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Experiences of Parents of Children With Late-Onset Pompe Disease Diagnosed By Newborn Screening

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DEDICATION

This thesis project is dedicated to the families and individuals within the Pompe disease community. I cannot thank you enough for being so open and vulnerable with me. Your commitment to your children and the community is incredible. Thank you for sharing your experiences with me. I hope I represent them well.

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ABSTRACT

Pompe disease is an autosomal recessive lysosomal and glycogen storage disorder. It is classified as either infantile-onset Pompe disease (IOPD), which is characterized by severe muscle weakness and enlarged heart shortly after birth, or late-onset Pompe disease (LOPD), which is characterized by more slowly progressive weakness without obvious symptoms at birth. Pompe disease was added to the Recommended Uniform Screening Panel (RUSP) for newborn screening (NBS) in 2015 as early treatment with enzyme replacement therapy is lifesaving for children with IOPD. However, most patients identified via newborn screening have LOPD, which does not require immediate treatment and may not present until childhood or adulthood. There are not yet clear guidelines for management and treatment of children with LOPD diagnosed via NBS which creates a challenge for both clinicians and parents.

This study explored the experiences of parents whose children were diagnosed with LOPD by NBS. Surveys containing multiple choice and free text questions were collected from 42 parents to assess their experiences with diagnosis and follow up, access to services, and the emotional impact of the diagnosis. The majority of parents (70.7%, 29/41) stated their anxiety levels decreased over time since their child's diagnosis. Out of those parents who saw a genetic counselor and commented on that experience, 71.9% (23/32) stated meeting with a genetic counselor impacted their ability to manage their child's diagnosis. The primary areas of genetic counseling impact included accessibility, providing resources, aiding in understanding of diagnosis, making a treatment plan, and

supporting parental mental health. Parents emphasized the necessity of healthcare provider knowledge on conditions like LOPD, the prolonged feeling of uncertainty years after diagnosis, and the benefit of having a good support group and healthcare team on anxiety levels. Knowledge of parental experiences and needs is important as more individuals with late-onset conditions continue to be identified by NBS. Information on how to improve these experiences can help healthcare providers better serve individuals and families affected by these conditions.

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LIST OF ABBREVIATIONS

ACMG ..... American College of Medical Genetics

ERT ..... Enzyme replacement therapy

GAA ..... Acid alpha-glucosidase

HCP ..... Healthcare provider

HRSA ..... Health Resources & Services Administration

IOPD ..... Infantile-onset Pompe disease

LOPD ..... Late-onset Pompe disease

NBS ..... Newborn screening

PD ..... Pompe disease

PT ..... Physical therapy

RUSP ..... Recommended Uniform Screening Panel

SPSS ..... Statistical Package for Social Sciences

CHAPTER 1: BACKGROUND

1.1 Late-onset Pompe Disease Overview

Pompe disease (PD) is a rare glycogen and lysosomal storage disorder characterized by progressive muscle weakness and respiratory failure. The condition affects approximately 1 in 23,000 people in the United States (Park, 2021). PD is caused by biallelic disease-causing variants in the *GAA* gene, leading to a deficiency of acid alpha-glucosidase (GAA), also known as acid maltase (Atherton et al., 2017). This causes glycogen to progressively build up in lysosomes, causing damage to skeletal and cardiac muscle. There are two primary forms of PD: infantile-onset Pompe disease (IOPD) and late-onset Pompe disease (LOPD), the latter being the focus of this study. The most notable differences in IOPD and LOPD are in symptom presentation. IOPD presents before the age of one and involves hypertrophic cardiomyopathy. Other IOPD symptoms include failure to thrive, muscle weakness, respiratory distress, macroglossia, and absent deep tendon reflexes. IOPD is more severe and rapidly progressive than LOPD and requires treatment in the form of enzyme replacement therapy (ERT) as early as possible. The muscle weakness can progress to respiratory insufficiency and left ventricular outflow obstruction when untreated. Without treatment, individuals die by two years of age (Chien et al., 2013; Kishnani et al., 2009).

LOPD may present at any age and does not present with cardiomyopathy within the first year of life. LOPD is more slowly progressive; thus, symptoms are not evident at birth. Additionally, symptom onset and presentation can vary significantly between

affected individuals, even within the same family. The age of onset can range anywhere from the first year of life to the sixth decade of life. The most common symptoms of LOPD include respiratory insufficiency and progressive proximal muscle weakness. Typically, the earlier that symptoms present, the faster the disease progresses. Without treatment, this progression often leads to individuals using wheelchairs, as the muscle weakness is primarily in the lower limbs. Fatigue follows, along with pain, joint contractions, increased respiratory infections, increased risk of heart rhythm disturbances, and sleep apnea. Scoliosis is also common in individuals with LOPD. Treatment for LOPD includes ERT, along with other interventions to assist in alleviating symptoms. Overall life expectancy may be shortened depending on age of onset, symptom progression, and treatment status (Chan et al., 2017; Hamed et al., 2021).

1.2 History of Newborn Screening

Newborn screening (NBS) was implemented to identify individuals with serious genetic conditions so they may be treated earlier and have improved survival. NBS began in the 1960s, originally used for identifying infants with phenylketonuria at birth. Screening for this condition started with measuring the amount of phenylalanine in dried blood spots, a practice that continues today (McCandless et al., 2020).

As NBS expanded, there was a need to provide guidelines for what was becoming population-based health screening. The World Health Organization published guidelines titled “Principles and Practice of Screening for Disease” in 1968 that have largely been referred to as the “Wilson and Jungner criteria” for population-based health screening (Wilson et al., 1968). The criteria have guided NBS practices for decades and illustrate several important points to be considered before adding a condition to the panel and

proceeding with NBS. These include, but are not limited to, the condition being an important health problem, there being an available treatment, understanding the natural history, having a balanced cost of diagnosis and treatment, and having an acceptable test for the condition. Notably, the criteria emphasize the need for follow-up after screening, not relegating the screening to a moment in time, but as a continuous process (Wilson et al., 1968).

NBS includes a newborn hearing exam, a congenital heart defects screen, and a biochemical screen for genetic disorders. The biochemical screen is typically performed using dried blood spots, similar to the original phenylketonuria test. The Health Resources & Services Administration (HRSA) recommends that initial dried blood spot samples should be collected within 48 hours of birth and should arrive at NBS laboratories within 24 hours after collection. All positive results should be communicated to healthcare providers (HCPs) within 7 days after birth, though time-critical conditions should be within 5 days (HRSA, 2017). The dried blood spot evaluation is typically done at a separate laboratory (McCandless et al., 2020). It is important to note that NBS is not diagnostic. When a newborn screens positive for a condition, diagnostic testing is necessary to confirm the infant is affected.

While the conditions included on and practices for NBS are state-designed and managed, there are national guidelines for the programs. The Recommended Uniform Screening Panel (RUSP) was designed by the American College of Medical Genetics as commissioned by the Maternal and Child Health Bureau in 2006 (American College of Medical Genetics [ACMG], 2006). The RUSP is a guideline of recommended genetic conditions to be included on NBS programs throughout the United States, as an attempt

to standardize and provide guidance to states developing such programs. Also included in the RUSP guidelines are recommended policies and procedures, standards for state NBS programs, and a decision matrix for NBS expansion. Primarily focused on inborn errors of metabolism that present at birth and have significant time constraints for treatment, the RUSP originally was intended to be a resource for states in evaluating what conditions are necessary on NBS.

In evaluating conditions, they consider the clinical characteristics, the logistics of screening for the condition, and available treatment and management. The original RUSP included 29 mandated conditions (ACMG, 2006). As treatments, technology, and advocacy have increased in the years since, more conditions continue to be added to the RUSP. Currently, there are 37 core conditions and 26 secondary conditions listed on the RUSP (HRSA, 2022). Core conditions are those that are specifically recommended to be included on NBS panels, whereas secondary conditions are those that may be found incidentally while screening for a core condition (HRSA, 2022). The conditions included on the panel are primarily metabolic conditions, but also include hematologic disorders and endocrinopathies. The ability to test for these conditions in a timely manner came largely from the development of tandem mass spectrometry technology in the 1980s and its subsequent implementation in NBS in the 1990s. This allowed for multiple conditions to be screened at once with small amounts of dried blood (Garg & Dasouki, 2006).

For a condition to be added to the panel, it must be nominated by a multidisciplinary team. This may include researchers or clinicians, advocacy organizations, and other interested individuals, though any group may nominate a condition. Nominations are reviewed by a committee within the HRSA, which manages

the RUSP. After committee approval, nominations are sent to an external group for an evidence-based review. The review is re-evaluated by the committee and a recommendation is made on whether to add the condition to the RUSP, ultimately concluding with the Health and Human Services secretary making a final decision. On average, this process takes 3-4 years after the committee receives the initial nomination (HRSA, 2022).

Today, NBS programs remain state-specific and are constantly changing with the help of passionate families and providers, along with increasing technology and available treatments. As it expands, it is essential to continue to evaluate the utility of conditions screened for in these programs and maintain up to date on advancements that can affect patients and their families. NBS is now encompassing many conditions that were not originally thought of as traditional inborn errors of metabolism, which includes storage disorders with varied ages of onset. As some ages of onset for these conditions, such as PD, can be at birth and be severely life-limiting, nominating and accepting these conditions on the RUSP has become much more common. This brings with it a new concern of identifying individuals who present much later in life, but have the condition diagnosed at birth. Identifying these children years before they show symptoms was not the initial goal of NBS and leads to questions about utility of treatment that are not present with the early onset forms of the disease.

1.3 Newborn Screening for Pompe Disease

PD was added to the RUSP in 2015, leading many states to add the condition to their panels in the years since. Prior to its implementation in the United States, Taiwan began screening for PD in 2005 by measuring GAA activity in dried blood spots at birth.

This was the first large-scale program for NBS of PD and led to several studies being published that allowed for other countries, including the United States, to adopt the condition into their NBS programs as well (Chien et al., 2008). Taiwan was also one of the first countries to show that early treatment of Pompe disease with the approved ERT allowed for increased survivability (Chien et al., 2013). This paved the way for groups here in the United States to nominate the condition with the evidence that treatment is both available and effective, and that NBS is a powerful tool to aid in that treatment initiation. As of this paper's submission, NBS for the condition has been implemented in 38 states and continues to be piloted in many more. The condition is screened for by analyzing the amount of the GAA enzyme in dried blood samples by fluorometry, tandem mass spectrometry, or digital microfluidic fluorometry (Sawada et al., 2020).

