Masthead Logo

Brigham Young University
BYU ScholarsArchive

All Theses and Dissertations

2018-04-01

Psychiatric Symptom Severity Following Pediatric Traumatic Brain Injury: A Meta-Analysis

Benjamin Douglas Eschler
Brigham Young University

Follow this and additional works at: https://scholarsarchive.byu.edu/etd

BYU ScholarsArchive Citation

Eschler, Benjamin Douglas, "Psychiatric Symptom Severity Following Pediatric Traumatic Brain Injury: A Meta-Analysis" (2018). *All Theses and Dissertations*. 7305.
https://scholarsarchive.byu.edu/etd/7305

This Thesis is brought to you for free and open access by BYU ScholarsArchive. It has been accepted for inclusion in All Theses and Dissertations by an authorized administrator of BYU ScholarsArchive. For more information, please contact scholarsarchive@byu.edu, ellen_amatangelo@byu.edu.

Psychiatric Symptom Severity Following Pediatric Traumatic Brain Injury: A Meta-Analysis

Benjamin Douglas Eschler

A thesis submitted to the faculty of
Brigham Young University
in partial fulfillment of the requirements for the degree of

Master of Science

Shawn D. Gale, Chair
Derin J. Cobia
Dawson Hedges

Department of Psychology

Brigham Young University

Copyright © 2018 Benjamin Douglas Eschler

All Rights Reserved

ABSTRACT

Psychiatric Symptom Severity Following
Pediatric Traumatic Brain Injury:
A Meta-Analysis

Benjamin Douglas Eschler
Department of Psychology, BYU
Master of Science

Objectives**:** A meta-analysis was conducted to determine the average effect size of internalizing and externalizing symptoms after pediatric traumatic brain injury across a range of severity (mild, moderate, and severe). Two-meta-regressions were also conducted to determine the role of age at injury at time since injury on these effect sizes.

Participants and Methods: 9725 titles and abstracts were collected from PubMed, PsycInfo, and Web of Science. Of these, 63 full-text articles were examined for inclusion criteria to determine eligibility for the study. To be included, the studies needed to be published prior to March 2017 in English, needed to have a control group of either orthopedically injured or typically developing peers, and required a reliable and valuable measure of internalizing and externalizing symptoms in children. Studies were excluded for non-accidental head injuries or if the sample recruited was outside the range of 2-17 years old at the time of injury. The analysis was based on 16 studies including 1083 cases of mild TBI, 184 cases of moderate TBI, 214 cases of severe TBI, and 1605 control cases.

Results: Analyses revealed a large effect size for internalizing symptoms of children with mild TBI (Hedge's $g = -0.624$, $p = 0.009$), a small effect size for moderate TBI (Hedge's $g = -0.238$, $p = 0.029$), and a large effect size for severe TBI (Hedge's $g = -0.923$, $p < .001$). These findings indicate that parents rate children's internalizing symptoms more severely for brain injured children than for typically developing or non-brain injured peers. These children may be experiencing more severe symptoms such as anxiety and depression regardless of injury severity. For externalizing symptoms, analyses demonstrated a moderate effect size for mild TBI (Hedge's $g = -0.531$, $p = 0.003$), a small effect size for moderate TBI (Hedge's $g = -0.257$, $p = 0.007$), and a large effect size for severe TBI (Hedge's $g = -0.909$, $p < .001$). Thus, children who experienced a TBI demonstrated externalizing symptoms including hyperactivity and impulsivity with the largest effect size associated with severe TBI. The results of the meta-regressions indicated that only injury severity was a significant predictor of symptom severity.

Conclusions: Using meta-analytic methods, we found that children who experience traumatic brain injury are rated as exhibiting more severe internalizing and externalizing symptoms across levels of severity. This effect was largest for severe injury and smallest for moderate injury. Caregivers and healthcare practitioners can use this information to better screen for and treat internalizing and externalizing symptoms in children after a traumatic brain injury.

