-Odom, J. N., Taylor, R., Ejem, D., ... & Rocque, G. B. (2019). Disparities in Hospice Utilization for Older Cancer Patients Living in the Deep South. *Journal of Pain and Symptom Management*, *58*(1), 86-91.

Turner, M. R., Hardiman, O., Benatar, M., Brooks, B. R., Chiò, A., De Carvalho, M., ... & Nicholson, G. (2013). Controversies and priorities in amyotrophic lateral sclerosis. *The Lancet Neurology*, *12*(3), 310-322.

Umberson, D., Thomeer, M. B., Reczek, C., & Donnelly, R. (2016). Physical illness in gay, lesbian, and heterosexual marriages: Gendered dyadic experiences. *Journal of Health and Social Behavior*, *57*(4), 517-531.

van Es, M. A., Hardiman, O., Chiò, A., Al-Chalabi, A., Pasterkamp, R. J., Veldink, J. H., & Van den Berg, L. H. (2017). Amyotrophic lateral sclerosis. *The Lancet*, *390*(10107), 2084-2098.

Vennila, V., Madhu, V., Rajesh, R., Ealla, K. K. R., Velidandla, S. R., & Santoshi, S. (2014). Tetracycline-induced discoloration of deciduous teeth: case series. *Journal of International Oral Health: JIOH*, *6*(3), 115.

Virnig, Beth A., A. Marshall McBean, Sara Kind, and Rishi Dholakia. "Hospice use before death: variability across cancer diagnoses." *Medical Care* 40, no. 1 (2002): 73-78.

Voustianiouk, A., Seidel, G., Panchal, J., Sivak, M., Czaplinski, A., Yen, A., ... & Lange, D. J. (2008). ALSFRS and appel ALS scores: discordance with disease progression. *Muscle &*

Nerve: Official Journal of the American Association of Electrodiagnostic Medicine, *37*(5), 668-672.

Waite, L. J., & Gallagher, M. (2001). *The Case for Marriage: Why Married People are Happier, Healthier, and Better off Financially*. Random House Digital, Inc..

Wang, M.-D., Little, J., Gomes, J., Cashman, N. R., & Krewski, D. (2017). Identification of risk factors associated with onset and progression of amyotrophic lateral sclerosis using systematic review and meta-analysis. *NeuroToxicology*, *61*, 101–130. https://doi.org/10.1016/j.neuro.2016.06.015

Warner, D. F., & Brown, T. H. (2011). Understanding how race/ethnicity and gender define age-trajectories of disability: An intersectionality approach. *Social Science & Medicine*, *72*(8), 1236-1248.

Washington, K. T., Bickel-Swenson, D., & Stephens, N. (2008). Barriers to hospice use among African Americans: a systematic review. *Health & Social Work*, 33(4), 267-274.

Watanabe, H., Atsuta, N., Nakamura, R., Hirakawa, A., Watanabe, H., Ito, M., … Sobue, G. (2015). Factors affecting longitudinal functional decline and survival in amyotrophic lateral sclerosis patients. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, 16(3–4), 230–236. https://doi.org/10.3109/21678421.2014.990036

Weisskopf, M. G., Cudkowicz, M. E., & Johnson, N. (2015). Military Service and Amyotrophic Lateral Sclerosis in a Population-based Cohort. *Epidemiology* (Cambridge, Mass.), 26(6), 831–838. https://doi.org/10.1097/EDE.0000000000000376

Williams, D. R., & Collins, C. (2001). Racial Residential Segregation: A Fundamental Cause of Racial Disparities in Health. *Public Health Reports*, *116*(5), 404–416. https://doi.org/10.1093/phr/116.5.404

Williams, D. R., & Jackson, P. B. (2005). Social sources of racial disparities in health. *Health Affairs*, *24*(2), 325-334.

