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Parents' Perceptions of Activity Restrictions in Children with Epilepsy: First Two Years Post-Diagnosis

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A thesis submitted in partial fulfillment of the requirements for the degree in Master of Science

PARENTS' PERCEPTIONS OF ACTIVITY RESTRICTIONS IN CHILDREN WITH EPILEPSY: FIRST TWO YEARS POST-DIAGNOSIS

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Abstract

Children with epilepsy are less physically and socially active than their peers. The objective is to explore whether parents represent a barrier to children's activity, by examining associations between child and family factors and parents' perceptions of epilepsy-related activity restrictions. Data were from the Health Related Quality of Life in Children with Epilepsy Study, a longitudinal study of children 4-12 years old with new-onset epilepsy. Parents reported on activity restrictions and family factors and neurologists reported on epilepsy-related characteristics at baseline, 6, 12, and 24 months. Linear mixed models were used to model relationships among child and family factors and parents' perceptions of activity restrictions. Parents' response rate was 82%. There was significant non-linear improvement in activity restriction over time. Significant child factors suggest that perceptions are largely influenced by seizure-related risks. Significant family factors suggest an opportunity through parental education to reduce unnecessary activity restrictions in children with epilepsy.

Keywords

child, epilepsy, activity restrictions, parent, caregiver, childhood activities, physical activity, social activity, parental overprotection, longitudinal study, mixed modeling, growth curve modeling

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List of Abbreviations

AEDs	antiepileptic drugs
ADHD	attention deficit hyperactivity disorder
AIC	Akaike's Information Criteria
AICC	finite-population-corrected Akaikes Information Criteria
AR (1)	Autoregressive Order 1
ATP	adenosine triphosphate
BIC	Schwarz's Bayesian Information Criterion
BMI	body mass index
CACN	Canadian Association of Child Neurology
CBCL	Child Behavior Checklist
CES-D	Center for Epidemiologic Studies-Depression Scale
CHQ	Child Health Questionnaire
CSP	Child Seizure Profile
EEG	electroencephalogram
Family APGAR	Adaptability, Partnership, Growth, Affection and Resolve
FCC	family centered care
FILE	Family Inventory of Life Events and Changes
FIRM	Family Inventory of Resources for Management
GABA	gamma-aminobutyric acid
GASE	Global Assessment of Severity of Epilepsy
GTCS	generalized tonic-clonic seizure
HARCES	Hague Restrictions in Childhood Epilepsy Scale
HASS	Hague Seizure Severity Scale
HRQL	health-related quality of life
HERQULES	Health-related Quality of Life in Children with Epilepsy Study
ILAE	International League Against Epilepsy
LR	likelihood ratio
MAR	missing at random
SAS	Statistical Analysis Software
SD	standard deviation
SE	standard error

SEM	standard error of measurement
SPSS	Statistical Package for the Social Sciences
UN	Unstructured
QOLCE	Quality of Life in Childhood Epilepsy

Chapter 1

Introduction and Research Objectives

1.1 Overview

This thesis examines activity restrictions associated with childhood epilepsy, as perceived by parents of children with epilepsy (over the first two years post-diagnosis). It has been reported that children with epilepsy are less physically active (Yu et al., 2008; Wong & Wirrell, 2006) and socially involved (McCusker et al., 2003; Sabaz et al., 2003a) than their peers without epilepsy. This is a concern because physical and social activities play an important role in healthy growth and development. As a population, these children also experience a higher proportion of emotional, behavioural, cognitive, and social difficulties than other children their age (Rodenburg et al., 2005a; Mcdermott et al., 2009; Shinnar & Pellock, 2002). It is possible that their relative lack of engagement in normal childhood activities contributes to the development of these co-morbid conditions. It may also be the case that these co-morbidities are part of the reason children with epilepsy are less active. According to clinical guidelines and based on past research, there is no reason that the majority of children with epilepsy should have more activity restrictions than other children their age (Commission of Pediatrics of the ILAE, 1997). In most cases these children are only at minimally greater risk during a given activity than the general population and the potential benefits of the activity largely outweigh the risks.

Usually parents or guardians play a key role as gatekeepers to their children's activities. They influence what activities their child engages in and how frequently. For this reason, parents' perception of the extent to which their children's activities should be restricted, based on how much risk they believe an activity entails, may be one of the main reasons

children with epilepsy are less active. In childhood epilepsy, the child's parent can act as a barrier to their participation in social and physical activities. This claim is based on past research that has found anxiety to be high in these parents, and that they tend to adapt restrictive or overprotective parenting styles (Chapieski et al., 2005; Rodenburg et al., 2005b; Shore et al., 2010; Williams et al., 2003).

This study aims to describe parents' perceptions of their child's activity restrictions associated with epilepsy to provide preliminary information as to whether parents do in fact act as a barrier to activity and whether the opportunity exists to remove some level of unnecessary activity restrictions.

1.2 Background Information

1.2.1 Incidence & Prevalence of Epilepsy in Childhood

Epilepsy is defined by the International League Against Epilepsy (ILAE) as a chronic neurological condition, characterized by recurrent seizures and is the most common neurologic disease in childhood (Casetta et al., 2011). Incidence rates are highest in early childhood, decline steadily moving into late adolescence, and peak again in the elderly. The decreasing incidence from childhood to adolescence is related to the decline in the diagnosis of epilepsies caused by congenital, developmental and genetic conditions beyond childhood (Kotsopoulos et al. 2002). The incidence of childhood epilepsy in Canada is 41 per 100,000 children per year (Camfield C. S. et al., 1996). Worldwide incidence rates range from 41 to 124 per 100,000 children per year (Pellock, Dodson & Bourgeois, 2001). The lowest rates are found in developed countries, which are approximately half those in developing countries. Incidence has also been found to be

higher consistently in males than females. These differences in incidence rates are likely due to the greater number of epilepsies associated with trauma and infections in developing countries and to gender differences in the incidence of risk factors for epilepsy, such as higher incidence of head injury and central nervous system infection in males, respectively (Kotsopoulos).

Estimates of the prevalence of childhood epilepsy vary depending on how epilepsy is defined. In studies defining epilepsy as seizures or seizure medication within the previous 3 years, prevalence estimates have ranged from 2.8 to 5.7 per 1000 (Pellock, Dodson & Bourgeois, 2001). According to Shinnar & Pellock (2002) epilepsy affects 0.5 to 1% of all children through the age of 16 years. Given its incidence and prevalence, epilepsy is a relatively common childhood condition that impacts many children and their families across Canada and worldwide.

1.2.2 Outcomes in Childhood Epilepsy

Childhood epilepsy is a complex and diverse disorder making it difficult for parents and health care professionals to know how to care for the child with epilepsy. It is a convulsive disorder with unpredictability regarding when seizures occur, resulting in added burden to the child and family. There is variability among cases regarding etiology, epilepsy syndrome, seizure type, and how the epilepsy affects the individual in various health domains. Collectively these children have been found to have disproportionately more emotional, behavioral, and cognitive difficulties than children in the general population (Rodenburg et al., 2005a; Mcdermott et al., 2009; Shinnar & Pellock, 2002). Common cognitive impairments found in children with epilepsy include

deficits in the areas of attention, memory, and academic achievement, as well as lower mean IQ scores (Evangelos & Gkampeta, 2011; Stores, 1978; Stefan & Pauli, 2002). They also experience problems with social development and stigma (Drazkowski, 2003; Baker et al., 1997). The stigma associated with epilepsy often results in individuals with epilepsy having poorer self-esteem, higher suicide rates, and fewer close relationships (Baker et al., 1997).

Prognostic studies that have followed children with epilepsy from the onset of epilepsy report that the majority of patients become seizure free within a few years of diagnosis (Shinnar & Pellock, 2002). Most children respond well to treatment and are able to gain adequate seizure control through the use of antiepileptic drugs (AEDs). Of those who become seizure free, approximately 60% successfully discontinue medication**.** On the other hand, approximately 20-30% of children with epilepsy are unresponsive to treatment with AEDs and have persistent seizures (Mikati at al., 2010). In many cases, seizures do not persist into adulthood, but there is evidence that childhood epilepsy is associated with adverse long-term psychosocial outcomes, even in those who attain remission (Shinnar & Pellock, 2002). The occurrence of childhood seizures appears to have a negative impact on education, employment, marriage, and fertility later in life (Sillanpaa et al., 1998). It is evident that childhood epilepsy can negatively impact a child's health-related quality of life (HRQL) through a number of different mechanisms, so investigating potential ways to minimize this impact, such as maximizing the child's involvement in normal childhood activities, is important.

1.2.3 Physical Activity in Childhood Epilepsy

Children and adolescents with epilepsy have been found to be less physically active than their peers without epilepsy (Yu et al., 2008; Wong & Wirrell, 2006). This is a concern because of the key role physical activity plays in healthy growth and development (Malina, Bouchard, & Bar-Or, 2004. p. 6). Physical activity is also associated with improved cardiovascular fitness, decreased all-cause mortality, and reduced risk of becoming overweight or obese in the general population (Warburton et al., 2006).

Physical activity is likely more important for children with epilepsy than other children their age because many potential benefits from physical activity, if realized, would lessen some co-morbidities associated with epilepsy. For example, in the general population physical activity has been found to reduce depression, improve self-esteem, and improve cognitive functioning (Arida et al., 2010). Physical inactivity has also been shown to be associated with a higher prevalence of co-morbidities, such as behavioural and emotional difficulties in the general population (Kantomaa et al., 2008). Physical activity can also be used to counter the effect of bone mineral density loss associated with some AEDs (Samaniego & Sheth, 2007), which increases the risk of osteoporosis and pathological fractures in adulthood. Finally, and maybe most importantly, there is growing evidence that engagement in physical activity or exercise is associated with reduced seizure frequency (Arida et al., 2008).

1.2.4 Social Activities in Childhood Epilepsy

There is a large social component to many physical activities in which children and adolescents with epilepsy are less involved (Yu et al., 2008; Wong & Wirrell, 2006).

They are also reported to be less involved in other predominantly social activities and social play than other children their age (Drazkowski, 2003). Studies using the Child Behavior Checklist (CBCL) have found that children with epilepsy have low levels of participation in the social activities domain compared to normative data (McCusker et al., 2003; Sabaz et al., 2003a).

Participation in social activities is crucial for a child's social, emotional, and cognitive development (Sigelman & Rider, 2011, p. 467). Through social play children learn how to interact with others, and appropriate social behaviors such as sharing, cooperating, and respecting the property of others. Involvement in social activities also leads to peer acceptance, which works against stigma and promotes self-esteem (Sigelman & Rider, 2011, p. 467). Finally, missing out on opportunities to develop social skills during childhood is likely to make the transition from childhood through adolescence and into adulthood more difficult.

1.2.5 Role of Parents in Determining Participation in Activities by Children with Epilepsy

In the past, children with epilepsy were often discouraged from participating in physical activity largely because of fears held by their clinicians and parents. The greatest fears continue to be that physical activity will induce seizures, increase seizure frequency and increase the risk of injury if a seizure occurs during an activity (Arida et al., 2008). While clinicians are beginning to encourage physical activity, parents often continue to adopt restrictive and/or protective parenting styles that are not justified based on the characteristics of their child's epilepsy (Chapieski et al., 2005; Rodenburg et al., 2005b; Shore et al., 2010; Williams et al., 2003). It is widely speculated that one of the primary

reasons children with epilepsy are less physically active is that their parents restrict them from participating (Dubow & Kelly, 2003; Arida et al., 2008). Limited parental understanding of their child's epilepsy may help explain overprotective parenting styles (Norzilla, Azizi, & Motilal, 1997; McNelis et al., 2007). Overprotective parenting is likely to limit the child's participation in both physical and social activities.

Parents act as gatekeepers to their child's involvement in physical and social activities. They are primarily responsible for the child's safety and well-being, and thus for determining what activity restrictions are necessary. In most situations they are also in a position to enforce these restrictions. Additionally, they have influence over what restrictions are placed on the child when under the supervision of others, such as teachers and coaches. While parents are not the only determinant of activity participation in childhood, they are on the front line and in their position of influence can act as a barrier to, or facilitator of, normal childhood activities. The presence of seizures in children adds complexity in determining the appropriate activity restrictions and may inherently lead the parent to be a barrier, rather than facilitator to physical activity.

1.2.6 Activity Restrictions in Childhood Epilepsy

Activity restrictions determined by parents are put in place out of concern for the child's physical and emotional well-being. All children are expected to be given some restrictions, but children with epilepsy may need additional restrictions because of their seizures. If a seizure occurs during an activity, the child could be at an elevated risk of sustaining an injury depending on the type and severity of the seizure, the nature of the activity and whether the child's body is in a vulnerable position when the seizure occurs.

To optimize children's HRQL, it is important that any decisions about restricting physical and social activities are informed by considering the potential risks and benefits associated with an individual child's epilepsy condition. In the majority of cases, the child with epilepsy is only at minimally greater risk than their peers without epilepsy (Commission of Pediatrics of the ILAE, 1997), and additional restrictions are not justified.

1.3 Research Objectives

Research Questions

1. What are parents' perceptions regarding activity restrictions for children with epilepsy over the first two years post-diagnosis?

2. To what extent are child and family factors associated with parents' perceptions regarding level of activity restriction in childhood epilepsy?

Objectives

1. To examine the pattern of parents' perceptions regarding activity restrictions associated with epilepsy in childhood over the first 24-months post-diagnosis.

   Hypothesis: Parents' perceptions regarding activity restrictions will change significantly over time. Over time they will perceive fewer activity restrictions being necessary.

2. To identify child characteristics significantly associated with parents' perceptions of activity restrictions in children with epilepsy.

   Hypothesis 1: Characteristics of the child (age, sex, epilepsy severity, epilepsy syndrome type (generalized vs. focal onset), number of current AEDs, side effects of AEDs, falls or injuries during seizures, co-morbid conditions, timing of seizures, convulsive status epilepticus, and family history of epilepsy) will be

significantly associated with parents' perceptions over the first 24-months post-diagnosis.

3. To identify family factors significantly associated with parents' perception of level of activity restriction.

   Hypothesis: Family factors (parental worry and concern, parental depression, family resources, family functioning, family demands, annual household income, and parent age, sex, marital status, employment status and highest level of education) will be significantly associated with parents' perceptions over the first 24-months post-diagnosis.

4. To examine whether child and family characteristics interact to explain parents' perception of level of activity restriction.

   Hypothesis: The effect of important child or family factors on perception of activity restrictions will differ depending on the level of the other factor (epilepsy severity, presence of a co-morbid condition, family resources, and parental worry and concern).

Chapter 2

Review of the Literature

2.1 Search Strategy and Organization of Literature Review

The primary goal of the literature review was to review previous studies that assessed parent perceived activity restrictions in children or adolescents with epilepsy. To gain a comprehensive understanding of the subject, publications addressing several related topics were reviewed and are presented in this chapter as follows. A review of guidelines is presented first, to provide rationale to support the notion that children with epilepsy should be more active, and identify common themes found in recommendations on activity restrictions for children with epilepsy. Previous studies examining level of physical activity participation, risks and benefits of physical activity, and theories on how physical activity affects seizure frequency in individuals with epilepsy are then reviewed. Similarly, previous studies examining level of involvement in social activities and, risks and benefits of social activities are reviewed. Additionally a section provides an overview of research assessing parent adaptation to having a child with epilepsy to gain an understanding of why parents might act as a barrier to their child's participation. Finally, previous studies that have examined activity restrictions in children with epilepsy are reviewed, with a focus on those findings specifically pertaining to each of the research objectives in this thesis. All searches included the electronic databases OVID (MEDLINE & EMBASE), CINAHL, and Web of Science. For full details of the search strategies utilized in this literature review refer to Appendix A.

2.2 Published Guidelines for Activity Restrictions in Children with Epilepsy

Published guidelines are valuable tools to guide clinicians and parents of children with epilepsy in determining appropriate activity restrictions for an individual child. These guidelines identify factors that should influence parents' decisions regarding their own child's activity restrictions. They include a focus on the risks that common childhood activities entail based on past research and clinical experience. Four published articles discuss managing the lifestyle of a child with epilepsy, aimed primarily at clinicians (Drazkowski, 2003; Parker, 1999; Camfield & Camfield, 2005; Indian Academy of Pediatrics, 2009), one article presents guidelines for determining activity restrictions, with a focus on risk (Commission of Pediatrics of the ILAE, 1997), and two focus on which activities should and should not be restricted in childhood epilepsy (Livingston, 1971; O'Donohue, 1983). While some of these articles are more dated, their recommendations continue to represent the standard protocol for activity restrictions in children with epilepsy.

Four common themes emerged in articles reviewing recommendations on activity restrictions for children with epilepsy. The first is that children with epilepsy are only at minimally greater risk than their peers of incurring an injury during the vast majority of activities (Drazkowski, 2003; Parker, 1999; Commission of Pediatrics of the ILAE, 1997; Livingston, 1971; O'Donohue, 1983). The second is that the parent of a child with epilepsy often adapts an overprotective parenting style, which leads to unnecessary activity restrictions being put in place (Commission of Pediatrics of the ILAE, 1997; Livingston, 1971; O'Donohue, 1983). Thirdly, restrictions should balance the need to

encourage the child's continued self-development against the need to protect the child and others from physical and emotional injury (Drazkowski, 2003; Parker, 1999; Commission of Pediatrics of the ILAE, 1997; Livingston, 1971). That is, it is important to balance the potential risks of the activity with the potential benefits. Fourth, the parent should exercise common sense in individualizing activity restrictions for his/her child (Drazkowski, 2003; Parker, 1999; Camfield & Camfield, 2005; Indian Academy of Pediatrics, 2009; Commission of Pediatrics of the ILAE, 1997; O'Donohue, 1983). These themes suggest that the majority of children with epilepsy should be no less active than other children their age and that in many cases they are likely less active than recommended.

2.3 Physical Activity in Childhood Epilepsy

2.3.1 Level of Physical Activity in Children with Epilepsy

Collectively, children with chronic conditions, such as epilepsy, have been found to have lower levels of physical activity involvement than their peers. Arim et al. (2012) found that children with neurodevelopment disorders (ex. cerebral palsy, intellectual disability, and autism spectrum disorder) (n=286) were less likely to participate in organized sports or physical activities than healthy children (n=7314). Similarly, findings from the 1983 Canada Fitness Survey indicated that children and adolescents living with a chronic condition participated in less physical activity than the general population (Malina, Bouchard, & Bar-Or, 2004, p. 612). This study sample was representative of children and adolescents living in Ontario, Canada.

It has been widely cited that people with epilepsy as a group are, on average, less physically active than the general population (Bjorholt et al., 1990; Steinhoff et al., 1996; Ablah et al., 2009; Hinnell et al., 2010). Most studies that have assessed level of physical activity in individuals with epilepsy have focused on adults. There is a lack of quantitative evidence on physical activity in children with epilepsy. Based on a review on physical activity and epilepsy, Dubow & Kelly (2003) concluded that people with epilepsy exercise less frequently than those without. This is despite individuals with epilepsy having similar views on sports and physical activity based on a study where adults with and without epilepsy agreed that sports are fun, suitable, and healthy for individuals with epilepsy (Steinhoff et al., 1996).

While the pervasive clinical impression is that children with epilepsy are less physically active, only a limited number of studies have actually assessed the difference in level of physical activity between children and adolescents with epilepsy and their peers without epilepsy. In the only study that examined younger children, Wong & Wirrell (2006) examined whether children and teens with epilepsy participate in fewer physical activities than their siblings without epilepsy. No significant group difference was found in the number of hours spent in any of the activities between cases (n=79) and controls (n=99). However, in the 13 to 17 age group, children with epilepsy (n=28) spent significantly less time in group activities and total sport activities (individual and group sports), but not in sedentary activity or individual sports than controls (n=36). Yu et al. (2008) found that teens with epilepsy (n=44) felt less positive about their health ($p<0.02$), and were less physically active ($p<0.03$) than controls (n=119), as measured by the Positive Health and Physical Activity subscales of the Health Behaviour in School-Aged Children

questionnaire. Gordon et al. (2010) used the Canadian Community Health Survey, Cycle 3.1, to compare the activity profiles of individuals with epilepsy (n=341), aged 12 to 39 years, with the general population (n=53,211). There was no difference in reported monthly frequency of leisure physical activity greater than 15 minutes, but individuals with epilepsy had a greater frequency of walking ($p<0.001$), and those without epilepsy had a greater frequency of ice hockey, weight training, and home exercise ($p\leq0.001$). These activities carry moderate to low risk for individuals with epilepsy supporting the notion that individuals with epilepsy are less active than they could be.

Overall there is some evidence that teens and adolescents with epilepsy are less physically active than their peers, but only one study examined children younger than 12 years old, and did not find a significant difference in this age cohort. Preliminary evidence suggests children and adolescents with epilepsy may be less active, but further work is required to validate previous findings. Publications reviewing physical activity and epilepsy make the assumption that children with epilepsy are less active, despite the lack of empirical evidence (Arida et al., 2008; Howard et al., 2004; Dubow & Kelly, 2003). In their review, Howard et al. (2008), state that children and adults with seizure disorders play sports and participate in recreational activities less frequently than the general population. Similarly, Arida et al. (2008) and Dubow & Kelly (2003) state that despite shifts in medical recommendations, the fact remains that people with epilepsy continue to be less active and less fit than the general population.