Keywords: pediatric, traumatic brain injury, psychiatric symptoms, internalizing, externalizing

TABLE OF CONTENTS

Abstract ii

List of Tables v

List of Figures vi

Psychiatric Symptom Severity Following Pediatric Traumatic Brain Injury: A Meta-Analysis 1

Specific Aims and Hypotheses 5

Methods 6

Identification and Selection of Source Studies 6

Inclusion Criteria 6

Procedure 7

Group Categorization by Injury Severity 8

Analytic Procedure 9

Aim 1 9

Aims 2 and 3 9

Results 10

Search Results 10

Meta-Analyses 12

Internalizing Problems Across Group Severity.. 12

Internalizing Problems by Group Severity. 13

Externalizing Problems Across Group Severity. 15

Externalizing Problems by Group Severity. 16

Meta-Regressions 18

Effect of Time Since Injury. 18

Effect of Age at Injury 19

Discussion 21

Conclusion 24

References 26

LIST OF TABLES

Table 1 *Sample Size And Measures Collected From Each Source Study* 11

Table 2 *Results Of Meta-Regression Investigating The Effects Of Time Since Injury On The Effect Size Of Internalizing Problems With GCS As An Ovariate* 18

Table 3 *Results Of Meta-Regression Investigating The Effects Of Time Since Injury On The Effect Size Of Externalizing Problems With GCS As A Covariate.* 19

Table 4 *Results Of Meta-Regression Investigating The Effects Of Age At Injury On The Effect Size Of Internalizing Symptoms With GCS As A Covariate.* 20

Table 5 *Results Of Meta-Regression Investigating The Effects Of Age At Injury On The Effect Size Of Externalizing Symptoms With GCS As A Covariate.* 20

LIST OF FIGURES

Figure 1. Procedure for the systematic literature search. 8

Figure 2. Funnel plot for all studies included in analyses of internalizing symptoms. 12

Figure 3. Overall internalizing symptoms across group severity. 13

Figure 4. Summary of internalizing symptoms by group severity. 14

Figure 5. Funnel plot for all studies included in the analysis of externalizing symptoms. .. 15

Figure 6. Overall externalizing symptoms across group severity. 16

Figure 7. Summary of externalizing symptoms by group severity 17

Psychiatric Symptom Severity Following Pediatric Traumatic Brain Injury: A Meta-Analysis

Traumatic brain injury (TBI) is the most common cause of death and disability in children and adults (Ghaiar, 2001). Each year, approximately 0.4% of children will sustain a TBI that can lead to lasting complications (Max, 2014). The public health burden of TBI is especially high in children and adolescents (Thurman, 2016). Rates of disability are unknown but may be around 20% for those children who are hospitalized following TBI (Thurman, 2016). Some estimates suggest that around one-third of individuals will sustain a TBI between birth and age 25 (McKinlay et al., 2008). Approximately 5.3 million Americans are currently living with TBI related difficulties (CDC, 2013). American emergency rooms triage over 473,000 children with TBI each year (Barlow, Crawford, Brooks, Turley, & Mikrogianakis, 2015).

The leading cause of TBI in children under 5 years old is falls, while motor vehicle accidents are the leading cause for adolescents over 15 years old (Thurman, 2016). The majority of TBIs are handled in an outpatient setting, while around 38% are admitted to the hospital for observation (McKinlay et al., 2008). Severity of TBI is usually assessed in the acute phase, normally within a few hours to a few days after the injury. Severity of injury is often indicative of long-term outcomes, with more severe injury predicting worse outcomes (Thurman, 2016). The Glasgow Coma Scale is one of the more commonly used ratings of TBI severity, and evaluates individuals based on eye opening responses, verbal responses, and motor responses (Jones, 1979), with a lower score indicative of more severe injury. Other indicators of severity include the incidence and duration of loss of consciousness and posttraumatic amnesia (Thurman, 2016). Eighty to ninety percent of pediatric TBI in the United States are mild (Faul et al., 2010).

TBI often leads to alteration in brain function that contribute to difficulties in cognition or sensorimotor difficulties (Bruns & Hauser, 2003). Some research implicates changes in IQ related to injury severity in TBI. A study by Anderson and colleagues (2000) found that increases in injury severity predicted lower IQ performance, and that a younger age at injury was similarly linked to a worse prognosis for severe TBI. This study with IQ emphasizes that there are potentially devastating outcomes following pediatric TBI that are possibly moderated by severity of injury and age at injury. Additional studies have demonstrated that, even for children who had above average premorbid functioning, TBI can severely alter their developmental trajectory (Babikian et al., 2015; Gamino et al., 2009). Children who sustain TBI may appear to demonstrate cognitive recovery back to baseline, but often plateau and fail to meet developmental milestones (Gamino et al., 2009). This phenomenon has been coined "neurocognitive stall." Additionally, many children and adolescents also experience significant chronic behavioral problems following TBI (Babikian et al., 2015).