Individuals with IOPD or LOPD have lower levels of GAA than expected, ultimately leading to both subtypes of the condition being screened for at birth. If a baby screens positive, the initial blood test is followed by biochemical tests confirming the enzyme deficiency, a cardiac evaluation to assess heart size and function, and gene sequencing of the *GAA* gene to identify the variants as well as to screen for pseudodeficiency alleles. Psuedodeficiency alleles are those that appear to lower GAA levels in biochemical testing, but ultimately do not lead to disease manifestation, which can lead to a false positive NBS. If GAA is deficient and cardiomyopathy is present, a diagnosis of IOPD can be made (Burton et al., 2017). There have been genotype-phenotype correlations established, which allows for some level of prediction in certain cases as to whether a diagnosis is late-onset or infantile-onset without knowledge of symptoms. Cardiac involvement is indicative of IOPD regardless of the genotype

(Peruzzo et al., 2019). Due to the clinical features and severity of IOPD, its inclusion on NBS allows for more immediate treatment and overall improved clinical outcomes and survivorship. The ability to have cardiac evaluations prior to symptom progression is a large benefit to identifying the condition at birth.

Before NBS, the diagnostic odyssey for individuals with LOPD could span years. Studies have noted that diagnostic odysseys ranged from less than a year to 40 years, with most individuals being diagnosed more than 5 years after symptom onset (Lagler et al., 2019; Lisi & Ali, 2021). The length of time between symptom onset and diagnosis can influence effectiveness of treatment and quality of life. In this way, LOPD identification at birth can lead to increased treatment effectiveness. However, there is additional controversy in PD's placement on NBS, along with other conditions that have late-onset counterparts such as Gaucher disease. It is unclear if early identification before apparent symptoms is beneficial for individuals with LOPD long term. There is still limited information on how effective treatment is before symptoms appear. Early symptom onset has been described in several studies and continues to be a growing research subject, with more understanding now that onset may be earlier than previously thought for most individuals with LOPD (Herbert et al., 2019; Huggins et al., 2022; Rairikar et al., 2017).

Studies performed interviewing individuals and families affected by this diagnosis support its placement on the NBS panels, emphasizing the importance of a shorter diagnostic period and access to treatment (Lisi et al., 2016). Lisi & Ali, (2021) described the NBS opinions of adults affected by LOPD along with other late-onset lysosomal storage conditions. All 13 individuals with LOPD interviewed for the study supported the condition's placement on NBS, specifically citing early treatment and shortened

diagnostic odyssey as benefits (Lisi & Ali, 2021). As it continues to be added to more NBS panels across the United States, more children will be diagnosed with LOPD before they have any noticeable symptoms. Identifying unmet needs of parents of these children, along with the patients themselves as they get older, is important as NBS continues to expand.

While many have supported its placement on NBS, the condition's implementation does not come without frustrations, as IOPD and LOPD cannot be differentiated on initial screens. In fact, most positive newborn screens for PD are later categorized as LOPD after further testing (Ross & Clarke, 2017). Due to the difference in clinical presentation at birth, parental expectations and emotional needs may be different between cases of IOPD and LOPD. Previous work has shown that many parents of children with IOPD have reported feeling grateful for the screening diagnosis and are focused on determining the best course of action for treatment of their child. Parents of children with LOPD diagnosed by NBS have expressed additional frustration with the result and feelings of uncertainty with expectations for their child's future (Pruniski et al., 2018).

Additionally, as this is a recent implementation in most states and regards a condition that may have subtle symptoms throughout childhood, it is possible that older siblings of children diagnosed by NBS also have the condition but are not aware of it. This leads to a unique issue of both health and psychosocial concerns for patients and families, who now may be facing a new diagnosis in multiple children. HCPs must understand this nuance when in discussion with families and affected individuals.

1.4 Treatment for PD

The primary form of treatment for PD is ERT, a treatment where a deficient enzyme in the body is replaced so that symptoms can be reduced, usually done intravenously. In PD, GAA is replaced by a human recombinant enzyme. The two current approved treatments are alglucosidase alfa, which was approved by the FDA in 2006 for IOPD and LOPD, and avalglucosidase alfa, which was approved in 2021 for LOPD. Both ERT treatments reduce the build-up of glycogen in the muscles. Alglucosidase alfa does this through cleaving glycogen and thus improving lysosome function in clearing the glycogen amounts but has been shown to have reduced efficacy in skeletal muscles, resulting in higher doses given (Dhillon, 2021; Khan et al., 2020; Schoser et al., 2017). Avalglucosidase alfa is similarly a human recombinant enzyme but was designed to also increase mannose-6-phosphate levels in attempts to increase uptake of the enzyme in skeletal muscles and be more efficient at clearing glycogen (Dhillon, 2021). ERT has been shown to reverse cardiomyopathy in IOPD and improve clinical features associated with PD if started in a timely manner prior to or soon after symptom onset (Dornelles et al., 2021). Treatment with ERT is a life-saving necessity in children with IOPD and should be started immediately after diagnosis, either clinically or via NBS. Individuals with LOPD may not require treatment at the time of their diagnosis, depending on age of onset and symptom severity. This makes timing an important factor in treatment decisions. Surveillance for symptoms is vital to implementing treatment in a timely manner.

Symptom surveillance includes respiratory assessments, skeletal evaluations for scoliosis, pulmonary function tests, feeding assessments, and cardiac evaluations (Cupler

et al., 2012). Physical therapy is also often prescribed to improve existing muscle weakness and prevent further progression. This surveillance is life-long and often imposes a significant time and financial burden on families.

On top of these aforementioned appointments, ERT is a treatment that is time intensive and financially straining. Infusions take hours and happen weekly or every other week, presenting a significant time burden (Hundsberger et al., 2019). ERT is also a significant financial burden on families. Studies looking at IOPD have found that supportive care costs over $41,000 for less than six months, and treatment can be up to $379,000 annually without insurance. In IOPD, all of these treatments are implemented immediately and have been shown to decrease symptoms and increase survivability (Richardson et al., 2021; Schoser et al., 2019).

With IOPD, there is the greatest benefit to the patient when treatment starts as early as possible (Chien et al., 2015). As it is variable in both expression and onset, LOPD treatment recommendations before symptom onset have historically been unclear when compared to IOPD recommendations. This question of when to start treatment for pre-symptomatic individuals is not unique to NBS; incidental diagnoses from other testing such as whole-exome sequencing and expanded carrier screening also presents questions of how to proceed after prematurely identifying people with a condition.

Before its presence on NBS, treatment for LOPD began at the time of diagnosis in symptomatic individuals. After starting ERT, several assessments must be continually performed annually or sometimes multiple times a year. These include muscle testing, formal pulmonary function tests, timed walk tests, quality of life surveys, and laboratory tests involving creatine kinase measurement and ERT antibody titers (Marques, 2022).

Data is still unclear on when treatment is most effective for LOPD but initiating it prior to clear symptom-onset can be a significant cost for families that otherwise may not have undergone treatment until later in life with uncertain prognosis benefits.

Historically, it has been thought that symptoms of LOPD do not appear until late childhood and beyond. More recent evidence shows musculoskeletal symptoms can be observed even within the first year of life. Huggins et al. (2022) describes a varying clinical phenotype among 20 children 6-21 months of age diagnosed with LOPD. In all patients observed, postural and kinematic concerns were seen, even in those with normal disease biomarkers and normal scores on standardized functional assessments. This study supports previous evidence of clinical features of newborns and infants with LOPD, which noted other specific features such as swallowing difficulties, delayed motor milestones, and proximal weakness that otherwise would have gone unnoticed (Herbert et al., 2019; Rairikar et al., 2017). Other studies have shown that while noticeable symptoms may not be present, there are subclinical signs of muscle damage in these children as shown with MRI, ultrasounds, and muscle biopsies (Burton et al., 2017). This disrupts the notion that LOPD does not affect individuals until they have outwardly noticeable features and urges reconsideration of treatment protocols.

Studies have found that the use of ERT in individuals with LOPD improves quality of life, decreases ventilator use, and increases the ability to walk farther distances (Dornelles et al., 2021). However, ERT may not be helpful for up to one-third of individuals with LOPD, creating a time and financial burden that may not be necessary or advantageous for these patients (Toscano et al., 2013). Due to its inclusion on NBS, more individuals with LOPD are being identified before they have clear clinical features

(Kronn et al., 2017). The early signs of LOPD, such as subtle muscle weakness, can be mistaken for hypotonia or developmental delay in childhood. Because of this, it has been difficult for parents to identify what signs are concerning in their children, and when treatment should be sought out, even though an early diagnosis is meant to be advantageous in treatment timing (Lee et al., 2022).

A study regarding ERT efficacy in muscle tissue of infants diagnosed with LOPD in Taiwan showed that ERT may be most helpful when individuals are asymptomatic, but signs of the disease can be measured (Raben et al., 2010). This data is helpful but may not be as applicable to the United States, as the common intervening sequence splice site pathogenic variant c.-32-13T>G is not found in Taiwanese populations (Kronn et al., 2017). However, there are not clear guidelines for how to distinguish between individuals who are symptomatic or asymptomatic as early symptoms can be subtle or may be subclinical. This makes it challenging to decide when, and if, to initiate treatment with ERT. Beyond the parental/caregiver uncertainty in symptom onset, HCPs have also expressed a lack of knowledge in when and how treatment should be provided to this group of individuals. In a study done by Davids et al. (2021) out of 78 HCPs, less than 75% believed their state had sufficient resources for patients with LOPD, and more than 60% of providers cited their uncertainty of when to begin treatment as a barrier to LOPD care. A similar percentage of providers cited the lack of education about lysosomal storage disorders for pediatricians as a barrier. This overlap in uncertainty between medical professionals and parent understanding is not easily resolved, and further contributes to the high emotions experienced by parents and caregivers months after diagnosis.

1.5 Parental Emotions and Needs

Recently, there have been studies identifying some of the emotions experienced by parents of children with LOPD identified by NBS at the time of diagnosis, primarily with focus on uncertainty and fear. It has been shown that being "patients in waiting" may lead to parents easily becoming overly concerned for their child and not knowing what signs to be worried about (Pruniski et al., 2018). Two more studies did further qualitative interviews with parents of children with LOPD diagnosed by NBS to support and further elucidate the findings of Pruniski et al. (2018). One study conducted by Prakash et al. (2022) interviewed parents of 9 children and further emphasized the anxiety and frustration parents faced regarding the "lack of information, guidance, and psychosocial support." The parents also stated that while they support PD being included on NBS, more support is critical (Prakash et al., 2022). Another study conducted by Crossen et al. (2022) assessed 8 mothers' experiences on NBS for LOPD through interviews. Emotions such as grief, sadness, and gratitude were all expressed. The mothers described support in the forms of Facebook parent groups, family and friends, religion, and providers all as essential to their emotional wellbeing. This study also highlighted parents' desires to hear the NBS result from someone familiar with PD rather than being told to do research on their own (Crossen et al., 2022).

