12-4-2023

Duchenne Muscular Dystrophy: Age, Disease Stage, and Patient-Reported Quality of Life

Sheila Jagers
Walden University

Walden University

College of Health Sciences and Public Policy

This is to certify that the doctoral dissertation by

Sheila Jagers

has been found to be complete and satisfactory in all respects,
and that any and all revisions required by
the review committee have been made.

Review Committee
Dr. Tolulope Osoba, Committee Chairperson, Public Health Faculty
Dr. Hadi Danawi, Committee Member, Public Health Faculty

Chief Academic Officer and Provost
Sue Subocz, Ph.D.

Walden University
2023

Abstract

Duchenne Muscular Dystrophy: Age, Disease Stage, and Patient-Reported Quality of Life

by

Sheila Jagers

MBA, Eastern Michigan University 2000

BS, Howard University 1987

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Public Health

Walden University

November 2023

Abstract

Duchenne muscular dystrophy (DMD), a severe form of muscular dystrophy, is a rare neuromuscular disease that predominantly impacts males and is characterized by progressive muscle weakness, loss of ambulation, cardiac complications, and respiratory disease. Although several investigators have evaluated the influence of DMD on patient-reported quality of life (PRQoL), only a few studies exist investigating PRQoL in the adult DMD population. This cross-sectional quantitative analysis examined the association between age, disease stage, and PRQoL as the outcome and the covariates of education and ethnicity. The Ferrans et al. PRQoL model grounds this study, which expanded Wilson and Cleary's model by clarifying individual and environmental factors. A secondary dataset *(N* = 83) from the NeuroQOL Clinical Validation Study, a subset of the Patient-Reported Outcomes Measurement Information System, was used for descriptive and ordinal logistic regression analyses that were conducted. The results revealed that the variable Hispanic/non-Hispanic (0,1) and PRQoL was statistically significant *(p* = .001), indicating that non-Hispanic DMD male patients have a statistically significant better PRQoL than Hispanic DMD male patients. However, the models for the independent variables age (logit = .092, SE = .062, Wald = 2.206, *p* = .137) and disease stage (logit = -.004, *SE*=.151, Wald=.001) *p* = (.978) revealed no significant associations. These findings indicate the need for additional research to investigate other factors that may impact PRQoL. This study contributes to positive social change by highlighting the need for initiatives that address PRQoL in DMD male patients of Hispanic descent.

Duchenne Muscular Dystrophy: Age, Disease Stage, and Patient-Reported Quality of Life

by

Sheila Jagers

MBA, Eastern Michigan University, 2020

BS, Howard University 1987

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Public Health

Walden University

November 2023

Dedication

Above all, I dedicate this project to God Almighty. He gave me the strength, wisdom, and the resources to complete this journey. Also, I dedicate this dissertation to my loving and supportive mother, Jacqueline Stemley, and my sister, Dawn Godfrey, for her emotional and financial support. To my Children, Joshua Harris, and Brittney Harmon, for their encouragement and who will now address me as Dr. Mom. Next, to my mentor and friend Darryl Allen Bridges, who has supported and encouraged me through all the challenges of Doctoral school, work, and life.

Acknowledgments

I am grateful to my chair, Dr. Tolulope Osoba, and committee member, Dr. Hadi Danawi, for their guidance and support throughout the dissertation journey. Also, thank you, Dr. Zin M. Htway, for countless hours helping with the methodology sections.

Table of Contents

List of Tables

List of Figures

Chapter 1: Introduction to the Study

Introduction

Muscular dystrophy (MD) refers to a group of more than 30 genetic diseases that cause progressive weakness and degeneration of skeletal muscles (Sahay et al., 2019). All mutations progressively weaken muscles and eventually impact ambulation (Sahay et al., 2019). There are several types of MD; however, the most common types are: Duchenne muscular dystrophy (DMD), Becker muscular dystrophy (BMD), congenital muscular dystrophy, facioscapulohumeral muscular dystrophy (FSHD), and limb-girdle muscular dystrophy (LGMD) (Jacques et al., 2019). The most severe form of MD is DMD, a rare neuromuscular disease caused by a mutation of the X-chromosome and is marked by progressive muscle weakness associated with increased disability (Mullin et al., 2021). Although females may be carriers, they are usually mildly affected; Duchenne syndrome typically affects males (Sahay et al., 2019). In fact, DMD affects one in 3,600 to 6,000 live male births (Gocheva et al., 2019). Historically, by age nine, DMD males require wheelchairs for mobility (Szabo et al., 2022). In later stages, they develop respiratory and cardiac complications, resulting in death at the mean age of 19 years (Szabo et al., 2022). At this time, there is no cure; however, primary interventions of oral corticosteroids, ventilation, and rehabilitation management are linked to increased longevity, with a median survival rate of 28.1 years (95% CI 25.1, 30.3) in patients born after 1990 (Broomfield et al., 2021).

Four phases categorize DMD disease progression: early ambulatory (childhood), late ambulatory (late childhood/adolescent/young adult), early nonambulatory (adolescent/young adult), and late nonambulatory (adult) (Szabo et al., 2022). The limited

availability of quantitative studies investigating the natural history of DMD progression hinders the progression of disease treatment and quality of life outcomes (Mullin et al., 2021). Gocheva et al. (2019) showed that decreased motor function is a common condition associated with late-stage disease in the second decade of life and is a significant factor in PRQoL outcomes.

According to Medina et al. (2019), as the disease progresses, so does the economic burden of disease management; there is a 5.7-fold increase in cost from the early ambulatory phase to the non-ambulatory phase. Physical impairments seriously impact the patient-related quality of life (PRQoL), leading to psychological, functional, and social disorders and economic dilemmas (Medicina et al., 2020). Consequently, Szigyarto and Spitali (2018) posited that as the DMD population ages, we must understand the late-stage health profile and appropriate care for this emerging population.

According to El-Aloul et al. (2020), disease progression is associated with sleep disturbances, motor function, and decreased ability to conduct activities of daily living (ADLs), as evidenced by long-term survivors and caregivers. Similarly, Birnkrant et al. (2018) and Houwen-van Opstal et al. (2021) posited that due to progressive muscular degeneration, affected males endure secondary life-limiting conditions such as pain, insomnia, and gastric distress. DMD is considered the most common pediatric neuromuscular disorder, and advances in medical treatment have increased longevity beyond the second decade of life (Szabo et al., 2022). In light of advances in medical management, there has been an increased emphasis on the quality of life (QoL) in the adult population, precisely, the effect of disease progression on daily functioning, social adjustment, and overall well-being.

Chapter 1 covers a summary of the research literature on DMD, research gaps in adult males surviving beyond 18 years of life, the rationale for the study, the research and social problem, the purpose of the study, research questions, the Ferrans et al. (2005) conceptual HRQoL model, assumptions, scope, and delimitations impacting internal and external validity, limitations of secondary research and potential biases, and the implications for positive social change.

Problem Statement

Limited empirical research examines the association between age, disease progression, healthcare access, and patient-reported Quality of Life (PRQoL). Existent research documented the impact of PRQOL on DMD in children and adolescents (Crisafulli et al., 2020; Ryder et al., 2017). Natural history disease studies highlighted the importance of patient-reported outcomes, including HRQoL; however, little is known regarding factors that impact HRQoL in adult males with DMD (Otto et al., 2017; Szabo et al., 2022). Several investigators have studied the influence of DMD on PRQoL in children and adolescents, yet few studies evaluated QoL at the advanced stages of the disease, specifically in the adult population (Crisafulli et al., 2020). Moreover, less is known about the impact of QoL on the nonambulatory adult phase.

Purpose of the Study

My dissertation aimed to assess the association between age at diagnosis, disease stage, healthcare access, and the outcome of PRQoL in the adult population. I will use a quantitative cross-sectional approach to indicate any significant association between the independent variables of age, disease progression, and healthcare access and the outcome of the PRQoL for DMD adult males. In observational studies, PROs are recommended as

assessment instruments (Ferizovic et al., 2022; Otto et al., 2017). The health-related quality of life (HRQoL) construct has become an essential framework for health research, healthcare services, and health organizations (Ferizovic et al., 2022; Otto et al., 2017). Further research is required to identify the association between age, disease stage, healthcare access, and PRQoL to support public health initiatives for DMD males transitioning into adulthood. Hence, this study will fill the gap in research by focusing on factors affecting PRQoL in adults 18 years old and over.

Research Questions and Hypotheses

My dissertation aims to determine if there is a statistically significant association between the independent variables of age at diagnosis, disease stage, and healthcare access and the outcome of PRQoL of the DMD adult male. The following bivariate questions will guide this study:

RQ1: Is there an association between age at diagnosis and PRQoL among male DMD adult patients?

$H_0$1–There is no association between age at diagnosis and PRQoL among male DMD adult patients.

H_a1– There is an association between age at diagnosis and PRQoL male DMD adult patients.

RQ2: Is there an association between disease stage and PRQoL male DMD adult patients?

$H_0$2– There is no association between disease stage and PRQoL among male DMD adult patients.

H_a2– There is an association between disease stage and PRQoL among male DMD adult patients.

RQ3: Is there an association between healthcare access and PRQoL male DMD adult patients?

$H_0 3$– There is no association between healthcare access and PRQoL among male DMD adult patients.

$H_a 3$– There is an association between healthcare access and PRQOL among male DMD adult patients.

RQ4: Is there any association between age at diagnosis, disease stage, healthcare access, gender, race, ethnicity, education, income, and PRQOL among male DMD adult patients?

$H_0 4$- There is no statistically significant variation between PRQOL and age, gender, ethnicity, education, age at diagnosis, disease stage, and healthcare access male DMD adult patients.

$H_a 4$: There is a statistically significant variation between PRQOL and age, gender, race, ethnicity, education, age at diagnosis, disease stage, and healthcare access male DMD adult patients.

Theoretical Foundation for the Study

The Ferrans et al.'s (2005) PRQoL model grounds this study, which expanded Wilson and Cleary's model by clarifying individual and environmental factors (Bakas et al., 2012). "Ferrans' revised model is based on the ecological model of McLeroy and colleagues," to clarify the multiple layers of influence on health outcomes at both

individual and environmental levels in PRQoL (Ferrans et al., 2005, p. 337; McLeroy et al., 1988).

> McLeroy and colleagues' model indicates five levels of influence: (a) intrapersonal factors (characteristics of the individual), (b) interpersonal factors (formal and informal social support systems), (c) institutional factors (organizations such as schools and healthcare facilities), (d) community factors (relationships among institutions and informal social networks in a defined area), and (e) public policy [local, state, and national laws and policies] (Ferrans et al., 2005, p. 377).

Ferrans et al. (2005) classified the characteristics of the individual as demographic, developmental, psychological, and biological factors that influence health outcomes. In contrast, characteristics of the environment are either social or physical" (Ferrans et al., 2005). “Social and environmental characteristics are the interpersonal or social influences on health outcomes, including family, friends, and healthcare providers” (Ferrans et al., 2005, p. 337). This framework provides structure to my study because it emphasizes how patients value and prefer the overall quality of life.

The logical connections between the framework and my study's nature include physical impairments and psychological factors that negatively influence PRQoL. Characteristics of the individual encompass age, race, ethnicity, gender, and genetic diseases, commonly linked to illness (Ferrans et al., 2005). In contrast, biological function is influenced by both individuals and the environment (Ferrans et al., 2005). The quality of the environment, such as access to healthcare and the availability of neurologists, can influence age at diagnosis and disease stage at diagnosis. In contrast, biological function refers to the continuum that supports life, explaining disease severity,

disease progression, and the perception of health. “Alterations in the biological function directly or indirectly impact all components of health, such as functional status” (disease stage), symptoms (ambulatory status, cardiomyopathy, respiratory function), and overall quality of life (Ferrans et al., 2005, p. 338). Social factors, including race-ethnicity, healthcare access, and cultural beliefs, influence adherence to treatment, when and where treatment is sought, and consequently impact age at diagnosis, disease stage, healthcare access, and PRQoL (see Table 1).

Table 1

Matching Ferrans et al. (2005) Conceptual Framework with Study Variables

Ferrans et al. (2005) Conceptual Model of HRQoL	Study Variables	Coding Scheme PROMIS and Neuro-QOL
1- Intrapersonal (characteristic: Biological Function)	1- Age	Age: Continuous (in years)
2- Institutional (subset: Biological Function)	2- Healthcare Access (Insurance Type)	Categorical: 1=Private/Commercial, 2=Medicaid, 3=Uninsured, 4= Military/Tricare
23- Intrapersonal (characteristic: Functional Status)	3- Disease stage (Physical mobility) Measures reflecting physical functional status consist of two measures, Upper Extremity Function, Activities of daily living (ADL), and Lower Extremity Function	Ordinal: 5 = Without any Difficulty 4 = With a Little Difficulty 3 = With Some Difficulty 2 = With Much Difficulty 1 = Unable to Do
4- Interpersonal: (characteristic: Overall Quality of Life (QOL).	4- PRQoL: Measures reflecting PRQoL are (1) the Ability to Participate in Social Roles and Activities, (2) Satisfaction with social roles and activities, and (3) Positive Affect & Well-Being)	Ordinal: (1) Ability to participate in social roles and activities: (3)Positive Affect & Well-being 1 = Never 2 = Rarely 3 = Sometimes 4 = Often 5 = Always Ordinal: (2) Satisfaction with social roles and activities 1 = Not at all 2 = A little bit 3 = Somewhat 4 = Quite a bit 5 = Very much

Note: For an explanation of composite scoring for the Physical function construct, see appendix H and Appendix I for PRQoL construct.

Rationale for Composite Variables

Impaired physical mobility, most often seen in people with DMD, limits the body's independent and purposeful physical movement of one or more extremities. The physical restrictions result in negative consequences on an individual's physical function, such as upper extremity function, fine motor, and ADL (one's ability to carry out various activities involving digital, manual, and reach-related functions, ranging from fine motor to self-care); lower extremity function (the ability to carry out various activities involving the trunk region and increasing degrees of bodily movement, ambulation, balance, or endurance). Thus, the independent variable disease stage is a composite of two measures:(1) Upper Extremity Function (fine motor, activities of daily living) and (2) Lower Extremity Function(mobility). Schalet et al. (2021, p. 11) conceptually defined physical function as a composite of two measures (see Appendix E):

1. "Upper extremity function: One's ability to carry out various activities involving digital, manual and reach-related functions, ranging from fine motor to self-care (activities of daily living)"; and
2. "Lower extremity function: One's ability to carry out various activities involving the trunk region and increasing degrees of bodily movement, ambulation, balance, or endurance."

DMD Disease stage progression is characterized by muscle weakness, which limits activities of daily living (ADLs), upper extremity muscle function, and lower limb function (Kaat et al., 2019). Moreover, muscle weakness impairs the ability to walk or perform functional tasks, such as ADLs (Jacques et al., 2019). Consequently, researchers have used a composite of ADLs and upper and lower extremity measurements to operationalize

physical function (Jacques et al., 2019; Kaat et al., 2019). Also, the PROMIS uses a single physical function score (item bank) for adults consisting of three subsets (ADLs, upper extremity, and lower extremity/mobility (Cella et al., 2019; Kaat et al., 2019). Thus, I chose to use a composite of upper extremity function (fine motor, ADL) and lower extremity function (mobility) to characterize the physical function.

At the same time, subjective PRQoL is conceptualized as a multidimensional construct of discrete domains that include psychological well-being, social relationships, functional roles, and perceptions of life satisfaction (Gil-González et al., 2020). Consequently, the outcome variable PRQoL is a composite of three measures conceptually defined by Schalet et al. (202, p. 11):

1. Ability to Participate in Social Roles and Activities: Degree of involvement in one's usual social roles, activities, and responsibilities, including work, family, friends, and leisure
2. Satisfaction with social roles and activities: Satisfaction with involvement in one's usual social roles, activities, and responsibilities, including work, family, friends, and leisure and
3. Positive Affect & Well-Being: Aspects of a person's life that relate to a sense of well-being, life satisfaction, or an overall sense of purpose and meaning.

The disease stage (physical function) consists of two measures that use an ordinal scale of one to five (see Table 2); consequently, the composite score range is two to ten. Meanwhile, the PRQoL variable is a composite of three measures with an ordinal scale of one to five (see Appendix H). The composite score range is 23 to 115. A common practice for controlling a type 1 error rate is using composite variables, multicollinearity

for regression analysis, or organizing multiple highly correlated variables into more digestible or meaningful information (Dong et al., 2019; Song et al., 2013).

Table 1

Rational for Composite Variables

Study Variable	Composite Measure	Operational Definition	Activity Examples
Disease Stage Upper Extremity ADL	Upper Extremity Function(Fine Motor Skills, ADL)	One's ability to carry out various activities involving digital, manual, and reach-related functions, ranging from fine motor to self-care (activities of daily living)	Dexterity: Griping objects, buttoning shirt, keypad usage; ADL; errands, bathing, brushing teeth
Disease Stage Lower Extremity	Lower Extremity Function (Mobility)	One's ability to carry out various activities involving the trunk region and increasing degrees of bodily movement, ambulation, balance, or endurance	Mobility: Walking for at least 15 minutes, arising, getting out of bed
Patient-Reported Quality of Life (PRQoL) (1)	Ability to Participate in Social Roles and Activities	Degree of involvement in one's usual social roles, activities, and responsibilities, including work, family, friends, and leisure	Perform daily routines, keep work responsibilities, and leisure activities, keep social commitments
PRQoL (2)	Satisfaction with Social Roles and Activities	Satisfaction with involvement in one's usual social roles, activities, and responsibilities, including work, family, friends, and leisure	Ability to meet friends, attend outside-of-home events, satisfied with ability to work and household activities
PRQoL (3)	Positive Affect and Well-Being	Aspects of a person's life relate to well-being, life satisfaction, or an overall sense of purpose and meaning.	feeling hopeful, life satisfaction, life purpose, life balance, meaningful life

Note: From "Neuro-QOL: Quality of life item banks for adults with neurological disorders: item development and calibrations based upon clinical and general population testing," by Gershon et al. (2012).

Nature of the Study

By utilizing a cross-sectional research design, my study will assess if there is an association between age at diagnosis, disease stage, healthcare access, and PRQoL in adult male DMD patients. This study will follow the strengthening the reporting of observational studies in epidemiology (STROBE) guideline, consisting of 22 items in the STROBE Statement, with recommendations about what should be included in a more accurate and complete description of observational studies (Cuschieri, 2019). The STROBE guidelines aim to strengthen the quality of reporting in observational studies. I utilized a quantitative approach to evaluate the association between age, disease progression, healthcare access, and PRQoL in DMD adults in their twenties and thirties.

My study used three patient-identified database links in the Patient-Reported Outcomes Measurement Information System v1.0/1.2 (PROMIS) Global Health instruments to assess an individual's physical, mental, and social health. PROMIS measures are general, not disease-specific, and are therefore universally applicable within and across disease populations (Cohen et al., 2021). The dataset for my dissertation PROsetta Stone Wave 2 consists of a merged dataset linking PROMIS "measures in the Social, Sleep, Cognition, and Psychological Well Being subdomains and related instruments from Toolbox and Neuro-QOL, as well as between the PROMIS Global and VR-12 forms using a unique response identification number (Cella, 2017). In summary, my dissertation dataset is one merged database.

1. Patient-Reported and Parent Proxy Global Outcomes Measurement Information System (PROMIS) assesses the child's overall physical, mental, and social health

evaluations. The seven-item pediatric and parent proxy global health index includes a single factor that results in one global score (0-100).

2. Quality of Life in Neurological Disorders (Neuro-QOL): Neuro-QOL: Item banks include self-report physical, mental, and social health. Also included is a domain-specific to targeted diseases (Duchene Muscular Dystrophy)
3. NIH Toolbox for the Assessment of Neurological and Behavioral Function® (N.I.H. Toolbox®): includes diverse populations (race and ethnicity), children and adults ages three to 85, and access, cognition, motor, sensation, and emotion. NIH performance measures: mean=100 (SD=15), unadjusted scale score, age-adjusted scale score, and fully adjusted scale score. Raw scores are also available to match PROMIS: T-score mean =50 (SD=10).

The PROMIS study was chosen because the questions in the survey were related to the critical variables of the research study. It provided sufficient data to answer the research questions and hypotheses.

Definition of Terms

Ability to participate in social roles and activities: The degree of involvement in one's usual social roles, activities, and responsibilities, including work, family, friends, and leisure" (Gershon, 2012, p. 11).

Cardiomyopathy: Involves problems with the heart muscle that can make it harder for the heart to pump blood (Merriam-Webster, n.d.).

Duchenne muscular dystrophy (DMD) diagnosis: The diagnosis is based on a thorough clinical evaluation, a detailed patient history, and various specialized tests, including molecular genetic tests (Jacques et al., 2019).

Duchenne muscular dystrophy (DMD) disease progression: The diseases is classified into four stages: (1) the early phase lasts until around age seven, (2) the transitional stage, ages six to nine, (3) loss of ambulation, and (4) the adult phase, age 15 and over (Landfeldt et al., 2020).

Duchenne muscular dystrophy (DMD): A genetic disease caused by a mutation of the dystrophin protein, which causes progressive muscle degeneration and weakness (Morrison, 201; Brusa et al., 2020).

Dystrophin: A protein that helps maintain the shape and structure of muscle fibers (Frew et al., 2017).

Functional status: Is "the capacity to engage in activities of daily living and social activities" (Starfield et al., 1995).

Healthcare access: It is classified by insurance types, such as commercial insurance, military, government insurance (Medicare, Medicaid), and self-pay.

Health-related quality of life (HRQoL): This is a domain that includes physical, psychological, and social domains of health influenced by a person's experiences, beliefs, expectations, and perceptions (Frew et al., 2017).

Health status: A person's current state of health, including functional status, morbidity, physiologic outcomes, and some notion of well-being ((Merriam-Webster, n.d.).

Lower extremity function: "One's ability to carry out various activities involving the trunk region and increasing degrees of bodily movement, ambulation, balance or endurance" (Gershon et al., 2012, p 11).

Motor function: Indicates the current physical health status, disease burden, and long-term health outcomes and is integrally related to daily functioning and quality of life (Cella,2017).

Neuromuscular disorders: Refer to inherited and acquired medical conditions associated with the peripheral nervous system (PNS), including the anterior horn cell, the peripheral nerve, the neuromuscular junction, and muscles (Dowling et al., 2018).

Neuro-QoL™ (Quality of Life in Neurological Disorders): Is a measurement system that evaluates and monitors the physical, mental, and social effects experienced by adults and children living with neurological conditions (National Institute of Neurological Disorders and Stroke (NINDS, 2015).

Patient-Reported Quality of Life (PRQoL): Is the Quality of life components reported by the patient, including health conditions and behaviors (Post, 2014).

Positive Affect & Well-Being: "Aspects of a person's life that relate to a sense of well-being, life satisfaction, or an overall sense of purpose and meaning" (Gershon et al., 2012, p. 11).

Satisfaction with social roles and activities: "The Satisfaction with involvement in one's usual social roles, activities, and responsibilities, including work, family, friends, and leisure" (Gershon et al., 2012, p. 11).

Socioeconomic status: The Social standing or class of an individual or group. It is often measured as a combination of education, income, and occupation (National Institute of Health [NIH], 2021).

Upper extremity function: "One's ability to carry out various activities involving digital, manual and reach-related functions, ranging from fine motor to self-care such as activities of daily living" (Gershon et al., 2012, p. 11).