Children with TBI are more likely to be socially ostracized and to experience general psychopathology relative to their peers (Yeates et al., 2013). Some estimates suggest a higher frequency of pre-existing psychiatric disorders in mild TBI than in severe TBI (Bloom et al., 2001). It is possible that children who are highly impulsive or more likely to engage in risk-taking behaviors often have diagnoses of disorders such as ADHD (Gerring et al., 1998). Epidemiological data following a birth cohort supports the theory that children who have TBI are more likely to experience behavioral difficulties pre-injury (Bijur et al., 1988). The term novel psychiatric disorder (NPD) refers to the development of any psychiatric disorder following TBI that was not present prior to injury (Max, 2014). One of the problems in determining accurate estimates of NPD after TBI is the variability in diagnostic approaches. The gold standard for

NPD assessment is for trained professionals to conduct a semi-structured interview that is supported by questionnaires to generate the psychiatric diagnoses (Max, 2014). Studies following this technique have demonstrated that approximately 49% of children with TBI developed a NPD in the first three months after injury compared to 9% of orthopedically injured peers (Max et al., 2012). Perhaps due to the heterogeneous damage from a TBI, NPDs commonly include personality change (not a personality disorder), internalizing disorders (such as anxiety and depression), and externalizing disorders (such as ADHD and oppositional defiant disorder) (Bloom et al., 2001; Max et al., 2000).

The specific categorization of psychiatric diagnoses is constantly evolving with each new edition of the DSM (Diagnostic and Statistical Manual) published by the American Psychiatric Association (APA). A diagnosis often requires that an individual endorses a determined number of symptoms and that the symptoms impair the individual's life in at least one domain (American Psychiatric Association, 2013). These diagnoses are often broadly grouped into externalizing and internalizing disorders. An externalizing disorder is characterized by primarily external, or behavioral, symptoms such as hyperactivity and aggression (McMahon, 1994). Internalizing disorders are characterized by internal, often unobservable, symptoms such as anxiety, fear, shyness, low self-esteem, and depression (Ollendick & King, 1994). Many questionnaires have been developed to assist clinicians as they make diagnostic decisions in children and adolescents. The Behavior Assessment System for Children (BASC) and the Child Behavior Checklist (CBCL) are two such measures. The BASC and CBCL both have parent, teacher, and child (self-report) versions (Doyle & Ostrander, 1997). These questionnaires evaluate multiple emotional and behavioral domains, and provide T-scores which allow children to be compared to a normative sample (Doyle & Ostrander, 1997). These measures are useful as they provide an

estimate of the severity of the symptomatology across many categories, such as anxiety, depression, atypicality, hyperactivity, and inattention regardless of whether the child meets criteria for a diagnosis of a psychiatric disorder. Additionally, the CBCL and BASC provide an overall rating for externalizing and internalizing problems that are represented as deviations from the mean (McMahon, 1994). The second edition of the BASC was normed with a sample of over 4,000 children from age 2 to 18 (Tan, 2007) while the CBCL was normed on a sample of approximately 700 children (Achenbach & Rescorla, 2001), both demonstrating adequate levels of reliability and validity across multiple samples.

While the BASC, CBCL, and other similar questionnaires provide estimates of deviations from the mean of a typically developing cohort, the standard practice for research is to recruit a sample of typically developing (TD) or orthopedically injured (OI) children to use as control subjects. Typically developing groups are often thought to be more similar to groups used for norms on tests, and are often much easier to recruit relative to the time and expense of OI groups (Mathias, Dennington, Bowden, & Bigler, 2013). Individuals with OIs are often included as a comparison group given the shared characteristics with those who sustain a TBI (i.e., more impulsive, male, and have shared hospitalization and injury mechanisms) that are potential confounds when using a TD group (Mathias et al., 2013). Most studies use either a TD or an OI group, but rarely contain both. In a recent study (Mathias et al., 2013), large samples of TD and OI adults were recruited as comparison groups in the evaluation of TBI. The study found that, when recruited appropriately, OI and TD control groups did not significantly differ from one another on many variables of interest including demographic, medical, cognitive, and psychosocial domains. Mathias and colleagues cautioned that TD groups are more likely to have equal gender distributions which is atypical from most TBI groups (which favor males) and

should put an emphasis on recruiting TD groups with a higher proportion of males. Thus, according to the research performed to date, no statistical difference has been found between TD and OI control groups on various demographic or cognitive domains, and they may be considered equivalent.