These feelings have been described similarly in parents waiting for confirmatory results from NBS exams for other conditions (Tluczek et al., 2005), and in those with genetic variants that have uncertain clinical outcomes (Macklin et al., 2018). With an LOPD diagnosis, parents must deal with both of those uncertainties and waiting periods; first, waiting for confirmation of a diagnosis, then waiting for symptoms to appear. While

PD is included on many NBS panels in the United States, many laboratories do not have molecular analysis capabilities to confirm the biochemical result and thus must send samples elsewhere to be sequenced, leading to an increased wait time between the initial screen positive and confirmatory diagnostic testing (Burton et al., 2017). Parents must come to terms with the emotions of having their apparently healthy child be diagnosed with a serious genetic condition, as well as understanding that there are no easy answers to what their child will experience and how they can help. These delays in the diagnosis itself are then more likely to increase fear and feelings of uncertainty in parents.

As described earlier, Davids et al. (2021) surveyed HCPs on their opinions regarding providing care for patients with PD and found that many providers felt HCPs were unable to comprehensively care for patients with LOPD. Some of the barriers included needing additional education about lysosomal storage disorders, needing official clinical practice guidelines, and uncertainty about when to begin treatment. Another study published in 2019 by Bansal et al. surveyed pediatric residents to assess their knowledge and attitude of NBS. Only 62% of residents from this study felt comfortable counseling an NBS result, and more than half did not know the appropriate follow-up for an abnormal result (Bansal et al., 2019). This highlights the importance of having access to genetics providers who can provide that appropriate care and shows where gaps in care may be for families who screen positive for any condition on NBS, but especially those conditions that are newer to the screen.

Despite general guidance being published by the Pompe Disease NBS Working Group in 2017, many unknowns about LOPD follow up care remain (Kronn et al., 2017). These barriers certainly add to the emotional distress levels of parents when trying to care

for their child. Not being able to consistently turn to healthcare professionals for guidance on an unfamiliar condition their child is identified to have can make this period especially overwhelming. Parental needs will not be fulfilled until provider needs are further met with resources and knowledge on how to care for these patients.

1.6 Genetic Counseling for LOPD

Genetic counselors are healthcare professionals that perform roles in helping individuals "understand and adapt to the medical, psychological, and familial implications of the genetic contributions to disease" (National Society of Genetic Counselors' Definition Task Force et al., 2006). Thus, genetic counselors are in a unique position of providing both clinical and emotional support to patients and their families. As PD is a genetic condition, it benefits patients and families to discuss the nuances of the condition in terms of inheritance, natural history, and management with professionals who study it. This can aid in parent and sibling understanding when the condition is first identified at birth and clarify next steps. As genetic counselors are well-suited to also address psychological considerations of a condition, evaluating and supporting parents and their emotional spectrums is a key part of the role.

Families often meet with a genetics team after initial disease diagnosis for this reason. This initial meeting can be surrounded by heavy emotion and upheaval of the life that parents imagined for themselves and their child. Many other factors may contribute to high emotional states or implement further barriers, such as language barriers, low health literacy levels, financial stress, and family system strain among countless other factors. Having medical professionals who are up to date on recommendations and research is imperative for continuing care and building a trustworthy relationship within

healthcare, as evidenced by the need for more pediatrician education and guidelines in Davids et al. (2021).

Those providing genetics services must be able to counsel on the management of the condition, identify other family members that may require testing, the risk of recurrence, and finding a supportive community within which to find solace. Beyond this, providing resources to help reduce those previously mentioned barriers and not rushing the family through information is all part of the role of a genetic counselor. This genetics team may be visited for years to come as guidelines change and the child continues management, and thus is an important part of the healthcare journey that the patient and their families undertake. Therefore, having a good initial NBS experience with genetics providers is essential for the continued rapport between family and the medical team and to build trust in the healthcare system. Establishing genetics professionals can do better to improve that initial impression and the care that follows is imperative to the good healthcare of patients and their families.

Beyond this, genetic counselors and other genetics providers are outnumbered by the number of families that may benefit from their services. This leads to many families hearing about genetic conditions for the first time from other providers such as pediatricians and nurses who may not feel as comfortable discussing genetics topics without guidance from a geneticist or genetic counselor (Davids et al., 2021).

1.7 Rationale

Previous studies have identified that parents of children with LOPD diagnosed by NBS experience strong emotions and concern over their children related to their condition (Crossen et al., 2022; Prakash et al., 2022; Pruniski et al., 2018). Studies have

also shown that HCPs do not feel able to adequately provide for patients with LOPD due to many of the same reasons that parents experience anxiety (Davids et al., 2021). To our knowledge, this study is the first of its kind looking at more than 10 individuals within this population assessing how anxiety levels can change over time and how genetic counseling may influence those levels. There is limited knowledge on what resources and information are helpful not just at the time of diagnosis, but also throughout the years afterwards. This study will provide genetic counselors and those providing genetic services with better insight into what parents of children with LOPD may find useful both initially and beyond, and how those change over time. This is a unique data set that presents advantages in understanding the current benefit of genetic counseling to these families. By getting this knowledge directly from parents to create a set of recommendations for genetics providers, part of the care barriers described previously can be reduced.

1.8 Purpose of Present Study

The aim of this study was to assess the emotional distress of parents of children who received a diagnosis of LOPD via NBS and investigate how genetic counseling impacts those parents' emotions. Additionally, this study aimed to identify which genetic counseling resources are helpful and how genetic counseling may improve patient and parent experiences with an LOPD diagnosis.

We predicted that genetic counseling impacts the levels of emotional distress in parents of children with LOPD diagnosed by NBS. We also predicted that there are areas of genetic counseling that can be improved to better help parents manage their child’s diagnosis and their own mental wellbeing. Results from this study may indicate a need

for the development of genetic counseling practice recommendations for individuals with LOPD and their parents. The objectives were as follows:

1. Analyze the changes in parental emotional distress and coping levels from initial diagnosis to subsequent follow up visits;
2. Identify unmet needs of parents of children with LOPD diagnosed on NBS; and
3. Develop a set of genetic counseling recommendations to improve patient care and parental well-being after LOPD and other late-onset disease diagnoses that may be utilized by genetic counselors and other HCPs involved in patient care.

CHAPTER 2:

EXPERIENCES OF PARENTS OF CHILDREN WITH LATE-ONSET POMPE DISEASE DIAGNOSED BY NEWBORN SCREENING[1]

[1] Paltzer, A., Zvejnieks, D., Huggins, E., Kishnani, P., Linebaugh, E. To be submitted to *Journal of Genetic Counseling*

2.1 Abstract

Pompe disease is an autosomal recessive lysosomal and glycogen storage disorder. It is classified as either infantile-onset Pompe disease (IOPD) which is characterized by severe muscle weakness and enlarged heart shortly after birth, or late-onset Pompe disease (LOPD), which is characterized by more slowly progressive weakness without cardiomyopathy or obvious muscle weakness at birth. Pompe disease was added to the Recommended Uniform Screening Panel (RUSP) for newborn screening (NBS) in 2015 as early treatment with enzyme replacement therapy is lifesaving for children with IOPD. However, most patients identified via NBS have LOPD, which does not require immediate treatment and may not present until childhood or adulthood. There are not yet clear guidelines for management and treatment of children with LOPD diagnosed via NBS which creates a challenge for both clinicians and parents.

This study explored the experiences of parents whose children were diagnosed with LOPD by NBS. Surveys containing multiple choice and free text questions were collected from 42 parents to assess their experiences with diagnosis and follow up, access to services, and the emotional impact of the diagnosis. The majority (70.7%, 29/41) of parents stated their anxiety levels decreased over time since their child's diagnosis. Out of those parents that saw a genetic counselor and explicitly commented on that experience, 71.9% (23/32) stated meeting with a genetic counselor impacted their ability to manage their child's diagnosis. The primary areas of genetic counseling impact included accessibility, providing resources, aiding in understanding of diagnosis, making a treatment plan, and supporting parental mental health. Parents emphasized the necessity

of healthcare provider (HCP) knowledge on conditions like LOPD, the prolonged feeling of uncertainty years after diagnosis, and the benefit of having a good support group and healthcare team on anxiety levels. Knowledge of parental experiences and needs is important as more individuals with late-onset conditions continue to be identified by NBS. Information on where to improve can help HCPs better serve individuals and families affected by these conditions.

2.2 Introduction

Pompe disease (PD) is an autosomal recessive lysosomal and glycogen storage disorder involving progressive muscle weakness and respiratory failure. The condition has two major types, late-onset Pompe disease (LOPD) and infantile-onset Pompe disease (IOPD) and affects approximately 1 in 23,000 people in the United States (Park, 2021). The primary differences between the two is that IOPD presents at birth with enlarged heart and rapidly progressing muscle weakness, whereas LOPD can present at any time with more slowly progressive muscle weakness without an enlarged heart at birth. IOPD can also present with failure to thrive and absent deep tendon reflexes. LOPD further involves fatigue, chronic pain, and skeletal abnormalities (Chan et al., 2017; Hamed et al., 2021). The condition is caused by pathogenic variants in the *GAA* gene leading to a deficiency of acid alpha glucosidase, also known as acid maltase or GAA. This is an enzyme involved in glycogen breakdown, leading to glycogen build-up in the skeletal and cardiac muscles. IOPD is typically fatal by two years of age in those that do not receive treatment. The condition is also life-limiting in individuals with LOPD depending on age of onset, severity of symptoms, and treatment status (Atherton et al., 2017), though individuals with LOPD are expected to live into late adulthood.

After diagnosis, most patients and families meet with a team of medical genetics specialists. One member of that team is typically a genetic counselor. Genetic counselors are healthcare professionals that perform roles in helping individuals "understand and adapt to the medical, psychological, and familial implications of the genetic contributions to disease" (National Society of Genetic Counselors' Definition Task Force et al., 2006). The team helps coordinate medical management and treatment when indicated for both forms of the condition, along with providing disease education throughout the lifespan.

In 2015, PD was added to the Recommended Uniform Screening Panel (RUSP), a national guideline in the United States that guides states on which conditions to include on their NBS panels. This has led to 38 states adding PD to their NBS panels in the years since (NewSTEPs, 2023). PD is screened for by measuring the amount of GAA in dried blood spots at birth. As both IOPD and LOPD have lower amounts of GAA, both conditions are screened for at birth (Burton et al., 2017). This has led to individuals being diagnosed with LOPD months, or even years, before having apparent symptoms of the condition, as the majority of those diagnosed with PD have LOPD versus IOPD.

