Exploring the experiences of adolescents and young adults with phenylketonuria and glycogen storage disease 1a through the healthcare transition

by

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ABSTRACT

The healthcare transition (HCT) is often precarious for patients diagnosed with chronic medical conditions as adolescent and young adult patients are required to independently manage their condition after relying heavily on parents for their disease management prior to the transition. The HCT is the coordinated and planned process that addresses the medical, psychosocial, and educational needs of patients as they transfer from pediatric to adult healthcare. The transition to adult care is significant due to the striking dissimilarities between the pediatric and adult care cultures. It is well known that patients with chronic diseases, such as inborn errors of metabolism (IEM), are at risk for declining disease management throughout the HCT, which is consequently associated with worse health outcomes. Patients with phenylketonuria (PKU) and glycogen storage disease 1a (GSD1a), two relatively common IEM characterized by a high management burden, are known to struggle with disease management during the HCT. Unfortunately, there are substantial gaps in our understanding of the patient-reported factors influencing readiness and capacity for disease management during the HCT, especially in patients with IEM. Due to the substantial effort associated with managing these conditions, patients with PKU and GSD1a have valuable knowledge regarding the factors influencing their management and the support they require to effectively navigate the HCT.

Semi-structured interviews with participants identified that experiences with the HCT were highly variable among participants, though they similarly identified a lack of support and information from their healthcare providers. Participants also described feeling isolated by their condition which impacted their mental health. The complexity of participants' evolving lives was an additional barrier to appropriate management as participants made management compromises to integrate their management with their everyday lives. Participants hoped to find balance between their management and mental health. Relationships with healthcare providers and parental involvement were also identified as highly influential on participants' willingness and capacity for disease management.

Overall, this study describes patients' perceptions of the HCT and the factors influencing their management throughout the HCT. The data presented herein were foundational to generating patient-centred recommendations to improve the HCT and ultimately promoting better health outcomes for future patients.

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DEDICATION

To Kristjan, with love.

This thesis was only possible because of your infallible support.

And now, on to the next adventure!

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LIST OF ABBREVIATIONS

AYA	adolescents and young adult(s)
BH4	tetrahydrobiopterin
CAPHC	Canadian Association of Paediatric Health Centres
EA	emerging adulthood
G6Pase	glucose-6-phosphatase
G6PC1	glucose-6-phosphatase catalytic subunit 1
GSD1	glycogen storage disease 1
GSD1a	glycogen storage disease 1a
HCT	healthcare transition
IEM	inborn error(s) of metabolism
IPA	interpretative phenomenological analysis
mg	milligram(s)
NBS	newborn screening
PAH	phenylalanine hydroxylase
Phe	phenylalanine
PKU	phenylketonuria
PPR	patient-provider relationship
Tbsp	Tablespoon
w/	with

CHAPTER 1: INTRODUCTION & LITERATURE REVIEW

1.1. INTRODUCTION

The transition from adolescence to adulthood is often a vulnerable time for adolescents and young adults (AYA) as they are faced with taking up new responsibility for themselves, making independent decisions and becoming self-sufficient (Keller, Cusick, & Courtney, 2007). The transition into adulthood is additionally complicated for those diagnosed with chronic medical conditions as they must also undergo the healthcare transition (HCT). The HCT is the process leading up to, throughout, and after the transfer of care from pediatric to adult healthcare (see *Section 1.3*). This transition is significant as the cultures of the two settings vary considerably. Research focused on the health care transition of AYA diagnosed with chronic diseases shows that the HCT is associated with declining self-management (disease management activities, see *Section 1.4*) (Anthony et al., 2009; Kaufman, Pinzon, Society, & Committee, 2007; MacLusky & Keilty, 2018), which underlies worse health outcomes and negative quality of life (Chan, 2021; Chu, Maslow, von Isenburg, & Chung, 2015). AYA diagnosed with inborn errors of metabolism (IEM), which are chronic metabolic diseases that require substantial time and effort to manage effectively, are often diagnosed through newborn screening (NBS) or in early childhood (Kruszka & Regier, 2019; Saudubray & Garcia-Cazorla, 2018). As such, much of the disease burden is managed by the patient's caregivers. Consequently, AYA with chronic diseases often struggle to become independent from their parents and begin self-management (Garbade et al., 2021). Phenylketonuria (PKU) and glycogen storage disease 1a (GSD1a) are two relatively common IEM characterized by a high management burden (see *Sections 1.5* and *1.6*). When managed correctly, individuals are expected to follow normal development and can lead independent adult lives (Ford, O'Driscoll, & MacDonald, 2018; Garbade et al., 2021). PKU and GSD1a patients are known to struggle with self-management (Feillet, MacDonald, Hartung, & Burton, 2010; Garbade et al., 2021), and therefore may be particularly vulnerable during the HCT. Overall, there is a prominent gap in our current knowledge surrounding the self-management of patients with IEM during the HCT. As such, there is a need to gain more insight into the factors influencing AYA patient readiness for self-management so that they may be better supported during the transition to adult care. Given the high management burden associated with PKU and GSD1a, patients with these conditions likely have valuable insight from which recommendations can be made to support future AYA patients with IEM who are undergoing the HCT.

While the remaining sections of this chapter provide relevant background information, context for the current research project, and, at times, a critique of the healthcare system, this information is largely presented from the healthcare providers' perspective. This study and its resulting recommendations were purposefully designed to focus on patients' perspectives of the issues at hand as the patient-perspective is most appropriate for ensuring patients' biggest concerns are targeted and future improvements to the HCT are relevant to the PKU and GSD1a populations.

1.2 THE TRANSITION FROM ADOLESCENCE TO ADULTHOOD

Emerging adulthood (EA) is an influential life stage for AYA (Zarrett & Eccles, 2006). This time of discovery affords many AYA opportunities to make independent choices and explore, however, it is also associated with significant challenges and changes. EA is considered a critical developmental period. Arguably, no other life stage, other than infancy, is characterized by the same degree of physical, cognitive, emotional and social changes (Wood et al., 2017). These developmental changes also occur concurrently as AYA learn to navigate social, emotional and practical challenges such as identity formation, academic and career pressures, financial independence, mental health, and health and lifestyle choices. EA is often associated with loss of supports that were afforded by school, family, and other social structures. At this time, AYA are expected to become more autonomous, though their brains are not yet fully developed and they are still learning new competencies that enable them to become self-sufficient adults (Wood et al., 2017). Indeed, AYA are considered to have unique developmental needs (Arnett, 2000; Twiddy, Hanna, & Haynes, 2017). The changes and challenges that AYA face during EA, which are briefly detailed below, likely contribute to the precariousness of the HCT as these changes and challenges influence AYA patients' readiness and capacity to self-manage.

AYA in EA may experience significant biological changes including changes in hormones, brain development and physique (Hochberg & Konner, 2020; Zarrett & Eccles, 2006). Interestingly, the frontal cortex, the part of the brain responsible for impulse and emotional control, is still developing during EA (Hochberg & Konner, 2020). This is an important consideration as AYA are often coping with emotional changes such as mood swings and increases in emotional intensity throughout this time (Zarrett & Eccles, 2006). AYA are also experiencing cognitive changes as they develop skills for abstract thinking, critical reasoning and information processing (Zarrett & Eccles, 2006). In addition to biological and psychological changes, AYA may also face

changes in their social circles and supports as they develop new relationships, lose previous relationships or experience restructuring of on-going relationships (Wood et al., 2017; Zarrett & Eccles, 2006). These changes likely contribute to the challenges AYA typically face during EA.

A key feature and challenge of EA is the search for identity. Personal and social factors interact to influence the developing identity. Once formed, identity dictates behaviour, character, and roles AYA hold in their social circles (Wood et al., 2017). Additionally, many AYA make choices about their education and career, while also juggling their first experiences with financial independence (Twiddy et al., 2017; Wood et al., 2017). During this time, AYA, especially those with chronic medical conditions (Berens, Wozow, & Peacock, 2020), are more likely to develop mental health concerns, which may be exacerbated by experimentation with drugs, alcohol, and eating and exercise habits (Wood et al., 2017; Zarrett & Eccles, 2006).

Consideration of this notable life stage is important for healthcare providers who interact with AYA patients with chronic diseases as these various changes and challenges likely have unique impacts on this population. In fact, a 2017 study by Twiddy, Hanna and Haynes focused on the needs of emerging adults with chronic pain, discussed how the identities AYA develop contribute to the ways in which they manage their condition (*e.g.* their coping style) (Luyckx et al., 2008; Twiddy et al., 2017). Even choices about career and education may be impacted for individuals with chronic medical conditions. Patients with GSD1a reported having concerns that their medical needs would prevent them from having the specific career they wish to pursue (United States Food and Drug Administration, 2021b). Wood *et al*. (2017) highlighted that chronic medical conditions often "*significantly impact the developmental trajectory of emerging adults during this life stage"*. More specifically, AYA with chronic medical conditions may delay the undertaking of adult roles, as defined by society, and are more vulnerable to problems, such as gaps in medical care, during this transitional time (Wood et al., 2017).

The HCT is a critical event in the care of AYA with chronic medical conditions as they are developing the skills required to self-manage. The HCT occurs synchronously with the transition from adolescence to adulthood; which in itself is a highly influential time that is foundational to behaviours and choices that may influence the rest of an individual's life (Hendricks, Monaghan, Soutor, Chen, & Holmes, 2013). This notion is distinctly relevant for AYA with chronic medical conditions, like PKU and GSD1a, as they are learning the self-management skills necessary to independently care for themselves. Of course, managing PKU and GSD1a does not occur in a

vacuum. Therefore, learning the skills to self-manage in the context of the typical challenges associated with EA create an additional layer of complication for patients navigating the HCT.

1.3. THE HEALTHCARE TRANSITION

The ideal HCT is a co-ordinated and planned process that addresses the medical, psychosocial and educational needs of AYA as they move from the pediatric to the adult healthcare setting (Berens et al., 2020; Blum et al., 1993; Schraeder et al., 2021). As mentioned above, this transition is significant as the cultures of pediatric and adult healthcare are strikingly dissimilar. In pediatric care, primary caregivers (referred to as parents in the remainder of this thesis) provide consent, make decisions and perform disease management for the patient. Moreover, care is typically more holistic and team-based and greater efforts are made to follow-up with parents' and patients' management. Under adult healthcare, patients are required to be autonomous and self-advocating (Castillo & Kitsos, 2017; Kaufman et al., 2007; Rosen, 1995). Throughout the HCT, AYA patients are expected to learn the knowledge and skills needed to independently manage their condition (see *Section 1.4*). The American Academy of Pediatrics states that the goal of the HCT is to "*maximize lifelong functioning and quality of life"* and is considered successful when uninterrupted, high-quality and developmentally appropriate care is offered as patients move from adolescence to adulthood (American Academy of Pediatrics, 2002).

With improved medical knowledge and technology, >90% of pediatric patients with childhood onset conditions are expected to live into adulthood and thus are likely to complete a HCT (Bensen, Steidtmann, & Vaks, 2014). Despite the ubiquitousness of the HCT, current research continues to identify inadequacies in transition processes. In fact, ~60% of AYA are suspected of receiving insufficient care and attention during the HCT (Bensen et al., 2014; McManus et al., 2013). Inadequate care may be attributed to the lack of standardization in the HCT process as different provincial health regions or healthcare facilities promote different transition guidelines (see *Section 1.3.1*). Consequently, there is substantial variability in the HCT across disease contexts and the country (Vaks et al., 2016). Ideally, the HCT consists of three phases, including 1) the preparatory phase, in which pediatric patients learn the skills and knowledge to manage their condition, 2) the transfer of care, at which point patients switch from pediatric to adult services, and 3) the integration phase in which the outcomes of the HCT are assessed (***Figure 1-1***) (Berens et al., 2020). It is recommended that a period of overlap occurs around the transfer of care in which

the patient is overseen by both teams to ensure stable integration (Meranda, Lorraine, Sarah, & Kaberi, 2017; Philpott, 2011). Though as previously mentioned, there is a high degree of variability in clinical practice, which creates significant challenges for AYA undergoing the HCT and under adult care.

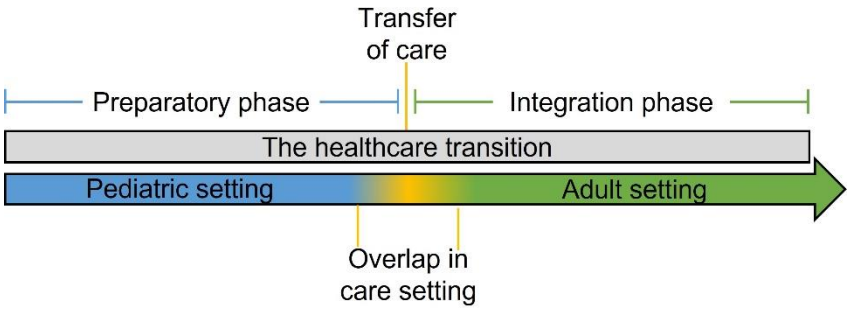

Figure 1-1. Progression of the HCT.
Schematic outlining the various stages of the HCT. The preparatory phase occurs in the pediatric setting (blue) and the integration phase (green) occurs in the adult healthcare setting. The transfer of care represents the switch from pediatric to adult care, and ideally there is a period of overlapping care (yellow) before and after the transfer of care.

Current research on the HCT highlights barriers and challenges within the HCT at the patient, provider and healthcare system levels (Kiana et al., 2021). AYA patients with chronic pain report that they struggle with balancing their self-management alongside their growing adult responsibilities. This struggle is perceived as a barrier to a successful HCT as their new responsibilities and pain cyclically impacted their ability to address either challenge (Murray et al., 2022). AYA patients also report a lack of preparedness for the HCT and feeling as though they were removed from the decision regarding when or how the HCT should proceed (A. L. Bennett, Moore, Bampton, Bryant, & Andrews, 2016; Lanzkron et al., 2019). Moreover, patients also report the value of the relationships and trust they built with their pediatric team. Consequently, there is resistance to leave the pediatric setting and fear of the unknown regarding expectations for the adult healthcare setting (Gray et al., 2015; Lanzkron et al., 2019; Rohatinsky, Risling, Kumaran, Hellsten, & Thorp-Froslie, 2018). From the provider perspective, a 2021 survey-based study investigating the barriers to the HCT as perceived by providers in rheumatology identified that 63% of participants did not discuss the HCT with their patients, while only 17% have established HCT protocols. Moreover, participants identified a deficit in the number of available adult providers (Kiana et al., 2021). Other HCT research showed that families and healthcare providers

both identified a need for improved communication between the pediatric and adult providers at all stages of the transition to promote continuity of care (Kung et al., 2016; Miller et al., 2009; Suris, Akré, & Rutishauser, 2009). Many studies also report that providers lack exposure and training in complex childhood-onset conditions. Consequently, providers are unfamiliar with the long-term complications and surveillance protocols (DiFazio, Harris, Vessey, Glader, & Shanske, 2014; Kiana et al., 2021). At the healthcare system level, there are calls to identify patient-specific outcome measures to assess the success of the HCT as there is little consensus on this matter, to date (Coyne, Hallowell, & Thompson, 2017; Schraeder et al., 2021). Without appropriate measures of success, patients may continue to experience gaps in care as there are no means to properly identify where supports are lacking. A 2017 study involving 22 healthcare sites in the United States identified that one of the most common barriers to the HCT is poor integration of transitional care services (Scott et al., 2017). They describe insufficient information sharing and discrepancies in the progress of the HCT in practice (Scott et al., 2017). The lack of standardization is understood to be a barrier to a successful transition. However, in a 2016 systematic review of primary care interventions to improve the HCT, Bhawra *et al*. (2016) identified that approaches to the HCT may need to be adapted to the disease context.

Given the ubiquitousness of the barriers identified in the literature, it is not surprising that AYA undergoing the HCT experience declining self-management (Anthony et al., 2009; Kaufman et al., 2007; MacLusky & Keilty, 2018), and as a result, worse health outcomes and negative quality of life (Chan, 2021; Chu et al., 2015). More specifically, PKU patients demonstrate decreases in metabolic control from childhood to adulthood, and are known to discontinue contact with their healthcare team (Peres et al., 2021). The HCT is also reported to be a vulnerable time for patients with sickle-cell disease as they are more likely to present to the emergency department compared to those who have not transitioned to adult care (Hemker, Brousseau, Yan, Hoffmann, & Panepinto, 2011). A systematic review by Sheehan, While and Coyne (2015) focusing on the impact of the HCT in type 1 diabetes patients determined patients often cease contact with their clinics and have greater difficulty maintaining glycemic control as adults. As such, it is imperative that research related to the HCT continues to be prioritized so that the challenges and shortcomings of the current HCT processes are rectified. Previous studies show that patients who have a successful HCT have improved outcomes including satisfaction, independence, and continuity and adherence of care (Kiana et al., 2021), though data remains limited. In fact, in a 2017 systematic

review, Gabriel *et al*. identified 43 out of 3844 peer-reviewed articles meeting their criteria for appropriate reporting of patient outcomes in the HCT. Of the 43 studies identified, two-thirds of those report improved adherence to care, health status, quality of life and self-management skills following a successful HCT (Gabriel, McManus, Rogers, & White, 2017).

The HCT is a new, but budding field of study. However, it is undeniable that there are substantial gaps in our understanding regarding the support patients require throughout this vulnerable time. Barriers have been associated with the HCT at multiple levels (*i.e.* patient, provider, healthcare system) and each level must be addressed in order to fully support patients throughout the HCT. A predominant challenge in initiating first steps to improve the HCT is determining which barriers are the most disruptive, and consequently, will incite the greatest positive impact on the experiences of AYA patients, once they are addressed. Therefore, this study, which is focused on investigating patient readiness for self-management during the HCT represents a strong initial step to begin addressing these challenges. Participants will identify the barriers and facilitators that were most impactful to them, and therefore warrant the most attention. Moreover, experiences of the participants herein have the potential to address the shortcomings of the HCT on multiple levels (*i.e.* patient, provider, healthcare system), and therefore offer widespread recommendations to make the greatest impacts on patient outcomes.

1.3.1. The healthcare transition guidelines in the literature

Given the precariousness of the HCT, there are growing efforts to develop resources, such as guidelines, recommendations, and quality standards, directing healthcare facilities to ensure a successful HCT and transfer of care. These resources have been created by national organizations, provincial health regions, major healthcare facilities, and principal investigators working in this research area, and are either focused general populations who may be undergoing a HCT, or are population specific (*e.g.* transplant recipients, disease specific, etc.)

In 2016, the Canadian Association of Paediatric Health Centres (CAPHC) published general guidelines which included 19 evidence-based recommendations to address barriers occurring at multiple hierarchical levels, including those experienced by patients and their families, by healthcare providers, and those that are inherent within the healthcare system (Canadian Association of Paediatric Health Centres, 2016). The CAPHC states that HCT guidelines are imperative to *"support a successful transition framework from paediatric to adult care that results in individuals who are better equipped to navigate the system and better able to manage their own*

health" (Canadian Association of Pediatric Health Centres, 2016). The CAPHC guidelines provide person-centred, clinical and system level recommendations to address the barriers mentioned above. The initial recommendations were made in Spring 2014, and the final recommendations were decided in Fall 2015. The person-centred recommendations speak to the importance of a HCT process that is youth and family centred, and that is amenable to accommodating personal choice and the complexities of patients' needs. Additionally, they recommend that the HCT should take a holistic approach that considers the *"physical, developmental, psychosocial, mental health, educational, lifestyle, cultural and financial needs"* (Canadian Association of Pediatric Health Centres, 2016) of AYA during the HCT. The proposed clinical recommendations focus on the significance of continuity of care, the collaboration between relevant stakeholders, and assessing patient readiness as a means of addressing gaps in knowledge and skills. Lastly, the system level recommendations focus on the importance of providing ongoing education, data collection and analysis to evaluate the HCT at the population level (Canadian Association of Pediatric Health Centres, 2016).

The CAPHC guidelines are firmly rooted in the literature and consider the complexity of patients' lives by acknowledging the interaction between EA and the HCT. However, arguably, the final recommendations are too generalized and do not contain the same detail of information as their initial recommendations. Therefore, the specific information required to act on these guidelines is missing. For example, they do not make concrete recommendations for the ages at which the HCT should begin and end. Nor do they specify how patient education should be provisioned (*e.g.* defined step-wise process with age-appropriate information).

The Canadian Paediatric Society released a position statement in 2022 that outlines 6 recommendations for the general population undergoing a HCT (Toulany, Willem Gorter, & Harrison, 2022). In their statement, the Canadian Paediatric Society acknowledged that the HCT should be flexible in nature as chronological age does not always correlate with ability. The society also identified the importance of a primary care provider throughout the transition to facilitate communication, ensure continuity of care and bolster patient education. The recommendations made by the society emphasize that care throughout the HCT should be "*continuous, comprehensive, coordinated, developmentally appropriate and meets the needs of all participants"* (Toulany et al., 2022). They recommend that patients build autonomy in a stepwise process, which occurs with concurrent changes in the parent/caregiver roles. Moreover, they

recommend pediatric and adult care providers develop strategies to ensure appropriate care and develop novel measures to assess the quality of the HCT on a population level. Lastly, they also call for increases in funding and educational initiatives (Toulany et al., 2022).

Like the recommendations proposed by the CAPHC, those proposed by the Canadian Paediatric Society address challenges with the HCT on multiple levels, which is essential to ensure that patients undergoing the HCT are protected. However, most of these recommendations ask for large-scale changes that likely take years to implement and have minimal focus on information that is immediately actionable and implementable on an individual level by healthcare providers. Furthermore, while the society includes important points, like a stepwise education plan, that were missed by the CAPHC, these guidelines do not sufficiently detail by what means patients should be educated, and what information should be included in their education.

Major Canadian healthcare centres and provincial health services have published their own guidelines for the HCT. The Hospital for Sick Children in Toronto (SickKids) released guidelines targeted to healthcare providers for AYA who have undergone organ transplants (SickKids Transplant Clinical Committee, 2021). These guidelines outline age-appropriate tasks that should be initiated or completed during specified age ranges. While the guidelines were originally released for a specific subset of patients, the guiding principles and recommendations could easily be employed as general guidelines for any AYA undergoing an HCT. The SickKids guidelines encourage providers to begin considering the HCT before the patient is 10 years of age and encourages providers to involve parents at this early stage. As patients age, providers are encouraged to educate patients about their condition and medications with more detail, visit with patients independently and address parents' concerns surrounding allowing their child to develop responsibility in their management. Ultimately, patients' knowledge and responsibility continue to build so that at the transfer of care, patients have an appropriate understanding of their health history, the potential short and long-term medical complications they may face and steps to follow if they experience complications (SickKids Transplant Clinical Committee, 2021). While these guidelines outline actionable steps to be taken at various stages throughout the HCT, they are relatively one-dimensional as the guidelines address the HCT from a medical model, focusing strictly on medical knowledge, which fails to address the psychosocial aspects of the HCT.