Specific Aims and Hypotheses

The overarching goal of this project is to conduct a meta-analytic review of psychiatric symptom severity following pediatric traumatic brain injury by synthesizing all available published research. Given this objective, the following aims and hypotheses are:

Aim 1: Determine the overall effect size of psychiatric symptom severity in children with TBI compared to non-head injured peers according to injury severity group.

Hypothesis 1: A significant, detectable dose-response effect will be observed in psychiatric symptom severity in relation to injury severity.

Aim 2: Determine the effect of time since injury on psychiatric symptom severity effect size following pediatric traumatic brain injury.

Hypothesis 2: Time since injury will act as a significant moderator of severity of internalizing and externalizing problems. Specifically, there will be an increase in severity of psychiatric symptoms related to a longer time post-injury.

Aim 3: To determine the effect of age at injury on psychiatric symptom severity effect sizes following pediatric traumatic brain injury.

Hypothesis 3: Age at injury will act as a significant moderator of psychiatric symptom severity and contribute to the severity of internalizing and externalizing problems. Specifically, a younger age at injury will predict poorer outcomes and more severe ratings of psychiatric symptoms.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used to ensure clarity and ease of reproducibility (Moher et al., 2009).

Identification and Selection of Source Studies

Electronic databases Web of Science, PubMed, and PsycInfo were searched for relevant articles. Web of Science was searched first, followed by PubMed, and PsycInfo was the last database searched. A search was conducted to find articles relating to pediatric TBI and psychiatric symptom severity using the following search terms: "(pediatric OR child OR adolescen*) AND (TBI OR "head injury" OR "brain injury" OR "traumatic brain injury") AND (psychiat* OR depress* OR anx* OR externalizing OR internalizing) NOT (adult*)".

Inclusion Criteria

Peer-reviewed articles published through March 2017 were considered for inclusion. A lower limit was not set on the date of publication, but all studies that met inclusion criteria were published between 1998 and 2016. Studies requirements were: publication in a peer-reviewed journal, written in English, include children from ages 2-17 years, and inclusion of a control group of non-head injured peers in the analyses. Control groups included were either typically developing without a history of trauma, or orthopedically injured with no history or indication of head-injury. All studies had to contain (1) means and standard deviations (or standard errors), (2) correlation coefficients, (3) *t* or *Z* values, and (4) *F* ratios, or odds ratios in order to compare psychiatric symptom severity between groups. While we were open to considering studies that did not report means and standard deviations, but included remaining criteria, all did report means and standard deviations or standard errors. No studies reported *t, Z, F*-values or odds ratios, thus these were not used in the calculation of effect sizes.

Procedure

After identifying studies that met the inclusion criteria described above, two trained members of the research group independently reviewed and extracted relevant data including: author names and publication year, sample size, statistical results related to measures of psychiatric symptom severity, Glasgow coma scale (GCS) scores, age at testing, and age at injury. The reviewers then discussed any discrepancies in the extracted data for correction. In studies that included multiple time points, the most recent data (i.e., those at the latest time point) were utilized. See Figure 1 for an illustration of the data extraction process.

