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An 8-year longitudinal assessment of health-related quality of life in children with epilepsy

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Abstract

This study estimated the course of health-related quality of life (HRQL) over 8 years among children newly diagnosed with epilepsy. Levels of HRQL in children newly diagnosed with epilepsy were assessed over 8 years and compared to levels reported for peers in the general population. Data came from the Health-Related Quality of Life in Children with Epilepsy Study, a multi-center prospective study of children in Canada with epilepsy. Parents of children with epilepsy reported their children were comparable to (or better than) their counterparts in the general population on the majority of individual health concepts 8 years post diagnosis. On average, fewer family resources, the presence of parental depressive symptoms, and cognitive problems are significantly associated with worse HRQL over time. Future research should focus on interventions that target parental depressive symptoms and family resources to improve the HRQL of individuals with childhood-onset epilepsy.

Keywords: Childhood epilepsy, health-related quality of life, HRQL, QOL, longitudinal, child health questionnaire, CHQ, family environment, cognitive comorbidities

Summary for Lay Audience

Children newly diagnosed with epilepsy have poorer well-being related to their overall health, also known as, health-related quality of life (HRQL), than their peers in the general population, but little is known about whether this remains the case in the long-term. Also, little is known about the factors associated with the course of HRQL for children with epilepsy in the long-term. The aim of this thesis was to evaluate the course of HRQL over the long-term in children who have been newly diagnosed with epilepsy. This thesis compared levels of HRQL in children eight years after a diagnosis of epilepsy to levels of HRQL in children in the general population. This thesis also identified factors that contribute to change in HRQL over time in children with epilepsy. Overall, parents of children with epilepsy reported their children's HRQL 8 years after diagnosis was similar to the general population. However, some are experiencing worse or no change in HRQL. Additionally, family environment, and their children having cognitive problems were associated with HRQL over time. Taken together, over the long-term children with epilepsy are doing well, however, some are at risk for poor HRQL. The current results are important in recognizing what factors other than seizure experience are related to HRQL over time. Understanding that there is a potential need to identify those at risk for poor HRQL early after diagnosis may help parents and clinicians to make decisions regarding these children's health care.

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List of Abbreviations

AED	Antiepileptic Drug
AIC	Akaike Information Criterion
APGAR	Family Adaptability, Partnership, Growth, Affection and Resolve
BIC	Bayesian Information Criterion
CES-D	Center for Epidemiological Studies Depression Scale
CHQ PF50	Child Health Questionnaire Parent Form
CWE	Children with Epilepsy
FILE	Family Inventory of Life Events and Changes
FIRM	Family Inventory of Resources for Management
GASE	Global Assessment of Severity of Epilepsy
HERQULES	HEalth-Related QUality of Life in children with Epilepsy Study
HRQL	Heath-Related Quality of Life
MCID	Minimal Clinically Important Difference
QOL	Quality of Life
SEM	Standard Error of Measurement
QOLCE	Quality of Life in Childhood Epilepsy Questionnaire
WHO	World Health Organization

Chapter 1

1 Introduction

1.1 Thesis Overview

This chapter describes background information regarding important subject areas explored throughout the thesis including an overview of childhood epilepsy, the importance of quality of life measurements, and the benefits of longitudinal research. Chapter Two presents a review of the literature that is specific to the research aims of the study. Chapter Three includes a description of the purpose of the study and research objectives. Chapter Four describes the study design and methods used to address the outlined objectives. Chapter Five presents the results from the analyses. Chapter Six provides a discussion of the results, conclusions based on the findings and the implications of the current research.

1.2 Background

1.2.1 Epilepsy Overview

Epilepsy is characterized as a brain disease that includes a predisposition to generating epileptic seizures. The definition of epilepsy by the International League Against Epilepsy was revised in 2014 to be that one of three conditions must be met: two unprovoked seizures less than 24 hours apart; one unprovoked seizure with evidence of the probability of further seizures; or the diagnosis of an epilepsy syndrome (Fisher et al., 2014). Seizure types are characterized in order to select appropriate therapies and offer common language. The classification of seizures was revised in 2017 to include three types: focal onset, generalized onset and unknown onset (Fisher et al., 2017). Six groupings of causes of epilepsy have been identified: structural, genetic, infections, metabolic, immune and unknown (Scheffer et al., 2017).

The World Health Organization (WHO) has estimated that around 50 million people worldwide have epilepsy, making it one of the most common neurological diseases (World Health Organization, 2019). Other estimates have suggested that the global

burden of epilepsy may be even higher with values closer to 65 million people with epilepsy worldwide (Ngugi, Bottomley, Kleinschmidt, Sander, & Newton, 2010).

Epilepsy affects all ages, sexes, races, income groups and geographical locations (World Health Organization, 2019). Geographically, the incidence and prevalence of epilepsy have been reported to be lower in developed countries and highest in rural areas of underdeveloped countries (Camfield & Camfield, 2015). Furthermore, epilepsy carries neurological, cognitive, psychological and social consequences (World Health Organization, 2019). For example, roughly half of people with epilepsy have comorbid physical or psychiatric conditions. The most common psychiatric comorbidities are depression and anxiety (Wei & Lee, 2015). Examples of physical comorbidities include abnormal bone health and polycystic ovary syndrome (Coppola et al., 2009; El-Khayat et al., 2004). Additionally, having physical and psychiatric comorbidities in people with epilepsy is associated with poorer health outcomes and decreased quality of life (World Health Organization, 2019).

Importantly, epilepsy is a treatable condition. Up to 70% of people with epilepsy could become seizure free with appropriate diagnosis and treatment; however, without access to care people with epilepsy may remain untreated and face stigma and discrimination (World Health Organization, 2019).

1.2.2 Childhood-Onset Epilepsy

The incidence of epilepsy is generally higher in the youngest and oldest age groups in the population (Fiest et al., 2016). The incidence of epilepsy is highest within a child's first year of life and often declines to adult levels by around the age of 10 years old (Camfield & Camfield, 2015). In at least 50% of childhood epilepsy the cause is unknown (Camfield & Camfield, 2015). From a public health standpoint, the majority of cases of childhood-onset epilepsy are not currently preventable (Camfield & Camfield, 2007), however, as 70% of people with epilepsy become seizure free, an emphasis on diagnosis and treatment over time is essential (World Health Organization, 2019).

The impact of a diagnosis of epilepsy is associated with direct and indirect costs. Direct costs include health care costs associated with assessment, diagnosis, and treatment; whereas, indirect costs include side effects that prevent the person from reaching their full potential (Chomba, Haworth, Atadzhanov, Mbewe, & Birbeck, 2008; World Health Organization, 2019). Additionally, direct costs can occur not only due to epilepsy-related treatment, but also due to comorbidities. Comorbid conditions are common among children with epilepsy, with population estimates reaching upwards of 70% (Pastor, Reuben, Kobau, Helmers, & Lukacs, 2015; Sillanpää & Cross, 2009). Comorbidities among children with epilepsy can be categorized into neurological/cognitive, psychological/behavioural, and physical (Wei & Lee, 2015). Among all comorbidities, intellectual disability is the most common in children with epilepsy (30-40%) (Reilly et al., 2014; Wei & Lee, 2015). Additionally, children with epilepsy have significantly more sleep problems than the general population (Wei & Lee, 2015). Among psychiatric/behavioural comorbidities, Autism Spectrum Disorder (ASD) (as high as 32%) (Clarke et al., 2005), Attention Deficit Hyperactivity Disorder (ADHD) (12-39%) (Reilly, 2011), depressive and anxiety disorders (12-24%) are the most common (Caplan et al., 2005; Wei & Lee, 2015). Furthermore, physical comorbidities associated with seizure medication may have a long-term effect on the physical health and quality of life of children with epilepsy (Wei & Lee, 2015).

The high prevalence of comorbid conditions among children with epilepsy and the positive prognosis of reduction of seizures in the long term, highlights the need to not solely focus on seizure-related clinical factors when treating epilepsy. Studying the whole picture of the child’s health, including comorbid conditions and health-related quality of life (HRQL), to measure outcomes through childhood and into adulthood is very important.

1.2.3 Health-Related Quality of Life in Children with Epilepsy

The WHO defines Quality of Life (QOL) as "an 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. QOL is a broad ranging concept that is affected by the relationship between a person's physical health, psychological state, level

of independence, social relationships, personal beliefs and their relationship to salient features of their environment" (WHO, 1995, p. 1405). HRQL is the facet of QOL that is directly relevant to delivery of health care. Hays and Reeve (2016) defined HRQL as a focus on how a person assesses their functioning in life and their perceived well-being in physical, mental and social domains of health. Functioning refers to a person's ability to carry out a defined activity while perceived well-being refers to a person's subjective feelings. HRQL highlights the importance of connecting well-being and functioning in daily life to health concerns. Understanding the connection between QOL and health can in turn influence how health care is delivered.

With respect to the treatment of childhood epilepsy, treatment has shifted from focusing on management of seizures to incorporating measurements of (HRQL) (Jones, 1998; Schachter, 2000). Treatment of epilepsy should be considered a multi-faceted process with an emphasis on community-based care (World Health Organization, 2019). Ultimately, the goal of treatment is to optimize HRQL (Thurman et al., 2011). Understanding the course of HRQL for individuals with disease is integral to families and clinicians. For families, understanding the potential impact of epilepsy on HRQL can aid in predicting what life may look like for those with epilepsy to aid in planning for the future. For clinicians, it means identifying children at risk for poor HRQL and working with families to allocate additional resources aimed at achieving more positive outcomes.

To optimize HRQL, it is important that we have an agreed-upon way to meaningfully interpret scores derived from HRQL questionnaires. Specifically, we need to know how large the changes observed in HRQL scores must be to be viewed as meaningful. In the absence of methods to practically interpret HRQL scores observed in children with epilepsy such as minimal clinically important difference (MCID), one way to attach meaning to HRQL scores is to use relative comparisons between children living with epilepsy and healthy age-matched counterparts in the general population or children living with other chronic health conditions. To compare across different populations requires the use of a generic measure of HRQL, as opposed to disease-specific measures. One such generic measure that has been used in childhood chronic diseases is the Child Health Questionnaire (CHQ) (Landgraf, Abetz, & Ware, 1996).

HRQL in children with epilepsy has been described in the HEalth-Related QUality of Life in children with Epilepsy Study (HERQULES) (Speechley et al., 2012). HERQULES is a multi-center prospective cohort study of children with new-onset epilepsy in Canada that measured HRQL at six time points across a 10-year span. A total of 374 children were included in the sample at baseline. In the first phase of HERQULES, the course of HRQL in children with epilepsy throughout the first two years post-diagnosis was described. It was determined that 56% of children with new-onset epilepsy experienced either no clinically important improvement (37%) or a clinically important decline (19%) in the psychosocial health subscale of HRQL over the first two years since diagnosis. On a physical health subscale, 61% experienced either no clinically important improvement (43%) or a clinically important decline (18%) over the first two years (Speechley et al, 2012). Furthermore, it was determined that at diagnosis, compared to a population-based normative sample from the United States (Landgraf, Abetz and Ware, 1996), children with newly diagnosed epilepsy had lower HRQL on most domains measured. Two years later, ratings were more similar to the population-based normative sample, except for psychosocial health (Speechley et al, 2012). The second phase of HERQULES extended the window of observation from the 2-year follow up to 8-10 years later—presenting the opportunity to describe the long-term course of HRQL. To date the long-term HRQL in this sample has been reported using a disease-specific measure of HRQL (Puka et al., 2020), but what remains to be assessed is the long-term course of HRQL, using a generic measure and comparing these outcomes to a same-aged sample from the general population. Similarly, the long-term follow up presents the opportunity to assess the baseline factors associated long-term HRQL.

1.2.4 Longitudinal HRQL in Children with Epilepsy

The study of HRQL in children with epilepsy (CWE) is often conducted using cross-sectional or short-term cohort studies. Cross-sectional study designs provide snapshots of patients' HRQL but do not provide information on the course of HRQL in the long-term. It has been reported that the ultimate goal of treatment of childhood epilepsy is to optimize HRQL and understanding what factors are associated with increased HRQL over the long term is pertinent to the overall picture of the course of epilepsy in children

(Thurman et al., 2011). Longitudinal research has the potential to offer information to parents regarding prognosis and the potential course for their child's HRQL later in life. Additionally, understanding what factors are associated with positive HRQL, may aid parents to make informed decisions regarding modifiable attributes of their child's life such as their child's health care or family environment that may benefit their child throughout the course of their life. The proposed thesis research will extend the description of the course of HRQL to the long term.

Chapter 2

2 Literature Review

This chapter provides an overview of health-related quality of life (HRQL), the Child Health Questionnaire (CHQ), and factors affecting HRQL in children with epilepsy. A comprehensive search strategy was completed, searching both PubMed and PsycINFO. Overall, the search included studying HRQL of childhood epilepsy, the Child Health Questionnaire, and instances where the Child Health Questionnaire was used to evaluate the outcome associated with childhood epilepsy or other chronic health conditions in children and adolescents. Studies included for review were limited to those where the age range of the sample was between 5 and 18 years. In total, 341 unique papers were identified, extracted, and read. Additional relevant articles were assessed through review of reference lists.

The first section focuses on the definition and measurement of HRQL (Section 2.1). The second section draws attention to one specific measure of HRQL, the Child Health Questionnaire (Section 2.2). The third section focuses on the association between HRQL (Section 2.3), family environment (Section 2.3.1), parental mood (Section 2.3.2) and the effect of psychiatric comorbidities (Section 2.3.3) on children with epilepsy. The final section outlines limitations in the literature to date (Section 2.4).

2.1 What is Health-Related Quality of Life?

HRQL is the facet of QOL that is directly relevant to delivery of health care. Different definitions of HRQL may focus solely on areas of quality of life that are related to health, disregarding concepts like the economy and politics (Karimi & Brazier, 2016). Other definitions, such as those proposed by Hays and Reeve (2016), define HRQL as a focus on how a person assesses their functioning in life and their perceived well-being in physical, mental and social domains of health. In this case, functioning refers to a person's ability to carry out a defined activity; whereas, perceived well-being would refer to a person's subjective feelings. Overall for the context of this thesis, HRQL highlights the importance of connecting well-being and functioning in daily life to health concerns.

In other terms, HRQL refers to the impact, both subjective and objective, of impairment as it relates to a disease, health policy or treatment (Spieth & Harris, 1996). Studying and evaluating HRQL using a patient's self-reported experiences can provide a subjective record that compliments a patient's diagnosis and prognosis. The coordination between subjective measurements and objective measurements can impact a patient's healthcare decisions. Monitoring and understanding HRQL over time in certain diseases, can lead to identification of patients at risk for poorer HRQL and predict health outcomes, including health care costs (Ryan et al., 2016). Understanding the connection between QOL and health can in turn influence how health care is delivered.

2.1.1 Measuring Health-Related Quality of Life in Children

Measuring HRQL in children involves assessing functioning that is directly affected by an illness or its treatment. Therefore, it is pertinent to identify what areas of functioning are being measured and how those areas align with the definition of HRQL. In assessing areas of functioning, measurements can focus on the multi-dimensionality of HRQL or alternatively, consider more specific, individual domains of HRQL. Typically, most descriptions of HRQL refer to four core domains of quality of life: disease state and physical symptoms, functional status, psychological functioning, and social functioning (Spieth & Harris, 1996).

In addition to measuring the individual domains or the multi-dimensionality of HRQL, it is important that researchers have an established method by which to meaningfully interpret scores derived from HRQL measures. Specifically, we need to know how large the changes observed in HRQL scores must be to be viewed as meaningful. One way to attach meaning to HRQL scores is to use relative comparisons between children living with a certain disease and healthy age-matched counterparts in the general population or children living with other chronic health conditions. To compare across different populations requires the use of a generic measure of HRQL, as opposed to a disease-specific measure (Miller, Palermo, & Grewe, 2003). Additionally, the use of a generic measure provides information on the relative burden of a certain disease or chronic condition that cannot be concluded using a disease-specific measure (Asmussen et al., 2000). A disease-specific measure may be more sensitive in identifying specific illness

related predictors, however (Miller et al., 2003). The use of disease-specific versus generic HRQL measures has been investigated in food allergic patients where disease-specific measures highlighted clinically important impairments and the use of generic measures was found to be indispensable for comparing between different diseases and complimenting clinical findings (Flokstra-de Blok et al., 2010). It has been recommended that when studying HRQL, both generic and specific perspectives be included to visualize the whole picture and aid patients (Miller et al., 2003).

The measurement of HRQL usually requires patients' self-report based on their reflections of their life and overall functioning. HRQL measures are developed and considered for use based on four aspects: relevant age range, reliability, validity and the extent to which the measures coincides with the researchers' definition of HRQL (Janssens, Gorter, Ketelaar, Kramer, & Holtslag, 2008).

Studying HRQL in children poses certain challenges. For example, often an adult, in most cases, the parent of the child is required to report on behalf of the child. However, there are measurements that include versions to be completed by children and versions completed by parents, such as, the Child Health Questionnaire-Child-Form and CHQ-Parent-Form, versions of the DISABKIDS, versions of the KINDL-R, the KIDSCREEN, and versions of the PedsQL (Hullmann, Ryan, Ramsey, Chaney, & Mullins, 2011). Child-report questionnaires often have the option to be administered through a self-administered questionnaire or an interviewer-administered format. Studies have found that there are differences between child and parent reports of HRQL (Baca, Vickrey, Hays, Vassar, & Berg, 2010). It has been established that the perspective of a parent may be different than their child. To gain the full picture, both perspectives should captured whenever possible (Baca et al., 2010; Fong et al., 2018) . It should be clearly stated, when solely the parents' or children's report is analyzed. Using a measure that has demonstrated acceptable levels of validity and reliability is an important consideration is selecting a measure of a children's HRQL (Hullmann et al., 2011).

2.2 The Child Health Questionnaire (CHQ)

A review of all generic HRQL measures for children aged 5-18 identified a total of 14 measures, including, Child Health and Illness Profile Adolescent and Child Edition (CHIP-AE/CE), Child Health Questionnaire—Child and Parent Forms (CHQ-CF87/PF50/PF28), DISABKIDS, Functional Status II (FS II)(R), Health Utilities Index Mark 2 (HUI 2), KIDSCREEN 52/27, KINDL, Pediatric Quality of Life Inventory (PedsQL), The Netherlands Organization (TNO) Institute of Prevention and Health and the Leiden University Hospital (TNO-AZL), TNO-AZL Children's Quality Of Life (TACQOL), and Youth Quality of Life Instrument—Research Version (YQOL-R) (Janssens et al., 2008). The measure used for this thesis is one of these, the Child Health Questionnaire Parent Form-50 (CHQ PF-50) (Landgraf et al., 1996). The CHQ-PF50 is a 50-item, generic, well-validated and reliable measure with strong psychometric properties (Hullman et al, 2011). The questionnaire is validated for parent-report of HRQL for children ages 5-18 with various acute and chronic health conditions and from the general population. Additionally, the CHQ has been studied in diverse populations. Upon completion, the questionnaire results in two summary scores, psychosocial and physical health, and fourteen subscale scores (Landgraf et al., 1996). The CHQ allows for a detailed look at individual domains of HRQL that illuminates individual aspects of HRQL that are comprised to assist in specially targeting them in an intervention (Landgraf et al., 1996).

2.2.1 Description of the CHQ Scales

The CHQ-PF50 contains 50-items. The response options for the CHQ are ordinal level and vary by the item. Each item consists of 4–6 response options. Additionally, each scale consists of varying numbers of items. Most scales use a recall period of four weeks. The change in health subscale has a recall period of one year, and both the family cohesion and general health scales refer to the child's health "in general".