Alberta Health Services has created guidelines for AYA who can live independently as adults and for AYA who will be dependent on parents as adults (Alberta Health Services, 2022). These

guidelines are similar to those created by SickKids as they outline specific tasks to be initiated or completed by specified age ranges. However, where the SickKids guidelines are lacking, the Alberta Health Services guidelines have addressed these gaps by equally emphasizing the importance of proficiency in medical knowledge and skill, as well as the psychosocial aspects of having a chronic condition, such as integrating self-management in social contexts (Alberta Health Services, 2022). It is not explicitly stated for whom the Alberta Health Services guidelines are targeted (*e.g.* provider, parent, patient), however they are lacking with respect to recommendations on how the pediatric and adult healthcare teams should be communicating and collaborating throughout the transition and what information should be passed on to ensure continuity of care.

Interestingly, all of these guidelines lack guidance for steps to follow when patients have not followed a traditional HCT process. Of course, well-implemented guidelines should ensure that all patients are prepared and able to complete the HCT at the expected time. However, as described in *Section 1.3,* the HCT is often influenced by other consequences of participating in the world. More specifically, there is no information regarding patients who may not have been able to maintain self-management or are returning to care as an adult from a prolonged absence. These patients may not have developed the knowledge that would typically be established during their time in pediatric care, and adult care providers may be unfamiliar with ways to address these gaps.

There are multiple HCT guidelines available in the literature currently, each with their own strengths and limitations. Additional research is required to address the limitations of the available guidelines and take steps towards integrating disease-specific best-practice guidelines into standard care. As stated above, the guidelines proposed by CAPHC are relatively strong guidelines that could be used as a foundation from which more specific guidelines and resources are developed. While further improvements to the guidelines could be made based on the shortcomings identified above, it is essential that the targeted patient populations are given platforms, such as this research study, to voice their opinions on the critical elements of the HCT that should be included in future guidelines. Development of patient-driven and disease specific HCT guidelines will ensure that patients receive the appropriate care, tailored information and will promote a successful HCT by mitigating gaps in care.

1.4. SELF-MANAGEMENT

The term self-management is typically employed in the context of treating chronic health conditions (*e.g.* diabetes, spina bifida, heart disease). The term was first coined in the 1960s and was used to imply that patients were active participants in treatment (Lorig & Holman, 2003). The term self-management has since been used widely across healthcare and the definition has continued to evolve. Unfortunately, while the term is employed uninhibitedly throughout the literature, self-management remains poorly conceptualized and defined, though the notion of patient involvement has been unvarying (Lorig & Holman, 2003). Self-management is most commonly understood, both in the literature and for the purpose of this thesis, as the process of conducting the day-to-day activities required for patients to manage or maintain their physical and mental health and wellbeing in the context of a chronic condition (Coleman & Newton, 2005; Grady & Gough, 2014; O'Connell, Mc Carthy, & Savage, 2018). Self-management activities may include symptom management, following medication schedules, maintaining a proper diet, coping with the psychosocial impacts of the condition and engaging with the healthcare system (Grady & Gough, 2014; Dena Schulman-Green et al., 2012). Self-management is championed as a means to reduce disease burden and improve patients' overall health and quality of life (O'Connell et al., 2018; Wagner et al., 2001; Zwerink et al., 2014).

In 2011, Udlis (2011) conducted an in-depth analysis of self-management literature to better define the concept and identified several antecedents, dimensions and consequences of self-management in the context of chronic illness. The antecedents to self-management were determined to be self-efficacy, support, intention, mutual investment and information (Udlis, 2011). To elaborate on each antecedent, patients must believe that they are capable of self-managing in order to have the motivation to effectively self-manage (Ebrahimi Belil, Alhani, Ebadi, & Kazemnejad, 2018; Sarkar, Ali, & Whooley, 2009; Udlis, 2011). Patients also require support from their healthcare providers, families and social circles to successfully manage (Dineen-Griffin, Garcia-Cardenas, Williams, & Benrimoj, 2019; Udlis, 2011). Self-management is more likely to be successful when patients have defined goals and plans to reach their goals. And, mutual investment, or a partnership between the patient and provider is essential for building trust between each party, which in turn promotes effective management (Dang, Westbrook, Njue, & Giordano, 2017; Eton et al., 2017; Udlis, 2011). Arguably, information is the foundation for self-management as knowledge regarding the impact of chronic illness on health, treatment options

and psychosocial supports, are imperative for making autonomous, well-informed decisions about managing one's own illness (Udlis, 2011; Vainauskienė & Vaitkienė, 2021). Perhaps equally as important as the availability of information, is the way the information is provisioned. It is well known that information presented in a way that facilitates learning, and is tailored to the individual's needs, improves satisfaction and application of the information (Farley, 2020; Harvey & Lawson, 2009; Harvie, 2021; Udlis, 2011).

Research focused on self-management in the context of childhood onset conditions identified the importance of building the precursors to self-management in early childhood (Sawin et al., 2021; Tuohy et al., 2019). Sawin *et al*. (2021) stated that for patients diagnosed with spina bifida, the *"building blocks for self-management begin in childhood"* as early education promotes a successful HCT (Peterson, Rauen, Brown, & Cole, 1994). The importance of this is highlighted by studies with patients with type 1 diabetes. Patients who had not developed appropriate self-management skills were more likely to have reduced metabolic control (Cameron, Garvey, Hood, Acerini, & Codner, 2018; Campbell et al., 2014). Research in the cystic fibrosis realm identified that children without self-management skills experience negative thought patterns towards their treatment plan which subsequently influenced their behaviour towards their treatment (Downs, Roberts, Blackmore, Le Souëf, & Jenkins, 2006), and likely had detrimental impacts for their management compliance as they grew older.

Ultimately, promoting self-management in all patients is essential for empowering patients to manage their condition independently and effectively. As a result, patients are afforded the tools to improve their health and quality of life (Coleman & Newton, 2005).

1.5. PHENYLKETONURIA

1.5.1. Epidemiology

PKU, also known as phenylalanine hydroxylase (PAH) deficiency, is a genetic condition characterized by aberrant phenylalanine (Phe) metabolism. PKU is among the most common inborn errors of amino acid metabolism and occurs ~1 in every 10,000 live births (van Spronsen, Hoeksma, & Reijngoud, 2009). As of 2020, the global prevalence of PKU was estimated to be 1:24,174 (Hillert et al., 2020). However, the incidences of PKU vary widely between ethnicity and geographic region. Interestingly, PKU is the most commonly inherited genetic condition among Europeans (Hillert et al., 2020), with the highest prevalence in Italy (1:4,000) and Ireland (1:4,545)

and the lowest PKU rates recorded in Denmark (1:13,434) and Finland (1:112,000). The lowest PKU prevalence was observed in Asia, in which the prevalence was reported to be 1:227,273. In Canada, the prevalence of PKU was estimated to be 1:15,000 (Hillert et al., 2020).

1.5.2. Diagnosis

PKU is most often diagnosed during the neonatal period (the first 4 weeks of life) through NBS programmes (Reiger & Greene, 2000; van Spronsen et al., 2009). NBS programmes were developed to systematically test babies shortly after birth to identify those with congenital disorders that required early intervention to prevent permanent disability or death (Grosse, 2015). The Guthrie test, developed by Dr. Robert Guthrie in 1963, was the foundation for modern day PKU testing and NBS programmes (Brosco & Paul, 2013; Guthrie, Susi, & Scriver, 1998; van Spronsen et al., 2021). The Guthrie test was an easy and inexpensive test that required a blood sample from a newborn's heel that was applied to a test card. A disk was punched out from the dried blood spot which was subsequently incubated in a petri dish plated with bacteria and a growth inhibitor. In the presence of high Phe levels, the growth inhibitor becomes inactivated and the bacteria are able to grow (Blumenfeld, Wallace, & Anderson, 1966). While the use of dried blood spots has persisted, the methods employed to test the blood spots have evolved. Now fluorimetric microassays, a chromatography-based approach with fluorimetric detection, and tandem mass spectrometry are employed in NBS programmes to quantify Phe levels (van Spronsen et al., 2021). These approaches are more sensitive than the Guthrie test and tandem mass spectrometry enables simultaneous measurement of multiple amino acids. Consequently, the diagnostic criteria for PKU include a Phe concentration >120 micromoles per litre and a Phe to tyrosine ratio of >1.5 (van Spronsen et al., 2021).

1.5.3. Molecular Pathogenesis

PKU is caused by pathogenic variants in *PAH* which is located on chromosome 12q23.2 and is comprised of 13 exons and 12 introns (***Figure 1-2***) (Alibakhshi, Moradi, Biglari, & Shafieenia, 2018). *PAH* mRNA encodes a 52 kDa enzyme, also called PAH, comprised of 452 amino acids (***Figure 1-2***) (G. Ho & Christodoulou, 2014). The PAH polypeptide can be divided into three main domains which include the regulatory domain (amino acids 1 – 142), located at the N-terminal tail, the catalytic domains (amino acids 143 – 410) and the oligomerization domain (amino acids 411 – 452), located at the C-terminal tail (***Figure 1-2***) (Blau, 2014; G. Ho & Christodoulou, 2014). The regulatory domain is posited to control access to the catalytic domain active site (Wang, Gu,

& Kaufman, 2001), while the catalytic domain contains binding sites for co-factor and substrate (Flydal & Martinez, 2013). The oligomerization domain enables tetramerization of PAH monomers to create a functional enzyme (Flydal & Martinez, 2013).

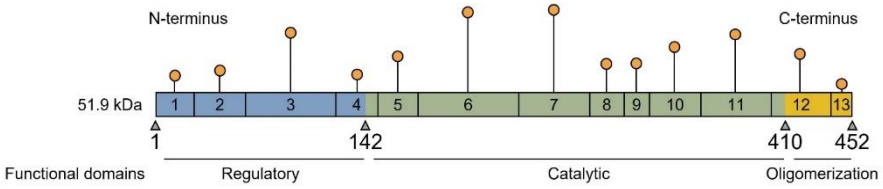

Figure 1-2. Primary PAH protein structure and mutation frequency.
Diagram showing the primary structure of PAH (National Library of Medicine, last updated 2023b). Exons are numbered and delineated by black outline. PAH is a 52 kDa protein with 3 functional domains including the regulatory (blue), catalytic (green) and oligomerization (orange) domains. Amino acids numbers denoting the boarders of each domain are indicated by grey arrows. Height of orange lollipops indicates the mutational frequency in each exon.

PAH is active in select tissues including kidneys, gallbladder and spermatids, but is predominantly active in the liver (Uhlén et al., 2015). PAH catalyzes the hydroxylation of Phe to tyrosine (***Figure 1-3A***), which is the rate limiting step of Phe metabolism. PAH loss of function underlies PKU pathogenesis as reduced activity causes accumulation of Phe to toxic concentrations and reduced tyrosine levels (***Figure 1-3B***). Excess Phe is subsequently converted to phenylpyruvate and phenylketones (*i.e.* phenylacetate and phenyllactate). While the exact pathogenic mechanism of elevated Phe concentrations is unknown, it has been suggested that high Phe levels saturate the transport proteins responsible for transporting amino acids across the blood-brain barrier. Consequently, protein synthesis in the brain is impeded and is suspected to underlie the neurobehavioural outcomes associated with PKU (see *Section 1.5.4*) (Kliegman et al., 2020; van Spronsen et al., 2009).

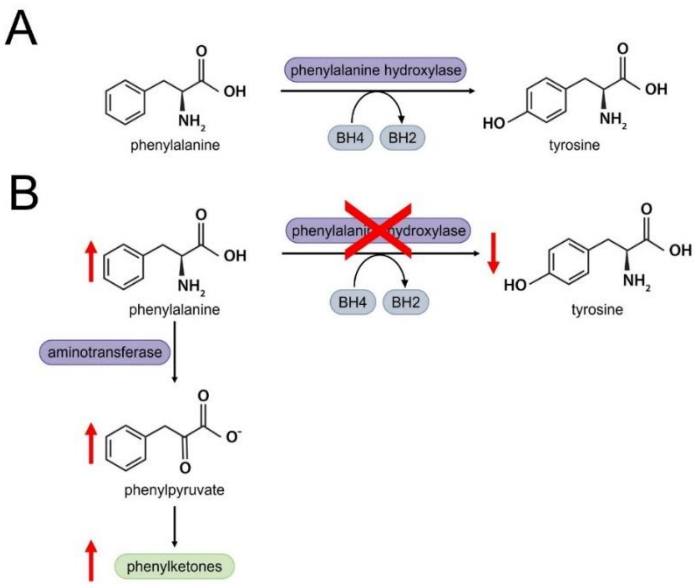

Figure 1-3. PAH activity regulates Phe abundance.
(A) Schematic depicting Phe metabolism. PAH catalyzes Phe hydroxylation to tyrosine. Tetrahydrobiopterin (BH4) acts as a co-factor by binding PAH and stabilizing the protein to catalytic activity. ***(B)*** Schematic depicting aberrant Phe metabolism. Deficient PAH activity induces an increase in Phe levels and a subsequent decrease in tyrosine. Excess Phe is converted to phenylpyruvate and phenylketones (*i.e.* phenylacetate and phenyllactate).

Disease phenotypes associated with the *PAH* gene are inherited in an autosomal recessive manner (Reiger & Greene, 2000; van Spronsen et al., 2021). To date, >1,000 pathogenic alterations and >2,600 pathogenic genotypes have been identified in individuals with PKU (Garbade et al., 2019; Hillert et al., 2020). While pathogenic variants have been noted throughout the entire *PAH* gene, most pathogenic variants occur within the catalytic domain, as depicted by ***Figure 1-3***. Disease severity is dictated by the degree of residual PAH activity, with plasma Phe concentrations >1,200 micromoles per litre categorized as "classic" PKU (the most severe form) (G. Ho & Christodoulou, 2014).

1.5.4. Disease Manifestation

As described in *Section 1.5.3*, the mutational spectrum observed in PKU underlies varying degrees of PAH activity. As such, PKU is phenotypically heterogeneous, and risk of adverse outcomes is negatively correlated with residual PAH activity (T. Chen et al., 2018; G. Ho & Christodoulou, 2014; Reiger & Greene, 2000). Moreover, clinical presentation varies depending on age of diagnosis and level of disease management (*Section 1.5.5*) (Reiger & Greene, 2000; van

Spronsen et al., 2021). If untreated, due to late diagnosis or management difficulties, individuals invariably develop severe and irreversible neurodevelopmental (*e.g.* intellectual disability, impaired growth, seizures) and psychiatric (*e.g.* autism, aggression, irritability, impulsivity, psychosis) sequelae (Ashe et al., 2019; Reiger & Greene, 2000), which may be attributed to white matter disturbances observed on brain imaging (van Spronsen et al., 2021). Persistent hyperphenylalaninemia (high Phe levels) may also cause decreases in melanin production, musty body odor, eczema and blindness (Reiger & Greene, 2000; van Spronsen et al., 2021). Contrastingly, if treated from an early age, and individuals maintain adequate management, particularly before 6 years old, the severity of neurodevelopmental and psychiatric manifestations is significantly reduced (Ashe et al., 2019). However, individuals with PKU are still more likely to develop certain psychological problems (*e.g.* anxiety, depression) compared to others with chronic diseases (Reiger & Greene, 2000). Extensive research has determined that individuals who strictly comply to treatment develop and maintain a normal intelligence quotient throughout their lifetime (Ashe et al., 2019; Burgess et al., 2021; Hood, Grange, Christ, Steiner, & White, 2014; Reiger & Greene, 2000; Waisbren et al., 2007). Individuals with a relaxed adherence to treatment may experience small decreases in intelligence, executive functioning (*e.g.* attention span, information-processing abilities) and motor reaction time (Reiger & Greene, 2000).

Impact of Maternal PKU on Pregnancy

It is imperative that pregnant individuals with PKU strictly follow a low-protein diet and monitor their blood Phe concentration to decrease the risks of abnormal fetal development (Rohde et al., 2021; van Spronsen et al., 2009). High maternal Phe levels are associated with microcephaly, intellectual disability/developmental delay, impaired growth and congenital heart disease in the fetus (Prick, Hop, & Duvekot, 2011; Rohde et al., 2021). Previous research has demonstrated that the risk for maternal PKU-related fetopathy is ~90% in pregnancies affected by hyperphenylalaninemia (Caletti et al., 2020). More specifically, the risk for microcephaly is 67%, while the risks for intellectual disability and birth differences are >90% and ~12%, respectively (Reiger & Greene, 2000). Given the strong associations between hyperphenylalaninemia and abnormal fetal development, it is recommended that PKU patients planning a pregnancy maintain a low-protein diet that is more stringent than what is typically recommended (see *Section 1.5.5*) for several months prior to conception (Reiger & Greene, 2000; Rohde et al., 2021).

1.5.5. Treatment

With the advent of NBS programmes, the incidence of severe intellectual disability due to PKU is predicted to be less than 1 in 1,000,000 (Reiger & Greene, 2000). This is attributable to the early diagnosis and subsequent early management of hyperphenylalaninemia (Reiger & Greene, 2000). Dietary treatment of PKU has long been established as the primary means for preventing symptoms (Burgard et al., 1999).

Dietary treatment is effective for treating PKU as Phe is an essential amino acid (*i.e.* is not synthesized by the body) and therefore, must be obtained through diet. Phe is naturally abundant in high protein foods such as meat, fish, dairy, soy, grains and legumes (Ashe et al., 2019; MacDonald et al., 2020; van Spronsen et al., 2021). Consequently, to mitigate the symptoms associated with PKU, individuals must adhere to a low-protein diet for their lifetime. The amount of protein consumed per day is tracked to ensure that blood Phe concentrations remain within the target range. Children under 12 years old, and individuals planning a pregnancy should aim to have their blood Phe concentration between 120 – 360 micromols per litre (~12 milligrams per kilogram per day), while adults should aim to be between 120 – 600 micromols per litre (~25 milligrams per kilogram per day) (Camp et al., 2014; Macleod & Ney, 2010). To ensure that all other nutritional needs are met, specialized low-protein foods and Phe-free amino acid formulas have been developed and are typically integrated into the diet (***Table 1-1***) (MacDonald et al., 2020). Though financial support varies between Canadian provinces, many low-protein foods and formula are covered by provincial healthcare programmes (Canadian PKU and Allied Disorders, 2016).

Table 1-1. Example of the typical daily diet for an individual with PKU[A].

Meal	Food[B]	Phe[C]
Breakfast	3/4 cup cheerios	133 mg
	1/8 cup almond milk	8 mg
	1 cup formula	0 mg
Snack	Apple sauce	6 mg
Lunch	Cheese sandwich (low protein bread/vegan cheese/mayonnaise/lettuce)	4 mg
	1/2 cup carrot sticks	18 mg
	1 cup formula	0 mg
	1 medium apple	7 mg
Snack	Celery, cucumber, 1 tbsp mayonnaise w/ dill	8 mg
Dinner	Low protein egg omelet with veggies	10 mg
	1/4 cup hashbrowns	53 mg
	1 tbsp ketchup	7 mg
Snack	1 cup formula	0 mg
	Total Phe	254 mg

[A]Courtesy of Nicole Aylward (metabolic dietician)
[B]Tbsp, tablespoon; w/, with
[C]Phe, phenylalanine; mg, milligrams; target Phe range is 250 – 350 mg/day, though levels differ for children and adults

In 2007, Kuvan (sapropterin dihydrochloride) became the first drug approved for PKU treatment by the United States Food and Drug Administration (Wiedemann, Oussalah, Jeannesson, Guéant, & Feillet, 2020). Kuvan is a synthetic formulation of BH4, a cofactor required for PAH activity (***Figure 1-3***). It is suggested that excess BH4 from Kuvan increases activity of residual PAH and/or stabilizes mutant PAH (Sanford & Keating, 2009). Kuvan revolutionized PKU treatment as some individuals greatly improved their Phe tolerance and were able to significantly expand their low-protein diet while on daily doses of the drug. However, many individuals may only minimally increase their Phe tolerance and are still required to monitor blood Phe concentrations, while a subset of individuals do not respond to Kuvan at all.

More recently, a second drug, Palynziq (pegvaliase-pqpz), was approved for PKU treatment. Palynziq is an injectable drug, taken daily, in which the active component is a pegylated Phe ammonia lyase. The enzyme converts excess Phe to ammonia and trans-cinnamic acid which are respectively metabolized in the liver and excreted in the urine (Hydery & Coppenrath, 2019). While Palynziq has also enabled select individuals to expand their low-protein diet, the drug is not without its complications. Clinical trials revealed that patients experienced highly heterogeneous immunological responses. All patients developed antibodies against the drug, which put them at

risk for allergic reactions including skin rashes, joint stiffness and anaphylaxis (Mahan, Gandhi, & Anand, 2019; van Spronsen et al., 2021). Patients must continue with treatment for several months to overcome the short-term immune-mediated responses and begin to experience treatment effects (van Spronsen et al., 2021). Despite the advances in drug treatments, a cure for PKU has yet to be identified.

1.5.6. Self-Management

As described in *Section 1.4*, self-management is the process by which individuals with chronic diseases, such as PKU, cope and manage their disease in their everyday life. Self-management activities involve symptom management, adhering to treatment regimens, navigating the healthcare system, and coping with the psychosocial impacts of the disease (Lorig & Holman, 2003; D. Schulman-Green, Jaser, Park, & Whittemore, 2016). PKU, in particular, is associated with a high management burden primarily due to the dietary restrictions that require extensive education and planning (MacDonald, Gokmen-Ozel, van Rijn, & Burgard, 2010; Ten Hoedt et al., 2011). While it is believed that diet management is the primary element of PKU self-management, PKU patients are faced with tasks within each of the self-management elements mentioned previously (***Figure 1-4***).

