Comparing Psychosocial Impacts of Spinal Muscular Atrophy Diagnoses Before and After Newborn Screening Implementation

by

Ariel Ann Breeze

BS in Biology, University of Kentucky, 2019

Submitted to the Graduate Faculty of the

School of Public Health in partial fulfillment

of the requirements for the degree of

Master of Science and Master of Public Health

University of Pittsburgh

2023

UNIVERSITY OF PITTSBURGH

SCHOOL OF PUBLIC HEALTH

This thesis was presented

by

Ariel Ann Breeze

It was defended on

June 12, 2023

and approved by

Hoda Abdel-Hamid, MD, FAAN; Director, Pediatric Neuromuscular Program, UPMC Children's Hospital of Pittsburgh; Director, Pediatric EMG Laboratory, UPMC Children's Hospital of Pittsburgh; Director, Pediatric MDA Clinic, UPMC Children's Hospital of Pittsburgh; Associate Professor, Pediatrics and Neurology

Robin E. Grubs, MS, PhD, LCGC; Associate Professor, Human Genetics

Thesis Advisor: Kelsey Bohnert, MS, MRes, CGC; Laboratory Services, UPMC Children's Hospital of Pittsburgh; Adjunct Instructor, Human Genetics

Comparing Psychosocial Impacts of Spinal Muscular Atrophy Diagnoses Before and After Newborn Screening Implementation

Ariel Ann Breeze, MS, MPH

University of Pittsburgh, 2023

Spinal muscular atrophy (SMA), a progressive neuromuscular condition, was recently added to state newborn screening (NBS) panels. While families have been found to support NBS for SMA, most studies have examined families' opinions regarding program implementation as opposed to the diagnostic process. The aims of this study were to examine the psychosocial impact of receiving a diagnosis of SMA, experiences with the healthcare system, and opinions on NBS. The goal was to identify gaps in support and ways that healthcare providers can improve outcomes for families by examining differences in those who were diagnosed before and after NBS for SMA. Seven semi-structured interviews were conducted with parents and caregivers of children with SMA to explore perspectives of the diagnostic odyssey. Through inductive thematic analysis with semantic identification, six overarching themes emerged: (1) communicating diagnosis and management: recommendations for healthcare providers, (2) navigating uncertainty: understanding and addressing informational needs, (3) finding community: importance of seeking support and becoming advocates, (4) processing change: evolving expectations for a child's future, (5) feeling overwhelmed: initial parental experiences following their child's diagnosis, and (6) experiencing loss: coping with guilt and the loss of expectations for a healthy child. Participants whose children were diagnosed via NBS discussed issues related to uncertainty and feelings of being overwhelmed more frequently compared to those whose children were diagnosed symptomatically. Given the psychosocial impact affected families have described, it is critical that

genetic counselors take an active role in the discussion of NBS results and SMA diagnoses. Genetic counselors can provide psychological support and accurate information about genetic conditions in a manner which will positively impact families. They are also in a unique position to collaborate with primary care providers to ensure that families are receiving accurate information about NBS-related conditions at multiple timepoints, therefore maximizing satisfaction and minimizing psychosocial harm. This project benefits the public health sector by identifying key roles for genetic counselors to play in not discussing health problems with the community but also by informing, educating, and empowering individuals.

Table of Contents

List of Tables

List of Figures

1.0 Introduction

Spinal muscular atrophy (SMA) is a progressive neuromuscular condition that is inherited in an autosomal recessive manner, affecting approximately 1 in 11,000 individuals worldwide (Cure SMA). The most common cause of SMA involves homozygous deletions or pathogenic variants within the *SMN1* gene located on chromosome 5q13 (Darras 2015). There are five types of SMA related to 5q13, decreasing in severity: type 0, type I, type II, type III, and type IV. Additionally, there are several types of SMA that do not involve chromosome 5q13, but these are beyond the scope of this study and involve different genes and inheritance patterns (Harms et al. 2010). The number of *SMN2* copies can vary by individual, modifying disease presentation for those affected with *SMN1*-related SMA (Hale et al. 2021). Both *SMN1* and *SMN2* play a role in the production of the survival motor neuron (SMN) protein, with most of this protein produced by *SMN1*. SMN is important for maintaining motor neurons that transmit neurological signals from the brain and spinal cord to cause the contraction of skeletal muscles. Pathogenic variants in *SMN1* lead to deficiency in SMN protein and motor neuron death. This causes many of the signs and symptoms of SMA, including progressive muscle weakness. This muscle weakness is proximal, affecting the individual's legs and arms near the midline of the body (Darras 2022).

Historically, there was extensive interest in adding SMA to the newborn screening (NBS) panel among patients and families, but initial review by the Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children (ACHDNC) rejected an early request in 2008 based on a lack of formal treatment options. Several years later, multiple treatment options started to receive approval from the Food and Drug Administration (FDA) once clinical trials demonstrated promising results. Nusinersen (Spinraza) is an antisense oligonucleotide while

onasemnogene abeparvovec-xioi (Zolgensma) involves viral gene therapy. Most recently, risdiplam (Evrysdi), an *SMN2*-directed RNA splicing modifier, was approved for patients and involves oral administration (Ratni et al. 2018). These treatment modalities led to a formal re-review resulting in SMA being added to the Recommended Uniform Screening Panel (RUSP) in 2018 (Butterfield 2021). The Association of Public Health Laboratories (APHL) has a database which collects information on genetic conditions that have been detected by NBS in each of the 48 states that screen for SMA. This repository revealed approximately 45 detectable cases between 2018 and 2021 (Hale et al. 2021).

Families have typically responded positively to adding SMA and other genetic conditions to NBS panels. Boardman et al. (2017) found that 70% of affected individuals and their family members supported NBS as it could lead to improved clinical outcomes and life expectancy for patients. This support is not without caveats, including psychological distress with positive screening results, insufficient information provided at diagnosis, limited access to specialists, and barriers to comprehension (Kariyawasam et al. 2021). To date, there has been little research focused on addressing these concerns. Many studies that have assessed patient attitudes about NBS for SMA have examined families' opinions regarding implementation of the program itself as opposed to the diagnostic process.

Studies have assessed which of the therapy options are most frequently used. Most families chose gene therapy via Zolgensma as their treatment due to the frequency of administration and delivery method (Deng et al. 2022). Zolgensma is a one-time intravenous infusion in comparison to Spinraza, which is administered via intrathecal injections on a regular basis (Mendell et al. 2017). Some families are delayed in pursuing treatment options and understanding the reasons for this delay has not been addressed in the current literature.

With SMA having been added to the RUSP in 2018, there exists an opportunity to compare families' experiences with the diagnosis prior to and following the implementation of NBS for SMA. This project was designed to address the gaps and build on the current literature regarding the impact of SMA diagnosis via NBS by directly comparing experiences at various points within the diagnostic process and exploring families' treatment considerations. This was done by conducting interviews to obtain information regarding these families' firsthand experiences. The Muscular Dystrophy Association (MDA) Clinic at the Children's Hospital of Pittsburgh maintained a database of individuals diagnosed with SMA. These families were contacted and invited to participate in an interview as part of the study.

1.1 Specific Aims

Specific Aim 1: Conduct qualitative interviews with families who have had a child diagnosed with spinal muscular atrophy before and after the condition was added to the newborn screening panel in Pennsylvania.

Specific Aim 2: Analyze interview transcripts through thematic analysis to examine the psychosocial impact of receiving a diagnosis of spinal muscular atrophy, experiences with the healthcare system during this period, and opinions on newborn screening.

Specific Aim 3: Use the data to identify gaps in support and ways that healthcare providers can help improve outcomes for families affected by spinal muscular atrophy.

2.0 Manuscript

2.1 Background

Spinal muscular atrophy (SMA) is a progressive, autosomal recessive condition affecting the central and peripheral nervous system. This condition leads to weakness and atrophy in the proximal skeletal muscles. SMA is one of the leading causes of infant mortality worldwide with a high carrier frequency compared to other genetic conditions (Pearn 1978). The most common cause of SMA is associated with pathogenic variants on chromosome 5q13, and there are five subtypes: type 0, I, II, III, and IV. The subtypes range on a continuum differing in both severity and age of onset, with type 0 being the most severe and the earliest onset and type IV being the mildest with the latest onset (Dubowitz 1999). With increased knowledge of molecular genetics and the development of various treatment modalities, the classification of patients into these various subtypes has become complicated.

Most SMA cases are caused by a homozygous deletion of the *SMN1* (survival of motor neuron 1) gene located on chromosome 5q13. *SMN1* produces the survival motor neuron (SMN) protein which is responsible for maintaining motor neurons throughout an individual's body. Individuals have two forms of the *SMN* gene, designated as *SMN1* and *SMN2* (survival of motor neuron 2). *SMN1* produces the full-length SMN protein whereas *SMN2* is a paralogous gene that differs from *SMN1* via substitution of cytosine with thymine in a splicing enhancer. This substitution allows the occasional exclusion of exon 7, resulting in a nonfunctional protein. Therefore, the severity, subtype, and age of onset of SMA is partially determined by *SMN2*. There is a negative correlation between *SMN2* copy number and severity of SMA (Lefebvre et al. 1997).

Prior to the discovery of *SMN2* as a paralogous modifier to *SMN1*, classification into subtypes was based on the degree of severity (Kolb & Kissel 2015). Certain features may lead clinicians to investigate a diagnosis. These include loss of motor skills, proximal muscle weakness, hypotonia, decreased or absent deep tendon reflexes, specific muscle contractions within the tongue, hand tremors, recurrent lower respiratory tract infections, and suggestive electromyogram findings (Mercuri et al. 2018). Implementation of molecular genetic testing allowed for confirmatory testing strategies in symptomatic individuals. The diagnostic process for SMA is changing rapidly with the advent of newborn screening (NBS), offering the opportunity for early detection prior to symptom onset.

Previous literature has evaluated parent and caregivers' experiences of having a child diagnosed with SMA. Parents have reported feeling that it took a significant amount of time and many visits with various healthcare specialists to receive an official diagnosis due to a lack of awareness regarding SMA, difficulty in recognizing abnormal development in infants, and the consideration of differential diagnoses. Many parents were unaware of the condition unless they had a child previously diagnosed. One family interviewed by Qian et al. (2015) reported 3-4 years spent attempting to find a diagnosis for their child. Because of the variation in developmental milestones, many parents and healthcare providers may interpret some delay as normal, further increasing the time until diagnosis. SMA symptoms also overlap with those of other neuromuscular conditions. One parent reported their child's neurologist considered a diagnosis of muscular dystrophy rather than SMA because the neurologist reportedly did not understand the child's presentation as consistent with type III SMA (Qian et al. 2015). Duchenne muscular dystrophy (DMD) is similar to SMA in that both conditions are described by muscle weakness and motor regression; however, DMD is unique in that affected individuals will have significantly

elevated serum creatine kinase levels (Bushby et al. 2010). Ultimately, due to these factors, families can wait months or years before receiving a diagnosis for their child.

Familial concerns regarding the diagnosis of SMA include not only the length of time, but also the way information is transmitted to parents and caregivers. Most parents interviewed by Qian et al. (2015) felt their child's healthcare team delivered this diagnosis poorly, spending little to no time discussing the diagnosis and providing no hope or positivity. Many parents reported receiving the diagnosis via a phone call or an office visit lasting less than five minutes (Qian et al. 2015). These approaches to delivering the diagnosis could harm the rapport between parents and their child's physician particularly when this communication violates respect of patient autonomy (Fernandes et al. 2022). It has been recommended that pediatricians receive education on both SMA and delivering life-altering diagnoses in a knowledgeable, sensitive fashion (Qian et al. 2015). Anestis et al. (2020) conducted a systematic review involving the delivery of motor neuron diseases with dementia (MNDD) and concluded that adoption of a patient-centered approach to communicating the diagnosis must be implemented and that healthcare professionals must provide basic information about the condition, an overview of available treatments, symptoms and prognosis, and references to reliable sources with which to receive information.

Historically, SMA management was symptomatic, with standardized care recommendations not being established until 2007 (Wang et al. 2007). These guidelines were revised with the development of three different Food and Drug Administration (FDA)-approved treatments. The first of these therapies, nusinersen (more commonly known as Spinraza), was approved by the FDA in 2016 and has since been approved by similar organizations worldwide. Spinraza is an antisense oligonucleotide that targets *SMN2* splicing, leading to increased production of SMN protein (Passini et al. 2011). The second therapy made available was

onasemnogene abeparvovec-xioi (more commonly known as Zolgensma), approved by the FDA for children under 2 years of age in 2019. Zolgensma is a form of viral gene therapy that functions via an adeno-associated virus serotype 9 (AAV9) which delivers a one-time dose to patients that crosses the blood-brain barrier to replace the non-functional *SMN1* gene (Sumner & Crawford 2018). The most recent therapy, risdiplam (more commonly known as Evrysdi), was approved by the FDA in 2020. Evrysdi uses small molecules that can cross the blood-brain barrier and modify splicing of exon 7 in *SMN2*, again resulting in increased production of SMN2 protein (Ratni et al. 2018).

One method in which the time to reach a diagnosis of SMA can be reduced is via implementation of newborn screening (NBS). NBS is a public health genetics service that provides screening to newborns for various genetic conditions which may lead to severe disability or death if left untreated, providing the opportunity for early treatment to be implemented that maximizes clinical benefit (Hale et al. 2021). The Department of Health and Human Services (DHHS) is the government entity that oversees recommendations for which conditions should be included on NBS panels. The Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) specifically develops these recommendations and includes these conditions in the Recommended Uniform Screening Panel (RUSP) (Hale et al. 2021). There are currently 35 core conditions on the RUSP.

Although SMA was added to the RUSP in July 2018, it was not the first time SMA was brought to the attention of the ACHDNC. A preliminary review was conducted in 2008 with the ACHDNC denying the inclusion of SMA based on the lack of a beneficial therapeutic measure (Butterfield 2021). However, the introduction of novel therapies allowed for a revaluation of the inclusion of SMA on NBS. After the ACHDNC added SMA to the RUSP, states began adding the

condition to their NBS panels. Per Cure SMA, 48 states screen for the condition as of September 2022. At least 45 cases of SMA were diagnosed via NBS between 2018 and 2021 (Hale et al. 2021). Pennsylvania was one of the first states to implement SMA as a mandated condition to screen for on its NBS panel in 2019. Currently, there are over 400 individuals living with SMA in Pennsylvania with approximately 12 affected infants born each year (Cure SMA, 2021).

Newborn screening results for SMA can be complicated by a variety of factors. There are multiple screening modalities available to examine *SMN1* and *SMN2* in newborns. All states currently screening for SMA on their NBS panels use qualitative polymerase chain reaction (qPCR) to detect whether there exists a deletion involving exon 7 in *SMN1*. Some states repeat this screening modality whereas others implement second- and third-tier screening strategies to obtain additional information about SMA in infants. Pennsylvania has implemented a two-tiered approach to SMA screening. Initial testing is performed with qPCR for *SMN1*, and then multiplex ligation PCR amplification (MLPA) is performed to determine the *SMN2* copy number. (Hale et al. 2021). Despite this information, NBS remains a screening test. As such, any diagnosis must be confirmed through clinical genetic testing.

Lack of awareness about what genetic conditions are included on NBS may lead to psychosocial distress and confusion at the time of diagnosis. For example, one study found that 48% of parents hoped for a false-positive result in their seemingly healthy infant and 45% of parents reported that receiving condition-specific information prior to undergoing NBS could have reduced the initial shock with their newborn's positive result (Kariyawasam et al. 2021). Families and caregivers may experience significant emotional distress following the sudden shock and stress associated with a serious diagnosis. Kariyawasam et al. (2021) found that 41% of parents reported their own barriers to comprehension at the time of diagnosis, including a heightened

emotional reaction and the complexity of difficult genetic concepts. Additionally, only 59% of parents felt that the information they received regarding SMA following positive NBS was sufficient (Kariyawasam et al. 2021). It is important to better understand where these gaps exist in receiving a diagnosis of SMA via NBS to better improve this process for the well-being of patients and their families.

When awareness is present, 70% of affected individuals and their family members have been found to support NBS for SMA (Boardman et al. 2017). Families and caregivers of patients with conditions identifiable by NBS focus primarily on the reduced diagnostic odyssey as an advantage of the program. The diagnostic odyssey expands beyond molecular screening results to also include management, uncertainty, and confirmation. Bush et al. (2022) refers to this expansion as the diagnostic odyssey continuum. This continuum is further described by the implications following medical management as well as psychosocial considerations.

Medical management implications arising from NBS can be addressed at both the provider and the parent level. Ensuring that primary care providers, pediatricians, and students in healthcare disciplines are appropriately educated about newborn screening with specialized training in patient-centered communication can help mitigate confusion and difficulty understanding diagnosis and medical management for affected families (Bush et al. 2022). Having well-informed medical professionals on a care team leads to efficient care and better understanding. Patient-centered communication is a key competency for medical students identified by the Accreditation Council for Graduate Medical Education. Affected families have also requested accessible educational resources, empowerment programs for developing advocacy skills, and ease of access to multidisciplinary medical specialists (Bush et al. 2022). Newborn screening resources offered

across states are not equitable. These disparities result from a lack of common educational goals identified by NBS programs (Potter et al. 2014).

Psychosocial implications arising from NBS can be best addressed by offering various resources to parents and caregivers. These resources include long-term counseling, patient navigator and complex care programs with transition services, and peer support services (Bush et al. 2022). Access to genetic and psychological counseling programs may help minimize the negative impacts of positive newborn screening results. Patient navigators can help parents and caregivers manage their children's care beyond an initial diagnosis whereas peer support programs connect families to others with similar experiences. Few studies have investigated the psychosocial impact that positive NBS results have on families and caregivers. A pilot NBS program developed by Kariyawasam et al. (2021) found that parents unanimously supported NBS for SMA based primarily on the benefits of early intervention for accessing treatment and increasing surveillance. In this pilot program, over 200,000 newborns in Australia were screened over a two-year period with 18 positive results arising among infants. Kariyawasam et al. (2021) then assessed notable benefits and challenges in the diagnostic journey via questionnaires, which uncovered complications related to a lack of information provided prior to NBS and comprehension difficulties.

Patients' perspectives have been assessed in relation to NBS for SMA as well. Affected individuals tend to place more emphasis on quality of life as opposed to the diagnostic odyssey. According to Boardman et al. (2018), 74% of affected adults supported newborn screening for SMA regardless of whether the specific subtype can be determined. Adults with severe forms of SMA were more likely to report a higher quality of life in comparison to those with mild forms. This is because individuals with more severe subtypes of the condition were diagnosed as children

and therefore had increased access to disability services in comparison to those who may not have been diagnosed until adolescence or adulthood due to having a milder subtype. According to Boardman et al. (2018), adults with milder types of SMA also reported a lower quality of life. This is consistent with previous literature highlighting the experiences of adults who have become disabled later in life. Symptom onset in adulthood is typically associated with grief and a loss or shift of a patient's expectations and plans for their future (Locock et al. 2009). NBS offers families a method for diagnosing SMA early in life, allowing for early treatment and potentially maximizing quality of life.

