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Long-Term Behavioural Problems in Youth with Childhood-Onset Epilepsy

Rebecca Grace Couper, *The University of Western Ontario*

Supervisor: Speechley, Kathy, *The University of Western Ontario*

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Abstract

Children with epilepsy are impacted far beyond having seizures, as children with epilepsy often have more psychiatric and behavioural problems than the general population. Whether these problems remain at elevated rates in the long-term is unclear. This study revealed that the prevalence of long-term behavioural problems in youth with childhood-onset epilepsy did not differ significantly from the assessment normative data. Multivariable regression was used to assess associations of baseline and current characteristics with long-term behavioural problems. No associations with baseline characteristics were found, but current attitude towards epilepsy was associated with total, internalizing, and externalizing behavioural problems while seizure control was associated with internalizing behavioural problems. These findings show that long-term behavioural problems in youth with childhood-onset epilepsy are not significantly elevated, and though there are not any associations with baseline characteristics, there are some associations with current characteristics that could make identifying and reducing behavioural problems easier.

Keywords: epilepsy, children, youth, behavioural problems, long-term

Summary for Lay Audience

The impact of childhood-onset epilepsy goes far beyond a child having seizures, impacting children's quality of life, as well as that of their parents. Up to 80% of children with epilepsy (CWE) may face cognitive, psychiatric, and/or behavioral comorbidities. It has been suggested that risk factors of behavioral problems in CWE are a combination of neurological, seizure, family, and child variables. The main objectives of this thesis were to determine the prevalence of behavioural problems in youth 10 years after a diagnosis of childhood-onset epilepsy and to explore which factors might be related to behavioural problems. A list of 112 behavioural and emotional problems, where respondents rate whether their own behaviour matches those in the list, was used to assess behavioral problems in a health-related quality of life in children with epilepsy study. Long-term behavioural problems in youth with childhood-onset epilepsy were not significantly different than those found in the general population. No factors from the time of diagnosis were found to be associated with behavioural problems, however significant associations were found with the youth's attitude towards epilepsy which was measured at the same time as the behavioural problems; approximately 10 years after the onset of epilepsy. In addition, the amount of time since the youth last had a seizure was associated with certain behavioural problems, where those who had not had a seizure for at least two years were less likely to have behavioural problems. Although no factors from when the children were diagnosed with epilepsy were associated with behavioural problems later in adolescence, measuring attitudes towards epilepsy could help determine which youth might benefit from interventions to lessen behavioural problems.

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List of Abbreviations

APGAR	Family Adaptability, Partnership, Growth, Affection, and Resolve
ASEBA	Achenbach System of Empirically Based Assessment
ASM	Antiseizure medication
AYA	Adolescent and young adult
BECRS	Benign epilepsy of childhood with Rolandic spikes
CBCL	Child Behaviour Checklist
CES-D	Center for Epidemiologic Studies Depression Scale
CWE	Children with Epilepsy
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders (4^{th} edition)
EEG	Electroencephalogram
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
ILAE	International League Against Epilepsy
PSS	Parental Stress Scale
QOLIE	Quality of Life in Epilepsy Inventory
SES	Socio-economic status
TRF	Teacher's Report Form
YSR	Youth Self-Report

Chapter 1 : Introduction and Background

This thesis explores long-term behavioural problems in youth with childhood-onset epilepsy and their potential associations with demographic, clinical, and family factors from baseline and 10 years after the onset of epilepsy. Chapter 1 provides background information on the burden associated with the disorder of epilepsy, the influence epilepsy may have on behaviour in youth with epilepsy, and assessment tools used to measure behaviour.

1.1 Introduction

Epilepsy is a neurological disorder characterized by recurrent seizures, and a seizure occurs when there is excessive electrical discharge in the brain. It directly affects nearly 50 million individuals globally (1) and the overall prevalence of epilepsy in Canada is estimated to be 0.4%. Of those diagnosed with epilepsy in Canada, 57% were diagnosed before the age of 20 years (2). The impact of childhood-onset epilepsy goes far beyond a child having seizures (3), impacting children's quality of life, as well as that of their parents. Evidence indicates that up to 80% of children with epilepsy may face cognitive, psychiatric, and/or behavioural comorbidities (4).

The unpredictable nature of seizures and the stigma associated with epilepsy have been assumed to influence psychosocial development (3), whereby epilepsy can have adverse effects on child development and quality of life for children with epilepsy. Children with epilepsy who had been more impacted by their neurologic disability saw themselves as less intelligent and less popular and had lower quality of life scores (5). Children with epilepsy have also demonstrated lower academic achievement when compared to children with asthma (6) and less social competencies compared to their siblings (7). Longitudinal studies have shown that these struggles can remain throughout the child's life, as children with epilepsy have high rates of social problems in adulthood, even if they are in remission (8). Behavioural problems in children with epilepsy have been found to significantly impact family life, more so than cognitive problems, neurological disability, or epilepsy alone, and parents of children more impacted by epilepsy saw their child as less rewarding and adaptable (5).

Adolescence, already a difficult stage of rapid physical, psychological, and social development, is further complicated by the demands of epilepsy (9). Risk-taking behaviour, such as delinquency, alcohol and drug misuse, can develop during adolescence and can have a major impact on health in adolescence and adulthood of healthy children. A relationship between risk-taking behaviour and health is seen clearly in adolescents with chronic illnesses, and how the individual and their family react to the illness and treatment can influence the progress of normal developmental tasks (10). The presence of behavioural problems may lead to an increased risk for school dropout (11), high risk behaviours, and non-compliance with treatment recommendations (12), making this life stage even more challenging for individuals with epilepsy.

1.2 Background

1.2.1 Epilepsy

Epilepsy was defined by the International League Against Epilepsy (ILAE) in 2005 as a brain disorder characterized by a predisposition to epileptic seizures where at least two unprovoked seizures occur >24 hours apart. In 2014, the definition of epilepsy was expanded for purposes of clinical diagnosis to also include either one unprovoked seizure and a probability of further seizures similar to the general recurrence risk of at least 60% after two unprovoked seizures occurring over the next 10 years, or a diagnosis of an epilepsy condition (13). There are several considerations taken into account in diagnosing epilepsy including seizure type, epilepsy type, and epilepsy syndrome which allows etiology to be considered at each step. As a first step, seizures are classified into focal onset, generalized onset, and unknown onset types. Type of epilepsy is then explored if a diagnosis of seizure has been made and there is access to imaging. These categories include focal, generalized, combined generalized and focal, and unknown, where types of epilepsy can include multiple types of seizures. The process of classifying an epilepsy syndrome incorporates seizure types, EEG, and imaging features that occur together, and can include age-dependent features and comorbidities. Six etiologic groups exist including structural, genetic, infectious, metabolic, immune, and unknown. Recognizing which etiologic group a patient’s epilepsy falls into can assist in determining a treatment plan (14).

Most patients with epilepsy are initially treated using anti-seizure medication, where the type of medication is dictated by the types of epilepsy and syndrome in addition to other drug-specific variables, patient-specific variables, and country-specific regulations and variables (15). The physician and patient, or the patient's guardian also tend to consider the risk of seizure recurrence, potential side effects of medication, and potential duration of treatment. There is no specific protocol for discontinuing medication, but some of the provincial guidelines include waiting a year or two after seizure freedom is achieved before discontinuing medication, and having medication discontinued slowly and under supervision (16). Epilepsy is considered resolved when an individual reaches 10 years of seizure freedom with at least 5 years free of anti-seizure medication or when the upper age limit for an age-dependent epilepsy syndrome has passed (13).

1.2.2 Prevalence of Behavioural Problems in Children with Epilepsy

Many studies have shown a higher prevalence of behavioural problems in children with epilepsy compared with population-based normative samples (17–22), matched controls (23–26), children with asthma (27,28), and their siblings (29,30). An early study of child mental health found that 28.6% of children with uncomplicated epilepsy had psychopathology including behavioural problems; nearly five times that of healthy children (31). Similar results were found using the 1999 British Child and Adolescent Mental Health Survey, where 37% of children with epilepsy had a psychiatric disorder compared to 11% in children with diabetes and 9% in control children (32). More recent studies of behavioural problems in children with epilepsy have found similar rates of behavioural problems. (17,24,29,33–43).

A British population-based cohort study found that although 80% of children with active epilepsy had a diagnosed (DSM-IV) behavioural disorder and/or cognitive impairment, only a third had previously been diagnosed with a behavioural disorder. It was hypothesized that not many children with epilepsy were assessed by mental health professionals, as the neurobehavioural symptoms are often overshadowed by seizures (4). Similar results were found in a cross-sectional study in the United States where approximately 60% of the 114 children who participated had a DSM-IV psychiatric diagnosis, yet more than 60% had not received any

mental health treatment (44). This leaves many children who are already struggling with a neurologic disorder with unmet mental health needs when they could likely benefit from early identification and treatment.

1.2.3 Assessment Tools

The Achenbach System of Empirically Based Assessment (ASEBA) is a common assessment tool to detect behavioural problems and provides a plethora of data including average population behaviour scores as well as suggested cut-off scores indicative of at-risk and clinical levels of problems. Information on internalizing, externalizing, and total problems is also given and can be further divided into eight subscales. In addition to the Child Behaviour Checklist (CBCL), which is completed by parents, Achenbach has a system of scales including the Youth Self-Report (YSR) which is completed by children and adolescents aged 11 to 18, and the Teacher Report Form (TRF) completed by teachers (45). Assessment tools differ from diagnostic tools such as the Diagnostic and Statistical Manual for Mental Disorders (DSM-5) (46) which is used to define and classify mental disorders including behavioural problems to improve diagnoses, treatment, and research. The DSM-5 categorizes and allows for a diagnosis, while the ASEBA is a screening questionnaire with profiles to help identify problem areas though no diagnosis is made. Most other studies that assess behavioural problems in children with epilepsy use screening questionnaires, such as the Strengths and Difficulties Questionnaire, rather than diagnostic measures. This study used the YSR; where youth describe their own functioning, which allows problem areas to be highlighted.

Chapter 2 : Purpose and Objectives

This chapter presents the purpose of the thesis and outlines the objectives.

2.1 Purpose

The purpose of this thesis is to assess long-term behavioural problems and its' associated factors in youth with childhood-onset epilepsy. It has been noted that behavioural problems are more prevalent in children with epilepsy compared to the general population, but very few studies have explored the prevalence of behavioural problems several years post-diagnosis and factors associated with the problems. The few studies that have focused on long-term behavioural problems in children with epilepsy have tended to explore epilepsy, child, or family characteristics separately but have rarely explored the relative contributions of a comprehensive set of factors. Assessing long-term behavioural problems and associated factors in children with epilepsy could provide guidance for targeted interventions during childhood to prevent long-term behavioural problems in adolescence and early adulthood.

2.2 Research Objectives

1) To describe the prevalence of self-reported total, internalizing, and externalizing behavioural problems (approximately ten years after diagnosis of epilepsy) in adolescents with childhood onset epilepsy
2) a) To identify the current demographic, clinical, and family characteristics (eight to ten-years after the diagnosis of epilepsy) associated with long-term behavioural problems
   b) To identify the demographic, clinical, and family characteristics at the time of epilepsy onset associated with long-term behavioural problems

Chapter 3 : Literature Review

This chapter reviews the literature on characteristics that may be associated with behavioural problems in children with epilepsy. Studies were found in June 2020 using MEDLINE (Ovid and ProQuest), CINAHL, and PsychINFO (Ovid) electronic databases with search terms (epilepsy OR epileptic OR seizures) AND (child OR children OR childhood OR adolescent OR pediatrics OR paediatrics) AND (behavioural problems OR behavioral problems OR problem behaviour OR problem behavior). Sections include epilepsy-related factors (seizure severity, seizure control, epilepsy duration and age of onset, types of seizures and epilepsy, anti-seizure medication), child characteristics (sex, age group, IQ and learning difficulties, and early temperament/behavioural issues/attitude), and family-related factors. The literature review also includes an overview of existing long-term behavioural studies in children with and without epilepsy, and limitations of existing literature.

3.1 Potential Factors Associated with Behavioural Problems

3.1.1 Epilepsy-Related Factors

Seizure Severity

Although seizure severity is not often included as an epilepsy-related factor in studies assessing behavioural problems, it seems to nearly always be a risk factor of behavioural problems. A cross-sectional study in the United States with 164 children with epilepsy aged 9 to 14 found a significant association between seizure severity which was graded using the Seizure Severity Scale and total, internalizing, and externalizing behavioural problems as assessed by the Child Behavior Checklist (21). Similar results were found in a four-year study conducted with 136 children with epilepsy, where there was an increase in behavioural problems over time for girls with high seizure severity, while most other groups in the study showed improvement over time, demonstrated by a decline in behavioural problems (27). Seizure severity was measured using a scale that considers the type of seizure, frequency, and number and side effects of antiepileptic drugs, where a high seizure severity was given if at least a “moderate problem” was scored in all categories. Only one study that included seizure severity did not find an association with

behavioural problems (47) where seizure severity and control were only associated with one of seven behaviour subscales, however over half of the sample had minimal severity and sample sizes for higher severity categories were quite small. Despite most studies finding an association between seizure severity and behavioural problems, it often is not included as an epilepsy-related factor.

Seizure Control

The control of seizures is often associated with behavioural problems in studies that consider epilepsy factors, though some studies did not find an association. Many studies have found more behavioural problems for children with uncontrolled or more frequent seizures compared to those with controlled seizures (7,48–54). For example, a cross-sectional study in India with 140 children with epilepsy aged 2 to 14 found that children with uncontrolled epilepsy had more behavioural problems as assessed using the CBCL compared to those who had not had a seizure for at least six months prior to the study (55). Similar results have been reported in other countries using various behaviour assessment tools, including in Kenya where the Child Behavior Questionnaire (23) was used and Indonesia where the Strengths and Difficulties Questionnaire was used (25).

