

Experiences of Parents of Children Diagnosed with Inherited Metabolic Diseases (IMD) in Canada: Qualitative Description and Identification of Patient- and Family-Centred Outcomes

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ABSTRACT

Objectives: The objectives of this thesis were to: (i) understand the experiences of parents/caregivers of children with inherited metabolic diseases (IMDs), including perceptions of the health care system; and (ii) identify important patient/family-centred outcomes for measurement in future studies.

Methods: A qualitative study used semi-structured interviews to gain in-depth insight into caregivers' experiences. In an adapted meta-synthesis study, the qualitative findings were integrated with the results of related research to identify priority outcomes.

Results: Twenty-one caregivers were interviewed. Participants described adjusting to the management of their child's illness through specific coping strategies but reported stress related to social development. While generally satisfied with disease-specific care, participants described negative experiences with non IMD-specific health services. Health-related quality of life, parental coping, and specific experiences with health care emerged as high-priority outcomes.

Conclusions: This project contributes to the limited published literature on caregiver experiences with pediatric IMD and informs future patient-centred research.

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CHAPTER ONE: INTRODUCTION

Patient-Centred Outcomes

In recognition of the importance of considering patients' preferences, values, and role in decision-making about their health (1), the measurement of patient-centred outcomes has become a priority for health research (2–4). As described by Sacristán, incorporating patient-centred outcomes into evaluative research helps to ensure that the evidence used to inform care represents the priorities of patients and their families and accurately reflects and responds to their experiences (1). According to the US-based Patient-Centered Outcomes Research Institute, patient-centred outcomes research allows patients and their caregivers to communicate and pursue informed decisions when assessing health care options (3). This is facilitated by empirical research that incorporates the voices of patients, caregivers, and the larger healthcare community (3).

Patient-centred outcomes are challenging to incorporate into rare disease research. This is in part because understanding of the natural history of rare diseases is often limited (5). It is also a consequence of the small body of evidence documenting which outcomes are most important for rare diseases, given the small and heterogeneous cohorts of patients available for study (6).

Inherited Metabolic Diseases (IMDs)

IMDs (also known as inborn errors of metabolism) are a large and heterogeneous class of more than 400 rare single gene diseases that are characterized by defects in specific proteins and enzymes, resulting in interference with normal functions (7,8). The clinical features of IMDs

vary across diseases and according to specific patient characteristics and can encompass acute episodic illnesses or more chronic manifestations that may or may not be progressive (9). Although IMDs are individually rare (birth prevalence of about 1:10,000 to 1:1,000,000), they have an important impact on affected individuals and their families and are collectively of public health importance (8,9). Currently, many newborn screening programs across the world target IMDs for early detection in order to provide a window of opportunity for treatment (9,10). IMDs are commonly treatable when diagnosed early with the implementation of effective treatment, however, treatments can be onerous for patients and families, and costly for the health care system (9).

Previous Literature on Patient and Family Experiences with IMDs

The following summarizes the small body of existing literature on the experiences of parents/caregivers specific to caring for a child with an IMD. This literature encompasses both qualitative and quantitative studies and has examined a range of diseases, including urea cycle disorders, amino acid disorders, lysosomal storage disorders, and other IMDs (e.g., galactosemia, mucopolysaccharidosis).

As chronic illnesses that often require daily home management as well as on-going medical care, IMDs affect not only the child but also the function of the entire family unit (11). Family impacts described in the literature include psychological functioning of the parents or siblings, changes in employment activities, economic status, parents' relationships with one another, and a family's relationship with society (12). The impact of having a child with an IMD has rarely been explored from families' perspectives. This exploration is essential if we are to

ensure that interventions for IMDs are evaluated in a way that incorporates outcomes and experiences that are most important to them. Fundamentally, parental functioning influences the health and development of the child and thus, it is important for health care professionals to consider the well-being of both the child and the parents in order to deliver the best possible care (12–14).

1. Parents' overall mental health and functioning

Parents of children with metabolic diseases have reported impacts of their child's illness and care in areas of their cognitive functioning, sleep, pain, social functioning, daily activities, sexuality, energy, and positive and negative emotions (14,15). Caregiving for a child with an IMD has been described as increasing parental stress, parental anxiety, and parental depression; this can have long-term effects including effects on a parent's marital status, development of other siblings, and relationships with others (11,13,16–18). Predictors of stress for parents include the developmental level of the child or child's adaptive functioning, difficulties meeting the child's health care needs, and social support (19). Parents of younger children with IMDs have been found susceptible to a lower parental quality of life as younger children need more support and supervision, and require constant regulation and management concerning diet and nutrition, which are often critical components to disease management for IMDs (13). Grant and colleagues' study of parents of children with mucopolysaccharidosis III (MPS III) concluded that emotional support from a partner, family, friends or other sources, and loss of friendship because of the child's illness are prominent in predicting parental health related quality of life (17).

2. Marital stress

Marital strain and discord have been associated with parents' lack of time for their own personal and social needs, and the experience of constant stress when caring for a child with an IMD (11,16).

3. Financial stress

A common parent-reported outcome in the literature is financial stress – including stress associated with the challenge of paying medical bills, finding and affording suitably qualified childcare staff, and paying for education and transportation costs (12,16,18)

4. Diagnostic experiences

Because of the low prevalence of IMDs and associated scarcity of available information and treatments, IMDs are often associated with misdiagnosis and uncertainty of prognosis – factors that add to the burden of caregiving stress for the parents (11,17). Parents have expressed the disadvantages of a delayed diagnosis and communicated that early diagnosis enables timely start of treatment as well as information useful for reproductive decision making (16). Parents reported feelings of concern, fear, sadness and fear of death when their child's diagnosis of an IMD was confirmed (11,18).

5. Experiences with the health care and education systems

Caregivers of children with IMDs have reported experiencing a difficult time interacting with the health care system. For example, in a study with families whose children were affected by maple syrup urine disease, parents felt frustrated in having more knowledge of the disease than some physicians, due to the rarity of their child's condition, and some felt that there was a

lack of competence from health care professionals (18). Moreover, parents' experiences interacting with the education system have been reported as mixed. In the same study described above, while some parents described positive experiences, others reported having a difficult time interacting with the education system including school teachers (18).

6. Feeding challenges

Many IMDs are treated with highly specialized and restrictive diets, particularly disorders of protein metabolism. Feeding difficulties are thus a common challenge in children with an IMD (20,21). Caregivers have stated that children are challenged by poor appetite, restricted food variety, and lengthy meal times (13,22). In addition, some children with phenylketonuria, which is one of the more common IMDs, are more likely to vomit, exhibit negative behaviour, get distracted and self-feed less often, and eat less in comparison to healthy children (13,14). Thus, parents and caregivers spend considerable time on dietary concerns (12–14).

7. Social challenges for the child and parents

Social challenges have been documented in several studies of children with IMDs. For example, patients suffering from Niemann-Pick disease type B, a relatively rare inherited lysosomal storage disorder, emphasized as stressors their limited physical activity, social isolation, and peer rejection as experienced between the ages of 10-16 years (23). Extending from this, time for leisure and relationships with friends may be compromised for children with an IMD, which presents additional social challenges (15). In parallel, a lack of perceived social support has been identified an important indicator of both patient and parental stress;

psychological and social support including close family relationships, friends, religious groups, medical professionals, and support groups are sources patients and their families use to cope with the disease (12,23). It has been documented that immigrant children suffering from phenylketonuria and their families are disproportionately affected by barriers to care related to language, psychosocial adjustment, economics, education and culture, which are associated with poorer adherence to treatment (24). Lastly, Hatzmann and others concluded that emotional support and friendship are positive predictors of quality of life (14).

8. Positive psychosocial impacts

While IMDs present challenges for patients and their families, it is interesting to note that caring for a child with an IMD can also have positive psychosocial effects. Studies have identified that some parents felt the diagnosis brought family members closer, and allowed them to be more compassionate and patient, caring, and appreciative of life and family (11,18).

The Canadian Inherited Metabolic Diseases Research Network (CIMDRN)

CIMDRN was established to develop research and generate evidence in the area of pediatric IMDs. It is a multidisciplinary practice-based research network that aims to develop evidence-based approaches to improve interventions and outcomes for children affected by IMDs and their families (5). This involves the integration of data on interventions, outcomes, and patient characteristics in order to identify patterns of care that are associated with best outcomes (5). The outcomes of interest to the network are guided by Berwick and colleagues' "triple aim" (25), which considers and recognizes the importance of clinical outcomes, patient and family experiences and perspectives, and health system impacts.

In addition to the collection of clinical data from the medical charts of participating children, part of CIMDRN's research program involves collecting data directly from the parents/caregivers of children with IMDs, regarding their experiences with illness and care, including self-reported outcomes such as quality of life. This thesis project was conducted within this component of CIMDRN's research program. The quantitative experiential data that will eventually be collected from CIMDRN's participating parents via questionnaires will be linked with clinical data in order to incorporate patient/family-reported outcomes into the network's research to evaluate care (5). To develop CIMDRN's questionnaire/s for parents/caregivers, CIMDRN investigators identified a need to generate evidence documenting those outcomes that are high priorities for measurement. A series of relevant studies was launched. This thesis aims to both contribute empirical data and also integrate the full series of studies.

The first CIMDRN study in the series was a broad scoping review, designed to identify a range of relevant patient- and family-centred outcomes and related self-administered measures, from published reports describing complex, chronic paediatric diseases (6). Because of the limited number of studies specific to IMDs, this scoping review included a broader range of diseases (e.g., cerebral palsy, cystic fibrosis, diabetes, Down Syndrome, epilepsy) with clinical similarities to IMDs (6). The second CIMDRN study of interest here was a qualitative interview study, conducted to elicit the views of representatives from patient support and advocacy organizations regarding the most important outcomes to families living with a child diagnosed with an IMD (26).