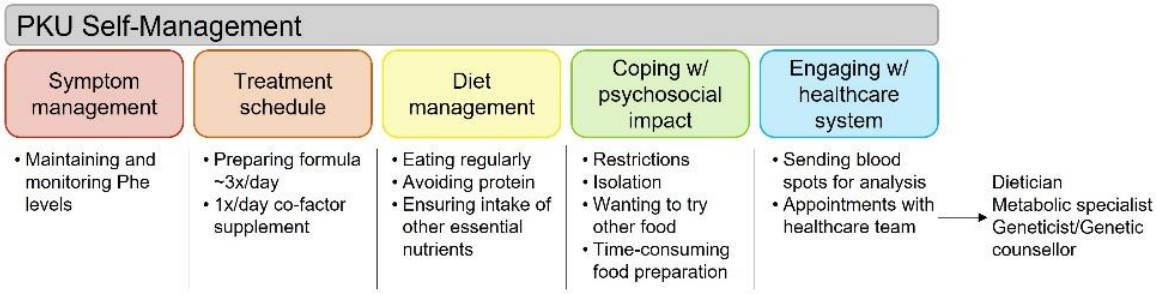

Figure 1-4. Self-management for PKU.
Schematic outlining examples of self-management activities for individuals with PKU. Activities include symptom management, maintaining treatment schedules, diet management, coping with the psychosocial impacts of the disease and engaging with the healthcare system. Self-management varies between patients and can be adapted based on each patients' biology and life circumstances.

Symptom management includes maintaining Phe levels within the target range. Phe levels are typically monitored monthly using blood spot cards that are sent for laboratory analysis (van Wegberg et al., 2017; Vockley et al., 2014). Blood spots may be requested as frequently as 1-2 times per week during pre-conception and pregnancy or other medically unstable times. Treatment

regimens require PKU patients to consume their formula regularly to supplement the micronutrients missing in their diet. Additionally, for patients using pharmaceuticals, it is essential that they follow their medication schedule to maintain their Phe allowance and prevent symptoms. As described in *Section 1.5.5*, self-management for PKU also includes maintaining a low-protein diet and manually tracking the amount of protein and Phe that is consumed each day. Diet maintenance may also include purchasing specialized low-protein foods. Compliance with the low protein diet has proven to be challenging for PKU patients. In fact, factors such as the burden of meal preparation, the impacts of the diet in social settings and influences from peers, among other concerns, have been associated with poor adherence (Bilginsoy, Waitzman, Leonard, & Ernst, 2005; Macdonald et al., 2008; Nevins, 2005; Olsson, Montgomery, & Alm, 2007). The European and American guidelines for PKU management recommend various types of medical follow-up for PKU patients (Lowe, DeLuca, & Arnold, 2020; van Wegberg et al., 2017; Vockley et al., 2014). In addition to regular follow-up with providers in a metabolic clinic, it is recommended that PKU patients have routine nutritional monitoring through bloodwork, neurocognitive and mental health assessments and assessment of bone health. The frequency of these assessments is dependent on age and pregnancy (Lowe et al., 2020; van Wegberg et al., 2017; Vockley et al., 2014). Individuals with PKU must also engage in activities that help them cope with the psychosocial impacts of their PKU, as it is well known that PKU is associated with anxiety, depression, hyperactivity, antisocial behaviour, poor impulse control and attention difficulties (see *Section 1.5.4*) (Gentile, Ten Hoedt, & Bosch, 2010; Reiger & Greene, 2000; van Spronsen et al., 2021). Children with PKU also experience bullying regarding their diet which often leads to disordered eating (Ford et al., 2018). For biologically female patients, self-management activities may also involve careful planning to ensure pregnancy occurs while blood Phe concentrations are well controlled.

Typically, the degree of self-management for individuals with PKU changes throughout their lifetime. As patients get older, it is expected that their understanding of the disease increases and they become responsible for a greater proportion of the required day-to-day management (Feillet et al., 2010; Vegni, Fiori, Riva, Giovannini, & Moja, 2010). The *Cristine M. Trahms Program for Phenylketonuria* at the University of Washington proposed a self-management timeline for children and teenagers with PKU (***Figure 1-5***). The timeline highlights age-appropriate knowledge and activities that children and teenagers can learn to empower them to self-manage and transition to adult healthcare.

PKU SELF-MANAGEMENT TIMELINE

Age	Tasks
0-6 months	Parents learn about and adjust to PKU
6-7 months	Parents start to offer low-protein solid foods Introduce cup with water
8-9 months	Parents introduce finger foods
10-15 months	Parents consider final weaning from bottle (discuss transition with clinic staff)
2-3 years	Learn the concept of "formula first" Learn to distinguish "yes" and "no" foods Transition from Phenyl-Free 1 to Phenyl-Free 2
4-5 years	Begin to learn to count foods – "how many" Begin to use scale – "how much"
5-6 years	Assist in formula preparation Learn how to deal with other children's curiosity about PKU
7-10 years	Prepare formula with decreasing supervision Choose after school snack Learn to pack school lunch Begin to list foods on food record Begin weighing food regularly on scale
10-12 years	Begin to prepare and consume formula independently each day (with parental monitoring) Prepare simple entrees independently Know what blood levels are ideal
13-14 years	Increasing self-monitoring (with continued parent support) in formula preparation and consumption Independently manage total phe intake for the day Learn menu planning Responsible for food records
15-17 years	Competent to perform and primarily responsible for all aspects of self-management with continued parent support Able to perform own filter paper blood sample or schedule blood draw Able to explain the basics of PKU – "What is it?" Responsible for remembering recent blood levels
18 years	Transition to adult-based clinic care Ready to live independently, including: – Formula preparation and consumption – Food preparation and records – Monthly serum phe – Setting and keeping own appointments on regular basis Parents act as consultants

Figure 1-5. Proposed self-management timeline for individuals with PKU.
Image of the self-management timeline proposed by the *Cristine M. Trahms Program for Phenylketonuria* at the University of Washington (2008). In the earliest months to years of a child's life, their PKU management is controlled by their parents. As the child ages, they are expected to assume more responsibility and autonomy until they are prepared to transfer to the adult healthcare system.

The self-management tasks for PKU are extensive, and it is well known that PKU patients often struggle with maintaining appropriate management. The underlying factors impacting self-management adherence are diverse, and therefore it is imperative to gain insight directly from patients regarding their support needs for managing during the HCT.

1.6. GLYCOGEN STORAGE DISEASE 1A

1.6.1. Epidemiology

Glycogen storage disease 1 (GSD1), also known as von Gierke disease, and is an IEM characterized by aberrant glycogen catabolism which limits available glucose for energy production. GSD1 occurs in all ethnic groups and the overall disease incidence is ~1 in 100,000 live births (Bali, El-Gharbawy, Austin, Pendyal, & Kishnani, 2006; Kishnani et al., 2014). The disease incidence is highest in the Ashkenazi Jewish population, but is found worldwide, and occurs in 1 in every 20,000 live births (Ozen, 2007). Ethnic group-specific pathogenic variants account for 90-100% of known disease alleles (Kishnani et al., 2014). GSD1a, a subtype of GSD1, accounts for 80% of GSD1 cases (Bali et al., 2006; Kishnani et al., 2014).

1.6.2. Diagnosis

Early diagnosis and treatment of GSD1a is essential for mitigating significant negative impacts on organ function, and ultimately improve prognosis. While GSD1a is not part of NBS programmes, the most severely affected individuals will present in the neonatal period. However, it is most common for affected individuals to present between 3 to 4 months of life. Diagnosis of GSD1a is typically based on clinical presentation (see *Section 1.6.4*), biochemical findings and genetic testing (see *Section 1.6.3*). GSD1a should be suspected when a patient presents with signs of hypoglycemia (pallor, breathing disturbances, jitteriness, reduced level of consciousness, seizure), hepatomegaly and growth failure, while suggestive biochemical findings include low blood glucose and elevated blood lactate, triglyceride, and uric acid levels. The diagnosis can be confirmed via molecular testing if biallelic disease-causing variants are identified in the underlying gene or if a patient shows deficient enzyme activity (see *Section 1.6.4*) following a liver biopsy. Most patients with GSD1a have <10% normal enzyme activity. Molecular testing is the preferred method of diagnosis as it is less invasive than a liver biopsy and is becoming increasingly sensitive (Bali et al., 2006; Froissart et al., 2011; Kishnani et al., 2014; Rake et al., 2002).

1.6.3. Molecular Pathogenesis

Pathogenic variants in *G6PC1* (*glucose-6-phosphatase catalytic subunit 1*), located on chromosome 17q21.3, underlie GSD1a pathogenesis. *G6PC1* is comprised of 5 exons and 4 introns, from which the resulting mRNA encodes a 40.5 kDa enzyme named glucose-6-phosphatase (G6Pase) (Bali et al., 2006). G6Pase is comprised of 357 amino acids organized into 9 transmembrane regions (***Figure 1-6***). G6Pase is responsible for removing the phosphate molecule from glucose-6-phosphate to generate free glucose, which is a key step in maintaining a normal blood sugar level via glycogenolysis and gluconeogenesis (Ozen, 2007; Plona, Eastman, & Drumm, 2021; Yang Chou & Mansfield, 1999). Glycogenolysis is the stepwise breakdown of glycogen (a large multibranched molecule serving as energy storage) into glucose monomers (***Figure 1-7***). Glycogenolysis enables the rapid access of glucose stored in the liver between meals, and energy for muscle contraction during exercise (Blanco & Blanco, 2017; Paredes-Flores & Mohiuddin, 2022). Gluconeogenesis, which occurs in the liver and kidneys, is the *de novo* synthesis of glucose molecules from smaller substrates, such as lactate and amino acids, rather than the breakdown of larger carbohydrate macromolecules. Gluconeogenesis is triggered during prolonged fasting and vigorous exercise once glycogen stores have been depleted (Engelking,

2015; Hanson & Owen, 2013). Impaired G6Pase activity inhibits glycogenolysis and gluconeogenesis, so ultimately, glycogen stores cannot be metabolised to release glucose monomers, nor can glucose monomers be anabolised from other substrates. Further, aberrant glycogenolysis induces accumulation of glucose-6-phosphate which is shunted to alternative pathways, resulting in accumulation of lactate, lipids and uric acid (see *Section 1.6.2*) (Ross et al., 2020). G6Pase is most highly expressed in the liver, kidneys and intestines (Parikh & Ahlawat, 2022; Plona et al., 2021). As such, G6Pase deficiency induces glycogen and fat accumulation in those tissues.

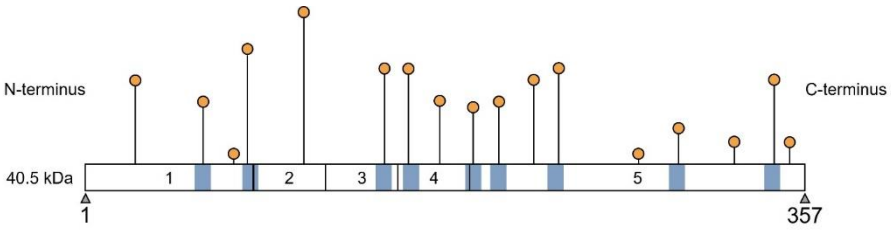

Figure 1-6. Primary G6Pase protein structure and mutation frequency.
Diagram showing the primary structure of G6Pase (National Library of Medicine, last updated 2023a). Exons are numbered and delineated by black outline. G6Pase is a 40.5 kDa protein with 9 transmembrane regions (blue). Amino acid numbers are indicated by grey arrows. Heigh of orange lollipops indicate the mutational frequency in each exon.

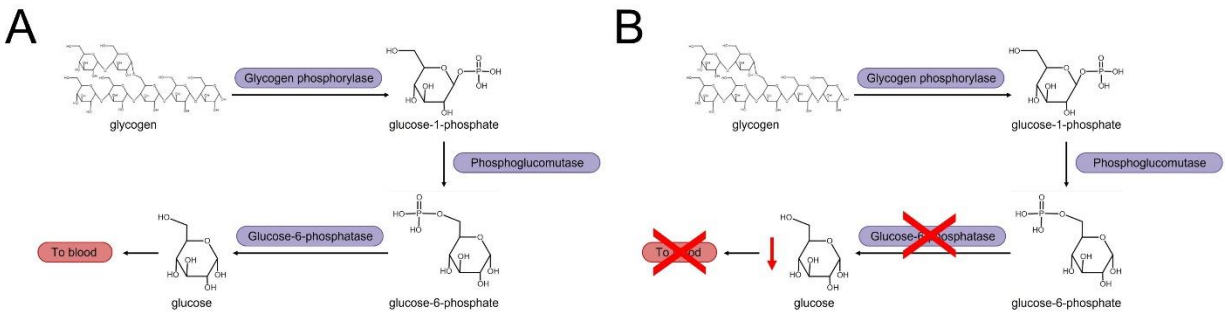

Figure 1-7. G6Pase activity regulates blood glucose concentration.
(A) Schematic depicting glycogenolysis. G6Pase catalyzes the dephosphorylation of glucose-6-phosphate to glucose. Glucose is subsequently absorbed into the bloodstream to maintain blood glucose concentrations. ***(B)*** Schematic depicting aberrant glycogenolysis. Deficient G6Pase activity prohibits adequate release of glucose from glycogen stores and results in a decrease in blood glucose concentration.

Disease associated with *G6PC1* alterations is inherited in an autosomal recessive pattern (Bali et al., 2006; Froissart et al., 2011; Parikh & Ahlawat, 2022; Weinstein, Steuerwald, De Souza, & Derks, 2018). More than 150 alterations have been identified in individuals with GSD1a though only a subset are classified as disease-causing, while the remaining are determined to be of uncertain significance (Plona et al., 2021). Pathogenic variants have been recorded throughout the *G6PC1* gene (***Figure 1-6***). Overall, a genotype-phenotype correlation has been difficult to discern (Plona et al., 2021), though it has been identified that Japanese individuals who are homozygous for the c.648G>T variant may have a milder hypoglycemic phenotype, but may be more likely to develop hepatocellular carcinoma.

1.6.4. Disease Manifestation

As described above, the genetic heterogeneity observed in the *G6PC1* gene does not account for the clinical heterogeneity recognized in this population. While GSD1a is a highly clinically variable condition, infants with GSD1a typically present once the interval between feeds increases (*e.g.* when they sleep through the night), around 3-4 months of age (Bali et al., 2006). As described in *Section 1.6.2*, infants present with signs of hypoglycemia and abnormal biochemical profiles. Affected infants are said to have doll-like facial features (*e.g.* round face, full cheeks) and hepatomegaly may cause a protuberant abdomen (Bali et al., 2006; Ozen, 2007; Rake et al., 2002). Individuals may experience tremors, irritability, abnormal sweating, and may have blue tinged skin. In prolonged periods of hypoglycemia, patients may experience seizures and permanent cognitive impairment. When blood glucose levels cannot be normalized, patients may experience a metabolic crisis that leads to death (Hicks, Wartchow, & Mierau, 2011; Ozen, 2007). Individuals who experience long-term complications may have short stature, osteoporosis, delayed puberty, high blood pressure, hepatocellular carcinoma, pancreatitis, myocardial infarction, and ovarian cysts (Bali et al., 2006). When managed adequately, patients experience typical growth patterns and are expected to live independent adult lives (Garbade et al., 2021). However, despite metabolic control, liver adenomas and kidney disease may still develop (Bali et al., 2006).

1.6.5. Treatment

Diet management has been the predominant treatment for GSD1a for more than 50 years (Ross et al., 2020). While recent advances in gene therapy will likely alter the way in which GSD1a is treated, currently, prevention of GSD1a manifestations is accomplished via therapeutic diet (Ozen, 2007; Rake et al., 2002). It is recommended that individuals with GSD1a limit consumption of

lactose, galactose, fructose, and sucrose as each of these saccharides cannot be metabolized due to the G6Pase deficiency (Froissart et al., 2011; Kishnani et al., 2014). As such, table sugar, fruit, and dairy are contra-indicated, and the therapeutic diet should consist primarily of carbohydrates in the form of simple dextrose or dextrose polymers (60-70% of total calories), protein (10-15% of total calories) and fat. In general, individuals are expected to maintain this diet for their lifetime (Kishnani et al., 2014).

Blood glucose concentrations are monitored throughout the day to ensure levels are within the targeted range (4 millimoles per litre – 6 millimoles per litre). In addition to altering the types of foods that are consumed, it is essential that meals and snacks are eaten every 1-2 hours to maintain blood glucose in infancy and can be extended to every 3-4 hours in older children once cornstarch therapy (discussed subsequently) is initiated (***Table 1-2***). Supplements may be recommended to avoid deficiencies of other important micronutrients (Kishnani et al., 2014). It is recommended that individuals consume uncooked cornstarch mixed with fluid every 3-6 hours depending on age as this allows less frequent feeding (Correia et al., 2008; Ross et al., 2020). Cornstarch is a complex carbohydrate that is slowly metabolised to maintain normoglycemia (Y.-T. Chen, Cornblath, & Sidbury, 1984). Maintaining appropriate blood glucose levels during sleep is a major concern with GSD1a. Patients who are too young to receive cornstarch treatments require a gastrostomy tube with a continuous pumping system with water and dextrose being delivered throughout the night until they are old enough to being cornstarch treatments. Patients who receive cornstarch treatments are often required to wake up 1-3 times per night to receive their cornstarch dose (Correia et al., 2008). Since cornstarch is not very palatable, gastrostomy tubes are also often used for delivery of doses. The challenges associated with ensuring cornstarch is consumed every 3-6 hours spurred the development of artificial cornstarch derivatives (*e.g.* Glycosade) that require a single dose to sustain normal blood glucose levels throughout the night. The development of artificial slow-release carbohydrate supplements was a pivotal development in GSD1a treatment, and while dietary management remains the mainstay of GSD1a management, advances in enzyme replacement therapies and molecular genetics may impact management decisions for individuals with GSD1a in the future.

Table 1-2. Example of the typical daily diet for an individual with GSD1a[A]

Time and meal	Food[B]
7:00 am	36 g cornstarch (mixed w/ water)
8:00 am Breakfast	Eggs and toast
11:00 am	28g cornstarch (mixed w/ water)
12:00 pm Lunch	Rice, meat and veggies
3:00 pm	28g cornstarch (mixed w/ water)
5:30 pm Dinner	Pasta, meat and veggies
7:00 pm	28g cornstarch (mixed w/ water)
8:30 pm Snack	Crackers
11:00 pm	cornstarch or Glycosade

[B]Courtesy of Nicole Aylward (metabolic dietician)
[A]g, grams; w/, with

1.6.6. Self-Management

GSD1a patients have reported their disease as having a moderate management burden as it requires significant time and space to address the various medical and psychosocial aspects associated with having a rare genetic condition (Garbade et al., 2021). Recall the different elements of self-management described in *Section 1.4*, comprehensive management of GSD1a requires individuals to accomplish various tasks within each of these elements (***Figure 1-8***).

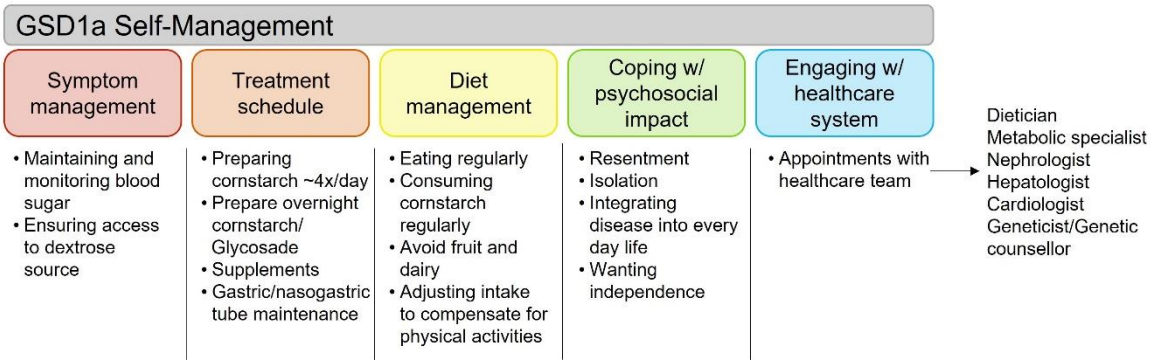

Figure 1-8. Self-management for GSD1a.
Schematic outlining examples of self-management activities for individuals with GSD1a. Activities include those listed in the coloured boxes, and examples of each are listed underneath. Self-management will vary between patients and based on each individuals' biology and life circumstances.

As depicted by ***Figure 1-8,*** self-management activities for GSD1a are abundant. Symptom management is accomplished by maintaining blood glucose levels with frequent monitoring via a glucometer before meals and cornstarch intake. Regular consumption of meals and cornstarch

doses (*i.e.* maintaining a treatment schedule) is critical for preventing symptoms. As described in *Section 1.6.5*, individuals are required to carefully time cornstarch treatments throughout the day and night to prevent hypoglycemia, and daily supplements may be required to avoid nutrient deficiencies. Diet management requires individuals to eat regularly and limit dietary intake of fruit and dairy. Self-management of GSD1a not only includes tasks to maintain physical health, but also requires coping with various psychosocial impacts of the disease. For example, GSD1a patients were reported by Garbade *et al*. (2021) to experience anxiety, fear and rage in relation to their disease. Moreover, a study by Flanagan *et al*. (2015) identified that 14.8% and 11.1% of GSD1a children and adolescents, respectively, were considered to have eating disorders and maladjusted attitudes towards food and eating. Self-esteem, with respect to physical appearance, was also considered to be lower compared to counterparts from the general population (Flanagan et al., 2015). Overall, patients report experiencing mental health problems as a by-product of coping (or lack thereof) with their disease (United States Food and Drug Administration, 2021a). Lastly, as described in *Section 1.6.4*, GSD1a is a multisystem condition that warrants surveillance by a multidisciplinary team (Kishnani et al., 2014). The American College of Medical Genetics and Genomics have detailed specific requirements for GSD1a patients' medical care (Kishnani et al., 2014). Patients should work closely with a metabolic dietician to establish an appropriate diet or address feeding issues (Kishnani et al., 2014). Liver imaging should be done once a year to assess development of liver adenomas. Renal function should be assessed every 6-12 months during routine visits with nephrology. Hematological studies should be conducted every 6-12 months to assess for anemia. Bone density should be assessed every 1-2 years, and echocardiograms should be completed every 3 years (Bali et al., 2006; Kishnani et al., 2014). In addition to specialist care, the American College of Medical Genetics and Genomics recommend that patients engage with their primary care providers for early evaluation and treatment should they become ill (Kishnani et al., 2014). Other specialists or allied health professionals (*e.g.* social worker, genetic counsellor, psychologist) may be consulted as needed. While many appointments and tests can be co-ordinated to occur during the same visit, engaging with the healthcare system may take substantial time away from school or work (Garbade et al., 2021).