In the few long-term studies that have been conducted, seizure status has been shown to affect at least some types of behaviour problems. A two-year study of 224 children with new-onset epilepsy found that children who had experienced at least one seizure since the previous assessment (6- to 12-month period between assessments) consistently scored higher on the total and internalizing CBCL scales across the study period (48). One study analyzing outcomes of behavioural problems an average of seven years after epilepsy surgery in childhood found that patients who had been seizure-free for at least a year prior to follow-up had a significant improvement in externalizing behaviours (54). Similarly, a prospective cohort study that followed children for eight to nine years after an initial diagnosis of epilepsy determined that children who had not been seizure-free for at least five years had higher scores in total and externalizing behaviour problems compared to those who had been seizure-free for five years (7).

Conversely, numerous studies have found no correlation between seizure control and behavioural problems (18,20,56–58). In a cross-sectional study in England of 47 children with epilepsy and an average age of 11 years, there was no difference in behavioural problems between children who had been seizure-free for at least six months and those who had not been seizure-free (58). Similarly, a three-year prospective study in the United States with 73 children with idiopathic epilepsy determined that although children with epilepsy had more behavioural problems than children with migraines and healthy controls, seizure frequency was not related to behavioural scores on the CBCL at any time during the study (56). Most studies that did not find a correlation between seizure control and behavioural problems defined seizure control as the frequency of seizures rather than complete freedom, such that most children were still having *some* seizures.

Another seizure variable that has been shown to be associated with behavioural problems is the presence of prior unrecognized seizures. In a cross-sectional study of 192 children with epilepsy, children with prior unrecognized seizures had significantly more behavioural problems than children who did not have prior unrecognized seizures (28). A three-year prospective cohort study with 300 children with epilepsy had similar findings, where children who had previously unrecognized seizures were at higher risk for behavioural problems at the study's baseline (29). Authors hypothesized that less involved parents might not notice a seizure, and those children might demonstrate more behavioural problems due to less parental supervision.

Epilepsy Duration and Age of Onset

Studies have shown mixed results regarding whether age of epilepsy onset is related to behavioural problems. Numerous cross-sectional studies have found no difference in behavioural problems by children's age at their diagnosis of epilepsy (20,47,59,60). Most of these studies used the CBCL to assess behavioural problems and participants had an average age of approximately 10 years. A 3-year longitudinal study with children with epilepsy aged 8 to 13 also found no relationship between age of epilepsy onset and behavioural problem scores using the CBCL and TRF measures (56).

Inconsistent results were seen across studies that found a relationship between age of onset and behavioural problems whether a younger age or older age of onset was associated with more

behavioural problems. A British birth cohort followed for 16 years which used the Teacher's Bristol Social Adjustment Guide and Rutter Scale-B measurements, found that behavioural disorders were associated with an earlier diagnosis of seizures (61). Other studies have also found specific behavioural problems (24,51,62), worse cognitive and behavioural outcomes (53), and poorer assessment scores on the Strengths and Difficulties Questionnaire (63) to be associated with an earlier age of onset. Fewer studies have found a positive relationship between age of onset and behavioural problems and where this is the case, older age tends to be associated with internalizing behavioural problems (52,57) and total behavioural problems (58).

Similarly, some studies have seen more behavioural problems with a longer duration of epilepsy (51,64,65). Even in a cross-sectional study with young children aged one to five, patients with a longer duration of epilepsy had more behavioural problems (66).

Types of Seizures and Epilepsy

Studies have shown mixed results regarding associations of types of seizures and long-term behavioural problems; this may partially be explained because there are numerous methods to classify seizures and epilepsy. Studies that have classified seizures into generalized and focal/partial have had fairly consistent results indicating that children with focal seizures tend to have more behavioural problems on at least some behavioural problems subscales (23,25,47,49,50,67). In one of these cross-sectional studies where 106 children with idiopathic epilepsy were assessed for behavioural problems, children with benign focal epilepsy demonstrated more behavioural problems compared to children with generalized epilepsy (50). A small study in Egypt found that children with focal seizures had more internalizing behavioural problems, while those with general tonic-clonic seizures had more externalizing behavioural problems (38). Fewer studies found no differences in behavioural problems for children by general and partial seizure types (36,56,61,68) and some found no differences in any seizure-related variables (69,70).

Epilepsy has been categorized in various ways across studies; however idiopathic epilepsy (i.e. where the cause of seizures is known) is usually one of the categories. Children with idiopathic epilepsy have been reported to have fewer behavioural problems than a comparison group with

non-idiopathic (51,71), cryptogenic (i.e. of obscure or unknown origin) (72), or symptomatic (cause is known) (22,62,73) epilepsy. Other studies have reported no difference in behavioural problems when comparing those with idiopathic epilepsy to those with non-idiopathic epilepsy (29,40,48,74,75). Some of those studies had small sample sizes and might not have had sufficient power to detect differences between sub-samples.

Focal site is another method used to categorize epilepsy. Most studies found that the site of focus made no difference in behavioural problems in children with epilepsy, where almost all studies included temporal as one of the focal sites and the participants were candidates or recipients of surgery (18,39,53,54,76). Two studies found differences in behavioural problems by focal site. One study found that the temporal site of interictal EEG abnormalities contributed to the risk for psychiatric comorbidities (51), while the other found children with frontal lobe epilepsy had lower scores on some subscales of behavioural problems compared to children with temporal lobe epilepsy or generalized absence epilepsy (77).

Anti-Seizure Medication

Anti-seizure medication has been found to be associated with behavioural problems in children with epilepsy in many studies, though some found no differences in behavioural problems by medication use. Where associations were present, medications tended to have lengthy lists of potential side effects including impaired attention and vigilance, impaired psychomotor speed, and secondary effects on other functions (78). In addition, many anti-seizure medications can impact cognitive function and behaviour, especially when given at high doses or as polytherapy (79).

Numerous studies have found that taking anti-seizure medication worsens behavioural problems in children, specifically taking multiple medications. Several cross-sectional studies have found some specific behavioural problems were elevated in patients using polytherapy compared to patients only using one medication (50,51,62,65,66). Similarly, numerous longitudinal studies have found an association between the continued use of anti-seizure medications and total behavioural problems (7,48,53) and one study found that an increase in number of medications

over six months was associated with an increase in attention problems over the course of the study (39).

Alternatively, numerous cross-sectional studies have reported no significant differences in behavioural problems by anti-seizure medication use including those that found no differences between monotherapy and polytherapy (55,58,59). Most of these studies had relatively small sample sizes, however some longitudinal studies revealed similar results where no differences in behavioural problems were observed across medication use or drug conditions (29,54,67,72). Some of these studies assessed specific types of anti-seizure medications, such as comparing the use of phenytoin and carbamazepine, rather than considering the number of total anti-seizure medications. As there are numerous types of anti-seizure medications and methodologies for drug trials are not uniform, it is difficult to assess anti-seizure medication-related behavioural and psychiatric side effects (80).

3.1.2 Child Characteristics

Sex

Many studies have found the development or presence of behavioural issues to be unrelated to sex of the child (23,29,41,53,62). These studies vary in follow-up times; some are cross-sectional while others are longitudinal with follow-up as long as three years, and most had sample sizes of at least 100 children with epilepsy. Nevertheless, few studies have reported differences in behavioural problems between boys and girls with epilepsy. In the studies where differences were seen, males were often found to have more behavioural problems compared to females, at least in most behavioural problem subscales as seen in numerous cross-sectional studies (22,40,67). One study with 112 children with epilepsy found an interaction between seizure type and sex, where boys with partial seizures had significantly higher behavioural scores than boys with generalized seizures and girls with either seizure type (67). Another study with 409 children with epilepsy reported higher externalizing behaviour problems scores for boys and higher internalizing behaviour problem scores in girls (22). Few studies demonstrated more behavioural problems in females, except for one study in the United States where only a subgroup of females had more problems. That study found an increase in behavioural problems over four years of

girls whose seizure severity remained high from baseline to follow-up, while other gender and severity subgroups showed improvement (27).

Age

Inconsistent results have been reported regarding the relationship between age and behavioural problems in children with epilepsy, but it is generally agreed that children of different ages exhibit different types of behavioural problems. A cross-sectional study with 140 children with epilepsy found there were differences by age group in behavioural problem types assessed using the CBCL. Younger children with epilepsy, aged two to five, had clinically abnormal scores for externalizing behaviour problems, while older children, aged 6 to 14, had abnormal scores for both internalizing and externalizing behaviour domains (55). A year-long study that followed over 300 children who underwent epilepsy surgery reported an older age at evaluation was associated with worse cognitive and behavioural problems as measured with multiple assessments (53).

Conversely, using the Rutter Parent Scale, which assesses behavioural problems and psychopathology in children, a cross-sectional study in the United Kingdom of 248 children with new-onset epilepsy reported that younger children (8 to 11 years) had significantly more behavioural and emotional problems than older children aged 12 to 15 years, although their quality of life scores were comparable (81). No associations between age and behavioural problems in children with epilepsy were reported in two studies, though both studies recognized that their findings were not common among the majority of studies that considered age as a potential influence on behavioural problems (39,41).

Cognitive Difficulties

Low IQ, learning difficulties and neurological impairments have been identified as factors that may be associated with behavioural problems. A cross-sectional study with 61 children with epilepsy found low IQ to be associated with internalizing behavioural problems and developmental delay to be associated with both internalizing and externalizing behavioural

problems (24). A cross-sectional study in the United States grouped 164 children with epilepsy by IQ into low, middle, and high groups. Low IQ was classified as a score below 85 which included an IQ as low as 56, while middle IQ was 85 to 100 and high IQ was 101 to 130. Although all three IQ groups had more children in the CBCL 'at risk' score range for behavioural problems than the standardized population values, the low IQ group had the most behavioural and mental health problems (21). Similarly, processing speed was determined to be a risk factor for behavioural problems in children with epilepsy (29) and a correlation was found between special education programs and behavioural problems (72). Other similar factors associated with more behavioural problems include developmental delay (24), executive functioning (82), and cognitive impairment (23,42,83). However, two other studies found no difference in behavioural problems across IQ groups in children with epilepsy (55,84). Possible explanations for the lack of relationship may be that the effect of IQ could have been mediated through other baseline measures (84) or because there were fewer children in the sub-groups (55).

Early Temperament, Behavioural Issues, and Attitude

Most longitudinal studies have reported an association between pre-diagnostic temperament and future behavioural problems. A three-year longitudinal study conducted with 229 children with epilepsy and using the TRF and CBCL to assess behaviour at multiple time points found that early temperament was associated with behavioural problems three years after onset (82). In other studies, long-standing behavioural problems or pre-diagnostic learning and behavioural issues were found to be related to more behavioural problems later in time (36,54,72,74). One seven-year prospective study found that more behavioural problems at baseline was the most consistent predictor of improved behaviour, which was hypothesized to reflect regression toward the mean or an overall trend of improved behaviour over time (54).

Another factor that is likely related to behavioural problems in children with epilepsy is the child's attitude or response towards the diagnosis of epilepsy and living with epilepsy. Two longitudinal studies in the Netherlands found that children with epilepsy who presented with behavioural problems had difficulty adapting to adversity and had poor reactions to their diagnosis (72,74). Similarly, there have been reports that children with negative feelings and

attitudes towards epilepsy are more likely to have fewer coping behaviours (85). A cross-sectional study with 173 children with newly diagnosed epilepsy found that children's attitude acted as a mediator in the relationship between stigma and mental health outcomes including behavioural problems, suggesting a positive attitude towards epilepsy may lessen behavioural problems (86).

3.1.3 Family Characteristics

Other factors that could contribute to behavioural problems in children with epilepsy are those external to the child including family characteristics such as family mastery or having a sense of control, child-parent relationships, family stress, and family resources. Families of children with epilepsy report lower levels of esteem and communication, less social support from extended family, and poorer financial well-being (20). When asked about their experience with children with epilepsy, parents reported limiting family outings, discomfort with others caring for their child, and sleeping with their child as they were fearful of seizure activity at night as some of the ways their child's epilepsy affects their family (87). Nearly all studies that considered family characteristics found behavioural problems to be associated with poorer familial relationships, less resources, and more stress.

All studies that have considered parental adaptation as a potential factor of behavioural issues have found correlations in at least some subgroups of behavioural problems. Two longitudinal studies concluded that a higher prevalence of behavioural problems was found in children whose parents had a difficult time continuing habitual parenting after their child was diagnosed with epilepsy (74,88). Adaptation issues were also found to be risk factors for more behavioural problems (20,42) and over-controlling parenting has been found to lead to more behavioural problems (89). It has been shown that some parents have altered their parenting style and tended to lower their expectations for their child with epilepsy (90), which can influence the child's behaviour (91).

Like parental adaptation, studies that have explored relationships between children with epilepsy and their parents have shown behavioural problems to be associated with poorer relationships.

One study in the United States with 51 dyads of children with epilepsy and their mothers used problem-solving tasks to observe child-mother interactions to assess whether they were related to behaviour problems (92). The results suggested that the interactions were related to children's behavioural problems, particularly for boys where low maternal support was associated with behavioural problems. The results for girls showed lower maternal support led to fewer externalizing problems, which led the authors to hypothesize that maternal behaviour could be more influential for boys than for girls. A lack of child satisfaction with their family relationships was also found to be a risk factor for more behavioural problems in a three-year prospective study with 300 children with epilepsy (29). Whether a parent accepts their child with epilepsy can influence behavioural problems, where acceptability issues were correlated with more externalizing behavioural problems (38). Similar findings were seen in a cross-sectional study in the Netherlands, where parental rejection was correlated with higher levels of internalizing and externalizing behavioural problems (19).

Most studies that have assessed socioeconomic status (SES) have found more behavioural problems when SES was low. Studies that used education level of the primary caregiver to reflect SES, found relationships with behavioural problems. A three-year study with 300 children with epilepsy determined that lower caregiver education was a key risk factor for behavioural problems (29), and a cross-sectional study with 224 children with new-onset epilepsy found lower caregiver education levels to correspond with more behavioural problems (33). Lower SES was associated with more behavioural problems in children with epilepsy in other cross-sectional studies (93,94) and a one-year cohort study, where more behavioural problems were correlated with lower SES and maternal education (69). Only a handful of studies failed to find a negative relationship between SES and behavioural problems and include studies from less developed countries. A study in Africa found no correlation between income and behavioural problems in children (41) while a study in India found that belonging to a higher income group was associated with psychopathology in children with epilepsy, suggesting families of lower socioeconomic status receive more social supports from extended family and neighbours despite financial challenges (64).