Rationale for the Thesis Project

Although the above studies for CIMDRN identified many outcomes describing complex, chronic pediatric diseases and salient experiences from the perspectives of patient support groups, there remain knowledge gaps about the outcomes that are most relevant to children with an IMD and their families (6,26). Specifically, the authors of those previous studies argued that a study that directly involves parents of affected children is critical to understanding the most important outcomes for future research (6,26). In particular, patient-centred outcomes that describe perceived experiences with illness and care are best reported by patients themselves or by a family member/caregiver if a patient is unable to self-report (27). Thus, there is a need to gain deeper insight into parents'/caregivers' perspectives in order to inform the development of a future questionnaire that aims to focus on the highest priority outcomes from their perspectives.

In addition, as described above, the literature describing family experiences with pediatric IMDs is scarce. Thus, a study that investigates those experiences in depth, from the perspectives of parents/caregivers across a range of pediatric IMDs and in different health care settings, promises to create new knowledge and contribute to that literature, aside from its specific contribution to CIMDRN's development of a questionnaire.

Purpose and Objectives

The overall aim of this thesis project is to improve the evidence base for the patient-centred management of pediatric IMDs by adding parent and family insights on important outcomes, and by supporting the development of an instrument for use in a long-term cohort study.

Thus, the objectives of this project are:

- 1) To gain an in-depth understanding of parents'/guardians' personal experiences of having a child living with an IMD, and their perceptions of their interactions with the health care system in the management of the IMD; and
- 2) To use this understanding, and the results of related, but separate, studies, to identify a set of priority patient- and family-centred outcomes and other important constructs for potential inclusion in a survey instrument for ongoing administration to parents of children with IMDs.

Structure of the thesis

Chapter two presents *Project 1: Caregiver interview study*, which addresses objective 1. It provides an in-depth understanding of caregivers' experiences with IMDs with respect to the daily management of disease, its impact on child and family life and perceptions of interacting with the health care system. Chapter three presents *Project 2: Meta-synthesis*, which addresses objective 2. It builds on the findings from the first reported study and also draws on the findings on three other related studies to identify important outcomes and constructs of families' experiences with IMDs that can be prioritized for measurement in a questionnaire for families

of children with IMDs. Lastly, Chapter four presents an overall discussion and interpretation for the thesis.

CHAPTER TWO: PROJECT 1, CAREGIVER INTERVIEW STUDY

Introduction

This study was designed to address the first objective of this thesis: To gain an in-depth understanding of parents'/guardians' personal experiences of having a child living with an IMD, and their perceptions of their interactions with the health care system in the management of the IMD. It involved primary data collection from parents/caregivers, with the intention of addressing a major gap in the existing literature, as identified in Chapter 1.

Methods

This study used a qualitative design, specifically one-on-one semi-structured telephone interviews. Interviews are useful for a range of purposes that include exploring attitudes and perceptions that underlie different health behaviours (28). Particularly, interviews allow the interviewees themselves to interpret, evaluate and describe their personal experiences, defined as the "insider's perspective" (29). This enables the respondent to define a problem in their own terms and can permit the researcher to explore respondents' experiences and modify the researcher's pre-conceptions of the matter (30). Outcomes that describe parents'/guardians' experiences were explored, thus, a qualitative interview design was well suited to address this research objective.

Sample selection and recruitment

The CIMDRN study population was composed of parents/caregivers of child participants enrolled in an on-going cohort study. The cohort study invites the participation of children born between 2006 and 2015, diagnosed with one of 30 IMDs (listed in Appendix A), and receiving

care at one of 14 participating specialist metabolic clinics in Canada (5). The sampling frame for the present study included parents/legal guardians of children who had been enrolled in the larger cohort study at four of the participating clinics: the Children's Hospital of Eastern Ontario (Ottawa), British Columbia Children's Hospital (Vancouver), Montreal Children's Hospital (Montreal), and the Izaak Walton Killam Health Centre (Halifax). Eligible parents/guardians had consented to be contacted to participate in an interview and/or questionnaire study and had been nominated by their families as the most knowledgeable of the child's disease and care.

From the sampling frame, I used a purposive sampling method to select potential participants to be invited for the present study, in order to achieve a diverse sample of parents/guardians of children receiving care at different centres, with different diseases (IMDs) and of different ages (31). The eventual sample size was dependent on data saturation (32). Based on previous experience, the research team anticipated approximately 15-25 interviews. Recruitment was initiated in phases (5-10 participants at a time). Selected eligible participants were invited by telephone or email. Participants provided written informed consent prior to the interview. Three attempts were made to contact participants and a voice message was left with each contact where relevant. After three attempts with no response or if a participant declined participation, they were not contacted further.

Interviews

Interview guide

An interview guide (Appendix B) was developed, based on a broad scoping review of the literature (6), and revised through discussion with my supervisors and other members of the

research team with methodological and clinical expertise. Topics initially covered by the guide were: diagnostic experiences; general health and overall well-being; physical health; social health and relationships; mental health; treatment experiences and interactions with the health care system. Because this study was intentionally conducted in parallel with Project 2 (chapter 3), findings from the latter were considered for inclusion as the set of interviews progressed.

Analysis

Thematic content analysis, specifically qualitative description, was used to summarize the interview data. This method was appropriate because qualitative description is a low inference method where the expected outcome is a descriptive summary that is close to the original interview data (29,31,33).

Five members of the research team collaborated with me on an initial analysis of the first three interview transcripts, to identify broad categories and to review the interview guide and the coding. I coded all subsequent interviews, with review and verification by my supervisor (BP). The data were then organized into themes and analysis took place alongside the interview process so that emerged themes were incorporated into subsequent interviews (34). Several discussions among team members were held to review the transcripts, discuss emerging themes, assess the degree of saturation, and identify priorities for participant recruitment. The '10 +3 criterion' (31) was used to adjust recruitment according to saturation: ten initial interviews were planned, with further interviews added in groups of three until sufficient saturation was judged to be achieved. The analysis was supported by NVivo software.

Ethics

Ethics approval for this study was received from the Children's Hospital of Eastern Ontario Research Ethics Board, the Ottawa Health Science Network Research Ethics Board, the University of British Columbia / Children's and Women's Health Centre of British Columbia Research Ethics Board, the Montreal Children's Hospital's Clinical Ethics, and Izaak Walton Killam Health Care Research Ethics Board.

Results

Interview/participant characteristics

From 36 recruitment invitations, we received signed informed consent from 23 potential participants. I interviewed all participants that provided consent to allow their voices to be heard, given their interest in the study, even though data saturation with respect to main themes was judged to have been achieved with 13 interviews. I also proceeded to complete 21 interviews in order to enrich the data across the diverse set of diseases involved. Two participants who initially consented failed to respond to the telephone call at the scheduled interview time and did not respond to follow-up telephone calls, so were subsequently excluded from the study. A pilot interview was conducted with a parent of a child with an IMD in order to pre-test the interview guide (33); data from the pilot interview were not included in the analysis for the final study. All interviews were audio-recorded and subsequently transcribed.

The majority of participants were mothers of a child with an IMD. Thirteen diseases were represented, including amino acid disorders, urea cycle disorders, fatty acid oxidation disorders, organic acid disorders and other metabolic diseases. The age of the affected children

whose parents were interviewed ranged from 1 year to 7 years. The average interview length was 55 minutes.

Themes

The themes that emerged fell into the two broad categories on which the interviews focused: (1) experiences with disease and its management at home and in the community; and (2) experiences with the health care system.

1. Experiences with disease and its management at home and in the community

Three themes emerged within this category: the "new normal" and proactive coping; social stressors; and parent advocacy.

a. *The "new normal" and proactive coping*

The daily management of their child's IMD was described by many caregivers as intense, due to the need for the child (and sometimes the entire family) to learn to adhere to very restricted diets and treatment regimens. For example, many parents expressed difficulties associated with the early stages of adjusting to the disease management:

"...it was a really big adjustment for our family just learning new ways, like new ways of eating I guess, because we were not, we're not vegetarians." (participant 11, amino acid disorder)

"I would say the worst of it was when he was a newborn because they told us that we had to feed him exactly every 3 hours." (participant 18, fatty acid oxidation disorder)

"Initially it was really hard and I've just learned to accept, we've worked it out, we know what works for us...so we just take food with us wherever we go..." (participant 21, fatty acid oxidation disorder)

Some parents took a leave of absence or even sacrificed their careers to learn and adapt to the complexities of the disease:

"I never went back to work. I was a [occupation] and made more money than my husband. I gave up my job to take care of (child)...." (participant 10, other disease category)

"I took an extra year off just to make sure that I understood her diet properly and to make sure that I found a daycare that's going to be convenient." (participant 11, amino acid disorder)

However, participants often reported that they eventually adjusted well to the complex day-to-day management, so that it became the 'new normal' for their family:

"We don't know anything else... it keeps the family on a very strict routine because we know we have to get that breakfast, lunch and dinner into them. So, it's a very timetabled thing." (participant 04, amino acid disorder)

"But we have no choice...they're going to have to deal with that all their life and...they don't know any better...some people tell us we're lucky because we haven't had a kid that doesn't have it, so we don't know how it is like, how easy it would be if they wouldn't have [disease]." (participant 17, amino acid disorder)

Indeed, some participants expressed that it was challenging to consider how the disease impacted their family life, since it was now all they knew:

"Nowadays it's one of my routines. I know what he has...it's very simple for me right now, I know how to calculate and everything... We're so used to it you know?" (participant 16, amino acid disorder)