Fourteen health concepts are considered in the CHQ. A brief description of each of these health concepts developed by Landgraf et al. (1996) is provided in Table 2.1.

Table 2.1: Description of CHQ Health Concepts

Health Concept Name	Description of Health Concept
Physical functioning	Measures the presence and extent of physical limitations due to health-related problems. Self-care, mobility and activities varying in severity of strenuousness are included. A four-level response continuum that ranges from "yes, limited a lot" to "no, not limited" is provided.
Role/Social Limitations-Physical	Measures the extent of limitation in school-related activities and activities with friends related to physical health problems. A four-level response continuum that ranges from "yes, limited a lot" to "no, not limited" is provided.
General Health	Subjective assessment of overall health and illness. Responses to statements of their child's past, future and current health, using a five-level continuum from "definitely true" to "definitely false", are provided.
Bodily Pain/Discomfort	This scale is included as an indicator of physical health. Items are designed to assess both intensity and frequency of general pain and discomfort. The degree of bodily pain or discomfort is assessed along a six-level response continuum that ranges from "none" to "very severe".
Parental Impact-Time	Captures the extent of limitations in personal time experienced by the respondent, be it parent or guardian, due to the following areas: child's physical health, emotional well-being, attention or learning abilities, child's ability to get along with others, and general behaviour. A four-level response continuum that ranges from "yes, limited a lot" to "no, not limited" is provided.
Parental Impact-Emotional	Captures the amount of distress experienced by the respondent for each of the following areas: child's physical health, emotional well-being, attention or learning abilities, child's ability to get along with others, and general behaviour. Responses along a five-level continuum from "none at all" to "a lot" are provided.
Role/Social Limitations-Emotional	Designed to measure limitations in the kind, amount and performance of schoolwork and activities with friends due to emotional difficulties. A four-level response continuum that ranges from "yes, limited a lot" to "no, not limited" is provided.
Role/Social Limitations-Behavioural	Similar to that of the social limitations-emotional, designed to measure limitations due to solely behavioural difficulties. A four-level response continuum that ranges from "yes, limited a lot" to "no, not limited" is provided.

Self Esteem	The scale captures satisfaction with school and athletic ability, looks/appearance, ability to get along with others and family, and life overall. A five-level response continuum that ranges from “very satisfied” to “very dissatisfied” is provided.
Mental Health	Measures the frequency of both negative and positive states of mental health. Frequency is measured using a five-level continuum that ranges from “all of the time” to “none of the time”.
General Behaviour	Measures overt behaviour as a component of mental health. The frequency of behavioural problems and ability to get along with others are measured using a five-level response continuum that ranges from “very often” to “never. A global item is also provided that rates the child’s behaviour overall, along a five-level continuum that ranges from “excellent” to “poor”.
Family-Limitations in Activities	Designed to assess the frequency of disruption in “usual” family activities. Reponses are provided using a five-level response continuum ranging from “very often” to “never”.
Family-Cohesion	A global family cohesion item is provided, and the respondent is asked to rate how well his/her family “gets along with one another” using a five-level continuum that ranges from “excellent” to “poor”.
Change in Health	A global change in health score over the previous year is included along a five-level response continuum that ranges from “much better now” to “much worse now”.

In addition to the 14 health concepts in Table 2.1 measured using the CHQ, two aggregate scores are derived, the psychosocial and physical health summary scores. Scores are transformed to a 0-100 scale with a mean of 50 and standard deviation of 10 (Landgraf et al., 1996).

When using the CHQ as a tool, studies decide to incorporate all fourteen subscales, some of the scales, or to focus solely on the summary scores. For example, Bruijn et al., (2009) presents results from all of the subscales but focuses on differences within mental health, parental impact time and family cohesion whereas Baildam et al., (2011) included multiple different questionnaires within their study, but focused solely on the family activity subscale from the CHQ. Studies may also report all subscale measurements but focus on the two summary scores for general results (de Wit et al., 2008)

2.2.2 Psychometric Properties of the CHQ

The CHQ has strong psychometric properties. It is feasible to use. A study of Dutch school children, showed that <2% of data were missing on the CHQ-PF50, and that the scale with the most missing items was the single item scale "Family cohesion" (4%) (Raat, Landgraf, Bonsel, Gemke, & Essink-Bot, 2002).

As for reliability, internal consistency for the CHQ-PF50 has been rated as good. Cronbach's alpha coefficient for Dutch schoolchildren was calculated to range from 0.39–0.96 for an average of 0.72 for the subscales (Raat et al., 2002). Additionally, Cronbach's alpha coefficient has been computed for United States schoolchildren (0.66-0.94), children with ADHD (0.56-0.89), children with epilepsy (0.71-0.94) and children with juvenile rheumatoid arthritis (0.60-0.90) (Landgraf et al., 1996).

Convergent validity was found to be acceptable, with correlations ranging from 0.21–0.49 for parallel domains on the CHQ compared to the Health Utilities Index (HUI) (Hullmann et al., 2011; Raat et al., 2002). Discriminant validity was also found to be moderate to strong (Hullmann et al., 2011; Raat et al., 2002).

2.2.3 The CHQ as a Generic Measure of HRQL

Using a generic measure makes it possible to directly compare HRQL across chronic conditions and with normative populations. Normative data make it possible to interpret a child's health score, or the average of a group, compared with groups of other children. To make relevant comparisons, a valid norm from a well-defined representative sample, that was taken from a population of interest in required. The CHQ-PF50 manual presents a set of general population normative data from the United States. The norms were estimated from responses to the National Survey of Functional Health Status (NSFHS), a 1994 cross-sectional survey (Landgraf, Abetz, and Ware, 1996). It is important to note that another version of the CHQ, the CHQ-PF28, is embedded within the CHQ-PF50 and is commonly used as a shorter version of the CHQ-PF50 (Houben-van Herten, Bai, Hafkamp, Landgraf, & Raat, 2015; Vet et al., 2016).

Since publication of the CHQ and its U.S. normative data, additional populations have been studied. In 2000, Australian populations norms were published from a representative sample of parents of school-aged children (Waters, Salmon, Wake, Hesketh, & Wright, 2000). Additionally, in 2003, a random national sample of Australian school-aged children was obtained and socioeconomic differences were investigated (Spurrier, Sawyer, Clark, & Baghurst, 2003). In 2015, a population study in the Netherlands published normative data from the Dutch population (Houben-van Herten et al., 2015). Having access to multiple sets of normative data allows for studies to compare not only within one country but to expand globally. For example, Attention-Deficit/Hyperactivity Disorder (ADHD) has been studied in the Canadian population, however, without Canadian norms, both U.S. and Australian norms were compared to compliment results found in Canada (Klassen, Miller, & Fine, 2004).

A generic questionnaire also allows for comparisons between the general population and a population with a chronic disease. Comparing people with chronic diseases and their counterparts in the general population provides a method to understand the impact a chronic disease may have on HRQL in an individual. Additionally, understanding how those with a chronic disease differ from the general population in particular domains of HRQL may aid parents and health care practitioners to make informed decisions regarding a child's health care. The CHQ has been used across many health conditions to compare to normative populations. For example, the CHQ assessed differences between children with cystic fibrosis (Britto et al., 2002), cerebral palsy (Bjornson et al., 2008; Davis et al., 2009), tooth disease (Burns, Ryan, & Ouvrier, 2010), leukemia (Gordijn et al., 2013), septic shock (Buysse et al., 2008) and human immunodeficiency virus (HIV) infected children (Byrne & Honig, 2006). In addition to using published population normative data, studies also have the opportunity of assembling their own reference populations and comparing them with their study sample (de Wee et al., 2011).

In addition to normative data from the general population, generic measures provide benchmarks for clinical conditions. The CHQ provides five clinical condition benchmarks including, asthma, ADHD, epilepsy, psychiatric disorder, and juvenile rheumatoid arthritis (Landgraf, Abetz and Ware, 1996). Including clinical condition data

allows for comparisons not just with the general population and globally, but also within different chronic conditions.

When a family has a child with a health condition, comparisons can be made between the HRQL of the child with the condition and another child within the family, used as sibling controls. Insight into sibling differences can help teams studying health conditions to provide family-oriented care. Chiou, Jang, Liao, & Yang,. (2010), compared children who have survived leukemia, their siblings, and aged-matched controls. Providing a control group within the family attempts to control for characteristics of the family environment such as family functioning that may be directly associated with HRQL. It was reported that the HRQL of children with leukemia was worse than their siblings and other children in the community. It was concluded that, pediatric leukemia survivors carried a burden on HRQL into their teen years as reflected by worse HRQL than both types of controls. Findings comparing both within the community and within families guide the support required by a population (Chiou et al., 2010).

2.2.4 Determining Clinical Relevance of CHQ scores

To determine whether scores derived from self-report questionnaires are clinically different, a minimal clinically important difference (MCID) is often used. An MCID is defined as "the smallest difference in score in the domain of interest that patients perceive to be beneficial and that would mandate, in the absence of troublesome side effects and excessive costs, a change in the patient's management". MCIDs allow for health practitioners to assign significance to an observed score that includes both a patient's perception and their clinical characteristics (Jaeschke, Singer, & Guyatt, 1989). To date, a minimal clinically important difference has not been established for the CHQ-PF50.

In the absence of an agreed upon MCID for a given measurement, other methods are used to determine if scores in a sample are indicative of a clinically important difference. Common distribution-based methods include Standard Error of Measurement (SEM), use of effect sizes, and standard deviation (Rai, Yazdany, Fortin, & Aviña-Zubieta, 2015). The SEM estimates the average number of points by which an observed score differs from the true scores. SEM is estimated by standard deviation of the measure multiplied

by the square root minus its reliability coefficient (Anastasi & Urbina, 1997). The SEM criterion has been established for identifying clinically meaningful intra-individual change in reliable and valid HRQL instruments (Wyrwich, Tierney, & Wolinsky, 1999). The SEM-based criterion has been used previously in earlier HERQULES analyses to evaluate scores derived from the CHQ-PF50 (Speechley et al., 2012). Another distribution method uses standard deviation as a measure of variability interpreting scores greater than or equal to 0.5 standard deviations as clinically different (Rai et al., 2015). A similar rule exists for use of effect sizes.

2.2.5 Longitudinal Studies Using the CHQ

Longitudinal studies have the potential to offer information to parents regarding long term prognosis associated with their child's epilepsy diagnosis. Extending prospective studies longitudinally, past one or two years, offers the ability to chart the course of HRQL in a child's life into adulthood. Using a relevant, valid and reliable measure, such as the CHQ repeatedly over time in the same population can begin to answer questions regarding the course of HRQL.

The CHQ is validated for use of participants aged 5-18 (Landgraf, Abetz, and Ware, 1996). In the case of longitudinal research, participants may surpass the age of 18 and no longer be within the validated use of the questionnaire. There are various ways to deal with these challenges. One method is to only consider those below the upper age limit for data analysis (Hesketh, Wake, & Cameron, 2004). Another option is to use the CHQ for those at or below 18 years of age and include an adult self-report questionnaire of HRQL such as the WHOQOL (World Health Organization Quality of Life) for those above the age of 18 (Zuidema et al., 2018).

Numerous examples of longitudinal studies using the CHQ exist in the literature (Ferro, Landgraf, & Speechley, 2013; Speechley et al., 2012). For example, Randhawa, Cetto, Chilvers, Georgalas, & Narula (2011), followed children undergoing adenotonsillectomies over four years. Measurements were taken pre-surgery and again at follow up, in the long term. Results concluded that the benefits of surgery are persistent at 4-year follow-up. Another example using multiple measurements

includes a study that compared subjects born extremely premature with those born at full-term. Participants were assessed at both 10 and 18 years of age and developmental trajectories were developed using scores from the CHQ. Results suggested that a longitudinal perspective is required when addressing health and well-being questions in those who are born extremely prematurely (Vederhus et al., 2015). The previous studies focus on measurements taken at two time points. However, multiple measurements can be taken across time to form a more descriptive course of HRQL. For example, DeMatteo et al., (2014), studied HRQL in children after sustaining a brain injury, at three time points over the span of five years. Including multiple time points allowed for the authors to discuss changes not only between baseline and five years, but also include the difference between baseline and eight months post injury (DeMatteo et al., 2014). Another study measured HRQL in children with physical disabilities at three data points over 18 months (Law et al., 2014). Results from the study highlighted factors that predicted changes in HRQL over time and indicated how this knowledge could inform clinical services and policy developments.

2.2.6 Summary of the Benefits of the CHQ

The CHQ provides a generic measure of HRQL for use with children in the general population or those experiencing a health condition. The CHQ is a versatile tool that can be used longitudinally for measuring the course of HRQL over time and to compare results from a sample with a health condition to age-counterparts in the general population. Combining the ability to measure over time, identify predictive factors, and compare to normative populations, the CHQ has the potential to inform parental decisions, influence health interventions, and potentially provide suggestions for health policy decisions.

2.3 Health-Related Quality of Life in Children with Epilepsy

Epilepsy is characterized as a brain disease that includes a predisposition to generating epileptic seizures (Fisher et al., 2014). The treatment of childhood epilepsy has shifted from focusing on management of seizures to incorporating measurements of HRQL (Jones, 1998; Schachter, 2000). Research has found that children with epilepsy have

diminished HRQL compared to healthy children (Bansal, Azad, Gudala, & Dasari, 2017; Cianchetti et al., 2015). Therefore, in addition to focusing on minimizing seizures, an emphasis on improving HRQL has been acknowledged as essential (Cianchetti et al., 2018; Sabaz et al., 2003; Taylor, Jacoby, Baker, & Marson, 2011). Epilepsy has been shown to impair HRQL in children, but also, within their families, which may not be related to the severity of the epilepsy itself (Cianchetti et al., 2015). It has been highlighted that attention to seizure control in a clinical setting will not address the full range of QOL-related problems within children with epilepsy and their families (Austin, Smith, Risinger, & McNelis, 1994).

Additionally, comorbidities are common amongst patients with epilepsy and therefore, treatment of epilepsy should be considered a multi-faceted process with an emphasis on community-based care (World Health Organization, 2019). Managing comorbidities is essential throughout all levels of care, including primary, specialist and therapeutic care. Availability of community-based care allows for all people in need of epilepsy services to access them and manage comorbidities (World Health Organization, 2019).

The Health-Related Quality of Life in Children with Epilepsy Study (HERQULES) assessed HRQL in a group of children newly diagnosed with epilepsy and followed them longitudinally for up to 10 years. Data derived from the CHQ-PF50 determined that, with regards to psychosocial health, 56% of children with epilepsy in the study experienced either no clinically important improvement (37%) or a clinically important decline (19%). On the physical health subscale, 61% experienced either no clinically important improvement (43%) or a clinically important decline (18%) (Speechley et al., 2012). It was also determined that at diagnosis, children with newly diagnosed epilepsy have lower HRQL on most domains measured compared to a population normative sample from the United States (Speechley et al., 2012). Two years later, ratings were more similar to the population normative sample, but not for measures of psychosocial health. Additionally, after controlling for baseline HRQL, cognitive problems, poor family functioning, and high family demands were risk factors for low HRQL two years later (Speechley et al., 2012). Within the HERQULES sample, child and family risk factors at diagnosis have been found to predict HRQL 2 years post-diagnosis which allowed for identification of

those at risk for lower HRQL soon after diagnosis (Ferro, Landgraf, et al., 2013). Self-reported HRQL has also been found to be directly related to health care costs. Children with poor, declining HRQL incur higher health care costs compared to those with stable, high HRQL (Ryan et al., 2016). Research targeting the identification of potentially modifiable traits is important as it can offer insight into how we might improve HRQL in children diagnosed with epilepsy. By identifying children at risk for compromised HRQL soon after diagnosis of epilepsy, an opportunity is presented to target families for health care resources aimed at improving HRQL (Speechley et al., 2012).

Controlling seizures is an essential factor in treating epilepsy. However, ultimately the goal of treatment is to optimize HRQL over the long term (Thurman et al., 2011). Assessing HRQL may offer a way to identify a subset of patients at risk who could benefit from interventions aimed at improving HRQL.

2.3.1 The Role of Family Environment in determining HRQL of Children with Epilepsy

When studying children diagnosed with epilepsy, the importance of expanding the focus beyond epilepsy-related factors has been widely accepted. A variety of aspects of the family environment may affect HRQL in children diagnosed with epilepsy. A combination of clinical and family factors have been reported previously from the HERQULES sample, to be associated with HRQL in children with epilepsy and understanding these associations has implications for research and healthcare decisions (Ferro et al., 2014).

Studies have emphasized a range of family factors that play a role in the HRQL of children with epilepsy. Having fewer family resources has been found to be associated with diminished HRQL in children with epilepsy (Conway et al., 2016). In addition, family functioning and family demands were identified as risk factors for HRQL in the same sample as the current study (Speechley et al., 2012). Additionally, a recent study assessed the effects of family management styles on children's HRQL (Im, Cho, & Kim, 2019). Family management styles are defined as a family's response to a health-related challenge, in this case, a diagnosis of epilepsy in a child. Family management styles

incorporate how the family copes, adapts and functions in response to the health-related challenge. Adopting an easy family management style was determined to be the most important factor in predicting HRQL of children with epilepsy (Im et al., 2019). An easy family management style reflects the extent to which a parent perceives the child's daily life as 'normal' despite having epilepsy (Im et al., 2019). Results that highlight the effect of family factors on a child's HRQL call for comprehensive interventions that focus on the family environment as well as epilepsy factors (Im et al., 2019). Ultimately, comprehensive interventions that involve children and their families are important in addressing the non-medical aspects of family experiencing a epilepsy diagnosis (Conway et al., 2016; Jain, Subendran, Smith, & Widjaja, 2018).

2.3.2 Parental Mood and Mental Health

Parental mood and mental health have been shown to affect parental HRQL as well as their child's HRQL. Terms such as caregiver mood, parental coping, emotional impact, psychosocial health, parental anxiety and depression are commonly used across the literature to characterize parents' mood and mental health.

Caregiver mood has been found to be a correlate of caregiver HRQL, actually more important than the child's seizure related variables (Jain et al., 2018). In addition to caregiver mood, mother's depressive symptoms have been investigated. In the HERQULES sample, a substantial proportion of mothers of children with epilepsy were found to be at risk of depression, and that risk remained stable over the long term (Ferro, Avison, Campbell, & Speechley, 2011; Puka, Ferro, Anderson, & Speechley, 2018). The family environment, including parental depressive symptoms, at time of diagnosis can have long term effects on mothers of CWE (Puka, Ferro, et al., 2018). Research supports that HRQL of CWE is dynamic and understanding the role of parental HRQL on child's HRQL and vice versa is pertinent on establishing viable interventions (Puka, Tavares, Anderson, Ferro, & Speechley, 2018). A bidirectional relationship between child's HRQL and parental HRQL has been elucidated and should be considered when studying HRQL in children with epilepsy (Jain et al., 2018).

Understanding the HRQL of parent's with CWE is essential. However, it is also essential to understand how parents' mood and mental health may affect their children's HRQL and vice versa. Overall, studies have concluded that parental mood and mental health is a contributing factor to HRQL in CWE (Connolly et al., 2006; Jain et al., 2018; McLaughlin, Schraegle, Nussbaum, & Titus, 2018; Puka, Ferro, Anderson, & Speechley, 2019; Taylor et al., 2011; Yong, Chengye, & Jiong, 2006). For example, among children diagnosed with benign rolandic epilepsy, the emotional impact on a parent of a child experiencing epilepsy was the major factor in determining the child's quality of life, even greater than the child's cognition (Connolly et al., 2006). Similarly, it has been reported that children with epilepsy, two years post-diagnosis, compared to the general population maintain lower scores on the emotional impact of epilepsy on parents, (Speechley et al., 2012). Taylor et al. (2011), highlighted that an important step when determining if a patient with new-onset epilepsy is at risk of poor HRQL is to consider the psychosocial status of the family as well as the child's psychosocial status. One psychosocial factor that has been investigated is anxiety. It has been found that among CWE, parental anxiety outweighed children's epilepsy-related clinical characteristics as a predictor of children's HRQL (Yong et al., 2006).