Overall, ***Figure 1-8*** is a gross over-simplification of GSD1a management. Patients may struggle to maintain glycemic control, cope with their disease, or attend healthcare appointments for any number of reasons (Derks et al., 2021). In theory, the steps to maintain glycemic control

are straightforward, but many patients struggle to achieve adequate blood glucose levels (United States Food and Drug Administration, 2021a). A study by Rake *et al*. (2002) reported that despite appropriate diet management, ~55% of GSD1a patients experienced hypoglycemia necessitating hospitalization (Rake et al., 2002). Moreover, patients are known to have variable biological responses to cornstarch and have expressed concerns regarding the palatability of cornstarch which often results in poor compliance (Garbade et al., 2021). In fact, when asked about the impacts of cornstarch on their quality of life, patients reported that the frequency and volume of cornstarch they must consume negatively impacts their quality of life as it takes time away from work, school, social events, sleep and raises concerns about weight gain (United States Food and Drug Administration, 2021a). GSD1a patients also report that coping with certain aspects of their disease gives rise to complicated emotions towards their management (Derks et al., 2021).

Figure 1-8 also fails to acknowledge that patients' disease presentation often changes as patients get older, which requires them to adapt their management accordingly. For example, despite adequate management, some patients will still experience long-term complications of GSD1a. It is well known that liver adenomas, which may progress to malignancy, are often detected between the ages of 10-30 years and patients may also develop progressive renal failure (Bali et al., 2006) both of which require patients to change their management accordingly (*e.g.* additional healthcare appointments, learning to cope with potential outcomes, *etc*.). In addition to the challenges associated with the biological reasons for adapting management, there are also other circumstances in which patients' management may need to be adapted or their management is seen as a complicating factor that the general population would not have to consider. To illustrate, patients who wish to travel must consider the logistics of bringing supplements and cornstarch doses for the totality of their trip or know whether they have access to their same brand of cornstarch during their travels. Garbade *et al*. (2021) identified that a subset of patients felt that the efforts associated with travelling to be too high and could not participate in certain activities during their trip. While the American College of Medical Genetics and Genomics outlined the baseline of care for GSD1a patients, there is a substantial amount of adjustment required by patients to accommodate their management in their lives.

CHAPTER 2: STUDY RATIONALE, RESEARCH QUESTION & AIMS

2.1 RATIONALE

The HCT is a vulnerable time for any AYA diagnosed with a chronic condition. However, AYA diagnosed with conditions characterized by a high management burden, such as IEM, are known to be vulnerable to declining management during the HCT. Indeed, our literature review suggests that individuals with PKU and GSD1a, two relatively common IEM, struggle with self-management during the transition to adult care. Unfortunately, current literature focused on the HCT of AYA with PKU and GSD1a is sparse. Much of the research that has been completed to date includes retrospective chart reviews and interviews lacking detail regarding the patient-perceived factors impacting their readiness and ability to self-manage. Therefore, there is a prominent gap in our current understanding of the self-management support required for individuals with IEM during the HCT. As such, additional research is required to describe the support needed specifically by AYA with PKU and GSD1a during the HCT. PKU and GSD1a are ideal IEM for the current study as they are relatively common conditions compared to other metabolic conditions and therefore have a larger population from which to recruit participants. Additionally, individuals with PKU and GSD1a are more likely to have the cognitive capacity to conduct their own self-management compared to individuals with other IEM.

Given the gaps in current literature, this study seeks to explore patient's experiences with self-management including, but not limited to, the evolution of their self-management over their lifetime, how they learned to manage their disease and their feelings of readiness and comfort with respect to becoming more independent in their self-management.

2.2 RESEARCH QUESTION & AIMS

The current study sought to answer, "what are the patient-reported factors influencing one's readiness and capacity to self-manage their disease when transferring from pediatric to adult care?" To answer this research question, I sought to complete three research aims.

Aim 1: Identify patients' current perceptions of the HCT.

Aim 2: Explore patients' past and/or current experiences with self-management during the HCT.

Aim 3: Understand how healthcare providers can support patients with respect to readiness and self-management during the HCT.

CHAPTER 3: METHODOLOGY AND METHODS

3.1. SAMPLING STRATEGY

Participants were recruited across Canada, by way of convenience sampling, in partnership with various patient groups and agencies identified through Google searches and the search feature on social media platforms (*e.g.* Facebook, Twitter, Instagram). Variations of search terms such as "PKU support group" or "GSD1a support group" were employed to identify putative partners. Groups and agencies were manually vetted to determine their relevance to the current study. Members of The Canadian Association of Genetic Counsellors and the Dieticians of Canada were also contacted via listserv as they are integral members of the healthcare team for these patient populations.

A total of 8 patient groups and organizations were identified and contacted, including 4 patient groups on Facebook, 1 national organization through Instagram, 1 national organization through LinkedIn, and 2 healthcare provider networks through email blast (***Table 3-1***).

Table 3-1. Patient Organizations from which Participants were Recruited

Group Name	Contact Method[A]
CanPKU	LinkedIn, Email
Canadian Association of Glycogen Storage Diseases	Email, Instagram
The Canadian Association of Genetic Counsellors	Email
Dieticians of Canada	Email
Phenylketonuria (PKU) World Wide Support Group!	Facebook
PKU (Phenylketonuria) recipes and tips , chat and advice	Facebook
Raise Awareness for Phenylketonuria (PKU)	Facebook
glycogen storage disease	Facebook

[A]Study inforgraphics were publicized for recruitment using these same methods

Leaders of the patient groups or agencies were contacted with information regarding the objectives of the study and were asked for assistance in disseminating the study information either by posting the information on their social media accounts or through email blasts. Leaders were provided with an infographic (Appendix A) outlining the research question, goals, eligibility criteria, type of participation (*i.e.* semi-structured interview), type of compensation for participation and contact information. Infographics were generated in Canva (canva.com) and downloaded as a .png formatted file.

The recruitment period began July 29th, 2022, at which point the study infographics were published using the various methods outlined in ***Table 3-1***, and ended December 17th, 2022. The

response rate for the recruitment strategies employed was not identified given that the nature of the methods utilized (*i.e.* social media, listservs) make calculating a rate virtually impossible. Once the infographics were made public, individuals interested in participating contacted me directly by email. Once initial contact was made, the putative participants were screened based on the inclusion criteria (***Table 3-2***). Participants were recruited into four separate groups based on their diagnosis (PKU vs. GSD1a) and age. The peri-transition group included individuals who were 16-20 years old, while the post-transition group included individuals aged 21-35 years. If the putative participant was determined to be eligible, the study invitation letter and consent forms (Appendix A) were emailed to them for review.

Table 3-2. Inclusion criteria used to determine eligibility to participate.

✓ Have been diagnosed with PKU or GSD1a
✓ Are between 16 and 35 years old
✓ Were born in Canada or are a Canadian citizen
✓ Healthcare is primarily received from a Canadian facility
✓ Can speak and understand English

Overall, 22 potential participants inquired about participating and ultimately, 13 interviews were conducted. Briefly, 4 PKU and 2 GSD1a participants were lost to follow-up, 2 inquiries were determined to be disingenuous, and 1 PKU participant was ineligible as they were not Canadian.

The putative participant and I met by phone or Zoom to review the consent forms. If consent was obtained, the consent forms were signed on the participant's behalf and the interview was conducted immediately following. All participants were assigned a unique ID number and were recorded in a master list that included demographic information such as their first name, age, location and diagnosis. The master list was generated in a password protected excel document and signed consent forms were compiled in a password protected folder, both of which were saved on Microsoft Teams.

3.2. QUALITATIVE INTERVIEWS

The current study seeks to gain a rich understanding of patient experiences with self-management as they undergo the HCT. As such, semi-structured interviews were selected as the data collection tool as they are amenable to gathering data from a population of individuals who may have had diverse experiences with self-management and the HCT. Semi-structured interviews are also flexible tools that are permissive to exploration of topics important to the participant, as questions may be modified based on the participant's responses, while also ensuring that data is collected specific to the research topics (Jonathan A. Smith & Osborn, 2003).

3.2.1. Interview guide development

An interview guide (Appendix A) was designed for each transition group (*i.e.* peri-transition and post-transition), though similar themes were explored within each guide. As described above (see *Section 1.3*), the HCT has been explored in depth in the context of other chronic conditions. As such, the interview guides for the current study were adapted from quantitative surveys and qualitative interviews previously reported in the literature (Mogre, Johnson, Tzelepis, & Paul, 2019; Sallay, Klinovszky, Csuka, Buzás, & Papp-Zipernovszky, 2021; Swarna Nantha, Chelliah, Haque, Yen, & Md Zain, 2021). Each guide consisted of 8-9 questions, with follow-up questions, that explored topics related to self-management in childhood and present day, feelings of readiness, navigating the healthcare transition and supports. To further refine the interview guide (*e.g.* assess the language employed, the question appropriateness, etc.), the interview guides were sent to the Youth Research Advisory Council at the Children's Hospital Research Institute of Manitoba for feedback. The interview guides were reviewed in a one-hour meeting with 6 council members, the council leader, and myself. The refined interview guide, with feedback incorporated from the research council, was subsequently employed in the first two interviews of the data collection phase (see *Section 3.2.2*). Following transcription and analysis of the first two interviews, to further optimize the interview guides and promote trustworthiness of the data, the guides and interviews were reviewed to ensure the guides elicited appropriate data. The interview guides were adapted accordingly and were employed in all subsequent interviews.

3.2.2. Conducting interviews

To gain first-hand accounts and rich descriptions of patients' experiences during the HCT, participants partook in a semi-structured interview. Participants had the option to complete the interview by phone or by Zoom. A total of 7/13 interviews were conducted by phone, and 6/13 interviews were conducted over Zoom. Interviews lasted an average of 50 minutes and 20 seconds

and ranged from 38 minutes to 62 minutes. All interviews were audio recorded, with permission of the participant, for downstream transcription, coding and analysis. The interview guide employed during the interview was selected based on the participant's transition status (*i.e.* peri-transition *vs.* post transition) (Appendix A). While interview guides were employed during each interview, the line of questioning was largely guided by the participant as questions were re-ordered or altered based on the participant's previous answers to elicit more detailed, in-depth narratives. Participants were mailed a $25 pre-paid Visa gift card honorarium as a sign of appreciation for their time. Following each interview, the audio recording was named with the interview date and the participant's assigned ID code. All interview recordings were saved in a password protected folder on Microsoft Teams.

3.2.3. Interview transcription

Audio recordings were transcribed by myself or a professional transcription service (Transcript Heroes). To make transcripts more concise, broken speech (*e.g.* "um", "ah") was removed and recordings were transcribed to read like written English. Transcript Heroes' employees were required to sign a confidentiality agreement. Transcription provided by Transcript Heroes was audio verified upon receipt. Transcripts were subsequently uploaded to qualitative analysis software for downstream coding and thematic analysis.

3.3. INTERPRETIVE PHENOMENOLOGICAL ANALYSIS

This exploratory study followed a phenomenological methodological framework in which an experience is understood on an individual basis rather than being understood in the context of pre-existing ideas of what the experience should be. More specifically, this study employed interpretative phenomenological analysis (IPA), which builds on the phenomenological framework by incorporating the understanding that an individual's lived experience is interpretative as humans are inherently *"sense-making organisms"* (J. A. Smith & Osborn, 2015). Consequently, IPA requires the primary researcher to make sense of the participant who is making sense of their experience (J. A. Smith & Osborn, 2015). Overall, IPA focuses on individual experiences to gain insight into the shared experiences of the group (Neubauer, Witkop, & Varpio, 2019; Ravitch & Carl, 2021; Jonathan A. Smith & Osborn, 2003) which is ingrained in its idiographic nature (J. A. Smith & Osborn, 2015).

IPA is an appropriate methodology for the current study given that the study population is small, and therefore the unique experiences of each participant will be more evident. Moreover, the resulting recommendations generated from the data are not meant to provide a standard of care for the HCT, but provide guidance to healthcare providers on possible considerations given the diversity of experiences in the study population. IPA is not employed to identify the average experience of a population, rather highlight the shared and unique experiences between the participants (Jonathan A. Smith, Flowers, & Larkin, 2009).

3.3.1. Data analysis

Transcripts were uploaded to Dedoose (qualitative analysis software) for analysis. Following audio verification, each transcript was analyzed separately. Each transcript was read twice in entirety to promote familiarity and active engagement with the data (Alase, 2017; Creswell & Creswell, 2013; Jonathan A. Smith et al., 2009). Throughout the first two read throughs, I created experiential statements that identified points of interest with the aim of producing an extensive set of comments on the data (Creswell & Creswell, 2013). Experiential statements employed similar language and reflected the original meaning of the experiences as shared by the participant. Additionally, some comments included speculative interpretation in which the language, context and abstract ideas are considered concurrently to gain deeper understanding of the meaning of the participant's experiences. There is no requirement in IPA to divide the transcript into meaning units and comment on each unit (Jonathan A. Smith et al., 2009). Subsequently, experiential statements were consolidated into personal experiential themes. Personal experiential themes reduced the amount of detail while preserving the complexity of the participant's experiences and reflected how the participant made sense of their experience. Similar to experiential statements, personal experiential themes reflected the language and thoughts of the participant but included additional insight by incorporating the interpretation of the primary researcher (Jonathan A. Smith et al., 2009). Personal experiential themes were consolidated into separate lists for each participant for downstream comparison and analysis. Finally, personal experiential themes are compared between participants to identify group experiential themes. Group experiential themes are generated to highlight the shared and unique experiences between the participants (Jonathan A. Smith et al., 2009). Insights on the negative and positive aspects of self-management during the HCT, and the types of support required by individuals with PKU and GSD1a will be interpreted from the group experiential themes to produce recommendations for improving self-management

during the HCT. Recommendations will be compiled and provided to all relevant stakeholders, including participants, research partners (patient groups and agencies), and healthcare providers involved in the care of these patient populations.

3.4. STUDY RIGOUR

To ensure study rigour (*i.e.* quality of the research process), and consequently trustworthiness of the study findings, a number of elements were strategically integrated into the study design and process to meet the standards expected of a rigorous qualitative study (credibility, transferability, dependability and confirmability) (Shenton, 2004). Credibility of the study and data is established in many ways. Select examples include the purposeful selection of the methods (*i.e.* semi-structured interviews) employed to ensure alignment of the methods and methodology (see *Section 3.2*) (Ravitch & Carl, 2021; Shenton, 2004; Tracy, 2010). Moreover, the first two interviews of the data collection phase acted as a piloting phase in which the interview guide and transcripts were scrutinized to identify whether the questions were eliciting the intended information (see *Section 3.2.1*.). Detailed description of participant experiences and discussing participant experiences that do not conform to the shared experiences of the study population also lend credibility to the current study (Ravitch & Carl, 2021; Shenton, 2004; Tracy, 2010). To instill transferability, detailed descriptions of the study context (see *Chapter 2*) and the data (see *Sections 4.2-4.4*) were included herein so that future research can employ aspects of the study design and findings while considering the specific context of the current study (Ravitch & Carl, 2021; Shenton, 2004; Tracy, 2010). Dependability is imparted in this research by clearly outlining the purpose for the strategies employed for data collection, and the data demonstrates the utility of these strategies. Additionally, generating an audit trail for the data collection and analysis processes also ensures study dependability (Ravitch & Carl, 2021; Shenton, 2004; Tracy, 2010). Confirmability, or the effort to remain neutral by acknowledging and challenging personal biases (Ravitch & Carl, 2021; Shenton, 2004; Tracy, 2010), is accomplished through reflexivity and external audits. Reflexivity is the active and systematic process of assessing one's identity and positionality, and how these may impact data collection and analysis (Ravitch & Carl, 2021; Tracy, 2010). Memos were written before and after each interview to practice reflexivity. External audits were conducted by research team members other than myself. Auditors examined data samples to determine whether the data supported my interpretations.

CHAPTER 4: RESULTS

4.1. PARTICIPANT DEMOGRAPHICS

There was a total of 13 participants included in this study, as outlined in ***Figure 4-1*** below. The majority of study participants (10/13) were diagnosed with PKU and 100% of participants with PKU were part of the post-transition group (*i.e.* 21-35 years old). Of the remaining 3 participants, those diagnosed with GSD1a, 1 participant was part of the peri-transition group (*i.e.* 16-20 years old) and 2 were part of the post-transition group.

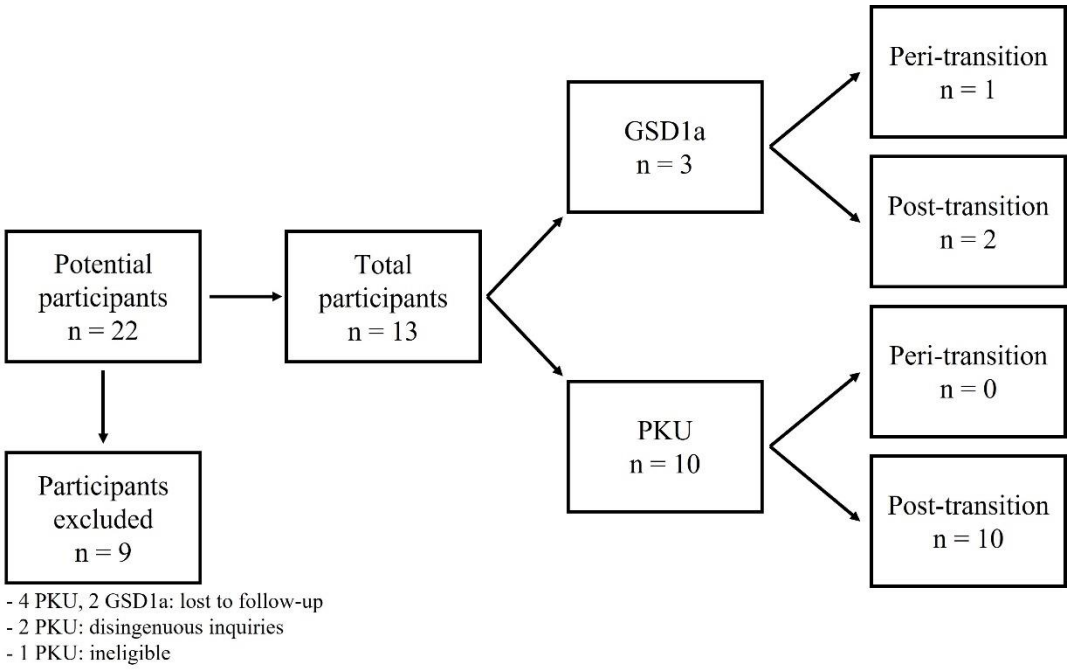

Figure 4-1. Participant recruitment and demographics.
Schematic detailing recruitment results and patient demographics. Of 22 potential participants, 9 individuals were excluded for various reasons, including being lost to follow-up, disingenuous inquiries and ineligibility. The remaining participants included 3 individuals with GSD1a (1 peri-transition; 2 post-transition) and 10 individuals with PKU (0 peri-transition, 10 post-transition).

4.2. OVERVIEW OF RESULTS

The results of this study are presented in two separate, but interrelated categories including the features of the HCT (see *Section 4.3*) and the patient reported factors influencing self-management and the HCT (see *Section 4.4*) (***Figure 4-2***). Group experiential themes were identified within each category, though overall, participant experiences were diverse.

Within the features of the HCT, two main themes were identified. The first theme (*Section 4.3.1*), "Variability of the healthcare transition," highlights that participants' experiences

with the HCT were not uniform. More specifically, some participants experienced significant changes in how care is conducted between pediatric and adult healthcare while others did not recognize any discernable differences. Additionally, some participants experienced changes in self-management, while others were able to maintain their management throughout the transition. The second theme (*Section 4.3.2*), "Informational needs and gaps in support," describes the uncertainty that many participants experienced due to lack of information regarding the transition itself, risks for the future, and how to integrate management into their changing lives. Participants also highlighted that there were gaps in support regarding healthcare, informational and mental health needs. Overall *Section 4.3* discusses participants' perceptions of the HCT, which is critical to provide a conceptual framework for the factors participants report to impact their self-management and the HCT.

Section 4.4 discusses the participant-reported factors impacting the HCT, in which there were four main themes identified. Firstly, "Psychosocial concerns and mental health" (*Section 4.4.1*) describes participants' struggles with coping with feeling limited and different from their peers and the mental health concerns that develop, whether they are related or unrelated to their disease. *Section 4.4.2* "Evolving self-management" details participants' experiences with adapting their management as they get older, which typically results in declining management. The third theme (*Section 4.4.3*), "Importance of the patient-provider relationship" sheds light on the perceived importance of rapport and open communication with the healthcare team, and the participant's desires to be treated as an individual rather than as a general PKU or GSD1a patient. Lastly, "Parental involvement" (*Section 4.4.4*) highlights the significant role parents have in teaching patients, either directly or indirectly, about management, and participants' feelings about their parents' sustained involvement in their management after beginning independent management.

Discussing these themes independently provides a foundational understanding of the HCT and patient experiences with self-management during the transition and facilitates generation of recommendations based on the results. However, ***Figure 4-2*** demonstrates how many of these themes are interrelated, which will be discussed further in the sections below. It is important to note that the influence of the subjects of each theme will likely differ depending on the individual. While group experiential themes were identified, it must be noted that experiences within each theme were diverse and patient experiences that contradict the identified themes will also be

presented to represent the expansive spectrum of experiences within the PKU and GSD1a communities. Quotes from the data are presented with participant identifiers and their diagnosis.

