

**EMOTIONAL AND BEHAVIORAL OUTCOMES OF TRAUMATIC BRAIN INJURY IN
CHILDREN AND ADOLESCENTS**

by

Christopher Aaron Taylor

BS, Health Information Management, University of Pittsburgh, 2004

Submitted to the Graduate Faculty of
the Graduate School of Public Health in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy

University of Pittsburgh

2010

UNIVERSITY OF PITTSBURGH
GRADUATE SCHOOL OF PUBLIC HEALTH

This dissertation was presented

by

Christopher Aaron Taylor

It was defended on

March 5, 2010

and approved by

Dissertation Committee Chair

Stephen R. Wisniewski, PhD

Professor, Department of Epidemiology
Graduate School of Public Health, University of Pittsburgh

P. David Adelson, MD

Professor, Department of Neurological Surgery
School of Medicine, University of Pittsburgh

Sue R. Beers, PhD

Associate Professor, Department of Psychiatry
School of Medicine, University of Pittsburgh

Anthony Fabio, PhD, MPH

Assistant Professor, Department of Neurological Surgery
School of Medicine, University of Pittsburgh

Thomas J. Songer, PhD, MPH, MSc

Assistant Professor, Department of Epidemiology
Graduate School of Public Health, University of Pittsburgh

Copyright © by Christopher Aaron Taylor

2010

EMOTIONAL AND BEHAVIORAL OUTCOMES OF TRAUMATIC BRAIN INJURY IN CHILDREN AND ADOLESCENTS

Christopher Aaron Taylor, PhD

University of Pittsburgh, 2010

Each year in the United States more than one-quarter million children suffer a traumatic brain injury. Previously published research has shown that children who survive a TBI event are more likely to exhibit symptoms of emotional and behavioral disorders in the months and years following their injury. This research seeks to add to the field by examining the prevalence of clinically significant symptoms of these outcome disorders and identify factors related to the presence of these disorders. Through a three-manuscript format, this dissertation examines the prevalence of depression, anxiety, Attention-Deficit Hyperactivity Disorder (ADHD), Oppositional Defiant Disorder (ODD), and Conduct Disorder (CD) symptoms in the young injury survivors as well as depression, anxiety, and poor quality of life in their primary caregivers. This study aimed to describe the distribution of the symptoms of these disorders and identify factors related to both the injury and home recovery environment that are associated with their presence. The first manuscript, focusing on depression and anxiety in the injured youth, found a 5.9% prevalence of both depression and anxiety. More severe injury is associated with increased depressive symptoms. Anxiety symptoms in the child are positively correlated with depression symptoms in the caregiver. The second manuscript found a 35.7% prevalence of ADHD in this cohort, a rate higher than expected in the general population. While no factors were significantly associated with ADHD, this is a significant finding because several years had passed since the injury event. No child was reported having symptoms of ODD/CD. Lastly, the

third manuscript focused on the primary caregivers of the brain-injured youth. More than half of all caregivers in this study reported symptoms of a low or very low quality of life. This work has public health significance in that the identification of factors associated with worse outcomes can improve public health by identifying patients and families who may need additional follow-up because of their increased risk. Additionally, these measures will help to improve long-term outcomes in survivors of TBI, and identify caregivers who may need additional assistance in their caregiving responsibilities and may face poor outcomes as well.

TABLE OF CONTENTS

ACKNOWLEDGMENTS	XIII
1.0 DISSERTATION OVERVIEW AND OBJECTIVES.....	1
1.1 SPECIFIC AIMS	1
2.0 INTRODUCTION.....	3
2.1 TRAUMATIC BRAIN INJURY IN CHILDREN	3
2.2 DEPRESSION AND DEPRESSIVE DISORDERS	4
2.2.1 Symptoms and Diagnosis.....	4
2.2.2 Depression and Traumatic Brain Injury in Children and Adolescents.....	5
2.2.2.1 Prevalence.....	6
2.2.2.2 Temporal Relationship.....	6
2.2.2.3 Relationship with Injury Severity	7
2.2.2.4 Suspected Risk Factors.....	7
2.3 ANXIETY AND ANXIETY-RELATED DISORDERS.....	8
2.3.1 Symptoms and Diagnosis.....	9
2.3.2 Anxiety and Traumatic Brain Injury in Children and Adolescents	9
2.3.2.1 Prevalence.....	9
2.3.2.2 Temporal Relationship.....	10
2.3.2.3 Relationship with Injury Severity	10

2.3.2.4	Suspected Risk Factors.....	11
2.4	ATTENTION-DEFICIT HYPERACTIVITY DISORDER.....	12
2.4.1	Symptoms and Diagnosis.....	13
2.4.2	Attention-Deficit Hyperactivity Disorder and Traumatic Brain Injury in Children	13
2.4.2.1	Prevalence.....	14
2.4.2.2	Relationship with Injury Severity	15
2.4.2.3	Suspected Risk Factors.....	16
2.5	OPPOSITIONAL DEFIANT DISORDER AND CONDUCT DISORDER	17
2.5.1	Symptoms and Diagnosis.....	17
2.5.2	Oppositional Defiant Disorder and Conduct Disorder and Traumatic Brain Injury in Children and Adolescents	18
2.5.2.1	Prevalence.....	18
2.5.2.2	Relationship with Injury Severity	19
2.5.2.3	Suspected Risk Factors.....	19
2.5.2.4	Co-morbidity	20
2.6	CAREGIVING FOR CHILD AND ADOLESCENT SURVIVORS OF TRAUMATIC BRAIN INJURY.....	20
2.7	SUMMARY	21
2.8	LITERATURE REVIEW SUMMARY TABLES.....	23
3.0	ARTICLE ONE: DEPRESSION- AND ANXIETY-RELATED OUTCOMES OF TRAUMATIC BRAIN INJURY IN CHILDREN AND ADOLESCENTS.....	32
3.1	ABSTRACT	32

3.2	INTRODUCTION	33
3.3	METHODS	35
3.3.1	Study Design	35
3.3.2	Data Collection	36
3.3.3	Statistical Methods	39
3.4	RESULTS	39
3.5	DISCUSSION	41
3.5.1	Strengths and Limitations	44
3.5.2	Conclusion	45
3.6	TABLES AND FIGURES	46
4.0	ARTICLE TWO: BEHAVIOR-RELATED OUTCOMES OF TRAUMATIC BRAIN INJURY IN CHILDREN AND ADOLESCENTS	57
4.1	ABSTRACT	57
4.2	INTRODUCTION	58
4.3	METHODS	60
4.3.1	Study Design	60
4.3.2	Data Collection	61
4.3.3	Statistical Methods	63
4.4	RESULTS	64
4.5	DISCUSSION	65
4.5.1	Strengths and Limitations	66
4.5.2	Conclusion	67
4.6	TABLES AND FIGURES	68

5.0 ARTICLE THREE: CONSEQUENCES OF CAREGIVING FOR YOUNG SURVIVORS OF TRAUMATIC BRAIN INJURY	76
5.1 ABSTRACT	76
5.2 INTRODUCTION	77
5.3 METHODS.....	79
5.3.1 Study Design	79
5.3.2 Study Population	79
5.3.3 Data Collection	80
5.3.4 Statistical Methods.....	82
5.4 RESULTS.....	82
5.5 DISCUSSION.....	84
5.5.1 Strengths and Limitations	86
5.5.2 Conclusion.....	88
5.6 TABLES AND FIGURES.....	89
6.0 GENERAL DISCUSSION	103
6.1 SUMMARY	103
6.2 STRENGTHS AND LIMITATIONS	107
6.3 FUTURE RESEARCH DIRECTIONS.....	108
6.4 PUBLIC HEALTH SIGNIFICANCE	109
BIBLIOGRAPHY	110

LIST OF TABLES

Table 1. Findings from Literature Examining TBI and Depression in Brain-Injured Youth	23
Table 2. Findings from Literature Examining TBI and Anxiety in Brain-Injured Youth	26
Table 3. Findings from Literature Examining TBI and ADHD in Brain-Injured Youth.....	29
Table 4. Findings from Literature Examining TBI and ODD/CD in Brain-Injured Youth.....	31
Table 5. Comparison of enrolled participants with unenrolled subjects from potential recruitment pool	53
Table 6. Demographic, Injury, and Outcome Characteristics.....	54
Table 7. Correlation Coefficients of Depression and Anxiety.....	55
Table 8. Differences in Depression and Anxiety T-scores by Category.....	56
Table 9. Demographic, Injury, and Outcome Characteristics.....	73
Table 10. Correlation Coefficients of ADHD.....	74
Table 11. Differences in ADHD by Category	75
Table 12. Demographic, Injury, and Environmental Characteristics.....	100
Table 13. Correlation Coefficients of Caregiver Depression, Anxiety, and Quality of Life.....	101
Table 14. Differences in Caregiver Outcomes by Category	102
Table 15. Summary of Findings.....	106

LIST OF FIGURES

Figure 1. Study Recruitment Flow Diagram.....	46
Figure 2. Distribution of the GOS-E Peds score at time of eligibility interview.....	47
Figure 3. Distribution of Total GCS for enrolled child participants at time of injury.....	48
Figure 4. Distribution of T-scores from the Beck Depression Inventory for Youth (BDI-Y).....	49
Figure 5. Distribution of T-scores from the Multidimensional Anxiety Scale for Children (MASC) Anxiety Disorder Index.....	50
Figure 6. Scatterplot of Age of Child at Interview (in years) vs. BDI-Y T-score	51
Figure 7. Scatterplot of CES-D Total Score (in caregivers) vs. MASC Anxiety Index T-score.	52
Figure 8. Study recruitment flow diagram.....	68
Figure 9. Distribution of GOS-E Peds score at time of eligibility interview.....	69
Figure 10. Distribution of Total GCS score at time of injury.....	70
Figure 11. Distribution of the CPRS-R:S ADHD Index T-score	71
Figure 12. Scatterplot of BAI Total Score (in caregivers) vs. ADHD Index T-score	72
Figure 13. Study recruitment flow diagram.....	89
Figure 14. Distribution of GOS-Peds score at time of eligibility interview	90
Figure 15. Distribution of Total GCS score at time of injury.....	91
Figure 16. Distribution of total scores from the Beck Anxiety Inventory (BAI)	92

Figure 17. Distribution of total scores from the Centers for Epidemiologic Studies – Depression (CES-D) scale	93
Figure 18. Distribution of the QoLI raw score	94
Figure 19. Scatterplot of Age of Child and Interview (in years) vs. BAI total score	95
Figure 20. Scatterplot of Age of Child at Interview (in years) vs. QoLI T-score.....	96
Figure 21. Scatterplot of Time since injury (in years) vs. CES-D total score	97
Figure 22. Scatterplot of Age of Child at Injury (in years) vs. CES-D total score	98
Figure 23. Scatterplot of FBI total score vs. QoLI T-score	99

ACKNOWLEDGMENTS

Research is not performed in isolation, and I would like to thank the many people who assisted me with this research endeavor.

Firstly, I would like to thank the families that volunteered to participate in this study. These families have turned a terrible life-changing event into a desire to help others. This work would not have been possible without them.

I would also like to thank my advisor, Dr. Stephen Wisniewski, who provided exceptional guidance with this work while being supportive and very patient. Also, I would like to thank Dr. Anthony Fabio for his outstanding guidance at the Center for Injury Prevention and Control (CIRCL) and for his willingness to be so involved with this work and offer helpful suggestions.

Additionally, I would like to thank Dr. David Adelson for his assistance with this research, Dr. Sue Beers for her excellent willingness to explain both the patient-related and psychological aspects of this work, and Dr. Thomas Songer for this ability to provide timely thoughts and advice on this project.

I would also like to thank those at the Center for Aging and Population Health who supported me both personally and professionally over these last six years. Drs. Anne Newman and Robert Boudreau have been excellent mentors to me and have shown me, by their examples, how to be a true scientist. Additionally, Dr. Nancy Glynn has not only been a wonderful mentor

and a great example of a scientist and leader, but she has also been a true friend to me and never doubted my abilities to succeed as a young professional.

I owe my family and friends a great thank you as well for their endless support and love throughout my time at the University of Pittsburgh. They never once doubted by ability to succeed nor my capability to persevere, and my love for them is unending.

Finally, my friend, Scott Kimball, and grandparents, Rosealene and Gerald Altemus, also loved me and greatly supported me and this work, but sadly all passed away before it was complete. I would like to dedicate this work to them.

1.0 DISSERTATION OVERVIEW AND OBJECTIVES

1.1 SPECIFIC AIMS

There are several aims of this research study. This study aims to examine factors associated with emotional and behavioral outcomes of traumatic brain injury in children and adolescents.

With respect to emotional outcomes, the specific aims of this research are to (1) examine the distribution of symptoms of depression and anxiety, (2) estimate the prevalence of depression and anxiety in the studied population, (3) examine the co-occurrence of depression and anxiety, and (4) examine the correlation of factors associated with the presence or absence of depression and anxiety symptoms.

With respect to behavioral outcomes, the specific aims of this research are to (1) examine the distribution of symptoms of disruptive behavior disorders (DBD), including Attention-Deficit Hyperactivity Disorder (ADHD), Oppositional Defiant Disorder (ODD), and Conduct Disorder (CD), (2) estimate the prevalence of these DBDs in the studied population, (3) examine the co-occurrence of ADHD, ODD, and CD, and (4) examine the correlation of factors associated with the presence or absence of these disorders.

Finally, with respect to caregivers of the brain injured youth, the specific aims of this research are to (1) examine the distribution of symptoms of depression and anxiety, (2) estimate the prevalence of depression and anxiety in the studied population, (3) examine the co-

occurrence of depression and anxiety, (4) examine the quality of life of these caregivers, and (5) examine the correlation of factors associated with the presence or absence of depression and anxiety symptoms and quality of life score.

2.0 INTRODUCTION

Every year in the United States approximately 1.4 million people experience a traumatic brain injury (TBI)¹. These injuries result in 50,000 deaths and 235,000 inpatient hospitalizations¹. Of these hospitalized survivors, 35% experience long-term disability as a result of TBI, and it is estimated that 2% of the US population is living with disability as a result of TBI².

Of the more than one million TBIs that occur each year, nearly one-third involve children under the age of 15¹. Five percent of these children die as a direct result of TBI. Those who do survive may experience chronic disability due to TBI-associated cognitive deficits, impaired motor skills, behavioral and psychiatric dysfunction as well as poor academic achievement³⁻⁵. Caregivers for persons with any chronic condition are at increased risk for poorer general health, increased stress, depression, and decreased life satisfaction⁶. Because of the pervasive effects that TBI can have on survivors and those who provide care for them, it is important that the field of public health closely examine the consequences of these injuries in order to ensure that the appropriate aftercare and follow-up is recommended and provided to this vulnerable population.

2.1 TRAUMATIC BRAIN INJURY IN CHILDREN

Traumatic brain injury is “a blow or jolt to the head or a penetrating head injury that disrupts the function of the brain⁷.” While TBI can be devastating to anyone regardless of age, TBI in

children and youth can be especially problematic because injury can alter brain development⁷. While the exact mechanisms of how the brain adapts after injury are not entirely known, it has been clearly demonstrated in the literature that brain injury can greatly affect a child's ability to think, reason, understand, and cope. Research has shown that these inabilities are manifested in any number of psychiatric and behavioral sequelae including depression, anxiety, attention disorders, disruptive behavior disorders, and changes in personality. While studies have repeatedly demonstrated a link between TBI and psychiatric and behavioral disorders, little research has been done examining the prevalence of these conditions several years since the time of injury. There is no research examining the prevalence of depression, anxiety, or disruptive behavior disorders more than two years after TBI. Additionally, studies sometimes overlook examining possible characteristics that may be associated with injury. While studies regularly focus on injury severity, age at injury, and gender, other factors including socioeconomic factors, family characteristics, pre-injury factors—such as psychiatric history— which can influence recovery, as well as characteristics associated with the injury survivor's primary caregiver and recovery environment are sometimes overlooked. Additionally, there has been very little research done studying the effects of caregiving for these young injury survivors.

2.2 DEPRESSION AND DEPRESSIVE DISORDERS

2.2.1 Symptoms and Diagnosis

According to the Diagnostic and Statistical Manual of Mental Disorders—Fourth Edition (DSM-IV), depression is a mood disorder where symptoms of depressed mood, which include feelings

of sadness, irritability and hopelessness, can affect a person's ability to function in his or her everyday life^{8, 9}. Depressed individuals may become overly critical of themselves and lose interest in previously pleasurable activities⁸. As well, depression in children can lead to problems with concentration and focus in addition to a loss of motivation and energy, and changes in personal hygiene and sleep patterns⁸. The prevalence of major depression in children and adolescents aged 9 through 17 as a whole has been estimated at five percent¹⁰. Furthermore, depression can increase the risk of suicide and suicidal thoughts which is the third leading cause of death in teenagers 15 years of age and older¹¹.

While only a physician or psychologist can diagnose depression, symptoms of depression can be evaluated through a variety of subjective and objective questionnaires that are scored to determine if a subject meets criteria, which suggest possible depression. In research studies, the use of symptom surveys and interviews are often used as a more convenient way to assess depressive symptoms rather than a structured psychiatric interview—the gold standard for diagnosis.

Treatment for depression includes anti-depressant medications, psychotherapy, and electroconvulsive therapy. Untreated depression can lead to suicide.¹²

2.2.2 Depression and Traumatic Brain Injury in Children and Adolescents

While several studies have examined factors associated with TBI and depression, the links between TBI and depression in children has not been extensively explored.

2.2.2.1 Prevalence

In general, children who suffer from chronic medical conditions are more likely to develop symptoms of depression compared to healthy peers¹³. In fact, one study in a pediatric population found that one-quarter of severe TBI survivors had a diagnosis of an ongoing depressive disorder and indicated that this may be an underestimate as children who exhibit externalized symptoms (such as aggression) may not be initially perceived as depressed¹⁴. Another study, while written by the same lead author, shows a similar statistic with 22% of TBI survivors reportedly having a post-injury depressive diagnosis¹⁵. Additionally, a study of young TBI survivors found a 13% prevalence of depression at one-year follow-up in 14-18 year-olds¹⁶. One study found a very high prevalence (63.2% of moderate-to-severe brain injuries) at six months, though this outlying rate includes diagnoses of both depressive and anxious disorders¹⁷.

2.2.2.2 Temporal Relationship

In a series of published articles that followed one particular cohort of young TBI survivors over a period of time, it was found that the prevalence of depressive symptoms in injury survivors lessened over time in most children, though some children still had depressive symptoms at least two years post-injury¹⁸⁻²². In fact, Max *et al.* suggested that the depressive symptoms could endure past the end of the two-year follow-up point though few studies have presented results based on a post-injury follow-up of more than two years. Additionally in this study, while some diagnoses had been resolved by the time of follow-up—possibly indicating some sort of time-injury mediation with respect to depression¹⁵ where a child more fully recovers from his or her injury over time or may come to grips with the limitations of injury months or years later¹⁵. This last finding parallels another article which notes the relative stability of an

increased number of depressive symptoms over time in TBI survivors compared to the return-to-baseline trend of non-TBI controls²³.

2.2.2.3 Relationship with Injury Severity

A previous review of research revealed contradictory conclusions, while in some studies mild head injury can have devastating effects on emotional and cognitive²⁴ functioning, other studies demonstrated that after controlling for pre-injury psychiatric history, mild head injury bestows no risk for additional psychiatric disease^{18, 25}. Kirkwood, *et al* demonstrated that severe TBI bestowed 2- to 6-times increased odds of exhibiting depressive symptoms when compared to controls with orthopedic injuries²³. Luis, *et al* found that increased injury severity is significantly related to the presence of incident post-TBI depression¹⁷. In contrast, studies have found associations between moderate and severe TBI (i.e. Glasgow Coma Scale score) and psychiatric dysfunction (including depression) in nearly all published studies. One exception found no relationship between GCS and an incident anxiety or depressive disorder, but reported a relationship between higher Glasgow Outcome Scale (GOS) and depression¹⁶.

2.2.2.4 Suspected Risk Factors

Low socioeconomic status (SES) has been found to be related to depressive symptoms in children following TBI²³. In addition to SES, Geraldina *et al.* found that male gender and increased neurological impairment were most predictive of psychological problems after TBI in children, though this observation was broad and not specific to depression alone¹⁶.

Age at injury may also be related to depression after TBI. One study specifically examining the relationship between age at injury and post-TBI mood disorders found that older [adolescent] TBI survivors (14-18 years old) were less likely to express internalized symptoms,

such as withdrawal, compared to younger injury survivor at one-year post-TBI¹⁶. While this work of Geraldina *et al* does not focus specifically on depression, guilt and suicidal ideation are internalized symptoms of depression. In contrast, though, another cohort—also followed-up at one year—found no such association with age and the development of an incident post-injury depressive or anxiety disorder¹⁹. The effect of age on TBI recovery remains unclear and requires further study and potentially longer follow-up.

It is critical to study the wide variety of factors that can be associated with injury and depression, as many factors have not been examined fully or replicated in multiple studies. As well, because of the lack of studies that examine TBI survivors longitudinally over an extended period of follow-up of more than two years, it is equally important to investigate depressive symptoms several years after injury to begin to understand how far-reaching the effects of TBI may be.

2.3 ANXIETY AND ANXIETY-RELATED DISORDERS

According to the DSM-IV, anxiety is a disorder where excessive and uncontrollable reactions resulting manifests with a wide range of physical and affective symptoms as a result of exposure to a typically non-threatening stimulus⁸. It is the most common emotional affliction in children and adolescents aged 9 to 17 years with an estimated 13 in every 100 children affected⁸. In general, boys are less affected than girls. Additionally, about half of all children with an anxiety disorder also have a concurrent mental or behavioral problem, such as depression.²⁶

2.3.1 Symptoms and Diagnosis

Symptoms of anxiety in children and adolescents include fear, worry, or an overall, unrealistic worry about everyday activities.⁸ Generally, different symptoms of anxiety can be grouped into a specific anxiety disorder. Common anxiety disorders include Separation Anxiety Disorder, Panic Disorder, Obsessive-Compulsive Disorder (OCD), Post-Traumatic Stress Disorder (PTSD), and Generalized Anxiety Disorder. All of these disorders include fear and worry, but the types of anxious thoughts, causes, and expression of anxious emotions are expressed in different ways.

Anxiety disorders can be treated with various treatments including cognitive behavioral therapy, family therapy, biofeedback, and medication. If left untreated, anxiety can lead to impaired interactions with peers, low self-esteem, alcohol or drug use, academic issues, and continued anxiety-related difficulties in adulthood.²⁶

2.3.2 Anxiety and Traumatic Brain Injury in Children and Adolescents

2.3.2.1 Prevalence

The majority of studies explicitly mentioning an anxiety disorder focus on PTSD. In a study examining children recovering from TBI, 13% met full PTSD diagnostic criteria at follow-up, though follow-up was relatively close to the time of injury (one month) in some cases²⁷. Furthermore, a similar study again comparing brain-injured youth ($N=81$) to orthopedic controls found that 31% of children reported symptoms of post-traumatic stress at the end of one-year post-injury²⁸—a rate higher than the average rate in the general population.

2.3.2.2 Temporal Relationship

The prevalence of anxiety and anxiety-related disorders can vary over time as new cases arise and other cases resolve. A study of young brain injury survivors over time found 86% with at least one PTSD-related symptom at three-month follow-up²² with a drop to 12% at two years²⁹. This same longitudinal examination found prevalence of (non-PTSD) anxiety-related diagnoses (e.g. separation anxiety disorder, panic disorder, generalized anxiety disorder, etc.) of 13.5%, 4.9%, and 14% at 3-, 6-, 12-month follow-up, respectively, indicating the presence of new and resolving cases at each time point^{18, 19, 22, 30}. In another study focusing on symptoms of post-traumatic stress, investigators found that the prevalence of those symptoms rose in the first three months post-injury. The number of symptoms reportedly dropped at both one-year and again at two-year follow-ups²⁹. Similarly, another study found the average anxiety score significantly increased over time post-injury with a comparative increase in the number of young survivors with at least ten anxiety-related symptoms³¹.

2.3.2.3 Relationship with Injury Severity

Moderate and severe brain injury may be associated with the post-injury development of anxiety disorders in children and adolescents³². In the first year post-injury, Rivara *et al.* found that children with more severe TBI were more likely to have symptoms of anxiety compared to the general pediatric population³³. However, in a study by Geraldina, *et al.*, the relationship between injury severity and anxiety was not found in another study where the children were examined within specific study-defined age ranges¹⁶. Additionally, TBI victims who reported symptoms of depression or an anxiety disorder at follow-up were more likely to have a higher average GCS at time of injury (14.24) compared to those with no post-injury onset of depression or anxiety disorder (12.32)¹⁷. One study that compared 61 children with TBI to controls with an

orthopedic injury found a non-statistically significant trend that suggested that children who experienced moderate and severe TBI in this cohort had more anxiety-related symptoms than those with mild injury¹⁷. Moreover, a study comparing severe and mild disability observed that children with higher levels of post-injury disability (based on the GOS) were more likely to have developed internalized symptoms of a mood or anxiety disorder (OR=17.51, $p=0.02$)¹⁶. In addition, results from a series of longitudinal assessments of 50 brain-injured children found that, in general, rates of incident psychiatric disorders—both depression- and anxiety-related—were higher for children with a severe injury compared to a mild or moderate injury regardless of whether or not the child had ever been diagnosed with a psychiatric disorder prior to injury^{18, 19, 22, 30}. A study exclusively examining PTSD found no relationship with PTSD and injury-related factors²⁷.

2.3.2.4 Suspected Risk Factors

Several risk factors for anxiety disorders and anxiety-related symptoms have been identified by studies examining children post-TBI and may have a relationship with younger age at injury in another study, as well³¹. In injured children age 7 to 13 years, children with increased levels of disability at follow-up reported fewer symptoms of anxiety. The authors, though, suggest this may be due to a decreased level of awareness and may not truly represent age at injury¹⁶.

A study of nearly 100 young TBI survivors found that post-injury depressive symptoms are related to post-injury anxiety symptoms³². Two studies found a significant relationship between pre-injury prevalence of anxiety symptoms and post-injury anxiety symptoms,^{31, 32} post-head injury depression, and female gender were all predictive of PTSD or PTS-related

symptoms³². As well, children are more at risk for developing symptoms of anxiety if they are from families with lower socioeconomic status²³ or were female³².

Furthermore, certain pathologic findings of brain injury may also be associated with the levels of anxiety symptoms. In the prior study cited study by Geraldina, *et al.* examining 14 to 18 year-olds as a separate age group found that frontal lobe damage is highly correlated with increased numbers of symptoms of anxiety¹⁶. Additionally, seventy-percent of children with a prefrontal injury showed a pathological score on the Test of Anxiety and Depression (TAD)¹⁶. Conversely, another study found that lesions in the orbitofrontal cortex (OFC) correlated to a significantly *decreased* risk for symptoms of anxiety (excluding PTSD-related symptoms). The authors suggested that the OFC's relationship to the amygdale and its fear-based reaction control may alter how the brain reacts to fear in OFC-damaged individuals. As well, this study found a positive association between PTSD symptoms and the presence of temporal lobe injury³⁴.

2.4 ATTENTION-DEFICIT HYPERACTIVITY DISORDER

The DSM-IV defines Attention-Deficit Hyperactivity Disorder (ADHD) as a mental disorder characterized by attention-related problems and hyperactivity with individuals frequently exhibiting both features. Children with ADHD find it difficult to pay attention and/or control impulsive behavior.⁸

2.4.1 Symptoms and Diagnosis

Symptoms of ADHD related to inattention include being easily distracted, failing to pay attention, and an inability to follow instructions. Hyperactivity-impulsivity-related symptoms include restlessness, fidgeting, difficulty waiting taking turns, and running, talking, or other inappropriate actions when calm behavior is expected. It is estimated that about two million children and adolescents in the US—roughly 3-5%—have ADHD⁸.

Suggested possible causes of ADHD include environmental agents, genetics, and brain injury. Additionally, many children with ADHD also have co-morbid condition such as Tourette Syndrome, Oppositional Defiant Disorder, Conduct Disorder, Anxiety, Depression, Bipolar Disorder, as well as learning disabilities.⁸ Max *et al.* found that both Personality Change Disorder³⁵ and Oppositional Defiant Disorder (ODD)^{14, 36} are significantly associated co-morbid conditions in young TBI survivors who have post-injury ADHD.

