The role of coping strategies in the association between caregiving complexity and quality of life among caregivers of children with inherited metabolic diseases

BY

Alana Fairfax

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Preface

The two manuscripts presented in this thesis are co-authored by the student (AF); her supervisor, Dr. Beth Potter, her co-supervisor, Dr. Jamie Brehaut, and her thesis advisory committee member, Dr. Ian Colman. Lindsey Sikora is a co-author on the first manuscript and Dr. Stephen Hawken is an additional co-author on the second manuscript. The student is the primary author of both manuscripts and was responsible for conducting a review of the literature, planning the methodology used in the systematic review and the secondary data analysis, the completion of the review and data analysis, and drafting the manuscripts. The thesis supervisor, co-supervisor, thesis advisory committee member, and additional named individuals provided guidance throughout the review, data analysis, and manuscript writing process. Ethical approval from all relevant Research Ethics Boards was obtained for completion of the second manuscript.

Abstract (150 words)

We investigated the association of coping with quality of life (QoL) among parents of children with chronic illnesses, particularly inherited metabolic diseases (IMD); and whether coping may modify the association between caregiving complexity and parental QoL. In project 1, we systematically reviewed studies of parents of children with chronic illness. Among 10 eligible studies, we identified some evidence that adaptive coping strategies were positively associated with parental psychological QoL. In project 2, we analyzed data from a cross-sectional mailed Canadian survey of parents of children <12 years of age with IMD. Among 113 respondents, greater emotion-focused coping was associated with lower mental QoL (all parents) and higher depressive symptoms (parents of children >=5 years). Analysis of significant interactions between coping and caregiving complexity did not reveal clear trends. Understanding the association of parental coping with QoL may help to inform interventions to promote parental health as part of family-centred care.

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TABLE OF CONTENTS

Chapter 1 – Introduction

Inherited Metabolic Diseases (IMD)

Inherited metabolic diseases (IMD) are a group of >500 rare single gene disorders that occur due to a disrupted metabolic pathway (1,2). The onset of clinical manifestations can vary from hours or months after birth to years, depending on each disease and patient characteristics (3). These manifestations vary among and within the specific diseases but can include acute episodes of metabolic crisis or chronic, and often multi-organ sequelae (3). IMD are often severe within pediatric populations diagnosed with these conditions (1) and have important impacts for children and their families (4). Intensive monitoring and management is frequently necessary to avoid cognitive and physical development complications (5). For some IMD, poor outcomes can occur despite early treatment interventions (6,7).

While individually rare, collectively IMD have a birth prevalence of approximately 1 in 2,500-5,000 live births (1,8). This may be an underestimate of the true disease burden as many cases go undiagnosed due to a scarcity of metabolic specialists (especially in rural or remote areas) able to confirm a diagnosis or because death may occur before a diagnosis is made (1). The number of IMD being diagnosed is increasing over time (1,2,9), as a result of population-wide newborn screening and advances in diagnostic capabilities, improved reporting techniques, and increased awareness regarding IMDs (1). Morbidity and mortality rates have decreased and many individuals with IMDs are living longer and more meaningful lives (1,10). This in turn has important implications for health services and for those providing care for individuals diagnosed with IMDs (1).

Impact of pediatric illness on caregivers: disease severity and caregiving complexity

Pediatric chronic illness affects not only the child but the entire family (11,12). Caregivers (which will be used synonymously with "parents" throughout this document, reflecting that children are sometimes cared for by guardians other than a parent) of children with chronic illness report the diagnostic stage (i.e., the time during and immediately after a diagnosis is made) in particular to be a stressful and traumatic experience (13,14). In addition to typical parenting duties, parents of children who are ill often take on the role of medical experts, care coordinators, and medical advocates for their children (15–18). Children with chronic illness often require assistance with everyday activities such as dressing, bathing, and eating, responsibilities that are typically assumed by the parent (19). Thus, parents of children with complex medical needs report significant emotional and social impacts (20–22). Several parent, child, and family characteristics can impact parenting behaviours (23) and parenting a child with a chronic health complication likely influences these behaviours (24). Research suggests that caregivers of chronically ill children experience more challenges compared to caregivers of children without chronic illness. Some of these challenges include financial constraints, lack of social support, increased levels of depressive symptoms, and physical and mental health decline (25–32).

It may be hypothesized that parents of children who are more severely ill would experience greater caregiving burden and stress relative to parents of children with milder chronic illness. Indeed, Barakat et al (13) found that among caregivers of children with sickle cell disease, disease-related parenting stress was directly associated with disease severity and healthcare utilization. However, across a range of pediatric chronic illnesses, findings regarding the predictive value of disease severity for caregivers' well-being are inconsistent (12,33,34).

Child behavioural problems have been frequently reported as an important predictor of parental well-being (22,26,35), yet while it is likely that behaviour problems may contribute to increased parent distress, it is also likely that increased parent distress may affect child behaviour or be associated with parent-reported perceptions of child behaviour (26). Furthermore, while some caregivers may not adapt well to caring for their child with relatively mild disease severity, others who care for more severely ill children may not be distressed. For these reasons, there is support for the hypothesis that caregiving burden or complexity, which is related to the volume and intricacy of caregiving tasks associated with caring for a child rather than a simple conception of disease severity, may be a better indicator of the impact of care provision on a parent's quality of life (36). Specifically, caregiving complexity or burden is defined by the stress or demand experienced by a caregiver and the time spent caring for the child (37,38).

The role of support from health care providers and other sources

Over the past few decades there has been a societal shift that places greater importance on community-based rehabilitation programs and family-centred care, which has been described as a "partnership approach to health care decision-making between the family and health care provider" (Kuo et al., p. 297) (39) and is considered the standard of pediatric care (39). Family-centred care permits parents to have a greater role in decision making in many aspects of their child's health, often facilitated by a partner relationship between health care provider and family that ensures that parents are respected, supported and provided with needed information (26,39). Strategies to facilitate family-centred care for children with chronic illnesses or disabilities include co-developed care plans, a 'Medical Home', a designated key provider, emphasis on effective coordination of care, and a strong focus on the needs of the entire family (18,40–42). Family-centred caregiving has many benefits, such as significant reductions in non-urgent

emergency department visits in children (43), increased parent confidence and competence in infant caregiving and greater willingness to ask for help from health care providers (44–47), and significant improvements in growth parameters and earlier discharge of very low birth weight infants (48).

Systemic challenges occur within the current health care system that can decrease the effectiveness of family-centred care. One such challenge is a lack of care coordination (49), particularly for children who need to see multiple sub-specialists. In a US study, effective care coordination was positively associated with family-reported receipt of family-centred care that led to several positive outcomes such as satisfaction with care, decreased family financial burden and impact on parental employment, and fewer emergency department visits and absences from school (50). Health care providers themselves may face barriers in providing adequate support to families as part of family-centred care. Fostering good partnerships with families takes time and providers may not be compensated nor have the time needed to develop these relationships (51–55). This may make it difficult for health care providers to offer families adequate support and information to enable them to provide the best possible care to their child.

Despite these challenges, support from health professionals has been found to have an important positive influence on parental coping strategies once caregivers learn to navigate their child's illness and corresponding needs (14,56). Support from other family members and individuals has also been found to be significantly related to positive coping methods (56). Thus, to help decrease distress linked to the complexity of caregiving by facilitating positive coping and family adaptation strategies, parents of children with chronic illness require support both from health care providers and from support groups, programs, and/or informal networks of family and friends.

Coping and how it relates to quality of life

Coping strategies are a potentially important influence on caregiver health and well-being, with evidence suggesting that positive coping strategies may have protective value for parents (57,58). According to Lazarus and Folkman's Transactional Model of Stress and Coping (59), coping can be defined as cognitive and behavioural management techniques that are constantly changing and used to decrease or tolerate an external or internal stressor that is appraised as exceeding one's resources or abilities (59). The categorization of coping strategies differs within the literature (60) and often depends on the author and measurement tool used. One way coping strategies can be categorized is into emotion-focused coping, which includes "cognitive and behavioural efforts directed at reducing or managing emotional distress" (Folkman and Lazarus, p. 225) (61), and problem-focused coping which includes "cognitive problem-solving efforts and behavioral strategies for altering or managing the source of the problem" (Folkman and Lazarus, p. 224) (61). The coping process is thought to be situation dependent, indicating that both the stressor itself and the interaction between the stressor and the environment contribute to the coping strategy used (62). Thus, the way individuals deal with stress will differ as people develop their own habitual ways to deal with adversity.

Coping and quality of life in caregivers of children with chronic illness

Some evidence suggests that maladaptive coping strategies (e.g., these may include emotion-focused or escape-avoidance strategies) are associated with a greater level of stress and decreased mental health (62–66), while adaptive coping strategies (e.g., these may include problem-focused or planful problem-solving strategies) are associated with lower stress levels and increased well-being of parents of chronically ill children (65–70). One study found that the type of coping strategy used by parents of children with disabilities had a greater influence on

perceived stress than the actual stressor itself (71). Therefore, if caregivers can adopt adaptive coping strategies, rather than maladaptive ones, this may improve their quality of life and, in turn, their ability to care for their child (66,67,72,73).

Coping and quality of life for caregivers of children with IMD

With regards to IMD specifically, little is known regarding the well-being of parents of children with IMD and the factors that contribute to parental well-being. The World Health Organization (WHO) defines quality of life (QoL) as "the individual's perception of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns" (WHOQOL Group, p. 551) (74). Fabre et al (75) examined the QoL of parents of children affected by IMD who experience diet restrictions (including children with organic acidurias, urea cycle defects or maple syrup urine disease). They found this population of parents to have lower QoL than parents of children with certain other chronic illnesses (such as Down syndrome and sickle cell disease) or children without chronic illness (75). This finding is consistent with other studies that have examined the well-being of parents of children with IMD (76–78). Hatzmann et al (77) examined predictors of health-related QoL of parents of children with IMD and found psychosocial determinants (emotional support and loss of friendship) to be more important in predicting health-related QoL of parents than socio-demographic and medical-related variables. Increased levels of emotional support were associated with increased QoL while loss of friendship was negatively associated with QoL (77).

ten Hoedt et al (78) examined the health-related QoL of parents of children with two specific IMD, phenylketonuria (PKU) and galactosemia, and found the health-related QoL of this parent population comparable to that of children without illness and significantly better than that

of parents of children with other metabolic disorders. In parents of children with galactosemia, emotional support was a significant positive predictor of mental health-related QoL (78). Among children with PKU, child's age and emotional support were positively associated with parent mental health while loss of friendship displayed a negative association with parent mental health (78). This is supported by a more recent examination of parental QoL of children with PKU, where parents were found to be coping well and perceived their QoL as being quite positive (79). In that study, family stress and perceived social support were the greatest predictors of parent QoL, being negatively and positively associated with QoL, respectively. These findings suggest that the impact of caregiving for pediatric IMD may depend on the specific caregiving needs of the child, which supports our previous discussion about the potential importance of caregiving complexity. While nearly all children with IMD have special dietary needs, there are differences in the need for health care services and home management across and within groups of IMD (e.g., fatty acid oxidation disorders, amino acid disorders, urea cycle defects), and these needs may influence caregiver well-being.

Some evidence suggests that when parents of children with chronic illness have trouble coping with their caregiving demands, this may be associated with greater anxiety and worry in their children (80). A recent study by Brown et al (10) examined the relationship between parental functioning and child's cognitive, social, and behavioural functioning in a sample of parents of children with IMD specifically. They found that poor parental coping was associated with increased emotional symptoms in children and that poor family management was associated with increased externalising behaviours in children, such as hyperactivity and conduct disorder (10). This supports a previous study from outside the IMD literature, whereby Barakat et al (13) found that increased disease-related parenting stress of caregivers of children with sickle cell

disease at baseline was associated with increased disease severity and greater health care utilization after one year follow-up. These studies support the notion that the functional well-being of parents can influence the health and development of a child with a chronic illness. Thus, the well-being of the parent is not only important for the parent's own health but also to support the well-being of the child (77,79).

The Canadian Inherited Metabolic Diseases Research Network (CIMDRN)

The Canadian Inherited Metabolic Diseases Research Network (CIMDRN) is a multidisciplinary, pan-Canadian network that aims to develop evidence-based approaches to improve patient and family experiences, improve clinical health outcomes and manage health system impacts on families whose children have IMD (81). To date, over 650 children with IMD and their parents are enrolled in CIMDRN's consent-based research program from 14 clinical centres across Canada. Participating children are born between 2006 and 2015 and have been diagnosed with one of 31 IMDs that are part of the research network's program. CIMDRN's work includes clinical data collection and administrative data analysis as well as qualitative research and surveys with participating families.

A recent qualitative study conducted by CIMDRN found that parents of children with IMD used a range of pro-active coping strategies and viewed these strategies as critical to their adjustment to the complex management of their child's illness (82). From these findings, the investigators developed a self-administered questionnaire that was pilot tested via cognitive interviews in a small sample of parents of children enrolled in CIMDRN and formed the basis for part of this thesis.

Rationale for the Thesis Project

There is limited evidence surrounding the impact of IMD on the well-being of the parents of children diagnosed with these conditions, and the factors that may influence parental well-being. There is growing evidence of the need to consider the well-being of caregivers of children with chronic illness (83). A greater understanding of the factors that are associated with QoL, including the potential role of coping strategies, is needed to better support this parent population. The causal mechanisms involved in studying the well-being of caregivers of children with chronic illness is complex. We recognize that a number of causal pathways could be hypothesized and evaluated. For example, it is possible that greater mental and physical health could improve one's ability to cope with a stressful situation. However, we chose to focus on one small piece of this system to better understand whether coping, as a potentially modifiable factor, is associated with quality of life in this population, and whether coping may also act as a modifier of the association between caregiving complexity and quality of life.

A noticeable limitation to current literature surrounding the well-being of caregivers of children with IMD is the common presentation of bivariate associations. For example, the above overview of the literature highlights the potential for adaptive or problem-focused coping strategies to mitigate the negative influence of caregiving stress on parental quality of life. However, to our knowledge, coping has rarely been investigated as an effect modifier (84) of the association between caregiving complexity and parental well-being in the literature on pediatric chronic illness (Figure 1).

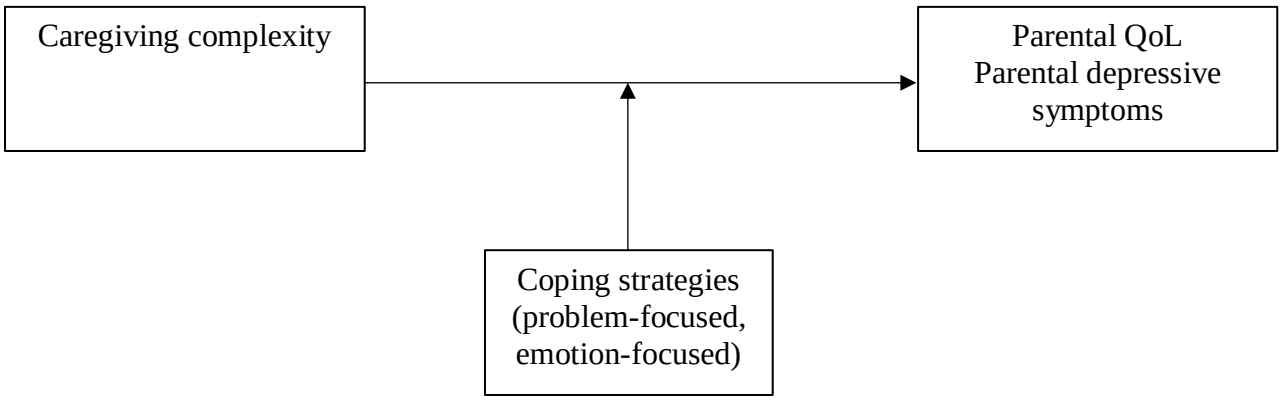

Figure 1. Coping strategies as potential effect modifiers in the association between caregiving complexity and parental QoL.

Purpose and objectives

The objectives of my thesis project were to:

1) Synthesize existing research about the association between coping strategies and QoL among parents and caregivers of children with chronic illnesses or disabilities; and the role of coping strategies as a potential effect modifier of the association between caregiving complexity and QoL in this population of parents (Figure 1).

Hypothesis: We hypothesized that adaptive and/or problem-focused coping styles would be associated with greater caregiver QoL. We also hypothesized that coping would be an effect modifier of the association between caregiving complexity and QoL.

2) Among parents and caregivers of children with IMD, empirically investigate the association between coping strategies and QoL and between coping strategies and depressive symptoms; and, the role of coping strategies as a potential effect modifier of

the association between caregiving complexity and both QoL and depressive symptoms (Figure 1).

Structure of the Thesis

This thesis has four chapters. Chapter 1 has provided an introduction to the topic, the rationale for the thesis, and the specific objectives and hypothesis. Chapter 2 presents a manuscript describing a systematic review with a narrative synthesis regarding the association between coping strategies and quality of life in parents of children with chronic illness or disability. Chapter 3 presents a manuscript describing a secondary data analysis of results from a survey of Canadian parents/caregivers of children with IMD. It examines the role of coping strategies in the association between caregiving complexity and both QoL and depressive symptoms. Lastly, Chapter 4 presents an integrative discussion that interprets the results of the two manuscripts together, discusses the strengths and limitations of the thesis, and provides direction for future study.

INTERFACE

This article synthesizes existing literature regarding the association between coping strategies and QoL in parents of children with chronic illness, and the potential role that coping strategies may play in the association between caregiving complexity and QoL. The student (AF) was responsible for conducting the systematic review searches, screening of citations and articles for eligibility, extraction of relevant data from included studies, and evaluating the content of included studies. AK contributed to the screening of retrieved citations and articles for eligibility and extraction of information from included studies. LS contributed to the search strategies and methodology used to complete this review. JB, IC, PC, and BKP contributed to the design and supervision of the study, the analysis of included information, and the interpretation of findings and major revisions to the manuscript. This manuscript has been submitted to *BMC Pediatrics*; it has been formatted accordingly.

Chapter 2 - A systematic review of the association between coping strategies and quality of life among caregivers of children with chronic illness and/or disability: Manuscript #1

Alana Fairfax[1], Jamie Brehaut[1,2], Ian Colman[1], Lindsey Sikora[3], Alessia Kazakova[1], Pranesh Chakraborty[4], Beth K Potter[1], in collaboration with the Canadian Inherited Metabolic Diseases Research Network.

Affiliations:
1 School of Epidemiology and Public Health, University of Ottawa, Ottawa ON, Canada
2 Ottawa Hospital Research Institute, Ottawa ON, Canada
3 Health Sciences Library, University of Ottawa, Ottawa ON, Canada
4 Children's Hospital of Eastern Ontario, Ottawa ON, Canada

ABSTRACT

Background: Parents of children with chronic illness have reported decreased psychological and physical quality of life (QoL) relative to parents of children without such illness, which may be associated with the extent of complexity involved in the caregiving role. Given that coping strategies have been reported to influence QoL, our goal was to synthesize existing research about the association between coping strategies and QoL in caregivers of children with chronic illness. We were particularly interested in whether coping strategies may modify or mediate the association between caregiving complexity and QoL.

Methods: We developed an electronic search strategy to identify relevant citations in Medline, EMBASE, PsycINFO and CINAHL. Two reviewers independently assessed retrieved citations against pre-specified inclusion criteria in two stages of screening. One reviewer abstracted data on study characteristics, methods to address confounding, measurement tools, risk of bias, and results with respect to associations of interest. A second reviewer validated extracted data. We summarized results narratively.

Results: 2,245 citations were screened and 163 full-text articles were reviewed. The 10 articles that met inclusion criteria addressed 5 diseases or disease groups and included a total of 1,988 caregivers. Nine of the 10 included studies were cross-sectional. We identified some evidence that coping was associated with QoL: in several studies, coping strategies considered to be adaptive were positively associated with psychological QoL while maladaptive strategies were negatively associated with psychological QoL. Only two studies considered coping as a third variable in the association between parental QoL and caregiving complexity, with inconsistent findings and challenges in interpreting cross-sectional associations. The variability among instruments used to measure key constructs, particularly coping strategies, made it difficult to synthesize results across studies.

Conclusions: This review highlights that positive coping strategies may be associated with better psychological QoL among parents of children with chronic illness but highlights important research gaps related to the consistent and clear measurement of coping strategies and their prospective association with measures of QoL. Further understanding how coping strategies are associated with QoL may inform the development of interventions to support families of children with chronic illness.

KEYWORDS: caregiver health, caregiving complexity, quality of life, coping, systematic review

Manuscript status: Submitted to *BMC Pediatrics.*

BACKGROUND

Pediatric chronic illness affects not only the child but the entire family [1,2]. In Canada, the setting for this study, 3.7% of children 15 years or younger were reported to have a disability [3] and 500,000 children were estimated to have a long-term chronic illness or mental illness [4]. Among children with chronic illness, nearly half experience severe disease and 8% experience ongoing activity limitations [4–6]. The number of children with diagnosed disability is likely to increase over time as children with chronic illness are living longer and healthier lives [4–6]. For example, many children diagnosed with illnesses that were once considered severely life-limiting, such as cystic fibrosis or muscular dystrophies, are now living into adulthood [7,8]. Care pathways for children with severe illness have gradually shifted away from hospital-based care and toward home-based care, often coordinated by parents and families [8]. Parents of children with chronic illness are thus not only primary nurturers in their children's lives but also key members of their children's health care teams [8].

Parents of children with chronic illness can experience increased caregiver challenges relative to parents of children without such needs, including increased medical related costs, challenges with child care and constrained employment opportunities [5,9–14]. These challenges, combined with direct parental responsibilities in health care, may increase caregiver burden for parents of children with chronic illnesses [15]. Evidence suggests that the challenges experienced by caregivers of children with chronic illness have an impact on overall caregiver health [12,16–20]. For example, a Canadian study found that caregivers of children with chronic health problems had more than twice the odds of having symptoms of depression, physical limitations, and chronic health problems of their own compared to caregivers of healthy children [21]. When caregiver health of children with chronic health problems was examined over 10

years, poorer self-reported caregiver health was associated with child health needs for the entirety of the 10 years [15]. Additionally, caregivers of children with severe health problems reported worse general health than caregivers of children with less severe health problems, who, in turn, reported worse health compared with caregivers of healthy children [15]. Findings from these studies support the idea that caregiver health is associated with caregiving complexity [15].

Factors that affect the well-being of parents or caregivers of children with chronic illness are not well documented [22]. One area of study has been the potential association of coping strategies with caregiver well-being [23]. A challenge to understanding how coping may relate to the well-being of caregivers of children with chronic illnesses is that there is not a consensus in the literature regarding how coping is conceptualized and measured [24–26]. Coping strategies are thought to be context dependent, indicating that both the stressor and the environment in which the stressor is presented contribute to the coping strategy used [27]. However, habitual coping strategies are also believed to develop and these differ among families [27]. Most instruments designed to measure coping responses classify these into specific strategies, approaches, or styles of coping using subscales [28–32]. However, their classification systems differ. For example, some authors distinguish between adaptive or positive coping strategies (e.g., maintaining social connections) and maladaptive or negative strategies (e.g., substance use) [33,34]; some distinguish between problem-focused coping (e.g., planning or problem-solving) and emotion-focused coping (e.g., escape-avoidance) [35]; and some describe different approaches to coping that would nevertheless all be considered adaptive, in that higher scores on any subscale within a measurement instrument would be interpreted as positive in terms of managing stress [36]. These classification systems imply different overall conceptions of how people cope with stressful situations and, in some cases, different assertions about which

approaches may be assumed to be "better" with respect to successful stress management and well-being. These differences in measurement also render it challenging to make comparisons across studies.

Our goal was to synthesize existing research about the association between coping strategies and quality of life (QoL) in caregivers of children with chronic illness or disability. Based on Carona et al [23], Dardas and Ahmad [22], and Lyons et al [37] we were particularly interested in whether coping strategies may modify the association between caregiving complexity and QoL and/or whether coping strategies would play another role as a third variable in that relationship (for example, mediating or acting as an intermediate variable in the association between caregiving complexity and QoL). It has been argued that because different diseases may have similar social and psychological impacts on caregivers and families, a 'non-categorical' approach (i.e., one that does not focus on a specific diagnosis but rather on a set of common challenges) is best when studying such impacts [38–40]. To align with this recommendation, we chose to focus on chronic pediatric illnesses that would be likely to be diagnosed early in childhood, have important impacts on caregivers with respect to the need for chronic or long-lasting home management, and require ongoing pediatric specialist care (i.e., medical, surgical, or nutritional intervention). To the best of our knowledge this is the first systematic review to consider the association between coping strategies and caregiver QoL in this population.