Assumptions

In my dissertation, I assumed that the data collected by the NIH Toolbox for the Assessment of Neurological and Behavioral Function were accurate and reflected the assumptions of my study. Also, I assumed the data was collected as described in the dataset's documentation. Furthermore, it is assumed that the Neuro-QoL instrument represents the variables relevant to my study: age, disease stage, healthcare access, and the outcome variable PRQoL. These assumptions are necessary because I relied on the secondary data provided by the NIH Toolkit for analysis of the relationship between age, disease stage, healthcare access, and PRQoL in health-related diseases such as DMD.

Scope and Delimitations

PROMIS®, Neuro-QoL™, and the self-report patient-reported outcome (PRO) measures of NIH Toolbox® use a T-score metric in which 50 is the mean of a relevant reference population, and 10 is the standard deviation (SD) of that population. The NIH Toolbox performance tests of cognitive, motor, and sensory function use standard scores but not T-scores. Health Measures is the official information and distribution center for PROMIS®, Neuro-QoL, N.I.H. Toolbox®, and ASCQ-Me® developed and evaluated with NIH funding. Likewise, (Valentine et al., 2019) validated the Neuro-QoL for common neurological conditions with state-of-the-science methods to be psychometrically sound.

There are difficulties in measuring QoL in children; however, studies show that children reliably report their own QoL from age eight (Powell et al., 2020). Comparable

measurement of QoL from childhood into adulthood has methodological challenges, which could be mitigated by using a suitable Patient Reported Outcome Measure (PROM) across ages, such as Neuro-QoL (Powell et al., 2020). Response shift is also a potential problem with any PROM. Response shift (Vanier et al., 2021) is an effect occurring whenever observed change (e.g., change in patient-reported outcome measures (PROM) scores is not fully explained by target change (i.e., change in the construct intended to be measured). Distinguishing the measure (PROM) from the underlying target construct (PRQoL) at two-time points delineates the plausible primary paths and clarifies the model's underlying assumptions (Vanier et al., 2021). Lastly, because this is a cross-sectional study, causal conclusions are limited.

Limitations

A potential disadvantage of secondary survey data is that it may not address my dissertation's research questions. Also, survey data potentially contains recall bias. Moreover, patient-reported outcomes measurement development for rare diseases has lagged behind more common diseases (Valentine et al., 2019). Because the design of the original study is cross-sectional, causation cannot be ascertained. Therefore, further research is needed to confirm causality between age, disease stage, healthcare access, and PRQoL in adult DMD males.

The outcome variable (PRQoL) is a composite of the Ability to Participate in Social Roles and Activities, Satisfaction with social roles and activities, and Positive Affect & Well-Being. Song et al. (2013) and Dong et al. (2019) asserted that using composite variables is common for controlling Type I error rates, addressing multicollinearity for regression analysis, or organizing multiple highly correlated

variables into more digestible or meaningful information. However, combining related variables into a composite variable can include alterations of the relationship strength with outside variables (e.g., outcome variables), changes in statistical power, over-reduction or loss of information, and challenges in interpreting the composite variable itself or the relationships with outside variables.

PRQoL and HRQoL in several peer-reviewed studies are used interchangeably. QoL has validated instruments with numerous definitions with and without "the "HRQoL qualifiers (Costa et al., 2021); many instruments attempt to measure it. Therefore, interpreting any empirical statement about QOL will depend on how it is defined and assessed (Costa et al., 2021). Patient-reported outcome (PRO) measures are an established method for tracking outcomes in DMD; however, it is time-consuming and results in barriers to implementation. Regardless of barriers, Medina et al. (2019) patient-reported outcomes (PROs) support patient-centered care, provide patients with an alternative means of communication, and provide clinicians with visual, quantitative values that may provide further insight into the natural history of the disease.

Significance

The impact of disease on health-related quality of life and understanding the association of health-related quality of life to motor function can provide helpful information for medical care, education, and welfare decision-making (Gocheva et al., 2019). Because DMD is associated with increased accumulation of disability and morbidity, as life expectancy improves, additional efforts maintain and promote patient quality of life, particularly mental well-being, in advanced stages of the disease, particularly in patients (Landfeldt et al., 2020). Insights from this study potentially

highlight the patient-specific quality of life factors that affect the PRQoL of adult males with DMD. Physical impairments increase with age; given the extended life expectancy, additional efforts are required to maintain and promote patient quality of life, especially in advanced stages of the disease, such as normative aspirations: employment and independent living (Landfeldt et al., 2020). A fundamental component of normalcy is the opportunity to socialize and have relationships (Hoskin, 2021). Public health initiatives are essential to support positive health outcomes as these patients transition to adulthood.

Summary

Chapter one discussed the problem and purpose of exploring age, disease stage, and healthcare access in PRQoL outcomes in the adult male surviving the second decade of life. I also discussed the background of the study, the research questions, the conceptual framework, and the nature of the study. I provided the assumptions, the scope and delimitations, and limitations that may affect the study. Within Chapter one, I also discussed the background of the study, the research questions, the conceptual framework, and the nature of the study. I provided the assumptions, the scope and delimitations, and limitations that may affect the study.

DMD is a debilitating genetic neuromuscular disease that majority impacts males. Innovative treatments have increased longevity extending into the second decade of life. However, social interventions have not met the demands of this growing population. This quantitative study investigates the association between age, disease progression, and healthcare access of DMD adult males' patient-reported quality of life outcomes. Previous research examined PRQoL in DMD pediatric populations, but less research extends into the adult population (Szabo et al., 2022). My literature review illustrated

limited information regarding age at diagnosis, disease stage, health care access, and PRQoL in adult DMD males. Thus, it is essential to investigate further the disease impact of DMD on the PRQoL of adult males.

The independent variables for my study are age at diagnosis, disease stage, and healthcare access in DMD adult males are related to questions one, two, and three. One dependent variable for my study is the patient-reported quality of life, measured using a composite variable. I utilized secondary data for this study provided by the National Institutes of Health [NIH] (2021) tool kit, which minimized resource constraints in data retrieval and design methodology. Within Chapter one, I also discussed the background of the study, the research questions, the conceptual framework, and the nature of the study. I provided the assumptions, the scope and delimitations, and limitations that may affect the study.

Chapter 2 contains a comprehensive review of the literature on the effects of DMD, treatment models, literature search strategies, and theoretical foundations that frame the study. Literature reviews pertinent to PRQoL outcomes are at the core of this study. The first section describes DMD, including etiology, diagnosis, disease progression, associated complications, and comorbidities. Second, the current practice of disease management and established clinical guidelines were reviewed. The third section includes a broad overview of PRQoL and considerations when measuring this construct. Finally, the chapter addressed known factors associated with PRQOL in adult males aged 18 and over.

Chapter 2: Literature Review

Restatement of the Problem and Purpose

DMD is a rare form of MD, estimated to impact between 1 in 3,500 and 5,000 live male births (Ferizovic et al., 2022). Although patients with DMD are diagnosed at approximately four years old, many are symptomatic earlier due to symptoms of proximal muscle weakness, displayed as delayed physical milestones: walking, running, and climbing stairs (Ferizovic et al., 2022). Patients begin to show signs of disease progression in their early teens and become nonambulatory, followed by increasing loss of upper limb strength and function (Ferizovic et al., 2022). As the disease progresses, patients experience respiratory and cardiac medical declines, eventually requiring mechanical ventilation support for survival, and have an increased risk of cognitive decline and psychological problems (Ferizovic et al., 2022). Consequently, the estimated median life expectancy at birth is 30 years (Landfeldt et al., 2020). Currently, there is no cure for DMD; the standard of care is palliatively aimed at managing symptoms and promoting the patient's QoL.

Adult males with DMD endure physical degeneration, which potentially alters their ability to perform activities of daily living, participate in social roles and activities, be satisfied with social roles and activities, and have a positive effect. These changes might significantly affect the patient's quality of life. Health organizations, physicians, social workers, educators, and DMD caregivers have provided feedback that early diagnosis, early intervention, and healthcare access positively impact the patient-reported quality of life outcomes. However, there is limited empirical research correlating the association of age at diagnosis, disease stage, and healthcare access. Hence, this study

will fill the gap in research by focusing on factors affecting PRQoL in adults 18 years old and over. My study aims to quantitatively assess the association between age, disease stage, healthcare access, and patient-reported quality of life (QOL).

Synopsis: Current Literature that Established Relevance of the Problem

Natural history studies highlight the importance of PRQoL outcomes; however, little is known about the factors such as age, disease progression, and healthcare access that impact PRQoL in adult males. Previous research on the hypothesized link between age, disease stage, and healthcare access to PRQOL outcomes has led to several investigational studies (Counterman et al., 2020; Jacques et al., 2019; Liang et al., 2019; Park et al., 2019). While several studies have investigated the association of the independent variables (age, disease stage, healthcare access) or a combination of the independent variables, after an extensive review of the literature, the results of my literary search failed to identify any studies linking all three independent variables age, disease stage, and healthcare access to PRQoL outcomes in adults with DMD. Studies by Counterman et al. (2020), Obeidat et al. (2021), and Vaidya and Boes (2018) examined the relationship between age at diagnosis and quality of life in children with DMD; still, they did not address QoL in adults during the later stages of the disease.

In contrast, using data from a clinical trial, Szabo et al. (2022) evaluated the association between the mean health state utility values by age and ambulatory status in placebo-treated ambulant DMD males; the authors found that the mean PRQoL utility values declined more in older DMD males compared to young DMD males. At the same time, Counterman et al. (2020) identified a correlation between age at diagnosis to healthcare access.

Fatigue, pain, and physical mobility impact activities of daily living (ADLs) and ultimately impact PRQoL. Jacques et al. (2019) and Powell et al. (2019) evaluated muscle weakness, ambulation, and pain in DMD patients and QoL; they also ascertained an association between disease stage and ADL performance in long-term survivors and caregivers. Moreover, Andreozzi et al. (2022), Birnkrant et al. (2018), El-Aloul et al. (2020) and Houwen-van Opstal et al. (2021), investigated the association between disease stage, disease severity, and HRQoL. Likewise, Gocheva et al. (2019) assessed the association between motor function (ambulatory, nonambulatory) and PRQoL. Regarding healthcare access, Szabo et al. (2022) conducted a qualitative study to identify societal value perspectives beyond healthcare cost and the importance of attributes that enhance QoL.

The full range of factors that affect QoL in DMD is currently unknown. The perspective from which QoL is measured may also differ. Additionally, a definitive list of factors that impact the QoL of the DMD patient is unknown because the perspective of how QoL is measured differs (Kwon et al., 2022; Uttley et al., 2018). Numerous studies investigate the quality and validity of instruments in capturing PRQoL in DMD patients. Rowen et al. (2021) investigated a preference-based measure for capturing people with DMD quality of life using a new measure, the DMD-QoL.

Comparatively, Powell et al. (2020) utilized a mixed-method approach to assess the content and face validity of the DMD-QoL, a fourteen-item QoL patient-reported outcome measurement (PROM) for boys and men with DMD. Propp et al. (2019) evaluated a patient-reported outcome measure that comprehensively captures the health-related priorities of children with DMD; however, this instrument does not incorporate

the adult DMD male. Propp et al. (2019) also utilized the priority framework of outcomes assessment to develop a priority framework of outcomes measurement (PROM) that comprehensively addresses the disease related PRQoL priorities of children and parents with DMD but omits the DMD adult.

Preview of the Major Sections of the Chapter

The major sections of this chapter are devoted to the literature search strategy, theoretical foundation, a literature review related to the key variables, and the summary and conclusions. The first section describes DMD, including etiology, diagnosis, disease progression, and disease management. Next, the risk factors for disease progression are discussed. The third section includes a broad overview of Ferrans et al. (2005) HRQoL conceptual model and considerations when measuring this model. Finally, the chapter discusses known factors associated with HRQOL in adult males with DMD. A discussion of each independent variable, study design, and theoretical framework is included in the literature review.

Literature Search Strategy

In my preliminary literature search, I searched for relevant literature using the Thoreau search engine, which queries several databases simultaneously, including MEDLINE with Full Text/PubMed, CINAHL, PsycINFO, Socindex, ScienceDirect, Academic Search, and Education Source. The search was limited to peer-reviewed scholarly articles limited to the years 2017-2022, using the search terms Duchene (30,951 results); Duchene + quality of life or well-being, or life satisfaction (1,259 results); Duchene + quality of life or well-being, or life satisfaction+ child or pediatric or pediatric or children (663 results);); Duchene + quality of life or well-being, or life satisfaction+

child or pediatric or pediatric or children + quantitative or statistic or correlation (266 results); Duchene + quality of life or well-being, or life satisfaction+ child or pediatric or pediatric or children + quantitative (104 results).

I further searched the same databases for muscular dystrophy, age at diagnosis, early intervention, DMD, QoL, HRQoL, and PRQoL (see Appendix A). Also, additional searches were conducted to delineate the research variables age, QoL, and healthcare access (see Appendix B). Finally, I reviewed published books and approved dissertations for scholarly literature needed for my research.

Theoretical Framework

Theoretical constructs provide an integrative approach to hypothesis testing (Jespersen et al., 2018). The health-related quality of life model incorporates health aspects that influence an individual's quality of life (Jespersen et al., 2018). Also, QoL is broadly accepted as a multidimensional construct, including physical, mental, and social dimensions (Jespersen et al., 2018). Matching variables to constructs identify what needs to be assessed and provide a better understanding of the HRQoL phenomenon (see Table 1). Although HRQoL is used in the literature interchangeably with QoL, Faison et al. (2016) asserted that HRQoL pertains to the QoL of an individual's state of health over time. For purposes of my research study, HRQoL is patient-reported. Consequently, HRQoL is used interchangeably with PRQoL.

According to Bakas et al. (2012), the most used HRQoL models were based on work by Wilson and Cleary, the revised model by Ferrans et al. (2005) and the World Health Organization (WHO). Ferrans and Power's Health-Related Quality of Life guided and informed the potential relationship between age, disease stage, healthcare access, and

PRQoL in DMD adult males. Bakas et al. (2012) concluded that Ferrans and Powers' revision of Wilson and Cleary's model appears to have the most significant potential to guide HRQOL research and practice and recommend Ferrans et al. (2005) model due to the addition of the individual and environmental characteristics to the standard Wilson and Cleary model which better explains HRQoL concepts.

Assessment of Health-Related Quality of Life

As a quantitative indicator of health-related quality of life (HRQoL), the health utility reflects people's preference for a specific health condition (Zhou et al., 2021). Traditionally, health utility is measured on a scale from zero to one, where zero represents death, and one represents total health (Zhou et al., 2021). Low utility values represent poor health, and a negative value is perceived as worse than death (Zhou et al., 2021). There are several preference-based measurement tools for health utility. Health utility questionnaires are primarily condition-specific or generic (Jespersen et al., 2018). There is considerable variability between disease-specific and generic instruments in measuring HRQoL in pediatric and adult populations. One strength of generic measures is that it provides a method to compare various disease groups to health controls (Solans et al., 2008). In contrast, disease-specific instruments expand on generic QoL instruments by incorporating attributes or conditions common to the disease (Szabo et al., 2022).

Ferrans et al. (2005) Health-Related Quality of Life Model

As previously stated in Chapter 1, Ferrans et al. (2005) PRQoL model grounds this study, which expanded Wilson and Cleary's model by clarifying individual and environmental factors (Bakas et al., 2012). Ferrans' "revised model is based on the ecological model of McLeroy and colleagues" (McLeroy et al., 1988; Ferrans et al., 2005,

p. 337), as modified by Eyler et al. (2002) to clarify the multiple layers of influence on health outcomes at both individual and environmental levels in PRQoL (Ferrans et al., 2005). Ferrans and Powers' HRQoL model operationalizes QoL as the subjective evaluation of wellness and life satisfaction, including physical function, physiological, psychological, sociological, emotional, and cognitive (Faison et al., 2016). Patient-reported outcomes of HRQoL provide crucial information on disease burden that is patient-specific. The HRQoL model offers insights into individual and environmental characteristics influencing health behaviors and outcomes.

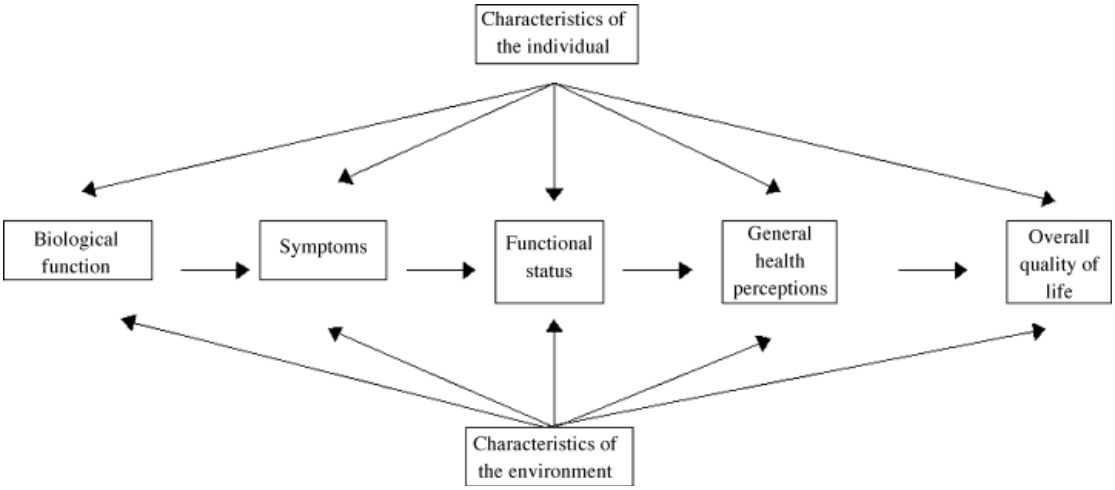
Applicability of the Five Domains of Ferrans et al. (2005) HRQOL Model

Among the five main concepts of the conceptual model, Ferrans et al. (2005) proposed that a sequence of unidirectional associations began with biological function, extended through symptoms, functional status, and general health perceptions, and ended with overall QOL. DMD disease onset is in early childhood, and disease severity increases with age, potentially negatively impacting HRQoL across the continuum. The HRQoL model was an appropriate framework for this research because it measures QoL outcomes across the lifespan using individual and environmental characteristics (Duangchan & Matthews, 2021). The five health outcomes align with the natural history of DMD: biological function and demographics (age, race, ethnicity, healthcare access, inherited X-linked recessive gene); symptoms (ambulatory status, upper body strength, respiratory status, cardiac symptoms); functional status (ability to perform activities of daily living [ADLs], loss of ambulation, disease severity, physical ability); general health perceptions (overall health typically assessed with a single ranked question); overall quality of life]subjective well-being and “life satisfaction determined by” an individual's

"evaluation of attributes of various domains of life" (Ferrans et al., 2005, p. 341). I drew from the five domains of the HRQoL model to align the RQs and the conceptual framework for this study (see Figure 1).

Figure 1

Health Related Quality of Life



Note: This figure illustrates the revised Wilson and Cleary model for health-related quality of life. Adapted from "Linking Clinical Variables with Health-Related Quality of Life: A Conceptual Model of Patient Outcomes," by I. B. Wilson and P. D. Cleary, 1995.

Literature Review Related to the Key Variables and Concepts

Health-Related Quality of Life and DMD

My study aimed to determine if there was a statistical significance between age, disease stage, and healthcare access on the predictions of PRQoL of the DMD adult male. Natural history studies highlight the importance of patient-reported Quality of life (PRQoL) outcomes; however, little is known about the factors such as age, disease progression, and healthcare access that impact PRQoL in adult males.

Age and PRQoL

The birth prevalence of DMD is estimated to be one in every 3,500 live male births. The age of onset is usually between 3 and 5 years of age (Ferizovic et al., 2022).

There is reason to believe that age at diagnosis impacts the PRQoL of male adult patients in that delayed diagnosis negatively impacts PRQoL (Szabo et al., 2022). Comparatively, Liang et al. (2019) discovered a statistically significant association between age and the clinical disease stage of boys with DMD; the higher the age or severity of the disease was negatively associated with the social and emotional functioning of patients and families. Existent research exemplified that DMD children and adolescents experience lower overall HRQoL comparative to their age groups without the disease (Bray et al., 2020; Brogna et al., 2019; Jacques et al., 2019; McDonald & Mercuri, 2018; Nagy et al., 2019). However, there is a paucity of evidence investigating the association between age and QoL in adult patients (Uttley et al., 2018). Thus, robust studies are required that investigate PRQoL age at diagnosis and rates of disease progression (Powell et al., 2019).

Physical dysfunction, such as missed milestones, manifests in children with DMD as early as two years due to an absence of the dystrophin protein, which causes muscle damage and progressive weakness (Rowen et al., 2021). Over time, gradual impairments impact mobility, respiratory, and cardiac dysfunction, thus, resulting in a shortened life expectancy at a median of 30 years. Based on the degenerative natural history of DMD, age is frequently used as a proxy for disease severity. Older age, longer illness duration, and greater disease severity are associated with lower perceived health-related quality of life (HRQOL) in individuals with neurodegenerative diseases (Bann et al., 2015; Carlton et al., 2022). Consequently, increasing age is often associated with worsening HRQoL; however, the association between age and decreased HRQoL has not been well defined. Likewise, the transition period between the teenage years to the twenties has profound implications due to increased independence and adult role attainment, which may impact

their QoL (Peay et al., 2022). In a self-reported survey on adult transition, males with Duchenne and Becker muscular dystrophy (DBMD) aged 16-30 reported self-care, social, employment, and economic challenges to adult role attainment (Jacques et al., 2019; Peay et al., 2022). For example, in a subset analysis of the Muscular Dystrophy Surveillance Tracking and Research Network (MD STARnet) Health Care Transitions and Other Life Experiences Survey, Peay et al. (2022) found that in patients with DMD (*n*=45), seven percent reported being to perform activities of daily living (ADLs), 76 percent reported spending social time with friends; four percent reported being employed full or part-time, and 33 percent reported students.

DMD and Adulthood

As DMD males transition into adulthood, limiting factors, including physical and medical complications, hamper the transition from adolescence to adulthood, as young DMD males rely on others to support ADLs. Reduction of ambulation reduces independence and potentially increases the risk of social isolation from peers (Weerkamp et al., 2022). After high school, personal contact and social engagement become more challenging in young adulthood for patients with DMD (Weerkamp et al., 2022). With disease progression, adult patients have an increased risk of depression and anxiety; adults report increased anxiety when transitioning to a wheelchair or ventilatory support (Weerkamp et al., 2022). As previously mentioned, the literature on the psychosocial aspects of DMD is diverse, as many adult males are psychosocially well-adjusted (Andrews & Wahl, 2018; Obeidat et al., 2021; Peay et al., 2022). It is assumed that DMD patients learn to adjust in the advanced stages of the disease (Weerkamp et al., 2022).

These findings emphasize the importance and the challenge of assessing HRQoL with adjusting to a chronic and progressive disorder from childhood into adulthood.

Disease Stage and PRQOL

Muscle weakness is a defining characteristic of Muscular Dystrophy (MD); however, quantitative methods evaluating QoL in adults with DMD are limited (Jacques et al., 2019; Powell et al., 2019). Irrespective of MD classification, all MDs typically involve declining muscle strength and eventual loss of ambulation, which may impact the perception of QoL (Powell et al., 2019). Also, Powell et al. (2019) research to date has focused on the progressive loss of muscular function with MD rather than on associations between QoL and objective measures of muscle strength in the adult MD population. Powell et al. (2019) conducted an investigational study of 75 males, including DMD patients; participants completed a survey that measured QoL, Knee-Extension Maximal Voluntary Contraction (KEMVC), Fatigue, Pain, Self-Efficacy, and Activities of Daily Living (ADL). Within the domain of MD classifications, Powell et al. (2019) identified differences in the domain of mental health perceptions; consequently, the authors discovered a necessity for research that provides an in-depth understanding of the mental well-being, independence, and management of fatigue and pain, which are required to improve QoL for adults with MD.