Similarly, studies that have assessed familial stressors, including fewer resources or other stressful events, found more behavioural problems when familial stress was elevated. A cross-sectional study that assessed child adaptation and family resources in childhood epilepsy found there were fewer behavioural problems in children where better family system resources were present, which include assets available to the family to help meet demands they encounter (20).

A lack of parental well-being is another factor potentially associated with behavioural problems in children with epilepsy, as seen in a cross-sectional study from the Republic of Korea with nearly 300 adolescents, where an association was found between parental depressive mood and internalizing problems (95) and in a two-year prospective study that found higher parent worry scores were related to more behavioural problems (96). In addition, a one-year study with young children with epilepsy found maternal anxiety levels to be positively related to total, internalizing, and externalizing behavioural problem scores (69).

3.2 Behaviour Changes Over Time in Children with Epilepsy

Most longitudinal studies that observed behavioural problems in children with epilepsy found either a decrease or no change in behavioural problems over time, though some found an increased risk of problems over time. Some shorter longitudinal studies of three to four years in length have reported a decline in behavioural problems of children with epilepsy, indicating an improvement, even though the prevalence of behavioural problems in children with epilepsy remained higher than those of children with asthma or their siblings (29,97). A six-year prospective cohort study with 69 children with epilepsy aged 8 to 18 found that behavioural problems did not worsen over the study period as assessed using the CBCL (98), while similar results were found in other studies of varying lengths (48,54,74,99,100).

Conversely, other studies have found an increase in behavioural problems over approximately 15 years (35,61). A 16-year study that followed a British birth cohort of over 17 000 children (almost 1000 of whom had childhood seizures and 66 diagnosed with epilepsy) found the association between epilepsy and emotional/behavioural problems was most significant at 16 years having increased from the risk of problems at age 7, suggesting an increasing risk over

time (61). The author proposed an accumulation of brain damage, cumulative effects of living with epilepsy, or hormonal changes during adolescence could be involved in an increasing risk as time passes.

3.3 Long-term Behavioural Problems in Children in the General Population

Most studies that have evaluated long-term behavioural problems in children of the general population have found that at least some level of behavioural problems in children continued into adulthood. A 24-year longitudinal study that observed a cohort of over 1000 children found that those with anxiety, oppositional defiant disorder, or conduct problems in childhood were at a greater risk for psychopathology in adulthood, while children with psychopathology were more likely to meet criteria for a DSM-IV diagnosis 24 years later (101). Similarly, a 14-year longitudinal population cohort study with over 1500 children aged 4 to 16 found that children with higher levels of parent-reported behavioural and emotional problems at the start of the study were at a 2- to 6-fold increased risk for psychological disorders later (102). Conversely, a two-year study with pre-school aged children found problem behaviours decreased over the study period, similarly to normative declines when children with a mean age of four years were assessed using numerous scales to compare earlier behaviour to later academic and socio-behavioural performances (103). It is suggested that there is much variability in the development of young children's problem behaviours and substantial between-child variation in changes of problem behaviours (103).

A Norwegian population-based cohort of 921 children collected parent-reported questionnaires approximately every two years from age 1.5 years to 14.5 years, where responses from the children were also collected beginning at age 12.5. Five trajectories were seen: high stable, where behavioural problems remain high throughout the study period, which represented 18% of children; high childhood limited, where many behavioural problems at onset significantly reduced to low levels in adolescence, representing 5% of children; medium childhood limited, where levels remain somewhat elevated into adolescence, representing 31%; adolescent onset, where fewer behavioural problems in childhood increase into adolescence, with 30%; and low stable, where behavioural problems remain low throughout the study, which represented 16% of

individuals. Family stress and maternal age were found to be the factors that separated children in the high stable class from other classes, where externalizing problems were seen consistently throughout childhood and adolescence (104).

3.4 Limitations of Previous Studies

Behavioural problems have been shown to be more prevalent in children with epilepsy compared to the general population for many years now. One major limitation has been the cross-sectional nature of many of the studies assessing behavioural problem thus precluding the exploration of risk factors for behaviour problems. For example, children with new-onset epilepsy might exhibit more behavioural problems as they were just diagnosed with a neurological disorder, so the level of problems might not accurately reflect behavioural problem levels before or after the diagnosis. Studies that assess behavioural problems over time tend to have a follow-up period of only a few years, which might not be representative of the remaining childhood period. The studies that have longer follow-up periods tend to have small sample sizes, or specific samples such as children eligible for surgery or those with a single type of epilepsy. In addition, some studies recruit patients from specific settings, such as hospitals or tertiary care centres, where children with difficult cases of epilepsy might make up the majority of the sample. Using specific settings or selecting certain patients limits the generalizability to all children with epilepsy.

Another limitation of some studies is their retrospective nature. These studies are limited to using medical records which might be missing formal diagnoses, rather than using standardized assessments or data collection forms collected prospectively using consistent methodology. Collecting data from only one individual (usually the mother) can also hinder the accuracy of the information received, as children can act differently in different scenarios, such as at school, or might not choose to share their thoughts and feelings with their family.

There are many factors that could potentially influence levels of behavioural problems in children, but it is not often that familial, child, and epilepsy factors are all considered in one study. Certain familial factors such as family mastery or parental stress are often seen to have at

least some effect on children's behavioural problems, although most studies have not considered such factors in addition to epilepsy-related variables. There has also been a lack of studies using a life course framework, where comprehensive factors from across the lifespan are explored (105). This framework would explore lifelong effects of factors from birth, such as low birth weight, to current characteristics to extensively investigate many factors and changes shown over a lifetime.

Chapter 4 : Methods

4.1 Data Source – HERQULES

This thesis used data collected in the HEalth-Related QUality of Life in children with Epilepsy Study (HERQULES), a large multicenter prospective cohort study of 373 children with newly diagnosed epilepsy (106). HERQULES used a two-stage clustered sampling strategy to first contact paediatric neurologists who subsequently recruited parents of children with new-onset epilepsy across Canada. The sampling frame of paediatric neurologists was created from the list of members of the Canadian Association of Child Neurology, which included the vast majority of those practicing in Canada at the time, and was completed with the assistance of an expert panel. From the total of 72 neurologists, 53 agreed to participate. Paediatric neurologists recruited parents of children 4 to 12 years of age who were diagnosed with a new-onset epilepsy, over an 18-month period beginning in 2004. Inclusion criteria were as follows: a new case of epilepsy where a previous diagnosis had not been previously confirmed and seen for the first time by a participating neurologist within the data collection period; the diagnosis was made between the ages of 4 and 12 years; and the parent or caregiver was primarily responsible for the child's care for a minimum of six months before the start of the study and would continue to for the duration of the study. The person who identified as the child's primary caregiver will be referred to as the parent for the remainder of the thesis. Exclusion criteria were as follows: a previous confirmation of an epilepsy diagnosis by another physician; a diagnosis of any other progressive or degenerative neurological disorder; a diagnosis with other major co-morbid non-neurological disorders that could impact quality of life; and the parent or caregiver had insufficient English language skills to complete questionnaires. Out of the 455 eligible families, 373 were recruited and 282 were retained for the first two years of follow-up. Research ethics board approval was obtained from 17 boards across Canada. Participating parents and neurologists received a token of appreciation at each time point.

A second phase of HERQULES was added to collect data on current state of health approximately 8 and 10 years after the child's initial diagnosis. Consent to contact the physician responsible for the epilepsy care of the adolescents and young adults (AYAs), for those still

receiving such care, was obtained from the children and/or parents depending on the AYA's age. A token of appreciation was sent to participating AYAs, parents, and physicians. The second phase only required research ethics approval from the Western University Health Science Research Ethics Board, rather than having to get REB approval from all recruitment sites, as relationships with the families were already established. At the 8-year follow-up, responses were received from 192 parents and 154 AYAs, while the 10-year follow-up had 173 parent responses and 131 AYA responses.

The Youth Self-Report (YSR) was designed to be completed by individuals aged 11 to 18 so it was included in the HERQULES self-report questionnaires only for youth younger than age 18 years. HERQULES had separate questionnaires for youth aged 11 to 17 years and young adults aged 18 years or older. The age limit of the YSR did not perfectly align with questionnaire age limits as behavioural problems were not the primary outcome of HERQULES. Although the YSR can be completed by 18-year-olds, the HERQULES questionnaire age groups did not allow for those 18 years old to do so. An assessment for those over 18 years old exists however, the Adult Self-Report does not appear to be widely used and was not included in the young adult questionnaire. Eligibility for analyses in this thesis was restricted to families of youth in HERQULES who were younger than 18 years old at the 8-year follow-up and are referred to as the eligible baseline subsample throughout the thesis. The birthdate of the oldest individual who completed the YSR at the 8-year follow-up was used to separate individuals who would have been eligible to complete the YSR in the youth (11-17 years old) questionnaire at an 8-year or 10-year follow-up. There was one individual whose age would have placed them in the youth questionnaire group but who had completed the young adult (18+ years old) questionnaire so that individual was removed from the eligible subsample. The eligible baseline subsample included 309 families of the 373 families in the HERQULES baseline sample.

4.2 Measurement

Questionnaires were mailed to parents and neurologists as soon as possible after diagnosis (referred to as baseline) and 6 months, 1 year, 2 years, 8 years, and 10 years later. At the 8- and 10-year follow-up, those children with epilepsy who were now AYAs were also asked to

complete questionnaires focused on their health and well-being. There were two questionnaires for AYAs depending on their age: one for those aged 11 to 17 and one for those 18 years or older. Questionnaires for parents included topics such as the child's health-related quality of life and their family environment, allowing changes to be tracked across the study's timeline. Questionnaires for neurologists focused on characteristics of the children's epilepsy and co-morbidities at each follow-up point, and questionnaires for AYAs focused on their health-related quality of life. Parents were to return their completed questionnaires, which each took approximately 45 to 60 minutes to complete, by mail to the HERQULES office. AYAs were given the option of completing their questionnaires online or using a paper copy to mail back. Physician forms, which took 5 to 7 minutes to complete were faxed back to the HERQULES office. Each measure completed by parents, AYAs, or physicians that is used in this thesis is reported below. A timeline of when each measure was collected is displayed in Table 4.1.

4.2.1 Children's Self-Assessed Behavioural Problems

Behavioural problems were reported by youth using the Youth Self- Report (YSR); a list of 112 behavioural and emotional problems in which respondents rate whether their own behaviour matches the problem presented. Data from the last available time point were used. The YSR was designed to be used for individuals aged 11 to 17, so only youth under 18 years of age completed the YSR in this study. Behaviour over the previous 6 months is rated using a three-point graded scale and includes 0 = item is not true, 1= somewhat or sometimes true, 2=very or often true. The scores can be used to determine elevated behavioural problems on syndrome scales (anxious/depressed, withdrawn/depressed, somatic complaints, social problems, thought problems, attention problems, rule-breaking behaviour, aggressive behaviour) or in higher order factors (internalizing and externalizing problems). The items addressing internalizing behaviours section are focused on syndromes of anxious/depressed, withdrawn/depressed, and somatic complaints syndromes while the items on externalizing behaviours are focused on syndromes characterized by rule breaking and aggressive behaviours.

YSR scores are reported as T-scores relative to the population norms standardized with a mean of 50 and standard deviation of 10, where higher scores indicate greater problems. T-scores will

simply be referred to as scores for the remainder of the thesis. Scores on the composite scales of total, internalizing, and externalizing behavioural problems can be categorized relative to population normative data such that scores below 60 are 'normal', scores between 60 and 63 are 'borderline', and scores above 63 are 'clinical'. Scores of 60 or higher correspond with the 84th percentile or higher of the normative data from the YSR, indicating a 'normal' score is anything below the 84th percentile. Subscales have slightly different scoring, where 'borderline' encompasses scores between 65 and 69, and 'clinical' covers scores over 69. The 'normal' scores for subscales include scores below the 93rd percentile of the YSR normative population. HERQULES used the 1991 version of the YSR and was scored using the 2001 version. According to the ASEBA Manual, "Data that were obtained on the 1991 forms can be scored according to the new scales by treating the changed problems as missing" (107). The method to handle missing data is not explicitly stated in the ASEBA Manual, so for this thesis missing items were given the average score of the subscale to which they belonged and were used to calculate total, externalizing, and internalizing scores. Six items were changed in the 2001 version, where three items were added to the rule-breaking behaviour subscale, two items were added to the attention problem subscale, and one item was added to the withdrawn/depressed subscale. These subscales are not individually reported here but solely used to calculate total, internalizing, and externalizing scales. Subscales that remained the same in the two versions are anxious/depressed, somatic complaints, social problems, thought problems, and aggressive behaviour. These subscales were assessed individually and were also used to calculate total, internalizing, and externalizing scores. Although raw scores differed between versions, percentiles and T-scores remained similar. Estimated Pearson correlations between raw subscale scores for the new YSR scales and 1991 versions ranged between 0.88 and 0.99 for problem scales and were 0.99, 0.97, and 1.00 for internalizing, externalizing, and total problems, respectively. Content validity has been demonstrated by ASEBA as scale items have been in development since the 1960s and have changed over the years, such as eliminating items that failed to discriminate between groups of children. The validity of the Child Behavior Checklist; the parent-reported version of the YSR, for children with epilepsy was supported in a study of children who had undergone epilepsy surgery (17). Even though some aspects of a seizure could be misidentified as behavioural problems, such as nervous movements or stares blankly, the difference in scores when including and excluding ambiguous items was not significant.

As only youth under 18 years of age were eligible to complete the YSR, there is a smaller sample with YSR scores at the 10-year follow-up as some participants had "aged out" of the YSR. Results from the 8-year follow-up were included as the final time point for those participants who were 18 or older by the 10-year follow-up as well as for those whom that was the last completed questionnaire returned.

4.2.2 Demographic and clinical characteristics

Severity of Epilepsy

The severity of epilepsy was classified by physicians using the Global Assessment of Severity of Epilepsy (GASE) Scale (108). It is a single-item measure where physicians rate the overall severity of epilepsy by answering the question "Taking into account all aspects of this patient's epilepsy, how would you rate the severity of his/her last visit?". Response options are as follows: (7) extremely severe, (6) very severe, (5) quite severe, (4) moderately severe, (3) somewhat severe, (2) a little severe, (1) not at all severe. The GASE has demonstrated moderate to strong validity, modest test-retest reliability, and good response to change over time (109).