In addition, parental coping is another factor of parental mood and mental health that has been investigated to influence HRQL. McLaughlin et al., (2018), demonstrates the unique role that parental coping has in youth with epilepsy's HRQL; such that, parental coping is significantly related and predicts lower scores of HRQL in youth with epilepsy.

Overall, understanding that parental mood and mental health affects CWE's HRQL highlights the need for family-based interventions and addressing the whole family during treatment (McLaughlin et al., 2018). Addressing non-medical features that have potential to be modifiable shows promise for improving parental mood and mental health with the hope, of in turn, of improving children's HRQL (Jain et al., 2018).

In conclusion, research supports that HRQL of children with epilepsy is a multi-dimensional patient reported outcome that is associated with psychosocial health, family environment and parental mental health. Therefore, targeting interventions to include the

family unit may be useful when addressing a child's HRQL (Im et al., 2019; Jain et al., 2018; Puka, Tavares, et al., 2018).

2.3.3 Psychiatric Comorbidities and Psychosocial Factors

In general, 70% of people with epilepsy become seizure free over time, placing an emphasis on understanding long term effects of comorbidities that may persist after seizures are gone (World Health Organization, 2019). Amongst children with epilepsy, comorbid conditions are common, with population estimates reaching upwards of 70% (Pastor et al., 2015; Sillanpää & Cross, 2009). Psychiatric comorbidities are the most prevalent comorbidities in children with epilepsy with reported prevalence reaching between 29-40%, which is higher than in the general population (Global Burden of Disease Collaborative Network, 2017). Identifying psychosocial problems at diagnosis of epilepsy in children is needed to address psychiatric comorbidities (Reilly et al., 2015; Taylor et al., 2011). This section will focus on psychosocial factors and psychiatric comorbidities.

Children with new-onset epilepsy, particularly those with comorbidities, are at risk for reduced HRQL at the time of diagnosis. Psychosocial support has been identified as key to addressing reduced HRQL in children (Taylor et al., 2011). Results from Baca, Vickrey, Caplan, Vassar, & Berg (2011), were consistent with the need to expand the focus from solely seizure related factors. Baca et al., (2011) determined that psychiatric comorbidities are associated with long-term HRQL in children with epilepsy. Furthermore, resolution of seizures does not ensure that comorbidities cease to affect children with epilepsy; importantly, the association of psychiatric comorbidities with worse HRQL is stronger than the association of seizure remission status with better HRQL (Baca et al., 2011). Additional studies have supported that the effect of epilepsy on HRQL in children arises through psychiatric factors (Bilgic, Isik, Sivri Colak, Derin, & Caksen, 2018). Highlighting the importance of non-seizure related factors, such as psychosocial aspects of health leads to identifying predictors that may be amenable to change and influence how we treat children diagnosed with epilepsy (Ferro et al., 2017).

Mood disorders such as, depressive and anxiety disorders, are some of the most common psychological comorbidities (Wei & Lee, 2015). Depression and anxiety are reported in 12-26% of children with epilepsy (Wei & Lee, 2015). Depressive symptoms have been found to be the strongest predictor of HRQL in children with epilepsy, over and above clinical and seizure factors (Sano et al., 2014). Specifically, symptoms of depression were more predictive of HRQL than seizure type, seizure duration and number and effects of anti-epileptic drugs (AEDs). That is not to say that number of AEDs did not have an effect, but the effect of AEDs was not as strong as depressive symptoms on HRQL (Sano et al., 2014). Symptoms of anxiety have been found to be independently and significantly related to QOL in children with epilepsy (Reilly et al., 2015). Understanding how psychosocial factors and mood disorders affect children with epilepsy may lead to changes in treatment and interventions when a child is diagnosed with epilepsy.

Overall, research has shown that psychiatric comorbidities are the most prevalent comorbidities in children with epilepsy (Global Burden of Disease Collaborative Network, 2017). Experiencing psychiatric comorbidities can negatively affect children's HRQL (Bilgic et al., 2018). Additionally, information collected through the measurement of psychosocial factors can be used to identify children at risk for diminished HRQL (Taylor et al., 2011; World Health Organization, 2019). Understanding the effects of modifiable factors, identifying them in patients, developing treatments and intervening early is pertinent to improving quality of life of children with epilepsy (Taylor et al., 2011).

2.3.4 Longitudinal Studies of Childhood-Onset Epilepsy

Cross sectional designs have often been adopted in studying the effects of epilepsy on children's HRQL. Studies identify a group of children recently diagnosed with epilepsy, evaluate their HRQL, compare them to the general public and/or identify predictive factors of HRQL (Momeni, Ghanbari, Bidabadi, & Yousefzadeh-Chabok, 2015; Sabaz et al., 2003). These studies have identified important factors related to HRQL and highlighted the impact of an epilepsy diagnosis on children and their families (Momeni et al., 2015; Sabaz et al., 2003). The importance has been recognized of conducting of longitudinal studies that focus on HRQL over time (Momeni et al., 2015) as well as those

that focus on identifying predictors of HRQL over time that are amenable to change through intervention (Ferro et al., 2014; Ferro, Landgraf, et al., 2013).

Longitudinal studies of children with epilepsy are sparse but do exist. For example, a long-term study from Nova Scotia identified a cohort of children diagnosed with idiopathic generalized epilepsy from 1977 to 1985. In 2008 to 2009, patients were contacted and asked questions that focused on social and medical outcomes. It was determined that 75% of those who responded obtained complete remission at follow up, an average of 22 years after diagnosis. The study also identified that unsatisfactory social outcomes and learning problems were common (Camfield & Camfield, 2010). This study also provided valuable information regarding remission status in a specific type of epilepsy. However, it lacked a comprehensive measure of HRQL, and measurements were not taken consistently throughout the follow up period.

Another study was published from a population based cohort in Finland (Sillanpaa, Haataja, & Shinnar, 2004). This study followed children younger than 16 years old with active epilepsy between 1961 to 1964. Participants were followed prospectively until 1997. Participants were contacted and questionnaires on HRQL and psychosocial health outcomes were completed. Participants were compared to population-based controls. Results highlighted that subjects on medication, regardless of remission status had lower scores on general and epilepsy-specific measures of QOL than controls or those off medication. It was determined that childhood-onset epilepsy had persistent long-term impacts on HRQL, especially amongst those still on medication (Sillanpaa et al., 2004).

Studies such as Sillanpaa et al., (2004) and Camfield and Camfield (2010) provided essential information regarding the long-term impact of an epilepsy diagnosis in childhood. However, neither study was able to collect repeated measurements throughout the follow up period and thus information is unavailable on the course of HRQL leading up to the final long-term assessment.

2.4 Limitations of Previous Studies

Studies of HRQL in children with epilepsy are often conducted using cross-sectional or short-term cohort designs (Momeni et al., 2015; Sabaz et al., 2003). Cross-sectional studies can provide important information regarding a child and their families experiences with an epilepsy diagnosis and their HRQL. However, cross-sectional studies are unable to provide information regarding the impact of epilepsy on HRQL over time. In contrast, longitudinal research has the potential to offer information to parents regarding prognosis and the potential course for their child's HRQL later in life. Currently, most longitudinal research in children with epilepsy relies on retrospective cohorts, comparing with age-matched controls, or single measurements from a cohort in the past (Camfield & Camfield, 2010; Sillanpaa et al., 2004). Additionally, to compare to normative populations with the intent to understand the impact of epilepsy on children, requires the use of a generic measure of HRQL, as opposed to disease-specific questionnaires.

The second phase of HERQULES extended the window of observation from the 2-year follow up, to 8-10 years later—presenting the opportunity to describe the long-term course of HRQL. To date results from that study have only been reported using a disease-specific measure of HRQL (Puka et al, 2020), but what remains to be assessed is the long-term course of HRQL, using a generic measure and comparing these outcomes to a normative sample.

To date, little is known about the factors associated with the course of HRQL for children with epilepsy in the long-term. Important steps in understanding the course of HRQL in the long-term include, measuring how levels of HRQL in children with epilepsy compare to levels in the general population and what factors contribute to improvement, decline or stable HRQL in children with epilepsy. Understanding what factors are associated with positive HRQL and how children with epilepsy compare to their age-matched peers, may aid parents to make informed decisions regarding their child's health care.

Chapter 3

3 Study Purpose and Research Objectives

3.1 Study Purpose

Children with epilepsy have poorer health-related quality of life (HRQL) than their peers in the general population (Bansal et al., 2017). To date, most of what we know about HRQL in children with epilepsy is based on cross-sectional or short-term follow-up after diagnosis. Far less is known about the long-term course of HRQL for those with childhood-onset epilepsy and the factors associated with it. The proposed research will contribute to understanding long-term HRQL associated with childhood-onset epilepsy, how HRQL in the long term compares to levels in the general population, and what factors contribute to improvement, decline or stability in HRQL over time.

Understanding what factors are associated with positive HRQL and how those with childhood-onset epilepsy compare to their age-matched peers may aid parents and clinicians in knowing what to expect and making informed decisions regarding health care for these children.

3.2 Research Objectives

The overall aim of the thesis is to describe the long-term course of HRQL in those diagnosed with childhood-onset epilepsy. There are three research objectives:

1. To evaluate HRQL associated with childhood-onset epilepsy eight years post-diagnosis.

   Related to this objective is one specific research question:

   1.1. How do average levels of HRQL in those with childhood-onset epilepsy eight years later compare to levels reported for age-matched peers in the general population?

2. To describe the course of HRQL over 8 years after the diagnosis of childhood-onset epilepsy.

   Related to this research objective are three specific research questions:

   2.1. What is the unadjusted average estimated course of HRQL from baseline to eight years later?
   2.2. Which characteristics around the time of diagnosis of childhood-onset epilepsy are associated with physical and psychosocial health summary subscale scores for HRQL eight years later?
   2.3. What is the average estimated course of HRQL from baseline to eight years later, while accounting for associated baseline characteristics?

3. To determine the change in HRQL over the 8 years following a diagnosis of childhood-onset epilepsy.

   Related to this objective, the change in HRQL will be explored through two research questions:

   3.1. For what proportion of those with childhood-onset epilepsy does HRQL eight years after diagnosis improve, worsen or not change from that reported around the time of diagnosis?
   3.2. For what proportion of those with childhood-onset epilepsy does HRQL eight years after diagnosis improve, worsen or not change from that reported two years post-diagnosis?

Chapter 4

4 Methods

This chapter presents details of the methods used for this project. The chapter starts with an overview of the source of the data. A brief description of the sampling method and study design is included. Following the study design, a description of the measurement tools used is provided. The chapter concludes with a description of the statistical methods.

4.1 Study Design and Sample

The data used for this research come from the HEalth-Related QUality of Life in Children with Epilepsy Study (HERQULES), which is a multi-center prospective cohort study of children with epilepsy in Canada. The study recruited families of newly diagnosed cases of epilepsy in children, recorded details regarding their epilepsy, measured their health-related quality of life (HRQL), documented other factors such as family environment, and followed the cohort for about 10 years since diagnosis.

For the first stage of sampling, all paediatric neurologists who were members of the Canadian Association of Child Neurology or added to the sampling frame by a panel of experts were invited to the study. A total of 72 members were contacted, of whom 53 (74%) agreed to participate. Research ethics approval was obtained from the 17 applicable research ethics boards across Canada (Western University Health Science Research Ethics Board file #10069E).

The second stage of sampling included recruiting eligible patients to be included in the study. Inclusion criteria for the HERQULES cohort were a new case of epilepsy in a child aged 4-12 years with no prior epilepsy diagnosis; parents were required to have primary responsibility over the child at least for the prior six months and have sufficient English language skills to complete questionnaires. Families were not eligible if their child had an additional diagnosis of a progressive or degenerative neurological disorder

or other major comorbid non-neurological physical disorder likely to impact their HRQL, such as asthma requiring daily medication or renal failure. Once identified as eligible for the study, parents received information regarding the study with detailed information regarding what participation would entail.

In the first phase of HERQULES, parents completed questionnaires, by mail, at four time points: at the time of diagnosis (baseline), 0.5, 1, and 2 years post-diagnosis. The questionnaires were designed to measure their child's HRQL, family factors, and demographic information. Parents' questionnaire took approximately 45-60 minutes to complete at each time. Parents also provided consent for their child's neurologist to provide clinical information at the same times. Neurologists provided clinical information such as severity of epilepsy, seizure type, and treatment. Physicians' questionnaire took approximately 5-7 minutes to complete each time. At baseline, the sample consisted of 456 eligible children; parents of 374 (82%) returned completed initial questionnaires. At the 2-year follow-up, 283 (62%) parents returned questionnaires. Throughout HERQULES, the Tailored Design Method was followed to optimize the response rate and quality of data obtained (Dillman, 2007).

In the second long-term follow-up phase of HERQULES, families were contacted for follow up at approximately the 8- and 10-years post-diagnosis, at which time self-report by the adolescents and young adults with epilepsy was introduced. Data from parents/caregivers and the participants' neurologists were collected using a mailed survey at both the 8- and 10-year follow-up. Due to the established approval across Canada from the first phase of HERQULES, approval for second phase of HERQULES was required only from the Western University Health Sciences Research Ethics Board (file #102819). At the 8-year follow-up, 168 parents returned completed questionnaires of participants who were still less than 18 years old.

My role in in the study entailed: developing research objectives for this thesis, conducting a literature review of the topics pertinent to the proposed research objectives, conducting statistical analyses under the supervision of my thesis supervisory committee, interpreting

and summarizing the results of the statistical analyses, and making conclusions based on the results.

4.2 Measures

Below is a description of the measurement tools used in HERQULES that pertain to the current project. The description of these tools is organized into parent report and physician report instruments. The baseline parent report questionnaire is included in Appendix A.

4.2.1 Parent Report

Sociodemographic Information

Sociodemographic information collected from parents included: child's sex and date of birth and parent's age, sex, marital status, employment status, education and annual household income. The current study dichotomized marital status into married or not married, with a value of one indicating married, and employment status into employed or not employed, with a value of one indicating that the parent is employed part or full time. Higher values for both education and income in the current study indicate higher levels of education and income. Values for income started at 10 000 dollars or less and increased by 10 000-dollar increments until 99 000 dollars followed by a final option of greater than 100 000 dollars.

Health-Related Quality of Life

Child Health Questionnaire-Parent Form (CHQ PF-50)

The CHQ is a generic health status tool (Landgraf, Abetz, & Ware, 1996). The questionnaire is validated for parent-report of HRQL for children ages 5-18 years in the general population as well as those with various acute and chronic health conditions.

The CHQ-PF-50 is the 50-item, parent-report version. The response options for the CHQ are ordinal and vary by the item. Each item consists of 4–6 response options. Additionally, each scale consists of a varying number of items. Most scales have a recall period of four weeks. The change in health subscale has a recall period of one year, and

both the family cohesion and general health scales rely on the child's health "in general". From the questionnaire, two summary scores, psychosocial and physical health, and fourteen subscale scores can be calculated for a detailed assessment of individual domains of HRQL to help target and develop specific interventions (Landgraf, Abetz and Ware, 1996). Each summary score is standardized and weighted with a mean of 50 and a standard deviation of 10. For each subscale and summary score, the higher the score, the more positive the outcome. For example, a higher score on the bodily pain sub-scale is interpreted positively as less pain and limitations due to pain.

The CHQ PF-50 is a well-validated and reliable measure (Hullmann et al., 2011; Landgraf et al., 1996). Internal consistency and test-retest reliability have been found to be good across normative samples and those with health conditions (Landgraf et al., 1996; Raat, Bonsel, Essink-Bot, Landgraf, & Gemke, 2002). In the first phase of HERQULES, Cronbach's alpha coefficients ranged from 0.86 to 0.89 (Speechley et al., 2012). Cronbach's alpha is a measure of internal consistency, specifically, determining whether a scale is reliable and that a set of items are measuring the same construct (Cronbach, 1951). Cronbach's alpha is measured on a scale from zero to one. A Cronbach's alpha closer to one typically indicates a higher degree of internal consistency (Cronbach, 1951). Construct and convergent validity have been evaluated. Construct validity has been found to be good (Brunner et al., 2009; Drotar, Schwartz, Palermo, & Burant, 2006). Convergent validity is considered good based on associations observed between scores on the CHQ PF-50 compared to other pediatric quality of life measures (Brunner et al., 2009). A confirmatory factor analysis of the CHQ in the HERQULES sample provided evidence that the higher-order summary factor structure of the CHQ is robust over time (Ferro, Landgraf, et al., 2013).

Family Environmental Factors

Family Adaptability, Partnership, Growth, Affection, and Resolve (Family APGAR)

The Family Adaptability, Partnership, Growth, Affection, and Resolve (Family APGAR) scale assesses satisfaction with family relationships (Smilkstein, 1978). It has five-items and uses a five-point Likert scale (0–4) with higher scores indicating greater satisfaction.

The APGAR has been shown to be valid and reliable in clinical and research settings (Smilkstein, 1978; Smilkstein, Ashworth, & Montano, 1982). In the current sample, Cronbach's alpha coefficient was 0.87 (95% CI: 0.85-0.89)

Family Inventory of Resources for Management (FIRM)

The Family Inventory of Resources for Management (FIRM) assesses what social, psychological, community and financial resources, families have available to aid them in adapting to stressful events (McCubbin, Thompson, & McCubbin, 1996). Respondents rate how each statement describes their family situation with response options ranging from 0 (not at all) to 3 (very well). The FIRM has 24 questions that are summed for a total score. Higher scores indicate greater resources. The FIRM has demonstrated adequate reliability and validity (McCubbin et al., 1996). In the current sample, Cronbach's alpha coefficient was 0.90 (95% CI: 0.88-0.91).

Family Inventory of Life Events and Changes (FILE)

The Family Inventory of Life Events and Changes (FILE) is a 71-item self-report questionnaire of family stress in the previous year across nine domains (McCubbin et al., 1996). Scores are tabulated for each domain and a total "pile-up" scale by counting the number of events experienced. The FILE's reliability and validity are well-established (McCubbin et al., 1996). In the current sample, Cronbach's alpha coefficient was 0.84 (95% CI: 0.82-0.86).

Center for Epidemiological Studies Depression Scale (CES-D)

The Center for Epidemiological Studies Depression Scale (CES-D) is a 20-item measure that assesses frequency of symptoms of depression over the past week (Radloff, 1977). The CES-D uses a four-point Likert scale, with total scores ranging from 0-60. The total score is calculated by summing all item responses, with a higher score indicating greater impairment. The factor structure of the CES-D has been established in adult women from the HERQULES sample; providing support that the scale is longitudinally invariant and changes in scores over time reflect true changes in depressive symptoms (Ferro &

Speechley, 2013). In the current sample the Cronbach's alpha coefficient was 0.97 (95% CI: 0.96-0.98).