METHODS

Protocol and registration

The protocol for this review was written following the PRISMA-P (Preferred Reporting Items for Systematic Reviews and Meta-Analyses- Protocol) checklist [41]. The protocol is registered with PROSPERO under the following registration number: CRD42017069316.

Search strategies and screening against eligibility criteria

With a health sciences librarian (LS), we developed a search strategy to identify eligible studies from the following electronic databases: Medline (via Ovid), EMBASE (via Ovid), PsycINFO (via Ovid), and CINAHL (via EBSCOHost) (search strategy, supplementary appendix). A combination of Medical Subject Headings (MeSH) and text words focused on the following concepts: coping strategies, QoL, and childhood diseases that were of interest to our study aims. We searched diseases of relevance to the review using MeSH only (details below), while the remaining concepts were searched using both MeSH and text words. The search was limited to children under the age of 18 and only English-language articles were considered. Complete search strategies used in Medline and EMBASE can be found in Appendix A, presented at the end of Chapter 2.

Because of the non-specific nature of the search terms in this field, for feasibility, it became necessary to narrow the search strategy. Because we were interested in diseases that would present similar challenges with respect to caregiving, we chose to focus on chronic pediatric illnesses with the following characteristics: (1) the disease would likely be diagnosed early in childhood and would have long-term intense home management requirements with an important impact on caregivers (to operationalize this, we focused on diseases with long-lasting manifestations and with genetic, metabolic, and/or neurologic etiology) and (2) the disease would require care from pediatric specialists involving nutritional, surgical or medical intervention. We built the etiology component of this disease concept into our search strategy

using MeSH headings whereas the requirements for care and notion of a long-lasting condition were adjudicated at the screening stage.

The citation list and bibliographies of relevant articles were also searched for applicable studies. We completed a grey literature search in clinicaltrials.gov, the Global Rare Diseases (Patient) Registry and Data Repository, Health Canada's Trial Registries, World Health Organization (WHO) registry, and Google scholar. A combination of key text words that formed the databases search strategies were used to complete the search of grey literature.

In the first phase of screening, two reviewers (AF and AK) independently screened returned titles and abstracts using pre-specified eligibility criteria (Table 1). Any discrepancies between reviewers were discussed; if there was remaining uncertainty of a citation's relevance, it was retained and further considered in the second phase of screening. In the second phase, full-text manuscripts of citations deemed relevant during the first screening phase were independently screened by the same two reviewers. All discrepancies were resolved through discussion, with third party consultation when needed. The number of articles excluded during each screening phase as well as reasons for study exclusion during the second phase were described using a flow diagram following the PRISMA statement [42]. Cohen's kappa was used to measure inter-rater reliability during the second screening phase, with the following formula:

$$k = \frac{\Pr(a) - \Pr(e)}{1 - \Pr(e)}$$

where Pr(a) is the actual observed agreement between the reviewers and Pr(e) represents the chance agreement between the reviewers [43].

When screening against eligibility criteria (Table 1), to distinguish QoL from other related aspects of caregiver health, QoL was considered to have been measured if studies: 1) examined both physical and psychological caregiver health; and 2) used a QoL measurement

instrument. If only psychological well-being or physical well-being was assessed then the study was considered ineligible. Coping was considered to have been measured if the author/s 1) used a coping instrument that measured coping strategies used by the parent caregiver or 2) considered coping strategies to be measured in the parent. Caregiving complexity did not have to be measured for a study to be considered relevant for the review but was examined in association with QoL if measured.

Table 1. Eligibility criteria for systematic review of the association between coping strategies and quality of life among caregivers of children with chronic illness and/or disability

Population	Parents/guardians of children (≤18 years of age) with a chronic illness or disability for which the etiology/manifestations are genetic, metabolic or neurologic and specialist pediatric care is required, involving surgical, medical or nutritional intervention
Intervention	Not applicable
Comparator	Study quantitatively analyzes the relationship of coping with parents'/guardians' QoL, with or without examination of the association with caregiving complexity
Outcome	QoL
Study characteristics	Peer reviewed, English-language, full text article describing primary studies that include ≥ 5 participants

Data extraction and analysis

Two reviewers (AF and BP) piloted the data extraction form and then one reviewer (AF) extracted the data from relevant articles and another reviewer (AK) verified the extracted data. We abstracted information on study characteristics, measures used to assess coping strategies, QoL, and caregiving complexity, as well as relevant analyses used to assess the relationship among these variables. Due to clinical heterogeneity among diseases that were the focus of relevant studies and anticipated methodologic heterogeneity in concepts, measures, and analyses,

it was decided, a priori, to complete a narrative synthesis of relevant studies, rather than to quantitatively synthesize the findings.

Study quality assessment

The methodological quality of included studies was examined using the Quality Assessment Tool for Observational Cohort and Cross-sectional Studies, which was constructed by the National Heart, Lung and Blood Institute [44]. It consists of a 14-item checklist and a final quality rating of good, fair, or poor is given for each included study. Only one study in the final sample was a randomized controlled trial (RCT) and since the analyses of interest were not separated based on intervention group, we treated that study as observational for the purposes of quality appraisal in order to use the same appraisal tool across all studies. The quality of the RCT was also secondarily assessed using the Cochrane risk of bias tool for RCTs [45]. One reviewer critically appraised study quality (AF) and a second reviewer (AK) verified the assessments.

RESULTS

Search and screening

The Medline (1,367), Embase (1,185), PsycINFO (166), and CINAHL (354) searches yielded a total of 3,072 articles. Citations were imported into the review manager program, Covidence, where 817 duplicates were removed. An additional 10 duplicates were manually identified during the first phase of screening, yielding 2,245 unique citations from the initial search (Figure 1). Following the first screening phase, 167 citations were identified for full-text review, of which four were identified as duplicates. During the second screening phase 156 articles were excluded. Cohen's kappa during the second screening phase was calculated to be 0.8, which indicates a strong level of agreement between the reviewers [43]. The majority of excluded studies satisfied more than one reason for exclusion (Figure 1): 9 studies described

pediatric illnesses that were deemed ineligible for this review; 32 articles included populations that exceeded 18 years of age and did not report results separately for children aged 18 years and younger; one study was non-English; and 19 were abstracts only. A large number of excluded studies (89 studies) did not measure overall QoL in caregivers but most often measured only psychological well-being. Another large quantity (80 studies) did not satisfy the coping eligibility criteria and 12 articles had ineligible study designs (e.g., commentary, descriptive analysis only without examining the association between coping and QoL). The grey literature search yielded one relevant article. Two additional articles were manually identified through reference list searches of relevant studies. A total of 10 articles were included in the review for further analysis.

[Figure 1 approximately here]

Characteristics of the included studies

Of the 10 studies included, 5 disease groups were identified (Table 2, one study included both cerebral palsy and epilepsy): autism (3 studies), cerebral palsy (3 studies), diabetes (2 studies), epilepsy (2 studies), and hemophilia (1 study). Nine of the 10 included articles were cross-sectional studies, with one study being an RCT. Four studies were conducted in the USA while the remaining 6 studies varied geographically, representing Canada, Portugal, Spain, Jordan, Israel, and Iran. A total of 1,988 caregivers were included in the review. In nearly all of the included studies, the vast majority of study respondents were mothers (Table 2).

[Table 2 approximately here]

Instruments used to measure quality of life

A variety of instruments were used to measure QoL within the included studies (Table 3). The World Health Organization Quality of Life Assessment Questionnaire (WHOQOL-BREF)

[54] was used in three studies [22,23,47] (Table 3). The WHOQOL-BREF is comprised of 26 items and measures the following domains: physical health, psychological health, social relationships, and environment. Higher scores indicating better QoL. Of the studies using this QoL measurement instrument, one did not include the environment sub scale but provided all of the other sub scale scores [23], while one study used the overall QoL summary score and did not provide sub scale scores [22]. A third study reported all sub scale scores for the WHOQOL-BREF [47], supplementing the psychological health subscales from the WHOQOL-BREF with measures of depression (the Beck depression inventory, BDI [55]) and anxiety (the State Trait Anxiety Inventory, STAI [56]).

Three studies [49,51,52] used a version of the Medical Outcomes Study Short-Form Health Survey, one using the Short Form 36 (SF-36) [57] and two using the Short Form 12 (SF-12) [58]. The SF-36 and SF-12 are generic health related QoL measurement instruments. Both versions provide scores for eight health concepts (physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health) as well as summary scores for physical and mental health. Higher scores indicate better health.

Streisand et al [53] used a single psychological well-being item and one physical well-being item to measure the QoL of parents of children with diabetes. Each item asked respondents to rate their mental or physical health on a scale from 1 to 5. Higher scores indicated decreased parent psychological or physical well-being.

One study used the EuroQoL five-dimensional questionnaire (EQ-5D) [59] to measure parental QoL [50]. The EQ-5D is a generic health related quality of life questionnaire consisting of five health profile domains: mobility, self-care, usual activities, pain/discomfort, and

anxiety/depression. Each domain is assessed using a single item with a higher score indicating better health.

Hamama-Raz and Hamama [48] used the Quality of Life in Pediatric Epilepsy Scale – Parent Form [60] to assess parental QoL. The instrument is comprised of 16 items and four subscales: physiological, functional, psychological, and social QoL. An overall QoL score is also computed with higher scores indicating lower QoL.

The parents Diabetes Quality of Life Questionnaire [61] was used to assess parents' QoL in the study by Grey et al [46]. The instrument consists of 47 items and three subscales: diabetes life satisfaction, disease impact, and disease-related worries. Due to the high correlation between the disease-related worries and diabetes life satisfaction subscales, only the disease impact subscale was reported. Higher scores indicate increased negative impact.

Instruments used to measure coping strategies

Many self-reported instruments were used to measure caregiver coping strategies. Two studies [47,52] used the Coping Health Inventory for Parents (CHIP) [36]. The CHIP consists of 45 items and three subscales: 1) maintaining family integration, cooperation and optimistic definition of the situation, 2) maintaining social support, self-esteem, and 3) psychological stability, and understanding the healthcare situation through communication with other parents and consultation with the healthcare team. It is used to assess caregivers' appraisal of their coping responses to management of family life when they have a child with a serious/chronic illness. A higher score indicates better management.

Three studies [23,49,50] used the Brief Coping Orientation to Problem Experiences (brief-COPE) [32] to measure coping mechanisms used by caregivers. The tool contains 28 items organized into 14 subscales: active coping, planning, positive reframing, acceptance, humor,

religion, use of emotional support, use of instrumental support, self-distraction, denial, venting, substance use, behavioural disengagement, and self-blame. The 14 subscales can further be classified into two categories, adaptive and maladaptive coping [62]. Higher scores indicate more frequent use of the coping strategy. Two studies [49,50] reported adaptive and maladaptive coping category scores while Carona et al [23] used only the behavioural disengagement subscale of the brief COPE to measure caregiver coping mechanisms.

Dardas and Ahmad [22] used the revised ways of coping checklist [30] which contains 66 items and eight cognitive and behavioural subscale strategies: confrontive coping, distancing, self-controlling, seeking social support, accepting responsibility, escape avoidance, planful problem solving, and positive reappraisal. The questionnaire asks respondents to think of a specific stressful situation and then answer each statement accordingly. Individual subscale scores are reported with higher scores indicating more frequent use of the coping mechanism.

Streisand et al [53] used a single coping item from the National Survey of Children's Health (NSCH) to assess parental coping strategies. The NSCH surveyed mothers regarding the health and well-being of their children. The parent coping item asked respondents to rate how well they felt they were coping with the day-to-day demands of parenthood and raising children. Questions were measured on a four-point Likert scale with higher ratings indicating *decreased* coping.

The Coping Inventory for Stressful Situations-21 (CISS-21) [63] was used to measure parental coping strategies in one included study [51]. The CISS-21 contains 21 items and is made up of three subscales: task/problem-oriented, emotion-oriented, and avoidance-oriented coping. Higher scores indicate more frequent use of the coping strategy.

Hamama-Raz and Hamama [48] used the 20 item Perceived Ability to Cope with Trauma Scale (PACT) [64] to measure coping strategies in their caregiver sample. The PACT consists of two subscales, emotional processing and a forward focus, and creates a single flexibility score which represents a balance between the two subscales. Higher scores indicate greater use of the strategy or increased flexibility.

In one study, the Issues in Coping with IDDM-Parent Scale [65] was used to measure coping strategies of parents of children with type 1 diabetes [46]. The measurement instrument assesses how difficult and upsetting parents find coping with issues related to management of their child's type 1 diabetes. The measurement instrument contains two subscales, how difficult, and how upsetting. In the included study [46], the mean of the two scales was used as an overall coping score. Higher scores indicated that parents find it more difficult and more upsetting to cope with diabetes.

[Table 3 approximately here]

Quality assessment

The quality of included studies was generally fair or good. Table 4 displays the critical appraisal of study quality of all included studies using the NIH quality assessment tool for observational cohort and cross-sectional studies. All studies clearly defined the research question or objective and the study population of interest. Fifty percent participation rate was achieved in 4 studies, was not achieved in 3 studies and was not reported in 3 studies. All but one study [23] recruited participants from the same or similar populations; this study included children diagnosed with cerebral palsy and epilepsy and recruited participants using different methods. A majority (8/10) of studies did not report sample size justification, power description, or variance and effect estimates. All cross-sectional studies (9/10) did not assess the exposure of interest

prior to outcome measurement as assessments occurred at the same time; therefore these studies also received a "no" for sufficient timeframe to see an association between exposure and outcome and multiple exposure measurements. All studies clearly defined and consistently implemented exposure and outcome measures however one study [53] used single item questions, rather than validated instruments, to measure coping and QoL. Blinding of outcome assessors did not pertain to the cross-sectional studies and was not reported in the RCT. Similarly, loss to follow-up was not applicable to the cross-sectional studies and was less than 20% in the RCT. Seven studies considered potential confounding variables in the relationship between coping strategies and QoL.

The Cochrane risk of bias tool was also used to assess the quality of the one included RCT. A high or unclear risk of bias was determined for several reasons. The authors did not mention how randomization of study participants occurred. There was no mention of how blinding (if any) of participants to intervention group was done. In addition, whether or not outcome assessors were blinded was not reported.

[Table 4 approximately here]

Findings regarding the association between caregiving complexity/burden or disease severity and quality of life

Five studies analyzed the relationship of child disease severity and/or some form of caregiving complexity to QoL in caregivers of children with chronic illness [23,47,49,50,52] (Table 5). The following aspects of disease severity or caregiving complexity were addressed: overall disease severity [49,50]; caregiving burden or 'objective strain' [23,49,50]; caregiving demands [52]; and caregiving self-efficacy [47].

Results with respect to associations of these dimensions of caregiving with caregiver QoL were mixed but generally suggestive that greater caregiving complexity or burden may be

associated with poorer caregiver well-being. Specifically, with respect to *child disease severity*, one study found no significant association between disease severity and caregiver QoL [50], while a second found that disease severity was significantly and negatively associated with caregiver psychological QoL [49]. With respect to *objective strain (a subscale of the caregiver strain questionnaire) and/or caregiving burden*, two studies found these variables to be significantly and negatively associated with overall caregiver well-being [23,50] while another study found that caregiving burden was significantly and negatively associated with psychological QoL specifically [49]. With respect to *caregiving demands*, one study found that having fewer demands was significantly, directly, and positively associated with both psychological and physical QoL [52]. Finally, Guillamon et al [47] reported on *caregiving self-efficacy*, which was significantly and positively associated with environmental and psychological health sub scales of QoL and was also a significant negative predictor of caregiver anxiety.

Findings regarding the association between coping strategies and quality of life

Across the 10 studies included in the review, 7 found at least some evidence that there were significant associations between coping strategies used by caregivers and caregiver QoL, but this differed according to types of coping and components of QoL.

1. *Coping and global QoL*

Six studies reported overall QoL in association with coping strategies [22,23,46,48,50,51]. Two studies found no significant association between the two variables [46,50], while the remaining four found coping strategies to be a significant predictor of caregiver QoL [22,23,48,51]. While poor coping strategies (e.g., behavioural disengagement, escape avoidance, emotion-oriented) were negatively associated with QoL [22,23,51], strategies considered to be adaptive (e.g., problem-oriented, accepting responsibility) were also negatively

associated with QoL [22,51]. Greater use of flexibility as a coping strategy was found in one study to be significantly associated with better QoL [48].

2. *Coping and subscales of QoL*

Five of the included studies reported associations between coping and subscales scores for QoL [47–49,52,53]. Specifically, three studies separately reported on associations between coping and psychological and physical QoL [49,52,53]. Guillamon et al [47] used the WHOQOL-BREF mental health sub scale and the BDI-II [55] and STAI-Trait [56] to measure caregivers' psychological health and the remaining physical, environment, and social relationships sub scales of WHOQOL-BREF to measure what they considered to be overall QoL. Hamama-Raz and Hamama [48] reported psychological, physical, social, and functional sub scales scores, as well as total QoL.

Coping and physical aspects of QoL

Among studies that examined QoL sub scale scores separately in relation to coping, coping strategies were not significantly associated with physical health in 4 studies [47–49,52]. However, Streisand et al [53] found that a single coping item was significantly and positively associated with both psychological and physical well-being (both of which were also measured using a single item).

Coping and psychological and/or social aspects QoL

Three studies found that coping strategies were significantly associated with caregiver psychological QoL [48,49,52] while one study found no significant association [47]. Specifically, Raina et al [52] identified that greater use of stress management was positively and directly associated with psychological health; Khanna et al [49] found that greater use of

maladaptive coping strategies was directly and negatively associated with caregiver psychological health; and Hamama-Raz and Hamama [48] found that caregivers who used flexibility as a coping strategy had better psychological, functional, and overall QoL. In that study, flexibility was not associated with the social sub scale of QoL [48].

Findings regarding the role of coping strategies as a mediator or moderator of the association between caregiving complexity/burden or disease severity and quality of life

Two studies also examined coping strategies as a third variable in the association between disease severity or caregiving complexity and QoL [23,49]. Carona et al [23] found that behavioural disengagement coping among caregivers, which is characterized by "reducing one's effort to deal with the stressor or even quitting the attempts to achieve goals with which the stressor is interfering" (p. 321) mediated the association between caregiving complexity and QoL. Specifically, their findings suggested that among parents of children with cerebral palsy or epilepsy who experienced increased caregiving burden/complexity, this additional complexity may have impaired their ability to cope and, specifically, elicited greater use of behavioural disengagement coping strategies. These coping strategies were in turn associated with poorer QoL [23].

Khanna et al [49] found that maladaptive coping strategies, defined as "emotion-focused strategies that aim to regulate the distress associated with the problem" [35], did not mediate the association between disease severity and caregiver psychological QoL in their multivariable model, nor was this a reported pathway in their final structural equation model. In addition, in their study, both maladaptive and adaptive coping strategies, the latter defined as "problem-focused coping strategies used to directly address the problem causing distress" [35] had a direct positive effect on caregiving burden which, in turn, had a direct negative effect on psychological

QoL in the structural equation model (maladaptive coping also had a significant direct negative effect on psychological QoL in the final model) [49].

[Table 5 approximately here]

DISCUSSION

This review sought to better understand the role of coping strategies in the association between caregiving complexity and quality of life among caregivers of children with chronic pediatric illnesses. To our knowledge, this is the first review to consider these associations in this population.

Our findings generally support an association between coping strategies and psychological aspects of QoL. Adaptive coping strategies were positively associated with psychological aspects of QoL in several of the reviewed studies. Conversely, maladaptive coping strategies were negatively associated with psychological aspects of QoL. This finding is supported by a number of studies of families of children with intellectual disability (ineligible for our review as they frequently did not meet our inclusion criteria with respect to diseases requiring pediatric specialist interventions), which have reported improved caregiver well-being associated with problem-focused coping strategies [66,67], while emotion-focused strategies may be associated with poorer caregiver well-being [68].

In terms of overall QoL, both adaptive and maladaptive strategies were associated with decreased QoL in four studies. This may indicate that caregivers who use more coping strategies (both adaptive and maladaptive) may have a greater need to cope (more to cope with). This is consistent with findings from a review by Cousino and Hazen [69] that analyzed parenting stress among caregivers of children with chronic illness. In that prior review, only two studies

considered an association between coping and parenting stress [69]. One study found that greater use of emotion-focused strategies was associated with greater parental stress [70]. The other study found that parenting stress activated the use of both emotion- and problem-focused coping [71].

We identified only two studies that examined the role of coping strategies as a mediator or moderator of the association between caregiving complexity and QoL. One of these studies found behavioural disengagement coping to mediate the association between caregiving burden and QoL [23]. The second study did not find coping (adaptive or maladaptive strategies) to be a potential mediator in the association between disease severity and QoL using hierarchical regression [49]. In a further analysis, a structural equation model in the study by Khanna et al showed maladaptive and adaptive coping strategies to both have a direct effect on caregiving burden, indicating that the more use of either coping strategy was associated with increased caregiver burden [49]. Caregiver burden had a direct negative effect on psychological QoL. Maladaptive coping strategies also had a direct negative effect on caregiver psychological QoL. These findings suggest that coping strategies play an important role in the association between caregiving burden and psychological aspects of QoL but that the nature of this role may be complex and is currently not supported by extensive evidence.

While our focus was specifically on the potential role of coping as a moderator or mediator of the relationship between caregiving complexity or burden and caregiver QoL, one of the studies we reviewed [22] examined coping's role in the association between *stress* and parental QoL. They found that accepting responsibility (an example of problem-focused coping) mediated the association between stress and QoL. Furthermore, seeking social support (categorized as having properties of both problem- and emotion-focused coping) was a

moderator in the association between stress and QoL. Escape-avoidance (an example of emotion-focused coping) was also found to moderate the association. More specifically, seeking social support and escape-avoidance coping strategies were associated with improved QoL when used to manage parental stress [22].

Another study [37] assessed the impact of symptom severity and parental coping strategies on stress among parents of children with Autism Spectrum Disorders (ASD). That study also examined whether coping style had a moderating role in the association between symptom severity and parental stress. The authors found that emotion-oriented coping and a form of avoidance-oriented coping (distraction) both moderated this relationship. Parents who rated their child's symptoms as severe and used distraction style coping reported lower levels of parent and family stress. They suggested that distraction serves as a protective factor for parents as parents' demand can be greater when their child's symptoms are more severe. Parents who used more emotion-oriented coping reported more pessimism (a subscale of stress) as autism symptom severity increased. The findings suggested that parents who focus on the high severity of their child's symptoms may exhibit more pessimistic views and negative outcomes, which can further exacerbate the negative affective conditions [37].

This review identified just 10 studies that met our eligibility criteria, only two of which specifically examined the potential role of coping in the association between caregiving complexity or burden and caregiver QoL. In addition, although we identified some consistency in positive associations between use of positive or adaptive coping strategies and psychological QoL among parents of children with chronic illness, the findings of the studies we reviewed were challenging to synthesize due to great diversity in how disease severity, caregiving complexity, and coping strategies were measured. In particular, our findings corroborated that there is a lack

of conceptual clarity about parental coping: the 6 different instruments used to measure coping across the 10 studies did not consistently define coping or categorize it in terms of its dimensions. Future studies that focus on coping and QoL in this population should seek to better understand the conceptual underpinnings of this construct.

In addition to this challenge related to conceptual and measurement clarity/consistency, a second important issue across the studies we reviewed was the lack of prospective research: all but one of the studies we reviewed used cross-sectional study designs, making it difficult to determine if caregivers who use adaptive coping mechanisms are healthier as a result of their improved coping ability or if caregivers with greater QoL are able better able to respond to their environment due to their improved health. Similarly, the study by Khanna et al [49] positioned coping as having an influence on caregiving burden (rather than the reverse), which in turn influenced QoL, further demonstrating the need for prospective studies to clarify the inter-relationships between the complexity of caregiving needs, strategies for coping with such needs, and caregiver well-being.

Resolving these remaining research gaps is important because if coping does mediate or moderate the relationship between caregiving complexity and caregiver QoL for parents of children with chronic illness, this has implications for potential interventions. A Cochrane review of psychological interventions for parents of children and adolescents with chronic illness found little evidence regarding the efficacy of psychological therapies for parents on several outcome domains of functioning, such as parental mental health [1]. However, that review highlighted that parent mental health and adaptive behavior can improve when parents participate in problem solving therapy. Similarly, in studies of children with diabetes, promising results have been found regarding caregivers' response to interventions aimed at providing skills to manage

uncertainty [72], coping skills training, and education sessions [46]. These studies show the potential benefits that interventions such as group-based education or coping training sessions may have on caregivers of chronically ill children and highlight the importance of continuing to study how coping affects well-being.