Genetic counselors play a significant role in newborn screening for genetic conditions by supporting primary care physicians and pediatricians in understanding conditions added to the NBS panel, reporting NBS results to parents in an empathetic fashion, and developing and distributing educational materials (Marcus 2019). Genetic counselors may also work in a subspecialty focused on neurodegenerative conditions including SMA, where they provide support to parents and caregivers together with a neurologist to provide lifelong care. They may also offer carrier screening for SMA to parents interested in understanding the risks of having children with this condition.

The American College of Obstetricians and Gynecologists (2017) recommends that all individuals assigned female at birth should be offered carrier screening for SMA due to its high incidence in multiple ethnic groups. The primary goal of carrier screening is to detect carriers of certain genetic conditions to provide patients either planning a pregnancy or who are currently pregnant with helpful information to guide reproductive decision-making (Herington & Horton 2021). With this information, genetic counselors can provide accurate risk assessments and engage in a thorough discussion regarding reproductive options.

2.2 Materials and Methods

2.2.1 Research Study Approval

The Institutional Review Board at the University of Pittsburgh (Appendix A) approved this study and determined that it met the regulatory requirements for exempt research.

2.2.2 Study Design and Participant Recruitment

The purpose of this study was to interview parents and caregivers about their experience receiving their child's SMA diagnosis before and after the inclusion of SMA on the NBS panel in Pennsylvania. Participants were 18 or older with a child aged 17 or younger with SMA. There were no specific exclusion criteria outside of these requirements.

Participants were recruited through the Muscular Dystrophy Clinic at the Children's Hospital of Pittsburgh. Parents and caregivers of children with SMA were contacted by clinical staff via phone call to discuss the study. Interested participants were then contacted by the principal investigator to provide additional information about the study and complete a screening questionnaire. 25 families were contacted, representing 26 patients. Of those contacted, 13 families indicated interest though only nine returned calls to complete the initial screening questionnaire and be scheduled for a Zoom interview. Ultimately, seven interviews were conducted via Zoom in total.

2.2.3 Participant Interviews

Participants were interviewed via Zoom between February 2023 and April 2023 by the principal investigator of the study, a genetic counseling and public health genetics dual-degree student at the University of Pittsburgh. A genetic counselor through the Muscular Dystrophy Clinic was also present during the interviews to ask any follow-up questions and assist with debriefing following the interview. A script was first used to introduce the principal investigator and describe the overarching goals of the study. The principal investigator then reviewed a verbal consent script with each participant which included permission to record and transcribe audio from each interview. Information regarding risks and benefits of study participation as well as contact information for the principal investigator was also provided (Appendix D). Recordings and audio transcription were stored securely on a personal password-protected computer. A dynamic interview guide was devised with open-ended questions to aid in understanding participants' experiences in having a child diagnosed with SMA regardless of whether this diagnosis occurred before or after the implementation of NBS (Appendix E). The dynamic nature of the interview allowed for additional follow-up questions to gather further information as part of the qualitative research process. Interviews ranged in length from 35 minutes to one hour and 16 minutes. The average length of the interviews was one hour. The audio from each interview was uploaded to Otter, an artificial intelligence service providing automated transcription of recorded audio and video. The transcripts were then uploaded to a password-protected computer and any participant names or personal information were subsequently de-identified.

2.2.4 Thematic Analysis

Inductive thematic analysis with semantic identification as described by Braun & Clarke (2006) was used to examine the experiences and emotions of parents and caregivers who have children with SMA. Audio files from each interview were imported to Otter.ai for automated transcription. Each transcript was read thoroughly to de-identify names of both the participant and the child with SMA and to ensure accuracy in transcription. After ameliorating the transcripts by checking for typos and inconsistencies, the principal investigator read the documents to begin developing ideas for initial codes and themes. Interview transcripts were exported to Microsoft Word for the coding process. Codes were added line by line as different concepts emerged throughout the transcript. This process was repeated several times to parse out additional codes relevant to the specific aims and to begin identifying themes. A codebook was developed in Microsoft Excel to track data. The principal investigator met with the research team to review progress throughout the analysis. The mind mapping software MindMeister was utilized to compare codes through visual representation and develop themes in comparison to the specific aims of the project. Thematic analysis memos were created throughout the process to aid in describing potential themes as they would arise. The principal investigator worked with the research team to review the themes, subthemes, and associated codes to refine them throughout the analytic process.

2.3 Results

2.3.1 Participant Demographics

Seven parents and/or caregivers of children with SMA were interviewed for the purposes of this study. Participants' demographics are listed in Table 1. The introductory interview was completed for two additional participants who were ultimately not interviewed via Zoom. Ages of the seven affected children ranged from 6 months to 14 years and four were identified by NBS.

Table 1. Participant Demographics

Participant ID	Age of Affected Child	Identification Via NBS?	*SMN2* Copy Number
1001	3 years	Yes	3
1003	6 years	No	2
1005	4 years	No	2
1006	6 years	No	3
1007	14 years	No	3
1008	10 months	Yes	3
1009	6 months	Yes	2

2.3.2 Identified Themes

A codebook with 367 codes was developed and the thematic analysis ultimately identified six themes: communicating diagnosis and management: recommendations for healthcare providers, navigating uncertainty: understanding and addressing informational needs, finding community: importance of seeking support and becoming advocates, processing change: evolving expectations for a child's future, feeling overwhelmed: initial parental experiences following their

child's diagnosis, and experiencing loss: coping with guilt and the loss of expectations for a healthy child. These themes are summarized and further described in Table 2.

Table 2. Description of Identified Themes

Theme	Description
Communicating diagnosis and management: Recommendations for healthcare providers	Participants highlighted experiences they had as their child was being diagnosed as well as frustration associated with the diagnostic odyssey, including experiences with NBS. Participants additionally provided recommendations for physicians in diagnosing a child with SMA.
Navigating uncertainty: Understanding and addressing informational needs	Participants discussed their need to receive information in a way that did not create additional fear. Some of this need was met through the genetic counseling process. Participants also commented on fear of the unknown and of researching information on the internet. They also made recommendations for providers in attending to these needs.
Finding community: Importance of seeking support and becoming advocates	Participants discussed their involvement in support groups and in receiving support from loved ones. They also discussed the various ways in which advocacy can occur and the importance of any level of advocacy with rare diseases.
Processing change: Evolving expectations for a child's future	Participants commented on the ever-changing landscape of SMA with the advent of various treatment modalities. Participants also focused on positivity and hope that may follow the diagnosis as well as coping with these expectations as they evolve throughout the child's life.
Feeling overwhelmed: Initial parental experiences following their child's diagnosis	Participants commented on the psychological impact of diagnosis causing it to be difficult to absorb information. Participants additionally discussed the impact of feeling emotionally overwhelmed and the limited time to process the diagnosis to make timely decisions.
Experiencing loss: Coping with guilt and the loss of expectations for a healthy child	Participants focused on both the loss of expectations for having a healthy child and the desire for privacy in coping with such loss. Participants also mentioned shifting perceptions as the child ages associated with visual acknowledgment of limitations.

2.3.2.1 Communicating Diagnosis and Management: Recommendations for Healthcare Providers

During interviews, participants were asked about their experiences with healthcare providers, including the way the diagnosis was disclosed. They focused on which type of healthcare provider should provide a diagnosis of SMA, with participants discussing various experiences with primary care providers/pediatricians, neurologists, and neuromuscular specialists. Of note, these different types of healthcare providers may have different approaches and comfort levels in disclosing this information. Several participants began this discussion by describing initial negative interactions with healthcare providers related to the way in which the diagnosis was delivered. Participants discussed the psychological effect of healthcare providers instilling fear when delivering the diagnosis as well as frustration occurring once these providers discouraged feelings of positivity and hope after giving the diagnosis. Many participants concluded these discussions by noting that while they have found a positive medical home since the diagnosis, the frustration they felt with the lack of general knowledge of caring for a child with SMA and the time to diagnosis was significant. Additionally, one of the specific aims of the study was to identify participants' perspectives regarding NBS. While both groups highlighted tremendous support for NBS for SMA, they also addressed some negative perceptions as well as feelings of ambivalence. Participants also provided recommendations for providers in both diagnosing and caring for a child with SMA throughout their life to avoid negative impacts, basing these recommendations on both what healthcare providers should avoid based on negative experiences and what healthcare providers should continue to adopt based on positive experiences. This highlights the significant impact healthcare providers can have at the initial diagnosis. This theme was seen most often in participants whose children were diagnosed with SMA prior to its addition to the NBS panel.

Participants provided recommendations for which providers should provide the diagnosis. Some participants believed that a neuromuscular specialist is the best person to deliver a diagnosis of SMA. This is mostly the belief of participants who were diagnosed before the advent of NBS, who discussed the following:

> *"I mean, I don't want Joe Schmo from down the street telling me, but if I went to my kid's PCP office, and she was the one to tell me, I don't think I maybe would have took it as well." -1006*

Participants who underwent NBS discussed their concerns of receiving their child's diagnosis from a neuromuscular specialist who they did not know rather than from a healthcare professional with whom they have an established relationship. One participant felt that learning this information from a stranger might feel uncomfortable, though they recognized that their experience may be isolated:

> *"I think if I hadn't found out from the pediatrician, I would have been more taken aback. And then that news might have hit harder in a lot of different ways." -1009*

Participants whose children were diagnosed prior to the advent of NBS discussed the possible negative experience of receiving the diagnosis from primary care providers since such providers may lack significant information regarding SMA. One participant commented that despite their affected child being in their teens, their pediatrician remains uncertain of how the various treatments are administered:

> *"I don't know how familiar pediatricians might be in research studies or medications, or even how those medications are given because, I mean, they're complex…even so, now, when we talk with our pediatrician because we do talk, we keep them in the loop with all the different things, he'll kind of say something like, 'Look, remind me again, how does he get*

that?' We kind of talked about it because he gets Spinraza right now, so [he asks about] the process through interventional radiology and anesthesia, and all that kind of stuff." -1007

One participant whose child underwent NBS commented that despite having a positive experience with their child's pediatrician, there was still limited knowledge:

"My PCP had no idea what it was either. Like obviously they learned about it, but they never actually had to get into it. So, he was like, 'I can give you stuff from the internet, I can print you some stuff, but that's about as good as I might be able to give you." -1008

Participants were then asked about their opinions on NBS for SMA to better understand impacts of the diagnostic odyssey. All participants favored NBS for SMA to an extent, although some participants discussed that while the positives outweigh the negatives, the negatives persist. One participant noted, "it's a blessing more than a curse" (1009). One positive aspect of NBS discussed by participants centered on the amount of information parents can receive from this screening. One participant commented on this availability of information:

"I think if you can do something as simple as a blood test to test for as many different conditions as you can, at that very early part of life, is very beneficial. Obviously, it gives you answers that you can start now looking into. What do we need to do? How do we need to do this? What is this going to look like for us?" -1001

Other participants focused on how NBS allows families to be more prepared in raising a child with SMA. One participant mentioned how NBS provides parents with additional time, which is vital in decision-making related to treatment:

"But to look back on it, okay, I could have had another 18 months to sit here and research, you know, what the different treatments could be, what my different possibilities are, maybe

talk to more families and be able to have more personal stories to go off of versus just what the FDA is saying is okay." -1006

Another participant discussed that the availability of treatment is a benefit of identifying SMA by NBS:

"It is a lot easier because then you can get the Zolgensma treatment before anything actually does come about." -1008

Despite the overwhelming support and positivity surrounding NBS, participants also commented on negative aspects. Some participants with children diagnosed symptomatically have noted that while they support NBS, they would have more negative things to say had they been diagnosed that way. One participant described how NBS can take away from a period of blissful ignorance with the knowledge that an asymptomatic child has a diagnosis leading to significant worry and concern:

"I had almost two years of thinking my child was normal. And I'm sorry to use that word. But I don't know how else to say it. So, it was, you know, ignorance is bliss for me." -1007

The same participant expressed prior disapproval for NBS when there were no approved treatment modalities for SMA:

"But when there wasn't, when there was nothing to offer, it didn't make sense to have in the newborn screening, to be honest with you." -1007

Another participant commented on how diagnosis via NBS could be overwhelming in terms of the information provided so soon after birth, especially regarding disease severity:

"I mean, after you just have a kid, I don't think that's necessarily the information I want to be given right then and there." -1006

Both participants with children diagnosed symptomatically and via NBS provided recommendations for physicians in both diagnosing and caring for a child with SMA based on their experiences. While negative experiences certainly provided a basis for what healthcare providers should avoid doing, positive experiences also proved important in providing guidance for what healthcare providers should continue doing. First, participants feel that physicians should provide guidance to parents about what to expect throughout their child's journey. One participant commented on the utility of anticipatory guidance as provided by a neuromuscular specialist:

> *"But they printed out the web page and, you know, kind of gave us warning of like, 'there are parents on here who have children who weren't able to receive the treatment that we were seeking at that time'." -1009*

Participants also recommended that healthcare providers have immediate plans in place for next steps following the initial diagnosis and that appointments should be scheduled ahead of time to discuss results. Additionally, participants suggested that pediatricians and PCPs inform parents that treatment is available as soon as the diagnosis is disclosed, and that a follow-up visit be scheduled following the initial results disclosure to allow time to process the information and to consider possible questions. These recommendations were provided by those families who received a diagnosis via NBS. One participant recommended that PCPs provide additional steps for families to take during their initial appointment once SMA is considered as a possible diagnosis:

> *"Because even if I was told, 'Hey, give it two days, somebody's gonna call you, they'll help you walk through it,' I would have gone home so scared as all get out. But knowing that there was a plan in place would have helped." – 1009*

Participants also provided recommendations for aspects of care that would be beneficial to parents at the time of diagnosis. This includes being calm, compassionate, and respectful. One participant recommended that healthcare providers be honest in relaying a diagnosis of SMA following their experience with a neurologist:

> *"I feel like honesty's the best policy, and you know, sometimes we get some people that beat around bushes for things, but maybe just being open yet sympathetic in a manner which, I mean, you gotta get your point across. So, you can't be over the top." -1006*

Participants additionally highlighted the sense of isolation caused by feeling neglected by the healthcare team. One participant described the little assistance provided by their child's pediatrician:

> *"But it just kind of felt like everything was dumped in our laps with no help, no guidance, no nothing." -1009*

Participants also recommended that the healthcare team work together with the SMA community. One participant noted that this is a need that is currently not being met among neurologists:

> *"And if you say some of the same things or mutual things that we [support organizations] have said to them or say to them, it's immediately going to gain their trust, and then you could help them while we can't be there, save their child. And that's a huge step. That's a huge step that I feel like isn't bridged yet." -1003*

Participants additionally emphasized that all types of healthcare providers should recognize how overwhelming a diagnosis of SMA can be for their patients' families. One participant shared that after delivering such a difficult diagnosis, healthcare providers should avoid immediately asking individuals for questions:

"And I think the worst thing that someone says when you get thrown a bunch of information is, 'Do you have any questions?' Well, of course not. I'm trying to process everything you just told me; I have zero questions." -1009

Participants also focused on the negative psychological impact of healthcare providers instilling fear during the diagnosis. One participant shared the following about how the diagnosis of SMA was delivered by a neurologist:

"It was doom and gloom, there was absolutely no positivity." -1003

Some participants described feelings of frustration caused by healthcare providers discouraging positivity and hope in the face of a difficult diagnosis. One participant shared how they were told by a geneticist that their expectations were unreasonable:

"But you know, to be told we're not appreciating the severity of this while we're also coordinating surgery for her trach and G-tube and preparing to vet home nursing agencies just felt a little off balance…They thought we had, and I'm quoting, 'unreasonable expectations' for Spinraza and didn't appreciate the severity of [the child]'s condition. We were a little upset about that and kind of, again, I don't know if we were supposed to see this note. Maybe we weren't." -1005

Participants provided recommendations for healthcare providers to give support to parents through a difficult diagnosis. One participant described their healthcare team, including the neuromuscular specialist, as a family:

"I just gained the most amazing family that I never thought I was going to have, and this support system has just like literally opened the gates." -1006

Participants described the importance of having healthcare providers truly listen to parents regarding their child's diagnosis and that they should trust the parents' instincts in stressful

situations. They also recommended that parents reach out to healthcare providers to ask any questions as they arise. One participant discussed this recommendation specifically for neuromuscular specialists:

> *"I think even just saying like, 'I know you're gonna have questions, here's my contact information, which is just really helpful whether that's a personal like work cell phone that you use only specifically for those instances, your email, whatever the case may be." -1009*

Finally, participants described the utility of neuromuscular specialists making the ultimate treatment decisions on their behalf during a time of immense stress. They prefer to trust the experts based on their expertise, and so their guidance was highly desired. Participants also commented specifically on those feelings of relief associated with treatment onset. One participant stated:

> *"And so, when we got to it [treatment], it kind of felt like a weight was removed. You know, we're still going through it. But it was such a nice feeling." -1009*

2.3.2.2 Navigating Uncertainty: Understanding and Addressing Informational Needs

In comparison to the previous section, this theme captures in more detail how participants discussed their individual information-seeking behaviors with some participants wanting as much information as possible and others hoping to avoid information from unreliable online resources that could create more fear than hope. Fear of the unknown and uncertainty regarding SMA's prognosis arose throughout each participant interview and demonstrated the need for emphasis on this particular experience for families. While genetic counseling was noted as a beneficial process for learning information about SMA, some participants had little to no memory of their interaction with genetic counselors. Participants commented on the overall lack of knowledge among various healthcare providers regarding SMA and lack of information provided about the NBS process. This theme was identified more frequently in participants with children diagnosed via NBS.