4.2.2 Physician Report

Severity of Epilepsy (GASE)

The overall severity of epilepsy was measured at baseline using the Global Assessment of Severity of Epilepsy (GASE) Scale (Speechley et al., 2008). The GASE Scale is a single item, 7-point global scale created to provide clinicians with a simple and efficient tool that categorizes patients by severity of illness. The single question asked is: "Taking into account all aspects of this patient's epilepsy, how would you rate its severity at his/her last visit? Please check one answer". The response options are: (1) extremely severe, (2) very severe, (3) quite severe, (4) moderately severe, (5) somewhat severe, (6) a little severe, (7) not at all severe. The GASE is considered to have adequate construct validity, stability and responsiveness to clinical changes as well as good intra- and inter-rater reliability (Chan, Zou, Wiebe, & Speechley, 2015; Speechley et al., 2008).

Seizure Type

Neurologists reported epilepsy characteristics such as seizure type and epilepsy syndrome of each patient, according to International League Against Epilepsy (ILAE) classifications (ILAE, 1989). For the current analyses, values were collapsed into three epilepsy syndrome categories: generalized, focal/partial, and undetermined.

Behavioural Problems

The physician questionnaire included the following question: "Does the patient have behavioural problems?". If the answer was yes, then physicians reported on the severity of the behavioural problems on a 3-point scale, (1) mild, (2) moderate, (3) severe and provided the diagnoses. The current study dichotomized this variable as the presence or absence of behavioural problems.

Cognitive Problems

The physician questionnaire included the following question: “Does the patient have cognitive problems?”. If the answer was yes, then physicians reported on the severity of the cognitive problem on a 4-point scale, (1) borderline, (2) mild, (3) moderate, (4) severe and provided the diagnoses. The current study dichotomized this variable as the presence or absence of cognitive problems.

4.3 Methods of Statistical Analysis

All analyses were conducted using STATA/SE 13.0 software for Mac (StataCorp LP., College Station, TX, USA). Analyses are described below in the order of the three objectives and their respective research questions as presented in Chapter 1.

4.3.1 Objective 1

To evaluate HRQL associated with childhood-onset epilepsy eight years post-diagnosis.

The research question associated with Objective 1, (How do average levels of HRQL in those with childhood-onset epilepsy eight years later compare to levels reported for age-matched peers in the general population?) were addressed as described below

Summary statistics and frequency distributions of sample characteristics were used to describe the sample at baseline, 2-year and 8-year follow up. Scale scoring was completed as outlined by the CHQ User’s Manual (Landgraf et al., 1996). Reverse scoring was completed where necessary. Reverse scoring is the process of recoding the response options of an item in a questionnaire, so the numerical scoring runs in the opposite direction of the original question. This is done in the CHQ to ensure all items are positively scored, such that a higher numerical score indicates better health than a lower score. Scores are imputed, using mean substitution, for those individuals with missing items, provided that the respondents answered at least half of the items in the scale. Raw subscale scores were computed and then transformed to range from 0 to 100, with a higher score indicating better health. To calculate the two-summary score means (psychosocial and physical health) for the sample, ten of the CHQ scales are standardized

using means and standard deviations from the general U.S. population and six clinical samples. The scales are then aggregated using weights from the same normative and clinical data sets. Then, the aggregate scores are standardized using a linear T-score transformation—resulting in a mean of 50 and a standard deviation of 10. Then, CHQ subscale and summary scores were compared between the study sample and a population normative sample (Landgraf, Abetz, and Ware, 1996) using two sample t-tests. P-values are reported along with the confidence interval of the sample mean differences.

4.3.2 **Objective 2**

Assess the extent to which characteristics around the time of diagnosis with childhood-onset epilepsy are associated with HRQL eight years later. Furthermore, describe the course of HRQL over 8 years while accounting for associated characteristics.

The first research question associated with this objective (What is the unadjusted average estimated course of HRQL from baseline to eight years later?) was addressed by the analyses described here.

A mixed-effects model was used to examine the course of HRQL measured at baseline, 0.5, 1, 2, and 8 years later for the psychosocial and physical health summary scores (Laird & Ware, 1982). The model has the following form.

$$y_{ij} = b_{0j} + b_{1j}T_{ij} + b_{2j}T_{ij}^2 ,$$

with

$$b_{0j} = b_0 + u_{0j}, b_{1j} = b_1 + u_{1j}, b_{2j} = b_2 + u_{2j}$$

where y_{ij} is the outcome of subject j at occasion i, T_{ij} is the corresponding time since diagnosis and was treated as continuous, b_{0j} is the intercept, and b_{1j} and b_{2j} are the coefficients of linear and quadratic relationships between time and outcome. These coefficients have mixed effects that comprise a sample average fixed effect (b_0, b_1, b_2) and a subject-specific random effect (u_{0j}, u_{1j}, u_{2j}), which are assumed to be normally distributed with means of 0 and variance-covariance to be estimated. In this thesis, an unstructured variance-covariance matrix was adopted, because the variances of the

random effects are unlikely to be the same since they describe different aspects of the individual curves. Individual differences were assessed by estimating a random coefficient representing variability around the averaged intercept and the slope.

Therefore, the mixed-effects model consists of the fixed effects, given by $y = b_0 + b_1T + b_2T^2$, to describe the average curve, and the random effects to account for the individual departures from the average curve. One can recognize that in the fixed effect model, b_0 represents the average outcome at time 0, b_1 and b_2 together represent the outcome change per unit time, or the rate of the outcome changes over the follow up time.

Mixed effect models are a commonly used approach for the analysis of repeated-measures data and provide estimates of the average change in a sample, accounting for correlations between repeated measures, missing data, and variations in the measurements of time (Singer & Willett, 2003). No covariates were added to the model, solely the effect of time on HRQL was estimated.

The second research question associated with this objective (which characteristics around the time of diagnosis with childhood-onset epilepsy are associated with physical and psychosocial health summary subscale scores of HRQL measurements eight years later?) was addressed by the analyses described below.

Associations between baseline risk factors and the CHQ, physical and psychosocial health summary scores 8 years later were calculated using Pearson correlations and ANOVA. P values, r values, and F values are presented. r values indicate the strength of a linear association between two continuous variables. F values provide an indication of the significance of a group of categorical variables; such that, a high F value indicates a high joint effect of all groups compared to the outcome variable.

The third research question associated with this objective (what is the average estimated course of HRQL from baseline to eight years later, while accounting for associated baseline characteristics?) was addressed by the analyses outlined below.

To investigate the effect of baseline characteristics on the psychosocial and physical health summary scores over time, the model from the first question associated with Objective 2 was expanded. Specifically, the model takes the following form:

$$y_{ij} = b_{0j} + b_{1j}T_{ij} + b_{2j}T_{ij}^2 + a_1X_1 + a_2X_2 + \cdots + a_pX_p$$

where X_1 to X_p and a_1 to a_p denote p baseline characteristics and their corresponding effects on a trajectory. Factors retained in the final model were selected using the Akaike information criterion (AIC) and Bayesian information criterion (BIC) statistics, with smaller values suggesting better models. Residues from the models were subjected to examination of assumptions using scatter plots. The model included baseline characteristics selected from bivariate analyses with $p < 0.20$ used as the criterion (Maldonado & Greenland, 1993). The guideline of 10 observations per variable was also considered when deciding the maximum number of characteristics to be included in the mixed-effects model (Peduzzi, Concato, Feinstein, & Holford, 1995). Both linear and quadratic terms for time were considered.

4.3.3 **Objective 3**

To determine the change in HRQL over the 8 years since diagnosis.

The two research questions that are associated with this objective (For what proportion of those with childhood-onset epilepsy does HRQL eight years after diagnosis improve, worsen or not change from that reported around the time of diagnosis? And for what proportion of those with childhood-onset epilepsy does HRQL eight years after diagnosis improve, worsen or not change from that reported two years post-diagnosis?) were addressed by the analyses described below.

The two CHQ subscales psychosocial health and physical health were considered the outcomes to be assessed in two parallel analyses. Change scores from baseline to 8 years and 2 years to 8 years were computed for both the psychosocial and the physical health summary scores. As a minimal clinically important difference has not been established for the CHQ-PF50 to date, change scores greater than or equal to 0.5 of a standard deviation were considered clinically important (Rai et al., 2015). Scores were then

grouped as improved, worsened or no change. Proportions of the samples in each of these categories are reported along with confidence intervals.

Chapter 5

5 Results

This chapter presents the results for this thesis. The first section describes the characteristics of the sample studied. The following sections describe the findings related to each of the research objectives and the associated research questions.

5.1 Sample Characteristics

At baseline, 374 children were included in the sample. Children were on average, 7.5 years old (SD = 2.3) and 52.3% were male. The majority of primary caregivers participating were a biological parent (94.1%) and female (92.7%). Of parents, the majority was married (79.6%), employed (66.5%), and had obtained post-secondary education (66.5%). The characteristics of adolescents, their parents and their families at baseline, 2- and 8-year follow-ups are summarized in Table 5.1.

At the 2-year follow up, 281 children were included in the sample. 85.7% of the sample had physician report data (n = 241) for epilepsy specific characteristics. The majority was diagnosed with localization-related epilepsy syndrome types (60.2%). At 2 years post-diagnosis, 31% were experiencing seizures, 21-9% were reported to have behavior problems and 28.1% to have cognitive problems.

At the 8-year follow up, 191 adolescents were included in the sample. This thesis focuses on a sub-sample aged 18 years and younger at the 8-year follow up. A total of 168 adolescents, 18 years or younger, 88.0% of the sample at 8-year follow up, were included in the analyses reported here. The average age of these adolescents was 15.0 years old (SD = 2.1). At 8 years post-diagnosis, 54.8% of adolescents were male. Of the sample at 8 years post-diagnosis, only 21% had a physician report on epilepsy specific characteristics since the vast majority of adolescents were no longer receiving any care for epilepsy. Thus, epilepsy-related characteristics at the 8-year follow-up were not analysed.

When comparing baseline characteristics, parents who remained in the sample to participate in the 8-year follow-up, had more education ($p = 0.001$), a higher household income ($p < 0.0001$), lower scores on depression symptoms, higher family functioning scores ($p = 0.0415$), higher family resources scores ($p < 0.0001$), lower scores on family demands ($p = 0.0003$) and their children were older ($p = 0.0021$) and less likely to have a cognitive problems ($p = 0.001$) than those who participated in the study initially but were lost to follow-up. There were no baseline significant differences in the two groups on the age ($p = 0.2802$), employment ($p = 0.175$), or marital status ($p = 0.055$) of the parent or the child's diagnosed epilepsy syndrome ($p = 0.284$), number of AEDs taken ($p = 0.382$), frequency of seizures ($p = 0.226$), severity of epilepsy ($p = 0.069$), or whether the child had behavioural problems ($p = 0.160$).

Table 5.1: Summary characteristics of sample at baseline at 2 years and 8 years after diagnosis.

	Baseline (n = 374)	2 Years (n= 281)	8 Years (n=168)
Children's Characteristics			
Age in years, mean (SD)	7.5 (2.3)	10.0 (2.3)	15.0 (2.1)
Sex, % male	52.3	52.0	54.8
Epilepsy syndrome type, %			
Generalized epilepsies	38.8	37.3	—
Localization-related (partial/focal epilepsies)	59.3	60.2	—
Not determined whether focal or generalized	1.9	2.5	—
Taking antiepileptic drugs, %	67.1	75.4	—
Experiencing seizures, %	93.4	31.3	—
Severity of Epilepsy, GASE, mean (SD)	5.4 (1.2)	6.3 (1.0)	—
Comorbidities, %			
Behavioural problems, %	15.1	21.9	—
Cognitive problems, %	20.0	28.1	—
Family Characteristics			
Parent's age in years, mean (SD)	38.2 (6.1)	40.8 (5.6)	46.1 (5.4)
Parent's sex, % female	92.7	92.9	94.1
Parent's marital status, % married	79.6	82.1	82.1
Parent's employment status, % employed	66.5	75.7	82.7
Education, % post-secondary	66.5	75.0	82.6
Annual household income, %			
<$39,999	20.9	14.2	7.8
$40,000—59,999	20.1	17.1	9.6
$60,000—79,999	18.0	18.9	11.4
≥$80,000	34.9	41.6	67.4
Depressive symptoms, CES-D, mean (SD)	14.3 (10.3)	11.8 (9.9)	10.4 (9.2)
Functioning, Family APGAR, mean (SD)	13.9 (3.8)	14.1 (3.9)	14.5 (3.6)
Resources, FIRM, mean (SD)	50.1 (11.1)	50.7 (11.5)	52.7 (11.2)
Demands, FILE, mean (SD)	9.5 (6.5)	7.8 (5.7)	8.3 (5.8)

5.2 Objective 1

To evaluate health-related quality of life (HRQL) associated with childhood-onset epilepsy eight years post-diagnosis.

Presented here are the results from the research question associated with Objective 1, (How do average levels of HRQL in those with childhood-onset epilepsy eight years later compare to levels reported for age-matched peers in the general population?).

Average levels of HRQL in the HERQULES sample at 8 years post-diagnosis were compared to the normative data collected from a general United States (U.S.) population sample of women who were parents of 252 children aged 5-18 years using the Child Health Questionnaire Parent-Form (CHQ-PF50). Two-sample, independent, t-tests were completed comparing the normative sample and the epilepsy sample for each of the 14 CHQ subscales and the two summary scores.

Results are summarized in Table 5.2. The epilepsy sample scored higher than the normative sample on three scales, general health ($p = 0.0240$), bodily pain ($p = 0.0117$) and family-cohesion ($p = 0.0103$). The epilepsy sample scored lower than the normative sample on one scale related to child, role/social limitations—emotional-behavioral ($p = 0.0281$), and two scales related to family, family-limitations in activities ($p = 0.0047$), and parental impact-emotional ($p < 0.0001$). The largest difference between the normative sample and the epilepsy sample was on the emotional impact on parents, which was 10 points lower on average in the epilepsy sample compared to the normative population. There was no significant difference between the epilepsy and normative sample on the remainder of subscales or the two summary scales.

Table 5.2: Average levels of HRQL compared between HERQULES sample at 8 years and U.S. normative data

	HERQULES (8 years)				U.S. normative data (n = 252)		
CHQ Score	N	Mean	SD	CI (95%)	Mean	SD	P value
Physical Functioning	168	94.3	15.1	92.0-96.6	95.6	15.3	0.3955
Role/Social-Physical	166	92.3	21.8	88.9-95.6	93.2	20.3	0.6560
General Health	168	76.5	17.1	73.8-79.1	72.5	17.8	0.0240
Bodily Pain	166	85.2	21.0	82.0-88.5	80.2	19.2	0.0117
Family Activities	168	83.7	21.1	80.5-86.9	89.4	19.6	0.0047
Role/Social Emotional/Behavioural	166	87.6	24.9	83.7-91.4	92.1	19.6	0.0381
Parental Impact-Time	168	87.6	20.9	84.4-90.8	87.2	20.5	0.8590
Parental Impact-Emotional	168	69.0	26.6	64.9-73.1	79.1	19.9	<0.0001
Self Esteem	166	76.9	19.4	73.9-79.9	78.7	16.9	0.3161
Mental Health	167	78.0	16.8	75.4-80.5	78.2	13.0	0.8719
Behaviour	167	74.8	19.5	71.8-77.8	75.1	17.1	0.8719
Family Cohesion	168	77.3	20.7	74.1-80.4	71.9	21.2	0.0103
Physical Summary Score	164	53.7	8.9	52.3-55.1	52.7	9.4	0.2800
Psychosocial Summary Score	164	49.3	11.7	47.5-51.1	50.9	9.0	0.1199

5.3 **Objective 2**

To describe the course of HRQL over 8 years after the diagnosis of childhood-onset epilepsy.

The results from the research question associated with Objective 2 (What is the unadjusted average estimated course of HRQL from baseline to eight years later?) are presented here.

The unadjusted mixed-effects model tested the effect of changes in scores over time, without accounting for predictors of change. Separate parallel analyses were conducted for psychosocial and physical health summary scores. Both linear and quadratic terms for time were tested for each of the two models.

Psychosocial health scores were visually inspected using a scatter plot, which is presented in Figure 5.1. The quadratic term for time was statistically significant and remained in the model ($p = 0.002$) (Table 5.3). Individual differences among participants were assessed by estimating a random coefficient representing variability around the averaged intercept and the slope. The mean intercept of 46.7 describes the average psychosocial health score at baseline, the years term describes the gradient or rate of growth in the unit of years, and the quadratic years term represents the multiplicative acceleration in psychosocial health scores and the shape of the curve. The years term and the quadratic years term must be interpreted together. In the unadjusted model, the average psychosocial health score at baseline was 46.7, and adolescents' scores increased by 1.6 points each year. There was a decreasing growth rate over time, as indicated by a negative coefficient for the quadratic time, here being the years since diagnosis variable; indicating a slowing of growth over time. In other words, the results suggest that at time zero, if the slope of psychosocial health scores were to remain unchanged, scores would linearly increase by an average of 1.6 points each year. However, as the quadratic term is significant and negative, this indicates that for each year's increase—the slope reduces by the coefficient for the quadratic term of time multiplied by two, or, 0.32 of a psychosocial health unit. CHQ scores for psychosocial health appear to increase until 2 years post-diagnosis at which time HRQL remains stable until 8 years. The average psychosocial

health summary score growth curve model for unadjusted psychosocial health scores over 8 years is provided in Figure 5.1.

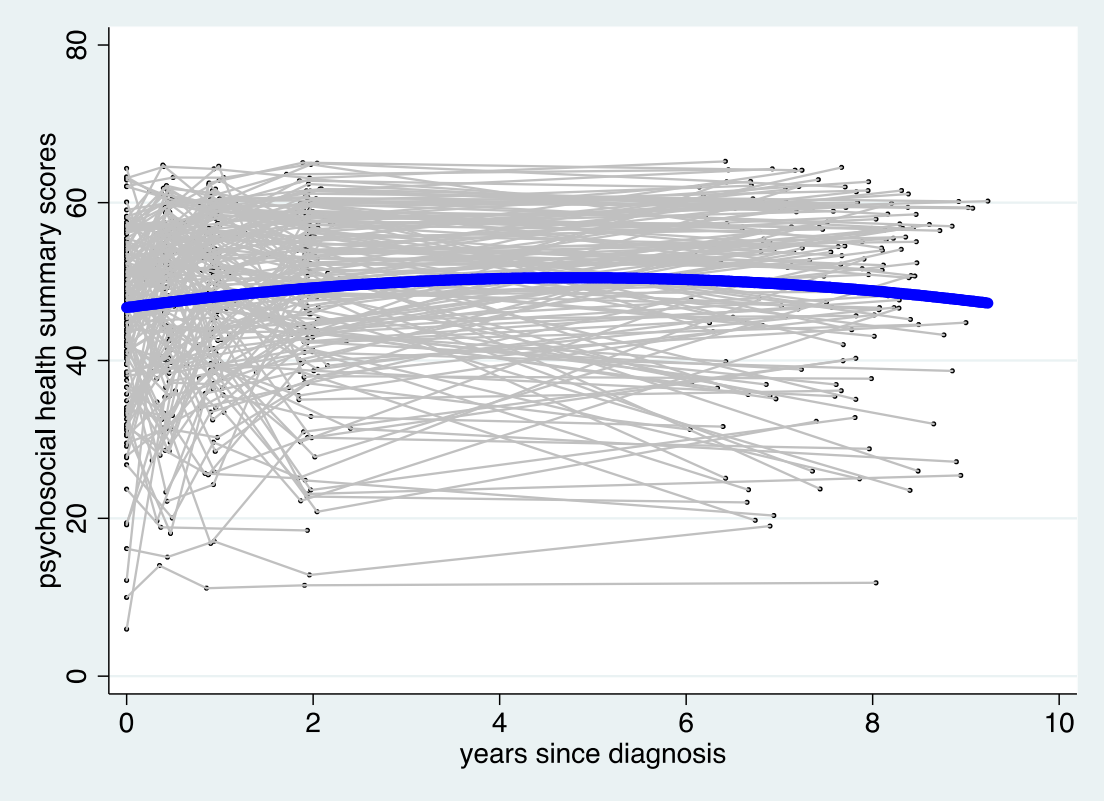

Figure 5.1: Scatter plot with connected lines and average psychosocial health summary score growth curve model for unadjusted psychosocial health scores over 8 years.