According to El-Aloul et al. (2020), DMD disease progression is associated with sleep disturbances, motor function, and decreased ability to conduct activities of daily living (ADLs), as evidenced by long-term survivors and caregivers. Similarly, Birnkrant et al. (2018, as cited in Houwen-van Opstal et al., 2021) posited that due to progressive

muscular degeneration, affected males endure secondary life-limiting conditions such as pain, insomnia, and gastric distress.

Wasilewska et al. (2020) list the milestones in DMD disease progression as loss of ambulation, loss of upper limb manipulation, malnutrition, heart failure, and respiratory insufficiency. Thus, it may be intuitive that HRQoL would decline with disease progression (adult-stage) due to disease progression; however, the relationship remains unclear (Szabo et al., 2022). Conflicts exist in the literature research regarding PRQoL and DMD, most likely due to the inconsistencies in the various definitions/constructs of HRQoL and the discrepancy in the methodology (i.e., instruments, information type). In a systematic review synthesizing the health state utility perspective of DMD patients and their families, Szabo et al. (2022) reported that patient and caregiver utilities trended lower with higher disease severity. Likewise, Insufficient evidence exists in the current body of research investigating the association between disease stage and PRQoL, specifically in the population over 20 years old; thus, to reflect the disease lifespan, future studies should include data characterized by age, ambulatory status, and disease severity to investigate the QoL as the impact as the disease progresses (Crisafulli et al., 2020; Solichin et al., 2021). Comparatively, In 2019, Gocheva et al. investigated the association between ambulatory and non-ambulatory DMD patients in PRQoL and motor function. Gocheva et al. (2019) found a discrepancy between the HRQoL index between DMD parents and their children; consistent with previous studies, parents evaluated their child's QoL as lower than their children's QoL rating, which is constant in other DMD studies and pediatric chronic illness. Gocheva et al. (2019) found

a gap in the research of longitudinal studies that provide insight into the intricacy of the association between health-related quality of life and functional performance.

Similarly, in a meta-analysis, Szabo et al. (2022) evaluated the health state utilities of DMD patients and their caregivers; they concluded that significant empirical evidence links disease progression with lower health utility scores. However, Szabo et al. (2022) posited that the body of evidence is limited in linking the late stages of the disease, particularly in non-ambulatory DMD patients. Likewise, Staunton et al. (2021) posited that no global impression of DMD disease-specific functional change dimensions exists that directly access the symptoms of disease progression and functional abilities necessary from the DMD patient perspective. The most frequently reported symptoms for ambulant individuals with DMD, caregivers, and clinicians were weakness, fatigue, cardiac difficulties, and pain. Across the domains of HRQoL (physical, mental, emotional, and social functioning), consistent differences in scores are observed in areas related to physical functioning (Bray et al., 2020; Lim et al., 2019). In a self-reported HRQoL study, DMD males reported their QoL as being poorer than the general population; however, the most significant deviation reported was in the physical function domain (Lim et al., 2019). Furthermore, in a cross-sectional study investigating The HRQoL of DMD patients and caregivers, Andreozzi et al. (2022) discovered a significant negative impact between DMD disease progression and patient HRQoL, as well as caregivers' ability to conduct their activities of daily living (ADLs).

Healthcare Access PRQoL

It is conceivable that insurance coverage impacts the age at which DMD is diagnosed. A recent study identified an association between race/ethnicity and age at

diagnosis. The estimated age of diagnosis for non-Caucasian patients was nine months later than for Caucasian patients (Counterman et al., 2020). The authors speculated that the disparity might be attributed to insurance type, as a significantly higher percentage of Caucasian (27%) patients were insured compared to non-Caucasians (13%) (Counterman et al., 2020).

Counterman et al. (2020) also identified a significant correlation between age at diagnosis and healthcare access (insurance type). This study provides insights into the socioeconomic factors associated with age at diagnosis that were not addressed in previous studies, including insurance type, education, unemployment rates, geographic location, and median household income. Regardless of disease type, insurance positively impacts childhood health and has lasting effects on adult QoL (Counterman et al., 2020).

As previously mentioned, DMD is a rare disease. Caregivers of children with rare diseases play a crucial role in their affected children's physical and emotional well-being (Boettcher et al., 2021). Rare disease caregivers share similar difficulties in caring for their affected children, Boettcher et al., 2021 including access to quality healthcare, disease-specific specialists, and overall healthcare access.

Covariates' Association with PRQoL: Age, Race, Ethnicity, Education, and Income

Socioeconomic status (income and education) may influence PRQoL. Patients with severe diseases from lower socioeconomic backgrounds experience reduced PRQoL than patients with high socioeconomic status (SES), independent of disease severity (Gocheva et al., 2019). Additionally, regarding race, Caucasian children are diagnosed with DMD earlier than Black and Hispanic children, and the gap widens later in the diagnostic process (Barnard et al., 2020). Inconsistent evidence exists evaluating the

influence of SES and psychosocial factors (social support, cultural climate) on PRQoL in DMD adult patients, thus warranting further investigation. Additionally, in a cross-sectional study evaluating the QoL of multiple sclerosis (MS) patients, Naseri et al. (2020) found that the severity of the disease, education, and age are related to the health condition of MS patients. Although the study population did not specifically mention DMD patients, DMD is a subset of MS.

Counterman et al. (2020) conducted a cohort study investigating associative factors that impact age at diagnosis in DMD patients without a known familiar history utilizing registry data (n= 1282); the study results illustrated that the mean age of diagnosis was 4.43 years. Non-Caucasian patients and patients from high-poverty neighborhoods were older at diagnosis ($p < .01$). Younger patients' birth age was associated with decreasing age of diagnosis ($p < .001$). Moreover, the authors identified a significant correlation between age at diagnosis and healthcare access. Moreover, the authors identified a significant correlation between age at diagnosis and healthcare access, thus, providing insight into socioeconomic factors such as insurance type, education, unemployment rates, geographic location, and median household income.

Summary

In this chapter, I reviewed the literature on the key study variables and Ferrans et al. (2005) HRQoL model, which formed the foundation of this investigation. Also, I reviewed the literature on the confounding variables of age, gender, race/ethnicity, income, and education. The full range of factors that affect QoL in DMD is currently unknown. Weerkamp et al. (2022) suggested that given the long lifespan of the DMD population, there is a growing need to assess psychosocial adjustment in the adult

population. The current body of evidence has established that DMD individuals report reduced HRQoL compared to their healthy counterparts from adolescence, teenager, and adulthood. Males in the advanced stages of the disease report lower levels of HRQoL in the physical domain. In addition to physical function, psychosocial function is also essential. In the psychosocial domain of HRQoL, health utilities are inconsistent, with some studies reporting better scores among older children and others reporting no differences. All patients, Dicker et al. (2018), especially those with chronic debilitating diseases, should benefit from healthcare accessibility and continuity of care.

Additionally, enhanced psychosocial care might reduce disease complications and improve PRQoL. DMD is considered the most common pediatric neuromuscular disorder, and advances in medical treatment have increased longevity beyond the second decade of life. Therefore, more emphasis on education, employment, independence, and social inclusion is required for DMD adult males to achieve optimal QoL. The full range of factors that affect QoL in DMD is currently unknown. Empathetically, a definitive list of factors that impact the QoL of the adult DMD patient is unknown; one reason is that the perspective of how QoL is measured differs (Kwon et al., 2022; Uttley et al., 2018). Thus, this study addresses the gap in the public health literature on the relationship between the independent variables of age, disease progression, healthcare access, and the dependent variable of HRQoL in adult DMD males.

Chapter 3 thoroughly addressed the research design, target population, secondary data collection analysis, recruitment, data access permissions, and reliability and validity of the data source.

Chapter 3: Research Method

Introduction

My study assessed the association between age at diagnosis, disease stage, healthcare access, and PRQoL in adult DMD males. I also examined the association between race, ethnicity, education, and income as covariates. In observational studies, PROs are recommended as assessment instruments (Ferizovic et al., 2022; Otto et al., 2017). The HRQoL construct has become an essential framework for health research, healthcare services, and health organizations (Ferizovic et al., 2022; Otto et al., 2017). I utilized a secondary database, the Patient-Reported Outcomes Measurement Information System (PROMIS), that included the following variables, DMD PRQoL outcomes, age, disease stage, and healthcare access to conduct a cross-sectional quantitative analysis. Chapter three encompasses the research design and study rationale, alignment of research questions and the study design, a definition of the study population, a description of the PROMIS secondary dataset, ethical considerations; the format of data analysis; and a summary of the chapter.

Research Design and Rationale

The research design is a quantitative analysis of a cross-sectional study utilizing a secondary database, the Patient-Reported Outcome Measurement Information System (PROMIS). Of particular importance to my study is the item banks of the Neuro-QoL, which is a clinically relevant psychometric health-related quality of life (HRQoL) survey instrument that focuses on six chronic neurological conditions: five adult conditions (stroke, multiple sclerosis, Parkinson's disease, epilepsy, and ALS) and two pediatric conditions [epilepsy and muscular dystrophy] (Gershon et al., 2012; Schalet et al., 2021).

An essential feature of the cross-sectional design is that it may be utilized to compare different populations and multiple variables within a particular time frame. Although cross-sectional studies do not ascertain cause and effect, they may determine a relationship between variables (Lavrakas, 2008). Moreover, Salkind (2010a) cross-sectional findings may be evaluated to design innovative studies for in-depth research.

Additionally, Dunn et al. (2015) and Moore et al. (2021) posited that compared to primary research, employing secondary data to evaluate a new hypothesis is advantageous because it requires less time and resources and allows access to large databases and longitudinal data. The PROMIS and Neuro-QoL item banks align with my dissertation because the iterative process incorporates patient-reported outcome measures, including the independent variables age, disease stage, and healthcare access, as well as the outcome variable HRQoL in my target population, muscular dystrophy (MD). While Neuro-QoL, item-response theory (ITR) patient-reported outcome measures align with my dissertation because it allows for real-time monitoring of QoL outcomes for comparative analysis (Gershon et al., 2012; Schalet et al., 2021). PROMIS database is founded on ITR, which has many advantages, such as allowing for the methodology of several measurement applications, including test construction, computer-based testing, equating, and identifying bias in item banks (Salkind, 2010b). Gershon et al. (2012) and Schalet et al. (2021) postulated that because patient-reported outcomes (PROs) are customized, cross-study comparisons are nearly unfeasible; however, PRO instruments that are designed using item response theory (ITR) enable cross-study comparisons.

Although IRT methods provide several advantages for survey research, there are limitations to widespread application. First, statisticians trained in classical test theory

may experience challenges due to the advanced knowledge of measurement theory IRT modeling requires (Lavrakas, 2008). Another potential obstacle is the large sample sizes required to provide a stable IRT parameter estimation; nevertheless, the practical applications of IRT modeling outweigh the challenges.

Independent Variables

The independent variables are age at diagnosis, disease stage, and healthcare access. Age is a continuous variable representing the participants' age at the time of the survey. The disease stage is an ordinal variable characterized by physical function, which consists of two measures (see Appendix F) :

1. Upper extremity function and ADLs are defined as "One's ability to carry out various activities involving digital, manual, and reach-related functions, ranging from fine motor to self-care (activities of daily living" (Gershon et al., 2012, p. 11).
2. Lower extremity function is defined as "One's ability to carry out various activities involving the trunk region and increasing degrees of bodily movement, ambulation, balance or endurance" (Gershon et al., 2012, p. 11).
3. Healthcare access, a categorical variable, is defined by insurance type, private/commercial, Medicaid, uninsured, and military/Tricare.

Composite scoring for the physical function construct will be measured as an average of the total responses to Upper extremity function/ADLs (eight questions) and Lower extremity function/mobility (eight questions) for a total of 16 questions, all affirmative with a range of 1-5 using a Likert scale; thus, reverse coding is not required (see Appendix H).

Dependent Variable, PRQoL

The dependent variable, PRQoL, represents (a) Ability to participate in social roles and activities, (b) Positive affect and Well-Being, and (c) Satisfaction with social roles and activities. Positive Affect and Well-Being describe "Aspects of a person's life relate to well-being, life satisfaction, or an overall sense of purpose and meaning" (National Institute of Neurological Disorders and Stroke [NINDS] (2015, Table 3, p. 6) . Whereas the Ability to Participate in Social Roles and Activities is indicative of the "degree of involvement in one's usual social roles, activities, and responsibilities, including work, family, friends, and leisure (NINDS, 2015, Table 3, p. 6). The

"Satisfaction with Social Roles and Activities Bank measures an individual's satisfaction" with involvement in one's usual social roles, activities, and responsibilities, including work, family, friends, and leisure" (NINDS, 2015 table 3, p. 7). See appendix I for the composite scoring rationale, questions, and examples for the PRQoL construct.

Research Questions and Hypotheses

My dissertation aimed to determine if age, disease stage, and healthcare access are statistically significant on the predictions of PRQoL of the DMD adult male. The following questions guide this study:

RQ1: Is there an association between age at diagnosis and PRQoL among male DMD adult patients?

$H_0$1–There is no association between age at diagnosis and PRQoL among male DMD adult patients.

H_a1– There is an association between age at diagnosis and PRQoL male DMD adult patients.

RQ2: Is there an association between disease stage and PRQoL male DMD adult patients?

$H_0$2– There is no association between disease stage and PRQoL among male DMD adult patients.

H_a2– There is an association between disease stage and PRQoL among male DMD adult patients.

RQ3: Is there an association between healthcare access and PRQoL male DMD adult patients?

$H_0$3– There is no association between healthcare access and PRQoL among male DMD adult patients.

H_a3– There is an association between healthcare access and PRQOL among male DMD adult patients.

RQ4: Is there any association between age at diagnosis, disease stage, healthcare access, gender, race, ethnicity, education, income, and PRQOL among male DMD adult patients?

$H_0$4-There is no statistically significant variation between PRQOL and age, gender, ethnicity, education, age at diagnosis, disease stage, and healthcare access male DMD adult patients.

H_a4: There is a statistically significant variation between PRQOL and age, gender, race, ethnicity, education, age at diagnosis, disease stage, and healthcare access male DMD adult patients.

Methodology

PROMIS Database

The Neuro-QOL aimed to develop a psychometrically HRQoL assessment tool for children and adults based on common neurological conditions (Gershon et al., 2012, as cited in Schalet et al., 2021). Based on extensive literary research, surveys, and consensus from patients and clinical providers, Gershon et al. (2012) selected five adult conditions (stroke, multiple sclerosis, Parkinson's disease, epilepsy, and amyotrophic lateral sclerosis) and two pediatric conditions (epilepsy and muscular dystrophy). Multiple methods and data sources were utilized to identify 17 domains of HRQoL, including a comprehensive literature search, thought leader interviews, surveys, and patient and caregiver focus groups (Gershon et al., 2012). Item development consisted of a six-step process: (a) expert analysis of existing instruments through literature search and previous item banking projects, (b) an iterative multistep process of assigning items to the Neuro-QoL domains, (c) post assignment of items to a domain area, (d) content experts conducted a systematic method of deleting individual items, (e) Evaluation of individual cognitive interviews, focus groups, and dataset analysis, and (f) instrument translation into English and Spanish (before field testing) (Gershon et al., 2012, p. 4). The dataset for my dissertation PROsetta Stone Wave 2 consists of a merged dataset linking PROMIS “measures in the Social, Sleep, Cognition and Psychological Well Being subdomains and related instruments from Toolbox and Neuro-QOL, as well as between the PROMIS Global and VR-12 forms using a unique response identification number (Cella, 2017).

PRO Rosetta Stone (PROsetta Stone ®) Database Validation

PROsetta Stone ® uses a psychometric process to establish a relationship between scores of two or more instruments measuring similar constructs (Schalet et al., 2021). Researchers have increasingly focused on linking patient-reported outcomes (PRO) data (Schalet et al., 2021). There are several benefits to linking PROs, "including the harmonization of data across studies, increasing power in hypothesis testing, aggregation of sum scores, and score conversion in clinical settings" (Schalet et al., 2021, p. 717, para 1). PROsetta Stone ®) used the equating method to link the Patient-Reported Outcomes Measurement Information System (PROMIS) outcomes (Cella et al., 2016). Equating is established when two tests "1) measure the same content/construct, 2) target very similar populations, 3) are administered under similar conditions such that the constructs measured are not differentially affected, 4) share common measurement goals, and 5) are equally reliable" (Cella et al., 2016, p. 1, para 1). Consequently, the test forms are considered interchangeable because equating adjusts for differences in difficulty (Cella et al., 2016). Several researchers have analyzed a multi-dimensional approach to measure validity and reliability, linking PRO and PROMIS instruments and confirmed validity (Amtmann et al., 2010; Cella et al., 2019; Choi et al., 2012; Schalet et al., 2021). Cella (2017a) assessed the validity and reliability of the Neuro-QoL instrument (see table applicable in assessing the QoL construct across several neurological conditions: the results were: internal consistency (Cronbach α) of the 13 short forms 0.85 to 0.97; correlations between short form and full-length item banks 0.88 to 0.99 (0.82-0.96, removal of mutual items).

Population

Data collection consisted of two waves; the first wave was split into two segments. Wave 1a consisted of clinical participants with neurological conditions, including stroke, multiple sclerosis, Parkinson's disease, epilepsy, amyotrophic lateral sclerosis, and muscular dystrophy patients, *n* = 533. Wave 1b consisted of an online survey; generic survey items were field tested on samples drawn for the United States (US) general population, *n* = 3,123 respondents. The second wave of field testing evaluated the reliability, validity, and responsiveness of the Neuro-QoL short forms and scales in clinical neurological populations [*n* = 581 adults and *n* = 113 pediatric patients] (Cella, 2017b, as cited in Schalet et al., 2021). It is of particular concern to my dissertation in wave two because the focus is neurological conditions and includes my target population of DMD males.

Sampling and Sampling Procedures (PROMIS: Neuro-QoL)

In wave two, adult participants (*n* = 580) were recruited from 12 academic clinical sites employing in-clinic recruitment and mailing informational letters to physician-identified patients. In wave two, sample demographics were male (46%), White (87%), African American (12%), and Asian (2%). The sample characteristics of the adult subset of muscular dystrophy are participants (*n*=51), male (84.3%), white (58.8%), and non-Hispanic (62.7%) with average age=16.3 [*SD*=3.4; range=10.1 to 21.9](Cella et al., 2016; Schalet et al., 2021). Research methods for the pediatric Neuro-QOL consist of generic and targeted measures, including "literature reviews, focus groups, cognitive interviews of children and consensus meetings were used to identify and finalize relevant domains and item content" (Cella et al., 2016, p. 1). Adults were randomly sampled via an internet

survey to access the pediatric population *n*=1018 children aged 10-17 years old drawn from the US general population for generic measures and 171 similarly aged children with muscular dystrophy or epilepsy for targeted measures (Cella et al., 2016). Of the 1018 children recruited, only 25 percent reported one neurological disorder, and eight percent reported two neurological conditions (Cella et al., 2016). Population statistics for the two pediatric conditions, epilepsy (*n*=61) and muscular dystrophy (*n*=51), Cella et al. (2016) confirmed that of the 51 muscular dystrophy participants, 65 percent were DMD.

Sampling Methods: Strengths and Weaknesses

PROMIS-Neuro QoL sampling procedures included the following recruitment methods, online-based, clinical on-site, and mailing. The online survey method is appropriate for cross-sectional research because the research can limit multiple responses by enabling cookies (Dun et al., 2015). Also, the researcher can send reminders or follow-up messages via email. However, the online methodology requires that investigators are trained in online technology. According to Nayak and Narayan (2019), overall, the benefits of online surveys and recruitment are increased response levels due to anonymity; elimination of data entry, fewer mistakes, missing data, and refusal compared to paper surveys; data collection from a large pool, and allowance of the advanced process such as branching and prompting of questions.

Conversely, the disadvantages of online sampling include the increased expense for small sample sizes, potential incompatibility across software systems, and decreased access to the technically disadvantaged and the population without internet access (Nayak & Narayan, 2019). Regarding mail-based sampling, a potential challenge is the misinformation of addresses and the reporting by parents of randomly selected children,

such as in proxy reporting (Jager et al., 2017). The probability sampling at neurological academic clinics ensured that each targeted neurologic condition was included; therefore, the sample was representative of the population (Jager et al., 2017). Regarding power, Cella et al. (2016) and Schalet et al. (2021) concluded that the nine Neuro-QoL measures demonstrated high internal consistency (Cronbach's alpha range from 0.81-0.98) and acceptable interclass correlation coefficients [ICC] (.61 to .97). Moreover, Lia et (2012) determined that the pediatric Neuro-QoL is a psychometrically comprehensive measurement tool for research studies.

Effect Size and Power Analysis

In statistics, effect size estimates the differences between group means and the relationship between variables. Effect size determines the magnitude of the relationship between variables (Baguley, 2009). Effect size is essential to my dissertation because it allows for comparative effects within and across studies, estimation of the (1 - β) power, and the sample size required to answer the research questions (Salkind, 2010a). G* Power version 3.1.9.7 software was used to calculate the sample size needed for this cross-sectional study (see Figure D1). Research questions one and two consist of one predictable variable and one outcome variable (composite scale 3-15); thus, a simple linear regression analysis is appropriate for both questions. Based on the G* Power analysis, statistical test multiple linear regression (MLR) with a medium effect size f^2 (0.15), α (.05), Power (.80), and one predictor, the estimated sample size is 55.

In contrast, the estimated sample size with a large effect size of f^2 (0.35) is 25 (see Figure D1). For research question three, the predictor variable consists of four categories of healthcare access (private/commercial, Medicaid, uninsured, military/Tricare); thus, an

appropriate statistical test is the Analysis of variance (ANOVA). Based on the parameters of f^2 (0.5), α (.05), Power (.80), and the number of groups (4), the estimated sample size is 48 (see Figure D2). Research question four has three predictor variables (age, disease stage, and healthcare access); thus, the power analysis is based on a multiple linear regression (fixed model deviation zero). Based on a large effect size f^2 (0.35), α (.05), Power (.80), and three predictor variables, the estimated sample size is 36 (see Figure D3). In summary, the effect sizes required for RQ1 and RQ2 are 55 for each question, RQ3 48, and Q4 36; thus, the minimal sample size required to evaluate all four research questions is 55.

Rationale for Moderate to Large Effect Size

By nature, rare disease research is challenging due to limited cases worldwide, problematic diagnoses, and limited availability of data resources (Kraemer & Blasey, 2016). However, predictor variables potentially have a critical impact on the dependent outcome. In Rare disease studies that investigated factors that impact PRQoL, researchers reported findings based on the importance of effect size in real-world situations (Kraemer & Blasey, 2016). I selected moderate to large effect sizes (.35 and .50) based on the following research findings (Multiple Linear Regression, Dependent Variable Quality of Life):

- Zöllner et al. (2021) examined predictors of health-related quality of life (HRQoL) using multiple linear regression (MLR) among. patients with Tuberous sclerosis complex (TSC, a rare disease) compared to patients with other chronological neurological disorders. The authors found significant results in medium to large effect sizes: active epilepsy (a large effect, $p<.001$) and neuropsychiatric manifestations (medium effect, $p< .003$) were

independently associated with adverse HRQoL outcomes, explaining 65 percent of the variance ($p<.001$).