There is approved treatment for PD in the form of enzyme replacement therapy (ERT). There are currently two approved ERT medications for PD, starting with alglucosidase alfa in 2006 (for IOPD and LOPD) and followed by avalglucosidase alfa in 2021 (for LOPD only). Both have shown to significantly improve most, if not all, clinical features associated with PD if started in a timely manner. ERT is both time-consuming and costly, requiring weekly or bi-weekly infusions and costing up to $379,000 annually without insurance (Richardson et al., 2021; Schoser et al., 2019). Treatment for IOPD is most effective when implemented immediately after diagnosis, making it important to

identify the condition at birth. Historically, ERT treatment for LOPD has been implemented at the time of symptom onset (Chien et al., 2015). As more individuals are diagnosed with the condition long before they have noticeable features, more research will need to be done on the efficacy of ERT and most effective timing strategies. Recent studies have shown that some children have signs of the condition both physically in muscle weakness and in biomarkers that otherwise would have gone unnoticed, allowing for treatment to be initiated sooner (Herbert et al., 2019; Huggins et al., 2022; Rairikar et al., 2017). Before NBS, diagnostic odysseys for LOPD ranged from less than a year to up to 40 years (Lagler et al., 2019; Lisi & Ali, 2021). Identifying the condition at birth may lead to advancements in treatment protocols and more information on the natural history of LOPD. Even so, the current lack of clarity for families and providers affected by this condition necessitates further exploration on what is helpful versus harmful regarding NBS for PD.

Recent studies have shown that parents of children with LOPD identified by NBS experience primarily uncertainty and fear at the time of diagnosis. Parents emphasized the need for further psychosocial support and provider knowledge while also being grateful for the diagnosis and access to treatment (Crossen et al., 2022; Prakash et al., 2022; Pruniski et al., 2018). The lack of HCP knowledge is supported by studies showing that the majority of HCPs feel their state is unable to sufficiently provide for children with LOPD and more than half of pediatric residents are uncomfortable talking about NBS results (Bansal et al., 2019; Davids et al., 2021). While the presence of LOPD on NBS is generally supported by individuals with the condition and families affected by it, more work needs to be done exploring how HCPs can better provide for this population

(Lisi & Ali, 2021; Lisi et al., 2016). Genetic counselors and other genetics providers are uniquely positioned to care for this patient population and provide both education and psychosocial support. This study marks the first research done assessing the efficacy of genetic counseling within this patient population and their families.

2.3 Materials and Methods

2.3.1 Participants

Approval for this study was obtained from the University of South Carolina Institutional Review Board (Pro00122436). Participants included in this study were parents of children diagnosed with LOPD by NBS. Some participants were also part of an IRB-approved Duke University study researching LOPD (Pro00100223). Participants were required to read and write in English. No other exclusionary criteria applied.

2.3.2 Research Methods

A message inviting individuals to participate in the survey was posted to several LOPD parent Facebook support groups. The invitation was also sent by email to parents enrolled in the previously mentioned Duke University study by one of the authors of this study, EH. Participation in the survey was voluntary and completing the survey served as consent to participate. The survey consisted of a combination of multiple choice and free response items. Qualtrics was used to design and collect survey data. The items inquired about initial experiences with the positive NBS and confirmatory testing, as well as questions around access to care, changes in anxiety levels since diagnosis, and the impact of genetic counseling. All participants remained anonymous during data analysis. Identifying information was collected from parents who were enrolled in the Duke study

but removed for subsequent analysis. No identifying information was collected from the parents recruited from Facebook support groups.

2.3.3 Data Analysis

Raw data were input into Microsoft Office Excel from Qualtrics for descriptive statistical analysis. Data from participants of the Duke University study were accessed through a secure shared drive before being input into Microsoft Office Excel. Further statistical analysis was performed using Kruskal Wallis tests through Statistical Package for Social Sciences (SPSS) software to determine relationships between specific dependent and independent variables. A p-value of ≤ 0.05 was considered statistically significant. Free-text questions were analyzed for themes by two authors of the study (AP and DZ). Themes were coded and analyzed for frequency using a grounded theory approach. Tables and figures were constructed with Microsoft Office Excel. Participants who completed less than 80% of the survey were excluded from analysis.

2.4 Results

2.4.1 Demographics

The survey sent out through Facebook support groups received 66 total responses. Responses that were at least 80% complete were included in analysis, which totaled to 28 responses. Twenty-five individuals (37.9%) did not complete any of the survey. The survey sent to parents who previously participated in the Duke University LOPD study received 14 responses, all of which were complete (100%). The total number of surveys analyzed was 42 between the two sets of data.

Most of the participants that took this survey were mothers of children with LOPD (41/42, 97.6%), with one father participating (1/42, 2.4%). Six children were

reported to be less than one year (14.3%), nineteen were reported to be 1-3 years (45.2%), and seventeen were reported to be 4+ years old (40.5%). Ages reflect the child's age at the time of survey completion.

2.4.2 Diagnostic Experiences

Parents first reported their experiences with NBS result disclosure (Table 2.1).

Table 2.1 Disclosure of NBS Results

Disclosure of NBS Result (n = 42)	Total (n)	Percentage (%)
Who first informed you of your child's positive NBS result?		
Geneticist	10	23.8%
Nurse	6	14.3%
Pediatrician	23	54.8%
NICU doctor	1	2.38%
Neonatal physician	1	2.38%
How long after birth did you receive the positive NBS result?		
3-5 days	10	23.8%
7+ days	30	71.4%
Over one month	2	4.76%
How long after NBS positive did you see a HCP to confirm?		
Within 48 hours (2 days)	14	33.3%
Within 3-5 days	11	26.2%
7+ days	13	31.0%
Over one month	3	7.14%
Unsure/I don't remember	1	2.40%

Most participants received their NBS positive result from a pediatrician and a week or more after birth. Participants further expanded on their positive and negative experiences with the screening disclosure, presented in Table 2.2 and Table 2.3.

Table 2.2 Positive NBS Disclosure Experiences

Theme	Frequency (n = 42)	Quotes
Information on Pompe/treatments	18 (42.9%)	"[It was helpful] knowing that if the time came, there was a treatment option available." "The most helpful information was that medicine has improved a lot and there are new treatments."
Encouraged not to Google/dated online information	16 (38.1%)	“They did not tell us how outdated Google was and didn’t have a lot of answers.” “I was told that the information [online] was old data and was not current. I was actually given very limited data on what [PD] was.”
Information on next steps provided	13 (31.0%)	"Most helpful was [the] name of [the] geneticist that would be our best point of contact."
More testing needed to confirm diagnosis	10 (23.8%)	“[I] was told that NBS came back flagged for [PD], but they need to run more tests to confirm diagnosis since sometimes these results can be false positives.”
Everything was helpful	4 (9.50%)	"We were given clear, concise, yet overwhelming info. Nothing we were told was not helpful."

Helpful information from the NBS results disclosure included information on PD and treatment, encouragement not to Google the condition or that online information was dated, information on next steps, and that more confirmatory testing was needed. Four parents mentioned that everything they were provided was helpful. Some parents found the advice not to search the condition online as helpful, and others stated it as very unhelpful. One parent mentioned, “We of course Googled it. We had zero knowledge about the disease, and didn’t realize that there were different types,” implying that the advice not to Google the condition should be supplemented with information to fill the knowledge gap. Others mentioned that they wished they had been told not to Google PD, saying “I wish I had been told NOT to look up Pompe disease before she started her

diagnosis journey because the information you come to first on the internet does not necessarily pertain to my child."

Table 2.3 Negative NBS Disclosure Experiences

Theme	Frequency (n = 42)	Quotes
Lack of guidance/information	17 (40.5%)	"All information that was given to me was extremely vague, not helpful, and we were terrified." "I didn't receive any information. I just held out hope that the test was wrong."
Lack of HCP knowledge	12 (28.6%)	"It's an uneasy feeling that even professionals in a highly regarded practice hadn't heard of Pompe disease before." "Our pediatrician was not familiar with Pompe, nor did he have any helpful information."
Uncertainty	12 (28.6%)	"Our pediatrician did not know what it was or what would happen when the results came back. I called [our state] department of health multiple times for answers and got vague indications that it was going to next steps of testing. It was a very scary and not transparent process."
Possibility of a false positive	8 (19.0%)	"Our pediatrician had no idea what it was and basically told us it could have been a lab mistake and not to worry [...] She tried to reassure us there was nothing wrong when there actually was."
Nothing was helpful	7 (16.7%)	"We were not given helpful information. No reputable websites to look at for up-to-date information, no handout with any information on Pompe disease, no information on what the next steps were."

Participants were also able to further comment on their experiences once diagnosis was confirmed, specifically what was helpful versus unhelpful. Themes from these comments are displayed in Table 2.4 and Table 2.5.

Table 2.4 Positive Confirmed Diagnosis Experiences

Theme	Frequency (n=42)	Quotes
Explanation of symptoms/labs	9 (21.4%)	"Handouts with Pompe disease information we could take home and read/reread/share with family [were helpful]."
Everything was helpful	8 (19.0%)	“All the information was helpful, our genetic counselor at the time was amazing.”
Specialist information	8 (19.0%)	"I felt like we were kind of guinea pigs. I asked what all this meant, and we were directed to the team at [specialty clinic]. Being connected [there] is what gave us hope and clarity." "We were given phone numbers and emails of the people we would need to talk with before we left so we didn't have to look them up."
Treatment information	6 (14.3%)	"It was helpful to know that there is a treatment for the disease because if not we could have been looking at a different future."
Comfort in prognosis of condition	5 (12.0%)	"I remember [our geneticist] saying 'She will outlive you' and that really helped. At that time, I was most worried about losing my daughter so her confidence in [her] life expectancy was what gave me the most ease."

Table 2.5 Negative Confirmed Diagnosis Experiences

Theme	Frequency (n = 42)	Quotes
Uncertainty	11 (26.2%)	"[It was unhelpful] that there was no way to tell how severe it would be, when the onset would be, and if we could do anything to help."
Too little/too much information	6 (14.3%)	"I do wish there was more of an information packet that gives up to date information." "The geneticist gave us way too much information about genetics and how things are passed on […] It was scary and overwhelming." "I was completely lost many times [;] they speak with a medical jargon that was way over our heads."
Nothing was helpful	4 (9.50%)	"I wouldn't say anything was helpful. The testing in [state] is extremely new and lacking […] through our research, we found a lot more about her specific variation than we were able to get from any other meeting."

Regarding resources provided at the time of diagnosis, 57.1% (24/42) of parents reported they did receive resources, 35.7% (15/42) reported they did not receive any resources, and 7.1% (3/42) reported they were unsure or didn't remember if they received any resources (Figure 1.1).