Table 5.3: Growth curve models of psychosocial health summary scores across 8 years in those with childhood-onset epilepsy

Variable	Level-1, Unadjusted regression, including quadratic term for time	Level-2, adjusted regression
	β (standard error) *P*	β (SE) *P*
Intercept	46.71 (0.77) *<0.0001*	34.30 (6.50) *<0.0001*
Years	1.57 (0.43) *<0.0001*	1.42 (0.43) *0.001*
Years^2	-0.16 (0.05) *0.002*	-0.14 (0.05) *0.006*
Age at baseline		-0.47 (0.62) *0.449*
Age at seizure onset		1.06 (0.61) *0.080*
Epilepsy severity (GASE)		0.04 (0.52) *0.943*
Parental Depressive Score (CES-D)		-0.11 (0.08) *0.181*
Family Functioning (APGAR)		0.28 (0.22) *0.205*
Family Resources (FIRM)		0.26 (0.09) *0.002*
Family Demands (FILE)		-0.07 (0.13) *0.572*
Cognitive Problems		-6.76 (1.91) *<0.0001*
Variance (Intercept)	77.74 (11.27)	45.80 (8.09)
Variance (Years)	4.32 (4.22)	3.51 (3.97)
Variance (Years^2)	0.05 (0.06)	0.04 (0.06)
Covariance (Intercept, Years)	0.72 (4.98)	1.37 (4.20)
Covariance (Intercept, Years^2)	-0.23 (0.59)	-0.36 (0.49)
Covariance (Years, Years^2)	-0.45 (0.51)	-0.33 (0.47)
Log restricted-likelihood (*P*)	-2896.36 (*0.0002*)	-2708.10 *(<0.0001*)
AIC	5812.72	5452.20
BIC	5859.79	5536.02

Note. For AIC (Akaike information criterion) and Bayesian information criterion (BIC) BIC the smaller the better.

Physical summary scores were visually inspected using a scatter plot (Figure 5.2), followed by including both linear and quadratic terms in the mixed model with results presented in Table 5.4. The quadratic term for the model was not statistically significant and thus removed from the model. The intercept, 51.8, describes the average physical score at baseline; the years term describes the gradient or rate of growth in the unit of years. On average, physical health summary scores increased by 0.3 units per year and that change was statistically significant ($p = 0.003$). The average physical summary score growth curve model for unadjusted physical scores over 8 years is shown in Figure 5.2.

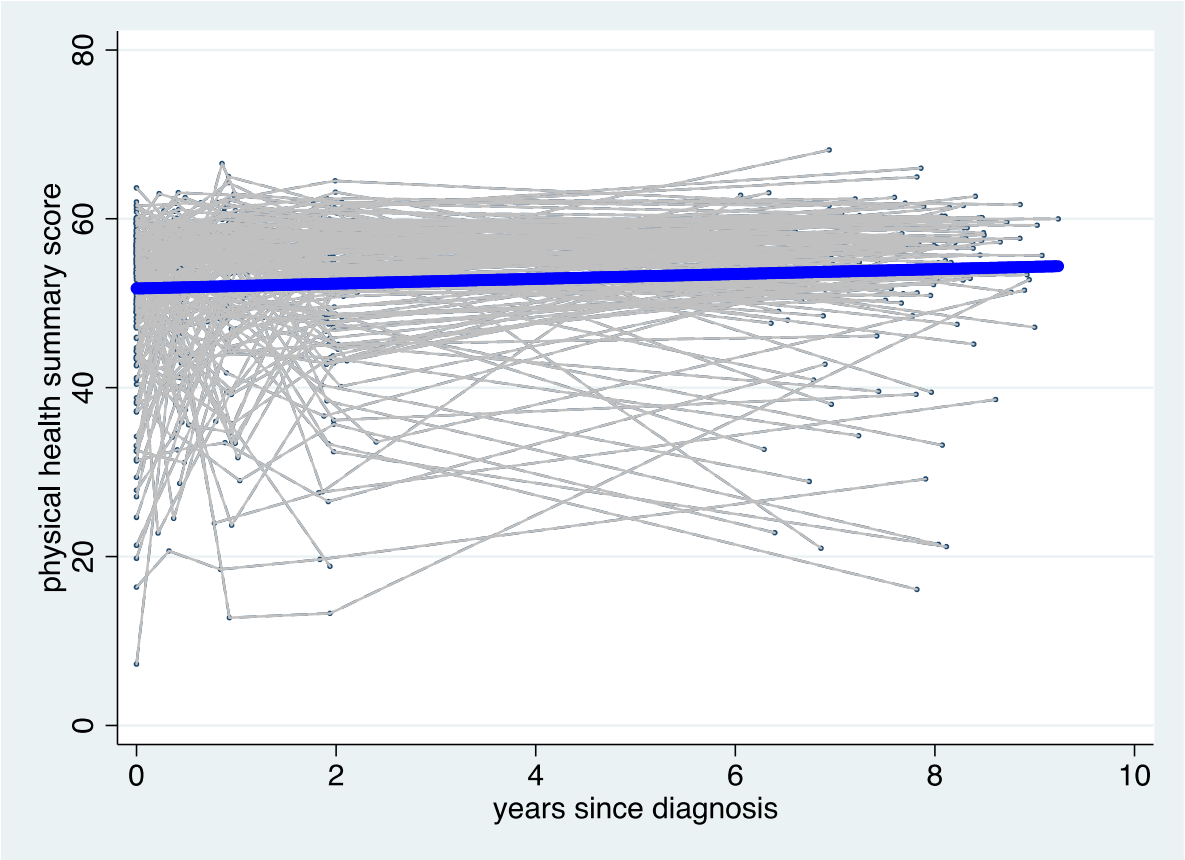

Figure 5.2: Scatter plot with connected lines and average physical health summary score growth curve model for unadjusted psychosocial health scores over 8 years.

Table 5.4: Growth curve models of physical summary scores across 8 years in those with childhood-onset epilepsy

Variable	Unadjusted regression, with quadratic term for time	Unadjusted regression, without quadratic term for time	adjusted regression
	β (standard error) *P*		β (SE) *P*
Intercept	51.24 (0.64) *<0.001*	51.75 (0.57) *<0.001*	57.55 (3.84) *<0.001*
Years	1.06 (0.45) *0.019*	0.28 (0.10) *0.003*	0.27 (0.10) *0.004*
$Years^2$	-0.10 (0.05) *0.062*		
Parental Depressive Score (CES-D)			-0.22 (0.06) *0.001*
Family Functioning (APGAR)			0.06 (0.17) *0.732*
Family Resources (FIRM)			0.02 (0.06) *0.35*
Cognitive Problems			-4.66 (1.48) *0.002*
Variance (Intercept)	47.25 (7.63)	41.13 (0.19)	33.55 (5.22)
Variance (Years)	10.15 (3.86)	0.46 (0.19)	0.47 (0.19)
Variance ($Years^2$)	0.11 (0.05)		
Covariance (Intercept, Years)	-8.56 (4.33)	-1.63 (0.81)	-1.63 (0.76)
Covariance (Intercept, $Years^2$)	0.77 (0.50)		
Covariance (Years, $Years^2$)	-1.02 (0.43)		
Log restricted-likelihood (*P*)	-2821.45 (*0.0071*)	-2826.85 (*0.0029)*	-2793.96 *(<0.0001*)
AIC	5662.90	5665.70	5607.91
BIC	5709.95	5693.93	5654.91

Presented here are the results for the second research question associated with Objective 2 (Which characteristics around the time of diagnosis with childhood-onset epilepsy are associated with physical and psychosocial health summary subscale scores of HRQL measurements eight years later?).

Parallel analyses were conducted for the CHQ psychosocial health and physical health summary scales. Unadjusted associations between baseline risk factors and psychosocial health scores 8 years post-diagnosis were assessed using Pearson correlations and ANOVA (Table 5.5). Children who were older at the time of epilepsy onset ($r = 0.18$, $p = 0.0210$), had higher scores on psychosocial health ($r = 0.53$, $p < 0.0001$), family functioning (APGAR; $r = 0.33$, $p < 0.0001$), and family resources (FIRM; $r = 0.45$, $p < 0.0001$), had no behavioural problems ($F = 15.00$, $p = 0.0002$), no cognitive problems ($F = 14.78$, $p = 0.0002$), and families with a higher income ($F = 1.91$, $p = 0.0487$) had higher psychosocial health scores 8 years later. In addition, children whose parents reported higher scores on depressive symptoms (CES-D; $r = -0.28$, $p = 0.0002$) and family demands (FILE; $r = -0.33$, $p < 0.0001$), had lower psychosocial health scores 8 years later.

Table 5.5: Associations between Baseline Risk Factors and 8-year CHQ Psychosocial Health Scores

	R	***P*-value**
Child age	0.10	0.2045
Age at seizure onset	0.18	0.0210
Number of antiepileptic drugs	-0.07	0.3558
Health-related quality of life, CHQ-Psych	0.53	<0.0001
Epilepsy severity, GASE	0.12	0.1317
Parent age	-0.02	0.8458
Parent depressive symptoms, CES-D	-0.28	0.0002
Family functioning, APGAR	0.33	<0.0001
Family resources, FIRM	0.45	<0.0001
Family demands, FILE	-0.33	<0.0001
	F (df)	***P*-value**
Child gender	0.96 *(1)*	0.3294
Seizure type	0.89 *(6)*	0.5054
Behavior problems	15.00 *(1)*	0.0002
Cognitive problems	14.78 *(1)*	0.0002
Marital status	0.78 *(4)*	0.3783
Employment status	1.19 *(4)*	0.2763
Education	1.40 *(5)*	0.2272
Annual household income	1.91 *(10)*	0.0487

Unadjusted associations between baseline risk factors and physical health scores 8 years post-diagnosis were assessed using Pearson correlations and ANOVA (Table 5.6). Children with higher physical scores ($r = 0.31$, $p < 0.0001$), family resources (FIRM; $r = 0.19$, $p = 0.0132$), and those without cognitive problems ($F = 9.14$, $p = 0.0029$) had higher physical health scores 8 years later. In addition, children whose parents reported having higher depressive symptoms scores at baseline (CES-D; $r = -0.20$, $p = 0.0096$) had lower scores on physical health 8 years later.

Table 5.6: Associations between Baseline Risk Factors and 8-year CHQ Scores-Physical Health

	R	***P*-value**
Child age	0.02	0.7952
Age at seizure onset	0.09	0.2723
Number of antiepileptic drugs	-0.01	0.9286
Health-related quality of life, CHQ-Physical	0.31	<0.0001
Epilepsy severity, GASE	0.09	0.2369
Parent age	-0.02	0.8134
Parent depressive symptoms, CES-D	-0.20	0.0096
Family functioning, APGAR	0.13	0.0857
Family resources, FIRM	0.19	0.0132
Family demands, FILE	-0.07	0.3926
	F (df)	***P*-value**
Child gender	0.34 *(1)*	0.5613
Seizure type	0.73 *(6)*	0.6292
Behavior problems	2.61 *(1)*	0.1081
Cognitive problems	9.14 *(1)*	0.0029
Marital status	0.78 *(4)*	0.3783
Employment status	1.19 *(4)*	0.2763
Education	0.64 *(5)*	0.6667
Annual household income	0.33 *(10)*	0.3331

The results for the third research question associated with Objective 2 (What is the average estimated course of HRQL from baseline to eight years later, while accounting for associated baseline characteristics?) are presented here.

Below are results for psychosocial and physical health summary scores analyzed using the mixed-effects models including baseline characteristics. Both linear and quadratic terms for time were tested in each model.

5.3.1 Psychosocial Summary Score Results

All baseline characteristics found to be significant in the unadjusted analysis were included in the adjusted model, to test the effect of time on psychosocial health summary scores as a function of baseline characteristics. Any characteristic that was found to have a p-value of less than 0.2 was recorded and added to the final model. The quadratic term was statistically significant and remained in the model. The final model tested the effect of time on psychosocial health scores as a function of child's age at epilepsy onset, age at onset of epilepsy, seizure severity (GASE), parent's score on depressive symptoms (CES-D), family functioning (APGAR), family resources (FIRM), family demands (FILE), and child's cognitive status.

The coefficient for time indicated that at time zero, if the slope of psychosocial health scores were to remain unchanged, scores would linearly increase by an average of 1.4 points each year. However, as the quadratic term is significant and negative, the quadratic term must be included in the interpretation, such that for each year increase, the slope reduces by the coefficient for the quadratic term of time multiplied by two, or, 0.28 of a psychosocial health unit. CHQ scores for psychosocial health appear to increase until 2 years post-diagnosis at which time HRQL remains stable until 8 years.

When entered into the final model, the coefficients for age at baseline, age at onset of epilepsy, baseline severity of epilepsy, parental depressive symptoms, family functioning, and family demands did not remain significant (Table 5.3). In other words, certain baseline variables such as age at diagnosis and parental depressive scores are associated

with final psychosocial health scores, but not over time. However, results indicate that family resources at baseline did have a significant and positive association with psychosocial health scores such that, for each family with a one-unit higher score in family resources at baseline, psychosocial health scores increase by a factor of 0.3 per unit of time (0.26, $p = 0.002$). Additionally, results indicate that presence of a cognitive problems at baseline had a significant and negative association with psychosocial health scores, such that if a child had cognitive problems at baseline, psychosocial health scores would be lower, on average, by a factor of 6.8 compared to those without cognitive problems. A graphical representation of the predicted growth curve across time is presented in Figure 5.3.

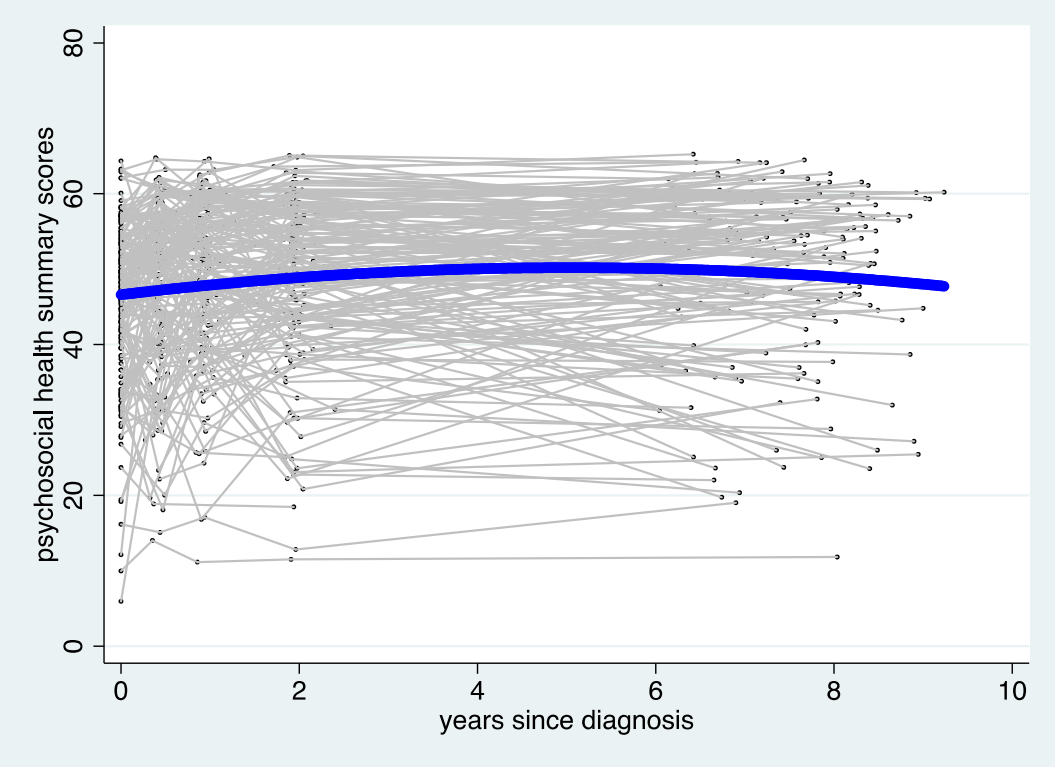

Figure 5.3: The average fitted growth curve model for adjusted psychosocial health scores over 8 years.

When examining information criteria, comparing the Level-1 unadjusted model and the Level-2 adjusted model, both the Akaike information criterion (AIC) and the Bayesian information criterion (BIC) decreased. The AIC and BIC for each model are presented in Table 5.3.

5.3.2 Physical Summary Score Results

For the physical health summary score, the adjusted model examined the effect of baseline characteristics on time trend of physical health summary scores. All baseline characteristics found to be significant in the unadjusted analysis were tested in the model independently. Any characteristic found to have a p-value of less than 0.2 was recorded and added to the final model. The final model tested the effect of time on physical health scores as a function of parent's depressive symptoms score (CES-D), family functioning (APGAR), family resources (FIRM), and child's cognitive status.

When modelling time, the quadratic term was not statistically significant and was not retained in the model. The coefficient for time was significant and positive, indicating that, on average, physical health summary scores increased by 0.27 units per year ($p = 0.004$).

When entered in the final model, the coefficients for family functioning, and family resources did not remain significant (Table 5.4). In other words, certain baseline variables such as family functioning and resources are associated with 8-year physical scores, but not over time. However, results indicate that parental depression scores at baseline did have a significant, negative association with the physical summary score, such that as parental depressive scores at baseline increase, physical health scores decrease by a factor of 0.22 per unit of time (0.22, $p = 0.001$). Additionally, results indicate that presence of cognitive problems at baseline had a significant, negative association with physical health scores such that, if a child had cognitive problems at baseline, physical health scores would be on average lower by a factor of 4.66 compared to those without cognitive problems, while all other factors are held constant. A graphical representation of the predicted growth curve across time is presented in Figure 5.4.

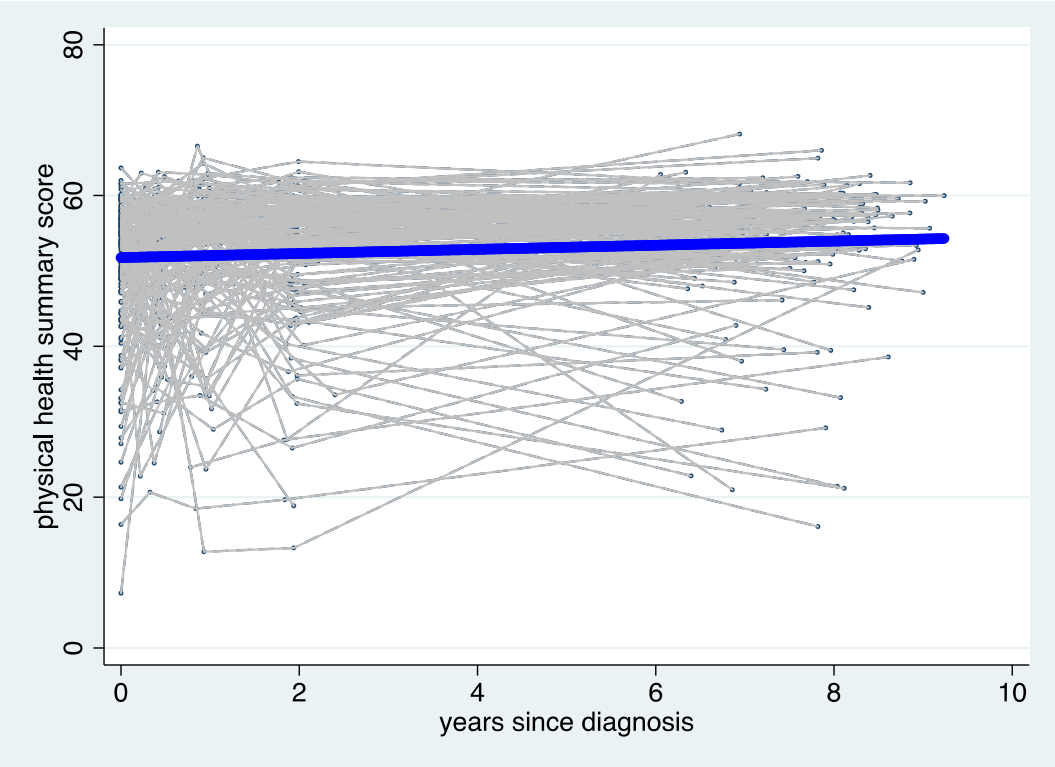

Figure 5.4: The average fitted growth curve model for adjusted physical health summary scores over 8 years.