2.3.2 Risks Associated with Physical Activity and Exercise in Children with Epilepsy

A parent's decision whether to allow their child to participate in sports and other physical activities should be grounded in whether the benefits outweigh the risks (Arida et al., 2008).The magnitude of risk for a person with epilepsy is determined by the likelihood of a seizure occurring while participating in an activity (Arida et al., 2008). The biggest concern for many parents of children with epilepsy is that their child is at elevated risk of incurring an injury during physical activity. An early study done by Aisenson (1948) reviewed the records of 960 pediatric patients to compare the incidence of potentially serious injuries in convulsive and non-convulsive children. Over a 16-year period, the injury rates in the two groups were nearly identical; 2.8% in 210 convulsive children and 2.9% in 750 non-convulsive children. A more recent study done by Kirsh & Wirrell (2000) assessed whether cognitively normal children with epilepsy (n=25) had a higher rate of accidental injury during daily activities than their age and sex matched friends without epilepsy (n=25). No significant differences were found in injury rates or severity of injury (injuries requiring medical treatment) comparing the two groups.

Closely tied to risk of injury during physical activity, is the concern that contact sports involving minor repeated head trauma will worsen seizure frequency and/or the severity of epilepsy. Arida et al. (2008) reviewed the relevant literature for evidence and found this concern to be a misconception. According to Dubow & Kelly (2003) there is no clinical or statistical evidence that repetitive head trauma from contact sports has a detrimental effect on seizure frequency. Similarly, it is a common concern that participation in physical activity itself will induce seizures. Arida et al (2008) reported

that seizures induced or exacerbated by exercise are relatively uncommon in individuals with epilepsy. Only in rare cases has physical activity been found to trigger seizures (Schmitt et al., 1994; Ogenyemi et al., 1988; Korczyn, 1979).

There are some specific physical activities that do carry substantial added risk for children with epilepsy. It has been reported that individuals with epilepsy are four times more likely to be involved in submersion incidents resulting in drowning or near drowning (Howard et al., 2004). Kemp & Sibert (1993) studied the records of the 306 children who drowned or nearly drowned in the UK in 1988 and 1989 and concluded that children with epilepsy are 7.5 times more likely to experience a submersion incident than a child without epilepsy. It was noted however, that none of the children with epilepsy who was supervised at the time of the incident died, suggesting that, when properly supervised, they are at no greater risk of drowning than the general population. While the risk of a submersion incident is greater than in the general population, it is still quite low. Recommendations suggest that swimming is safe in cases when the child has adequate seizure control and under appropriate supervision (Commission of Pediatrics of the ILAE, 1997). Along with swimming and water activities, activities involving heights, such as climbing and horseback riding, also bring an increased risk of serious injury or death in children with epilepsy (Commission of Pediatrics of the ILAE, 1997). In summary, research to date suggests that participation in physical activity carries minimal added risk for persons with epilepsy. The majority of the activities that do carry added risk, such as those involving heights are not common in childhood.

2.3.3 Benefits of Physical Activity and Exercise in Children with Epilepsy

In their review of physical activity and epilepsy, Arida et al. (2008) state that, "with few exceptions, regular physical exercise is beneficial to the individual with epilepsy". In the general population, physical activity has been found to decrease obesity, heart disease, diabetes, and hypertension (Poirier & Despres, 2001). These benefits are important to children with epilepsy, who have been found to have higher body mass indices (BMI's) than their peers (Wong & Wirrell, 2006). Exercise has also been shown to decrease stress and depression and improve self-esteem in the general population. These benefits are also important to individuals with epilepsy who tend to have poorer self-esteem and higher suicide rates, due to the stigma associated with epilepsy (Baker et al., 1997).

The question of whether physical activity has a positive or negative impact on seizure frequency remains unanswered. There is growing evidence, however, that it has a positive impact. Arida et al. (2008) concluded that physical activity can decrease seizure frequency, as well as lead to improved cardiovascular and psychological health. Nakken et al. (2005) found that 20 of 26 children had a decrease in epileptiform activity while exercising, as evidenced by a decrease in epileptiform discharges in electroencephalogram (EEG). Similarly, Gotze et al.'s (1967) examination of EEG readings found that physical activity tends to normalize the EEG in adults with epilepsy. In doing so, physical activity may raise the seizure threshold and reduce the likelihood of seizures. Overall, the many important physical and psychological benefits of physical activity appear to largely outweigh the risks for children with epilepsy. These benefits

include growing evidence that physical activity has an overall positive impact on the child's seizure frequency.

2.3.4 Theories on the Pathways through Which Physical Activity Affects Seizure Frequency

The exact mechanism through which physical activity affects seizure frequency remains unknown. There are physiological responses to exercise that can impact seizure occurrence and factors associated with physical activity that are known to trigger seizures, such as stress and fatigue. The main theory regarding why physical activity might decrease seizure frequency is the associated increase in mental activity. Arida et al. (2008) state that the increased vigilance and attention involved in exercise could explain the observed reduction in seizure frequency during physical activity. Along these lines, Howard et al. (2004) suggest that physical activity enhances alertness and focus, which increases an individual's seizure threshold.

Fatigue and stress resulting from physical activity are often raised as factors that may trigger seizures. Stress is one of the most commonly reported precipitants of seizures in people with epilepsy (Arida et al., 2009). However, according to Arida et al. (2009), psychological stress associated with physical activity, can trigger or inhibit seizures. The increased mental activity, concentration, and enjoyment experienced by individuals with epilepsy during physical activity may inhibit seizures, while the stress of competition may trigger seizures. Fatigue may also play a role in increasing seizure frequency post-exercise. Horyd et al. (1981) found that 65% (n=20) and Nakken (1997) found that 23% (n=26) of children with epilepsy had an increase in epileptiform discharges on EEGs immediately following exercise compared to baseline. A review by Howard, Radlogg, &

Sevier (2004) concluded there was no evidence that the stress of physical activity or post exercise fatigue act as seizure precipitants. While EEG activity may increase post-exercise, the actual occurrence of seizures resulting from fatigue post-exercise appears rare.

Other factors that have been found to trigger seizures include: hyperhydration, hypoglycaemia, hypoxia, hyponatraemia, hyperthermia, and hyperventilation (Arida et al., 2008; Dubow & Kelly, 2003). Hyperhydration is a well-known precipitant of seizures, and can result from excessive ingestion of water. Hypoglycaemia, resulting from low blood glucose, can also occur during prolonged physical exercise. Hyperthermia can occur when exercising in high temperatures and under humid conditions. Finally, hyperventilation is often mistakenly raised as a potential risk for triggering a seizure during physical activity. The increased ventilation that occurs during physical activity is a compensatory homeostatic mechanism, and the respiratory alkalosis of induced hyperventilation does not occur (Arida et al., 2008).

Theories have been proposed to explain how exhaustive or anaerobic exercise affects seizure frequency. One theory by Gotze et al. (1967) is that intense physical activity causes acidosis, which in turn reduces the irritability of the cortex and raises the seizure threshold. It is known that acidosis reduces the irritability of the cortex (Arida et al., 2009). Acidosis results in an increase in blood pH, which decreases the effectiveness of enzymes involved in gamma-Aminobutyric acid (GABA) metabolism. The resulting increase in GABA concentration in the brain has a natural anticonvulsant effect (Arida et al., 2009). Another theory is that extracellular adenosine, which is known to have an anticonvulsant effect, reduces seizure frequency during intense exercise. Adenosine is

produced during exercise as a by-product of adenosine triphosphate (ATP) utilization and energy metabolism. The increased activation of the brain during exercise is associated with an elevated metabolic rate, and thus, increases in adenosine concentration (Arida et al., 2009).

Additional theories exist on how low to moderate intensity or aerobic exercise affects seizure frequency. Arida et al. (2009) state that changes in the neurotransmitter systems resulting from physical exercise could reduce seizure frequency. Evidence suggests that brain neurotransmission is influenced by exercise, and the alterations could mediate the inhibitory/excitatory balance to reduce seizure frequency. The increase in norepinephrine following physical training that has been observed in rat models may lead to reduced seizure frequency (Brown & Huss, 1973; De Castro & Duncan, 1985).

The overall theme found in the literature is that participation in physical activity is more likely to inhibit than trigger seizures in individuals with epilepsy. During physical activities and immediately following there appears to be a reduction in seizure frequency in the majority of cases. To gain the benefits from physical activity in terms of its positive impact on seizure frequency, the child's participation must be ongoing, stressing the importance of minimizing activity restrictions in children with epilepsy.

2.4 Social Activities in Childhood Epilepsy

2.4.1 Involvement in Social Activities in Children with Epilepsy

It has been reported that people with epilepsy experience restrictions participating in social situations (Drazkowski et al., 2003). Clinical guidelines state social activities such as sleeping over at a friend's house, going to movies, parties and other events are normal

childhood activities that should be encouraged by the treating physician (Parker, 1999; ILAE Commission Report, 1997). Sabaz et al. (2003b) and McCusker et al. (2002) found that children with epilepsy had lower scores on the social activities domain of the Child Behaviour Checklist (CBCL) compared to normative data. McCusker et al. (2002) found that 38% (18 of 48) of their sample of children with intractable epilepsy scored in the clinically significant range of the social activities subscale of the CBCL. Children were considered in the clinically significant range if their T score (normal population mean of 50 (SD 10)) on the subscale was greater than 67. Additional studies however have not found a significant difference in the social activities domain comparing children with epilepsy to healthy controls (Tse et al., 2007; Caplan et al., 2005).

In a study by Pal et al. (2002) children living with epilepsy in rural India were found to be significantly less involved in social and recreational activities than healthy controls. In the general population, it has been observed that involvement in social activities or social interactions are important for children's social development and psychological well-being (Drewel & Caplan, 2007). Several studies have found that children with epilepsy have poorer social skills, suggesting that they are less involved in social activities where these skills are predominantly acquired and developed. Hamiwka et al. (2011) found that children with epilepsy had poorer social skills compared with healthy controls. They were found to be less cooperative, had greater difficulties helping others, sharing, and complying with rules and directions. Similarly, Rodenburg et al. (2005a) reviewed 46 studies, including 2,434 children with epilepsy, and concluded they were at an elevated risk for social difficulties compared with other children.

2.4.2 Risks and Benefits of Social Activities

The risks during social activities are minimal for the majority of children with epilepsy. The risk of physical injury during most social activities is low, but the risk of emotional injury to the child and others must be considered. To minimize risk it is important that the adults supervising the child are informed of the seizures and the appropriate action to take if one should occur (Parker, 1999; ILAE Commission Report, 1997). Siblings and friends should also be informed of the child's seizures to minimize the impact if one occurs.

Lack of participation in social activities during childhood can result in social deficits, leading to difficulties in the development and maintenance of interpersonal relationships. Withholding a child with epilepsy from participating in social activities can promote stigmatization (Drazkowski, 2003). According to a review by Drewel & Caplan (2007) children with epilepsy are less popular and socially accepted, have lower social competence and greater social problems, are more socially isolated and have more peer difficulties compared with healthy children or children with other health conditions, such as asthma. These social difficulties are also commonly associated with behavioural problems. Participation by children with epilepsy in social activities can work against social difficulties or be an effective tool for preventing social and behavior problems from developing.

Involvement in social activities is crucial for the development of appropriate social skills, which are necessary for an individual to behave competently and appropriately in social settings (Drewel & Caplan, 2007). Social skills are crucial for interacting with others and developing healthy relationships. Participation in normal childhood activities is important

for every child's sense of well-being. According to Drewel & Caplan (2007) instructing parents to arrange exposures to social situations for their child has yielded lessened social difficulties for both healthy children and children with central nervous system conditions. Social involvement also improves mood and provides an outlet for relieving emotional stress. Additional benefits of social activities in childhood include: learning to compromise and cooperate, learning empathy, flexibility, self-awareness, and self-regulation. Such capabilities are essential for successful social interactions later in life (Burdette & Whitaker, 2005). With minimal risks associated with social activities participation should be encouraged.

2.5 Parent Adaptation and Behaviors in Childhood Epilepsy

When a child is diagnosed with epilepsy, the family is faced with adapting to having a child with a chronic illness that is unpredictable. Parents' responses vary, and the way in which they respond to the change in their life will have consequences on the parent, the child, and on the family as a whole. Parents' realization that they may have to accept a new vision for their child is often accompanied by elevated levels of anxiety (Shore et al., 2010). There continues to be a lack of knowledge and understanding among many parents about epilepsy and how it affects the child. Common misconceptions contribute to the observed increased levels of anxiety, and frequently result in overprotective parenting styles and activity restrictions. Parents of children with epilepsy have been found to be more emotionally involved in their child with epilepsy, be more depressed, and worry more, all leading to increased activity restrictions (Shore et al., 2010).

Chapieski et al. (2005) examined the impact of maternal anxiety about a child's epilepsy on parental overprotection and the child's adaptive functioning. Subjects were mothers of a child diagnosed with epilepsy within the previous six months (n=56). Maternal anxiety was found to be significantly associated with overprotective and overly directive parenting styles at baseline and after one year. Maternal anxiety about the child's epilepsy decreased over time, but after one year it was still significantly associated with poorer child adaptive functioning. Maternal anxiety has been found to be influenced by the severity of the child's epilepsy (Chapieski et al., 2005), socioeconomic status, coping resources, and stress (Williams et al., 2003), but not seizure type or frequency (Chapieski et al., 2005; Williams et al., 2003). Williams et al. (2003) found that the child's quality of life, assessed with the Impact of Childhood Illness Scale, significantly decreased with increasing levels of parental anxiety. They suggested that parents with higher levels of anxiety are more likely to perceive higher risks for their children.

As well as increased anxiety, parents of children with epilepsy reportedly exhibit higher levels of stress and depression than the general population (Shore et al., 2010). In a study by Pekcanlar et al. (2011) mothers of children living with epilepsy had significantly higher state anxiety and depression scores than mothers of healthy children. Similarly, Wirrell et al. (2009) found that nearly two-thirds of mothers of children with intractable epilepsy scored in the clinical range for Total Stress, indicating higher than normal levels of parenting stress. Ferro et al. (2011a) found that 30-38% of mothers of children with epilepsy were at risk for clinical depression over the first two years post diagnosis. In addition, Ferro et al. (2011b) found that maternal depressive symptoms had a significant negative impact on the child's HRQL. Finally, Shore et al. (2004) found that more than

one-third of mothers to children with epilepsy suffered from depression and felt inadequate at managing their child's epilepsy and maintaining the family's usual leisure activities. Based on the findings of these studies, it is common for parents of children with epilepsy to experience psychological distress.

It is common for parents of children with epilepsy to worry that their child will die when a seizure occurs, that seizures result in a loss of intelligence, and that seizures will result in injury, and these concerns frequently result in overprotection and activity limitations (Williams et al., 2003; Commission of Pediatrics of the ILAE, 1997). Further, the parent's lack of knowledge and misconceptions about epilepsy has been associated with parental anxiety (Austin et al., 2008; Chapieski et al., 2005; Shore et al., 1998). In a longitudinal study by Shore et al. (2010), parents of children with epilepsy had information and support needs that were surprisingly high given that the sample was composed of children with relatively well-controlled seizures. Even after two years, one-third to one-half of parents reported needs for information and support, and continued to experience fears and concerns about their child's epilepsy. The parent's misconceptions about epilepsy are likely to lead to overprotective parenting behaviours, and unjustified activity restrictions. Wong & Wirrell (2006) found that ten of seventy-nine parents reported their child was limited in his/her ability to participate in physical activities, six of whom gave reasons that the authors did not believe warranted limitation; four parents stated that their children were limited simply because they had epilepsy, and two stated their child could not "get hit in the head," as this might worsen their seizures.

According to Coulter (1982) many parents of children with epilepsy react to their child's epilepsy with over-protectiveness. Rodenburg et al. (2005b) conducted a literature review

examining whether families of children with epilepsy differ on distinct family factors when compared to healthy children and children with another chronic illness. They found that, compared to each of these control groups, parents of children with epilepsy were more overprotective and less supportive of their child with epilepsy. The overprotective parenting style adopted by many parents of children with epilepsy is likely associated with their perceiving their child to have greater activity restrictions.

2.6 Activity Restrictions in Childhood Epilepsy

The primary search strategy yielded twenty-one articles examining parent-perceived activity restrictions in children and adolescents with epilepsy. Of these, 5 were validation studies, of the Quality of Life Childhood Epilepsy (QOLCE) questionnaire or the Hague Restrictions in Childhood Epilepsy Scale (HARCES), which presented results pertinent to the objectives of this thesis (Carpay et al., 1997; Sherman et al., 2002; Sabaz et al., 2000; Sabaz et al., 2003a; Connolly 2004). An additional four studies described activity restrictions in specific epilepsy subsamples (Sabaz et al., 2003b; Mathiak et al., 2010; van Empelen et al., 2007; Connolly et al., 2006). Of the remaining studies, eight assessed the effect of treatment on activity restrictions (four surgical (Griffiths et al., 2007; Zupanc et al., 2010; Sabaz et al., 2006; van Empelen et al., 2004) and four non-surgical (Conant et al., 2008; Jung et al., 2010; Gupta et al., 2004; Yoo et al., 2009), one study assessed the relationship between parent perceived AED complaints and activity restrictions (Carpay et al., 2002), two were studies of the relationship between cognitive impairment and activity restrictions in children with epilepsy (Sabaz et al., 2001; Sherman et al., 2006) and one study examined factors associated with activity restrictions in prevalent cases (Nadkarni et al., 2011).

Previous studies examining activity restrictions in children and adolescents with epilepsy have assessed activity restrictions using one of two parent-report measures: The Hague Restrictions in Childhood Epilepsy Scale (HARCES) or the Physical Restrictions subscale of the Quality of Life Childhood Epilepsy (QOLCE) questionnaire (Refer to Appendix B for copies of these scales). In this thesis the QOLCE Physical Restrictions subscale was used to assess activity restrictions. What the present study refers to as "parent-perceived activity restrictions" was referred to in previous studies as "physical restrictions".

In previous studies where the QOLCE was used, the primary objective of the study was to examine changes in, or factors associated with the child's HRQL. For this reason the majority of these studies did not examine factors associated with activity restrictions. In many cases the mean score of the Physical Restrictions subscale of the QOLCE is compared across groups or within a cohort over time. In those studies that used the HARCES, describing activity restrictions in children or adolescents with epilepsy was a primary objective. On the QOLCE, scores range from 0 to 100 and a higher score is better (higher functioning/less activity restrictions) and on the HARCES scores range from 10 to 40 and a higher score is worse (more severe disability/higher activity restrictions).

Changes in Parent-Perceived Activity Restrictions over Time. Nine previous studies have examined change in parent-perceived activity restrictions in children and adolescents with epilepsy over time. The majority of these studies compared mean activity restriction scores collected before and after the child receiving treatment aimed at improving the child's epilepsy. Gupta et al. (2004) & Jung et al. (2010) found parents'

perceptions of activity restrictions did not change significantly following short-term antiepileptic drug interventions (2 and 24 weeks), despite post-treatment improvements in areas such as attention, memory, language and behavior. On the other hand, Yoo et al. (2009) found a significant improvement in activity restriction scores (n=25) following eight weeks of Ritalin therapy in children with epilepsy and attention deficit hyperactivity disorder (ADHD). The reduction in perceived activity restrictions following therapy was likely a result of the Ritalin reducing the symptoms of ADHD, rather than due to changes in the children's epilepsy.

Conant et al. (2008) examined the effect of a 10-week karate class on the child's HRQL (n=9) and found that parents' perceptions of activity restrictions associated with epilepsy did not change significantly after the 10-week class. In a study that assessed test-retest reliability of the QOLCE, activity restriction scores reported by parents 2-4 weeks apart (n=39) were found to be highly correlated (Pearson's $r = 0.81$) (Connolly, 2004). In a similar study that assessed reliability of the HARCES, activity restriction scores assessed 1 year apart (n=78) were also highly correlated (Spearman's $r^2 = 0.75$) (Carpay et al., 1997). Finally, Sabaz et al. (2006) examined change in activity restrictions post-surgery, measured using the QOLCE, in children who had intractable seizures prior to surgery. Children were classified into one of two groups, those that became seizure free following surgery (n=20) and those who had persistent seizures (n=15). A significant improvement in mean activity restrictions score was found only in those who became seizure free, reflecting the importance of seizure frequency in affecting parent's perceptions.