Seizure Type

Physicians were asked to record the types of epilepsy syndrome and seizures the patient had, according to ILAE's classifications at the time those data were collected: primary generalized, absence, simple/complex partial, Benign epilepsy of childhood with Rolandic spikes (BECRS), secondarily generalized, BECRS + secondary generalized, and undetermined (110). These types were then used to create summary categories including generalized, partial, or unknown seizure types.

Seizure Freedom

At the 10-year follow-up, youth were asked "When was your last seizure?" with response options of less than 6 months ago, 6 months to less than a year ago, 1 year ago to less than 2 years ago, 2 years ago to less than 5 years ago, 5 years ago to less than 10 years ago, 10 years

ago or more, and I don't remember. Parents were also asked at the 10-year follow-up when their son's/daughter's most recent seizure was and were given the same response options as the youth. Youth responses were used if available, and parents' responses were used if the youth response was not available. This variable was dichotomized into less than 2 years ago or 2 years or more.

Medication Use

Physicians reported both the number of anti-seizure medications currently being taken by the child and the number of anti-seizure medications in total.

At the 10-year follow-up, youth were asked "Are you currently taking any medication(s) to treat epilepsy or seizures?" with response options of yes or no. If respondents answered "no", a follow-up question asked when the last time medication was taken for epilepsy or seizures. Options included: less than 6 months ago, 6 months to less than 1 year ago, 1 year to less than 2 years ago, more than 2 years ago, I have never taken medication for epilepsy or seizures, I don't remember.

Age at Diagnosis

The age at diagnosis was calculated for each participant using parent-reported date of birth variables and the date the patient was last seen by the physician. If the date was not provided by the physician, values were calculated using the child's date of birth and the date the parent completed their questionnaire.

Comorbidities

Physicians reported whether patients had behavioural problems and if so, rated the severity as severe, moderate, or mild. They also reported whether any diagnosis had been made. Physicians reported whether patients had cognitive problems and if so, rated the severity as severe, moderate, mild, or borderline. They also reported whether any diagnosis had been made. Responses were dichotomized into comorbidities present if either behavioural or cognitive

problems were present, or comorbidities absent if the patient did not have behavioural or cognitive problems.

At the 8- and 10-year follow-up, parents were asked if their child was ever diagnosed with other disorders or syndromes (developmental delay, a learning disability, attention deficit disorder or attention deficit hyperactivity disorder, Autism, pervasive developmental disorder or Asperger's syndrome, oppositional defiant disorder, conduct disorder, depression, and anxiety). Responses were dichotomized into comorbidities present if any of the diagnoses had a response of yes, or comorbidities absent if no diagnoses were reported.

Sex

Parents or guardians recorded the sex of the child as either male or female.

Attitude Towards Epilepsy

Youth's attitude towards epilepsy was measured using the Attitude Toward Epilepsy subsection of the QOLIE-AD-48 (Quality of Life in Epilepsy for Adolescents) survey given to the youth 11 to 17 years old at the 8- and 10-year follow-ups. The QOLIE-AD-48 was developed to assess health-related quality of life in adolescents with epilepsy (111). The Attitude Towards Epilepsy subsection's four questions are: "How good or bad has it been that you have epilepsy?", "How fair has it been that you have epilepsy?", "How happy or sad has it been for you to have epilepsy?" and "How bad or good have you felt it is to have epilepsy?". These questions ask how often in the past four weeks the individual has had certain attitudes and use a five-point response scale ranging from negative (1= very negative) to positive (5=very positive) attitudes. The QOLIE has demonstrated good internal construct validity, good internal consistency, and reliability with an overall Cronbach's alpha coefficient of 0.74, and a Cronbach's alpha for the attitude subscale used here of 0.83 (111).

4.2.3 Parent and family characteristics

Family Functioning (APGAR)

Family Functioning was measured using the Family APGAR questionnaire designed to assess the level of satisfaction in five areas of family relationships including adaptability, partnership, growth, affection, and resolve (112). Parents were asked to think about the five statements provided and to mark the honest answer that best describes their feelings most of the time. Response options were as follows: never, hardly, some of the time, almost always, and always. The APGAR has demonstrated validity and reliability in research and clinical settings with Cronbach's alpha measured at 0.86 (113).

Family Resources (FIRM)

The Family Inventory of Resources for Management (FIRM) is designed to assess families' accessibility of social, psychological, community, and financial resources to help manage family life or adapt to stressful events (114). Two subscales of the FIRM were used: Family Strengths: Mastery and Health (20 items), and Extended Family Support (4 items). These subscales were used as they have been found to be related to adaptation to childhood epilepsy (115). Participants were asked to read statements related to family life, then mark how much the statement described their own family situation using a scale from 0 to 3 where 0 was "not at all", 1 was "minimally", 2 was "moderately", and 3 was "very well". Cronbach's alpha was measured at 0.89 and had a significant positive correlation with family environment dimensions demonstrating good reliability and validity for the FIRM (114).

Parental Depressive Symptoms (CES-D)

The Center for Epidemiological Studies Depression Scale (CES-D) (116) was used to evaluate parents' depressive symptoms. This tool provided 20 statements to which the respondent noted how frequently they agreed with that statement in the past week, choosing from less than one day, 1 to 2 days, 3 to 4 days, or 5 to 7 days. High internal consistency, test-retest stability, concurrent validity, and construct validity were demonstrated for the CES-D (116).

Perceived Stress Scale (PSS)

Caregivers were asked about their feelings and thoughts during the month to determine their perceived stress levels. They were asked to indicate how often they felt or thought about 10 statements and were given five responses from which to choose: 0=Never, 1=Almost Never, 2=Sometimes, 3=Fairly Often, 4=Very Often. The PSS demonstrated adequate internal and test-retest reliability (117).

Socioeconomic Status (SES)

Previous studies have used numerous measures to represent socioeconomic status, including income and parental education. Primary caregivers were asked to select a category that corresponded to their yearly household income before taxes. At the 10-year follow-up, categories were as follows: less than $20,000, $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-$149,999, $150,00 or more, don't know. Caregivers recorded their education level by selecting the highest grade of school they have completed. Response options were as follows: less than 8 years, 8-12 years, completed high school, completed vocational/technical training, completed college/university, completed a master's or PhD degree.

Other Demographic Factors

Additional factors were used for the purpose of descriptive analysis but were not used in regression analyses. These factors were not described in the literature as potential contributors for more behavioural problems but were included in the descriptive analyses to provide a comprehensive picture of the families studied. Parents were asked to select a category that described their current marital status using the categories: married, widowed, divorced, separated, remarried, or never married. In addition, caregivers were asked about their current work status by selecting an option that best described their situation. In the first five timepoints, choices included: not working due to my child's health, not working for other reasons, looking for work outside the home, working full time or part time, full time homemaker, and student. The

sixth timepoint separated part-time and full-time work and did not include looking for work outside the home.

4.3 Statistical Analysis

Analyses were performed using SAS software version 9.4 for Windows (118). Descriptive analyses were performed for data collected at baseline, and the 8-year and 10-year follow-ups. Categorical variables were summarized using frequencies and proportions, while continuous variables were summarized using means and standard deviations. The outcome variable of interest, behavioural problems as measured by the YSR was analyzed for scores at the 10-year follow-up if available, otherwise scores at the 8-year follow-up were used.

Objective one (prevalence of long-term behavioural problems) was addressed using descriptive statistics. Mean estimates and 95% confidence intervals of scores for the total behavioural problems, internalizing problems, externalizing problems, and five of the eight subscales were attained. Proportions of youth who scored in the ‘borderline’ and ‘clinical’ ranges were also reported.

Objective two (factors associated with long-term behavioural problems from the final time point and at diagnosis) was addressed by bivariable and multiple regression analyses. Bivariable regression analysis was used to assess associations between long-term behavioural problems scores and each individual factor. Multiple regression analysis was then conducted to assess adjusted associations by considering child and familial variables from the bivariable analysis with $p<0.30$, intended to reduce Type II error due to small sample size, to look at individual effects of each factor while adjusting for other variables. Continuous variables were assessed with linear regression, and dichotomous and nominal variables were assessed with logistic regression.

4.4 Attrition Analysis

An attrition analysis was performed to describe any differences between the group of participants who participated in the 8-year or 10-year follow-up, specifically those who completed the YSR

at either or both time points, and the group of participants who were eligible to complete the YSR at either the 8-year or 10-year follow-up but did not. Baseline variables, including clinical (age at onset, medication use, severity of epilepsy, seizure type, comorbidities) and familial (family resources, family functioning, parental depression symptoms, income) were compared across groups. Continuous variables were compared using t-tests, while binary variables were compared using chi-square tests.

4.5 Missing Data

Complete case analysis (CCA) where only cases without missing variables are included, was used for baseline variables in objective two as the missingness of variables did not depend on the outcome (119). In addition, no auxiliary variables were necessary for the analyses of baseline variables, thus multiple imputation was not required. Values from the next time point were used if baseline values were missing in a few cases where possible. For example, if physician-reported values from baseline were missing, values reported at time two (six months) including age of onset replaced the missing data from time one (baseline). Similarly, parent-reported variables such as demographic and family characteristics were replaced with values from future time points if values remained consistent across other time points. Other variables such as severity and type of seizures were left as missing as these variables might not have remained constant between time points.

There were more missing data at the 8-year and 10-year follow-up. Although behavioural problem scores were reported at the 8-year and 10-year follow-up, some predictor variables were only collected at the 10-year follow-up. Retained individuals who were 18 years or older completed a different questionnaire than the 11 to 17 year age group, which did not include the YSR. Even if an individual had aged out of the 11 to 17 age group between the 8-year and 10-year follow-up period, characteristics only measured at the 10-year follow-up could be extracted from the 18 years and older questionnaire. Variables from the 10-year follow-up were used to calculate what the respondents' answers would have been if they had been asked at the 8-year follow-up. This allowed all variables to be estimated at the same time point, which was when the

YSR was completed. For example, when asked about their last seizure, a response of 4 years at the 10-year follow-up would have been 2 years at the 8-year follow-up.

Multiple imputation (MI) by the method of fully conditional specification (FCS) was used to handle missing values from the 8-year and 10-year variables. The FCS method is also commonly referred to as MICE, multiple imputation by chained equations, and sequential regression multivariate imputation (120). A salient feature of FCS is its ability to handle different variable types (continuous, binary, unordered categorical, and ordered categorical) because each variable is imputed using its own imputation model. Based on the assumption of data missing at random, analysis using MI was executed using three steps. First, the appropriate imputation model for each variable was defined and missing values from the original data set were independently imputed repeatedly. Next, each completed data set was analyzed and lastly, the results of the analysis in step two were used in multiple imputation calculations to determine parameters of interest. Variables from baseline were included as auxiliary variables in the imputation phase however, only variables from the 8-year and 10-year follow-up points were imputed. FCS was used as it allows for logistic regression to be used for binary and categorical variables.

Table 4.1: Measures by time of collection and missingness

Variable	Reported by	Time of Collection				Our sample (Sample to complete YSR) (N=128)
		Baseline (Eligible Baseline Subsample) (N=309)	8 years		10 years Total* (N=63)	
			Total (N=121)	Last point* (N=65)		
Behavioural Problem Scores (YSR)	Youth		121 (0 missing)	65 (0 missing)	63 (0 missing)	128 (0 missing)
Seizure type	Physician	306 (3 missing)				
Seizure severity (GASE)	Physician	298 (11 missing)				
Medication use**	Physician Youth	306 (3 missing)			60 (3 missing)	99 (29 missing)
Age at diagnosis	Calculated	309 (0 missing)				
Comorbidities (behavioural or cognitive problems)	Physician Parent	306 (3 missing)	112 (9 missing)	59 (6 missing)	60 (3 missing)	118 (10 missing)
Seizure freedom**	Youth Parent				63 (0 missing)	118 (10 missing)
Attitude towards epilepsy	Youth		117 (4 missing)	63 (2 missing)	62 (1 missing)	125 (3 missing)
Sex	Parent	308 (1 missing)				
Family Function (APGAR)	Parent	302 (7 missing)	112 (9 missing)	59 (6 missing)	60 (3 missing)	124 (4 missing)
Family Resources (FIRM)	Parent	298 (11 missing)	111 (10 missing)	58 (7 missing)	60 (3 missing)	124 (4 missing)
Parental Depression (CES-D)	Parent	299 (10 missing)	112 (9 missing)	59 (6 missing)	60 (3 missing)	124 (4 missing)
Parental Stress (PSS)**	Parent				60 (3 missing)	113 (15 missing)
Family income	Parent	287 (22 missing)	111 (10 missing)	59 (6 missing)	59 (4 missing)	117 (11 missing)
Highest education	Parent	302 (7 missing)	111 (10 missing)	59 (6 missing)	59 (4 missing)	123 (5 missing)
Work Status	Parent	301 (8 missing)	112 (9 missing)	59 (6 missing)	60 (3 missing)	124 (4 missing)
Marital Status	Parent	302 (7 missing)	112 (9 missing)	59 (6 missing)	60 (3 missing)	124 (4 missing)

* Used in our sample (N=128), ** Only taken at 10-year follow-up

Chapter 5 : Results

The study findings are presented in this chapter. Family characteristics of the sample retained are described, compared to those families who were lost to follow-up, and factors associated with long-term behavioural problems in youth with childhood-onset epilepsy are presented.

5.1 Sample Characteristics

Of the 162 youths aged 11 to 17 years who participated in the 8- or 10-year follow-up, 128 self-reported on the outcome of interest, behavioural problems using the YSR. These comprise the sample analyzed here, referred to as the subsample to complete the YSR or 'our sample'. The remaining 34 who completed sections of the follow-up questionnaire but did not complete the outcome of interest were excluded from the analyses. For 65 youths who had aged out of the 11 to 17 years age category by the 10-year follow-up or did not continue to the 10-year follow-up, YSR scores from the 8-year follow-up were analyzed. There were 56 youths who completed the YSR at both the 8-year and 10-year follow-up whose 10-year YSR scores were analyzed. An additional 3 youths became age-eligible and completed the YSR once at the 10-year follow-up, and another 4 youths were eligible to complete both the 8-year and 10-year follow-up, but only completed the 10-year follow-up, for a final sample of 128 youths with YSR scores. A study flow chart showing participants in our sample is explained in Figure 5.1.