Fit statistics as quantified by the AIC and BIC were improved by the adjusted models. Results in Table 5.4 showed that both AIC and BIC from adjusted model are smaller than that from the unadjusted models.

5.4 Objective 3

To determine the change in HRQL over the 8 years following a diagnosis of childhood-onset epilepsy.

5.4.1 Proportion of Change Across Eight Years After Diagnosis

The results for the first research question associated with Objective 3 (For what proportion of those with childhood-onset epilepsy does HRQL eight years after diagnosis improve, worsen or not change from that reported around the time of diagnosis?) are presented here.

The physical and psychosocial health summary scores derived from the CHQ were the two outcome measures used in two parallel analyses. Change scores from baseline to 8 years were computed for both the psychosocial and the physical health summary scores. As a minimal clinically important difference has not been established for the CHQ-PF50 to date, a change score greater than or equal to one half of a standard deviation of the change score was used to represent a clinically important difference.

Using the CHQ-psychosocial health summary score and standard deviation method, clinically important changes were calculated between baseline and 8 years later (Table 5.7). Based on one half of a standard deviation, a change in psychosocial health scores larger or equal to 5.5 psychosocial health units was considered a clinically important change. Across 8 years, 41% (95% CI: 22-48) of adolescents experienced a clinically important improvement, whereas 59% experienced either no clinically important change (37%, 95% CI: 30-45) or a clinically important decline (22%, 95% CI: 16-29).

Table 5.7: Change in psychosocial health summary scores (CHQ) from baseline to 8 years after diagnosis of epilepsy (n = 158)

Type of change	Number of adolescents	Proportion of adolescents (%)	CI (95%)
Decrease	35	22.15	16.30-29.38
Increase	64	40.51	33.06-48.42
No Change	59	37.34	30.08-45.22

Using the CHQ-physical health summary score and standard deviation method, clinically important changes were calculated between baseline and 8 years later (Table 5.8). Based on one half of a standard deviation, a change in physical health scores larger or equal to 5.3 physical health units was considered a clinically important change. Across 8 years, 36% (95% CI: 29-44) of adolescents experienced a clinically important improvement whereas 64% experienced either no clinically important change (54%, 95% CI: 46-61) or a clinically important decline (11%, 95% CI: 7-17).

Table 5.8: Change in physical health summary scores (CHQ) from baseline to 8 years after diagnosis of epilepsy (n = 158)

Type of change	Number of adolescents	Proportion of adolescents (%)	CI (95%)
Decrease	17	10.83	6.80-16.81
Increase	56	35.67	28.50-43.55
No Change	84	53.50	45.59-61.24

5.4.2 Proportion of Change Across Two to Eight Years After Diagnosis

The results for the second question associated with Objective 3 (For what proportion of those with childhood-onset epilepsy does HRQL eight years after diagnosis improve, worsen or not change from that reported two years post-diagnosis?) are presented here.

The physical and psychosocial health summary scores derived from the CHQ were the two outcome measures used in two parallel analyses. Change scores from 2-years to 8 years post-baseline were computed for both the psychosocial and the physical health summary scores. A change score greater than or equal to one half of a standard deviation of the change score was used to represent a clinically important difference.

Using the CHQ-psychosocial health summary score and standard deviation methods, clinically important changes were calculated between 2 years and 8 years post-diagnosis (Table 5.9). Based on one half of a standard deviation, a change in psychosocial health scores larger or equal to 4.8 psychosocial health units was considered a clinically important change. Across two to eight years post-diagnosis, 29% (95% CI: 22-36) of adolescents experienced a clinically important improvement whereas 72% experienced either no clinically important change (50%, 95% CI: 42-58) or a clinically important decline (22%, 95% CI: 16-29).

Table 5.9: Change in psychosocial health summary scores (CHQ) from 2 years to 8 years after diagnosis of epilepsy (n = 162)

Type of change	Number of adolescents	Proportion of adolescents (%)	CI (95%)
Decrease	35	21.60	15.88-28.69
Increase	46	28.40	21.92-35.90
No Change	81	50.00	42.28-57.71

Using the CHQ-physical health summary score and standard deviation methods, clinically important changes were calculated between 2 years and 8 years post-diagnosis (Table 5.10). Based on one half of a standard deviation, a change in physical health

scores larger or equal to 4.4 physical health units was considered a clinically important change. Across two to eight years post-diagnosis, 23% (95% CI: 17-30) of adolescents experienced a clinically important improvement whereas, 77% experienced either no clinically important change (58%, 95% CI: 50-65) or a clinically important decline (19%, 95% CI: 14-26).

Table 5.10: Change in physical summary scores (CHQ) from 2 years to 8 years after diagnosis of epilepsy (n = 162)

Type of change	Number of adolescents	Proportion of adolescents (%)	CI (95%)
Decrease	31	19.25	13.83-26.16
Increase	37	22.98	17.07-30.19
No Change	93	57.76	49.92-65.23

Chapter 6

6 Discussion

This chapter discusses the findings of this thesis. The first section summarizes and interprets the findings for each objective. The following sections, 6.2 and 6.3 describe the strengths and limitations of the thesis. The next section provides recommendations for future research. The final section presents conclusions and implications of this thesis.

6.1 Summary and Interpretation of Results

The purpose of this thesis was to describe the course of health-related quality of life (HRQL) in those diagnosed with childhood-onset epilepsy, how HRQL in the long term compares to levels in the general population, and what factors contribute to improvement, decline or stability of long-term HRQL. The following summarizes and interprets the findings for each research objective.

Objective 1

The purpose of Objective 1 was to evaluate the HRQL associated with childhood-onset epilepsy eight years post-diagnosis. The parents of children with epilepsy included in our sample reported their children were comparable to (or better than) their counterparts in the general population on the majority of individual health concepts with no differences in either of the two summary scores at 8 years post diagnosis. Parents of children with epilepsy did report that their children were doing more poorly compared to the available reports of parents of similarly-aged children from the general population on three health concepts, one related to the child (role-emotional-behavioural), and two related to the family (family limitations in activities, and parental impact-emotional). These findings are of clinical relevance as they provide parents and clinicians with information regarding long-term outcomes of children with epilepsy compared to their peers in the general population.

Prior research comparing the HRQL of epilepsy cohorts to the general population has suggested that HRQL in children with epilepsy is compromised compared to age-

matched healthy children (Miller et al., 2003; Momeni et al., 2015; Taylor et al., 2011). Compared with published normative data, children with epilepsy had poorer HRQL in scales specifically related to child's behaviour and the emotional well-being of parents (Taylor et al., 2011). Momeni et al., (2015), provided additional support that the health factor with the lowest score in their epilepsy sample was associated with the emotional well-being of the parents. Prior research has not reported results on longer term HRQL in adolescents with epilepsy compared to population counterparts. Previously, studies reported cross-sectional results at a single time point, compared with sibling controls, or did not focus on characteristics associated with HRQL (Baca et al., 2010; Connolly et al., 2006; Sillanpää, Haataja, & Shinnar, 2004). The current study provides HRQL results collected on the same cohort at multiple time points over the long term. Longitudinal research prospectively measuring factors of HRQL are limited and often have relatively short follow ups of less than three years (Austin et al., 2010; Modi, Ingerski, Rausch, & Glauser, 2011). Similarly, the first phase of HERQULES compared the current cohort with the general population up until two years post-diagnosis (Ferro et al., 2013; Speechley et al., 2012), but left the question of longer-term comparison unanswered. The current research extended the duration of follow up to eight years post-diagnosis, parents of children with epilepsy reported poorer outcomes on the same three health factors, the emotional and behavioural role on the child, family limitations in activities, and the emotional impact of their child's health on the parent, that were found to be poorer than the normative population at the 2-year follow-up (Speechley et al., 2012). The results from prior research, the first phase of HERQULES, and the present study are all consistent that, on average, parents of children with epilepsy experience greater emotional concern as a result of their child's physical and/or psychosocial health, compared to the population normative data.

The current results indicate that for our sample of children with epilepsy their parents report them as having comparable or better HRQL at 8 years post diagnosis than parents of those in the general population. Previous research has highlighted that parents of children with newly diagnosed epilepsy often report improved HRQL despite often poor seizure outcomes (Ferro, Camfield, et al., 2013). A potential explanation for why parents in our epilepsy sample did not report worse outcomes than the general population on

most of the HRQL individual domains or summary domain measurements may be the notion of the disability paradox (Albrecht & Devlieger, 1999). The disability paradox is defined as "the discrepancy between the objective limitations and suffering posed by certain disabilities, and the reasonable or excellent quality of life reported by some individuals living with them" (Carona, Pereira, Moreira, Silva, & Canavarro, 2013, p. 971). The paradox realizes that despite challenges associated with having a chronic illness or disability, psychological growth and inner strength potentially contribute to a balanced life perspective that in turn is reflected in positively reported HRQL (Albrecht & Devlieger, 1999; Carona et al., 2013). For example, consider the individual aspect of bodily pain; epilepsy is not characterized as a condition that is principally painful, a parent may be carefully monitoring a child's illness and they may rate their child's bodily pain incorporating a balance of other HRQL domains. The parent may consider a more balanced life perspective and perceive aspects of HRQL as more positive in their children compared to parents drawn from the general population. This perspective is supported in the current research; parents of those with epilepsy in our sample reported that their children experienced less pain or limitations due to pain after 8 years, compared to the general population. This finding is consistent with prior research that found the Child Health Questionnaire (CHQ) scale with the highest score among those newly diagnosed with epilepsy was that of bodily pain (Momeni et al., 2015).

Another potential interpretation for parents in the epilepsy sample reporting better outcomes than the general population on certain HRQL measurements over time may be due to parents positively recalibrating their assessment of their child's condition and HRQL over time (Sajobi, Speechley, et al., 2017). This concept is called positive response shift (Schwartz & Sprangers, 1999; Sprangers & Schwartz, 1999). At 8 years after diagnosis our sample of children with epilepsy had similar reports of psychosocial health compared to the general population. This was not the case at baseline or 2 years after diagnosis, wherein, parents of children with epilepsy reported their children to have poorer psychosocial health compared to the general population. A positive response shift over time can suggest potential benefits such that the parent's perception of the course of their child's HRQL is improving. For example, parents of children newly diagnosed with epilepsy may initially rate their child's HRQL as poor but then over time, they may adapt

and develop positive mechanisms of dealing with their child's circumstances and report better HRQL. Research concluding that response shift should be considered as a measurement bias has been contrasted by research highlighting a potential positive outcome of a positive response shift and emphasizing the parent's process adaptively responding to a child's diagnosis (Sajobi, Speechley, et al., 2017).

As the measure of HRQL analyzed here, the CHQ, is a generic measure, a reasonable question to ask is whether our finding that levels of HRQL in our sample of children with epilepsy were generally similar to their counterparts in the general population could be attributable to the CHQ being incapable of capturing deficits in aspects of HRQL that may be specific to epilepsy. We are reassured by other findings previously reported for the HERQULES sample that this is not likely the case. Specifically, using a well-validated epilepsy- specific measure of HRQL, the Quality of Life in Childhood Epilepsy Questionnaire (QOLCE), a similar pattern of findings resulted to those reported here; as assessed by parents using the QOLCE, HRQL also improved in the first two years after diagnosis and was sustained over the long term (Puka et al., 2020).

Of note, when validating the CHQ, data on children with epilepsy was collected to provide a clinical benchmark (Landgraf et al., 1996). Including benchmarks in the measure allowed for the questionnaire to compare their results from clinical samples to their normative sample. The CHQ manual provides evidence that the scales in the CHQ were able to discriminate between children with clinically defined conditions from a representative U.S. sample and that differences observed in the average score between groups exceeded measurement error (Landgraf et al., 1996).

Overall, results assessing HRQL using parent-report on the CHQ indicated that those with childhood-onset epilepsy, have comparable or better HRQL 8 years post-diagnosis than their counterparts in the general population. Overall, these results offer reassuring information to parents with children newly diagnosed with epilepsy about the potential for positive long-term outcomes. However, the results also point to the importance of monitoring particular aspects of HRQL related to a child's emotional and behavioural problems limiting their everyday activities, their health interrupting family activities, and

parents experiencing emotional worry as a result of their child's health, to identify those who could benefit from interventions targeted at improving any deficits observed.

Objective 2

The purpose of Objective 2 was to describe the course of HRQL over 8 years after diagnosis of epilepsy. First, the unadjusted average estimated course of HRQL from baseline to eight years later was described where both psychosocial and physical summary scores changed significantly.

When the growth curve over time was modelled for psychosocial health, the quadratic term of time was significant, suggesting that the score profile was not a simple linear one but rather showed curvature. Specifically, the levels of psychosocial health increased soon after diagnosis and then flattened after 2 years. As for physical health, there was a linear improvement over time. In other words, over the duration of follow up physical health scores increased.

The goal of the second and third questions associated with Objective 2 was to determine which characteristics around the time of diagnosis were associated with HRQL measured 8 years later and to estimate the average course of HRQL from baseline to eight years later while accounting for the identified, associated characteristics. Baseline characteristics that predicted psychosocial health over 8 years were family resources and presence of a cognitive problems in the child. Baseline characteristics that predicted physical health over 8 years were parental depressive scores and presence of cognitive problems in the child. Both psychosocial and physical health growth curves followed the same growth pattern suggested in the unadjusted analysis. In summary, a child having cognitive problems predicted both psychosocial and physical health over time; family resources predicted psychosocial health and parental depression predicted physical health.

Parental depressive symptoms and family factors have been found to contribute to HRQL in children with epilepsy (Connolly et al., 2006; Jain et al., 2018; Puka et al., 2019). Over two years, family environment was found to be associated with HRQL and play a

substantial role in children's HRQL (Speechley et al., 2012; Ferro, Camfield, et al., 2013). The current research extends past the 2-year follow up and provides a longer-term analysis of family factors that are related to HRQL over time. Consistent with our findings, a recent analysis of the HERQULES cohort across ten years supports that better family environment at the time of diagnosis is associated with better HRQL over the long-term (Puka et al., 2020).

Comorbid conditions among children with epilepsy are common (Pastor et al., 2015; Sillanpää & Cross, 2009). In the current research, having cognitive problems predicted both psychosocial and physical health over time. Reflecting on prior research, the presence of cognitive problems was associated with HRQL two years after diagnosis in the same cohort (Speechley et al., 2012). Moreover, problems associated with child behaviour and cognition were the strongest predictors of HRQL over 2 years post-diagnosis (Ferro, Camfield, et al., 2013). The current findings are also consistent with previously reported results from the HERQULES sample, using a disease-specific measure of HRQL, indicating that absence of comorbidities, such as cognitive problems at the time of diagnosis are associated with better HRQL over 10 years post diagnosis (Puka et al., 2020). The similarity in findings when using a generic and a disease-specific measure, both in the short- and long-term follow-up within this sample strengthens the suggestion that those baseline factors highlighted as potential targets for intervention given the persistence of association with HRQL over the long-term.

The presence of cognitive problems has been considered one of the strongest predictors of HRQL (Ferro et al., 2013; Puka et al., 2020; Speechley et al., 2012). Notably, Conway et al. (2016), emphasized the importance of both child cognition and family variables in the HRQL of children with epilepsy. Cognitive problems are not always considered modifiable; however, parent and family environment has been emphasized as a potential target for patient care and early intervention. Research has shown that parent and family environment has a great impact on a child's HRQL (Rodenburg, Meijer, Deković, & Aldenkamp, 2005). Research highlighting comprehensive care and interventions targeting potentially modifiable factors alongside medical interventions has been suggested to improve HRQL (Loiselle, Ramsey, Rausch, & Modi, 2016). Risk factors that have been

identified as modifiable and lead to improvement of unfavorable trajectories include those related to family environment and parental depressive symptoms. Moving towards family centered care can serve to intervene on risk factors that are amenable to change and improve HRQL trajectories (Ferro, Camfield, et al., 2013). In addition to providing targeted and comprehensive care, the timing for initiation of care is important. Research stresses the importance of identifying those at risk for reduced quality of life at the time of diagnosis, so that early intervention can begin (Taylor et al., 2011). The current research adds evidence that the changes in HRQL that occur during the first 2 years after diagnoses continue over the long term, and that targeting risk factors near the time of diagnosis may be important in identifying children at risk for poor HRQL and potentially improving HRQL over the long term.

Objective 3

The goal of Objective 3 was to determine the change in HRQL between time of diagnosis and 8 years later. This objective was split between assessing the change in HRQL, psychosocial and physical health separately, at time of diagnosis to 8-years later and additionally between 2 years later and 8 years later.

The interest in comparing baseline to 8 years and 2 years to 8 years stems from prior literature on the change in HRQL from baseline to 2 years. A prior study, Speechley et al (2012), assessed clinically important changes in both psychosocial and physical health scores over 2-years in children newly diagnosed with epilepsy.

The first question of Objective 3 assessed the proportion of those with childhood-onset epilepsy for which HRQL improved, worsened or stayed the same across 8 years. When assessing psychosocial health, just over 40% of participants experienced a clinically important improvement across 8 years. For physical health, more than one third of participants experienced a clinically important improvement.

The second question of Objective 3 assessed the proportion of those with childhood-onset epilepsy for whom HRQL improved, worsened, or stayed the same across the period of 2 years after diagnosis to 8 years after diagnosis. For psychosocial health, just under one

third of participants experienced a clinically important improvement. For physical health, just under one quarter experienced a clinically important improvement.

The study found that 28% of individuals experienced a clinically important improvement in psychosocial health and 23% of individuals experienced a clinically important improvement in physical health between the second and eight year after diagnosis. The comparison between the proportion who improved from baseline to 2 years and those that improved across the 8-year follow up is similar. A possible explanation may include that those who improved from baseline to 2 years may be closer to the high range of the CHQ and may have less room for further growth, resulting in ceiling effects. Additionally, the sample retained at 8-year follow up may have been more likely to represent a subsample of the initial cohort that fared better than those who were lost to follow up, thus resulting in similar findings over the full 8 years as between baseline and 2 years.

The proportion of youth who improved, worsened or remained stable over different periods of time may assist clinicians in discussing with families what is known about children with epilepsy, in terms of what can be reasonably expected regarding the course of HRQL over the years after diagnosis.