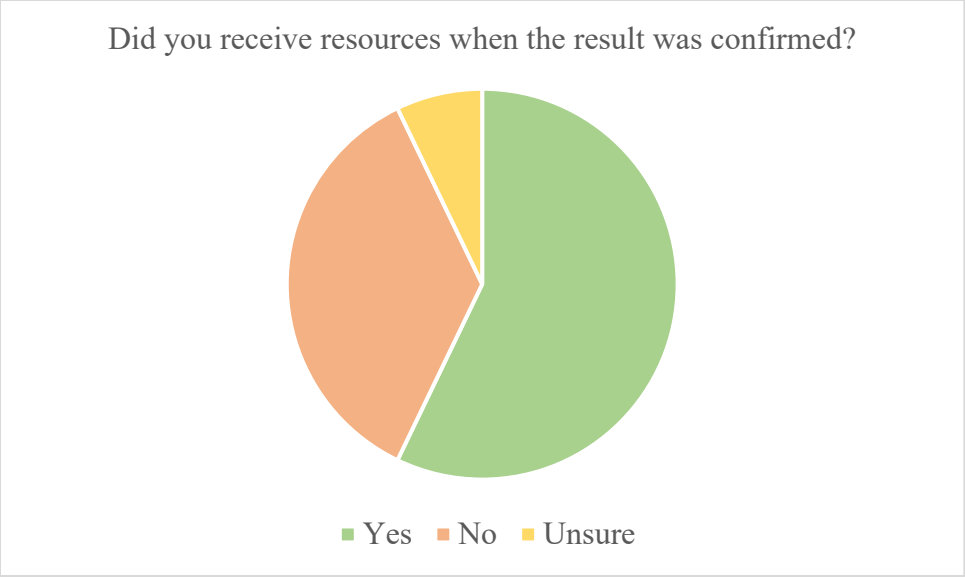

Figure 2.1 Pie chart displaying if resources were provided when LOPD diagnosis was confirmed.

We also asked what resources parents received and whether or not they were helpful. Twelve (28.6%) parents explicitly mentioned that information on specialists of LOPD was a helpful resource given at diagnosis. Eight (19%) parents wrote that they were provided with a pamphlet or paper detailing LOPD. One parent stated that "handouts were helpful to take home with us as we processed the diagnosis." Two other parents mentioned that the pamphlets were either "somewhat" or "not" helpful. Resources mentioned 1-2 times in the responses that were noted to be helpful include insurance resources, support group information, PT guides, and websites. Seven (16.7%) parents described a lack of resources provided. One parent described that the papers given to them were IOPD focused rather than LOPD. Others stated that the most resources they were provided were page dividers with a binder.

2.4.3 Familial Testing

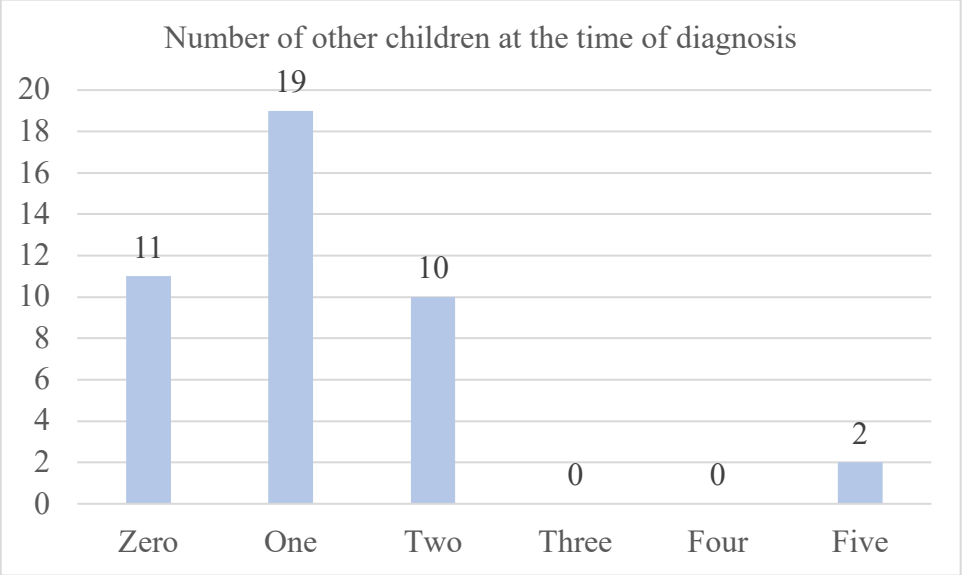

Figure 2.2 Bar chart describing the number of other children the participants had at the time of their child with LOPD's diagnosis.

Parents were also asked about other children in the family. Thirty-one parents (73.8%) had other children prior to their child with LOPD's diagnosis. Of those 31 parents with other children, 26 (83.9%) stated that testing other children for LOPD was a major concern at the time of their child's NBS result and diagnosis. Five out of the 31 parents (16.1%) stated that testing other children was not a main concern at the time of diagnosis and 11 parents (26.2%) did not have other children at the time. Five (11.9%) of the parents have another child with LOPD. It was not differentiated between when that child was born and/or tested for LOPD on this survey.

2.4.4 Access to Care

ERT status and ease of access to medical services such as ERT and physical therapy were assessed. One-fifth (20.6%, 7/42) reported their child was currently receiving ERT, 81% (34/42) reported their child was not currently receiving ERT, and 2.4% (1/42) reported that their child would begin ERT within the next 3 months.

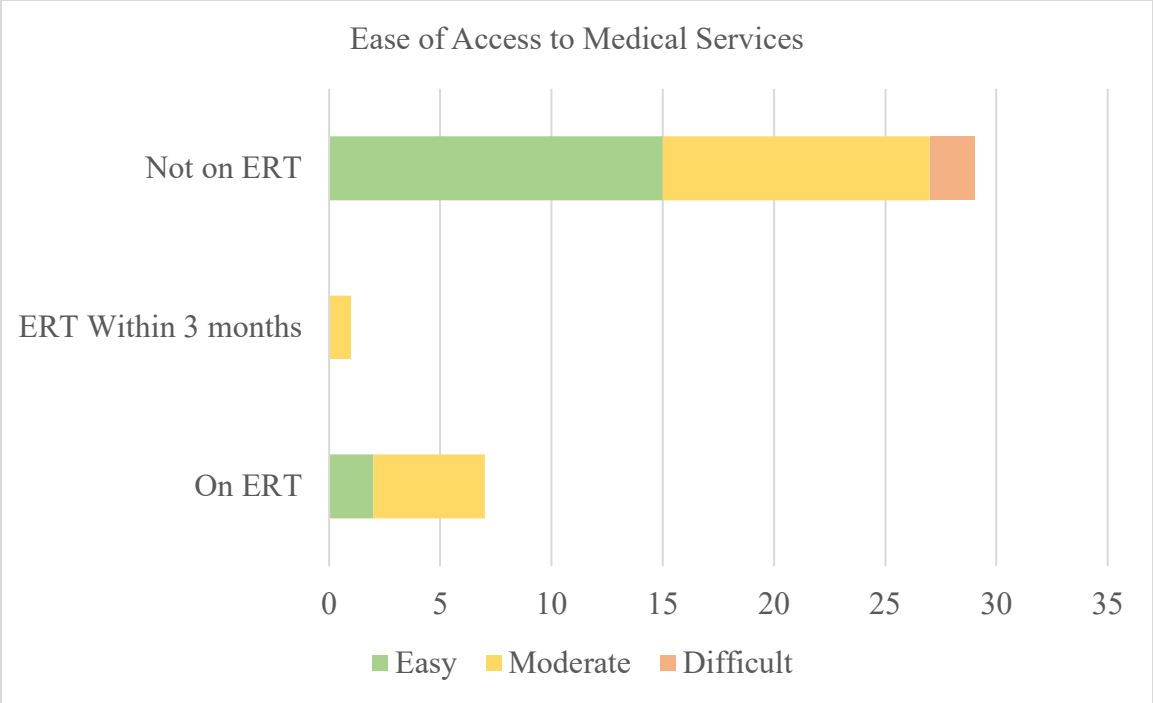

Figure 2.3 Bar chart describing ease of access to medical services. Medical services include ERT, physical therapy, and other appointments.

Of those not receiving ERT services, 51.7% (15/29) reported it has been easy getting medical services for their child at the recommended intervals, 41.4% (12/29) reported it has been moderate, and 6.9% (2/29) reported it has been difficult (Figure 2.3). Of those on ERT, 28.6% (2/7) reported it has been easy getting medical services and 71.4% (5/7) reported it has been moderate. The individual whose child was scheduled to begin ERT within 3 months of the survey completion reported it has been moderately difficult getting medical services. Combining all three groups, 46% (17/37) stated it was easy getting services, 48.6% (18/37) stated it was moderate, and 5.4% (2/37) stated it was difficult. No significant difference was seen between ERT status and ease of access to services (p-value=0.518, test statistic=1.316). Parents expanded upon their answers in a free response section (Table 2.6).

Table 2.6 Experiences Accessing Healthcare Services

Theme	Frequency (n = 42)	Quotes
Logistics of care as a barrier	15 (35.7%)	"There were a lot of tears [while setting up home infusions for ERT] because I was stressed about finding a nurse who could access my son's port and would travel to where we live." "We have received the medication late more than [once] and I have to [call] the pharmacy every month to make sure [the] shipment is on time." "The area where we live has zero resources. We tried using a PT here and they acted like our son didn't really need the help." "It's been hard feeling like no one really knows much about her diagnosis. Each appointment we've had, there's been some issue with someone not knowing how to code something in their system, or them not having a protocol set up, or the nurse literally never hearing of Pompe disease and giving us hope for a false positive. The whole thing has been very isolating and hard."
Great providers	13 (31.0%)	"The providers are excellent and even come to our home for services." "[Our team] has always been fantastic at communicating and being able to bring information and communicate with physical therapists here has been helpful in getting the care we need."
Insurance/financial difficulty	6 (14.3%)	"My insurance has been the most cumbersome." "With the ERT, the cost was quite expensive after insurance and until we got the financial assistance, it was quite difficult."
Long wait times	4 (9.52%)	"PT was easy to set up, just took a while for anything to actually get started." "Referrals and scheduling for specialist doctors has been hard (even before COVID) with months stretching out in-between appointments."
Easy to schedule appointments/access team	4 (9.52%)	“Having access to the geneticist at our local pediatric hospital has been very easy. We can get appointments when needed and they are very receptive to answering questions."
No services needed for now	4 (9.52%)	“We have not needed services, yet.”

2.4.5 Anxiety Changes

Parents were asked how their anxiety levels changed from time of diagnosis to today. Duke University study participants were asked this in a series of two questions. The first asked how their anxiety changed from time of diagnosis to after their first genetic counseling session at Duke University. The second question asked how their anxiety changed from the first genetic counseling session within the study to the most recent (Figure 2.4). This study did not ask about prior genetics visits at other clinics before or between Duke University study visits. Anxiety levels then directly relate to being seen at a specialty clinic rather than general genetics like other participants from Facebook support groups.