"We live in a new version of normal that is a heightened level of stress so... we live in the state of stress, it's just our new normal so I don't know that we notice it as much. It doesn't go away so it's just always there right?" (participant 15, amino acid disorder)

This adjustment to life with an IMD seemed to be accomplished through the use of a range of coping strategies. Specifically, respondents provided numerous examples of the organization, planning, and lifestyle changes they had undertaken in order to cope with disease management and establish routines. For example, for one family this included a choice to live close to the affected child's school:

"We are living in apartment in [area] and just a few steps from school...very close to the school just in case anything happened we can go to the school."(participant 06, other disease category)

For other families, it included selectively placing the child in a specific supportive day care and school:

"I drive 20 minutes of out my way...of where I work and live just so I can take them there [child's daycare]. I think, you know, I trust them so, you know and they're really good with the kids and it's a family-run daycare..." (participant 07, fatty oxidation disorder)

"... we were very, very careful with what we selected as far as preschool and home daycare and stuff and we sent them to a preschool and they were with family members before that so we had complete control." (participant 04, amino acid disorder)

Planning ahead and being prepared was also described as an important aspect:

"We do basically 2 trips to the grocery store every week, and everything is planned on a 7 day calendar...Friday, Saturday I'll sit down and I'll plan out the meals for the week."
(participant 21, fatty acid oxidation disorder)

Other lifestyle changes that included receiving support from extended family members and relatives were also described as a coping strategy to manage the disease:

"...both our moms have the scale at their house, they have food for her. And then, we are hoping to go [State] in Spring break so my mom is gonna come along just to help us out."
(participant 03, amino acid disorder)

"Our social life is pretty good because now we can drop him off at my in-laws, or my parents and we can go out, we can have a life." (participant 10, other disease category)

Moreover, parents credited social media and the internet for providing information, resources and connecting with other affected families:

"...the only thing is the support group on Facebook so if I have questions or whatnot it... it is nice to be able to go on there and get experiences from other parents." (participant 11, amino acid disorder)

"...for the first little while it was mainly just researching it on the internet..." (participant 09, fatty acid oxidation disorder)

For many families, vacations were described as challenging tasks that required a lot of planning and preorganization:

"...you kind of have to visualize what you're going to do...what you need to pack because it's not just packing your clothes, we have to pack all the food, we have to bring their bread we have to... So that's a challenge." (participant 17, amino acid disorder)

Another respondent described developing a spread sheet to manage health care appointments:

"I created a spreadsheet of all of our specialists, all the tests we have to do, so it's, you know it's an ongoing spreadsheet that I update... every 3, 4 months and the nice thing about it is that when I do update it...which is a lot of work but when I...do it then I know what I'm missing." (participant 10, other disease category)

b. Social Stressors

Despite these coping strategies, many caregivers reported feeling stress related to concerns about the social lives of their children, particularly surrounding situations where the child may be excluded because of necessary dietary restrictions. Social events that involve food

were described as a common challenge by several respondents. These challenges intensified during holidays and special events:

"...just going to children's birthday parties or things like that, it is getting a bit more difficult... she sees them eating this food, and then she'll look at hers and she knows that it's not the same right? Yeah so it is very, it is difficult..." (participant 11, amino acid disorder)

"...it's a bit hard during the holidays, because everything is related around food, and I find it hard, birthday parties...because we make their own cake and we were having issues with certain members of the family..." (participant 17, other disease category)

Often, caregivers described experiencing great difficulties accessing special medical foods that are similar to foods eaten by unaffected children – being able to identify with other children was depicted as an important for the social development of the affected child and a common concern for the parents:

"...but normality, being able to find something comparable to what all the other kids are eating, that's been a huge pain... "She gets a little sulky sometimes, because she knows she is not getting exactly the same thing the kids get but we go out of our way to find kind of like the replica..." (participant01, other disease category)

"When we go to Wal-Mart they've got a McDonalds there, she sees parents and their kids going to McDonalds...And she knows that when we walk into McDonalds the only thing she's able to get is a pop." (participant 13, fatty acid oxidation disorder)

Furthermore, feelings of isolation, frustration and a sense of not belonging were identified by some parents as a worry for their children, particularly at school:

"... when the food comes in the teachers tend to give them a pencil or an eraser and we have now a bucket-full of pencils and erasers and that is a measurement of how often that they are left out of these things..." (participant 04, amino acid disorder)

"the biggest thing, you know now she's in school...they have pizza days at school, and she can't have those... if we know it's pizza day we go and make up a big old pizza for her... But you know it's not the same. She knows it's not the same but she's happy that we do it... she sometimes feels like she is uh... a weirdo." (participant 13, fatty acid oxidation disorder)

c. The need for Parent Advocacy

Perhaps in part as a response to social challenges, a third theme, parent advocacy, emerged when considering children's access to special services and inclusion in activities, particularly in the context of managing the diet:

"...we just have to really advocate for her. We are part of a church, and our church in the infant nursery like would provide Ritz crackers for kids and like she can't have Ritz crackers and I didn't want them to handing out food so just kind of suggesting that they change the way they do things." (participant 03, amino acid disorder)

"We have Brownies and Sparks and the reason why I became a Unit Leader was because I needed to push the food out of weekly meetings because it was something, again, [child] would be exposed to it during the day." (participant 04)

Some caregivers also described advocating on a broader level, with the government, in order to access needed foods or services:

"...the only complaint I have about that is we...so we lobbied the [Provincial government]... we met with our MLA and we petitioned for coverage of low protein foods because [Province] was the only province without coverage." (participant 15, amino acid disorder)

Moreover, the rarity of IMDs was perceived to necessitate parents to advocate in school settings specifically around placing the child in the appropriate school that met the affected child's needs:

"...because the school board has never dealt with a child that has [disease]...I went in there with an 8 page letter...I kept telling the school board, if my son doesn't get the amount of hours that I requested, he will not go to your school." (participant 10 , other disease category).

2. Experiences with the health care system

The two themes that emerged within this category were: experiences with IMD-specific care; and experiences with non IMD-specific care.

a. Experiences with IMD-specific care

Parents commonly reported that affected children required frequent health care interactions involving multiple health care providers from various disciplines. Almost all of the affected children in this study received disease-specific care from specialist metabolic physicians and dietitians. Many participants were highly satisfied with the care that their child

received in the specialist metabolic clinic, with metabolic health care providers regarded as supportive, and dietitians in particular described as highly engaged with families:

"...our experience is amazing. We have a fantastic doctor and a fantastic dietitian. The backup dietitian and the backup doctor are equally as knowledgeable."(participant 15, amino acid disorder)

"...when we finally met (metabolic physician) ... he gave us the time. At no time did we ever feel that we... needed to hurry up and get out and we were extremely happy."(participant 13, fatty acid oxidation disorders)

"...the dietitians really help, like really help a lot, you know, um, really guiding me and everything with his intake with food and you know, trying new things." (participant 08, amino acid disorder)

Respondents also commonly expressed satisfaction with the coordination of care in this part of the health care system:

"Oh, when she was diagnosed it was great because [metabolic physician] and [dietitian] would come in together and we got a chance to see both. We have an option to see them separately. So yah, there is definitely a good coordination between them." (participant 01, other disease category).

"I think it's very well with coordination. I think for the... the metabolic it's okay. She's very connected." (participant 14, urea cycle disorder).

"I find the Metabolics Department to be really well, really effective, really coordinated and great systems in [Children's Hospital] so that part has been really great." (participant 15, amino acid disorder)

b. Experiences with non IMD-specific care

Although respondents expressed contentment with IMD-specific care, many participants reported negative experiences and dissatisfaction with non IMD-specific components of the health care system that were used frequently by their child, for example, the emergency department, the pharmacy, or the blood laboratory.

For many affected children, frequent blood draws were required and were described as highly stressful due to the inherent pain:

"There was a time we took [child] for a blood draw and I could hear her, and I could hear her screaming and [technician] was fishing in [child]'s arm for the vein. Like, excessively fishing and I asked her to stop. Blood draws were very, very difficult." (participant 05, urea cycle disorder).

A few parents expressed their concerns about the specific services in phlebotomy, including access to highly experienced professionals, late phlebotomy results, or inconvenient hours that affected parents' schedules:

"...my son is very small...They have to take a lot of blood. And the people, I don't think they have enough experience to poke a child so young....there's another team for the just for the young...But we cannot access to this team. " (participant 14, urea cycle disorder)

"...we do it at home with the finger. I receive the blood work of my son not on the second day, not on the third, later, so I don't know what's going on like, this week, my son could have the level very high for 1 week and I'm not gonna know, and the next week I'm going to receive the results." (participant 12, amino acid disorder).

"...having a clinic open Saturday mornings for even just one hour because we do blood work so regularly... it impacts a lot of people's schedules... eat up a lot of our vacation time, sick leave, parental leave, whatever we have... just for the blood work alone." (participant 04, amino acid disorder).

Respondents also communicated about the internal coordination of the hospital. This often included concerns with receiving the correct medication from the pharmacy and access to special medical foods for the affected child:

"...we were told not to use medication from home ...but the pharmacy, when she was in Emerg that afternoon, they were going to send up her meds from pharmacy, which they didn't..." (participant 05, urea cycle disorder)

"...but they didn't have any soy based formula at all. And we have since had her in the hospital as she got older but we don't let her eat anything from the hospital because there is always something in it that she can't eat." (participant 01, other disease category).