Yokoi, D., Atsuta, N., Watanabe, H., Nakamura, R., Hirakawa, A., Ito, M., Watanabe, H., Katsuno, M., Izumi, Y., Morita, M., Taniguchi, A., Oda, M., Abe, K., Mizoguchi, K., Kano, O., Kuwabara, S., Kaji, R., Sobue, G., & JaCALS. (2016). Age of onset differentially influences the progression of regional dysfunction in sporadic amyotrophic lateral sclerosis. *Journal of Neurology*, *263*(6), 1129–1136. https://doi.org/10.1007/s00415-016-8109-0

Yu, Y., Su, F.-C., Callaghan, B. C., Goutman, S. A., Batterman, S. A., & Feldman, E. L. (2014). Environmental Risk Factors and Amyotrophic Lateral Sclerosis (ALS): A Case-Control Study of ALS in Michigan. *PLOS ONE*, 9(6), e101186. https://doi.org/10.1371/journal.pone.0101186

APPENDIX A: SUPPLEMENTAL TABLES, CHAPTER ONE

Table A1.1 Model 1: Multinomial Logistic Regression Predicting the Reporting of Onset Location, Distal Risk Factors, Relative Risk Ratios (N=9789)

	Base Category: Limb			
	Bulbar		Global	
	Relative Risk Ratio	Confidence Interval	Relative Risk Ratio	Confidence Interval
Racial/Ethnic Minority	1.18	(.89, 1.58)	.90	(.53, 1.54)
Women	1.53 ***	(1.39, 1.69)	.57 ***	(.47, .69)
Education (ref= Tech, Trade, or Some College)				
High School or Less	1.23 *	(1.04, 1.46)	1.10	(.84, 1.45)
College or More	1.12	(.98, 1.27)	.77 *	(.63, .95)
Constant	.21 ***	(.18, .24)	.11 ***	(.09, .13)

*p < .05, **p < .01, ***p < .001

Table A1.2. Model 2: Multinomial Logistic Regression Predicting the Reporting of Onset Location, Distal Risk Factors, Veteran Status, Relative Risk Ratios (N=9789)

	Base Category: Limb			
	Bulbar		**Global**	
	Relative Risk Ratio	Confidence Interval	Relative Risk Ratio	Confidence Interval
Racial/Ethnic Minority	1.18	(.89, 1.58)	.89	(.52, 1.53)
Women	1.52 ***	(1.36, 1.69)	.49 ***	(.40, .60)
Education (ref= Tech, Trade, or Some College)				
High School or Less	1.23 *	(1.04, 1.46)	1.09	(.82, 1.52)
College or More	1.12	(.98, 1.27)	.77 *	(.63, .96)
Civilian	1.03	(.90, 1.18)	1.70 ***	(1.36, 2.12)
Constant	.20 ***	(.18, .24)	.08 ***	(.06, .10)

*p < .05, **p < .01, ***p < .001

Table A1.3. Model 3: Multinomial Logistic Regression Predicting the Reporting of Onset Location, Social Position, Veteran Status, Proximate Risk Factors, Relative Risk Ratios (N=9789)

	Base Category: Limb			
	Bulbar		Global	
	Relative Risk Ratio	Confidence Interval	Relative Risk Ratio	Confidence Interval
Racial/Ethnic Minority	1.19	(.89, 1.59)	.86	(.50, 1.47)
Women	1.51 ***	(1.35, 1.69)	.47 ***	(.39, .58)
Education (ref= Tech, Trade, or Some College)				
High School or Less	1.22 *	(1.03, 1.45)	1.14	(.86, 1.50)
College or More	1.14 *	(1.00, 1.30)	.69 ***	(.55, .86)
Civilian	1.05	(.92, 1.20)	1.64 ***	(1.31, 2.06)
Low Occupational Risk	.97	(.83, 1.13)	1.56 **	(1.18, 2.07)
Ever Smoked Cigarettes (ref=Never)	1.11	(1.00, 1.23)	.89	(.74, 1.07)
Ever Drank Alcohol (ref=Never)	.95	(.83, 1.08)	1.10	(.86, 1.41)
Constant	.20 ***	(.16, .25)	.06 ***	(.04, .09)

*p < .05, **p < .01, ***p < .001