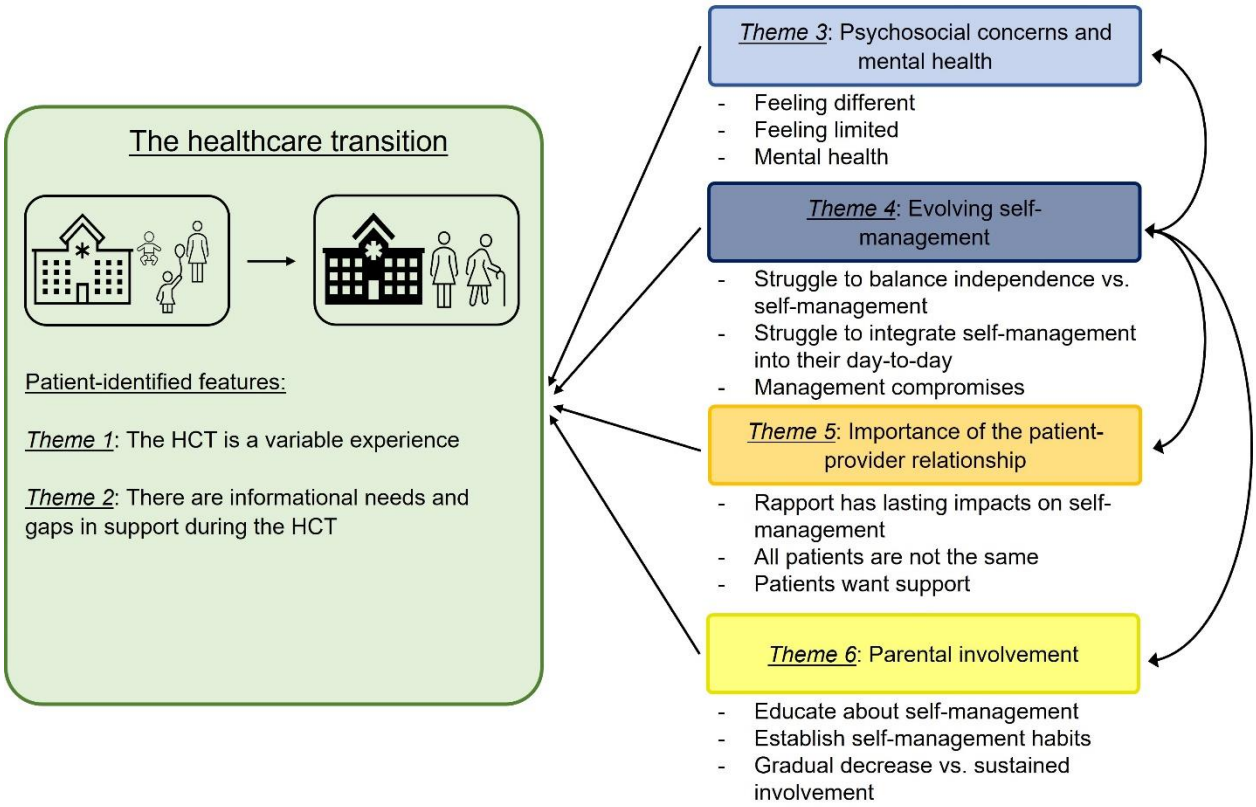

Figure 4-2. Perceptions of the HCT and factors influencing self-management.
Schematic outlining the participant-identified features of the HCT (green) and the factors reported to influence self-management (blue and yellow) and ultimately impact the HCT. Small boxes below themes 3-6 summarize the main points discussed in the associated themes.

4.3 FEATURES OF THE HEALTHCARE TRANSITION

4.3.1. Theme 1: Variability of the healthcare transition

Given that every province and/or healthcare facility have their own protocol for conducting the HCT with PKU and GSD1a patients, it is important to gain an understanding of how patients perceived their HCT. New insight from PKU and GSD1a patients may shed light on aspects of these protocols that are favourable or unfavourable for patients with these conditions. When asked about their perceptions of the HCT, participants focused largely on the differences (or lack thereof) they perceived between pediatric and adult healthcare, their feelings towards the HCT, and the changes in self-management that occurred throughout the HCT. Through their descriptions, it became clear that participants' experiences with the HCT were highly variable.

Participants were asked whether they perceived any differences between pediatric and adult healthcare. Many participants, GSD1a participants in particular, reported that they did not expect, nor experience significant differences. One participant reflected that while their doctors were different, *"[the doctors] goals towards getting me healthier was always, I would say, the same style of steps"* (P5_GSD1a) and so the focus of their health goals and treatment plan was unchanged, which contributed to the consistency between the two care settings. Another participant, who was approaching the transfer of care, spoke to the fact that they were already managing fairly independently, so they did not anticipate significant differences. Additionally, for one participant, it was not the lack of differences that made adult care seem similar to pediatric care. In fact, they highlighted that the transfer of care *"wasn't a big deal"* (P4_GSD1a) because they had already had many different providers and appointments throughout their life. However, they acknowledged that the transfer of care was still challenging, because a new provider is less familiar with their medical history.

Other participants did report differences between pediatric and adult care. Some felt like *"everything changed"* (P13_PKU) because the frequency of their visits with the clinic and other aspects of their management changed in adult care. Pediatric and adult care were frequently contrasted by participants by describing the pediatric system as being *"more personal"* (P4_GSD1a) or *"more detailed"* (P11_PKU) than adult care. One participant specifically elaborated on these similar sentiments by going as far as saying that they perceived that PKU adults *"aren't as important"* (P1_PKU) because *"they focus a lot on children"* and adults aren't afforded the same attention to their care.

Participants elaborated further on their feelings throughout the HCT. Interestingly, negative feelings regarding the HCT were discussed by participants whether they stayed at the same centre post-transition or were transferred to a new adult clinic. One participant, who did not change centres post-transition, described their experience with the HCT as *"going out into the world alone"* (P9_PKU), while another, who changed centres post-transition, shared that they were left in a situation in which they no longer had a respirologist, cardiologist or nephrologist as they transitioned to the adult healthcare system. Participants conveyed a sense of desertion by their healthcare team during the HCT and these experiences were often described as *"hard"* or *"scary"*. One PKU participant, who stayed at the same healthcare centre, shared that their experience had been reflected back to them by other people with PKU that they know. They stated: *"I found, and*

with people I've talked to with PKU, the hardest transition is those teenage years into young adulthood... I do think it's a difficult time". Participants described many reasons for which they struggled or had negative feelings towards the HCT. They reflected on gaps in care, as was mentioned above, but to elaborate further, many participants recalled that their transfer to adult care occurred synchronously with their return to care after a prolonged hiatus. These participants described feeling unprepared and anxious for the HCT. One participant acknowledged that they were *"not sure that it was at the time that I was exactly ready for that kind of change"* (P8_PKU), which was a sentiment reflected by many participants. They described that during the HCT they were required to start doing tasks that they didn't feel ready to do. Participants conceded that at a certain point, they had to be independent, but *"everyone has their own time…everyone matures at a different stage"* which contributed to the feelings of the HCT being difficult, and laden with fear and anxiety.

Those who had positive experiences with the HCT shared that they did not feel uncertain or unprepared throughout the HCT. Participants discussed that they felt comfort in the fact that their providers would not be changing. Others described the HCT as a *"soft"* or *"natural"* transition because self-management felt like it was *"second nature"* (P12_PKU).

Overwhelmingly, participants identified that they were vulnerable to declining self-management throughout the HCT. The ways in which participants experienced declining management (*e.g.* falling off diet, not attending appointments with healthcare providers, etc.) and the factors influencing management will be discussed more thoroughly in *Section 4.4*. But briefly, participants discussed experiencing fluctuations in their blood glucose and Phe levels throughout the HCT. One participant referred to their Phe levels as *"out of control"* (P9_PKU). While decreased self-management was by far the most common experience for participants, a couple participants shared that they were able to maintain their levels throughout the HCT. One participant elaborated that they worked to maintain their self-management throughout the HCT because if they did not, they were *"literally harming [themselves] and worsening the situation"* (P13_PKU).

Overall, these excerpts highlight the diverse experiences participants had throughout the HCT. Understanding the varying feelings regarding the transition, experiences within the process and management outcomes is a first step towards understanding the support patients may require navigating the HCT.

4.3.2. Theme 2: Informational needs and gaps in support

Though the experience of the HCT itself was variable among participants, it was frequently discussed that participants had many unanswered questions throughout the transition process. There was lack of information regarding the transfer of care during the HCT, the long-term impacts of their management style, how to incorporate their management into their everyday lives during EA, or how their management could be impacted by having children. While reflecting on their informational needs, participants simultaneously identified gaps in support from their healthcare providers.

When approaching the actual transfer of care within the HCT, participants reflected on a feeling of uncertainty or *"what's next?"* (P2_PKU), particularly for patients who were staying at the same healthcare centre. One participant highlighted her confusion: *"Like I go into a clinic where you guys see babies…I'm not a baby anymore. Like what happens next?"* (P2_PKU). Participants called for more transparency from healthcare providers during the HCT. Transparency was seen as a critical element of the HCT as it was emphasized that *"the transition is a huge deal"* (P2_PKU) and participants acknowledged that during the HCT, leading up to the transfer of care, AYA patients are *"…not really adults yet. We're kind of in this weird spot"* (P6_PKU) as they are teetering at the threshold between adolescence and adulthood. At this point, they are expected to be taking more responsibility for their own management but are also still actively learning how to manage their disease in an independent way.

Given that patients are still learning late in the HCT process, there is bound to be some uncertainty. For many participants, their parents single-handedly managed certain aspects of their management, like ordering medical foods. When it came time for participants to take over these aspects of their management, these tasks were still described as *"unknowns."* This may be partly explained by the fact that some participants shared that *"there was no official meeting to talk about transitioning"* (P9_PKU). For some, these unknowns perpetuated the limitedness described by participants, which is further explored in *Section 4.4.1*. But to illustrate, one participant recounted the point at which they were responsible for managing their financial account with the hospital so that they could access a greater variety of low-protein food products as only a subset were covered by the government. They stated: *"I never...got anything that wasn't free. I'd never wanted to approach that subject...you want what's free...it was an unknown. I just didn't need to resolve it. So, I left it that way"* (P6_PKU). For another participant, lack of information impacted their self-

management itself. They recalled that their parent co-ordinated their clinic visits throughout the HCT prior to the transfer of care. Unfortunately, following the initial appointment with their adult healthcare team, they did not return to the clinic for several years as they *"didn't know how to access the clinic"* (P9_PKU). These excerpts highlight how patients may avoid addressing these unknowns and consequently learn to navigate their condition in absence of these factors. Their avoidance to rectify these unknowns can likely be attributed to many underlying reasons, however, some participants identified experiencing *"a bit of anxiety when it comes to those unknowns"* (P6_PKU) which deterred them from learning the skills they identified they were lacking.

Topics relating to mental health concerns, such as anxiety and depression, were ubiquitous among the participants. The impact of mental health on self-management will be discussed in a subsequent section (*Section 4.4.1*), but another issue that resonated with participants was the lack of information about the risks for mental health concerns and means to access mental health supports. Many participants spoke with reproach as they shared that they were not aware that there was *"a stronger possibility"* (P11_PKU) of facing mental health challenges given their genetic condition. They reflected frequently on the fact that mental health *"wasn't something that was ever discussed"* (P4_GSD1a), and so having access to a mental health professional *"just wasn't something that ever happened"* (P4_GSD1a). As participants were looking back on their experience with mental health throughout the HCT, they emphatically suggested that *"[talking about mental health] would have been helpful"* (P10_PKU) and that it *"would be something that I would kind of give to patients transitioning"* (P4_GSD1a) when asked about how the transition process could have been better for them. Participants questioned whether they would have done better during the HCT if they had had more information and support surrounding their mental health. One participant expressed: *"I really wish I did have that opportunity because I could have done better"* (P10_PKU).

In addition to the uncertainty surrounding access to care in the adult healthcare setting and gaps in mental health support, participants expressed significant concerns regarding how their self-management may have to change, or how their self-management choices will impact them in the future. Pregnancy was often discussed by their healthcare team as soon as participants revealed that they were sexually active. Once participant stated that:

> *"they basically had it drilled into my head, that an unexpected pregnancy was a bad thing. And that having PKU as a woman meant I was going to have to deal with certain things if I got pregnant, they happened to leave out what they were. But basically, that if I was to find myself pregnant that would be what they called a PKU 911"* (P1_PKU).

However, this discussion was often lacking information and participants expressed that it was *"never really elaborated on when I was younger...it should have been something that was discussed"* (P4_GSD1a). When this participant became pregnant, they recalled that this lack of information caused them anxiety as they *"had to call them...all in a panic. And I was like, what's going to take place? And what are my sugars going to do?"* (P4_GSD1a). Others decided to address this information gap by learning from other people around them. One participant shared: *"I have had some of my PKU friends...have babies. So, I kind of know what to expect, going into it a little bit from their experiences"* (P1_PKU), while another identified that in their search to learn more information they noticed that *"there's a lot of women with PKU that are having unplanned pregnancies and so the supports I think should be there ahead of time to help women understand the consequences better and how to manage it"* (P10_PKU). These participants highlighted that while healthcare teams attempt to address their patients' concerns regarding pregnancy, patients may seek other means to answer their questions as their healthcare teams are not providing sufficient information.

Participants overwhelmingly discussed the dynamicity of their self-management and often experienced fluctuations in their level of compliance with their management, which will be further explored in *Section 4.4.2*. However, because of this, participants expressed concerns about how their management choices during the HCT would impact their long-term health. For most, the consequences of inadequate management during the HCT *"seem like a far way off"* (P8_PKU) or were *"not obvious"* (P9_PKU). However, many expressed that *"it's always sort of on the back of your mind"* (P9_PKU). One participant questioned whether they were *"doing something to my brain that is going to come back and bite me later"* (P2_PKU). Many participants reflected that it was scary for them not to know what the consequences of their choices were. For those who were already experiencing long-term consequences of their management choices, they expressed that if they had known about the consequences, they may have been motivated to make better choices. For example, one participant shared that *"if anyone told me I'd be getting kidney stones all the*

time, I definitely would've changed things because they're the worst things in the world" (P5_GSD1a).

Learning is an inherent process in the HCT, and in these excerpts, participants discuss the unanswered questions they had throughout the transition process. They identified informational needs, and consequently gaps in support regarding care in an adult healthcare setting, lack of information and support regarding mental health, and uncertainty about navigating potential future concerns like pregnancy and long-term health. The informational needs of these populations are diverse. Understanding what information patients perceive they are not receiving or recollecting is important as it may shed light on problems patients are likely to experience in the future and enables healthcare providers to mitigate these problems.

4.4 FACTORS INFLUENCING SELF-MANAGEMENT AND THE HEALTHCARE TRANSITION

Figure 4-2 illustrates the complexity of patients' lives. Of course, patients experience the typical growing pains of EA alongside the challenges of managing a rare genetic condition that requires substantial physical, emotional and mental space. Consequently, as patients are navigating their complex lives, they are influenced by their values, the events that are occurring in their life and the people surrounding them, which impact their response towards their management and the HCT. Therefore, it is important to look at the complexities of patients' lives during adolescence and early adulthood to understand what impact they may have on patients' readiness and capacity to self-manage during the HCT. Understanding the influence of these life factors is where the answer to the current research question lies.

4.4.1. Theme 3: Psychosocial concerns and mental health

Participants called attention to several psychosocial concerns occurring throughout the HCT, including during their school years and into adulthood. They described how these concerns impacted their perceptions of themselves and their management. It is important to consider how these factors would impact how patients navigate the HCT.

Participants repeatedly recalled feeling different from their peers or a desire to participate in the world like their peers, at all life stages. They emphatically stated that they *"didn't feel the same as others"* (P11_PKU) and *"wanted to be like every other person"* (P5_GSD1a). These feelings of otherness ultimately impacted their confidence and willingness to interact with their peers. One participant reflected about how it was scary for them to be different, which caused them to act

more withdrawn from their peers. Participants shared that the desire to fit in with their peers was underlaid by feelings of embarrassment or self-consciousness which were often related to the visual representations of their difference. One participant shared that they *"didn't know anyone else that had [a gastrostomy tube]"* which made them self-conscious during the summer. Others made comments about their embarrassment about drinking their formula at school or having to wear a medical alert bracelet.

While reflecting on their experiences during childhood and adolescence, participants shared that as they matured and gained more experience, they developed a more positive perception of their difference. They described their condition as a valuable *"uniqueness"* (P6_PKU) that enables them to mentor younger peers who are learning to manage their same condition. Despite this change in their own perception of their condition, participants discussed the challenges of being labelled as different or incapable compared to others around them. One participant stated that there are often *"prejudgements that you're not necessarily competent"* (P9_PKU) which encouraged them to be evasive about their condition with others. Other participants described these feelings of otherness in adulthood as being *"very isolating"* (P2_PKU).

In addition to feeling different, participants repeatedly discussed feeling limited by their diet which likely contributed to their perception of being different. Considering that therapeutic diets are the primary means of controlling PKU and GSD1a, it was unsurprising that participants discussed specific challenges with activities involving food. Though the individuals around them attempted to be inclusive by modifying meals, participants shared that it contributed to feelings of being different and left out. Events surrounding food were described as *"awkward"* (P11_PKU) because they were often not supposed to eat the food that was served. One participant spoke about how meals were often disheartening because they didn't *"want to sit here and eat PKU pasta while [everyone else is] eating steak and potatoes"* (P2_PKU). While the PKU participants had varying disease severity, many discussed how they felt especially limited by the small protein allowance their type of PKU afforded them. One participant recalled that as a teenager, it was *"pretty tricky"* (P12_PKU) to manage their diet due to the limited amount of protein they could have. They recalled that *"there was definitely days...where you couldn't have anything else for the rest of the day"* (P12_PKU). Participants also discussed the limitations of their diet in the context of what was covered by their respective provincial healthcare programmes. Those who had lived throughout the country identified that some provinces are much more limited in the medical foods

that are covered by their programmes. For some, this meant that other foods that were not covered were out of reach as they were *"really expensive"* (P10_PKU) and meant that they felt like they were eating *"the same couple of things over and over and over again"* (P10_PKU).

The idea of limitedness was pervasive in many social contexts for participants, as well. Participants shared that they felt like they were unable to participate in activities like their peers. After school activities, like contact sports, were advised against by many participants' healthcare teams. Being limited was difficult for participants in their younger years as they *"want[ed] to hangout...and play with friends"* (P5_GSD1a). One participant shared an experience in which they opted not to take part in an over-night school trip because they felt as though their management would take too much of the supervisors' time away from the other students on the trip. They stated that it *"really sucked…being left out"* (P2_PKU). The overall burden of managing a chronic condition in tandem with the rest of their lives was tiring for some, which meant that they *"miss[ed] out on some social opportunities"* (P8_PKU) due to low energy.

Psychosocial factors, like those described above or others that participants mentioned during the interviews but weren't discussed herein (*e.g.* loss, grief, childhood trauma), had impacts on participants' mental health. Concerns such as anxiety and depression were prevalent among participants. It is well known that improper diet management is associated with psychological symptoms such as anxiety and depression in individuals with PKU. Participants elaborated on the intricate interconnectedness of these psychosocial concerns, mental health, and self-management.

It was acknowledged by many PKU participants that there are certainly stressors for any AYA engaging in the world. However, they identified an additional layer of complexity for individuals with PKU as their *"self-awareness isn't at its best"* (P8_PKU) when their Phe levels are not controlled. One participant stated: *"there were certainly times that I feel like things became overwhelming and really upsetting, where if my levels had been managed well, it's probably something I could've handled"* (P8_PKU). Deciphering where the boundary lies between emotional responses that are suitable for the circumstances, or are exacerbated as a symptom of PKU, proved to be difficult for many participants. In fact, one participant shared that they could *"get overly emotional"* and that they *"don't know if that's part of just me being me, or if PKU sometimes plays into it"* (P2_PKU). Unfortunately, many participants mentioned that due to the association between diet management and mental health *"the automatic assumption was...you must be off your diet"* (P10_PKU) when they were experiencing emotions they attributed to be

typical for teenagers. Consequently, participants felt dismissed and that their struggles were written off. However, it was clear that for some there was a reciprocal relationship between their mental health and their self-management. They recognized that poor self-management affects their mental health, but actively working on improving their mental health *"definitely helps with following your diet"* (P10_PKU). The impacts of these psychosocial factors and mental health spurred development of maladaptive self-management behaviours. For example, it was common for management to go *"on the backburner"* out of a desire to *"live a normal life"* (P9_PKU).

The psychosocial and mental health issues exemplified in these excerpts illustrate the influence these factors can have on the HCT as patients may have greater challenges maintaining their self-management and ultimately, navigating the HCT. The issues identified by these participants suggest that healthcare providers should follow a holistic model of care that addresses the psychosocial support needs of AYA throughout the HCT.

4.4.2. Theme 4: Evolving self-management

Recall that EA is associated with various developmental changes and challenges as AYA gain more independence and responsibility. The HCT occurs synchronously with EA. During this time, patients are expected to take a more active role in their self-management. Therefore, it is important to gain a better understanding of the impacts EA on self-management and the HCT. Independence associated with EA was determined to have adverse effects on self-management. Often, participants acknowledged that greater freedom was associated with poor decisions regarding their management. They described an underlying curiosity about the foods that were contraindicated for their conditions. It was challenging to navigate the freedom of spending more time away from parental influences and the influence of their peers. Adolescents were considered not to be *"mentally prepared"* (P6_PKU) to balance their new freedom and make *"good choices"* (P8_PKU) with respect to their self-management. One participant described the consequences of this struggle by narrating their experience with spending more time out of their house, with access to their own money.

> *"When I started being out of the house a lot more on my own, my own access to money...that's when they started to fall downhill. I fell off my diet quite heavily by about 18...and that persisted, probably for a good 8 years"* P6_PKU

Other participants highlighted that balancing university on top of their management was particularly taxing. Considering the arduous university schedule, one participant described how they would inappropriately *"stretch"* (P4_GSD1a) the time between their cornstarch doses because there was no one to keep them accountable as they moved away from home for university. Consequently, the departure from the more *"controlled"* (P9_PKU) high school environment to the *"independence and freedom in university"* (P9_PKU) was often associated with dysregulated Phe or blood glucose levels due to the changes participants would make to their management.

Thus far, these excerpts demonstrate that many participants struggle to maintain their management as they gain more independence. These excerpts also allude to the fact that as patients are gaining independence and freedom, other aspects of their life are also changing (*e.g.* going away to university, starting a new job, etc.). Therefore, patients are required to learn how to incorporate their management into all the different aspects of their life. It was shared that it was challenging to incorporate management into the work setting, as schedules for part time jobs were inconsistent which made it difficult to develop a routine, which negatively impacted self-management. The burden of self-management was perceived as having an impact on virtually every social activity. One participant shared that *"it affected everything I was doing, whether I was going to an event or a party or anything like outside my own home"* (P6_PKU). Eating out was described as *"next to impossible"* (P12_PKU) by one participant.

Participants expressed their struggles with balancing self-management with increasing independence and integrating management into their everyday lives to their healthcare team. However, participants recalled that there was a lack of support from their healthcare providers to address their concerns. Self-management was inconvenient to perform in the context of inconsistent university and work schedules. Diet requirements were changing as participants took on manual labour jobs throughout the summer. And overall, participants were told that by their healthcare providers that they *"just have to do it"* (P2_PKU) or their providers were *"absent in it all...and were really not hitting the expectations...[with] just supporting me through this huge transition phase"* (P7_GSD1a).