It is important to explore the effect of attrition when interpreting these results. Of the original sample, parents of 43% who were 18 years old or younger were retained to the 8-year follow-up. When comparing baseline characteristics, compared to parents who began the study but were lost to follow-up before the 8-year follow-up, there were no baseline differences in terms of the child's diagnosed epilepsy syndrome, number of AEDs taken, frequency of seizures, severity of epilepsy, or whether the child had behavioural problems or on the age, employment, or marital status of parents. However, parents who completed all five questionnaires, had more education, higher household income, fewer depression symptoms, better family functioning, better family resources, fewer family demands and their children were older and less likely to have cognitive problems than other lost to follow-up. In interpreting the current findings, we do need to consider that those families that were more advantaged, based on sociodemographic factors, may have been more likely to stay in the study. In that case, the effect of attrition

bias in our sample may have resulted in an under-estimation of compromised HRQL and the proportion of those with clinically important improvements in HRQL we report may be larger in our study sample than if the entire baseline sample had been retained.

6.2 Strengths of the Current Research

One of the strengths of this research is the study design. HERQULES was a large, multi-center, prospective cohort study that recruited incident cases from across Canada with a diverse range in the type of epilepsy diagnosed. HERQULES was long term and followed a group of individuals from childhood, into adolescence and adulthood. This is the first study of its kind that not only measured relevant clinical variables but also the family environment in an assessment of the HRQL of children and their parents up to 10 years after the diagnosis of epilepsy.

Additionally, the measures used in the study were reliable and well validated and included both epilepsy-specific and generic measures of HRQL. Particularly the use of a robust generic measure, the CHQ, allowed for comparison with the general population throughout the duration of the 8-year follow up.

Methodologically, the use of a mixed effects methods strengthens the current study. Mixed effects models manage serial growth data, allowing the flexibility to simultaneously predict individual curves, model the average course and incorporate baseline variables into the model (Johnson, Balakrishna, & Griffiths, 2013). Furthermore, mixed effects models allow for heterogeneity among subjects in their trajectories of change and account for missing data (Singer & Willett, 2003).

Additionally, the study presents both research and clinically relevant data, growth modelling and proportions of change, respectively. Therefore, results can be used to influence future research as well as present information to clinicians working with children newly diagnosed with epilepsy.

6.3 Limitations of the Current Research

Although access to data from a long-term prospective study presented a unique opportunity, the current study has some limitations. First, as expected with the long-term follow-up of any cohort, there was attrition. The effect of attrition bias indicated a retention of families that tend to be more advantaged, which may mean that the sample on which the results are based is biased toward those likely to have more positive outcomes such as better HRQL. Thus, leading to an over-estimation of the long-term level of HRQL for those with childhood-onset epilepsy.

Another potential weakness is that patients were recruited from pediatric neurology practices across Canada. This may have resulted in a sample not fully representative of children newly diagnosed with epilepsy in Canada. This concern is somewhat mitigated, however, by the finding that family physicians refer over 80% of children diagnosed with epilepsy to a pediatric neurologist (Speechley, Levin, Wiebe, & Blume, 1999). Additionally, at the final follow-up, the majority of youth in this study were seizure free for over five years which is in accordance of reported the reported course of epilepsy into adulthood (Sillanpää & Schmidt, 2017).

It should also be noted that data analysed here were based on parent or physician report. In the final two follow-ups of HERQULES, self-report data were collected from the youth with epilepsy. It is generally agreed that it is important, whenever possible, to solicit both parent and child report of children's HRQL. Differences do exist between child and parent report of HRQL and it is important to understand both perspectives (Baca et al., 2010; Speyer, Herbinet, Vuillemin, Chastagner, & Briancon, 2009; Sundaram, Landgraf, Neighbors, Cohn, & Alonso, 2007) . It is the case, however, that young children are not always able to self-report on their HRQL due to lack of developmental maturity or illness (Puka et al., 2020). For the purposes of assessing the course of HRQL over the course of childhood and adolescence and incorporating parental and family measures, use of parent report at all time points provides consistency in the reporter that is essential for repeated measures (Fong et al., 2018; Matsumoto, Vitale, Hyman, & Roye, 2011). As the aim of the current study was to assess the course of

HRQL in children as young as four years of age at diagnosis of epilepsy across time, a parent report measure was required to provide a consistent proxy reporter.

Finally, as a Canadian normative population for the CHQ was not available, data from a U.S. normative sample was used to compare to our sample. Other researchers have compared Canadian data with U.S. norms as well as Australian norms (Klassen et al., 2004). In an ADHD study, U.S. and Australian norms did not significantly differ from one another (Klassen et al., 2004). The previous report from the HERQULES cohort used the published U.S. norms from the CHQ as the comparison (Speechley et al., 2012) and thus use of the same normative population provides consistency and ease of comparison between reports.

6.4 Recommendations for Future Research

Future research should focus on evaluating self-reported HRQL prospectively over the long term. Evaluating self-report measures will provide an understanding of how the individual diagnosed with epilepsy perceives their own HRQL over time. The current results are novel in that they provide a longer-term picture of HRQL that improves over the first two years and is sustained over the long term in those diagnosed with childhood onset epilepsy. Additionally, family environment and presence of cognitive problems was associated with HRQL over 2 years continues to predict HRQL in the long term. Understanding that there is a potential need to identify those at risk for compromised HRQL early after diagnosis presents the opportunity to target interventions that address modifiable factors, such as those associated with the family environment. Evaluating a family-centered approach may be such a recommendation.

6.5 Conclusions and Implications

In conclusion, after 8 years, HRQL in the epilepsy sample was the same or better on average compared to the normative population. However, almost a quarter are experiencing worse HRQL than baseline over the 8-year period and over a third experienced no clinically important change. Additionally, family resources, parental depressive symptoms, and cognitive comorbidities are associated with physical and

psychosocial health growth over time. Taken together, the long-term prognosis of childhood epilepsy is good; however, there is a subsample of youth who are at risk for compromises in long-term HRQL. The current research extends the follow up of HERQULES from 2 to 8 years and provides a more complete picture of HRQL for those newly diagnosed with epilepsy. For the first time, children newly diagnosed with epilepsy are compared to the general population across multiple time points over 8 years. The current results are important in ascertaining additional variables over and above seizure experience to identify those at risk for poor HRQL over the long term that may potentially benefit from early interventions targeting the child and their family unit.

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Appendices

Appendix A: HERQULES Parent Questionnaire

Child Health
Research Institute

HERQULES STUDY

Health Related Quality of Life in Children with Epilepsy: The First Two Years After Diagnosis Through Parents' Eyes

Parents' Questionnaire

Q1

Throughout this questionnaire when we refer to "your child", we are referring to your child with the initials ____ ____ . Please keep this child in mind when responding to the questions.

Children's Hospital
of Western Ontario
London Health Sciences Centre

Schulich
MEDICINE & DENTISTRY

Western

Q1

Study ID __ __ __ __

I have received $5.00 as a token of appreciation for my participation in the HERQULES Study with Dr. Kathy Nixon Speechley in London Ontario.

Date: _____ Initial: _____

INSTRUCTIONS

1. **Most of the questions in this booklet ask about your child's health and well-being. A few of the questions ask about your own health and well-being. Your individual answers will remain strictly confidential.**

2. **Answer questions by checking the appropriate box (☐ Yes ☐ No ☐ Don't know) or circling the appropriate number.**

3. **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 when your child does not have these problems.**

4. **There are no right or wrong answers. If you are unsure how to answer a question, please give the best answer you can. Write any comments you may have on the page beside the question.**

SECTION 1:

YOUR CHILD'S PHYSICAL ACTIVITIES

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

1.1. In his/her daily activities during the past 4 weeks, how often has your child:

	Very Often	Fairly Often	Some-times	Almost Never	Never	Not applicable
a. needed more supervision than other children his/her age?	☐	☐	☐	☐	☐	☐
b. needed special precautions (i.e. wearing a helmet)?	☐	☐	☐	☐	☐	☐
c. played freely in the house like other children his/her age?	☐	☐	☐	☐	☐	☐
d. played freely outside the house like other children his/her age?	☐	☐	☐	☐	☐	☐
e. gone swimming? (i.e. swam independently)	☐	☐	☐	☐	☐	☐
f. participated in sports activities (other than swimming)?	☐	☐	☐	☐	☐	☐
g. stayed out overnight (with friends or family)?	☐	☐	☐	☐	☐	☐
h. played with friends away from you or your home?	☐	☐	☐	☐	☐	☐
i. gone to parties without you or without supervision?	☐	☐	☐	☐	☐	☐
j. been able to do the physical activities other children his/her age do?	☐	☐	☐	☐	☐	☐

1.2. 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	Not applicable
a. felt tired	☐	☐	☐	☐	☐	☐
b. felt energetic	☐	☐	☐	☐	☐	☐

1.3. Is there anything else you would like to tell us about your child's activities?

WELL-BEING

Below is a list that describes how your child might feel in general.

1.4. 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	Not applicable
a. felt down or depressed?	☐	☐	☐	☐	☐	☐
b. felt calm?	☐	☐	☐	☐	☐	☐
c. felt helpless in situations?	☐	☐	☐	☐	☐	☐
d. felt happy?	☐	☐	☐	☐	☐	☐
e. wished s/he was dead?	☐	☐	☐	☐	☐	☐
f. felt in control?	☐	☐	☐	☐	☐	☐
g. felt tense and anxious?	☐	☐	☐	☐	☐	☐
h. felt frustrated?	☐	☐	☐	☐	☐	☐
i. felt overwhelmed by events?	☐	☐	☐	☐	☐	☐
j. worried a lot?	☐	☐	☐	☐	☐	☐
k. felt confident?	☐	☐	☐	☐	☐	☐
l. felt excited or interested in something?	☐	☐	☐	☐	☐	☐
m. felt pleased about achieving something?	☐	☐	☐	☐	☐	☐
n. got easily embarrassed?	☐	☐	☐	☐	☐	☐
o. felt different or singled out?	☐	☐	☐	☐	☐	☐
p. felt nobody understood him/her?	☐	☐	☐	☐	☐	☐
q. felt valued?	☐	☐	☐	☐	☐	☐
r. felt s/he was not good at anything?	☐	☐	☐	☐	☐	☐
s. felt no one cared?	☐	☐	☐	☐	☐	☐

1.5. Is there anything else you would like to tell us about how your child feels in general?

COGNITION

The following questions ask about some problems children have with concentrating, remembering, and speaking.

1.6. Compared to other children of his/her own age, how often during the past 4 weeks has your child:

	Very Often	Fairly Often	Some-times	Almost Never	Never	Not applicable
a. had difficulty attending to an activity?	☐	☐	☐	☐	☐	☐
b. had difficulty reasoning or solving problems?	☐	☐	☐	☐	☐	☐
c. had difficulty making plans or decisions?	☐	☐	☐	☐	☐	☐
d. had difficulty keeping track of conversations?	☐	☐	☐	☐	☐	☐
e. had trouble concentrating on a task?	☐	☐	☐	☐	☐	☐
f. had difficulty concentrating on reading?	☐	☐	☐	☐	☐	☐
g. had difficulty doing one thing at a time?	☐	☐	☐	☐	☐	☐
h. reacted slowly to things being said & done?	☐	☐	☐	☐	☐	☐
i. completed activities that needed organising/planning?	☐	☐	☐	☐	☐	☐
j. found it hard remembering things?	☐	☐	☐	☐	☐	☐
k. had trouble remembering names of people?	☐	☐	☐	☐	☐	☐
l. had trouble remembering where s/he put things?	☐	☐	☐	☐	☐	☐
m. had trouble remembering things people told him/her?	☐	☐	☐	☐	☐	☐
n. had trouble remembering things s/he read hours or days before?	☐	☐	☐	☐	☐	☐
o. planned to do something then forgot?	☐	☐	☐	☐	☐	☐
p. had trouble finding the correct words?	☐	☐	☐	☐	☐	☐
q. had trouble understanding or following what others were saying?	☐	☐	☐	☐	☐	☐
r. had trouble understanding directions?	☐	☐	☐	☐	☐	☐
s. had difficulty following simple instructions?	☐	☐	☐	☐	☐	☐
t. had difficulty following complex instructions?	☐	☐	☐	☐	☐	☐
u. had trouble understanding what s/he read?	☐	☐	☐	☐	☐	☐
v. had trouble writing?	☐	☐	☐	☐	☐	☐
w. had trouble talking?	☐	☐	☐	☐	☐	☐

1.7. Is there anything else you would like to tell us about your child's concentration, memory or speech?

YOUR CHILD'S SOCIAL ACTIVITIES

1.8. During the past 4 weeks, how often has your child's epilepsy:

	Very Often	Fairly Often	Some-times	Almost Never	Never	Not applicable
a. limited his/her social activities (visiting friends, close relatives, or neighbours)?	☐	☐	☐	☐	☐	☐
b. helped him/her to make friends?	☐	☐	☐	☐	☐	☐
c. affected his/her social interactions at school or work?	☐	☐	☐	☐	☐	☐
d. improved his/her friendships & relationships with others?	☐	☐	☐	☐	☐	☐
e. limited his/her leisure activities (hobbies or interests)?	☐	☐	☐	☐	☐	☐
f. isolated him/her from others?	☐	☐	☐	☐	☐	☐
g. improved his/her relations with family members?	☐	☐	☐	☐	☐	☐
h. made it difficult for him/her to keep friends?	☐	☐	☐	☐	☐	☐
i. frightened other people?	☐	☐	☐	☐	☐	☐

1.9. During the past 4 weeks, how limited are your child's social activities compared with others his/her age because of his/her epilepsy or epilepsy-related problems?

☐ Yes, limited a lot ☐ Yes, limited some ☐ Yes, limited a little ☐ Yes, but rarely ☐ No, not limited

1.10. During the past 4 weeks, how often has your child freely discussed his/her epilepsy with friends?

☐ Very often ☐ Fairly often ☐ Sometimes ☐ Almost Never ☐ Not applicable

1.11. During the past 4 weeks, how often has your child freely discussed his/her epilepsy with family?

☐ Very often ☐ Fairly often ☐ Sometimes ☐ Almost Never ☐ Not applicable

1.12. Is there anything else you would like to tell us about your child's social activities?

YOUR CHILD'S BEHAVIOUR

Below are statements that describe some children's behaviour.
Please try to answer all questions as well as you can, even if some do not seem to apply to your child.

1.13. Compared to other children his/her own age, how often during the past 4 weeks do each of the following statements describe your child?

	Very Often	Fairly Often	Some-times	Almost Never	Never	Not applicable
a. relied on you/family to do things for him/her that s/he was able to do him/herself	☐	☐	☐	☐	☐	☐
b. asked for reassurance	☐	☐	☐	☐	☐	☐
c. was socially inappropriate (said or did something out of place in a social situation)	☐	☐	☐	☐	☐	☐
d. wanted things to be perfect	☐	☐	☐	☐	☐	☐
e. did not give up easily	☐	☐	☐	☐	☐	☐
f. angered easily	☐	☐	☐	☐	☐	☐
g. hit or attacked people	☐	☐	☐	☐	☐	☐
h. swore in public	☐	☐	☐	☐	☐	☐
i. joined in activities with other children	☐	☐	☐	☐	☐	☐
j. feared unfamiliar places, situations or people	☐	☐	☐	☐	☐	☐
k. preferred his/her own company instead of seeking out others	☐	☐	☐	☐	☐	☐
l. was obedient	☐	☐	☐	☐	☐	☐
m. set high standards for self	☐	☐	☐	☐	☐	☐
n. did not worry about what others thought	☐	☐	☐	☐	☐	☐
o. get along with other children	☐	☐	☐	☐	☐	☐
p. wished s/he was someone or somewhere else	☐	☐	☐	☐	☐	☐
q. acted without thinking	☐	☐	☐	☐	☐	☐
r. demanded a lot of attention	☐	☐	☐	☐	☐	☐

Compared to other children his/her own age, how often during the past 4 weeks do each of the following statements describe your child?

	Very Often	Fairly Often	Some-times	Almost Never	Never	Not applicable
s. was decisive	☐	☐	☐	☐	☐	☐
t. was independent	☐	☐	☐	☐	☐	☐
u. preferred routines or disliked changes	☐	☐	☐	☐	☐	☐
v. did things just to prove s/he could	☐	☐	☐	☐	☐	☐
w. preferred the company of adults	☐	☐	☐	☐	☐	☐

1.14. Is there anything else you would like to tell us about your child's behaviour?

GENERAL HEALTH

1.15. Compared to other children his/her age, how do you think your child's health has been in the past 4 weeks? Please consider your child's epilepsy as part of his/her health when you answer this question.

☐ Excellent ☐ Very Good ☐ Good ☐ Fair ☐ Poor

1.16. Is there anything else you would like to tell us about how epilepsy has affected your child's health?

QUALITY OF LIFE

1.17. In the past 4 weeks what has your child's quality of life been?

☐ Excellent ☐ Very Good ☐ Good ☐ Fair ☐ Poor

1.18. Consider your child's present skills in thinking, learning, remembering, speaking and understanding. Taken together, do you think that your child is functioning:

- ☐ At the level expected for his/her age?
- ☐ Somewhat behind the level expected for his/her age?
- ☐ Significantly behind the level expected for his/her age?

SECTION 2:

2.1 The next questions ask about your interaction with your child's neurologist. Please think about your child's most recent visit to his/her neurologist for epilepsy care and circle the response that best represents your opinion.

a. To what extent was your child's main problem(s) discussed at that visit?

Completely Mostly A little Not at all

b. Would you say that your doctor knew that this was one of your reasons for coming in for that visit?

Yes Probably Unsure No

c. To what extent did the doctor understand the importance of your reason for coming in for that visit?

Completely Mostly A little Not at all

d. How well do you think your doctor understood you at that visit?

Very well Well Somewhat Not at all

e. How satisfied were you with the discussion of your child's problem?

Very satisfied Satisfied Somewhat satisfied Not satisfied

f. To what extent did the doctor explain this problem to you?

Completely Mostly A little Not at all

g. To what extent did you agree with the doctor's opinion about the problem?

Completely Mostly A little Not at all

h. How much opportunity did you have to ask your questions?

Very much A fair amount A little Not at all

i. To what extent did the doctor ask about your goals for your child's treatment?

Completely Mostly A little Not at all

j. To what extent did the doctor explain treatment?

Very well Well Somewhat Not at all

k. To what extent did the doctor explore how manageable this (treatment) would be for your child and you? He/she explored this:

Completely Mostly A little Not at all

l. To what extent did you and the doctor discuss your respective roles? (Who is responsible for making decisions and who is responsible for what aspects of your child's care?)

Completely Mostly A little Not at all

m. To what extent did the doctor encourage you to take the role you wanted in your child's care?

Completely Mostly A little Not at all

n. How much would you say that this doctor cares about your child as a person?

Very much A fair amount A little Not at all

SECTION 3:

3.1. The next set of questions asks about what social, psychological, community and financial resources families believe they have available to them in the management of family life. To complete this inventory you are asked to read the list of "Family Statements" one at a time. In each statement, "family" means your immediate family (mother and/or father and children.) Then ask yourself: *"How well does the statement describe our family situation?"*

Then make your decision by circling one of the following:

0 = Not At All	This statement does not describe our family situation. This does not happen in our family.
1 = Minimally	This statement describes our family situation only slightly. Our family may be like this once in a while.
2 = Moderately	This statement describes our family situation fairly well. Our family is like this some of the time.
3 = Very Well	This statement describes our family very accurately. Our family is like this most of the time.

Please read and record your decision for each of the statements below.