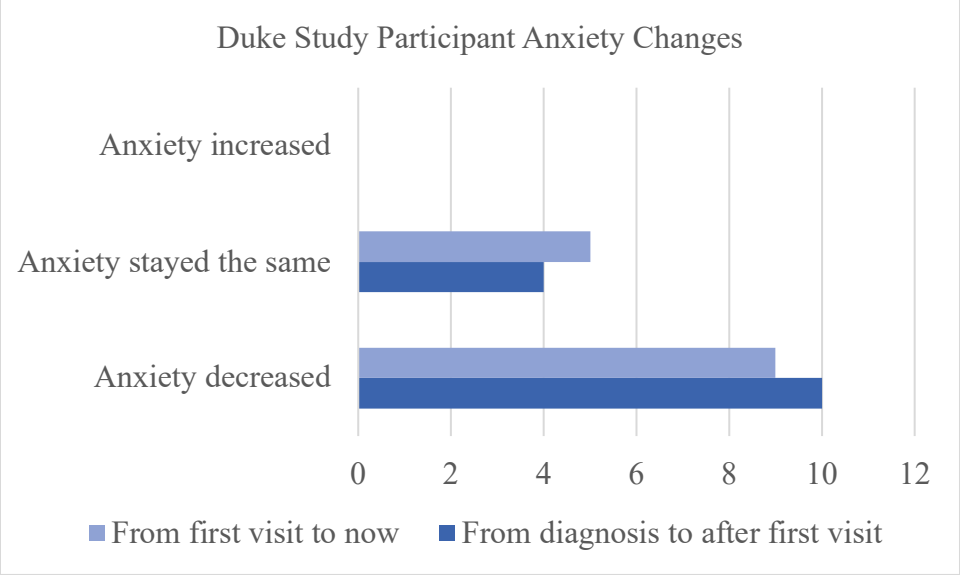

Figure 2.4 Bar chart describing Duke study participants' anxiety changes.

Most (71.4%, 10/14) study participants stated their anxiety levels decreased after their first visit at Duke University. Four (28.6%) participants stated their anxiety levels stayed the same after their first visit. Similarly, most (64.3%, 9/14) participants stated their anxiety levels have decreased in the time in-between the first study visit to now. Five (35.7%) stated their anxiety levels have stayed the same from their first visit to their

most recent study visit. Five participants had different answers between the two questions. Three participants stated their anxiety decreased after the first visit and has stayed the same since. Two participants stated their anxiety stayed the same after the first visit and has decreased since then.

All participants, including those in the Duke University study and those in Facebook support groups, were asked how their anxiety levels changed from the point of diagnosis to the time of survey completion. The majority (70.7%, 29/41) of parents stated their anxiety levels decreased over time since their child's diagnosis. A few (12%, 5/41) parents stated their anxiety increased over time. Some (17.1%) parents reported their anxiety levels are about the same as what they were at diagnosis. Free-text responses were further analyzed for themes that could contribute to the change or stagnation in anxiety levels (Table 2.7). There was no significant difference between anxiety change and current age of child (p-value = 0.692, test statistic = 0.736).

Table 2.7 Causes of Anxiety Changes

Theme	Frequency (n = 42)	Quotes
Increased knowledge	17 (40.5%)	"What has helped ease anxiety the most [has] been being well informed and understanding Pompe itself."
Great healthcare team	14 (33.3%)	"[The team is] caring, specific, understanding, etc. They make me and my child feel like people, not numbers." "Our team has been the most informative, and given us the most hope, while still being straightforward and explaining things in a way that we can understand." "There are concerns about the future, but we know that we have a very capable team who are being proactive."
Uncertainty	12 (28.6%)	"I had bad anxiety to begin with. It's worse now - I'm constantly wondering if she's meeting her milestones, or if she's lagging behind in anything. Every time we're waiting on a test result, I get anxious." "I think the anxiety of not knowing what to expect is always there when starting something new." "Fear of the unknown and what's to come will always be a part of this, but I feel like the more informed we are the better."
Progression/lack of symptoms	11 (26.2%)	"I feel so much better now after the reassurance from doctors that my daughter is doing well." "Seeing [my child] thrive because of the interventions that have been initiated so early allows me to find some peace amongst the chaos."
Support groups	7 (14.3%)	"My anxiety decreased after that first week as I joined social media pages for parents." "Through social media I have [met] so many other parents and grown adults with the condition." "The community I have found on Facebook has assured me my son has a great chance to live a somewhat normal and fulfilling life!"
Faith	3 (7.10%)	"My anxiety has decreased because I have put my fear in God's hands and I'm taking it one day at a time."

The only theme in Table 2.7 that was associated with increased anxiety levels was uncertainty. All participants who mentioned that uncertainty contributed to anxiety levels were included in the frequency total. This includes some participants whose overall anxiety levels have decreased over time.

2.4.6 Genetic Counseling Experiences

Figure 2.5 displays participant experiences with genetic counseling. A few participants (12%, 5/42) reported they had not met with or were unsure whether they had met with a genetic counselor. We asked directly if meeting with a genetic counselor impacted parents' abilities to manage their child's diagnosis. Those that had not met with a genetic counselor and/or did not comment on whether or not an impact was made were excluded from analysis. Of the 32 participants that saw a genetic counselor and directly commented on those experiences, 28.1% (n=9) stated seeing a genetic counselor did not impact their ability to manage their child's diagnosis and 71.9% (n=23) stated seeing a genetic counselor did impact their ability to manage their child's diagnosis. Two individuals (4.8%) stated their genetics team as a whole made an impact but did not specify genetic counselor.

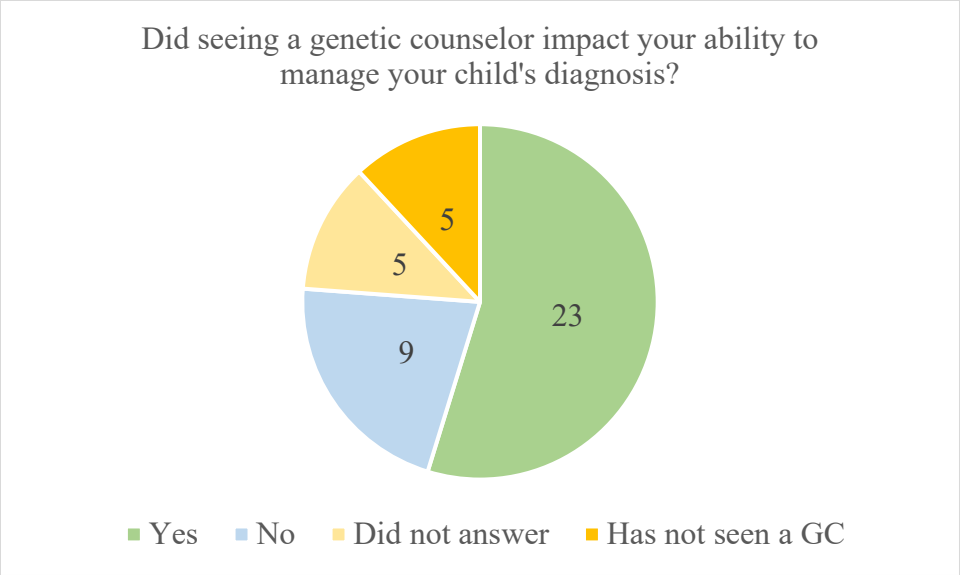

Figure 2.5 Pie chart describing impact of genetic counseling on diagnosis management.

For those that saw a genetic counselor, the primary areas of impact were ease of accessibility (4/34, 11.8%), providing resources (5/34, 14.7%), aiding in understanding of the diagnosis (15/34, 44.1%), making a treatment plan (7/34, 20.6%), and supporting the mental health of parents (5/32, 15.6%).

Participants were also asked if there was a member of their healthcare team who they routinely go to when they need something. Two-thirds (66.7%, 28/42) said they did have someone, 19% (8/42) said they did not have someone, and 14.3% (6/42) stated they were unsure if they had someone they routinely go to. The title of that person they routinely go to widely varied and included genetic counselors (11), nurses (4), physicians (9), clinical coordinators (6), and physician assistants (2). Some participants listed more than one individual.

At the end of the survey, participants had the chance to provide any other information they believed was important for us to know. Some parents re-emphasized the need for HCPs to be knowledgeable on the conditions on their state NBS panels. Others

specified the need for more resources to be made widely available for HCPs to disperse, including support groups, community resources, and overall, more medical information to provide at time of screen positive and diagnosis confirmation.

2.5 Discussion

2.5.1 Response Rate

Overall completion rate for the Facebook support group survey was 42.4% (28/66). Completion rate may be low for several reasons. Twenty-five individuals (37.9%) did not complete any of the survey. This may be because they realized they did not fall within the survey participant requirements after reading the description, or perhaps because they decided not to fill it out at that moment due to survey length or other factors. The biggest drop-off of participation happened at the first free-response question, implying some participants may have been willing to fill out a multiple-choice survey but not one with free-response questions.

2.5.2 Diagnosis Experiences

Most of this study's participants received their result from a pediatrician after a week or longer. The HRSA recommends that NBS results be disclosed to providers within a week after birth due to the timely nature of conditions on the panel (HRSA, 2017). The delay parents reported in receiving this result encourages re-evaluation of the efficacy of current NBS practices.

The most common helpful experiences reported by parents at time of receiving the screen positive result include information on next steps and further testing, information on the condition, treatment availability, and the directive not to search for the condition online. These findings have been similarly noted before as being involved in

NBS disclosures without qualifiers on benefit (Prakash et al., 2022). Helpful experiences at the time of confirming the diagnosis included specialist information, treatment information, comfort in disease prognosis, and explanation of symptoms and labs. Access to specialty care centers was highlighted as a helpful experience in Prakash et al. (2022), along with viewing treatment as a hopeful prospect; having specialist and treatment information as positive experiences at diagnosis aligns with those findings. Pruniski et al. (2018) discussed the process of normalization and relative adversity as being involved in coping with a diagnosis. The findings of being comforted in disease prognosis at time of diagnosis supports this previous research.

Uncertainty was the most common overall feeling mentioned throughout the NBS result and diagnosis. This finding has been well reported by previous studies and continues to be an important aspect of LOPD diagnosis that requires addressing (Crossen et al., 2022; Prakash et al., 2022; Pruniski et al., 2018). While HCPs and genetics providers cannot take that uncertainty away, acknowledging those feelings and providing ways to cope with them are action steps that can be taken to provide further support to parents.