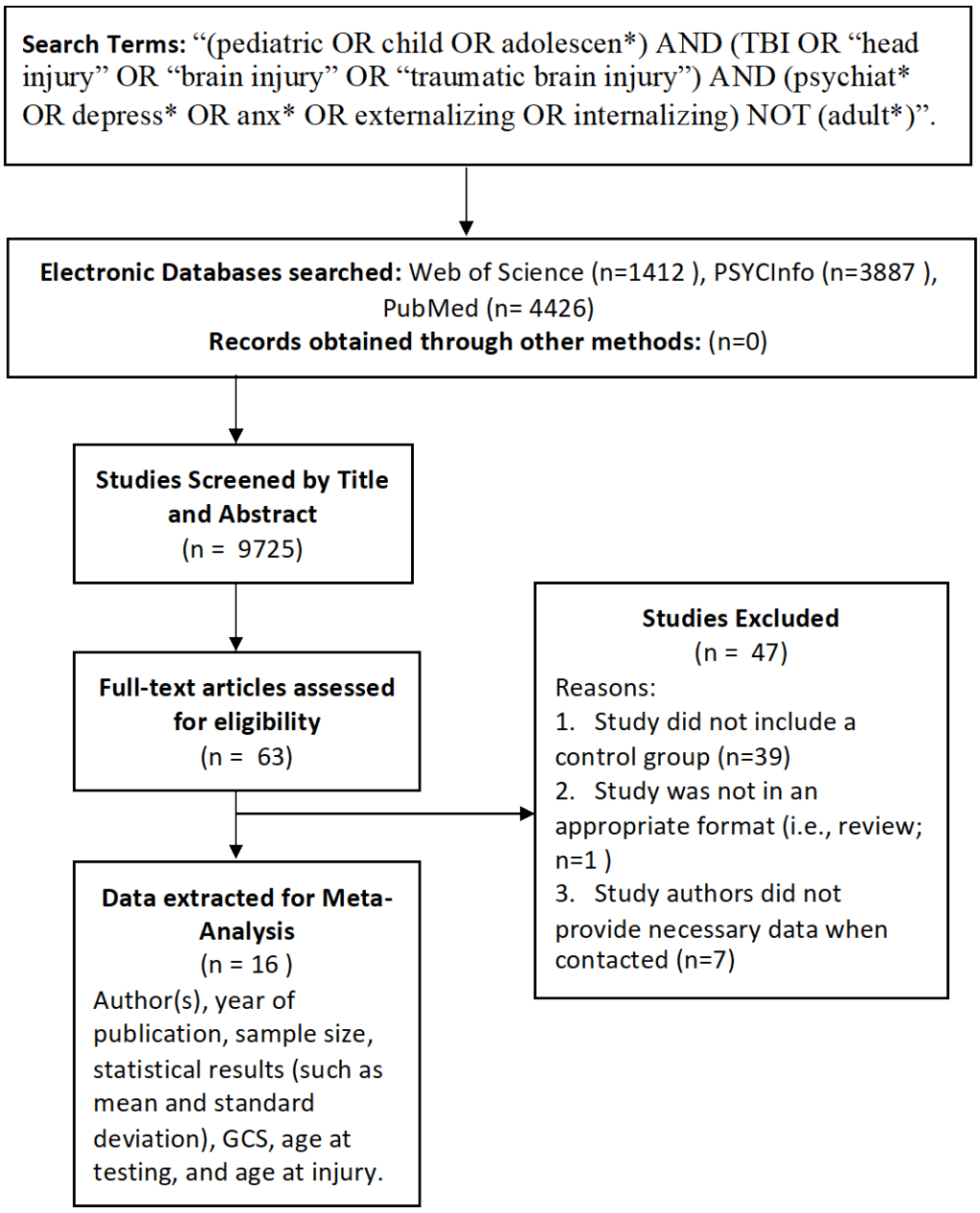


Figure 1. Procedure for the systematic literature search.

Group Categorization by Injury Severity

Based on published guidelines, groups from the 16 selected studies were categorized according to average GCS score: 3-8 = severe; 9-12 = moderate; 13-15 = mild (Beauchamp & Anderson, 2013). These groupings of injury severity are consistent with a majority of articles included in the peer-reviewed literature.

Analytic Procedure

We used Comprehensive Meta-Analysis version 3.0 (Biostat, Englewood, NJ) to calculate effect sizes, homogeneity statistics, and meta-regressions. This software also assisted with addressing publication bias through the calculation of a fail-safe N and funnel plots. Rosenthal's Fail-safe N is procedure that estimates the number of studies required to reach a *p*-value for statistically significant effect sizes above 0.05. Funnel plots display the relationship between study size, or precision, and effect size. We plotted effect sizes of the source studies on the x-axis and standard errors on the y-axis. Typically, a symmetrical distribution around the mean effect size exists if publication bias is not present. Asymmetry demonstrated by "missing" studies with large standard errors, but small effect sizes, in the context of fewer studies with large effect sizes suggests publication bias.

Aim 1. A summary Hedges *g* effect size for psychiatric symptom severity was calculated using a random-effects model from each individual source study. Effect sizes were obtained for each severity group (mild, moderate, and severe) and Q and I^2 tests were conducted to determine whether significant differences in effect sizes between severity groups exists.

Aims 2 and 3. A meta-regression analysis was employed for each injury severity group (mild, moderate, and severe). The effect size for psychiatric symptom severity served as the dependent variable in the meta-regressions. For each regression, age at injury and time since injury acted as independent variables, with GCS used as a covariate. Regression analyses assist in the determination of the variability and influence of age at injury and time since injury with the effect sizes.