- Schwartz et al. (2022), in a cohort study, assessed psychosocial factors associated with quality-of-life outcomes (QoL) of DMD patients and their caregivers using
- Linear modeling. The authors used ANOVA analysis to examine the differences in dependent variables by highest versus lowest-impact groups; Cohen's d (effect size, ES) results revealed that high-impact groups had more patient and caregiver comorbidities (large ES of $d\geq0.8$), higher body mass index, more DMD care recipients, and younger caregivers (medium ES of $d\geq0.5$).

Data Analysis Method Plan

My study planned to evaluate four research questions and hypotheses. I plan to conduct the following data analysis:

- RQ1, the independent variable, age, is continuous, and the outcome variable (PRQoL) is continuous (composite range 23-115). Simple linear regression (SLR) is an appropriate statistical test to analyze the relationship between age and PRQoL.
- RQ2, the predictor variable disease stage is a continuous (range 116-80) composite variable of the construct physical function (upper and lower extremity function, total questions 16, scale 1-5, see Appendix H) and one continuous outcome variable PRQoL (composite scale 23-115); thus, a simple linear regression analysis is an appropriate test (see Appendix I).

- RQ3, the predictor variable healthcare access consists of four categories (1=private/commercial, 2=Medicaid, 3=uninsured, 4=military/Tricare). Because the predictor variable is nominal and the dependent variable (PRQoL) is continuous, a one-way Analysis of variance (ANOVA) is an appropriate statistical test.
- RQ4 has three predictor variables (age, disease stage, and healthcare access) for a single dependent variable. A multiple linear regression analysis quantifies the association between each predictor variable and the dependent variable (criterion), simultaneously considering all other independent variables (Verbeke & Molenberghs, 2013). Consequently, MLR is a suitable test for modeling and interpreting the relationship between the three predictor variables and the dependent variable for RQ4.

Covariates' Association with PRQoL: Age, Race, Ethnicity, Education, and Income

Other studies observed that socioeconomic status (race, ethnicity, income, and education) influences PRQoL outcomes (Barnard et al., 2020; Counterman et al., 2020; Gocheva et al., 2019). Therefore, I will analyze age, education level, race, ethnicity, and income as covariates. Confounding variables are extraneous variables that have the potential to impact the study variables in a way that misrepresents the actual association between the predictor variables and the outcome variable (Pourhoseingholi et al., 2012; Zhao et al., 2020). To control for the potential confounding variables of age, education level, race, ethnicity, and income, I will conduct an Analysis of Covariance (ANCOVA) and MLR. ANCOVA may serve as an extension to multiple regression to assess

regression lines to see which have different Y intercepts with equal slopes (Pourhoseingholi et al., 2012; Zhao et al., 2020).

Assumptions Multiple Linear Regression (MLR)

For my dissertation, the dependent variable PRQoL is continuous (composite score 23-115), while the independent and covariates variables are age, disease stage, healthcare access, education level, income, race, and ethnicity. MLR methodology examines the relationship between multiple predictor variables, age, disease stage, healthcare access, and a response variable, PRQoL. However, utilization of the MLR model requires adherence to five main assumptions: (1) linearity, a linear relationship between each predictor variable and the response variable; (2) Multicollinearity, no high correlation between predictor variables; (3) Independence of errors: observations are independent (4) Homoscedasticity: residuals in the linear model have constant variance, and (5) Multivariate normality: the residuals are normally distributed (Osborne, 2017).

Assumptions ANOVA

Conducting an ANOVA is based on three primary assumptions: (a) the sample is based on a normally distributed population, (b) Independence: sample cases are independent, and (c) Homogeneity of variance: the variance among the groups should be approximately equal (Salkind, 2010b).

ANCOVA and Covariate Analysis

ANCOVA is a suitable linear statistical model for evaluating covariates (confounders); it combines ANOVA and linear regression and assesses the potential effect on the outcome variable after removing the variance that accounts for quantitative covariates (Pourhoseingholi et al., 2012; Zhao et al., 2020). A Linear regression analysis

examines the association between multiple covariates and a numeric outcome by isolating the relationship of interest and identifying the extent to which the confounders distort the relationship between predictor variables and the outcome variable (Pourhoseingholi et al., 2012, as cited in Zhao et al., 2020). MLR and ANCOVA are appropriate statistical methods to control confounders (Van Breukelen, 2022).

Descriptive Analysis

Descriptive statistics provide a method to describe the characteristics of your sample and evaluate variables for any violations of assumptions required by the statistical analysis (Pourhoseingholi et al., 2012; Zhao et al., 2020). Descriptive statistics provides a visual summary of the data using description tables and graphic descriptions (frequency distribution and outliers) to enhance understanding of the data and data cleansing (Pallant, 2010). Without descriptive data, it would be challenging to visualize or present data from a meaningful perspective (Pallant, 2010).

Missing Data (Item non-response) Analysis

Imputation techniques are appropriate for item non-response to avoid a reduction in sample size. I planned to conduct a missing data analysis to uncover the underlying rationale for the missing data and use the analysis as the criterion for selecting the appropriate imputation technique. I planned to use simple imputation for item non-response, attributing one value for each missing data point with the sample mean of that variable or the conditional sample mean after grouping cases (Lewis-Beck et al., 2004). Whereas in regression imputation, a regression of the non-response variable is estimated from complete cases; consequently, the prediction equation "is used to impute the estimated conditional mean for each missing value" (Lewis-Beck et al., 2004, p. 3 para1).

The imputation process is considered stochastic when randomly assigned residual or error terms (Lewis-Beck et al., 2004). An advantage of imputation is maintaining sample size; however, imputation may result in bias.

Threats to Validity

An essential threat to validity is the assumption involving science in discovering truth (Salkind, 2010c). Regarding psychometric concerns, the definition of validity is well-defined but abstract (Salkind, 2010a). Content validity requires representing selected items concerning what is to be measured (Salkind, 2010c). Lastly, construct analysis compares the construct to be measured with other existing constructs to verify its relative uniqueness (Salkind, 2010c). As previously mentioned, the reliability (internal consistency) of the Neuro-QoL short forms Cronbach's alphas range from .82 to .98 and ICC from .61 to .97 (Gershon et al., 2012; Schalet et al., 2021). The global QoL item bank "I am content with the quality of my life right now" reflected convergent validity was significantly significant [$p < .05$] (Gershon et al., 2012; Schalet et al., 2021). Confounding factors such as race/ethnicity, education, and income potentially impact the findings of the actual effect of the independent variables (Salkind, 2010c). Additionally, the primary research consisted of robust studies to confirm the reliability and validity of the survey instrument established by experts and peer reviewed procedures.

Ethical Considerations

Ethical Procedures

This current study adhered to several ethical procedures of IRB approvals, abidance to participating and recruiting human subjects, including vulnerable populations, data collection, confidentiality, and data storage, to assert compliance with

ethical standards. As guiding principles, I followed the Canadian Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (Canadian Institutes of Health Research, 2018), the American Psychology Association Ethical Principles of Psychologists and Code of Conduct (American Psychological Association [APA], 2016), and Walden University procedures.

Institutional Review Board (IRB) process. Before analyzing the PROMIS data sets, approval was obtained from the Walden University Institutional Review Board (approval no. 05-01-23-0993288) to ensure compliance with ethical guidelines, including the informed consent process, participant recruitment procedures of the primary study, data collection, confidentiality, analysis, storage, and proper permission to utilize questionnaires. Because this dissertation involved vulnerable populations, I completed and submitted Form D of Walden's IRB application process to ensure compliance with all criteria for at-risk populations.

Data Collection, confidentiality, and storage procedures. Before analyzing the PROMIS/Neuro QoL datasets, I will seek approval from the Walden University IRB and adherence to the Health Measures terms and conditions of use (see Appendix E). The POMIS database is governed by Harvard DataVerse Repository API Terms of Use and Harvard DataVerse Repository General Terms of Use (Hammer et al., 2020). All data sets governed by the Data verse repository are granted the Creative Commons (CC) Public Domain Dedication by default. Consequently, access to the PROMIS repositories is publicly available. The agreement for use requires materials from the datasets to cite the relevant source. Also, researchers are required to maintain the anonymity of human subjects. As a result, PROMIS datasets used unique patient identifiers to connect datasets

while maintaining anonymity. Wave-2 adult participants received a modest compensation of 20 dollars for the baseline assessment (Gershon et al., 2012; Schalet et al., 2021). Signed informed consent was obtained in English and Spanish language formats. Because of the patient's limited ability to consent, consent by proxy was employed. Of potential concern are the ability and challenges that proxies (parents and caregivers) face to make informed consent based on the participant's preferences (Shepherd et al., 2022). Essential components of "good" proxy consent include identifying the proxy's knowledge and understanding of participation, clarifying research outcomes, and potential social change (Shepherd et al., 2022). The primary dataset, the Neuro-QoL secondary dataset, received IRB approval from all participating academic institutions. Upon IRB approval, The Neuro-QoL dataset (Cella, 2017) will be downloaded and stored both on my password-protected laptop and OneDrive cloud storage as a backup. Per Walden University's storage requirements, survey data will be deleted from my laptop and OneDrive after five years.

Summary

This dissertation aims to assess the association between age at diagnosis, disease stage, healthcare access, and patient-reported quality of life (QOL) in adult males, utilizing secondary data from the Neuro-QoL data repository. Therefore, I discussed the research design and rationale, methodology (population, sampling procedures), description of the PROMIS secondary dataset, reviewed the research questions and hypothesis, as well as the ethical considerations for my dissertation.

Chapter 4: Results

Introduction

My study assessed the association between age at diagnosis, disease stage, healthcare access, and patient-reported quality of life (PRQoL) in adult DMD males. I also examined the association between race, ethnicity, education, and income as covariates. Assessing the associations between the predictor variables of age, disease stage, and the outcome variable of PRQoL may support public health initiatives for DMD patients transitioning into adulthood. In this chapter, I began with changes in my data analysis plan. Next, I described the dataset. Then, I reviewed the descriptive statistics, including the sample's baseline descriptives and demographic characteristics. Fourth, I presented the results of the inferential statistical analysis for each research question and hypothesis. Finally, I summarized the research findings.

Deviations from the Data Analysis Method

The changes to the original data analysis plan are due to limitations to the availability of data (missing questions) for my target population of MD, including DMD patients. The following are deviations from the data analysis plan as described in Chapter 3:

- RQ1: Is there an association between age at diagnosis and PRQoL among male DMD adult patients? The population age range for the target population is 10 to 22 years old. Consequently, including patients ages 10-22 years provides a more robust analysis of the disease's natural history or maturing adults. Thus, the deviation to RQ1 includes changing the wording from the adult male to include maturing males ages 10-22. The maturing or emerging adult stages include (late

childhood/adolescent/young adult). Age at diagnosis is unavailable and was substituted by the continuous variable age.

- RQ2: Is there an association between disease stage and PRQoL male DMD adult patients? The original plan was to create a composite variable for the disease Stage, including three measures: upper extremity function, a combination of daily living activities (ADL), and lower extremity function. Because the measures (questions) were missing for the DMD target audience, I substituted the disease state variable with the Patient-Reported Outcomes Management Information System (PROMIS) Global Health (06) variable: To what extent are you able to carry out your everyday physical activities such as walking, carrying groceries, or moving a chair (1=not at all, 2=a little, 3=moderately, 4= mostly, 5=completely)? Global Health (06) includes upper and lower extremity activities and ADLs; thus, the Global Health (06) variable is an appropriate measure of the variable disease stage.
- RQ3: Is there an association between healthcare access and PRQoL male DMD adult patients? The database does not contain data (variables) to measure healthcare access directly or by proxy; thus, the independent variable of healthcare access is eliminated from the analysis.
- RQ4: Is there any association between age at diagnosis, disease stage, healthcare access, gender, race, ethnicity, education, income, and PRQoL among male DMD adult patients? The outcome variable PRQoL consisted of three measures: ability to participate in social roles and activities, satisfaction with social roles and activities, and positive affect and well-being. However, the data is missing.

Consequently, the variable for PRQoL was substituted with the PROMIS Global Health (02): In general, would you say your quality of life is (1=poor, 2=fair, 3=good, 4=very good, 5=excellent).

- Covariates: Due to the absence of data and lack of proxies, the following covariates, race, income, and healthcare access were removed. The covariate gender was removed because the target audience only includes males.
- The statistical analysis was changed from Multiple linear regression to ordinal logistic regression due to the categorical scale of the dependent variable. Consequently, I ran an A-priori Sample Size Calculator for Multiple Regression. A power analysis calculator was utilized to estimate the minimum required sample size for a multiple regression study. The results of the analysis indicate a required sample size of 76 with an Effect size (*f*2): 0.15, Desired statistical power level: 0.8, Number of predictors: 3, and Probability level: 0.05. In contrast, an effect size of (*f*2):0.35, desired statistical power level: 0.8, number of predictors: 3, and probability level: 0.05, requires a minimum sample size of 36. In conclusion, the minimum sample size required for this study is 36 (Soper, 2023).

The PROMIS Global Health Scale refers to evaluations that measure health in general compared to specific elements of health and includes five primary health domains, physical function, fatigue, pain, emotional distress, and social health (Cella et al., 2019).

Data Collection Method

The PROMIS Quality of Life in Neurological Disorders "NeuroQOL Clinical Validation Study (aka Wave II)" served as the database for this study. I obtained the secondary data set from the Harvard Dataverse Health Measures database. The NIH

sponsored study (2015) was conducted in two waves: the first wave was split into two segments. Wave 1a consisted of clinical participants with neurological conditions, including stroke, multiple sclerosis, Parkinson's disease, epilepsy, amyotrophic lateral sclerosis, and muscular dystrophy patients, *n* = 533. Wave 1b consisted of an online survey; generic survey items were field tested on samples drawn for the United States general population, *n* = 3,123 respondents. The second wave of field testing evaluated the reliability, validity, and responsiveness of the Neuro-QoL short forms and scales in clinical neurological populations. In wave two, adult participants (*n* = 580) were recruited from 12 academic clinical sites employing in-clinic recruitment and mailing informational letters to physician-identified patients. In wave two, sample demographics were male (46%), White (87%), African American (12%), and Asian (2%). The sample characteristics of the adult subset of muscular dystrophy are participants (*n* = 51), male (84.3%), white (58.8%), and non-Hispanic (62.7%) with average age=16.3 [*SD*=3.4; range=10.1 to 21.9](Cella et al., 2010; Schalet et al., 2021).

Data Cleaning Method

IRB approval (number 05-01-23-0993288) was obtained from Walden University before accessing the dataset. The NeuroQoL dataset was filtered by my study variables, A1-age (re-labeled) age, A1_global02(re-labeled, PRQoL), A1_Global06 (relabeled Disease stage), A1-NQCF02 [neurological disease diagnosis] (=6, Muscular Dystrophy), A1_NQPEDSSD02 (re-labeled Gender, filter 1=male), A1_NQPEDSSD03 (re-labeled Hispanic/Spanish/Latino,1=yes,0=no), and A1_NQPEDSSD05 (relabeled School Attendance, 1=yes, 0=no).

Descriptive Statistic (Omnibus)

Table 3

Descriptive Statistics for the Diagnosed Neurological Condition

Diagnosed Neurological Condition

		N	%
MS		293	11.7%
PD		229	9.2%
ALS		136	5.4%
Stroke		190	7.6%
Epilepsy		339	13.6%
MD		99	4.0%
Missing	System	1212	48.5%
Total		2498	100%

Note: Muscular Dystrophy is 7. 7 valid percent (*n*=99) of the diagnosed neurological condition population.

Table 4

Descriptive Statistics of the Continuous Variable, Age

Age	N	Mean	Std Error
	99	15.93	.345

Table 5

Frequencies and Percentages, Age

Age

		Frequency	Percent	Valid Percent
Valid	10	6	6.1	6.1
	11	11	11.1	11.1
	12	2	2.0	2.0
	13	6	6.1	6.1
	14	10	10.1	10.1
	15	9	9.1	9.1
	16	10	10.1	10.1
	17	8	8.1	8.1
	18	11	11.1	11.1
	19	7	7.1	7.1
	20	9	9.1	9.1
	21	8	8.1	8.1
	22	2	2.0	2.0
	Total	99	100.0	100.0

Note: 74.7 percent of the population is 14 years old, and 25.3 percent is under 14.

Table 6

Frequency and Percentage Distribution of Gender

What is your Peds gender?

		Frequency	Percent	Valid Percent
Valid	Male	83	83.8	83.8
	Female	16	16.2	16.2
	Total	99	100.0	100.0

Note: 83.8 percent of the population is male, and females make up 16.2%

Table 7

Frequency and Percentage, Spanish/Hispanic/Latino Orgin

Are you of Spanish/Hispanic/Latino Peds origin?

		Frequency	Percent	Valid Percent
Valid	No	61	61.6	64.2
	Yes	34	34.3	35.8
	Total	95	96.0	100.0
Missing	System	4	4.0	
Total		99	100.0	

Note: 34 percent of respondents are of Spanish, Hispanic, or Latino Ethnicity, 61 percent are not of Spanish, Hispanic, or Latino ancestry, and four responses are missing.

Table 8

Frequency and Percentage of School Attendance (Education)

Are you attending school now (including home school)?

		Frequency	Percent	Valid Percent
Valid	No	14	14.1	14.7
	Yes	81	81.8	85.3
	Total	95	96.0	100.0
Missing	System	4	4.0	
Total		99	100.0	

Note: 81 percent of respondents are attending school, 14 percent are not attending school, and four responses are missing.

Table 9

Frequency and Percentage of Disease Stages

Disease Stage

		Frequency	Percent	Valid Percent
Valid	Not at all	31	31.3	35.6
	A little	12	12.1	13.8
	Moderately	15	15.2	17.2
	Mostly	17	17.2	19.5
	Completely	12	12.1	13.8
	Total	87	87.9	100.0
Missing	System	12	12.1	
Total		99	100.0	

Note: Respondents reported disease stage as a valid percent, not at all 35.6 percent, a little as 13.8 percent, moderately as 17.2 percent, mostly as 19.5 percent, and completely as 13.8 percent. Missing system data accounted for 12.1 percent.

Table 10

Frequency and Percentage Distribution of PRQoL

PRQOL

		Frequency	Percent	Valid Percent
Valid	Poor	3	3.0	3.1
	Fair	9	9.1	9.2
	Good	33	33.3	33.7
	Very good	32	32.3	32.7
	Excellent	21	21.2	21.4
	Total	98	99.0	100.0
Missing	System	1	1.0	
Total		99	100.0	

Note: PRQoL respondent valid percent: 12.3 percent rated QoL as poor or fair, 33.7 percent as good, 32.7 percent as very good, 21.4 percent as excellent, and missing data accounted for only 1 percent.

Descriptives Target population: Muscular Dystrophy, Males

Table 11

Descriptive Statistics for the Continuous Variable, Age

Descriptive Statistics

	N	Mean	Std. Deviation
Age	83	15.98	3.268

Note: The mean age is 15.98 with a standard deviation of 3.268, *n*=83

Table 12

Frequency and Percentage Distribution, Age

Age

	N	%
10	5	6.0%
11	6	7.2%
12	2	2.4%
13	6	7.2%
14	9	10.8%
15	8	9.6%
16	10	12.0%
17	8	9.6%
18	9	10.8%
19	6	7.2%
20	6	7.2%
21	6	7.2%
22	2	2.4%

Note: Of male MD respondents, 22.9 percent are between 10-13 years of age (*n*=38), and 77.1 percent are 14 to 22 years old (*n*=45)

Table 13

Frequency and Percentage, Males

Gender

	N	%
Male	83	100%

Note: Filtered for Males only (*n*=83)

Table 14

Frequency and Percentage Distributions of Disease Stages

Disease Stage

	N	%
Not at all	28	33.7%
A little	10	12.0%
Moderately	12	14.5%
Mostly	14	16.9%
Completely	7	8.4%
Missing System	12	14.5%
Total	83	100%

Note: Percent of Respondents reported disease stage as not at all 33.7 %, a little 12.0 %, moderately 14.5%, mostly 16.9 %, completely 8.4 %, system missing 14.5 %

Table 15

Frequency and Percentage of PRQoL Stages

PRQoL

		N	%
Poor		3	3.6%
Fair		8	9.6%
Good		25	30.1%
Very good		27	32.5%
Excellent		19	22.9%
Missing	System	1	1.2%
Total		83	100%

Note: 98.8 percent of male respondents (*n*=82) responded to the PRQoL measure (poor= 3.5%, fair=9.65, good=30.1%, very good 32.5%, and excellent 22.9%, system missing 1.2%).

Table 16

Frequency and Percentage of Spanish/Hispanic/Latino Patients

Spanish/Hispanic/Latino

		N	%
No		53	63.9%
Yes		26	31.3%
Missing	System	4	4.8%
Total		83	100%

Note: Non-Hispanic respondents account for 63.9 percent, Hispanic respondents account for 31.3 percent, and missing system data is 4.8 percent.

Table 17

Frequency and Percentage of School Attendance (Education)

School Attendance

		N	%
No		12	14.5%
Yes		67	80.7%
Missing	System	4	4.8%
Total		83	100%

Note: 80.7 percent of respondents attend school, whereas 14.5 percent are not in school.

Statistical Assumptions

I used ordinal logistic regression to address my study's research questions. Assumptions for ordinal logistic regression include:

1. an ordinal level dependent variable: assumption met the dependent variable is ordinal with five categories (1=poor, 2=fair, 3=good, 4=very good, 5=excellent).
2. that the independent variable(s) are continuous, ordinal, or categorical: assumption met, the independent variable age is continuous, and the independent variable disease stage is ordinal (1=poor, 2=fair, 3=good, 4=very good, 5=excellent).
3. No multicollinearity: assumption met as there is only one continuous independent variable (age). If you have one or no continuous independent variables, you do not need to test for multicollinearity (Williams & Quiroz, 2020).

4. The assumption of proportional odds was not met, as assessed by a full likelihood ratio test comparing the fit of the proportional odds model to a model with varying location parameters, $\chi^2(12) = 24.821$, $p = .016$. Consequently, the Test of Parrell lines for each predictor variable was run to test proportional odds. Age $\chi^2(3) = 5.043$, $p = .169$, ethnicity $\chi^2(3) = 6.562$, $p = .087$, and education, $\chi^2(3) = 4.044$, $p = .257$, met the assumption with $p > .05$. However, the disease stage, $\chi^2(3) = 13.430$, $p = .004$, predictor variable violated the proportional odds assumption $p<.05$. Consequently, RQ3 was revised by dropping the predictor variable disease stage $\chi^2(3) = 15.685$, $p = .074$, meeting the proportional odds assumption.

Ordinal Logistic Regression

Ordinal logistic regression was performed to evaluate the association between age, disease stage, education, ethnicity, and PRQoL. For this analysis, the significance values are $p<.05$, and the confidence intervals are 95% for the upper and lower limits.

Age and PRQoL

RQ1: Is there an association between age at diagnosis and PRQoL among male DMD adult patients?

$H_0$1–There is no association between age at diagnosis and PRQoL among male DMD adult patients.

H_a1– There is an association between age at diagnosis and PRQoL male DMD adult patients.

Results for Age and PRQoL

Ordinal logistic regression was performed to evaluate the association between age and PRQoL among DMD male patients. The ordinal logistic model was non-significant, $X^2(1)=2.224$, $p>.05$. The results of the Wald test in Table 18, show that the association between age and PRQoL did not add significantly to the prediction ($p>.05$). The independent variable, Age has a non-significant effect to the prediction of PRQoL among DMD males. The ordered odds estimate (.092), *SE* (.062), Wald (2.206) $p>.05$. The Wald test statistic for the predictor variable age is 2.206 with an associated p-value of .137; thus, I fail to reject the null hypothesis and conclude that the regression coefficient for age is not statistically different from zero in estimating PRQoL.