Family Statements:	**Not at all**	**Minimally**	**Moderately**	**Very Well**
a. Being physically tired much of the time is a problem in our family	0	1	2	3
b. We have to nag each other to get things done	0	1	2	3
c. We do not plan too far ahead because many things turn out to be a matter of good or bad luck anyway	0	1	2	3
d. Having only one person in the family earning money is (or would be) a problem in our family	0	1	2	3
e. It seems that members of our family take each other for granted	0	1	2	3
f. Sometimes we feel we don't have enough control over the direction our lives are taking	0	1	2	3
g. Certain members of our family do all the giving, while others do all the taking	0	1	2	3
h. We seem to put off making decisions	0	1	2	3
i. Our family is under a lot of emotional stress	0	1	2	3
j. Many things seem to interfere with family members being able to share concerns	0	1	2	3
k. Most of the money decisions are made by only one person in our family	0	1	2	3
l. It seems that we have more illness (colds, flu, etc.) in our family than other people do	0	1	2	3
m. In our family some members have many responsibilities while others don't have enough	0	1	2	3
n. It is upsetting to our family when things don't work out as planned	0	1	2	3
o. Being sad or "down" is a problem in our family	0	1	2	3
p. It is hard to get family members to cooperate with each other	0	1	2	3
q. Many times we feel we have little influence over the things that happen to us	0	1	2	3
r. We have the same problems over and over – we don't seem to learn from past mistakes	0	1	2	3

Family Statements:	**Not at all**	**Minimally**	**Moderately**	**Very Well**
s. There are things at home we need to do that we don't seem to get done	0	1	2	3
t. We seem to be so involved with work and/or school activities that we don't spend enough time together as a family	0	1	2	3
u. Our relatives seem to take from us, but give little in return	0	1	2	3
v. We try to keep in touch with our relatives as much as possible	0	1	2	3
w. Our relative(s) are willing to listen to your problems	0	1	2	3
x. Our relatives do and say things that make us feel appreciated	0	1	2	3

SECTION 4:

4.1. Over their life cycle, all families experience many changes as a result of normal growth and development of members and due to external circumstances. The following list of family life changes can happen in a family at any time. Because family members are connected to each other in some way, a life change for any one member affects all the other persons in the family to some degree.

*"**FAMILY**" means a group of two or more persons living together who are related by blood, marriage or adoption. This includes persons who live with you and to whom you have a long term commitment.*

Please read each family life change and decide whether it happened to any member of your family - **including you** - during the past 12 months and check **Yes** or **No**.

Did the change happen in your family:	During the Last 12 Months **Yes**	**No**	**Score**
I. Intrafamily Strains			
a. Increase of husband/father's time away from family			46
b. Increase of wife/mother's time away from family			51
c. A member appears to have emotional problems			58
d. A member appears to depend on alcohol or drugs			66
e. Increase in conflict between husband and wife			53
f. Increase in arguments between parent(s) and child(ren)			45
g. Increase in conflict among children in the family			48
h. Increased difficulty in managing teenage child(ren)			55
i. Increased difficulty in managing school age child(ren) (6-12 yrs)			39
j. Increased difficulty in managing preschool age child(ren) (2.5-6 yrs)			36
k. Increased difficulty in managing toddler(s) (1-2.5 yrs)			36
l. Increased difficulty in managing infant(s) (0-1 yr)			35
m. Increase in the amount of "outside activities" which the children are involved in			25
n. Increased disagreement about a member's friends or activities			35

Did the change happen in your family:	During the Last 12 Months Yes	No	Score
o. Increase in the number of problems or issues which don't get resolved			45
p. Increase in the number of tasks or chores which don't get done			35
q. Increased conflict with in-laws or relatives			40
II. Marital Strains			
a. Spouse/parent was separated or divorced			79
b. Spouse/parent had an "affair"			68
c. Increased difficulty in resolving issues with a "former" or separated spouse			47
d. Increased difficulty with sexual relationship between husband and wife			58
III. Pregnancy and Childbearing Strains			
a. Spouse had unwanted or difficulty pregnancy			45
b. An unmarried member became pregnant			65
c. A member had an abortion			50
d. A member gave birth to or adopted a child			50
IV. Finance and Business Strains			
a. Took out a loan or refinanced a loan to cover increased expenses			29
b. Went on welfare			55
c. Change in conditions (economic, political, weather) which hurts the family investments			41
d. Change in agriculture market, stock market, or land values which hurts family investments and/or income			43
e. A member started a new business			50
f. Purchased or built a home			41
g. A member purchased a car or other major item			19
h. Increased financial debts due to over-use of credit cards			31
i. Increased strain on family "money" for medical/dental expenses			23
j. Increased strain on family "money" for food, clothing, energy, home care			21
k. Increased strain on family "money" for child(ren)'s education			22
l. Delay in receiving child support or alimony payments			41
V. Work-Family Transitions and Strains			
a. A member changed to a new job/career			40
b. A member lost or quit a job			55
c. A member retired from work			48
d. A member started or returned to work			41
e. A member stopped working for extended period (e.g., laid off, leave of absence, strike)			51
f. Decrease in satisfaction with job/career			45
g. A member had increased difficulty with people at work			32
h. A member was promoted at work or given more responsibilities			40
i. Family moved to a new home/apartment			43
j. A child/adolescent member changed to a new school			24
VI. Illness and Family "Care" Strains			
a. Parent/spouse became seriously ill or injured			44
b. Child became seriously ill or injured			35

Did the change happen in your family:	During the Last 12 Months Yes	No	Score
c. Close relative or friend of the family became seriously ill			44
d. A member became physically disabled or chronically ill			73
e. Increased difficulty in managing a chronically ill or disabled member			58
f. Member or close relative was committed to an institution or nursing home			44
g. Increased responsibility to provide direct care or financial help to husband's and/or wife's parents			47
h. Experienced difficulty in arranging for satisfactory child care			40
VII. Losses			
a. A parent/spouse died			98
b. A child member died			99
c. Death of husband's or wife's parent or close relative			48
d. Close friend of the family died			47
e. Married son or daughter was separated or divorced			58
f. A member "broke up" a relationship with a close friend			35
VIII. Transitions "In and Out"			
a. A member was married			42
b. Young adult member left home			43
c. Young adult member began college (or post high school training)			28
d. A member moved back home or a new person moved into the household			42
e. A parent/spouse started school (or training program) after being away from school for a long time			38
IX. Family Legal Violations			
a. A member went to jail or juvenile detention			68
b. A member was picked up by police or arrested			57
c. A member ran away from home			61
d. A member dropped out of school or was suspended from school			38

SECTION 5:

5.1. Now we would ask that you think about the following and check the answer that best describes how you feel most of the time. Please be honest.

a) When something is bothering me, I can ask my family for help.

☐ Never ☐ Hardly ☐ Some of the time ☐ Almost always ☐ Always

b) I like the way my family talks things over and shares problems with me.

☐ Never ☐ Hardly ☐ Some of the time ☐ Almost always ☐ Always

c) I like how my family lets me try new things I want to do.

☐ Never ☐ Hardly ☐ Some of the time ☐ Almost always ☐ Always

d) I like what my family does when I feel mad, happy, or loving.

☐ Never ☐ Hardly ☐ Some of the time ☐ Almost always ☐ Always

e) I like how my family and I share time together.

☐ Never ☐ Hardly ☐ Some of the time ☐ Almost always ☐ Always

SECTION 6:

6.1. Now we'd like to ask some questions about you. Please read these sentences that say something about how people sometimes feel and circle the number of the category on this page that best indicates how often you have felt this way in the past 7 days.

0. Rarely or none of the time (less than one day)
1. Some or a little of the time (1-2 days)
2. Occasionally or a moderate amount of time (3-4 days)
3. Most or all of the time (5-7 days)

During the past seven days:

a)	I was bothered by things that usually don't bother me.	0	1	2	3
b)	I did not feel like eating; my appetite was poor.	0	1	2	3
c)	I felt that I could not shake off the blues even with help from my family or friends.	0	1	2	3
d)	I felt that I was just as good as other people.	0	1	2	3
e)	I had trouble keeping my mind on what I was doing.	0	1	2	3
f)	I felt depressed.	0	1	2	3
g)	I felt that everything I did was an effort.	0	1	2	3
h)	I felt hopeful about the future.	0	1	2	3
i)	I thought my life had been a failure.	0	1	2	3
j)	I felt fearful.	0	1	2	3
k)	My sleep was restless.	0	1	2	3
l)	I was happy.	0	1	2	3
m)	I talked less than usual.	0	1	2	3
n)	I felt lonely.	0	1	2	3
o)	People were unfriendly.	0	1	2	3
p)	I enjoyed life.	0	1	2	3
q)	I had crying spells.	0	1	2	3
r)	I felt sad.	0	1	2	3
s)	I felt that people dislike me.	0	1	2	3
t)	I could not get "going".	0	1	2	3

SECTION 7:

We would like to understand and measure the experiences of parents who have a child with epilepsy. In particular we wish to know about your perceptions of the care you have been receiving over the past year from the health care institution(s) that provide(s) services to your child for his/her epilepsy.

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** doctors, nurses, psychologists, therapists, social workers, etc.

ORGANIZATION:
refers to all staff from the health care institution(s), 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. We are interested in your personal thoughts and would appreciate your completing this questionnaire on your own without discussing it with anyone.

7.1. 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.

7. To a Very Great Extent
6. To a Great Extent
5. To a Fairly Great Extent
4. To a Moderate Extent
3. To a Small Extent
2. To a Very Small Extent
1. Not at All
0. Not Applicable

Indicate how much this event or situation happens to you.

IN THE PAST YEAR TO WHAT EXTENT DO THE **PEOPLE** WHO WORK WITH YOUR CHILD	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
a. help you to feel competent as a parent?	7	6	5	4	3	2	1	0
b. provide you with written information about what your child is doing in treatment?	7	6	5	4	3	2	1	0
c. provide a caring atmosphere rather than just give you information?	7	6	5	4	3	2	1	0
d. let you choose when to receive information and the type of information you want?	7	6	5	4	3	2	1	0

IN THE PAST YEAR TO WHAT EXTENT DO THE **PEOPLE** WHO WORK WITH YOUR CHILD	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
e. 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
f. 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
g. fully explain treatment choices to you?	7	6	5	4	3	2	1	0
h. provide opportunities for you to make decisions about treatment?	7	6	5	4	3	2	1	0
i. provide enough time to talk so you don't feel rushed?	7	6	5	4	3	2	1	0
j. plan together so they are all working in the same direction?	7	6	5	4	3	2	1	0
k. treat you as an equal 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
l. give you information about your child that is consistent from person to person?	7	6	5	4	3	2	1	0
m. treat you as an individual rather than as a "typical parent" of a child with epilepsy?	7	6	5	4	3	2	1	0
n. provide you with written information about your child's progress?	7	6	5	4	3	2	1	0
o. tell you about the results from assessments?	7	6	5	4	3	2	1	0

IN THE PAST YEAR TO WHAT EXTENT DOES THE **ORGANIZATION** WHERE YOU RECEIVE SERVICES	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
p. give you information about the types of services offered at the organization or in your community?	7	6	5	4	3	2	1	0
q. have information available about your child's epilepsy (e.g., its causes, how it progresses, future outlook)?	7	6	5	4	3	2	1	0
r. provide opportunities for the entire family to obtain information?	7	6	5	4	3	2	1	0
s. have information available to you in various forms, such as a booklet, kit, video, etc.?	7	6	5	4	3	2	1	0
t. 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

SECTION 8:

8.1. **In general, would you say your child's health is:** (check one box only)

☐ Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor

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

8.2. **During the past 4 weeks, has your child been limited in any of the following activities due to health problems?** (check one box on each line)

	Yes, limited a lot	Yes, limited some	Yes, limited a little	No, not limited
a. Doing things that take **a lot** of energy, such as playing soccer or running?	☐	☐	☐	☐
b. Doing things that take **some** energy, such as riding a bike or skating?	☐	☐	☐	☐
c. Ability (physically) to get around the neighbourhood, playground, or school?	☐	☐	☐	☐
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?	☐	☐	☐	☐

8.3. **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?** (check one box on each line)

	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 he/she could do	☐	☐	☐	☐
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 friends (it took extra effort)	☐	☐	☐	☐

8.4. **During the <u>past 4 weeks</u>, 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?** (check one box on each line)

	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 he/she could do	☐	☐	☐	☐
b. Limited in the **AMOUNT** of time he/she could spend on schoolwork or activities with friends	☐	☐	☐	☐

8.5. **During the <u>past 4 weeks</u>, how <u>much</u> bodily pain or discomfort has your child had?** (check one box only)

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

8.6. **During the <u>past 4 weeks</u>, how <u>often</u> has your child had bodily pain or discomfort?** (check one box only)

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

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

8.7. **How often during the <u>past 4 weeks</u> did each of the following statements describe your child?** (check one box on each line)

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

8.8. **Compared to other children your child's age, in general would you say his/her behaviour is**: (check one only)

☐ Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor

The following phrases are about children's moods.

8.9. **During the past 4 weeks, how much of the time did your child:** (check one box on each line)

		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?	☐	☐	☐	☐	☐

The following question asks 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.

8.10. **During the past 4 weeks, how satisfied do you think your child has felt about:** (check one box on each line)

		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?	☐	☐	☐	☐	☐

The following statements are about health in general.

8.11. **How true or false is each of these statements for your child?** (check one box on each line)

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

8.12. **Compared to one year ago, how would you rate your child's health now?** (check one box only)

☐	☐	☐	☐	☐
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

8.13. **During the <u>past 4 weeks</u>, how MUCH emotional worry or concern did each of the following cause YOU?** (check one box on each line)

	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	☐	☐	☐	☐	☐

8.14. **During the <u>past 4 weeks</u>, were you LIMITED in the amount of time YOU had for your own needs because of?** (check one box on each line)

	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	☐	☐	☐	☐

8.15. **During the past 4 weeks, how often has your child's health or behaviour:**
(check one box on each line)

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

8.16. **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?** (check one box only)

☐ Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor

These final few questions ask about your child and his/her family.

8.17. **Is your child:**

☐ Male ☐ Female

8.18. **What is your child's date of birth?**

☐☐ / ☐☐ / ☐☐
DAY MONTH YEAR

8.19. **Who lives with your child currently?**

Person	Their relationship to your child	Their Age	Their sex
1			☐ Male ☐ Female
2			☐ Male ☐ Female
3			☐ Male ☐ Female
4			☐ Male ☐ Female
5			☐ Male ☐ Female
6			☐ Male ☐ Female
7			☐ Male ☐ Female
8			☐ Male ☐ Female

8.20. **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:

_____

8.21. **Are you:**

☐ Male ☐ Female

8.22. **What is your date of birth?**

☐☐ / ☐☐ / ☐☐
DAY MONTH YEAR

8.23. **Which of the following best describes your current work status?** (check one box only)

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

8.24. **What is your relationship to this child?** (check one box only)

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

8.25. **What is the highest grade of school you have completed?**

- ☐ less than 8 years
- ☐ 8-12 years
- ☐ completed high school
- ☐ completed vocational/technical training
- ☐ completed college/university
- ☐ completed graduate school

8.26. **What is your current marital status?** (check one box only)

☐ Married	☐ Widowed	☐ Divorced	☐ Separated	☐ Remarried	☐ Never married

8.27. **Are you currently living with a spouse or partner?**

☐ Yes ☐ No ⟶ If no, go to question 8.30.

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

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

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

- ☐ less than 8 years
- ☐ 8-12 years
- ☐ completed high school
- ☐ completed vocational/technical training
- ☐ completed college/university
- ☐ completed graduate school

The next two questions will allow us to compare your family's health to that of other people in the study who are similar to you.

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

- ☐ 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 - $99,999
- ☐ $100,000 or more
- ☐ Don't know

8.31. **Thinking about your total family income, from which sources did your family receive income during the past year?** (check all that apply)

- ☐ Wages 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-annuation
- ☐ Dividends and interest on bonds, deposits, and saving certificates
- ☐ Other government sources such as welfare, mother's allowance, etc.
- ☐ Other sources(s), please specify: _____

8.32. **How long ago was your child *first* diagnosed with epilepsy?**

_____ Months ago or _____ Weeks ago

8.33. **Who *first* diagnosed your child with epilepsy?** (check one box only)

- ☐ Family Physician
- ☐ Neurologist
- ☐ Pediatrician
- ☐ Other (please specify) _____

8.34. **Did the doctor who first diagnosed your child with epilepsy prescribe any medications for seizures?**

- ☐ Yes
- ☐ No

8.35. **DATE THIS QUESTIONNAIRE WAS COMPLETED:**

☐☐ / ☐☐ / ☐☐
DAY MONTH YEAR

Thank you for participating in this study.

If there are any other issues concerning your child's health and quality of life that we did not ask but that you would like us to know about, please feel free to mention them below.

Curriculum Vitae

EMILY K. CHEMNITZ

EDUCATION

M.Sc. in Epidemiology Western University (2018-present)

- Epidemiology

B.Sc. (Hons) Brock University (2013-2018)

- Neuroscience (Neuropsychology stream)

HONOURS AND AWARDS

Department of Paediatrics, Western University Graduate Studentship Award……..2019
Children's Health Research Institute Graduate Research Fellowship……2018
NSERC Undergraduate Student Research Award…….....2018
Brock University-Science Fair Scholarship……..2013-2017
Deans Honour List (above 80%)……...2013-2017
Brock Scholars Award……...2013-2016
Eric John Memorial Bursary……...2013
Canada Wide Science Fair (Bronze)…….....2013
Niagara Regional Science and Engineering Fair (Bronze)…….2013

RESEARCH EXPERIENCE

Western University, Epidemiology and Biostatistics (September 2018-Current)
Research Assistant

- Supported a multi-disciplinary team of epidemiologists, researchers and physicians in the roll out of a mindfulness program targeted for children diagnosed with epilepsy
- Roles included: coding paper questionnaires into an online format, screening questionnaires, fulfilling research duties at the program in preparation for program evaluation

NSERC Undergraduate Student Research (May 2018-August 2018)
Research assistant and continuation of undergraduate thesis project

- Collected, inputted and performed preliminary analysis on data from undergraduate thesis project
- Assisted lab members in a variety of other research projects and completed administrative work pertinent to the continuation of ongoing projects

Undergraduate Thesis Project (September 2017-May 2018)
Individual differences in movie viewing patterns across age groups

- Designed, facilitated and analyzed a formal research project with the support of a supervisor
- Focus of research was neurocognitive aging, specifically, whether viewing patterns during a dynamic movie may have an effect on memory and age.

Research Assistant (January-April 2017)

Volunteer at Brock University

- Supported the primary researcher by facilitating a study with participants during the study phase of the research
- Research was focused in social psychology

Research Assistant (June 2014-August 2014)
Employed by Brock University

- Conducted and completed a literature review with a professor in the Kinesiology Department.

WORK EXPERIENCE

Niagara Region, Public Health (August 2017-August 2018)
Young Adult Peer Leader

- Partnered with two community-after school groups across the region to facilitate discussions and activities surrounding health-related topics. Worked with the students to develop their leadership, advocacy and self-empowerment skills to promote health within their communities.

Brock University (August 2015-February 2018)
International Plus Assistant/International Learning Programs Assistant

- Managed the International Plus Program and facilitated all related workshops. As well, provided support for the international learning programs at Brock University; including the Brock Exchange Program.

Niagara Region, Public Works (April 2015-August 2015)
Water-Wastewater Outreach Assistant

- Assisted in managing the water wagon program, including the schedules of two other workers, attending the events, and planning the promotional materials. Also, provided in office support and wrote for the internal newspaper.

Niagara Region, Public Health (April 2014-April 2015)
Community Awareness Educator

- Promoted the new Smoke-Free Outdoor Spaces By-Laws at community events and supervised a set of volunteers.

Niagara Region, Public Health (August 2011-August 2013)
Peer Leader

- Worked in a group of peers to advocate and promote healthy living amongst youth and young adults in the Niagara Region. Also, facilitated healthy living programming within schools.