Concerns about the care their child received at the emergency department was noted as an important dimension of experience for several participants. While a few positive experiences were noted, respondents commonly expressed their distress and dissatisfaction with the inconsistency in care received from the emergency department during a crisis:

"... I just have a lot of stress around mostly around the health care that we received there [emergency department] because I can't say that it's consistent at all...I feel like almost like I have to prove that they are sick..." (participant 02, fatty acid oxidation disorder)

This sometimes extended to worry about the capability of emergency professionals to manage the needs of patients with a rare (and unfamiliar to the provider) condition:

"We had to go to Emergency once and the ER doctor had never heard of [disease]. It was hard to explain while we were under stress." (participant 18, fatty acid oxidation disorder)

"When we go to the ER in crisis...we know what to say, we know what's going to work... we've come up against a couple of doctors in the ER that don't appreciate that, they want to be the ones to when they walk into the room, everyone looks to them for the answers."

(participant 21, fatty acid oxidation disorder)

Summary of key points

The interviews provided rich insights into parents'/guardians' personal experiences of having a child with an IMD, with respect to the impact of the disease and its management on child and family life, and their perceptions of interacting with the health care system.

Caregivers reported that they became well-adjusted to the complex daily management requirements of their child's disease and redefined their "new normal" through the use of different coping strategies. Despite coping strategies that appeared to allow for ease of managing daily routines, many respondents reported stress related to concerns about the social lives of their children that necessitated parent advocacy, particularly surrounding situations where the child may be excluded because of necessary dietary restrictions.

With regards to experiences with the health care system, most parents interviewed were highly satisfied with care received in the specialist metabolic clinic. However, participants often reported negative experiences with the non IMD-specific components of the health care system that were used frequently, such as the emergency department, pharmacy, or blood laboratory. While these were often single events, they were recounted commonly and described as an important source of stress for several participants.

CHAPTER THREE: PROJECT 2, META-SYNTHESIS STUDY

Introduction

Project 2 was designed to address the second objective of this thesis: to identify a set of priority patient- and family-centred outcomes and other important constructs for potential inclusion in a survey instrument for ongoing administration to parents of children with IMDs. It used a meta-synthesis approach to incorporate the findings of Project 1 with three other separate enquiries to create a unified perspective on the most important aspects of families' experiences with IMDs. In order to address overall objective 2, this project's sub-objectives were to:

- (i) synthesize and integrate the results of a scoping review, a literature scan, and a qualitative study (the latter involved representatives of patient advocacy organizations), all of which were part of CIMDRN's research program;
- (ii) integrate the results of the qualitative caregiver interview study (Project 1) into the above synthesis process during the progress of that study; and
- (iii) use the final synthesized findings across all four studies to identify important aspects of families' experiences with IMDs (patient- and family-centred outcomes and other important constructs) in order to eventually inform the development of a questionnaire.

Methods

Overall approach

Meta-synthesis has emerged as an approach to synthesizing qualitative research (35). Meta-synthesis is designed to "...integrate results from a number of different but inter-related

qualitative studies. The technique has an interpretive, rather than an aggregating, intent, in contrast to meta-analysis of quantitative studies" (35). While a gold standard approach has not been established for meta-synthesis studies, Sandelowski et al. (36), and Walsh and colleagues (35), described three types of meta-synthesis designs that have been used relatively widely: (i) integration of findings from multiple related studies that are led by the same investigator(s), to generate new insight into a phenomenon; (ii) synthesis of findings from a number of studies across a specific field that are led by different investigators; and (iii) synthesis of qualitative studies (with the synthesized studies either coming from the same or different investigators), but with the use of quantitative methods for the synthesis. While most of the approaches to meta-synthesis described in the literature are restricted to a synthesis of qualitative data, Mays et al. described the use of meta-synthesis methods to integrate findings from both quantitative and qualitative studies (37).

I adapted the designs described above to guide this work for the purposes of this project, which required integrating qualitative data and literature reviews. This adapted meta-synthesis was designed to provide a broad descriptive summary of the research phenomena (patient/family experiences living with pediatric IMDs and in dealing with the health care system)(36), while keeping in mind the ultimate goal of informing a survey instrument.

Component studies

Four studies comprised the 'sample' for Project 2 (further details are provided in Results):

- (i) a scoping review that was conducted to identify patient- and family-centered

outcomes and self-administered measures from published reports, including reports of studies related to a broad range of diseases with clinical similarities to IMDs (6);

(ii) a literature scan that summarized the current literature on experiences specific to caring for a child with an IMD (summarized in Chapter 1);

(iii) a qualitative study of patient advocates to elicit their views on important priorities of families living with a child diagnosed with an IMD (26); and

(iv) a qualitative study of parent and caregiver experiences (Project 1, Chapter 2).

Procedure

The essential approach was a compare and contrast analytic technique as described by Walsh and Downe (35) and Sandelowski and colleagues (36), the goal being to identify concordances, discordances, and relationships across the set of studies (35,36). This was an activity involving four participants from the research team, in which I took a leading role. In the first step, I summarised studies (i)-(iii) to clarify key themes and concepts, as a starting point for analysis. To accomplish the compare and contrast technique, a small group of researchers involved in each of the studies being integrated met on a roughly bi-weekly basis over a period of nine months. In an initial stage, through discussion, the group identified similarities, differences and gaps in knowledge across the results of studies (i)-(iii). As the analysis progressed, the results were used to inform component study (iv) (Project 1 reported in Chapter 2). As findings emerged from Project 1, they were integrated into the meta-synthesis analysis. The final step was to draft a summary description and table describing the synthesized findings, as well as a summary of important aspects of families' experiences with pediatric

IMDs. The summary and table were further reviewed and refined through discussion by the group, with additional input by my co-supervisor (BW) and TAC member (IG).

Results

1. Initial summaries of studies (i)-(iii)

Study (i): Scoping review

The first study was a scoping review that was conducted to identify a range of relevant patient- and family-centered outcomes and measures of those outcomes, from published reports that described complex, chronic paediatric diseases and relied on self-administered questionnaire methods with children or their family members (6). The scoping review went beyond IMDs to incorporate literature on related conditions because of the small body of literature specific to IMDs.

This review identified following five broad categories of outcomes (see Table 3.1):

- general health status and quality of life
- physical health and functional status
- social health and relationships
- mental health
- disease management and perceptions

The category of mental health appeared most frequently in the reviewed studies and child general health status and quality of life (HRQoL) was the most frequent single outcome measured (6). In addition, outcomes related to caregiver/child roles in disease management were also significant. However, outcomes related to physical health and functional status were

documented less often than the other categories (6). Lastly, the scoping review mainly identified studies that focused on the child as the primary unit of analysis.

Study (ii) Literature Scan

The second study was a literature scan that summarized the small body of published literature (n=14 papers) on experiences specific to caring for a child with an IMD, encompassing both qualitative and quantitative studies.

This review identified the following four themes (see Table 3.1; further details of this study are also reported in Chapter 1):

- uncertainty and dealing with the unknown as an important aspect of having a child with an IMD that can lead to parent stress
- IMDs impact not only the child but also the function of the entire family unit – distress to the psychological functioning of the parents and family
- emphasis on parental function and mental health as a key influence on the health and development of the affected child
- positive psychosocial effect of caring for a child with an IMD on the family

Study (iii) Qualitative study of patient advocates

The third study was a qualitative interview study that elicited the views of representatives from patient support and advocacy organizations regarding their perceptions of most important priorities of families living with a child diagnosed with an IMD (26).

This study identified the following four broad themes (see Table 3.1)

- overarching theme of uncertainty and the unknown
- challenges associated with an affected child's major life transitions (i.e., transition to day care, school and social development, transition to adolescence and adulthood)
- progress of entire rare diseases communities over time
- strong emphasis on concepts that impact the family

2. Compare and contrast meta-synthesis of studies (i)-(iii)

The theme of *uncertainty and dealing with the unknown* emerged as an important aspect of having a child with an IMD from both the literature scan (study ii) and the qualitative study of patient advocates (study iii). This included parents dealing with scarcity of available information on disease and treatment options, misdiagnosis that lengthens the diagnosis process, uncertainty of prognosis, and experiencing a difficult time interacting with professionals within the health care and education systems who are unfamiliar with the disease. These factors were perceived to increase the burden of caregiving stress for parents. The theme of uncertainty did not emerge clearly from the scoping review (i), which led us to hypothesize that it may be specific to the rare disease setting, perhaps particularly for IMDs.

A strong emphasis on concepts that impact the family in addition to the child was also identified from the literature scan (ii) and the qualitative study of patient advocates (iii). This contrasted with the scoping review's (i) main emphasis on the impact of the disease on the affected child with a strong prominence on mental health and social health outcomes. It also emerged from studies (ii) and (iii) that some outcomes and experiences that are relevant to

patients and families are disease-specific, and it may be difficult to generalize experiences across all IMDs. For example, feeding challenges were frequently mentioned in both studies (ii) and (iii), including lengthy meal times and restricted food variety. Highly specialized and restrictive diets are more common in children with disorders of protein metabolism (20–22) relative to some other IMDs so it was hypothesized that feeding challenges may be less salient to families dealing with other categories of IMDs, e.g., fatty acid oxidation disorders.

List of topics identified for inclusion in project 1

The findings of studies (i)-(iii) in relation to CIMDRN's objectives led us to identify some areas that have not been well-studied, but that were hypothesized as potentially important for the development of patient/parent-reported measures for use in studies designed to evaluate care. The following areas were identified and prioritized for querying within Project 1 – caregiver interview study (which became study (iv) for the meta-synthesis):

- parents' expectations from treatments
- role of parenting styles in influencing their perceptions of both the management of disease and the system of care
- families' experiences with access to services, including services outside of the hospital care system such as respite services, home care, and nursing care.

3. Integration of study (iv) into meta-synthesis

Study (iv) Qualitative study of parent and caregiver experiences

The fourth study was the qualitative interview study that explored parents'/guardians' personal experiences of having a child living with an IMD, and their perceptions of their interactions with the health care system in the management of the IMD (Project 1, Chapter 2).