Our review has important strengths, including its synthesis, for the first time, of studies reporting quantitative associations between caregiving complexity, coping, and QoL in parents of children with chronic illness; and our focus on assessing study quality and identifying important research gaps. However, findings from this review must be interpreted in light of its limitations. First, while attempts were made to include all relevant research, our search strategies were limited to English language articles only. Secondly, the inclusion criteria used in this review needed to be strict in order to develop a search strategy that was feasible given the non-specific language used to describe coping and well-being and the large literature on chronic pediatric illness in general. This narrowed the scope of the included articles, for example, in terms of the illnesses studied. We focused on illnesses that would be very likely to have an early, long-lasting, and important impact on caregivers in order to have the best chance of uncovering associations between caregiving complexity, coping, and QoL. The review was also restricted to studies that included quantitative measures of caregiver coping and quality of life. Findings from qualitative studies, particularly regarding caregivers of children with rare diseases, are essential to understanding factors that contribute to the well-being of caregivers who are often under studied in the literature but whose experiences are unique and important to consider. However, for our purposes, we were specifically interested in quantitative estimates of association and, particularly, studies that had examined coping as a potential mediating or moderating variable. Lastly, our conclusions are limited by the inherent limitations of the included articles, which, as

described, include a lack of consistency in defining and measuring key constructs, and the lack of prospective studies to clarify the temporal order of the associations identified.

CONCLUSIONS

Findings from our review support the hypothesis that positive or adaptive coping strategies may be positively associated with psychological QoL among caregivers of children with chronic illness. However, given the various instruments used to measure coping and differing ways to classify strategies, it is difficult to synthesize the role of coping strategies as they relate to caregiver burden and well-being. What remains unanswered is the role of coping strategies as a third variable in the association between caregiving complexity and QoL. A greater understanding of this relationship could help guide the development of intervention programs that improve caregiver well-being. Specifically, if future studies using prospective designs provide further evidence supporting a causal relationship, our findings highlight the potential value of interventions targeted at caregiver coping processes to help facilitate the use of adaptive strategies to improve caregivers' QoL.

LIST OF ABBREVIATIONS

ASD: Autism Spectrum Disorders

BKI: the Beck depression inventory

Brief Coping Orientation to Problem Experiences (brief-COPE)

CHIP: Coping Health Inventory for Parents

CISS-21: Coping Inventory for Stressful Situations-21

STAI: State Trait Anxiety Inventory

EQ-5D: EuroQoL five-dimensional questionnaire

MeSH: Medical Subject Headings

NSCH: National Survey of Children's Health

QoL: Quality of life

PACT: Perceived Ability to Cope with Trauma Scale

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PRISMA-P: Preferred Reporting Items for Systematic Reviews and Meta-Analyses- Protocol

RCT: randomized controlled trial

SF-36: Short Form 36 health survey

SF-12: Short Form 12 health survey

WHO: World Health Organization

WHOQOL-BREF: World Health Organization Quality of Life Assessment Questionnaire

DECLARATIONS

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and material

All data generated or analysed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

AF contributed to the conception and design of the study, the analysis and interpretation of the results, and drafting the manuscript. JB and IC contributed to the conception, design, and supervision of the study, the interpretation of the results, and revisions to the manuscript for important intellectual content. LS and PC contributed to the conception and design of the study, the interpretation of the results, and revisions to the manuscript for important intellectual content. AK contributed to the analysis and interpretation of the results and revisions to the manuscript for important intellectual content. BKP contributed to the conception, design and supervision of the study, the interpretation of the results, and drafting the manuscript. All authors approved the final submitted version of the manuscript.

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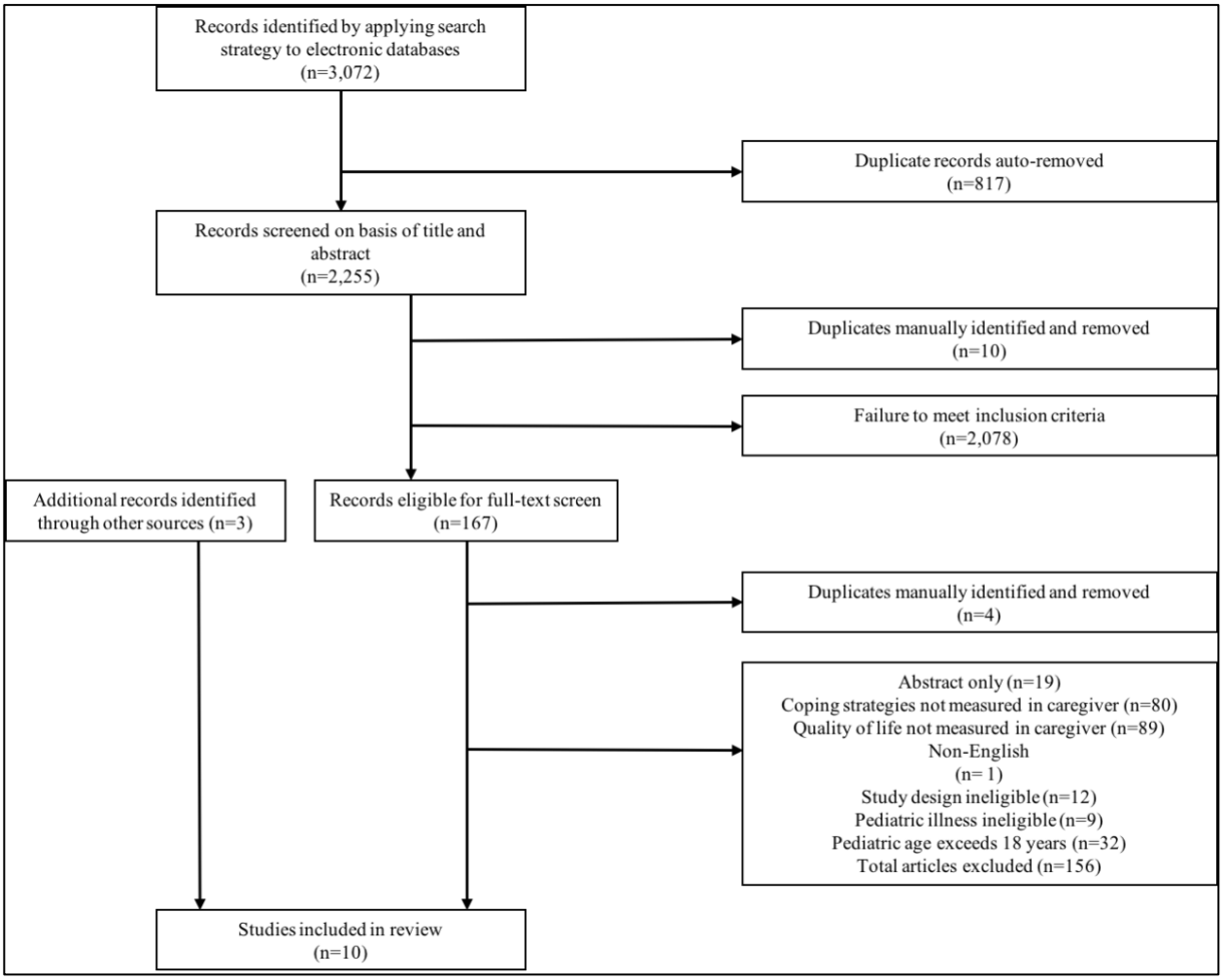

Figure 1. PRISMA flow diagram for the systematic review of the association between coping strategies and quality of life among caregivers of children with chronic illness and/or disability.

Table 2. Study characteristics of included studies.

Author, year (country)	Study design	Sample size	Illness	Inclusion criteria	Caregiver relation to child	Mean age of caregivers (SD or range)	Age of children
Carona et al., 2014 [23] (Portugal)	Cross-sectional	156 (epilepsy, n=65; cerebral palsy, n=91)	Epilepsy and cerebral palsy	Parent of a child aged 8-18 years who had been diagnosed with epilepsy or cerebral palsy by a physician, and assumed the primary caregiving role at the time of assessment.	Mother (87.7% epilepsy; 90.1% cerebral palsy)	42.42 years (7.20) epilepsy; 41.47 years (6.26) cerebral palsy	12.52 years (2.88) epilepsy; 12.07 years (2.82) cerebral palsy
Dardas & Ahmad, 2015 [22] (Jordan)	Cross-sectional	184	Autistic disorder	Parents of children under the age of 12 years with a clinical diagnosis of autistic disorder and could read and write in Arabic.	Mother, 62%	37 years (SD=7.6, range from 21-69)	6.3 years (SD=3, range= 2-12)
Grey et al., 2011 [46] (USA)	Randomized controlled trial	123 (coping skills training, n=75; group education, n=48)	Type 1 diabetes	Parent of a child who had been diagnosed with Type 1 diabetes for at least 6 months and between the ages of 1-12 years.	95% mothers, 3% fathers; 2% guardians (female)	37.3 years (SD=5.6, range=26-51)	8.1 (2.9) coping skills training; 7.9 (2.8) group education
Guillamon et al., 2013 [47] (Spain)	Cross-sectional	62	Cerebral palsy	Father or mother of a child with cerebral palsy (aged less than 18 years) and was the main caregiver.	Mother, 88.7%	40.95 years (SD=0.79, range=29.53)	7.69 years (SD=0.19, range=1-17)
Hamama-Raz & Hamama, 2015 [48] (Israel)	Cross-sectional	48	Epilepsy	Parents of children between 6-19 years of age, with Hebrew speaking ability, with only minor learning difficulties, with 1-4 seizures a year, and with the absence of other chronic illnesses.	Mother, 85.42%	42.90 years (SD=6.20)	13.71 years (SD=3.02, range=8-18)

Khanna et al., 2011 [49] (USA)	Cross-sectional	304	Autism	Primary caregivers of children with autism aged less than or equal to 18 years of age and had no more than one child diagnosed with autism.	Female, 93.1%; relationship not stated	38.9 years (SD=8.0)	7% <5 years of age; 44.1% 5-less than 10 years; 41.4% 10-less than 15 years; 6.6% 15-18 years of age
Khanna et al., 2013 [50] (USA)	Cross-sectional	316	Autism	Primary caregivers of children with autism who are aged 18 years or younger and have only one child with autism.	Mother, 91.5%	18-44 years, 69%; 45-64 years, 30.1%	<5 years, 16.8%; 5-10 years, 46.5%; 11-18 years, 36.1%
Motaharian et al., 2015 [51] (Iran)	Cross-sectional	49	Hemophilia	Primary caregiver (primary responsibility of providing care to child) of a child (less than 18 years of age) with hemophilia.	Male, 71.4% (relation not stated)	40 years or younger (44.9%); Older than 40 years (55.1%)	Twelve years or younger (46.9%); Older than 12 years (53.1%)
Raina et al., 2005 [52] (Canada)	Cross-sectional	468	Cerebral palsy	Primary caregiver who had a child who participated in the Ontario Motor Growth (OMG) study (explored patterns of gross motor development in children with cerebral palsy), lived with the child, and resided in Ontario.	Mother, 89.7%	40.3 years (SD=6.72)	10.6 years (SD=2.69)
Streisand et al., 2010 [53] (USA)	Cross-sectional	278	Diabetes (type 1 or type 2)	Parent or guardian who was the most informed about the child's health, child who was less than 18 years of age and was diagnosed with diabetes by a physician.	Mother (biological, step, foster, or adoptive), 100%	Not reported	12.1 years (SD=4.3, range=<1-17)

Table 3. Self-administered measurement tools used to examine coping strategies, quality of life, and caregiving complexity.

Measurement tool	Description of the tool	Reviewed studies using this tool
Quality of life instruments		
World Health Organization Quality of Life Assessment Questionnaire (WHOQOL-BREF) [54]	Latent variable composed of four subscales (physical, environmental, psychological, and social relationships) for a total of 26 items; higher score indicates better quality of life. Sub scale scores or a total overall scale can be computed.	[22,23,47]
Medical Outcomes Study Short Form 36 Health Survey (SF-36) [57]	Generic measure of health concepts related to functional status and well-being; comprised of 8 domains and provides summary score for physical and psychological well-being.	[52]
Medical Outcomes Study Short-Form Health Survey version 2 (SF-12v2) [58]	Comprised of 12 items and 8 health concept subscales, also gives a summary score for physical and mental health status. Physical component sumamry (PCS) is made up of the physical functioning, role physical, bodily pain and general health subscales whereas the mental component (MCS) is comprised of the vitality, social functioning, role emotional, and mental health subscales.	[49,51]
EuroQoL five-dimensional (EQ-5D) questionnaire [59]	Consists of five health profile domains: mobility, self-care, usual activities, pain/discomfort and anxiety/depression, each domain is assessed using a single item. A visual analogue scale is also used and ask caregivers to rate their current health status (range from 0-100).	[50]
Quality of Life in Pediatric Epilepsy Scale – Parent Form [60]	Comprised of four sub scales: psychological, physiological, functional, and social, with higher score indicating lower QoL.	[48]
Parents Diabetes Quality of Life Questionnaire [61]	Assesses parents' perceptions of the impact of diabetes treatment on their general satisfaction with life; comprised of three subscales: diabetes life satisfaction, disease impact, and disease-related worries.	[46]
Coping instruments		
Coping Health Inventory for Parents (CHIP) [36]	Comprised of 3 subscales: 1) maintaining family integration, cooperation and optimistic definition of the situation; 2) maintaining social support, self-esteem and psychological stability; 3) understanding the healthcare situation through communication with other parents and consultation with the healthcare team.	[47,52]

Brief COPE Inventory [32]	Comprised of 14 sub scales with two items each; broadly captures coping methods. Sub scales can be summarized into adaptive or maladaptive coping strategies.	[23,49,50]
Revised Ways of Coping Checklist [30]	Consists of 66 items separated into eight different cognitive and behavioural strategies (sub scales) used to cope with stressful encounters: confrontive coping, distancing, self-controlling, seeking social support, accepting responsibility, escape avoidance, planful problem solving, and positive reappraisal.	[22]
Calsbeek Coping Inventory for Stressful Situations (CISS) [63]	Comprised of 21 items in three domains: problem-oriented, emotion-oriented, and avoidance-oriented coping strategies.	[51]
Perceived Ability to Cope with Trauma Scale (PACT) [64]	Comprised of two sub scales: emotional processing and forward focus, single score used.	[48]
Issues in Coping with IDDM-Parent Scale [65]	Measures parents' issues in coping with their child's diabetes; Consists of two sub scales: how difficult and how upsetting parents find it to cope with issues related to management of child's Type 1 Diabetes.	[46]
Caregiving complexity/burden instruments		
Revised Burden Measure [73]	Latent variable composed of three subscales: Relationship Burden, Objective Burden, Subjective Burden.	[23]
Revised Scale for Caregiving Self-Efficacy [74]	Consists of three domains: obtaining respite, responding to disruptive patient behaviours, and controlling upsetting thoughts. Sub scale and overall scores.	[47]
Caregiver Strain Questionnaire [75]	Consists of three domains: objective strain, subjective internalized strain, and subjective externalized strain, an overall burden score is used.	[49,50]
Pediatric Evaluation of Disability Inventory (PEDI) [76]	Measures amount of caregiver assistance provided to a child during basic functional activities of daily living.	[52]

Table 4. Quality assessment for included studies: NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.

Quality Assessment Criteria	**Study**									
	Carona et al. (2014) [23]	Dardas &Ahmad (2015) [22]	Grey et al. (2011) [46]	Guillamon et al. (2013) [47]	Hamama-Raz & Hamama (2015) [48]	Khanna et al. (2011) [49]	Khanna et al. (2013) [50]	Motaharian et al. (2015) [51]	Raina et al. (2005) [52]	Streisand et al. (2010) [53]
Was the research question or objective in this paper clearly stated?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Was the study population clearly specified and defined?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Was the participation rate of eligible persons at least 50%?	✗	NR	✓	NR	✗	✗	NR	✓	✓	✓
Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	✗	✓	✓	✓	✓	✓	✓	✓	✓	✓
Was a sample size justification, power description, or variance and effect estimates provided?	✗	✓	✗	✗	✓	✗	✗	✗	✗	✗
For the analyses in this paper, were the exposure(s) of interest	✗	✗	✓	✗	✗	✗	✗	✗	✗	✗

measured prior to the outcome(s) being measured?										
Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	✘	✘	✓	✘	✘	✘	✘	✘	✘	✘
For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✘
Was the exposure(s) assessed more than once over time?	N/A	N/A	✓	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✘
Were the outcome assessors blinded to the exposure status of participants?	N/A	N/A	NR	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Was loss to follow-up after baseline 20% or less?	N/A	N/A	✓	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	✖	✖	✓	✓	✓	✓	✓	✖	✓	✓
Overall Quality	Good	Fair	Good	Good	Good	Good	Good	Poor	Good	Poor

NR: Not reported; N/A: Not applicable

Table 5. Variables of interest, approach to analysis, and main findings of included studies.

Author, year	Variables of interest	General approach to analysis	Main findings
Carona et al., 2014 [23]	Coping: behavourial disengagement (avoidant, emotion-focused strategy) QoL: overall QoL Caregiving complexity: caregiving burden measured	Structural equation modelling	(1) Caregiving burden directly and negatively predicted parents' QoL (2) Behavioural disengagement directly and negatively predicted parents' QoL (3) Caregiving burden had a significant indirect effect on parent's QoL via behavioural disengagement coping. (4) Coping had a mediating role in the association between caregiving burden and quality of life.
Dardas & Ahmad, 2015 [22]	Coping: eight sub scale measurements QoL: overall QoL	Bivariate and multivariable regression	(1) Escape avoidance and accepting responsibility coping strategies were significantly and inversely associated with QoL. (2) Accepting responsibility was found to mediate the association between stress and QoL. (3) Escape avoidance and seeking social support were found to moderate the relationship between stress and QoL.
Grey et al., 2011 [46]	Coping: issues in coping measurement (higher score=coping is more upsetting and difficult) QoL: Disease impact on general life satisfaction (higher score=greater negative impact)	Correlation	(1) While controlling for baseline coping, change in coping at 3 months was not significantly correlated with change in quality of life at 3, 6, or 12 months.
Guillamon et al., 2013 [47]	Coping: sub scale measurements of integration, social support, and understanding QoL: sub scale measurements of physical, social relationships, environment (considered QoL), and mental health, BDI, and STAI-Trait (considered to be mental health). Caregiving complexity: self-efficacy measured	Multivariable regression	(1) Coping strategies did not significantly predict any quality of life or mental health indicators. (2) Caregiving self-efficacy was a significant, positive predictor of the quality of life environment and mental health sub scales, and significantly predicted caregiver anxiety.
Hamama-Raz & Hamama, 2015 [48]	Coping: flexibility measurement QoL: sub scale measurements (physical, psychological, social, and functional) as well as overall QoL (higher score=lower QoL)	Correlation and multivariable regression	(1) Flexibility coping was significantly and inversely correlated with each QoL sub scale as well as overall QoL. (2) Flexibility coping was significantly and negatively associated with psychological, functional, and overall QoL

			(i.e., greater use of flexibility coping was associated with a decreased negative effect of QoL).
Khanna et al., 2011 [49]	Coping: adaptive and maladaptive sub scale measurements QoL: physical and psychological sub scale measurements Caregiving complexity: caregiving burden measured Disease severity: care recipient functional status	Multivariable regression and structural equation modelling	(1) Care recipient functional status, maladaptive coping, and caregiver burden were significantly and negatively associated with psychological QoL. (2) Maladaptive coping had a direct negative effect on psychological QoL. (3) Adaptive and maladaptive coping had a direct positive effect on caregiver burden which in turn had a direct negative effect on psychological QoL.
Khanna et al., 2013 [50]	Coping: adaptive and maladaptive sub scale measurements QoL: overall health-related QoL Caregiving complexity: three sub scale measurements- objective strain, subjective internalized strain, and subjective externalized strain Disease severity: parent-reported measurement of social interaction, communication, and restricted and repetitive behavior (overall score given)	Correlation and multivariable regression	(1) Objective and subjective internalized strain were significantly and inversely correlated with QoL. (2) Maladaptive coping was significantly and inversely correlated with QoL. (3) Objective strain was a significantly and negatively associated with QoL.
Motaharian et al., 2015 [51]	Coping: three sub scale measurements given (problem-, emotion-, and avoidance-oriented) QoL: overall QoL	Correlation and multivariable regression	(1) Emotion- and avoidance-oriented coping was significantly and inversely correlated with QoL. (2) Emotion- and avoidance-oriented coping were significantly and negatively associated with QoL in the regression model.
Raina et al., 2005 [52]	Coping: stress management QoL: sub scale measurements of physical and psychological QoL Caregiving complexity: caregiving demand	Structural equation modelling	(1) Stress management (coping) had a direct positive effect on caregiver psychological health. (2) Caregiving demand was directly and positively associated with physical and psychological health QoL of caregivers (greater score = less demand).
Streisand et al., 2010 [53]	Coping: single item, respondents asked how well they felt they were coping with the day-to-day demands of parenthood and raising children.	Bivariate associations and multivariable regression	(1) Coping was significantly associated with psychological and physical QoL in bivariate and multivariate models.

	QoL: Parent physical and psychological well-being measured using single item.		

Appendix A

Supplement 1: Medline and Embase Search Strategies

Medline Database Search Strategy

1. Adaptation, Psychological/
2. (psycholog* adj2 adapt*).tw.
3. Stress, Psychological/
4. Social Adjustment/
5. Social Support/
6. social support.tw.
7. social adjustment.tw.
8. coping behav*.tw.
9. coping strateg*.tw.
10. Resilience, Psychological/
11. resilience.tw.
12. or/1-11

13. Parents/
14. exp Parent-Child Relations/
15. parent*.tw.
16. Caregivers/
17. Spouses/
18. carer*.tw.
19. mother*.tw.
20. (mom or mum).tw.
21. father*.tw.
22. dad*.tw.
23. caregiver*.tw.
24. Legal Guardians/
25. guardian*.tw.
26. 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25

27. exp Metabolic Diseases/
28. exp Genetic Diseases, Inborn/
29. exp Nervous System Diseases/
30. 27 or 28 or 29

31. limit 30 to "all child (0 to 18 years)"

32. "Quality of Life"/
33. "Activities of Daily Living"/
34. exp Health Status/
35. exp Self Concept/
36. quality of life.tw.

37. QOL.tw.
38. well being.tw.
39. wellness.tw.
40. HRQOL.tw.
41. (activit* adj3 living).tw.
42. hope.tw.
43. life qualit*.tw.
44. (health adj2 level*).tw.
45. healthiness.tw.
46. good health.tw.
47. functional abilit*.tw.
48. health status.tw.
49. 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48

50. 12 and 26 and 31 and 49

51. limit 50 to english language

Embase Database Search Strategy

1. adaptive behavior/
2. (psycholog* adj2 adapt*).tw.
3. mental stress/
4. social adaptation/
5. social support/
6. social adjustment.tw.
7. social adaptation.tw.
8. social support.tw.
9. coping behavior/
10. coping behav*.tw.
11. coping strateg*.tw.
12. or/1-11

13. parent/
14. exp child parent relation/
15. parent*.tw.
16. caregiver/
17. caregiver*.tw.
18. spouse/
19. carer*.tw.
20. mother*.tw.
21. (mom or mum).tw.
22. father*.tw.
23. dad*.tw.
24. legal guardian/

25. guardian*.tw.
26. 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25

27. exp metabolic disorder/
28. exp genetic disorder/
29. exp neurologic disease/
30. 27 or 28 or 29

31. limit 30 to (infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)

32. "quality of life"/
33. daily life activity/
34. exp health status/
35. exp self concept/
36. quality of life.tw.
37. QOL.tw.
38. well being.tw.
39. HRQOL.tw.
40. (activit* adj3 living).tw.
41. hope.tw.
42. life qualit*.tw.
43. (health adj2 level*).tw.
44. healthiness.tw.
45. good health.tw.
46. functional abilit*.tw.
47. health status.tw.
48. 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47

49. 12 and 26 and 31 and 48

50. limit 49 to English language

Supplement 2: Email confirmation of article submission to BMC Pediatrics

Notification to co-authors of submission to BMC Pediatrics BPED-D-18-00675

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Fri, Aug 24, 7:42 AM

BPED-D-18-00675
A systematic review of the association between coping strategies and quality of life among caregivers of children with chronic illness and/or disability
Alana Fairfax; Jamie Brehaut; Ian Colman; Lindsey Sikora; Alessia Kazakova; Pranesh Chakraborty; Beth K. Potter

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INTERFACE

This article presents results from a secondary data analysis of a mailed survey sent to participating parents of children enrolled in a Canadian cohort study. The focus of our analysis was to examine the association between coping, caregiving complexity, and parent QoL and depressive symptoms. We also investigated our hypothesis that coping strategies were an effect modifier in the association between caregiving complexity and QoL in this parent population. Ethics approval was obtained from the Children's Hospital of Eastern Ontario Research Ethics Board, the Ottawa Health Science Network Research Ethics Board, and affiliated research ethics boards of participating centres.