The typical treatment for ADHD in children and adolescents is stimulant medication accompanied by behavioral therapy and lifestyle adjustments. Even if treated in adolescence, ADHD can continue be a problem in adulthood.³⁷ Untreated ADHD can lead to difficulty in social situations and inter-personal relationships.³⁷

2.4.2 Attention-Deficit Hyperactivity Disorder and Traumatic Brain Injury in Children

ADHD and its relationship with TBI have been studied through a wide range of studies of all types. While no pathologic feature related to brain anatomy in post-injury exams has yet been found^{38, 39}, there is strong evidence to suggest that some attention-related symptoms appear, or worsen, as a result of TBI after adjusting for other possible factors.

Generally, the literature makes a distinction between primary ADHD (PADHD)—which is present prior to TBI—and secondary ADHD (SADHD) subtypes that present after injury. While one study suggested that children with PADHD may be more at risk for certain types of injury⁴⁰—possibly as a result of ADHD-related behaviors—nearly all of the research examining associations between TBI and ADHD examine SADHD, the subtype resulting post-injury. There is some evidence to suggest that PADHD is pathologically different from SADHD as severe TBI survivors with SADHD were found in one study to have greater problems with memory, attention, and executive functioning than non-injured children with PADHD⁴¹. This is not to suggest that PADHD does not play a role in injury recovery, but this possible role of PADHD has not been wholly examined by the literature.

2.4.2.1 Prevalence

The prevalence estimates of SADHD with respect to TBI maintain around 20% at about one year post-injury. The few studies that have examined participants in a longitudinal manner post-TBI found that rates of new ADHD cases maintain throughout two years of follow-up. In a record review, Max *et al.* found that 10% of 50 children evaluated met criteria for pre-injury ADHD. Of those without a pre-injury suggestion of ADHD, 42% met ADHD criteria for a post-TBI diagnosis⁴². Levin *et al.* examined young TBI survivors without previously diagnosed ADHD and found a prevalence of 14.5% of ADHD one-year post-TBI. This rate rose to 18.3% at two years post-TBI. It is interesting to note that those who met criteria for ADHD before their injury accounted for 23% of this cohort that is considerably higher than the estimated prevalence of ADHD in the general population for the age range studied. This pre-injury rate was similar to that found by Gerring *et al.* (20%)⁴³. Additionally, Gerring *et al.* also found 18.8% of young survivors of moderate and severe TBI had symptoms of ADHD at one year post-injury⁴³.

Furthermore, Max *et al.* studied children over time post-injury. In the months following injury, they found new onset rates of ADHD of 16.2% and 9.8% for the first three²² and second three³⁰ months post-TBI, respectively. Additionally, the one-year incidence was 11.6% and 14.3% for two years of follow-up^{18, 19}. These results suggest that even two years post-injury, TBI survivors may still be at risk for developing ADHD as a result of their injuries.

Of note, one study found that young TBI survivors who had pre-injury ADHD and were being treated with ADHD medications developed fewer ADHD symptoms at two years follow-up than those who were not being receiving medication for pre-injury ADHD⁴⁴. In a cohort study examining children post-TBI, one-third of ADHD diagnosed in the first year post-TBI was resolved by 18-month follow-up³⁸ indicating that a secondary ADHD diagnosis may be transient in nature in some persons.

2.4.2.2 Relationship with Injury Severity

Severity of injury has been consistently examined in studies examining possible risk factors for SADHD. While several studies found that more severe injuries correspond to an increased risk for attention-related difficulties, including ADHD not all studies have come to the same conclusion. In a study examining post-injury attention-related deficits (not specifically ADHD symptoms), researchers found that children who sustain severe brain injuries show greater deficits in areas related to attention compared to children with mild or moderate injuries⁴⁵. Furthermore, additional reports on this cohort show that children with a severe TBI displayed the poorest attention-related skills at follow-up. Performance, however, did improve over time though attention-related difficulties did persist through two-years post-injury follow-up.⁴⁶ These results were similar to other work that showed severely injured TBI survivors showed

less improvement with respect to attention-related task scores than similarly aged children with less severe (i.e. mild or moderate) injuries⁴⁷.

Moreover, these results were similar to other work that also showed ADHD symptoms positively associated with severity of injury two years post-TBI with the prevalence of SADHD in severely injured children (38%) more than twice that of those with mild and moderate injuries (12.5%)³⁸. Conversely, severity of injury has been found not to be related to ADHD symptoms in both a longitudinal²¹ and cross-sectional⁴⁸ examination. Furthermore, one case-control study looking at post-TBI and post-orthopedic injury functioning found the rate of ADHD prevalence (pre- or post-injury) at 37.5% for those with the most severe injuries throughout a one-year follow-up⁴⁹. Finally, in an article comparing children with and without ADHD after severe TBI, of the 82 children examined, 14 met diagnostic criteria for SADHD at one-year follow-up⁴¹.

2.4.2.3 Suspected Risk Factors

Socio-economic status (SES) has also been found in one study to be a statistically significant independent predictor of ADHD at six month follow-up for new onset SADHD case in post-TBI children²⁰. In contrast, when SES was controlled for in another study—along with family psychiatric history, injury severity, and level of family functioning—only family functioning remained a significant predictor of ADHD two years post-TBI³⁸. However, another study also looking at family functioning and its relationship with TBI found no association with ADHD⁴². Additional studies found no associations with gender³⁸ nor family history of alcohol abuse⁴². One additional factor possibly related to attention-related difficulties post-TBI includes younger age at time of injury⁵⁰, though others have found no significant age-ADHD association⁴².

In terms of anatomical correlates, little conclusive evidence has been found though several studies have found evidence suggesting frontal brain anatomy may be related to ADHD incidence^{20, 39, 51, 52}. A study using brain-imaging MRI found the odds of developing SADHD were more than 3.6-times higher for children with injury to the thalamus compared and 3.15-times higher for those with basal ganglia injury compared to children without those respective injuries³⁹. As well, a neuroimaging study of 76 young TBI survivors found that injury in the right putamen legion was associated with post-injury ADHD, but the results were not significant after statistical adjustment⁵³.

2.5 OPPOSITIONAL DEFIANT DISORDER AND CONDUCT DISORDER

The DSM-IV defines both Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD) as disruptive behavior disorders where patterns of defiant, disobedient, and possibly hostile behavior beyond the bounds of normal conduct are exhibited. ODD and CD are not co-occurring diseases—a diagnosis of ODD will typically precede that of CD because of the time requirements of behavior exhibition.⁸

2.5.1 Symptoms and Diagnosis

Common behaviors of children with ODD include blaming others for their own mistakes, being easily annoyed, and angry, resentful, spiteful, or vengeful actions and behavior. A diagnosis of ODD is generally not considered until these symptoms are present for at least six months. The prevalence of ODD is estimated at 2-16% of all 9-17 year olds⁸.

Children and adolescents with CD display symptoms similar to ODD though often more intense. Symptoms of CD include overly aggressive behavior, bullying, lying, truancy, vandalism, stealing, and cruel behavior toward people and animals. The DSM-IV lays out a litany of persistent behaviors that commonly comprise the profile of a child with CD. Three or more symptoms must have been present in the past 12 months with at least one behavior present in the past 6 months. In left untreated, it is estimated that about half of all children with ODD will continue to express symptoms for at least three years with half of them going on to develop CD.⁵⁴

Youth diagnosed with ODD and CD typically experience academic difficulties and poor relationships with others and are at higher risk for injury, sexually transmitted disease, depression, and suicide²⁶. ODD and CD are usually treated with a combination of psychiatric medication and individual and/or family therapy.⁵⁵

2.5.2 Oppositional Defiant Disorder and Conduct Disorder and Traumatic Brain Injury in Children and Adolescents

Little research has been performed investigating the relationship between TBI and ODD/CD. As a result, little is known about possible risk factors for post-injury ODD/CD.

2.5.2.1 Prevalence

In one study 39% of those with an incident post-TBI psychiatric disorder presenting at an outpatient clinic had ODD or CD (about 3% prevalence)⁵⁶. A record review showed the prevalence of ODD or CD at 6% for a study of fifty injured children at one-year follow-up⁴².

2.5.2.2 Relationship with Injury Severity

In a cross-sectional record review, injury severity was not found to be associated with ODD/CD⁴⁸. However, in a longitudinal study by the same author, injury severity was found to be related to ODD but not until two years post-TBI⁵⁷. In that same longitudinal analysis, investigators found that the number of ODD symptoms of children who suffered a severe TBI increased at about the same rate as those with mild TBI. However, over two years of follow-up post-injury, the number of symptoms expressed by those with mild injury dropped, whereas the number of symptoms of those with severe injury maintained over that two year period⁵⁷. In contrast, another study examining ODD symptoms, researchers unexpectedly found that children with milder injuries expressed a greater ODD symptoms⁴².

2.5.2.3 Suspected Risk Factors

As with ADHD, family functioning was found to be associated with ODD/CD symptoms. Poorer family functioning was associated with higher occurrence of ODD/CD in two studies examining predictors of disruptive behavior disorders^{42, 57}. Also with ADHD, SES was inversely associated with number of ODD symptoms⁵⁷. A presence of family history of alcohol abuse was also higher in injured children with a history of ODD/CD compared to those with no ODD/CD history, but age at injury was significant in this cross-sectional examination⁴².

While no definite anatomical correlate of ODD/CD has been found, one study of looking at aggressive behaviors (aggressive behaviors are a hallmark symptom of conduct disorder) found that frontal lobe injury may be associated⁵⁸.

2.5.2.4 Co-morbidity

Post-injury symptoms of ODD/CD were related to the presence of SADHD^{14, 36, 42}. In fact, follow-up over time of one injured cohort showed that the presence of new ODD symptoms was significantly higher in children with SADHD compared to those without^{20, 21}. The National Institute of Mental Health estimates that one-third to one-half of youth with ADHD also have ODD³⁷.

2.6 CAREGIVING FOR CHILD AND ADOLESCENT SURVIVORS OF TRAUMATIC BRAIN INJURY

There is minimal research available of the effects that TBI can have on caregivers. Of this small pool of research available on caregivers of TBI survivors, very little is known about the effects that caregiving has on the caregivers of young TBI survivors. In general, studies have shown that the responsibility of providing care generally falls to spouses or parents⁵⁹. Consequences of being the primary caregiver of a TBI survivor include increased use in both prescription and non-prescription drugs and alcohol⁶⁰. Additionally, caregivers of those with chronic illness are at higher risk for reporting increased levels of stress, depression, decreased life satisfaction, and poorer general health⁶.

Ergh, *et al.*^{61, 62}, Marsh, *et al.*^{60, 63, 64} and Wade, *et al.*⁶⁵ have all cited that depression and anxiety are prevalent in the population of caregivers who provide care to both adult and child survivors of TBI. Most of this research examines the roles and effects of caregiving for adult TBI survivors with approximately one-third of caregivers reporting symptoms of depression or anxiety and both six months and one year post-injury^{63, 64}.

Despite the available studies on caregiving, little has been reported on the risk factors for depression and anxiety in caregivers of young survivors of childhood TBI. The rate of poor family functioning has found to be as high as 74% in one cohort of caregivers⁶⁶, and patients recovering in environments with poorer family functioning have been shown to be at more risk for injury-related distress⁶⁷⁻⁶⁹. This increased level of distress may, in turn, adversely affect the caregiver.

In addition to family functioning, social support has been shown to be related to caregiver mental health as well as caregiver quality of life and life satisfaction though this result was found in a cohort of caregivers of adult TBI survivors. Increased social support mediates caregiver burden and distress⁶². Additionally, the number of neuropsychological problems of the TBI survivor is positively related to caregiver burden⁶² and inversely related to life satisfaction⁶¹. Furthermore, the number of adverse effects that an injury survivor has experienced post-injury has been shown as a significant predictor of caregiver depression⁷⁰. Additionally, the perception of the condition of the injury victim is related to depression as a lower perceived amount of adverse effects related to the injury survivor is associated with a decreased rate of depression⁷⁰. Finally, the ratings of the children with TBI symptoms may be affected by the levels of depression and other emotional problems of the parents⁶⁵.

2.7 SUMMARY

It is evident that there is much research still to be done on the behavioral and emotional outcomes of TBI in children. While the research performed to date is solid in its methods, the results are contradictory and few studies can agree on any one set of risk factors. Additionally,

the studies published have been based on a relatively small number of patient cohorts who have been described and reported on several times using a variety of methodological approaches. Furthermore, these cohorts have been small in number, usually less than one hundred participants, and long-term follow-up is limited, particularly in children where the brain is still developing. No study has followed young TBI survivors past a two-year window so the prevalence of emotional and behavioral outcomes past two years post-TBI is unknown and factors that may contribute to these outcomes several years past injury have not been studied.

As well, there is almost no research on the effects of caregiving for young TBI survivors, and no study has studied both the emotional outcomes of injury and caregiving in a cohort of patients and caregivers. Such a study is very important because it will allow an examination of how various emotion and behavior studies in the young patient can potentially impact the well being of the caregiver, as well as examine the relationships between the emotional states of both caregiver and injured child.

2.8 LITERATURE REVIEW SUMMARY TABLES

Table 1. Findings from Literature Examining TBI and Depression in Brain-Injured Youth

Primary Author	Title	Design	Population	Sample Size	Major Findings
Geraldina P (2003)	Neuropsychiatric Sequelae in TBI: A comparison across different age groups	Cross-sectional	0 to 18 years at TBI (Mean Age = 11.67 at 1Y follow-up)	96	<ul style="list-style-type: none"> - Prevalence of depression in 14 to 18 year-olds was 13% depression (using TAD); 13.5% using CBCL. - Frontal lesions were significantly associated with anxiety and depression ($p = .05$). - Higher GOS is associated with anxiety and depression when compared to mild-level GOS children. - For 7 to 18 YO, poorer neurological exam score was associated with lower depression levels ($p = .039$). - Male sex is related to internalized behavior, but not anxiety and depression. - No correlation between any disorder and GCS.
Kirkwood M (2000)	Prevalence and Correlates of Depressive Symptoms Following Traumatic Brain Injuries in Children	Prospective cohort	6 to 12 YO at injury followed-up at 6- and 12-months post-TBI	51 w/ mod TBI 38 w/ sev TBI 55 w/ ortho inj	<ul style="list-style-type: none"> - Most participants did not display clinical levels of depressive symptoms. - Overall, depressive symptoms in TBI group stayed steady post-TBI, where those with orthopedic injury return more closely to baseline levels. - Children w/ severe TBI 2- to 6-times more likely to exhibit depressive symptoms than orthopedic controls. - Lower SES was associated with increased parent report of depressive symptoms. - Family functioning was NOT related to depressive symptoms in this study.

Table 1 (continued)

Primary Author	Title	Design	Population	Sample Size	Major Findings
Luis CA (2002)	Mood and anxiety disorders following pediatric traumatic brain injury: A prospective study	Prospective cohort	6-15 YO at time of injury assessed via phone 6-mo post-injury	45 w/ mild TBI 19 w/ mod-sev TBI 35 ortho ctrls	<ul style="list-style-type: none"> - Brain-injured children were at higher risk for developing depression compared to controls. - Increased injury severity (i.e. lower GCS) is related to development of an incident case of depression or anxiety. - For mild TBI, 35.7% and 21.4% with novel anxiety or depressive disorder, respectively. For moderate-severe TBI, novel depressive and anxiety disorder prevalence were 63.2% and 15.8%, respectively. 63.2% of moderate-severe group developed a new mood disorder diagnosis (38.1% of mild). - Multivariate analysis only accounted for 42% of variance in model.
Max JE (1997)	Traumatic Brain Injury in Children and Adolescents: Psychiatric Disorders in the First Three Months	Prospective cohort	6-14 YO at TBI (3-month FU)	26 w/ mild TBI 9 w/ mod. TBI 15 w/ sev. TBI (at Baseline) 17 w/ mild TBI 9 w/ mod. TBI 11 w/ sev. TBI (at 3-mo FU)	<ul style="list-style-type: none"> - Severity of Injury predicted any incident psychiatric disorder at 3-mo FU (p=.0233). - Lifetime presence of psychiatric disorder predicted incident psychiatric disorder at 3-mo FU (p=.0331). - Positive family psychiatric history predicted incident psychiatric disorder at 3-mo FU (p=.0292). - Family function predicted incident psych disorder at 3-mo FU (p=.0190). - SES predicted incident psych disorder at 3-mo FU (p=.0271). - 5 cases of Major Depression (13.5%) at 3-month FU.
Max JE (1997)	Traumatic Brain Injury in Children and Adolescents: Psychiatric Disorders in the Second Three Months	Prospective cohort	6-14 YO at TBI (6-month FU)	20 w/ mild TBI 9 w/ mod. TBI 12 w/ sev. TBI	<ul style="list-style-type: none"> - No incident or prevalent cases of Major Depression at 6-mo FU. - Severity of injury cont'd to predict incident psychiatric disorder at 6-mo FU (p=.012). - Family function cont'd to predict incident psychiatric disorder at 6-mo FU (p=.013). - Positive family psych history cont'd to predict incident disorders at 6-mo FU (p=.031 for first-degree relatives only). - Lifetime psych disorder no longer predicted incident psych disorders at 6-mo FU. - Age at TBI, gender, litigation status, temporal lobe lesions, and extrafrontal lesions did not predict "novel" disorder at 6-mo FU.

Table 1 (continued)

Primary Author	Title	Design	Population	Sample Size	Major Findings
Max JE (1998)	Traumatic Brain Injury in Children and Adolescents: Psychiatric Disorders at One Year	Prospective cohort	6-14 YO at TBI (12-month FU)	21 w/ mild TBI 9 w/ mod. TBI 13 w/ sev. TBI	<ul style="list-style-type: none"> - Severity of injury cont'd to predict any incident disorder at 12-mo FU (p=.059). - One case of depression disorder found at 12-mo FU. - Lifetime psych disorder cont'd to NO longer predict incident disorder at 12-mo FU. - Family function cont'd to predict any incident psych disorder at 12-mo FU (p=.027). - Positive family psych history cont'd to predict incident disorder at 6-mo FU (p=.011 for first-degree relatives only). - SES now predicts any incident disorder at 12-mo FU, though it did not predict at 6-mo FU (it did predict at 3-mo FU). - Age at TBI, gender, litigation status, temporal lobe lesions, and extrafrontal lesions did NOT predict incident disorders at 12-mo FU.
Yeates KO (2001)	Neurobehavioral Symptoms in Children Closed-Head Injuries: Changes in Prevalence and Correlates During the First Year Postinjury	Prospective cohort	6 to 12 YO at injury followed-up at 6- and 12-months post-injury	38 w/ mod CHI 31 w. sev CHI 53 w. ortho inj	<ul style="list-style-type: none"> - Prevalence of most neurobehavioral symptoms tended to peak at six-months and drop down at 12-months FU, but not to baseline prevalence. - Overall, those with severe injury had more emotional and behavioral symptoms at follow-ups than those with moderate injury. Both CHI groups had more emotional symptoms at FU than the orthopedic injury control group. - In models, injury severity was the strongest predictor of emotional and behavioral symptoms.

Table 2. Findings from Literature Examining TBI and Anxiety in Brain-Injured Youth

Primary Author	Title	Design	Population	Sample Size	Major Findings
Daviss WB (2000)	Predicting Post-Traumatic Stress After Hospitalization for Pediatric Injury	Prospective cohort	7-17 YO at TBI	48	<ul style="list-style-type: none"> - 45/48 (94%) met Criterion A for PTSD. - 6/48 (13%) met full PTSD diagnosis criteria. - PTSD score (CAPS-CA measure) was highly correlated with Total Problems (from CBCL) and parental distress. - No injury-related factors predicted PTSD.
Levi RB (1999)	Posttraumatic stress symptoms in children following orthopedic or traumatic brain injury	Prospective cohort	6 to 12 YO followed-up with at 6 and 12 months post-TBI	81 w/ TBI 59 ortho ctrls	<ul style="list-style-type: none"> - At 1Y, those with severe TBI reported higher number of PTS symptoms compared to moderate TBI or controls.
Max JE (1998)	Posttraumatic Stress Symptomatology after Childhood Traumatic Brain Injury	Prospective cohort	6 to 14 YO at time of injury followed-up at 3-, 6-, 12-, and 24-months post-TBI	26 w/ mild TBI 9 w/ mod TBI 15 w/ sev TBI	<ul style="list-style-type: none"> - 2/46 (4.3%) who had any FU met full criteria for PTSD and these were resolved by 3-month FU. - Definite increase in PTSD symptomatology in the first three months post-injury (86% with any PTSD symptomatology), but symptoms then decreased through 2Y FU (12% with any PTSD symptomatology).
Gerring JP (2002)	Clinical predictors of Posttraumatic Stress Disorder after closed head injury in children	Prospective cohort	4 to 19 YO at CHI followed-up for 1 year	95 w/ sev CHI	<ul style="list-style-type: none"> - Posttraumatic Stress Disorder (PTSD) was prevalent in 12/95 (12.6%); only 2 were concordant reports of both parent and child. - Significant predictors of PTSD include female gender and pre-injury anxiety symptoms. - PTS-related symptoms were significantly predicted by (1) injury severity, (2) pre-morbid prevalence of anxiety symptoms, (3) other psychiatric disorder diagnosis, and (4) post-CHI depression.

Table 2 (continued)

Primary Author	Title	Design	Population	Sample Size	Major Findings
Geraldina P (2003)	Neuropsychiatric Sequelae in TBI: A comparison across different age groups	Cross-sectional	0 to 18 years at TBI (Mean Age = 11.67 at 1Y follow-up)	96	<ul style="list-style-type: none"> - Prevalence of anxiety symptoms was 30% in 7 to 13 YOs; 11.3% in 14 to 18 YOs. - For 7 to 13 YO, presence of frontal lesions and poorer GOS is associated with presence of anxiety. - Participants with higher levels of disability often had lower levels of anxiety and vice-versa. - Presence of frontal lesions were significantly associated with both anxiety and depression ($p = .05$). - 14 to 18 year-olds have 13.5% prevalence of anxiety or depression (combined) (CBCL). - Higher GOS is associated with anxiety and depression when compared to mild-level GOS children. - For 14 to 18 YO, no significant relationship between anxiety and injury severity was observed. - Male sex is related to internalized behavior but not anxiety. - No correlation between any disorder and GCS.
Luis CA (2002)	Mood and anxiety disorders following pediatric traumatic brain injury: A prospective study	Prospective cohort	6-15 YO at time of injury assessed via phone 6-mo post-injury	45 w/ mild TBI 19 w/ mod-sev TBI 35 ortho ctrls	<ul style="list-style-type: none"> - Brain-injured children were at higher risk for developing anxiety compared to controls. - Increased injury severity (i.e. lower GCS) is related to development of incident anxiety. - For mild TBI, 35.7% with incident anxiety disorder, respectively. For moderate-to-severe TBI, anxiety disorder prevalence was 15.8% - Post-TBI stress levels are predictive of incident disorder, but stress may also be a reaction to new-onset mood disorders (esp. anxiety).

Table 2 (continued)

Primary Author	Title	Design	Population	Sample Size	Major Findings
Vasa RA (2002)	Anxiety after severe pediatric closed head injury	Prospective cohort	4 to 19 YO with severe TBI followed-up for 1 year	97	<ul style="list-style-type: none"> - Overall, the average anxiety score significantly increased from pre-injury to post-injury. - Increase in the number of children with many (10+) anxious symptoms from baseline to 1Y follow-up. - Overanxious symptoms were the most common class of anxiety-related symptoms to increase post-injury. - Pre-injury anxiety symptoms were predictive of post-injury symptoms making pre-injury anxiety a risk factor for post-injury symptoms and disorders. - Younger age at injury was predictive of increased post-injury anxiety symptoms (but not disorders). - Neither injury severity nor SES were predictive of post-injury anxiety symptoms (note only severe injuries were included).
Vasa RA (2004)	Neuroimaging Correlates of Anxiety after Pediatric Traumatic Brain Injury	Cross-sectional	4 to 19 YO with severe TBI followed-up for 1 year	95	<ul style="list-style-type: none"> - Damage in the temporal lobe was associated with Posttraumatic Stress Disorder (PTSD) symptoms. - Damage (i.e. greater number and volume of lesions) in the orbitofrontal cortex (OFC) is inversely related to anxiety. OFC is related to the amygdala and fear-based response so OFC damage may affect how the brain reacts to fears.

Table 3. Findings from Literature Examining TBI and ADHD in Brain-Injured Youth

Primary Author	Title	Design	Population	Sample Size	Major Findings
Slomine BS (2005)	Differences in attention, executive functioning, and memory in children with and without ADHD after severe traumatic brain injury	Prospective cohort	6-16 YO w/ severe TBI at one-year follow-up	82	<ul style="list-style-type: none"> - 13.5% (15/82) met criteria for pre-injury ADHD based on structured interview with caregiver (6/15 did not meet criteria 1-year post-TBI and were dropped from analysis). - 9/15 with pre-injury ADHD met criteria for ADHD 1-year post-TBI. - 14/82 developed ADHD after TBI (S-ADHD).
Max JE (1998)	Child and Adolescent Traumatic Brain Injury: Correlates of Disruptive Behavior Disorders	Record Review	Average of 6 YO at TBI	17 w/ mild TBI 12 w/ mod/sev TBI 21 w/ sev. TBI	<ul style="list-style-type: none"> - 10/50 met pre-injury ADHD criteria. - 21/50 met post-injury ADHD criteria (does not include those w/ pre-TBI ADHD). - ADHD not associated with any variables tested (family functioning [p<0.27], severity of injury [p>0.40], family hx EtOH abuse [p>0.35], age at injury [p=0.82]).
Gerring JP (1998)	Premorbid Prevalence of ADHD and Development of Secondary ADHD After Closed Head Injury	Prospective cohort	4 to 19 YO at CHI followed-up for 1 year	10 w/ mod CHI 84 w/ sev CHI	<ul style="list-style-type: none"> - Prevalence of pre-injury ADHD was 20% (95% CI: 12%, 30%) which was significantly higher than a non-injury reference group (4.5%). - Incidence (new ADHD cases w/ no pre-TBI ADHD) at 1Y FU was 19% (95% CI: 10%, 33%). This was also significantly higher than the reference population. - No difference between genders, SES or number of pre-injury psychiatric diagnoses (except ADHD) in ADHD prevalence/incidence. - Injured children who developed S-ADHD had greater levels of aggression, psychiatric comorbidity, and overall disability compared to those with no post-injury ADHD (S-ADHD) at FU. - Authors suggest behavioral inattentiveness and impulsivity (symptoms of ADHD) lead children into risky behavior resulting in a higher-than-average pre-injury prevalence of ADHD making ADHD a risk factor for CHI.

Table 3 (continued)

Primary Author	Title	Design	Population	Sample Size	Major Findings
Levin H (2007)	Symptoms of attention-deficit/hyperactivity disorder following traumatic brain injury in children	Prospective cohort	5-15 YO followed over two years post-TBI	114	<ul style="list-style-type: none"> - In children without pre-injury ADHD, only SES significantly predicted presence of SADHD. - Prevalence of ADHD in those w/o pre-TBI ADHD: 14.5% (1Y) to 18.3% (2Y). - Prevalence of ADHD in those w/ pre-TBI ADHD: 86.4% (1Y) to 96.2% (2Y). - Pre-TBI ADHD-ers who were treated compared to those not treated for ADHD pre-injury reported less ADHD symptoms at 2Y.
Max JE (2004)	Attention Deficit Hyperactivity Disorder in Children and Adolescents Following Traumatic Brain Injury	Prospective cohort	5 to 14 YO at TBI	57 w/ mild/mod. TBI 37 w/ sev. TBI 24 w/ ortho inj.	<ul style="list-style-type: none"> - S-ADHD occurred in 13/34 with severe TBI (38%). This rate was much less in those with mild/moderate injury (1/8, or 12.5%). - Of those with orthopedic injury, SADHD occurred in only 1/20 (5%). - Severity of injury (as a continuous variable of GCS) was associated with SADHD. - Gender was not significantly associated with SADHD. - SADHD resolved in one-third within 18-months post-TBI.
Max JE (1998)	Attention-Deficit Hyperactivity Disorder Symptomatology After Traumatic Brain Injury: A Prospective Study	Prospective cohort	6 to 14 YO at time of injury followed-up at 3-, 6-, 12-, and 24-months post-TBI	26 w/ mild TBI 9 w/ mod TBI 15 w/ sev TBI	<ul style="list-style-type: none"> - Change in ADHD symptomatology over 24-month FU was related to injury severity. - Family functioning was a significant predictor of overall ADHD symptomatology even after controlling for injury severity, family psychiatric history, and SES.
Herskovits EH (1999)	Is the Spatial Dist'n of Brain Lesions Associated with Closed-Head Injury Predictive of Subsequent Development of ADHD	Cross-sectional	4 to 19 YO with TBI and no prior history of pre-TBI ADHD	76	<ul style="list-style-type: none"> - 15/76 in sample developed SADHD after injury. - Children who developed SADHD had more lesions in the right putamen region than those who did not develop SADHD, but these results were no longer significant after adjustment for multiple comparisons.