Virtually every participant identified difficulties with their management. A significant portion of the day is consumed by thinking about self-management, as participants described their management as a *"second full-time job"* (P1_PKU), or *"one of the hardest diets to manage in the world"* (P8_PKU). For this reason, participants search for ways to *"just make stuff manageable"*

(P12_PKU) and consequently, adapt their management to fit into the different facets of their life. Participants identified various ways in which they adapted their management and diverse reasons for doing so. Those who felt they were particularly comfortable with their diet, managed by largely knowing what foods were compatible with their diets, and which foods should be avoided, rather than strictly tracking every meal. Participants also discussed how they took it upon themselves to change their protocols (*e.g.* how and when) for their formula and cornstarch doses. For other participants, their management was seen as a bargaining process. One participant described how they justify adapting their management:

> *"I could be cooking some...big steaks or something. I'll have a small one, but I'll have a really good small piece...I know I should not eat steak in any way shape or form, but then on the other side I'm also now eating low protein foods four or five days a week. I'm still drinking all of my formula. I'm doing meal prep, I'm baking low protein items..."* (P6_PKU)

Other participants emphasized that the burden of their self-management was *"a lot to handle and it is a lot to do everything"* (P2_PKU) and that there wasn't enough time in the day to strictly monitor their diets. Consequently, participants identified elements of their management that were more flexible and other elements in which *"if something is going to slip, what cannot stop?"* (P2_PKU). Participants reflected on the importance of finding balance between following their diet in a way that permitted them to live their lives, while also not limiting their function. They described their desire to find a *"happy medium"* (P10_PKU) with their diet, rather than their typical oscillation between completely on and off diet, as a means to finding overall *"peace of mind and happiness"* (P6_PKU) in their lives. While participants desired to find harmony between the complexity of their lives and their self-management, for some, the search for balance coupled with the inconvenience of management coalesced to promote management habits that were insufficient for mitigating PKU or GSD1a symptoms.

Not only do these excerpts highlight the challenges with integrating management into everyday life, *Theme 4* nicely illustrates the complexity of patients lives, how this complexity interacts with management and the gaps in support that participants have experienced. Considering the dynamicity of patients' lives and the consequent dynamicity of patients' self-management

during the HCT, it is imperative to explore these experiences as they likely identify challenges healthcare providers may face in supporting their patients through the HCT.

4.4.3. Theme 5: Importance of the patient-provider relationship

The criticality of the patient-provider relationship (PPR) was highlighted by participants of the current study. They identified that their readiness and willingness to independently manage their condition and ultimately complete the HCT was partly influenced by the dynamics between themselves and their providers.

Participants acknowledged the importance of the PPR as they recounted instances in which early experiences with their healthcare team impacted how they approached their management and interacted with their team in the future. When reflecting on the difficulties they sometimes faced with self-management, participants shared an unwillingness to discuss these hardships with their healthcare team because it was perceived that *"if you did one thing wrong, that is all they would focus on"* (P1_PKU). These types of interactions with their healthcare team precipitated in anxiety for years moving forward, even following staffing changes in which participants were no longer under the care of their initial providers. One participant, who was overwhelmed by their family circumstances and the burden of their self-management, shared that during the HCT, *"it was a lot easier to just lie and pretend and you get that one day of the year over with"* (P5_GSD1a). Another participant recounted a story in which an interaction with their healthcare team left them feeling alone and fearful, which resulted in their avoidance to measure their Phe levels and ultimately, prompted them to leave their clinic in their teens. They described their healthcare team as *"really punitive instead of supportive"* which meant that they did not feel comfortable being *"very transparent with them about what was going on"* (P8_PKU). Therefore, strong rapport and trust between patients and providers is crucial for eliciting honesty from patients.

One compromising element to the PPR that participants identified was the tendency for healthcare providers to treat all patients the same. Participants disliked that it seemed like providers put *"everybody into the same pocket"* (P2_PKU) and enforced the same goals on them that they would enforce on other patients. Participants emphasized that they are *"more than just [their condition]"* (P10_PKU). Therefore, their goals for self-management were likely different than other patients because of the interactions with the other complexities of their lives. It was important to participants that their providers *"meet them at where they're at with their needs"* (P10_PKU) and know that patients' goals may differ from the providers'. One participant stated that healthcare

providers should adjust their expectations for each patient *"because everybody seems to be unique and so everybody seems to handle the PKU differently and be affected differently. Kind of just not putting everybody into...the same spot"* (P2_PKU).

Participants also reflected positively on the importance of the PPR. Having a strong rapport with the healthcare team was believed to help with the HCT. Participants described feeling grateful to have a team that made them feel *"really comfortable"* (P11_PKU). Their healthcare team worked to build connections and trust with them. One participant described that the trust they built with their healthcare team allowed them to be open and honest with them, which was critical during the HCT. They shared: *"I'm spilling my beans...and I feel good being there...Medical people – doctors – should make sure that they build a connection between themselves and the patient. I think that's the most important thing"* (P13_PKU).

In addition to the quality of the PPR, participants wished for more communication with their healthcare providers throughout the HCT. Again, they recalled the *"chaos"* (P2_PKU) of their lives during the transition, and the process of figuring out how to self-manage. In doing so, they agreed that it would be beneficial to them if their healthcare team checked in with them more throughout the HCT.

The importance of the patient-provider relationship is further accentuated by the fact that many attribute their improved management to their healthcare team. Participants spoke about their success with getting back on diet, or their relief at feeling comfortable enough to return to their clinic after years away from care. One participant recounted the point at which a new provider reached out to them after the participant left their clinic because of a hurtful interaction with their past provider. They shared:

> *"Had they not reached out, I don't know how long it would've taken me before I would've been initiated back…it was a big relief to know that these are people that I could trust…people that I could be, you know, truthful with"* (P8_PKU).

Another participant attributed their current health to the strong relationships and open communication with their providers. They praised their team by saying:

> *"They always have been there and I've always had a lot of trust in them and what they're doing. And being with them my entire life, like going there my entire life I feel like has helped, probably helped me get to where I am. Because without them, I'm sure I wouldn't be doing as well as I am"* (P4_GSD1a).

The PPR is typically a longitudinal relationship that requires rapport to be built over time. Interestingly, participants acknowledged that they learned as they got older that their healthcare team was available to them as a support, and generally, not to criticize them. This idea also improved communication between participants and providers as participants realized that their healthcare team can only be helpful if patients are open and honest. One participant shared: *"when you're going to the doctors and lying to the doctors they can't tell you what you're doing wrong if you don't say you're doing anything at all"* (P5_GSD1a). As a natural consequence to this, participants described feeling more comfortable overall and were able to bring up sensitive topics like sex, drugs and alcohol.

Participants underscored the importance of the PPR and its impact on their self-management and the HCT. The PPR is critical for ensuring positive experiences and outcomes for patients. Building rapport between patients and providers promotes improved communication, satisfaction, self-management and HCT outcomes which are each stepping stones in providing patient-centred care.

4.4.4. Theme 6: Parental involvement

PKU and GSD1a are diagnosed within the first few days to months of life. Therefore, the majority of a patients' disease management is performed by their parent or caregiver. At the transfer of care, AYA have had varying degrees of independence with their self-management throughout the HCT. Participants identified various underlying reasons for the amount of independence they had developed throughout the HCT. One of the most prominent reasons, however, was parental involvement. Participants described their experiences with learning self-management from their parents during childhood and adolescence and reflected on sustained parental involvement following the transfer of care.

Parents played a predominant role in educating participants about their self-management, both directly and indirectly. For many participants, parents taught them how to perform certain management tasks from a young age. Parents played a part in teaching their children how to weigh their food, how to prepare their formula or cornstarch doses, or

to order their medical foods, among other self-management tasks. One participant was appreciative of their parent who taught them *"how to look up all my numbers in the book and how to weigh everything. I was involved in weighing my food from an even younger age"* (P1_PKU). One participant's experience was distinct compared to others. They recalled that their parental figure did not take the participant's disease management seriously. They encouraged the participant to lie to their healthcare team and did not facilitate their diet management. They shared: *"as a kid you're thinking that your parents are taking care of you properly and growing up you think that you're learning skills and stuff and, in reality, I was learning how not to take care of myself"* (P5_GSD1a). Given this experience, they learned that their management was not important and continued to struggle with their management into adulthood. Though this experience differed in some respects from the remaining participants, there is consistency in the fact that participants learned from their parental figure about managing their disease. Therefore, parents hold a significant influence on the future of their AYA child's management.

Many parents who undertook a direct teaching role were described by patients as reducing the amount of supervision they provided as the participant learned to appropriately self-manage. One participant described how their parent *"supervised me the first couple of times to make sure I was doing it right. Then I was on my own"* (P1_PKU). This experience also occurred in the context of attending healthcare appointments. Participants recalled that as they got older, their parent was less involved in their healthcare appointments. Parents would stay in the waiting room and, for some participants, eventually stop coming to appointments all together. Despite the ability to manage independently, participants described a tendency to *"try to dish it off to someone else"* (P12_PKU). Participants continued to rely on their parents for their management due to self-reported laziness, convenience, and to ensure that their management remained consistent.

However, parents were also reported to play an opposite role in teaching self-management skills. Participants shared that some aspects of their management were completely managed by their parents. Parents would take over ordering medical foods, making healthcare appointments, or formula preparation. One participant described that despite their healthcare team recommending that the participant become more independent with making their formula, their parent insisted on preparing it because they knew that the

participant was *"going to have to do it for the rest of [their] life…let them be a kid"* (P10_PKU). Participants who were not given the opportunity to learn self-management skills from their parents or relied on their parents for management during the HCT identified that they struggled with those aspects of management in adulthood. One participant described how *"all the doctors' appointments…was pretty much handled by [my parents]"* (P10_PKU) and attributed their difficult HCT to the fact that they *"didn't really know how to make those appointments or who to contact or what to do"* (P10_PKU) after transferring to adult care. Other participants discussed that their parents' control over their management left them *"second guessing"* because they had *"never really been someone...who did things on [their] own"* (P13_PKU). As adults, other participants continued to rely on others in their life for help with management. One participant shared that their parent was the one to do the participant's finger poke to test their blood, and now as an adult their partner has *"always done [the finger poke] for me"* (P3_PKU). Consequently, participants demonstrated the importance of learning all management skills so that they are empowered to self-manage as adults.

Further, management philosophies that were learned in childhood from parental figures, were often maintained throughout adulthood. One participant, who discussed the negative experiences with the way their parent managed their disease, reflected on the fact that they continue to prefer eating foods that are contraindicated for their diet as they were provided those foods in childhood and adolescence. They stated: *"I've always thought about my health but it's always been like, it is what it is. Like, if my own mom wasn't willing to take care of it why should I take care of it?"* (P5_GSD1a). Another participant shared that their parent didn't strictly track everything that the participant was eating as a child and *"as long as I was healthy and functioning and I didn't seem to be missing anything"* (P2_PKU) they were satisfied with that management philosophy. This participant continued to rely on this management style throughout adulthood, which highlights that parents are important figures in the self-management habits practiced by AYA later in life.

Some parents had sustained involvement in their child's management, as reported by many participants. Participants perceived their parent's engagement in their management as positive and negative. One participant who felt positively expressed that they *"couldn't imagine what it would be like if [their parent] wasn't so involved in what was going on"*

(P7_GSD1a) and expected that their parent would continue to be *"fairly involved in everything for a while to come"* (P7_GSD1a). Others remarked that they didn't feel ready at the time of transfer, so they appreciated that their parent continued to be involved. They felt that their parent was their *"safety net"* (P7_GSD1a) during a time in which their lives were changing and becoming more complex. Those who felt negatively shared that they felt their parents were too *"overprotective"* (P13_PKU) and were overwhelmed by constantly being overseen by their parents. They felt that this ultimately impacted their ability to become independent in their management. Others felt frustrated that their parents were staying involved even though they were adults. One participant recounted a time in which they were going on a trip as an adult and their parent was asking about the participant's management. They expressed their irritation, saying *"…like, I can do it myself. I'm fine...Like, I'm doing OK. Don't worry."* (P4_GSD1a), which suggests that they felt that their parent was overbearing.

Overall, parental involvement caused varying impacts on participants and their self-management. Parents hold valuable roles in teaching their children to self-manage appropriately. Their involvement is critical for establishing management habits, which has the potential to result in negative outcomes for their child. While participants' experiences with their parents differed, there is consistency regarding the significant influence that parental involvement has on the lives of patients as they learn self-management skills, navigate the HCT, and overall health outcomes.

CHAPTER 5: SUMMARY, DISCUSSION, FUTURE DIRECTIONS & SIGNIFICANCE

5.1. SUMMARY

Within this project, I employed semi-structured interviews and Interpretative Phenomenological Analysis to identify common experiences with self-management during the HCT among participants with PKU and GSD1a. Interviews explored self-management over participants' life time, participants' experience with the HCT, feelings of readiness for independent management, challenges participants faced, and support needs, among various other topics, to identify the patient-reported factors influencing their readiness and capacity to self-manage during the HCT. A total of 6 themes were identified (***Figure 4-2***). Two themes pertain to participants' experiences with the HCT, namely, "Variability of the healthcare transition" (*Theme 1*) and "Informational needs and gaps in support" (*Theme 2*) which provide important context to frame *Themes 3-6*. *Themes 3-6*, "Psychosocial concerns and mental health," "Evolving self-management," "Importance of the patient-provider relationship" and "Parental involvement", directly address the current research question. Feeling different, limited and mental health concerns throughout participants' lives and particularly at transitional life stages (*i.e.* the HCT) negatively influenced reduced self-management. Emerging adulthood, which occurs concurrently with the HCT, was associated with food curiosity and influence from peers that was associated with worse self-management. Moreover, balancing transitions with jobs and education proved to be quite challenging for participants and elicited management compromises. Negative experiences with healthcare providers were often associated with distrust and departures from care, while positive relationships were associated with patient satisfaction and improved outcomes. Lastly, parents were identified as predominant influences on self-management success. Collectively, these findings shed light on the challenges AYA with PKU and GSD1a may face throughout the HCT and are the foundation from which recommendations can be developed to better support patients' self-management throughout the HCT. Ultimately, these recommendations will improve health outcomes and patients' quality of life throughout and post-HCT.

5.2. DISCUSSION

Overall, participants recapitulations of their experience with self-management during the HCT called attention to the struggles that patients face while balancing factors such as emerging adulthood and the HCT. While this research in the context of PKU and GSD1a is novel, the challenges associated with self-management and the HCT have been studied extensively in other

disease contexts, such chronic kidney disease, cystic fibrosis and diabetes. Growing research in other disease contexts have identified similar challenges to those discussed herein. Moreover, it is becoming increasingly well-known that a disconnect exists between healthcare providers' perceptions of the barriers and facilitators to patients' self-management and patients' perceptions of the same. Therefore, the patient-driven recommendations based on the findings of the current study, which are supported by an extensive body of existing literature, are a strong initial step to begin improving patient experiences with self-management during the HCT.

5.2.1. Recommendations

While the results of this study provide a framework for numerous recommendations, I have developed 10 recommendations that address the main themes within this study and are supported in the literature. Moreover, many of the proposed recommendations are immediately implementable by healthcare providers which affords providers the opportunity to begin to improve patients' experiences with self-management during the HCT without delay.

Patient-driven recommendations to improve self-management during the HCT:

1. Develop a plan for the HCT early on with patients and their parents, and discuss the plan in detail.
2. Ask patients about whether they feel like they are getting the right support.
3. Acknowledge and discuss challenges with balancing emerging adulthood and self-management.
4. Have discussions about goal building and individualized management planning.
5. Engage in discussions regarding non-medical topics.
6. Integrate mental health screening and resources into appointments, if at all possible.
7. Develop, promote and encourage patients to attend disease-specific social activities.
8. Keep up to date on new medical foods and formulas. Have samples available, if at all possible.
9. Have recipes/resources available for patients.
10. Engage with parents regarding the importance of their child developing self-management skills and the support parents may need to facilitate their child's HCT.

These recommendations are based in the patient-centred care model (see *Section 5.2.2*), which advocates for patients to be active collaborators in their care with their healthcare providers. As

such, patients should be engaged in developing a plan for their HCT and their management goals. Parents are often integral to the patient's HCT, therefore they should be engaged in planning the progression of the HCT and their child's development. Though not explicitly explored throughout the interviews, many participants indicated that they left their clinic in their early teenage years, therefore, it is imperative that HCT-related interventions (*i.e.* HCT planning, goal building) be initiated at an early, but developmentally appropriate age. In keeping with the patient-centred care model, providers should attempt to build rapport with their patients so that they may meaningfully engage and inquire with patients about the challenges they are facing in EA and the types of support they may need as they progress through the HCT. Participants spoke extensively about the impacts of various psychosocial factors and their mental health on their management. They also revealed that they did not perceive that they were offered opportunities to discuss mental health with their healthcare team. As such, the integration of mental health screening and resources would be highly beneficial for patients given the inextricable connection between mental health and self-management. Diet management was the prominent topic discussed by participants. They shared the challenges they faced with feeling limited by their diets and how these limitations eventually impacted their management. By staying abreast with new food, formulas, complex carbohydrate developments, having sample products, having recipes, or information about diet-related workshops, providers can support patients to expand their diet variety and identify nutrition sources that are better suited to their patients.

Collectively, these recommendations represent initial steps for laying the foundation to improve HCT outcomes and patients' quality of life. The subsequent sections will consider the findings of the current study in the context of the current literature and provide additional support for the relevance of these recommendations.

5.2.2. Patient-centred care

As the medical field improves it's understanding of the provision of patient care and the multidimensional nature of patient well-being, models of patient care are continuously evolving to incorporate the latest understanding and best practices. Patient-centered care is increasingly becoming the predominant framework from which patient care is provided. Patient-centred care is defined as care that *"honors patients' preferences, needs, values and goals"* (Greene, Tuzzio, & Cherkin, 2012) by taking these factors into account during decision-making and delivery of healthcare (NEJM Catalyst, 2017; Lin & Hwang, 2020). Patients are recognized as active

collaborators in their care, and are treated from clinical, emotional, mental and social perspectives (NEJM Catalyst, 2017). As such, patient-centred care is based the biopsychosocial model (Greene et al., 2012), which is a holistic approach to patient care that considers how the individual patient's experience with disease is influenced by biological, psychological and social factors. As such, treatment for a given condition should include means to address the not only the biological aspects of disease, but the psychological and social concerns that contribute to disease (Borrell-Carrió, Suchman, & Epstein, 2004; Rosignoli et al., 2022).

The participants of this study nicely exemplified throughout their interviews the interactions between the biological, psychological, and social factors contributing to their experience of disease. As an example, recall that participants discussed how they often felt limited by the biological requirements to manage their disease (*e.g.* diet, formula/cornstarch), which often resulted in feelings of anxiety and depression and impacted the ways that participants felt like they could interact with their peers. Other PKU and GSD1a research identified similar interactions. The United States Federal Drug Administration conducted a listening session with adults with GSD1a, in which participants were asked a series of questions regarding their experience with GSD1a throughout their lifetime. Participants indicated that the most frustrating aspects of their conditions were the frequent hospitalizations which made it difficult for them to lead social and normal lives. Others spoke about how the negative impacts GSD1a has on their mental health as it is a consistent issue that impacts every aspect of their lives (United States Federal Drug Administration, 2021a). Vegni *et al*. (2010) conducted a qualitative study about the age-related experiences of living with PKU. They identified interactions between psychological and social factors that were common across all age groups. Participants discussed that they often had to make a choice regarding whether to reveal their PKU to those with whom they interacted. For example, they may have to choose between being perceived as being "normal" by their peers, but this may result in avoidance of social situations involving food, or to reveal their condition which may negatively impact how they are perceived by their peers (Vegni et al., 2010). The interconnectedness of the biological, psychological and social aspects of PKU and GSD1a, as demonstrated in the literature and by participants of the current study, strongly support the implementation of patient-centred care models for these populations. This model is further supported by the fact that the underlying principles of patient-centred care are well aligned with the needs identified by the participants herein.

The Picker Institute (2023), an international healthcare charity involved in research regarding patients' experiences with care, conducted several case studies to identify 8 principles of patient-centred care. The principles are as follows:

1) *Fast access to reliable healthcare advice:* patients should have access to the right care at the time that they need it.

2) *Continuity of care and smooth transition:* patients are entitled to continuity of information and seamless transitions.

3) *Involvement and support for family and carers:* patients' social support systems are invaluable and support for carers is integral to patient's care

4) *Emotional support, empathy and respect:* patients are entitled to holistic care that considers their emotional well-being as equal to their physical well-being.

5) *Attention to physical and environmental needs:* patients' care should be provided in a space that affords them privacy and dignity.

6) *Clear information, communication and support for self-care:* patients require easy access to reliable information that helps them make informed decisions about their care.

7) *Effective treatment by trusted professionals:* patients should receive effective care that is in line with their needs and preferences

8) *Involvement in decisions and respect for preferences:* patients are entitled to be active partners in their care.

The necessity of each of these principles is not only weaved throughout the predominant themes identified in this study, but also in the more individualistic experiences of participants that were not identified as primary themes. For example, a few participants were interested in increasing the amount they were exercising. Knowing that exercising more would likely influence their nutritional needs, they contacted their dieticians by email for advice, but did not receive responses for several weeks. The lack of response from the dietician violates the principles of 1, 6 and 7 listed above.

Overall, patient-centred care has been associated with increased patient satisfaction, improved PPR, increased engagement in care from patients, and increased quality of life (Sladdin, Ball, Bull, & Chaboyer, 2017). While the impacts of patient-centred care as it pertains to PKU and GSD1a

are largely unstudied, the impacts of patient-centred care have been studied extensively in other disease contexts. A 2022 systematic review of 20 randomised controlled trials and 4 quasi-experimental studies including 4,083 participants with type 2 diabetes identified positive correlations between patient outcomes and receipt of patient-centred care (Asmat, Dhamani, Gul, & Froelicher, 2022). More specifically, following three months of follow-up, participants who received patient-centred care interventions to promote self-management demonstrated statistically significant improvement in glycemic control compared to the control groups that received usual care. Of the 16 studies reporting on diet control, 69% reported statistically significant improvement, while 71% (5 out of 7) of studies reporting on physical activity also identified significant increases in populations receiving patient-centred care interventions compared to the control group (Asmat et al., 2022). Primary research conducted with patients with hypertensive nephropathy identified similar responses to patient-centred care interventions for self-management (Lee et al., 2021). Participants in the experimental group attended a 90-minute patient-centred care program that focused on an introduction to the condition and potential comorbidities, dietary precautions for patients, medication regimens, and stress management once a week for 4 weeks. Overall, the study findings showed improved disease control relative to the control group receiving usual care. Participants in the experimental group demonstrated enhanced blood pressure control lasting at least 6 months (*i.e.* until study end) post-intervention. The study results also showed improvement in the physical and mental contributors to quality of life (Lee et al., 2021). In a qualitative study, patients who were admitted to hospital reported that patient-centred care made them feel like they were receiving the time they deserved and wanted from their healthcare providers (Alharbi, Carlström, Ekman, Jarneborn, & Olsson, 2014). Others described feeling *"invisible"* when their providers would speak amongst themselves about the patient without involving the patient in the conversation, which is contrary to the patient-centred care model (Alharbi et al., 2014). These studies, particularly those that include conditions requiring dietary management, exhibit overlap in the types of self-management tasks, as well as the sentiments expressed by the participants of the current study. Arguably, these study findings support the use of patient-centred approaches in PKU and GSD1a care.