Of our sample, 53.9% were male and were diagnosed with epilepsy between the ages of 3.7 and 11.3 years, with an average age at diagnosis of 7.1 (SD: 1.9) years. At the final long-term follow-up of the study, over 80% of youth were not currently taking medication to treat epilepsy or seizures and 75.4% had not had a seizure in the previous two years. The youth reported a more positive attitude towards epilepsy using the QOLIE-AD-48 (mean score 54.9) than reported in published normative data (mean score of 39.8) (111). QOLIE-AD-48 subscale scores are transformed to range from 0 to 100 where higher values represent better functioning. All characteristics of the youth can be seen in Table 5.1.

Parents reported over half of youth had been diagnosed with at least one comorbidity including developmental delay, a learning disability, attention deficit disorder or attention deficit hyperactivity disorder, pervasive development disorder or Asperger's syndrome, oppositional defiant disorder, conduct disorder, depression, or anxiety.

Family characteristics at the 8-year or 10-year follow-up were also analyzed. The mean of the Family APGAR score was 14.9 [5.0 to 20.0], demonstrating relatively high family functioning in our sample. Using the CES-D, 18.8% of parents reported depressive symptoms that would be considered clinically significant (≥16) with an average score of 9.0 [0.0 to 38.0]. Level of family resources was relatively high, with a sample mean FIRM score of 53.3 on this measure that ranges between 0 and 72 with higher values indicating more resources. Over half of parents recorded household income as greater than $100,000 and almost 80% of parents were working part-time or full-time. Nearly 75% of parents had completed university, college, or graduate school and over 80% were married. Perceived stress of parents had a mean score of 12.2, where the normative data for the Perceived Stress Scale has a mean of 23.67, indicating the parents did not feel as though they had high stress in their lives. The PSS normative population was composed of college students and community members, and although the authors recognize their sample is restrictive, they believe their data would not significantly differ from the general population (117). All familial characteristics of our sample are reported in Table 5.2.

At the onset of epilepsy, 14.8% of the youth had behavioural or cognitive problems, as reported by their physician. Physicians diagnosed 35.2% of the children as having generalized seizures, 63.3% had partial seizures, and 1.6% had undetermined seizures. The number of anti-seizure medications the children were taking at the first report by physicians after diagnosis ranged from zero to two, where 36.7% were not taking any medication, 59.4% were taking one medication and 3.9% were taking two anti-seizure medications.

5.1.1 Missing Data

Of the 128 youths in our sample, 8.6% and 29.7% had some missing data at baseline and at the final follow-up, respectively. Tables 5.3 and 5.4 show a breakdown of missing data, including

proportions of the sample with missing variables. For example, in Table 5.3, 91.4% of the sample had no missing values, 4.7% were only missing a value for income, 3.1% were missing seizure severity, and 0.8% were missing both parental depressive symptoms and seizure severity. The higher percentage of missing data at the final timepoint is attributable to the fact that some variables were collected for the first time at the 10-year follow-up for which not all individuals were retained. For example, the variable measuring current medication use at the 10-year follow-up had nearly a quarter of the data missing. In addition, the status of complete data entails no missing data for either the parent or child questionnaires, requiring completed questionnaires from both individuals to have been returned.

5.2 Attrition Analysis

The attrition analysis compares participants who were eligible to complete the YSR at the 8-year or 10-year follow-up who were retained until the final time point or our sample, to those who did not remain in the study for its entirety. At the study baseline, 373 families participated in the HERQULES study, 309 of which had children who were eligible to complete the YSR at long-term follow-up. Flow charts with retention rates at each time point in the HERQULES study for parents and youth can be found in Figures 5.2 and 5.3, while Table 5.5 presents results of the attrition analysis.

No evidence was found to suggest the groups differ in terms of gender, age of epilepsy onset, seizure severity, seizure type, comorbidities, use of anti-seizure medication, family functioning, parent marital status, and parent employment status at the study baseline. Parents of families who were not retained until the long-term follow-up had fewer family resources, were more likely to have depressive symptoms, and were less educated compared to the parents of our sample.

5.3 Objective 1: Prevalence of Behavioral Problems

Long-term behavioural problems are reported below both as continuous and categorical variables, by considering the mean scores compared to the normative population and by considering the proportion of individuals who scored above the ‘normal’ threshold. The mean

scores for total, internalizing, and externalizing behaviour problem scales for our sample were all similar to the normative mean of 50 (SD: 10) with values of 50.5 (SD: 10.7), 51.9 (SD: 11.9), and 49.6 (SD:9.9), respectively. Distributions of total, internalizing, and externalizing problem scores can be seen in Figures 5.4, 5.5, and 5.6, respectively. The YSR normative mean for subscales is 55, which was close to the subscale means for our sample. The only significant difference in mean values was seen for the Aggressive Behaviour subscale, where our sample mean was lower than the normative mean at 53.7. Additional details of the YSR mean scores are found in Tables 5.6.

The proportions above the 'normal' threshold in our sample were higher than those of the normative population for the main scales of total, internalizing, and externalizing behavioural problems. YSR scores from our sample indicated that 21.9% recorded total behavioural problem scores above the threshold of 'normal'. The scores for internalizing problems were above 'normal' for 25%, while the scores for externalizing problems were above 'normal' for 17.2% of individuals. Above 'normal' consists of 'borderline' and 'clinical' scores. The 'normal' category for total, internalizing, and externalizing problems contain scores below the 84th percentile of normative scores, the 'borderline' category represents scores between the 84th and 90th percentile, and the 'clinical' category is for scores in the 90th percentile. The 'normal' categories for subscale scores contain scores below the 93rd percentile of the YSR normative sample, where the 'clinical' range represents above the 97th percentile. The anxiety/depressed, somatic complaints, social problems, thought problems, and aggressive behaviour subscale categorical scores did not significantly differ from the normative sample. When proportions of scoring categories were examined, no statistical differences were seen between our sample and the normative sample. Additional details of the YSR score categories are found in Table 5.7.

5.4 Objective 2

5.4.1 Objective 2A: Baseline Characteristics and Long-term Behavioural Problems

To address this objective, baseline characteristics were regarded as predictor variables while total, internalizing, and externalizing problem scores at the long-term follow-up were regarded separately as outcome variables. We pre-specified $p<0.30$ as the criterion to screen predictors in

the bivariate regression analyses, followed by using $p<0.05$ as the criterion in the multivariable analyses. For total behavioural problem scores, the bivariate analysis selected the type of seizure ($p=0.25$), anti-seizure medication ($p=0.13$), family resources ($p=0.08$), family functioning ($p=0.05$), and parent's level of education ($p=0.22$). For internalizing behavioural problem scores, the bivariate analysis resulted in no predictors. For externalizing behavioural problem scores, the bivariate analysis yielded gender($p=0.25$), type of seizure ($p=0.03$), seizure severity ($p=0.23$), family resources ($p=0.11$), and family functioning ($p=0.04$) as potential predictors. The multivariable analyses showed that no baseline characteristics were significantly associated with long-term total, internalizing, or externalizing problem scores as no p-values were less than 0.05. Detailed results are shown in Tables 5.8 and 5.9 for the bivariate and multivariable analyses, respectively.

5.4.2 Objective 2B: Current Characteristics and Long-Term Behavioural Problems

To address this objective, multiple imputation was used to handle nearly one third of the cohort where participants had missing data on at least one variable. For each analysis, 30 imputation replications were performed to match the proportion of cases with missing variables. The results showed that only attitude towards epilepsy at the long-term follow-up was significantly associated with total, internalizing, and externalizing behavioural problems measured at the same time. An association was observed between length of time since last seizure and internalizing behavioural problems. Detailed results are shown in Table 5.10. No other characteristics were significantly associated with total, internalizing, or externalizing behavioural problems.

Figure 5.1: Study flow chart for youth who completed YSR (our sample)

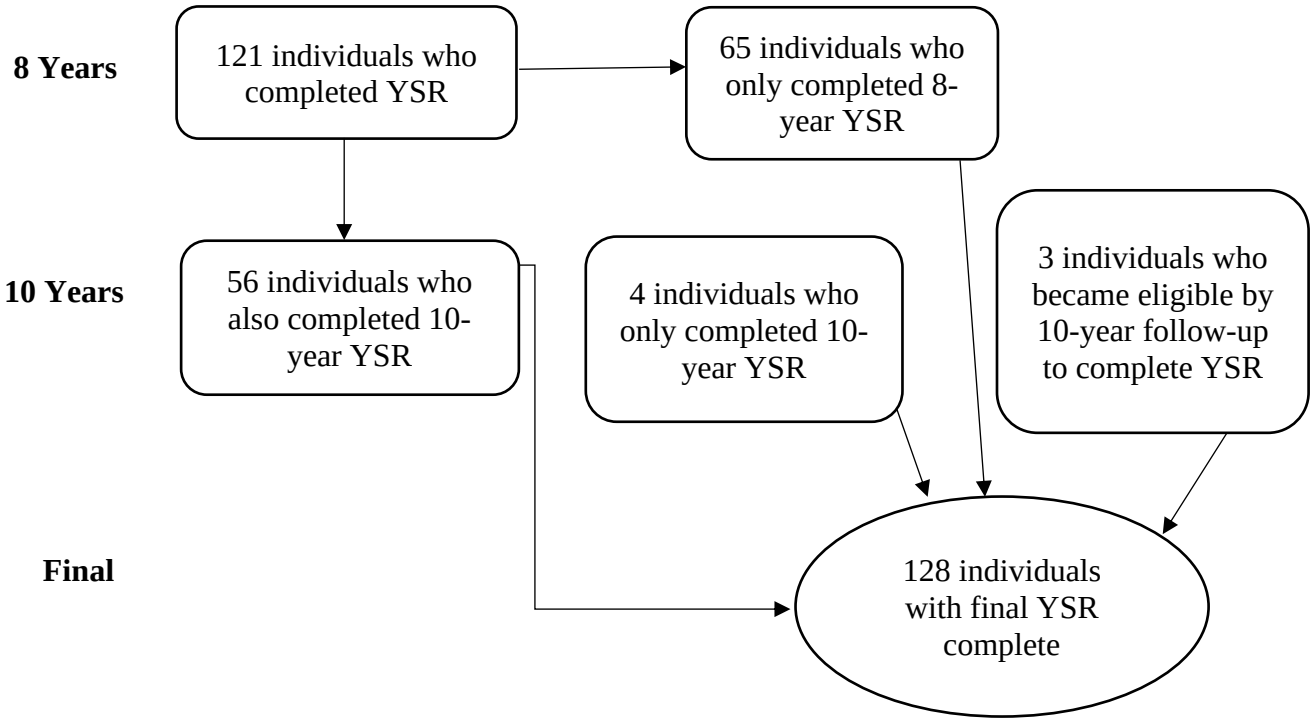
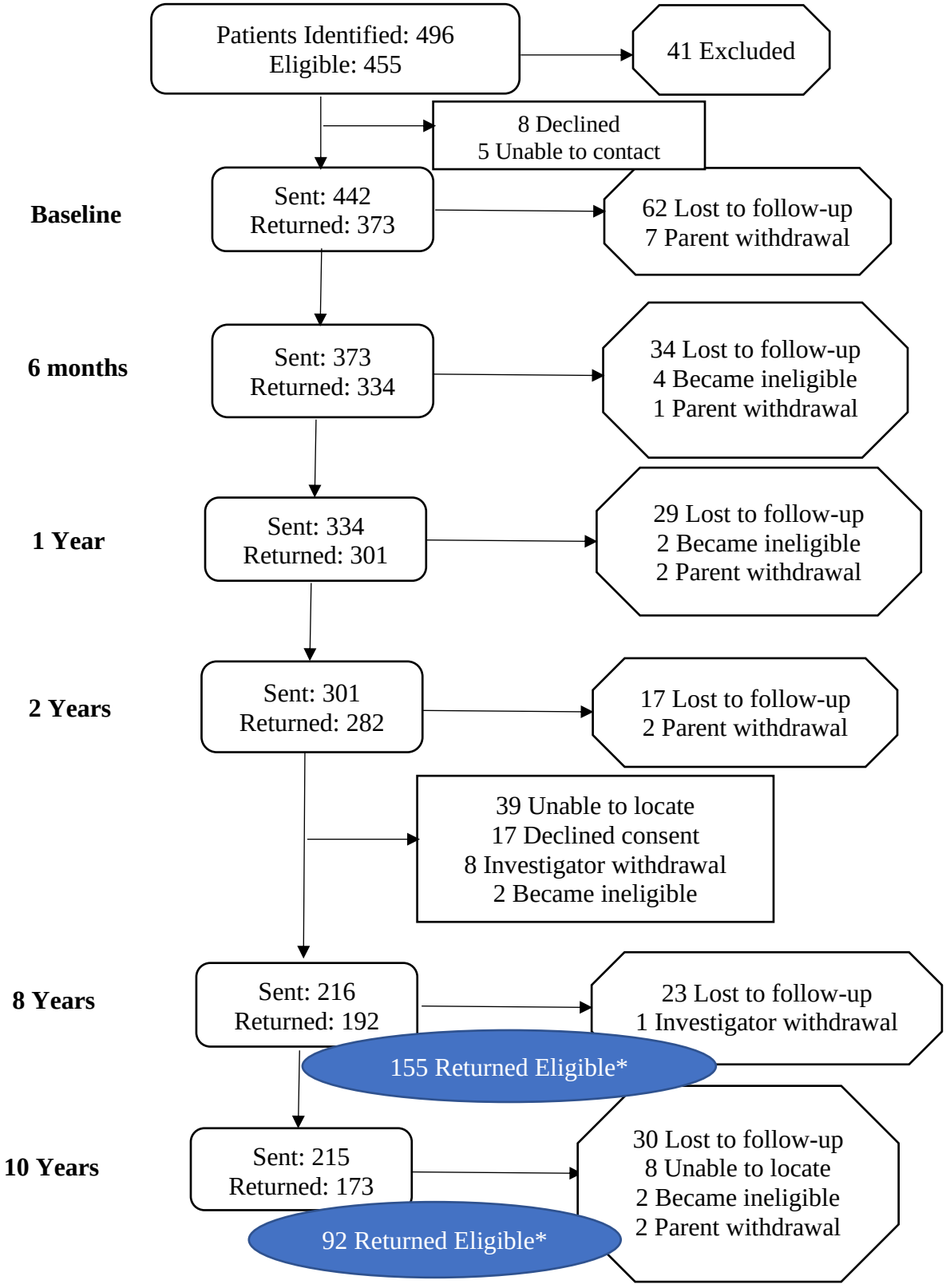
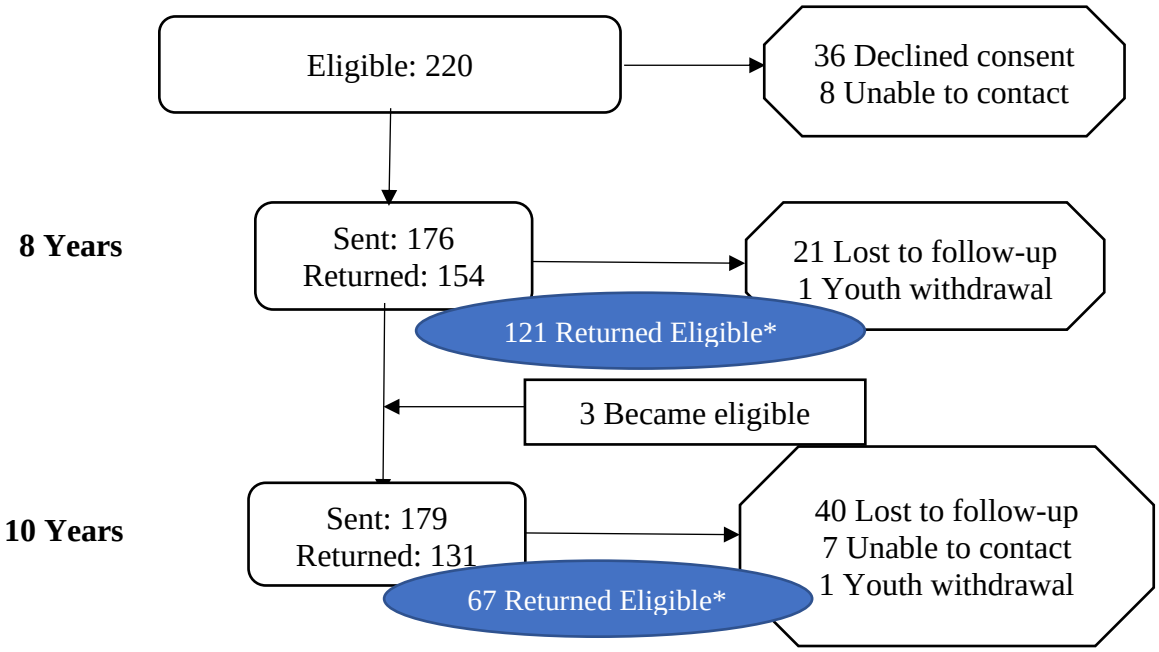