The student (AF) was responsible for conducting the survey analysis, interpreting the findings, and writing the manuscript. SH contributed to the methodology of the analysis. JB, IC, and BKP contributed to the design and supervision of the survey analysis, the interpretation of the findings, and major revisions of the manuscript. We plan to submit this manuscript to *Health and Quality of Life Outcomes*; it has been formatted accordingly.

Chapter 3 – Coping, caregiving complexity, and quality of life among parents of children with inherited metabolic diseases in Canada: a cross-sectional survey – Manuscript #2

Alana Fairfax[1], Jamie Brehaut[1,2], Ian Colman[1], Stephen Hawken[1,2], Beth K Potter[1], in

collaboration with the Canadian Inherited Metabolic Diseases Research Network

Affiliation:

1 School of Epidemiology, Public Health and Preventive Medicine, University of Ottawa, Ottawa, Ontario, Canada
2 Ottawa Hospital Research Institute, University of Ottawa, Ottawa, Ontario, Canada

Abstract

Background: Positive approaches to coping may be associated with better quality of life (QoL) among parents of children with chronic illness. We aimed to investigate the association between coping and QoL among parents of children with inherited metabolic diseases (IMD) in Canada. We also investigated whether coping strategies would be an effect modifier in the association between caregiving complexity and QoL in this population.

Methods: Parents of children under 12 years of age with an IMD who were enrolled in a cohort study at one of 13 participating centres were eligible to participate in this cross-sectional survey. We invited parents to complete a mailed questionnaire that included validated measures of parent QoL (SF-12), parental coping strategies (WAYS of coping scale), caregiving complexity (from the Child Health Questionnaire) and socio-demographic characteristics. We used multiple linear regression to investigate associations among these measures and to determine whether coping was an effect modifier of the association between caregiving complexity and QoL.

Results: 113 parents completed and returned questionnaires between January and July 2017 (response rate 37%). A majority of respondents were the female (88%) biological parent (98%) of a child with an IMD. Greater use of emotion-focused coping was significantly associated with lower mental QoL scores among parents of both younger (<5 years) and older (>=5 years) children and with higher depressive symptoms in parents of older children. We identified some statistically significant interactions between the use of problem-focused coping and caregiving complexity but stratified analyses did not reveal clear patterns.

Conclusions: Our findings align with studies in other areas of pediatric chronic illness in suggesting that greater use of emotion-focused coping strategies among parents of children with IMD may be associated with poorer mental QoL. The direction of this association requires further evaluation in longitudinal samples. Further research is also needed to better understand the role of coping, particularly problem-focused coping, as a possible effect modifier of the relationship between caregiving complexity and parental QoL. Understanding how coping

affects parental well-being can help to inform the development of interventions to promote the health of parent caregivers as part of family-centred care.

Keywords: Quality of life, coping, parents, inherited metabolic diseases

Background

Inherited metabolic diseases (IMD) are a group of >500 single gene diseases that result from a defect in metabolic pathways and are often diagnosed early in a child's life (1,2). Individually rare, IMDs collectively occur with a birth prevalence of about 1 in 2,500-5,000 live births (2). While clinical manifestations vary depending on the specific IMD and on patient and environmental factors (3,4), they often include episodes of acute and potentially life-threatening metabolic crises that require urgent medical care and/or chronic complications marked by multi-system sequelae (2). Treatment typically involves specialized and highly restrictive diets that require intense family management and can include expensive drugs and medical foods (4). In some cases, a large team of healthcare specialists is regularly involved in managing the care of children with IMD, with frequent visits to pediatric centres (5).

While caregiving is part of the normal role of a parent, this role increases in intensity when a child is diagnosed with an IMD or other chronic disease. In addition to learning how to care for a child with an IMD, parents may also experience guilt, anger, and worry about the future (6,7). Parents often take on the role of care coordinator for their child. Constant home management is also required for most children with IMD as poor treatment adherence can affect physical health and cognitive development (8). The long-term impact for parents and other family members is substantial and includes lifestyle changes due to dietary restrictions, close monitoring and management of treatment, and frequent trips to medical centres (6,9). The complex nature of caring for children with IMD may thus have important effects on caregiver quality of life (QoL) (9).

The degree of complexity associated with the caregiving role has been found to be an important predictor of poor psychological outcomes and caregiver well-being in caregivers of

children with chronic illness (10–12). Parents of children with metabolic disorders specifically have reported lower health-related QoL compared to parents of children without illness (13). IMD can lead to both financial and emotional stress (6,14,15), and negative social impacts have been reported (16). However, while a great deal of stress may be experienced by families of children with IMD, some families have reported that dealing with a child's chronic illness has brought their family closer together (6,17).

In the context of caregiving, stressors have been described as "the problematic conditions and difficult circumstances experienced by caregivers (i.e., the demands and obstacles that exceed or push to the limit one's capacity to adapt)" (18,19). Stress originates in the relationship between one's external environment and one's internal state and thus caregiving stress occurs "when the demands imposed by a patient's condition collide with a caregiver's subjective ability to respond, or when these demands obstruct the pursuit of other objectives" (20). This may be why some caregivers can adapt well to a complex caregiving role while others experience poor health outcomes (19).

Coping is an important consideration in understanding the well-being of caregivers (19). While coping strategies have been defined and classified in a number of different ways (21), one common approach has been to group such strategies into two broad categories: problem-focused coping and emotion-focused coping (22). Problem-focused coping involves modifying the stressor or problem and considering ways to improve the problem (22). Emotion-focused coping is described as managing the emotional response of the stressful situation (22). While one approach to coping is not superior to the other, within the coping literature there is a predominant view that emotion-focused coping strategies are frequently less adaptive relative to problem-focused strategies in the context of stressful situations (23). The coping process has been

hypothesized to alter the relationship between stressors and health (24) and, while coping strategies cannot change the external source of a stressor, they may influence the effect of the stressor on an individual (25). Despite coping strategies being reported as an important factor in the caregiving process (26–28), there is little evidence regarding their relationship with QoL in parents of children with IMD. In particular, to our knowledge no previous studies have empirically investigated whether coping affects the relationship between caregiving complexity and QoL in parents of children with IMD. Therefore, this study aimed to examine the role of coping strategies in the association between caregiving complexity and QoL among parents of children with IMD in Canada. It was hypothesized that coping strategies would be an effect modifier in this relationship.

Methods

Participants and Procedures

This study analyzed data from a cross-sectional mailed survey of parents or guardians of children with IMD in Canada (hereafter we refer to participants as "parents" given that 98% of respondents were the biological parent of a child with an IMD). The full survey aimed to ascertain patient and family experiences with disease management and with receiving health care and is part of a larger research program, the Canadian Inherited Metabolic Diseases Research Network (CIMDRN) (29). To date, >650 children with IMD and their parents are enrolled in CIMDRN's consent-based cohort from 13 clinical centres across Canada. Participating children are born between 2006 and 2015 and have been diagnosed with one of 31 IMD targeted by the cohort study (Table 1). Participating parents of children enrolled within CIMDRN (<12 years of age) and who consented to be contacted to participate in surveys were considered eligible for the

present study. The parent most knowledgeable about the child was asked to complete the questionnaire.

Table 1. Eligible IMD (18 of these 31 diseases were represented in the questionnaire study, shown in italics).

Amino acid disorders:
Phenylalanine hydroxylase deficiency
Homocystinuria
Maple syrup urine disease
Tyrosinemia Type I
Ornithine transcarbamylase deficiency
Urea cycle disorders:
Arginase deficiency
Argininosuccinic acidemia
Carbamyl phosphate synthetase deficiency
Citrin deficiency
Citrullinemia
Hyperornithinemia-Hyperammonemia-Homocitrullinuria syndrome
N-acetylglutamate synthetase deficiency
Fatty acid oxidation disorders:
Medium chain acyl-CoA dehydrogenase deficiency
Very long-chain acyl-CoA dehydrogenase deficiency
Carnitine uptake defect
Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency
Trifunctional protein deficiency
Organic acid disorders or 'other' IMD:
ß-Ketothiolase deficiency
Glutaric acidemia type I
HMG-CoA lyase deficiency
Isovaleric academia
3-Methylcrotonyl-CoA carboxylase deficiency
Methylmalonic acidemias
Propionic academia
Guanidinoacetate methyltransferase deficiency
Mucopolysaccharidosis type I
Farber disease
Galactoesmia
Glycogen storage disease type I
Multiple carboxylase/biotinidase deficiency
Pyridoxine-dependent epilepsy/Antiquitin deficiency

We contacted eligible participants up to four times by mail to invite their participation, using an approach modified from Dillman to maximize the response rate (30). A pre-notification

letter informed parents that they would receive a survey invitation package within the following days. Survey invitation packages included an invitation letter, an information sheet which explained the study in detail, a questionnaire cover letter, a questionnaire booklet, a pre-stamped return address envelope, and a $2 coffee shop gift card that was used as a token non-conditional incentive. Two reminder survey packages were mailed to those who had not yet responded, separated by two-week intervals. By completing and returning the survey, parents were considered to provide tacit consent to participate in the study.

The survey was initiated at each participating clinical centre as research ethics board approval was obtained at that centre, beginning in January 2017. Survey implementation has continued with ongoing enrollment in the larger cohort study. For completion of this thesis project, this analysis included responses to the survey received between January and July 2017.

Measures

All survey variables were derived from responses to questions on the self-report questionnaire (Appendix B, presented after Chapter 4); where possible, we measured constructs using previously validated instruments. For this project, we were interested in analyzing a subset of survey variables that captured parental QoL, parental coping, parental depression, and caregiving complexity. We also analyzed responses to questions collecting participant demographic information.

Parent quality of Life

QoL of parents of children with IMD was assessed using the Medical Outcomes Study Short-Form Health Survey 12 version 2 (SF-12v2) (31). The SF-12v2 health survey was modified from the SF-36 (32) to include one or two questions from each of the eight subscales that made up the SF-36, capturing the physical and mental health of a general population (31).

Specifically, the SF-12 includes two items from the following scales of the SF-36: physical functioning, role physical, role emotional and mental health. It includes one item from the scales: bodily pain, general health, vitality and social function. Questions ask respondents about their well-being during the preceding four weeks on a three-point or five-point Likert scale. The SF-12 generates a subscale score for each of the eight domain scales as well as two summary scores, a physical component summary score (PCS) and a mental component summary score (MCS). These two summary scores were used to represent physical and psychological QoL in this study, respectively. PCS and MCS scores can range from 0-100 with a higher score indicating better mental or physical QoL. All scoring of the SF-12v2 was completed using the QualityMetric Health Outcomes Scoring Software 5.0 (33).

Parent depressive symptoms

The Center for Epidemiologic Studies Depression Scale-Revised (CESD-R) (34) was used to assess parental depressive symptoms. It is an updated version of the CESD (35) which was developed to examine depressive symptomology in epidemiologic studies of the general population (35). It is a 20 item self-report instrument that measures nine primary symptoms of major depressive disorder defined by the American Psychiatric Association Diagnostic and Statistical Manual, fifth edition (DSM-V) (34). Participants were provided with instructions stating, “Below is a list of ways you might have felt or behaved. Please check the boxes to tell us how often you have felt this way in the past week or so”. Each item consists of five response options: “not at all or less than 1 day”, “1-2 days”, “3-4 days”, “5-7 days”, “nearly every day for 2 weeks”. The tool provides an overall summary score, ranging from 0-60, with a higher score indicating greater levels of depressive symptoms (36).

Caregiving Complexity

Caregiving complexity was measured using two subscales covering parental time-impact and parental emotion-impact. Both subscales differed slightly based on the age of the child: the Child Health Questionnaire (CHQ)-Parent Form 50 (37) was completed by parents of children 5 years of age or older and the Infant and Toddler Quality of Life (ITQOL) Parent Form (38) was completed by parents of children less than 5 years of age. In both instruments, parental time-impact is a measure of the degree of limitation to the parent/caregiver's personal time experienced due to the child's illness while parental emotion-impact assesses the degree of distress experienced by the parent/caregiver due to the child's health and illness (39). Each subscale of the CHQ contains three items while seven items comprise the ITQOL subscales. The emotion-impact subscale asks parents to consider "during the past 4 weeks, how much anxiety or worry did each of the following cause you?" Responses include a five-point Likert scale ranging from "none at all" to "a lot". The time-impact subscale asks "during the past 4 weeks, were you limited in the amount of time you had for your own personal needs due to problems with your child's:". Responses are assessed along a four-point Likert scale and included: "yes, limited a lot", "yes, limited some", "yes, limited a little", "no, not limited" (39). Scores for both subscales can range from 0-100, with higher scores indicating that parents are reporting *fewer* limitations in personal time or emotional stress or worry due to their child's health (40).

Parental Coping Strategies

The Revised Ways of Coping Checklist (41) was used to measure parent coping strategies and behaviours. The instrument is comprised of 66 items that ascertain respondents' use of eight cognitive and behavioural strategies to cope with stressful encounters. The following subscales form the measurement: problem-focused coping, wishful thinking, distancing, seeking

social support, emphasizing the positive, self-blame, tension reduction, and self-isolation (41). Respondents were asked to "think about a stressful situation that you have recently experienced in relation to your child's disease or in providing care for your child" and then rate the extent to which they used the strategy. Responses were on a four-point Likert scale, ranging from 0 (not used) to 3 (used a great deal). Higher scores indicate greater use of behaviours described by each respective scale during the stressful event.

Subscale items were categorized into two overall coping strategies, problem-focused and emotion-focused coping (42). Problem-focused coping includes items that describe cognitive problem-solving efforts and behavioural strategies for altering or managing the source of the problem (22,42). Emotion-focused coping is comprised of items that describe cognitive and behavioural efforts directed at reducing or managing emotional distress (22,42). Problem-focused coping comprised items on the problem-focused subscale. Emotion-focused coping comprised the following scales: wishful thinking, distancing, emphasizing the positive, self-blame, tension reduction, and self-isolation. For each strategy (problem- or emotion-focused coping), the items comprising the strategy were summed, yielding a score that could range from 0-33 for problem-focused coping, and from 0-72 for emotion-focused coping. Seeking social support includes items that could represent both emotion- and problem-focused coping and was therefore not included in either category (22,41,42).

Statistical Analysis

A descriptive analysis of participant characteristics and scores on the instruments described above was completed. Counts and percentages were calculated for categorical data while means, standard deviations, medians, and ranges were calculated for continuous variables.

We were interested in the association of each measure of caregiving complexity and coping (independent variables) with parental QoL or parental depressive symptoms (outcomes); we analyzed physical and mental QoL as separate outcomes. Given that all three outcomes (depression, physical QoL, mental QoL) were continuous measures, we used linear regression for our multivariable analysis (described below). Analyses were stratified by age of the child (< 5 years of >=5 years) because the measures of caregiving complexity were different for these age groups. As an initial step, Partial Spearman Rank correlations, which are pairwise correlations between the independent variable and outcome, adjusted for all other covariates, were calculated to determine those covariates that would be included in the final multiple regression models. The correlation coefficients were ranked by strength and the covariates with the greatest correlation coefficients with respect to the outcome were included in a given regression model in addition to the four primary independent variables (two measures of caregiving complexity and two measures of coping). Specifically, based on our limited sample sizes (n=46 and n=67 for parents of younger and older children, respectively), in order to keep the total number of independent variables in each multivariable regression model to a maximum of ten (with consideration of the degrees of freedom for each covariate), we included the three covariates that were most strongly associated with the outcome from the partial correlation analysis. The covariates included in each multivariable model are listed in the footnotes of Table 5 (sample of parents of children 5 years of age or older) and Table 6 (sample of parents of children less than 5 years of age).

Multiple linear regression was used to examine the associations of interest. In each final model, we included and retained all primary predictor variables (problem-focused coping, emotion focused coping, parent time-impact, and parent emotion-impact) and the three top ranked covariates from the partial correlation analyses. We also included pre-specified

interaction terms depending on their contribution to a given model. Specifically, with respect to interaction terms, to examine whether coping strategies were an effect modifier in the association between caregiving complexity (i.e., parent time impact and parent emotion impact) and the outcomes of interest (mental QoL, physical QoL, and depressive symptoms), a multiplicative term representing the interaction between each subscale of caregiving complexity and coping strategies (total of four interaction terms) was tested in the final regression model for each outcome. To determine which interaction terms were retained in the final model, backwards selection was used. All interaction terms were first added to the full model at the same time with the least significant interaction term eliminated first. Eliminated terms were then manually re-entered into the final main effects model individually to check for significance. If an interaction term was significant, the continuous effect modifying variable (the coping variable) was split into a categorical variable with four equal levels (quartiles). Then the linear association between the outcome of interest and main exposure (the caregiving complexity variable) was descriptively examined within each quartile of the effect modifier (coping strategies).

Item-missing data were managed using casewise deletion. Data cleaning and statistical analyses were conducted using SAS, version 9.4 (SAS Institute Inc., Cary, NC, USA). A two-sided p-value of 0.05 and 95% confidence limits were used to signify statistical significance in all analyses.

Ethical considerations

The survey study received ethics approval from the Children's Hospital of Eastern Ontario Research Ethics Board, the Ottawa Health Science Network Research Ethics Board, and the affiliated research ethics board of each participating centre.

Results

Survey Participation

By July 2017, the survey had been initiated at 8 centres, with 305 families invited to complete the questionnaire and 113 responses received (response rate of 37%, Figure 1).

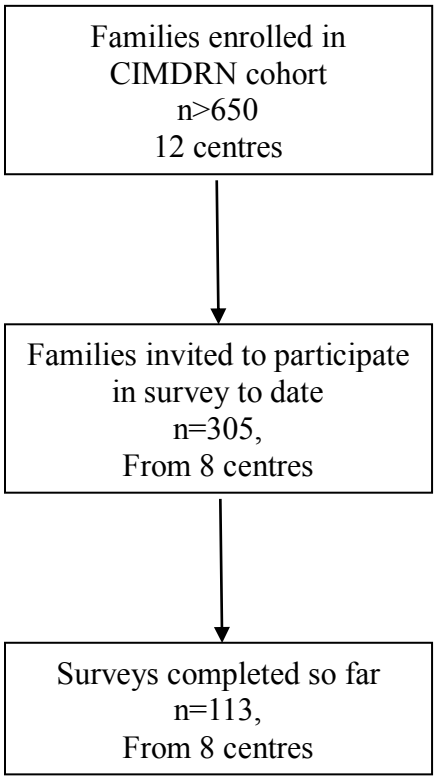

Figure 1. Family participation to date (survey is ongoing).

Sample Characteristics

Table 2 presents the demographic and clinical characteristics of participating families. A majority of respondents were female (88%) and the biological parent (98%) of the child with an IMD. Two thirds of parents (66%) were 35 years of age or older, with a mean age of 38 (SD=6). 85% of parents reported that they were married or common law, 64% were working full or part time, 74% completed some form of post-secondary education, and 54% lived in a large city. A minority of parents (21%) reported having more than one child diagnosed with an IMD. In these families, one child was designated a priori as the "index" child for the study and parents were

asked to consider this child when completing the survey. 55% of the children with IMD were female, 60% were 5 years of age or older, and just over a third (35%) were diagnosed with a fatty acid oxidation disorder (FAOD). All remaining results are presented stratified by the age of the child (younger than 5 years, or 5 years and older) given the use of different caregiving complexity measurement instruments based on child age.

Table 2. Participant demographic characteristics.

Respondents (n=113)	
Age	n (%)
25-29	10 (9)
30-34	28 (25)
35-39	26 (23)
40-44	32 (28)
45 years or older	17 (15)
Gender	
Male	13 (11)
Female	99 (88)
Relation to child	
Biological parent	110 (98)
Frequency Missing = 1	
Work status	
Not working	9 (8)
Working full or part-time	72 (64)
Full time homemaker	18 (16)
Other[†]	14 (12)
Marital status	
Married/Common Law	97 (86)
Divorced or separated	10 (9)
Never married	6 (5)
Highest level of education	
Completed high school or less	18 (16)
Completed vocational/technical training	11 (10)
Completed college/university	65 (59)

Completed graduate school	17 (15)
Frequency Missing = 2	
Annual household income	
Less than $50,000	20 (18)
$50,000 - $69,999	10 (9)
$70,000 - $89,999	12 (11)
$90,000 - $99,99	9 (8)
$100,000 or more	55 (49)
Don't know	6 (5)
Frequency Missing = 1	
Community	
Large city (population of 100,000 or more people)	59 (54)
Medium-sized city (population of at least 30,000 but less than 100,000 people)	18 (16)
Small community (population of at least 1,000 but less than 30,000 people)	29 (26)
Frequency Missing = 3	
Number of people in household	
Fewer than four	21 (19)
Four	52 (46)
Five	22 (20)
Six or more	17 (15)
Frequency Missing = 1	
Language most often spoken at home	
English	97 (87)
Other	15 (13)
Frequency Missing = 1	
Additional child(ren) diagnosed with IMD	
No	89 (79)
Yes	23 (21)
Frequency Missing = 1	
Child Characteristics	
Child gender	
Male	51 (45)
Female	62 (55)
Child birth year	
2006-2007	25 (22)
2008-2009	23 (20)

2010-2011	19 (17)
2012-2013	21 (19)
2014-2015	25 (22)
Disease category	
Fatty Acid Oxidation Disorders	40 (35)
Amino Acid/Urea Cycle Disorders	35 (31)
Other IMD	38 (34)

† Other includes looking for work outside the home, student, and other.

Mental QoL, Physical QoL, Depressive Symptoms, Coping Strategies, and Caregiving Complexity scores among IMD Parents

The mean, standard deviation (SD), median, quartiles, and potential ranges of observed variables are presented in Tables 3a and 3b. Parents in both samples (children < or >= 5 years of age) reported relatively low levels of depressive symptoms and reported their emotions to be more greatly impacted, rather than their time, by the demands of caring for their child.

Table 3 a). Descriptive statistics for observed variables in sample of parents with children 5 years of age or older.

Variable	N	Mean	SD	Median	25% Q1	75% Q3	Possible Minimum	Possible Maximum	Higher scores mean…
OUTCOMES									
QoL: Increased Mental Health	67	46.88	9.08	47.67	40.32	55.12	0	100	Better health
QoL: Increased Physical Health	67	56.04	5.67	57.12	53.04	59.78	0	100	Better health
Increased Depressive Symptoms	65	7.72	7.66	5	1	12	0	60	More depressive symptoms
REDUCED CAREGIVING COMPLEXITY									
Lower parent time-impact	66	79.63	25.31	88.89	66.67	100	0	100	Reduced impact on parent time (lower impact)
Lower parent emotion-impact	66	62.50	30	70.83	50	83.33	0	100	Reduced impact on parent emotions (lower impact)
COPING									
Greater problem- focused coping	59	12.44	7.01	13	7	18	0	33	Greater use of strategy
Greater emotion-focused coping	57	14.36	10.58	12	7	20	0	72	Greater use of strategy
Emotion-focused coping sub scales									
Wishful thinking	60	3.31	3.43	3	0	4.5	0	15	Greater use of strategy
Detachment	60	3.08	2.83	2	1	5	0	18	Greater use of strategy
Focus on positive	60	3.80	2.76	3.50	2	6	0	12	Greater use of strategy
Self-blame	60	1.48	1.74	1	0	2	0	9	Greater use of strategy
Tension reduction	61	1.55	1.51	1	0		0	9	Greater use of strategy
Keep to self	61	1.93	1.99	1	0	3	0	9	Greater use of strategy

* SD= standard deviation

Table 3 b). Descriptive statistics for observed variables in sample of parents with children less than 5 years of age.