Table 4. Findings from Literature Examining TBI and ODD/CD in Brain-Injured Youth

Primary Author	Title	Design	Population	Sample Size	Major Findings
Max JE (1998)	Child and Adolescent Traumatic Brain Injury: Correlates of Disruptive Behavior Disorders	Record Review	Average of 6 YO at TBI	17 w/ mild TBI 12 w/ mod/sev TBI 21 w/ sev. TBI	<ul style="list-style-type: none"> - 3/50 met pre-injury ODD/CD criteria. - 27/50 met post-injury ODD/CD criteria (does not include those w/ pre-TBI ODD/CD) - ODD/CD was significantly associated w/ poorer family functioning ($p < .00005$) with those with “novel” ODD/CD having poorer family functioning. - ODD/CD was significantly associated w/ more severe injury but in an unexpected direction: “novel” ODD/CD group had milder TBI than those with no ODD/CD. - ODD/CD was associated with family history of alcohol dependence/abuse ($p < .10$). - Age at injury, IQ, and language skills not associated with ODD/CD.
Max JE (1998)	Oppositional Defiant Disorder Symptomatology After Traumatic Brain Injury: A Prospective Study	Prospective cohort	6 to 14 YO at time of injury followed-up at 3-, 6-, 12-, and 24-months post-TBI	26 w/ mild TBI 9 w/ mod TBI 15 w/ sev TBI	<ul style="list-style-type: none"> - ODD symptomatology peaked at one-year post-TBI. - SES predicted change in number of ODD symptoms at each FU past 3 months. - Injury severity was NOT significant predictor until 24-month FU where those with severe TBI were much more likely to have continued ODD symptomatology. - Poorer family function predicted increased overall ODD symptoms in the first year post-TBI. - Imaging suggests that bicaudate ratio was related to change in ODD symptoms over time (same finding for ADHD in this cohort). Results for ODD nor ADHD were not specified as statistically significant.
Tateno A (2003)	Clinical correlates of aggressive behavior after traumatic brain injury	Cross-sectional	Adults (avg. 36 ± 15 yo), examined 6-mo post-injury	89 w/ TBI 26 injured controls	<ul style="list-style-type: none"> - 33.7% demonstrated aggressive behavior in the first 6 months post-TBI. - Aggressive behavior was significantly associated with (1) depression, (2) history of drug or EtOH abuse, and (3) frontal lobe lesions.

3.0 ARTICLE ONE: DEPRESSION- AND ANXIETY-RELATED OUTCOMES OF TRAUMATIC BRAIN INJURY IN CHILDREN AND ADOLESCENTS

Christopher A. Taylor¹, P. David Adelson², Sue R. Beers³, Anthony Fabio⁴, Thomas J. Songer¹, Stephen R. Wisniewski¹. (Authors listed alphabetically—Final order to be determined.)

¹ Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA

² Children's Neuroscience Institute, Phoenix Children's Hospital, Phoenix, AZ

³ Department of Psychiatry, School of Medicine, University of Pittsburgh, Pittsburgh, PA

⁴ Department of Neurological Surgery, School of Medicine, University of Pittsburgh, Pittsburgh, PA

Manuscript in preparation.

3.1 ABSTRACT

Background: While research exists that links higher prevalence of depression- and anxiety-related outcomes to brain injury, the results of these studies vary widely and the long-term associations between injury and these outcomes have not been fully examined. *Methods:* Participants included 13 young survivors of moderate and severe TBI and their caregivers recruited from a hospital-based pediatric neurological surgery practice. Children completed a telephone-based interview assessing symptoms of depression and anxiety. Caregivers completed

questionnaires on the child's family environment. *Results:* On average, the child participants were 13.8 ± 2.8 years old and at least four years post-injury. Prevalence of both depression and anxiety were each 5.9% based on testing and medical history. Child's age at the time of interview was positively correlated with depression symptoms ($\rho=0.56$, $p=0.04$). Also, children with more severe injuries had a higher mean depression score compared to those with moderate injuries ($p=0.05$). *Conclusion:* The prevalence of depression in this cohort was in line with expected values for a general adolescent population and much lower than previous studies examining children closer to the time of injury. Additionally, this study also found that increased injury severity was associated with a higher number of depression-related symptoms. No factors were found to be associated with anxiety in this population.

3.2 INTRODUCTION

Of the more than one million traumatic brain injuries that occur every year, nearly one-third involve children and adolescents¹. Young survivors of TBI have been shown to be at risk for chronic disability due to TBI-related cognitive deficits, impaired motor skills, and poor academic achievement³⁻⁵. Additionally, while studies have suggested a link between TBI and psychiatric and behavior disorders, little research has been done examining the prevalence of these conditions several years past the time of injury.

The prevalence of major depression in children and adolescents ages 9 to 17 is roughly 5 percent⁸. In contrast, one study found that one-quarter of survivors of severe TBI had a depression-related diagnosis¹⁴. Additional studies have found wide-ranging—though still higher-than-normal—prevalence rates of 13%¹⁶ and 22%¹⁵ in young mixed-severity TBI

survivors. Additionally, studies have found a relationship between prevalence and time elapsed since injury. In a series of published articles following one injured cohort over time, the prevalence of depressive symptoms in TBI survivors lessened over time in most children, though some still had depressive symptoms at the end of two-year follow-up¹⁸⁻²². Yet another study notes an increased, while relatively stable, number of depressive symptoms in young TBI survivors which is in contrast to orthopedically-injured controls whose prevalence of depressive symptoms returned to baseline levels at the end of follow-up²³.

Anxiety can lead to a greatly reduced quality of life due to an overall, unrealistic worry about everyday activities. Left untreated, anxiety can lead to impaired adult relationships, low-self-esteem, and drug or alcohol use²⁶. Additionally, about half of all children with an anxiety disorder also have a concurrent psychiatric or behavioral problem, such as depression²⁶. Anxiety is the most common emotional disorder in children and adolescents aged 9 to 17 years with an estimated 13% prevalence⁸. In contrast, a one-year follow-up of a brain-injured cohort found 31% with symptoms of an anxiety-related disorder²⁸—much higher than the general youth population. Other studies that followed cohorts longitudinally found resolved and newly presented cases of anxiety at each follow-up point through one-year post-TBI^{18, 19, 22, 30}.

It is already known that children who experience chronic medical conditions are more likely to develop symptoms of depression than their healthy peers¹³. Because of these risks, both depression and anxiety are important public health issues. It is important to understand if and how TBI-related dysfunction is related to these conditions that may put more children at risk for poor psychological outcomes. Published research articles have identified some risk factors for depression and anxiety in young survivors of TBI, though the magnitude and direction of some of these effects vary across study populations.

Injury severity is one factor that is examined in most TBI-related research studies. Increased severity of injury in survivors of childhood TBI is positively related with increased report of depressive^{16, 17, 23} and anxious^{18, 19, 22, 30} symptoms in nearly all studies examined. Additional factors that have been suggested to be associated with depressive symptoms include age¹⁶, gender^{16, 32}, socioeconomic status²³, increased neurological impairment¹⁶, and injury-related anatomical changes,¹⁶ though these findings are not conclusive and no studies examined these factors in injury survivors several years past the time of injury.

The specific aims of this research were to (1) examine the distribution of symptoms of depression and anxiety, (2) estimate the prevalence of depression and anxiety symptoms in the studied population as determined by standardized symptom surveys, (3) examine the co-occurrence of depression and anxiety, and (4) examine the correlation of factors associated with the presence or absence of depression and anxiety symptoms.

3.3 METHODS

3.3.1 Study Design

For this cross-sectional epidemiological study, participants were contacted for initial screening based on a search of medical records from a study-associated pediatric neurosurgeon (PDA). Based on a review of medical record information, parents of 93 children who met inclusion criteria were contacted with a letter outlining the details of the study. Inclusion criteria included (1) alive and living in the community, (2) between 8 and 17 years of age at the time of study enrollment, (3) experienced a moderate or severe TBI based on initial-injury GCS score, and (4)

spoke English with (5) at least six months post TBI. Potential participants were excluded from our mailing if the head trauma was thought to be the result of abuse. Families who did not respond to the mailing were contacted by telephone by a clinician with access to medical record and contact information. Parents who responded positively to the letter were contacted and screened. Children were asked to participate if they received a Glasgow Outcome Scale – Pediatrics (GOS–E Peds)⁷¹ score of 3 or better as part of the eligibility interview completed over the telephone with the primary parental caregiver. This score on this age-modified version of the Glasgow Outcome Scale (GOS) correlates to functioning at an upper moderate disability level or higher and indicates that the child likely had the capacity to participate in the outcomes assessment interview. Non-respondent families were ultimately contacted by mail three times to determine potential interest. Additionally, a clinical staff member attempted to contact non-responding families by telephone, but no families were ultimately recruited from this effort.

Participants who enrolled were mailed a packet of forms. Parents were asked to provide written informed consent for their child’s participation. Additionally, children were asked to assent to participation. This study was approved by the Institutional Review Board of the University of Pittsburgh (protocol number PRO08050341). Seventeen caregivers and 14 children were enrolled, though one child declined to participate in the outcomes assessment interview (Figure 1). Gift cards were provided to both parent and child enrolled participants.

3.3.2 Data Collection

Symptoms of depression and anxiety were obtained directly from enrolled child participants through telephone interview. To assess depression symptoms, child participants were administered Beck Depression Inventory for Youth (BDI-Y)⁷². The BDI-Y is a self-report

instrument used to measure symptoms of depression in children between 7 and 18 years of age. This symptom survey is comprised of 20 questions. Respondents utilize a five-item Likert scale to respond the question, and the total raw score is converted to a normalized sex- and age-specific T-score. The BDI-Y has demonstrated sufficient internal reliability (Cronbach alpha = 0.91) and test-retest reliability ($r > 0.75$).

To assess anxiety symptoms, child participants were administered the Multidimensional Adolescent Anxiety Scale (MASC)⁷³. The MASC is a self-report instrument used to measure symptoms of anxiety in children between 8 and 17 years of age. This symptom survey is comprised of 39 questions. Respondents utilize a five-item Likert scale to respond the question, and the total raw score is converted to a normalized sex- and age-specific T-score. The MASC has demonstrated satisfactory internal validity (Cronbach alpha ranges = 0.61) and test-retest reliability range from 0.64 to 0.71 depending sex and age.

Both the BDI-Y and MASC were administered with the using of a blinded response form. This blinded form included lead words for each statement and categories of response. This approach was utilized for two reasons. Permitting the child to write their answers helped alleviate the risk of a response bias where the child may feel anxious in verbally reporting their responses to the interviewer. Additionally, because only the first few words of each statement were included (e.g. “I am...”, “I feel...”, etc.) on each form, the privacy of the child was protected from their parents who were responsible for mailing the completed forms back to the study investigators. The psychometric properties of these testing instruments (Figure 1) are based on traditional administration of these measures. The [traditional] forms used to administer these tests are designed for direct completion by the child.

Socio-economic status (SES) was scored based on Hollingshead's criteria⁷⁴. The occupational scoring for the Hollingshead SES measure was modified from the original 1970s US Census data for use in this research to more adequately reflect modern employment. The measure of religious faith was scored after completion of the Santa Clara Strength of Religious Faith Questionnaire⁷⁵. A measure of the family's burden of injury was obtained by the use of the Family Burden of Injury Interview⁷⁶. A measure of family function was obtained by the General Functioning subscale of the McMaster Family Assessment Device⁷⁷. Medical history related to previous diagnoses of depression and anxiety was obtained by parental report. All of these measures were obtained via questionnaires completed by the primary caregivers of the injured children. Information relating to injury severity and other factors collected at the time of injury were obtained through the use of medical record data. The marker of clinically significant depression or anxiety symptoms was defined as having a current diagnosis based on self-report or a T-score ≥ 65 on the BDI-Y (depression) or a T-score ≥ 65 on the Anxiety Disorder Index on the MASC (anxiety).

A medical safety plan was developed and utilized. Participants without a previous diagnosis of these disorders with a T-score ≥ 65 on either testing instrument were contacted by a licensed psychologist (SRB). The psychologist discussed the results of the test with the parent or legal guardian of the child participants and provided referrals to appropriate care providers, when necessary.

3.3.3 Statistical Methods

T-scores for symptom surveys were determined by the publishers of the tests based on population norms. After the scoring of the surveys, raw scores are translated to T-scores. T-scores used in this analyses accounted for age and sex.

Measures of correlation were calculated between continuous outcomes scores (depression and anxiety T-scores) and continuous injury-related and demographic variables using Spearman correlation values. Additionally, differences between categories of injury-related variables were tested using non-parametric Wilcoxon comparisons. All analyses were performed using SAS 9.2 (Cary, NC).

3.4 RESULTS

Ninety-three families met the initial eligibility criteria based on age, time since injury, and injury severity. Of the 93 families to which letters were mailed, 27 responded positively and indicated an interest in being screened for eligibility (Figure 1). Of those 27, 20 were successfully contacted and screened and 7 were unable to be reached using the contact information provided in the reply form. Forty-four families did not respond to the mailing and were contacted by a member of the medical staff to determine their interest. None of these 44 non-responders were ultimately interested in participating in this study. All 17 screened caregivers were enrolled. One child was not eligible to participate due to an ineligible GOS-E Peds score (Figure 2). Additionally, 2 children were not interested in participating, and 1 additional child agreed to participate but did not wish to be interviewed as part of the depression and anxiety outcomes

assessment. Ultimately, data related to depression and anxiety symptoms were collected on 13 injured youth.

All enrolled participants—caregivers and young injury survivors—were non-Hispanic whites. All caregivers enrolled in this study were women, and just 3 of the 13 children were female (23.1%). Nine children (69.2%) suffered a severe TBI at time of admission to the hospital with injuries (Figure 3), on average, more than seven years ago (Table 6). No statistically significant differences were found between injury severity, age at injury, time passed since injury, race, or sex between enrolled study participants and those enrolled in this study (Table 5).

Of the thirteen young injury survivors enrolled, one (5.9%) was reported as having a current diagnosis of depression by a medical professional based on the parent-reported medical history. The average T-score was 51 (Figure 4). About one-half of the children screened had a BDI-Y T-score of greater than or equal to 50, and no T-score fell below 40 (Figure 4).

Additionally, one enrolled child (5.9%) also had a current diagnosis of an anxiety disorder by a medical professional at the time of this interview. The MASC Anxiety Disorder Index T-score ranged from 27–60 with no child earning a clinically significant T-score of ≥ 65 (Figure 5). Eight participants (62%) had MASC Anxiety Index T-scores of less than 50, indicating somewhat less anxiety than found in the general youth population. There was no co-occurrence of depression and anxiety.

The BDI-Y T-score and MASC Anxiety Disorder Index T-score were positively correlated ($\rho=0.30$), but the relationship was not statistically significant ($p=0.31$).

Spearman correlation statistics were generated (Table 8), and the age of the child at the time of this interview was positively correlated with depression ($\rho=0.56$, $p=0.04$) (Figure 6).

Caregiver total score on Center for Epidemiologic Studies–Depression (CES-D) scale—the caregiver measure of depressive symptoms—was also modestly correlated to the MASC ADI T-score ($\rho=0.47$, $p=0.10$) (Figure 7). Additionally, children with severe injuries had a higher mean BDI-Y T-score (52.9 ± 5.3) compared to enrolled children with a moderate TBI (47.5 ± 3.1 , $p=0.05$) (Table 9).

3.5 DISCUSSION

In this study, we evaluated the relationship between depression and anxiety in children who experienced moderate and severe TBI. We interviewed traumatically brain-injured children and their primary caregivers to determine the prevalence of depression and anxiety in the children as well as identify environmental and injury-related characteristics that may be associated with the depression and anxiety outcomes. Using correlation statistics, we identified a few variables that appear to be statistically related with these depression- and anxiety-related outcomes.

Based on the age- and sex-adjusted T-scores of the BDI-Y, one injured child (5.9%) was reported as having a diagnosis of a depression-related disorder. This prevalence of depression is much lower than what has been reported in studies of depressive outcomes in a TBI population, and more in line with the prevalence of the general population of 9–17 year olds¹⁰. Several previously published studies showed higher prevalence rates of depression. However, these studies were conducted within two years of injury, and most examined symptoms between six months and one year while study examined children whose injuries occurred four to twelve years prior to the interview. This may suggest that if the increased prevalence of depression-related symptoms occurs within the first few years post-injury is true for all child TBI populations, then

that prevalence may decrease over time to a value that is very similar to that of the general population of adolescents. However, only a longitudinal analysis with examinations over time can confirm this possibility.

Anxiety in this population of injured children is equal to that of depression with one child (5.9%) reported as having a current diagnosis. This is lower than the rates reported in previously published studies conducted within the first few months and years of follow-up and is also lower than the general population prevalence of 13% for 9–17 year olds. As with depression, it may be possible that the time since injury has resolved some symptoms of anxiety, some which were reported to be related to post-traumatic stress as a result of the traumatic injury event. As well, much of the anxiety-related symptoms present in the near-term after TBI is attributed to PTSD³². As time from the traumatic event passes, these PTSD symptoms may decrease. Again, longitudinal analyses with several follow-up time points can further elucidate this possibility.

The co-occurrence, or comorbidity, of depression and anxiety symptoms in children has been well-documented²⁶, however, no child enrolled in this study had a clinically significant amount of symptoms for both conditions—nor a caregiver-reported diagnosis of both disorders—to indicate any comorbidity in this study population. There is no answer to be found in these data to indicate why there are no comorbid presentations of depression and anxiety in this population, although the low prevalence of the outcomes and small sample size greatly limits the possibility of any such finding.

The age of the injured child at the time of the interview was positively associated with BDI-Y T-score. This relationship indicates that older children enrolled and interviewed in this study were likely to have a higher depression score than younger children interviewed. However, the age at the time of injury was not significantly associated with this depression score

($p=0.26$). This finding is not consistent with the work of Geraldina *et al.* that did find a relationship between age at injury and increased depression symptoms¹⁶. However, it does agree with Max *et al.* who found no relationship between age and depression¹⁹. This possibly suggests that, with this population, age at the time of injury is not associated with depressive outcomes as much as life events and situations which may become more apparent—and significant to the child—as they grow up in adolescence functioning in a way that may differ from many of their peers. However, there are no data in this study to support this suggestion any further, but it is an important area to examine in further research of this kind.

In addition to age, this study found that a more severe brain injury was significantly associated with a higher depression T-score (Table 3). This finding is in line with nearly all studies of this type that have consistently found that a more severe injury is related to increased depressive symptoms^{16, 17, 23}.

In contrast to depression, there were no environmental or injury characteristics strongly correlated with anxiety disorders in this study population. Furthermore, the CES-D total score for the caregiver was modestly associated with the child's anxiety score ($p=0.10$). It is not possible to determine, assuming this is a valid (rather than a spurious) relationship, any causality. There is also a small, suggestive association between caregiver and child depression scores ($p=0.18$), though this relationship may be the reaction of the caregiver to the situation of their wards. Finally, children who are reportedly receiving special education services have, on average, lower anxiety T-scores compared to those who do not receive those services. Again, there is no data to suggest a reason for this, and the information on special education services provided to the child is unknown. Anecdotally, based on casual information provided by the caregivers, the range of services greatly varies from full-time remedial classes for some children

to additional resources being available, if necessary, for others and can vary greatly by school district.

3.5.1 Strengths and Limitations

This research has many strengths that support the findings of this study. Firstly, the injury-related data are well documented and include important variables related to the injury event. Additionally, the outcome assessments—while not conducted in person—were collected in a way which minimized self-report bias by use of the blinded response interview with the child. Additionally, the caregiver-provided data was provided completely in a way that allowed the analysis to be performed in a way that includes as many data points as possible. Finally, this study included children whose injuries occurred at least four years ago. The authors are not aware of any other studies of childhood TBI survivorship that has included children this far past the time of injury.

The number of individuals who chose to participate in this study—while nearly 20% of the total potential pool of 93 participants—was relatively small. This small sample limits the statistical power to detect true differences between groups. It also calls into question the representativeness of the sample. The majority of the screened participants were moderately high functioning, leaving one to wonder if families with low functioning children felt they would not be helped by this study or if the study would be too burdensome given their current caregiving responsibilities. Additionally, there were very few participants who were very highly functioning. While the pool of potential TBI survivors were drawn from only those with moderate and severe injuries, it is possible that the families of children who are now high

functioning and several years post-injury would decide to rather not relive events associated with such a traumatic experience.

3.5.2 Conclusion

In conclusion, this study provides a novel look at depression- and anxiety-related outcomes several years after experiencing a childhood TBI. The prevalence of depression in this cohort was comparable to that of the similarly aged general population. The prevalence for anxiety was lower than that of the general population, and lower than that reported in any previous childhood head injury research. A few factors were significantly associated with depression and anxiety, including age, injury severity, and receipt of special education services.

These factors should be continued to be examined in future research as their significance may help researchers, physicians, and mental health professionals to more fully understand environmental and injury-related factors associated with these outcomes.

3.6 TABLES AND FIGURES

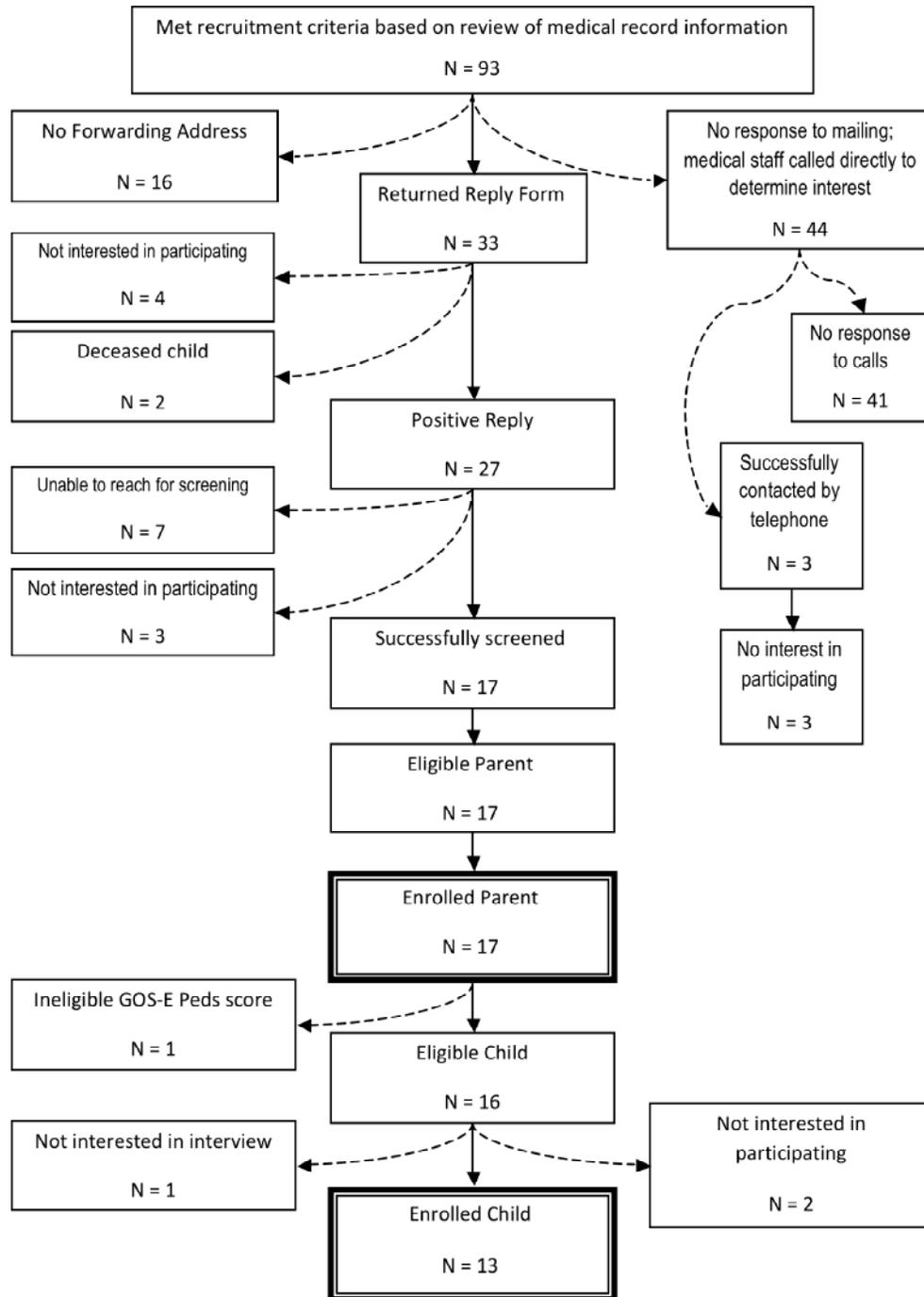


Figure 1. Study Recruitment Flow Diagram

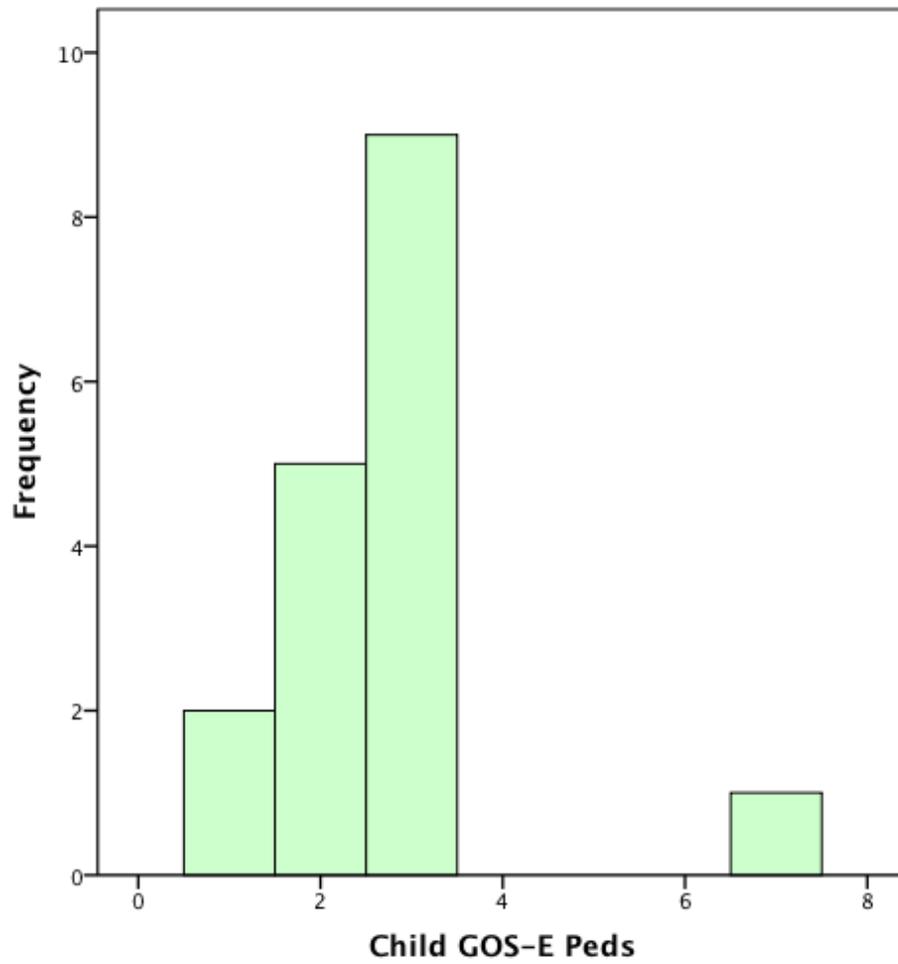


Figure 2. Distribution of the GOS-E Peds score at time of eligibility interview

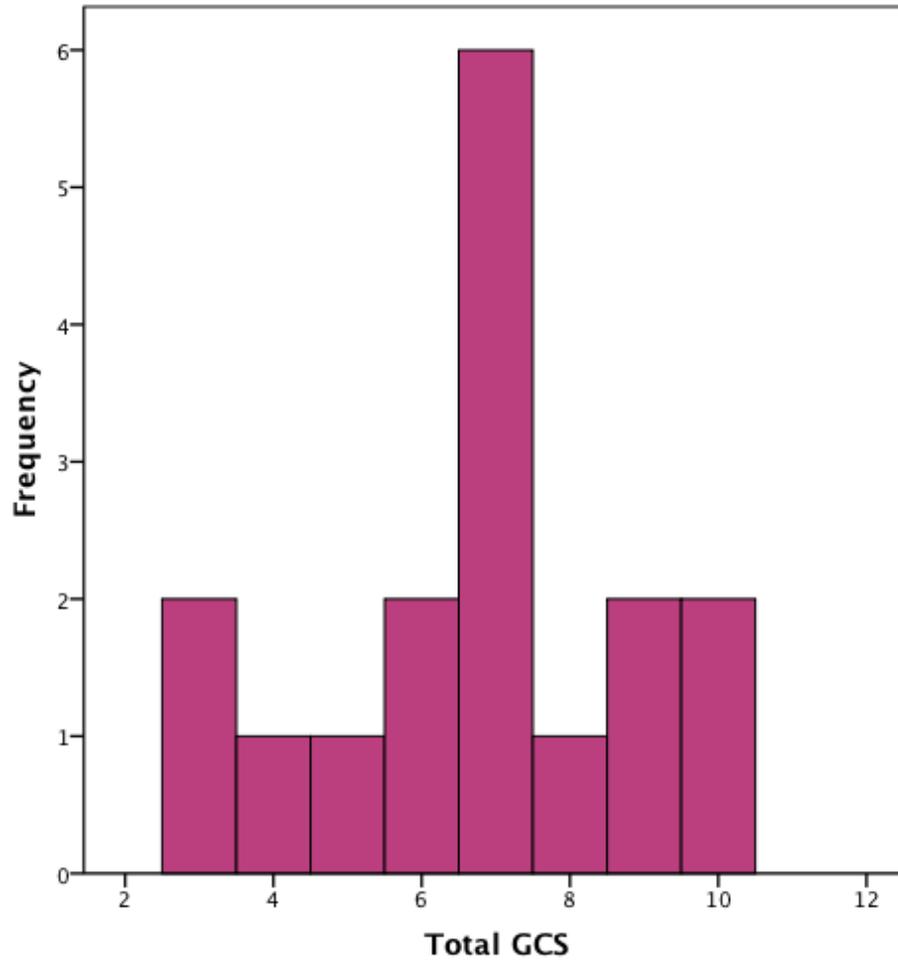


Figure 3. Distribution of Total GCS for enrolled child participants at time of injury