Families recommended healthcare providers provide further information on increasing life expectancies for children with SMA based on emerging treatments. One participant whose child was diagnosed via NBS commented:

> *"It would have been nice, I think, from our standpoint, having a newborn… Somebody saying, 'Hey, you know what? Life expectancies are a little longer.' I still don't know what that looks like in terms of children with SMA. I can't find any valid research to give me some sort of idea… I do know with gene therapy, after that their life expectancy is a little longer." -1001*

Participants highlighted that information-seeking needs can be met via the process of genetic counseling, which provided comprehensive information on the genetic component of SMA to parents and caregivers. As one participant shared:

> *"I think that the [genetic counselor] at the time was extremely comprehensive, very thorough, and like I said, really set us up for our free lab testing appointment. So, I think that worked out very well." -1007*

However, genetic counseling was not beneficial for all participants. One participant felt that the appointment was one requirement among many that needed to be fulfilled to obtain adequate care for their child with SMA rather than being an opportunity to gain helpful information:

> *"And behind the scenes we're kind of like…"Do we really care about going for this appointment? It was really just kind of like checking up to see, okay, everything looks good. It wasn't really anything too crazy. Yeah, it was, it was a genetic counselor. I'm looking at the note here…So I knew there was one follow up. I don't think we've had one since then. And it was just sort of another opportunity for questions or for them to kind of see how*

[our child] was doing and whatnot. I don't remember how long after discharge that was, but it was a thing that happened." -1005

Participants discussed the lack of knowledge, explanations, and appropriate informed consent for newborn screening as it pertains to SMA throughout the diagnostic journey. Despite some participants having a background in nursing, not a single participant had heard of SMA prior to their child's diagnosis. One participant whose child was diagnosed prior to NBS commented on the significant lack of information provided on SMA:

"There wasn't enough. There wasn't enough. There wasn't enough anything. There wasn't enough doctors that knew about it…There wasn't enough information I really had to depend on." -1003

Parents with children diagnosed before newborn screening had awareness of when SMA was added to the NBS panel in Pennsylvania and much of the associated details about the process. In contrast, participants who had children diagnosed via NBS knew less about the process. One participant whose child was diagnosed with NBS commented:

"I'll be honest, even with newborn screening, I didn't know what was looked at, what was addressed in that screening, anything. So. it was all brand new to both me and my husband." -1009

Participants additionally discussed the lack of written information provided on SMA, with some parents receiving no written information in the clinical setting. This led to some recommendations regarding the method with which written information should be provided. One such recommendation was that written information and resources should be personalized. One participant noted:

"So, I wish the information was maybe a little more individualized so the people that need the resources were getting it versus like, we didn't necessarily need everything. I think that was a downfall." -1006

Participants also felt that written information should be provided in small increments over time to avoid excessive information overload. As one participant discussed:

"I think to maybe get like, the stuff of the treatments and whatnot originally would have been amazing. And then a couple months down the road do like the comparison ones, and the things of that nature would have been less overwhelming versus when you're a mom with a kid with this disease…Please send me like the fun facts later on once this has all been processed." -1006

Participants overwhelmingly believed that healthcare providers should give this information to their patients at the time of the child's diagnosis, particularly when discussing treatment options. They also described the importance of being provided with reliable websites to obtain information rather than having to do their own research online. One participant noted:

"Or directing me to a website, you know, 'These are valid websites, these are the ones that you're going to get the correct information from.' That was something that would be helpful for me instead of trying to navigate through misinformation and that type of thing." -1001

Participants provided recommendations not only for healthcare providers, but also for parents who are interested in obtaining information. Multiple participants expressed the importance for parents to learn as much about their child as possible. However, one participant whose child was diagnosed prior to the implementation of NBS recommended that parents with

children newly diagnosed with SMA refrain from researching the condition online given the possibility of reading inaccurate or scary information. This participant stated:

> *"Um, it was more of a feeling like I've got to see what I'm not supposed to see. I thought it was gonna be excitement. And here, it was not excitement. It was just heartbreak." -1006*

Another participant whose child was diagnosed via NBS expressed similar fears:

> *"So, I don't Google because I'm scared of what could happen." -1009*

The desire for knowledge and information appeared to be related to fear of the unknown and grappling with a sense of uncertainty. Participants discussed significant concerns and worries about what steps should be taken in the future. The following participant whose child was diagnosed via NBS described this uncertainty:

> *"It was still scary, obviously, because you know, he didn't have treatment or anything yet, but I don't know what would happen. He hadn't went through anything yet. So, I know, there's like nothing really holding the SMA back from coming out full force." -1008*

Much of the uncertainty appeared to be related to the complexity associated with different SMA subtypes. One participant whose child was diagnosed prior to NBS focused on this as the source of their fear:

> *"I think the other thing that was hard as a parent is with SMA, there's the different levels. And I know that, you know, obviously one is diagnosed at birth, four is a later onset, two and three are kind of somewhere in between." -1007*

Other participants discussed the wide spectrum in clinical manifestations with SMA and the challenges this creates given an inclination to their own child's experience to that of another. One participant mentioned that this tendency to compare led them to avoid joining a SMA-related support group:

"I think I did that for a couple reasons, but the biggest one was because there is such a variation between how children are. I thought that would be more difficult for me to hear about. Maybe a type 1 or to hear about even an older type 2 who maybe wasn't progressing as well." -1007

This avoidance and fear was not reported in those participants whose child was diagnosed via NBS.

2.3.2.3 Finding Community: Importance of Seeking Support and Becoming Advocates

During interviews, discussions emerged that centered on the importance and utility of seeking support and becoming involved in advocacy work. Support stemmed from not only family members and friends, but also religion, the SMA community, and various support groups and organizations. However, participants described difficulties of presenting their child's diagnosis to others as well as the fear of comparing their own child's progress to that of other children with SMA. Consequently, some participants commented on their decision not to be part of any support groups. Additionally, participants focused on the implications of advocacy and the desire to make a difference, having expressed that any level of advocacy is critical. Participants described advocacy in a broad way that occurred in the healthcare system, support groups, legal processes, and research activities. The type and frequency of advocacy required for children with SMA extended beyond what many of the participants in this study initially expected at the time of their child's diagnosis, with some participants expressing how helpful it would have been to have someone to explain how to best advocate for their child. For participants in this study, advocacy did not exist solely at a societal level but additionally included advocating for themselves and their child. This theme was more frequently noted in participants whose children were diagnosed symptomatically.

Participants commented on receiving support from family and friends. One participant shared on how this support can prevent negative feelings from arising:

> *"And I have literally the best village. I mean, I have two amazing step-parents, both of my parents are absolutely amazing. My brother is amazing. And if it wasn't for them, I feel like it's very possible to go down a very dark hole." -1006*

Related to support, participants also commented on complicating factors surrounding family support. One of these factors occurs when family members and friends compare their loss to that of the participants.' This led to frustration due to how incomparable these losses felt to participants. One participant provided an example of this:

> *"Like, for example, my parents, my older brother had cancer whenever he was a young adult, and so they can understand that. But he got better. So, it was very hard to explain to people because they try to assimilate it to something else. And maybe I'm wrong, but it's hard. It's hard to compare it to something." -1007*

Another concept related to support involves the inevitability of preparing to inform family members about the diagnosis, including its life-limiting nature and the complexity of genetics. One participant commented on how the availability of an online seminar to direct family members to would allow them to prepare family members more easily:

> *"It would be easier with a webinar. Yeah, just to be like, 'Okay, if your kid's, you know, a type 1, this is what this means. Type 2, this is what this means, you know.' I mean, then they can actually listen, 'Okay, I heard that. [The child]'s a type 2. So, okay, now, I need to just listen to what they about type 2.' So, you could actually put it all together in one big webinar, like send it to them pretty much after their official diagnosis, so they know what to be listening for." -1008*

Participants additionally described finding support in their religious beliefs and communities. Some participants used this as a helpful mechanism to maintain positivity for both the family and their child while others used religion to help explain their child's genetic condition to them. One participant stated:

> *"And so, teeing up what he would say to his peers or to his friends, what he might share and how he wanted to share it [was important]. We're Catholic, we're pretty religious. And so, his answer was, 'Well, this is how God made me.' And you know, that is the truth." -1007*

The participants additionally described the strength and tenacity of the SMA community, referring to the community as aggressive in their advocacy and the close ties within such a small and tight knit group. Participants expressed an overwhelmingly positive perception of the community, with one even commenting that the journey would have been significantly lengthier and more difficult without the community. This participant said:

> *"With awful news comes a great family that you didn't even know you needed. And it doesn't matter what time of day it is, there's always somebody that's going to help you through it. And truly, you're never on this journey alone, ever." -1006*

Social media was also helpful for participants, with one stating, "What helped me was, honestly, and as cliché as this is, was social media, seeing how other people's daily lives looked with SMA" (1001). This provided a starting point to allow families to find other families on their own SMA journeys. Many support groups also take place over social media such as Facebook. One participant noted:

> *"There's just a lot of SMA Mom groups on Facebook. Facebook is the main one that I use, but there's just so many support groups or different things. Like they have support groups*

for all the different types, support groups for moms, support groups for dads. It's been kind of helpful." -1006

As mentioned previously, participants discussed the need for advocacy in a variety of unexpected ways. One participant shared concern regarding inaccessibility within the U.S.:

"I think the only other thing that this is, in general, you know, I think our world, our country isn't as accessible as everyone would like to think that it is. And so, this experience has been kind of eye opening, with places where we can go in, places where we can't, and just how our infrastructure doesn't necessarily support, you know, thinking about travel." -1007

Other participants commented that they found themselves frequently doing the jobs of others. For example, one participant noted:

"My wife and I have a saying, it's like, 'It has been zero days since I've had to do someone else's job for them'…We had to briefly become experts on billing codes because Radiology couldn't bill something for the same procedure the way somebody else did. So, it sat in limbo for two years before the hospital was sending us a bill with an overdue balance, and then they couldn't figure it out, and insurance couldn't figure it out. So, we had to call insurance, figure out the code they should have used, then get back to the hospital. And then they had to communicate that to Radiology because Radiology has their own separate billing team that you can't directly call." -1005

They also were forced to learn how to phrase questions in specific ways to receive understandable answers from specialists. Multiple participants discussed the utility of having someone teach newly diagnosed families how to advocate for their child. One participant shared how difficult learning to advocate can be:

"I mean, at the risk of sounding braggy, which I don't mean to, like my wife and I, we're pretty with it, on the ball, intelligent people. I mean, I think probably above average. I think that I would be frightened for a family that had to deal with this who was more in that average area. Again, that's not a takedown or whatever else, it's just that there's no reason it should be that difficult. You shouldn't have to be able to be a certain caliber to deal with those sorts of things...And there's no way to prepare. There's no way that parents are prepared for that right now. It needs to be like Advocacy 101. They do the NICU 101 courses at [some hospitals]." -1005

Regardless of the manifestation, participants suggested that any level of advocacy is important. Participants focused on the importance of advocating for their children within the healthcare system, starting with healthcare providers. One participant described why advocating for children with SMA is critical:

And if you're worried about that, step up and speak up, because your kid isn't going to be able to tell you, 'Hey, I couldn't move my leg yesterday or today,' you know, if you see something, don't be afraid to say, 'I think this is what's happening, please, let's move faster'." -1009

Similarly, participants focused on the importance of trusting their instincts when it feels as if something is wrong with their child. One participant noted:

"But you know, maybe just follow your gut when you get a positive on the screening, and you're not sure where to go, just follow your gut because it's going to lead you the right way. You're going to do what you need to do." -1009

Advocacy may be beneficial not only with healthcare providers, but also at the hospital level. One participant shared how a lack of advocacy can lead to suboptimal care:

"You have to staple yourself to that room. Because if you're not there, you can't be sure that the things you expect to happen will happen." -1005

Participants discussed the importance of advocacy in obtaining treatment for their children: not only for an individual's own child, but in some cases getting the specific treatment to their child's hospital for the first time as well as involvement in clinical trials. One participant described their experience in obtaining access to Spinraza for their child's hospital:

"And I got the Research Development information. And I went to the director of the hospital, and I laid it all out for him. And I'm like, 'You can do this. You can have Spinraza in your hospital. Like, we have the people, we have the money, we have the kids.' And they signed it." -1003

Additionally, participants discussed actions that were necessary to provide their child with the best possible care in accessible ways. One participant commented on rule breaking that was required for their child's situation:

"Do you know how many extra days we chose to stay in the hospital because we were at that cost? I swear it was like conspiracy. I'm like, '[Child's name], you are getting better. And we've been here for 19 days. I swear to Jesus, if they try to discharge us tomorrow, you're staying another day for free." -1003

In addition to advocacy within clinical settings, participants felt it was beneficial to engage in advocacy through support groups. One participant discussed volunteering with organizations which have helped them in the past, stating:

"I'm being able to help other people through what somebody else helped me through two years ago." -1006

Other participants detailed their specific activities with support organizations, with one participant discussing participation in a walk team to fundraise for the Muscular Dystrophy Association (MDA). Another participant recounted their advocacy work through the legal system specifically in having SMA added to the NBS panel, detailing their experiences in collaborating with the governor and various senators to fight for the condition to be added to the NBS panel in Pennsylvania. Participants also discussed advocacy through participation in research. One participant characterized the importance of research:

> *"Any research I can help in, any interviews, any of that type of thing that could help another child. To understand [the child] better, understand other children coming in, you know, to try your medications, whatever that may look like. I am totally on board with doing that." -1001*

2.3.2.4 Processing Change: Evolving Expectations for a Child's Future

Several participants described the importance of recognizing that SMA is a significantly different condition than it was over a decade ago with a much-improved prognosis following the development of various treatment modalities. Consequently, participants commented on the evolution of their expectations regarding their child's future in terms of the milestones and prognosis. For many participants, this led to an associated increase in positivity with the recognition that their children's prognosis may not be limited by their diagnosis. Much of this theme focuses on the future following their child's diagnosis, including a reset of expectations as additional treatments are developed and more information is learned about SMA. Participants additionally provided recommendations for other parents to help them recognize that the outlook of SMA is changing in a positive direction. This theme was more frequently noted in participants whose children were diagnosed symptomatically.

Participants discussed that children are exceeding expectations, feeling that children with SMA grow and strive for more beyond their diagnosis in terms of developmental milestones and symptom development. One participant discussed their disinterest in labeling their child with a particular subtype:

> *"In my parent heart, I didn't want anybody to label him as something, as a number. So, like, for example, when we went to the pulmonologist for the first time, it was [a doctor] who was phenomenal. I loved him and [the child] really loved him too. And he said, 'I understand your child has type 2 SMA', and I said, 'We don't know that yet'." -1007*

One participant focused on how unique each child with SMA can be:

> *"While SMA is a diagnosis, each kid is different, and they're going to meet different milestones regardless…You know, some kids may not be able to use their lower extremities at all." -1001*

The same participant discussed how children with SMA are not limited by their diagnosis, stating:

> *"Just because he has SMA doesn't mean he cannot do things." -1001*

Another participant provided recommendations for parents dealing with a new SMA diagnosis:

> *"Truly, the possibility of what these kids are going to be able to do is endless…do not stress so much about wanting your kid to be accepted." -1006*

Participants additionally discussed positivity and hope following a diagnosis of SMA. One participant described how much their child impresses them, saying:

> *"We're amazed on a daily basis with him." -1006*

Another participant commented on the present-day context of SMA with the availability of treatment, stating:

"I guess if you had to have SMA, this is probably one of the best times to have to have it." -1005

One participant discussed the excitement that can surround SMA in the present day:

"We started solid foods with him, which was really exciting, because I didn't know if that was going to be a possibility with his development, if that was going to be something we'd need to put off. And we haven't had to, and we haven't had issues. And it's just been awesome to be able to hit those kinds of mile markers with him. And it's just been really fun." -1009

Another participant focused on their gratitude not only that their child is still living, but that other parents will never have to experience a similar level of suffering:

"And you won't even know what my life looks like ever. And I'm so grateful. And I'm so glad, envious a little, but more grateful. And I consider that a blessing. And I'm still honored that [the child] is here and able to be a part of that big movement toward medicine. And people won't have to suffer. And people won't have to sit and wonder if their kid's gonna live through a silly little cold, you know." -1003

Another participant recognized that their biggest source of hope involved treatment:

"As far as the actual like, receiving the diagnosis, all that we were hoping for that whole time was something that we could treat, you know. Something that had a treatment, you know. Knowing about Spinraza at that time certainly wouldn't reverse the course of anything, but it could stabilize. And we would be able to make the most out of whatever that stabilization means from there." -1005

Participants focused on the development of several medications for SMA as well. For example, one participant stated:

"And, I mean, I used to advocate and be aggressive, but I don't anymore because medicine has changed so much and come so far in the last six years, that there are four medicines right now that you can give your child at birth." -1003

One participant commented that the treatment and outlook of SMA has changed significantly in a brief period:

"I think in such a short period of time, it's frankly unheard of. I mean, thinking about how much other, you know, disorders or diseases are out there, and how long they've been around, and that not much has happened and looking at SMA, it's like, amazing." -1007

This same participant shared how the present day is quite different from when their child was first diagnosed:

"Honestly, I think it's a little bit of a different time, to be honest with you. Because at the time of his diagnosis, truthfully, like I said, there wasn't even…I think there were trials in mice, or something along those lines, but not even in people." -1007

Participants additionally provided recommendations that other parents remain calm at the time of diagnosis given this changing landscape. One participant stated:

"It's easy to say, but I like to tell people to stay calm, even though it's hard to." -1008

Participants expressed relief they experienced following initiation of treatment, having noticed improvements in strength, dexterity, and movement following treatment, which thereby led to psychosocial relief. One participant provided their perspective of these improvements:

"The movement and control has just grown exponentially. So, we've seen a lot of improvement from newborn to symptomatic to he can sit between my legs and play with a toy and hold himself up." -1009

One participant focused on their child's improvement with Zolgensma, stating that, "he went from not being able to move them to kicking and putting pressure through his feet" (1009). Participants similarly commented on their experiences with Spinraza, including how anesthesia may be required for administration. One participant praised Spinraza:

> *"And it's [Spinraza] just kind of like this miracle drug has happened for us and gave us all these amazing results that we never thought we were going to have." -1006*

Additionally, multiple participants focused on the time-sensitive nature of treatment for SMA, describing the process as feeling rushed. One participant felt that parents' primary goal should be to do anything to help their child obtain and start treatment prior to allowing themselves to grieve:

> *"Don't cry beforehand because you're just wasting time. Minutes, seconds, literally months." -1003*

2.3.2.5 Feeling Overwhelmed: Initial Parental Experiences Following Their Child's Diagnosis

This theme is centered on initial parental experiences following a diagnosis of SMA, particularly those feelings associated with being overwhelmed. Nearly every participant, regardless of whether their child was diagnosed symptomatically or via NBS, felt overwhelmed at the time of diagnosis. These feelings of being overwhelmed made it difficult to comprehend information. Participants discussed the fast-paced nature of the diagnosis particularly in the context of children diagnosed via NBS, leading to little-to-no time to think through decisions about treatment. This theme was identified more frequently in participants with children diagnosed via NBS.

Participants discussed how the time following diagnosis can cause significant psychosocial stress leading to difficulty in absorbing and retaining information. One participant described how the information provided was overwhelming once the NBS results were disclosed:

"So, there was a lot of information kind of just given to us. And I mean, it just feels blurry. To be really honest, it happened so quickly." -1009

Some participants described feeling astounded by the amount of equipment required for a child with SMA, whereas others focused on the amount of information alone:

"And then they just hand you a pile of paperwork, and your brain feels like mush. You know, like, I can't read that. I can't figure any of this stuff out right now, I have no idea." -1003

Multiple participants mentioned that the time surrounding diagnosis was never-ending. Other participants focused on how their mind would quickly oscillate between pragmatic concerns to deep worries about their child's lifespan as soon as the diagnosis was made. Participants recommended that healthcare providers allow parents time to process a difficult diagnosis in their child prior to meeting with an array of providers during an initial appointment immediately following the diagnosis. Participants provided with this additional time following the diagnosis noted a more positive experience with having the opportunity to discuss the condition with their families and develop appropriate questions. One participant described the benefit of having time to process the diagnosis:

"So, when we spoke with the genetic counselor at CHOP, I was a little bit more calm. I was able to listen and take things in a little bit better. So, it wasn't like, you know, they explained it better. They handled it differently. My mindset was changed." -1009

Participants also commented on the importance of managing the diagnostic process and learning information about the prognosis in an incremental manner to diminish feelings of being overwhelmed. One participant focused on the positivity associated with these incremental steps:

"We will take whatever comes up with one issue at a time, just navigate through it." – 1001

Participants also provided recommendations to other parents with children diagnosed with SMA, stating that it is important to trust the experts and specialists taking care of their children:

"But especially if you're going to neurologists…or a children's facility, I'm sure they know what they're doing. And they know, you know, especially if it's an immediate problem, they'll take care of it. If they're relaxed, then you should try to relax because obviously everything's going to be taken care of." -1008

2.3.2.6 Experiencing Loss: Coping with Guilt and the Loss of Expectations for a Healthy Child

Participants described their loss of expectations for having a healthy child and the guilt associated with such a loss. When discussing this loss of expectations, some participants shared that they desired time from their loved ones to allow time to process such loss. Other participants mentioned how expectations of their child's wellbeing and future shifted as the child grew older. As their children aged, there was further visual acknowledgment of the child's limitations noted by strangers. This theme was seen more often in those individuals whose children were diagnosed before the implementation of NBS for SMA.