Variable	N	Mean	SD	Median	25% Q1	75% Q3	Possible Minimum	Possible Maximum	Higher scores mean…
OUTCOME									
QoL: Increased Mental Health	44	44.66	11.10	46.90	37.91	54.13	0	100	Better health
QoL: Increased Physical Health	44	55.59	5.79	57.01	51.80	59.56	0	100	Better health
Increased Depressive Symptoms	45	10.49	11.86	7	1	15	0	60	Greater depressive symptoms
REDUCED CARGIVING COMPLEXITY									
Lower parent time-impact	46	79.30	23.35	85.71	66.67	100	0	100	Reduced impact on parent time (lower impact)
Lower parent emotion-impact	46	67.70	27.17	75	46.43	89.29	0	100	Reduced impact on parent emotions (lower impact)
COPING									
Greater problem-focused coping	43	11.53	6.80	12	7	15	0	33	Greater use of strategy
Greater emotion-focused coping	43	17.69	12.39	17	9	24	0	72	Greater use of strategy
Emotion-focused coping sub scales									
Wishful thinking	45	4.55	4.44	3	1	7	0	15	Greater use of strategy
Detachment	44	3.77	3.50	3	1	5	0	18	Greater use of strategy
Focus on positive	44	4.29	3.10	3	2	7	0	12	Greater use of strategy
Self-blame	43	1.48	1.77	1	0	2	0	9	Greater use of strategy

Tension reduction	44	1.38	1.58	1	0	2	0	9	Greater use of strategy
Keep to self	45	2.02	1.71	2	1	3	0	9	Greater use of strategy

* SD= standard deviation

Correlation of Caregiving Complexity and Coping with Mental QoL, Physical QoL, and Depressive Symptoms among IMD Parents

Tables 4a and 4b provide the partial Spearman rank correlation coefficients between each outcome and explanatory variable, adjusted for all other potential covariates. With regards to the sample of parents of children 5 years of age or older, higher use of problem-focused coping, less parent emotion-impact, and having a child diagnosed with an "other" IMD (relative to an amino acid or urea cycle disorder) were significantly correlated with higher mental QoL (Table 4a). Higher use of emotion-focused coping, higher level of education, and homemaker versus other work status were significantly correlated with lower mental QoL. Higher use of emotion-focused coping, higher level of education, and homemaker versus other work status were also significantly correlated with greater depressive symptoms. No covariates were significantly correlated with physical QoL.

Higher mental QoL of parents of children younger than 5 years of age was significantly ($p<0.05$) correlated with higher use of problem-focused coping, lower parent time-impact, higher income, and homemaker versus other work status (Table 4b). Greater use of emotion-focused coping was significantly associated with lower mental QoL in parents of young children. Physical QoL and depressive symptoms were not significantly correlated with any covariates among children younger than 5 years of age.

Table 4 a). Partial Spearman rank correlation between covariates and each outcome measure in sample of parents with index child 5 years of age or older.

Variables	Outcome		
	Mental QoL (n=55)	**Physical QoL (n=55)**	**Depressive Symptoms (n=54)**
Greater problem-focused coping	*0.445***	*-0.031*	*-0.268*
Greater emotion-focused coping	*-0.427***	*-0.047*	*0.606‡*

Reduced caregiving complexity (lower time-impact)	*0.058*	*0.082*	*0.082*
Reduced caregiving complexity (lower emotion-impact)	*0.319**	*-0.022*	*-0.257*
Child gender			
Reference category=male			
Female	0.177	-0.079	-0.036
Increased child age	-0.014	-0.163	0.091
Caregiver gender			
Reference category=male			
Female	0.160	-0.172	-0.181
Increased caregiver age	0.025	0.023	-0.266
Higher income	0.265	-0.022	-0.107
Education			
Reference category=high school or less			
Technical training	*-0.390**	*0.161*	*0.454***
College/University	*-0.443***	*0.228*	*0.429***
Graduate school	*-0.395**	*0.236*	*0.235*
Work status			
Reference category=working full- or part-time			
Homemaker	*-0.418***	*0.198*	*0.464***
Other work status	*-0.106*	*0.101*	*-0.173*
Child diagnosis			
Reference category= Amino acid/urea cycle disorders			
FAOD	*0.008*	*-0.018*	*0.079*
Other IMD	*0.451***	*-0.208*	*-0.268*
Additional child diagnosed with IMD	0.109	-0.188	-0.184

Values in italics were included in multivariate regression models.
* p<0.05 **p<0.01 ‡ p<0.0001

Table 4 b). Partial Spearman rank correlation between covariates and each outcome measure in sample of parents with index child less than 5 years of age.

Variables	**Outcome**		
	Mental QoL (n=41)	**Physical QoL (n=41)**	**Depressive Symptoms (n=42)**
Problem-focused coping	*0.478**	*0.161*	*-0.271*
Emotion-focused coping	*-0.406**	*0.193*	*0.317*
Reduced caregiving complexity (lower time-impact)	*0.434**	*0.183*	*-0.312*

Reduced caregiving complexity (lower emotion-impact)	*0.082*	*0.051*	*-0.141*
Child gender			
Reference category=male			
Female	-0.107	*0.294*	-0.082
Child age	0.086	0.184	-0.077
Caregiver gender			
Reference category=male			
Female	-0.073	-0.120	*0.171*
Caregiver age	0.068	*0.253*	*-0.190*
Income	*0.397**	0.142	0.154
Education			
Reference category=high school or less			
Technical training	-0.084	-0.184	-0.058
College/University	-0.188	-0.075	0.031
Graduate school	-0.209	-0.079	0.136
Work status			
Reference category=working full- or part-time			
Homemaker	*0.408**	0.041	-0.059
Other work status	*0.350*	-0.161	-0.025
Child diagnosis			
Reference category= Amino Acid/Urea Cycle disorders			
FAOD	0.154	*-0.006*	*-0.077*
Other IMD	0.069	*0.379*	*-0.233*
Additional child diagnosed with IMD	*-0.223*	0.234	-0.149

Values in italics were included in multivariate regression models.
* $p<0.05$

Association between coping strategies, caregiving complexity, and mental QoL and depressive symptoms in parents of children 5 years of age or older

Table 5 describes the results of multivariable linear regression analyses conducted to assess the association between parent coping strategies, caregiving complexity, and two outcomes of interest, mental QoL and depressive symptoms, in parents of children 5 years of age or older. Given that none of the primary predictor variables was associated with physical QoL in this parent sample in the partial correlation analyses (Table 4a), we made a post-hoc decision to exclude this outcome from the reporting of the linear regression analysis (Appendix C, presented

after Chapter 4). Also based on the partial correlation analyses, the covariates selected for inclusion in the multivariable models for both mental QoL and depression were parental education, parental work status, and child diagnosis (IMD category).

Mental QoL

Table 5, model 4 describes the multivariable associations of coping and caregiving complexity variables as potential predictors with the outcome mental QoL among parents of children aged 5 years or older. Parents' greater use of emotion-focused coping strategies was associated with lower mental QoL (β= -0.414; 95% confidence interval -0.684, -0.145), while lower parent emotion-impact was not associated with mental QoL. There was a significant interaction between parents' greater use of problem-focused coping and lower parent time-impact. When we analyzed that interaction effect, in parents with lower levels of problem-focused coping (i.e., quartile 1 and quartile 2), lower parent time impact (a higher score on the time-impact variable) was associated with a higher self-reported score of mental QoL (quartile 1: β=0.250; quartile 2: β=0.130), while among parents who reported greater use of problem-focused coping (quartile 3 and 4), lower parent time impact was associated with a lower score of mental QoL (quartile 3: β= -0.072; quartile 4: β= -0.128) (Appendix C). These results related to the exploration of the interaction should be interpreted with caution due to our small sample size. Full models showing coefficients for all covariates are presented in Appendix C.

Depressive symptoms

Table 5, model 4 describes the multivariable associations of coping and caregiving complexity as potential predictors of depressive symptoms of parents of children 5 years of age or older. Parents' greater use of emotion-focused coping strategies (β=0.413; 95% confidence

interval 0.178, 0.649) was associated with greater depressive symptoms (Full models in Appendix C). No interaction terms were statistically significant.

Association between coping strategies, caregiving complexity, and mental QoL in parents of children younger than 5 years of age

Table 6 displays results of multivariable linear regression analyses conducted to assess the association between parent coping strategies, caregiving complexity, and mental QoL in parents of children younger than 5 years of age. Given that no primary predictor variables were associated with physical QoL or depressive symptoms in this parent sample, based on the partial correlation analyses, we chose post-hoc to exclude regression models for these outcomes from presentation here (see Appendix C). Also based on the partial correlation analyses, the covariates selected for inclusion in the multivariable model for mental QoL were household income, parental work status, and having more than one child diagnosed with an IMD.

Mental QoL

Table 6, model 4 describes the multivariable associations of coping and caregiving complexity as potential predictors of mental QoL among parents of children younger than 5 years of age. Lower parent time impact (β=0.329; 95% confidence interval 0.160, 0.498) was associated with higher mental QoL. Greater use of emotion-focused coping (β=-0.332; 95 confidence interval -0.580, -0.084) was associated with lower parent mental QoL in this sample. There was a significant interaction between lower parent emotion-impact and greater use of problem-focused coping in the association with mental QoL in this sample (Table 6). We found that at lower levels of problem-focused coping (quartiles 1 and 2), parents who reported lower parent emotion-impact had lower mental QoL (quartile 1: β=-0.059; quartile 2: β=-0.117). By contrast, at the highest level of problem-focused coping, parents who reported lower emotion-impact had higher mental QoL scores (quartile 4: β=0.105). It was not possible to analyze the

association between emotion-impact and mental QoL in parents who were in quartile 3 of problem-focused coping. These results related to the exploration of the interaction should be interpreted with caution due to our small sample size. Full models showing coefficients for all covariates are presented in Appendix C.

Table 5. Coping and caregiving complexity variables predicting mental QoL and depressive symptoms among parents of children 5 years of age or older: multivariable regression results.

Independent variables	Model 1 (coping strategies)	Model 2 (caregiving complexity)	Model 3 (coping and caregiving complexity)	Model 4 (coping and caregiving complexity with significant covariates)
Higher Level of Mental QoL (MCS)[a]				
↑ Problem-focused coping	0.391 (-0.044, 0.827)		0.347 (-0.068, 0.762)	0.683 (0.282, 1.085)
↑ Emotion-focused coping	-0.557 (-0.852, -0.262)*		-0.352 (-0.664, -0.039)*	-0.414 (-0.684, -0.145)*
↓ Parent emotion-impact		0.083 (-0.029, 0.196)	0.065 (-0.053, 0.183)	0.090 (-0.016, 0.195)
↓ Parent time-impact		0.092 (-0.002, 0.188)	0.082 (-0.050, 0.214)	0.078 (-0.041, 0.197)
Time impact x problem focused coping[b]				-0.014 (-0.027, -0.001)*
Greater Depressive symptoms (CESD-R)[c]				
↑ Problem-focused coping	-0.254 (-0.607, 0.098)		-0.236 (-0.581, 0.109)	-0.281 (-0.611, 0.048)
↑ Emotion-focused coping	0.527 (0.287, 0.766)*		0.436 (0.173, 0.698)*	0.413 (0.178, 0.649)*
↓ Parent emotion-impact		-0.091 (-0.176, -0.006)*	-0.108 (-0.206, -0.009)*	-0.080 (-0.172, 0.013)
↓ Parent time-impact		-0.025 (-0.126, 0.076)	0.052 (-0.059, 0.162)	0.009 (-0.097, 0.115)

[a] Additional covariates in Model 4: Disease category, education level, work status (Appendix C). Model 1: n=56, Adjusted R^2=0.1974; Model 2: n=66, Adjusted R^2=0.2228; Model 3: n=55, Adjusted R^2: 0.2913; Model 4: n=55, Adjusted R^2: 0.5342.

[b]Interaction effects: see Table 7, Appendix C.

[c]Additional covariates in Model 4: Disease category, education level, work status (Appendix C). Model 1: n=55, Adjusted R^2= 0.2881; Model 2: n=64, Adjusted R^2= 0.1529; Model 3: n=54, Adjusted R^2=0.3364; Model 4: n=54, Adjusted R^2= 0.5007.

Table 6. Coping and caregiving complexity in relation to mental QoL among parents of children less than 5 years of age: multivariable regression results.

Independent variables	Model 1 (coping strategies)	Model 2 (caregiving complexity)	Model 3 (coping and caregiving complexity)	Model 4 (coping and caregiving complexity with significant covariates)
Higher Level of Mental QoL (MCS)[a]				
↑ Problem-focused coping	0.746 (0.231, 1.261)*		0.813 (0.370, 1.255)*	0.775 (0.419, 1.132)
↑ Emotion-focused coping	-0.689 (-0.995, -0.383)*		-0.484 (-0.768, -0.200)*	-0.332 (-0.580, -0.084)*
↓ Parent emotion-impact		0.038 (-0.113, 0.189)	0.036 (-0.123, 0.195)	0.046 (-0.091, 0.183)
↓ Parent time-impact		0.290 (0.099, 0.480)*	0.241 (0.048, 0.434)*	0.329 (0.160, 0.498)*
Emotion impact x problem focused coping[b]				-0.027 (-0.041, -0.014)*

[a] Additional covariates in Model 4: Total household income, work status, additional child diagnosed with IMD (Appendix C). Model 1: n=41, Adjusted R^2=0.3215; Model 2: n=44, Adjusted R^2=0.3254; Model 3: n=41, Adjusted R^2: 0.5077; Model 4: n=41, Adjusted R^2: 0.7040.

[b] Interaction effects: see Table 8, Appendix C.

Discussion

Parents play a crucial role in the management of their child's health care, especially when a child is diagnosed with a chronic illness (43). The present study focused on mental and physical QoL, as well as depressive symptoms, among parents of children with IMD in Canada. The aims of the study were to investigate whether caregiving complexity and coping strategies were associated with parental QoL and depressive symptoms. In addition, we examined whether coping strategies modified the association between caregiving complexity and QoL. We found that greater use of emotion-focused coping was associated with lower mental QoL in parents of both younger and older children with IMD, and with higher depressive symptoms in parents of older children with IMD. The association between caregiving complexity and parent QoL was less consistent although parents of younger children with IMD who experienced a lower impact of caregiving in terms of their time had significantly higher mental QoL. We found some evidence that problem-focused coping strategies modified the association between caregiving complexity and mental QoL among parents of children with IMD but we were unable to fully explore the nature of this interaction effect.

Comparison of our sample with related studies on QoL and caregiving complexity

Parents in our sample reported lower mental and physical QoL relative to the U.S. population norm for the SF-12 (33) and when compared to another sample of parents of children with IMD that used the longer version (SF-36) of the QoL instrument used in our study (5). Other studies have assessed the QoL of parents of children with IMD using a variety of QoL instruments, rendering direct comparisons challenging (44,45). However, a study of parents of children with two specific IMD (phenylketonuria or galactosemia) reported that participating parents had comparable levels of QoL to parents of healthy children (44). Another study found

that parents of children with the IMD methylmalonic academia reported decreased QoL relative to parents of children with chronic illness living in a long-term care facility but comparable QoL to parents of children with chronic conditions living at home (45).

A number of studies have used the SF-12 (or another version of this instrument) to measure parent QoL in caregiver samples of children diagnosed with other (non-IMD) chronic illnesses; their results vary in comparison to our findings. For example, parents of children with a different genetic disorder (CDKL5) (46) reported lower mental QoL and comparable physical QoL to our parent sample. In another study, parents of children with a range of chronic illnesses or disabilities (47) reported both lower physical and lower mental QoL compared to our sample. In studies of parents of children with neurologic disorders (48), and parents of children with functional abdominal pain (49), participants reported lower physical QoL but similar mental QoL to parents in our sample. Parents of children with developmental coordination disorder (50) reported greater mental QoL and lower physical QoL when compared with our parent sample. A three-point difference in mean summary scores is considered clinically significant for the SF-12 (51) and was used when making the above comparisons.

With regards to the instruments we used to measure caregiving complexity, parents in our sample reported comparable time impact but a greater emotional impact of caregiving relative to a normative sample of parents of healthy children (40). This finding is surprising given the extensive home disease management requirements associated with IMD, including highly specialized diets. It may be that parents adapt to the burdensome nature of disease management. In a recent qualitative study of parents who were participants in the larger cohort invited to participate in our study, participants reported adjusting well over time to the daily requirements of managing their child's disease (52). A European study found that parents of children with the

IMD phenylketonuria reported very similar time- and emotion-impact scores to parents in our study (53). When compared to parents of children with other chronic illnesses, findings differed. For example, studies of parents of children with juvenile rheumatoid arthritis (40) and sickle cell disease (54) reported similar perceived impact on both subscales when compared to our parent sample. Parents of children with epilepsy as well as parents of children with attention deficit hyperactive disorder reported both their time and emotions to be more impacted than parents in our study (45).

Association of coping and caregiving complexity with parental QoL and depression

In this study, we found that coping strategies were associated with parents' mental QoL among parents of both older and younger children with IMD. Specifically, greater use of problem-focused coping was generally (although not always significantly) associated with higher mental QoL while greater use of emotion-focused coping was associated with lower mental QoL when adjusting for important covariates. These findings are supported by previous studies of parents caring for children with chronic illness (55–59) that found emotion-focused strategies to be less adaptive overall when coping with caregiving stress or that such strategies are used more often by caregivers who have lower QoL.

We note that in the broader literature on coping, it is recognized that neither problem- nor emotion-focused coping is superior for managing stressful situations (60). Rather, it has been suggested that when a direct action can change the situation, problem-focused strategies may be more adaptive. Contrarily, when it is appraised that nothing can be done to change the stressful situation, emotion-focused strategies are likely to be of greater benefit (60). We also note that an increase in emotion-focused coping does not necessarily imply a decrease in problem-focused

coping and often a combination of both strategies may be used to help individuals deal with a stressful situation (42).

With regards to parental depressive symptoms, in our study emotion focused coping was positively associated with greater depressive symptoms in parents of children older than 5 years of age with IMD. In a previous study that examined the association between caregiver depressive mood and coping strategies in parents of children with developmental delay (61), escape avoidance coping (classified as an emotion-focused strategy) was positively associated with parents' depressive mood while no significant association was found between problem-focused coping and depressive mood.

In our study, the association between caregiving complexity and parent QoL was less clear relative to the association between coping and QoL, although there was some evidence among parents of younger children with IMD that those who experienced a lower time-impact of caregiving had higher mental QoL scores. Several significant interaction terms between coping and caregiving complexity also emerged in the multivariable analyses. When we examined the interaction effects at various levels of the effect modifying variable, a few trends can be cautiously highlighted. For example, in the sample of parents of children older than 5 years of age, a lower reported time impact of caregiving for parents was associated with greater mental health only at lower levels of problem-focused coping. If this were confirmed in further studies, it may suggest that greater use of problem-focused coping can mitigate some of the challenges associated with the impact of caregiving on parents' time. In parents of children younger than 5 years of age, there was some evidence that a lower emotional impact of caregiving was associated with greater mental health only at a higher level of problem-focused coping; the

nature of this association is more challenging to interpret intuitively. These findings based on the interaction analysis should be interpreted with caution due to our small sample size.

The potential role of coping strategies as a third variable (either effect modifier or intermediate variable) in the association between a measurement of caregiving demands and QoL of parents of children with chronic illness has not been well documented. In a previous study of parents of children diagnosed with asthma, greater levels of caregiver burden were negatively and indirectly associated with parental QoL via decreased use of acceptance coping and increased use of denial coping (62). Within the autism spectrum disorder literature, coping strategies have been found to moderate the association between child symptom severity and stress (63), and between stress and parental QoL (59). For children diagnosed with neurodevelopmental conditions, caregiving burden had an indirect and negative effect on parents' QoL via a specific emotion-focused coping strategy, behavioural disengagement (63,64).

Limitations of the study

While a notable strength of this study is the multicentre design including a representative sample of children with IMD in Canada, a number of limitations should be considered. First, we do not have socio-demographic information regarding the non-responders or reasons why participation was declined; our relatively low response rate introduces the possibility of non-response bias. For example, it is possible that those with lower QoL or who experience greater caregiving complexity may have been less likely to participate, particularly considering that the majority of those who responded reported that they were living with a spouse or partner, and half reported a household income of $100,000 or greater.

A notable limitation was our small number of male respondents. It is possible that parents of different genders have different perspectives of the caregiving process and therefore differ in their reported experiences. Future research should seek to further understand the role of caregiver gender in the associations among caregiving complexity, coping, and quality of life; and investigate how the family as a unit (in addition to parents as individuals) copes with illness.

Another limitation was our small sample size, which corresponds to the relatively low prevalence of IMD in the population and was exacerbated in our analysis given that the instruments used to measure caregiving complexity differed between parents of younger and older children. While the subscales measured the same underlying construct in each sample, the uniqueness of the subscales meant we were unable to combine the two samples but rather, had to examine the associations of interest separately. Consequently, our two sample sizes were quite small and we were limited in the number of covariates we could include in our regression analyses. In addition, our small sample size made it difficult to evaluate significant interaction terms at various levels of our potential effect modifying variable. An additional limitation related to sample size was the need to group 31 individually rare IMD into three broad categories for analysis, which may have led us to miss heterogeneity within each disease category.

In addition, the classification of coping strategies and the many ways to categorize them makes it difficult to not only assess this complex variable but also to compare our findings to other studies within the literature. This has been reported as a limitation when examining coping strategies (21). The coping strategy instrument used in this study had eight subscales. Therefore, to accommodate our small sample sizes, we categorized these subscales into two coping variables – problem and emotion focused, consistent with previous reported practice (42). A

larger sample would have enabled us to evaluate each individual subscale and perhaps more fully understand how coping relates to parental well-being.

Given the cross-sectional study design, we are unable to establish causality nor the direction of any potential causal relationship. For example, it is possible that parents who experience lower mental QoL are inclined to rely more heavily on emotion-focused coping strategies, rather than emotion-focused coping itself contributing to QoL. Future studies should adopt a longitudinal design to better evaluate the role that coping strategies play in the relationship between caregiving complexity and QoL.

Conclusion

This study adds to the limited literature with regards to the role of coping strategies as potential moderators of caregiving complexity in association with parental QoL and depressive symptoms in a population of parents of children with IMD. Findings from this study are consistent with previous studies that problem focused coping may be associated with higher caregiver mental QoL while emotion focused coping is associated with lower mental QoL. Additional research, particularly using a longitudinal study design, would contribute to a greater understanding of how coping strategies may impact the relationship between the complexity of caregiving as experienced by parents and their resulting QoL. Such research has potential to provide important information on how best to support this parent population. Considering the health and psychological QoL of parents of children with IMD is an integral part of providing the best patient and family-centered care.

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List of Abbreviations

IMD: Inherited Metabolic Diseases

QoL: Quality of Life

CIMDRN: Canadian Inherited Metabolic Diseases Research Network

SF: Short Form Health Survey

PCS: Physical Component Summary

MCS: Mental Component Summary

CESD-R: Center for Epidemiologic Studies Depression Scale-Revised

CHQ: Child Health Questionnaire

ITQOL: Infant and Toddler Quality of Life

FAOD: Fatty Acid Oxidation Disorder

SD: Standard Deviation

Chapter 4: Final Discussion

Limited research has focused on the role coping strategies play with regards to parent quality of life (QoL) and caregiving complexity (i.e., the impact of caregiving with respect to parents' time and emotional stress) in parents of children living with a chronic illness. Understanding whether coping strategies are associated with parental QoL and whether such strategies are effect modifiers of the association between caregiving complexity and QoL can inform strategies to improve parental adaptation and well-being. For example, if particular approaches to coping have the potential to mitigate the influence of highly complex caregiving on parental QoL, then strategies to promote those coping approaches could be evaluated as interventions with families of children who have chronic illness. This project aimed to assess the role that coping strategies play in the association between caregiving complexity and parental QoL in parents of children with chronic illness and, specifically, children with inherited metabolic diseases (IMD) in Canada.

Findings and interpretation for the systematic review

In the first part of this thesis (Chapter 2), we conducted a systematic review to synthesize existing evidence regarding the association between coping strategies and QoL among parents or caregivers of children with chronic illness. Synthesizing findings across studies was challenging due to variability in the definition and measurement of key constructs, particularly coping strategies. For example, one means of classifying coping strategies is to categorize them into two groups – problem-focused and emotion-focused coping. Problem-focused coping can be defined as "cognitive problem-solving efforts and behavioural strategies for altering or managing the source of the problem" (59). Problem-focused coping is likely to be used when the situation is appraised as being modifiable – something can be done to change the situation. Emotion-focused

coping is defined as "cognitive and behavioural efforts directed at reducing or managing emotional distress" (59). Emotion-focused coping is likely to be used when it has been appraised that nothing can be done to change the situation or condition. While we report about coping strategies using this categorization method throughout this document, in the systematic review this was not consistently applied across all studies.

Among the 10 studies that met our inclusion criteria for the systematic review, we identified evidence of an association between coping strategies and caregiver psychological QoL but not between coping strategies and physical QoL. The lack of evidence supporting a relationship between coping and physical QoL is consistent with other studies of parents of children with chronic illness (85,86) and other caregiver populations (87) that did not find evidence of an association between coping and physical QoL. Conversely, some studies of adults who themselves have chronic conditions have found that specific coping strategies are associated with physical QoL (88). A recent review of coping in association with health in general identified coping as a potentially important contributor to both physical and psychological health (89) and other studies have found that problem-focused coping strategies were positively associated with physical activity in different populations (90) (91). Skinner et al., (60) further note that "how people deal with stress can reduce or amplify the effects of adverse life events and conditions not just on emotional distress and short-term function, but also long-term, on the development of physical and mental health or disorder" (p. 216). These findings suggest that while there is currently limited evidence, it may be important to continue to evaluate the role of coping strategies in association with physical QoL (in addition to psychological QoL) in parent caregivers.