Two studies have examined change in parents' perceptions of activity restrictions over time by measuring activity restrictions at baseline, and three more times over the course

of at least 24 months. Van Empelen et al. (2004) examined changes in activity restrictions, measured using the HARCES, following functional hemispherectomy surgery in 12 Dutch children. The child's caregiver provided data at 1-3 months prior to surgery, and, 6, 12, and 24 months post-surgery. Mean activity restriction scores significantly improved from 30.8(3.6) prior to surgery to 13.5(3.2) 6 months after surgery. From 6 to 24 months there was no significant change. In an additional study by van Empelen et al. (2007), mean activity restrictions scores, measured at baseline, 6, 12, and 24 months using the HARCES, did not change significantly over 24 months in children with intractable epilepsy ineligible for surgery (n=28). No intervention or treatment was implemented in this study.

Findings from previous studies suggest that without a major intervention such as surgery, parents' perceptions of activity restrictions do not change over time in prevalent cases of children with epilepsy. Following surgery, parents' perceptions were found to improve significantly; in the case of the van Empelen et al. (2007) study, parents' perceptions improved significantly 6 months post-surgery, but remained relatively constant beyond 6 months, representing non-linear change over time. The improvement following surgery is likely a result of the surgery positively affecting the child's epilepsy. A key difference between the present study and previous studies is that the sample consists of incident rather than prevalent cases of children with epilepsy. Post-diagnosis is a unique window for assessing change and previous studies have not assessed perceptions of activity restrictions starting at diagnosis. Following the diagnosis of epilepsy it takes time for the family to become familiar and comfortable with the condition. Over time some adjustment is likely. Immediately following the diagnosis the parents and physician are

likely to be most cautious and there is the most uncertainty about the child's epilepsy. For this reason activity restrictions might be expected to lessen from baseline to two years post-diagnosis, with the greatest change occurring from baseline to 6 months. In the present study it is believed that two years is a sufficient window of time to observe change should it occur. Ideally, the child's parent would perceive few restrictions associated with epilepsy soon after diagnosis and this would remain fairly consistent over time.

2.7 Child Factors Associated with Parent-Perceived Level of Activity Restriction

Seizure Frequency. Seizure frequency can vary greatly among children with epilepsy from several times a day to only a few times a year. Some children are very responsive to treatment and become seizure free over time while others are nonresponsive to AEDs and have persistent seizures. The primary goal of the majority of childhood epilepsy interventions is to improve seizure control (reduce seizure frequency), which makes this variable of particular interest in most studies assessing activity restrictions in children and adolescents with epilepsy.

Seizure frequency is often cited as the primary child factor that should affect decisions regarding the child's activity restrictions (Commission of Pediatrics of the ILAE, 1997; O'Donohue, 1983; Camfield & Camfield, 2005). A child with higher seizure frequency requires more activity restrictions if the seizures put the child at an elevated risk of incurring an injury. The ILAE guideline on Restrictions for Children with Epilepsy (1997) suggests that after a 1-year seizure-free interval it is reasonable to discontinue most epilepsy-related restrictions. Another guideline that focused on children with

childhood absence epilepsy states that most children gain complete seizure control within a few weeks at which point it is recommended that they resume participation in all normal activities (Camfield & Camfield, 2005). In most cases participation in normal activities is encouraged once seizures are well-controlled (Jung et al., 2010). Typically, having an occasional seizure is not a valid reason for major restriction of normal childhood activities.

In a study examining level of physical activity in children and teens with epilepsy, Wong & Wirrell (2006) found that children with a higher seizure frequency had a significantly greater BMI percentile for their age, but did not find a significant association between seizure frequency and participation in group, individual or total sports activity. The review of previous studies that examined activity restrictions found several with a significant positive association between seizure frequency and activity restrictions (Zupanc et al., 2010; Sherman et al., 2002; Sabaz et al., 2006; van Empelen et al., 2004; Griffiths et al., 2007; Carpay et al., 1997; Sabaz et al., 2003a; Nadkarni et al., 2011). However, some studies did not find a significant relationship between seizure frequency and activity restrictions (Jung et al., 2010; Sherman et al., 2006; Connolly et al., 2006).

In previous studies examining the effect of epilepsy surgery on activity restrictions, Zupanc et al. (2010), Sabaz et al. (2006), & Sabaz et al. (2003a) classified children and adolescents into two groups, based on whether they had a significant reduction in seizure frequency post-surgery. In all studies, the group with a greater reduction in seizure frequency had significantly fewer activity restrictions following surgery. Similarly, Sherman et al. (2002) grouped children with intractable epilepsy into high (n=22) and low (n=22) seizure frequency groups, and found that activity restriction scores, assessed

using the HARCES, were significantly higher in the high seizure frequency group. Griffiths et al. (2007) & van Empelen et al. (2004) found that activity restrictions, assessed using the QOLCE, improved significantly post-surgery, which was likely a result of an overall reduction in seizure frequency. Finally, Carpay et al. (1997) found a significant positive association between parent-estimated likelihood of a seizure occurring in the next month and HARCES score (n=122). Some studies have found no association between seizure frequency and activity restrictions, but none has found a significant negative association. Although findings are not entirely consistent, research to date suggests that seizure frequency is an important child factor in explaining parents perceptions of activity restrictions associated with epilepsy.

Epilepsy Syndrome (Partial, Generalized, or Undetermined). Type of epilepsy syndrome is relevant to the possibility of injury, and therefore plays an important role in determining risk. The ILAE classifies types of epilepsy syndromes most broadly according to the source of the seizure onset, into generalized epilepsies and localization-related (partial/focal) epilepsies (ILAE, 1989). Children are classified as having generalized epilepsies and syndromes if clinical seizure investigation indicates initial involvement of both cerebral hemispheres, and as having localization-related syndromes when findings at investigation indicate a localized seizure origin. A third classification, undetermined epilepsy syndromes, is used in cases where the child has both focal and generalized seizures together or in succession and has both focal and generalized EEG discharges, or when there are no positive signs of either focal or generalized seizure onset.

Seizures that are associated with a loss of consciousness put the child at the greatest risk during an activity (Commission of Pediatrics of the ILAE, 1997). However, focal, generalized, and undetermined epilepsies can all be associated with loss of consciousness, and both focal and generalized can develop into a generalized tonic-clonic seizure (GTCS). Partial epilepsy seizure types however, are often longer in duration than generalized. Because partial seizures often last longer, they put a child at a greater risk of injury if one occurs during an activity. Finally, the initial epilepsy syndrome at time of diagnosis is an important factor affecting seizure recurrence, with an initial partial seizure being more likely to recur than a generalized one (Drazkowski, 2003). According to Semah et al. (1998) a greater percentage of children with generalized epilepsies gain seizure control (>1 year without seizure) than children with partial epilepsies. A child with greater seizure control should need fewer activity restrictions.

Wong & Wirrell (2006) found no significant difference in physical activity levels comparing those who had a GTCS in the previous year (n=22) with those who had not (n=57). Despite the theoretical basis for activity restrictions being influenced by type of epilepsy syndrome, no previous study has examined the association between activity restrictions and syndrome type (partial, generalized, or undetermined). Sabaz et al. (2003a) did find that children with idiopathic epilepsies were reported to require significantly fewer activity restrictions than children with symptomatic epilepsies. The symptomatic epilepsies examined were all partial epilepsy syndromes providing some evidence that children with generalized epilepsies may be perceived to require fewer activity restrictions than partial syndromes.

Seizure Severity (Intensity of Seizures). O'Donohue (1983) stated that to determine appropriate activity restrictions for a child with epilepsy, one should take into account the severity of the child's seizures, since severe seizures put the child at a greater risk of incurring physical or emotional injury and therefore require more activity restrictions. Two such studies measured seizure severity using separate parent-report measures, the Hague Seizure Severity Scale (HASS) and an adapted version of the HASS. Carpay et al. (1997) found that parent-perceived seizure severity was not associated with mean activity restrictions score, assessed using the HARCES (n=122). Sabaz et al. (2000) found a significant negative partial correlation (controlling for age, age of seizure onset, gender, and IQ) between seizure severity and activity restrictions, assessed using the QOLCE (n=63). This finding indicates that an increase in severity of epilepsy was associated with an increase in activity restrictions (decrease in the Physical Restrictions subscale).

In a validation study of the QOLCE, Sabaz et al. (2003a) also found a significant negative partial correlation between seizure severity, assessed using the Child Seizure Profile (CSP), and activity restrictions, after controlling for age of seizure onset, IQ, family income, and number of AED's taken (n=71). In an additional study, Sabaz et al. (2003b) found that caregivers of children with symptomatic epilepsies (n=66) perceived their child to require more activity restrictions than caregivers of children with idiopathic epilepsies (n=48). They suggest this finding may be a result of children with symptomatic epilepsies having more severe seizures. Finally, Connolly et al. (2006) found that in children with benign rolandic epilepsy (n=30), which is a relatively less severe epilepsy syndrome, seizure severity, assessed using the CSP, was not correlated with activity

restrictions, assessed using the QOLCE. Overall, findings from previous studies suggest that seizure severity is positively associated with activity restrictions.

Antiepileptic Drugs (current number of AEDs, total number of AEDs, AED adherence, and side effects of AEDs). When considering the role of AEDs in affecting parent's perceptions of their child's activity restrictions, the number of current AEDs being taken and total number of AEDs ever taken are important considerations. They are indicators of how well controlled and/or severe the child's epilepsy is, with a higher number being correlated with worse control. The more well-controlled their epilepsy is, the less likely the child is to have a seizure during physical activity and thus the less risk of injury. A child's adherence to prescribed AEDs should also play into parents' perceptions of the necessary restrictions for the child (ILAE Commission Report, 1997). If the child is adhering to medication that effectively controls his/her seizures, he/she is less likely to have a seizure and thus incur an injury during activity than someone not adhering. Adherence to medication becomes more of an issue with increasing age, moving from childhood into adolescence and increasing independence. Finally, common adverse effects of AEDs, such as ataxia, tremors, sedation, drowsiness, poor concentration, and slowed reaction times can affect the child's ability to safely participate in physical activities (Drazkowski, 2003) and should therefore affect parent's perceptions.

Previous studies assessing activity restrictions in children and adolescents with epilepsy have not assessed the relationship between AED adherence and activity restrictions. The relationships between current and previous number of AEDs and activity restrictions have been assessed however. In a study by Griffiths et al. (2007), higher HARCES scores

correlated with higher number of current AEDs in surgical and nonsurgical groups. In an additional study by Sherman et al. (2006) the number of failed and current AEDs was significantly positively correlated with HARCES score. These findings indicate that a higher number of current and previous AEDs used are associated with greater activity restrictions. Another study by Carpay et al. (2002) found a significant positive correlation between complaints attributed to AEDs as perceived by the caregiver and HARCES score (n=108), suggesting that the presence of AED-related side effects increases parents' perceptions of activity restrictions.

Two previous studies examined the association between AEDs and activity restrictions by dichotomizing children based on prior and current AED use. Sherman et al. (2002) found that those with high prior AED use (≥5 ineffective AEDs, n=25) had significantly higher activity restrictions, assessed using the HARCES, than those with low prior AED use (<5 ineffective AEDs, n=19). Finally, in children with benign rolandic epilepsy (n=30), those who were currently on AEDs did not have significantly different activity restrictions scores on the QOLCE compared to those not currently on AEDs (Connolly et al., 2006). Several previous studies have found a positive relationship between current number of AEDs and activity restrictions, but none controlled for other epilepsy-specific variables in the analysis. It is possible that in these studies number of AEDs taken may have acted as a proxy for difficult to control epilepsy or epilepsy severity.

Timing and Location of Seizures. The timing of the child's seizures and where children are when seizures occur are important factors in determining activity restrictions. Children with epilepsy who have exclusively nocturnal seizures are at minimal to no risk during daytime activity. The timing of seizures in relation to waking and sleeping should

be taken into account when restricting the child's activities. It is interesting to note that most children with epilepsy experience fewer seizures when engaged in physical activities than when idle or at rest (O'Donohue, 1983). The only previous study that has assessed the relationship between activity restrictions and timing of seizures was conducted by Carpay et al. (1997). Using the HARCES to measure activity restrictions, they found the HARCES score and whether the child's seizures occurred at a fixed time of day or night (n=122) were not significantly related.

Co-morbid Conditions (Cognitive, Behaviour, or Motor Problems). Co-morbid diagnoses, both physical and psychological are relatively common in children with epilepsy. There is a high prevalence of ADHD in children with epilepsy compared to the general population, estimated between 12 and 17% (Reilly, 2011). Children with both ADHD and epilepsy are at higher risk of poorer HRQL compared to children with epilepsy alone (Sherman et al., 2007). Vallenga et al. (2005) state that approximately 30% of individuals with intellectual disability also suffer from epilepsy and that the percentage increases with the severity of the disability. Having an intellectual disability, or cognitive impairment, affects the child's decision-making ability, and increases the likelihood he/she will sustain an injury during an activity. Physical co-morbidity also puts the child at greater risk of injury during an activity. According to the ILAE Commissioners Report (1997) the presence of a physical or mental handicap in addition to the child's epilepsy may be a confounding factor in determining the need for restrictions. In general, a co-morbid diagnosis is likely to increase the need for activity restrictions in children with epilepsy.

Several previous studies have examined the relationship between co-morbid diagnoses and activity restrictions. Griffiths et al. (2007) found that higher HARCES scores correlated with lower functional independence in both surgery (n=51) and non-surgery (n=80) groups, while Sherman et al. (2006) noted a significant negative correlation between HARCES score and adaptive level (n=121). Finally, Sabaz et al. (2001) found that physical restrictions were significantly greater in children with intellectual disability (n=30) than those with normal IQ (n=64). These studies suggest that parents of children who have epilepsy and a co-morbid condition are likely to perceive greater need for activity restrictions than parents of children with epilepsy alone**.**

Age (Age at Epilepsy Onset) & Sex. Children younger than 8 years are often unable to understand the risk of activities, and stricter activity restrictions are necessary (ILAE Commission Report, 1997). Activities should be age-appropriate, and activity restrictions tend to become less strict with increasing age of the child. Age affects a child's capacity to make decisions, which affects their ability to participate in an activity safely. Girls are also more likely to have higher activity restrictions than boys, because girls are traditionally viewed as more fragile (McAuliffe, 2008, p. 437).

Two studies found no significant association between age and HARCES score or between sex and HARCES score in prevalent cases of children with epilepsy (Carpay et al., 1997; Griffiths et al., 2007). Similarly, Sherman et al. (2006) & Connolly et al. (2006) found no significant correlation between age of epilepsy onset and HARCES scores (n=121 & n=30). Sabaz et al. (2003a) found that age and sex were not correlated with activity restriction scores in a validation study of the QOLCE (n=71). Finally, Nadkarni et al. (2011) found that activity restrictions scores, assessed using the QOLCE, were not

significantly different in children 5-9 and 10-14 years old. Past research assessing activity restrictions suggests that age of epilepsy onset and sex are unrelated to parent's perceptions of activity restrictions associated with their child's epilepsy.

Duration of Epilepsy. The duration of a child's epilepsy is included in many studies of HRQL in childhood epilepsy, and is likely an important variable in explaining parent perceived activity restrictions. The longer a child has lived with epilepsy, the more likely he/she is to gain adequate seizure control (Shorvon & Luciano, 2007). Once seizures are controlled, the need for additional activity restrictions due to the child's epilepsy is minimal. Also, with increasing duration of the condition, the child's parent should become more familiar with the child's condition, and gain a better understanding of the risks an activity entails.

Several previous studies have assessed whether duration of epilepsy and activity restrictions are correlated in children and adolescents. Connolly et al. (2006) found no correlation between duration of epilepsy and activity restrictions in a sample of children with benign rolandic epilepsy (n=30). Similarly, Griffiths et al. (2007) found no significant correlation between duration of epilepsy and HARCES score, in children who underwent epilepsy surgery (n=51), or in children with epilepsy who did not undergo surgery (n=80). Sherman et al. (2006) found no significant correlation between epilepsy duration and HARCES score in 121 children and adolescents. However, Sherman et al. (2002) & Carpay et al. (1997) did find significant positive correlations between duration of epilepsy and HARCES score (n=44 & n=122). These studies suggest that a longer duration of epilepsy is associated with parents perceiving more activity restrictions in prevalent cases of children with epilepsy. This result is likely because children who are

diagnosed with epilepsy at a younger age tend to have more catastrophic epilepsy, in need of the greatest restrictions, and these cases tend to represent those with the longest durations (Shields, 2000).

Epilepsy Severity. Several factors should be considered in determining severity of epilepsy, including seizure frequency, severity and type, medication requirements and side effects, and impact on daily life activities to offer a full picture of the patient's condition. O'Donohoe (1983) suggests it is important that restrictions imposed on a child with epilepsy are in proportion with the severity of his/her epilepsy. Children with intractable or refractory epilepsy, whose epilepsy is not well controlled by treatment, are generally considered to have more severe epilepsy.

In a longitudinal cohort study, van Empelen et al. (2007) found that children with intractable epilepsy ineligible for surgery (n=28) had relatively severe activity restriction scores (Carpay et al., 1997). In studies by Sabaz et al. (2000) and Sabaz et al. (2001) mean scores on the QOLCE [Mean (SD)] were 51.45 (21.75) and 58.16 (21) respectively in children with refractory epilepsy. With a score of 100 indicative of no epilepsy-associated activity restrictions these scores are relatively poor and suggest that parents of children with refractory epilepsy perceive their child to require a relatively large number of epilepsy-associated activity restrictions compared to the majority of children with epilepsy.

Furthermore, Sabaz et al (2003a) found that activity restriction scores, assessed using the QOLCE, were significantly poorer on average for inpatients (n=43) than outpatients (n=28), reflective of differences in epilepsy severity. In an additional study by Sabaz et

al. (2003b), children with idiopathic epilepsy syndromes (n=48), which are typically less severe, were reported to require significantly fewer activity restrictions than those with symptomatic or more sever epilepsy syndromes (n=66). Similarly, Connolly et al. (2006) examined activity restrictions in children with less severe epilepsies and found that caregivers perceived relatively few epilepsy-related activity restrictions [79.95(21.12)]. These findings indicate that severity of the child's epilepsy significantly affects parents' perceptions of their child's activity restrictions.

Additional Child Factors Considered. There are other child factors that one might suggest could be related to parent perceived activity restrictions, such as convulsive status epilepticus, having a family member with epilepsy, and the frequency of falls or injuries during seizures. Their potential role in parents' perceptions has not been previously studied, however. Children who have convulsive status epilepticus, which are seizures that last long periods of time are expected to require greater activity restrictions. The parent of a child who has family history of epilepsy, may be more knowledgeable about epilepsy and how it affects the child. For this reason a family history of epilepsy could be associated with fewer parent perceived activity restrictions. Finally a greater number of falls or injuries during seizures could be associated with an increase in perceived activity restrictions because of the increased likelihood of an injury occurring.

2.8 Family Factors Associated with Parent Perceived Level of Activity Restriction

A limited number of studies have examined the association of family factors with parents' perceptions of their child's activity restrictions associated with epilepsy. Based on the literature, there are several family factors that are likely to influence parents'

perceptions of their child's activity restrictions. Parents of children with epilepsy have higher levels of anxiety and depression than controls (Shore et al., 2010; Chapieski et al., 2005). These factors are likely to affect the parent's perceptions regarding activity restrictions. According to Vallenga et al. (2006), if parents are anxious, the balance between protection and risk swings in favour of protection. Parents who have more depressive symptoms and/or higher levels of worry and concern may be more likely to perceive greater activity restrictions. In a cross-sectional study examining children with benign rolandic epilepsy (n=30), Connolly et al. (2006) found that emotional worry and concern, assessed using the Child Health Questionnaire (CHQ), was significantly positively correlated with activity restrictions, assessed using the QOLCE.

Several family variables including: family resources, functioning, and demands, and annual household income are likely associated with parental psychological adjustment and parenting styles. Parents who have poor psychological adjustment and/or adopt protective parenting styles may perceive more activity restrictions than those who adjust well. Chapieski et al. (2005) found that more family stresses (higher FILE scores) and fewer coping resources (Coping Resources Inventory) were significantly associated with higher levels of maternal anxiety about epilepsy and overprotective parenting styles. Similarly, greater family and social supports have been shown to reduce parenting stress in newly diagnosed epilepsy (Rodenburg, 2007). It is reasonable to suggest that families with fewer resources, poorer functioning, and more demands, may perceive their child to have more activity restrictions, although no previous studies have examined the association between these family variables and activity restrictions.

2.9 Interaction of Child and Family Factors and Parent Perceived Level of Activity Restriction

Whether the effects of child and family factors interact in explaining parent perceived level of activity restriction has not been assessed in previous studies. It is important that multiple effects are studied in research rather than the isolated effects of single variables (Pedhazur & Schmelkin, 1991). In addition, the presence of significant interactions will have important implications for the interpretation of the results. If interaction is present, the interpretation of a factor included in the interaction must include the other factor in the interaction. To more clearly understand the factors affecting parents' perception of activity restrictions it is important to assess whether child characteristics such as epilepsy severity and the presence of a co-morbid condition interact with key family factors such as, parental anxiety and family resources. Parents are expected to perceive the most activity restrictions in situations where the child has more severe epilepsy or has a co-morbid condition and there is more stress on the family in terms of fewer resources and higher parental anxiety.