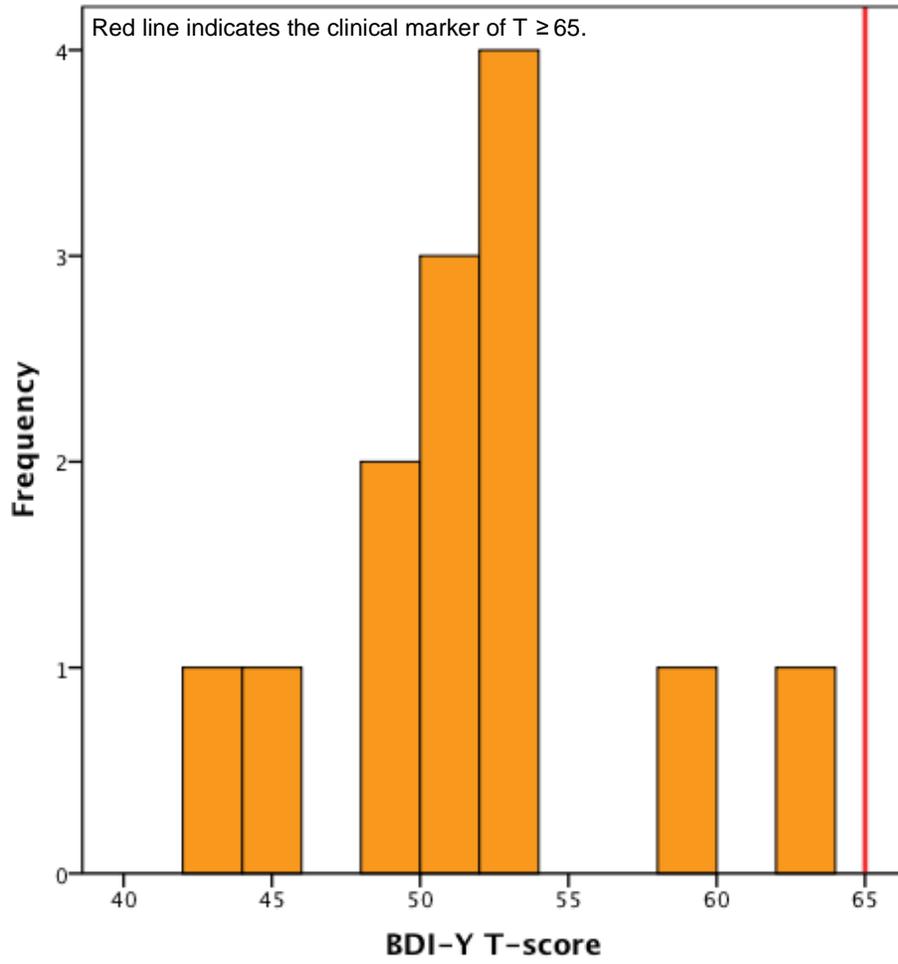


Figure 4. Distribution of T-scores from the Beck Depression Inventory for Youth (BDI-Y).

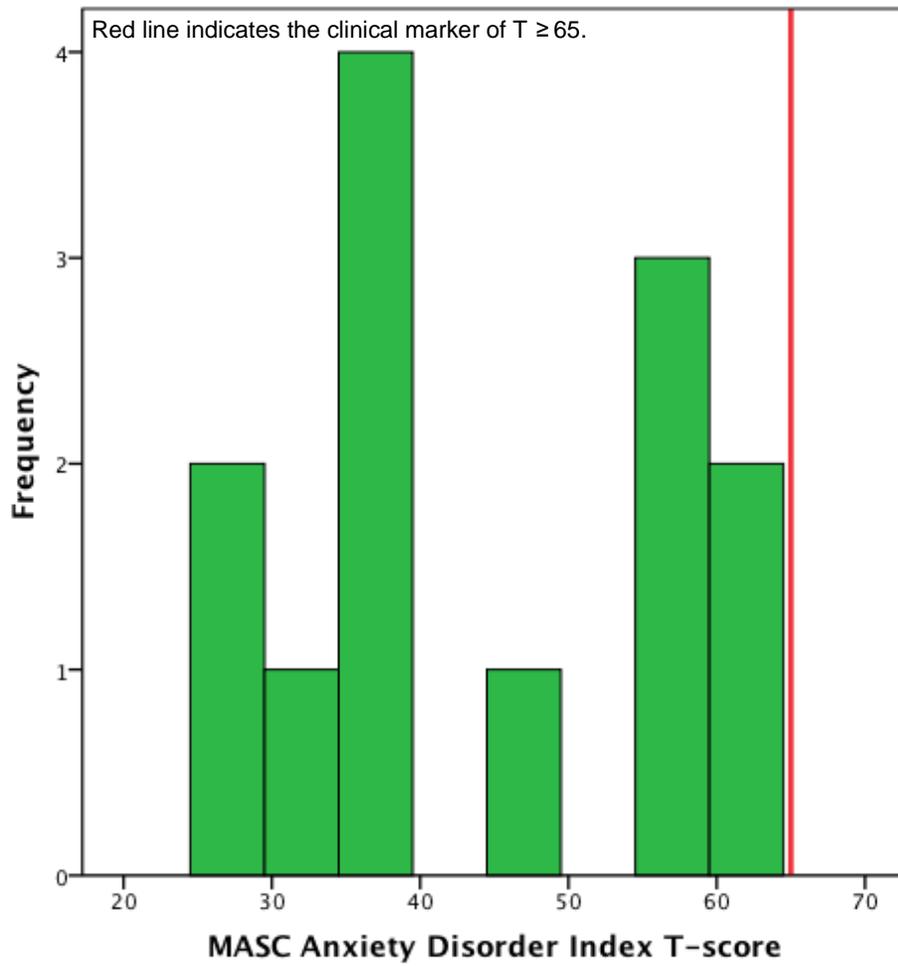


Figure 5. Distribution of T-scores from the Multidimensional Anxiety Scale for Children (MASC) Anxiety Disorder Index.

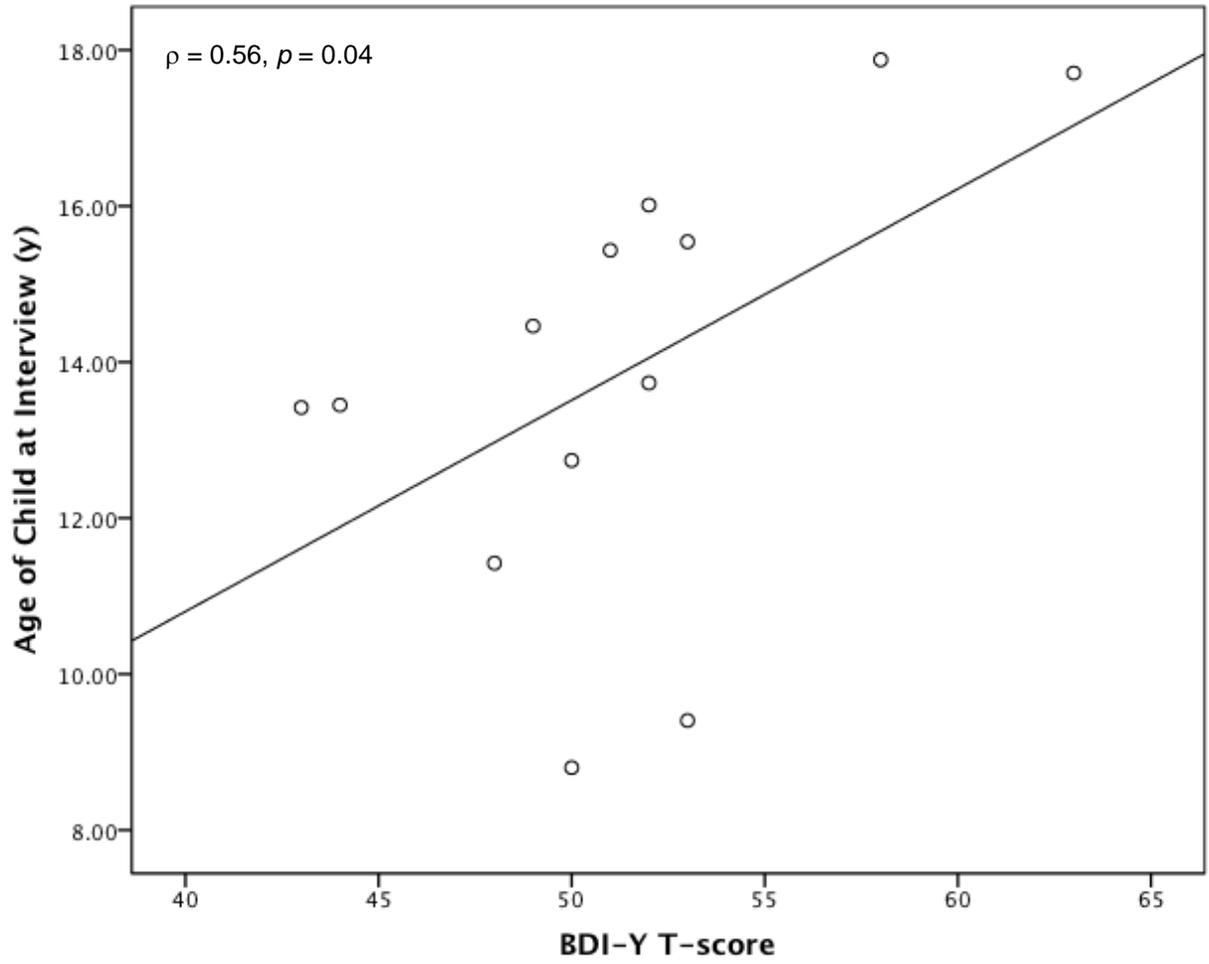


Figure 6. Scatterplot of Age of Child at Interview (in years) vs. BDI-Y T-score

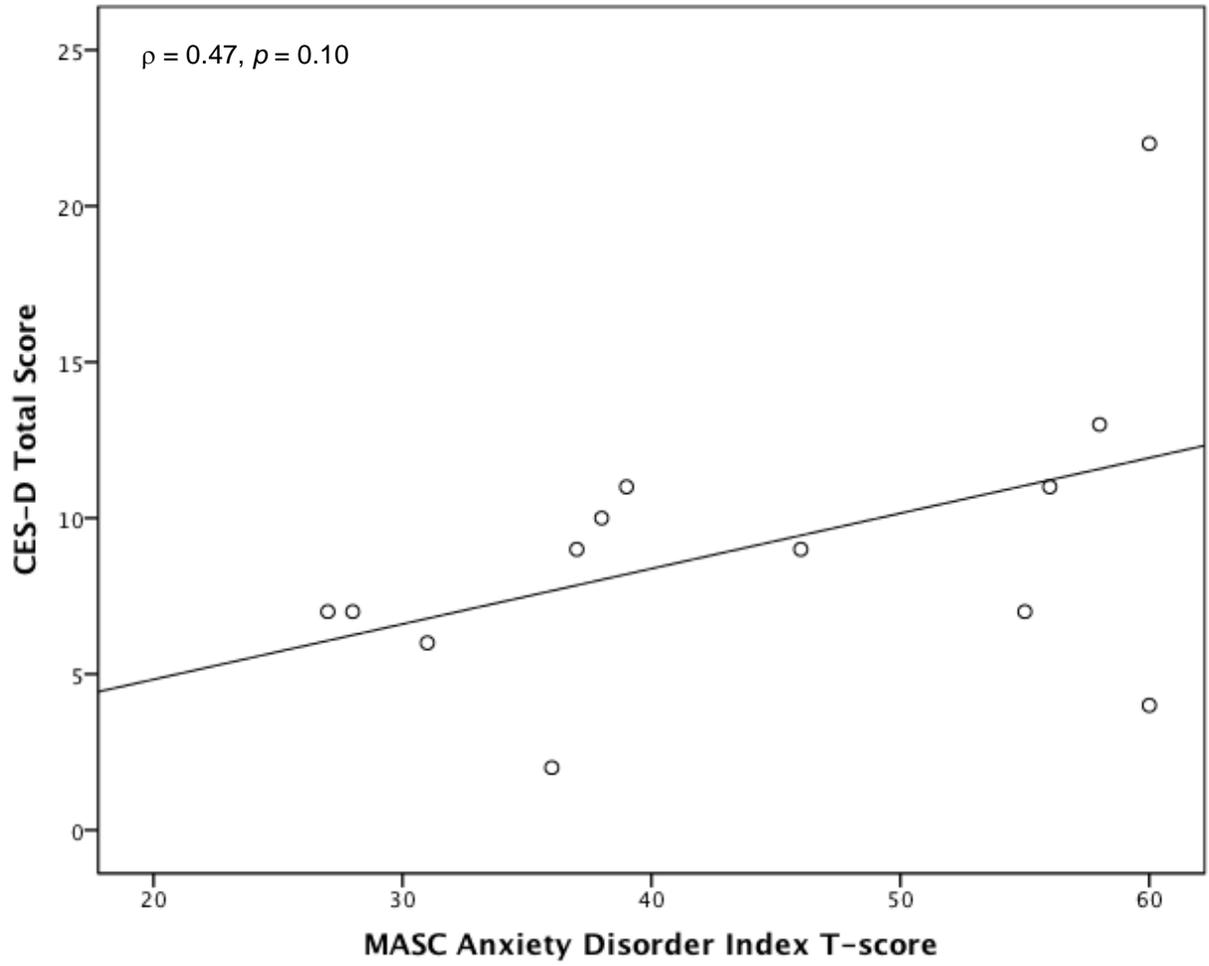


Figure 7. Scatterplot of CES-D Total Score (in caregivers) vs. MASC Anxiety Index T-score.

Table 5. Comparison of enrolled participants with unenrolled subjects from potential recruitment pool

Continuous Variables			
	Enrolled Participants	Unenrolled participants from same recruitment pool	<i>p</i>
Characteristic	Mean ± SD	Mean ± SD	
Age at interview (y)*	13.8 ± 2.8	13.6 ± 3.0	0.88
Age at injury (y)	7.0 ± 3.9	6.8 ± 3.6	0.82
Time since injury (y)	6.8 ± 2.9	6.8 ± 2.5	0.89
Glasgow Coma Scale	6.8 ± 2.1	7.1 ± 1.9	0.57
Categorical Variables			
Characteristic	N (%)	N (%)	<i>p</i>
<i>Sex</i>			0.16
Male	14 (82.4)	48 (63.2)	
Female	3 (17.6)	28 (36.8)	
<i>Race</i>			0.41
White	17 (100.0)	63 (82.9)	
Non-White	0 (100.0)	13 (17.1)	

* Median date of the assessment interview was used to determine the current age for subjects who did not enroll in the study.

Table 6. Demographic, Injury, and Outcome Characteristics

Continuous Variables		
Characteristic	Mean ± SD	Range
Age at interview (y)	13.8 ± 2.8	8.8 - 17.9
Time since injury (y)	7.5 ± 2.3	4.0 - 12.0
BDI-Y T-score	51.2 ± 5.2	43 - 63
MASC ADI T-score	43.9 ± 12.5	27 - 60
Family Burden of Injury score	19.4 ± 6.9	7 - 34
Family Functioning score	1.8 ± 0.5	1.0 - 2.6
Religious Faith score	21.8 ± 5.9	10 - 30
Hollingshead SES	40.0 ± 9.9	26 - 61
Categorical Variables		
Characteristic	N (%)	
<i>Sex</i>		
Male	10 (76.9)	
Female	3 (23.1)	
<i>Race</i>		
White	13 (100.0)	
Non-White	0 (0.0)	
<i>Glasgow Coma Scale</i>		
Moderate (9-12)	4 (30.8)	
Severe (3-8)	9 (69.2)	
<i>GOS-E Peds</i>		
Upper Good Recovery (1)	2 (15.4)	
Lower Good Recovery (2)	4 (30.8)	
Upper Moderate Disability (3)	7 (53.8)	
<i>Injury Mechanism</i>		
Fall	5 (38.5)	
Motor Vehicle Accident	3 (23.1)	
Car vs. Pedestrian	3 (23.1)	
Recreational	1 (7.7)	
Other	1 (7.7)	
Current Depression	1 (7.7)	
Current Anxiety	1 (7.7)	

Table 7. Correlation Coefficients of Depression and Anxiety

Characteristic	BDI-Y T-score		MASC ADI T-score	
	ρ	<i>p</i> -value	ρ	<i>p</i> -value
<i>Injured Youth Characteristics</i>				
Age at interview (y)	0.56	0.04	-0.32	0.28
Age at injury (y)	0.34	0.26	-0.39	0.19
Time since injury (y)	0.20	0.51	0.28	0.35
Total GCS	-0.60	0.03	-0.20	0.51
<i>Caregiver Characteristics</i>				
Caregiver Age at interview (y)	-0.10	0.75	-0.12	0.69
Family Burden of Injury score	0.17	0.58	0.41	0.16
Family Functioning score	-0.20	0.51	-0.22	0.47
Religious Faith score	0.06	0.84	0.28	0.36
Hollingshead SES	0.33	0.28	0.04	0.89
QOLI T-score	-0.03	0.92	0.28	0.35
BAI total score	-0.08	0.81	0.23	0.48
CES-D total score	0.40	0.18	0.47	0.10

Table 8. Differences in Depression and Anxiety T-scores by Category

Characteristic	N (%)	BDI-Y T-score		MASC ADI T-score	
		Mean + SD	p-value	Mean + SD	p-value
<i>Sex, child</i>			> 0.99		0.80
Male	11 (78.6)	51.3 + 6.0		44.7 + 12.2	
Female	3 (21.4)	51 + 2.0		41.3 + 15.6	
<i>Glasgow Coma Scale</i>			0.05		0.65
Moderate (9-12)	4 (28.6)	47.5 + 3.1		41 + 15.1	
Severe (3-8)	10 (71.4)	52.9 + 5.3		45.2 + 11.9	
<i>GOS-E Peds</i>			0.75		0.34
Upper Good Recovery (1)	2 (14.3)	50 + 1.4		42.5 + 21.9	
Lower Good Recovery (2)	4 (28.6)	53.5 + 6.7		50.3 + 9.5	
Upper Moderate Disability (3)	8 (57.1)	50.3 + 5.3		40.7 + 12.1	
Receives special education services			0.73		0.14
Yes	8 (57.1)	51.3 + 7.2		39.3 + 13.4	
No	6 (42.9)	51.2 + 1.9		49.3 + 9.7	
Lives with family members other than caregiver			0.30		0.22
Yes	12 (85.7)	50.2 + 4.2		41.5 + 4.2	
No	2 (14.3)	57.0 + 8.5		57.0 + 1.4	
Lives with sibling(s)			0.73		0.34
Yes	7 (50.0)	50.5 + 5.1		38.7 + 11.4	
No	7 (50.0)	51.9 + 5.7		48.4 + 12.3	
Lives with father/stepfather			0.27		0.94
Yes	10 (71.4)	49.4 + 3.7		43.7 + 12.2	
No	4 (28.6)	55.3 + 6.4		44.5 + 15.0	

4.0 ARTICLE TWO: BEHAVIOR-RELATED OUTCOMES OF TRAUMATIC BRAIN INJURY IN CHILDREN AND ADOLESCENTS

Christopher A. Taylor¹, P. David Adelson², Sue R. Beers³, Anthony Fabio⁴, Thomas J. Songer¹, Stephen R. Wisniewski¹. (Authors listed alphabetically—Final order to be determined.)

¹ Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA

² Children's Neuroscience Institute, Phoenix Children's Hospital, Phoenix, AZ

³ Department of Psychiatry, School of Medicine, University of Pittsburgh, Pittsburgh, PA

⁴ Department of Neurological Surgery, School of Medicine, University of Pittsburgh, Pittsburgh, PA

Manuscript in preparation.

4.1 ABSTRACT

Background: While research exists that links higher prevalence of disruptive behavior disorders to brain injury, the results of these studies vary widely and the association of identified risk factors associated with these outcomes is contradictory and possible long-term relationships have not been studied. *Methods:* Participants included 14 young survivors of moderate and severe TBI and their caregivers recruited from a hospital-based pediatric neurological surgery practice. Caregivers completed questionnaires on the child's family environment as well as symptom

surveys examining Attention-Deficit Hyperactivity Disorder (ADHD), Oppositional Defiant Disorder (ODD), and Conduct Disorder (CD). *Results:* On average, the child participants were 14.1±2.9 years old and, on average, 7.1±2.7 years post-injury. Prevalence of ADHD was 35.7%. There was no report of a current diagnosis of ODD or CD based on medical history or symptom survey score. There is a non-significant negative correlation between age at injury. *Conclusion:* The prevalence of ADHD is much higher than the 3-5% present in the general youth population, and the scores were—on average—higher than the population norms. No environmental or injury-related factors were statistically associated with these outcomes.

4.2 INTRODUCTION

Of the more than one million traumatic brain injuries that occur every year, nearly one-third involve children and adolescents¹. Young survivors of TBI have been shown to be at risk for chronic disability due to TBI-related cognitive deficits, impaired motor skills, and poor academic achievement³⁻⁵. Additionally, while studies have suggested a link between TBI and psychiatric disorders, little research has been done examining the prevalence of these conditions or factors associated with these outcomes several years past the time of injury.

Roughly 3% to 5% of children in the US have Attention Deficit Hyperactivity Disorder (ADHD)⁸. Studies that have reported the prevalence of ADHD—specifically Secondary ADHD (ADHD) that develops post-injury—show prevalence rates much higher than those of ADHD found in the general population—generally 10% to 15% prevalence⁴⁴. Some studies have followed cohorts longitudinally and found that incidence rates of about 10% for the first six months post-injury and nearly 15% for the first two years^{18, 19, 22, 30}. These results suggest that

even two years post-TBI, injury survivors may be at risk for developing ADHD at a rate higher than that of their healthy peers.

Some factors associated with ADHD have been identified, though they have not been examined reported on by many studies or over several years since injury. While several studies have found more severe injuries correspond to an increased risk for attention-related difficulties (not limited to ADHD)^{38, 45-47}, not all studies have come to this same conclusion^{21, 48}. The impact of injury severity and its affect on ADHD symptoms over several years has not been examined.

Low socioeconomic status (SES) has been associated as a factor²⁰, though another study did not find SES as significant after controlling for other factors³⁸. Additional correlates have been reported but they have not been found to be related to ADHD: family functioning⁴², family psychiatric history³⁸, and family history of alcohol abuse⁴². One study showed a significant relationship between younger age at injury and ADHD⁵⁰, but that result has not been replicated⁴². Lastly, pre-injury ADHD (known as Primary or PADHD) has been shown to be related to TBI with almost one-quarter of injured children in one study meeting criteria for ADHD at the time of injury.

In addition to ADHD, some research has suggested that Oppositional Defiance Disorder (ODD) and Conduct Disorder (CD) may be related to TBI in youth populations. Studies of TBI have shown an ODD/CD prevalence of 2%–6% prevalence^{42, 56}. However, little research has been conducted on these two closely related behavior disorders, and little is known about their relationships with TBI.

Injury severity has been found to be positively related with ODD/CD symptoms⁴⁸, though other studies did not confirm that result until two years post-injury⁵⁷. In fact, this study suggested that mild- and severe-TBI survivors had the same number of ODD/CD symptoms at

the first follow-up, but the number of symptoms decreased for the mild TBI group over time and the severe TBI group did not. Still, yet another study mild TBI survivors expressed greater ODD symptoms, though this group was not followed over time⁴².

Additional significant factors associated with ODD/CD include poor family functioning^{42, 57}, low SES⁵⁷, and family history of alcohol abuse⁴². Additionally, post-injury symptoms of ODD/CD were related to the presence of SADHD^{14, 36, 42}. The National Institute of Mental Health estimates that up to one-third of youth with ADHD also have some degree of ODD/CD³⁷ suggesting that this co-morbidity will be related to the ODD/CD symptoms.

The specific aims of this research were to (1) examine the distribution of symptoms of disruptive behavior disorders, including Attention-Deficit Hyperactivity Disorder (ADHD), Oppositional Defiant Disorder (ODD), and Conduct Disorder (CD), (2) estimate the prevalence of these DBDs in the studied population, (3) examine the co-occurrence of ADHD, ODD, and CD, and (4) examine the correlation of factors associated with the presence or absence of these disorders.

4.3 METHODS

4.3.1 Study Design

This is a cross-sectional epidemiological study. Participants were contacted for initial screening based on a search of medical records from a study-associated pediatric neurosurgeon (PDA). Based on a review of medical record information, parents of 93 cases who met our inclusion criteria were contacted with a letter outlining the details of the study. Inclusion criteria were met

if the child (1) was between 8 and 17 years of age, (2) experienced a moderate or severe TBI based on initial-injury GOS score, (3) was alive and living in the community, and (4) spoke English with (5) at least six months passed since injury. Potential participants were excluded from our mailing if the head trauma was thought to be the result of abuse. Parents who responded positively to the letter were contacted and screened. Children were asked to enroll if they were reported by their parent as having a Glasgow Outcome Scale – Pediatrics (GOS–E Peds) version score of three or better. This score correlates to functioning at an upper moderate disability level or higher and indicates that the child likely had the capacity to participate in the outcomes assessment interview. Non-respondent families were ultimately contacted by mail three times to determine potential interest. Additionally, a clinical staff member attempted to contact non-responding families by telephone, but no families were ultimately recruited from this effort.

Participants who enrolled were mailed a packet of forms. Parents were asked to provide written informed consent for their child’s participation. Additionally, children were asked to assent to participation. This study was approved by the Institutional Review Board of the University of Pittsburgh (protocol number PRO08050341) (Figure 8). Gift cards were provided to both parent and child participants.