This study identified the following five themes:

- use of proactive coping strategies to manage complex diet and lifestyle management routines and establish a "new normal"
- social stressors and challenges faced by the affected child that caused parental stress and impacted on the emotional well-being of the parents
- need for parent advocacy to ensure child's needs and access to services
- satisfaction with disease-specific components of care (i.e., metabolic physicians and dietitians)
- dissatisfaction with non disease-specific components of care (e.g., emergency department, pharmacies, blood laboratory)

The concept of proactive coping was not identified in studies (i) through (iii). While the literature scan (ii) and patient advocacy study (iii) identified challenges with school, the concept of the social well-being of the child was not dominant in the findings of those two studies. By contrast, several constructs and tools for measuring social well-being emerged from the scoping review and social health was one of the five outcome categories in that study. Also, the

distinction between perceptions of care within and outside the metabolic clinic was not identified in studies (i) through (iii).

Regarding the specific list of topics identified for further investigation in study iv, with respect to parenting styles, this emerged in the form of discussions about coping strategies and in the role of parental advocacy as central to successful disease management and inclusion of the child in social/school activities. With respect to parents' expectations from treatments, although this was discussed with the interviewees in study iv, the interview results did not support treatment expectations as a priority theme for parents. Instead, parents described their experiences in managing home treatments, concerns accessing drugs and medical formulas, and accessing health care services. Barriers such as long wait times, inadequate insurance coverage, lack of available medical foods and geographical challenges were factors described by participants as challenges and stressors that interfered with treatment adherence. With respect to parents' experiences with accessing services outside of hospital care, study iv identified that parents were most concerned about services that typically were part of hospital care but took place outside the IMD clinic (for example, the emergency department, pharmacy, and blood laboratory). When participants in study iv were asked about supports beyond hospital care, home care and respite care were rarely identified. Instead, many participants reported receiving less formal support from outside the health care system, including social support from family, friends, and social media. These informal support systems and services were described as important ways to cope with IMDs.

Table 3.1: Integrative summary of key outcomes

Study	Summary of key outcomes identified (i)-(iii)
Scoping Review (i)	<ul style="list-style-type: none"> • outcomes within the category of mental health documented most frequently • child HRQoL was most frequent single outcome measured • child mental health, and family function outcomes documented relatively often • child/caregiver roles in disease management also important • physical health and functional status not emphasized • frequent focus on child as the primary unit of analysis
Literature Scan of IMD Studies (ii)	<ul style="list-style-type: none"> • uncertainty and the unknown was a dominant theme in studies specific to IMDs and were described as a source of parent stress; whereas this was not identified by the scoping review • many IMD-specific studies focused on the impact of the disease on the overall family unit, in contrast to the scoping review, where the child was most often the unit of analysis • many constructs/outcomes were disease-specific and this may challenge generalizability across all IMDs
Patient Advocacy Study (iii)	<ul style="list-style-type: none"> • uncertainty and the unknown was again a dominant theme when considering patient support/advocacy groups' perspectives on important aspects of the experience of having a child with an IMD • a second theme addressed challenges with a child's life transitions (to daycare/school, in adolescence, and to adulthood) – this was new (did not emerge in studies i and ii) • a third key theme related to the progress of a rare disease community as a whole, with regards to advances in treatment and mobilization of support; speculation that this insight may be unique to the perspective of patient support/advocacy organizations • similar to study ii, there was a focus on the overall family unit in addition to the affected child • also similar to study ii, some constructs/outcomes were disease-specific and may challenge generalizability across all IMDs • additional areas identified for querying in parent/caregiver study (study iv): understanding of caregivers' expectations from treatments; role of parenting styles in influencing perceptions of management of disease and care; families' experiences with access to services, including services and supports outside of hospital care
Parent/caregiver Study (iv)	<ul style="list-style-type: none"> • proactive coping strategies used to manage daily life and establish a "new normal"; social challenges faced by the affected child that often caused parent stress and impacted parents' emotional well-being. • satisfaction with IMD-specialist care and dissatisfaction with non IMD-specific care • uncertainty and the unknown once again an identified theme that caused parent stress • focus on concepts that impact on the overall family unit in addition to the affected child • diet management and adherence are common challenges across majority of IMDs • insights identified from prioritized list of topics (parenting, treatment expectations, accessing care outside of hospital): role of parental advocacy central to successful disease management and inclusion of child in social activities; reported experiences

related to treatment management and concerns with access to drugs, medical formulas and health care services; reliance on informal support systems (e.g., family, friends, social media) outside of the health care system to cope with IMDs.

Integrative synthesis to identify priorities for future measurement

A number of aspects of families' experiences with IMDs emerged from the integration of findings in this meta-synthesis as priorities for future questionnaire-based studies. Specifically, through detailed discussions of the synthesis results with my thesis supervisors and advisory committee, and considering the objectives of the larger CIMDRN research network in the context of additional relevant literature, I identified eight major constructs that are priorities for measurement in questionnaires designed for parents/caregivers of children with IMDs (Table 3.2).

The first two selected constructs are health-related quality of life (HRQoL) of the caregiver/parent and of the child. HRQoL was not identified as a specific theme across all of the studies included in the meta-synthesis, with the exception of its frequent use as a measure of child well-being in the scoping review (study i). However, HRQoL is a multi-dimensional measure of well-being that encompasses mental and social well-being (as well as physical health) (38) both of which were collectively important across the meta-synthesis (Table 3.2). HRQoL has also been identified as important in the literature related to children with chronic diseases and their parents/caregivers (14,39).

Considerations of the impact of IMDs on an affected child's parents and on the entire family unit strongly emerged from studies ii and iii in the meta-synthesis and was also

important in study iv (Table 3.1). An emphasis on families is supported by the of IMD-specific literature (11,13,16–18,26), supporting the selection of family functioning/quality of family life as a family-level variable to accompany the above focus on child/parent HRQoL. With respect to parents, the impacts that were most strongly suggested as important in studies ii and iv were parental mental health and parental stress. Parental stress and mental health have also been identified as an important influence on the health and development of the child in the IMD-specific literature (11–14,16–18).

Proactive coping was identified as a common coping strategy used by parents in study iv (Table 3.1 and Chapter 2). This seemed to be a novel finding in the field of IMDs and its description as being critical to parents' management of their child's illness in that study that led the inclusion of parental coping in general and proactive coping in particular as research priorities, in part to determine whether its role generalizes beyond my study iv sample (Table 3.2). Similarly, parental advocacy was identified as a specific coping strategy important to the successful management of their child's disease by several participants in study iv and yet this has not been emphasized in the IMD literature, to my knowledge (Table 3.2).

With respect to satisfaction with care, interestingly, in study iv (Table 3.1, Chapter 2), caregivers reported positive experiences and interactions with health professionals in the metabolic clinic whereas many negative experiences were reported with other parts of the health care system. These findings support the literature that satisfaction is an important indicator of patient-centred care (40) but the differences that participants identified across different components of care appears to be a new finding regarding IMDs and this warrants

further investigation (Table 3.2). Families' access to and use of health care services, the sixth selected construct, was identified as a challenge and a stressor by several participants in study iv related to services both outside and within the hospital (Table 3.1). Sources of informal supports (e.g., family, friends and social media) were also noted as ways to cope with the disease. Thus, it is important to evaluate affected families' abilities to gain access to services, and to identify any specific barriers to accessing care (41).

Table 3.2: Selection of constructs to measure in questionnaire

Construct (n=8)	Definition	Meta-synthesis findings
HRQoL- parent/caregiver	<ul style="list-style-type: none"> Caregivers’ own reported assessments of their well-being or lack of well-being. This can include physical, emotional, social (functional capacity/functional status) dimensions (42–44). 	<ul style="list-style-type: none"> Caregiver HRQoL was not a dominant theme across the four synthesized studies. However, as a multi-dimensional construct, HRQoL encompasses both mental and social health (along with physical functioning) and is a well-recognized measure of overall well-being. Parental/family social/mental health and well-being were important in study ii and study iv.
HRQoL- child	<ul style="list-style-type: none"> A child’s own reported assessment of their well-being or lack of well-being; or, a parent’s proxy report of a child’s well-being or lack of well-being. This can include physical, emotional, social (functional capacity/functional status) dimensions (42–44). 	<ul style="list-style-type: none"> Child HRQoL was frequently cited in study i. As per above, as a multi-dimensional construct, HRQoL encompasses both mental and social health (along with physical functioning) and is a well-recognized measure of overall well-being. Mental health emerged as a dominant category of outcomes in study i, which focused mainly on the child as the unit of analysis. The affected child’s social health was an important theme in study iv.
Family function and quality of family life	<ul style="list-style-type: none"> Manner in which a family operates as a whole unit through communication and management of their surrounding environment (45). 	<ul style="list-style-type: none"> IMDs’ impact on an affected child’s entire family strongly emphasized in studies ii and iii. There was evidence of psychological distress on the child’s family members identified in studies ii and iv.
Parents’ mental health/ parents’ stress	<ul style="list-style-type: none"> Demands from being a parent/caregiver to a child with an illness that can be associated with 	<ul style="list-style-type: none"> Parents’ mental health and parents’ stress were identified in studies ii and iv as important

	adverse psychological consequences, expressions of emotional and physical strains and/or feelings of anger, loneliness and fatigue stress (46).	dimensions of the caregiving experience.
Parental coping	<ul style="list-style-type: none"> • Coping refers to the manner in which individuals respond to stressful events through the use of different strategies or efforts to regulate the self and the surrounding environment (47). • Proactive coping is a strategy that involves anticipating probable risks and stressors that may cause harm and taking actions beforehand to prevent or reduce their impact(48,49). 	<ul style="list-style-type: none"> • Proactive coping emerged as a strategy used by families in study iv to manage complex daily routines associated with managing the child's disease. • Important to understand the range of coping strategies used by other affected families and whether proactive coping is generalizable beyond this study.
Parent advocacy	<ul style="list-style-type: none"> • Advocacy that is involved around areas that affect a person with a disease or disability and their family members with a specific focus on concerns, needs and requirements of a person with a chronic disease/disability(50). 	<ul style="list-style-type: none"> • Parental advocacy also identified as a coping strategy in study iv related to the management of the child's disease, including the child's inclusion in social activities and access to clinical interventions.
Satisfaction with care	<ul style="list-style-type: none"> • Extent of the degree of convergence between a patient and their family's experiences with a specific intervention compared with needs and expectations(51). 	<ul style="list-style-type: none"> • A difference in satisfaction with care in the metabolic specialist clinic vs. other systems of the health care system emerged in study iv. • Satisfaction with care is an important indicator of patient-centred health care and the differences identified from study iv require further exploration.