One participant discussed how the loss of expectations affected their ability to cope and how the diagnosis led to the realization that their child's daily activities were not typical developmental tasks associated with childhood:

"Like your typical two-year-old, right? You're setting your daughter up for dance, or you're going to T-ball, and for me it was 'okay, now we have to go find a therapist. Now we need to get OT, speech.' You know, there's all these things that we now need to align where I thought my biggest battle was going to be finding a baseball bat, not finding a therapist to help my kid." -1006

Participants additionally commented on the shifting perceptions of others as the child grows older, leading to a recognition of their child's physical limitations. Participants described how physical limitations and the presence of mobility devices such as wheelchairs serve as visual acknowledgements of the child's diagnosis. One participant discussed this change:

"Now you're realizing, okay, I have a child with a physical limitation. And I have to now navigate our house or car…It's also a visual acknowledgement that something is different. You know, whenever he's little, you could just carry him around and nobody knew. But then when you have him in a wheelchair, it makes it more real for not just you all, but for everyone. And so, it's just a different shift in experiences and that actually forced him to grow up pretty quickly because then he needed to figure out, 'How do I handle kids my own age, younger or older, who just stare?' We always, without fail, will be somewhere and you'd overhear a child, and they're not out of line by any means, but saying to their parent, 'Mommy, why is that boy in that wheelchair?'" – 1007

Participants commented on the desire to have time to process their child's diagnosis to best aid in coping with such a loss of expectations. One participant described their decision to not share their child's diagnosis with all their family members:

"So, at first, I will say I asked my parents not to say anything because I didn't have the answers. And I didn't know everything. And I asked them to kind of wait until I was ready to have that conversation with our loved ones." -1009

This loss of expectations led some participants to consider the future, which generated uneasy questions in the current moment:

"The long-term care, the what ifs, those are something that's definitely going to be needed. And then who do we talk to, who helps us navigate that? Who gives us the information? So, it's all a lot of trying to look into the future, to be prepared for things and not be blindsided." -1001

2.4 Discussion

One goal of this project was to conduct interviews with parents and caregivers of children with SMA. Thematic analysis identified six themes related to the psychosocial impacts of an SMA diagnosis: communicating diagnosis and management: recommendations for healthcare providers, navigating uncertainty: understand and addressing informational needs, finding community: importance of seeking support and becoming advocates, processing change: evolving expectations for a child's future, feeling overwhelmed: initial parental experiences following their child's diagnosis, experiencing loss: coping with guilt and the loss of expectations for a healthy child.

While the overarching point of comparison was between participants whose children were diagnosed with SMA symptomatically and those whose children were diagnosed through NBS, participant interviews revealed that NBS itself was not a notable component of their journey. This project has highlighted the outcome that NBS is not as defining of an event for families as

compared to other variables. Factors including temporality, administered treatment type, age of diagnosis, and age of treatment initiation all arose as potential points of comparison in which more meaningful differences may arise. Most differences in theme interpretation can be attributed to one of these above factors, with participants whose children were diagnosed symptomatically tending to have older children that either began treatment at later time periods or were excluded from specific treatment modalities and received a diagnosis at an older age compared to those participants whose children were diagnosed by NBS. These factors served as confounding variables in determining explicit differences between participant groups.

2.4.1 Communicating Diagnosis and Management: Recommendations for Healthcare Providers

One of the specific aims of this project was to identify gaps in support for parents and caregivers and discuss recommendations for how healthcare providers can improve the process of diagnosing SMA. Most participants described a combination of positive and negative experiences throughout their child's diagnostic odyssey, and this led to the development of a theme initially based on negative experiences to determine what actions healthcare providers should avoid. However, through refinement of the theme, both positive and negative experiences were used to determine recommendations for healthcare providers. This also lent itself towards a discussion of the general frustration associated with a rare disease's diagnostic journey.

Currently, pediatricians receive the NBS results and relay this information to parents. As a result, it was important to examine individuals' experiences in learning this information from different providers (neuromuscular specialists versus primary care providers or pediatricians) to better understand not only whether their experience was positive or negative, but also

recommendations for who should be providing the diagnosis. Families with children diagnosed via NBS tended to prefer receiving the diagnosis from a pediatrician or PCP as opposed to those families whose children were diagnosed symptomatically that preferred diagnoses to instead be provided by neuromuscular specialists. It is important to note that while families who underwent NBS for SMA did prefer receiving the diagnosis from a pediatrician, this preference was limited to two participants. One participant described this preference as based on having a previous relationship with her child's pediatrician. This would not be the case for many newly diagnosed families, particularly when starting a family. Therefore, discussions on provider preference in disclosure may have been biased by the small sample size. This study also explored the perspective of NBS of those participants whose children were diagnosed before SMA was added to the NBS panel and participants whose children were diagnosed by NBS. While all participants did support NBS, some discussed negative aspects of the screening as well. Perspectives did not exist as simply a dichotomy, however, with one participant noting ambivalence towards the process and describing NBS as "both a blessing and a curse" (1009).

Discussions related to recommendations for healthcare providers in giving a diagnosis and providing care occurred more frequently in interviews with participants whose children were diagnosed prior to the implementation of NBS for SMA; this may be due to the early identification of the condition via NBS. Early identification significantly decreased the chances for a lengthy diagnostic odyssey to occur because there is no need for an evaluation to include multiple differential diagnoses. Participants with children diagnosed via NBS did, however, provide specific recommendations for pediatricians and PCPs to set up follow-up appointments following the initial diagnosis to provide families with the opportunity to ask additional questions later and provide next steps in a timely fashion, provide access to neuromuscular specialists one-on-one

instead of with a large group of healthcare providers all at once, and to avoid asking parents what questions they have immediately following an overwhelming diagnosis. NBS itself was discussed more often by participants whose children were diagnosed via NBS likely because these participants underwent this experience firsthand. These participants listed more positive aspects of NBS compared to those with children diagnosed symptomatically, who listed more negative aspects of NBS. Participants with children diagnosed via NBS also displayed more feelings of ambivalence towards NBS.

These findings have been identified in previous studies. Fernandes et al. (2022) conducted a study focused on the positive and negative aspects of the way their child's (or the patient's own) diagnosis of SMA was communicated to them. Negative aspects included healthcare providers disclosing little to no information, a significant focus on negativity, and relaying the diagnosis in a cold fashion. Participants in the study also provided recommendations to healthcare providers on disclosing the diagnosis to families and patients including the importance of listening, providing sufficient information, acting in a compassionate manner, and maintaining a sense of optimism when possible (Fernandes et al. 2022). The present study provided further recommendations for healthcare providers not previously addressed in the literature, including providing information to parents about what to expect, providing the diagnosis immediately without delay, and working together with the SMA community. Krosschell et al. (2022) identified similar findings regarding physical therapy best practices for patients with SMA, noting the importance of collaborating with advocacy groups to develop guidance for best practices for patients. The current study presents a previously underreported focus for families affected by SMA and provides additional steps in allowing for healthcare providers to enhance rapport and trust with these families.

Additionally, previous research discovered similar views of NBS. Prior to the implementation of NBS for SMA, Boardman et al. (2017) found that 70% of affected families and adults support NBS due to the availability of increased support, life expectancy, the possibility of further research, and prevention of difficult symptoms. Qian et al. (2015) found similarly positive impressions on NBS, but participants also expressed that NBS could negatively impact parents' relationship with the affected child, parents might prefer to be unaware of cases with mild symptoms, and NBS could generate excessive expenses for the health system. Kariyawasam et al. (2021) focused their research on perspectives of parents who were part of a pilot NBS program for SMA, discovering that while they supported the program, 45% of participants felt that much of their distress was attributed to lack of information provided about SMA. The present study is unique in that perspectives of participants both with children diagnosed before and after NBS implementation have been gathered to gain a greater understanding of the parental perspective of NBS. Sims et al. (2022) described families' experiences and needs following positive NBS results for sickle cell trait (SCT). This research highlighted several recommendations for healthcare providers in disclosing such results, including a lack of information provided, limited information on the prognosis and rare outcomes, and the desire to be provided with more information about how to discuss the results with their child in the future. These families also requested support resources, which were often not provided. Thus, there exists a need to ensure that families receiving positive result disclosures from NBS are receiving information that will be most relevant to them in terms of information seeking, family planning, and helpful resources. This project confirms this need.

2.4.2 Navigating Uncertainty: Understanding and Addressing Informational Needs

Participants within the study described their various information-seeking behaviors following their child's SMA diagnosis in conjunction with their desire to learn information about the diagnosis in a safe and efficient fashion. There were different needs discussed by participants, which sometimes were unmet and may have led to additional suffering. A related subtheme that emerged through the study involved participants describing that this research often led to more pain than useful knowledge, particularly due to information on life expectancy. Especially with the current era of NBS, it is critical for parents to receive written information at the time of diagnosis regarding SMA to provide relevant and up-to-date information in a safe and compassionate manner. Nearly every participant discussed fear of the future, most of which is caused by uncertainty surrounding the diagnosis. Regardless of whether a child was diagnosed via NBS or symptomatically, this uncertainty remained and was sometimes even more prevalent for those participants who received a diagnosis via NBS. This uncertainty was caused by the lack of predictability in SMA subtypes when treatment is initiated prior to symptom development. Treatments have been in existence for a short period of time, making it difficult to predict the child's prognosis.

This theme was likely found more frequently in those participants whose children were diagnosed via NBS because their children were asymptomatic at the time of diagnoses. The other group of participants had their children diagnosed following a diagnostic odyssey and at least some degree of symptom development, which could reduce some uncertainty. Participants whose children were diagnosed via NBS additionally expressed the most concerns over researching SMA on the internet in comparison to those diagnosed symptomatically. This may again be attributed to the asymptomatic nature of the diagnosis and this group of participants not expecting any

diagnosis. Prior studies focusing on uncertainties following NBS have been conducted, but have focused on genetic conditions in which NBS does not provide a definitive diagnosis unlike SMA. Boardman & Clark (2022) identified the term "genetic nomadism" to refer to constant oscillation between having a diagnosis of cystic fibrosis and having a child without a genetic condition as a source of uncertainty for what the future may hold.

These findings are consistent with prior research on parents' and affected individuals' experiences and needs with SMA. Research conducted by Qian et al. (2015) discovered that parents with children affected by SMA felt helpless due to the uncertain trajectory of their child's prognosis and life expectancy. In this study, participants echoed similar concerns, describing their own information-seeking behaviors as being caused primarily by the fear of the unknown. This study also highlighted parents' tendency to focus on the inability to plan when dealing with an uncertain diagnosis, leading to many unanswered questions (Qian et al. 2015). Other studies have explored uncertainty for positive NBS results in other conditions. Prakash et al. (2021) explored this concept with Pompe disease, a lysosomal storage condition complicated by the inability to distinguish between infantile- and late-onset forms of the condition. Participants described a lack of provided information on newborn screening itself as well of inadequate, outdated information available online. This study found that parents expressed a high desire to seek resources and educate themselves, highlighting the importance of information-seeking behaviors in NBS-related conditions. Pompe disease with its two forms offers a reliable comparison to SMA as well. While parents are provided with some information about what their child's prognosis may be based on *SMN2* copy numbers, this is far from certain and leads to fear among families. Providing a reliable source of information on SMA is critical in order to ease some of this uncertainty for families.

2.4.3 Finding Community: Importance of Seeking Support and Becoming Advocates

Participants focused on the importance of seeking support through various sources when dealing with a complex diagnosis. Each participant mentioned support groups and organizations to various extents and some participants discussed how these groups can benefit families, friends, and the SMA community. However, it appeared that formal support groups were not helpful for everyone; some individuals benefitted more from one-on-one support with other families, or simply with their own family members and friends. Each participant additionally commented on the utility of advocacy and giving back to others, clarifying that advocating for your child through the healthcare system looks vastly different than advocacy through clinical trials or through various support groups. Participants also commented on the unexpected manifestation of advocacy, including the lack of accessibility in the United States and how this is something many parents do not realize until having a child with a disability.

This theme was noted to occur more frequently in interviews with participants whose children were diagnosed symptomatically and may reflect their children were diagnosed at a time point where there was less information available regarding SMA in comparison to children diagnosed after the implementation of NBS. This lack of available information may have led participants to seek information and support from other sources, such as other parents in support groups. These participants' children were also diagnosed at a period when the diagnosis was sometimes given too late for some treatment options or when no treatment options existed. In these stressful situations, participants may have been more eager to seek support in comparison to those participants who underwent NBS. Participants with children diagnosed prior to NBS had more robust discussions surrounding support groups as well as the strength and tenacity of the SMA community. While participants whose children were diagnosed via NBS did discuss the

importance of receiving support, this was less of a focus for these families despite reporting significant psychosocial distress associated with their child's diagnosis. The present study has uncovered the possibility of a previously unaddressed need to provide resources for support groups and organizations to families with SMA at the time of diagnosis. Additionally, the children of participants that were diagnosed symptomatically are much older than those diagnosed via NBS in this study, and so there would have been increased time to become involved in both support groups and advocacy work. Participants with children diagnosed prior to NBS had more robust discussions related to concerns about accessibility and the manifestation of advocacy in numerous unique ways. Some participants were heavily involved in having SMA added to the NBS panel in Pennsylvania as well. While these unique advocacy roles did not disappear with the implementation of NBS for SMA, the participants in this study who had children diagnosed via NBS did not encounter advocacy surrounding a lengthy diagnostic odyssey. Additionally, this group of participants all have very young children. Much of this need for advocacy may not arise until the child has aged to the point where accessibility issues arise, and it is possible for some of these participants that physical limitations may never develop given the implementation of early treatment, though much remains unknown given how recently SMA treatments were developed.

Minimal research has been conducted to describe the impact of support from family, friends, and the community on the psychological well-being of parents and caregivers of patients with SMA. However, there is research available on the role of genetic counselors in providing support. Genetic counselors can adopt unique roles in newborn screening that include providing psychosocial support at the time of diagnosis and offering resources to guide families to both appropriate information and trusted support groups. Marcus et al. (2019) reports the role of genetic counselors in the public health sector is vast and can include developing educational resources,

consulting newly diagnosed families on the behalf of their primary care provider, and providing psychosocial support throughout the diagnosis. Additionally, there are many studies which have focused on the value of support groups for parents. Jackson et al. (2018) focused their research on the perspective of parents with children who have severe intellectual and/or developmental disabilities. They found that positive components of support groups included the value of having a shared experience with others in similar situations, an opportunity to help others and give back to the community, feelings of positivity following each meeting, building connections with other families, and using this as an opportunity to act. The researchers also inquired about reasons families may choose not to join a support group, including difficulty in finding others with similar experiences in the context of rare diagnoses, feeling that support groups do not make a difference, frequency of comparing their child's experience to that of others, experiencing negative emotions, and having support elsewhere. These experiences echo those of families with SMA. While most parents feel that support groups are beneficial, there are circumstances in which seeking support from other sources may be more helpful. Given the prevalence of positive experiences with support groups in the rare disease community, it is important that families are given resources delineating these sources of support to best improve psychological concerns.

Little research has focused on the implications and importance of advocacy within the SMA community. Most available studies focus on the efforts of SMA advocacy groups in helping to develop best practice guidelines or development of disease registries. However, there does exist research on the various roles of rare disease advocacy groups in general. Patterson et al. (2023) discovered that the major priorities for these organizations are to support rare disease research, provide information to families and healthcare providers, raise awareness, provide social support to affected families, provide services to families, and advocate to government organizations.

Halley et al. (2023) focused on disparities associated with rare diseases and ways that stakeholders can advance equity; specifically, these researchers felt that organizations should provide resources and strategies for families to engage in self-advocacy because this can help to address challenges, improve patient outcomes, and increase awareness within the medical community. The available research does not focus on patient attitudes and outcomes associated with becoming involved with advocacy, and so the present study provides further detail to better understand the psychological impact of advocacy work for families with SMA.

2.4.4 Processing Change: Evolving Expectations for a Child's Future

For several participants, it was important to recognize that SMA was at one time viewed as severe and significantly impactful on their child's future and quality of life. With the implementation of various treatment modalities and early diagnosis via NBS, the landscape has changed significantly, and many families no longer consider SMA severely life-limiting. With this recognition came the additional knowledge that children with SMA are unique and are not bound by their diagnosis, having their own unique behaviors and having no limitations to the milestones they are able to reach. While it was difficult for participants to remain positive, they recognized the positive progression of SMA treatment and experienced more days full of happiness compared to days with fear. As a result, participants recommended that other parents who have a child with a rare condition try to remain calm after receiving a diagnosis. These feelings are addressed most often by participants with children diagnosed symptomatically prior to the approval to Zolgensma. Treatment has shifted the landscape of SMA, and the positivity displayed by parents when discussing treatments helped to highlight this shifting landscape.

While evidence of this theme was found in interviews with both groups of participants, it was found more frequently with participants whose children were diagnosed symptomatically especially as it related to thoughts on treatment. It is possible that this group had either been diagnosed during a period where there were less treatment options available, or they had closer connections with individuals whose children were diagnosed before Spinraza received FDA approval. These participants displayed more positivity and hope following the shock of the initial diagnosis, increased awareness of how the landscape of SMA has changed more positively from a previously bleak diagnosis, and emphasized the importance of obtaining treatment as quickly as possible. They also had more commentary on Spinraza considering the age of their affected children. Because these participants experienced their child's diagnosis at a time where the prognosis was less positive, they were able to describe evolved expectations for their affected child. Participants whose children were diagnosed via NBS, on the other hand, displayed more recognition that their children are not limited by their prognosis and commented further on the utility of having neuromuscular specialists assist them in making treatment decisions. Consequently, these participants did not discuss evolving expectations as frequently as their children were diagnosed at a point early enough to begin treatment prior to symptom onset and at a time when there are multiple treatment options available. Therefore, participants whose children were diagnosed via NBS did not receive the SMA diagnosis during a time when the outlook was more dismal for certain types of SMA.

Prior research has focused on the perspectives of neuromuscular specialists and their perspectives on the evolving list of available treatments for SMA. It was discovered that parents and caregivers benefit from additional counseling and time to prepare for engaging in treatment decisions due to the sheer number of factors involved in decision-making with these various

treatment modalities (Ramos-Platt et al. 2022). These factors include early initiation of treatment, route of administration, manifestation of symptoms, whether anesthesia is required, long-term data availability, and anecdotal evidence. Zolgensma, one of the available treatments, is only administered once whereas Evrysdi is administered orally. These treatments are evolving in ways which can improve quality of life for participants. Mueller (2022) coined the term "prognostic imagination" defined as a method in allowing families to envision their lives given a diagnosis and is subject to change with evolving information on symptomatic management, treatment options, and further research. It is critical that healthcare providers create a space for open communication about these evolving expectations to help families better understand their children's condition and cope with potential stressors in a healthier fashion.