4.3.2 Data Collection

Observed symptoms related to ADHD were gathered from the Conners’ Parent Rating Scale Revised Short (CPRS:R-S) form⁷⁸. The CPRS-R:S is a parent-report instrument used to measure symptoms of ADHD in children between 3 and 17 years of age. This symptom survey is comprised of 27 questions. Respondents indicate how often a particular activity is observed

utilizing Likert scale categories. The total raw score is converted to a normalized sex- and age-specific T-score. The CPRS-R:S has demonstrated adequate internal validity (Cronbach alpha > 0.89) and test-retest reliability ($r = 0.80$).

Assessment ODD and CD was performed using the Child Symptom Inventory (CSI)⁷⁹ in children 12 years of age or younger. The ODD and CD sections of this instrument contain 8 and 15 questions, respectively. The CSI has demonstrated adequate internal validity (Cronbach alpha > 0.80) and test-retest reliability ($r = 0.80$ (ODD) and $r = 0.46$ (CD)).

The Adolescent Symptom Inventory (ASI)⁷⁹ was used for participants older than 12 years. The ODD and CD sections of this instrument also contain 8 and 15 questions, respectively. The ASI has also demonstrated adequate internal validity (Cronbach alpha > 0.80) and test-retest reliability ($r > 0.70$ (ODD) and $r > 0.64$ (CD)).

Socio-economic status (SES) was scored based on Hollingshead's criteria⁷⁴. The occupational scoring for the Hollingshead SES measure was modified from the original 1970s US Census data for use in this research to more adequately reflect modern employment. The measure of religious faith was scored after completion of the Santa Clara Strength of Religious Faith Questionnaire⁷⁵. A measure of the family's burden of injury was obtained by the use of the Family Burden of Injury Interview⁷⁶. A measure of family function was obtained by the General Functioning subscale of the McMaster Family Assessment Device⁷⁷. Medical history related to previous diagnoses of depression and anxiety was obtained by parental report. All of these measures were obtained via questionnaires completed by the primary caregivers of the injured children. Information relating to injury severity and other factors collected at the time of injury were obtained through the use of medical record data.

A marker of clinically significant ADHD symptoms was defined as having a current diagnosis based on self-report or a T-score ≥ 65 on the CPRS-R:S ADHD Index. ODD or CD were considered to be present if any of the symptoms of these disorders were reported to be present in the child.

A medical safety plan was developed and utilized. Participants without a previous diagnosis of these disorders with a T-score ≥ 65 on the CPRS-R:S ADHD Index or symptoms suggesting the presence of ODD or CD based on the CSI/ASI instrument were contacted by a licensed psychologist (SRB). The psychologist discussed the results of the test with the parent and made referrals to appropriate care providers when necessary.

4.3.3 Statistical Methods

T-scores for symptom surveys were determined by the publishers of the tests based on population norms. After the scoring of the surveys, raw scores are translated to T-scores. T-scores used in this analyses accounted for age and sex.

Measures of correlation were calculated between the continuous ADHD outcome score and continuous injury-related and demographic variables using Spearman correlation values. Additionally, differences between categories of injury-related variables were tested using non-parametric Wilcoxon comparisons. All analyses were performed using SAS 9.2 (Cary, NC).

4.4 RESULTS

Ninety-three families met the initial eligibility criteria based on age, time since injury, and injury severity. Of the 93 families to which letters were mailed, 27 responded positively and indicated an interest in being screened for eligibility (Figure 8). Of those 27, 20 were successfully contacted and screened and 7 were unable to be reached using the contact information provided in the reply form. Forty-four families did not respond to the mailing and were contacted by a member of the medical staff to determine their interest. None of these 44 non-responders were ultimately interested in participating in this study. All 17 screened caregivers were enrolled. One child was not eligible to participate due to an ineligible GOS-E Peds score (Figure 10). Additionally, 2 children were not interested in participating, and 1 additional child agreed to participate in this study but did not wish to be interviewed as part of a telephone-based depression and anxiety outcomes assessment. Ultimately, because data related to the disruptive behavior disorders was parent-reported, information was collected on 14 injured youth.

All enrolled participants—caregivers and injury survivors—were non-Hispanic whites. All caregivers enrolled in this study were women, and just three of the fourteen children used in this analysis were female (21.4%). Ten children (71.4%) experienced a severe TBI (Figure 11) with 7.1 ± 2.7 years passed since the event. No statistically significant differences were found between time passed since injury, current age, age at injury, sex, and race between enrolled participants and subjects from the recruitment pool of 93 individuals who did not participate in this study⁸⁰.

Of the fourteen injury survivors included in this study, five (35.7%) met the criteria for having a current indication of ADHD. More than two-thirds of enrolled children were reported as having an ADHD Index T-score of more than 50, which shows a distribution with more

ADHD symptoms than the general population (Figure 12). No caregiver reported having a child exhibiting symptoms of ODD or CD and, thusly, these outcomes were excluded from further analysis. No parents reported having children with pre-injury diagnoses of ADHD.

Spearman correlation statistics were generated (Table 11). There were no characteristics examined in this study that had a statistically significant relationship with the ADHD Index T-score. However, the Spearman correlation statistic between caregiver anxiety (BAI) and the ADHD Index T-score was relatively large ($\rho=0.40$, $p=0.20$) (Figure 13). There were no statistically significant differences between categories of environmental and injury-related characteristics (Table 12).

4.5 DISCUSSION

In this study, we evaluated the relationship between behavioral outcomes in children who experienced TBI. Utilizing questionnaires, caregivers of young injury survivors provided objective information related to the child's symptoms of ADHD, ODD, and CD.

The 35.7% prevalence of ADHD in this study cohort is significantly higher than that found in the general population of US peers which is generally between 3-5%⁸. This prevalence is also higher than any prevalence reported in previously published childhood TBI studies. This is especially surprising given the fact that this study was performed so long after the time of injury. This cohort's ADHD prevalence is close to double those previously reported, all within two years of injury^{18, 19, 42, 43}. This suggests that TBI may result in the development of new ADHD symptoms even several years post-injury.

The absence of children with ODD or CD symptoms may suggest that symptoms of these conditions are quite diminished after several years following injury. Conversely, it is also possible that caregivers with children who exhibit such intense symptoms as those hallmark to ODD/CD may have decided to forego participating in this study because the responsibility of caring for a child with such symptoms can be understandably burdensome.

Previous injury factors associated with ADHD in other studies were not duplicated with this analysis. Studies disagreed on the relationship between ADHD symptoms and injury severity, this study did nothing to further the argument toward one end or another. There is no difference between those with moderate and severe injuries and their reported ADHD symptoms. An expanded examination of raw GCS score was also non-significant.

4.5.1 Strengths and Limitations

This research has many strengths that support the findings of this study. Firstly, the injury-related data are well documented and include important variables related to the injury event. Additionally, the outcome assessments—while not conducted in person—were collected using validated studies for objective parental report. Additionally, the caregiver-provided data was collected completely in a way that allowed the analysis to be performed in a way that includes as many data points as possible. Finally, this study included children who injuries occurred at least four years ago. The authors are not aware of any other studies of childhood TBI survivorship that has included children this far past the time of injury.

The number of individuals who chose to participate in this study—while nearly 20% of the total potential pool of 93 participants—was relatively small. This small sample limits the statistical power to detect true differences between groups. It also calls into question to

representativeness of the sample. The majority of the screened participants were moderately well functioning, leaving one to wonder if families with poor-functioning felt they would not be helped by this study or if the study would be burdensome given their current caregiving responsibilities. Additionally, there were very few participants who were very well functioning. While the pool of potential TBI survivors were drawn from only those with moderate and severe injuries, it is possible that the families of children who are now very well functioning and several years post-injury would decide to rather not relive events associated with such a traumatic experience.

4.5.2 Conclusion

In conclusion, this study provides a novel look at outcomes of disruptive behaviors (ADHD, ODD, and CD) several years after experiencing a childhood TBI. The prevalence of ADHD in this cohort was much higher than those reported in similar studies collected relatively closer to the injury event and that of the similarly aged general population. Because of the paucity of epidemiologic data showing strong and significant factors related to these disruptive behavior disorders, research should continue in this area. Future research should focus on not only those factors studied previously, but also on new and novel ideas that have not been collected or analyzed in the published data record.

It is important to continue this research as future consistent and significant findings may help researchers, physicians, and mental health professionals to more fully understand environmental and injury-related factors associated with these outcomes.

4.6 TABLES AND FIGURES

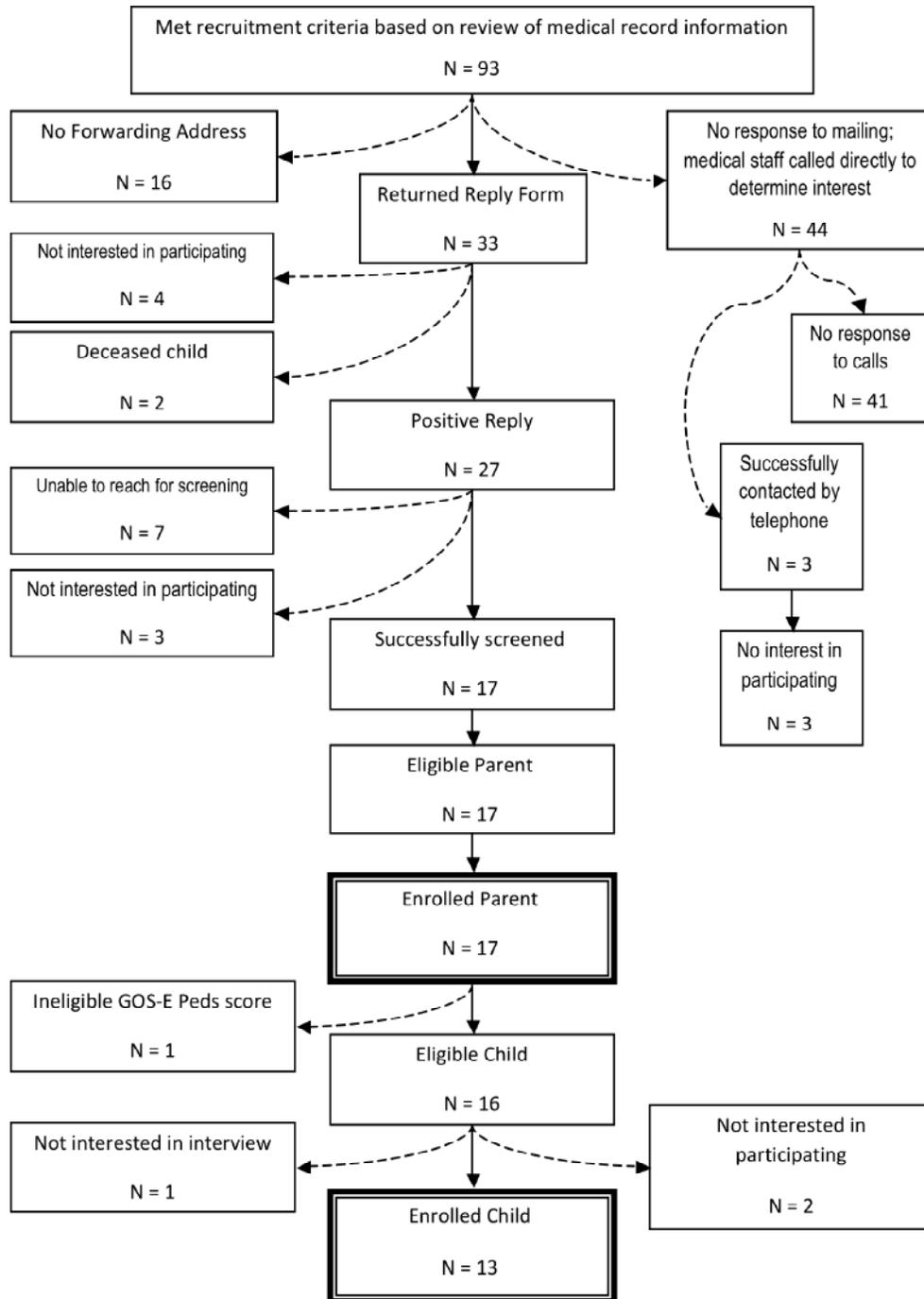


Figure 8. Study recruitment flow diagram

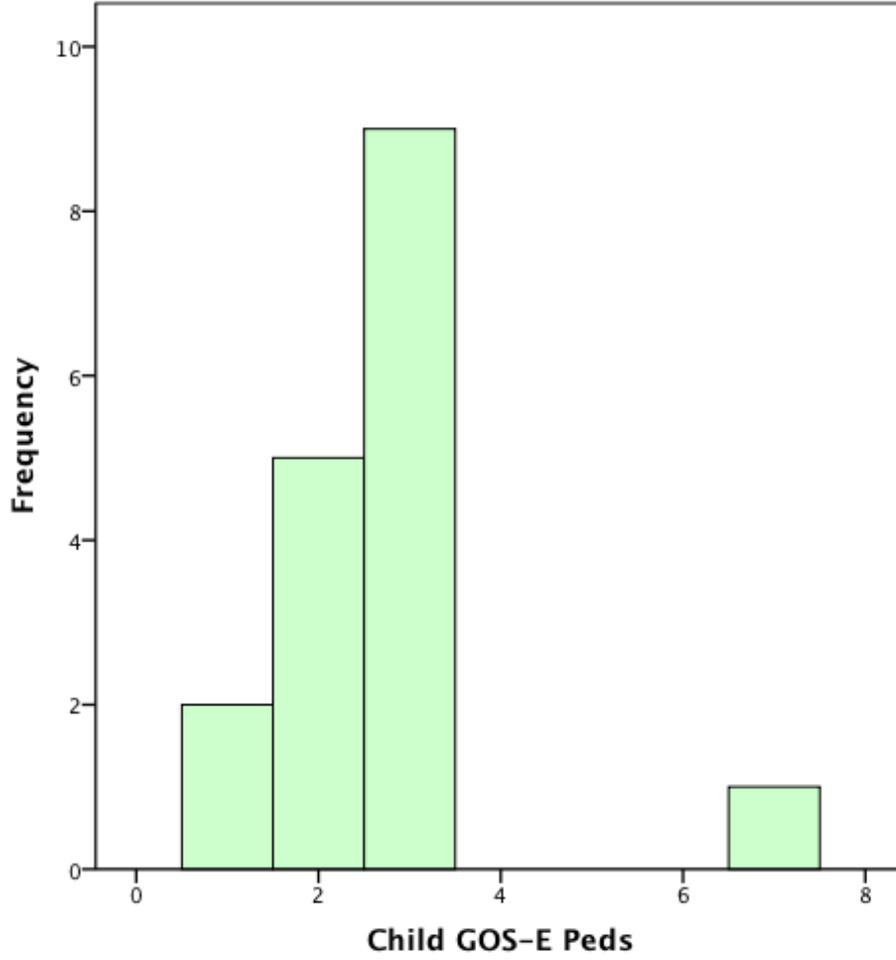


Figure 9. Distribution of GOS-E Peds score at time of eligibility interview

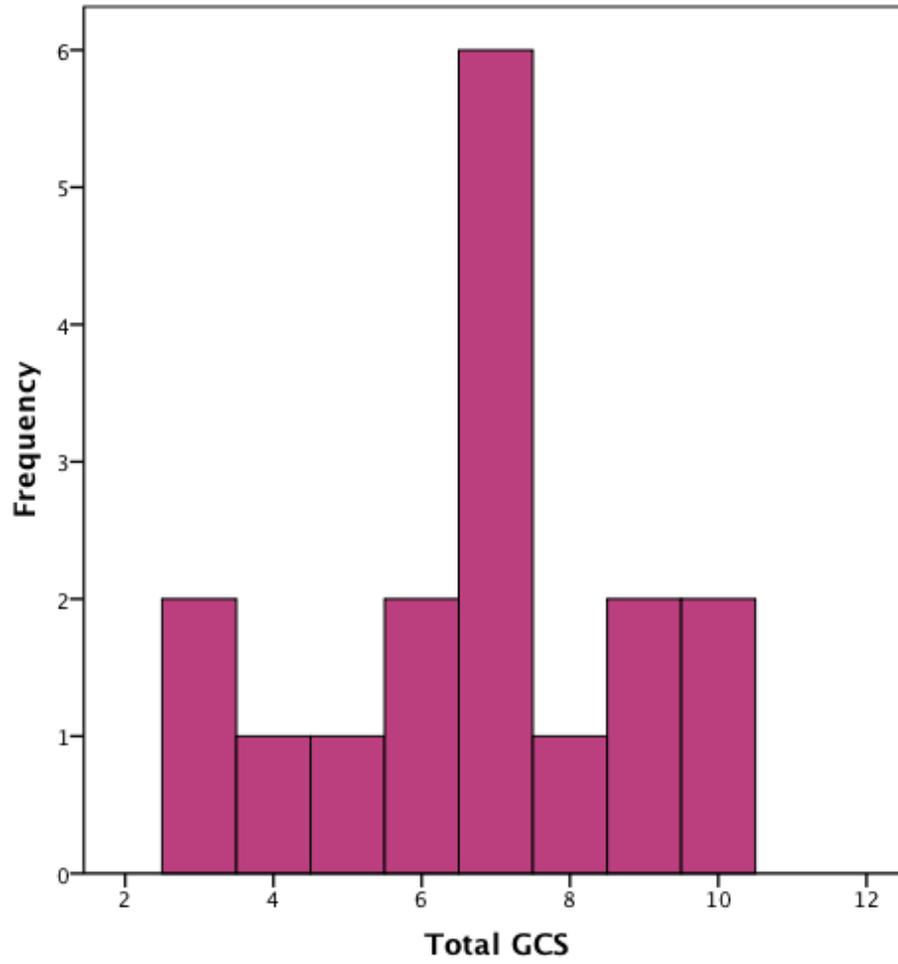


Figure 10. Distribution of Total GCS score at time of injury

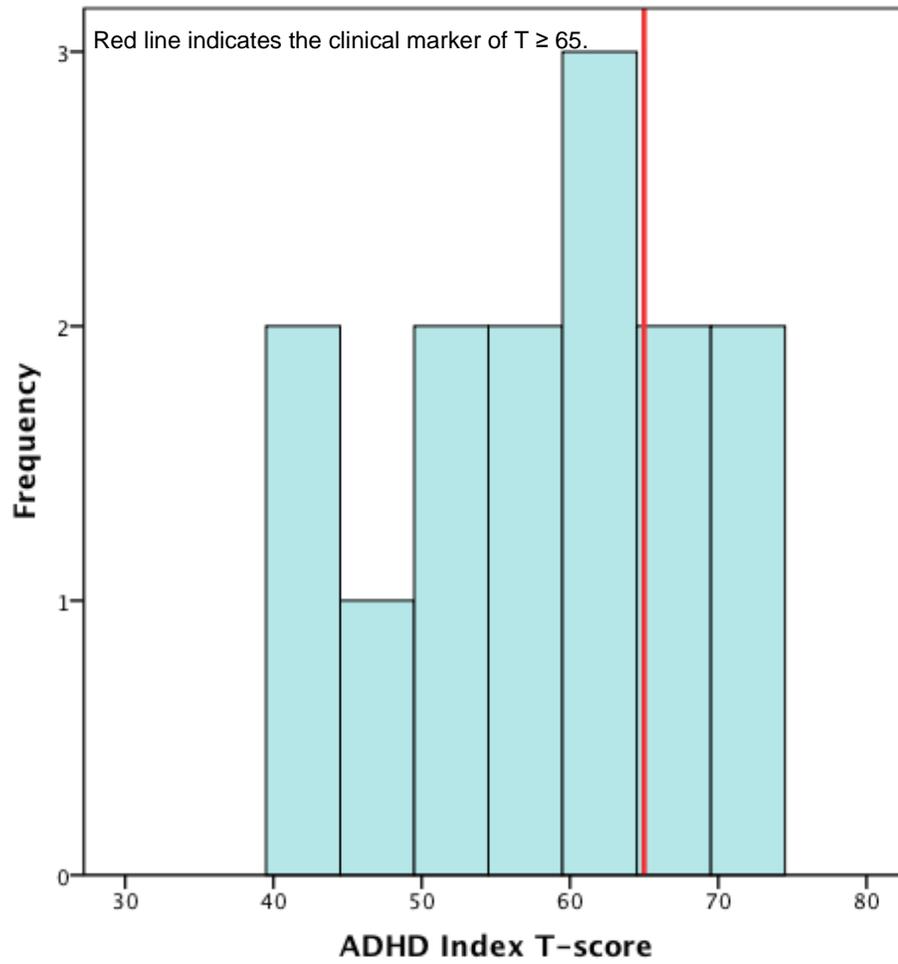


Figure 11. Distribution of the CPRS-R:S ADHD Index T-score

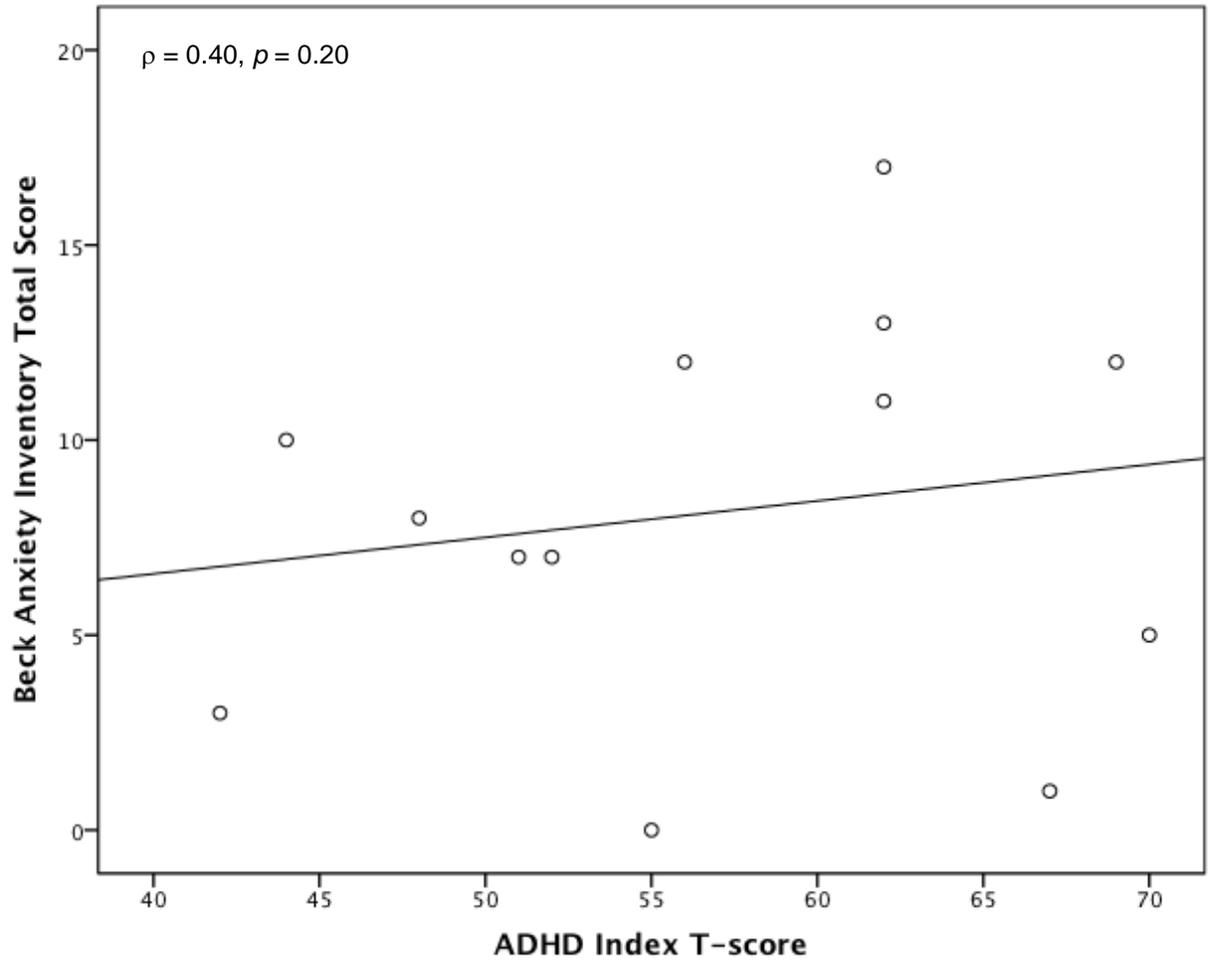


Figure 12. Scatterplot of BAI Total Score (in caregivers) vs. ADHD Index T-score

Table 9. Demographic, Injury, and Outcome Characteristics

Continuous Variables		
Characteristic	Mean ± SD	Range
Age at interview (y)	14.1 + 2.9	8.8 - 17.9
Time since injury (y)	7.1 + 2.7	1.7 - 12.0
ADHD Index T-score	57.9 + 9.6	42 - 70
Family Burden of Injury score	21.3 + 9.7	7 - 46
Family Functioning score	1.8 + 0.5	1.0 - 2.6
Religious Faith score	21.2 + 6.0	10 - 30
Hollingshead SES	40.4 + 9.6	26 - 61
Categorical Variables		
Characteristic	N (%)	
<i>Sex</i>		
Male	11 (78.6)	
Female	3 (21.4)	
<i>Race</i>		
White	14 (100.0)	
Non-White	0 (0.0)	
<i>Glasgow Coma Scale</i>		
Moderate (9-12)	4 (28.6)	
Severe (3-8)	10 (71.4)	
<i>GOS-E Peds</i>		
Upper Good Recovery (1)	2 (14.3)	
Lower Good Recovery (2)	4 (28.6)	
Upper Moderate Disability (3)	8 (57.1)	
<i>Injury Mechanism</i>		
Fall	5 (35.7)	
Motor Vehicle Accident	3 (21.4)	
Car vs. Pedestrian	3 (21.4)	
Recreational	2 (14.3)	
Other	1 (7.1)	
Current ADHD	5 (35.7)	
Current ODD	0 (0.0)	
Current CD	0 (0.0)	

Table 10. Correlation Coefficients of ADHD

Characteristic	CPRS-R:S ADHD Index T-score	
	ρ	<i>p</i>-value
<i>Injured Youth Characteristics</i>		
Age at interview (y)	-0.36	0.22
Age at injury (y)	-0.17	0.58
Time since injury (y)	-0.05	0.86
<i>Caregiver Characteristics</i>		
Caregiver Age at interview (y)	-0.27	0.37
Family Burden of Injury score	0.07	0.82
Family Functioning score	-0.18	0.56
Religious Faith score	0.22	0.46
Hollingshead SES	0.04	0.89
QOLI T-score	-0.11	0.73
BAI total score	0.40	0.20
CES-D total score	0.17	0.59

Table 11. Differences in ADHD by Category

Characteristic	N (%)	CPRS-R:S ADHD Index T-score	
		Mean + SD	p-value
<i>Sex, child</i>			0.54
Male	11 (78.6)	54.0 + 9.8	
Female	3 (21.4)	58.9 + 9.8	
<i>Glasgow Coma Scale</i>			0.94
Moderate (9-12)	4 (28.6)	58.8 + 8.9	
Severe (3-8)	10 (71.4)	57.5 + 10.2	
<i>GOS-E Peds</i>			0.13
Upper Good Recovery (1)	2 (14.3)	50.0 + 8.5	
Lower Good Recovery (2)	4 (28.6)	67.8 + 4.3	
Upper Moderate Disability (3)	8 (57.1)	55.9 + 9.7	
Receives special education services			0.85
Yes	8 (57.1)	57.0 + 10.7	
No	6 (42.9)	59.0 + 8.6	
Lives with family members other than caregiver			> 0.99
Yes	11 (78.6)	58.0 + 8.8	
No	3 (21.4)	57.0 + 18.4	
Lives with sibling(s)			0.95
Yes	7 (50.0)	57.7 + 7.5	
No	7 (50.0)	58.0 + 11.9	
Lives with father/stepfather			0.68
Yes	10 (71.4)	58.9 + 9.4	
No	4 (28.6)	55.3 + 11.0	

5.0 ARTICLE THREE: CONSEQUENCES OF CAREGIVING FOR YOUNG SURVIVORS OF TRAUMATIC BRAIN INJURY

Christopher A. Taylor¹, P. David Adelson², Sue R. Beers³, Anthony Fabio⁴, Thomas J. Songer¹, Stephen R. Wisniewski¹. (Authors listed alphabetically—Final order to be determined.)

¹ Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA

² Children's Neuroscience Institute, Phoenix Children's Hospital, Phoenix, AZ

³ Department of Psychiatry, School of Medicine, University of Pittsburgh, Pittsburgh, PA

⁴ Department of Neurological Surgery, School of Medicine, University of Pittsburgh, Pittsburgh, PA

Manuscript in preparation.