Patient-centred care is at the heart of all recommendations proposed in *Section 5.2.1*, as they are reminiscent of the Picker Institute principles listed above. However, the importance of the PPR in patient-centred care is poorly emphasized by the Picker Institute. As was described by the

participants of the current study, the PPR influences whether patients are honest about their management and even whether they choose to stay under care at their clinic. As such, the PPR may be an essential foundation from which patient-centred self-management and care can be built. Central to a beneficial and successful PPR, and thus patient-centred care, is the importance of a strong rapport between patient and provider. In fact, Lin and Hwang (2020) stated that *"knowing the patient as a person allows [healthcare providers] to understand what is crucial to the patient's adherence, so the [patient-centred care] approach states the importance of allowing patients to have the opportunity to share their illness experiences*". Thus, it is likely that strong rapport influences patients' willingness to share their experiences, which ultimately facilitates successful self-management.

5.2.2.a Rapport with healthcare providers improves management

A positive PPR underlies many of the principles of patient-centred care discussed above. Strong rapport between patients and providers facilitates exchange of information, management of patients' emotions and decision making (Świątoniowska-Lonc, Polański, Tański, & Jankowska-Polańska, 2020). As such, the PPR is central to patient education, and virtually all aspects of self-management. Moreover, providers and patients are able to build a mutual understanding of the patient's goals for self-management to ensure that the patient receives care that is most relevant to them (Świątoniowska-Lonc et al., 2020). Eton *et al*. (2017) stated that in addition to the reasons previously discussed, relational skills (*i.e.* establishing rapport and trust, communication, expressing non-judgmental acceptance) enables providers to practice from a biopsychosocial lens, which is associated with holistic care and improved outcomes as described above (Charlton, Dearing, Berry, & Johnson, 2008; Eton et al., 2017).

The relationship between patients and providers is built upon trust, communication and shared decision making (Greene et al., 2012; Świątoniowska-Lonc et al., 2020). Relationships lacking these elements often have detrimental impacts for patients. Participants of the current study demonstrated the importance of the PPR to their self-management. Those who had negative experiences with their providers shared that they were less likely to be honest about their management, and many chose to leave their clinic for several years before returning as adults. Contrastingly, those who had positive interactions felt that the trust and respect that was built between themselves and their providers promoted conditions that helped patients feel comfortable with being honest about their management and willing to ask questions. While the importance of

the PPR for patients with PKU and GSD1a has not been previously reported in the literature, the PPR has been investigated in other disease contexts.

A 2022 study by Mathew *et al*. investigated the specific aspects of the PPR that promote self-management in patients diagnosed with type 2 diabetes (Mathew et al., 2022). The authors identified that patients who trusted their healthcare providers were more likely to initiate and adhere to the recommendations for insulin. Additionally, patients who felt comfortable enough to express the challenges they were facing with their insulin were able to collaborate with their provider to develop an individualized plan for their insulin needs, moving forward, which had positive impacts on their glycemic control (Mathew et al., 2022). Interestingly, patients with hypertension who are seen in a secondary healthcare setting (*i.e.* in specialty clinics, rather than by their primary care provider) are less likely to maintain aspects of their management such as fluid restrictions and attending follow-up appointments (Świątoniowska-Lonc et al., 2020). Świątoniowska-Lonc *et al.* (2020) identified that in this patient cohort, the PPR, and specifically the quality of communication, was a *"significant predictor of adherence"* to self-management. Moreover, Brenk-Franz *et al*. (2017) argue that to promote self-management, it is essential for providers to learn the interaction style of each of the patients, which is determined by bolstering their relationship. Patients who were perceived as exhibiting an anxious or insecure attachment style were found to have poorer coping and dietary control, as well as less hope and self-efficacy. The authors highlight, as others mentioned previously, that communication is an essential aspect of the PPR (Brenk-Franz et al., 2017). In a study with emerging adults diagnosed with diabetes, AYA patients described the importance of going beyond informational content during the appointments with their providers. Or in other words, they want their providers to convey interest in them as individuals, and that they are not just a number on a patient list. AYA who felt like their provider cared about them showed increased receptivity to their provider's advice (Wolf, Martyn, Haw, & Kimble, 2023). These findings are highly relevant to the current study as participants herein discussed the importance of being considered as an individual, and that poor communication impacted the level of honesty from participants with their providers and adherence to their management.

There are many ways in which providers can build rapport and a trusting relationship with their patients. Effective communication, including verbal and non-verbal, is thought to be a central pillar of rapport building (Butt, 2021). Showing interest and asking about patients' lives is an

alternative approach for history taking, and also affords patients the opportunity to discuss what is important to them, and what is happening currently in their lives. Butt (2021) shared that this type of conversation is helpful to get a sense of the patient's health awareness, baseline understanding of their disease and provides a frame of reference for medical advice so recommendations fit within the context of the patient's life (Butt, 2021). In a study focused on newly diagnosed HIV patients, Dang *et al*. (2017) identified three actionable pieces that providers can do to promote trust and build rapport. The authors identified that patients want their providers to provide reassurance to reduce their fears and stress. Reassurance was associated with increased emotional and mental strength and patient resilience. Additionally, patients wanted providers to tell them they are within their right to ask questions. Patients reported feeling anxious about asking questions to their providers as they did not want to be seen as being a difficult patient or offend their provider. Simply asking patients if they have questions multiple times throughout their appointment provided a great deal of comfort (Dang et al., 2017). Open body language, direct body orientation, smiling, head nodding, eye contact, facial expressions, vocal tone are also known to be beneficial for building rapport (Duggan, Bradshaw, Swergold, & Altman, 2011). However, Duggan *et al*. cautions providers not to overstep rapport boundaries, which consequently conveys negative perceptions of the patient. For example, exaggerated tone, excessively simplified vocabulary, exaggerated body language and exaggerated praise can be considered paternalistic and detrimental to the PPR (Duggan et al., 2011).

Overall, patients value rapport between themselves and their providers. When providers actively work to build trust and respect with their patients, and provide holistic care, patients feel better supported and are better able to complete their self-management. By fostering the PPR, providers create an environment that empowers and motivates patients, and ultimately leads to improved health outcomes.

5.2.3. Integration of mental health support

As described in *Section 1.1*, AYA in EA are at an increased risk for mental health concerns (Wood et al., 2017; Zarrett & Eccles, 2006). Chronic medical conditions and mental health appear to have bidirectional effects. It is well known that AYA diagnosed with chronic conditions are at an even higher risk for mental health concerns compared to their AYA peers (Berens et al., 2020; Canadian Mental Health Association, 2008). Chronic medical conditions in AYA are associated with limitations impacting their capacity to participate in typical social situations (*e.g.* school,

socializing with friends), which consequently increases risks for conditions like anxiety and depression (Adams, Chien, & Wisk, 2019; Houtrow, Jones, Ghandour, Strickland, & Newacheck, 2012). Additionally, depression and anxiety are associated with negative health outcomes such as decreased adherence to treatment plans, decreased quality of life and increased hospitalizations (Quittner et al., 2020). Therefore, detection and treatment of mental health concerns may be a complimentary approach to improve the health of PKU and GSD1a patients.

Participants of this study described their own experiences with the reciprocal effects of their PKU or GSD1a and mental health. The association between neuropsychological concerns (*e.g.* anxiety, depression) are described in *Section 1.5.4*, and PKU participants described their experiences with anxiety as a result of high Phe levels. Mental health concerns were also prevalent among GSD1a participants. Participants identified many disease-associated factors that challenged their mental health, including the sense of otherness and limitedness, and the challenges with balancing their condition with everything else in their lives. They further elaborate that their mental health challenges impacted their capacity for self-management, which in turn would negatively impact their disease.

Calls for integration of mental health screening have been made in other disease contexts as well. Patients with inflammatory bowel disease were determined to be at a particularly high risk of developing mental health concerns before the age of 18, which indicates a significant need for mental health support. Bennett and Pfefferkorn (2019) suggest that *"an integrated mental health and digestive health model is the simplest, and best, solution."* Integrating mental health resources (*e.g.* assessment, counselling, tools) reduces barriers for patients who are interested in accessing mental health supports (Bensemann, Zeng, & Hamer, 2022; Funk, Saraceno, Drew, & Faydi, 2008). Research has indicated that integration of mental health screening into healthcare appointments for other chronic healthcare concerns is beneficial. A 2018 study by Myers *et al*. assessed the integration of mental health counselling with chronic disease care from the patient perspective. Participants were screened for depression and alcohol use during their usual appointment for their chronic condition. The majority of participants appreciated screening and acknowledged that they were unlikely to independently seek or request services, outside of their healthcare appointments, due to limited understanding of mental health concerns (Myers et al., 2018). In another study, the authors assessed the integration of mental health screening into 84 different cystic fibrosis clinics across the United States (Quittner et al., 2020). They identified

several noteworthy successes following integration of the new screening programmes. Providers improved their understanding of the relationship between mental and physical health and that mental health is essential for overall health of patients and there was increased collaboration between the clinics and community mental health providers, among many other successes. From the patient perspective, integration of mental health screening helped normalize and destigmatize mental health issues, identified patients with anxiety and depression who were previously missed in other contexts, created an open dialogue, and increased awareness of the mental health support available (Quittner et al., 2020).

The benefits of integrating mental health screening and resources into chronic disease clinics are clear. However, participants of this study identified how PKU and GSD1a affect everyone in different ways. Participants also discussed their diverse life experiences. As such, it is likely that PKU and GSD1a patients would benefit from diverse mental health interventions (*e.g.* formal counselling, workbooks, apps, peer support groups) as not all approaches will be suitable for every patient. In fact, a few participants identified that interacting with other patients with PKU and GSD1a would be highly beneficial to them. However, they wished to have options with respect to how they can connect with other patients, so they can interact with others on their own terms.

5.2.3.a The benefits of peer support for individuals with chronic conditions

Social support is the perception or realization of support when it is needed from others, including family members, friends, peers, patient organizations, and the community (Strom & Egede, 2012; Yang et al., 2021). Social support benefits patients by providing advice on coping, positive communication regarding their condition and decreasing stress, among many other benefits (Gallant, 2003; Sacco & Yanover, 2006; Strom & Egede, 2012). Peer support is a specific type of social support which is thought to be particularly beneficial for patients with chronic diseases (Embuldeniya et al., 2013). Peer support is provided by individuals who have similar characteristics to the individuals being supported. Support is based on experiential knowledge of the condition that the person seeking support is also experiencing. Research suggests that peer support may influence physical and mental health outcomes for those seeking support (Dennis, 2003; Embuldeniya et al., 2013; Gallant, 2003; Yang et al., 2021).

In the present study, participants overwhelmingly identified concerns regarding the perception that they were different from their peers, and a sense of isolation as their condition often resulted in feeling let out. Additionally, a few participants spoke emphatically about their desire to connect

with other individuals with PKU and GSD1a throughout the HCT, though these results were not discussed in *Chapter 4*. Participants expressed sentiments that are similar to what is known in the literature which shows that connecting with other individuals affected with the same conditions, and having shared experiences in coping with these conditions, strengthens bonds between individuals. In their 2013 article synthesizing knowledge on the impact of chronic disease peer support interventions, Embuldeniya *et al*. demonstrated that peer support interventions were beneficial for both those seeking and providing support as the interventions afforded participants a sense of connection, combatted isolation and enabled participants to find meaning in their condition. Ultimately, peer support interventions empowered patients and changed their outlook on the disease, which in turn was positively impactful for participants' mental health (Embuldeniya et al., 2013).

Peer support is also associated with other benefits that go beyond its direct effects on patients' mental health. In their work focused on patients who seek peer support through social media, Kjærulff *et al*. (2023) suggested that these peer interactions are valuable for preparing patients to actively participate in their clinical encounters with their providers. Patients are provided with information, vocabulary and encouragement from their peers which empowers patients to interact with their providers and address their concerns (Kjærulff, Andersen, Kingod, & Nexø, 2023). Yang *et al*. (2021) stated that a relationship exists between social support and diet self-management in diabetes patients as social support levels indirectly affect adherence to diet control. Moreover, they established that social support was directly associated with self-efficacy (*i.e.* an individual's confidence in their ability to achieve a certain outcome) and diet-promoting behaviours (Yang et al., 2021). Given the current understanding of the impact of social and peer support on management of chronic conditions, it is likely that PKU and GSD1a patients would benefit substantially by having access to varying types of peer support interventions as the participants in the present study relayed similar issues to those identified in the literature.

Given the experiences of the participants of this study, and what is known in the literature, the interconnectedness of physical and mental health is undeniable. Therefore, it is essential that both physical and mental health be considered to provide comprehensive care for PKU and GSD1a patients. Integrating mental health screening, support services or other mental health resources into PKU and GSD1a patients' routine care throughout the HCT, in a time in which they are most

vulnerable to mental health concerns, will ensure the provision of holistic care necessary to facilitate a successful HCT.

5.2.4. Importance of dietary resources

Research in PKU and GSD1a management and treatment continues to progress. While new drugs and gene therapies are at, or soon to be at, the cutting edge of treatment, dietary management remains the central pillar of PKU and GSD1a management. Given the importance of following food restrictions and regularly incorporating formula/cornstarch throughout the day, it is imperative that PKU and GSD1a patients have access to information and products that promote patients' willingness and capacity to follow their nutritional recommendations. Primary articles regarding the association between diet and maintenance of self-management in PKU, GSD1a or other chronic conditions requiring dietary restrictions are seemingly limited. However, a small number of articles quote that PKU and GSD1a patients struggle with palatability of formula or cornstarch and medical foods (Derks et al., 2021; Giovannini, Verduci, Salvatici, Paci, & Riva, 2012; Gloria Ho et al., 2016). Moreover, Bilginsoy *et al*. (Bilginsoy et al., 2005) identified that PKU patients and their caretakers are often dissatisfied with the variety of medical PKU foods available (Bilginsoy et al., 2005). A study by Ho *et al*. (2016) identified that patients often feel limited due to lack of information about the nutritional contents of food items, and overall uncertainty, which limits the variety of foods patients consume. Clinicians report that the effects of dietary restrictions on patients' social lives, limited food variety and palatability have substantial negative influences on diet management for PKU and GSD1a patients (Bilginsoy et al., 2005; Gloria Ho et al., 2016; MacDonald et al., 2010; MacDonald et al., 2012).

For the participants of this study, the impacts of their diet management were widespread. They described influences from their dietary restrictions and formula or cornstarch as being interwoven with mental health, social interactions, and everyday life. Their dietary restrictions contributed to feeling left out at social gatherings, reluctance to participate in social gatherings involving foods, food fatigue from eating the same food items repeatedly and food curiosity. Formula and cornstarch contributed to feelings of otherness and embarrassment and were not palatable nor convenient for participants to incorporate into their daily lives. For most participants, these impacts resulted in poor health outcomes as participants would either make compromises on their management that were not sufficient to mitigate disease symptoms or would eliminate aspects of their management all together. As such, these participants experiences and knowledge from the

literature, though limited, strongly suggest that steps should be taken to ensure that AYA with PKU and GSD1a have the resources needed to meet their dietary needs in a fulfilling way throughout the HCT. Ultimately, providing AYA patients with dietary resources, including information, free samples, recipes, cooking classes and workshops during the HCT will promote appropriate diet management (Casey, 2013; Gloria Ho et al., 2016; MacDonald et al., 2010) during a transitional period that is characteristically challenging for patients to maintain their dietary requirements.

To address these concerns, participants of this study spoke briefly about various meal-planning apps, cooking classes and workshops that had been helpful for them in the past. Again, information regarding the effectiveness of these types of dietary resources on diet management in PKU and GSD1a, is virtually non-existent, or anecdotal at best. However, there are many resources, such as cookbooks and recipe blogs, available online, and many patient organizations host their own diet-focused events. Given the sheer volume of diet (mis)information available for PKU and GSD1a online, it is likely beneficial for patients to receive a list of vetted and reliable resources from providers.

Though the available literature is limited, participants of this study undoubtedly identified a need for additional support regarding their dietary management as they too commented on the monotony and palatability of their diets. By ensuring that patients have access to reliable information, samples to limit the financial burden of trying new foods or formulas, and practical skills that enable them to expand their dietary preferences, patients may be more willing and capable of maintaining their diet management during the HCT.

5.2.5. Parents as facilitators of self-management

It is expected that AYA will assume responsibility for managing their own activities of daily living as they transition into adulthood, and expectations are no different for AYA diagnosed with chronic medical conditions like PKU and GSD1a. As described in *Chapter 1*, PKU and GSD1a are diagnosed in the first few days to months of life. Therefore, parents or caregivers are burdened with the task of performing their child's disease management. As patients mature and prepare throughout the HCT, the role of the parent/caregiver must evolve to enable patients to learn to independently self-manage (SickKids Transplant Clinical Committee, 2021). Ideally, parents provide and demonstrate care to their child so that the child can subsequently perform the task while under direct supervision. Provision of tasks should be done incrementally. Eventually, the

child should be capable of performing their care accurately without supervision of their parent (SickKids Transplant Clinical Committee, Kayle, Tanabe, Shah, Baker-Ward, & Docherty, 2016; Nightingale, McHugh, Kirk, & Swallow, 2019; 2021). Healthcare providers have some influence over this process by encouraging parents to relinquish control over certain tasks, and teaching AYA patients the skills and knowledge to empower them to begin managing independently (Nightingale et al., 2019). However, parents must be the at the forefront of their child's development as interactions with healthcare providers are often limited outside appointment times. Participants of this study described the prominent influence that their parents had over the HCT as they were learning to self-manage.

In the context of this study, parents were described as having integral roles in teaching participants how to track their diet and prepare their formula or cornstarch. It is interesting that participants described that while their parents helped them become independent in some aspects, there were other tasks that remained under their parents' control, which subsequently impacted their capacity to perform those tasks independently in the adult healthcare setting. Parents who were not managing the participant's condition or would not let the participants manage at all also had a significant impact on the participants' health outcomes and self-efficacy. Participants also had varying opinions about their parents' sustained involvement in their care after the transfer to adult care. Collectively, participants described the process of switching management responsibility from parents to themselves as complex.

The underlying reasons that account for the ways in which parents choose to support their child in learning self-management throughout the HCT is beyond the scope of this project. However, participants of this study highlighted areas in which parents may require additional support to facilitate the progressive switch in management responsibilities. Therefore, this information warrants incorporation into the recommendations as the parental role appeared to have profound impacts on participants. There is growing research regarding the challenges that parents face in relinquishing control of their child's management, which reinforces the notion that parents have a substantial role in teaching management and creating the foundation for health behaviours that persist into adulthood. In fact, research suggests that *"the approach, communication style and attitudes adopted by parents could influence how a child assumed self-management responsibility"* (Husted, Esbensen, Hommel, Thorsteinsson, & Zoffmann, 2014; Nightingale et al., 2019). Furthermore, in the review by Nightingale *et al.*, they identified that patients felt better

supported throughout the HCT when their parents conveyed encouragement, trust and a belief that the patient could manage independently (Nightingale et al., 2019). While some parents are willing to let go, others are more reluctant to give up control over disease management. Parental challenges associated with relinquishing control over self-management are known to impact the HCT (Buford, 2004; Kayle et al., 2016; Lerch & Thrane, 2019). Parents of children with asthma described negative emotions (*e.g.* fear, uncertainty, anger, guilt) towards the demands of their child's illness, particularly during times in which they felt they could not get the child's symptoms under control. For some parents, this meant that they managed in a way that lacked focus on prevention of symptoms. It has been reported that some parents find it difficult to maintain their child's management at home, so they adapt the management to minimize the intrusiveness of the condition (Nightingale, Friedl, & Swallow, 2015). In their systematic review, Lerch and Thrane (2019) identified that parents struggle with the pace and extent to which they should pass responsibility to their child. Additionally, parents reported feeling uncertain about how to transmit the knowledge and intuition they have developed to their child. Parents were hesitant to make changes that would negatively impact their routines and child's health (Kayle et al., 2016; Lerch & Thrane, 2019).

Parents play a critical role in their child's development of independent self-management, but the experiences of the participants of the current study and the literature suggest that parents also require support from healthcare providers throughout the HCT. Therefore, not only is it prudent to have on-going conversations with parents about the importance of teaching their child to manage independently, but parents also likely require their own education and mental health support throughout the HCT (Nightingale et al., 2015). Just as patients' lives are diverse and complicated, so are parents' lives. Parents have their own values, health beliefs and parenting styles that influence the ways in which they choose to manage their child's care (Buford, 2004) and therefore likely require diverse options for learning how to transfer responsibility to their child (Nightingale et al., 2015). In the literature, parents have asked for education in group and one-on-one settings in which information is provided verbally, visually and written formats, as well as reliable information that is accessible online. Parents requested opportunities to connect with other parents of children diagnosed with the same condition. Importantly, parents' needs and preferences for learning and support varied over time as they become more confident and their child's needs changed (Nightingale et al., 2015).

While this study does not focus on the experiences of parents throughout the HCT, participants highlighted the intersectionality of their own experiences and their parents' experiences during the HCT. As such, it is well within the scope of this study to make recommendations suggesting increased support for parents during the HCT given the critical importance of their role as described by the participants of this study.

5.2.6. Limitations

While this exploratory study was instrumental in identifying patient-reported factors influencing their readiness and capacity for self-management during the HCT, it is not without its limitations. Firstly, the use of social media for recruitment can be extremely advantageous for reaching many individuals. However, eventually, the study advertisements become buried by other posts which decreases the response rate. Response rates may have also been impacted by the time at which posts were made. For example, more or fewer individuals would likely see a post depending on whether the post was made at a peak time during the day or evening. To further critique the recruitment methods, the study materials were produced in English only and were publicized by groups who were mostly, if not completely, English speaking. Therefore, this study is missing valuable experiences from the PKU and GSD1a populations of French-speaking areas of Canada. Additionally, while it was important to recruit participants from across Canada to gain a more expansive understanding of the factors influencing self-management, this may also represent a limitation to this study due to the differences in healthcare between provinces. For example, the transfer of care standards (*e.g.* changing hospitals vs. remaining at the same hospital as an adult) and/or provincial funding may have been confounding variables impacting patients' experiences throughout the HCT.