Figure 5.2: HERQULES parent retention flow chart



*Returned Eligible are parents of youth eligible to complete the YSR (<18 years of age)

Figure 5.3: HERQULES youth and young adult retention flow chart



*Where Returned Eligible are youth who were eligible to complete the YSR (<18 years of age)

Figure 5.4: Distribution of total behavioural problem scores

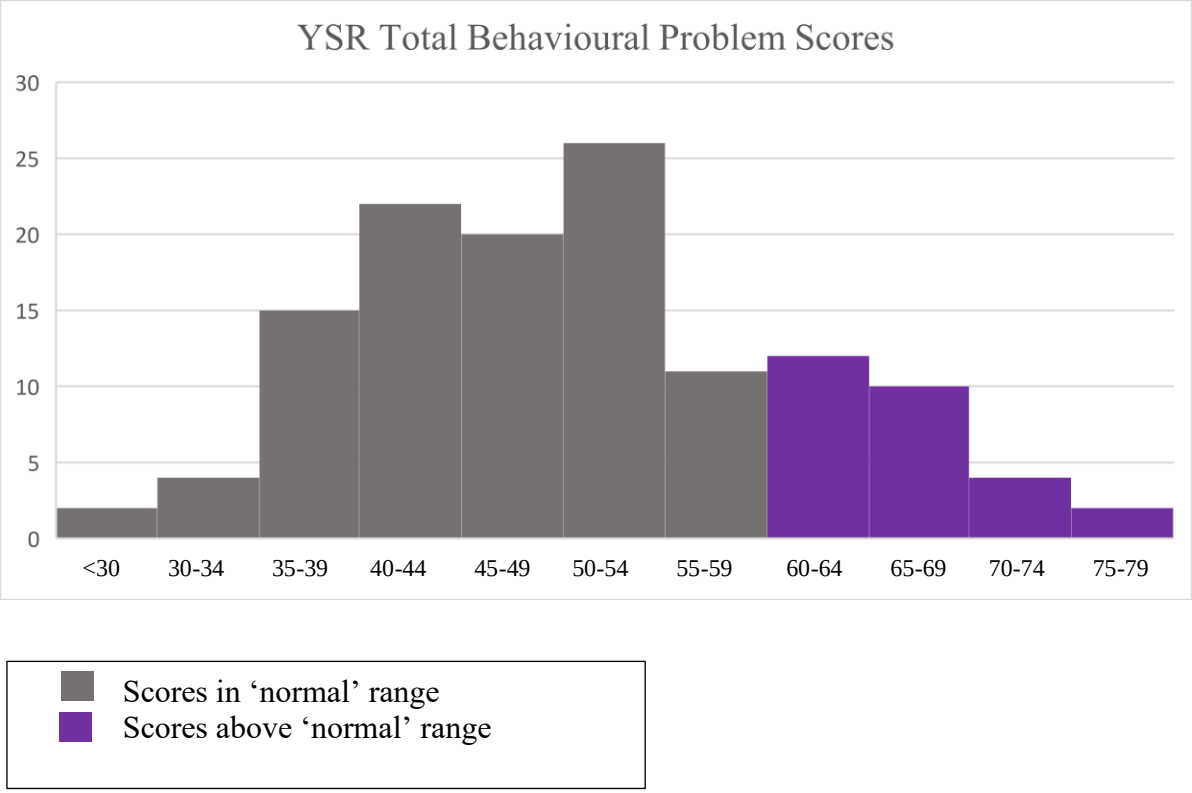


Figure 5.5: Distribution of internalizing behavioural problem scores

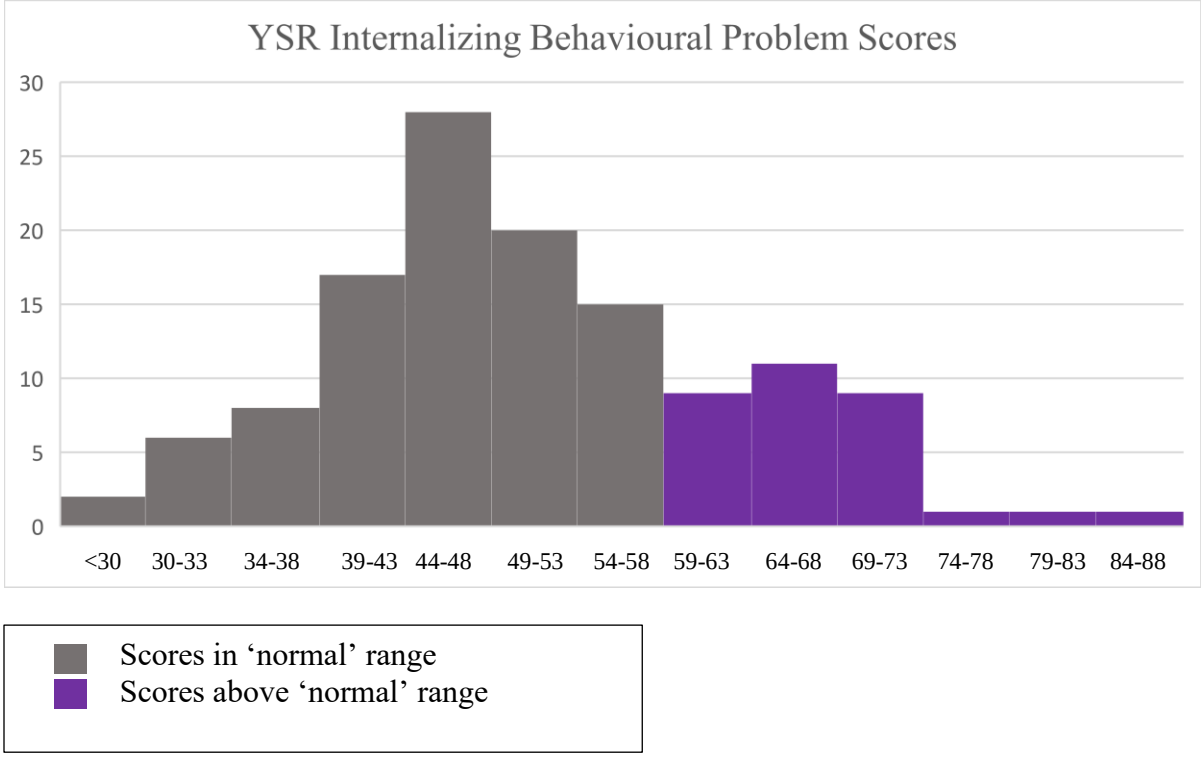


Figure 5.6: Distribution of externalizing behavioural problem scores

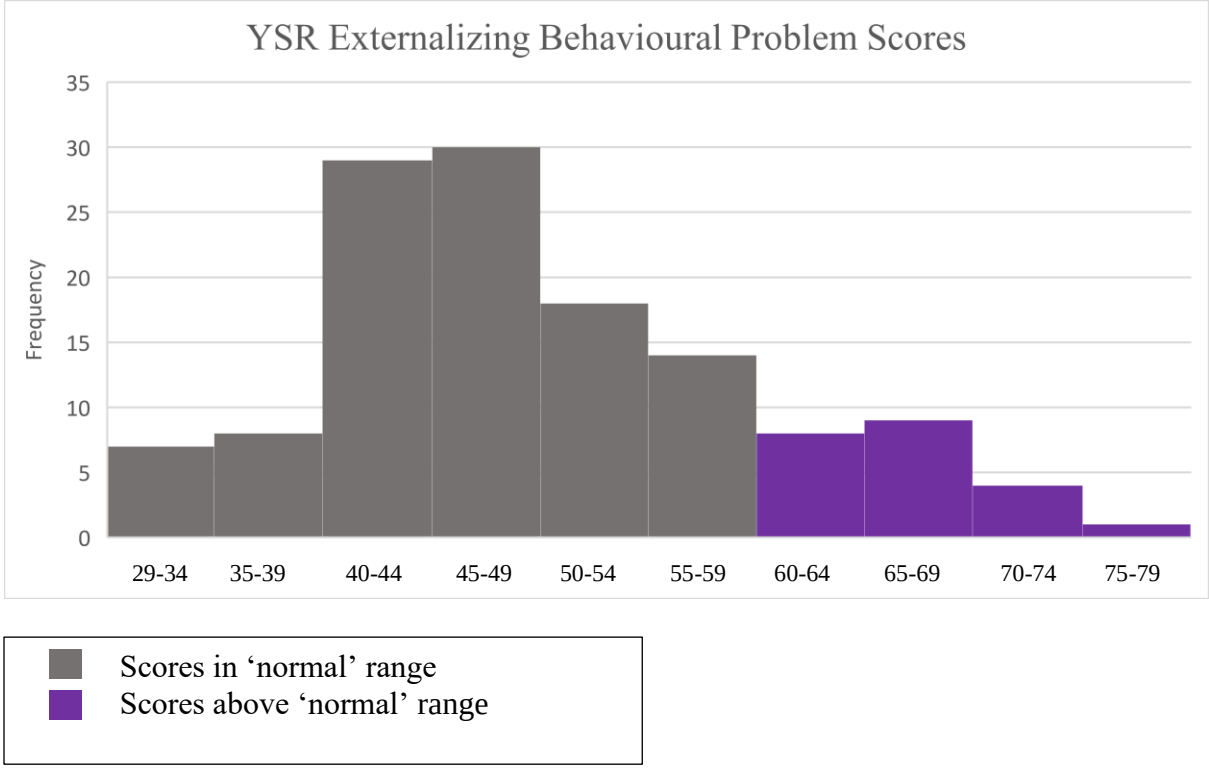


Table 5.1: Youth characteristics from our sample at 10-year follow-up (n=128)

Attitude towards epilepsy: mean (SD) [range]	54.9 (22.7) [0.0, 100.0]
Gender: Frequency (%)	
Male	69 (53.9)
Female	59 (46.1)
Comorbidities: Frequency (%)	
Present	68 (55.3)
Absent	55 (44.7)
Last Seizure: Frequency (%)	
< 2 years ago	19 (16.1)
2+ years ago	89 (75.4)
Don't know	10 (8.5)
Medication Use to Treat Epilepsy or Seizures*: Frequency (%)	
Currently taking medication	19 (19.2)
Not currently taking medication	80 (80.8)

*23% missing data

Table 5.2: Family characteristics from our sample at 10-year follow-up (n=128)

Family Functioning: mean (SD) [range]	14.9 (3.9) [5.0, 20.0]
Family Resources: mean (SD) [range]	53.3 (10.6) [26.0, 72.0]
Parental Depressive Symptoms: mean (SD) [range]	9.0 (8.2) [0.0, 38.0]
Parental Perceived Stress: mean (SD) [range] *	12.2 (7.0) [0, 33]
Household Income: Frequency (%)	
<$10,000 to 39,999	14 (11.6)
$40,000 to 69,999	16 (13.2)
$ 70,000 to 99,999	22 (18.2)
$100,000 +	69 (57.0)
Parent Highest Level of Education: Frequency (%)	
High school or less	16 (13.0)
Post-secondary	107 (87.0)
Parent Employment Status: Frequency (%)	
Not working	27 (21.8)
Full-time or part-time work	97 (78.2)
Parent Marital Status: Frequency (%)	
Married	100 (80.7)
Not married	24 (19.3)