2.10 Limitations of Previous Studies Assessing Activity Restrictions

No previous study has examined parent perceived activity restrictions in children with epilepsy by identifying the sample at time of diagnosis and then following subjects prospectively. Therefore the associations between child and/or family factors and parents' perceptions of activity restrictions in children with epilepsy have not been previously assessed in the first years post-diagnosis. Previous studies have generally assessed outcomes following surgery, effects of a specific treatment, or only focused on a specific subsample of the childhood epilepsy population. Most previous studies have

been cross-sectional in design, and the majority has studied small, generally convenience samples, composed of prevalent cases. Furthermore, the main focus of many studies to date has been on HRQL, rather than specifically on activity restrictions. For this reason, many studies have done limited analyses on activity restriction scores and often only report descriptive statistics. The current study seeks to address the limitations of previous studies.

Chapter 3

Methodology

This chapter describes the secondary data set used in this study, with a focus on the study design, sample, data source, and data collection and management strategies. The measures used to collect family and child factors are then reviewed. Finally the procedure and statistical analyses used to describe the characteristics of the sample studied and assess each of the thesis objectives are discussed.

3.1 Study Design, Sample and Data Source

The data used in this study came from the Health-related Quality of Life in Children with Epilepsy Study (HERQULES), a multi-centre prospective cohort study that followed children with epilepsy ages 4 to 12 over the first two years post-diagnosis (Speechley et al., 2003). The primary objective of that study was to assess the course of health-related quality of life in children with epilepsy and examine the determinants of HRQL over a two-year period. Data were obtained from the child's primary caregiver and pediatric neurologist at baseline, 6, 12, and 24 months. Approval for HERQULES protocol was obtained from all relevant research ethics boards across Canada (see Appendix C for approval at The University of Western Ontario).

A two-stage clustered sampling strategy was used in HERQULES. All paediatric neurologists in Canada were invited to participate in the study. The membership list of the Canadian Association of Child Neurology (CACN) was used as the sampling frame. The list was reviewed by a panel of paediatric neurology leaders in Canada to add names of a few neurologists who were not on the list and exclude a few who were not currently

practicing. At the outset of the study all 72 practicing paediatric neurologists were invited to participate and 74% did. This group of neurologists consecutively sampled all their patients eligible for the study based on the inclusion and exclusion criteria over a 36 month period from April 2004 to April 2007.

Inclusion Criteria:

1. New case of epilepsy (2 or more unprovoked seizures), in whom diagnosis of epilepsy had not been previously confirmed, seen for the first time by a paediatric neurologist within the data collection period.
2. Epilepsy first diagnosed between the ages of 4 and 12 years.
3. Parent/caregiver (survey respondent) must have been primarily responsible for the child's care for at least the past six months and continue to be for the duration of the study.

Exclusion criteria:

1. Diagnosis of epilepsy previously confirmed by another physician
2. Diagnosed with other progressive or degenerative neurological disorder.
3. Diagnosed with other major co-morbid non-neurological disorders that would have an impact on quality of life (e.g. asthma requiring daily medication).
4. Parent/caregiver has insufficient English language skills to complete questionnaires.

A total of 456 eligible families were approached to participate in HERQULES and agreed to have the neurologist forward their contact information to the HERQULES office.

Data Collection Strategy. Within a few days of the child's appointment with their neurologist the primary caregivers were mailed a letter of information inviting their participation and explaining what participation entailed. Since the vast majority of primary caregivers were parents, they will be referred to as such for the rest of the thesis.

Parents were then contacted a few days later via telephone by the study coordinator to determine their participation status and those who agreed were mailed self-administered questionnaires at baseline (as soon as practical after diagnosis), and again approximately 6, 12, and 24 months later. Time points for data collection were chosen based on a number of a priori considerations in the absence of any standard protocol. Data were collected as soon after diagnosis as possible to capture the immediate impact of diagnosis. Following baseline, 6 and 12 months were chosen since the first year is considered the most dynamic time in terms of management and family adaptation. After the first year the situation is likely to stabilize making 24 months an appropriate next measurement time. Consideration was given to making sure times were close enough together to avoid missing potential important fluctuations in scores and far enough apart to allow detectable changes to occur and not burden the respondents. The questionnaire took 45-60 minutes to complete and was rated at a grade 7 reading level using the Flesch-Kincaid Grade Score (Kincaid et al. 1975).

Of the 456 eligible families, 443(97%) parents verbally consented over the telephone and 374 returned the completed baseline survey (response rate = 82%). The Tailored Design Method was used to encourage high participation and retention rates (Dillman, 2000). Attrition rates at each subsequent time point are shown in Appendix D. Participating neurologists completed a brief questionnaire describing the clinical features of each child's epilepsy at the same four time points. Over 98% of the completed parent-report questionnaires have coinciding physician forms for each measurement occasion.

Data Management. Clinical data obtained from the child's neurologist were recorded manually at each site and faxed or mailed to the HERQULES office in the Department of

Pediatrics at the Children's Hospital of Western Ontario in London, Canada. Parent surveys were mailed directly to the HERQULES office for data entry, analysis, and quality control. Every returned questionnaire was examined for completeness and any identifying information was removed.

Data were entered by graduate students of the Department of Epidemiology and Biostatistics at the University of Western Ontario, London Ontario using the Statistical Package for the Social Sciences (SPSS) data entry program. Decisions made during the process of data entry were recorded for quick reference. Data verification was then performed on 100% of the data by research assistants other than those who initially entered the data. They maintained data correction logs and any corrections were made by the student who originally entered the data. This process ensured that the data were accurate and of good quality.

Missing Data. On the Physical Restrictions subscale of the QOLCE the majority of missing data resulted from responses of 'non-applicable' to scale items. The mean substitution method suggested by Wirrell et al. (2005) was used to handle missing data on the QOLCE. If more than 20% (2 items) of the items were missing the summary score was not calculated for that child. For all additional measures utilized in this study the guidelines for scoring provided by the instrument developers were followed.

3.2 Measures

3.2.1 Parent Report

Children's Activity Restrictions

Parents' perceptions of children's activity restrictions were assessed using the 10-item Physical Restrictions subscale of the Quality of Life in Childhood Epilepsy Questionnaire (QOLCE). The QOLCE is an epilepsy-specific parent-report measure of health-related quality of life with 76-items assessing the five domains of physical, cognitive, social, and behavioral function, and emotional well-being. The Physical Restrictions Subscale focuses on the frequency of restrictions related to the child's epilepsy using a five-point Likert response scale ranging from "very often" to "never" and a time reference of the previous four weeks. The activity restriction score calculated ranges from 0 (low functioning) to 100 (high functioning). As outlined earlier, the Physical Restrictions subscale of the QOLCE was adapted from The Hague Restrictions in Childhood Epilepsy Scale (HARCES), a parent-report measure which has also been validated for use in children and adolescents with epilepsy (Carpay et al., 1997). The Physical Restrictions subscale and HARCES are displayed in Appendix B.

Several studies have validated the QOLCE subscale in samples of children with epilepsy. The Physical Restrictions subscale has been shown to have high internal consistency reliability (Cronbach's alpha $\geq$0.85) and good convergent and discriminant validity (Sabaz et al., 2000; Sabaz et al., 2003a). Connolly (2004) also demonstrated that the Physical Restrictions subscale has high test-retest reliability (Pearson Correlation = 0.81). In HERQULES, Cronbach's alpha of the Physical Restrictions subscale was 0.88.

Family Demands

The Family Inventory of Life Events and Changes (FILE), a 71-item self-report measure was used to record the normative and non-normative life events experienced by the

family in the last 12 months (McCubbin, Thompson, & McCubbin, 1996). Each item is answered either yes or no, with yes answers receiving a value of 1, with scores ranging from 0 to 71. Higher scores indicate higher demands on the family or more change. Studies have shown the FILE to be both valid and reliable (McCubbin, Thompson, & McCubbin, 1996). In HERQULES, Cronbach's alpha was 0.84.

Family Resources

Level of resources available to aid families' adaptation to stressful events was assessed using two subscales from the Family Inventory of Resources for Management (FIRM): family mastery and health and extended family social support, since they have been found to be associated with adaptation to childhood epilepsy (Austin et al., 1992). Scores on individual items, which range from 0 (not at all) to 3 (very well), are summed to give a total FIRM score. The FIRM score can range from 0 to 72, and was reverse coded so that a higher score indicates greater family resources. The FIRM has demonstrated adequate reliability and validity properties (McCubbin, Thompson, & McCubbin, 1996). In HERQULES, Cronbach's alpha was 0.90.

Family Functioning

The Family Adaptability, Partnership, Growth, Affection, and Resolve scale (APGAR) was used to assess parents' satisfaction with family relationships. It is a 5-item instrument that uses a 5-point Likert scale (0 = Never to 4 = Always), designed to measure the family member's satisfaction with five aspects of family functioning. A score of 0 to 20 is possible with a higher score indicating better family functioning. It has been found to have satisfactory internal consistency reliability, test-retest reliability and validity (Austin

& Huberty, 1989; Smilkstein, Ashworth, & Montano, 1982). In HERQULES, Cronbach's alpha was 0.87.

Parental Depression

The Center for Epidemiologic Studies-Depression Scale (CES-D) was used to assess parental depression. It is a 20-item scale designed to measure current level of depressive symptoms (with emphasis on depressed mood), by referring to the previous seven days. Items are scored on a 4-point Likert scale from 0 (rarely or none of the time) to 3 (most or all of the time). This scale has been widely used and validated in general population surveys (Radloff, 1977). The total score can range from 0 to 60 with a score of ≥16 considered indicative of clinically relevant depression. In HERQULES, Cronbach's alpha was 0.91.

Parental Worry and Concern

The Parental Impact-Emotional subscale from the Child Health Questionnaire (CHQ-PF50) was used to assess parental worry and concern. This subscale has 3 items and uses a 5-point Likert scale (1 = none at all to 5 = a lot). Parents are asked how much worry or concern the child's health, emotional well-being or behaviour, and attention or learning abilities, has caused them during the past four weeks. Items are summed for a summary score between 0 and 100, with higher scores indicative of less worry and concern. Asmussen et al. (2000) found that the parental impact-emotional scale had acceptable internal consistency reliability with a Cronbach alpha of 0.74 and intraclass correlation coefficient (ICC) of 0.82 (95% confidence interval (CI) = 0.73-0.89). In HERQULES, Cronbach's alpha was 0.84.

Other Information about Parents and Families

Sociodemographic information was acquired through parent-report including: parents' current marital status, current employment status, highest level of education completed and household income. Current marital status was coded as married, widowed, divorced, separated, remarried, or never married. Current employment status was measured using 6 categories (not working due to my child's health, not working for "other" reasons, looking for work outside the home, working full or part-time, full time homemaker, and student). Highest level of education completed was also measured using 6 categories (less than 8 years, 8-12 years, completed high school, completed vocational/technical training, completed college/university, completed graduate school). Total yearly household income was measured in intervals of $10,000, from less than $10,000 to $100,000 or more.

3.2.2 Neurologist Report

Clinical Epilepsy Characteristics

Information collected from physicians included: type of epilepsy syndrome, seizure intensity and frequency, epilepsy severity, number of anti-epilepsy drugs (AEDs) prescribed total and currently, any side effects of AEDs, presence of co-morbidities (cognitive, behavioural, or motor problems), timing of seizures (exclusively nocturnal or not), occurrence of convulsive status epilepticus, family history of epilepsy, and falls or injuries during seizures. Seizure frequency and intensity, side effects of AEDs, and falls or injuries during seizures were measured on a 7-point Likert scale (1 = none or never to 7 = extremely frequent, severe or high). The neurologist was asked to respond to the

questions based on information from the patient's most recent visit.

Neurologists' responses regarding the types of seizures and epileptic syndrome children experienced were coded using the ILAE's 1981 classification of seizures (ILAE, 1981) and the ILAE 1989 classification (ILAE, 1989), respectively. For the purposes of this study, a summary variable was created classifying seizures as: generalized, partial or undetermined. For co-morbid conditions, the neurologist responded yes or no to whether the child had a behavioral, cognitive, or motor problem. If the response was yes to a behavioral or motor problem they proceeded to identify the problem as mild, moderate, or severe, and for a cognitive problem they further identified it as borderline, mild, moderate, or severe. For the results presented here, if the child was reported to have at least one of the three problems he/she was deemed to have a co-morbid condition at that time, irrespective of severity. Family history of epilepsy was recorded as binary, with the neurologist responding yes or no to the question, "does this patient have any family with epilepsy?".

Severity of epilepsy was measured using the Global Assessment of Severity of Epilepsy (GASE) scale. The scale was developed as a neurologist report to assess the overall severity of epilepsy in children (Speechley et al., 2008). The neurologist is asked to respond to the question, "taking into account all aspects of this patient's epilepsy, how would you rate its severity now?". Severity is then rated on a 7-point Likert scale (1 = extremely severe to 7 = not at all severe). In an initial assessment of the validity of the GASE, inter-rater reliability and test-retest reliability were high, and there was preliminary evidence of construct validity (Speechley et al., 2008). A summary table of the scales used in the analyses is found in Appendix E.

3.3 Conceptual Model

The conceptual model guiding this thesis is displayed in Figure 3.1. This model illustrates that there are three levels of factors, child, parent and family, which can affect parents' perceptions of their child's activity restrictions associated with epilepsy. For the purposes of this thesis, parent and family factors have been referred to collectively as 'family factors'. Child factors, in particular epilepsy-related variables should be the most important in affecting parents' perceptions. There are several, such as epilepsy severity and syndrome type that are important to consider based on guidelines of necessary activity restrictions in childhood epilepsy, as outlined in the literature review (Section 2.7). The presence of a co-morbid condition was also important to include, because of its associations with activity restrictions and childhood epilepsy.

Also as outlined in the literature review (Section 2.8), there is some evidence to suggest that characteristics of the parent, such as level of depressive symptoms or anxiety can impact parents' perceptions of their child's activity restrictions. Parent and family variables are also being examined in this thesis to provide preliminary evidence regarding whether parents might act as a barrier to their child's activity involvement. Finally, factors that describe the family environment, including family demands, functioning, and resources were included. The family environment is important to consider, because it has been shown to be associated with overprotective parenting (Chapieski et al., 2005) and can impact parents' psychological state (Rodenburg et al., 2007). Several indicators of socioeconomic status were also included, (annual household income, current employment and education status) because socioeconomic circumstances are known to influence health (Galobardes et al., 2007).

3.4 Procedure and Statistical Analysis

For all statistical analyses SAS software Version 9.2 was used. A two-sided p-value <0.05 was considered statistically significant for all analyses.

3.4.1 Descriptive Statistics

Univariable analyses were used to examine characteristics of the sample (mean and standard deviation (SD), frequencies, percentages) and descriptive statistics of the outcome, activity restrictions, at each time. Bivariable analyses (t- and χ^2 tests) were used to examine whether those lost to follow up differed from those remaining in the study at 24 months on baseline characteristics.

3.4.2 Analyses to examine the pattern of parents' perceptions regarding activity restrictions associated with epilepsy in childhood (Objective 1)

To examine the distribution of perceptions of activity restriction scores over the four time points, box and whisker plots were produced. Growth curve modeling (Chen & Cohen, 2006) was then used (PROC MIXED) to assess the pattern of parents' perceptions regarding activity restrictions associated with epilepsy over the first two years post-diagnosis. This modeling strategy is used to assess the overall time trend for the sample, in terms of the average change over time and average score at baseline (intercept). In addition, a quadratic term (time^2) can be added to the model to assess whether the average time trend is non-linear. An advantage of using PROC MIXED is that it permits the inclusion of individuals not assessed at all time points. The assumption of data missing at random (MAR) was examined by plotting individual trajectories of activity

restriction scores over time (Hopwood et al. 1994). The time when parents completed each questionnaire, measured in weeks since diagnosis, was used to model time.

Different covariance structures were specified and compared using model fit criteria to determine which fit the data best. Covariance structures that were tested included: compound symmetry, autoregressive order 1, Toeplitz, and unstructured (Wolfinger, 1996). The compound symmetry structure assumes that the correlation between two separate measures is constant regardless of how far apart the measurements are. Autoregressive order 1 (AR(1)) assumes homogeneous variances and correlations that decline exponentially with time, so that measurements taken closer together are more highly correlated than those taken further apart. Similar to the AR(1) structure, Toeplitz assumes all measurements next to each other have the same correlation, measurements two apart have the same correlation different from the first, and measurements three apart have the same correlation different from the first two, etc. Finally the unstructured structure is the most liberal, allowing every term to be different but requires fitting the most parameters of any structure. Theoretically we believed that either the Toeplitz or AR(1) covariance structure would fit the data best. To compare the fit of the unconditional linear and non-linear growth models, the likelihood ratio (LR) test or chi-square statistic was used. For determining which covariance structure fit the data best, the Akaike's information criteria (AIC), Schwarz's Bayesian information criterion (BIC), and the finite-population-corrected Akaike's information criteria (AICC) were used (Burnham & Anderson, 1998).

3.4.3 Analyses to identify child and family factors associated with parents' perceptions of their child's activity restrictions associated with epilepsy (Objective 2 & 3)

To model the associations of child and family factors with activity restrictions, linear mixed modeling was used (PROC MIXED). The conceptual model is displayed in Figure 3.1. Model building steps proposed by Cheng et al. (2009) were followed as a guideline. Initially a maximum model was specified by identifying child and family factors believed to play a role in affecting parents' perceptions of their children's activity restrictions associated with epilepsy. Factors included in the maximum model are displayed at the end of the chapter in Table 3.1. Prior to testing the main effects for child and family factors the interaction terms of interest were tested and significant interactions (Objective 4) remained in the model moving forward. In addition to the interactions between child and family factors, the interactions between time and time-invariant covariates were also tested. These interaction terms capture the association of change in activity restrictions over time with a time-invariant predictor. That is, they are used to identify whether the association between the predictor and outcome is significantly different over the two-year period.

Two effects, between ($\bar{X}_{¡}$) and within-subject ($\bar{X}_{¡j}$ - $\bar{X}_{¡}$), were used to model time-varying covariates. In the analysis of clustered (repeated measures) data, it has been shown that assuming the two effects are identical can result in misleading interpretations (Neuhaus & Kalbfleisch, 1998; Shen et al., 2008). In practice, it has been shown that the two effect estimates are often different. The between-subject effect is time-invariant and estimates that the average activity restriction score (Y) will differ by x units between two children

whose average X differs by 1 unit. The within-subject effect is time-varying and estimates that for a given child their activity restriction score (Y) will increase/decrease by an average of x units for each 1 unit increase in X.

The fixed effects for modeling time were determined in the first research objective. A covariate for time (in weeks since diagnosis) and a quadratic term for time (time^2) were included to represent the nonlinear time trend. To determine whether to fit a random intercept model or a random intercept and slopes model, the appropriateness of assuming compound symmetry was addressed in the first objective by comparing the fit of different covariance structures. Because compound symmetry, assuming changes in all subjects' activity restriction were the same over time, did not fit the data best, a random intercepts and slopes model was chosen. The compound symmetry structure was checked again, against other structures, for appropriateness in the final mixed model. In addition, since the subjects were nested within treating physicians or health centers, the clinical site was included as a nested random effect to account for clustering. Each clinical site corresponded to a unique physician and the average number of children per site was 7 (range 1-30).

The predictor selection strategy used was backward elimination. Starting with the maximum model, predictors with the least value were sequentially deleted. A select number of predictors were identified a priori that were negated from deletion because of their theoretical importance in their relationship with parents perceptions of their child's activity restrictions associated with epilepsy (child's age, epilepsy severity, presence of a co-morbid condition, parental worry and concern, parent's highest level of education completed and annual household income). Parent education and annual household

income were chosen as indicators of socio-economic status. Education is often used as a generic indicator of socioeconomic position and is thought to capture the knowledge-related assets of an individual (Galobardes et al., 2007). Of the remaining predictors, those with a significance level ≥0.20 were sequentially eliminated.

To avoid collinearity, a linear regression model was initially fitted on the outcome that included all covariates in the maximum model (Refer to Figure 3.1) and collinearity diagnostics were conducted on them. Predictors were sequentially removed based on tolerance and variance inflation factor values and scientific understanding of the topic. Seizure frequency and intensity were excluded from the outset since these variables are integrated into the measure for severity of epilepsy. Once the final model was fitted, the assumptions that random effect terms and residuals are normally distributed were evaluated using normal probability plots (Der & Everitt, 2006, p. 312).