Another common negative experience was lack of HCP knowledge on the condition as well as lack of guidance and information given to parents. This supports and enhances previous research performed by Crossen et al. (2022) that emphasized parents' desires to hear genetic testing and screening results from individuals who are familiar with the conditions rather than being told to do research on their own. Crossen et al. (2022) also highlighted parents' emphasis on the importance of provider education on NBS disorders. It is helpful to know that parents are looking for more information and

resources at the time of the positive screen even if in many cases the result is not a true positive. For those that ultimately receive a diagnosis of LOPD or otherwise, their initial experiences may lead to mistrust or low confidence in the healthcare system.

Further resources should be made available to HCPs disclosing NBS results. Research done by Davids et al. (2021) has shown that one-fourth of HCPs do not feel their state has the appropriate resources to provide for newborns diagnosed with LOPD. HCPs also cited multiple barriers for providing for newborns diagnosed with LOPD at birth, including uncertainty by HCPs of when to begin treatment, a lack of clinical practice guidelines and recommendations available, and the need for additional education about LSDs for pediatricians (Davids et al., 2021). Additional research has shown that more than half of pediatric residents are unaware of the correct follow-up for an abnormal NBS result, and more than a third do not feel comfortable counseling on an NBS result (Bansal et al., 2019).

More commitment to provider education should be undertaken to ensure that HCPs are comfortable disclosing NBS results and know the appropriate avenues of referral. This may be seen in the addition of genetics specific courses during medical school or residency training or having genetics providers give continuing education on related topics. NBS state programs and testing centers may also provide specific educational materials for providers for each condition so that providers feel comfortable talking about the results with parents and caregivers. All HCPs are able to provide genetic counseling to some extent; having the tools to do so is one step in ensuring families are receiving the care they need.

At the time of diagnosis, 35.7% of individuals reported they received no resources. A lack of resources has been previously reported, with Prakash et al. (2022) stating that many parents had to seek out resources on their own and Crossen et al. (2022) reporting online search engines such as Google as a primary source of information for parents. This study expanded upon previous work done regarding resources given to parents at the time of diagnosis. Knowledge that more than a third of parents did not receive resources at diagnosis encourages a change in how HCPs provide for families with this diagnosis. Providers should be ready and willing to not only provide information to parents at the time of screen positive and throughout diagnosis, but also have resources for parents on hand so that they do not feel they have to turn to the internet where much of the information is outdated. Prakash et al. (2022) has published a list of resources for families and providers related to LOPD that may be referenced.

2.5.3 Access to Care

The majority of participants reported their child was not receiving ERT. As many of these children are likely not showing apparent symptoms and with the unclear treatment guidelines, this was an expected result. Most participants also described their access to care as either easy or moderate. While no significant difference was seen between how parents with children on ERT responded versus those whose children are not on ERT, we had very few parents with children on ERT respond to the survey. More research can be done in the future to further clarify the differences in treatment access between those on ERT and those not as more individuals identified by NBS start treatment as their symptoms present over time.

The most common positive theme that parents reported in accessing care was having good experiences with their providers. Participants described satisfactory care in several ways, including having a team who is compassionate, dedicated, accessible, and knowledgeable. Crossen et al. (2022) mentioned that some parents found support from their providers in the form of education, psychosocial support, and reassurance; this can be extended to the care patients and their families receive from providers. Many parents described various barriers in access to care, even for those that reported overall easy access. The logistics of care, including but not limited to, scheduling appointments and access to knowledgeable medical professionals, was the most reported difficulty in access to care. Scheduling difficulties and taking time off work for appointments were also noted by some parents in Crossen et al. (2022).

Financial and insurance strain was a theme in this study. Several parents mentioned this specifically as being a barrier to care. This is the first study within this population to our knowledge that has reported on parents currently or previously experiencing financial strain due to LOPD management. Previous studies have reported that parents of children with LOPD anticipate insurance difficulties in the future but had not experienced them yet (Crossen et al., 2022; Prakash et al., 2022; Pruniski et al., 2022). Support services and ERT treatments are estimated to be upwards of $450,000 a year without insurance for individuals with IOPD, though those numbers vary significantly with symptom presentation and services required (Richardson et al., 2021; Schoser et al., 2019). Numbers for LOPD are not as accessible but are likely similar once ERT begins. Being diagnosed at birth leads to additional financial burdens since ERT and surveillance can be started immediately instead of waiting until the diagnostic odyssey

concludes, possibly years after symptom-onset. As this is a newer situation, it is uncertain how much difference this increased surveillance and ERT will make in clinical outcomes for those with LOPD, particularly since it is not yet recommended that infants diagnosed with LOPD begin ERT at time of diagnosis. A few parents mentioned resources for financial aid and support from ERT companies which significantly reduced costs and may be avenues other providers can be attentive to when caring for these families.

2.5.4 Anxiety Changes

Most parents reported that their anxiety levels decreased since their child's diagnosis. To our knowledge, this is the first study directly examining this factor as it relates to time. Prakash et al. (2022) described parental emotions leveling out over time, but not anxiety-specific feelings and what elements aided in changing or not changing those levels. There was no significant difference between anxiety level change and age of child. This implies that time may not be a significant factor in aiding parents' initial decrease in anxiety levels, but rather other factors such as getting more information from HCPs and finding community are enough to aid in decreasing emotional distress at any point in time.

Coping strategies including finding support groups, family support, faith, having provider reassurance, getting more education, and addressing psychosocial concerns have been reported to aid in acceptance of an LOPD diagnosis by NBS (Crossen et al., 2022). This study affirms those previously identified themes, with the most common causes of decreased anxiety levels being increased knowledge, an accessible and reliable healthcare team, and the satisfactory health status of the child with LOPD. The latter theme regarding child health status refers to parents being reassured by either a lack of

symptoms in their child, not receiving ERT, and/or gaining control over enzyme levels. While parents benefit from psychosocial support as well, information is what truly led to their anxiety levels decreasing. This emphasizes the benefit of providing parents with the knowledge that they need to understand the condition and their child's health throughout the entire diagnostic process, including at NBS positive.

Many parents, regardless of anxiety level change, reported a continued sense of uncertainty after diagnosis. Several parents mentioned that uncertainty contributed to their feelings of anxiety. This further emphasizes the need to continue to support parents after diagnosis and throughout their child's life by being accessible and providing psychosocial support to continue to validate parents' feelings of uncertainty and hopefully help address their levels of anxiety.

2.5.5 Genetic Counseling Recommendations

The primary goals of genetic counseling involve helping individuals and their families understand and manage genetic conditions through education and psychosocial support. The areas of impact stated by parents included providing resources, aiding in understanding of diagnosis, making a treatment plan, and supporting the mental health of parents. These areas support the goal of genetic counseling. This suggests that for those that benefit from genetic counseling, it has a significant impact on their ability to support their child, understand the diagnosis, and receive support for their own health. It also gives guidance for where genetic counseling can improve in the future for this population, as many individuals did not explicitly state what was helpful about genetic counseling or that it did not have an impact for them.

To our knowledge, this is the first study assessing genetic counseling impact in this patient population. Most participants that saw a genetic counselor and commented on the experience stated that seeing a genetic counselor had an impact on their ability to manage their child's diagnosis. While the majority stated genetic counseling did have an impact, there was a large percentage of parents who are not getting what they should be out of genetic counseling. This study identifies areas where genetic counseling can continue to improve and be a resource for families. Parents in this study stated that at the time of NBS positive, information on PD and treatments was the most helpful. Genetic counselors and other providers speaking with family members should be up to date on treatment status for these conditions and be able to give a breakdown of what this condition is. Receiving news that your child may have a genetic disorder is rarely a positive experience; having knowledgeable providers and tangible next steps can make that experience more manageable.

Some individuals stated they received no resources at the time of diagnosis. Of those that did receive resources, a few stated that they were unhelpful or not specific to LOPD. Genetic counselors and those providing genetic counseling services should be aware of the current resources available for conditions on NBS, particularly with LOPD and other late-onset conditions that may have fewer resources online or may not be as prominent. Many parents stated that while online searches revealed outdated information, they were not aware of other places to search for more updated information. HCPs, including genetic counselors and those providing genetic counseling, have a responsibility to provide resources to their patients and families.

While resources include the ones directly mentioned by participants in this study, such as support groups and websites for families, they can also address some of the barriers to care that families have faced. Some participants mentioned facing struggles dealing with insurance coverage, finding local providers who are knowledgeable on LOPD, and navigating pharmacies. Genetic counselors and other genetics providers can aid in not only providing information on the condition itself, but additionally in giving families actionable resources to reduce the number of barriers they experience when accessing care in their area.

Based on this study's data, we have constructed a list of recommendations for genetic counseling of LOPD that may be utilized by genetics and non-genetics professionals alike. While not stated directly in the recommendations, we strongly recommend all HCPs who disclose NBS results to be up to date on information and resources regarding the condition they are discussing. Genetics professionals should additionally aid in provider education when possible, particularly when a new condition is added to NBS panels. The recommendations are listed below.

- **Genetic counseling for LOPD and other late-onset conditions should include information about the condition, information on treatment, and provide aid in the form of resources and psychosocial support.** Specialist contact information may also be helpful to provide in general genetics and pediatric clinic settings. Resources may include, but are not limited to, physical papers on LOPD to take home, support group information, financial aid assistance, and trustworthy online sites that can be shared with other family and friends. Relevant resources should be provided at both screen positive and confirmed diagnosis.

- **Genetics providers should aid in initiating and coordinating cascade sibling testing.** The majority of parents who had other children at the time of their child's NBS diagnosis stated testing other children was a major concern at the time of diagnosis. This conversation should be initiated by providers, and parents should understand all options for testing other family members. Genetic counselors in particular can aid parents in understanding inheritance of the condition and coordinating genetic testing of other relatives.
- **HCPs should assess the amount of information parents would like to know at the time of initial appointment.** Parents reported receiving both too much and too little information at time of screen positive and diagnosis. Education must be tailored to each individual and may be spread over multiple appointments if that is what is most effective.

2.6 Limitations

This study is limited by a small sample size. While it is the largest study of its kind within this population, more research needs to be done with a larger group of individuals to be able to make more generalizable recommendations. Additionally, comprehensive demographic data was not collected. Future studies should further assess if there are relationships between NBS and follow-up experiences and demographic data to see if there may be populations of people receiving inequitable care. It should also be noted that the use of the statistical Kruskal Wallis test using age of the child as an independent variable was analyzed as though the differences between the options were equal for the sake of determining relationships, which they are not. The data collected from the Duke University study group may be skewed as they received care at a specialty

center. This study did not ask other participants about their association with specialty centers and the benefits and barriers associated with that.