Secondly, this group of 13 participants likely accounts for only a minuscule proportion of the PKU and GSD1a populations in Canada. Though the participants unequivocally identified common experiences within the HCT, they also presented a diverse sampling of experiences. Therefore, the recommendations presented above, which address the common themes identified by participants, may be generalizable to the wider population of PKU and GSD1a AYA, but there are undoubtedly additional support needs required by PKU and GSD1a AYA patients who were not included in this study. Therefore, their needs may not be represented in the recommendations. This presents an opportunity for future research. Moreover, this study is lacking participants from the peri-transition age group, which impacts the types of insights received throughout this study.

While the post-transition group can provide insight retrospectively, and shed light on what could have been helpful, the peri-transition group can provide information based on the biggest concerns that they have while actively participating in the HCT.

Thirdly, due to the wide scope of this project (*i.e.* aimed to identify any and all patient-reported factors influencing self-management) it was not feasible to explore each identified factor in-depth. Consequently, future research can be conducted to assess the patient and provider-perceived appropriateness and effectiveness of the recommendations.

5.3. FUTURE DIRECTIONS

To the best of my knowledge, this study was the first to investigate the patient-reported factors influencing self-management in the context of the HCT for PKU and GSD1a patients. As such, it is imperative that the patient-driven recommendations described in *Section 5.2.1* are disseminated to the relevant healthcare providers, as well as the PKU and GSD1a communities that hope to benefit from the results of this research. To disseminate my findings to the healthcare community, publication in a peer-reviewed journal and presentation at national or international academic conferences would be highly beneficial. To disseminate these findings to patients and parents in the PKU and GSD1a communities the current recommendations will be presented using an infographic to be distributed via social media and email listervs. In addition, this exploratory study has laid groundwork for future research projects that could occur in short-, mid-, and long-term timelines.

In Harrison and Graham's (2021) textbook focused on knowledge translation in healthcare, they identified steps to implementing best-practice changes. Following identification and clarification of the issues, they propose building solutions and field testing the solutions. The recommendations in *Section 5.2.1* are a first step to building solutions. Future work to be completed in a short-term timeline could involve individual clinics identifying the ways in which the proposed recommendations could be included in their practice. For example, should integration of mental health screening and resources include collaboration with counsellors or other mental health professionals, or is it sufficient for the primary specialist of the appointment to ask their patient a pre-determined set of questions? Once appropriate solutions have been identified, they can be field tested in clinic. At this point, it is critical that providers, and most importantly patients, have opportunities to provide their impressions and feedback on the utility of the recommendations. Providers can provide insight into whether the recommendations are practical

to implement, while patients can speak to whether the recommendations addressed the gaps that were identified by participants in this study. Building solutions and field testing can be an iterative process. Once solutions have been appropriately tailored to the clinic and the population they serve, the recommendations and solutions can be implemented, evaluated and sustained (Harrison & Graham, 2021).

Many of the proposed recommendations in *Section 5.2.1* could be enhanced by the development of accompanying interventions. For example, participants who felt different from their peers may benefit from attending social events with other AYA who are diagnosed with their same condition. As such, future work that could be completed in a mid-term timeline could include developing different disease-specific opportunities for patients to connect with each other. Given that the populations of PKU and GSD1a patients in each province is likely small, it would be beneficial to develop both virtual and in-person opportunities that enables connection between patients from specific regions or patients from across the country. These opportunities should not be limited to events focused solely on learning and developing skills and should include events meant to simply offer a group of individuals with shared experience an excuse to come together and socialize. Examples of these interventions could include, but are certainly not limited to, virtual formal support groups, online or in-person cooking classes, art nights, book clubs or workshops. Any interventions that are created should be developed by a multi-disciplinary team and include a patient-partner in some capacity to ensure that a diversity of opinions and expertise are considered. This will help ensure that the interventions are appropriately targeted to the intended population. It is also critical that individuals in attendance be offered the opportunity to provide feedback on the interventions so that they can be appropriately adapted and improved.

Future work to be completed during a long-term timeline could include research focused on developing standardized, but disease-specific guidelines for the HCT. While the current study is not sufficient on its own to be a basis for HCT guidelines, the long-term timeline for this suggestion provides time for additional studies to be conducted to generate greater evidence to formulate best-practice guidelines. As described in *Section 1.3.1*, there are many generalized guidelines in the literature that can act as an outline for PKU and GSD1a specific guidelines. Guideline development should involve a multi-disciplinary team including all specialists relevant to PKU and GSD1a care, as well as one or more patient partners. It is imperative that guidelines be targeted to patients, parents, and providers. Information that could be included in these guidelines are flexible timelines

for provision of information and the progressive transfer of responsibility to patients, disease-specific skills and information that should be provided to patients and parents and how communication between pediatric and adult providers should be facilitated, among others.

Overall, the future work that comes from this project is not limited to the suggestions above. This project provides evidence that acts as a launching pad for smaller-scale clinic-specific research projects or contributes to the rationale for larger-scale country-wide research.

5.4. SIGNIFIANCE

The transition from adolescence to adulthood is already a complex transition owed to the challenges of EA. It is well known that this transition is additionally complicated for individuals with PKU and GSD1a as they are also undergoing the HCT. AYA PKU and GSD1a patients are known to struggle with self-management during this transition. The work presented in this thesis is an important step towards understanding the patient-reported factors influencing patient's readiness and capacity for self-management during the HCT. I have identified 6 keys themes from this work which includes 2 themes related to patients' perceptions of the HCT, and 4 themes related to the factors influencing their self-management. Identification and preliminary exploration of these themes is critical to better understand the needs of PKU and GSD1a patients so that steps can be taken to ensure patients feel supported and empowered to maintain their self-management throughout the HCT. While this project focused on the needs of patients with PKU and GSD1a, this work may also benefit individuals with rarer IEM in which it is more difficult to pursue research due to the limited population. Overall, these participants' experiences were invaluable for creating recommendations to ensure the health and well-being of future AYA transferring to adult care.

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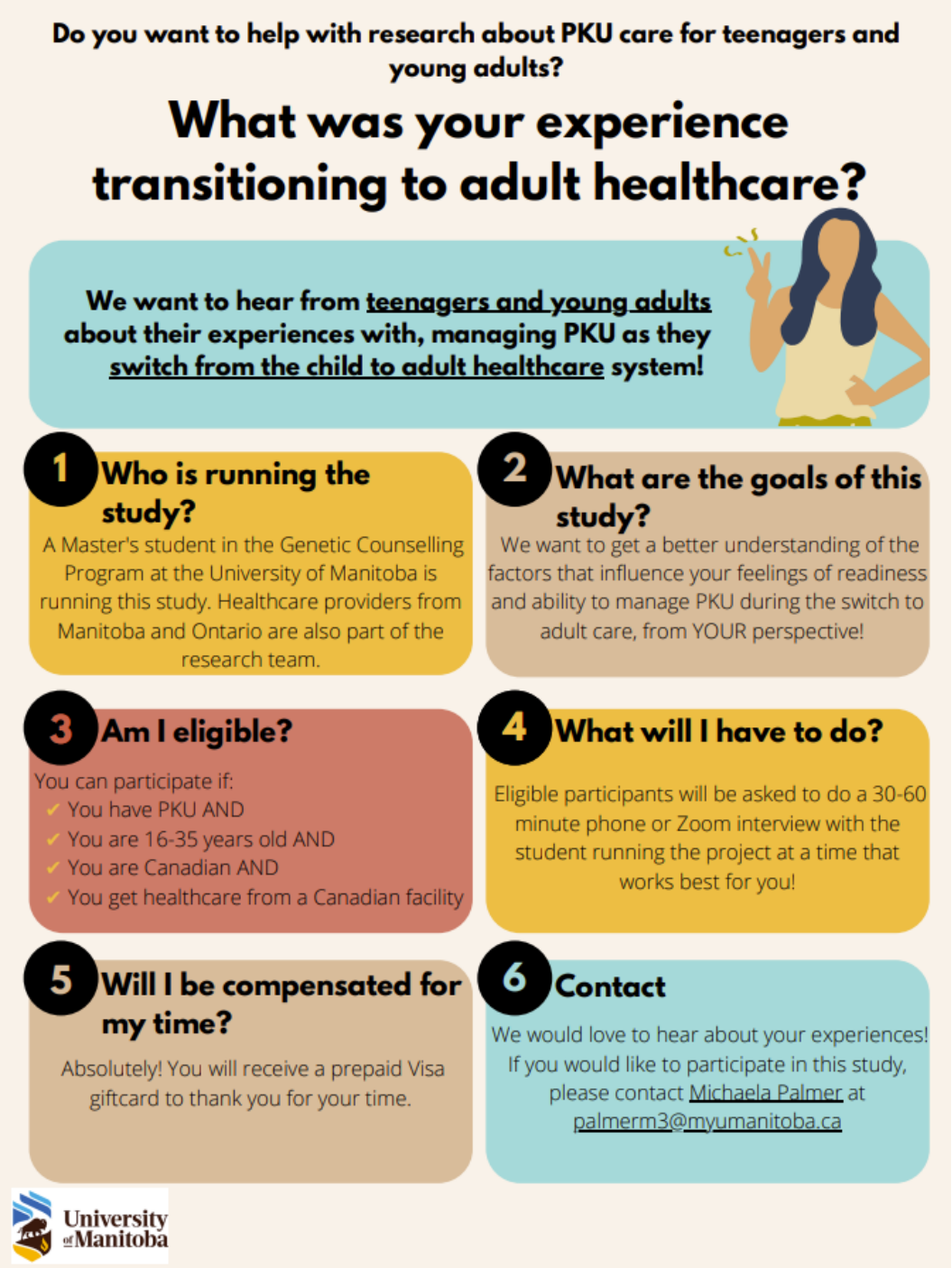
APPENDIX A

STUDY INFOGRAPHIC



Supplementary Figure 1: Infographic advertising the current study.
Image of the infographic provided to PKU-related patient groups and agencies to advertise the research study. Dimensions of the infographic were altered depending on the platform in which they were shared. Similar infographics were designed and shared for GSD1a.

INVITATION LETTER

Dear (Participant),

We are reaching out to you because you expressed interest in our research project asking about your experience managing your condition during the transition from child to adult healthcare. Thank you for you reaching out to us! We have attached some consent forms for you (*and your parent/guardian*) to review if you need more information about the research study. If you are eligible to participate based on your answers to questions 1-5 written below, we would like to set up a time to review the consent forms and do the interview with you. We anticipate that the interview will take no longer than 60 minutes. Please email or call us back with the following information:

1. Do you or your dependent have PKU or GSD1a?
2. Are you or your dependent between the ages of 16 and 35 years?
3. Are you or your dependent Canadian?
4. Do you or your dependent receive healthcare from a Canadian facility?
5. Do you or your dependent speak and understand English?
6. Your preferred method of contact for the consent review and interview: telephone or videoconferencing.
7. A preferred date and time to review the consent form and complete the interview.

Once we have this information, we will follow-up with you to confirm the information and meeting date.

If you wish to fill out the consent form in advance, please send the signed copy back to us at this email address (palmerm3@myumanitoba.ca). However, you do **not** have to complete the consent to participate in research form prior to setting up an interview time. The consent form will be verbally reviewed before the interview begins. You do **not** have to consent to the interview after the forms are reviewed and you may withdraw your consent at any time.

If you have any questions or concerns, please do not hesitate to contact us. Contact information is also included in the consent form.

Sincerely,

Michaela Palmer

University of Manitoba

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RESEARCH PARTICIPANT INFORMATION AND CONSENT FORM
Individual Interview

Title of Study: Exploring the experiences of adolescents and young adults with phenylketonuria and glycogen storage disease 1a through the healthcare transition.

Principal Investigator: Michaela Palmer, MSc, Genetic Counselling Student, Department of Biochemistry and Medical Genetics, Rady Faculty of Health Sciences, University of Manitoba

Co-Investigator: Dr. Patrick Frosk, PhD, MD, FRCPC, FCCMG

Advisory Committee: Dr. Allison Dart, PhD; Dr. Gayle Halas, PhD; Melanie Napier, MSc., CGC

You are being asked to participate in a research study involving an individual interview exploring the experiences of teenagers and young adults diagnosed with phenylketonuria (PKU) or glycogen storage disease 1a (GSD1a; Von Gierke disease) as they manage their condition during the transition from child-focused to adult-focused healthcare. Please take your time to review this consent form and discuss any questions you may have with the study staff, your friends or family before you make your decision. This consent form may contain words that you do not understand. Please ask the study staff to explain any words or information that you do not clearly understand.

Purpose of this Study

This research study is being conducted to study the experiences of patients with PKU or GSD1a with self-management during the transition from the child-focused to adult-focused healthcare setting. We want to learn about the patient-reported factors the influence someone's feelings of readiness and ability to self-manage (e.g. follow their diet, interact with their healthcare team) their PKU/GSD1a. We hope that participants will share the challenges and successes they have had during this transition, and whether or how they had to become more independent when managing their PKU/GSD1a. We hope that this study will reveal the important elements of the healthcare

transition that are needed to ensure the health and well-being of future teenagers and young adults who are transitioning to adult care.

Participants Selection

You are being asked to participate in this study because you identified as a someone with PKU or GSD1a. You are eligible to participate in this study if you meet all of the following criteria:

- You have been diagnosed with PKU or GSD1a
- You are between the ages of 16 and 35 years old
- You receive healthcare from a Canadian facility
- You speak and understand English

Study procedures

You will be asked to participate in one 60 minute interview which are meant to be a discussion between you and the principal investigator about the research topic. You will be asked questions about your feelings of readiness, challenges, successes, learning experiences, and self-management during the transition to adult care. Interviews will be phone or video conference calls and will be audio recorded. The principal investigator may take notes during the interview. The recording will be transcribed by the principal investigator or a professional transcribing service (Transcript Heroes) for further analysis. Names may be used during the interview but will be removed from the transcripts and final documents. The audio recordings and related documents will be kept on a secure hard drive in a secure location accessible only to the principal investigator and supervisor. The audio tapes will be stored in locked files before and after being transcribed. Tapes will be destroyed within seven years of completing the transcriptions and the transcriptions will be destroyed seven years after the completion of this evaluation. Final results will be provided to the participants by email or mail, depending on patient preference, within one year of the study's completion.

Risks and Discomforts

Participation in this study presents no more than minimal risk. However, it is possible that taking part in the interview could cause distressing thoughts and feelings. You do not have to answer any questions that make you feel uncomfortable or that you find upsetting. Should you need any additional help or support, we will refer you to Klinic Crisis Line or help you find other counselling help.

Your confidentiality may be broken if you describe one of the following:

- You say something about harming yourself or others.
- You tell me about the abuse or neglect of a child.
- You report inappropriate or incompetent practice of a healthcare professional

Benefits

There will be no direct benefit to you for your participation in the study. We hope that information obtained from this study will help us gain a better understanding of experiences of teenagers and young adults with PKU or GSD1a transitioning from child to adult care and help improve this process for future patients.

Costs

There is no cost to you to attend the interview.

Payment for participation

You will be given a $20 prepaid Visa giftcard for participating in an interview.
You will receive no payment or reimbursement for any expenses related to taking part in this study.

Confidentiality

We will do everything possible to keep your personal information confidential. Your name will not be used at all in the study records. A list of names and addresses of participants will be kept in a secure file so we can send you a summary of the results of the study. If the results of this study are presented in a meeting, or published, nobody will be able to tell that you were in the study as all personal information with be coded. Please note that although you will not be identified as the speaker, your words may be used to highlight a specific point. The collection and access to personal and health related information will be in compliance with provincial and federal privacy legislations.

Audiotapes of the interview will be typed and used to prepare a report. The audiotapes and typed notes will be kept for seven years in a secure hard drive in a locked office as per the Masters in Genetic Counselling Program requirements. Only the principal investigator and supervisor will have access to them and know your name. Additionally, the Health Research Ethics Board (HREB) of the University of Manitoba may require access to these files for quality assurance purposes

(contact information for HREB below under "Questions"). The collection and access to personal information will comply with provincial and federal privacy legislations.

Permission to Quote:
We may wish to quote your words directly in reports and publications resulting from this. With regard to being quoted, please check either yes or no for each of the following statements:

Researchers may publish documents that contain quotations by me under the following conditions:	
☐ Yes ☐ No	I agree to be quoted directly if my name is not published (I remain anonymous).
☐ Yes ☐ No	I agree to be quoted directly if a made-up name (pseudonym) is used.

Voluntary Participation/Withdrawal from the Study
Your decision to participate in this study is voluntary. You may refuse to participate or withdraw from the study at any time, within three months following the interview, by contacting the principal investigator, Michaela Palmer. If you withdraw from the study, all data you provided will be destroyed. Your decision not to participate or to withdraw from the study will not affect your medical care.

Questions
If any questions come up during or after the study contact the principal investigator and/or the supervisor.

Michaela Palmer
Email: palmerm3@myumanitoba.ca
Telephone: 204-789-3774

Patrick Frosk
Email: pfrosk@hsc.mb.ca
Telephone: 204-787-4454

For questions about your rights as a research participant, you may contact The University of Manitoba, Bannatyne Campus Research Ethics Board Office at (204) 789-3389

Consent Signatures:

1. I have read all 4 pages of the consent form.

2. I have had a chance to ask questions and have received satisfactory answers to all of my questions.
3. I understand that by signing this consent form I have not waived any of my legal rights as a participant in this study.
4. I understand that my records, which may include identifying information, may be reviewed by the research staff working with the Principal Investigator and the agencies and organizations listed in the Confidentiality section of this document.
5. I understand that I may withdraw from the study at any time and my data may be withdrawn prior to publication.
6. I understand I will be provided with a copy of the consent form for my records.
7. I agree to participate in the study.

Participant printed name: _____ Date _____
(day/month/year)

Participant phone number: _____

PARENT/GUARDIAN CONSENT

Parent/Guardian name: _____ Date _____

(day/month/year)

Participant name: _____

Parent/Guardian phone number: _____

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has knowingly given their consent

Printed Name: _____ Date _____
(day/month/year)

Signature: _____ Role in the study: _____

PERI-TRANSITION INTERVIEW GUIDE

PKU/GSD1a over the years

- How did PKU/GSD1a impact your daily activities and well-being as a child/young teen? (10-15 years old)?
    - What parts of your PKU/GSD1a management were doing?
    - How was it different from your experience now?
- Over the years, have interactions with your healthcare team/doctor changed?
    - How has it changed?
    - What do you think about these changes or lack of changes?
        - How do they make you feel?

The healthcare transition

- At most centres that manage metabolic diseases there is a different group of doctors that care for kids and adult patients. Has this process of transitioning to the adult health care system started yet for you?
    - What kinds of preparations have been made with your health care team? With your parents/caregivers and can you tell me a bit about those discussions? Do you know what the plan is for when you transition to adult health care?
        - how old were you when you started to transition from pediatric to adult healthcare?
        - Are you staying at the same hospital/facility?
        - Will you have the same healthcare team?
        - Have you thought about what the biggest changes/differences will be between the two settings?
            - What do you think they will be?
    - Have you had/do you recall any discussions about your changing responsibilities leading up to the transition?

Feelings of readiness and self-management

- When you think about all the things involved in managing your PKU/GSD1a, like coping emotionally, eating the right foods or talking with your doctors, how do you think your PKU/GSD1a management is going, in your own opinion?

    - What do you consider to be good management?
    - Can you tell me about a time when you felt like you didn't have good management?
        - How did you improve your management?
- Do you feel ready to take on more responsibility/independence with respect to your disease when you transition to adult health care?
    - How did/will you learn about what you needed to do to self-manage?
    - What aspects of your self-management do you feel comfortable with?
        - How did you come to feel so comfortable with this?
    - What aspects of your self-management do you feel uncomfortable with?
        - What about this makes you feel uncomfortable?
        - Do you have any questions about your self-management that you feel still need to be answered by your healthcare team?
- What kinds of challenges do you think you might encounter in managing your disease once you transition to adult health care?
    - Will your parent/caregiver's participation in your PKU/GSD1a management change?
    - What are some of your biggest concerns regarding self-management during this time?

<u>Supports</u>

- What would you like health care providers to do to support the transition process?
- Is there anything else you want to tell me about feeling ready to face this change to adult care? Anything else you'd like to share about feeling ready to self-manage your condition?

POST-TRANSITION INTERVIEW GUIDE

PKU/GSD1a over the years

- How did PKU/GSD1a impact your daily activities as a child/young teen (10-15 years old)?
    - What parts of your PKU/GSD1a management were doing?
    - How was it different from your experience following your transition (18-20)? Is it different than what your experience is now?

The healthcare transition

- I'd like to hear a bit more about your transition from the pediatric to adult healthcare settings.
    - how old were you when you transitioned from pediatric to adult healthcare?
    - did you stay at the same hospital/facility?
    - did you have the same healthcare team?
    - With these in mind, what would you say are the biggest changes/differences you have experienced between adult and pediatric care?

Feelings of readiness and self-management

- I'd like to ask a bit more about what happened to prepare you for the change from pediatric to adult care:
    - Do you recall any discussions about your changing responsibilities leading up to the transition?
        - What were these discussions about?
        - What did you wish was discussed?
    - Did you feel ready to take on more responsibility/independence with respect to your disease when you transitioned to adult health care?
        - What do you think you needed in order to feel ready to self-manage?
- How did you manage your disease during the transition?
    - How did you learn about what you needed to do to self-manage?
    - How did your parent's/caregiver's participation in managing your PKU/GSD1a change?
    - How did the transition impact your Phe levels/blood sugar?

    - What were some of your biggest concerns regarding self-management during this time?
    - How confident were you that you could manage your disease as you transitioned to adult health care?
- In what ways did your self-management change after you transitioned to adult health care?
    - Did you find it harder or easier to manage your disease?
    - How well do you feel your PKU/GSD1a was managed before, during and after your transition?
    - Do you think your attitude and approach to self-management has changed over this transition period?
        - Tell me a bit more about that? (Perhaps even ask for some examples of how things have changed from pediatric to adult management.)
- Can you tell me about a time during transition that you were feeling unprepared or uncertain about what to do?
    - Is there something you wish you had during the transition that you didn't?
    - Was there something that happened/was discussed that you felt wasn't helpful?

<u>Supports</u>

- How do you think healthcare providers can support patients during the transition process?
- Is there anything else you want to tell me about feeling ready to face this change to adult care? Anything else you'd like to share about feeling ready to self-manage your condition?
    - What advice would you give to other patients as they prepare to transition to adult care?