5.1 ABSTRACT

Background: Each year in the United States, more than one quarter million of children and adolescents experienced a TBI. However, little research exists on the caregivers of these young injury survivors. *Methods:* Participants included 17 caregivers of young survivors of moderate and severe TBI recruited from a hospital-based pediatric neurological surgery practice. Caregivers completed questionnaires on the child's family environment as well as symptom surveys related to depression, anxiety, and quality of life. *Results:* The prevalence of depression

in this cohort was 23.5% based on testing and medical history; prevalence of anxiety was 18.8%. More than half of all caregivers reported symptoms of a low or very low quality of life. Both depression and anxiety were negatively associated with age at the time of injury. Levels of good family functioning decreased as the child's level of recovery decreased. *Conclusion:* The prevalence of depression in this cohort of caregivers is higher than that of the general adults population of about five percent. The 18% prevalence of anxiety was nearly identical to that found in the general population. The large number of caregivers with low or very low quality of life, as well as the increased prevalence of depression, indicate the need to follow these caregivers and determine examine their needs, even several years post-injury.

5.2 INTRODUCTION

Of the more than one million traumatic brain injuries that occur every year, nearly one-third involve children and adolescents¹. Because of their age, these young injury survivors heavily rely on family-based caregivers during their recovery, unfortunately very little is known about the effect and burden that caregivers of young TBI survivors may experience.

Studies have shown that the responsibility of providing care generally falls to spouses or parents⁵⁹. Some consequences for the caregivers of adult TBI survivors include increased use of both prescription and non-prescription drugs and alcohol⁶⁰. Additionally, caregivers of those with chronic illness are at higher risk for reporting increased levels of stress, depression, decreased life satisfaction, and poorer general health⁶. However, there is little research specific to the caregivers of young TBI survivors. Several studies have shown Ergh^{61, 62}, Marsh^{60, 63, 64} and Wade⁶⁵ indicate that depression and anxiety are prevalent in the population of caregivers

who provide care to survivors of TBI⁶⁰⁻⁶⁵. Most of this research examines the roles and effects of caregiving for adult TBI survivors with approximately one-third of caregivers reporting symptoms of depression or anxiety and both six months and one year post-injury^{63, 64}. Little though has been reported on risk factors for depression and anxiety in caregivers of TBI survivors, specifically child survivors. The rate of poor family functioning has found to be as high as 74% in one cohort of caregivers⁶⁶, and patients recovering in environments with poorer family functioning have been shown to be at more risk for injury-related distress⁶⁷⁻⁶⁹. This increased level of distress may, cyclically, further adversely affect the caregiver and the family unit. In addition to family functioning, social support has been shown to be related to caregiver mental health as well as caregiver quality of life and life satisfaction though this result was found in a cohort of caregivers of adult TBI survivors. Increased social support mediates caregiver burden and distress⁶² while the number of neuropsychological problems of the TBI survivor is positively related to caregiver burden⁶² and inversely related to life satisfaction⁶¹.

Furthermore, the number of adverse effects that an injury survivor has experienced post-injury has been shown as a significant predictor of caregiver depression⁷⁰. Additionally, the perception of the condition of the injury victim is related to depression, as a lower perceived amount of adverse effects related to the injury survivor is associated with a decreased rate of depression⁷⁰.

The specific aims of this research were to (1) examine the distribution of symptoms of depression and anxiety, (2) estimate the prevalence of clinically significant depression and anxiety in the studied population, (3) examine the co-occurrence of depression and anxiety, (4) examine the quality of life of these caregivers, and (5) examine the correlation of factors

associated with the presence or absence of depression and anxiety symptoms and quality of life score.

5.3 METHODS

5.3.1 Study Design

In this cross-sectional epidemiological study, the hypothesis was that caregivers of young survivors of TBI report higher prevalence of depression and anxiety than reported in the general population. Additionally, we hypothesized that characteristics of the home environment, such as perceived family burden and family functioning, as well as quality of life are related to these outcomes.

5.3.2 Study Population

Participants were contacted for initial screening based on a search of medical records from a study-associated pediatric neurosurgeon (PDA). Based on a review of medical record information, parents of 93 cases who met our inclusion criteria were contacted with a letter outlining the details of the study. Inclusion criteria were met if the child (1) was between 8 and 17 years of age, (2) experienced a moderate or severe TBI based on initial-injury GOS score, (3) was alive and living in the community, and (4) spoke English with (5) at least six months passed since injury. Potential participants were excluded from our mailing if the head trauma was thought to be the result of abuse. Parents who responded positively to the letter were contacted

and screened. Children were asked to enroll if they were reported by their parent as having a Glasgow Outcome Scale – Pediatrics (GOS–E Peds) version score of three or better which correlates to functioning at an upper moderate disability level or higher and indicates that the child likely had the capacity to participate in the outcomes assessment interview. Non-respondent families were ultimately contacted by mail three times to determine potential interest. Additionally, a clinical staff member attempted to contact non-responding families by telephone, but no families were ultimately recruited from this effort.

Participants who agreed to be enrolled were mailed a packet of forms that were to be mailed back to the study principal investigator. This study was approved by the Institutional Review Board of the University of Pittsburgh (protocol number PRO08050341). Gift cards were provided to both parent and child participants.

5.3.3 Data Collection

Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression (CES-D) scale⁸¹. The CES-D is a self-report instrument used to measure symptoms of depression in adults. This symptom survey is comprised of 20 questions. Respondents indicate how often a particular activity represents them. The CES-D has demonstrated adequate internal validity (Cronbach alpha ranges from 0.84 to 0.90) and test-retest reliability ($r > 0.41$).

Symptoms of anxiety were assessed using the Beck Anxiety Inventory (BAI)⁸². The BAI is a self-report instrument used to measure symptoms of anxiety in adults. This symptom survey is comprised of 21 questions. Respondents indicate how often they agree with a particular statement using a Likert scale. The BAI has demonstrated adequate internal validity (average Cronbach alpha = 0.92) and test-retest reliability ($r = 0.75$).

Additionally, caregiver quality of life measured by the Quality of Life Inventory (QOLI)⁸³. The QOLI is a self-report instrument used to measure quality of life in adults. This survey is comprised of 32 questions. Respondents indicate how important a particular aspect to their life is and to what extent they are satisfied or dissatisfied with that area. The QOLI has demonstrated adequate internal validity (Cronbach alpha ranges = 0.80) and test-retest reliability ($r = 0.75$).

Injury burden was determined using the Family Burden of Injury Interview (FBII)⁸⁴. The Santa Clara Strength of Religious Faith Questionnaire (SCSRFQ)⁸⁵ evaluated a measure of religious faith. Family functioning was measured by the general function subscale of the McMaster family functioning assessment device⁷⁷. All of these measures were completed by self-report of the enrolled caregiver.

Socio-economic status (SES) was scored based on Hollingshead's criteria⁷⁴. The original Hollingshead SES occupational scoring was modified from the original 1970s US Census algorithm to reflect modern employment. The measure of religious faith was scored after completion of the Santa Clara Strength of Religious Faith Questionnaire⁷⁵. A measure of the family's burden of injury was obtained by the use of the Family Burden of Injury Interview⁷⁶. A measure of family function was obtained by the General Functioning subscale of the McMaster Family Assessment Device⁷⁷. Medical history related to previous diagnoses of depression and anxiety was obtained by parental report. All of these measures were obtained via questionnaires completed by the primary caregivers of the injured children. Information relating to injury severity and other factors collected at the time of injury were obtained through the use of medical record data.

The marker of clinically significant depression was defined as having a self-report of depression diagnosed by a medical professional or a CES-D score greater than 16. The marker of clinically significant anxiety symptoms was defined as a having a self-report of anxiety diagnosed by a medical professional or a BAI score greater than or equal to 23.

A medical safety plan was developed and utilized. Caregivers without a previous diagnosis of anxiety or depression who score greater than 16 of the CES-D or greater than 23 on the BAI were contacted by a licensed psychologist who discussed the results with the participant. The psychologist referred the participant to an appropriate care provider when necessary.

5.3.4 Statistical Methods

Measures of correlation were calculated between the continuous depression, anxiety, and quality of life outcome score and continuous injury-related and demographic variables using Spearman correlation values. Additionally, differences between categories of injury-related variables were tested using non-parametric Wilcoxon comparisons. All analyses were performed using SAS 9.2 (Cary, NC).

5.4 RESULTS

Ninety-three families met the initial eligibility criteria based on age, time since injury, and injury severity. Of the 93 families to which letters were mailed, 27 responded positively and indicated an interest in being screened for eligibility (Figure 14). Of those 27, 20 were successfully contacted and screened and 7 were unable to be reached using the contact information provided in

the reply form. Forty-four families did not respond to the mailing and were contacted by a member of the medical staff to determine their interest. None of these 44 non-responders were ultimately interested in participating in this study. All 17 screened caregivers were enrolled. One child was not eligible to participate due to an ineligible GOS-E Peds score (Figure 15). Additionally, 2 children were not interested in participating, and 1 additional child agreed to participate in this study but did not wish to be interviewed as part of a telephone-based depression and anxiety outcomes assessment. Ultimately, because data related to the disruptive behavior disorders was parent-reported, information was collected on 14 injured youth. Child and adolescent anxiety and depression data were collected on 13. Nearly three-quarters of participating children were classified with severe injuries at the time of TBI (Figure 16).

All enrolled participants—caregivers and young injury survivors—were non-Hispanic whites. All caregivers enrolled in this study were women, and all but one was the mother of the TBI survivor.

The distribution of BAI raw scores shows that nearly every caregiver receiving a score less than 15, which indicates minimal or mild anxiety (Figure 17). There was no depression-anxiety comorbidity in this caregiver population. For the enrolled caregivers, four (23.5%) indicated a current diagnosis of depression (Figure 18). The distribution of CES-D scores was skewed indicating that most of the caregivers did not report many depression-related symptoms (Figure 18). Three caregivers indicated an anxiety disorder (18.8%) (Table 12).

The distribution of the QoLI T-score shows one-quarter of caregivers in this study population have a score centered around 42, with more than half reporting lifestyle attributes indicative of a low or very low quality of life (Figure 19).

Caregiver anxiety, as measured by the BAI, showed a near significant association with the child's age at interview ($\rho = -0.46, p = 0.07$) (Figure 20). Age at interview had a very similar relationship with the QoLI T-score ($\rho = -0.45, p = 0.07$) (Figure 21).

Spearman correlation statistics were generated (Table 13). Time since injury was also associated with CES-D total ($p = 0.01$) (Figure 22). The age of the child at the time of injury was statistically associated with total CES-D score ($p = 0.05$) (Figure 23). Additionally, when examining the means between categories of GOS-E Peds score, there was a significant difference with respect to CES-D. However, this significant difference is the result of one data point with a poor GOS-E Peds score and high depression level.

FBII score was highly associated with QoLI T-score, ($\rho = 0.46, p = 0.06$) (Figure 24). QoLI T-score was also higher for caregivers with no additional children in the household. Nearly half of all caregivers earned a Low or Very Low quality of life score. Only one caregiver reported a high quality of life.

Family functioning differed by gender of the child with households having an injured young boy reporting more family dysfunction than those with an injured young girl (2.1 vs. 1.1, $p = 0.02$) (Table 14). Family functioning also differed across GOS-E Peds score with a trend of increasing family dysfunction as the level of recovery decreased.

5.5 DISCUSSION

In this study, we evaluated the relationship between depression and anxiety in caregivers of children who experienced childhood TBI. We provided questionnaires to primary caregivers that assessed symptoms of depression and anxiety as well as a variety of factors that reflect the

environment in which they live and provide care for the injured children. Using correlation statistics, we identified variables that appear to be statistically related with these depression- and anxiety-related outcomes. Additionally, we sought to assess each caregiver's quality of life and determine what factors are associated with a good or poor quality of life as well as how quality of life may be associated with depression and anxiety.

In this study of caregivers, four caregivers of the 17 enrolled (23.5%) met our criteria for a depressive condition. This prevalence is higher than those reported in the caregiver literature⁶⁰⁻⁶⁵ as well as that expected in the generation population (1 in 18, or 5.3%²⁶). This finding is interesting given that most of these caregivers are caring for children who have reached a good or moderately good level of recovery several years post-injury. Published literature focused on caregivers with children in the post-acute or near post-acute stages of recovery, generally six months to one year post-TBI. However, the injuries for these children occurred, on average, seven years prior to the study, and some as long as twelve years ago. The correlation statistics relating depression and time since injury is statistically significant and positively correlated with increasing time since injury associated with higher depression scores. While the rate is higher, it is not possible to know if these cases of depression are the result of the caregiving environment or not. The especially high rate of depressive symptoms this far past the time of injury event is definitely worthy of further investigation in future studies.

For anxiety disorders, the results appear much more typical of that reported in the literature. Three of 17 (18.8%) caregivers reported anxiety diagnoses which is very much aligned with the 18.1% prevalence found in the general population of adults⁸⁶. This rate is lower than those reported for caregivers closer to the time of injury, and suggests that anxiety symptoms, unlike depression, in caregivers decrease over time after injury.

Age at the time of injury is negatively associated with total CES-D score. This finding is interesting as it demonstrates that caregivers whose children were very young at injury may have higher rates of depression symptoms. This suggests that the injury of a young child may have more emotional impact on the caregiver than that of an older child.

Another intriguing finding is the relationship between the FBII and the QoLI scores. There is a significant, positive correlation ($\rho=0.46$, $p=0.06$) between these values that suggest that a greater perceived burden at the time of injury is associated with a higher (current) quality of life. This is an incongruent finding. The FBII asks for information from the six months immediately following the injury event, whereas the quality of life measure is based on the caregiver's current situation. While the statistic is significant, it may be that the relationship is, in fact, spurious. Future longitudinal studies of caregivers with more accurate data collected at the time of injury may help further elucidate this finding.

Nearly half of all caregivers participating in this study reported that environments were suggestive of low or very low quality of life. While it is not possible to know if this quality of life is directly related to caregiving responsibilities, this is a notable finding. This suggests that there may be a need to provided resources to caregivers to help them improve their quality of life. Low quality of life can be associated with increased fatigue and depression (though that finding was not significant in this study), and this may affect the caregiver's ability to provide care.

5.5.1 Strengths and Limitations

This research has many strengths that support the findings of this study. Firstly, the injury-related data are well documented and include many variables related to the injury event.

Additionally, the outcome assessments—while not conducted in person—were collected using validated studies for objective reporting of the caregiver’s depressive and anxious symptoms as well as quality of life. This study included children whose injuries occurred at least four years ago. The authors are not aware of any other studies of childhood TBI survivorship that has included children, and caregivers of these children, this far past the time of injury.

The number of individuals who chose to participate in this study—while nearly 20% of the total potential pool of 93 participants—was relatively small. This small sample limits the statistical power to detect true differences between groups. It also calls into question the representativeness of the sample. The majority of the screened participants were relatively well functioning, leaving one to wonder if families with poor-functioning felt they would not be helped by this study or if the study would be burdensome given their current caregiving responsibilities. Additionally, there were very few participants who were very well functioning. While the pool of potential TBI survivors were drawn from only those with moderate and severe injuries, it is possible that the families of children who are now very well functioning and several years post-injury would decide to rather not relive events associated with such a traumatic experience.

Also, there may be a self-report bias in the reporting of depression and anxiety symptoms, and quality of life assessment where the caregiver may feel uncomfortable reporting their true symptoms and feelings.

While the FBII asked about data in the six-month period following injury, potentially significant amounts of time from the injury have passed, and this measure may be subject to a recall bias.

5.5.2 Conclusion

In conclusion, this study—while small—provides a novel look at outcomes of depression, anxiety, and quality of life in caregivers of children who experienced a TBI several years ago. The prevalence of depression and depressive symptoms in this cohort of caregivers is much higher than the values previously reported in caregiver literature as well as that of the general population of US adults. Additionally, nearly half of these caregivers enrolled in this study reported symptoms of low or very low quality of life. These findings are particularly poignant given that nearly all of the children are moderately well functioning several years post-injury.

These findings support the idea that more focus should be placed on caregivers of injured youth, as this group has shown that depressive symptoms and poor quality of life exist even several years past the time of injury. Future research should focus on perceived needs of these caregivers in order to more fully understand the needs of this community and the recovery environment in which young survivors of TBI live.

5.6 TABLES AND FIGURES

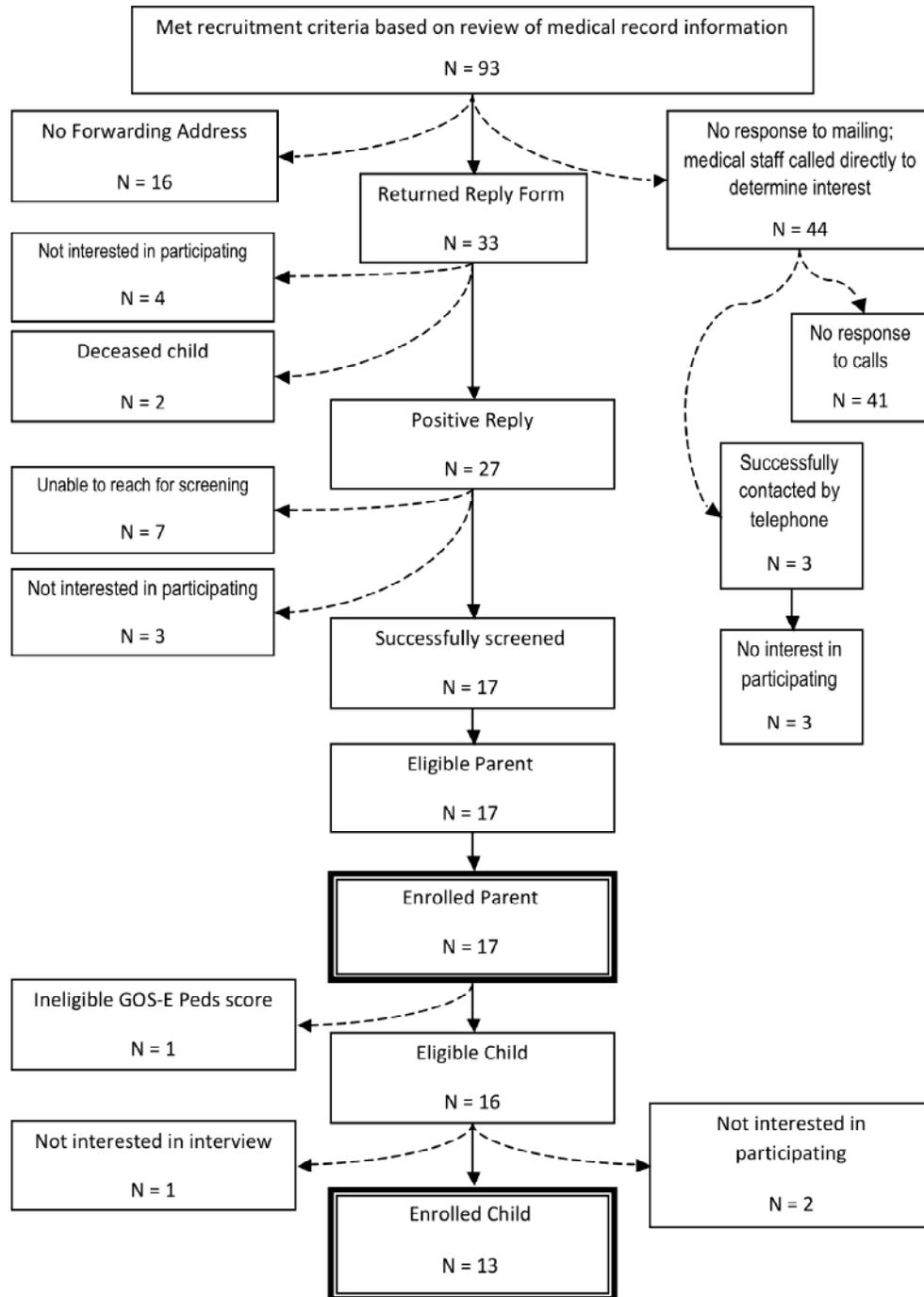


Figure 13. Study recruitment flow diagram

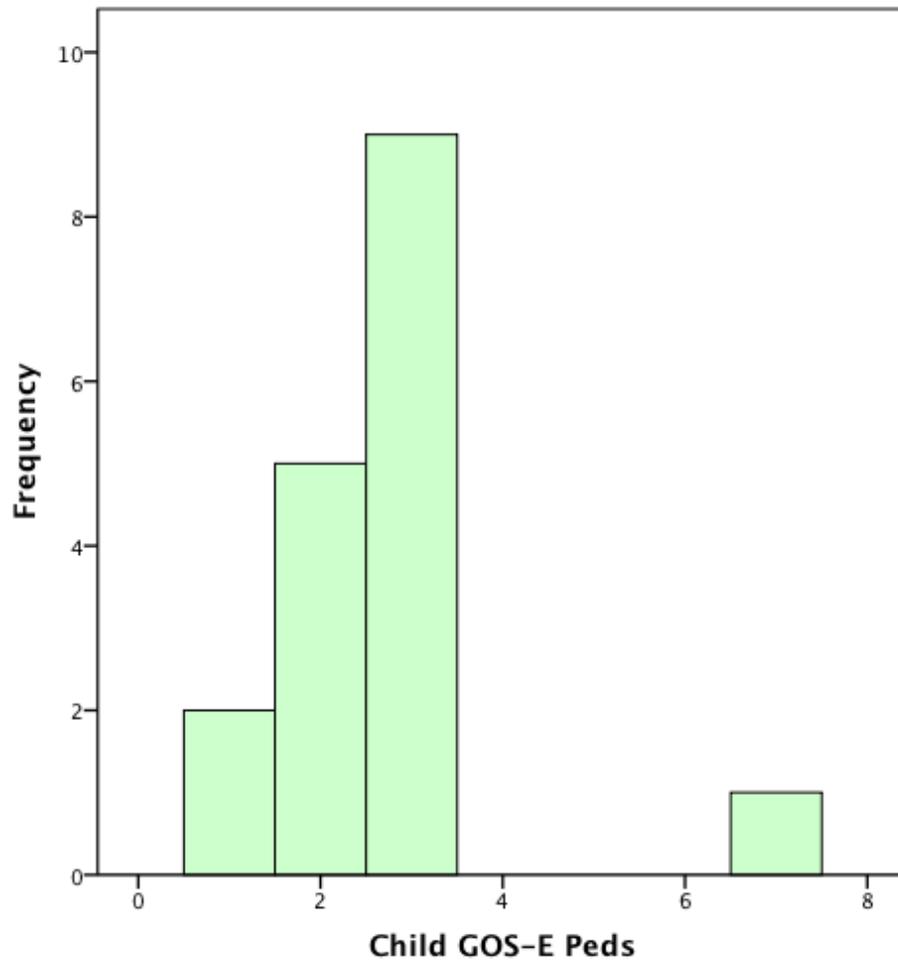


Figure 14. Distribution of GOS-Peds score at time of eligibility interview

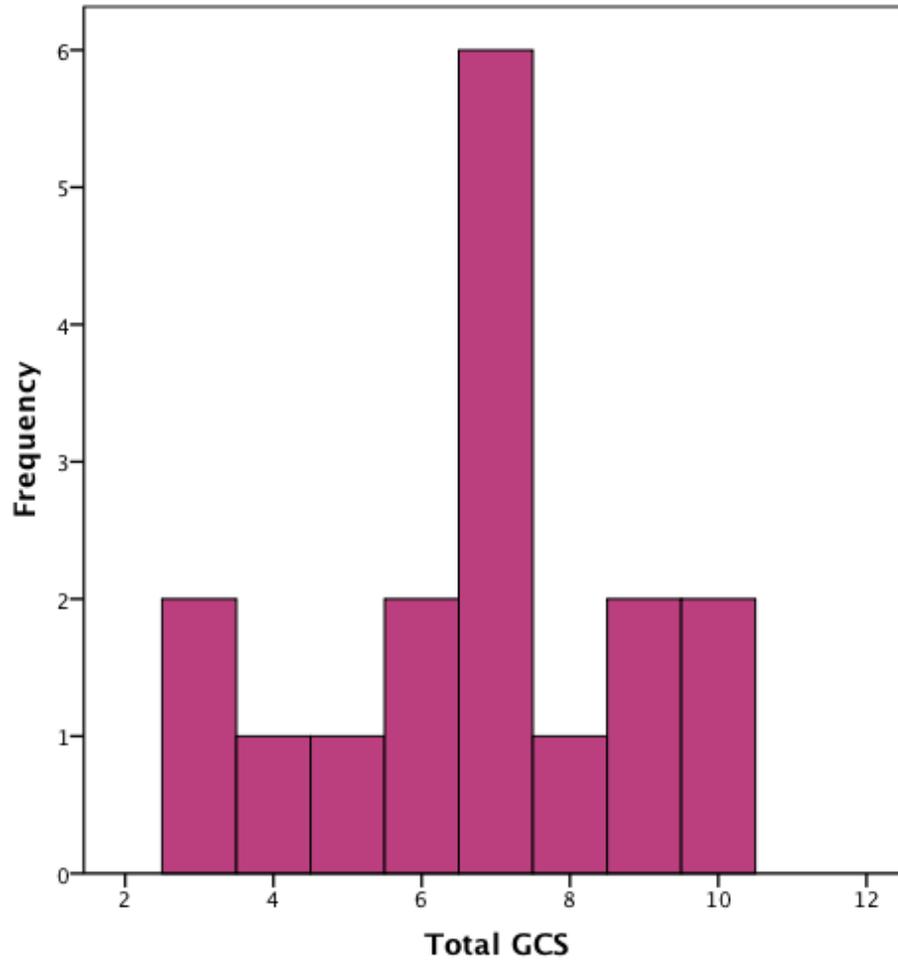


Figure 15. Distribution of Total GCS score at time of injury

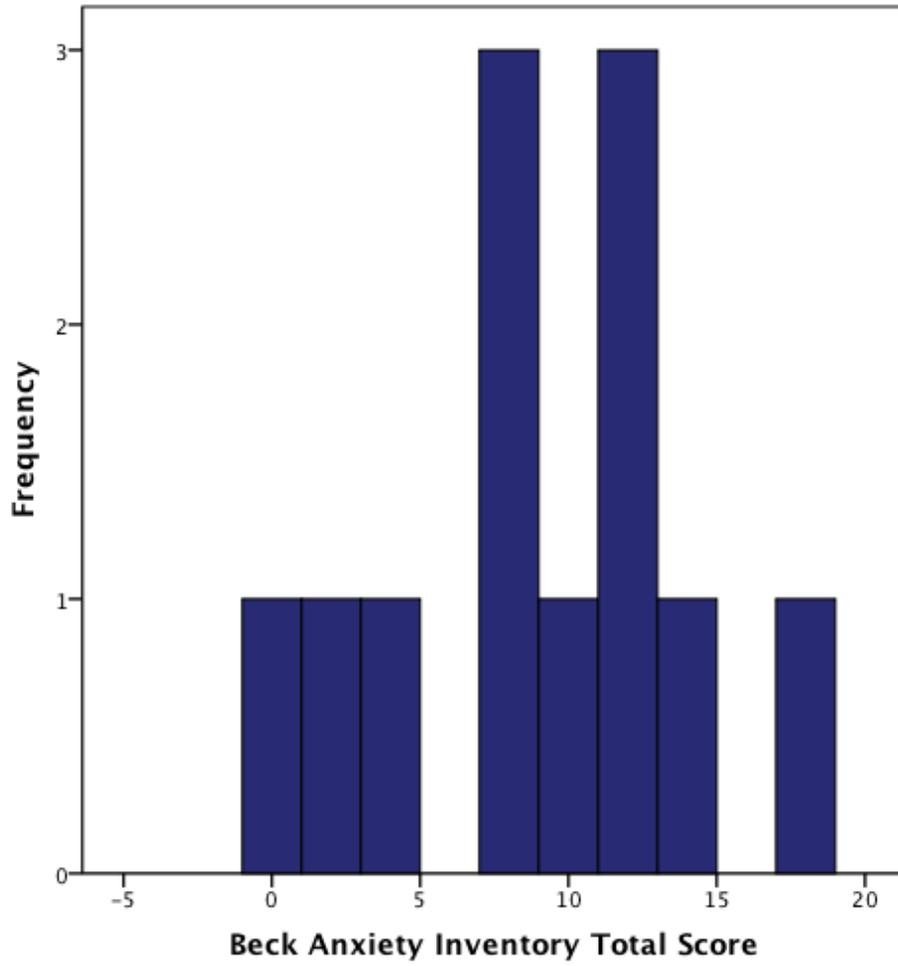


Figure 16. Distribution of total scores from the Beck Anxiety Inventory (BAI)