2.4.5 Feeling Overwhelmed: Initial Parental Experiences Following Their Child's Diagnosis

Participants highlighted the severity and impact of feeling overwhelmed in impairing coping strategies and the ability to care for their children. Mental noise may have been a component of this overwhelming feeling. As described by mental noise theory, individuals begin experiencing significant levels of emotional and/or mental agitation which impacts their ability to process vital information, especially once this information carries significant risk to an individual or a loved one (Covello 2022). This makes it difficult to comprehend information, leading to information blending and diminished information retention, feelings of being overwhelmed, feeling like the world has stopped, and the lack of time and ability to undergo an in-depth decision-making process. Both parents with children diagnosed by NBS and those diagnosed symptomatically experienced this but in different ways; it appeared that parents of children

diagnosed via NBS had more difficulty in grappling with being overwhelmed and with mental noise.

This theme was most likely discussed more frequently with participants whose children were diagnosed by NBS because the diagnosis was provided right after the baby was born and asymptomatic. The other participants received their child's diagnosis after noticing initial symptoms and working diligently to advocate for their child's healthcare needs. Receiving such an unexpected diagnosis may have led to feelings of being overwhelmed. Additionally, participants whose children's diagnosis was identified by NBS commented more frequently on how the diagnostic process can be viewed as fast-paced and that it is critical to trust the experts with their child's care. Participants whose children were diagnosed symptomatically, in contrast, had a lengthy time towards diagnosis and developed subsequent distrust in many healthcare providers following the diagnostic odyssey. Kariyawasam et al. (2021) found that participants who received a positive SMA NBS result experienced negative emotions including anxiety, anger, sadness, and confusion, and these types of emotions may contribute to feeling overwhelmed following a NBS diagnosis.

This identified theme is consistent with previous research on both parents' and patients' experiences with SMA. Qian et al. (2015) found that participants focused on limited social activities due to the overwhelming nature of SMA. Other studies have focused similarly on parent experiences following cystic fibrosis (CF) diagnoses via NBS. Jessup et al. (2015) found that families experienced impaired receptivity followed by the diagnosis which involved feelings of being overwhelmed, fear, disbelief, and shock. These researchers suggested that important information be repeated with assessment of parents' well-being and approaching sense of being overwhelmed. The current project explored overwhelming aspects of the diagnostic journey in

SMA and found that feelings of being overwhelmed extended into other areas of care, including treatment decisions. It is critical that healthcare providers actively listen to parents with newly diagnosed children to help mediate these overwhelming feelings.

2.4.6 Experiencing Loss: Coping with Guild and the Loss of Expectations for a Healthy Child

Participants consistently discussed coping with the loss of expectations for having a healthy child by describing those previous expectations and the plans that had been made for their child's future. Having those future expectations taken away and changed entirely appeared to have an impact on the emotional well-being of the participants and affected their coping processes. Some participants moved beyond the initial grief associated with this loss, and spoke about how this loss continued to grow through time. As a child ages, physical symptoms may become more noticeable and highlight a difference visually noticeable to others. This lends itself to a second stage of the loss of expectations manifested by the adoption of new equipment to improve mobility and questions being asked by others outside of the child's immediate family.

This theme was found more frequently in discussions with those participants whose children were diagnosed before SMA was added to the NBS panel in Pennsylvania and may reflect that participants whose children were diagnosed via NBS had less postnatal time with their children before the diagnosis was made. These participants learned within one week of their child's birth that this diagnosis exists, therefore having less time to form expectations in comparison to participants who had several months or years with a healthy child. Additionally, part of this theme involves visual acknowledgment of physical limitations. Children diagnosed via NBS were much younger than those who were diagnosed symptomatically, and so their families had less

opportunity to see these physical symptoms manifest. Regardless of their age, these children also received treatment at a younger age and may never manifest significant symptoms.

Previous studies have identified similar themes when interviewing both parents and patients with SMA. von Gontard et al. (2012) acknowledged the difficulty for families in coping with a diagnosis of SMA, discovering that a primary source of stress results from the child's physical inabilities and characteristics. Loss of expectations is a type of anticipatory grief by Lindemann (1944) in the context of separation during war but has since evolved to focus on the grief experienced by parents of terminally or chronically ill children. Regardless of the age of onset of an inherited condition, previous studies have found that families will alter rules around social interaction and beliefs following a loss of expectations (Rolland 1990). The current study found similar results, with some participants commenting on the importance of preparing how to interact with others and preparing for the shift in interaction as a child's physical limitations become more evident. Rolland (1990) recommends that families dealing with inherited conditions can maximize coping by acknowledging the possibility that loss may occur, maintaining positivity and hope, and encouraging adaptability as time progresses. There is potential for healthcare providers to give support to families who are struggling to deal with this anticipatory loss and move past any potential blame-guilt cycles.

2.4.7 Study Limitations

2.4.7.1 Data Saturation

One limitation of this study was that this study did not achieve appropriate data saturation. Novel codes emerged during each interview, which made the creation of themes challenging. Further research and refinement of themes is required by conducting studies with more

participants. This will help ensure further data saturation once all themes related to the psychosocial impact of diagnosis, experiences with the healthcare system, opinions on NBS, gaps in support, and recommendations for healthcare providers to improve outcomes for families have been appropriately identified and developed. Data saturation is a critical component of qualitative research to ensure that researchers are no longer identifying additional information through further interviews that would alter the conceptual framework developed through the analysis (Guest et al. 2020). It is important to note theoretical sample size sufficiency as well. Vasileuiou et al. (2018) identified that data saturation is difficult to achieve in part due to the presence of multiple definitions as well as how difficult it can be to achieve. These researchers recommend that studies instead identify sample size sufficiency with a predetermined consideration of the appropriate number of interviews and ample justification for the sample size.

Seven participants were interviewed for this study. While the sample size is small with seven participants in total, there existed sufficient variation in the children's ages (ranging from 6 months to 14 years). Four participants had children diagnosed prior to the implementation of NBS for SMA while three participants had children diagnosed following the adoption of NBS. One participant whose child was diagnosed via NBS only became a caregiver for their child within the last year and lacked information related to the initial diagnosis. This may have had some impact on the differences noted between the two groups.

2.4.7.2 Convenience Sampling

Participants in this study were selected via convenience sampling. Convenience sampling does not hinge upon probability and involves subject enrollment due to their availability and accessibility (Elfil & Negida 2017). All study participants were recruited from patient lists at the Muscular Dystrophy Clinic within the Children's Hospital of Pittsburgh. The clinical team initially

contacted families seen recently who have children diagnosed with SMA. Families not participating in the Muscular Dystrophy Clinic were not contacted. Not all families choose to regularly follow up with the Muscular Dystrophy Clinic either due to mild symptom progression, poor rapport built with the team, or the child may be deceased. Additionally, children with SMA exist internationally. Working with various support organizations such as Cure SMA may have led to participation from various regions and provided more robust data as well as improved data saturation via an increased number of interviews.

2.4.8 Future Research

Results of this study highlighted recommendations for communicating the diagnosis and management based on firsthand experiences of the diagnostic odyssey, psychological impact of having a child with SMA through the navigation of uncertainty, the importance of seeking support and becoming advocates, evolution of expectations, and feelings of being overwhelmed. Additionally, participants focused on coping with the loss of expectations for a healthy child. However, additional research should be performed to gather information from more families to reach data saturation and to identify, develop, and refine themes. A greater number of participants could be contacted through popular support organizations such as Cure SMA to reach families worldwide. This study was also time-constrained, and so having additional time to complete interviews could have led to greater participation among recruited subjects.

Another future direction identified through participant interviews is the experiences of foster and adoptive parents. One participant recently became a foster parent with plans to adopt a child with SMA. This participant identified unmet needs from the healthcare team, having received minimal information about the diagnosis aside from the name and lacking relevant medical history

to explain how the child was diagnosed. This participant demonstrated resiliency and had many more questions and needs compared to other participants. Future studies could focus on the experiences of foster and adoptive parents of those children with SMA and other rare genetic conditions to best identify what healthcare providers can do to better ease this transition. There also exists an opportunity to engage with individuals outside of the nuclear family. During participant interviews, discussions centered on informing other family members such as grandparents and aunts and uncles, about the diagnosis. These family members serve not only as critical support systems to parents and caregivers, but also remain a major part of affected individuals' lives. It is critical to better understand these individuals' perspectives and address their needs as well.

Additional studies could discuss specific recommendations for not only what pieces of information parents and caregivers found to be beneficial, but also what information led to more harm. Throughout participant interviews, families highlighted specific recommendations for information they received that was helpful following their child's diagnosis. Some participants discussed that this information was helpful overall, but at times proved to be overwhelming. Future interviews could ask more detailed questions about what information families received at the time of diagnosis and specifically what may have proved to be harmful or unhelpful. This would be beneficial in helping to tailor written information to families' needs.

Further research should focus on the mental noise component of the diagnosis as this may be a significant barrier in allowing parents and caregivers to process their child's diagnosis appropriately. According to Covello (2022), moments of stress can lead to difficulty hearing and comprehending information and may lead families to focus only on what they hear first. This mental noise can reduce individuals' ability to process information by approximately 80%.

Participants in this project were not explicitly asked about their experiences with mental noise. Future research could explore this concept more to determine the impact of mental noise in processing NBS results.

Finally, future studies may be conducted to better understand and bridge the gap between the SMA community and the healthcare team. One participant in the study commented on how this is a large need yet to be filled and would allow for patients to receive the best possible care. Additional research could involve qualitative research via either interviews or focus groups with healthcare providers in the neuromuscular space to understand their perspectives on SMA support groups and previously developed rapport. It would also be beneficial to gain perspectives from leaders of SMA support organizations to determine their perspectives in collaborating with neuromuscular specialists to provide the best care and support to affected individuals and their families.

2.5 Conclusion

One of the specific aims of this study was to examine the psychosocial impact on parents of having a child diagnosed with SMA, experiences with the healthcare system, and opinions on NBS. Participants provided detailed accounts regarding the diagnostic odyssey and experiences with the healthcare system, describing the journey as often overwhelming and time-consuming. Despite the newfound relief associated with the development of various treatments for SMA, these psychosocial concerns remain for families regardless of whether their child was diagnosed symptomatically or with NBS. This study was data-driven; while one of the primary objectives of the study was to examine perceptions and differences pertaining to NBS, this was not a large part

of the participants' journeys. Participants with children diagnosed via NBS focused less on the technology itself and more on the way the diagnosis was communicated, similarly to families diagnosed prior to the advent of NBS. Those participants whose children were diagnosed before SMA was added to the NBS panel appeared to have a more positive perspective of this technology which could be in part due to an increased amount of information known about NBS in this group. Another specific aim of this study was to identify gaps in support and ways that healthcare providers can help improve outcomes for families. Participants provided recommendations for physicians and other members of the healthcare team for both diagnosing and caring for a child with SMA, focusing on ways to address information-seeking behaviors, aspects of providers' demeanor, importance of working with the SMA community, and even commenting on which type of physician should be providing the diagnosis. These recommendations were based on both negative and positive experiences shared by the participants and included the following: providing anticipatory guidance to families about what to expect throughout SMA's prognosis, making a preliminary plan with families about next steps within the diagnosis, immediately discussing the availability of treatment, scheduling follow-up appointments following the initial results disclosure, disclosing the diagnosis in a compassionate and respectful manner, collaborating with the SMA community, maintaining recognition that the diagnosis can be overwhelming, and providing support to families at the time of diagnosis by maintaining an open line of communication. The overarching goal of this study was to better understand the familial impact of receiving a diagnosis of SMA and how these psychosocial difficulties might compare depending on whether the child was diagnosed before or after the implementation of NBS for the condition to better determine what changes healthcare providers could implement to improve the way in which the diagnosis is given to newly diagnosed families. Given the negative psychological impact

described by affected families, it is critical that genetic counselors take a more active role in the diagnosis as it pertains to conditions on the NBS panel. Genetic counselors are in a unique position to provide significant psychosocial support and accurate information about SMA and other genetic conditions in a way which may positively impact families. Additionally, genetic counselors may have the opportunity to work further with primary care providers and pediatricians to ensure that families are receiving accurate and helpful information at multiple timepoints. Each participant was asked about their experiences with genetic counselors and while some noted the utility of the knowledge provided, most participants did not consider genetic counselors to be a key player in the diagnostic journey. This absence may have worsened outcomes following the initial diagnosis for families with negative experiences. Further research may be conducted to better understand these differences on a larger scale outside of the Western Pennsylvania region using these methods as a preliminary framework to guide further discussion and discover additional ways to reduce psychosocial distress for parents and caregivers.

3.0 Research Significance to Genetic Counseling and Public Health

The primary goal of this study was to interview parents and caregivers of children diagnosed with SMA and analyze audio transcripts to assess differences in experiences between those receiving a diagnosis prior to and following the implementation of NBS for SMA. Thematic analysis of the interviews highlighted which factors surrounding a diagnosis of SMA have been mitigated with the advent of NBS and which could be improved upon, increased understanding parents' and caregivers' treatment decisions, and the utility of resources currently being offered to families of affected individuals.

Genetic counselors have the opportunity to be one of the first healthcare providers to deliver an SMA diagnosis to families. Firsthand perspectives of the diagnostic experience will allow genetic counselors working in neuromuscular settings to identify which processes could be improved to better assist families in terms of psychosocial impact as well as information gathering. The results of this study may inform how genetic counselors can deliver this difficult news particularly in cases of long-term follow-up. Results from this study highlighted parents' desire to be allowed time to process the news, and so allowing the opportunity for additional follow-up after receiving the diagnosis may allow for better understanding and the opportunity to enhance trust and rapport. Genetic counselors are often involved in the development of condition-related brochures and resources, and the data gathered from this study may help guide which information may be most beneficial to families. The absence of genetic counselors while disclosing a diagnosis of NBS-related conditions may lead to worsened psychosocial outcomes. The potential for genetic counselors to collaborate with providers disclosing positive NBS results may be beneficial in ameliorating many negative outcomes that can be associated with difficult diagnoses.

This project has relevance to public health. One of the ten essential public health services described by the Centers for Disease Control and Prevention (CDC) is to diagnose and investigate health problems and health hazards in the community (CDC 2021). Newborn screening is one of the most successful projects in the area of public health genetics and involves the diagnosis of genetic conditions that, while individually rare, impact the public on a much larger scale when considered in combination. Participants in this study provided recommendations for what healthcare providers could avoid doing when providing a diagnosis. Genetic counselors have a unique opportunity to play a key role in newborn screening by aiding in the diagnosis and providing both the time and the information requested by families in a compassionate manner.

Another key tenet of public health is to inform, educate, and empower individuals about health issues (CDC 2021). This service requires equitable access to both care and health resources. The participants in this study were asked about SMA resources they were provided with at the time of diagnosis, and they expressed a desire to learn more about the genetic basis of SMA both at the time of diagnosis and even in the present day, years after the initial diagnosis. Genetic counselors and other healthcare professionals can be instrumental in improving the resources and information that families and caregivers receive when their child is diagnosed with SMA, combining helpful documents and brochures provided by support organizations such as Cure SMA and the pharmaceutical companies with available treatments. This study supports the importance of informing, educating, and empowering the public on relevant health concerns. Participants expressed a need for this information and discussed the importance of tailoring this information for families based upon not only their own health literacy, but the specific subtype of SMA seen in the affected child as well. Personalization of these resources was discussed as a recommendation for pediatricians and PCPs in providing the diagnosis on multiple occasions, both in those families

diagnosed before and after the implementation of NBS for SMA. This personalization would be beneficial not only for parents and caregivers of affected individuals, but could also be helpful in informing extended family members about the diagnosis when these individuals were not in the room at the initial visit to discuss the diagnosis. Additional studies could focus specifically on improving the health literacy and accessibility of these resources and designing methods to combine helpful information from a multitude of such resources.

4.0 Public Health Essay: Assessing the Readability of Fact Sheets Distributed by Pharmaceutical Companies to Families and Caregivers Impacted by SMA

4.1 Background

SMA is a genetic condition that involves progressive weakness and atrophy of the proximal skeletal muscles. There are five types of SMA currently delineated which vary in both severity and age of onset: types 0, I, II, III, and IV. Three treatment modalities have been approved by the FDA for SMA (Spinraza, Zolgensma, and Evrysdi) with each therapy harboring a unique mechanism of action. Carrier screening is offered routinely for SMA, contributing to the perception that SMA is a significant public health concern. In fact, the American College of Obstetricians and Gynecologists (2017) currently recommends that all patients considering carrying a pregnancy for family planning purposes be offered carrier screening for SMA due to its high incidence in multiple ethnic groups. Additionally, SMA is on the newborn screening panel in 48 states (Cure SMA 2022). Previous literature has focused on eliciting the opinion of parents who have a child with SMA in adding the condition to the Recommended Uniform Screening Panel (RUSP). While most parents have been found to support NBS for SMA, most parents preferred carrier screening and/or prenatal testing to allow for earlier preparation (Kariyawasam et al. 2021). However, there had been little research performed that examines the diagnostic odyssey for parents. Research has found negative responses to NBS implementation include psychological distress with positive screening results, insufficient information provided at the time of diagnosis, delayed access to specialist care, and barriers to comprehension (Kariyawasam et al.

2021). Despite these known concerns, there has been little research focused on addressing them or understanding them further.

Given the severe prognosis of SMA if left untreated, families are often told to decide on a treatment type quickly following their child's diagnosis. There are three treatment options currently available for SMA: Spinraza, Zolgensma, and Evrysdi. Because of the importance of timing in treatment initiation, the first information that families are presented with are typically brochures and fact sheets related to each of these three treatments. As barriers to comprehension has been noted as a negative perspective of NBS for SMA, these brochures could either help educate families about the condition or hinder their understanding (Kariyawasam et al. 2021). The American Medical Association (AMA) recommends that all health education materials should be available at or below the sixth-grade reading level, while the National Institutes of Health (NIH) recommends that health education materials be provided at an eighth-grade reading level (Rooney et al. 2021). Brochures for these three treatment modalities can subsequently be analyzed to see if they are beneficial or harmful for parents in better understanding their child's healthcare needs and treatment options using the reading level as a point of comparison.

The aim of this project is to examine existing fact sheets and brochures created by pharmaceutical companies with FDA approved treatments for SMA for both readability and accessibility to see where improvements can be made. Results from this project can inform future efforts to evaluate resources for readability and improve accessibility for families.

4.1.1 Research Question

Research Question 1: Which pharmaceutical company with FDA-approved treatment for SMA provides users with the most accessible brochures in terms of readability measures?