Therefore, I failed to reject the null hypothesis and conclude that there is no association between age and PRQoL among maturing male DMD patients.

Table 18

Parameter Estimates for Age and PRQoL

Parameter Estimates

							95% Confidence Interval	
		Estimate	Std. Error	Wald	df	Sig.	Lower Bound	Upper Bound
Threshold	[A1_PRQoL = 1]	-1.851	1.116	2.749	1	.097	-4.039	.337
	[A1_PRQoL = 2]	-.448	1.010	.197	1	.657	-2.428	1.531
	[A1_PRQoL = 3]	1.184	1.007	1.383	1	.240	-.789	3.157
	[A1_PRQoL = 4]	2.666	1.042	6.542	1	.011	.623	4.709
Location	A1_Age	.092	.062	2.206	1	.137	-.029	.213

Link function: Logit.

Results: Disease Stage and PRQoL

RQ2: Is there an association between disease stage and PRQoL male DMD adult patients?

$H_0$2– There is no association between disease stage and PRQoL among male DMD adult patients.

H_a2– There is an association between disease stage and PRQoL among male DMD adult patients.

An ordinal logistic regression analysis investigated the association between disease stage and PRQoL among DMD male patients. The predictor variable, Disease stage (five categories), in the ordinal logistic regression, did not add significantly to the model $X^2(1)= (65.164)$, $p>.05$. Results in Table 19 show that the predictor variable, disease stage did not add significantly to the prediction of PRQoL ($p>.05$). The ordered odds estimate (-.004), *SE* (.151), Wald (.001) $p>.05$. Therefore, I failed to reject the null hypothesis and conclude that there is no association between disease stage and PRQoL among maturing male DMD patients.

Table 19

Parameter Estimates Disease Stage and PRQoL

Parameter Estimates

							95% Confidence Interval	
		Estimate	Std. Error	Wald	df	Sig.	Lower Bound	Upper Bound
Threshold	[A1_PRQoL = 1]	-3.551	.808	19.295	1	.000	-5.135	-1.967
	[A1_PRQoL = 2]	-2.074	.529	15.369	1	.000	-3.111	-1.037
	[A1_PRQoL = 3]	-.381	.444	.737	1	.391	-1.251	.489
	[A1_PRQoL = 4]	1.146	.464	6.090	1	.014	.236	2.055
Location	A1_DiseaseSTAGE	-.004	.151	.001	1	.978	-.300	.292

Link function: Logit.

Results: Age, Disease Stage, Ethnicity, Education, and PRQoL

RQ3: Is there an association between healthcare access and PRQoL male DMD adult patients?

$H_0$3– There is no association between healthcare access and PRQoL among male DMD adult patients.

H_a3– There is an association between healthcare access and PRQOL among male DMD adult patients.

An ordinal logistic regression analysis investigated the association between age, disease stage, ethnicity, education, and PRQOL among maturing DMD male patients. The predictor variables age (continuous: 10-22), disease stage (five categories), and covariates education (dichotomous: yes, no), and ethnicity (Spanish: yes, no) in the ordinal logistic regression analysis, $p<.05$ would lead one to conclude that at least one of the regression coefficients in the model is not equal to zero, $x^2(4)= (10.488)$, $p=(.033)$. Parameter estimates in Table 20 show that age, disease stage, and education did not add significantly to the model. The covariate variable, ethnicity (non-Spanish), added significantly to the prediction, with an estimated log-odds estimate= [1.676], *SE* [.554], Wald [9.140][$p=.003$). The results indicate that non-Spanish DMD male patients have a statistically significantly better PRQoL than Spanish DMD male patients.

Table 20

Parameter Estimates Age, Disease Stage, Education, Ethnicity, PRQoL

Parameter Estimates

							95% Confidence Interval	
		Estimate	Std. Error	Wald	df	Sig.	Lower Bound	Upper Bound
Threshold	[A1_PRQoL = 1]	-2.165	1.497	2.090	1	.148	-5.100	.770
	[A1_PRQoL = 2]	-.544	1.367	.158	1	.691	-3.224	2.137
	[A1_PRQoL = 3]	1.356	1.368	.982	1	.322	-1.326	4.038
	[A1_PRQoL = 4]	3.064	1.411	4.714	1	.030	.298	5.829
Location	A1_DiseaseSTAGE	-.086	.169	.257	1	.612	-.418	.246
	A1_Age	.051	.078	.417	1	.518	-.103	.204
	[A1_School=0]	-1.082	.716	2.286	1	.131	-2.484	.321
	[A1_School=1]	0[a]	.	.	0	.	.	.
	[A1_SpanishHispanicLatino=0]	1.676	.554	9.140	1	.003	.589	2.762
	[A1_SpanishHispanicLatino=1]	0[a]	.	.	0	.	.	.

Link function: Logit.

a. This parameter is set to zero because it is redundant.

Results for Revised RQ3: Age, Ethnicity, education, and PRQoL

RQ3: Is there an association between healthcare access and PRQoL male DMD adult patients?

$H_0$3– There is no association between healthcare access and PRQoL among male DMD adult patients.

H_a3– There is an association between healthcare access and PRQOL among male DMD adult patients.

An ordinal logistic regression analysis investigated the association between age, ethnicity, education, and PRQOL among maturing DMD male patients. The predictor variables age (continuous: 10-22), and covariates education (dichotomous: yes, no), and ethnicity (Spanish: yes, no) in the ordinal logistic regression analysis, $p<.05$ would lead one to conclude that at least one of the regression coefficients in the model is not equal to

zero, $x^2(3)= (16.767)$, $p=(.001)$. Parameter estimates in Table 21 show that age and education did not add significantly to the model. The covariate variable, ethnicity (non-Spanish), added significantly to the prediction, with an estimated log-odds estimate= [1.946], *SE* [.504], Wald [14.896][p=.001). The results indicate that Non-Spanish DMD, male patients, have a statistically significantly better PRQoL than Spanish DMD male patients.

Table 21

Parameter Estimates Age, Education, Ethnicity, PRQoL

Parameter Estimates

							95% Confidence Interval	
		Estimate	Std. Error	Wald	df	Sig.	Lower Bound	Upper Bound
Threshold	[A1_PRQoL = 1]	-.996	1.244	.642	1	.423	-3.433	1.441
	[A1_PRQoL = 2]	.585	1.158	.256	1	.613	-1.684	2.855
	[A1_PRQoL = 3]	2.507	1.189	4.450	1	.035	.178	4.837
	[A1_PRQoL = 4]	4.159	1.246	11.134	1	.001	1.716	6.602
Location	A1_Age	.086	.070	1.491	1	.222	-.052	.224
	[A1_SpanishHispanicLatino=0]	1.946	.504	14.896	1	.000	.958	2.935
	[A1_SpanishHispanicLatino=1]	0[a]	.	.	0	.	.	.
	[A1_School=0]	-.475	.633	.563	1	.453	-1.715	.765
	[A1_School=1]	0[a]	.	.	0	.	.	.

Link function: Logit.

a. This parameter is set to zero because it is redundant.

Summary

This study evaluated whether the independent variables, age, disease stage, and education and ethnicity covariates are associated with the dependent variable Patient-Reported Quality of Life (PRQoL) among maturing DMD male patients. From the inferential statistics, RQ1, the association between age and PRQoL among maturing DMD males (Table 18, p=137) was non-significant (p>.05), which led to the acceptance of the null hypothesis and the conclusion that there is no association between age and

PRQoL among maturing DMD male patients. Likewise, in RQ2, the association between disease stage and PRQoL among maturing DMD males (p=.978, Table 19) was non-significant (p>.05), which led to the acceptance of the null and the conclusion that there is no association between disease stage and PRQoL among maturing DMD male patients. In the modeling question (RQ3), the assumption of proportional odds was not met ; there was a statistically significant association (p=between age, disease stage, ethnicity, and PRQoL among maturing DMD male patients (x^2 (12)=24.821, p=.016). Consequently, the Test of Parrell lines for each predictor variable was run to test for proportional odds, which led to dropping the variable disease stage (x^2 (3)13.430, p=.004). The ordinal logistic regression analysis evaluating the association between age, ethnicity, education, and PRQoL was statistically significant, x^2(3)= (16.767), p=(.001), which would lead one to conclude that at least one of the regression coefficients in the model is not equal to zero, which led to the rejection of the null and accept the alternative hypothesis, there is a statistically significant association between age, ethnicity, education, and PRQoL among maturing DMD male patients. The parameter estimates for RQ3 (Table 20) show that age and education did not add significantly to the model. However, the covariate variable, ethnicity, added significantly to the prediction, with an estimated log-odds estimate= [1.946], *SE* [.504], Wald [14.896][p=.001}(Table 21). Overall, the results indicate that non-Spanish DMD male patients have a statistically significantly better PRQoL than Spanish DMD male patients.

In Chapter 5, I will interpret the findings of the analysis, discuss the study limitations, discuss any additional findings, reintroduce the social change implications, address the appropriateness of the Ferrans et al. (2005) Conceptual Model of HRQoL for

the DMD male population, potential research implications, and recommendations for further research.

Chapter 5: Discussion, Conclusions, and Recommendations

Introduction

DMD is the most severe form of MD and causes progressive neuromuscular weakness, eventually impacting ambulation (Sahay et al., 2019). Although females may be carriers, DMD mainly impacts males. DMD has an estimated birth prevalence of 1:5000 live males (Szabo et al., 2022). As the disease progresses, there is a 5.7-fold increase in the economic burden (Wasilewska et al., 2020). Moreover, physical impairments gravely influence the PRQoL, leading to psychological, functional, and social disorders and economic dilemmas (Wasilewska et al., 2020). There is no cure for DMD; however, medical advances such as early diagnosis and treatment and novel medicines have extended the life expectancy of DMD patients beyond 18 years old (Landfeldt et al., 2020). Consequently, given the increase in life expectancy beyond the second decade, additional initiatives are required to maintain and enhance PRQoL, particularly mental well-being, normative aspirations, employment, and independent living (Landfeldt et al., 2020). There is a gap in the literature regarding factors such as age, disease stage, education, and ethnicity that impact the PRQoL of the maturing DMD male patient.

In this study, I proposed to determine whether there was an association between age, disease stage, and the outcome of PRQoL among maturing DMD male patients. The modeling analysis included the covariates of education and ethnicity. I conducted a descriptive analysis of the study variables and covariates.

Also, I performed an ordinal logistic regression to evaluate the association between age and PRQoL among maturing DMD male patients. The association between

age and PRQoL was not statistically significant (p>.05); therefore, the null hypothesis was accepted. I concluded that there is no association between age and PRQoL among maturing male DMD patients. A second ordinal logistic regression analysis evaluated the association between disease stage and PRQoL among maturing DMD male patients. The predictor variable, disease stage, did not add significantly to the prediction of PRQoL (p>.05). Therefore, I accept the null hypothesis and conclude that there is no association between disease stage and PRQoL among maturing male DMD patients. To answer the modeling question, an ordinal logistic regression analysis was conducted to investigate the association between age, ethnicity, education, and PRQOL among maturing DMD male patients. The predictor variables age (continuous: 10-22), and covariates education (dichotomous: yes, no), and ethnicity (Spanish: yes, no) in the ordinal logistic regression analysis, $p < .05$ would lead one to conclude that at least one of the regression coefficients in the model is not equal to zero. Parameter estimates show that age and education did not add significantly to the model. The covariate variable, ethnicity (non-Spanish), added significantly to the prediction, with an estimated log-odds estimate= [1.946], *SE* [.504], Wald [14.896][p=.001). The results indicate that non-Spanish DMD male patients have a statistically significantly better PRQoL than Spanish DMD male patients.

Interpretation of the Findings

Limited empirical research examines the association between age, disease stage, healthcare access, and PRQoL. Existent research documented the impact of PRQoL on the DMD children and adolescent population (Crisafulli et al., 2020). However, little is known about the factors that impact the PRQoL in the advanced stages of the disease.

This study's findings indicate that non-Hispanic DMD male patients have a statistically significantly better PRQoL than Hispanic DMD male patients. Likewise, Gocheva et al. (2019) discovered that independent of disease severity, patients from lower Socioeconomic status (ethnicity, income, education) experience reduced PRQoL compared to patients with high socioeconomic status (SES). Within Muscular Dystrophy (MD) registries, it was determined that 7.5% of individuals with DMD identified as Black and 20.5% identified as Latino/Hispanic (Barnard et al., 2020). Thus, the inclusion of racial/ethnic diversity in research studies is warranted to understand better and support diversity in DMD public health initiatives. My study indicates the need for further research evaluating the association between ethnicity and PRQoL in the maturing DMD adult male.

This study did not show a statistically significant association between age and PRQoL. In previous studies, older age was associated with lower PRQoL in individuals with neurological diseases such as DMD (Carlton et al., 2022). Conversely, many DMD adult males are psychosocially well-adjusted and report high levels of PRQoL (Andrews & Wahl, 2018; Peay et al., 2022). The assumption is that DMD patients learn to adjust to the complexities of disease progression (Weerkamp et al., 2022). My findings align with the disparities in associating age with PRQoL in the maturing DMD male patient; further research is required. Also, this study did not show a statistically significant association between disease stage and PRQoL. In the same manner, Szabo et al. (2022) postulated that although it may be intuitive that PRQoL would decline with disease progression, the relationship remains unclear. Conversely, a cross-sectional study by Andreozzi et al.

(2022) discovered a significant negative impact between DMD disease progression and PRQoL.

This study was based on Ferrans et al. (2005) Health-Related Quality of Life (HRQoL), which expanded Wilson and Cleary's model by clarifying individual and environmental factors (Bakas et al., 2012). Policymakers, researchers, and healthcare providers view HRQoL as a construct of interest (Costa et al., 2021). Ferrans et al. (2005) HRQoL consists of five main concepts: biological function, symptoms, functional status, general health perceptions, and overall Quality of Life (QoL). The five constructs align with the natural history of DMD: biological function and demographics (age, race, ethnicity, healthcare access); symptoms (ambulatory status, upper body strength, respiratory status, cardiac symptoms); functional status (ability to perform activities of daily living [ADLs], loss of ambulation, disease severity, physical ability); general health perceptions (overall health typically assessed with a single ranked question); overall quality of life, subjective well-being and "life satisfaction determined by" an individual's "evaluation of attributes of various domains of life" (Ferrans et al., 2005, p. 341). I drew from the five domains of the HRQoL model to align the RQs and the conceptual framework for this study(See Table 22). The logical connection between the Ferrans et al. (2005) Health-Related Quality of Life (HRQoL) framework includes physical impairments and psychological factors influencing PRQoL.

Table 22

Matching Ferrans et al. (2005) Conceptual Framework with Study Variables

Ferrans et al. (2005) Conceptual Model of HRQoL	Study Variables	Coding Scheme PROMIS and Neuro-QOL
1- Intrapersonal (characteristic: Biological Function)	1- Age	Age: Continuous (in years)
2- Intrapersonal (characteristic: Biological Function)	2- Ethnicity	Categorical: Hispanic: Non-Hispanic=0, Hispanic= 1
3- Institutional (characteristic: Functional capacity/social environmental factors)	3. Education (School Attendance) "Are you attending school now?'	Categorical: No =0, Yes=1
4- Intrapersonal (characteristic: Functional Status)	4- Disease stage (Physical mobility) Measures reflecting upper and lower extremity physical function Global 06: "To what extent are you able to carry out everyday activities such as walking, climbing stairs, carrying groceries, or moving a chair?	Ordinal: 5 = Completely 4 = Mostly 3 = Moderately 2 = A little 1 = Not at all
5- Interpersonal: (characteristic: Overall Quality of Life (QOL).	5- PRQoL: Measures reflecting PRQoL Global 02: "In general, would you say your quality of life is?"	Ordinal: 5 =Excellent 4 =Very good 3 =Good 2 = Fair 1 = Poor

Limitations of the Study

Several limitations to this study need to be considered when interpreting the findings. By utilizing a secondary data set PROMIS, Nuero-QoL, there may be bias regarding the delineation of DMD diagnosis from other sub-types of Muscular Dystrophy. Thus, the analysis may include non-DMD patients, resulting in an overrepresentation of the sample population. Second, by design, survey data may be susceptible to recall bias and misreporting of information. Also, causation cannot be ascertained because the original study is cross-sectional. Furthermore, The Neuro-QoL

validation participants were recruited from several clinical sites: Ann & Robert H. Lurie Children's Hospital of Chicago, Cleveland Clinic Foundation, Dartmouth-Hitchcock Medical Center, NorthShore University Health System, Northwestern University Feinberg School of Medicine, Rehabilitation Institute of Chicago, University of California-Davis, University of Chicago, University of Puerto Rico, and University of Texas Health Science Center; thus, the reported findings may not be generalizable to all populations.

Recommendations

Additional research is required to verify the findings from this study regarding the factors associated with PRQoL in maturing DMD male patients. Future research should include the utilization of a DMD disease-specific measurement instrument. The progressive nature of DMD results in a loss of ambulation around the time that a DMD patient's peers would be gaining independence; consequently, a disease-specific preference-based instrument that captures the full range of effects that impact DMD patients (Szabo et al., 2022). A disease-specific instrument should include aspects identified as significant by DMD patients, such as the impact of hope, fear, fatigue, social participation, and dignity (Szabo et al., 2022). Moreover, there is a need for diverse representation in rare disease studies. According to Barnard et al. (2020), there is a limited representation of black and Hispanic participants in DMD observational studies, indicating that these studies are at risk of selection bias. Additionally, future research is required to evaluate QoL instruments that explore dimensions specific to the Hispanic population.

The current study focused on age and disease stage's impact on PRQoL among maturing DMD male patients. Additional research is required to investigate other factors that may impact PRQoL, such as social support systems and social media utilization. Social support is "one's perception that they are being cared for and that assistance would be available when needed" (Mo et al., 2022, p. 2). One study conducted in Hong Kong with 941 adult participants established a positive association between social support and PRQoL (Mo et al., 2022). Also, in a cross-cultural study, Rodriguez et al. (2022) evaluated the services provided by two different cultural models (Mexico-Spain) to determine how the services impact the financial and emotional relationship between DMD patients and caregivers. Rodriguez et al. (2022) discovered that caregivers in Mexico have a greater well-being than caregivers in Spain, which may be attributed to Mexico's substantial cultural support system.

Social media platforms allow patients to discuss their health concerns and connect with similar patients. In a cohort study of 230 multiple myeloma (MM) patients, Gries and Fastenau (2020) concluded that Patient-oriented social media platforms contribute to patient well-being and PRQoL. Existing literature on the influence of social media usage (SMU) and subject well-being (SWB) is inconclusive, thus requiring additional research to establish an agreement in this area of research (Sheldon & Titova, 2023). Future healthcare initiatives for Hispanic DMD patients and caregivers should focus on social determinants of health, social support systems, and clinical outcomes like PRQoL.

Implications

The nature of rare diseases (RD), including DMD, requires target dissemination of research to Patient Advocacy groups. Patient Advocacy groups such as the National

Organization for Rare Disorders (NORD), CureDuchenne, Muscular Dystrophy Association (MDA), and Parent Project Muscular Dystrophy (PPMD)--provide social support, patient education, research grants, funding support, and raise awareness for RD patients, caregivers, and healthcare providers. I plan to present my research at patient advocacy forums. Of particular interest is the Akari Foundation, which is dedicated to supporting DMD Hispanic immigrant and low-income families. Successful dissemination of information requires the use of several methods across time. I will use the following methods: (a) sharing information through social media or on an organization's website and (b) disseminating information on an organization's website (caregiver groups, rare disease organizations, public health forums). The results of this study indicate that Hispanic/Latino DMD participants experience a lower PRQoL score compared to non-Hispanic/Latino DMD participants; thus, indicating a need for increased representation in research studies of the Hispanic population. Moreover, the findings indicate a need for initiatives that address PRQoL in maturing DMD male patients but emphasize a greater need in the Hispanic/Latino community.

Conclusions

In this study, I evaluated whether associations existed between age, disease stage, and PRQoL. The ordinal logistic regression analysis performed for the independent variable age did not indicate an association with PRQoL. Likewise, The ordinal logistic regression analysis performed for the independent variable disease stage did not indicate an association with PRQoL. However, this study demonstrated an association between Hispanic/Latino ethnicity and PRQoL among maturing DMD male patients. It remains unclear in the literature whether there is an association between age, disease stage, and

PRQoL in maturing DMD male patients. Identifying whether an association exists may lead to initiatives addressing the needs of maturing DMD male patients that enhance PRQoL. Therefore, I encouraged researchers to increase the recruitment of Hispanic/Latino DMD participants. Also, I recommend crafting QoL instruments tailored to the Hispanic Culture. Lastly, I recommend additional research investigating two other factors that may impact PRQoL: social support systems and social media utilization. The co-existence of the disease burden and the vulnerability of Hispanic DMD patients require innovative strategies to enhance PRQoL utilities that offer tailored interventions for social support, healthcare, and public health policy. Therefore, it is essential that healthcare providers, policymakers, patient advocacy groups, and public health officials collaborate to enhance the well-being of the Hispanic DMD population.