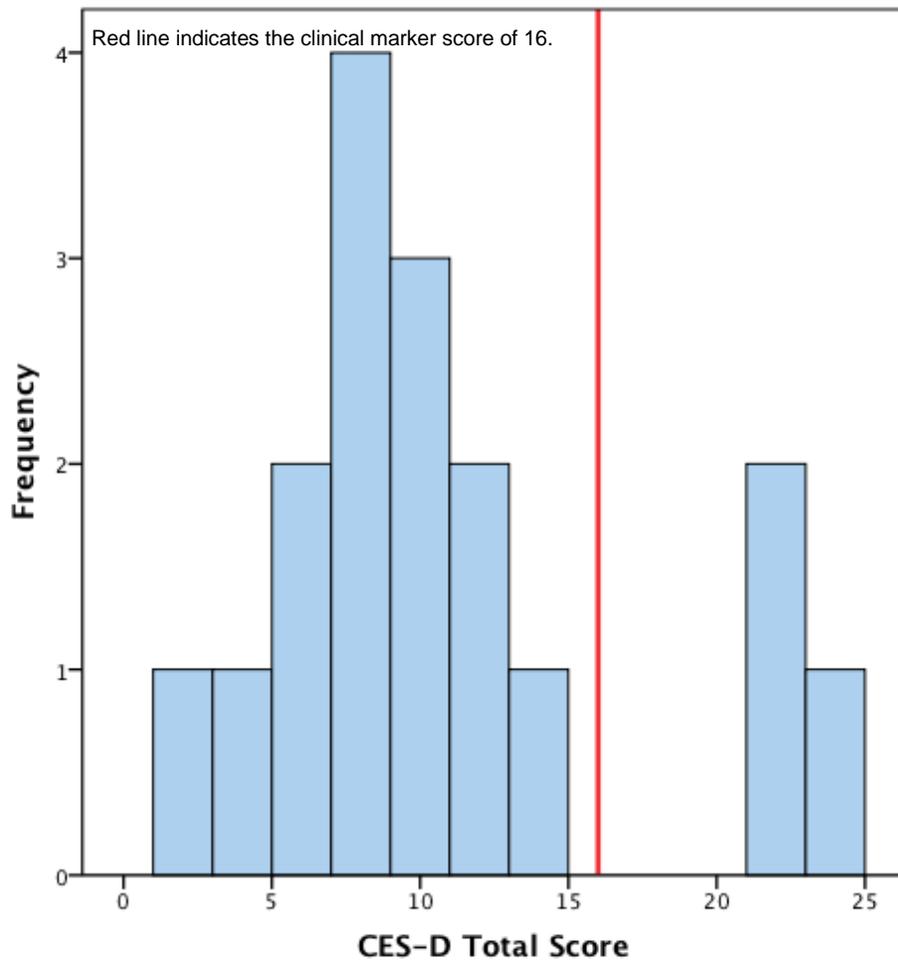


Figure 17. Distribution of total scores from the Centers for Epidemiologic Studies – Depression (CES-D) scale

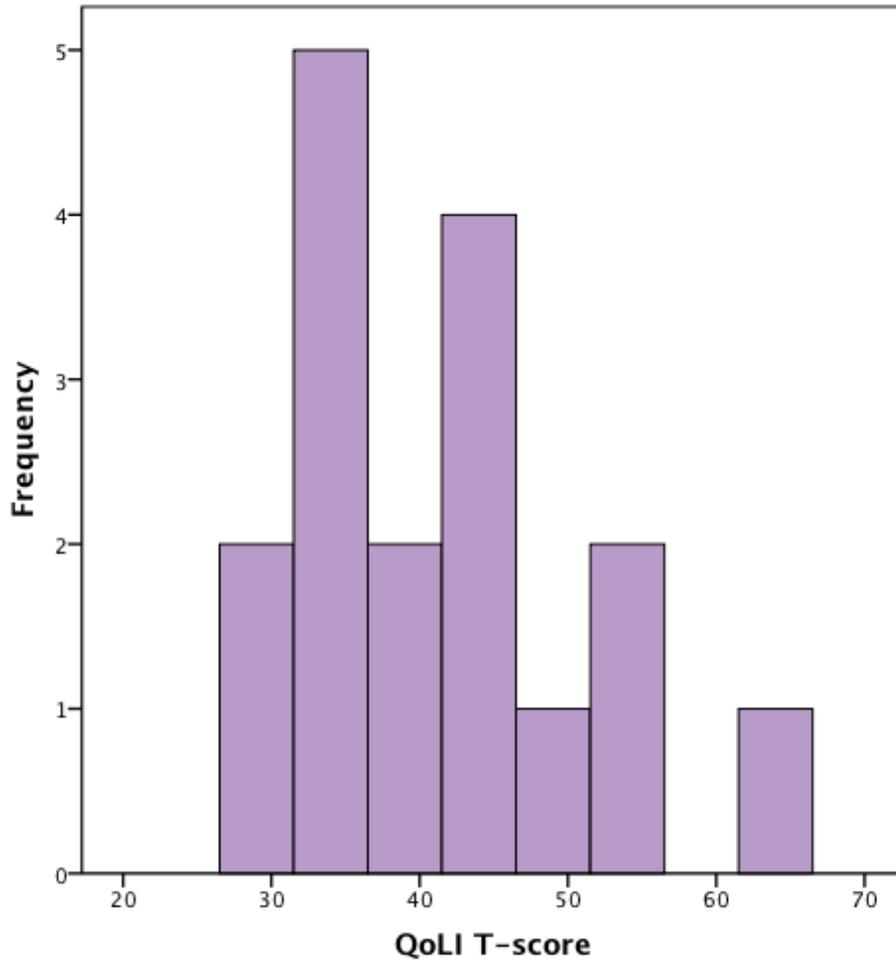


Figure 18. Distribution of the QoLI raw score

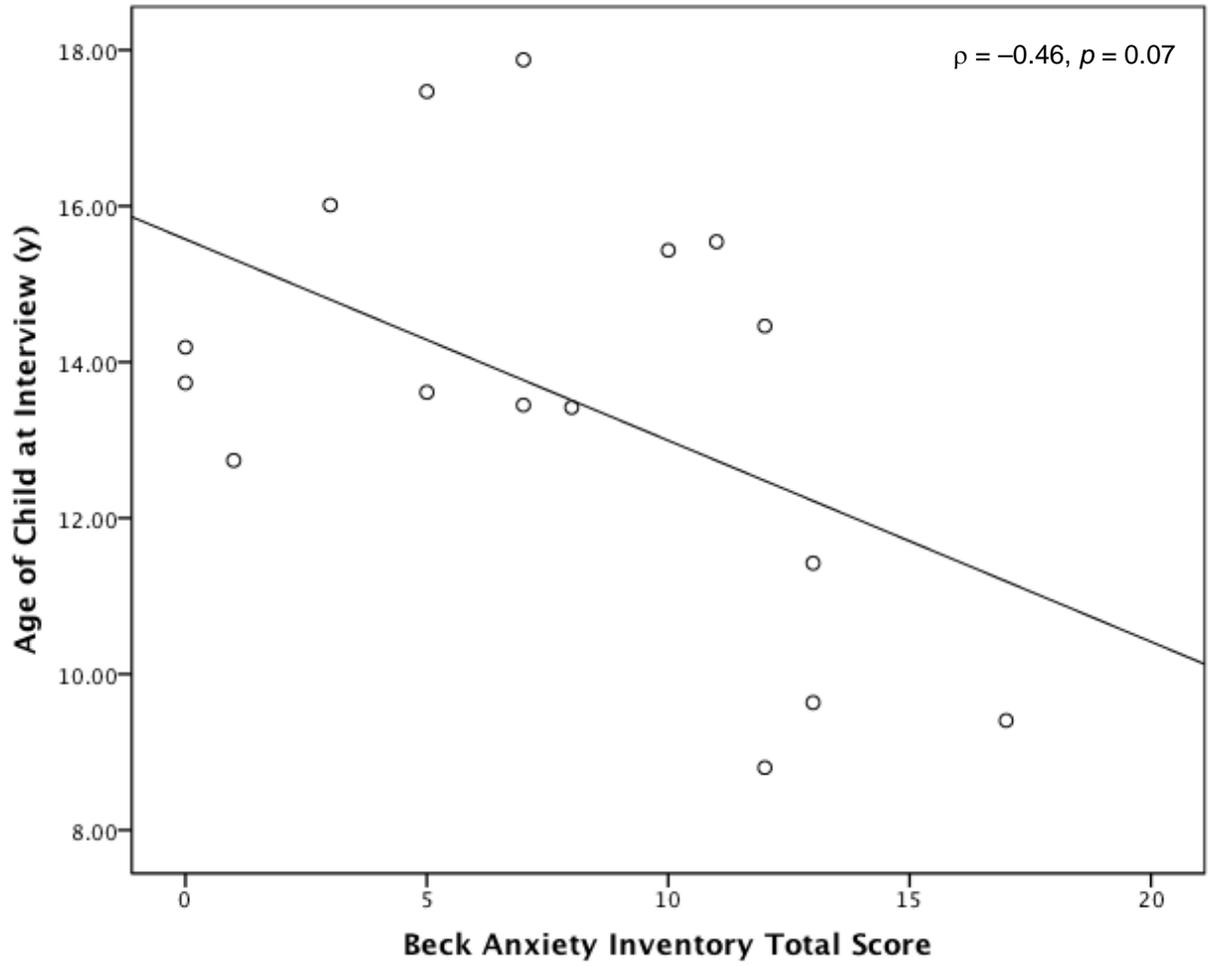


Figure 19. Scatterplot of Age of Child and Interview (in years) vs. BAI total score

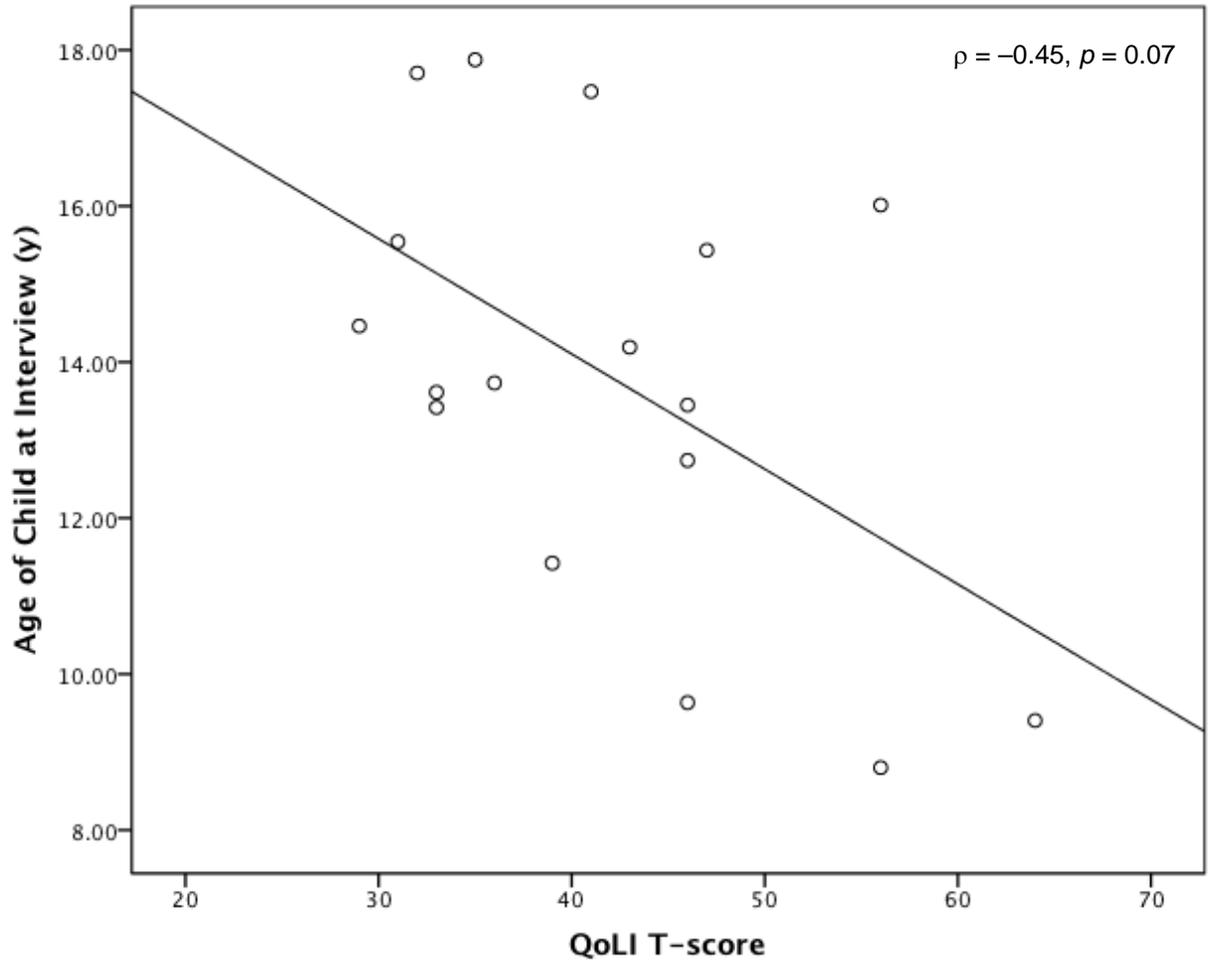


Figure 20. Scatterplot of Age of Child at Interview (in years) vs. QoLI T-score

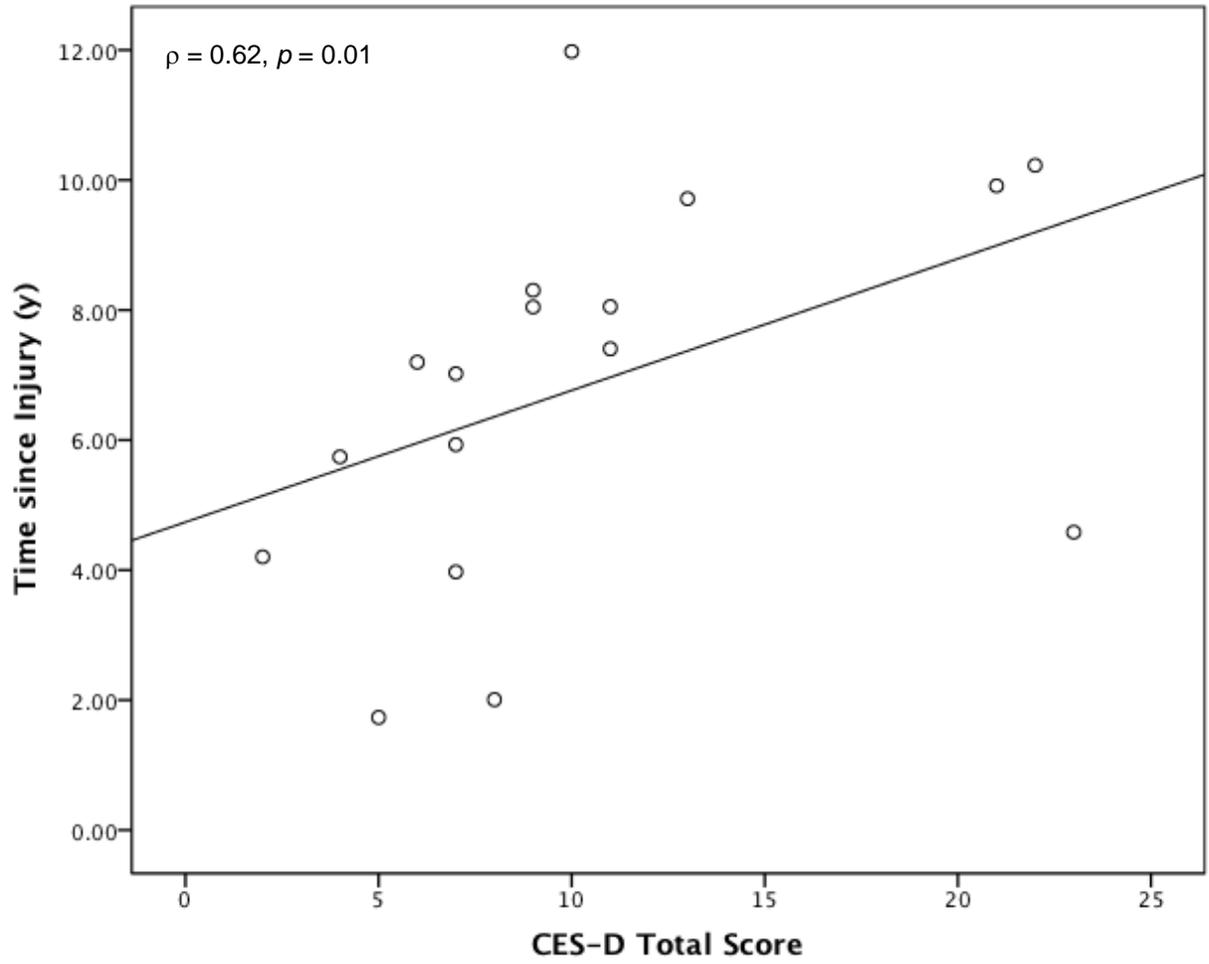


Figure 21. Scatterplot of Time since injury (in years) vs. CES-D total score

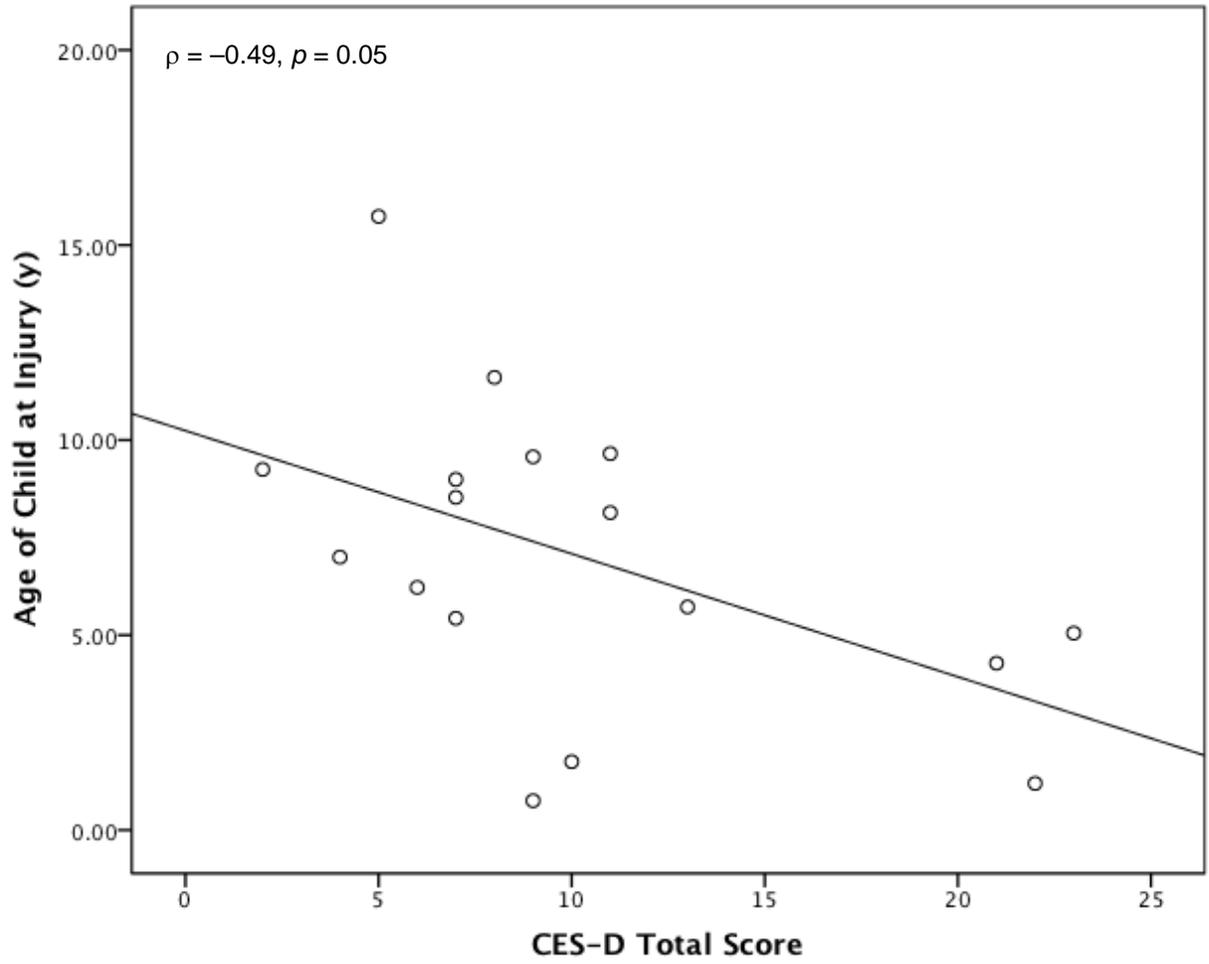


Figure 22. Scatterplot of Age of Child at Injury (in years) vs. CES-D total score

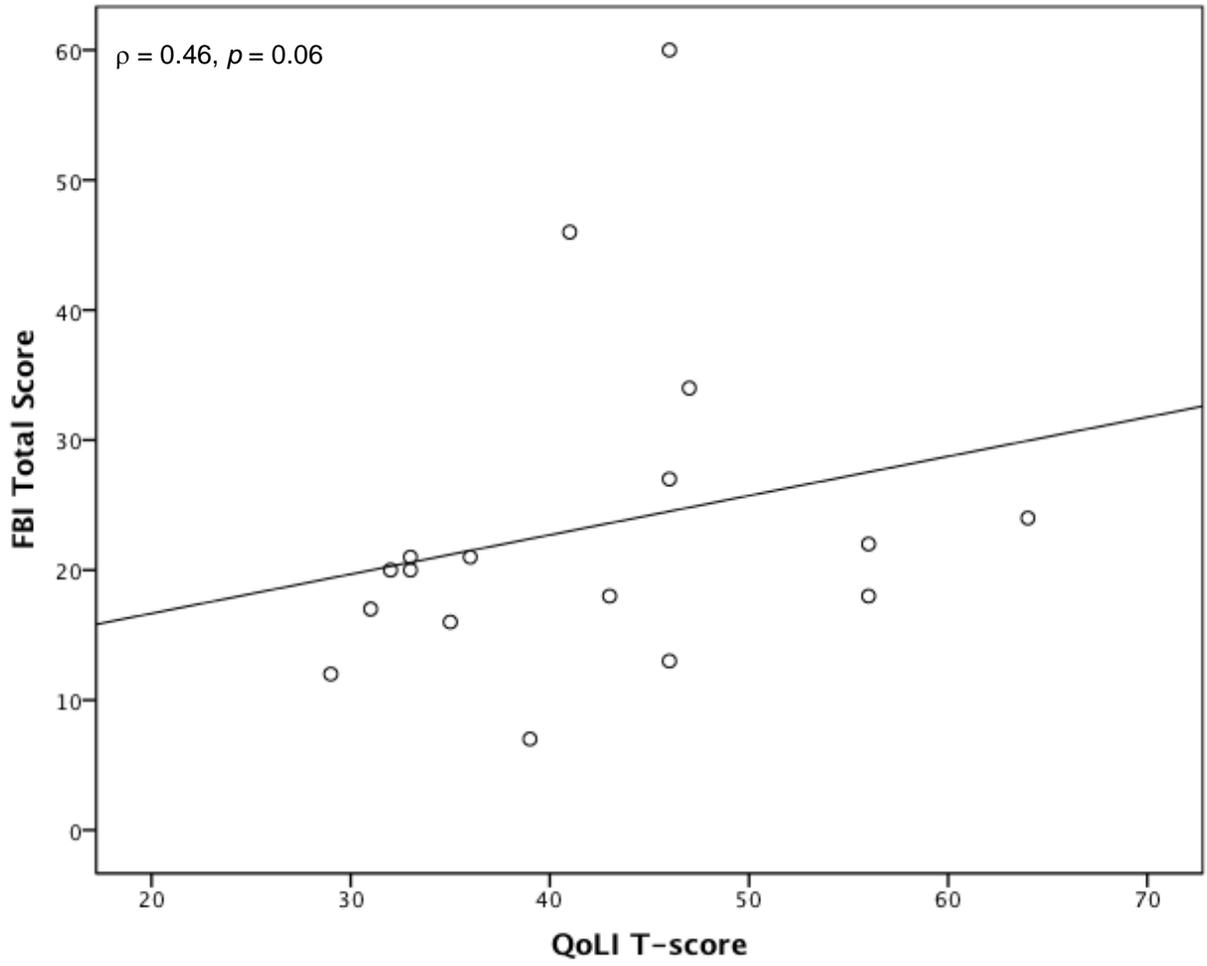


Figure 23. Scatterplot of FBI total score vs. QoLI T-score

Table 12. Demographic, Injury, and Environmental Characteristics

Continuous Variables		
Characteristic	Mean ± SD	Range
Age at interview, child (y)	13.8 + 3.0	8.8 - 17.9
Age at interview, caregiver (y)	40.0 + 7.3	28.7 - 55.7
Time since injury (y)	6.8 + 2.9	1.7 - 15.7
CES-D Total score	10.3 + 6.2	2 - 23
BAI Total score	7.8 + 5.1	0 - 17
Family Burden of Injury score	23.3 + 12.9	7 - 60
Family Functioning score	1.9 + 0.5	1.0 - 2.6
Religious Faith score	20.6 + 6.5	7 - 30
Hollingshead SES	40.1 + 9.3	26 - 61
Quality of Life Index T-score	41.9 - 10.0	29 - 64
Categorical Variables		
Characteristic	N (%)	
<i>Sex, child</i>		
Male	12 (80.0)	
Female	3 (20.0)	
<i>Sex, caregiver</i>		
Male	0 (0.0)	
Female	17 (100.0)	
<i>Race, child</i>		
White	17 (100.0)	
Non-White	0 (0.0)	
<i>Race, caregiver</i>		
White	17 (100.0)	
Non-White	0 (0.0)	
<i>Glasgow Coma Scale</i>		
Moderate (9-12)	4 (26.7)	
Severe (3-8)	11 (73.3)	
<i>GOS-E Peds</i>		
Upper Good Recovery (1)	2 (13.3)	
Lower Good Recovery (2)	4 (26.7)	
Upper Moderate Disability (3)	8 (53.3)	
Vegetative State (7)	1 (6.7)	
<i>Quality of Life Index T-score</i>		
Very Low QoL	7 (41.2)	
Low QoL	2 (11.8)	
Average QoL	7 (41.2)	
High QoL	1 (5.9)	
<i>Injury Mechanism</i>		
Fall	6 (35.3)	
Motor Vehicle Accident	4 (23.5)	
Car vs. Pedestrian	4 (23.5)	
Recreational	2 (11.8)	
Other	1 (5.9)	
Current Depression	4 (23.5)	
Current Anxiety	3 (18.8)	

Table 13. Correlation Coefficients of Caregiver Depression, Anxiety, and Quality of Life

Characteristic	CES-D total score		BAI total score		QOLI T-score		FBI total score		FAF mean score	
	ρ	<i>p</i> -value	ρ	<i>p</i> -value	ρ	<i>p</i> -value	ρ	<i>p</i> -value	ρ	<i>p</i> -value
<i>Injured Youth Characteristics</i>										
Age at interview (y)	0.00	> 0.99	-0.46	0.07	-0.45	0.07	-0.25	0.34	-0.06	0.81
Age at injury (y)	-0.49	0.05	-0.29	0.28	-0.38	0.14	-0.12	0.66	0.20	0.45
Time since injury (y)	0.62	0.01	-0.12	0.66	-0.15	0.58	-0.31	0.23	-0.33	0.20
<i>Caregiver Characteristics</i>										
Caregiver Age at interview (y)	-0.05	0.85	0.03	0.92	-0.36	0.15	-0.02	0.94	-0.29	0.26
Family Burden of Injury score	-0.03	0.92	-0.02	0.94	0.46	0.06	-	-	0.10	0.69
Family Functioning score	-0.15	0.56	-0.36	0.17	0.11	0.68	0.10	0.69	-	-
Religious Faith score	-0.03	0.92	-0.36	0.17	0.26	0.32	0.17	0.52	-0.36	0.15
Hollingshead SES	0.19	0.50	0.25	0.38	-0.12	0.67	0.09	0.75	0.05	0.87
QOLI T-score	-0.09	0.73	0.10	0.70	-	-	0.46	0.06	0.11	0.68
BAI total score	0.26	0.33	-	-	0.10	0.70	-0.02	0.94	-0.36	0.17
CES-D total score	-	-	0.26	0.33	-0.09	0.73	-0.03	0.92	-0.15	0.56

Table 14. Differences in Caregiver Outcomes by Category

Characteristic	N (%)	CES-D total score		BAI total score		QOLI T-score		FBI total score		FAF mean score	
		Mean + SD	p-value	Mean + SD	p-value	Mean + SD	p-value	Mean + SD	p-value	Mean + SD	p-value
<i>Sex, child</i>			0.54		0.33		0.25		0.58		0.02
Male	14 (82.3)	10.3 + 6.8		7.0 + 5.4		43.3 + 9.8		23.8 + 13.6		2.1 + 0.4	
Female	3 (17.7)	10.3 + 3.1		11.0 + 1.0		35.7 + 9.9		21.0 + 11.5		1.1 + 0.2	
<i>Glasgow Coma Scale</i>			0.95		0.11		0.47		0.27		0.25
Moderate (9-12)	4 (23.5)	11.0 + 7.4		11.3 + 2.2		39.3 + 11.9		15.5 + 7.2		1.7 + 0.3	
Severe (3-8)	13 (76.5)	10.1 + 6.1		6.6 + 5.4		42.8 + 9.7		25.7 + 13.5		1.96 + 0.5	
<i>GOS-E Peds</i>			0.02		0.26		0.79		0.29		0.09
Upper Good Recovery (1)	2 (11.8)	10.0 + 4.2		11.0 + 1.4		38.0 + 12.7		23.0 + 15.6		1.2 + 0.3	
Lower Good Recovery (2)	5 (29.4)	14.8 + 6.2		9.0 + 6.1		40.2 + 10.1		16.8 + 5.8		1.8 + 0.5	
Upper Moderate Disability (3)	9 (52.9)	6.4 + 2.5		5.9 + 5.0		43.3 + 10.9		22.9 + 9.6		2.1 + 0.4	
Vegetative State (7)	1 (5.9)	23.0		13.0		46.0		60.0		2.4	
Receives special education services			0.16		0.15		0.38		0.84		0.09
Yes	11 (64.7)	9.4 + 6.7		6.1 + 4.3		40.0 + 8.3		24.6 + 14.9		2.1 + 0.4	
No	6 (45.3)	12.0 + 5.3		10.5 + 5.7		45.5 + 12.6		20.8 + 8.8		1.6 + 0.5	
Lives with family members other than caregiver			0.38		0.88		0.54		0.58		0.71
Yes	14 (82.3)	10.2 + 6.8		7.8 + 5.4		42.9 + 10.3		23.0 + 14.0		1.9 + 0.5	
No	3 (17.7)	10.7 + 2.5		7.5 + 3.5		37.3 + 8.4		24.7 + 8.1		1.8 + 0.7	
Lives with sibling(s)			0.24		0.96		0.06		0.45		0.74
Yes	9 (52.9)	12.7 + 7.3		7.7 + 5.1		37.0 + 5.7		24.2 + 17.2		1.9 + 0.5	
No	8 (47.1)	7.6 + 3.5		7.9 + 5.6		47.5 + 11.2		22.3 + 6.3		1.9 + 0.5	
Lives with father/stepfather			0.23		0.44		0.21		0.96		0.52
Yes	11 (64.7)	9.5 + 6.5		7.0 + 5.8		44.6 + 10.4		21.3 + 9.8		2.0 + 0.5	
No	6 (45.3)	11.8 + 5.9		9.4 + 3.4		37.0 + 7.6		27.0 + 9.8		1.8 + 0.6	

6.0 GENERAL DISCUSSION

6.1 SUMMARY

This dissertation investigated the association between TBI and subsequent emotional and behavioral outcomes in young injury survivors and their caregivers. The analyses were performed in a cohort of 14 young injury survivors and 17 primary caregivers.