4.2 Available SMA Treatments

4.2.1 Spinraza

Nusinersen, marketed as Spinraza, was developed by Biogen. It is an antisense oligonucleotide that binds to a repressor within exon 7 of *SMN2* to enhance exon 7 inclusion, thereby leading to increased production of SMN protein (Li 2020). Spinraza is the first SMA treatment modality to be approved by the FDA, receiving approval in 2016. It is delivered to patients via intrathecal (IT) infusion to maximize its potential for crossing the blood-brain barrier (Li 2020). Deng et al. (2022) discovered that approximately 5.6% of parents with children with SMA diagnosed via NBS chose Spinraza as their child's therapy. This decision was made after the child was found to be ineligible for Zolgensma following initial screening labs (Deng et al. 2022).

4.2.2 Zolgensma

Onasemnogene abeparvovec-xioi, marketed as Zolgensma, was developed by Novartis. It is an AAV9-based gene therapy that works via a single intravenous injection (Mendell et al. 2017). Zolgensma was approved by the FDA in 2019. Its mechanism of action allows the gene therapy to cross the blood-brain barrier and target neurons throughout the central nervous system and spinal cord, allowing for both sustained and quick SMN expression (Mendell et al. 2017). Deng et al. (2022) found that approximately 72.2% of parents of children with SMA diagnosed via NBS chose Zolgensma for their child's treatment due to the low frequency of administration, avoidance of intrathecal infusion, and early data on symptomatic improvement.

4.2.3 Evrysdi

Risdiplam, marketed as Evrysdi, was developed by PTC Therapeutics. It is an RNA splicing modifier that is directed towards *SMN2* and is administered orally (Dhillon 2020). Evrysdi was approved by the FDA in 2020. Its mechanism of action allows the small molecule to improve the ability of *SMN2* to produce functional SMN protein, thereby bypassing pathogenic variants in *SMN1* (Dhillon 2020). Deng et al. (2022) found that 11.1% of parents of children with SMA diagnosed via NBS chose Evrysdi for their child's treatment.

4.2.4 Use of Multiple Treatments

Some patients with SMA use multiple modes of treatment to achieve higher efficacy. Zolgensma is currently only administered once whereas Spinraza is administered through multiple loading doses and Evrysdi is administered daily. Additionally, each of these therapies maintains a different mechanism of action, which may help to increase uptake of SMN protein (Cure SMA 2020). Mirea et al. (2021) evaluated data on affected children treated first with Spinraza and then with Zolgensma and compared this group to children who received only Spinraza. These researchers discovered that combination therapy improved multiple symptoms, including respiratory management. Additionally, Oechsel & Cartwright (2021) investigated data on affected children treated first with Zolgensma and then with Evrysdi. These patients each improved following initiation of Zolgensma, but started Evrysdi after improvement plateaued. This study found that SMA symptoms improved one month after starting Evrysdi. The most effective use of combination therapy has not yet been identified (Oeschsel & Cartwright 2021). However, the available research highlights significant potential for efficiency in managing symptoms of SMA.

4.3 Methods

The three available SMA therapies (Spinraza, Zolgensma, and Evrysdi) are supplied by pharmaceutical companies such as Genentech and Novartis. Each company has created its own set of fact sheets and brochures associated with the specific treatment modality. These brochures were obtained and downloaded in PDF form from the patient-centered websites developed by each company. The brochures were read to assess layout, illustrations, messaging, information, and cultural appropriateness. Additionally, the text from these brochures was then uploaded to Readable, an online database which assesses various readability measures. This study focused specifically on the Flesch-Kincaid grade level, Gunning Fog index, SMOG index, spelling issues, grammar issues, percentage of sentences with over 30 syllables, percentage of words with over 12 letters, adverbs, passive voice percentage, and the number of words per sentences. The Flesch-Kincaid grade level is a literacy metric that measures the reading level of a body of text with its corresponding output being equivalent to a grade level within the United States education system. The Gunning Fog index is another readability estimate that incorporates measures such as number of sentences and word lengths, whereas the SMOG Index provides a readability score that considers the number of years of education a reader would need to understand a text document. According to Readable, brochures should aim to have zero spelling errors or grammar issues. Additionally, less than 6% of sentences should have over 30 syllables, less than 3% of words should have more than 12 letters, less than 4% of the documents should contain adverbs, less than 3% of documents should be written in passive voice.

There are three primary fact sheets distributed by Spinraza which are grouped into the population of individuals treated: infants, children, and adults. These fact sheets vary in length from 30 to 32 pages. Zolgensma, on the other hand, offers patients eight brochures ranging from

2 to 30 pages in length. Zolgensma's brochures are grouped based on patient point of interaction. These brochures include information on SMA, prenatal diagnosis, information for caregivers, treatment descriptions, and long-term care with the length varying depending on what information is being covered. Evrysdi offers families four fact sheets which range from 9 to 47 pages. Overall, these brochures are divided based on logistical aspects of treatment. These fact sheets include information about treatment itself, insurance navigation and financial options, and instructions for use. Regardless of the treatment mode or specific brochure, each of the evaluated brochures are targeted for parents and caregivers of affected patients.

Each document from the different pharmaceutical companies was analyzed separately with the readability metrics from each brochure combined at the end to create an overall average for all brochures corresponding to each treatment. For example, each of the three brochures provided for Spinraza were analyzed individually through Readable to assess different readability measures. Metrics from each of the three brochures were then combined to produce an average for all of the brochures. This allowed for more direct comparison between the three overarching companies by providing a single score to compare across the companies.

Qualitative information regarding these brochures was assessed using the Modified Instrument for Assessing User-Friendliness developed by Arnold et al. (2006). This instrument evaluates five specific areas: layout, illustrations, messaging, information, and cultural appropriateness. Cultural appropriateness involves avoidance of harmful stereotypes and inclusivity in terms of available languages.

4.4 Results

4.4.1 Comparison Across Brochures

Figure 1 shows the comparison between the Flesch-Kincaid grade level, sentences with over 30 syllables, and words per sentence in each of the fact sheets provided for Spinraza designed for three different age groups. Each brochure is similar, though the brochure developed for infants receiving treatment has a lower Flesch-Kincaid grade level and the lowest number of sentences with over 30 syllables. The number of words per sentence is highest in the brochure developed for adults receiving treatment.

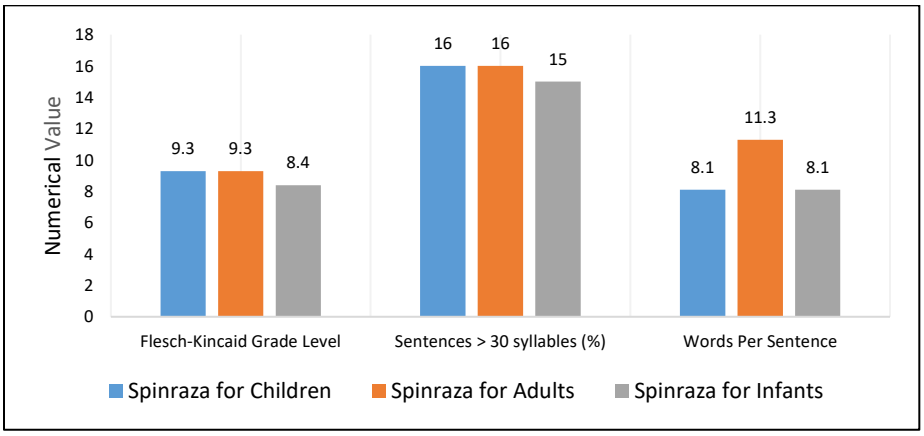

Figure 1. Comparison of Readability Statistics in Spinraza Resources

Figure 2 focuses on the comparison of readability statistics in the brochures and fact sheets distributed for Zolgensma. The statistics are similar between all three resources, though the brochure focused on prenatal diagnoses has a larger percentage of sentences over 30 syllables in length.

Figure 3 compares readability statistics in the fact sheets provided for Evyrsdi, the newest therapy developed for SMA. Like Zolgensma, the brochures are similar to one another. However, the resource focused on providing instructions for use of the medication has the highest percentage of sentences over 30 syllables in length (30%).

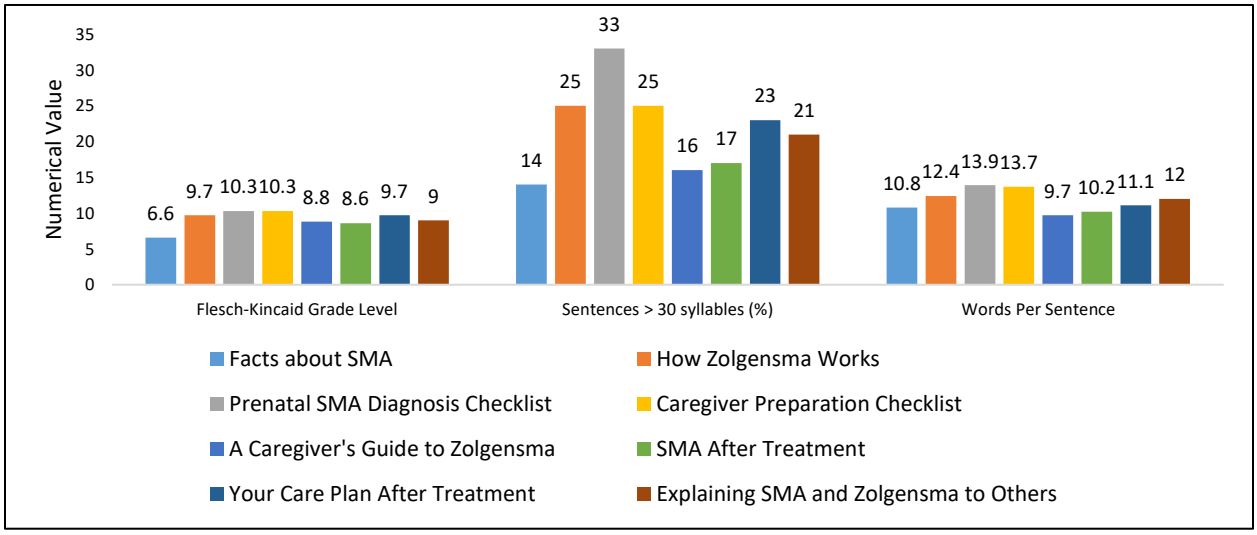

Figure 2. Comparison of Readability Statistics in Zolgensma Resources

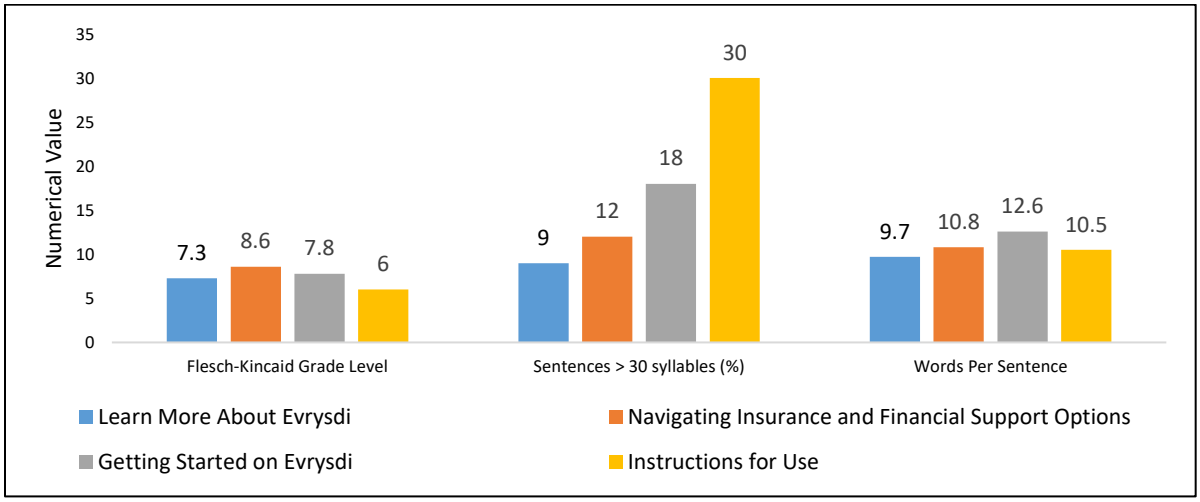

Figure 3. Comparison of Readability Statistics in Evrysdi Resources

4.4.2 Comparison Across Pharmaceutical Companies

Figures 4 and 5 depict the comparison of various readability measures obtained from the brochures created by the pharmaceutical companies associated with Spinraza, Zolgensma, and Evrysdi. Cliches and the percentage of words larger than 12 letters were omitted from the figure because there were zero cliches or large words in any of the documents provided. Spinraza brochures had the highest percentage of grammatical issues, and the lowest percentage of long sentences, adverbs, and number of words per sentence. Zolgensma's fact sheets had the highest Flesch-Kincaid grade level as well as Gunning Fog and SMOG indices, the lowest percentage of spelling issues, the highest percentage of long sentences and passive voice count, and the highest number of words per sentence. Brochures distributed for Evyrsdi had the lowest Flesch-Kincaid grade level along with Gunning Fog and SMOG indices, the highest percentage of spelling issues and adverb use, the lowest percentage of grammatical issues, and the lowest instances of passive voice count.

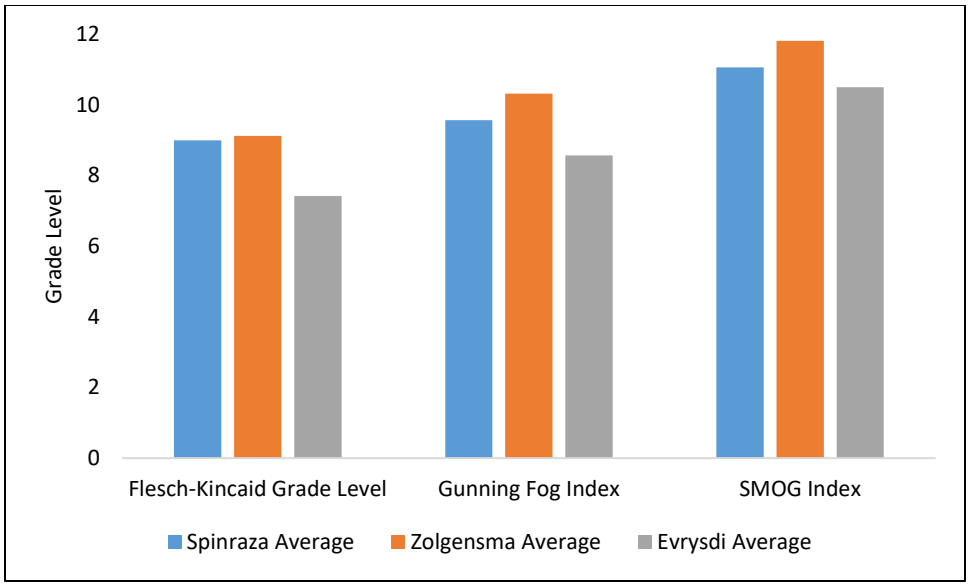

Figure 4. Comparing Readability Measures Across SMA Therapy Brochures

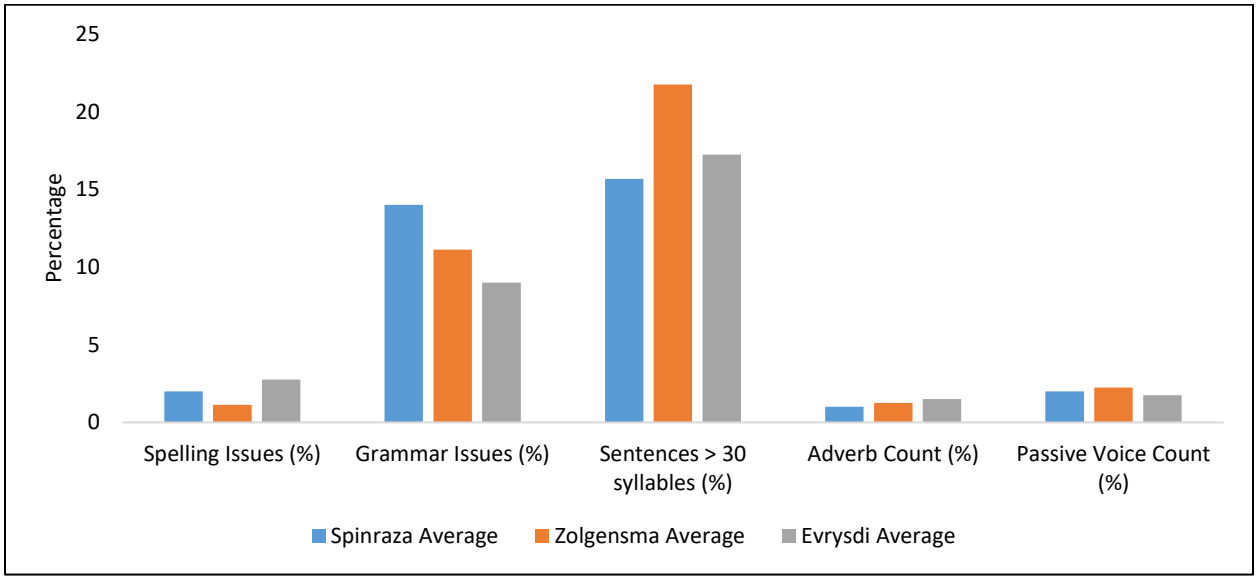

Figure 5. Comparing Spelling and Grammatical Errors Impacting Readability Among SMA Therapy Brochures

4.4.3 Qualitative Assessment

Arnold's Modified Instrument for Assessing User-Friendliness (2006) evaluates five specific areas: layout, illustrations, messaging, information, and cultural appropriateness. Table 3 summarizes qualitative findings from each of the three treatment types. The brochures provided for Spinraza have a clean layout which allows for easier readability with font sizes larger than 12 points, avoidance of unnecessary specialty fonts, ample white space, and use of bullets and boxes. Some of the paragraphs are large with over six lines of text. All illustrations serve a clear purpose and can be easily understood. The messaging in these brochures is appropriate with short, explanatory headings and action messages presented early in the text. However, it would often require reading multiple paragraphs to receive the bulk of information. The information is manageable in terms of short sentences with some unknown phrases being defined. Outside of this instrument, it is important to note that there is a table of contents at the beginning of each brochure, but that this is not easily navigable online, making these large booklets more difficult to search through. These brochures are also not currently available in another language.

Each fact sheet provided for Zolgensma has a clean layout. The font sizes are larger than 12 points and there are no specialty fonts or unnecessary italics incorporated. There is ample white space in these documents, but bullets and boxes are used more sparingly. Some paragraphs are large, with information spanning over nine lines in length at times. All the illustrations are helpful, but there does appear to be a lack of images in some of the brochures. For example, there are no images available on the "Caregiver Preparation Checklist" brochure. The messaging in these fact sheets were appropriate with short, explanatory headings often in the form of a question and action messages presented early and the most essential information being discussed early. The information is manageable with short sentences and complicated terms being consistently defined.

There is an interactive table of contents available for the larger documents that is simple to navigate. Each brochure is available in both English and Spanish.