Access to care/services and supports outside the hospital setting

- Extent to which the affected child and his or her family has the ability to gain access to health care; dependent on predisposing characteristics i.e., age, sex, enabling resources such as availability of services, physicians, insurance and health needs (41).
 - Use of health care services outside primary hospital care to treat the affected child or to treat family members(e.g., nursing care, respite services, long-term care).
 - Access to care and services were described as a challenge in study iv with respect to access to services that were part of the hospital (outside the IMD department) and some services outside of the hospital.
 - Study iv also identified families' use of informal support (e.g., family, friends, social media) as ways to cope with the disease.
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CHAPTER FOUR: DISCUSSION

The first part of this thesis examined caregivers' experiences of living with a child diagnosed with an IMD and their perceptions of interacting with the healthcare system, using in-depth semi-structured interviews. The findings from this study suggested that participants generally coped well with the complex daily management of the disease through the use of different proactive coping strategies to establish routines, and they expressed satisfaction with the care received in the specialist metabolic clinic from metabolic physicians and dietitians. However caregivers reported stress related to their concerns about the social lives of their children, particularly surrounding situations where the child may be excluded because of dietary restrictions necessary as part of their child's care that often required parent advocacy. They also reported negative experiences with some non disease-specific components of the health care system that were used frequently, such as the emergency department, pharmacy, and blood laboratory.

The second part of this thesis, a meta-synthesis, synthesized and integrated the findings of four studies conducted within a program of research focused on rare metabolic diseases. These studies included a scoping review, a literature scan of IMD studies, and two qualitative studies (including the qualitative study described in Chapter 2). I used an adapted meta-synthesis approach to identify patient- and family-centred outcomes and other important constructs to eventually inform the development of a questionnaire for families of children with IMDs participating in the larger program of research that includes this thesis project.

Strengths and Limitations

The parent/caregiver study is one of the only studies that have explored caregivers' experiences of living with a child diagnosed with an IMD. A strength was its wide representation of IMDs. However, the wide heterogeneity of IMDs may result in lack of depth, neglecting important experiences that may be specific to one or more diseases. Although face-to-face interviews may have some advantages with respect to establishing rapport with respondents (28), because the sample was geographically dispersed and for the convenience of parents and caregivers, I chose telephone interviews. In addition, I talked with parents who expressed interest in being interviewed and were able to devote the time to the study. Thus, my findings may not be transferrable to families struggling to cope with the disease management.

To ensure rigor in the qualitative study, I performed constant comparison analysis where broad emerged themes from coded transcripts were explored in future interviews to establish credibility of the findings (34). Negative cases, i.e., those that are inconsistent with the emerging findings, were sought in the analysis of the interviews and discussed with respect to whether they warranted changes in the interpretation of the study's findings (52). For example, while majority of the participants credited the social media and the internet as a mechanism to receive support and connect with similar families, a few respondents described negative experiences associated with the use of social media and internet. Recognizing the negative cases helped to ensure that I refined the analysis until most of the available data were summarized (52). Lastly, to ensure quality of the interviews two researchers (BP and BW)

listened to one or more of the interview recordings and the research team read all transcripts in detail.

The meta-synthesis project also had several limitations. Importantly, the limitations of the four synthesized studies were carried over into the meta-synthesis findings. For example, the scoping review had some limitations with its search strategy that may have resulted in missing some studies (6). The literature scan of IMDs presented some methodological challenges, such as missing information on how some of the outcomes were reported in the studies, potential challenges related to inaccuracy in participants' responses in questionnaires, and a wide range of assessed outcomes, which posed challenges for summarizing the data (53). The patient advocacy study provided the perspectives of patient support groups, as opposed to insights from affected families (26). A limitation of the caregiver interview study was that it potentially missed the experiences of families that are struggling most to cope with the disease and its management, as I only interviewed participants who expressed interest and were able to devote their time to participate in a telephone interview.

Further, two of synthesized studies were themselves syntheses of publications, and in conducting the compare and contrast exercise, I did not refer to the original sources, relying solely on the synthesized findings. Thus, I may have missed some potential insights from the original sources, although this was mitigated to some extent since members of the meta-synthesis research team were also the lead investigators for the scoping review and literature scan. The studies synthesized were also diverse in their designs and methods. This made it difficult to ascribe differences in the findings to a particular study feature (e.g., study design, methods of collecting data, diseases or populations studied). Finally, qualitative studies, by

their nature, are typically not designed for synthesis purposes and researchers may believe that summarizing and synthesizing qualitative data make it difficult to retain an individual study's original meaning (35,36). A gold standard approach to meta-synthesis has not been developed and I adapted existing published approaches to my specific study objectives. Thus, the methods I used were exploratory and I cannot be certain that a different group of investigators, using a different adaptation of this design, would arrive at the same conclusions. I recommend further studies of methods for meta-synthesis that approach similar research questions using diverse methods.

A strength of Project 2 was the consultation with multiple sources, i.e., integration of the existing literature and interviews with both patient support organizations and families of affected IMD children to identify important characteristics of IMD for development of constructs for further study (54). Another strength was the analysis of similarities and differences across the four major studies, which served to broaden our interpretations of families' experiences with IMDs (36).

Interpretation of findings from Project 1 and comparison with the broader literature on patient and family experiences

Many participants in the caregiver/parent interview project reported the use of coping strategies, particularly proactive coping to deal with the daily management of their child's disease. Proactive coping, also commonly referred to as "future-oriented thinking", includes a set of strategies that involve anticipating probable risks and stressors that may cause harm and taking actions beforehand to prevent or reduce their impact (48,49). This seemed to contribute to life being described as routine or 'normal' despite what frequently included quite complex

daily requirements. The published literature on experiences specific to caring for a child with an IMD is scarce. Grant and colleagues' (17) study of parents of children with MPS III described their use of a range of strategies that included proactive coping, other positive coping strategies (e.g., religion, emotional/social support), and strategies such as substance use. In addition, close family relationships are referred to as a vital coping mechanism (23). Social media and the internet have gained attention for their role in parents' seeking information and connecting with others (26). This aligns with the findings in my study – almost all caregivers described seeking support from extended family and friends and many credited the internet and social media as a mechanism to obtain more information and to connect with other families affected by the disease.

Social challenges were identified as an important dimension of experience for affected children and were prioritized as concerns by the parents we interviewed. Henderson et al. (23) similarly emphasized the social challenges and peer rejection that are often experienced by individuals with a specific IMD, Niemann-Pick disease; these feelings of isolation and loneliness are predicted to exacerbate during adolescence. The emotional responses related to feelings of isolation and peer rejection may be more prevalent in children affected by Niemann-Pick disease relative to some other IMDs due to the physical restrictions and fatigue that characterize this disease(23). While Niemann-Pick disease was not among those we studied, we nevertheless identified social concerns as central to the experiences of many families with IMDs. Likewise, in a study of the perspectives of patient advocacy organizations related to IMDs (study iii in Project 2), Khangura et al., (26) found that participants often described families'

challenges associated with a child's social development, and this often connected with life transitions, such as the transition to school and transition through adolescence.

Parent advocacy was an important theme in my study and emerged in part in relation to the social challenges described above and also extended to advocacy around access to care. I did not identify advocacy as a theme in other related literature. While I did not collect socioeconomic data for the study sample, I hypothesize that collectively, the parents I interviewed tended to be relatively socio-economically advantaged, with access to more resources, because many conveyed the importance of their education and income as factors in contributing to successful coping with their child's illness. Thus, if the participants in my study had greater access to resources, they may have also had greater capacity to participate in advocacy activities. Supporting this notion, a common parent-reported theme in the literature but not in Project 1 is financial stress (12,16,18) that may indicate the experiences of families that are having difficulties coping with the disease. Further, the families I interviewed often communicated their interest and their belief in the importance of this research in furthering current knowledge of IMDs; and it may be hypothesized that families with such commitment to research also tend to commit to advocating for their child's needs and care.

In addition, I identified a difference in caregivers' satisfaction with IMD- specific and non-specific components of the health care. In the literature, caregivers of children with IMDs have reported both positive and negative experiences interacting with the health care system (18), however, to my knowledge, this study is the first to specifically identify differences in disease-specific and non-disease-specific services. The complexity in care characterized by multiple needs in different areas of functioning for children with IMDs, and their nature as rare

diseases requiring highly specialized services, may be responsible for the central organization of disease-specific care in specialist metabolic clinics. In this study, most parents reported feeling content with the coordination of care within those clinics, a factor that has been documented in the literature to determine satisfaction in care (55). Further research that explores IMD families' experiences, interactions and relationships with metabolic providers may identify factors that lead to satisfaction in care within this system.