The first paper of this dissertation focused on depression- and anxiety-related outcomes in the brain-injured children and adolescents. In this article, we found the prevalence of depression in these children was much lower than rates previously reported in the literature for children with TBI and much more in line with the prevalence found in the general child and adolescent population. The prevalence of anxiety was found to be lower than both that any prevalence rate reported in the literature as well as the observed rate in the general youth population. This paper also found that age at injury is not associated with the increased presence of depressive or anxious symptoms. Age at the time of interview was positively correlated with depressive symptoms which may suggest that life events and the pitfalls of adolescence may play a significant role in this population who is several years post-injury. Injury severity was found to be associated with increased depressive symptoms, but not for symptoms of anxiety.

Few factors were strongly associated with anxiety. Additionally, the caregiver CES-D total score was associated with anxiety, but is most likely not reflective of the child, but more

likely a reflection on the caregiver's functioning. Children who receive special education services are more likely to have a lower number of anxiety-related symptoms, though the reasoning behind this finding is not clear especially in light of the wide variety of services that a child may or may not receive.

The second paper examined the relationship between the disruptive behavior disorders of ADHD, ODD, and CD and their association with brain injury in children. Within this study population, there was a large number of children with previously diagnosed ADHD or clinically significant levels of ADHD as reported on the CPRS:R-S symptom survey. This 35.7% prevalence is much higher than the 5% rate found in the general youth population, and much higher than rates reported in previous studies. This is also surprising given that this youth population is several years from the time of injury suggesting that the symptoms did not abate over time, and ADHD may have become more prevalent over time when compared to research conducted in just one or two years post-TBI. There were not statistically significant findings with respect to the ADHD, but there is a pattern that may suggest that injury at earlier ages may be associated with more ADHD symptoms.

There were no children who met the criteria for ODD or CD, which may suggest that symptoms of these conditions decrease over time. However, this may also be the result of volunteer bias on the part of the caregivers.

The third paper focused on outcomes of depression and anxiety and quality of life in the caregivers of brain-injured youth. This study found a prevalence of depression (23.5%) in this caregiver population that is higher than that in the few published studies that examined caregivers of young injury survivors. This finding is important since there has been several elapsed since the time of injury and most of the children of these caregivers are moderately well

functioning. In fact, the correlation between time elapsed since injury and depressive symptoms is positively associated and statistically significant possibly suggesting that depressive symptoms increased over time in this population.

The prevalence of anxiety in this population is very close to that found in the general population of adults, and lower than those rates reported closer to the time of injury in previously published reports suggesting a possible diminishment of symptoms of over time.

This caregiver analysis also found that nearly 50% of the enrolled caregivers were symptoms of low or very quality of life. This is a notable finding, and coupled with the findings related to depression, suggest that future research should continue to focus on caregivers of this type so additional resources can be provided to them as part of their child's recovery and treatment plan.

Table 15. Summary of Findings

Outcomes	Prevalence	Association with Injury Severity	Association with Time since Injury	Other Associated Risk Factors
Depression (Child)	5.9%	More severe injury is associated with increased depression symptoms	No statistically significant relationship	None
Anxiety (Child)	5.9%	No statistically significant relationship	No statistically significant relationship	Caregiver depression score is positively associated with anxiety symptoms
ADHD (Child)	35.7%	No statistically significant relationship	No statistically significant relationship	No statistically significant relationship
ODD/CD (Child)	0%	N/A	N/A	N/A
Depression (Caregiver)	23.5%	No statistically significant relationship	Increasing time since injury is positively associated with increased depression symptoms	Earlier age of child at injury is associated with increased depression symptoms
Anxiety (Caregiver)	18.8%	No statistically significant relationship	No statistically significant relationship	Earlier age of child at interview is associated with increased anxiety symptoms
Poor Quality of Life (Caregiver)	52.9%	No statistically significant relationship	No statistically significant relationship	Earlier age of child at interview is associated with poor quality of life

6.2 STRENGTHS AND LIMITATIONS

The number of individuals who chose to participate in this study—nearly 20% of the total potential pool of 93 participants—was relatively small. This small sample limits the statistical power to detect true differences between groups. It also calls into question to representativeness of the sample. The majority of the screened participants were moderately well functioning, leaving one to wonder if families with poor-functioning felt they would not be helped by this study or if the study would be burdensome given their current caregiving responsibilities. Additionally, there were very few participants who were very well functioning. While the pool of potential TBI survivors were drawn from only those with moderate and severe injuries, it is possible that the families of children who are now very well functioning and several years post-injury would decide to rather not relive events associated with such a traumatic experience.

Additionally, there may be a self-report bias in the reporting of caregiver outcomes, as the caregiver may feel uncomfortable reporting their true symptoms and feelings. Moreover, the FBII asked about data in the six-month period following injury. Because the time of the injury event was several years ago, this measure is subject to a recall bias because of the time that has since elapsed. As well, this study is cross-sectional in its design, limited the findings to associations because the temporality of cause-and-effect analysis is not available.

However, this research has many strengths that support the findings of this study. Firstly, the injury-related data are well documented and include many variables related to the injury event. Additionally, the outcome assessments—while not conducted in person—were collected using validated measures for objective and subjecting collection of this study's outcomes.

Additionally, this study included children whose injuries occurred at least four years ago with the average time elapsed since injury much greater than those previously reported in the published literature. Because this study was able to enroll both children and their caregivers as participants, an additional strength of this research is its ability to analyze and compare both injury survivors and their caregivers to determine possible interactions between injury and the recovery environment.

6.3 FUTURE RESEARCH DIRECTIONS

This research is one small piece of a growing field of injury research. Because this study is cross-sectional in design, future studies should expand upon the point-in-time analysis toward a longitudinal design. This longitudinal design would have the advantage of increased statistical power and the ability to analyze causality-based hypotheses.

Future analyses of this type would be strengthened by data collected at the time of injury. A well-constructed study of this type would also include a long period of follow-up assessment with periodic assessment of psychological outcomes, injury recuperation, and recovery environment. A study of this type would be able to monitor the symptoms of psychological outcomes in both injured patient and caregiver and determine factors both predictive and associative with these outcomes. This powerful next step would help contribute to a more fully supportive recovery environment for both the injury survivor and caregiver.

6.4 PUBLIC HEALTH SIGNIFICANCE

At its simplest, the ultimate goals of public health are to prevent disease and promote health. This study examined the factors associated with outcomes from TBI in young children and their caregivers. This study was able to identify factors in these populations that differ from that of the general population. Additionally, this research was able to identify, through statistical methods, factors that may be associated with these outcomes. These results, when published in the literature, will add to the growing field of epidemiologic studies examining the outcomes of brain injury. The identification of factors associated with disease is paramount in order to help prevent disease and promote health in individuals who are most at risk. Furthermore, the identification of factors associated with worse outcomes can help identify patients and families who may need additional follow-up because of their increased risk. These measures will help to improve long-term outcomes in survivors of TBI. Through these means, public health knowledge about this subject can be advanced, and significance through this work can be achieved.

BIBLIOGRAPHY

1. Langlois JA R-BW, Thomas KE. *Traumatic Brain Injury in the United States: Emergency Department Visits, Hospitalizations, and Deaths*. Atlanta, GA: Centers for Disease Control and Prevention, National Center for Injury Prevention and Control;2006.
2. Thurman DJ, Alverson C, Dunn KA, Guerrero J, Sniezek JE. Traumatic brain injury in the United States: A public health perspective. *J Head Trauma Rehabil*. Dec 1999;14(6):602-615.
3. Kraus JF. Epidemiology of Head Injury. In: Cooper PR, ed. *Head Injury*. Baltimore: Williams and Wilkins; 1987:1-19.
4. Kraus JF. Epidemiological features of brain injury in children: Occurrence, children at risk, causes, and manner of injury, severity, and outcomes. In: Broman SH, Michel ME, eds. *Traumatic Brain Injury in Children*. New York: Oxford University Press; 1995:22-39.
5. Kraus JF, Fife D, Conroy C. Pediatric brain injuries: the nature, clinical course, and early outcomes in a defined United States' population. *Pediatrics*. Apr 1987;79(4):501-507.
6. Biegel DE, Sales E, Schulz R. *Family Caregiving in Chronic Illness: Alzheimer's Disease, Cancer, Heart Disease, Mental Illness and Stroke*. Newbury Park, CA: Sage Publications, Inc.; 1991.
7. *Facts about Traumatic Brain Injury*: Centers for Disease Control and Prevention;2006.
8. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 4th ed. Washington, DC: American Psychiatric Press, Inc.; 2000.
9. World Health Organization. Depression.
http://www.who.int/mental_health/management/depression/definition/en/. Accessed November 10, 2007.
10. Shaffer D, Gould MS, Fisher P, et al. Psychiatric diagnosis in child and adolescent suicide. *Arch Gen Psychiatry*. Apr 1996;53(4):339-348.
11. Hoyert DL, Kochanek KD, Murphy SL. Deaths: final data for 1997. *Natl Vital Stat Rep*. Jun 30 1999;47(19):1-104.
12. National Institute of Mental Health. *Depression*: Department of Health and Human Services;2008. 08 3561.
13. Bennett DS. Depression among children with chronic medical problems: a meta-analysis. *J Pediatr Psychol*. Apr 1994;19(2):149-169.
14. Max JE, Koele SL, Smith WL, Jr., et al. Psychiatric disorders in children and adolescents after severe traumatic brain injury: a controlled study. *J Am Acad Child Adolesc Psychiatry*. Aug 1998;37(8):832-840.

15. Max JE, Lindgren SD, Knutson C, Pearson CS, Ihrig D, Welborn A. Child and adolescent traumatic brain injury: psychiatric findings from a paediatric outpatient specialty clinic. *Brain Inj.* Oct 1997;11(10):699-711.
16. Geraldina P, Mariarosaria L, Annarita A, et al. Neuropsychiatric sequelae in TBI: a comparison across different age groups. *Brain Inj.* Oct 2003;17(10):835-846.
17. Luis CA, Mittenberg W. Mood and anxiety disorders following pediatric traumatic brain injury: a prospective study. *J Clin Exp Neuropsychol.* May 2002;24(3):270-279.
18. Max JE, Robin DA, Lindgren SD, et al. Traumatic brain injury in children and adolescents: psychiatric disorders at two years. *J Am Acad Child Adolesc Psychiatry.* Sep 1997;36(9):1278-1285.
19. Max JE, Robin DA, Lindgren SD, et al. Traumatic brain injury in children and adolescents: psychiatric disorders at one year. *J Neuropsychiatry Clin Neurosci.* Summer 1998;10(3):290-297.
20. Max JE, Schachar RJ, Levin HS, et al. Predictors of attention-deficit/hyperactivity disorder within 6 months after pediatric traumatic brain injury. *J Am Acad Child Adolesc Psychiatry.* Oct 2005;44(10):1032-1040.
21. Max JE, Schachar RJ, Levin HS, et al. Predictors of secondary attention-deficit/hyperactivity disorder in children and adolescents 6 to 24 months after traumatic brain injury. *J Am Acad Child Adolesc Psychiatry.* Oct 2005;44(10):1041-1049.
22. Max JE, Smith WL, Jr., Sato Y, et al. Traumatic brain injury in children and adolescents: psychiatric disorders in the first three months. *J Am Acad Child Adolesc Psychiatry.* Jan 1997;36(1):94-102.
23. Kirkwood M, Janusz J, Yeates KO, et al. Prevalence and correlates of depressive symptoms following traumatic brain injuries in children. *Child Neuropsychol.* Sep 2000;6(3):195-208.
24. Beers SR. Cognitive effects of mild head injury in children and adolescents. *Neuropsychol Rev.* Dec 1992;3(4):281-320.
25. Massagli TL, Fann JR, Burington BE, Jaffe KM, Katon WJ, Thompson RS. Psychiatric illness after mild traumatic brain injury in children. *Arch Phys Med Rehabil.* Sep 2004;85(9):1428-1434.
26. *Mental Health: A Report of the Surgeon General.* Rockville, MD: Department of Health and Human Services;1999.
27. Daviss WB, Mooney D, Racusin R, Ford JD, Fleischer A, McHugo GJ. Predicting posttraumatic stress after hospitalization for pediatric injury. *J Am Acad Child Adolesc Psychiatry.* May 2000;39(5):576-583.
28. Levi RB, Drotar D, Yeates KO, Taylor HG. Posttraumatic stress symptoms in children following orthopedic or traumatic brain injury. *J Clin Child Psychol.* Jun 1999;28(2):232-243.
29. Max JE, Castillo CS, Robin DA, et al. Posttraumatic stress symptomatology after childhood traumatic brain injury. *J Nerv Ment Dis.* Oct 1998;186(10):589-596.
30. Max JE, Lindgren SD, Robin DA, et al. Traumatic brain injury in children and adolescents: psychiatric disorders in the second three months. *J Nerv Ment Dis.* Jun 1997;185(6):394-401.
31. Vasa RA, Gerring JP, Grados M, et al. Anxiety after severe pediatric closed head injury. *J Am Acad Child Adolesc Psychiatry.* Feb 2002;41(2):148-156.

32. Gerring JP, Slomine B, Vasa RA, et al. Clinical predictors of posttraumatic stress disorder after closed head injury in children. *J Am Acad Child Adolesc Psychiatry*. Feb 2002;41(2):157-165.
33. Rivara JM, Jaffe KM, Polissar NL, Fay GC, Liao S, Martin KM. Predictors of family functioning and change 3 years after traumatic brain injury in children. *Arch Phys Med Rehabil*. Aug 1996;77(8):754-764.
34. Vasa RA, Grados M, Slomine B, et al. Neuroimaging correlates of anxiety after pediatric traumatic brain injury. *Biol Psychiatry*. Feb 1 2004;55(3):208-216.
35. Max JE, Koele SL, Castillo CC, et al. Personality change disorder in children and adolescents following traumatic brain injury. *J Int Neuropsychol Soc*. Mar 2000;6(3):279-289.
36. Max JE, Lansing AE, Koele SL, et al. Attention deficit hyperactivity disorder in children and adolescents following traumatic brain injury. *Dev Neuropsychol*. 2004;25(1-2):159-177.
37. National Institute of Mental Health. *Attention Deficit Hyperactivity Disorder*. Bethesda, MD: National Institute of Mental Health, US Department of Health and Human Services.
38. Max JE, Arndt S, Castillo CS, et al. Attention-deficit hyperactivity symptomatology after traumatic brain injury: a prospective study. *J Am Acad Child Adolesc Psychiatry*. Aug 1998;37(8):841-847.
39. Gerring J, Brady K, Chen A, et al. Neuroimaging variables related to development of Secondary Attention Deficit Hyperactivity Disorder after closed head injury in children and adolescents. *Brain Inj*. Mar 2000;14(3):205-218.
40. DiScala C, Lescohier I, Barthel M, Li G. Injuries to children with attention deficit hyperactivity disorder. *Pediatrics*. Dec 1998;102(6):1415-1421.
41. Slomine BS, Salorio CF, Grados MA, Vasa RA, Christensen JR, Gerring JP. Differences in attention, executive functioning, and memory in children with and without ADHD after severe traumatic brain injury. *J Int Neuropsychol Soc*. Sep 2005;11(5):645-653.
42. Max JE, Lindgren SD, Knutson C, Pearson CS, Ihrig D, Welborn A. Child and adolescent traumatic brain injury: correlates of disruptive behaviour disorders. *Brain Inj*. Jan 1998;12(1):41-52.
43. Gerring JP, Brady KD, Chen A, et al. Premorbid prevalence of ADHD and development of secondary ADHD after closed head injury. *J Am Acad Child Adolesc Psychiatry*. Jun 1998;37(6):647-654.
44. Levin H, Hanten G, Max J, et al. Symptoms of attention-deficit/hyperactivity disorder following traumatic brain injury in children. *J Dev Behav Pediatr*. Apr 2007;28(2):108-118.
45. Catroppa C, Anderson V. Attentional skills in the acute phase following pediatric traumatic brain injury. *Child Neuropsychol*. Dec 1999;5(4):251-264.
46. Catroppa C, Anderson V. A prospective study of the recovery of attention from acute to 2 years following pediatric traumatic brain injury. *J Int Neuropsychol Soc*. Jan 2005;11(1):84-98.
47. Wassenberg R, Max JE, Lindgren SD, Schatz A. Sustained attention in children and adolescents after traumatic brain injury: relation to severity of injury, adaptive functioning, ADHD and social background. *Brain Inj*. Aug 2004;18(8):751-764.
48. Max JE, Lindgren SD, Knutson C, Pearson CS, Ihrig D, Welborn A. Child and adolescent traumatic brain injury: correlates of injury severity. *Brain Inj*. Jan 1998;12(1):31-40.

49. Max JE, Koele SL, Lindgren SD, et al. Adaptive functioning following traumatic brain injury and orthopedic injury: a controlled study. *Arch Phys Med Rehabil.* Aug 1998;79(8):893-899.
50. Kaufmann PM, Fletcher JM, Levin HS, Miner ME, Ewing-Cobbs L. Attentional disturbance after pediatric closed head injury. *J Child Neurol.* Oct 1993;8(4):348-353.
51. Hesslinger B, Tebartz van Elst L, Thiel T, Haegele K, Hennig J, Ebert D. Frontoorbital volume reductions in adult patients with attention deficit hyperactivity disorder. *Neurosci Lett.* Aug 16 2002;328(3):319-321.
52. Lee JS, Kim BN, Kang E, et al. Regional cerebral blood flow in children with attention deficit hyperactivity disorder: comparison before and after methylphenidate treatment. *Hum Brain Mapp.* Mar 2005;24(3):157-164.
53. Herskovits EH, Megalooikonomou V, Davatzikos C, Chen A, Bryan RN, Gerring JP. Is the spatial distribution of brain lesions associated with closed-head injury predictive of subsequent development of attention-deficit/hyperactivity disorder? Analysis with brain-image database. *Radiology.* Nov 1999;213(2):389-394.
54. Lahey BB, Loeber R, Quay HC, Frick PJ, Grimm J. Oppositional defiant and conduct disorders: issues to be resolved for DSM-IV. *J Am Acad Child Adolesc Psychiatry.* May 1992;31(3):539-546.
55. American Academy of Child & Adolescent Psychiatry. FAQs on Oppositional Defiant Disorder. http://www.aacap.org/cs/resource_center/odd_faqs. Accessed 10/21/2008.
56. Max JE, Dunisch DL. Traumatic brain injury in a child psychiatry outpatient clinic: a controlled study. *J Am Acad Child Adolesc Psychiatry.* Mar 1997;36(3):404-411.
57. Max JE, Castillo CS, Bokura H, et al. Oppositional defiant disorder symptomatology after traumatic brain injury: a prospective study. *J Nerv Ment Dis.* Jun 1998;186(6):325-332.
58. Tateno A, Jorge RE, Robinson RG. Clinical correlates of aggressive behavior after traumatic brain injury. *J Neuropsychiatry Clin Neurosci.* Spring 2003;15(2):155-160.
59. Knight RG, Devereux R, Godfrey HP. Caring for a family member with a traumatic brain injury. *Brain Inj.* Jun 1998;12(6):467-481.
60. Marsh NV, Kersel DA, Havill JH, Sleigh JW. Caregiver burden at 1 year following severe traumatic brain injury. *Brain Inj.* Dec 1998;12(12):1045-1059.
61. Ergh TC, Hanks RA, Rapport LJ, Coleman RD. Social support moderates caregiver life satisfaction following traumatic brain injury. *J Clin Exp Neuropsychol.* Dec 2003;25(8):1090-1101.
62. Ergh TC, Rapport LJ, Coleman RD, Hanks RA. Predictors of caregiver and family functioning following traumatic brain injury: social support moderates caregiver distress. *J Head Trauma Rehabil.* Apr 2002;17(2):155-174.
63. Marsh NV, Kersel DA, Havill JA, Sleigh JW. Caregiver burden during the year following severe traumatic brain injury. *J Clin Exp Neuropsychol.* Jun 2002;24(4):434-447.
64. Marsh NV, Kersel DA, Havill JH, Sleigh JW. Caregiver burden at 6 months following severe traumatic brain injury. *Brain Inj.* Mar 1998;12(3):225-238.
65. Wade SL, Taylor HG, Drotar D, Stancin T, Yeates KO. Family burden and adaptation during the initial year after traumatic brain injury in children. *Pediatrics.* Jul 1998;102(1 Pt 1):110-116.

66. Ponsford J, Olver J, Ponsford M, Nelms R. Long-term adjustment of families following traumatic brain injury where comprehensive rehabilitation has been provided. *Brain Inj.* Jun 2003;17(6):453-468.
67. Groom KN, Shaw TG, O'Connor ME, Howard NI, Pickens A. Neurobehavioral symptoms and family functioning in traumatically brain-injured adults. *Arch Clin Neuropsychol.* Nov 1998;13(8):695-711.
68. Gan C, Campbell KA, Gemeinhardt M, McFadden GT. Predictors of family system functioning after brain injury. *Brain Inj.* Jun 2006;20(6):587-600.
69. Testa JA, Malec JF, Moessner AM, Brown AW. Predicting family functioning after TBI: impact of neurobehavioral factors. *J Head Trauma Rehabil.* May-Jun 2006;21(3):236-247.
70. Hanks RA, Rapport LJ, Vangel S. Caregiving appraisal after traumatic brain injury: The effects of functional status, coping style, social support and family functioning. *NeuroRehabilitation.* 2007;22(1):43-52.
71. Beers SR, Hahner TP, Adelson PD. Validity of a pediatric version of the Glasgow Outcome Scale--Extended (GOS-E Peds). *Journal of Neurotrauma.* October 2005 2005(22):1224.
72. Smith SD, Schwartz RC, George RG, Panke D. Convergent validity of the Beck Depression Inventory for Youth. *Psychol Rep.* Jun 2004;94(3 Pt 2):1444-1446.
73. March JS, Parker JD, Sullivan K, Stallings P, Conners CK. The Multidimensional Anxiety Scale for Children (MASC): factor structure, reliability, and validity. *J Am Acad Child Adolesc Psychiatry.* Apr 1997;36(4):554-565.
74. Hollingshead AB. A Four-Factor Index of Social Status. New Haven, CT: Department of Sociology, Yale University; 1975.
75. Plante TG, Boccaccini MT. The Santa Clara Strength of Religious Faith Questionnaire. *Pastoral Psychology.* May 1997;45(5):375-387.
76. Taylor HG, Drotar D, Wade SL, Yeates K, Stancin T, Klein S. Recovery from traumatic brain injury in children: The importance of the family. In: Broman SH, Michel ME, eds. *Traumatic Head Injury in Children.* New York: Oxford University Press; 1995:188-216.
77. Epstein NB, Baldwin LM, Bishop DS. The McMaster Family Assessment Device. *Journal of Marital and Family Therapy.* 1983;9(2):171-180.
78. Conners CK, Sitarenios G, Parker JD, Epstein JN. The revised Conners' Parent Rating Scale (CPRS-R): factor structure, reliability, and criterion validity. *J Abnorm Child Psychol.* Aug 1998;26(4):257-268.
79. Sprafkin J, Gadow KD, Salisbury H, Schneider J, Loney J. Further evidence of reliability and validity of the Child Symptom Inventory-4: parent checklist in clinically referred boys. *J Clin Child Adolesc Psychol.* Dec 2002;31(4):513-524.
80. Taylor CA, Adelson PD, Beers SR, Fabio A, Songer TJ, Wisniewski SR. *Emotional and Behavioral Consequences of Traumatic Brain Injury.* Pittsburgh, PA: Epidemiology, University of Pittsburgh; 2010.
81. Radloff LS. The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. *Applied Psychological Measurement.* 1977;1(3):385-401.
82. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. *J Consult Clin Psychol.* Dec 1988;56(6):893-897.
83. Frisch MB, Clark MP, Rouse SV, et al. Predictive and treatment validity of life satisfaction and the quality of life inventory. *Assessment.* Mar 2005;12(1):66-78.

- 84.** Burgess ES, Drotar D, Taylor HG, Wade S, Stancin T, Yeates KO. The family burden of injury interview: reliability and validity studies. *J Head Trauma Rehabil.* Aug 1999;14(4):394-405.
- 85.** Sherman AC, Simonton S, Adams DC, et al. Measuring religious faith in cancer patients: reliability and construct validity of the Santa Clara Strength of Religious Faith questionnaire. *Psychooncology.* Sep-Oct 2001;10(5):436-443.
- 86.** Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry.* Jun 2005;62(6):617-627.