Brochures presented for Evyrsdi are organized and clear with a layout that contributes to readability. The font sizes are larger than 12 points, and no specialty fonts or unnecessary capitalization is included. There is ample white space in these documents, and bullet points and boxes are used well. Some paragraphs span over five lines as well. Illustrations are plentiful with each image helping to clarify meaning within the text. The messaging in these brochures is clear, with short, explanatory headings and action messages presented early and often. The information itself is manageable, particularly when viewed online. Consumers can click on any green term in some of these documents and be redirected to a page in the document that defines the potentially unknown terms. There is additionally an interactive table of contents for most of the brochures. Of note, these fact sheets are only available in English.

The fact sheets provided for Spinraza, Zolgensma, and Evrysdi provide families and caregivers with similar levels of information, including information about the genetic cause of SMA, disease prognosis, how the treatment modality works (including the preparation and/or aftermath of the medication itself), clinical trials results, and safety data. Each treatment company also provides varying information about the support they offer families. Zolgensma is unique in that it provides families and caregivers with checklists to bring to their children's appointments to confirm dates and times of appointments and treatments to help maintain a sense of organization.

Table 3. Qualitative Assessment Based on Arnold's Modified Instrument for Assessing User-Friendliness

Treatment Type	Layout	Illustrations	Messaging	Information	Cultural Appropriateness
Spinraza	Font size larger than 12pt, no specialty fonts, ample white space, use of bullets and boxes, large paragraphs (>6 lines)	Serve clear purpose, easily understood	Explanatory headings, early action messages, requires reading multiple paragraphs to understand	Short sentences, unknown phrases are defined	Unavailable in languages other than English
Zolgensma	Font size larger than 12pt, no specialty fonts or italics, ample white space, bullets and boxes used sparingly, large paragraphs (>9 lines)	Helpful, some brochures have minimal images	Explanatory headings in the form of a question, early action messages, essential information discussed early	Short sentences, consistent definitions	Each brochure is available in both English and Spanish
Evrysdi	Font size larger than 12pt, no specialty fonts or unneeded capitalization, ample white space, use of bullets and boxes, large paragraphs (>5 lines)	Plentiful and meaningful	Explanatory headings, early action messages	Manageable with interactive glossary online	Unavailable in languages other than English

4.5 Discussion and Conclusions

Previous literature has shown that parents respond positively to the consideration of adding SMA and other genetic conditions to NBS panels. This support is not without caveats, including psychological distress associated with positive screening results, insufficient information provided at the time of diagnosis, limited access to specialists, and barriers to comprehension (Kariyawasam

et al. 2021). Despite these known barriers, there has been little research focused on addressing such concerns. Instead, most studies have examined families' opinions on implementation of the program itself as opposed to the diagnostic process and individual experiences. Consequently, one primary goal of this study was to evaluate the existing brochures distributed by the pharmaceutical companies providing SMA therapies. As the data in Figure 1 show, barriers to comprehension are a valid concern for families affected by SMA. The average Flesch-Kincaid grade level for brochures developed by Spinraza and Zolgensma are at the ninth-grade level whereas those for Evrysdi are at a seventh-grade reading level. The AMA recommends that all health-related educational materials should be provided below the sixth-grade reading level whereas the NIH recommends that these materials be provided below the eighth-grade level (Rooney et al. 2021). This is importance because in the United States, 36% of adults have limited health literacy, which is defined as reading below the eighth-grade level (Kutner et al. 2006). Given such a significant percentage, it is critical for reading materials to be below an eighth-grade reading level to ensure maximal comprehension. None of the brochures provided for any of the three treatment types follow AMA recommendations, while only those for Evrysdi follow NIH recommendations.

The three therapies available for SMA provide families and caregivers with information at comparable readability levels across multiple indices. As Figure 4 highlights, Evrysdi provides this information in the most accessible format in terms of Flesch-Kincaid grade level, Gunning Fog index, SMOG index, Flesch reading ease, and overall reach. The brochures created for Evrysdi also have the smallest percentage of grammar issues and passive voice count. However, only Zolgensma provides brochures in an additional language aside from English. While not quantifiable in comparison to those readability measures, this is a critical component in terms of accessibility. Sentell & Braun (2021) investigated low health literacy and limited English

proficiency (LEP) as important barriers to healthcare that often occur simultaneously. Ultimately, the researchers found that LEP leads to a greater risk of negative healthcare outcomes than low health literacy. As such, it is critical to provide health-related educational materials to families in multiple languages. Other studies have investigated whether providing such materials in languages other than English would improve patients' knowledge and health outcomes. Perera et al. (2011) found that Sri Lankan patients had significantly higher levels of understanding regarding their health when provided with a discharge summary in their native language. Providing health education materials for complex conditions will help reduce barriers to understanding for families whose first language is not English and therefore improve cultural sensitivity of these brochures.

Brochures were analyzed individually in Figures 1-3, comparing Flesch-Kincaid grade level, sentences over 30 syllables, and the number of words per sentence to examine for any potential skewing of results. There are more resources for Zolgensma than Spinraza or Evrysdi (eight brochures versus three or four). It was important to determine whether there was any specific brochure with a significantly better or worse readability measure that may have impacted the overall average scores. Figure 1 focuses primarily on Spinraza, highlighting that brochures designed for children and adult treatment are at a ninth-grade reading level whereas those for infants are at an eighth-grade reading level. Figure 2 focuses on Zolgensma, showing that brochures are as low as a sixth-grade reading level and as high as a tenth-grade reading level. The brochure with the lowest reading level is entitled "Facts About SMA". This brochure is four pages in length and provides families with information about the inheritance pattern, carrier frequency, disease prevalence, prognosis without treatment, symptoms, and illustrations explaining SMN protein levels and the five subtypes. The Flesch-Kincaid reading level is likely lower due to the focus on illustrations and having many complex terms defined. The brochures with the highest

reading level are the two checklists for prenatal diagnoses and caregiver preparation. These brochures do not define complex terms, with terms such as creatinine and systemic corticosteroid being used freely. There may be an assumption that prior to reading these checklists, the patient has already met with a specialist. However, patients can easily find this information available online. The complexity of these documents could create more confusion for families. Figure 3 shows the results for Evrysdi. The brochure focused on providing instructions for use is at a sixth-grade reading level whereas those involving navigation of insurance and financial support are at an eighth-grade reading level. Instructions for the medication could be the most important piece of information for families to understand to ensure that patients are being treated properly, and so this piece having the lowest grade level is unsurprising. The document focuses on instructions for use described storage of the medication and instructions for oral administration without any focus on genetics or the treatment's mechanism of action. Of note, however, this document has a significant percentage of sentences with more than 30 syllables compared to the other documents provided for Evrysdi. These sentences are quite lengthy, but are supported with helpful illustrations and bold text to highlight the most important information. Several sentences could be broken down into two or more sentences, however, and this change could decrease the Flesch-Kincaid reading level further.

There are several areas of improvement that exist in the fact sheets and brochures developed by the pharmaceutical companies providing treatments for SMA, including the lack of accessibility for individuals whose first language is not English. Only Zolgensma offers their fact sheets in another language (Spanish). The European Medicines Agency (2022) offers product information for Spinraza, Zolgensma, and Evrysdi in all official European Union languages, including Spanish and French, for a total of 24 languages. However, these are 48-page documents

with no images and significant text, contributing to further inaccessibility. Other potential improvements include decreasing the current Flesch-Kincaid grade level along with other indices. Spinraza and Zolgensma both provide brochures that are, on average, at a reading level above a threshold that is accessible to most individuals while resources for Evrysdi may still be difficult to understand for many individuals based on AMA Guidelines (Rooney et al. 2021). This could be mediated by decreasing sentence and paragraph length while using words and phrases that are less complex. For example, the Caregiver Preparation Checklist provided by the pharmaceutical company distributing Zolgensma has the highest Flesch-Kincaid grade level in part due to sentences such as the following: *Caregivers and close contacts of patients should follow infection prevention practices (e.g., hand hygiene, coughing/sneezing etiquette, limiting potential contacts)* (Novartis Gene Therapies, Inc. 2023). This sentence could be rephrased to read more similarly to: *Anyone who comes into regular contact with patients receiving Zolgensma should wash their hands, cover their mouths when coughing or sneezing, and limit the amount of other people they meet with.*

Various institutions including the AMA, NIH, and Centers for Disease Control and Prevention (CDC) provide recommendations for creating and revising written health materials. These guidelines focus on general content of the materials, text construction, and visual presentation (Williams et al. 2016). In terms of general content, it is recommended that these brochures focus on no more than three concepts, limit information to what is most important, use words that do not require medical training, ensuring content is age- and culturally appropriate, and noting action steps at both the beginning and end of the document. Recommendations for text construction include the following: maintaining information between a sixth- and eighth-grade reading level, using one- or two-syllable words, short paragraphs, active voice, and a clear topic

sentence at the beginning of each paragraph, providing examples and patient stories, using second-person language, including the most important points at the beginning, grabbing the reader's attention early, providing information in a stepwise fashion, using bulleted lists, avoiding abstract words, maintaining consistency, emphasizing benefits, and respecting the audience. Recommendations for visual presentation additionally include use of appealing colors and photos with concise captions, avoiding graphs and charts if possible, using 40-50% white space, avoiding all capital letters and frequent italics, using a font size larger than 12-point, bolding headings and subheadings, spelling out fractions and percentages with images, justifying the left margin, and avoiding text on shaded backgrounds or patterns.

To be considered user-friendly, it is critical that information be manageable (Arnold et al. 2006). At over 30 pages, these brochures could frustrate and confuse families. Zolgensma's brochures are shorter and more easily digestible, which could be partially attributed to having a larger offering of resources. Dividing the content into separate brochures as opposed to maintaining it within one document with a table of contents could make information more manageable for patients and caregivers.

4.5.1 Future Research

While barriers to comprehension are a major concern for families and caregivers, this issue is not unique to NBS or SMA. Kumar et al. (2011) used the Parental Health Literacy Activities Test (PHLAT) to assess both health literacy and numeracy of parents and caregivers to newborns within the general population especially as it pertains to tasks necessary in caring for infants, including nutrition, growth and development, safety, and medical care. Naturally, these difficulties may extend into the realm of newborn screening. Genetic literacy is less commonly understood in

comparison to general health literacy, contributing to further barriers in comprehension. Information from the Health Information National Trends Survey has identified information on genetic literacy in the general population (Krakow et al. 2019). This survey revealed that 57% of participants are aware of genetic testing. Similarly, other studies have focused on measurement of genetic literacy through a survey designed to assess general knowledge of genetics as well as the ability to apply information to human health decisions (Little et al. 2022). They discovered that while genetic literacy has improved over time, skills and knowledge could still improve. High genetic literacy was considered as answering over 70% of questions correctly. 18.8% of participants demonstrated high genetic literacy in terms of skills while 23.7% demonstrated high genetic literacy with knowledge. The researchers recommend that educational interventions be implemented to improve genetic literacy in the general public.

Further studies should be conducted to assess where improvements can be made not only in brochures for SMA, but for all conditions found on NBS panels. This will allow for improved health outcomes for affected infants and decreased psychosocial harm to parents and caregivers. Arnold et al. (2006) assessed newborn screening brochures from 48 states and Puerto Rico using the Flesch reading ease (FRE) formula and user-friendliness. In this analysis, the average FRE score of all written materials was 53.26, corresponding to a 10^{th}- to 12^{th}-grade reading level. 8% of brochures scored below the eighth-grade reading level. There is significant room for improvement in these brochures in reducing the reading difficulty level and focusing on issues related to layout, illustrations, messaging, information, and cultural sensitivity.

Additionally, it is important to note that these Flesch-Kincaid grade level calculations are limited in that some terms related to genetics and health are difficult, if not impossible, to simplify in plain language. For example, the term “chromosome” is highly complex and cannot be omitted

without losing meaning. Further studies could focus on assessing readability if certain complicated terms are removed from the calculations, such as the drug name.

4.5.2 Limitations

There are several limitations to this analysis. One major limitation in examining these resources is the lack of comparison between different treatments. Notable, these brochures function as a marketing tool for each company. This can make choosing a treatment increasingly difficult for parents and caregivers. Instead of having one document to provide comparisons and differences, families may have to sift through three individual brochures spanning over 30 pages in length. This study did not assess brochures provided by clinical teams. SMA-related treatment brochures distributed to both healthcare providers and patients include data on study results regarding the specific treatment modality. One study found that following positive newborn screening results, most families and caregivers chose Zolgensma for treatment; 72% of families chose Zolgensma, 12% chose Evrysdi and 6% chose Spinraza (Deng et al. 2022). These families still desired supplemental information in the form of brochures or videos to aid in treatment decisions and medical options. As further therapies are developed, the need for better comparison tools will increase as well. It is critical to improve understanding of the available treatments to facilitate decision-making and to decrease barriers to comprehension for families and caregivers impacted by SMA.

Appendix A IRB Approval

University of Pittsburgh | Institutional Review Board
Office of Research Protections

EXEMPT DETERMINATION

Date:	October 11, 2022
IRB:	STUDY22080128
PI:	Ariel Breeze
Title:	Comparing Psychosocial Impacts of Spinal Muscular Atrophy Diagnoses Following Newborn Screening Implementation

The Institutional Review Board reviewed and determined the above referenced study meets the regulatory requirements for exempt research under 45 CFR 46.104(d).

Determination Documentation

Determination Date:	10/11/2022
Exempt Category:	(2)(ii) Tests, surveys, interviews, or observation (low risk)
Approved Documents:	• Verbal Consent Script, Category: Waiver Script; • Interview Guides, Category: Data Collection; • Participant Follow-up Call, Category: Recruitment Materials; • Participation Verbal Consent, Category: Recruitment Materials; • Recruitment Flyer, Category: Recruitment Materials;

If you have any questions, please contact the University of Pittsburgh IRB Coordinator, Ali Arak. **NOTE**: Modifications are only required if they will affect the exempt determination. It is important to **close your study when finished** by submitting a Continuing Review.

Please take a moment to complete our Satisfaction Survey as we appreciate your feedback.

Appendix B Participation Request Script

Participation Request Script for the CHP Team:

I am calling to ask for your assistance with a research study that is being conducted by a genetic counseling student at the University of Pittsburgh. The purpose of this research is to study the impact of diagnosis with and without newborn screening of spinal muscular atrophy. Parents who have children with SMA that have been diagnosed either with newborn screening or after symptoms have been presented are being asked to participate. Specifically, the hope is to learn how the diagnostic process can be improved for families affected by SMA.

In order to conduct this study, an interview will take place with interested families. These interviews can take place either virtually or over the phone. The interview will be recorded and will take approximately one hour to complete. Questions asked will focus on your experiences and feelings surrounding your child's diagnosis. Most of these questions will be open-ended and will allow you to give as much detail as you feel comfortable sharing. You also have the option to refuse to answer any questions. Individual interview responses will be kept strictly confidential.

We would appreciate your help with this project. Your decision to participate is completely voluntary. Is this something you would be interesting in participating in?

[If yes]

We also have some screening questions to help determine eligibility for this research study:

- How old is your child with SMA?
- Was your child diagnosed pre-symptomatically or after symptoms had already begun?
- How many copies of *SMN2* was your child found to have?

The genetic counseling student will be reaching out to you to discuss this further and set up a time that works best for you. Is there a time of day that works best for you for a follow-up call?

Thank you for your willingness to participate. The genetic counseling student will be reaching out to you soon.

Appendix C Participant Follow-up Call Script

Script for Participant Follow-up Calls

Hello, may I speak with _____? My name is Ariel Breeze, and I am calling from the Muscular Dystrophy Program at the Children's Hospital of Pittsburgh regarding the spinal muscular atrophy research study you were recently contacted about. Is this something you would still be interested in participating in?

I'm calling mainly to introduce myself because I will be the person conducting all the interviews. We are conducting the interviews over Zoom.

If you are interested, I would like to set up a day and time for this interview. Is there a date and time of day that works best for you and your schedule? Date: _____ Time: _____

Since we will be meeting over Zoom for this interview, could I get an email address from you that you check regularly that I can send the link to? I will be sending the link following this phone call. Email address: _____

If you have any questions for me at all, please feel free to call me at (412) 254 – 4095. Again, my name is Ariel. Thank you so much for taking the time to speak with me today and for your willingness to participate in this study.

Appendix D Study Introduction and Verbal Consent Script

Study Introduction

Hello, and thank you for your willingness to chat with me and participate in this study. My name is Ariel Breeze, and I am a Master of Science in Genetic Counseling and Master of Public Health student at the University of Pittsburgh. My goal today is to learn about your experiences in having a child diagnosed with spinal muscular atrophy to understand more about what this process has been like for families and what we can do in a healthcare setting to help improve this process. I have been working with Dr. Abdel-Hamid and Kelsey Bohnert with the MDA Clinic to reach out to families that have had children diagnosed with SMA and will now be conducting interviews with interested family members.

Since this is a research study, it is important to address some specific points. First, participation in this study is completely voluntary. You may leave this Zoom call at any time. Your decision to participate or not participate will not affect your current or future relationship with UPMC or the University of Pittsburgh.

Second, while there are no foreseeable risks associated with participating, there are also no direct benefits. Your confidentiality is also very important. Because of this, I have taken several measures to protect your confidentiality. Your name and any identifiable information will only be visible to myself and members of the research team. I will be recording the audio of our conversation today as well. This audio will be used to create anonymous transcripts in which all information will be de-identified. The original audio recordings will be deleted following transcription, and the transcripts will be saved securely on a personal password-protected computer.

My role here is to get to know you and understand your experiences in your child's diagnosis. Kelsey will also be here with her camera off and will be muted during the interview, but if you have any questions or concerns, she is available to help at any time.

You are encouraged to ask questions about any aspect of this research study by contacting the principal investigator, myself, at (412) 254-4095 or her mentor, Robin Grubs, MS, PhD, LCGC at (412) 624-4695. You may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, questions, obtain information, offer input, or discuss situations in the event that the research team is unavailable.

Do you have any questions about the study or the information I just went over?

Are you willing to participate in this study?

Appendix E Dynamic Interview Guide

Interview Guide for All Participants
Date: _____
Study Participant ID: _____
Confirmation of Verbal Consent: ___

1. I would like to start off by learning more about your child. Could you tell me a little bit about them?

2. What did you know about spinal muscular atrophy prior to [child's name]'s diagnosis?

3. Tell me about how you first found out about [child name's] diagnosis of spinal muscular atrophy. Describe for me your thoughts and feelings initially following this diagnosis.

4. How did this diagnosis affect your treatment decisions for [child's name], and what other factors did you consider?

5. How did you feel about the way you were told about [child's name]'s diagnosis? What about this process made you feel comfortable and what made you feel uncomfortable?

6. What would you recommend to doctors on the process of telling parents about their child's diagnosis of spinal muscular atrophy? (Who should provide that information, how many appointments should the parents have with relevant physicians, should written information be provided?)

7. Did you receive any written information about spinal muscular atrophy following the diagnosis, and was this helpful? (Was there too much or not enough information? Are there any other resources that would have been helpful at the time of the diagnosis?)

8. What would you say to a family who has just received a diagnosis? What have you learned that you wished you had known then?

9. How have you been coping with or adapting to [child's name]'s diagnosis since that day?

Bibliography

Anestis, E., Eccles, F., Fletcher, I., French, M., & Simpson, J. (2020). Giving and receiving a diagnosis of a progressive neurological condition: A scoping review of doctors' and patients' perspectives. Patient Education and Counseling, 103(9), 1709–1723. https://doi.org/10.1016/j.pec.2020.03.023.