Our review found that coping strategies considered to be positive or adaptive were frequently associated with higher psychological QoL while negative or maladaptive strategies were frequently associated with lower psychological QoL. These findings align with results from other caregiving research, for example among studies of caregivers of children with intellectual disabilities (92,93), and suggest that coping strategies could be a promising area for the development of interventions to support parents.

Only two of the studies we reviewed investigated coping strategies as a third variable (i.e., mediator or effect modifier) in the association between caregiving complexity and caregiver QoL among parents of children with chronic illness. Their findings were inconsistent and it was challenging to interpret the nature and direction of the relationships among variables in part due to the use of cross-sectional study designs. In addition to a need for prospective research to address this challenge, our review findings point to a need for further conceptual clarity regarding the definition, dimensions, and measurement of coping.

Integration with the secondary analysis study

In the second part of this thesis (Chapter 3), we analyzed data from a cross-sectional mailed survey of parents of children under 12 years of age who were receiving care for an IMD in Canada. Specifically, we investigated the association between parental coping and parental QoL among the 113 parent participants in the survey, and we hypothesized that coping strategies would be an effect modifier in the association between caregiving complexity and QoL. Aligned with the findings from the systematic review, we found that while coping was not significantly associated with parent physical QoL, it was associated with mental QoL. Specifically, greater use of emotion-focused coping was associated with lower parental mental QoL among parents of both younger (<5 years) and older (≥5 years) children. Greater use of emotion-focused coping

was also associated with higher depressive symptoms among parents of older children. With regards to caregiving complexity, decreased time impact of caregiving was associated with greater mental QoL in parents of children younger than 5 years of age.

Our consistent finding of a negative and significant association between emotion-focused or maladaptive coping and parental mental QoL has been reported elsewhere (35,94,95). Emotion-focused coping strategies are conceptually aimed at reducing emotional distress but do not attempt to change the source of the stress. It has been reported that individuals will use emotion-focused coping strategies when they do not think anything can be done to change the situation. Contrarily, people have reported using problem-focused strategies when they think the demands of the situation can be modified (59).

Keeping this in mind, it may not be surprising that adapting in an emotion-focused way may be associated with poorer mental QoL, as this approach would not be expected to alleviate environmental stressors. For instance, distancing or detaching oneself from a situation (examples of emotion-focused strategies) can lead to a decrease use of problem-focused strategies, and has been associated with poor psychological outcomes (96). Furthermore, the use of wishful thinking (an example of emotion-focused coping) is often used when a poor outcome is anticipated (97). This can lead to self-failure due to the expectation of an undesirable outcome. Meanwhile, the use of problem-focused strategies (such as planful problem-solving) may indicate a proactive role in disease management. For instance, parents of children who use problem-focused coping, and specifically attributes of the planful problem-solving strategy, may be more likely to advocate for their child or follow strict treatment regimes (89). These are actions that may result in improved health outcomes for both the child and the caregiver. It should be noted that people often use a combination of emotion- and problem-focused strategies to deal with a stressful

situation and there is not a consensus that problem-focused strategies are preferred, since both types of strategies have been identified useful in improving psychological well-being (61,97). An additional important caveat to these interpretations is that neither our survey analysis findings or the findings from the systematic review provide direct causal evidence, particularly given the cross-sectional nature of all of the data sources we investigated. For example, it may be that parents who already have poorer mental QoL are more likely to use emotion-focused rather than problem-focused coping strategies. Or it may be that the nature of some stressors in this population do not offer opportunities for problem-focused coping and so emotion-focused coping is a reflection of a more difficult set of circumstances that also lead to poorer mental QoL.

From our survey analysis, we found some support for the hypothesis that problem-focused coping strategies may be an effect modifier of the association between some measures of caregiving complexity and mental QoL: we identified a significant statistical interaction between coping and the time impact of caregiving for older children and between coping and the emotional impact of caregiving for younger children. However, stratified analyses to further explore the nature of these interactions did not reveal clear trends, perhaps due to our small sample size. Among parents of children 5 years of age or older, we did find that a lower time impact of caregiving was associated with higher mental QoL when parents reported less problem-focused coping but with lower mental QoL with greater use of problem-focused coping. If this were confirmed in further studies, it may suggest that greater use of problem-focused coping can mitigate some of the challenges associated with the impact of caregiving on parents' time.

Our secondary analysis finding that coping strategies may be an effect modifier in the association between caregiving complexity and QoL is supported by prior research. For example,

within the autism literature, a number of studies have examined the role of coping strategies as potential modifiers of associations between child symptoms severity or stress and parental adjustment or QoL (66,95,98), with varying results. Two studies examined the association between child symptom severity and stress or maternal adjustment (66,98). Lyons et al (98) found emotion-oriented strategies moderated the relationship between stress and child symptom severity, indicating that parents who frequently use emotion-oriented strategies reported significantly more pessimism stress as symptom severity increased. Smith et al (66) found that lower emotion-focused coping and greater problem-focused coping was associated with increased maternal adjustment, irrespective of the level of symptom severity. Dardas and Ahmad (95) found that seeking social support and escape-avoidance coping, a strategy considered to be emotion-focused, moderated the association between parental stress and QoL. In that study, when parents reported greater use of both strategies to deal with stressful situations, this was significantly associated with greater QoL (95).

In summary, our systematic review and secondary analysis support the hypothesis that increased use of some coping strategies, including problem-focused strategies, is associated with improved psychological QoL among parents of children with chronic illness and that increased use of other strategies, including emotion-focused strategies, is associated with decreased psychological QoL. While these findings are consistent with a number of previous studies related to caregiving for children with chronic illness (35,92,93,95,99), Yeh (100) found that parenting stress initiated the use of both problem- and emotion-focused coping in caregivers of children with cancer. This could suggest that when faced with a stressful situation, parents may use a combination of different strategies to process the event and react in a suitable way.

A structured review of previously published qualitative studies (101) examined parents' experiences of living with a child with a long-term condition. From the 34 qualitative studies, the authors identified adaptation and coping to be a prominent feature associated with living with a child with a complex and long-term disorder. The review authors highlighted that while some parents adjusted well (102–104), improving their communication and organizational skills as a result of caring for their child (105,106), others experienced negative physical and emotional impacts (107–111). Our systematic review and survey analysis contribute to this body of literature by providing quantitative evidence that corroborates the importance of considering the ways in which parents of children with chronic illness adapt, and specifically the coping strategies they use, as potential contributors to their well-being. If our findings are supported by further evidence, particularly from prospective studies, the results highlight coping as a potential target for interventions designed to support families of children with chronic conditions including IMD. In particular, interventions that encourage the use of problem-focused strategies could be developed and evaluated with respect to their potential to improve parental adaptation and QoL.

Limitations and Directions for Future Research

One of the challenges with our secondary data analysis was the relatively small sample size, particularly for exploring interactions between caregiving complexity and coping. A larger sample size would enable these interactions to be explored and facilitate the inclusion of additional covariates in each regression model. For this reason, the findings of our interaction analysis must be interpreted with caution. In addition, we evaluated only two general approaches to coping (problem-focused and emotion-focused) in part because our sample size precluded separately evaluating all eight subscales of the Ways of Coping Checklist (WOCC). Although

the approach we used is consistent with the way in which coping has been defined and measured in previous studies (61), looking at each subscale separately as an additional analysis could provide more insight into the role of more specific strategies. In particular, we excluded the subscale that measures the strategy 'seeking social support', since this is not clearly a problem-focused nor an emotion-focused strategy. Using social support as a coping strategy has been reported as an important way for parents of chronic illness (77,112,113) and more specifically, other IMD, to deal with the stress associated with caring for their child (78,79,114). It has been found to be an important predictor of health related QoL in a sample of parents of children with IMD (77) and informal support systems were reported to be important in a sample of parent participants who took part in a recent qualitative study from the same cohort that formed the sampling frame for our survey (82).

In general, within the current coping literature there is lack of consistency with regards to the way coping strategies are described, defined, and measured. This proved to be problematic in the systematic review, while trying to synthesize existing evidence with regards to the way caregivers of children with chronic illness cope. For example, in parallel with the above discussion of our survey analysis, some previous studies separately examined several different coping subscales while others attempted to categorize the strategies into adaptive/maladaptive or problem- or emotion-focused coping. As described above, categorizing strategies in this way may lead to an over-simplification of the nature of coping and the degree to which it is helpful or adaptive (60,115–117). For example, some responses that are classified as maladaptive (e.g., behavioural disengagement, avoidance) are typically considered to be counter-productive but may be beneficial to use in some situations (118). Additionally, some strategies, such as seeking social support, may indicate the use of both emotion- and problem-focused coping (119). Future

studies should seek to clarify the conceptual underpinnings of coping as it relates to caregiving for children with chronic illness.

The use of cross-sectional study designs was a limitation in both our systematic review and survey analysis. A majority of the studies included in our review were cross-sectional in nature. In addition, chapter 3 of this project involved secondary data analysis of a cross-sectional survey. As described above, cross-sectional designs do not provide strong evidence in support of causal relationships. Therefore, our findings related to the associations of interest do not directly indicate that the caregiving complexity associated with caring for a child with a chronic illness, or coping strategies used by parents, causes increased or decreased parent QoL. An important gap in the literature is the question of whether or how coping affects parent QoL over time; prospective studies are needed to better understand the nature and direction of the associations among caregiving complexity, coping, and QoL. Longitudinal studies are also important because coping has been described as a dynamic process (117,120). The challenges associated with caring for children with IMD likely change over time. For example, the stress experienced by parents following diagnosis may be different than that after 5 years of disease management, which could differ still during metabolic decomposition or 10 years of managing disease treatment regimes. Examining coping strategies prospectively will provide greater insight into the adaptation process during these different stages in life; this will allow for better targeted caregiver intervention and support.

From this project, there is some evidence to support the role of coping strategies as a potential effect modifier in the association between caregiving complexity and parental QoL. An important direction for future research, particularly with a large sample size and prospective design, will be to further investigate this hypothesis. If future research corroborates our findings,

interventions that encourage the use of appropriate coping strategies may help parents learn to manage their caregiving demands and stress and reduce poor psychological outcomes (121,122). In particular, interventions that limit the use of emotion-focused strategies and promote the use of problem-focused coping strategies may be a means to promote parent QoL and reduce depressive symptoms (123).

Conclusion

Caregiving for a child who is chronically ill has been associated with stress and with adverse psychosocial outcomes (31,77,124–127). The findings of the two components of this thesis project highlight that specific groups of coping strategies may be associated with psychological QoL among parents of children with IMD or other chronic illnesses. Greater use of strategies considered to be less adaptive (particularly emotion-focused coping in our study of parents of children with IMD) may be associated with poorer psychological QoL while those considered to be more adaptive may be associated with improved QoL. We identified limited evidence that some coping strategies may also modify the association between the complexity of caregiving and QoL for parents of children with an IMD; and we highlight a need to further investigate this possibility. Collectively our findings support the development and evaluation of interventions that may help parents to develop adaptive coping strategies, suggesting the potential for such interventions to promote improved QoL, allowing parents to fulfill their goals while also meeting the medical, emotional, and developmental needs of their children. IMD are a group of rare diseases that often require lifelong treatment and intense home management. Interventions targeted at improving parental adaptation may help to improve the well-being of both parents and children, as a component of family-centred care.

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Appendix B

Supplement 1. CIMDRN patient and family experiences survey

Canadian Inherited Metabolic Disease Research Network
Patient and family experiences survey

We are inviting you to participate in a survey about your experiences as a parent or guardian of a child with an inherited metabolic disease (IMD). You are being invited because you have at least one child enrolled in the clinical data collection study of the Canadian Inherited Metabolic Disease Research Network (CIMDRN) and you indicated that you would like to be contacted to be invited to participate in a survey. We are interested in your child's health and well-being, your experiences with the health care system for your child's disease, and your own health and well-being.

Completing and returning this questionnaire indicates that you consent to participate in this survey study. If you wish to participate, please complete this questionnaire and mail it back to us using the pre-stamped envelope we provided.

INSTRUCTIONS:

1) **Throughout this questionnaire when we refer to "your child", we are referring to your child who has an IMD and was born in the year ####.**

2) If you have more than one child with an IMD who is also a participant in CIMDRN, we have included a shorter questionnaire in this package for your other child (or children) with an IMD who is a CIMDRN participant. Please complete that questionnaire as well.

3) This questionnaire should be completed by the parent or guardian in the household who is most knowledgeable about your child.

4) Please answer the questions by checking the appropriate box (☑) or by circling the appropriate number.

5) There are no right or wrong answers. If you are unsure how to answer a question, please give the best answer you can. Your individual answers will remain confidential.

6) Certain questions may look alike but each one is different. Some questions may ask about problems that your child does not have. Please try to answer each question as it is important for us to know that your child does not have these problems.

7) Some sections of this questionnaire have their own instructions. Please read all instructions carefully as you answer the questions.

Study ID: _____

Part 1: Child health questionnaire

The following questions ask about your child's health and well-being. If you are unsure how to answer a question, give the best response you can. It is very important that you fill in each question.

Your child's global health

		Excellent	Very good	Good	Fair	Poor
1.1	In general, would you say your child's health is:	☐	☐	☐	☐	☐

Your child's physical activities

The following questions ask about physical activities your child might do during a day.

		Yes, limited a lot	Yes, limited some	Yes, limited a little	No, not limited
1.2	During the past 4 weeks, has your child been limited in any of the following activities due to health problems?				
	a. Doing things that take a lot of energy, such as playing	☐	☐	☐	☐
	b. Doing things that take some energy such as riding a bike or skating?	☐	☐	☐	☐
	c. Ability (physically) to get around the neighbourhood,	☐	☐	☐	☐
	d. Walking one block or climbing one flight of stairs?	☐	☐	☐	☐
	e. Bending, lifting, or stooping?	☐	☐	☐	☐
	f. Taking care of him/herself, that is, eating, dressing, bathing, or going to the toilet?	☐	☐	☐	☐

Your child's everyday activities

		Yes, limited a lot	Yes, limited some	Yes, limited a little	No, not limited
1.3	During the past 4 weeks, has your child's school work or activities with friends been limited in any of the following ways due to EMOTIONAL difficulties or problems with his/her BEHAVIOUR?				
	a. Limited in the KIND of schoolwork or activities with friends	☐	☐	☐	☐
	b. Limited in the AMOUNT of time he/she could spend on schoolwork or activities with friends	☐	☐	☐	☐
	c. Limited in PERFORMING schoolwork or activities with	☐	☐	☐	☐

1.4 During the past 4 weeks, has your child's school work or activities with friends been limited in any of the following ways due to problems with his/her PHYSICAL health?

	Yes, limited a lot	Yes, limited some	Yes, limited a little	No, not limited
a. Limited in the KIND of schoolwork or activities with friends	☐	☐	☐	☐
b. Limited in the AMOUNT of time he/she could spend on schoolwork or activities with friends	☐	☐	☐	☐

Pain

1.5 During the past 4 weeks, how much bodily pain or discomfort has your child had?

None	Very mild	Mild	Moderate	Severe	Very severe
☐	☐	☐	☐	☐	☐

1.6 During the past 4 weeks, how often has your child had bodily pain or discomfort?

None of the time	Once or twice	A few times	Fairly often	Very often	Every/almost every day
☐	☐	☐	☐	☐	☐

Behaviour

Below is a list of items that describe children's behaviour or problems they sometimes have.

1.7 How often during the past 4 weeks did each of the following statements describe your child?

	Very often	Fairly often	Some--times	Almost never	Never
a. Argued a lot?	☐	☐	☐	☐	☐
b. Had difficulty concentrating or paying attention?	☐	☐	☐	☐	☐
c. Lied or cheated?	☐	☐	☐	☐	☐
d. Stole things inside or outside the home?	☐	☐	☐	☐	☐
e. Had temper tantrums or a hot temper?	☐	☐	☐	☐	☐

1.8 Compared to other children your child's age, in general would you say his/her behaviour is:

Excellent	Very good	Good	Fair	Poor
☐	☐	☐	☐	☐

Well-being

The following phrases are about children's moods.

1.9 During the past 4 weeks, how much of the time do you think your child:

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Felt like crying?	☐	☐	☐	☐	☐
b. Felt lonely?	☐	☐	☐	☐	☐
c. Acted nervous?	☐	☐	☐	☐	☐
d. Acted bothered or upset?	☐	☐	☐	☐	☐
e. Acted cheerful?	☐	☐	☐	☐	☐

Self-esteem

The following ask about your child's satisfaction with self, school, and others. It may be helpful if you keep in mind how other children your child's age might feel about these areas.

1.10 During the past 4 weeks, how satisfied do you think your child has felt about:

	Very satisfied	Somewhat satisfied	Neither satisfied nor dissatisfied	Somewhat dissatisfied	Very dissatisfied
a. His/her school ability?	☐	☐	☐	☐	☐
b. His/her athletic ability?	☐	☐	☐	☐	☐
c. His/her friendships?	☐	☐	☐	☐	☐
d. His/her looks/appearance?	☐	☐	☐	☐	☐
e. His/her life overall?	☐	☐	☐	☐	☐

Your child's health

The following statements are about health in general.

1.11 How true or false is the statement for your child?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a. My child seems to be less healthy than other	☐	☐	☐	☐	☐
b. My child has never been seriously ill	☐	☐	☐	☐	☐
c. When there is something going around my	☐	☐	☐	☐	☐
d. I expect my child will have a very healthy life	☐	☐	☐	☐	☐
e. I worry about my child's health more than other	☐	☐	☐	☐	☐

1.12 Compared to one year ago, how would you rate your child's health now:

Much better now than 1 year ago	Somewhat better now than 1 year ago	About the same now as 1 year ago	Somewhat worse now than 1 year ago	Much worse now than 1 year ago
☐	☐	☐	☐	☐

You and your family

1.13 During the past 4 weeks, how MUCH emotional worry or concern did each of the following cause YOU?

	None at all	A little bit	Some	Quite a bit	A lot
a. Your child's physical health	☐	☐	☐	☐	☐
b. Your child's emotional well-being or behaviour	☐	☐	☐	☐	☐
c. Your child's attention or learning abilities	☐	☐	☐	☐	☐

1.14 During the past 4 weeks, were you LIMITED in the amount of time you had for your own needs because of:

	Yes, limited a lot	Yes, limited some	Yes, limited a little	No, not limited
a. Your child's physical health	☐	☐	☐	☐
b. Your child's emotional well-being or behaviour?	☐	☐	☐	☐
c. Your child's attention or learning abilities	☐	☐	☐	☐

1.15 During the past 4 weeks, how often has your child's health or behaviour:

	Very often	Fairly often	Some-- times	Almost never	Never
a. Limited the types of activities you could do as a	☐	☐	☐	☐	☐
b. Interrupted various everyday family activities (eating meals, watching tv)?	☐	☐	☐	☐	☐
c. Limited your ability as a family to "pick up and go"	☐	☐	☐	☐	☐
d. Caused tension or conflict in your home?	☐	☐	☐	☐	☐
e. Been a source of disagreements or arguments in	☐	☐	☐	☐	☐
f. Caused you to cancel or change plans (personal or work) at the last minute?	☐	☐	☐	☐	☐

1.16 Sometimes families may have difficulty getting along with one another. They do not always agree and they may get angry. In general, how would you rate your family's ability to get along with one another?

Excellent	Very good	Good	Fair	Poor
☐	☐	☐	☐	☐

Part 2: Experiences with care in the metabolic clinic

*The following questions ask about your experiences with care for your child. First, we wish to know about your perceptions of the care you have been receiving over the **past year** from the health care organization that provides specialized metabolic services to your child. In the questions below, when we ask about the "organization", we mean the **metabolic clinic** where your child receives care.*

The care that you and your child receive from this organization may bring you into contact with many individuals. The questions on this form are grouped by who these contacts are, as described below.

***PEOPLE**: refers to those individuals who work directly with you or your child. These **may include** metabolic physicians, dietitians, nurses, genetic counsellors, etc.*

***ORGANIZATION**: refers to all staff from the health care organization, whether involved directly with your child or not. In addition to health care people they **may include** support staff such as office staff, housekeepers, administrative personnel, etc.*

The questions are based on what parents, like yourself, have told us about the way care is sometimes offered.

*For each question, please indicate how much the event or situation happens to you. You are asked to respond by circling **one** number from 1 (Not at All) to 7 (To a Very Great Extent) that you feel best fits your experience. Please note that the zero value (0) is used only if the situation described does not apply to you.*

When answering these questions, we would like you to think about your child's metabolic clinic as the health care organization.

***PEOPLE**: refers to those individuals who work directly with you or your child. These **may include** metabolic physicians, dietitians, nurses, genetic counsellors, etc.*

IN THE PAST YEAR, TO WHAT EXTENT DO THE PEOPLE WHO WORK WITH YOUR CHILD...	Indicate how much this event or situation happens to you.							
	To a Very Great Extent	To a Great Extent	To a Fairly Great Extent	To a Moderate Extent	To a Small Extent	To a Very Small Extent	Not at All	Not Applicable
2.1 ...help you to feel competent as a parent?	7	6	5	4	3	2	1	0
2.2 ...provide you with written information about what your child is doing in treatment?	7	6	5	4	3	2	1	0
2.3 ...provide a caring atmosphere rather than just give you information?	7	6	5	4	3	2	1	0

IN THE PAST YEAR, TO WHAT EXTENT DO THE PEOPLE WHO WORK WITH YOUR CHILD...	Indicate how much this event or situation happens to you.							
	To a Very Great Extent	To a Great Extent	To a Fairly Great Extent	To a Moderate Extent	To a Small Extent	To a Very Small Extent	Not at All	Not Applicable
2.4 ...let you choose when to receive information and the type of information you want?	7	6	5	4	3	2	1	0
2.5 ...look at the needs of your "whole" child (e.g., at mental, emotional, and social needs) instead of just at physical needs?	7	6	5	4	3	2	1	0
2.6 ...make sure that at least one team member is someone who works with you and your family over a long period of time?	7	6	5	4	3	2	1	0
2.7 ...fully explain treatment choices to you?	7	6	5	4	3	2	1	0
2.8 ...provide opportunities for you to make decisions about treatment?	7	6	5	4	3	2	1	0
2.9 ...provide enough time to talk so you don't feel rushed?	7	6	5	4	3	2	1	0
2.10 ...plan together so they are all working in the same direction?	7	6	5	4	3	2	1	0
2.11 ...treat you as an <u>equal</u> rather than just as the parent of a patient (e.g., by not referring to you as "Mom" or "Dad")?	7	6	5	4	3	2	1	0
2.12 ...give you information about your child that is consistent from person to person?	7	6	5	4	3	2	1	0
2.13 ...treat you as an individual rather than as a "typical" parent of a child with a disease?	7	6	5	4	3	2	1	0
2.14 ...provide you with written information about your child's progress?	7	6	5	4	3	2	1	0
2.15 ...tell you about the results from assessments?	7	6	5	4	3	2	1	0

***ORGANIZATION**: refers to all staff from the health care organization, whether involved directly with your child or not. In addition to health care people they **may include** support staff such as office staff, housekeepers, administrative personnel, etc.*

IN THE PAST YEAR, TO WHAT EXTENT DOES THE ORGANIZATION WHERE YOU RECEIVE SERVICES...	**Indicate how much this event or situation happens to you.**							
	To a Very Great Extent	To a Great Extent	To a Fairly Great Extent	To a Moderate Extent	To a Small Extent	To a Very Small Extent	Not at All	Not Applicable
2.16 ...give you information about the types of services offered at the organization or in your community?	7	6	5	4	3	2	1	0
2.17 ...have information available about your child's disease (e.g., its causes, how it progresses, future outlook)?	7	6	5	4	3	2	1	0
2.18 ...provide opportunities for the entire family to obtain information?	7	6	5	4	3	2	1	0
2.19 ...have information available to you in various forms, such as a booklet, kit, video, etc.?	7	6	5	4	3	2	1	0
2.20 ...provide advice on how to get information or to contact other parents (e.g., organization's parent resource library)?	7	6	5	4	3	2	1	0

Part 3. Satisfaction and experiences with metabolic and other health services

*In this section, we ask further questions about your satisfaction and experiences with the care your child has received within **the metabolic clinic.** We then ask about your experiences with other health services your child may have received. Please check the box next to the answer that best describes your experience.*

3.1 In the **past year**, about how many times have you visited the metabolic clinic for your child's care?

- ☐ Not at all in the past year →→ If Not at all, go to question # 3.7
- ☐ 1-2 times
- ☐ 3-5 times
- ☐ 6-9 times
- ☐ At least 10 times

3.2 How would you rate your overall satisfaction with your experience in the metabolic clinic for your child's care, in the past year?