References

American Psychological Association. (2016). Revision of ethical standard 3.04 of the "Ethical Principles of Psychologists and Code of Conduct" (2002, as amended 2010). *American Psychologist, 71*, 900. Retrieved from https://www.apa.org/ethics/code

Amtmann, D., Cook, K. F., Jensen, M. P., Chen, W. H., Choi, S., Revicki, D., Cella, D., Rothrock, N., Keefe, F., Callahan, L., & Lai, J. S. (2010). Development of a PROMIS item bank to measure pain interference. *Pain*, *150*(1), 173–182. https://doi.org/10.1016/j.pain.2010.04.025

Andreozzi, V., Labisa, P., Mota, M., Monteiro, S., Alves, R., Almeida, J., Vandewalle, B., Felix, J., Buesch, K., Canhão, H., & de Zarate, I. B. O. (2022). Quality of life and informal care burden associated with Duchenne muscular dystrophy in Portugal: The COIDUCH study. *Health Quality of Life Outcomes*, *20*(1), 36. https://doi.org/10.1186/s12955-022-01941-x

Andrews, J. G., & Wahl, R. A. (2018). Duchenne and Becker muscular dystrophy in adolescents: current perspectives. *Adolescent Health, Medicine and Therapeutics*, *9*, 53–63. https://doi.org/10.2147/AHMT.S125739

Baguley, T. (2009). Standardized or simple effect size: what should be reported? *British Journal of Psychology,100*(3), 603–617. https://doi.org/10.1348/000712608X377117

Bakas, T., McLennon, S. M., Carpenter, J. S., Buelow, J. M., Otte, J. L., Hanna, K. M., Ellett, M. L., Hadler, K. A., & Welch, J. L. (2012). Systematic review of health-related quality of life models. *Health and Quality of Life Outcomes,10*, 134.

https://doi.org/10.1186/1477-7525-10-134

Bann, C. M., Abresch, R. T., Biesecker, B., Conway, K. C., Heatwole, C., Peay, H., Scal, P., Strober, J., Uzark, K., Wolff, J., Margolis, M., Blackwell, A., Street, N., Montesanti, A., & Bolen, J. (2015). Measuring quality of life in muscular dystrophy. *Neurology, 84*(10), 1034–1042. https://doi.org/10.1212/WNL.0000000000001336

Barnard, A. M., Riehl, S. L., Willcocks, R. J., Walter, G. A., Angell, A. M., & Vandenborne, K. (2020). Characterizing enrollment in observational studies of Duchenne muscular dystrophy by race and ethnicity. *Journal of Neuromuscular Diseases, 7*(2), 167–173. https://doi.org/10.3233/JND-190447

Birnkrant, D. J., Bushby, K., Bann, C. M., Apkon, S. D., Blackwell, A., Brumbaugh, D., Case, L. E., Clemens, P. R., Hadjiyannakis, S., Pandya, S., Street, N., Tomezsko, J., Wagner, K. R., Ward, L. M., Weber, D. R., & D.M.D. Care Considerations Working Group. (2018). Diagnosis and management of Duchenne muscular dystrophy, part 1: Diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. *The Lancet Neurology, 17*(3), 251-267. https://doi.org/10.1016/S1474- 4422(18)30024-3

Boettcher, J., Boettcher, M., Wiegand-Grefe, S., & Zapf, H. (2021). Being the pillar for children with rare diseases - a systematic review on parental quality of life. *International Journal of Environmental Research and Public Health, 18*(9), 4993. https://doi.org/10.3390/ijerph18094993

Bray, N., Spencer, L. H., & Edwards, R. T. (2020). Preference-based measures of health-related quality of life in congenital mobility impairment: A systematic review of

validity and responsiveness. *Health economics review*, *10*(1), 9. https://doi.org/10.1186/s13561-020-00270-3

Brogna, C., Coratti, G., Pane, M., Ricotti, V., Messina, S., D'Amico, A., Bruno, C., Vita, G., Berardinelli, A., Mazzone, E., Magri, F., Ricci, F., Mongini, T., Battini, R., Bello, L., Pegoraro, E., Baranello, G., Previtali, S. C., Politano, L., … Mercuri, E. (2019). Long-term natural history data in Duchenne muscular dystrophy ambulant patients with mutations amenable to skip exons 44, 45, 51 and 53. *PloS One*, *14*(6), e0218683. https://doi.org/10.1371/journal.pone.0218683

Bronfenbrenner, U. (1977). Toward an experimental ecology of human development. *American Psychologist*, 513-531. Retrieved from http://jmsw.org/hdf/facultystaff/Tudge/

Broomfield, J., Hill, M., Guglieri, M., Crowther, M., & Abrams, K. (2021). Life expectancy in Duchenne muscular dystrophy: Reproduced individual patient data meta-analysis. *Neurology*, *97*(23), e2304–e2314. https://doi.org/10.1212/WNL.0000000000012910

Brusa, R., Magri, F., Bresolin, N., Comi, G. P., & Corti, S. (2020). Noncoding RNAs in Duchenne and Becker muscular dystrophies: Role in pathogenesis and future prognostic and therapeutic perspectives. *Cellular and Molecular Life Sciences : CMLS*, *77*(21), 4299–4313. https://doi.org/10.1007/s00018-020-03537-4

Canadian Institutes of Health Research. (2018). Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research Council, Tri-Council Policy Statement: Ethical Conduct for Research Involving

Humans. Retrieved from https://ethics.gc.ca/eng/policy-politique_tcps2-eptc2_2018.html

Carlton, J., Powell, P. A., & Project HERCULES Carer Group (2022). Measuring carer quality of life in Duchenne muscular dystrophy: A systematic review of the reliability and validity of self-report instruments using COSMIN. *Health and Quality of Life Outcomes*, *20*(1), 57. https://doi.org/10.1186/s12955-022-01964-4

Cella, D. (2017a). NeuroQOL clinical validation study (aka Wave II). *Harvard Dataverse*. https://doi.org/10.7910/DVN/WLFEUV

Cella, D. (2017b). NeuroQOL wave 1b. *Harvard Dataverse*. Retrieved from https://doi.org/10.7910/DVN/TLCDRX

Cella, D., Choi, S. W., Condon, D. M., Schalet, B., Hays, R. D., Rothrock, N. E., Yount, S., Cook, K. F., Gershon, R. C., Amtmann, D., DeWalt, D. A., Pilkonis, P. A., Stone, A. A., Weinfurt, K., & Reeve, B. B. (2019). PROMIS® adult health profiles: Efficient short-form measures of seven health domains. *Value in Health*, *22*(5), 537-544. https://doi.org/10.1016/j.jval.2019.02.004

Cella, D., Riley, W., Stone, A., Rothrock, N., Reeve, B., Yount, S., Amtmann, D., Bode, R., Buysse, D., Choi, S., Cook, K., DeVellis, R., DeWalt, D., Fries, J. F., Gershon, R., Hahn, E. A., Lai, J. S., Pilkonis, P., Revicki, R., … PROMIS Cooperative Group, C. G. (2010). The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008. *Journal of Clinical Epidemiology*, *63*(11), 1179–1194.

Cella, D., Schalet, B. D., Kallen, M., Lai, J. S., Cook, K. F., Rutsohn, J., & Choi, S. W. (2016). PROSetta Stone® analysis report: A Rosetta Stone for patient reported outcomes. Chicago, IL: Department of Medical Social Sciences, Feinberg School of Medicine, Northwestern University. Retrieved from https://static1.squarespace.com/static/60c7c36a1afd4a3ab90af0a6/t/60c8fd649abf4b38eff96a76/1623784809470/PROsetta+Stone+Analysis+Report_Vol+2_09_15-2016.pdf

Choi, S. W., Podrabsky, T., McKinney, N., Schalet, B. D., Cook, K. F., & Cella, D. (2012). Prosetta Stone® Methodology: A Rosetta Stone For Patient Reported Outcomes. Chicago, IL: Department of Medical Social Sciences, Feinberg School of Medicine, Northwestern University.

Cohen, M. L., Lanzi, A. M., & Boulton, A. J. (2021). Clinical Use of PROMIS, Neuro-QoL, TBI-QoL, and other Patient-Reported Outcome Measures for Individual adult Clients with Cognitive and Language Disorders. *Seminars in Speech and Language*, *42*(3), 192–210. https://doi.org/10.1055/s-0041-1731365

Costa, D., Mercieca-Bebber, R., Rutherford, C., Tait, M. A., & King, M. T. (2021). How is quality of life defined and assessed in published research? *Quality of Life Research: An International Journal of Quality-of-Life Aspects of Treatment, Care, and Rehabilitation*, *30*(8), 2109–2121. https://doi.org/10.1007/s11136-021-02826-0

Counterman, K. J., Furlong, P., Wang, R. T., & Martin, A. S. (2020). Delays in diagnosis of muscular dystrophy: An evaluation of genotypic and sociodemographic factors. *Muscle Nerve, 61*(1), 36-43 https://doi.org/10.1002/mus.26528

Crisafulli, S., Sultana, J., Fontana, A., Salvo, F., Messina, S., & Trifirò, G. (2020). Global epidemiology of Duchenne muscular dystrophy: An updated systematic review and meta-analysis. *Orphanet Journal of Rare Diseases, 15*, 1-20. https://doi.org/10.1186/s13023-020-01430-8

Cuschieri, S. (2019). The STROBE guidelines. *Saudi Journal of Anesthesia*, *13*(1), S31–S34. https://doi.org/10.4103/sja.SJA_543_18

Data Verse Community Norms. (2022). Data verse community norms. Retrieved from https://dataverse.org/best-practices/dataverse-community-norms

Dicker, D., Nguyen, G., Abate, D., Abate, K. H., Abay, S. M., Abbafati, C., Abbasi, N., Abbastabar, H., Abd-Allah, F., Abdela, J., Abdelalim, A., Abdel-Rahman, O., Abdi, A., Abdollahpour, I., Abdulkader, R. S., Abdurahman, A. A., Abebe, H. T., Abebe, M., Abebe, Z., … Murray, C. J. L. (2018). Global, regional, and national age-sex-specific mortality and life expectancy, 1950–2017: A systematic analysis for the Global Burden of Disease Study 2017. *The Lancet*, *392*(10159), 1684–1735. https://doi.org/10.1016/S0140-6736(18)31891-9

Dong, L., Martinez, A. J., Buysse, D. J., & Harvey, A. G. (2019). A composite measure of sleep health predicts concurrent mental and physical health outcomes in adolescents prone to eveningness. *Sleep Health*, *5*(2), 166-174.

Dowling, J. J., D Gonorazky, H., Cohn, R. D., & Campbell, C. (2018). Treating pediatric neuromuscular disorders: The future is now. *American Journal of Medical Genetics Part A*, *176*(4), 804–841. https://doi.org/10.1002/ajmg.a.38418

Duangchan, C., & Matthews, A. K. (2021). Application of Ferrans et al.'s conceptual model of health-related quality of life: A systematic review. *Research in Nursing Health. 44*(3), 490–512. https://doi.org/10.1002/nur.22120

Dunn, S. L., Arslanian-Engoren, C., DeKoekkoek, T., Jadack, R., & Scott, L. D. (2015). Secondary data analysis as an efficient and effective approach to nursing research. *Western Journal of Nursing Research*, *37*(10):1295-1307. doi:10.1177/0193945915570042

Faison, Y., Burns, D., & Weed, D. (2016). Application of Ferrans and Powers Quality of Life Model to improve diabetes health outcomes. *Holistic Nursing Practice*, *30*(3), 131–138. https://doi.org/10.1097/HNP.0000000000000149

Faul, F., Erdfelder, E., Lang, A.-G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, *39*, 175-191.

Ferizovic, N., Summers, J., de Zárate, I. B. O., Werner, C., Jiang, J., Landfeldt, E., & Buesch, K. (2022). Prognostic indicators of disease progression in Duchenne muscular dystrophy: A literature review and evidence synthesis. *PLoS One*, *17*(3), 1–38. https://doi.org/10.1371/journal.pone.0265879

Frew, J. W., Davidson, M., & Murrell, D. F. (2017). Disease-specific health-related quality of life patient-reported outcome measures in Genodermatoses: A systematic review and critical evaluation. *Orphanet Journal of Rare Diseases*, *12*, 1–10. https://doi.org/10.1186/s13023-017-0739-5

Gershon, R. C., Lai, J. S., Bode, R., Choi, S., Moy, C., Bleck, T., Miller, D., Peterman, A., & Cella, D. (2012). Neuro-QOL: Quality of life item banks for adults with neurological disorders: item development and calibrations based upon clinical and general population testing. *Quality of Life Research: an International Journal of Quality-of-life Aspects of Treatment, Care, and Rehabilitation*, *21*(3), 475–486. https://doi.org/10.1007/s11136-011-9958-8

Gil-González, I., Martín-Rodríguez, A., Conrad, R., & Pérez-San-Gregorio, M. Á. (2020). Quality of life in adults with multiple sclerosis: A systematic review. *BMJ Open*, *10*(11), e041249.

Gocheva, V., Schmidt, S., Orsini, A. L., Hafner, P., Schaedelin, S., Rueedi, N., Weber, P., & Fischer, D. (2019). Association between health-related quality of life and motor function in ambulant and nonambulant Duchenne muscular dystrophy patients. *Journal of Child Neurology*. 2019;34(14):873-885. doi:10.1177/0883073819865681

Gries, K. S., & Fastenau, J. (2020). Using a digital patient powered research network to identify outcomes of importance to patients with multiple myeloma. *Journal of Patient-Reported Outcomes*, *4*(1), 74. https://doi.org/10.1186/s41687-020-00242-5

Hanmer, J., Jensen, R. E., & Rothrock, N. (2020). A reporting checklist for HealthMeasures' patient-reported outcomes: ASCQ-Me, Neuro-QoL, NIH Toolbox, and PROMIS. *Journal Patient-Reported Outcomes*, *4*, 1-7. https://doi.org/10.1186/s41687-020-0176-4

Hoskin, J. (2021). Troubling norms? Adults and teenagers with a life-limiting impairment in Denmark and England talk about their lives, support, and plans. *European Journal of Special Needs Education, 36*(3), 329-343. https://doi.org/10.1080/08856257.2020.1754545

Houwen-van Opstal, S. L., Heutinck, L., Jansen, M., Krom, Y. D., Cup, E. H., Hendriksen, J. G., Willemsen, M. A. A. P., Verschuuren, J. G. M., Niks, E. H., & de Groot, I. J. (2021). Occurrence of symptoms in different stages of Duchenne muscular dystrophy and their impact on social participation. *Muscle & Nerve, 64*(6), 701-709.

Jacques, M. F., Stockley, R. C., Onambele-Pearson, G. L., Reeves, N. D., Stebbings, G. K., Dawson, E. A., Groves, L., & Morse, C. I. (2019). Quality of life in adults with muscular dystrophy. *Health & Quality of Life Outcomes, 17*(1). https://doi:10.1186/s12955-019-1177-y

Jager, J., Putnick, D. L., & Bornstein, M. H. (2017). II. More than just convenient: The scientific merits of homogeneous convenience samples. *Monographs of the Society for Research in Child Development, 82*(2), 13–30. https://doi.org/10.1111/mono.12296

Jespersen, L. N., Michelsen, S. I., Holstein, B. E., Tjørnhøj-Thomsen, T., & Due, P. (2018). Conceptualization, operationalization, and content validity of the EQOL-questionnaire measuring quality of life and participation for persons with disabilities. *Health Quality of Life Outcomes, 16*, 199. https://doi.org/10.1186/s12955-018-1024-6

Kaat, A. J., Buckenmaier, C. T., Cook, K. F., Rothrock, N. E., Schalet, B. D., Gershon, R. C., & Vrahas, M. S. (2019). The expansion and validation of a new upper extremity item bank for the Patient-Reported Outcomes Measurement Information System®(PROMIS). *Journal of Patient-Reported Outcomes*, *3*, 1-8.

Kraemer, H., & Blasey, C. (2016). The "rules of the game". *How Many Subjects*, 1-21. SAGE Publications, Ltd. https://dx.doi.org/10.4135/9781483398761

Kwon, J., Freijser, L., Huynh, E., Howell, M., Chen, G., Khan, K., Daher, S., Roberts, N., Harrison, C., Smith, S., Devlin, N., Howard, K., Lancsar, E., Bailey, C., Craig, J., Dalziel, K., Hayes, A., Mulhern, B., Wong, G., … Petrou, S. (2022). Systematic review of conceptual, age, measurement, and valuation considerations for generic multidimensional childhood patient-reported outcome measures. *PharmacoEconomics*, *40*, 379–431. https://doi.org/10.1007/s40273-021-01128-

Lai, J. S., Nowinski, C., Victorson, D., Bode, R., Podrabsky, T., McKinney, N., Straube, D., Holmes, G. L., McDonald, C. M., Henricson, E., Abresch, R. T., Moy, C. S., & Cella, D. (2012). Quality-of-life measures in children with neurological conditions: pediatric Neuro-QOL. *Neurorehabilitation and Neural Repair*, *26*(1), 36–47. https://doi.org/10.1177/1545968311412054

Landfeldt, E., Thompson, R., Sejersen, T., McMillan, H. J., Kirschner, J., & Lochmüller, H. (2020). Life expectancy at birth in Duchenne muscular dystrophy: A systematic review and meta-analysis. *European Journal of Epidemiology*, *35*(7), 643–653. https://doi:10.1007/s10654-020-00613-8

Lavrakas, P. J. (2008). Encyclopedia of Survey Research Methods. SAGE Publications, Inc. Retrieved from https://dx.doi.org/10.4135/9781412963947

Lewis-Beck, M. S., Bryman, A., & Liao, T. F. (2004). Regression models for ordinal data. In *The SAGE encyclopedia of social science research methods, 1*, 942-942. https://dx.doi.org/10.4135/9781412950589.n833

Liang, R., Chan, S. H. S., Ho, F. K. W., Tang, O. C., Cherk, S. W. W., Ip, P., & Lau, E. Y. Y. (2019). Health-related quality of life in Chinese boys with Duchenne muscular dystrophy and their families. *Journal of Child Health Care*, *23*(3), 495-506. https://doi.org/10.1177/1367493519857423

Lim, Y., Kreider, C. M., Alvarez, M., & Bendixen, R. M. (2019). HRQoL in Barth Syndrome: Agreement between child self-reports and parent proxy-reports and its relationship to parental HRQoL. *Journal of Human & Clinical Genetics, 1*(2), 10.29245/2690-0009/2019/2.1104. https://doi.org/10.29245/2690-0009/2019/2.1104

McDonald, C. M., & Mercuri, E. (2018). Evidence-based care in Duchenne muscular dystrophy. *The Lancet Neurology*, *17*(5), 389-391

McLeroy, K. R., Bibeau, D., Steckler, A., & Glanz, K. (1988). An ecological perspective on health promotion programs. *Health education quarterly, 15*(4), 351–377. https://doi.org/10.1177/109019818801500401

Medina, L. D., Torres, S., Alvarez, E., Valdez, B., & Nair, K. V. (2019). Patient-reported outcomes in multiple sclerosis: Validation of the Quality of Life in Neurological Disorders (Neuro-QoLTM) short forms. *Multiple Sclerosis Journal - Experimental, Translational, and Clinical.* https://doi.org/10.1177/2055217319885986

Merriam-Webster. (n.d.). Cardiomyopathy. In *Merriam-Webster.com dictionary*. Retrieved July 24, 2022, from https://www.merriam-webster.com/dictionary/cardiomyopathy

Mo, P. K., Wong, E. L., Yeung, N. C., Wong, S. Y., Chung, R. Y., Tong, A. C. Y., Ko, C. C. Y., Li, J., & Yeoh, E. K. (2022). Differential associations among social support, health promoting behaviors, health-related quality of life and subjective well-being in older and younger persons: a structural equation modelling approach. *Health and Quality of Life Outcomes*, *20*(1), 38. https://doi.org/10.1186/s12955-022-01931-z

Moore, E., Thomas, K., & Gephart, S. (2021). Fresh perspectives on an old method. *CIN: Computers, Informatics, Nursing*, *39*(8), 393-399. doi: 10.1097/CIN.0000000000000796.

Mullin, A. P., Corey, D., Turner, E. C., Liwski, R., Olson, D., Burton, J., Sivakumaran, S., Hudson, L. D., Romero, K., Stephenson, D. T., & Larkindale, J. (2021). Standardized data structures in rare diseases: CDISC user guides for Duchenne muscular dystrophy and Huntington's disease. *Clinical and Translational Science*, *14*(1), 214-221.

Nagy, S., Schmidt, S., Hafner, P., Klein, A., Rubino-Nacht, D., Gocheva, V., Bieri, O., Vuillerot, C., Bonati, U., & Fischer, D. (2019). Measurements of motor function and other clinical outcome parameters in ambulant children with Duchenne muscular dystrophy. *Journal of Visualized Experiments: JoVE*, (143), 10.3791/58784. https://doi.org/10.3791/58784

Naseri, A., Nasiri, E., Talebi, M., Karimi, K., & Talebi, M. (2020). Does the type of disease-modifying drugs impact the quality of life in patients with relapsing-remitting multiple sclerosis? *Romanian Journal of Neurology*, *19*(3), 171–178.

National Institute of Health. (2021). "Muscular Dystrophy: Hope Through Research". *National Institute of Neurological Disorders and Stroke,* 13 (77), Retrieved from NIH. National Institute of Neurological Disorders and Stroke

National Institute of Neurological Disorders and Stroke (NINDS). (2015). User Manual for the Quality of Life in Neurological Disorders (Neuro-QoL) Measures, Version 2.0.

Nayak, M. S. D. P., & Narayan, K. A. (2019). Strengths and weaknesses of online surveys. *Technology*, *6*(7), 0837-2405053138.

Obeidat, H. M., Al Hadid, L. A., Al-Sagarat, A. Y., & Khrisat, M. (2021). Lived experience of Jordanian parents having a child with Duchenne muscular dystrophy. *Journal of Pediatric Nursing*, *57*, 5–10. https://doi.org/10.1016/j.pedn.2020.11.001

Osborne, J. (2017). Basic estimation and assumptions. SAGE Publications, Inc. https://dx.doi.org/10.4135/9781071802724

Otto, C., Steffensen, B. F., Højberg, A. L., Barkmann, C., Rahbek, J., Ravens-Sieberer, U., Mahoney, A., Vry, J., Gramsch, K., Thompson, R., Rodger, S., Bushby, K., Lochmüller, H., & Kirschner, J. (2017). Predictors of health-related quality of life in boys with Duchenne muscular dystrophy from six European countries. *Journal of Neurology*, *264*(4), 709–723. https://doi.org/10.1007/s00415-017-8406-2

Pallant, J. (2010). SPSS survival manual: A step-by-step guide to data analysis using SPSS. Maidenhead: Open University Press/McGraw-Hill.

Park, Y. E., Kim, D. S., Choi, Y. C., & Shin, J. H. (2019). Progression of GNE myopathy based on the patient-reported outcome. *Journal of Clinical Neurology (Seoul, Korea)*, *15*(3), 275–284. https://doi.org/10.3988/jcn.2019.15.3.275

Peay, H. L., Do, B. T., Khosla, N., Paramsothy, P., Erickson, S. W., Lamb, M. M., Whitehead, N., Fox, D. J., Pandya, S., Kinnett, K., Wolff, J., & Howard, J. F. (2022). Role attainment in emerging adulthood: Subjective evaluation by male adolescents and adults with Duchenne and Becker Muscular Dystrophy. *Journal of Neuromuscular Diseases*, *9*(3), 447–456. https://doi.org/10.3233/JND-210709

Post, M. W. (2014). Definitions of quality of life: What has happened and how to move on. *Topics in Spinal Cord Injury Rehabilitation*, *20*(3), 167–180. https://doi.org/10.1310/sci2003-167

Pourhoseingholi, M. A., Baghestani, A. R., & Vahedi, M. (2012). How to control confounding effects by statistical analysis. *Gastroenterology and Hepatology from Bed to Bench*, *5*(2), 79–83.

Powell, P. A., Carlton, J., & Rowen, D. (2019). Producing a preference-based quality of life measure for people with Duchenne muscular dystrophy: A mixed-methods study protocol. *BMJ Open, 9*(3). doi:10.1136/ bmjopen-2018-023685

Powell, P. A., Carlton, J., Rowen, D., Chandler, F., Guglieri, M., & Brazier, J. E. (2021). Development of a new quality of life measure for Duchenne Muscular Dystrophy using mixed methods. *Neurology*, *96*(19), e2438 e2450; doi: 10.1212/WNL.0000000000011896

Powell, P. A., Carlton, J., Woods, H. B., & Mazzone, P. (2020). Measuring quality of life in Duchenne muscular dystrophy: a systematic review of the content and structural validity of commonly used instruments. *Health and Quality of Life Outcomes*, *18*(1), 1-26.