3.4.4 Analyses to identify whether child and family factors interact to explain parents' perception of level of activity restriction (Objective 4)

The mixed model approach was used to identify whether child and family factors interact to explain parents' perceptions of their child's activity restrictions associated with epilepsy. To test for significant interactions, the interactions that were identified a priori as potentially important were tested in the maximum model prior to examining the associations between child and family factors and activity restriction (Objective 2 & 3). Interaction terms were tested in the maximum main effects model after collinearity diagnostics had been conducted. Four interaction terms examining the interaction of child and family factors were tested; between presence of a co-morbid diagnosis and parent

worry and concern, between presence of a co-morbid diagnosis and family resources, between epilepsy severity and parent worry and concern, and finally, between epilepsy severity and family resources. The between-subject effects for child and family factors were used in the interaction terms. Including the interactions of time and time-invariant covariates a total of 26 interactions were tested in this study.

Significant interactions were further investigated by the interaction term approach suggested by Van Ness & Allore (2006). In the only significant interaction, the presence of a co-morbid condition was treated as the moderator, and parental worry and concern was treated as the main predictor. In the interaction term approach, by modeling the presence of a co-morbid condition as binary and using 0/1 coding to indicate the presence or absence of a co-morbid condition, then the parameter estimate and standard error of the parental worry and concern predictor are interpretable as their values at the 0 level. By rerunning the model using inverted coding for the modifier, the results provide information comparable to the 1 level of the modifier.

Figure 3.1: Conceptual Model

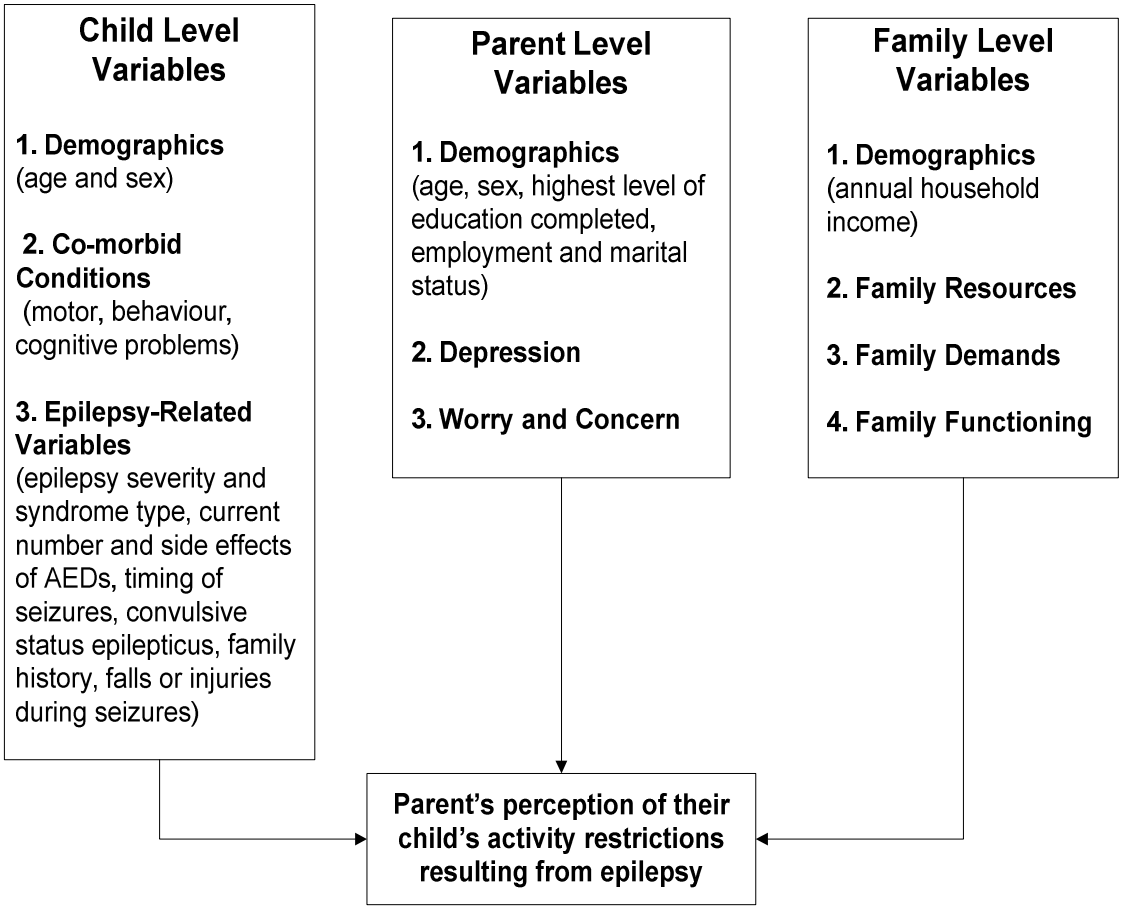


Table 3.1: Covariates Included in the Maximum Main Effects Model

Child Factors	Family Factors
Age*	**Parental worry and concern**, CHQ *
Sex	**Parent education**
Co-morbid conditions (motor, behavior,	Family Resources, FIRM *
cognitive problems)*	Family Demands, FLES *
Epilepsy severity	Family Functioning, APGAR *
Current # of AEDs *	Annual household income
Falls or injuries during seizures *	Parental Depression, CESD *
Side effects of AEDs *	Parent age *
Epilepsy syndrome	Parent sex
Exclusive nocturnal seizures	Parent employment status
Convulsive status epilepticus	Parent marital status
Family history of epilepsy	

Note: *indicates that the factor was included in the model as two separate effects, a time invariant effect, and a time-varying effect (between- and within-subject effects).
Factors specified a priori to stay in the model are bolded.
Parent education (completed college/university or did not), current employment status (employed or unemployed), and marital status (married or not married) were modeled as dichotomous

Chapter 4

Results

This chapter presents the results, beginning with characteristics of the child, parent, and family environment, in addition to descriptive statistics of the activity restriction scores at each time. The results addressing each of the three objectives are then sequentially presented. Tables and Figures are found at the end of the chapter.

4.1 Sample Characteristics

A total of 374 families participated in this study. Baseline and 24 month characteristics of the children with epilepsy are shown in Tables 4.1. The average age of children [Mean(SD)] at baseline was 7.5(2.3) years and almost half were male. Almost two-thirds of the children had partial seizures and the vast majority were actively having seizures at his/her last visit. According to neurologist report, over one third of the children had at least one of behavior, cognitive or motor problems. The mean score on the epilepsy severity scale, the GASE, was 5.4(1.2), which represents mild epilepsy. Twenty-one percent of children had exclusively nocturnal seizures and only five percent were reported to have convulsive status epilepticus.

Characteristics of the families and parents at baseline and 24 months are displayed in Table 4.2. The mean age of the parent respondents was 37.5(6.4) years and the majority were female. Of the parents who responded at baseline, almost all were the child's biological parent (94%) and 3% were the adoptive parent. Two-thirds of parents completed post high school education, two-thirds were working full or part time and 80% were married. The mean score on the Parental Impact-Emotional subscale of the CHQ

was 46.5(27.9). Parents reported having moderate to high levels of worry and concern on average. The mean score on the CES-D was 14.3(10.3), and 37.5% scored in the clinically significant range for clinical depression. The average CES-D score in this sample was greater than found in the general population, indicating greater depressive symptoms on average, and similar to that reported by mothers of adolescents with epilepsy in the United States (Dunn et al., 1999).

Focusing on family level factors, just over half of families had an annual household income ≥$60,000. Mean scores describing the family environment in terms of family functioning, family demands, and family resources indicate that these families were, on average, functioning well, had few demands, and adequate resources.

Results of the attrition analysis that compared subjects who were lost to follow up (n=91) with those who completed the parent-report questionnaire at time four (n=283) on baseline characteristics are displayed in table 4.3. Children who completed the follow-up did not significantly differ from those lost to follow-up on any of the child characteristics that were tested. Parents who completed the follow-up were significantly older at baseline and significantly more likely to be married. They were also significantly more likely to have an annual household income ≥ $80,000 and have completed college or university compared to parents lost to follow-up. Finally, those who completed the follow-up were significantly more likely to score lower on the CES-D scale, indicating lower levels of depression at baseline than those who were lost to follow-up. Focusing on the family environment, those who completed follow-up had significantly more family resources (FIRM) and fewer family demands (FILE).

Descriptive statistics for parents' perceptions of their children's activity restrictions scores at the four time points are displayed in Table 4.4. Parents' mean activity restriction score [Mean(SD)] at baseline was 62.9(18.5) and two years post-diagnosis was 74.1(18.6). The number of parents' who completed the activity restrictions measure at baseline, 6, 12, and 24 months was 364, 328, 295, and 274.

4.2 Pattern of parents' perceptions regarding activity restrictions associated with epilepsy in childhood over the first 24-months post-diagnosis (Objective 1)

The box and whisker plot displayed in Figure 4.1 visually displays how the distribution of activity restriction scores changed from baseline to 6, 12, and 24 months. Activity restriction scores improved over time, with a greater proportion of scores closer to higher functioning (fewest restrictions) and measures of central tendency (mean and median) improving from baseline to 24 months. Activity restriction scores also became less variable from baseline to 24 months. The assumption of data MAR, required by repeated measures analysis, appeared satisfied based on the plot of individual trajectories. Individuals with missing data did not appear to have different trajectories than those who completed the study (data not shown).

After testing the unconditional linear growth model, a quadratic term for time ($time^2$) was added to test for non-linear change in parent's perceptions. There was a significant negative quadratic change in perceptions over time ($p=0.0002$). Model fit significantly improved comparing the linear model with the model including the quadratic term (Chi-square = 13.3, df = 1, $p<0.0001$). Based on AIC, AICC, and BIC values, the covariance structures, autoregressive order 1 [AR(1)], Toeplitz, and unstructured, fit the data

similarly. The AIC and AICC values were slightly better for the UN specification, but the BIC value was better for the AR(1) specification. To minimize loss of power, the AR(1) covariance structure was chosen. Fit statistics comparing the different covariance structures are presented in Appendix H.

The random variance and fixed effects estimates from fitting the unconditional non-linear growth model with time in weeks are presented in Table 4.5. The significant Time² effect indicates that the overall time trend is non-linear, with parents perceiving their child needing fewer activity restrictions because of their epilepsy over time on average. The difference in average activity restriction score from one measurement time to the next decreases in magnitude. By 24 months the improvement in scores over time tapers off. The observed and model predicted average time trends are presented in Figure 4.2.

4.3 Child and family factors associated with parents' perceptions of child's activity restrictions associated with epilepsy (Objective 2 & 3)

Collinearity diagnostics were conducted after fitting the maximum main effects model. Based on pairwise correlations and variance inflation values, the decision was also made to delete the within-subject effects for child's age and parent's age. It is believed that the between-subject effects for age sufficiently account for the child and parent age effects of interest. Parental depression (between-subject effect), was then removed based on the tolerance and variance inflation factor values. Following collinearity diagnostics, interaction terms were tested (Objective 4) and the only significant interaction (parental worry and concern and presence of a co-morbid condition) was kept in the model testing main effects.

Fitting the mixed model, data from 339 of the 374 cases who responded at baseline were used. The 35 cases not utilized by the PROC MIXED procedure had substantial missing values for the independent variables included in the final model. Based on the results from the first objective, time and quadratic time (time^2) were included as fixed effects for time. Both effects were significant in the final model. A random intercept and slope model was fitted to allow heterogeneity in both slopes and intercepts, rather than assuming compound symmetry. Originally the autoregressive, order 1 covariance structure was specified, based on the results of objective 1. However, the final covariance structure selected was unstructured (UN), because it improved convergence and the AIC, AICC, and BIC values (Appendix I). The site the family was sampled from was included in the final model to account for clustering, because it improved model fit criteria and impacted the fixed effect estimates (Appendix J). With clinical site included as a nested random effect the between- and within-subject effects for epilepsy severity went from nonsignificant to significant. The site may account for differences between different neurology practices, for example in advice given about necessary restrictions, as well as in differences between geographic locations. Normal probability plots showed that the assumptions of normally distributed random effect terms (time and intercept) and residuals are satisfied (Refer to Appendix K).

Child Factors. The predictors that remained in the final model following backward elimination are displayed in Table 4.6. Child factors significantly associated with parents' perceptions of their child's activity restrictions due to epilepsy include (effect estimate (SE)), average child's age during the study period (0.84(0.35)), epilepsy severity (2.03(1.01), between-subject effect), epilepsy severity (0.99(0.49), within-subject effect),

and exclusively nocturnal seizures (3.93(1.61)). In addition, children with generalized epilepsy syndromes were perceived to require significantly fewer activity restrictions than those with partial syndromes (3.06(1.53)). Finally, the presence of a co-morbid condition (-15.73(4.30), between-subject effect) was statistically significant and interacted with parental worry concern (0.17(0.08)).

Children who were older were perceived to require fewer restrictions. An increase in an individual child's epilepsy severity over the study period was significantly associated with an increase in parent's perception of their child's activity restrictions and a child who had a greater average severity of epilepsy over the study period was perceived to require more restrictions. The presence of a co-morbid condition was significantly associated with an increase in perceived activity restrictions and moderated the relationship between activity restrictions and parental worry and concern. Finally, children with exclusively nocturnal seizures were perceived to require fewer restrictions than those whose seizures were not exclusively nocturnal. Additional child factors that remained in the model ($p<0.20$) but were not significant included convulsive status epilepticus, family history of epilepsy, side effects of AEDs (within-subject effect), and falls or injuries during seizures (both effects).

Family Factors. Family factors that were significantly related to parents' perceptions of their child's activity restrictions due to epilepsy were average parent age over the study period (-0.31(0.14)), annual household income (0.50(0.23), between-subject effects), parental worry and concern (between subject effect = 0.19(0.05), within-subject effect = 0.10(0.02)), and family resources (0.21(0.07), within-subject effect). Parents' highest level of education completed was not significantly associated with activity restrictions.

The between-subject effect of parental worry and concern was moderated by the presence of a co-morbid condition. If a co-morbid condition was present, parental worry and concern had a greater effect on parents' perceptions (Section 4.4).

Parents who were older perceived their child to require more activity restrictions. An indicator of socioeconomic status, higher annual household income was associated with fewer perceived activity restrictions. Parents with an average lower level of worry and concern perceived significantly fewer activity restrictions and a decrease in worry and concern was significantly associated with a decrease in activity restrictions over the first two year post epilepsy diagnosis. Finally, an increase in family resources over the first two years post-diagnosis was significantly associated with an improvement in activity restrictions. Other family factors that remained in the final model but were not significant were family functioning and current employment status. None of the interactions between time and time-invariant covariates (child and family factors) that were tested was statistically significant.

4.4 Interaction of child and family factors associated with parents' perceptions of their child's activity restrictions associated with epilepsy (Objective 4)

The only significant interaction term was the presence of a co-morbid condition and parental worry and concern (effect estimate = 0.17 (SE = 0.08), $p<0.05$). The effect parental worry and concern had on parents perceptions' differed depending on whether their child had a co-morbid condition or not. For parents of a child with a co-morbid condition, parental worry and concern had a greater effect on parent's perceptions of their child's activity restrictions (0.37 (0.06), $p<0.05$) compared to parents of a child without a

co-morbid condition (0.19 (0.05), $p<0.05$). The effect is in the same direction (quantitative interaction); a decrease in parental worry and concern is associated with a decrease in perceived activity restrictions, but the magnitude of the effect is greater for parents who have a child with a co-morbid condition (Figure 4.3). No other interaction terms that were tested were significant.

Table 4.1: Child Factors at Baseline and 24 Months

Variable		Baseline (n=374)	24 Months (n=274)
Age		7.5(2.3)	9.5(2.3)
Sex, n(%)			
	Male	196(52.4)	146(51.6)
	Female	178(47.6)	137(48.4)
Epilepsy Severity, GASE		5.4(1.2)	6.3(1.1)
Seizure Frequency		3.3(1.7)	1.5(1.0)
Seizure Type, n(%)			
	Partial	221(59.6)	195(58.4)
	Generalized	143(38.5)	133(39.8)
	Undetermined	7(1.9)	6(1.8)
Co-morbid Condition*, n(%)			
	Yes	120(36.0)	121(38.2)
	No	213(64.0)	196(61.8)
Exclusively Nocturnal Seizures, n(%)			
	Yes	78(21.2)	49(15.9)
	No	290(78.8)	259(84.1)
Convulsive Status Epilepticus, n(%)			
	Yes	18(4.9)	11(3.6)
	No	353(95.1)	298(96.4)
Current # of AEDs		0.7(0.5)	0.9(0.6)
Side Effects of AEDs		1.5(1.1)	1.5(1.0)
Falls or Injuries During Seizures		1.6(1.1)	1.2(0.5)
Family History of Epilepsy			
	Yes	137(38.9)	109(37.5)
	No	215(61.1)	62.5(182)

For continuous variables, values represent mean (standard deviation).

*Co-morbid condition was present if the child's neurologist reported the child having at least one of behavioral, motor or cognitive problem.

Table 4.2: Parent and Family Factors at Baseline and 24 Months

Variable	Baseline (n=374)	24 Months (n=274)
Age	37.5(6.4)	40.3(5.6)
Sex, n(%)		
Male	27(7.0)	20(7.0)
Female	347(93.0)	262(93.0)
Highest Level of Education Completed, n(%)		
Primary School	42(11.2)	16(5.7)
High School	83(22.2)	55(19.5)
Technical Training	49(13.1)	32(11.4)
College/University	200(53.5)	179(63.5)
Annual Household Income, n(%)		
Less than $20,000	34(8.0)	10(3.8)
$20,000-$39,999	50(14.2)	30(11.5)
$40,000-$59,999	75(21.4)	50(19.2)
$60,000-$79,999	68(19.4)	53(20.4)
≥ $80,000	81(37.0)	117(45.0)
Employment Status, n(%)		
Employed	249(67.1)	214(77.0)
Not Employed	35(9.4)	19(6.8)
Homemaker	80(21.6)	43(15.5)
Student	7(1.9)	2(0.7)
Marital Status, n(%)		
Married	298(79.7)	232(82.3)
Not married	76(20.3)	50(17.7)
Parental Impact-Emotional (CHQ)	46.5(27.9)	65.4(26.7)
CES-D (Parental Depression)	14.3(10.3)	11.8(9.9)
FIRM (Family Resources)	50.1(11.1)	50.7(11.5)
Family APGAR (Family Functioning)	13.9(3.8)	14.1(3.9)
FILE (Family Demands)	9.5(6.5)	7.8(5.7)

For continuous variables, values represent mean (standard deviation).

Table 4.3: Comparison of Participants who Completed the Study (n=283) and Those Lost to Follow-up (n=91) on Baseline Characteristics

Variable	Study Sample	Completed Follow-up	Lost to Follow-up	t/χ^2	P-value
Child					
Age, years	7.5(2.3)	7.5(2.3)	7.3(2.4)	0.62	0.53
Male, n(%)	196(52.4)	147(51.9)	49(53.9)	0.10	0.75
Epilepsy Severity, GASE	5.4(1.2)	5.4(1.1)	5.3(1.3)	1.04	0.30
Seizure Frequency	3.3(1.7)	3.2(1.6)	3.4(1.7)	-0.83	0.41
Partial Seizures, n(%)	221(59.6)	171(60.6)	50(56.2)	0.59	0.75
Co-morbid Condition*, n(%)	120(36.0)	90(34.0)	30(44.1)	2.42	0.12
Nocturnal Seizures, n(%)	78(21.2)	63(22.3)	15(17.4)	0.95	0.33
Current # of AEDs	0.7(0.5)	0.7(0.5)	0.8(0.5)	-1.18	0.24
Side Effects of AEDs	1.5(1.1)	1.5(1.2)	1.3(1.0)	1.33	0.18
Falls/Injuries During Seizures	1.6(1.1)	1.6(1.1)	1.7(1.2)	-0.90	0.37
Parent					
Age, years	37.5(6.4)	38.2(5.6)	35.9(7.1)	3.27	**0.001**
Female, n(%)	347(93.0)	265(93.6)	82(90.1)	1.28	0.26
Parental Impact-Emotional	46.5(27.9)	46.9(28.2)	45.1(26.9)	0.52	0.60
Parental Depression, CESD	14.3(10.3)	13.4(10.2)	17.2(10.2)	-3.08	**0.002**
Married, n(%)	289(79.7)	240(84.8)	58(63.7)	18.88	**<0.001**
Employed, n(%)	249(67.1)	193(68.2)	56(61.5)	1.37	0.24
College/University, n(%)	200(53.5)	162(57.2)	38(41.8)	6.64	**0.01**
Family					
Resources, FIRM	50.1(11.1)	51.0(11.4)	47.2(9.9)	2.80	**0.005**
Functioning, APGAR	13.9(3.8)	14.1(3.9)	13.3(3.4)	1.71	0.09
Demands, FILE	9.5(6.5)	8.9(6.0)	11.3(7.6)	-2.99	**0.003**
Income ≥80,000, n(%)	130(37.0)	109(38.5)	21(23.1)	7.24	**0.007**

For continuous variables, values represent mean (standard deviation).
*For co-morbid condition must have at least one of motor, cognitive or behavior problem.