- ☐ Very dissatisfied
- ☐ Somewhat dissatisfied
- ☐ Neither satisfied nor dissatisfied
- ☐ Somewhat satisfied
- ☐ Very satisfied

3.3 When considering your answer to question 3.2, how important were each of the following factors in contributing to your overall level of satisfaction?

	Essential	Very important	Somewhat important	Not important
a. Location of the clinic in relation to home	☐	☐	☐	☐
b. Wait time to get an appointment	☐	☐	☐	☐
c. Wait time to see a health care provider	☐	☐	☐	☐
d. Metabolic health care providers' knowledge about your child's needs	☐	☐	☐	☐
e. Appropriate treatment for your child's	☐	☐	☐	☐
f. Metabolic health care providers' communication with you / your child	☐	☐	☐	☐
g. Amount of time that metabolic health care providers spend with you / your	☐	☐	☐	☐
h. Attitude of metabolic health care providers	☐	☐	☐	☐
i. Communication and coordination of metabolic health care providers with	☐	☐	☐	☐
j. Attention to non-medical needs (for example, comfort in waiting area)	☐	☐	☐	☐

3.4 In the past year, have you had an experience at the metabolic clinic for your child's care that was either *so positive* or *so negative*, you were still thinking about it one week later?

☐☐ Yes, a positive experience
☐☐ Yes, a negative experience
☐☐ No

If you answered YES to question 3.4, please briefly describe the experience:

_____

_____

_____

_____

3.5 How do you typically travel from your home to the metabolic clinic for your child's care?

☐☐ Drive own vehicle
☐☐ Use general public transit (e.g., bus or subway)
☐☐ Use special transport services (e.g., equipped with wheel chair accessibility)
☐☐ Other (please specify):_____

3.6 About how long does it take you to travel from your home to the metabolic clinic for your child's care?

☐☐ Less than 30 minutes
☐☐ At least 30 minutes but less than one hour
☐☐ From 1 to 2 hours
☐☐ More than 2 hours

Next, the following questions ask about your experiences with ***the emergency department.*** *Please check the box next to the answer that best describes your experience.*

3.7 In the **past year**, about how many times have you visited the emergency department for your child's care?

☐☐ Not at all in the past year →→ If Not at all, go to question # 3.11
☐☐ 1-2 times
☐☐ 3-5 times
☐☐ 6-9 times
☐☐ At least 10 times

3.8 How would you rate your overall satisfaction with your experience in the emergency department for your child's care, in the past year?

☐☐ Very dissatisfied
☐☐ Somewhat dissatisfied
☐☐ Neither satisfied nor dissatisfied
☐☐ Somewhat satisfied
☐☐ Very satisfied

3.9 When considering your answer to question 3.8, how important were each of the following factors in contributing to your overall level of satisfaction?

	Essential	Very important	Somewhat important	Not important
a. Wait time to see a physician	☐	☐	☐	☐
b. Health care providers' knowledge about	☐	☐	☐	☐
c. Appropriate treatment for your child's health problem	☐	☐	☐	☐
d. Health care providers' communication	☐	☐	☐	☐
e. Attitude of health care providers	☐	☐	☐	☐
f. Communication and coordination of	☐	☐	☐	☐
g. Pain management for your child	☐	☐	☐	☐
h. Attention to non-medical needs (for	☐	☐	☐	☐

3.10 In the past year, have you had an experience at the emergency department for your child's care that was either *so positive* or *so negative*, you were still thinking about it one week later?

☐☐ Yes, a positive experience
☐☐ Yes, a negative experience
☐☐ No

If you answered YES to question 3.10, please briefly describe the experience:

_____

_____

_____

_____

*Next, we wish to ask about your experiences with **the blood laboratory** (the place where you take your child for blood to be drawn for laboratory tests). Please check the box next to the answer that best describes your experience.*

3.11 In the past **year**, about how often have you visited a blood laboratory for your child to have blood drawn (for a blood test)?

☐☐ Not at all in the past year →→ If Not at all, go to question # 3.15
☐☐ 1-2 times
☐☐ 3-5 times
☐☐ 6-9 times
☐☐ 10-19 times
☐☐ At least 20 times

3.12 How would you rate your overall satisfaction with your experience at the blood laboratory, in the past year?

☐☐ Very dissatisfied
☐☐ Somewhat dissatisfied
☐☐ Neither satisfied nor dissatisfied
☐☐ Somewhat satisfied
☐☐ Very satisfied

3.13 When considering your answer to question 3.12, how important were each of the following factors in contributing to your overall level of satisfaction?

	Essential	Very important	Somewhat important	Not important
a. Hours of operation	☐	☐	☐	☐
b. Wait time to have blood drawn	☐	☐	☐	☐
c. Wait time to receive test results	☐	☐	☐	☐
d. Amount of blood needed	☐	☐	☐	☐
e. Complications or side effects associated with blood draw	☐	☐	☐	☐
f. Health care providers' communication	☐	☐	☐	☐
g. Attitude of health care providers	☐	☐	☐	☐
h. Pain management	☐	☐	☐	☐
i. Attention to non-medical needs (for example, comfort in waiting area)	☐	☐	☐	☐

3.14 In the past year, have you had an experience at the blood laboratory that was either *so positive* or *so negative*, you were still thinking about it one week later?

☐☐ Yes, a positive experience
☐☐ Yes, a negative experience
☐☐ No

If you answered YES to question 3.14, please briefly describe the experience:

_____

_____

_____

_____

*The following questions ask about your experiences when **your child stayed overnight in the hospital.** Please check the box next to the answer that best describes your experience.*

3.15 In the past **year**, about how often has your child stayed overnight in the hospital (please count the number of separate times that your child went to the hospital and was admitted overnight, not the number of nights that he or she stayed)?

☐☐ Not at all in the past year →→ If Not at all, go to question # 3.19
☐☐ 1 time
☐☐ 2 times
☐☐ 3-5 times
☐☐ At least 6 times

3.16 How would you rate your overall satisfaction with your experience with the care your child received while in the hospital overnight, in the past year?

☐☐ Very dissatisfied
☐☐ Somewhat dissatisfied
☐☐ Neither satisfied nor dissatisfied
☐☐ Somewhat satisfied
☐☐ Very satisfied

3.17 When considering your answer to question 3.16, how important were each of the following factors in contributing to your overall level of satisfaction?

	Essential	Very important	Somewhat important	Not important
a. Health care providers' knowledge about	☐	☐	☐	☐
b. Appropriate treatment for your child's health problem	☐	☐	☐	☐
c. Duration of hospital stay	☐	☐	☐	☐
d. Health care providers' communication with you / your child	☐	☐	☐	☐
e. Attitude of health care providers	☐	☐	☐	☐
f. Communication and coordination of health care providers with each other, for providers directly involved in your child's care while in hospital	☐	☐	☐	☐
g. Coordination with services at the hospital outside of direct care for your pharmacy)	☐	☐	☐	☐
h. Pain management for your child	☐	☐	☐	☐
i. Attention to non-medical needs (for	☐	☐	☐	☐

3.18 In the past year, have you had an experience with the care that your child received while in the hospital overnight that was either *so positive* or *so negative*, you were still thinking about it one week later?

☐☐ Yes, a positive experience
☐☐ Yes, a negative experience
☐☐ No

If you answered YES to question 3.18, please briefly describe the experience:

_____

_____

_____

_____

*The following questions ask about your experiences with **the pharmacy that you use most often for your child's medications and/or medical foods or supplements.** Please check the box next to the answer that best describes your experience.*

3.19 In the **past year**, about how often have you visited the pharmacy to order orreceive medications or medical foods or supplements for your child?

☐☐ Not at all in the past year →→ **If Not at all, go to Part 4 on the next page**
☐☐ One time
☐☐ More than one time, but less frequently than once per month
☐☐ At least once per month but less frequently than once per week
☐☐ At least once per week

3.20 How would you rate your overall satisfaction with your experience at the pharmacy, in the past year?

☐☐ Very dissatisfied
☐☐ Somewhat dissatisfied
☐☐ Neither satisfied nor dissatisfied
☐☐ Somewhat satisfied
☐☐ Very satisfied

3.21 When considering your answer to question 3.20, how important were each of the following factors in contributing to your overall level of satisfaction?

	Essential	Very important	Somewhat important	Not important	Not applicable
a. Hours of operation	☐	☐	☐	☐	☐
b. Pharmacy team's knowledge about your child's needs	☐	☐	☐	☐	☐
c. Availability of the medications or medical foods or supplements your	☐	☐	☐	☐	☐
d. Timely access to medications or medical foods or supplements	☐	☐	☐	☐	☐
e. Expenses that you had to cover in accessing medications or medical	☐	☐	☐	☐	☐
f. Correct product and dose received	☐	☐	☐	☐	☐
g. Pharmacy team's communication	☐	☐	☐	☐	☐
h. Attitude of pharmacy team	☐	☐	☐	☐	☐

3.22 In the past year, have you had an experience with the pharmacy that was either *so positive* or *so negative*, you were still thinking about it one week later?

☐☐ Yes, a positive experience
☐☐ Yes, a negative experience
☐☐ No

If you answered YES to question 3.22, please briefly describe the experience:

_____

_____

_____

_____

Part 4. Family experiences with care coordination

*The following questions ask about your experiences with the **coordination** of health care for your child. We are interested in how different health care services and providers work together.*

4.1 Your child's **main provider** is the doctor, physician assistant, nurse or other health care provider who knows the most about your child's health, and who is in charge of your child's care overall. Which of the following best describes your child's main provider?

☐☐ Physician in the metabolic clinic
☐☐ Dietitian in the metabolic clinic
☐☐ Nurse in the metabolic clinic
☐☐ Other provider in the metabolic clinic
☐☐ Family physician from outside the metabolic clinic
☐☐ Pediatrician from outside the metabolic clinic
☐☐ Other provider from outside the metabolic clinic
☐☐ Other (please specify): _____

*The questions in this section of the survey will refer to this provider as "**the main provider**." Please think of that person as you answer the questions.*

Getting help to manage your child's care

These first questions are about the people who may help you manage care, treatment and services for your child.

4.2 In the last 12 months, did your child visit more than one doctor's office or use more than one kind of health care service, such as physical or speech therapy, or community service, such as home health care or transportation services?

☐☐ Yes
☐☐ No

4.3 Did anyone in the main provider's office help you to manage your child's care or treatment from different doctors or care?

☐☐ Not applicable: my child did not visit more than one doctor's office or use more than one service
☐☐ No
☐☐ Yes – if yes, who helped you the most? (please check one only)
- ☐☐ Your child's main provider
- ☐☐ Another doctor, dietitian, or nurse in the main provider's office
- ☐☐ A clerk or receptionist in the main provider's office
- ☐☐ A care coordinator in the main provider's office
- ☐☐ A social worker in the main provider's office
- ☐☐ A care manager or case manager in the main provider's office
- ☐☐ Someone else in the main provider's office

4.4 Did anyone outside the main provider's office help you to manage your child's care or treatment from different doctors or care providers?

☐☐ Not applicable: my child did not visit more than one doctor's office or use more than one service
☐☐ No
☐☐ Yes – if yes, who helped you the most? (please check one only)
- ☐☐ Another doctor, dietitian, or nurse from a different office/clinic
- ☐☐ A care coordinator who isn't a part of the main provider's staff
- ☐☐ A social worker who isn't a part of the main provider's staff
- ☐☐ A care or case manager who isn't a part of the main provider's staff
- ☐☐ Someone else who isn't a part of the main provider's office

4.5 If someone helped you manage your child's care in the last 12 months, thinking of the person who helped you the MOST (from within or outside your main provider's office), did the person who helped you with managing your child's care…

	Yes definitely	Yes somewhat	No	Not applicable (did not need this or no one helped me)
a. Know the important information about your	☐	☐	☐	☐
b. Seem informed and up-to-date about the care your child got from other providers?	☐	☐	☐	☐
c. Support your decisions about what is best	☐	☐	☐	☐
d. Help you to get appointments to visit other providers?	☐	☐	☐	☐
e. Help you to get special medical equipment that your child needed like a special bed,	☐	☐	☐	☐

4.6 In the last 12 months, did you know how to contact the person who helped you most with managing your child's care when you needed help or had a question?

☐☐ Yes
☐☐ No
☐☐ Not applicable (no one helped me to manage my child's care)

4.7 Overall, how often did you get the help you needed to manage your child's care or treatment from **different** doctors or care providers in the last 12 months?

- ☐☐ Never
- ☐☐ Sometimes
- ☐☐ Usually
- ☐☐ Always
- ☐☐ Not applicable (my child did not receive treatment from different doctors or care providers in the last 12 months)

4.8 Overall, how satisfied or dissatisfied were you with help you received in managing your child's care or treatment in the last 12 months?

- ☐☐ Very satisfied
- ☐☐ Somewhat satisfied
- ☐☐ Somewhat dissatisfied
- ☐☐ Very dissatisfied
- ☐☐ Not applicable (my child did not receive treatment from different doctors or care providers in the last 12 months)

Your child's care from specialists and receipt of community services

The next few questions ask about your experiences with getting care for your child from specialists. We are also interested in your experiences with getting community services for your child.

4.9 Specialists are doctors like surgeons, heart doctors, allergy doctors, mental health doctors, and other doctors who specialize in one area of health care. During the last 12 months, did the main provider tell you that your child needed to see a specialist from outside the metabolic clinic?

- ☐☐ Yes
- ☐☐ No

4.10 Did the person who helped you with managing your child's care contact you to make sure your child got an appointment to see a specialist?

- ☐☐ Yes
- ☐☐ No
- ☐☐ Not applicable (my child did not need to see a specialist or no one helped me to manage my child's care)

4.11 Community services are services to help maintain your and your child's health and well-being, which may or may not be ordered by one of your child's doctors. This can include things like home health care, early intervention programs, respite care, help with transportation, and parent or caregiver support services. In the last 12 months, did you or your child need or use community services?

- ☐☐ Yes
- ☐☐ No

4.12 Which community services did you or your child receive over the past 12 months, related to your child's care? (Please check all that apply)

- ☐☐ Home health care (e.g., nursing support, personal support worker)
- ☐☐ Community-based early intervention programs (e.g., for speech and language)
- ☐☐ Community source for special medical equipment like a special bed, wheelchair, orthotics, or feeding tube supplies, to be used at home
- ☐☐ Special transportation accommodations (e.g., paratransit)
- ☐☐ Received help paying for special transportation
- ☐☐ Respite care
- ☐☐ Other (please specify):_____
- ☐☐ None of these (we did not need nor use community services related to my child's care)

4.13 In the past 12 months, did you have problems accessing any of the community services that you or your child needed? (Please check one response)

- ☐☐ Not applicable (we did not need community services related to my child's care)
- ☐☐ No
- ☐☐ Yes -- If yes, how would you describe the problems you experienced in accessing community services for you or your child? (Please check one or both)
  - ☐☐ Financial barriers (e.g., related to insurance coverage)
  - ☐☐ Non-financial barriers (e.g., long wait times)

If yes (you experienced problems in accessing services), please briefly describe the problems you experienced in accessing community services:

_____

_____

_____

4.14 Did the person who helped you with managing your child's care help you to get the community services you or your child needed?

- ☐☐ Yes
- ☐☐ No
- ☐☐ Not applicable (no one helped me to manage my child's care or my child did not need community services)

4.15 In the past 12 months, which of the following expenses have you or others in your household paid **from your personal or family income** to care for your child?

- ☐☐ Home health care (e.g., nursing support, personal support worker)
- ☐☐ Community-based early intervention programs (e.g., for speech and language)
- ☐☐ Other (e.g., occupational therapy)
- ☐☐ Medical equipment (e.g., special bed, wheelchair, orthotics, feeding tube supplies)
- ☐☐ Special transportation accommodations (e.g., paratransit)
- ☐☐ Respite care
- ☐☐ Medications
- ☐☐ Medical foods or supplements
- ☐☐ Other (please specify): _____
- ☐☐ None

Summaries of your child's visits and care plans

The next set of questions asks about different ways in which you might get information about the care your child is receiving. We are interested in summaries you might have received after visiting the main provider's office or between visits, and written care plans that your provider may have created.

4.16 A written visit summary sums up what happened during your child's visit to a health care provider. A written visit summary can be available on paper, on a web site, through an app, or sent by email. In the last 12 months, did anyone at the main provider's office give you a written visit summary after your child's visits?

☐☐ No
☐☐ Yes – If yes, how often did the written visit summaries you got from the main provider's office include…

	Never	Sometimes	Always	Not applicable
a. A list of your child's health problems at	☐	☐	☐	☐
b. An up-to-date list of all the prescription your child is taking?	☐	☐	☐	☐
c. An up-to-date list of all the over-the-	☐	☐	☐	☐
d. A list of your child's allergies?	☐	☐	☐	☐
e. The names of all the specialist doctors	☐	☐	☐	☐
f. The plan for follow-up care for your child after the visit?	☐	☐	☐	☐
g. What to do if your child had a problem	☐	☐	☐	☐

4.17 In the last 12 months, how often was the written visit summary you got from the main provider's office easy to understand?

☐☐ Never
☐☐ Sometimes
☐☐ Always
☐☐ Not applicable (I did not receive a written summary from the main provider's office)

4.18 In the last 12 months, how often was the written visit summary you got from the main provider's office useful to you and your family?

☐☐ Never
☐☐ Sometimes
☐☐ Always
☐☐ Not applicable (I did not receive a written summary from the main provider's office)

4.19 In the last 12 months, did the main provider's office have a web site or app you could use between visits to look up information about your child's visits and health care?

☐☐ Yes
☐☐ No
☐☐ I don't know if my child's main provider's office has a web site or app

4.20 A shared care plan is a written document that contains information about your child's active health problems, medicines he or she is taking, special considerations that all people caring for your child should know, goals for your child's health, growth and development, and steps to take to reach those goals. Has the main provider created a shared care plan for your child?

☐☐ Yes
☐☐ No
☐☐ I don't know if my child's main provider has created a shared care plan for my child

4.21 An emergency care plan is a written document that contains important information about your child's health, treatment and medications. It also includes special considerations that all people caring for your child should know, for example, how your child lets you know he or she is in pain, or how to communicate with your child if he or she can't hear or speak. Families often bring the emergency care plan when they take a child to an emergency room or urgent care clinic. Has the main provider created an emergency care plan for your child?

☐☐ Yes
☐☐ No

Coordination with school

The next set of questions asks about your child's experiences in school.

4.22 In the last 12 months, did your child attend school?

☐☐ Yes
☐☐ No →→ If No, go to Part 5 on the next page

4.23 In the last 12 months, have you encountered any problems with the day-to-day management of your child's condition at school?

☐☐ Yes – if yes, which of the following problems have you encountered? (please check one only)
- ☐☐ Availability of appropriate foods at school
- ☐☐ Availability of appropriate storage for special food brought from home
- ☐☐ Administration of medication, supplements, or medical foods by school staff
- ☐☐ Challenges in communicating with school staff about your child's day-to-day needs
- ☐☐ Challenges in receiving support/cooperation from school staff with your child's day-to-day needs

☐☐ No

4.24 Because of his or her health condition does your child have any difficulty learning, understanding, or paying attention in class?

☐☐ Yes
☐☐ No →→ If No, go to Part 5 on the next page

4.25 In the last 12 months, did anyone from the main provider's office contact staff at your child's school to make sure they understood how your child's health condition affected his or her ability to learn, understand or pay attention in class?

☐☐ Yes
☐☐ No
☐☐ I don't know

Part 5: Your health and well-being

*This section asks for your views about **your** health. This information will help keep track of how you feel and how well you are able to do your usual activities. For each of the following questions, please mark the one box that best describes your answer.*

5.1 In general, would you say your health is:

Excellent	Very good	Good	Fair	Poor
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

5.2 The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☐ 2	☐ 3
b Climbing several flights of stairs	☐ 1	☐ 2	☐ 3

5.3 During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Accomplished less than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Were limited in the kind of work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

5.4 During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Accomplished less than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Did work or other activities less carefully than usual	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

5.5 During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

5.6 These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks…

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a Have you felt calm and peaceful?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Did you have a lot of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c Have you felt downhearted and depressed?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

5.7 During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Part 6: Parent / caregiver behaviours

To respond to the following statements, please take a few moments and ***think about a stressful situation that you have recently experienced in relation to your child's disease or in providing care for your child****.*

By "stressful" we mean a situation that was difficult or troubling for you, either because you felt distressed about what happened, or because you had to use considerable effort to deal with the situation. As you respond to each of the following statements, please keep this stressful situation in mind. Please read each item below and indicate to what extent you used it in the situation.

		Not used 0	Used somewhat 1	Used quite a bit 2	Used a great deal 3
6.1	Just concentrated on what I had to do next – the next step.	0☐	1☐	2☐	3☐
6.2	I tried to analyze the problem in order to	0☐	1☐	2☐	3☐
6.3	Turned to work or substitute activity to take my mind off things.	0☐	1☐	2☐	3☐
6.4	I felt that time would make a difference – the	0☐	1☐	2☐	3☐
6.5	Bargained or compromised to get something positive from the situation.	0☐	1☐	2☐	3☐
6.6	I did something which I didn't think would work,	0☐	1☐	2☐	3☐
6.7	Tried to get the person responsible to change his or her mind.	0☐	1☐	2☐	3☐
6.8	Talked to someone to find out more about the	0☐	1☐	2☐	3☐
6.9	Criticized or lectured myself.	0☐	1☐	2☐	3☐
6.10	Tried not to burn my bridges, but leave things	0☐	1☐	2☐	3☐
6.11	Hoped a miracle would happen.	0☐	1☐	2☐	3☐
6.12	Went along with fate;; sometimes I just have bad	0☐	1☐	2☐	3☐
6.13	Went on as if nothing had happened.	0☐	1☐	2☐	3☐
6.14	I tried to keep my feelings to myself.	0☐	1☐	2☐	3☐
6.15	Looked for the silver lining, so to speak;; tried to look on the bright side of things.	0☐	1☐	2☐	3☐
6.16	Slept more than usual.	0☐	1☐	2☐	3☐
6.17	I expressed anger to the person(s) who caused the problem.	0☐	1☐	2☐	3☐

		Not used 0	Used somewhat 1	Used quite a bit 2	Used a great deal 3
6.18	Accepted sympathy and understanding from someone.	0☐	1☐	2☐	3☐
6.19	I told myself things that helped me to feel better.	0☐	1☐	2☐	3☐
6.20	I was inspired to do something creative.	0☐	1☐	2☐	3☐
6.21	Tried to forget the whole thing.	0☐	1☐	2☐	3☐
6.22	I got professional help.	0☐	1☐	2☐	3☐
6.23	Changed or grew as a person in a good way.	0☐	1☐	2☐	3☐
6.24	I waited to see what would happen before doing anything.	0☐	1☐	2☐	3☐
6.25	I apologized or did something to make up.	0☐	1☐	2☐	3☐
6.26	I made a plan of action and followed it.	0☐	1☐	2☐	3☐
6.27	I accepted the next best thing to what I wanted.	0☐	1☐	2☐	3☐
6.28	I let my feelings out somehow.	0☐	1☐	2☐	3☐
6.29	Realized I brought the problem on myself.	0☐	1☐	2☐	3☐
6.30	I came out of the experience better than when I went in.	0☐	1☐	2☐	3☐
6.31	Talked to someone who could do something concrete about the problem.	0☐	1☐	2☐	3☐
6.32	Got away from it for a while;; tried to rest or take a vacation.	0☐	1☐	2☐	3☐
6.33	Tried to make myself feel better by eating, drinking, smoking, using drugs or medication, etc.	0☐	1☐	2☐	3☐
6.34	Took a big chance or did something very risky.	0☐	1☐	2☐	3☐
6.35	I tried not to act too hastily or follow my first hunch.	0☐	1☐	2☐	3☐
6.36	Found new faith.	0☐	1☐	2☐	3☐
6.37	Maintained my pride and kept a stiff upper lip.	0☐	1☐	2☐	3☐