Arnold, C. L., Davis, T. C., Frempong, J. O., Humiston, S. G., Bocchini, A., Kennen, E. M., & Lloyd-Puryear, M. (2006). Assessment of Newborn Screening Parent Education Materials. Pediatrics, 117(Supplement_3), S320–S325. https://doi.org/10.1542/peds.2005-2633L.

Boardman, F. K., Young, P. J., & Griffiths, F. E. (2018). Impairment Experiences, Identity and Attitudes Towards Genetic Screening: The Views of People with Spinal Muscular Atrophy. Journal of Genetic Counseling, 27(1), 69–84. https://doi.org/10.1007/s10897-017-0122-7.

Boardman, F., & Clark, C. (2022). 'We're kind of like genetic nomads': Parents' experiences of biographical disruption and uncertainty following in/conclusive results from newborn cystic fibrosis screening. Social Science & Medicine, 301, 114972. https://doi.org/10.1016/j.socscimed.2022.114972.

Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology*, *3*(2), 77-101. doi:10.1191/1478088706qp063oa.

Bush, L., Davidson, H., Gelles, S., Lea, D., & Koehly, L. M. (2022). Experiences of Families Caring for Children with Newborn Screening-Related Conditions: Implications for the Expansion of Genomics in Population-Based Neonatal Public Health Programs. International Journal of Neonatal Screening, 8(2), 35. https://doi.org/10.3390/ijns8020035.

Bushby, K., Finkel, R., Birnkrant, D. J., Case, L. E., Clemens, P. R., Cripe, L., Kaul, A., Kinnett, K., McDonald, C., Pandya, S., Poysky, J., Shapiro, F., Tomezsko, J., & Constantin, C. (2010). Diagnosis and management of Duchenne muscular dystrophy, part 1: Diagnosis, and pharmacological and psychosocial management. The Lancet Neurology, 9(1), 77–93. https://doi.org/10.1016/S1474-4422(09)70271-6.

Butterfield, Russell J. "Spinal Muscular Atrophy Treatments, Newborn Screening, and the Creation of a Neurogenetics Urgency." Seminars in Pediatric Neurology 38 (July 2021): 100899. https://doi.org/10.1016/j.spen.2021.100899.

Cardarelli, R., Licciardone, J. C., & Taylor, L. G. (2006). A cross-sectional evidence-based review of pharmaceutical promotional marketing brochures and their underlying studies: Is what they tell us important and true? BMC Family Practice, 7, 13. https://doi.org/10.1186/1471-2296-7-13.

Carrier screening for genetic conditions. Committee Opinion No. 691. American College of Obstetricians and Gynecologists. Obstet Gynecol 2017;129:e41–55.

Centers for Disease Control and Prevention. (2021, December 20). *The Public Health System & the 10 Essential Public Health Services*. https://www.cdc.gov/publichealthgateway/publichealthservices/pdf/Ten_Essential_Services_and_SDOH.pdf.

Covello, V. T. "An Overview of Risk Communication," in Communicating in Risk, Crisis, and High Stress Situations: Evidence-Based Strategies and Practice , IEEE, 2022, pp.33-67, doi: 10.1002/9781119081753.ch3.

Cure SMA (2020 March). *Scientific Considerations for Drug Combinations.* https://curesma.wpengine.com/wp-content/uploads/2020/03/03042020_Scientific-Considerations-for-Drug-Combinations_Final_Updated.pdf.

Cure SMA. (2021 June). *SMA Fact Sheet: Pennsylvania*. https://www.curesma.org/wp-content/uploads/2021/06/SMA-State-Fact-Sheet_June2021_PA_v2.pdf.

Cure SMA. (2022, September 26). *Newborn screening for SMA*. https://www.curesma.org/newborn-screening-for-sma/.

Darras, B. T. (2015). Spinal Muscular Atrophies. Pediatric Clinics of North America, 62(3), 743–766. https://doi.org/10.1016/j.pcl.2015.03.010.

Deng, Stella, Bo Hoon Lee, and Emma Ciafaloni. "Parent Perceptions in Choosing Treatment for Infants With Spinal Muscular Atrophy Diagnosed Through Newborn Screening." Journal of Child Neurology 37, no. 1 (January 1, 2022): 43–49. https://doi.org/10.1177/08830738211040292.

Dobrow, M. J., Hagens, V., Chafe, R., Sullivan, T., & Rabeneck, L. (2018). Consolidated principles for screening based on a systematic review and consensus process. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne, 190(14), E422–E429. https://doi.org/10.1503/cmaj.171154.

Dubowitz, V. (1999). Very severe spinal muscular atrophy (SMA type 0): An expanding clinical phenotype. 3.

Elfil, M., & Negida, A. (2017). Sampling methods in Clinical Research; an Educational Review. Emergency, 5(1), e52.

Ema. (2022, July 5). Evrysdi. European Medicines Agency. Retrieved November 30, 2022, from https://www.ema.europa.eu/en/medicines/human/EPAR/evrysdi.

Fernandes, I. A. M., Menezes, R. O. A., & Rego, G. (2022). Communication of the Diagnosis of Spinal Muscular Atrophy in the Views of Patients and Family Members, a Qualitative Analysis. International Journal of Environmental Research and Public Health, 19(24), 16935. https://doi.org/10.3390/ijerph192416935.

Guest, G., Namey, E., & Chen, M. (2020). A simple method to assess and report thematic saturation in qualitative research. PLOS ONE, 15(5), e0232076. https://doi.org/10.1371/journal.pone.0232076.

Hale, Kshea, Jelili Ojodu, and Sikha Singh. "Landscape of Spinal Muscular Atrophy Newborn Screening in the United States: 2018–2021." International Journal of Neonatal Screening 7, no. 3 (June 24, 2021): 33. https://doi.org/10.3390/ijns7030033.

Halley, M. C., Halverson, C. M. E., Tabor, H. K., & Goldenberg, A. J. (2023). Rare Disease, Advocacy and Justice: Intersecting Disparities in Research and Clinical Care. The American Journal of Bioethics, 0(0), 1–10. https://doi.org/10.1080/15265161.2023.2207500.

Harms, M. B., Allred, P., Gardner, R., Fernandes Filho, J. A., Florence, J., Pestronk, A., Al-Lozi, M., & Baloh, R. H. (2010). Dominant spinal muscular atrophy with lower extremity predominance. Neurology, 75(6), 539–546. https://doi.org/10.1212/WNL.0b013e3181ec800c.

Herington, E., & Horton, J. (2021). Genetic Carrier Screening for Cystic Fibrosis, Fragile X Syndrome, Hemoglobinopathies, and Spinal Muscular Atrophy. Canadian Agency for Drugs and Technologies in Health. http://www.ncbi.nlm.nih.gov/books/NBK584540/.

Jackson, J. B., Steward, S. R., Roper, S. O., & Muruthi, B. A. (2018). Support Group Value and Design for Parents of Children with Severe or Profound Intellectual and Developmental Disabilities. Journal of Autism and Developmental Disorders, 48(12), 4207–4221. https://doi.org/10.1007/s10803-018-3665-z.

Jessup, M., Douglas, T., Priddis, L., Branch-Smith, C., & Shields, L. (2016). Parental Experience of Information and Education Processes Following Diagnosis of Their Infant With Cystic Fibrosis Via Newborn Screening. Journal of Pediatric Nursing, 31(3), e233–e241. https://doi.org/10.1016/j.pedn.2015.11.010.

Kariyawasam, Didu S. T., Arlene M. D'Silva, Janine Vetsch, Claire E. Wakefield, Veronica Wiley, and Michelle A. Farrar. "'We Needed This': Perspectives of Parents and Healthcare Professionals Involved in a Pilot Newborn Screening Program for Spinal Muscular Atrophy." EClinicalMedicine 33 (March 1, 2021). https://doi.org/10.1016/j.eclinm.2021.100742.

Kolb, S. J., & Kissel, J. T. (2015). Spinal Muscular Atrophy. Neurologic Clinics, 33(4), 831–846. https://doi.org/10.1016/j.ncl.2015.07.004.

Krakow, M., Ratcliff, C. L., Hesse, B. W., & Greenberg-Worisek, A. J. (2017). Assessing Genetic Literacy Awareness and Knowledge Gaps in the U.S. Population: Results from the Health Information National Trends Survey. Public Health Genomics, 20(6), 343–348. https://doi.org/10.1159/000489117.

Krosschell, K. J., Dunaway Young, S., Peterson, I., Curry, M., Mazzella, A., Jarecki, J., & Cruz, R. (2022). Clinical and Research Readiness for Spinal Muscular Atrophy: The Time Is

Now for Knowledge Translation. Physical Therapy, 102(10), pzac108. https://doi.org/10.1093/ptj/pzac108.

Kumar, D., Sanders, L., Perrin, E. M., Lokker, N., Patterson, B., Gunn, V., Finkle, J., Franco, V., Choi, L., & Rothman, R. L. (2010). Parental Understanding of Infant Health Information: Health Literacy, Numeracy and the Parental Health Literacy Activities Test (PHLAT). Academic Pediatrics, 10(5), 309–316. https://doi.org/10.1016/j.acap.2010.06.007.

Kutner M, et al. (2006) The health literacy of America's adults: results from the 2003 National Assessment of Adult Literacy. Washington, National Center for Education Statistics. Available at http://nces.ed.gov/pubs2006/2006483_1.pdf.

Lefebvre, S., Burlet, P., Liu, Q., Bertrandy, S., Clermont, O., Munnich, A., Dreyfuss, G., & Melki, J. (1997). Correlation between severity and SMN protein level in spinal muscular atrophy. Nature Genetics, 16(3), Article 3. https://doi.org/10.1038/ng0797-265.

Li, Q. (2020). Nusinersen as a Therapeutic Agent for Spinal Muscular Atrophy. Yonsei Medical Journal, 61(4), 273–283. https://doi.org/10.3349/ymj.2020.61.4.273.

Lindemann, E. (1944). Symptomatology and management of acute grief. American Journal of Psychiatry, 101(2), 141–148. https://doi.org/10.1176/ajp.101.2.141

Little, I. D., Koehly, L. M., & Gunter, C. (2022). Understanding changes in genetic literacy over time and in genetic research participants. American Journal of Human Genetics, 109(12), 2141–2151. https://doi.org/10.1016/j.ajhg.2022.11.005.

Locock, L., Ziebland, S., & Dumelow, C. (2009). Biographical disruption, abruption and repair in the context of Motor Neurone Disease. Sociology of Health & Illness, 31(7), 1043–1058. https://doi.org/10.1111/j.1467-9566.2009.01176.x.

Marcus, G. (2019). The Role of the Genetic Counselor in Newborn Screening. North Carolina Medical Journal, 80(1), 39–40. https://doi.org/10.18043/ncm.80.1.39.

Mendell, J. R., Al-Zaidy, S., Shell, R., Arnold, W. D., Rodino-Klapac, L. R., Prior, T. W., Lowes, L., Alfano, L., Berry, K., Church, K., Kissel, J. T., Nagendran, S., L'Italien, J., Sproule, D. M., Wells, C., Cardenas, J. A., Heitzer, M. D., Kaspar, A., Corcoran, S., … Kaspar, B. K. (2017). Single-Dose Gene-Replacement Therapy for Spinal Muscular Atrophy. New England Journal of Medicine, 377(18), 1713–1722. https://doi.org/10.1056/NEJMoa1706198.

Mercuri, Eugenio. "Spinal Muscular Atrophy: From Rags to Riches." Neuromuscular Disorders 31, no. 10 (October 2021): 998–1003. https://doi.org/10.1016/j.nmd.2021.08.009.

Mercuri, E., Finkel, R. S., Muntoni, F., Wirth, B., Montes, J., Main, M., Mazzone, E. S., Vitale, M., Snyder, B., Quijano-Roy, S., Bertini, E., Davis, R. H., Meyer, O. H., Simonds, A. K., Schroth, M. K., Graham, R. J., Kirschner, J., Iannaccone, S. T., Crawford, T. O., … Szlagatys-Sidorkiewicz, A. (2018). Diagnosis and management of spinal muscular atrophy: Part 1: Recommendations for diagnosis, rehabilitation, orthopedic and nutritional

care. Neuromuscular Disorders, 28(2), 103–115. https://doi.org/10.1016/j.nmd.2017.11.005.

Mirea, A., Shelby, E.-S., Axente, M., Badina, M., Padure, L., Leanca, M., Dima, V., & Sporea, C. (2021). Combination Therapy with Nusinersen and Onasemnogene Abeparvovec-xioi in Spinal Muscular Atrophy Type I. Journal of Clinical Medicine, 10(23), 5540. https://doi.org/10.3390/jcm10235540.

Mueller, R. (n.d.). Prognostic imagination: Genetic counseling amidst therapeutic innovation and evolving futures. Journal of Genetic Counseling, n/a(n/a). https://doi.org/10.1002/jgc4.1660.

Novartis Gene Therapies, Inc. (2023 March). *Zolgensma (onasaemnogene abeparvovec-xioi): Care preparation checklist.* https://www.zolgensma.com/pdf/caregiver-preparation-checklist.pdf.

Oechsel, K. F., & Cartwright, M. S. (2021). Combination therapy with onasemnogene and risdiplam in spinal muscular atrophy type 1. Muscle & Nerve, 64(4), 487–490. https://doi.org/10.1002/mus.27375.

Passini, M. A., Bu, J., Richards, A. M., Kinnecom, C., Sardi, S. P., Stanek, L. M., Hua, Y., Rigo, F., Matson, J., Hung, G., Kaye, E. M., Shihabuddin, L. S., Krainer, A. R., Bennett, C. F., & Cheng, S. H. (2011). Antisense Oligonucleotides Delivered to the Mouse CNS Ameliorate Symptoms of Severe Spinal Muscular Atrophy. Science Translational Medicine, 3(72), 72ra18-72ra18. https://doi.org/10.1126/scitranslmed.3001777.

Patterson, A. M., O'Boyle, M., VanNoy, G. E., & Dies, K. A. (2023). Emerging roles and opportunities for rare disease patient advocacy groups. Therapeutic Advances in Rare Disease, 4, 26330040231164424. https://doi.org/10.1177/26330040231164425.

Pearn, J. (1978). Incidence, prevalence, and gene frequency studies of chronic childhood spinal muscular atrophy. Journal of Medical Genetics, 15(6), 409–413.

Perera, K. Y. S., Ranasinghe, P., Adikari, A. M. M. C., Balagobi, B., Constantine, G. R., & Jayasinghe, S. (2012). Medium of Language in Discharge Summaries: Would the Use of Native Language Improve Patients' Knowledge of Their Illness and Medications? Journal of Health Communication, 17(2), 141–148. https://doi.org/10.1080/10810730.2011.585926.

Potter, B. K., Etchegary, H., Nicholls, S. G., Wilson, B. J., Craigie, S. M., & Araia, M. H. (2015). Education and Parental Involvement in Decision-Making About Newborn Screening: Understanding Goals to Clarify Content. Journal of Genetic Counseling, 24(3), 400–408. https://doi.org/10.1007/s10897-014-9780-x.

Prakash, S., Penn, J. D., Jackson, K. E., & Dean, L. W. (2022). Newborn screening for Pompe disease: Parental experiences and follow-up care for a late-onset diagnosis. Journal of Genetic Counseling, 31(6), 1404–1420. https://doi.org/10.1002/jgc4.1615.

Qian, Y., McGraw, S., Henne, J., Jarecki, J., Hobby, K., & Yeh, W.-S. (2015). Understanding the experiences and needs of individuals with Spinal Muscular Atrophy and their parents: A qualitative study. BMC Neurology, 15, 217. https://doi.org/10.1186/s12883-015-0473-3.

Ratni, H., Ebeling, M., Baird, J., Bendels, S., Bylund, J., Chen, K. S., Denk, N., Feng, Z., Green, L., Guerard, M., Jablonski, P., Jacobsen, B., Khwaja, O., Kletzl, H., Ko, C.-P., Kustermann, S., Marquet, A., Metzger, F., Mueller, B., … Mueller, L. (2018). Discovery of Risdiplam, a Selective Survival of Motor Neuron-2 (SMN2) Gene Splicing Modifier for the Treatment of Spinal Muscular Atrophy (SMA). Journal of Medicinal Chemistry, 61(15), 6501–6517. https://doi.org/10.1021/acs.jmedchem.8b00741.

Rolland, J. S. (1990). Anticipatory Loss: A Family Systems Developmental Framework. Family Process, 29(3), 229–244. https://doi.org/10.1111/j.1545-5300.1990.00229.x.

Rooney, M. K., Santiago, G., Perni, S., Horowitz, D. P., McCall, A. R., Einstein, A. J., Jagsi, R., & Golden, D. W. (2021). Readability of Patient Education Materials From High-Impact Medical Journals: A 20-Year Analysis. Journal of Patient Experience, 8, 2374373521998847. https://doi.org/10.1177/2374373521998847.

Sentell, T., & Braun, K. L. (2012). Low Health Literacy, Limited English Proficiency, and Health Status in Asians, Latinos, and Other Racial/Ethnic Groups in California. Journal of Health Communication, 17(sup3), 82–99. https://doi.org/10.1080/10810730.2012.712621.

Sims, A. M., Cromartie, S. J., Gessner, L., Campbell, A., Coker, T., Wang, C. J., & Tarini, B. A. (2022). Parents' Experiences and Needs Regarding Infant Sickle Cell Trait Results. Pediatrics, 149(5), e2021053454. https://doi.org/10.1542/peds.2021-053454.

Sumner, C. J., & Crawford, T. O. (2018). Two breakthrough gene-targeted treatments for spinal muscular atrophy: Challenges remain. The Journal of Clinical Investigation, 128(8), 3219–3227. https://doi.org/10.1172/JCI121658.

Vasileiou, K., Barnett, J., Thorpe, S., & Young, T. (2018). Characterising and justifying sample size sufficiency in interview-based studies: Systematic analysis of qualitative health research over a 15-year period. BMC Medical Research Methodology, 18(1), 148. https://doi.org/10.1186/s12874-018-0594-7.

von Gontard, A., Rudnik-Schöneborn, S., & Zerres, K. (2012). Stress and coping in parents of children and adolescents with spinal muscular atrophy. *Klinische Pädiatrie*, *224*(04), 247–251. https://doi.org/10.1055/s-0032-1304577.

Wang CH, Finkel RS, Bertini ES, Schroth M, Simonds A, Wong B, Aloysius A, Morrison L, Main M, Crawford TO, Trela A, and Participants of the International Conference on SMA Standard of Care. Consensus statement for standard of care in spinal muscular atrophy. J Child Neurol. 2007;22:1027-1049.

Williams, A. M., Muir, K. W., & Rosdahl, J. A. (2016). Readability of patient education materials in ophthalmology: A single-institution study and systematic review. BMC Ophthalmology, 16(1), Article 1. https://doi.org/10.1186/s12886-016-0315-0.

Wilson, J. M. G., & Jungner, G. (n.d.). PRINCIPLES AND PRACTICE OF SCREENING FOR DISEASE. 168.