Table 4.4: Parents' Perceived Activity Restriction Scores at Baseline, 6, 12, and 24 Months

Time	RR (%)	n	Missing*	Mean (SD)	Median	Interquartile Range
Baseline	82	374	10	62.86(18.51)	65.0	22.5
6 Months	90	336	8	68.58(19.17)	72.2	25.0
12 Months	91	304	10	73.45(18.41)	75.0	25.0
24 Months	94	283	9	74.12(18.57)	77.5	22.5

Note: RR=Response Rate, n = sample size, SD=Standard Deviation.
*Missing represents the number of parents' who returned the parent-report questionnaire (n), but did not complete the activity restrictions subscale of the QOLCE.

Table 4.5: Individual Growth Model for Longitudinal Change in Activity Restriction Scores

Effect	Unconditional Non-linear Model Estimate (SE)
Random Variance	
Intercept	212.99 (21.62)***
Linear Slope (time)	0.002 (0.002)
AR(1)	0.18(0.08)*
Residual	133.25(13.66)***
Fixed Effects	
Intercept	61.18(1.03)***
Time	0.30 (0.03)***
Time²	-0.0017 (0.00027)***

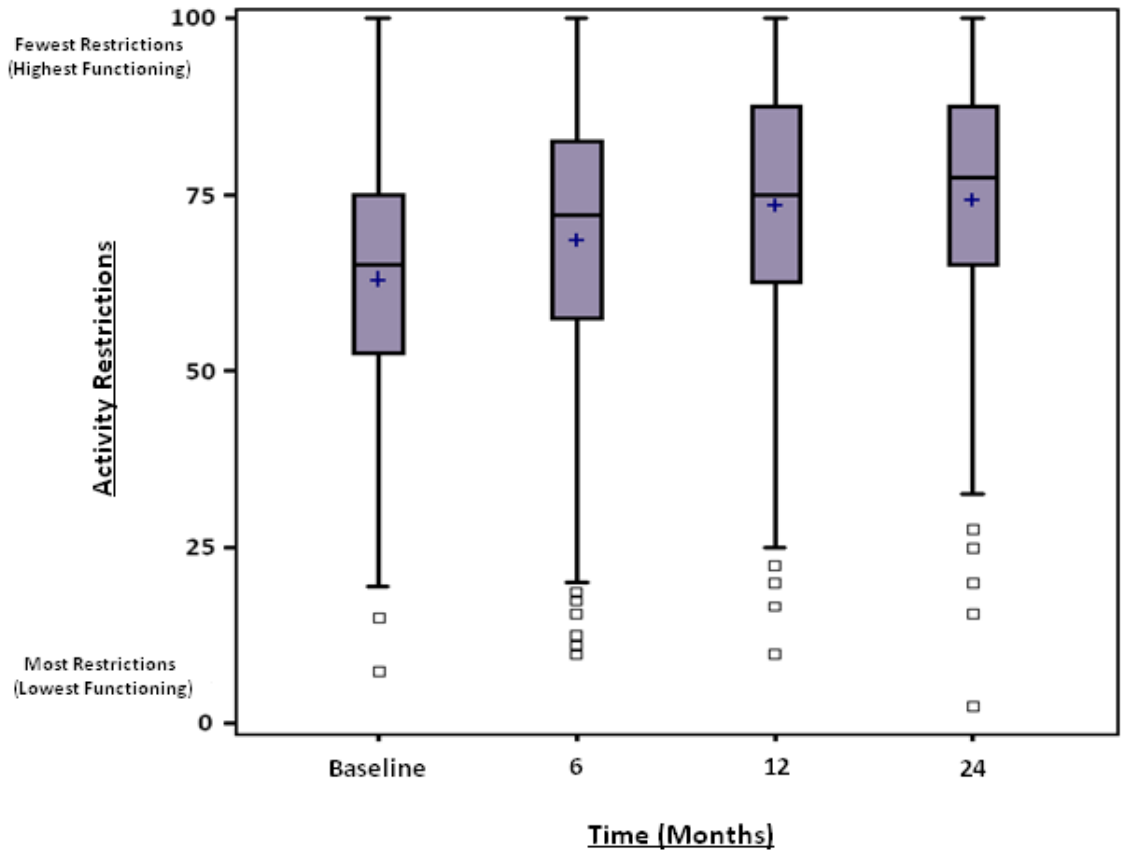
Note. SE= standard error, *p<0.05 **p< 0.001; ***P<0.0001
Predictive Model: $Y(tweeks)= 61.18+ 0.30t-0.0017t^2$

Table 4.6: Results of Fitting a Non-Linear mixed Effects model Including Child and Family Factors, and Interaction Terms on Activity Restrictions using Backward Elimination

Effect	Between-Subject	Within-Subject
Child Factors		
Child Age	**0.84(0.35)**	
Epilepsy Severity (GASE)	**2.03(1.01)**	**0.99 (0.49)**
Co-morbid Condition	**-15.73(4.30)**†	
Side Effects of AEDs		0.63 (0.43)
Convulsive Status Epilepticus	4.14(2.85)	
Exclusively nocturnal seizures	**3.93 (1.61)**	
Falls or injuries during seizures	-2.14(1.40)	-1.08(0.64)
Family History of Epilepsy	-2.01(1.29)	
Generalized Epilepsy Syndrome*	**3.06 (1.53)**	
Undetermined Epilepsy Syndrome*	6.45(3.80)	
Family Factors		
Parent Age	**-0.31(0.14)**	
Parental Worry and Concern, CHQ	**0.19(0.05)**†	**0.10 (0.02)**
Family Resources, FIRM	0.11(0.09)	**0.21 (0.07)**
Family Functioning, APGAR		0.27(0.20)
Annual Household Income	**0.50(0.23)**	
Highest Level of Education Completed[n]	0.53(1.23)	
Employment Status[a]	1.67(1.20)	
Interactions		
Co-morbid Condition x Parental worry and concern	**0.17(0.08)**	

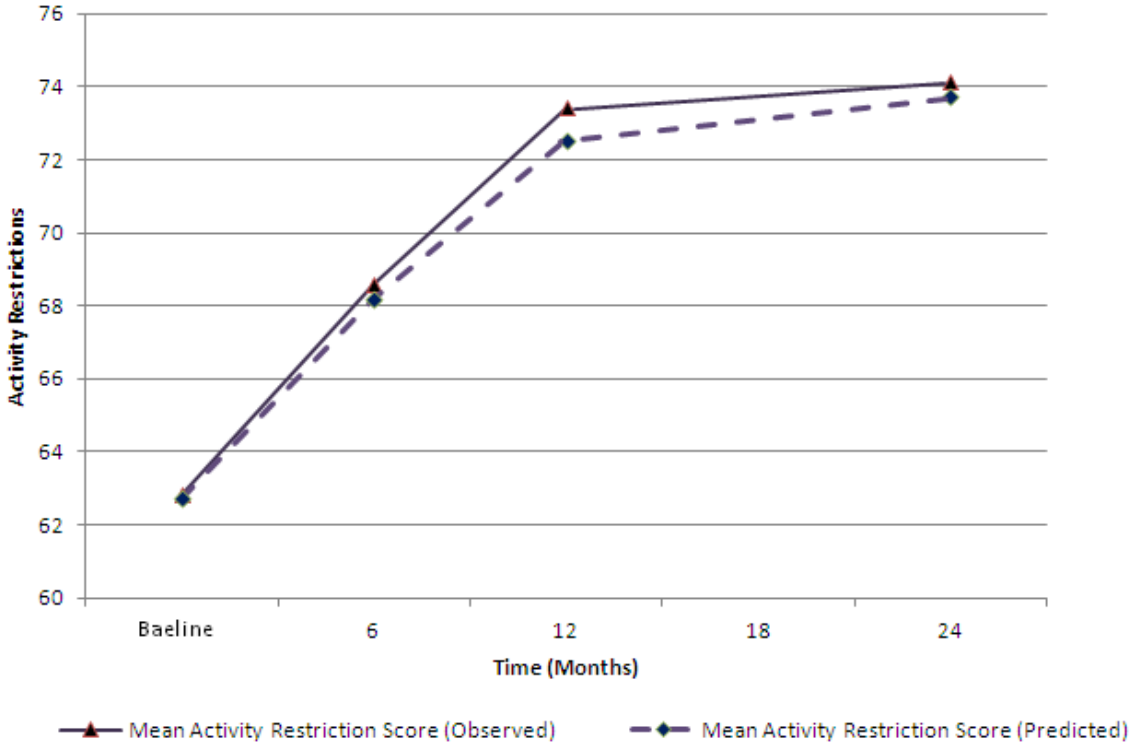
Effects represent, Estimate(Standard Error).
Significant results are bolded ($p<0.05$)
Exclusively nocturnal seizures, convulsive status epilepticus and co-morbid diagnosis are binary (Yes/No) with reference group, No.
† = effect included in interaction term in the model.
Reference groups: *partial epilepsy syndromes, [n] completed college/university [a]unemployed.
Positive values indicate a one unit change in the predictor is associated with an improvement in or fewer perceived activity restrictions.

Figure 4.1: Box and Whisker Plot Showing Change in Distribution of Parent Perceived Activity Restriction Scores from Baseline to 24 Months



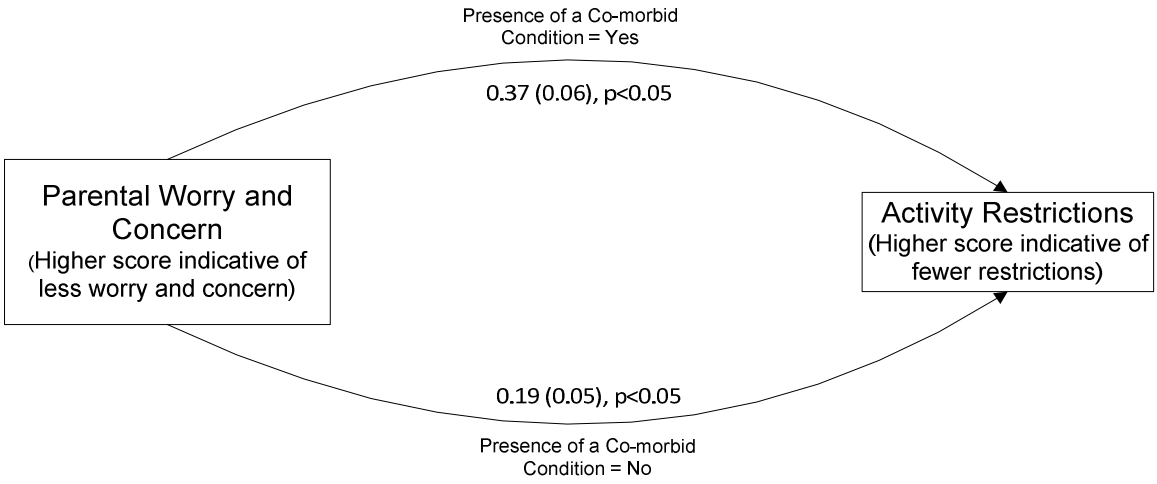
Note: Mean = +, Median = center most horizontal line, Outliers = □

Figure 4.2: Observed and Model Predicted Mean Activity Restriction Scores from Baseline to 24 Months



Note. For Time the average date of completion in weeks was used to calculate the model predicted scores (Time 1 = 5.3 weeks, Time 2 = 27.7 weeks, Time 3 = 55.1 weeks, Time 4 = 107.8 weeks)

Figure 4.3: Presence of a Co-morbid Condition Moderating the Effect of Parental Worry and Concern on Parent's Perceptions of Activity Restrictions



Chapter 5

Discussion

This chapter summarizes the results of this study and the potential implications of the findings. The strengths and limitations of the study are then discussed, followed by conclusions and future directions.

5.1 Study Purpose

The purpose of this study was to examine trajectories and predictors of parents' perceptions of their child's activity restrictions in the first two years post epilepsy diagnosis. The focus was on activity restrictions that the parent believed their child required because of his/her epilepsy. By assessing predictors of parents' perceptions this thesis provides preliminary evidence as to whether the parent of a child with epilepsy may act as a barrier to their participation in physical and social activities, which are important to healthy growth and development in childhood. Ideally parents' perceptions would have been associated with exclusively epilepsy-related variables or important child factors and not characteristics of the family or parent. The significant association of family factors could indicate that parents unnecessarily restrict their child from normal childhood activities.

While there is a strong suggestion in the literature that children with epilepsy are less active than their peers (Wong & Wirrell, 2006; Yu et al., 2006; Dubow & Kelly, 2003; Arida et al., 2008), no previous study has examined why this difference may exist. Childhood is a critical period for physical and psychological growth and development

and the main factor determining activity participation during this period is parents' decision. They are in a position to facilitate or restrict their child's participation. Moving into adolescence, the influence on activity involvement begins to shift from the parent to the child's peer group. It is important that a child with epilepsy and their parents understand the degree to which epilepsy may impact their ability to participate, which emphasizes education as a critical component of patient care (Austin et al., 2002; Long et al., 2000).

5.2 Summary of Results

Initial findings were that parents' perceptions of restrictions lessened on average from the point of epilepsy diagnosis to 24 months, although the change tapered off after 1 year. This suggests that there may be opportunity, in the first year following diagnosis to positively influence their perceptions. This trend was expected, as physicians and parents alike are likely to be most cautious in the first months following diagnosis. Additionally, in the majority of cases, the child's epilepsy will become increasingly well-controlled over time (Shorvon & Luciano, 2007). Changes in epilepsy-related factors and important family factors likely explain, at least partially, some of why their perceptions improved on average over the study period. In this study, an improvement in an individual child's severity of epilepsy over the two year period was significantly associated with parents' perceiving fewer restrictions. In addition, a decrease in a parent's level of worry and concern and an increase in a family's level of resources, over the 24 months, were significantly associated with parents' perceptions of fewer restrictions. The parent's level of worry and concern is a factor that could be positively affected early on post-diagnosis through education and discussion during the medical encounter to change perceptions.

While it is expected that parents will take some time to become comfortable with their child's epilepsy and how it will affect their child's life, fewer unnecessary restrictions will be perceived the sooner this adaptation occurs. The longer that the unnecessary activity restrictions persist, the greater the impact is likely to be on the child's HRQL.

There is no well-established guideline for identifying a clinically important difference for the QOLCE subscales. Speechley et al. (2012) used a standard error of measurement (SEM) to identify clinically meaningful change. Scores of at least 1 SEM are interpreted as clinically important when used with robust HRQL measures (Kleinbaum & Klein, 2002). In this study the average activity restrictions score changed more than 1 SEM (8.24), from 62.9(18.5) at baseline to 74.1(18.6) at 24 months post-diagnosis, indicating a clinically significant improvement in parents perceptions in the first two years post-diagnosis. This standard error of measurement value was calculated by Speechley et al. (2012) using the same dataset analyzed in this thesis.

The finding that parent's perceive fewer activity restrictions on average over the first two years post-diagnosis suggests that the duration of epilepsy is significantly negatively associated with parents' perceptions of restriction. This is unlike previous studies, which either did not find a significant correlation (Griffiths et al., 2007; Connolly et al. 2006; Sherman et al., 2006), or found that a longer duration of epilepsy was associated with greater activity restrictions (Sherman et al., 2002; Carpay et al., 1997). In the present study, by sampling incident cases, the children's epilepsy is less well established. In prevalent cases perceptions may have become more or less stable beyond two years post-diagnosis. Also children diagnosed with epilepsy under 4 years old, who represent the most catastrophic cases of epilepsy (Shield, 2000) were excluded in this study. In the

studies that found a significant positive association children diagnosed at a very young age would likely make up the majority of those children with the longest duration of epilepsy, influencing the direction of this association. None of the child or family factors interacted with time in this study. The effect that individual factors had on parents' perceptions was relatively constant over the first two years post-diagnosis. This finding suggests that the child and family factors found to be associated with parents' perceptions are consistent regardless of time since diagnosis in the first two years post-diagnosis.

The child factors, average age, presence of a co-morbid condition (cognitive, motor, or behavior problems), timing of seizures (exclusively nocturnal seizures versus not), type of epilepsy syndrome, average epilepsy severity and a change in epilepsy severity over the 24 months were significantly associated with parent's perceptions of their child's activity restrictions. As hypothesized, younger children were perceived to require significantly more activity restrictions. Despite previous studies not finding a significant association between activity restrictions and age (Sabaz et al., 2003a; Carpay et al., 1997; Griffiths et al., 2007; Nadkarni et al. 2011), it was hypothesized in this thesis that parents would perceive greater restrictions for younger children, because they are less capable of judging risk and more vulnerable to injury than older children. The lack of a significant result in previous studies may have been because the previous study samples were not restricted to younger children and included adolescents. The effect age has on parents' perceptions may disappear once the child reaches adolescence.

Also as hypothesized, children who had exclusively nocturnal seizures were perceived to require fewer restrictions. The only previous study to include seizure timing as a factor did not find an association (Carpay et al., 1997). Children who have exclusively nocturnal

seizures are at minimal risk during daytime activities and should require fewer restrictions. Children with generalized epilepsy syndromes were perceived to require fewer restrictions than those with partial epilepsies. This finding may be because generalized syndromes are associated with better seizure control outcomes, on average, than partial syndromes (Semah et al., 1998).

The presence of a co-morbid condition was associated with greater activity restrictions and interacted with parental worry and concern. This finding is consistent with previous studies (Sherman et al., 2006; Sabaz et al., 2001). Adjusting for the presence of a co-morbid condition in the model was important, because of its association with activity restrictions. If it was not included in the model it would have acted as a confounder in the association of activity restrictions and other factors. Finally, a decrease in epilepsy severity over the 24 months was significantly associated with a decrease in perceived activity restrictions and less severe average epilepsy severity was associated with fewer restrictions. The association of these epilepsy-related variables and the presence of a chronic condition with parents' perceptions coincide with recommendations on activity restrictions for children with epilepsy presented in published guidelines (ILAE Commission Report, 1997).

Unlike previous studies, seizure frequency was not included as a child factor, but overall severity of epilepsy rated by the child's neurologist was included. This variable incorporates seizure frequency and was believed to be more important in the association with activity restriction. Overall severity of epilepsy should be the most important individual variable considered when determining necessary activity restrictions for an individual child with epilepsy. According to O'Donohoe (1983), restrictions imposed on

a child with epilepsy should be in proportion with the severity of his/her epilepsy. A single covariate that assesses severity of epilepsy has not been examined in previous studies because a validated measure has not previously existed.

The variables seizure frequency and intensity, previously found to be positively associated with activity restrictions, were incorporated into the severity of epilepsy measure utilized here, which was found to be significantly positively associated with activity restrictions. The association of epilepsy severity is consistent with previous studies that found groups of children with more severe epilepsies were perceived to require significantly more restrictions (Sabaz et al., 2003a; Sabaz et al., 2003b). Higher current number of AEDs (Griffiths et al., 2007; Sherman et al., 2006) and side effects of AEDs (Carpay et al. 2002) were previously found to be positively associated with activity restrictions, but were not significant in the present study. It is possible that these effects were captured by the epilepsy severity variable. In previous studies that did not control for other epilepsy-related variables, current number of AEDs may have acted as a proxy for epilepsy severity with a greater number of AEDs indicative of a greater severity of epilepsy.

Similar to previous studies, sex of the child (Carpay et al., 1997; Griffiths et al., 2007; Sabaz et al., 2003a) was not significant. The perception that girls are more fragile than boys may be less common than it previously was thought. Other child factors that were examined but were not found to be significant include: convulsive status epilepticus, family history of epilepsy, and frequency of falls or injuries during seizures. These factors are likely less important in affecting parents' perceptions of their child's activity restrictions than those that were significant, such as epilepsy severity and syndrome type

that have a greater impact on risk of injury during activity (ILAE Commission Report, 1997). The frequency of falls or injuries during seizures was expected to be strongly associated with parents' perceptions of activity restrictions because in theory it should directly reflect risk, but may be less important than epilepsy severity and timing of seizures which might capture *severity* of injuries from falling rather than just *frequency*.

One of the objectives of this study was to determine if family, in addition to, child factors were associated with parents' perceptions. Controlling for important child factors, there were statistically significant associations between several family factors and parents' perceptions. Parent age and annual household income over the 24 months were significantly positively associated with perceived activity restrictions. The finding that older parents are more likely to perceive greater restrictions for their child may be because they are more likely to be rigid or have more traditional way of thinking and/or are less capable of getting involved themselves with their child's activity, because of their health status or time constraints. The relationship with annual household income, suggests that families with lower socioeconomic status perceive fewer restrictions.

As hypothesized, an increase in family resources over the 24 months, as assessed with the FIRM, was significantly negatively associated with perceived activity restrictions. Both a change in parental emotional worry and concern and average level of parental worry and concern over the 24 months were significantly positively associated with parent's perceptions. For a parent of a child with a co-morbid condition, parental worry and concern had a greater effect on parent's perceptions of their child's activity restrictions.

Few studies have examined the association between family factors and activity restrictions. The only previous study that examined parental-impact emotional (worry and concern) found it to be significantly positively correlated with parents' perceived activity restrictions (Connolly et al., 2006). In their study, Nadkami et al. (2011) examined maternal education, and found that literate mothers perceived significantly more activity restrictions, assessed using the QOLCE, than illiterate mothers. In the present study there was no significant difference in perceptions comparing parents who had completed college/university to lower levels of education completed.