*11.7% missing data

Table 5.3: Missing data patterns of our sample at baseline

Variable	Proportions of Our Sample with Missing Values			
	Group A **(Complete Cases)** **91.4%** (117 of 128)	Group B **4.7%** (6 of 128)	Group C **3.1%** (4 of 128)	Group D **0.8%** (1 of 128)
Gender	X	X	X	X
Parental depressive symptoms	X	X	X	Missing
Family functioning	X	X	X	X
Family resources	X	X	X	X
Income	X	Missing	X	X
Parental employment status	X	X	X	X
Parental education	X	X	X	X
Marital status	X	X	X	X
Seizure type	X	X	X	X
Seizure severity	X	X	Missing	Missing
Anti-seizure medication	X	X	X	X
Age of onset	X	X	X	X
Comorbidities	X	X	X	X

X = variable had value completed
Missing = variable had not been completed (missing value)

Table 5.4: Missing data patterns of our sample at 10-year follow-up

Variable	Proportions of Our Sample with missing values										
	Group A **(Complete cases) 70.3%** (90 of 128)	Group B **14.1%** (18 of 128)	Group C **4.7%** (6 of 128)	Group D **2.3%** (3 of 128)	Group E **2.3%** (3 of 128)	Group F **2.3%** (3 of 128)	Group G **0.8%** (1 of 128)	Group H **0.8%** (1 of 128)	Group I **0.8%** (1 of 128)	Group J **0.8%** (1 of 128)	Group K **0.8%** (1 of 128)
Attitude towards epilepsy	X	X	X	X	X	Missing	X	X	X	X	X
Family functioning	X	X	X	X	Missing	X	X	X	X	X	Missing
Family resources	X	X	X	X	Missing	X	X	X	X	X	Missing
Parental depressive symptoms	X	X	X	X	Missing	X	X	X	X	X	Missing
Parental stress	X	X	Missing	Missing	Missing	X	X	X	Missing	Missing	Missing
Income	X	X	X	X	Missing	X	Missing	Missing	X	Missing	Missing
Parental education	X	X	X	X	Missing	X	X	Missing	X	X	Missing
Comorbidities	X	X	X	X	Missing	X	X	X	Missing	X	Missing
Last seizure	X	X	Missing	X	Missing	X	X	X	Missing	X	X
Medication	X	Missing	Missing	X	Missing	X	Missing	X	Missing	X	X

X= variable had value completed (not missing)
Missing= variable had not been completed (missing value)

Table 5.5: Attrition analysis comparing retained and lost to follow-up groups

	Lost to follow-up (under 18 at follow-up) N=181	Completed follow-up (Our Sample) N=128	p (t-test) or p (chi-square)
Gender	N=180	N=128	0.70
Male	93 (51.7%)	69 (53.9%)	
Female	87 (48.3%)	59 (46.1%)	
Age of Onset (years)	N=181 7.08 (SD 1.90)	N=128 7.15 (SD 1.89)	0.74
Type of Seizure	N=181	N=128	0.92
Generalized	62 (34.3%)	45 (35.2%)	
Partial	117 (64.6%)	81 (63.3%)	
Unknown	2 (1.1%)	2 (1.6%)	
Seizure Severity (GASE scale)	N=179 2.58 (SD 1.21)	N=123 2.49 (SD 1.05)	0.51
Comorbidities (Cognitive or Behaviour)	N=181	N=128	0.09
No	140 (77.4%)	109 (85.2%)	
Yes	41 (22.7%)	19 (14.8%)	
Anti-Seizure Medication Use	N=181	N=128	0.83
0	65 (35.9%)	47 (36.7%)	
1	111 (61.3%)	76 (59.4%)	
2	5 (2.8%)	5 (3.9%)	
Family Resources (FIRM scale)	N=173 50.79 (SD 10.86)	N=128 53.30 (SD 10.59)	0.05
Family Functioning (Family APGAR scale)	N=176 13.94 (SD 3.84)	N=128 14.54 (SD 3.88)	0.18
Parental Depressive Symptoms	N=174 13.70 (9.52)	N=127 11.48 (SD 8.50)	0.04
Parent's marital status	N=176	N=128	0.25
Married	144 (81.8%)	111 (86.7%)	
Not married	32 (18.2%)	17 (13.3%)	
Parent's highest level of education	N=176	N=128	0.05
High School or less	58 (33.0%)	29 (22.7%)	
Post-Secondary Education	118 (67.1%)	99 (77.3%)	
Parent's employment status	N=176	N=128	0.80
Working full- or part-time	122 (69.3%)	87 (68%)	
Not working	54 (30.7%)	41 (32.0%)	
Family Income	N=165	N=122	0.12
<$10,000 to 39,999	32 (19.4%)	13 (10.7%)	
$40,000 to 69,999	55 (33.3%)	37 (30.3%)	
$ 70,000 to 99,999	40 (24.2%)	33 (27.1%)	
$100,000 +	38 (23.0%)	39 (32.0%)	

Table 5.6: Youth Self Report (YSR) mean results at 8-year or 10-year follow-up compared to YSR normative population

Score Group	Our Sample Mean (SD) [range] (n=128)	Normative mean	p-value (from one-sample t-test)
YSR Total Problems	50.5 (10.7) [26, 75]	50	0.60
YSR Internalizing Problems	51.9 (11.9) [27, 88]	50	0.08
YSR Externalizing Problems	49.6 (9.9) [29, 77]	50	0.62
Anxiety/Depression	55.0 (7.4) [50, 92]	55	0.96
Somatic Complaints	55.9 (8.7) [50, 93]	55	0.25
Social Problems	55.3 (7.0) [50, 75]	55	0.68
Thought Problems	54.1 (5.8) [50, 73]	55	0.09
Aggressive Behaviour	53.7 (6.1) [50, 75]	55	0.02

Table 5.7: Youth Self Report (YSR) 'above normal' scores at 8-year or 10-year follow-up compared to YSR normative population

Score Group	Our Sample Groups: Frequency (%)	Normative "Above Normal" proportion	p-value (from Chi-squared test)
YSR Total Problems	Above Normal: 28 (21.9%) Normal 100 (78.1) Borderline 10 (7.8) Clinical 18 (14.1)	16%	p=0.29
YSR Internalizing Problems	Above Normal: 32 (25%) Normal 96 (75.0) Borderline 7 (5.5) Clinical 25 (19.5)	16%	p=0.11
YSR Externalizing Problems	Above Normal: 22 (17.2%) Normal 106 (82.8) Borderline 6 (4.7) Clinical 16 (12.5)	16%	p=0.82
Anxiety/Depression	Above Normal: 18 (14.1%) Normal 110 (85.9) Borderline 9 (7.0) Clinical 9 (7.0)	7%	p=0.10
Somatic Complaints	Above Normal: 17 (13.3%) Normal 111 (86.7) Borderline 9 (7.0) Clinical 8 (6.3)	7%	p=0.14
Social Problems	Above Normal: 17 (13.3%) Normal 111 (86.7) Borderline 7 (5.5) Clinical 10 (7.8)	7%	p=0.14
Thought Problems	Above Normal: 11 (8.6%) Normal 117 (91.4) Borderline 9 (7.0) Clinical 2 (1.6)	7%	p=0.67
Aggressive Behaviour	Above Normal: 13 (10.2%) Normal 115 (89.8) Borderline 9 (7.0) Clinical 4 (3.1)	7%	p=0.42

Table 5.8: Bivariate regression analysis for each baseline variable and outcome

	Total Problems (Parameter Estimates)	Internalizing Problems (Parameter Estimate)	Externalizing Problems (Parameter Estimate)
Gender	-0.17 (p=0.93)	-0.11 (p=0.96)	-2.02 (p=0.25)
Age of Onset	-0.14 (p=0.77)	-0.13 (p=0.82)	0.15 (p=0.75)
Type of Seizure	2.23 (p=0.25)	1.26 (p=0.56)	3.85 (p=0.03)
Seizure Severity	-0.28 (p=0.76)	0.17 (p=0.87)	-1.01 (p=0.23)
Comorbidities	1.87 (p=0.52)	-0.36 (p=0.91)	1.18 (p=0.65)
Anti-Seizure Medication	2.60 (p=0.13)	1.21 (p=0.53)	0.70 (p=0.66)
Family Resources	-0.16 (p=0.08)	-0.05 (p=0.62)	-0.13 (p=0.11)
Family Functioning	-0.50 (p=0.05)	-0.24 (p=0.39)	-0.46 (p=0.04)
Parental Depressive Symptoms	0.09 (p=0.42)	0.07 (p=0.59)	0.03 (p=0.74)
Parent's Highest Level of Education	-2.94 (p=0.22)	0.92 (p=0.73)	-2.02 (p=0.35)
Family Income	-0.61 (p=0.52)	-0.35 (p=0.74)	-0.40 (p=0.64)

Table 5.9: Multivariable regression analysis for baseline variables and each outcome (using results from bivariate analysis with p<0.30)

Variable	Total Problems (Parameter Estimates)	Internalizing Problems (Parameter Estimates)	Externalizing Problems (Parameter Estimates)
Gender (ref=2)	Not included in analysis	Not included in analysis	2.29 (p=0.17)
Type of Seizure (ref=gen) Partial Unknown	 2.01 (p=0.29) 6.08 (p=0.41)	Not included in analysis	 3.32 (p=0.06) 3.64 (p=0.69)
Seizure Severity	Not included in analysis	Not included in analysis	-1.29 (p=0.11)
Anti-Seizure Medication	2.27 (p=0.18)	Not included in analysis	Not included in analysis
Family Resources (FIRM)	-0.09 (p=0.42)	Not included in analysis	-0.02 (p=0.86)
Family Functioning (APGAR)	-0.24 (p=0.45)	Not included in analysis	-0.53 (p=0.06)
Parent's Highest Level of Education	-3.22 (p=0.15)	Not included in analysis	Not included in analysis

Table 5.10: Multiple imputation analyses for 8-year or 10-year follow-up variables and each outcome

Variable	Total Problems	Internalizing Problems	Externalizing Problems
Attitude Towards Epilepsy	-0.10 (p=0.01)	-0.10 (p=0.04)	-0.12 (p<0.01)
Parental Depressive Symptoms	0.01 (p=0.98)	0.17 (p=0.45)	-0.17 (p=0.39)
Family Functioning (APGAR)	0.07 (p=0.83)	-0.03 (p=0.93)	0.37 (p=0.20)
Family Resources (FIRM)	-0.12 (p=0.37)	0.03 (p=0.85)	-0.23 (p=0.053)
Parental Stress	0.05 (p=0.82)	0.04 (p=0.88)	0.12 (p=0.60)
Family Income (ref=<$39,999)			
$40,000 to 69,999	-2.67 (p=0.48)	-0.23 (p=0.96)	-3.64 (p=0.30)
$ 70,000 to 99,999	-3.15 (p=0.40)	1.63 (p=0.71)	-6.27 (p=0.07)
$100,000 +	-2.31 (p=0.47)	2.07 (p=0.58)	-2.85 (p=0.35)
Education (ref = High School or less)	-3.08 (p=0.29)	-2.35 (p=0.47)	-2.25 (p=0.41)
Comorbidities (ref=No)	2.60 (p=0.16)	2.65 (p=0.21)	0.65 (p=0.71)
Last seizure (ref=less than 2 year)			
2+ years ago	-4.09 (p=0.30)	-9.54 (p=0.03)	0.58 (p=0.86)
Don’t remember	0.46 (p=0.92)	-4.93 (p=0.33)	0.08 (p=0.98)
Medication (ref=currently taking)	0.97 (p=0.80)	4.41 (p=0.31)	-0.42 (p=0.90)

Chapter 6 : Discussion

This chapter provides a summary of the results and discusses the strengths and limitations of this study. The implications of this study and future research recommendations are also suggested.

6.1 Summary of Results

The aims of the thesis were to assess the prevalence of long-term behavioural problems in youth with childhood-onset epilepsy and to explore associations between long-term behavioural problems and child and family factors. Associations between epilepsy-related, child, and family factors from the time of diagnosis and behavioural problems measured approximately 10 years after epilepsy-onset were examined. Additionally, associations between characteristics measured approximately 10 years after diagnosis and long-term behavioural problems were examined.

6.1.1 Prevalence of long-term behavioural problems

Previous studies have demonstrated elevated behavioural problems in children with epilepsy, but whether such problems remain an issue in the long-term is unclear. The first objective of this thesis was to assess the prevalence of behavioural problems approximately 10-years after the diagnosis of childhood-onset epilepsy. The prevalence of total, internalizing, and externalizing behavioural problems was 21.9%, 25.0%, and 17.2% respectively, where behavioural problems were measured using scores above the 'normal' threshold of the YSR. According to the YSR handbook, the normal category contains scores below the 84th percentile, indicating that approximately 16% of their normative US population sample fall in the above normal (borderline or clinical) range. The most recent normative US population was composed of youth from the general population in 1999 and 2000 using probability sampling. Although the prevalence for total, internalizing, and externalizing behavioural problems found in our study demonstrated proportions larger than the normative population, the differences were not significant for any scales. For subscales, the range of 'normal' scores for the anxiety/depression, somatic complaints, social problems, thought problems, and aggressive behaviour subscales includes values less than the 93rd percentile of the YSR normative data, indicating 7% of the normative

sample is in the borderline or clinical categories. There was 14% of scores above normal in the anxiety/depression subscale for our sample compared to the normative sample. Although the proportion of our sample with borderline or clinical scores for the anxiety/depression subscale was more than the normative sample, the difference was not statistically different at the 5% significance level, perhaps due partially to the size of our sample. All other proportions of above normal scores for subscales did not differ from the normative sample.

Some studies have found elevated rates of attention problems in children with epilepsy. Even in youth who were seizure-free, a significant difference was found in the proportion of abnormal scores for attention problems measured 8 years after epilepsy surgery (54). Unfortunately, attention problems could not be calculated for this thesis. There were too many differences in the attention problems subscale in the older version of the YSR completed by the youth and the newer version used for scoring that could have misclassified the significance of problems.