Propp, R., McAda, L., Davis, A. M., Salbach, N. M., Weir, S., Encisa, C., & Narayanan, U. G. (2019). Development and content validation of the Muscular Dystrophy Child Health Index of Life with Disabilities questionnaire for children with Duchenne muscular dystrophy. *Developmental Medical Child Neurology*, *61*(1), 75-81. doi:10.1111/dmcn.13977

Rodríguez, A. A., Amayra, I., López-Paz, J. F., Martínez, O., García, M., Salgueiro, M., Al-Rashaida, M., Luna, P. M., Pérez-Nuñez, P., Passi, N., García, I., & Ortega, J. (2022). The role of associations in reducing the emotional and financial impact on parents caring for children with Duchenne muscular dystrophy: A cross-cultural study. *International Journal of Environmental Research and Public Health*, *19*(19). https://doi.org/10.3390/ijerph191912334

Rowen, D., Powell, P., Mukuria, C., Carlton, J., Norman, R., & Brazier, J. (2021). Deriving a preference-based measure for people with Duchenne muscular dystrophy from the DMD-QoL. *Value in Health: The Journal of the International Society for Pharmacoeconomics and Outcomes Research*, *24*(10), 1499–1510. https://doi.org/10.1016/j.jval.2021.03.007

Ryder, S., Leadley, R. M., Armstrong, N., Westwood, M., de Kock, S., Butt, T., Jain, M., & Kleijnen, J. (2017). The burden, epidemiology, costs, and treatment for Duchenne muscular dystrophy: an evidence review. *Orphanet Journal of Rare Diseases, 12*, 1–21. https://doi:10.1186/s13023-017-0631-3

Sahay, K. M., Smith, T., Conway, K. M., Romitti, P. A., Lamb, M. M., Andrews, J., Pandya, S., Oleszek, J., Cunniff, C., & Valdez, R. (2019). A review of MD S'AR net's research contributions to Pediatric-Onset Dystrophinopathy in the United States; 2002-2017. *Journal of Child Neurology, 34*(1), 44-53. https://doi.org/10.1177/0883073818801704

Salkind, N. J. (2010a). Sample. In Encyclopedia of research design (Vol. 1, pp. 1395-1299). SAGE Publications, Inc., https://dx.doi.org/10.4135/9781412961288.n395

Salkind, N. J. (2010b). Threats to validity. *Encyclopedia of Research Design*, 1, 1509-1512. SAGE Publications, Inc. https://dx.doi.org/10.4135/9781412961288.n462

Salkind, N. J. (2010c). Validity of measurement. Encyclopedia of Research Design, 1, 1592-1596. SAGE Publications, Inc. https://dx.doi.org/10.4135/9781412961288.n487

Schalet, B. D., Sangdon, L., Cella, D., & Choi, S. W. (2021). Linking scores with patient-reported health outcome instruments: A validation study and comparison of three linking methods. *Psychometrika, 86*(3), 717-746.

Schwartz, C. E., Stark, R. B., Borowiec, K., & Rapkin, B. D. (2022). Drivers of caregiver impact in Duchenne muscular dystrophy: a cohort study. *J Patient Rep Outcomes, 6*, 22 https://doi.org/10.1186/s41687-022-00421-6

Sheldon, K. M., & Titova, L. (2023). Social media use and well-being: testing an integrated self-determination theory model, *MediaPsychology,* doi:10.1080/15213269.2023.2185259

Shepherd, V., Hood, K., & Wood, F. (2022). Unpacking the 'black box of horrendousness': A qualitative exploration of the barriers and facilitators to conducting trials involving adults lacking capacity to consent. *Trials, 23*(1), 471. https://doi.org/10.1186/s13063-022-06422-6

Solichin, I., Prabowo, I., Laras, S., Putra, N. H. D., & Rhatomy, S. (2021). Early ambulatory Duchenne muscular dystrophy: First symptomatic stage of ambulation - A case report. *International Journal of Surgery Open, 33*. https://doi.org/10.1016/j.ijso.2021.100349

Song, M. K., Lin, F. C., Ward, S. E., & Fine, J. P. (2013). Composite variables: When and how. *Nursing Research*, *62*(1), 45–49. https://doi.org/10.1097/NNR.0b013e3182741948

Soper, D. S. (2023). A-priori sample size calculator for multiple regression [Software]. Available from https://www.danielsoper.com/statcalc

Starfield, B., Riley, A. W., Green, B. F., Ensminger, M. E., Ryan, S. A., Kelleher, K., Harris, S., Johnston, D., & Vogel, K. (1995). The adolescent child health and illness profile. *Medical Care, 33*(5), 553-566. doi:10.1097/00005650-199505000-00008

Staunton, H., Trennery, C., Arbuckle, R., Guridi, M., Zhuravleva, E., Furlong, P., Fischer, R., & Hall, R. (2021). Development of a Clinical Global Impression of Change (CGI-C) and a Caregiver Global Impression of Change (CaGI-C) measure for ambulant individuals with Duchenne muscular dystrophy. *Health Qual Life Outcomes, 19*, 184. https://doi.org/10.1186/s12955-021-01813-w

Suarez, A., Reilly, C., & Fajgenbaum, D. C. (2019). Quantitative analysis of a rare disease network's international contact database and E-repository provides insights into biobanking in the electronic consent era. *Orphanet Journal of Rare Diseases, 14*(1), N.PAG. https://doi.org/10.1186/s13023-019-1145-y

Szabo, S. M., Audhya, I. F., Malone, D. C., Feeny, D., & Gooch, K. L. (2022). Characterizing health state utilities associated with Duchenne muscular dystrophy: A systematic review. *Quality of Life Research: An International Journal of Quality-of-Life Aspects of Treatment, Care & Rehabilitation. https*://doi:10.1007/s11136-019-02355-x

Szigyarto, C. A., & Spitali, P. (2018). Biomarkers of Duchenne muscular dystrophy: Current findings. *Degenerative Neurological and Neuromuscular Disease, 8*, 1–13. https://doi.org/10.2147/DNND.S121099

Uttley, L., Carlton, J., Woods, H. B., & Brazier, J. (2018). A review of quality-of-life themes in Duchenne muscular dystrophy for patients and caregivers. *Health and Quality of Life Outcomes, 16*(1), 237. https://doi.org/10.1186/s12955-018-1062-0

Vaidya, S., & Boes, S. (2018). Measuring quality of life in children with spinal muscular atrophy: A systematic literature review. *Quality of Life Research, 27*, 3087–3094. https://doi.org/10.1007/s11136-018-1945-x

Valentine, T. R., Weiss, D. M., Jones, J. A., & Andersen, B. L. (2019). Construct validity of PROMIS® Cognitive Function in cancer patients and non-cancer controls. *Health Psychology, 38*(5), 351–358. https://doi.org/10.1037/hea0000693

Van Breukelen, G. (2022). The SAGE encyclopedia of research design. SAGE Publications, Inc. https://dx.doi.org/10.4135/9781071812082

Vanier, A., Oort, F. J., McClimans, L., Ow, N., Gulek, B. G., Böhnke, J. R., Sprangers, M., Sébille, V., Mayo, N., & Response–Shift in Sync Working Group. (2021). Response shift in patient-reported outcomes: definition, theory, and a revised model. *Quality of Life Research: An International Journal of Quality-of-Life Aspects of Treatment, Care, and Rehabilitation, 30*(12), 3309-3322. https://doi.org/10.1007/s11136-021-02846-w

Verbeke, G., & Molenberghs, G. (2013). Generalized linear mixed models—overview. SAGE Publications Ltd, https://dx.doi.org/10.4135/9781446247600

Wasilewska, E., Małgorzewicz, S., Sobierajska-Rek, A., Jabłońska-Brudło, J., Górska, L., Śledzińska, K., Bautembach-Minkowska, J., & Wierzba, J. (2020). Transition from childhood to adulthood in patients with Duchenne muscular dystrophy. *Medicina (Kaunas, Lithuania), 56*(9), 426. https://doi.org/10.3390/medicina56090426

Weerkamp, P. M. M., Collin, P., Maas, R. J., Vermeulen, R. J., Klinkenberg, S., & Hendriksen, J. G. M. (2022). Psychosocial adjustment in adults with Duchenne muscular dystrophy: A pilot study on a shortened parent-report questionnaire. *Neuromuscular Disorders, 32*(2), 159-165. https://doi.org/10.1016/j.nmd.2021.10.008

Williams, R. & Quiroz, C. (2020). Ordinal regression models. SAGE Publications, Inc. http://dx.doi.org/10.4135/9781526421036

Wilson, I. B., & Cleary, P. D. (1995). Linking clinical variables with health-related quality of life. A conceptual model of patient outcomes. *JAMA*, *273*(1), 59–65.

Zhao, Q., Adeli, E., & Pohl, K. M. (2020). Training confounder-free deep learning models for medical applications. *Nature Communications, 11*(1), 6010. https://doi.org/10.1038/s41467-020-19784-9

Zhou, T., Guan, H., Wang, L., Zhang, Y., Rui, M., & Ma, A. (2021). Health-related quality of life in patients with different diseases measured with the EQ-5D-5L: a systematic review. *Frontiers in Public Health*, *9*, 675523.

Zöllner, J. P., Conradi, N., Sauter, M., Knuf, M., Knake, S., Kurlemann, G., Mayer, T., Hertzberg, C., Bertsche, A., Immisch, I., Klein, K. M., Marquard, K., Meyer, S., Noda, A. H., von Podewils, F., Schäfer, H., Thiels, C., Zukunft, B., Schubert-Bast, S., … Strzelczyk, A. (2021). Quality of life and its predictors in adults with tuberous sclerosis complex (TSC): A multicentre cohort study from Germany. *Neurological Research and Practice*, *3*(1), 35. https://doi.org/10.1186/s42466-021-00130-3

Appendix A: Keyword Search Two

Database	Search Terms	Results	Notes
Health Science	Muscular Dystrophy AND (diagnosis or diagnosing or diagnostics)	2,231	Broad search; scientific (biomarkers); narrow by using multiple terms
Health Science	Muscular Dystrophy AND age of diagnosis	88	More focused; Several DMD age of diagnosis
Health Science	Muscular Dystrophy AND (early diagnosis or early intervention)	129	More focused; Several DMD early diagnoses found
Health Science	Muscular Dystrophy AND (early diagnosis or early intervention) outcomes, benefits, effects, Impact, or effectiveness	18	Focused on biomarkers for diagnosis; broadened terms
Health Science	Muscular Dystrophy AND early diagnosis or early identification or early detection	179	Removal of the keywords" outcomes or benefits or effects or impact or effectiveness" enhanced variable selection
Health Science	DMD AND (quality of life or well-being or well-being or health-related)	133	Added insights into the QOL of DMD patients
Health Science	DMD, QoL quality of life or health-related quality of life(PRQOL), parents, caregivers, mother, father, or parent	46	Provided additional insight into the QOL of parents, caregivers, and patients

Appendix B: Key Word Search Three

Concept 1: Quality of Life
1st search box: Duchenne muscular dystrophy OR dmd OR Duchenne syndrome OR Duchenne's
2nd search box: quality of life OR well-being
**Thoreau, 2017-present, Results 737*
Concept 2: Age (Adult)
1st search box: Duchenne muscular dystrophy OR dmd OR Duchenne syndrome OR Duchenne's
2nd search box: quality of life OR well-being
3rd search box: adult*
**Thoreau, 2017-present, Results 178*
Concept 3: Health access (Insurance)
1st search box: Duchenne muscular dystrophy OR dmd OR Duchenne syndrome OR Duchenne's
2nd search box: Insurance
**Thoreau, Results 103*
Concept 4: Age at diagnosis
1st search box: Duchenne muscular dystrophy OR dmd OR Duchenne syndrome OR Duchenne's
2nd search box: age of diagnosis OR age at diagnosis
**Thoreau, Results 114*

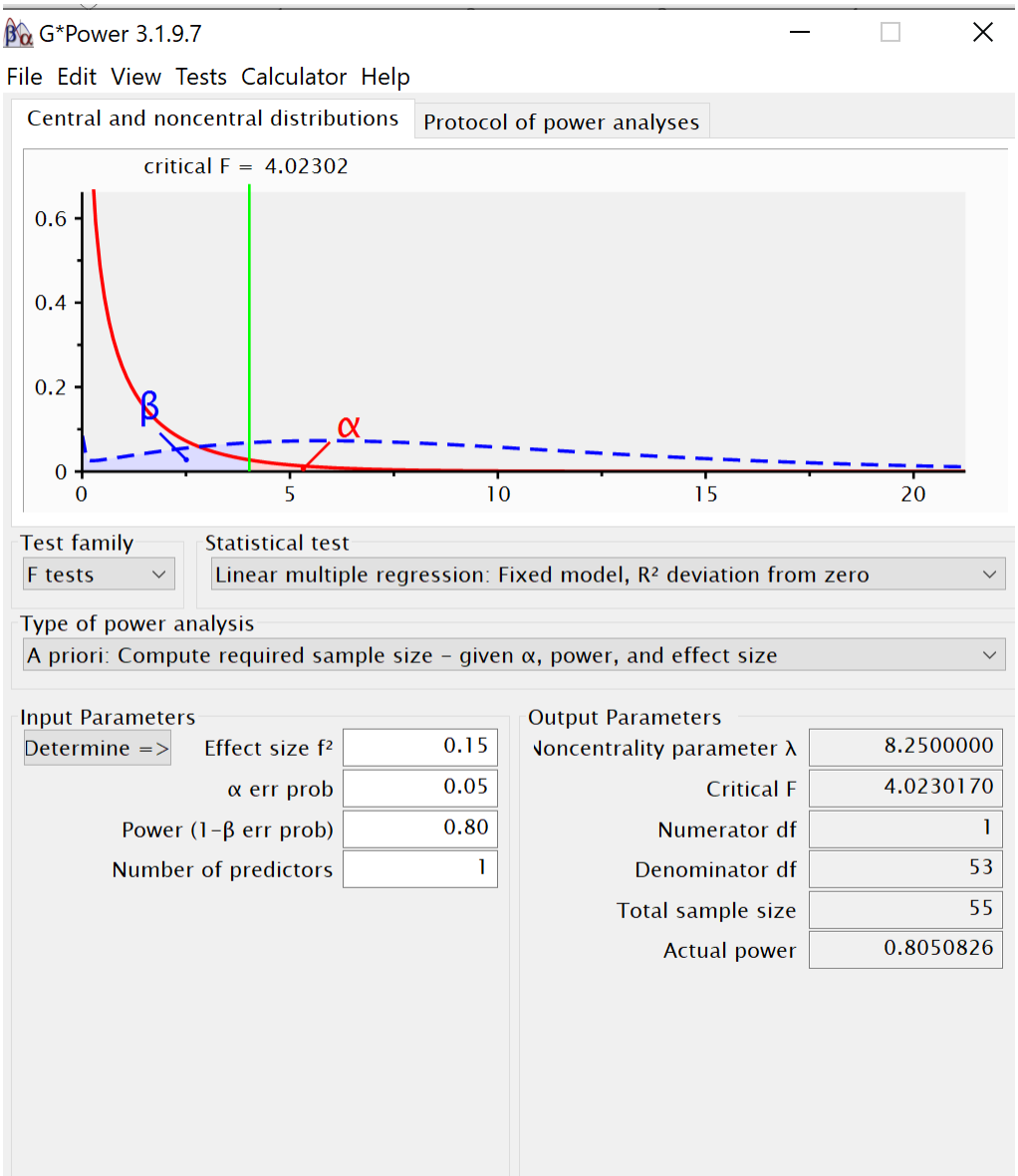
Appendix C**:** Matching Ferrans et al. (2005) Conceptual Framework with Study Variables

Ferrans et al. (2005) Conceptual Model of HRQoL	**Study Variables**	**Coding Scheme** **PROMIS and Neuro-QOL**
1- **Intrapersonal** (characteristic: Biological Function)	1- Age	Age: Continuous (in years)
2- **Institutional** (subset: Biological Function)	2- Healthcare Access (Insurance Type)	Categorical: 1=Private/Commercial, 2=Medicaid, 3=Uninsured, 4=Military/Tricare
3- **Intrapersonal** (characteristic: Functional Status)	3- Disease stage (Physical mobility) Measures reflecting physical functional status consist of three measures, Upper Extremity Function, Activities of daily living (ADL), and Lower Extremity Function	Ordinal: 5 = Without any Difficulty 4 = With a Little Difficulty 3 = With Some Difficulty 2 = With Much Difficulty 1 = Unable to Do
4- **Interpersonal**: (characteristic: Overall Quality of Life (QOL).	4- PRQoL: Measures reflecting PRQoL are (1)the Ability to Participate in Social Roles and Activities, (2) Satisfaction with social roles and activities, and (3) Positive Affect & Well-Being)	Ordinal: (1)Ability to participate in social roles and activities (3)Positive Affect & Well-being 1 = Never 2 = Rarely 3 = Sometimes 4 = Often 5 = Always Ordinal: (2)Satisfaction with social roles and activities 1 = Not at all 2 = A little bit 3 = Somewhat 4 = Quite a bit 5 = Very much

Appendix D: Data Analysis Effect Size

Figure D1

Medium Effect Size RQ1



Large Effect Size (RQ1 & RQ2)