Family factors that had not been examined previously, and were not significantly associated with parents' perceptions in the present study, were: parent's sex, employment status, marital status, depression, family functioning, and family demands. There were very few male respondents (<10%), so the sample size for fathers was likely too small to make comparisons with mothers. Current employment and marital status were not significant but may have impacted parents' level of worry and concern and family resources, which were both significant. Family functioning and demands are distal factors that ideally should not have influenced parents' perceptions, but were included because they have been shown to influence parents' psychological state (Rodenburg et al., 2007) and be associated with overprotective parenting (Chapieski et al., 2005).

Compared to previous studies that examined activity restrictions without implementing an intervention, the mean score of the sample at 24 months (74.12(18.57)) was relatively high (Sabaz et al., 2003a; Sabaz et al., 2003b; Connolly 2004; Sabaz et al., 2000) The only study that had a similar cross-sectional mean score was done by Connolly et al. (2006), examining children with benign rolandic epilepsy (75.95(21.12)). The high score

found at 24 months was likely because the sampling strategy utilized resulted in a sample composed of children with relatively less severe epilepsy than the majority of previous studies. The sample was restricted to children at least 4 years old, and the most catastrophic cases of childhood epilepsy occur by age 4 (Shield, 2000). In addition, at the time of diagnosis children with other major co-morbid disorders that would have an impact on quality of life were excluded, which could have contributed to a less severe cases of epilepsy.

The results of the attrition analysis showed that participants lost to follow-up did not differ significantly from those who completed the 24 month questionnaire on any child characteristics at baseline. Parents lost to follow-up were significantly younger, reported higher depressive symptoms, were less likely to be married and less likely to have completed a college/university education than those who completed the study. They also had fewer resources, more demands and lower household incomes at baseline on average than parents who completed the study, suggesting that these families were probably functioning poorly relative to those who remained in the study. Based on the findings that fewer resources (a decrease in resources over time) and lower incomes are associated with greater restrictions, the attrition may have implications for interpreting the findings. Although no important child characteristics differed, based on differences in family factors, the average decrease in activity restrictions that was observed may not have been as great if these families stayed in the study.

5.3 Implications

The results of this study provide preliminary evidence suggesting that parents of children with epilepsy may unnecessarily restrict their child from physical and social activities. This claim is based on the finding that factors not related to the child's epilepsy, but of the parent and family, were associated with parent's perceptions of their child's activity restrictions. Thus, there may be an opportunity to remove unnecessary activity restrictions placed on children with epilepsy in the first two years after diagnosis, and possibly beyond, by targeting the parents. Parents could be targeted for educational interventions through discussion and education with their neurologist or other members of the health care team. In addition to educating the family about necessary activity restrictions resulting from epilepsy, the benefits of activity involvement should be emphasized to parents, including the possible positive impact on seizure frequency as a means of motivating parents to follow through with removing unnecessary restriction.

Previous studies have identified that individuals and parents of children with epilepsy lack knowledge about epilepsy (Long et al., 2000; Frizzell et al., 2011; Shore et al., 2010). Several studies have evaluated the efficacy of educational programs developed to improve patients' and their families' knowledge and understanding about their epilepsy (Way & Pfafflin, 2002; Helgeson et al., 1990; Lewis et al., 1989; Austin et al., 2002). These studies have consistently found that educational sessions significantly improve knowledge. Lewis et al (1989) found that a family-focused educational program enhanced parent and children's knowledge in many areas related to management of seizures and unnecessary restriction of their social and play activities. The findings of this

thesis reinforce the importance and need for families with a child with epilepsy to be educated about epilepsy.

Clinical recommendations state the majority of children with epilepsy should not be held back from physical and social activities and that the potential benefits of activity for these children largely outweigh the risks. Based on these recommendations and the mild severity of epilepsy in the sample studied here, there may be room for additional improvement in parents' perceptions following 24 months post-diagnosis. In the first two years of treatment, the long-term pattern of seizure control is largely established (Hauser et al., 1996). Not only may there be opportunity to remove some level of unnecessary restrictions in the first two years after diagnosis by targeting the parents, there may also be opportunity beyond the two year mark and in prevalent cases.

This study has also identified characteristics of families and parents that can be used to target particular families who are at the greatest risk of restricting their child or being misinformed of what restrictions are necessary. These factors include; older parents, families with higher annual household incomes, families with fewer resources, and parents who display greater levels of worry and concern. It is important that educating a family about epilepsy is personalized and put in a context that is relevant to the family and individual. Frizzell et al. (2011) found that following two 2-hour personalized education programs administered to adolescents with epilepsy (n=30), their general knowledge of epilepsy, self-knowledge of syndrome, attitudes towards epilepsy, and seizure self-efficacy significantly improved.

Incorporating a discussion of activity restrictions as part of family centered care (FCC) should be considered as an option to remove unnecessary restrictions placed on children with epilepsy. FCC is based on the understanding that the family is the child's primary source of strength and support and that they play a vital role in ensuring the health and well being of children (American Academy of Pediatrics, 2012). This type of care is grounded in information sharing, collaboration, and a mutually beneficial partnership, among the child, the family and health care providers. The family and providers work together, making the caregiver an integral part of the health care team. FCC has been shown to be associated with improved health and well-being, improved satisfaction, and greater efficiency for children with special needs and their families (Kuhlthua et al. 2011). Providing an opportunity for parents to discuss their concerns and experiences about their child's participation in physical and social activities can be beneficial to all parties involved. The health care professional can effectively incorporate information provided by parents and address their concerns when advising them, in order to remove unnecessary activity restrictions in children with epilepsy.

5.4 Strengths and Limitations

This study had several strengths. It was the first to examine child and family factors associated with parent's perceptions of their child's activity restrictions in the first 24 months post-epilepsy diagnosis. No previous prospective study has followed a sample from diagnosis, examining activity restrictions in incident cases. In addition, the focus of previous studies has been on child factors and in cases where family factors were examined only a select few were included and assessed using correlations. By restricting the sample to newly diagnosed children, trends and trajectories early in the illness process

were identified and it provided an ideal window of opportunity for interventions aimed at improving child health-related quality of life.

The design of this study had several strengths which allowed it to overcome some of the methodological shortcomings of previous research. Previous studies examining activity restrictions in children with epilepsy were relatively small-scale, regional, cross-sectional, and focused on specific subsamples of children with epilepsy. This study's relatively large sample size and strong response and retention rates increase the external validity of the findings. The HERQULES data set was collected using a repeated measures design, which increases the validity of the results and allowed us to assess change over time and both between- and within-subject effects. The measure used to assess activity restrictions was a well-validated and reliable instrument. In addition, using neurologist report to collect child factors minimized potential bias from parent-report. Finally, using multilevel modeling made it possible to retain subjects in the analysis for whom complete data were not available.

There are also a few limitations that need to be considered. The study sample was recruited from paediatric neurology practices and may not be representative of all families with a child with epilepsy, potentially limiting external validity. However, due to the feasibility constraints in designing population-based studies, more practical strategies to get a representative sample are required. Speechley et al. (1999) demonstrated that in the absence of a population-based registry, it is feasible to recruit a representative population-based sample of recently diagnosed children with epilepsy by targeting paediatric neurologists. In that study, family physicians practicing in southwestern Ontario, reported they refer between 80-99% of their patients with childhood epilepsy to

a paediatric neurologist. The study sample was also limited to children who were diagnosed with epilepsy between the ages of 4 and 12 years, so it is not known whether the results of this study are generalizable to older and younger children. Generalizability is also limited to parents and children of parents with sufficient English language skills.

An additional limitation of this study is that there was no measure of how much activity the children actually participated in. The assumption is being made that parents' perceptions of their child's activity restrictions directly affects the frequency of the child's involvement. In reality, we cannot know whether their perceptions directly translate into action. This assumption is believed to be reasonable given the influence of the parent over their child in childhood. The child's parents are in the unique position to facilitate or restrict their child's involvement in physical or social activities, which makes them the ideal person to target for increasing activity involvement of children with epilepsy. Also, it is reasonable to assume that if a parent believes their child is able to participate they are more likely to encourage or facilitate their child's involvement and less likely to act as a barrier.

There were also some variables omitted in this study that may have been important predictors of parents' perceptions of activity restrictions, including, family size, birth order, and presence of other children in the family with epilepsy. A final limitation is that there was no measure of how much restriction parents perceived their child to require prior to their diagnosis of epilepsy.

5.5 Conclusions and Future Directions

This study demonstrated that parents of children with epilepsy may unnecessarily restriction their child from participating in physical and social activities, which are an important part of healthy growth and development in childhood. In addition to several important child factors, several family factors were significantly associated with parents' perceptions, providing evidence that parents may prevent their child from participation if they perceive their child is more restricted because of their epilepsy than he/she really is. This finding is supported by previous studies that have found parents of children with epilepsy tend to adopt overprotective parenting styles (Chapieski et al., 2005; Rodenburg et al., 2005b; Shore et al., 2010; Williams et al., 2003).

In this study many of the most important epilepsy-related variables that were hypothesized to be associated with parents' perceptions were significant, suggesting that restrictions may be well adapted to seizure-related risk. This finding is contrary to Carpay et al. (1997) who concluded, based on their study findings, that restrictions probably were not optimally adapted to seizure-related risks. This is an encouraging finding, suggesting an increase in parents' knowledge. However, two years post-diagnosis, and after relative stability of parents' perceptions, there was room for additional improvement in their perceptions. This finding may indicate a lack of understanding by the parent of how epilepsy affects their child's ability to participate, suggesting they believe that more total activity restrictions are necessary than recommended by clinical guidelines (Commission of Pediatrics of the ILAE, 1997). This is consistent with previous study findings that individuals with epilepsy and parents of children with epilepsy are not that knowledgeable about epilepsy (Shore et al., 2010; Long et al., 2000).

The findings of this study stress the importance of educating the child and their family about how epilepsy affects them, the risks and benefits of activity and what activity restrictions are necessary. It is important that parents of children with epilepsy are educated and have easy access to information. Educational interventions have been shown to be effective (Frizzell et al., 2011; Helgeson et al., 1990; May & Pfafflin, 2002), and are an important part of patient care. If there is an opportunity to remove unnecessary restrictions by targeting the parents it provides a means by which the potentially negative impact on development (physical and social) from lack of activity involvement can be reduced. Removing unnecessary restrictions could also decrease co-morbidities in children with epilepsy and lead to improvements in their HRQL.

This study was only able to provide preliminary evidence as to whether parents of children with epilepsy are limiting their child's participation in normal childhood activities. The goal of this study was to examine parent's perceptions of their child's activity restrictions and from their perceptions and factors associated with those perceptions speculate whether they might unnecessarily restrict their child from participation. A future study designed purposefully to determine what the barriers to physical and social activities are in younger children with epilepsy would provide stronger evidence to what specific barriers exist. Once these barriers to activity are identified they can be targeted to increase participation, as a means of improving the child's HRQL.

Through future research there is an opportunity to build on the findings presented in this thesis. A future study examining activity restrictions in prevalent cases of children with epilepsy would determine with more certainty whether there is an opportunity to remove

unnecessary restrictions in children who have been living with epilepsy for various lengths of time. Another direction of future research could be to assess the effectiveness of parent targeted interventions, such as incorporating a discussion of activity restrictions during family centered care, aimed at removing unnecessary restrictions. Specifically, a study could examine whether restrictions are impacted by the intervention and if there is an impact on child health outcomes. Future research should also assess the child's perspective on their activity restrictions, and their belief of how restricted they are and/or what restrictions are necessary because of their epilepsy. Finally it is important to examine other potential barriers to activity, such as the children themselves, stigma, and health care providers.

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Appendices

APPENDIX A: Literature Search Strategy

A.1: Activity Restrictions Search Strategy

The search strategy shown in Appendix A.2 was used to identify any published article that assessed activity restrictions in children or adolescents with epilepsy. The electronic databases MEDLINE and EMBASE were searched simultaneously using the OVID system. Search strategies using the same key words were also used to search the additional databases of CINAHL and Web of Science. Different combinations of the following keywords were used: child, children, childhood, adolescent, childhood epilepsy, epilepsy, HARCES, hague restrictions in childhood epilepsy scale, QOLCE, quality of life in childhood epilepsy questionnaire, physical restrictions, activities of daily living, motor activity, physical activity, exercise, sports, (See Appendix A.2). Where appropriate all Medical Subject Heading (MeSH) terms were exploded to broaden the search for relevant studies. The keywords: assessment, evaluation, measurement were also used to narrow down the search results to studies that actually quantitatively assessed the restriction. In addition, the references of relevant articles were reviewed to identify further studies examining physical restrictions in childhood epilepsy. The result of each stage of the search methodology is illustrated in Appendix A.2.

To be included in the literature review the article had to meet the following criteria: (1) report on parent-reported activity restrictions in childhood epilepsy (2) the sample included children or families of children with epilepsy ≤18 years of age; and (3) be written in English. Articles were excluded from the review if they: (1) were not written in English (2) did not focus on a childhood epilepsy population (3) did not include a measure of activity restrictions. A detailed account of the excluded articles is shown in Appendix A.2.

The final literature review consisted of 21 article assessing activity restrictions in children or adolescents with epilepsy. Of the 21articles, 8 were studies of the effect of treatment on activity restrictions (4 surgical and 4 non-surgical treatments), 1 study assessed the

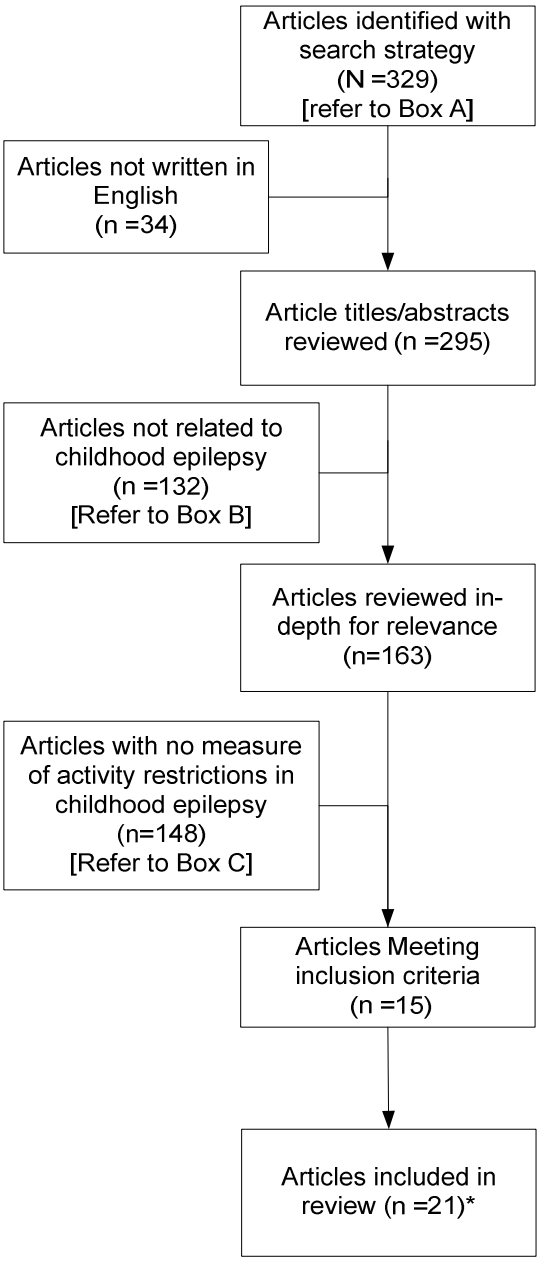
relationship between activity restrictions and parent-perceived AED complaints, 1 examined the association between specific parent and child factors, and activity restrictions, 2 were studies of the relationship between activity restrictions & cognitive impairment in children with epilepsy, and 5 were studies assessing activity restrictions in specific epilepsy subsamples. An additional 4 studies were designed to validate either the QOLCE or HARCES.

A.2: Details of Search Strategy for Articles Assessing Physical Restrictions in Childhood Epilepsy Using OVID (MEDLINE & EMBASE)

1. Children OR child OR childhood OR adolescent OR adolescen*
2. childhood epilepsy OR epilepsy OR epileps* OR epilep*
3. physical restrictions OR activities of daily living OR motor activity OR physical activit* OR exercise OR sports
4. HARCES OR QOLCE OR hague restrictions in childhood epilepsy scale OR quality of life in childhood epilepsy questionnaire
5. (#1) AND #2
6. (#3) AND #5
7. (#4) OR #6
8. Assessment OR evaluation OR measurement
9. (#8) AND #7

Databases: OVID (Medline, EMBASE), CINAHL, Web of Science. (*) used to search for variations of the preceding root word. Search utilized Boolean operators: AND, OR.

A.3: Search Process to Identify Articles Assessing Activity Restrictions in Children with Epilepsy for Review



Details of articles deemed irrelevant for current analysis

Box A.
- OVID; MEDLINE & EMBASE (n=186)
- WebofScience (n=110)
- CINAHL (n=32)

Box B.
- Adult sample (n=43)
- Childhood condition other than epilepsy (n=70)
- Physiology of neurologic conditions (12)
- Animal study (n=3)
- Reviews of research methodology Issues (n=3)
- Drug Review (n=1)

Box C.
- No assessment of activity restrictions (n=146)
- Recommended guidelines of activity restrictions for children with epilepsy (n=2)

*Additional articles identified through reviewing references of articles meeting inclusion criteria (n=15) and additional articles identified (n=6)

A.4: Additional Search Strategies for Articles on Recommended Activity Restrictions, Articles Assessing Physical and Social Activities and Articles Assessing Parent Adaptation in Childhood Epilepsy

All additional searches for articles also utilized the databases OVID, CINAHL, and Web of Science. A condensed version of the search strategy shown in Figure 3, that excluded the fourth line of keywords, was used to identify studies that assessed the effect of physical activity or exercise in children with epilepsy. It was also used to identify articles assessing the risks or benefits of physical activity in this population. Closely tied to the search strategy shown in Figure 3, was a search aimed at identifying articles that present guidelines of activity restrictions in childhood epilepsy. The keywords, *management, recommendation* and guideline** were utilized in addition to those displayed in Figure 3. Seven articles reviewing what restrictions are indicated or recommended for children with epilepsy were included. There were also three articles included that focused on recommendations for sports participation in childhood epilepsy.

The next additional search was focused on identifying all articles that assessed level of physical activity in childhood epilepsy, as well as articles reviewing the risks and benefits of physical activity for children with epilepsy. Different combinations of the following keywords were used: *child, children, childhood, adolescent, childhood epilepsy, epilepsy, motor activity, physical activity, exercise, sport*, health behaviour, risk* and benefit**. Articles included were limited to those written in English. Three articles fitting these criteria were identified. Do to the lack of literature on level of physical activity in childhood epilepsy, an additional convenience search was done to identify articles assessing level of physical activity in chronic childhood conditions collectively. The key phrase, 'chronic childhood conditions', was substituted in place of epilepsy OR childhood epilepsy in the search strategy.

A similar search was aimed at identifying articles that assessed participation in social activities, as well as risks and benefits of social activity participation for children with epilepsy. Different combinations of the following keywords were used: *child, children, childhood, adolescent, childhood epilepsy, epilepsy, social (play, participation,*

involvement, activit), 'child behaviour checklist', CBCL, leisure activity, and recreational activity.*

Finally, a search was conducted to identify articles assessing parent adjustment to childhood epilepsy, with a focus on common parenting practices in childhood epilepsy. The goal of this search was to get a general grasp on the main themes found in the literature. Different combinations of the following keywords were used: *parent, caregiver, childhood epilepsy, epilepsy,* adaptation, parent* adjustment, maternal anxiety, overprotection, parenting style*.