		Not used 0	Used somewhat 1	Used quite a bit 2	Used a great deal 3
6.38	Rediscovered what is important in life.	0☐	1☐	2☐	3☐
6.39	Changed something so things would turn out all right.	0☐	1☐	2☐	3☐
6.40	Avoided being with people in general.	0☐	1☐	2☐	3☐
6.41	Didn't let it get to me;; refused to think too much about it.	0☐	1☐	2☐	3☐
6.42	I asked a relative or friend I respected for advice.	0☐	1☐	2☐	3☐
6.43	Kept others from knowing how bad things were.	0☐	1☐	2☐	3☐
6.44	Made light of the situation;; refused to get too serious about it.	0☐	1☐	2☐	3☐
6.45	Talked to someone about how I was feeling.	0☐	1☐	2☐	3☐
6.46	Stood my ground and fought for what I wanted.	0☐	1☐	2☐	3☐
6.47	Took it out on other people.	0☐	1☐	2☐	3☐
6.48	Drew on my past experiences;; I was in a similar situation before.	0☐	1☐	2☐	3☐
6.49	I knew what had to be done, so I doubled my efforts to make things work.	0☐	1☐	2☐	3☐
6.50	Refused to believe that it had happened.	0☐	1☐	2☐	3☐
6.51	I made a promise to myself that things would be different next time.	0☐	1☐	2☐	3☐
6.52	Came up with a couple of different solutions to the problem.	0☐	1☐	2☐	3☐
6.53	Accepted it, since nothing could be done.	0☐	1☐	2☐	3☐
6.54	I tried to keep my feelings from interfering with other things too much.	0☐	1☐	2☐	3☐
6.55	Wished that I could change what had happened or how I felt.	0☐	1☐	2☐	3☐
6.56	I changed something about myself.	0☐	1☐	2☐	3☐
6.57	I daydreamed or imagined a better time or place than the one I was in.	0☐	1☐	2☐	3☐

		Not used 0	Used somewhat 1	Used quite a bit 2	Used a great deal 3
6.58	Wished that the situation would go away or somehow be over with.	0☐	1☐	2☐	3☐
6.59	Had fantasies or wishes about how things might	0☐	1☐	2☐	3☐
6.60	I prayed.	0☐	1☐	2☐	3☐
6.61	I prepared myself for the worst.	0☐	1☐	2☐	3☐
6.62	I went over in my mind what I would say or do.	0☐	1☐	2☐	3☐
6.63	I thought about how a person I admire would	0☐	1☐	2☐	3☐
6.64	I tried to see things from the other person's point of view.	0☐	1☐	2☐	3☐
6.65	I reminded myself how much worse things could	0☐	1☐	2☐	3☐
6.66	I jogged or exercised.	0☐	1☐	2☐	3☐

Part 7. Parent / caregiver feelings

	Below is a list of the ways you might have felt or behaved. Please check the boxes to tell us how often you have felt this way in the past week or so.	LAST WEEK				Nearly every day for 2 weeks
		Not at all *or* Less than 1 day	1-2 days	3-4 days	5-7 days	
7.1	My appetite was poor.	☐	☐	☐	☐	☐
7.2	I could not shake off the blues.	☐	☐	☐	☐	☐
7.3	I had trouble keeping my mind on what I was doing.	☐	☐	☐	☐	☐
7.4	I felt depressed.	☐	☐	☐	☐	☐
7.5	My sleep was restless.	☐	☐	☐	☐	☐
7.6	I felt sad.	☐	☐	☐	☐	☐
7.7	I could not get going.	☐	☐	☐	☐	☐
7.8	Nothing made me happy.	☐	☐	☐	☐	☐
7.9	I felt like a bad person.	☐	☐	☐	☐	☐
7.10	I lost interest in my usual activities.	☐	☐	☐	☐	☐
7.11	I slept much more than usual.	☐	☐	☐	☐	☐
7.12	I felt like I was moving too slowly.	☐	☐	☐	☐	☐
7.13	I felt fidgety.	☐	☐	☐	☐	☐
7.14	I wished I were dead.	☐	☐	☐	☐	☐
7.15	I wanted to hurt myself.	☐	☐	☐	☐	☐
7.16	I was tired all the time.	☐	☐	☐	☐	☐
7.17	I did not like myself.	☐	☐	☐	☐	☐
7.18	I lost a lot of weight without trying to.	☐	☐	☐	☐	☐
7.19	I had a lot of trouble getting to sleep.	☐	☐	☐	☐	☐
7.20	I could not focus on the important things.	☐	☐	☐	☐	☐

Part 8: You and your child

Finally, we would like to ask you questions about you and your child

8.1 Who lives with your child currently (please include **yourself** in the table below)?

Person	Relationship to your child	Age in years	Has this person been diagnosed with the same disease as your child?
1			☐☐ Yes ☐☐ No
2			☐☐ Yes ☐☐ No
3			☐☐ Yes ☐☐ No
4			☐☐ Yes ☐☐ No
5			☐☐ Yes ☐☐ No
6			☐☐ Yes ☐☐ No
7			☐☐ Yes ☐☐ No
8			☐☐ Yes ☐☐ No

8.2 How would you describe the size of the community where your child lives?

☐☐ Large city (population of 100,000 or more people)
☐☐ Medium-sized city (population of at least 30,000 but less than 100,000 people)
☐☐ Small community (population of at least 1,000 but less than 30,000 people)
☐☐ Rural area (population of less than 1,000 people)
☐☐ Other (please specify)_____

8.3 Is anyone helping you to complete this questionnaire?

☐☐ No
☐☐ Yes →→ If yes, who is helping you?
☐☐ Your spouse/partner
☐☐ Your child
☐☐ Other →→ If other, please specify:

_____

8.4 What is your relationship to this child? (Please check only one box)

☐☐ Biological parent
☐☐ Step parent
☐☐ Foster parent
☐☐ Adoptive parent
☐☐ Guardian
☐☐ Other (please explain below)

_____

_____

8.5 What is your gender?

☐☐ Male
☐☐ Female
☐☐ Other gender

8.6 What is your current age in years?

☐☐ Younger than 20 years
☐☐ 20-24
☐☐ 25-29
☐☐ 30-34
☐☐ 35-39
☐☐ 40-44
☐☐ 45-49
☐☐ 50 years or older

8.7 Which of the following best describes your current work status? (Please check only one box)

☐☐ Not working due to my child's health
☐☐ Not working for other reasons
☐☐ Looking for work outside of home
☐☐ Working full or part-time (either outside the home or at a home-based business)
☐☐ Full time homemaker
☐☐ Student
☐☐ Other (please specify):_____

8.8 What is the highest grade of school you have completed?

☐☐ Less than 8 years
☐☐ At least 8 years but did not complete high school
☐☐ Completed high school
☐☐ Completed vocational/technical training
☐☐ Completed college/university
☐☐ Completed graduate school

8.9 What is your current marital status? (Please check only one box)

☐☐ Married/Common Law
☐☐ Widowed
☐☐ Divorced
☐☐ Separated
☐☐ Never married

8.10 Were you born in Canada?

☐☐ Yes
☐☐ No →→ If no, please respond to the following two questions:

a. In what country were you born? (Please write name of country):

_____

b. In what year did you immigrate? (Please specify year):

_____

8.11 What language do you speak most often at home? (Please check only one box)

☐☐ English
☐☐ French
☐☐ Other (please specify):_____

8.12 Are you currently living with a spouse or a partner?

☐☐ Yes
☐☐ No →→ If no, go to question # 8.16

8.13 Which of the following best describes your spouse's/partner's current work status? (Please check only one box)

☐☐ Not working due to my child's health
☐☐ Not working for other reasons
☐☐ Looking for work outside of home
☐☐ Working full or part-time (either outside the home or at a home-based business)
☐☐ Full time homemaker
☐☐ Student
☐☐ Other (please specify):_____

8.14 What is the highest grade of school your spouse/partner has completed?

☐☐ Less than 8 years
☐☐ At least 8 years but did not complete high school
☐☐ Completed high school
☐☐ Completed vocational/technical training
☐☐ Completed college/university
☐☐ Completed graduate school

8.15 Was your spouse/partner born in Canada?

☐☐ Yes
☐☐ No →→ If no, please respond to the following two questions:

a. In what country was he or she born? (Please write name of country):

_____

b. In what year did he or she immigrate? (Please specify year if known):

_____

8.16 In which category is your total yearly **household** income before taxes? (Please check only one box)

- ☐☐ Less than $10,000
- ☐☐ $10,000 -- $19,999
- ☐☐ $20,000 -- $29,999
- ☐☐ $30,000 -- $39,999
- ☐☐ $40,000 -- $49,999
- ☐☐ $50,000 -- $59,999
- ☐☐ $60,000 -- $69,999
- ☐☐ $70,000 -- $79,999
- ☐☐ $80,000 -- $89,999
- ☐☐ $90,000 -- $99,99
- ☐☐ $100,000 or more
- ☐☐ Don't know

8.17 Thinking about your total family income, from which sources did your family receive income during the past year? (Please check all of the boxes that apply)

- ☐☐ Wage and salaries
- ☐☐ Income from self-employment
- ☐☐ Family allowance (baby bonus)
- ☐☐ Unemployment insurance or strike pay
- ☐☐ Worker's compensation
- ☐☐ Old Age Security, Guaranteed Income Supplement, Canada or Quebec Pension Plan, Retirement Pension Plan, Super-annulation
- ☐☐ Dividends and interests on bonds, deposits, and savings certificates
- ☐☐ Other government sources such as welfare, mother's allowance, etc.
- ☐☐ Other source(s), please specify: _____

We wish to express our sincere appreciation to you for participating in this study. Thank you!

Appendix C

Supplement 1. Full multivariate regression models and stratified analyses

Table 5 a). Multivariate regression of psychological QoL and covariates of interest in parents of children 5 years of age or older.

Independent variables	**Mental QOL (MCS)**			
	Model 1 (coping strategies) n=56 Adjusted R^2: 0.1974	Model 2 (caregiving complexity) n=66 Adjusted R^2: 0.2228	Model 3 (coping and caregiving complexity) n=55 Adjusted R^2: 0.2913	Model 4 (coping and caregiving complexity with significant covariates) n=55 Adjusted R^2: 0.5342
↑ Problem-focused coping	0.391 (-0.044, 0.827)		0.347 (-0.068, 0.762)	0.683 (0.282, 1.085)*
↑ Emotion-focused coping	-0.557 (-0.852, -0.262)*		-0.352 (-0.664, -0.039)*	-0.414 (-0.684, -0.145)*
↓ Parent emotion-impact		0.083 (-0.029, 0.196)	0.065 (-0.053, 0.183)	0.090 (-0.016, 0.195)
↓ Parent time-impact		0.092 (-0.002, 0.188)	0.082 (-0.050, 0.214)	0.078 (-0.041, 0.197)
Child characteristics				
Disease category				
Amino acid/ Urea cycle disorders (REF)	-	-	-	-
FAOD				-0.314 (-4.888, 4.259)
Other IMD				7.336 (2.175, 12.496)*
Caregiver characteristics				
Highest level of education				
High school education or less (REF)	-	-	-	-
Vocational/technical training				-9.067 (-16.139, -1.994)*

College/University				-5.897 (-10.817, -0.978)*
Graduate school				-6.257 (-12.760, 0.245)
Work status				
Working full- or part-time (REF)	-	-	-	-
Full-time homemaker				-9.561 (-15.220, -3.902)*
Other work status				-4.247 (-10.688, 2.194)
Time impact x problem focused coping				-0.014 (-0.027, -0.001)*

p<0.05, 95% confidence interval

Table 5 b). Multivariate regression of physical QoL and covariates of interest in parents of children 5 years of age or older.

Independent variables	**Physical QOL (PCS)**			
	Model 1 (coping strategies) n=56 Adjusted R^2: -0.0023	Model 2 (caregiving complexity) n=66 Adjusted R^2: -0.0080	Model 3 (coping and caregiving complexity) n=55 Adjusted R^2: 0.2913	Model 4 (coping and caregiving complexity with significant covariates) n=55 Adjusted R^2: -0.0935
↑ Problem-focused coping	0.154 (-0.121, 0.429)		0.152 (-0.133, 0.437)	0.055 (-0.266, 0.376)
↑ Emotion-focused coping	-0.124 (-0.310, 0.061)		-0.133 (-0.348, 0.081)	-0.125 (-0.351, 0.100)
↓ Parent emotion-impact		-0.026 (-0.094, 0.041)	-0.009 (-0.090, 0.072)	-0.026 (-0.116, 0.064)
↓ Parent time-impact		0.049 (-0.032, 0.129)	0.003 (-0.087, 0.094)	0.025 (-0.078, 0.128)
Child characteristics				
Disease category				
Amino acid/ Urea cycle disorders (REF)	-	-	-	-
FAOD				0.607 (-3.338, 4.551)
Other IMD				-2.312 (-6.778, 2.155)

Caregiver characteristics				
Highest level of education				
High school education or less (REF)	-	-	-	-
Vocational/technical training				2.813 (-3.291, 8.916)
College/University				2.338 (-1.880, 6.555)
Graduate school				3.791(-1.800, 9.382)
Work status				
Working full- or part-time (REF)	-	-	-	-
Full-time homemaker				-0.116 (-5.011, 4.779)
Other work status				1.539 (-3.882, 6.959)

p<0.05, 95% confidence interval

Table 5 c). Multivariate regression of depressive symptoms and covariates of interest in parents of children 5 years of age or older.

Independent variables	**Depressive symptoms (CESD-R)**			
	Model 1 (coping strategies) n=55 Adjusted R^2: 0.2881	Model 2 (caregiving complexity) n=64 Adjusted R^2: 0.1529	Model 3 (coping and caregiving complexity) n=54 Adjusted R^2: 0.3364	Model 4 (coping and caregiving complexity with significant covariates) n=54 Adjusted R^2: 0.5007
↑ Problem-focused coping	-0.254 (-0.607, 0.098)		-0.236 (-0.581, 0.109)	-0.281 (-0.611, 0.048)
↑ Emotion-focused coping	0.527 (0.287, 0.766)*		0.436 (0.173, 0.698)*	0.413 (0.178, 0.649)*
↓ Parent emotion-impact		-0.091 (-0.176, -0.006)*	-0.108 (-0.206, -0.009)*	-0.080 (-0.172, 0.013)
↓ Parent time-impact		-0.025 (-0.126, 0.076)	0.052 (-0.059, 0.162)	0.009 (-0.097, 0.115)
Child characteristics				
Disease category				

Amino acid/ Urea cycle disorders (REF)	-	-	-	-
FAOD				0.829 (-3.237, 4.896)
Other IMD				-3.916 (-8.508, 0.676)
Caregiver characteristics				
Highest level of education				
High school education or less (REF)	-	-	-	-
Vocational/technical training				8.455 (2.187, 14.722)*
College/University				5.294 (0.918, 9.671)*
Graduate school				3.464 (-2.272, 9.201)
Work status				
Working full- or part-time (REF)	-	-	-	-
Full-time homemaker				7.666 (2.625, 12.708)*
Other work status				-4.255 (-9.828, 1.319)

p<0.05, 95% confidence interval

Table 6 a). Multivariate regression of psychological health and covariates of interest in parents of children less than 5 years of age.

Independent variables	**Mental QOL (MCS)**			
	Model 1 (coping strategies) n=41 Adjusted R^2: 0.3215	Model 2 (caregiving complexity) n=44 Adjusted R^2: 0.3254	Model 3 (coping and caregiving complexity) n=41 Adjusted R^2: 0.5077	Model 4 (coping and caregiving complexity with significant covariates) n=41 Adjusted R^2: 0.7040
↑ Problem-focused coping	0.746 (0.231, 1.261)*		0.813 (0.370, 1.255)*	0.775 (0.419, 1.132)*
↑ Emotion-focused coping	-0.689 (-0.995, -0.383)*		-0.484 (-0.768, -0.200)*	-0.332 (-0.580, -0.084)*
↓ Parent emotion-impact		0.038 (-0.113, 0.189)	0.036 (-0.123, 0.195)	0.046 (-0.091, 0.183)

↓ Parent time-impact		0.290 (0.099, 0.480)*	0.241 (0.048, 0.434)*	0.329 (0.160, 0.498)*
Caregiver characteristics				
Total household income				
<$50,000 (REF)	-	-	-	-
$50,000-$99,999				5.706 (-0.928, 12.339)
$100,000 +				7.667 (0.688, 14.647)*
Don't know				7.086 (-2.731, 16.904)
Work status				
Working full- or part-time (REF)	-	-	-	-
Full-time homemaker				5.390 (0.012, 10.768)*
Other work status				6.949 (1.255, 12.642)*
Additional child diagnosed with IMD				-5.893 (-12.370, 0.584)
Emotion impact x problem-focused coping				-0.027 (-0.041, -0.014)*

p<0.05, 95% confidence interval

Table 6 b). Multivariate regression of physical health and covariates of interest in parents of children less than 5 years of age.

Independent variables	**Physical QOL (PCS)**			
	Model 1 (coping strategies) n=41 Adjusted R^2: -0.0321	Model 2 (caregiving complexity) n=44 Adjusted R^2: -0.0278	Model 3 (coping and caregiving complexity) n=41 Adjusted R^2: -0.0142	Model 4 (coping and caregiving complexity with significant covariates) n=41 Adjusted R^2: 0.0597
↑ Problem-focused coping	0.126 (-0.212, 0.464)		0.109 (-0.228, 0.447)	0.044 (-0.315, 0.402)

↑ Emotion-focused coping	-0.007 (-0.208, 0.193)		0.036 (-0.181, 0.253)	0.131 (-0.122, 0.383)
↓ Parent emotion-impact		0.044 (-0.054, 0.141)	0.097 (-0.025, 0.218)	0.058 (-0.081, 0.197)
↓ Parent time-impact		-0.033 (-0.156, 0.089)	-0.069 (-0.217, 0.078)	0.027 (-0.152, 0.206)
Child characteristics				
Gender: female				3.676 (-0.417, 7.769)
IMD diagnosis				
Amino acid/Urea Cycle disorders (REF)	-	-	-	-
FAOD				-0.300 (-5.764, 5.165)
Other IMD				3.931 (-1.555, 9.416)
Caregiver characteristics				
Caregiver age				
40 years or older (REF)	-	-	-	-
35-39 years				-3.083 (-10.804, 4.638)
30-34 years				-3.011 (-10.859, 4.837)
25-29 years				-4.120 (-12.126, 3.886)

p<0.05, 95% confidence interval

Table 6 c). Multivariate regression of depressive symptoms and covariates of interest in parents of children less than 5 years of age.

Independent variables	**Depressive Symptoms (CESD-R)**			
	Model 1 (coping strategies) n=42 Adjusted R^2: 0.2579	Model 2 (caregiving complexity) n=45 Adjusted R^2: 0.1960	Model 3 (coping and caregiving complexity) n=42 Adjusted R^2: 0.3438	Model 4 (coping and caregiving complexity with significant covariates) n=42 Adjusted R^2: 0.4820

↑ Problem-focused coping	-0.564 (-1.152, 0.024)		-0.594 (-1.151, -0.037)*	-0.627 (-1.194, -0.060)*
↑ Emotion-focused coping	0.692 (0.343, 1.042)*		0.533 (0.181, 0.885)*	0.306 (-0.087, 0.698)
↓ Parent emotion-impact		-0.092 (-0.268, 0.084)	-0.094 (-0.294, 0.107)	-0.004 (-0.209, 0.201)
↓ Parent time-impact		-0.153 (-0.358, 0.052)	-0.096 (-0.320, 0.128)	-0.187 (-0.429, 0.055)
Child characteristics				
IMD diagnosis				
Amino acid/Urea Cycle disorders (REF)	-	-	-	-
FAOD				-5.241 (-13.775, 3.293)
Other IMD				-6.687 (-15.091, 1.718)
Caregiver characteristics				
Gender: female				4.54 (-6.653, 15.733)
Caregiver age				
40 years or older (REF)	-	-	-	-
35-39 years				-3.341 (-14.726, 8.043)
30-34 years				-0.112 (-11.465, 11.242)
25-29 years				5.146 (-7.171, 17.462)
Time impact x problem-focused coping				-0.056 (-0.108, -0.005)*
Emotion impact x problem-focused coping				0.072 (0.021, 0.122)*

p<0.05, 95% confidence interval

Table 7. Stratified multivariable regression model of parent time-impact predictor variables for each quartile of problem focused coping for mental QoL in parents of children 5 years of age or older.

Independent variables	Model 1[a] – Q1 level of problem focused coping	Model 2[b] – Q2 level of problem focused coping	Model 3[c] – Q3 level of problem focused coping	Model 4[d] – Q4 level of problem focused coping
Mental QoL (MCS)				
↓Parent time-impact	0.250 (-0.334, 0.835)	0.130 (-0.098, 0.358)	-0.072 (-2.286, 2.142)	-0.128 (-1.071, 0.814)

[a] n=16, adjusted R^2=0.5872; [b] n=15, adjusted R^2=0.4171; [c] n=12 *(missing=3)*, adjusted R^2=0.7963; [d] n=12 *(missing=1)*, adjusted R^2=0.6432

Table 8. Stratified multivariable regression models of caregiving complexity variables for each quartile of problem focused coping for mental QoL and depressive symptoms in parents of children less than 5 years of age.

Independent variables	Model 1[a] – Q1 problem-focused coping	Model 2[b] – Q2 problem-focused coping	Model 3[c] – Q3 problem-focused coping	Model 4[d] – Q4 problem-focused coping
Mental QoL (MCS)				
↓Parent emotion impact	-0.059 (-1.526, 1.407)	-0.117 (-2.995, 2.760)	Could not be determined	0.105 (-0.688, 0.897)
Depressive symptoms				
↓Parent time impact	Could not be determined	-0.274 (-2.512, 1.965)	-0.491 (-9.490, 8.509)	-0.322 (-1.215, 0.571)
↓Parent emotion impact	Could not be determined	0.034 (-1.825, 1.893)	-0.098 (-6.359, 6.163)	0.181 (-0.687, 1.050)

[a] n=10, adjusted R^2=0.9070; [b] n=11 (*missing=1)*, adjusted R^2=0.0582; [c] n=9 (*missing=1)*; [d] n=11, adjusted R^2=0.4146 [e] n=10; [f] n=12; adjusted R^2=-0.2594; [g] n=9 *(missing=1)*, adjusted R^2=0.1188; [h] n=11, adjusted R^2=0.2882

Appendix D

Supplement 1: Assessment of learning outcomes

Program Learning Outcomes for Graduate Programs in Epidemiology

Self-assessment

Attribute	**Learning Outcomes**	
	Master's Program	
	Graduating students will be able to:	**Self-assessment**
Application of knowledge	1. Evaluate and critically appraise the strengths and limitations of an epidemiologic study from its design to the conclusions drawn. 2. Critically and systematically synthesize existing knowledge about a health topic. 3. Proficiently use statistical software to analyze epidemiologic data.	In conducting a systematic review, I screened more than 150 full-text articles against our inclusion criteria to determine relevant studies. The quality of included studies was appraised using the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional studies. This tool helped me evaluate the strengths and limitations of each relevant study was evaluated, considering methodological rigor, sample size and power, and biases. I also examined self-reported outcome measures used in the included studies which identified a current gap in the coping literature. The completion of a secondary data analysis enabled me to clean, organize, and analyze data from a self-reported survey of parents of children with IMD. I wrote code that allowed me to describe the parent sample and also conduct correlation and multivariable regression analyses. Important covariates were accounted for and the evaluation of coping strategies as an effect modifier in the association between caregiving complexity and QoL was examined.

Engaged scholarship, knowledge translation, and communication	4. Define the core components of engaged scholarship 5. Describe best practices for facilitating uptake of evidence into policy, programs, patient care, and/or the design or analysis of future research. 6. Prepare a clearly written and logically argued report from epidemiologic analyses. 7. Effectively disseminate and communicate epidemiologic evidence to academic and non-academic audiences in written and oral formats. 8. Describe the implications of epidemiologic evidence for policy, programs, patient care, and/or future research.	I frequently attended lectures and rounds presented by researchers in the School of Epidemiology and Public Health and also at the Ottawa Hospital Research Institute. A wide variety of research topics were presented on, from which I could learn more about methodological and study design and consider how this could be applied to my own projects. Synthesizing existing evidence of studies that quantitatively examined the association between coping strategies and QoL enabled me to identify a current gap in the literature. There is an inconsistency in the way coping is operationalized. This makes it difficult to synthesize and examine coping strategies in associations with important outcomes such as caregiver QoL mental health. Consistent coping definitions, categorizations, and measurements would improve health care providers ability to support parents of children with chronic illness through different interventions. Results from each project of this thesis were presented to a variety of audiences such as researchers, clinicians, and students.
Autonomy, professional capacity, leadership and mentorship	9. Identify and adhere to ethical principles relevant to epidemiologic research that apply locally, nationally, and internationally, including the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS). 10. Adhere to principles of academic integrity according	Analyzing a small sample size required me to be aware of the sensitive nature of the data sometimes meant collapsing levels of categorical variables that would otherwise be interesting to examine. Frequent consultation with my TAC was necessary during the completion of this project, especially with regards to model building and the evaluation of interaction terms with a small sample size while also

	to the policies of the University of Ottawa. 11. Appreciate the value of and participate in an interdisciplinary research community in their chosen field of health research. 12. Commit to proactively seeking new knowledge and being aware of current issues of debate in their chosen field of health research.	refraining from over analyzing results of analyzes with limited power.