In a previous study focused on a single IMD (maple syrup urine disease), a few positive experiences with care were reported by families, such as health care professionals' eagerness to learn about the disease (18). However, in that study, many families reported negative incidents and dissatisfaction with care, with parents describing stressful interactions with health care professionals (18). In particular, parents in that study reported feeling disrespected, some indicated that they felt that health care professionals were incompetent, and caregivers felt frustrated in having more knowledge of the disease (18). Similarly, my study identified some comparable negative interactions, particularly in emergency departments, blood laboratories, and pharmacies. A study that identified predictors of patient dissatisfaction within emergency care reported discontent with health care professional's competence and attitude during an emergency visit as a strong predictor of satisfaction (56) – a finding that is consistent with my study. The findings from my study point to the potential benefit of a coordinated approach to care that includes the non disease-specific elements of care as well as specialist metabolic care, in order to adequately support the needs of children and their caregivers. Social stressors on parents are important for health care providers to consider with respect to the social and emotional responses associated with disease management. The successful use of a

range of proactive coping strategies among study participants suggests the potential value of promoting their use, and this is an important direction for future study.

These findings also connect to a broader literature on childhood chronic illness and disability, i.e., beyond IMDs, much of which relates to neurodevelopmental disorders. The work of Ruth Stein and others support a 'non-categorical' approach to research and care (57). Such an approach recognizes that caregiving for children across diverse chronic conditions presents similar psychosocial and social challenges and supports interventions that target these challenges regardless of the underlying diagnosis (58). In support of this non-categorical approach, there are many similarities between my findings with respect to caregiving for children with IMDs (e.g., challenges associated with daily routines, social challenges and health care experiences) and those identified in this broader literature. In particular, several frameworks such as Wallander and Varni's disability stress coping model (59) and Raina's caregiving process model (60) have been developed to describe the experiences of children and their families in coping with and managing chronic childhood illness. The disability stress coping model identifies risk factors (e.g., poverty, lack of social support, lower socioeconomic status (SES) and poor family functioning) that are related to poor child and parent psychosocial adjustment (61). On the contrary, resistance factors (e.g., higher SES, support from extended family and adaptive coping mechanisms) are correlated with better child and parent psychosocial adjustment (61). Social support, coping strategies and the ability to access resources are additional resistance factors in the model that are postulated to help caregivers to manage and cope with their child's disease – factors that were also identified in my study. Similarly, in my study, many participants acknowledged their proactive coping strategies

including receiving help through informal support systems and their ability to gain access to resources as factors that helped in the management of their child's disease. Further, many conveyed the importance of their education and income in contributing successful coping with their child's illness. Thus, the findings from my study relate to the disability-stress coping model. .

Raina's caregiving process model describes the caregiving process and caregiving burden among those who care for children with chronic illnesses, including the complex stress processes and factors that are related to caregiving (60). This model also focuses on demographic characteristics (SES, income, education) that influence the caregiving situation and on the use of coping/support systems. Caregiver strain is described as an important influence on caregiver health in the caregiving process model (60). In my study, caregiver strain was present in the form of managing the complex day-to-day complex diet and the negative health care experiences with other parts of the hospital. In addition, Raina et al's model postulates that child characteristics and behavioural problems are strongly influential in predicting the health of the caregivers (62) . I did not identify behavioural problems or behavioural issues in my interviews with parents of children with IMDs. This could be due to a difference in the disease manifestations of IMDs versus the neurodevelopmental disorders that are the focus of the caregiving process model and associated literature.

Despite some similarities to the broader literature related to the experiences of children with chronic illness and their families, I did identify aspects of patient and family experiences related to IMDs that appeared to be unique to these diseases. This included the impact of coping with severe dietary restrictions and experiences arising due to the rarity of IMDs,

including uncertainty and lack of familiarity of IMDs to many health care providers. In addition, IMDs in Canada and many other developed countries are uniquely managed within speciality metabolic clinics, where affected children receive care provided mainly by metabolic physicians and metabolic dietitians. Thus, studying the specific health care experiences and needs for this population has the potential to best inform interventions to improve care.

Beyond child health, the chronic care model (CCM)(63,64) is an evidence-based framework developed to improve the quality of chronic illness management, particularly within primary care, with associated literature focusing mainly on adult populations. Interestingly, this model describes some similar issues and experiences to those that I identified among caregivers of children with IMDs. Specifically, a few components of the CCM framework that relate to my findings include the clinical information system, the self-management support and the community support components. Many participants in my study described the lack of care coordination in parts of the health care system outside the metabolic clinic (e.g., the emergency department, blood laboratory, pharmacy etc.). In response to challenges in care coordination that have been observed in the broader chronic illness literature (65), the CCM suggests need for improvements to clinical information systems so that different parts of the health care system can communicate and work together. Another component to the CCM, self-management support, incorporates patient-centred interventions such as self-management skill building and patient activation with supports from health care professionals, community members and extended family in order to better manage chronic illnesses (63). In my study, home management of IMDs was described as complex and intense; dietitians were described as playing a strong role in providing support through phone calls and emails to help families

effectively manage at home. A difference relative to the CMM is that I interviewed parents who were largely responsible for managing the child's disease whereas the CCM focuses on patient self-management. Finally, improvements in community supports is another patient-centred component of the CMM that may be relevant for children with IMDs and their families. Specifically, many participants in my study described the benefits of connecting with other families of affected children to share their experiences, often through social media. Thus, strategies for improving care for children with IMDs may be informed by research focused on other chronic illnesses in children and adults.

Interpretation of findings from Project 2 and connection with patient-reported outcomes initiatives

Although many common themes emerged from the meta-synthesis, each synthesized study provided valuable insights that were not uncovered by the others. The scoping review went beyond IMDs and included reports on other complex, chronic paediatric diseases that are clinically similar to IMDs. Another difference that characterizes this study in comparison to others was its exclusive focus on previous studies that collected data using self-administered questionnaires, which may place a greater emphasis on outcomes that have published validated measures (6). On the contrary, the literature scan of IMDs studies included both qualitative and quantitative studies and was much smaller (n= 14 synthesized studies versus n=304 studies in the scoping review), but included disease-specific experiences in greater detail. The third study, which was qualitative, provided insight into family experiences with an IMD from the perspectives of patient support organizations. The representatives from this

study had a unique view of patient and family experiences as they considered the needs of multiple families and were well-positioned to provide broader insights about the progress of entire rare disease communities (e.g., status of interventions and support for diseases that were the focus of their work). In addition, the patient support groups provided insights on experiences related to the transition of adolescence because they were situated to provide perspectives from older children.

Finally, the fourth study incorporated provided in-depth perspectives of individual families, including those not connected with patient support groups.

There is a growing body of literature highlighting the importance of patient-centred outcomes in health research, including patient-reported outcomes that directly measure the experiences of patients and their families from their own perspectives (66–68). Incorporating patient/family-reported outcomes in studies that evaluate care for rare diseases may be particularly important because for rare diseases it may be especially challenging to optimize outcomes across the "triple aim" (simultaneously improving patient/family experiences and clinical outcomes while managing health system impacts) (5,25). Thus, understanding the impact of interventions on outcomes that are prioritized by patients and families can help to inform decisions about necessary trade-offs among these aims (5,69). However, while measuring patient-reported outcomes in studies involving rare diseases is important, multiple challenges exist (70). Many of these challenges are inherent to the nature of rare diseases rather than being specific to the development of questionnaire-based outcome measures. For example, these challenges include the existence of few previously published disease-specific instruments given a small body of research on any one rare disease, and the small number of

patients available for study, which leads to imprecision in measurement (70). Further, the heterogeneity in clinical presentation that is characteristic of many rare diseases, including IMDs, poses a challenge in identifying specific outcomes that have relevance across patients even within one disease category. The National Institutes of Health (NIH)'s Patient Reported Outcomes Measurement Information System (PROMIS) has suggested developing concept-specific (e.g., anxiety, pain, mobility) questionnaires as opposed to disease-specific tools because of the lack of available disease-specific measures (71). This approach would also address the challenge of heterogeneity within and across diseases.

The Patient Reported Outcomes Measurement Information System (PROMIS) is a system of standard and validated patient-reported tools supported by the NIH and relevant to patients across the health care system (i.e., not disease-specific), designed to evaluate and inform patient-centred health care (63). The PROMIS pediatric self- and proxy- reported health framework identified physical health, mental health and social health outcome domains as most relevant (72). Most of the constructs that emerged from this thesis project, as described in Table 3.2, Chapter 3, align with the PROMIS pediatric framework. Exceptions were our identification of parental coping and experiences with health care as important patient-reported outcomes for children with IMDs and their families. This may highlight important aspects of patient and family experiences that are specific to IMDs, since intense lifelong management and frequent interactions with multiple care providers reflect the complex health needs of families of affected children. Although physical health and functional status were inquired during our interviews with caregivers, this outcome was not frequently mentioned as salient to overall quality of life among the participants in our qualitative study, nor was it a

focus of the findings of the literature review studies synthesized in Chapter 3. This may be due to the nature of our qualitative study, which exclusively included families of children with complex physical health problems, and thus, impaired physical health may have been perceived as a “given” by participants, rather than a feature they needed to share in a study about overall family experiences. With respect to the literature we reviewed, it may be that physical health is often measured by health care professionals rather than self-reported (73), so that it was largely excluded from our scoping review and literature scan, which focused on patient/family-reported experiences.

Implications and directions for future research

The knowledge generated from this study shed light on salient patient- and family-centered outcomes and experiences of caregivers of children with IMDs. This work has provided the foundation for the future development of questionnaires for caregivers of children with IMDs to quantitatively ascertain key aspects of their experiences with the disease and with the health care system. For example, the interview results have prompted the planning of questions that will seek to understand families' satisfaction and experiences with different parts of health care services, including non IMD-specific care. Further research should focus on operationalizing the identified constructs from this thesis either through existing validated scales or through the development of new measures.