APPENDIX B: HARCES and Physical Restrictions subscale of the QOLCE

The HARCES					
Question		*Response Category*			
		1	**2**	**3**	**4**
1	How much extra supervision is needed in your child's daily activities?	None	A Little	Some	A Lot
2	Does your child require special precautions in daily activities (such as wearing a helmet)?	Never	Some-times	Usually	Always
3	*Does the epilepsy influence the freedom of your child:* To play in the house?	*Not at All*	*A Little*	*Some*	*A Lot*
4	To play outside?	"	"	"	"
5	To go swimming?	"	"	"	"
6	To participate in sports activities (excluding swimming)?	"	"	"	"
7	In traffic (such as riding a bicycle)?	"	"	"	"
8	To stay elsewhere overnight (with friends or family)?	"	"	"	"
9	To go to parties?	"	"	"	"
10	To participate in physical education?	"	"	"	"
Each question has four adjectival response categories providing a score of 1 (most favorable) to 4 (most unfavorable)					

QOLCE Section 1.1
YOUR CHILD'S PHYSICAL ACTIVITIES
The following questions ask about physical activities your child might do.
1.1 In his/her daily activities during the past 4 weeks, how often has your child:

		Very Often	Fairly Often	Some-times	Almost Never	Never	N/A
a.	Needed more supervision than other children his/her age?	"	"	"	"	"	"
b.	Needed special precautions (i.e. wearing a helmet)?	"	"	"	"	"	"
c.	Played freely in the house like other children his/her age?	"	"	"	"	"	"
d.	Played freely outside the house like other children his/her age?	"	"	"	"	"	"
e.	Gone swimming? (i.e. swam independently)	"	"	"	"	"	"
f.	Participated in sports activities (other than swimming)?	"	"	"	"	"	"
g.	Stayed out overnight (with friends or family)?	"	"	"	"	"	"
h.	Played with friends away from you or your home?	"	"	"	"	"	"
i.	Gone to parties without you or without supervision?	"	"	"	"	"	"
j.	Been able to do the physical activities other children his/her age do?	"	"	"	"	"	"

APPENDIX C: Ethics Approval from the University of Western Ontario

Office of Research Ethics

The University of Western Ontario
Room 00045 Dental Sciences Building, London, ON, Canada N6A 5C1
Telephone: [redacted] Fax: [redacted] Email: [redacted]
Website: www.uwo.ca/research/ethics

Use of Human Subjects - Ethics Approval Notice

Principal Investigator: Dr. K.N. Speechley
Review Number: 10069E
Revision Number:
Protocol Title: Health-Related Quality of Life in Children with Epilepsy: The First Two Years After Diagnosis Through Parents' Eyes
Department and Institution: Paediatrics, Children's Hospital of Western Ontario
Sponsor: CIHR
Approval Date: 18-Nov-03
End Date: 31-Mar-08
Documents Reviewed and Approved: UWO Protocol, Letters of Information & Consent
Documents Received for Information:

This is to notify you that the University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) which is organized and operates according to the Tri-Council Policy Statement and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has received and granted expedited approval to the above named research study on the date noted above. The membership of this REB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

This approval shall remain valid until end date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the UWO Updated Approval Request Form.

During the course of the research, no deviations from, or changes to, the protocol or consent form may be initiated without prior written approval from the HSREB except when necessary to eliminate immediate hazards to the subject or when the change(s) involve only logistical or administrative aspects of the study (e.g. change of monitor, telephone number). Expedited review of minor change(s) in ongoing studies will be considered. Subjects must receive a copy of the signed information/consent documentation.

Investigators must promptly also report to the HSREB:

a) changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;

b) all adverse and unexpected experiences or events that are both serious and unexpected;
c) new information that may adversely affect the safety of the subjects or the conduct of the study.

If these changes/adverse events require a change to the information/consent documentation, and/or recruitment advertisement, the newly revised information/consent documentation, and/or advertisement, must be submitted to this office for approval.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interset, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

Chair of HSREB (Expedited): Dr. Paul Harding

Karen Kueneman, BA (Hons), Ethics Officer HSREB (Expedited)
E-mail: [redacted]

Faxed (Y)N
Date: Nov. 19/03

Office of Research Ethics

The University of Western Ontario
Room 4180 Support Services Building, London, ON, Canada N6A 5C1
Telephone: [illegible] Fax: ([illegible] Email: e[illegible]
Website: www.uwo.ca/research/ethics

Use of Human Subjects - Ethics Approval Notice

Principal Investigator: Dr. K.N. Speechley
Review Number: 10069E **Revision Number:** 5
Review Date: August 20, 2008 **Review Level:** Expedited
Protocol Title: Health-Related Quality of Life in Children with Epilepsy: The First Two Years After Diagnosis Through Parents' Eyes
Department and Institution: Paediatrics, Children's Hospital of Western Ontario
Sponsor: CIHR
Ethics Approval Date: August 20, 2008 **Expiry Date:** September 30, 2009
Documents Reviewed and Approved: Revised study team.
Documents Received for Information:

This is to notify you that The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced revision(s) or amendment(s) on the approval date noted above. The membership of this REB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the UWO Updated Approval Request Form.

During the course of the research, no deviations from, or changes to, the protocol or consent form may be initiated without prior written approval from the HSREB except when necessary to eliminate immediate hazards to the subject or when the change(s) involve only logistical or administrative aspects of the study (e.g. change of monitor, telephone number). Expedited review of minor change(s) in ongoing studies will be considered. Subjects must receive a copy of the signed information/consent documentation.

Investigators must promptly also report to the HSREB:

a) changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;
b) all adverse and unexpected experiences or events that are both serious and unexpected;
c) new information that may adversely affect the safety of the subjects or the conduct of the study.

If these changes/adverse events require a change to the information/consent documentation, and/or recruitment advertisement, the newly revised information/consent documentation, and/or advertisement, must be submitted to this office for approval.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

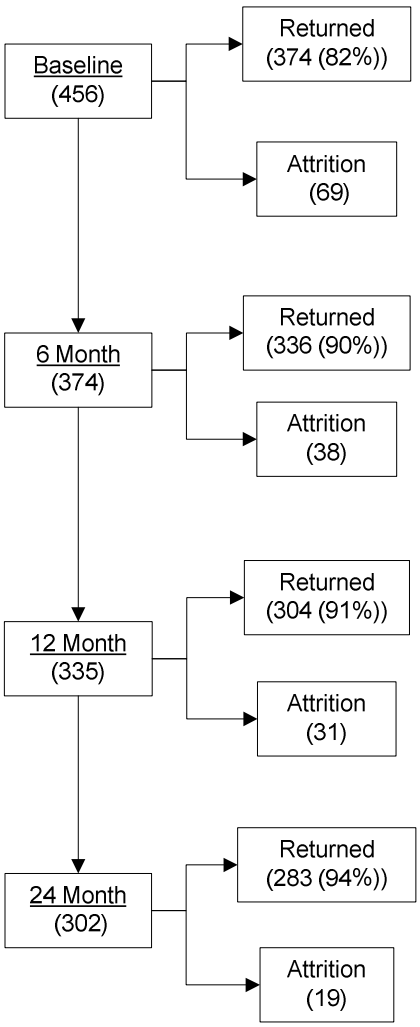
Chair of HSREB: Dr. Paul G. Harding

Ethics Officer to Contact for Further Information			
☐ Janice Sutherland	☐ Elizabeth Wambolt	☑ Grace Kelly	☐ Denise Grafton

This is an official document. Please retain the original in your files.

cc: ORE File
LHRI

APPENDIX D: Parent Response Rates and Attrition at Baseline, 6, 12, and 24 Months



APPENDIX E: Description of Measures

Family Factors	Measures	Informant and Description
Family Demands	Family Inventory of Life Events & Changes (FILE) (McCubbin et al.1996)	Parent Report 71 items – normative and non-normative life events experienced in previous 12 months (yes/no responses)
Family Resources	Family Inventory of Resources for Management (FIRM) (McCubbin et al.1996)	Parent Report 2 subscales predictive of adaptation: Family Strengths (20 items) & Extended Family Social Support (4 items) (Austin,1992) – level of resources available to aid families adaptation to stressful events 4-point likert scale (0 = not at all to 3 = very well)
Family Functioning	Family Adaptability, Partnership, Growth, Affection, and Resolve scale (APGAR) (Austin & Huberty, 1989)	Parent Report 5 items – satisfaction with family relationships 5-point likert scale (0 = never to 4 = always)
Parent Depression	Centre for Epidemiological Studies Depression Scale (CES-D) (Radloff, 1977)	Parent Report 20 items - current level of depressive symptoms, referring to previous 7 days 4-point likert scale (0 = rarely or none of the time to 3 = most or all of the time)
Parent Worry and Concern	Parental Impact-Emotional subscale of the Child Health Questionnaire (CHQ) (Asmussen et al. 2000)	Parent Report 3 items – how much worry or concern child's health, emotional well-being or behavior, and attention or learning abilities, has cause them during past 4 weeks 5-point likert scale (1 = none at all to 5 = a lot)
Demographics	Parent's age, sex, education, employment status, marital status, annual household income	Parent Report .

Child Factors	Measures	Informant and Description
Sex, Age		Parent Report
Severity of Epilepsy	Global Assessment of Severity of Epilepsy scale (GASE) (Speechley et al. 2008)	Neurologist Report 1 item – "taking into account all aspects of this patient's epilepsy, how would you rate its severity now?" 7-point likert scale (1 = extremely severe to 7 = not at all severe)
Other Epilepsy Characteristics	Type of epilepsy syndrome, seizure intensity and frequency, total and current number of AEDs, timing of seizures (exclusively nocturnal or not), convulsive status epilepticus (yes/no),	Neurologist Report

	family history of epilepsy (yes/no), falls or injuries during seizures and side effects of AEDs	
Co-morbid Conditions	Presence of behavioural, motor, or cognitive problems	Neurologist Report 3 single item questions (yes/no)

Outcome	**Measures**	**Informant and Description**
Parents' Perceptions of Activity Restrictions	Physical Restrictions subscale of the Quality of Life in Childhood Epilepsy (QOLCE) (Sabaz et al. 2000)	Parent Report 10 items 5-point Likert scale (5 = very often to 1 = never)

APPENDIX F: Parent-Report Measures

Family Inventory of Life Events and Changes (FILE)

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

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

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

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

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

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

Family Inventory of Resources for Management (FIRM)

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

Then make your decision by circling one of the following:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Center for Epidemiologic Studies Depression Scale (CES-D)

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

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

During the past seven days:

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

Parental Impact-Emotional subscale of the Child Health Questionnaire (CHQ)

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

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

Current Marital Status

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

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

Highest Level of Education Completed

What is the highest grade of school you have completed?

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

Current Employment Status

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

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

Annual Household Income

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

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

APPENDIX G: Physician Report Form

Study I.D _ _ _ _

PHYSICIAN FORM

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

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): _____
2. Date form completed (dd/mm/yy): _____
3. Seizure type(s): _____ _____
   _____ _____
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: _____

PLEASE TURN OVER TO COMPLETE

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 H: Unconditional Linear Growth Model; Model Fit Statistics for Different Covariance Structures

Toeplitz

-2 Res Log Likelihood	10267.8
AIC (smaller is better)	10277.8
AICC (smaller is better)	10277.8
BIC (smaller is better)	10297.4

Autoregressive Order 1

-2 Res Log Likelihood	10271.1
AIC (smaller is better)	10279.1
AICC (smaller is better)	10279.1
BIC (smaller is better)	10294.8

Compound Symmetry

-2 Res Log Likelihood	10284.0
AIC (smaller is better)	10290.0
AICC (smaller is better)	10290.0
BIC (smaller is better)	10301.8

Unstructured

-2 Res Log Likelihood	10254.0
AIC (smaller is better)	10278.0
AICC (smaller is better)	10278.2
BIC (smaller is better)	10325.0

APPENDIX I: Model Fit Statistics of Final Mixed Model with Different Covariance Structures

Toeplitz

-2 Res Log Likelihood	8029.4
AIC (smaller is better)	8033.4
AICC (smaller is better)	8033.4
BIC (smaller is better)	8041.1

Autoregressive Order 1

-2 Res Log Likelihood	8133.7
AIC (smaller is better)	8137.7
AICC (smaller is better)	8137.7
BIC (smaller is better)	8145.3

Compound Symmetry *Problems with convergence*

-2 Res Log Likelihood	7894.9
AIC (smaller is better)	7900.9
AICC (smaller is better)	7900.9
BIC (smaller is better)	7912.4

Unstructured

-2 Res Log Likelihood	7893.4
AIC (smaller is better)	7901.4
AICC (smaller is better)	7901.4
BIC (smaller is better)	7916.7

APPENDIX J: Comparing Final Models with Clinical Site as a Nested Random Effect of Not

J.1: Clinical Site NOT included as nested random effect

Fit Statistics

-2 Res Log Likelihood	7893.4
AIC (smaller is better)	7901.4
AICC (smaller is better)	7901.4
BIC (smaller is better)	7916.7

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
3	287.65	<.0001

Solution for Fixed Effects

Standard

Effect	Estimate	Error	DF	t Value	Pr > |t|
Intercept	32.7753	9.4128	327	3.48	0.0006
tweek	0.2095	0.03976	277	5.27	<.0001
tweek*tweek	-0.00115	0.000317	277	-3.62	0.0003
AVage	0.8430	0.3460	354	2.44	0.0153
AVgase	2.1670	1.0008	354	2.17	0.0310
dfgase	1.0209	0.4862	354	2.10	0.0365
AVcdigzerono	-14.8636	4.2568	354	-3.49	0.0005
AVPE	0.2004	0.04858	354	4.13	<.0001
AVcdigzerono*AVPE	0.1577	0.07444	354	2.12	0.0349
dfside_effects	0.7118	0.4310	354	1.65	0.0995
status	4.0698	2.8593	354	1.42	0.1555
nocturn	3.9014	1.6065	354	2.43	0.0157
AVfalls_seizures	-1.9594	1.3926	354	-1.41	0.1603
dffalls_seizures	-1.0247	0.6407	354	-1.60	0.1107
history	-1.9529	1.2851	354	-1.52	0.1295
gorp_1	3.3601	1.5247	354	2.20	0.0282
gorp_3	6.3956	3.8089	354	1.68	0.0940
AVp1age	-0.3360	0.1407	354	-2.39	0.0174
income	0.4780	0.2341	354	2.04	0.0419
education	0.4983	1.2311	354	0.40	0.6859
employment	1.8995	1.1966	354	1.59	0.1133
dfAPGAR	0.2730	0.1991	354	1.37	0.1712
dfPE	0.1025	0.02296	354	4.46	<.0001
AVFIRM	0.09887	0.08463	354	1.17	0.2435
dfFIRM	0.2029	0.07345	354	2.76	0.0060

J.2: Clinical Site included as nested random effect

Fit Statistics

-2 Res Log Likelihood	7817.0
AIC (smaller is better)	7825.0
AICC (smaller is better)	7825.0
BIC (smaller is better)	7840.3

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
3	288.43	<.0001

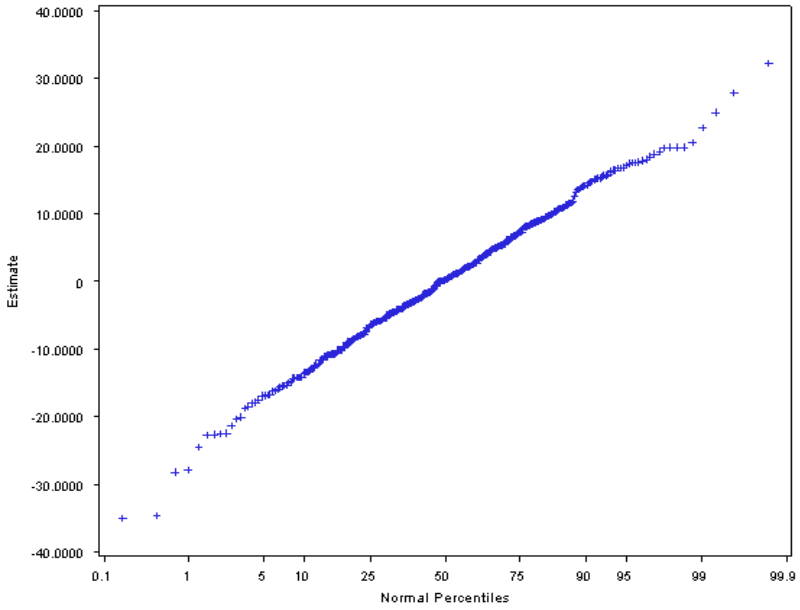
Solution for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept	32.5212	9.4508	326	3.44	0.0007
tweek	0.2088	0.03993	271	5.23	<.0001
tweek*tweek	-0.00116	0.000319	271	-3.64	0.0003
AVage	0.8447	0.3481	352	2.43	0.0157
AVgase	2.0331	1.0094	352	2.01	0.0448
dfgase	0.9858	0.4864	352	2.03	0.0434
AVcdigzerono	-15.7306	4.2987	352	-3.66	0.0003
AVPE	0.1939	0.04900	352	3.96	<.0001
AVcdigzerono*AVPE	0.1725	0.07514	352	2.30	0.0222
dfside_effects	0.6304	0.4327	352	1.46	0.1461
status	4.1385	2.8530	352	1.45	0.1478
nocturn	3.9321	1.6050	352	2.45	0.0148
AVfalls_seizures	-2.0845	1.3985	352	-1.49	0.1370
dffalls_seizures	-1.0775	0.6398	352	-1.68	0.0930

history	-2.0140	1.2894	352	-1.56	0.1192
gorp_1	3.0562	1.5349	352	1.99	0.0472
gorp_3	6.4484	3.7951	352	1.70	0.0902
AVp1age	-0.3141	0.1415	352	-2.22	0.0271
income	0.5000	0.2346	352	2.13	0.0337
education	0.5298	1.2325	352	0.43	0.6675
employment	1.6697	1.1971	352	1.39	0.1640
dfAPGAR	0.2721	0.1996	352	1.36	0.1737
dfPE	0.1003	0.02297	352	4.37	<.0001
AVFIRM	0.1147	0.08565	352	1.34	0.1814
dfFIRM	0.2118	0.07346	352	2.88	0.0042

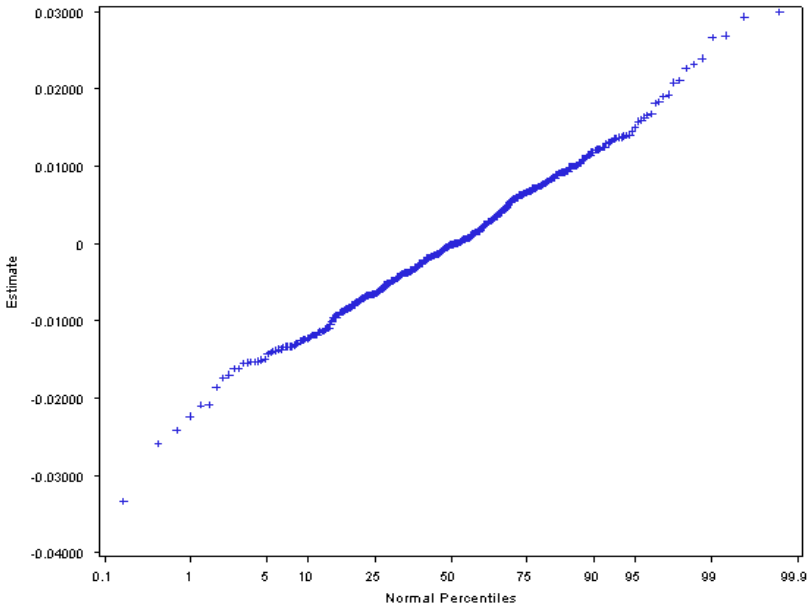
APPENDIX K: Normal Probability Plots of Predicted Random Intercepts, Random Slopes, and Residuals for Final Fitted Model

Effect = Intercept



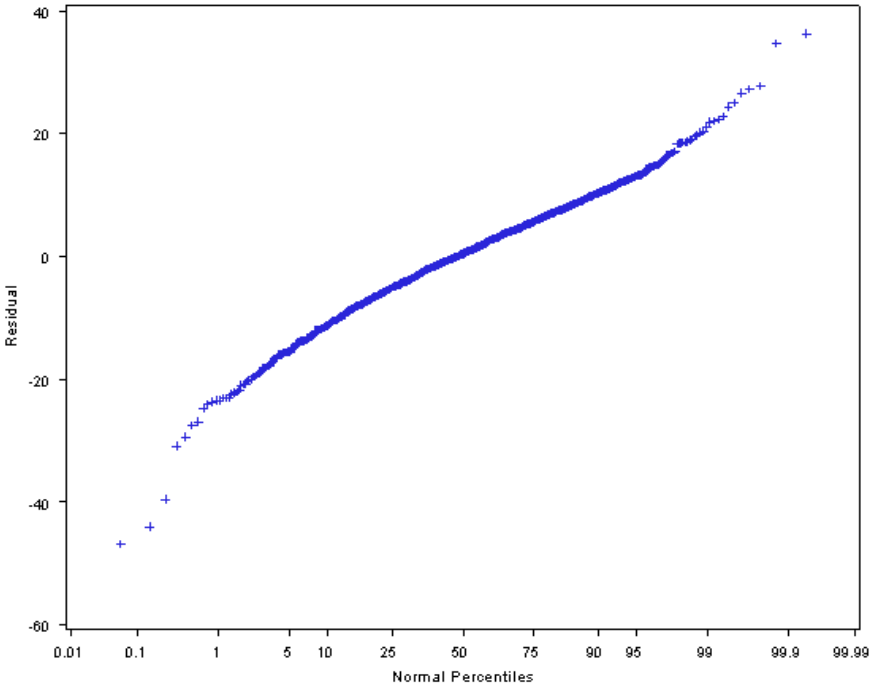
Probability plot of predicted random intercepts for final fitted model

Effect = Time (Weeks)



Probability plot of predicted random slopes for final fitted model

Residuals



Probability plot of predicted residuals for final fitted model

Curriculum Vitae

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