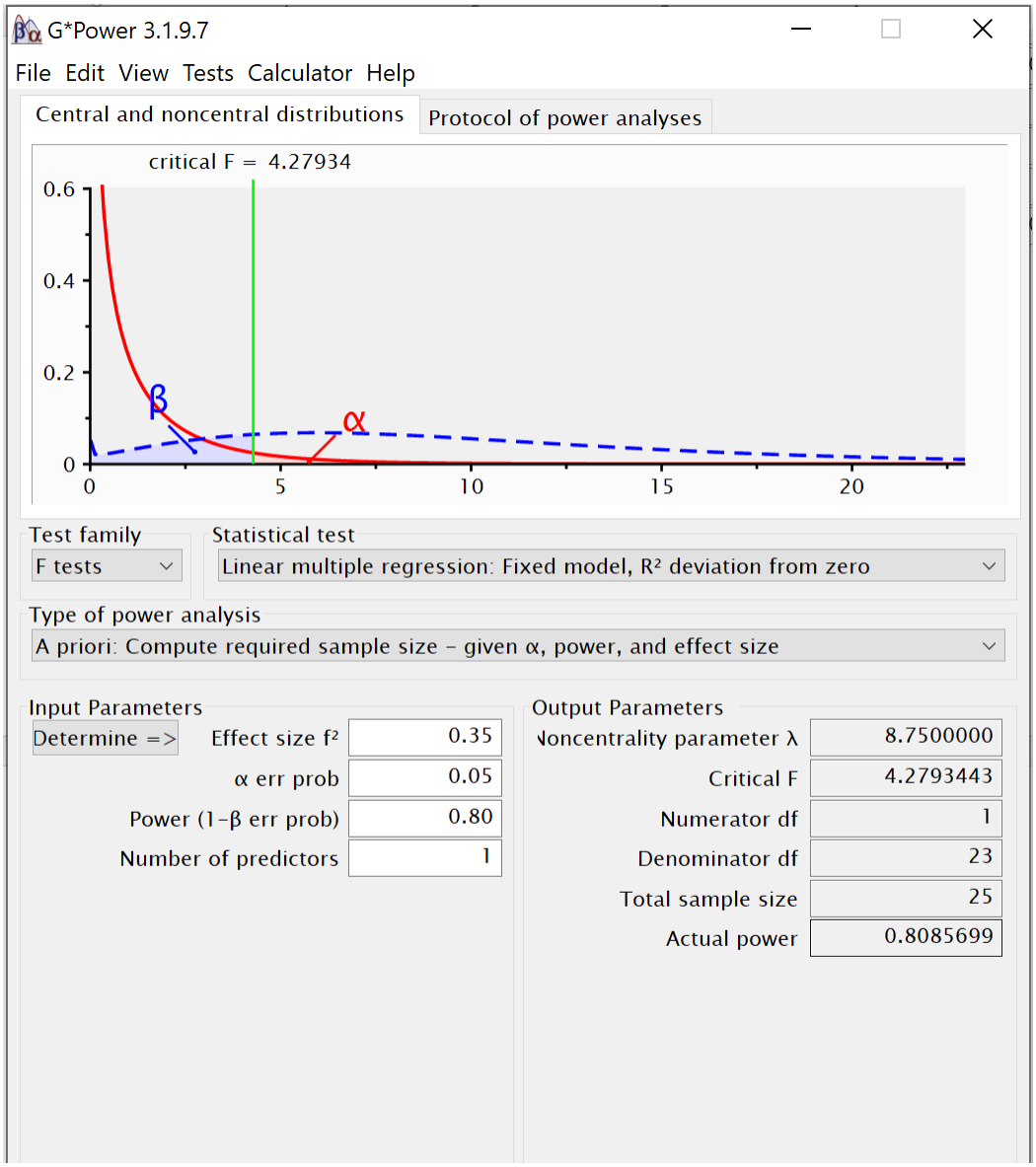


Figure D2

RQ3

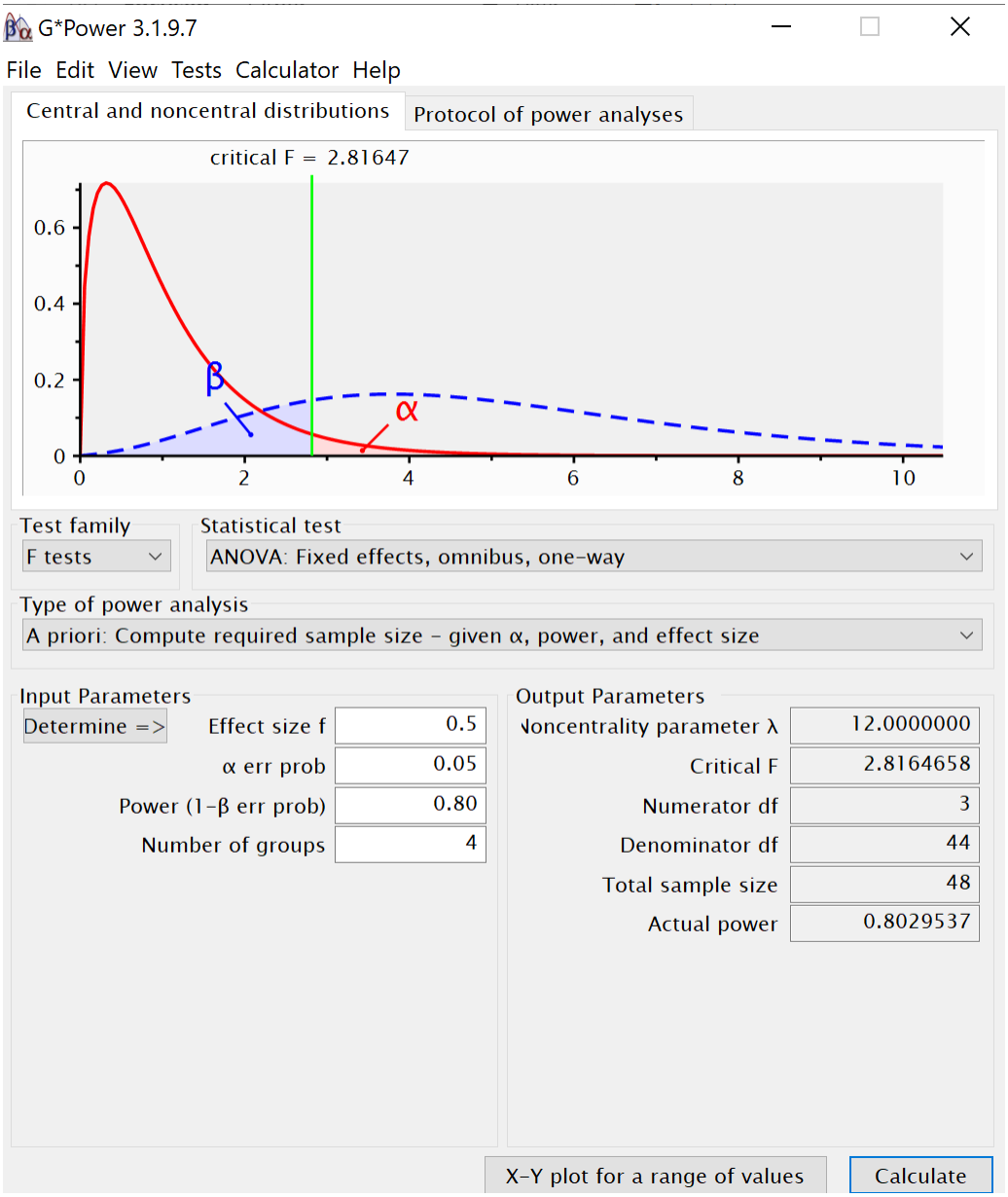
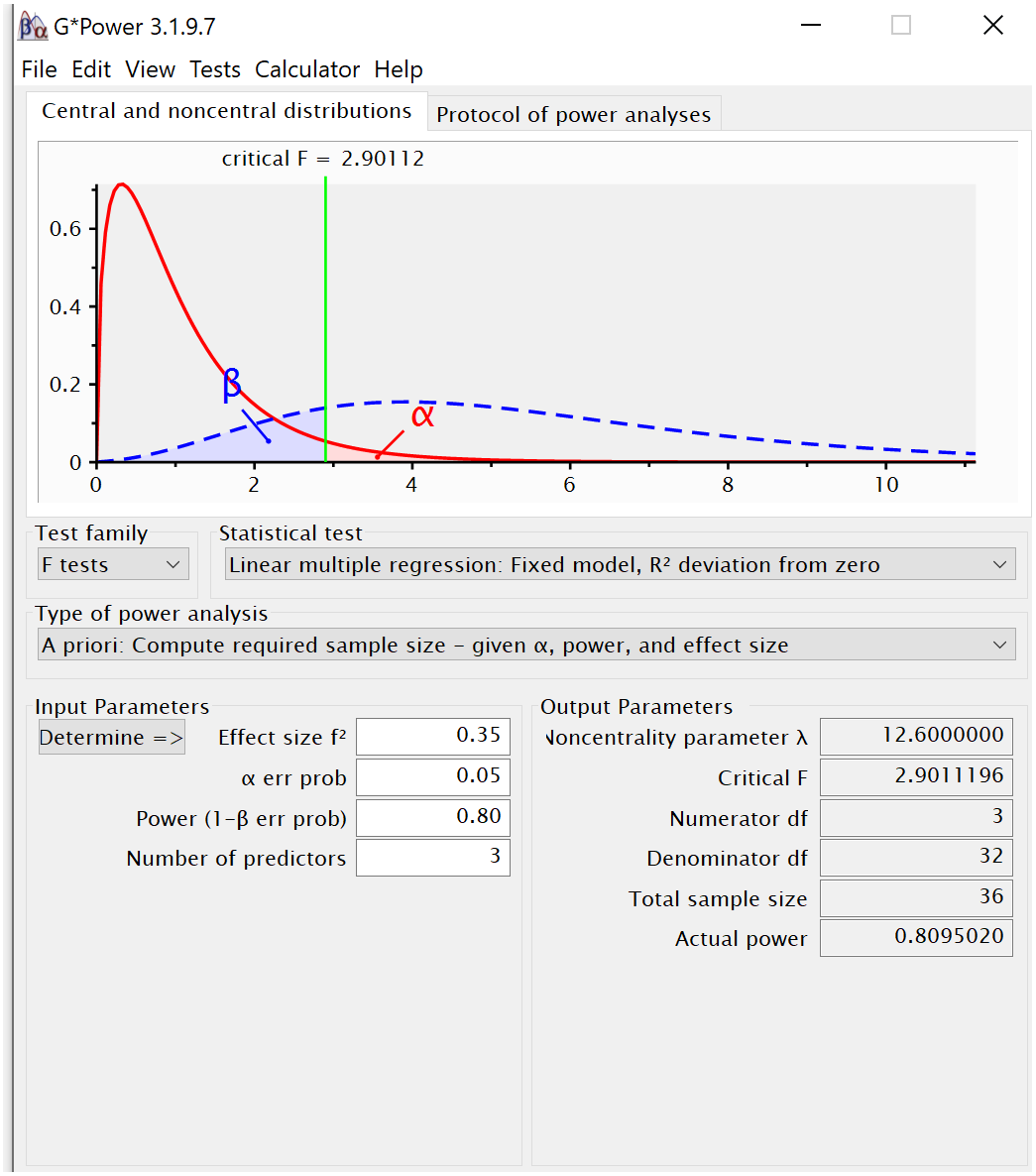


Figure D3

MLR Fixed Model Deviation Zero Large Effect Size



Faul et al. (2007).

Appendix E: Dataverse Community Norms

CC0 Waiver for Datasets

All datasets added in a Dataverse repository are default granted the CC0 Public Domain Dedication. The Dataverse software uses the CC0 waiver by default for all datasets (4.0 and on) because of its name recognition in the scientific community, making it a familiar option for data (for which, in general, copyright does not apply), and is in use by repositories as well as scientific journals that require the deposit of open data. For more information on the CC0 waiver, please visit the Creative Commons website (https://creativecommons.org/share-your-work/public-domain/cc0). Data depositors can opt out of using the CC0 waiver for their datasets if needed.

*The Dataverse Project asks that all users who download datasets from a Dataverse repository follow the following Community Norms.**

Crediting any research used with data citations

Any materials (books, articles, conference papers, theses, dissertations, reports, and other such publications) created that employ, reference, or otherwise utilize the data (in whole or in part) gathered from deposited datasets should credit the source with the appropriate data citation generated by the Dataverse repository (found on the dataset page). These citations include the data authors, data identifier, and other information per the Joint Declaration of Data Citation Principles (https://www.force11.org/datacitationprinciples) for all research data.

To find out more, visit our Data Citation Best Practices guide (https://dataverse.org/best-practices/data-citation).

Maintaining the anonymity of human subjects

Users of the Service should not abuse the available data that relate to human subjects and use the materials to:

1. obtain information that could directly or indirectly identify any research subjects, or obtain information to attempt to directly or indirectly identify any research subjects;

2. produce and/or publish connections among datasets that could identify individuals or organizations; or

3. obtain (additional) information about or (additional) means of contact for already-identified subjects.

* Legal Disclaimer: these Community Norms are not a substitute for the CC0 or custom licenses applicable to each dataset. Please be advised that the Community Norms are not a binding contractual agreement and that downloading datasets from a Dataverse repository does not create a legal obligation to follow these policies.

Third-Party API Applications

If you are interested in building an API application designed (exclusively or not) to allow and provide access to Harvard Dataverse Repository and its materials and services, please keep in mind that such applications:

1. Must ensure that all users of the application read and agree to both the Harvard Dataverse Repository API Terms of Use (https://dataverse.org/best-practices/harvard-api-tou) and Harvard Dataverse Repository's General Terms of Use (https://dataverse.org/best-practices/harvard-dataverse-general-terms-use);

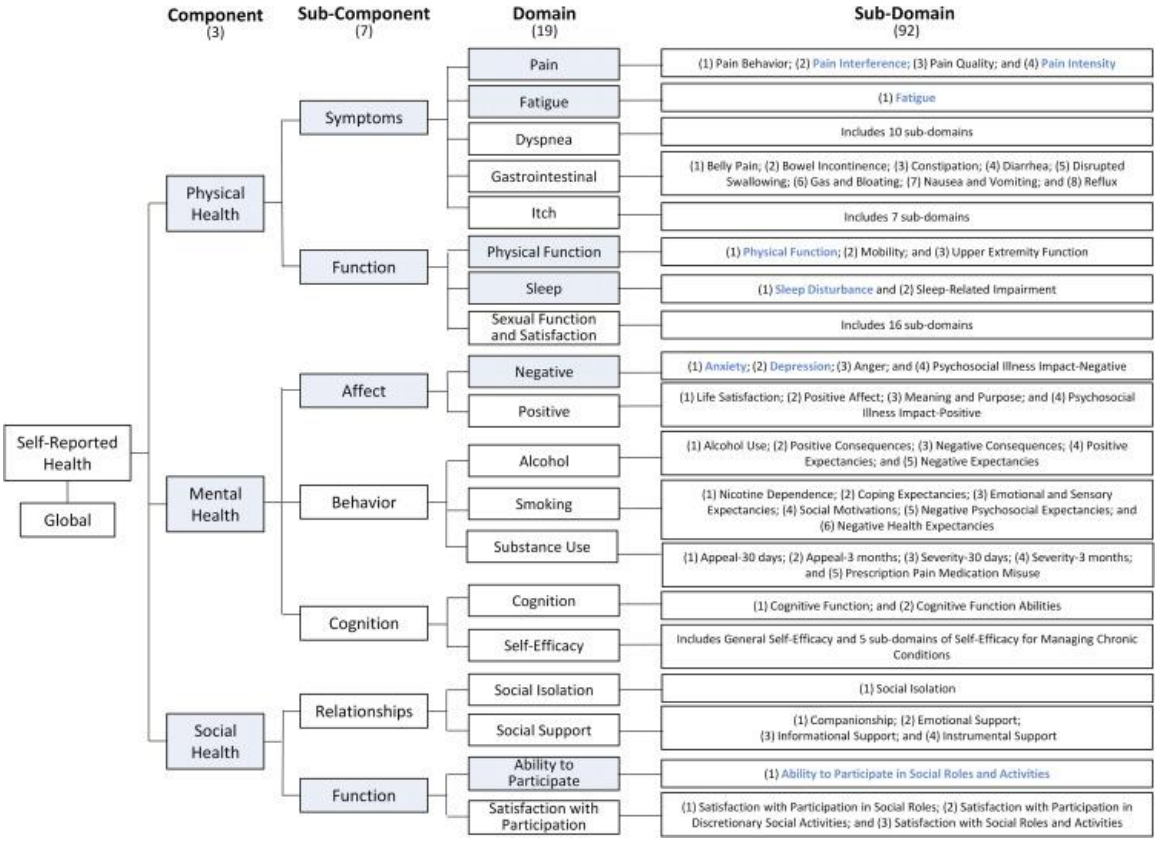
2. Must post both the Harvard Dataverse Repository API Terms of Use and Harvard Dataverse Repository General Terms of Use in an adequately noticeable and conveniently-accessible place so that all users of the application and easily find and view it;

3. Acknowledge and agree that the Harvard Dataverse Repository is not otherwise affiliated with any third-party Dataverse Project API applications that provide access to the Harvard Dataverse Repository and, therefore, will not be held responsible or liable (in whole or in part) for any suits or damages incurred by the third-party Dataverse Project API application owners, administrators, and affiliates; and

4. Must publish its third-party non-affiliation status concerning the Harvard Dataverse Repository in its application and disclaim any special relationship with the Harvard Dataverse Repository outside of the ones

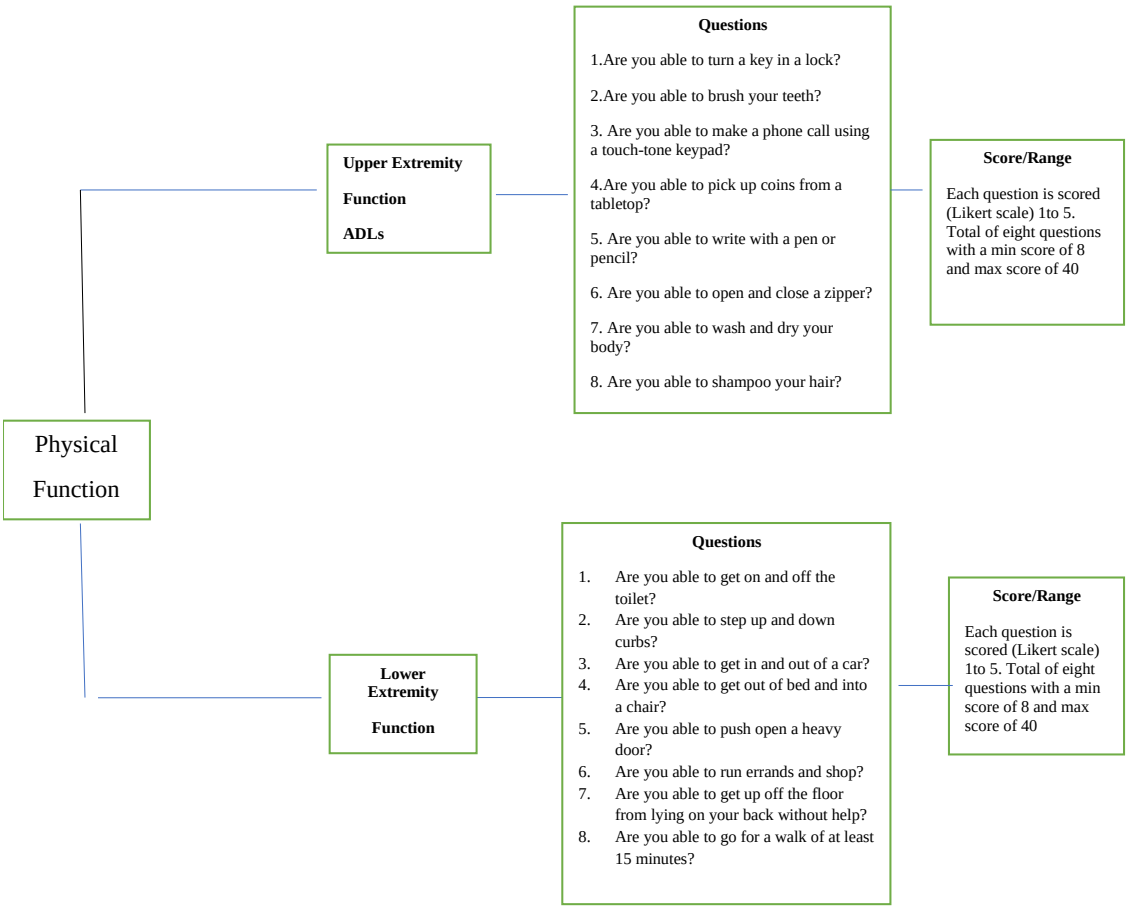
arising out of the obligations agreed upon from this Terms of Use and the Harvard Dataverse Repository General Terms of Use agreements.

Appendix F: Taxonomy of the current PROMIS domain Framework



Taxonomy of the current PROMIS domain framework. (Adapted with permission; see HealthMeasures.net/PROMIS for updated information.

Appendix G: Physical Function Composite Score



Note: Composite scoring for Physical function consists of eight questions for upper extremity function/ADLs (range min score 16 to max 40) plus eight questions for lower extremity function (range min score 16 to max 40) equals a total physical function score (range min 32 to max 80).

Appendix H: Physical Function Composite Score

Questions	**Code/Scale**	**Response (score)**
Upper Extremity Function -Fine Motor, ADL	Scale 1-5	
1. Are you able to turn a key in a lock?	1=Unable to do; 2=With much difficulty; 3=With some difficulty,4= With little difficulty, 5=Without any difficulty	1
2. Are you able to brush your teeth?	1=Unable to do; 2=With much difficulty; 3=With some difficulty,4= With little difficulty, 5=Without any difficulty	1
3. Are you able to make a phone call using a touch-tone keypad?	1=Unable to do; 2=With much difficulty; 3=With some difficulty,4= With little difficulty, 5=Without any difficulty	1
4. Are you able to pick up coins from a tabletop?	1=Unable to do; 2=With much difficulty; 3=With some difficulty,4= With little difficulty, 5=Without any difficulty	1
5. Are you able to write with a pen or pencil?	1=Unable to do; 2=With much difficulty; 3=With some difficulty,4= With little difficulty, 5=Without any difficulty	1
6. Are you able to open and close a zipper?	1=Unable to do; 2=With much difficulty; 3=With some difficulty,4= With little difficulty, 5=Without any difficulty	1
7. Are you able to wash and dry your body?	1=Unable to do; 2=With much difficulty; 3=With some difficulty,4= With little difficulty, 5=Without any difficulty	1
8. Are you able to shampoo your hair?	1=Unable to do; 2=With much difficulty; 3=With some difficulty,4= With little difficulty, 5=Without any difficulty	1
Example score	**Mean** =(sum)/#of questions [8/8/]=1.0	**Sum total 8**
Lower Extremity Function Mobility		Score (Answer)
1. Are you able to get on and off the toilet?	1=Unable to do; 2=With much difficulty; 3=With some difficulty,4= With little difficulty, 5=Without any difficulty	1
2. Are you able to step up and down curbs?	1=Unable to do; 2=With much difficulty; 3=With some difficulty,4= With little difficulty, 5=Without any difficulty	1
3. Are you able to get in and out of a car?	1=Unable to do; 2=With much difficulty; 3=With some difficulty,4= With little difficulty, 5=Without any difficulty	1
4. Are you able to get out of bed and into a chair?	1=Unable to do; 2=With much difficulty; 3=With some difficulty,4= With little difficulty, 5=Without any difficulty	1
5. Are you able to push open a heavy door?	1=Unable to do; 2=With much difficulty; 3=With some difficulty,4= With little difficulty, 5=Without any difficulty	1
6. Are you able to run errands and shop?	1=Unable to do; 2=With much difficulty; 3=With some difficulty,4= With little difficulty, 5=Without any difficulty	1
7. Are you able to get up off the floor from lying on your back without help?	1=Unable to do; 2=With much difficulty; 3=With some difficulty,4= With little difficulty, 5=Without any difficulty	1
8. Are you able to go for a walk of at least 15 minutes?	1=Unable to do; 2=With much difficulty; 3=With some difficulty,4= With little difficulty, 5=Without any difficulty	1
	Mean =(sum)/#of questions [8/8/]=1.0	**Total 8**
Respondent answers 1 to all 16 questions, Total combined score for physical function =16	Upper extremity/ADL + Lower extremity	**16**

Note: Total Score Range: Upper Extremity/ADLs plus Lower extremity function for a total of 16 Questions with a Score Range from 16-80	**Mean** =(sum)/#of questions [16/16]=1.0	Mean 1

Appendix I: Patient-Reported Quality of Life (PRQoL) Composite Score

Measure/Questions	**Code/Scale**	**Responses Score**
(1) Ability to Participate in Social Roles and Activities	**Scale (1-5)**	**Response scores (Example)**
1. I am able to socialize with my friends	1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Always	2
2. I am unable to do all of my regular activities with friends	1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Always	2
3. I can keep up with my social commitments.	1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Always	2
4. I am unable to participate in leisure activities.	1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Always	2
5. I am unable to perform my daily routines	1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Always	2
6. I can keep up with my work responsibilities (include work at home)	1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Always	2
Total 6 questions (range 1-5)	**Mean =(sum)/#of questions [12/6]=2**	**Total score 12**
2. Satisfaction with Social Roles and Activities	**Code/Scale**	**Response scores (Example)**
1. I am bothered by my limitations in regular family activities	1=Not at all, 2.=A little bit, 3=Somewhat, 4= Quite a bit, 5=Very much	2
2. I am disappointed in my ability to socialize with my family.	1=Not at all, 2.=A little bit, 3=Somewhat, 4= Quite a bit, 5=Very much	2
3. I am bothered by limitations in my regular activities with friends.	1=Not at all, 2.=A little bit, 3=Somewhat, 4= Quite a bit, 5=Very much	2
4. I am disappointed in my ability to meet the needs of my friends.	1=Not at all, 2.=A little bit, 3=Somewhat, 4= Quite a bit, 5=Very much	2
5. I am satisfied with my ability to do things for fun outside of my home.	1=Not at all, 2.=A little bit, 3=Somewhat, 4= Quite a bit, 5=Very much	2
6. I am satisfied with the amount of time I spend doing leisure activities	1=Not at all, 2.=A little bit, 3=Somewhat, 4= Quite a bit, 5=Very much	2
7. I am satisfied with how much of my work I can do (include work and home)	1=Not at all, 2.=A little bit, 3=Somewhat, 4= Quite a bit, 5=Very much	2
8. I am satisfied with my ability to do household chores or tasks.	1=Not at all, 2.=A little bit, 3=Somewhat, 4= Quite a bit, 5=Very much	2

Total of 8 Questions (range 1-5)	**Mean =(sum)/#of questions [16/8]=2**	**Total score 16**
Questions	**Code/Scale**	**Response scores (Example)**
3. Positive Affect and Well-Being		
1. I had a sense of well-being.	1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Always	3
2. I feel hopeful.	1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Always	3
3. My life was satisfying.	1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Always	3
4. My life had purpose.	1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Always	3
5. My life had meaning.	1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Always	3
6. I felt cheerful.	1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Always	3
7. My life was worth living.	1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Always	3
8. I had a sense of balance in my life.	1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Always	3
9. Many areas of my life were interesting to me.	1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Always	3
Total of 9 Questions (scale 1-5)	**Mean =(sum)/#of questions [27/9]=3**	**Total score 27**
Composite of three measures Total questions 23	**Score range 23-115**	**Total all three measures =55**
Ability to Participate in Social Roles and Activities + Satisfaction with Social Roles and Activities + Positive Affect and Well-Being	**Mean =(sum)/#of questions [55/23]=2.39**	

Appendix J: Sociodemographic Variables

Variable Name	Item Stem	Responses
Socio01	What is your telephone area code (where you are currently located)?	textbox=textbox
Socio02	What is your age?	textbox=textbox
Socio03	What is your gender?	1=Male
		2=Female
Socio04	Are you of Spanish/Hispanic/Latino origin?	0=No
		1=Yes
Socio05	What is your racial or ethnic background? (Please check all that apply)	1=White
		2=Black or African-American
		4=Asian
		8=American Indian/Alaska Native
		16=Native Hawaiian/Other Pacific Islander
Socio06	What is your current relationship status?	1=Never Married
		2=Married
		3=Living with partner in committed relationship
		4=Separated
		5=Divorced
		6=Widowed
Socio07	What is the highest grade in school that you completed?	1=5th grade or less
		2= 6th grade
		3=7th grade
		4=8th grade
		5=Some high school
		6=High school grad/GED
		7=Some college/Technical degree/AA
		8=College degree (BA/BS)
		9=Advanced degree (MA, PHD, MD)
Socio08	What is your current occupational status? (Please check all that apply)	1=Homemaker
		2=Unemployed
		4=Retired
		8=On disability
		16= On Leave of absence
		32=Full-time employed

		64=Part-time employed
		128=Full-time student
Socio09	What is your family household income (from all sources)?	1=Less than $20,000
		2=Between $20,000 and $49,999
		3=Between $50,000 and $99,999
		4=$100,000 or more

Appendix K: Social Change: Advocacy Groups

1. Muscular Dystrophy Association (MDA) is dedicated t to advocating for policies and programs that help save and improve the lives of kids and adults with neuromuscular disease. Advocacy Blog https://www.votervoice.net/MDA/blogs and Quest Media, an MDA platform for awareness, targets experts, thought leaders, and members of the neuromuscular disease community about topics that matter to them and the larger community of individuals with disabilities.
2. The American Public Health Association (APHA) Genomic forum engages public health and healthcare communities and others in projects and activities that increase the awareness, knowledge, and skills of genetic services as these services relate to the ethical, legal, and social issues surrounding genetics/ genomics/ epigenetics, and the relationships and relevance of genomics to public health, health care, and health disparities. https://www.apha.org/APHA-Communities/Forums/Genomics-Forum
3. The Global Network for Rare Diseases (GNRD) is an initiative in collaboration with the World Health Organization (WHO) aimed at developing a person-centered global network of care and expertise for all Persons Living with Rare Diseases (PLWRD) worldwide. https://www.rarediseasesinternational.org/global-collaborations-tools/
4. Communicate research findings and connect with advocacy groups on Social media outlets:
    - Rare Disease International (Facebook, Linkin)
    - Parent Project Muscular Dystrophy: www.parentprojectmd.org
    - CDC: www.cdc.gov/ncbddd/musculardystrophy
    - World Duchenne Organization: www.worldduchenne.org