The interview study, although focusing on some disease-specific experiences, highlighted persistent themes related to coping, social distress and experiences with care. Additional research that focuses on both disease-specific and generalizable experiences can

further our knowledge and understanding of the impact of these chronic diseases in order to inform patient-centred care. With respect to the meta-synthesis study, it would be interesting to explore whether our adapted meta-synthesis technique may be valuable in other research areas, including other studies that seek to develop a questionnaire.

Conclusion

Before this thesis, there was limited evidence on experiences that are important to patients and families living with an IMD. This study provided a detailed understanding of this phenomenon and additionally, through a primary qualitative study, identified aspects of their experience that parents of children with IMDs prioritize, yet that may not have been emphasized in the existing literature. In addition to contributing to the future development of a questionnaire, the findings of this thesis emphasize that for child patients with IMDs and their families, the use of proactive strategies are important ways to cope with the challenges of the disease and this points to the potential for future interventions focused on such coping strategies. Social stressors are associated with disease management and are important to parents/caregivers, highlighting a need to address this dimension of their experience. Finally, the results of the interview study with respect to experiences with care point to a need to better coordinate care across the entire health care system, including those components that are not specific to the management of IMDs.

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Appendix A: CIMDRN Disease List



Disease List

Emerging Team in Rare Diseases: Long-term follow-up of children with inborn errors of metabolism (IEM) in Canada

AMINO ACID / UREA CYCLE DISORDERS:

- **Phenylalanine hydroxylase (PAH) deficiency: phenylketonuria (PKU) and non-PKU hyperphenylalaninemia (non-PKU HPA)**
- **Arginase (AG) deficiency**
- **Argininosuccinic acidemia (argininosuccinate lyase deficiency, ASA)**
- **Carbamyl phosphate synthetase (CPS1) deficiency**
- **Citrin deficiency**
- **Citrullinemia (argininosuccinic acid synthetase deficiency)**
- Homocystinuria: CBS deficiency
- **Hyperornithinemia-Hyperammonemia-Homocitrullinuria (HHH) syndrome**
- Maple syrup urine disease (MSUD)
- **N-acetylglutamate synthetase (NAGS) deficiency**
- **Ornithine transcarbamylase (OTC) deficiency**
- Tyrosinemia (Type I)

ORGANIC ACID DISORDERS:

- β -Ketothiolase (BKT) deficiency
- Glutaric acidemia type I (GAI)
- HMG-CoA lyase Deficiency
- Isovaleric acidemia (IVA)
- 3-Methylcrotonyl-CoA carboxylase (3MCC) deficiency
- Methylmalonic acidemias (methylmalonyl-CoA mutase deficiency; cobalamin defects)
- Propionic acidemia (PA)

FATTY ACID OXIDATION DISORDERS:

- **Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency**
- **Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency**
- Carnitine uptake defect (CUD)
- Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency
- Trifunctional protein (TFP) deficiency

OTHER

- **Mucopolysaccharidosis type I (MPS 1)**
- Pyridoxine-dependent epilepsy
- Galactosemia (GALT), excluding epimerase and kinase deficiency
- Glycogen storage disease type 1 (GSD1, types A and B)
- Multiple carboxylase deficiency (MCD)/Biotinidase deficiency
- **Guanidinoacetate methyltransferase deficiency (GAMT)**

*Priority diseases (BOLD) for in-depth longitudinal data collection

Appendix B: Interview Guide

Patient and Family Experiences Interview Guide

[Following the initial introduction of CIMDRN, this project's purpose, their consent to be interviewed and arrangement of a suitable time to call – all prior to the interview, either by phone or e-mail].

Preamble Items-

- Hello – this is [name of interviewer] calling from the Canadian Inherited Metabolic Diseases Research Network.
- Thank you very much for agreeing to speak with me today about your child's, and your family's experiences of living with [the disease of interest].
- I have a few questions for you today to gain a better sense of what is important to your child, you and your family to live with and manage [the disease of interest]; but first, do you have any questions about CIMDRN or our interest in consulting with parents of patients?
- Because our larger study is specifically interested in paediatric patients and their families, my questions today are generally interested in your child with [the disease of interest] and your family. That is, the questions will ask both about your child and your family and what experiences or aspects of life are most important to both your child and your family. We are also interested in your experiences with the health care system in supporting care for your child.
- As mentioned previously, the interview is expected to take about an hour and your answers will be confidential.

Patient and family experiences

1) When was your child diagnosed with *[the disease of interest]*? Would you please describe the process of the diagnosis for your child, yourself and your family?

- *[If further prompt is necessary]*: That's really helpful. I'm also wondering how you learned about the diagnosis, who gave you the information; was it by telephone or in person?
- *[If relevant]*: How did you find your interactions with health professionals and the health care system around the time of diagnosis? Was it helpful?

2) Was there a waiting period during the diagnostic process, where you experienced uncertainty about the diagnosis of *[the disease of interest]*?

- *[If yes]*: Can you tell me about that time? How did it impact your family?

- *[If further prompt is necessary]*: This could include impact on daily life, time spent in with health care providers, or impact on feelings and emotions of family members.
- *[If relevant]*: Did you receive any specific support from health care providers in dealing with this waiting? What support did you receive? Was it helpful?

3) What would you characterize as some of the most important impacts on daily life for your child, yourself and your family living with *[the disease of interest]*?

- *[If further prompt is necessary]*: This could include such things as how [disease] affects general health, quality of life, ability to carry out the kinds of activities in which you or your child participate.
- *[If respondent has addressed only the child or only the family]*: That's really helpful. I'm also wondering what sorts of things are considered important to [EITHER] your child [OR] yourself and your family in terms of well-being.

4) What are some of the primary concerns regarding your child with *[the disease of interest]*, and yourself and/or your family around physical health and function in daily activities?

- *[If further prompt is necessary]*: This could include such things as mobility (moving around), pain, cognitive function (thinking abilities for example language, memory, problem solving, and decision making skills), sleeping and/or feeding problems.
- *[If respondent has addressed only the child or only the family]*: That's really helpful. I'm also wondering what sort of things are considered important to [EITHER] your child [OR] yourself and your family in terms of physical health and function in daily activities.

5) How would you characterize the importance of social health (ability to create and maintain healthy relationships) for your child and yourself and/or your family living with *[the disease of interest]*?

- *[If further prompt is necessary]*: This might include such things as social life, unaffected sibling's life, whether loneliness and isolation are concerns for your child and you as a family, how well your child is able to 'fit in' at school or in social groups and how concerns about the future as an adult contribute to these, or whether and/or how your family draws from the support of others.
- *[If respondent has addressed only the child or only the family]*: That's really helpful. I'm also wondering what sorts of things are considered important to [EITHER] your child [OR] yourself and your family as far as relationships and social needs or experiences.

6) Are there support systems that you rely on in coping with *[the disease of interest]* for your child, yourself and your family?

- *[If further prompt is necessary]*: This might include friends, family/relatives, family support group, social workers, psychologist, spiritual/religious groups, internet etc.

7) *[If relevant, depending on age]*: How do you/did you feel about your child transitioning to day care or school with *[the disease of interest]*?

- *[If further prompt is necessary]*: This could include concerns with respect to the caregiver's or teacher's knowledge of the disease, adherence to prescription diet at school or day care, maintaining academic standards of the school, ability to form relationships at school/day care, etc.

8) How would you describe the mental health of your child and yourself and/or your family?

- *[If further prompt is necessary]*: This could include things like anxiety, depression, coping skills, emotional distress, behavior problems and the available support to manage these problems.
- *[If respondent has addressed only the child or only the family]*: That's really helpful. I'm also wondering what sorts of things are considered important to [EITHER] your child[OR]yourself and/or your family in terms of mental health.

9) How do you and your child feel about the treatments for *[the disease of interest]*?

- What do you and/or your family, and child expect from treatment/therapy?
- Are the treatments and/or therapies considered burdensome?
- Does your child and you and/or your family have trouble coping with the administration of and/or consistently taking these treatments*[i.e., adherence]*?
- Do you think adherence to treatment (taking the treatment as planned or as recommended by your child's health care providers) is an issue at all?
- *[If respondent replies yes]*:What factors make adherence to the planned or recommended treatment more challenging?
- How does insurance coverage for the costs of treatments and therapies affect these issues?
- Do you think that healthcare providers can do anything to help improve adherence to treatment or therapy?

10) How would you describe your experiences with the health care system, or what is it about health care that is important to you and your child?

- E.g., does the rarity of *[the disease of interest]* factor into the quality of care, for instance, emergency room clinicians being unfamiliar with *[the disease of interest]*?

- What are your experiences with the coordination of care for your child with the different members of your health care team?

11) Could you please describe your enrolment process into this study and how you felt about the consent process?

- E.g., length of time, clarity of information, amount of information, etc.
- Do you have any suggestions on how the consent process could be improved?
- *[If further prompt is necessary]*: What worked well for you? What did not?
- What are some reasons you decided to participate in research?

12) How did you feel about the experience of participating in this interview?

[If further prompt is necessary]: This could include things like length, detail, or the kinds of questions that I asked.

13) Do you have anything more to add or other areas of experience that you know are particularly important to your child with *[the disease of interest]* and your family?

Concluding items

- We really appreciate the time you've devoted to speaking with us today.
- With your permission, we will be contacting you after we have analyzed all of the interviews to get your feedback on our early findings..
- If you'd like more information about CIMDRN, please visit our website at www.cimdrn.ca.
- And please don't hesitate to contact me at any time in follow up to this discussion.