CHAPTER 3: CONCLUSION

This study further informs providers on the complex experiences of parents with children with LOPD diagnosed by NBS. The findings presented here support previous research done by Pruniski et al. (2018), Prakash et al. (2022), and Crossen et al. (2022) which emphasized the levels of stress experienced by this parent population and the necessity of re-evaluation of current healthcare processes involving them. To our knowledge, this is the first study in this patient population reporting on changes in levels of anxiety and the impact of genetic counseling on navigating a positive LOPD NBS diagnosis. This is also the largest study to date within this patient population. Our findings emphasize the importance of increased provider knowledge when disclosing NBS results and further encourage HCPs to provide resources throughout the diagnosis process and continue to support families well after a diagnosis as feelings of uncertainty remain. Our study may be used as a reference by genetics and non-genetics providers alike in determining how best to provide for this population at various points in their medical journey. More research should be done as more newborns are diagnosed with LOPD so we may better serve this population in the future.

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APPENDIX A: FACEBOOK SUPPORT GROUP SURVEY

Start of Block: Introduction Block

Q25 Thank you for participating in this survey. The purpose of this study is to better understand the experiences of parents whose children have been diagnosed with late-onset Pompe disease by newborn screening.

All responses from this survey will be kept anonymous and cannot be linked back to you. Your participation in this research is voluntary. By completing this survey, you are consenting to participate in this study which has been approved by the University of South Carolina Institutional Review Board.

If you have any questions regarding the research, you may contact the primary investigator at any time:

Allie Paltzer
Genetic Counseling M.S. Candidate
Allison.Paltzer@uscmed.sc.edu

Your responses are very much appreciated. Thank you for your participation!

End of Block: Introduction Block

Start of Block: Information Block

Q1 Please confirm you are a parent or guardian of a child with late-onset Pompe disease who was diagnosed by newborn screening:

○ I confirm that I am a parent or guardian of a child with late-onset Pompe disease diagnosed by newborn screening (1)

Page Break

Q2 What is your relationship to the child with Pompe disease?

- ○ Mother (1)
- ○ Father (2)
- ○ Other (please specify) (3) _____

Q3 How old is your child now?

- ○ Less than one year (1)
- ○ 1-3 years (2)
- ○ 4+ years (3)

Q4 Who first informed you of your child's positive newborn screen result?

- ○ Geneticist (1)
- ○ Pediatrician (2)
- ○ Nurse (3)
- ○ Unsure/Don't remember (4)
- ○ Other (please specify) (5) _____

Q5 How long after birth did you receive the positive newborn screen result?

- ○ Within 48 hours (2 days) (1)
- ○ Within 3-5 days (2)
- ○ A week or more (3)
- ○ Unsure/Don't remember (4)
- ○ Other (please specify) (5) _____

Q6 Thinking about when you first received the positive newborn screen result, what information was given to you at that time was helpful? Please be as specific as you'd like.

_____

_____

_____

_____

_____

Q7 Thinking about when you first received the positive newborn screen result, what information was given to you at that time was NOT helpful? Please be as specific as you'd like.

_____

_____

_____

_____

_____

Page Break

Q8 How long after receiving the positive newborn screen result did you see a healthcare provider to confirm the diagnosis?

- ○ Within 48 hours (2 days) (1)
- ○ Within 3-5 days (2)
- ○ A week or more (3)
- ○ Unsure/Don't remember (4)
- ○ Other (please specify) (5) _____

Q9 Thinking about when the diagnosis was CONFIRMED, what information was given to you that was helpful? Please be as specific as you'd like.

_____

_____

_____

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_____

Q10 Thinking about when the diagnosis was CONFIRMED, what information was given to you that was NOT helpful? Please be as specific as you'd like.

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Q11 Thinking about when the diagnosis was CONFIRMED, were you given any resources?

- ○ Yes (1)
- ○ Unsure/Don't remember (2)
- ○ No (3)

Q12 If you selected YES, please describe the resources and whether or not they were helpful.

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Page Break

Q13 At the time of your child's diagnosis, how many other children did you have? (E.g., 1, 2, 3, etc.)

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Q14 At the time of your child's diagnosis, would you consider having your other children tested for Pompe disease a major concern at that time?

- It was a major concern for me at that time. (1)
- It was NOT a major concern for me at that time. (2)
- I did not have any other children at the time. (3)

Q15 Do you have any other children with Pompe disease?

- Yes (1)
- No (2)

Page Break

Q16 Is your child who was diagnosed by newborn screening receiving treatment with enzyme replacement therapy?

- ○ Yes (1)
- ○ No (2)
- ○ Not at this time, but there are plans to start within the next 3 months (3)

Q17 Overall, has it been easy, moderate, or difficult getting medical services like physical therapy and/or enzyme replacement therapy for your child at the recommended intervals?

- ○ Easy (1)
- ○ Moderate (2)
- ○ Difficult (3)

Q18 Please elaborate on your previous answer. What has been easy about getting services? What has been difficult? Please be as specific as you'd like.

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Page Break

Q19 Thinking about the time between the initial diagnosis and now, have your anxiety levels changed?

- ○ Yes, my anxiety has increased/got worse. (1)
- ○ Yes, my anxiety decreased/got better. (2)
- ○ No, my anxiety levels stayed the same or about the same. (3)

Q20 Please explain the factors that you think have caused your anxiety levels to increase, decrease, or stay the same. Please be as specific as you'd like.

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Q21 Have you met with a genetic counselor at any point since your child's diagnosis?

- ○ Yes (1)
- ○ Unsure (2)
- ○ No (3)

Q22 If yes, thinking about the time(s) you met with a genetic counselor, what impact did genetic counseling have on your ability to manage your child's diagnosis? If there was no impact, please type "no impact."

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Q23 Is there a person on your genetics team who you routinely go to when you need something? If yes, please list that person's title (i.e. nurse, clinic coordinator, genetic counselor, etc.).

- Yes (1) _____
- Unsure (2)
- No (3)

Page Break

Q24 Is there anything else you would like us to know that we have not asked about? Please be as specific as you'd like.

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End of Block: Information Block

APPENDIX B: DUKE STUDY SURVEY

Start of Block: Default Question Block

Q1 Please type your child's first and last name. The questions in this survey all refer to your child that is enrolled in the Late-Onset Pompe Disease Newborn Screening Study at Duke University.

_____

Q2 What is your relationship to the child with Pompe disease?

- ○ Mother (1)
- ○ Father (2)
- ○ Other (please specify) (3) _____

Q3 How old is your child now?

- ○ Less than one year (1)
- ○ 1-3 years (2)
- ○ 4+ years (3)

Q4 Who first informed you of your child's positive newborn screen result?

- ○ Geneticist (1)
- ○ Pediatrician (2)
- ○ Nurse (3)
- ○ Unsure/Don't remember (4)
- ○ Other (please specify) (5) _____

Q5 How long after birth did you receive the positive newborn screen result?

- ○ Within 48 hours (2 days) (1)
- ○ Within 3-5 days (2)
- ○ A week or more (3)
- ○ Unsure/Don't remember (4)
- ○ Other (please specify() (5)

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Q6 Thinking about when you first received the positive newborn screen result, what information was given to you at that time was helpful? Please be as specific as you'd like.

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Q7 Thinking about when you first received the positive newborn screen result, what information was given to you at that time was NOT helpful? Please be as specific as you'd like.

_____

Q8 How long after receiving the positive newborn screen result did you see a healthcare provider to confirm the diagnosis?

- ○ Within 48 hours (2 days) (1)
- ○ Within 3-5 days (2)
- ○ One week or more (3)
- ○ Unsure/Don't Remember (4)
- ○ Other (specify) (5) _____

Q9 Thinking about when the diagnosis was CONFIRMED, what information was given to you that was helpful? Please be as specific as you'd like.

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Q10 Thinking about when the diagnosis was CONFIRMED, what information was given to you that was NOT helpful? Please be as specific as you'd like.

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Q11 Thinking about when the diagnosis was CONFIRMED, were you given any resources?

- ○ Yes (1)
- ○ Unsure/Don't Remember (2)
- ○ No (3)

Q12 If you selected YES, please describe the resources and whether or not they were helpful.

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Q13 At the time of your child's diagnosis, how many other children did you have?

- ○ None (1)
- ○ 1 (2)
- ○ 2 (3)
- ○ 3 (4)
- ○ 4 (5)
- ○ 5+ (6)

Q14 At the time of your child's diagnosis, would you consider having your other children tested for Pompe disease a major concern at that time?

- ○ It was a major concern for me at that time. (1)
- ○ It was NOT a major concern for me at that time. (2)
- ○ I did not have any other children at the time. (3)

Q15 Do you have any other children with Pompe disease?

- ○ Yes (1)
- ○ No (2)

Q16 Is your child (who is enrolled in the research study) receiving treatment with enzyme replacement therapy?

- ○ Yes (1)
- ○ No (2)
- ○ Not at this time, but there are plans to start within the next 3 months (3)

Q17 Overall, has it been easy, moderate, or difficult getting medical services like physical therapy and/or enzyme replacement therapy for your child at the recommended intervals?

- ○ Easy (1)
- ○ Moderate (2)
- ○ Difficult (3)

Q18 Please elaborate on your previous answer. What has been easy about getting services? What has been difficult? Please be as specific as you'd like.

_____

Q19 How did you find out about the newborn screening research study at Duke University?

- ○ Genetic counselor (1)
- ○ Geneticist (2)
- ○ Pediatrician (3)
- ○ Found it myself online (4)
- ○ Other (please specify) (5) _____

Q20 Thinking about the first study visit at Duke, did your anxiety levels change after the completion of the first visit?

- ○ Yes, my anxiety increased/got worse. (1)
- ○ Yes, my anxiety decreased/got better. (2)
- ○ No, my anxiety level stayed the same or about the same. (3)

Q21 Thinking about the time between the first study visit at Duke and your most recent study visit, have your anxiety levels changed (i.e. since the start of the study)?

- ○ Yes, my anxiety has increased/gotten worse. (1)
- ○ Yes, my anxiety has decreased/gotten better. (2)
- ○ No, my anxiety levels have stayed the same or about the same. (3)

Q22 Please explain the factors that you think have caused your anxiety levels to increase, decrease, or stay the same. Please be as specific as you'd like.

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Q23 Thinking about the time(s) you met with a genetic counselor during the study visits at Duke University, what impact did genetic counseling have on your ability to manage your child's diagnosis? If there was no impact, please type "no impact."

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Q24 Does your child have a geneticist that they routinely see outside of Duke University?

- ○ Yes (1)
- ○ No (2)
- ○ Unsure (3)

Q25 Is there a person on your genetics team (at Duke University or your local team) who you routinely go to when you need something? If yes, please list that person's title (i.e. nurse, clinic coordinator, genetic counselor, etc.)

- ○ Yes (1) _____
- ○ No (2)
- ○ Unsure (3)

Q26 Is there anything else you would like us to know that we have not asked about? Please be as specific as you'd like.

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End of Block: Default Question Block