In addition to looking at the proportions of abnormal scores, mean scores of behavioural problems were compared to the YSR normative data. Mean scores of our sample were all similar to the means of the normative population, where normative means were 50 for the total, internalizing, and externalizing problems and 55 for the five subscales. A significant difference was found in the aggressive behaviour mean score of our sample, which had a value of 53.7; significantly lower than that of the normative population, indicating our sample had less aggressive behaviour. A consistent finding, a lower mean score for the aggressive behaviour problem subscale, was found in a long-term study of children who had epilepsy surgery approximately 8-years prior to behavioural problem measurements. Although youth who were seizure-free had a mean value of 53.3 for the aggressive behaviour subscale, they also had lower mean scores for many subscales compared to normative data (54). It is not clear why a significant difference was seen only for the aggressive behaviour subscale in our sample, while the externalizing behavioural problem score was not significantly different from the normative mean.

Overall, long-term behavioural problems of our sample were not significantly different than mean scores of the YSR normative population. Although previous studies have demonstrated

children with new-onset epilepsy may have more behavioural problems when diagnosed, these promising results of average behavioural problem levels in youth with childhood-onset epilepsy indicate behavioural problems do not remain higher than in the general population.

6.1.2 Associations between baseline characteristics and long-term behavioural problems

The bivariate analyses between each baseline variable and long-term behavioural problem scores indicated potential associations ($p<0.30$) of total behavioural problems with type of seizure, anti-seizure medication, family resources, family functioning, and parent's level of education; of externalizing behavioural problems with sex, type of seizure, seizure severity, family resources, and family functioning; while no potential associations were observed for internalizing behavioural problems. When the multivariable analyses were performed using the significant variables achieving $p<0.30$ in the bivariate analyses, no variables were significantly associated with total, internalizing, or externalizing behavioural problem scores.

It was rather surprising to find no baseline variables associated with long-term behavioural problems. The lack of association between behavioural problems and sex could be influenced by the YSR assessment already taking sex into account. The YSR takes sex into account when calculating scores, where females have slightly higher internalizing raw scores corresponding to the same scores in males, while males have slightly higher externalizing raw scores that correspond to equivalent scores in females. Epilepsy-related variables have been indicative of behavioural problems in past studies, but not seen here. It is possible that certain seizure variables, such as the number of anti-seizure medications, seizure severity, and seizure types changed after the initial visit. Numerous studies have found relationships between family factors and short-term behavioural problems. Those results were not found in our study with long-term behavioural problems, perhaps as parents have adapted to their child's epilepsy or behavioural problems. Habitual parenting was highlighted as a factor towards behavioural problems in children with epilepsy, where increased habitual parenting after a diagnosis with epilepsy was found in children with less behavioural problems. As our study examined behavioural problems after a decade, it is likely that parenting behaviours would have changed over time, introducing a new style of parenting that works better for their family.

These results indicate that no clinical, familial, or child factors from diagnosis were significantly related to behavioural problems measured 10-years post-diagnosis. Unfortunately, we were unable to detect any clear indications at the time of diagnosis to predict more long-term behavioural problems.

6.1.3 Associations between current characteristics and long-term behavioural problems

Current factors and long-term behavioural problems were analyzed using MI, and one variable was associated with all behavioural problem scales. Attitude towards epilepsy was significantly associated with total, internalizing, and externalizing behavioural problems. This relationship indicated that the more positive the youth's attitude towards epilepsy, the less behavioural problems were seen or that the youth with fewer behavioural problems had better attitudes towards epilepsy. Specifically, for every point towards a more positive attitude towards epilepsy, a reduction of 0.10, 0.10, and 0.12 points, was seen in the total, internalizing, and externalizing problem scale scores, respectively. These results were also seen in other studies, as children with negative attitudes are more likely to have fewer coping behaviours (85). In addition, another study's results suggested attitude towards epilepsy partially mediated some negative health outcomes, including behavioural problems that were associated with stigma (86). If attitude towards epilepsy is reflective of the impact that childhood-onset epilepsy has on youth, the youth in our sample appear to have not been majorly impacted by their epilepsy diagnosis.

A significant association was also observed between seizure control and behavioural problems, where individuals who had their last seizure more than two years ago had less internalizing behavioural problems compared to individuals who had a seizure more recently. This was also found when measuring long-term anxiety and depression in youth with pediatric-onset epilepsy, where more problems were seen in patients who were still having seizures, regardless of surgery status (121). Although seizure freedom has previously been found to be associated with fewer behavioural problems, this relationship was not found in the current thesis for total or externalizing behavioural problems, potentially due to the quality of our measure of seizure freedom. While our data were composed of results from the 8-year and 10-year follow-up,

seizure freedom was reported by youth and parents retrospectively only at the 10-year follow-up, potentially introducing some error into the estimate of length of time since the youth's last seizure. It was necessary to categorize the length of time since the last seizure variable as less than or more than two years ago, which in turn, made it not possible to have more accurate data on whether the youth were currently having seizures. Even if more precise times were available, there were only 19 individuals who had seizures in the previous two years, so further classification by time would have produced a further problem of even smaller cell sizes. The association between length of time since last seizure and internalizing behavioural problems could represent anxiety associated with the possibility of another seizure happening, however the lack of association with total and externalizing behavioural problems could indicate the youth had developed other coping mechanisms for living with epilepsy rather than acting out. It is also possible that our sample of older youth had more time to adapt to life with seizures and were generally less affected by them.

It is not surprising that there were more current characteristics associated with behavioural problems compared to characteristics from baseline, as current characteristics were measured at the same time as behavioural problems. It is reasonable that proximal factors are likely to be more relevant than distal ones. Our results showed significant associations between seizure control and internalizing behavioural problems as well as between attitude towards epilepsy and total, internalizing, and externalizing behavioural problems. Perhaps if all children, with and without epilepsy, were better educated about epilepsy and seizures, the stigma associated with epilepsy and the attitude of children with epilepsy could improve, which in turn could lessen behavioural problems.

6.2 Strengths

Strengths of this thesis include the combination of demographic, clinical, and family factors, the length of prospective follow-up in the HERQULES study, and the validity of instruments used. Previous studies that look at behavioural problems in children with epilepsy tended to consider either demographic, clinical, or family characteristics, but rarely explored multiple domains. Another strength of this study is the follow-up period of ten years. It is rare for studies that look

at behavioural problems to have results from beyond a few years, let alone a decade. This allows for a broader view of childhood rather than only considering the time directly after the child's onset of epilepsy. Most factors considered in this study were assessed using validated measures, including the outcome measured by the Achenbach system of tests, which has been used in many studies with children with epilepsy. In addition, this study recruited patients from across Canada, a large country which varies in demographics, cultures, and rurality, broadening the range of applicability of study results.

6.3 Limitations

A key limitation of this study is that the primary outcome of behavioural problems as measured by the Achenbach System of Empirically Based Assessment (ASEBA) was only measured during the long-term follow-up rather than throughout the study. It is ideal when using ASEBA that multiple informants complete assessments to provide a more comprehensive picture of behavioural problems across different aspects of children's lives. This study collected youth self-reports only; thus, behavioural problems were measured solely from the child's perspective. Another limitation with using the YSR was the age restriction. The YSR was designed to be completed by youth aged 11 to 17, restricting the sample size of the outcome variable as any young adults retained until the 8-year or 10-year follow-up period were ineligible due to their older age to complete the YSR. Just like behavioural problems were only assessed at the final follow-up, some potential predictors were also only collected at one time. Potential predictors that were solely collected at the 10-year follow-up included length of time since the youth's last seizure and when the youth last took medication for seizures. Many of the respondents who were only eligible to complete the YSR at the 8-year follow-up also completed all other components of the questionnaire for young adults 18 years or older at the 10-year follow-up. This allowed use of some data collected at 10-years to act as proxy measures for what those values would have been at the 8-year follow-up. For example, youth report at the 10-year follow-up regarding length of time since last seizure could be used to calculate what the value would be if provided at the 8-year follow-up. A challenge for many studies that explore epilepsy in children is the resolution of seizures, and youth without seizures discontinuing regular follow-up from a

physician. This makes it more difficult to keep seizure-related information up to date, such as when medication was last taken.

Another potential limitation could be the differences found in families retained and those who were not retained until the 8-year or 10-year time point. Those who were not retained had fewer family resources, were more likely to have depressive symptoms, and were less educated. As these factors have been previously associated with more behavioural problems, it is possible that our study results might have had slightly more elevated long-term behavioural problems if more families had been retained.

6.4 Recommendations for Future Research

Future prospective research on long-term behavioural problems in children with epilepsy should consider measuring behavioural problems beginning at baseline to see if there are changes over time, in addition to measuring behavioural problems from the perspective of the child as well as the parent. Studies with longer follow-up periods would be beneficial, as many studies only follow children with epilepsy for a few years, due largely to limitations of resources and difficulty of tracking participants. Specifically looking into adulthood and whether behavioural problems continued could allow further interventions to be put in place sooner after an epilepsy diagnosis. Other psychological factors such as use of resources, educational programs, or psychological counselling could be measured in addition to family, clinical, and child characteristics.

6.5 Implications and Conclusions

This thesis found no statistical evidence to suggest that the prevalence of behavioural problems 10-years after childhood-onset epilepsy was different from the prevalence of behavioural problems in the YSR normative population. Evidence was found to suggest that attitude towards epilepsy and seizure control at long-term follow-up were the only characteristics from baseline or follow-up associated with long-term behavioural problems. Additional studies exploring long-term changes in behavioural problems prospectively over time in children with epilepsy would

be beneficial to explore if behavioural improvements occur. It would also allow researchers and clinicians to better pinpoint where the most behavioural problems are in childhood and its associated variables at different developmental stages. Identifying individuals with poorer attitude towards epilepsy, even a decade after their diagnosis with epilepsy, could assist in targeted interventions to reduce behavioural problems. This thesis provides some evidence that long-term behavioural problems in youth with childhood-onset epilepsy are not significantly different than those in the general population, which could be promising to families and children with epilepsy.

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Appendices

Appendix A: Physician Form

Patient's Date of Birth (dd/mm/yy): _____ Site #:_____

Please answer the following questions based on information from this patient's most recent visit and return upon completion

1. Date of patient's last visit (dd/mm/yy): _____ or Date of Telephone F/U (dd/mm/yy)_____

2. Date form completed (dd/mm/yy): _____

If information for 3 thru 7 is unchanged from baseline (diagnosis) visit, please check here and proceed to 8. ☐

3. Seizure type(s): 1) _____ 2)_____
   3)_____ 4)_____
4. Epilepsy syndrome: _____
5. Convulsive status epilepticus:
   ☐ No
   ☐ Yes
6. Exclusive nocturnal seizures:
   ☐ No
   ☐ Yes
7. Age of first seizure (excluding febrile seizure): _____ yrs
8. Does this patient have any family with epilepsy?
   ☐ No
   ☐ Yes
9. Number of AEDs currently: _____
10. Number of AEDs total: _____
11. Is this patient of school age?
    ☐ No
    ☐ Yes → Grade: ___ ☐ regular class ☐ regular class with resource ☐ special class

12. Does the patient have behavioural problems?
☐ No (normal)
☐ Yes → Please check one: ☐ mild ☐ moderate ☐ severe

Diagnosis: _____

13. Does the patient have cognitive problems?
☐ No (normal)
☐ Yes → Please check one: ☐ borderline ☐ mild ☐ moderate ☐ severe

Diagnosis: _____

14. Does this patient have motor problems?
☐ No
☐ Yes → Please check one: ☐ mild ☐ moderate ☐ severe

Diagnosis: _____

15. Other neurological deficits? Please specify: _____

_____

16. 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.

☐ Extremely severe
☐ Very severe
☐ Quite severe
☐ Moderately severe
☐ Somewhat severe
☐ A little severe
☐ Not at all severe

17. Rate the following aspects of this patient's epilepsy at his/her last visit.

Check one box using the following 7-point scale:
1 = none or never
7 = extremely frequent, severe or high

	1	2	3	4	5	6	7
Frequency of seizures							
Intensity of seizures							
Falls or injuries during seizures							
Severity of post-ictal period							
Amount of antiepileptic drugs							
Side effects of antiepileptic drugs							
Interference of epilepsy or drugs with daily activities							

Appendix B: Select questionnaires from parent form

Family Inventory of Resources for Management (FIRM): Family Strength: Mastery and Health and Extended Family Support Subscales

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

Family Statements:	Not at all	Minimally	Moderately	Very Well
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
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

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

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

Center for Epidemiological Studies Depression Scale (CES-D)

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

Curriculum Vitae

Name

R Grace Couper

Post-Secondary Education and Degrees

Western University
London, Ontario, Canada
2019-2021 MSc. (Candidate)

McMaster University
Hamilton, Ontario, Canada
2013-2018 BTech

Awards and Honours

Department of Epidemiology and Biostatistics
Western Graduate Research Scholarship
2019-2021

Related Work Experience

Research Assistant
Neuroepidemiology Research Unit
Lawson Health Research Institute
2021

Teaching Assistant
Western University
2021

Research Assistant
Western University
2019-2021

Research Assistant
MacPherson Institute, McMaster University
2018

Publications

Amin Reza Rajabzadeh, Jennifer Long, **Rebecca Grace Couper**, Ana Gomez Cardoso. Using Engineering Design Software to Motivate Student Learning for Math-Based Material in Biotechnology Courses. International Journal of Engineering Education.

R Grace Couper, Dr. Jennifer Long. Diversifying the Engineering Voices: Bringing Diverse Professionals to the Classroom Through Video Interviews. Proceedings 2017 Canadian Engineering Education Association Conference

Presentations

R Grace Couper, GY Zou, Karen Campbell, Kathy Speechley. Long-Term Behavioural Problems in Children with Epilepsy. Child Health Research Day 2021. May 19, 2021 (Poster presentation)

R Grace Couper, GY Zou, Karen Campbell, Kathy Speechley. Long-Term Behavioural Problems in Children with Epilepsy. London Health Research Day 2021. May 11, 2021 (Poster presentation)

R Grace Couper, Jennifer Long. Diversifying the Engineering Voices: Bringing Diverse Professionals to the Classroom Through Video Interviews. Canadian Engineering Education Association Conference, 2017. Toronto, Canada (Oral presentation)