Results

Search Results

Selected search terms resulted in a total of 9,725 full articles for review (Web of Science = 1,412, PubMed = 4,426, and PsycInfo = 3,887). Titles and abstracts of each article were then reviewed for the identified inclusion criteria. This resulted in 63 articles (Web of Science = 29, PubMed = 21, and PsycInfo = 13) which were subjected to full-text review of inclusion criteria. Of these, a total of 16 articles met full inclusion criteria (**Table 1**).

Table 1
Sample Size And Measures Collected From Each Source Study

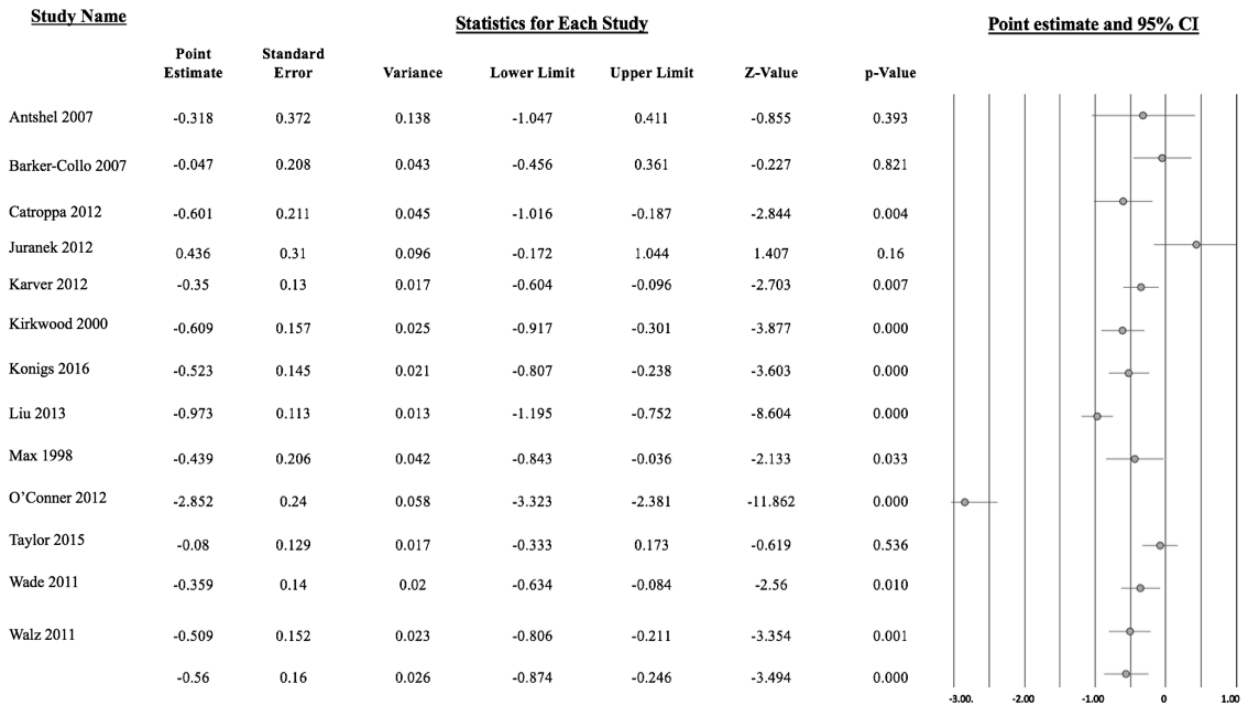
	Control Group	Mild	Moderate	Severe		
Article	N (type)	N	N	N	Measure	Categorization
Antshel, 2007	23 (TD)	41			BASC-2	Int. and Ext.
Barker-Collo, 2007	16 (OI)	38	28	2	CBCL	Int. and Ext.
Bellerose, 2015	50 (TD)	51			CBCL	Ext.
Catroppa, 2012	19 (TD)	7	20	13	BASC-2	Int. and Ext.
Ganesalingam, 2006	65 (TD)	65			BASC-2	Ext.
					ECBI	Ext.
Juranek, 2012	20 (OI)			21	SCARED-R	Int.
Karver, 2012	75 (OI)	49		19	CBCL	Int. and Ext.
Kirkwood, 2000	55 (OI)		51	38	CDI	Int.
Konigs, 2016	52 (OI)	75		37	CBCL	Int. and Ext.
Liu, 2013	558 (TD)	167			CBCL	Int. and Ext.
Max, 1998	24 (OI)	24		23	CDI	Int.
	24 (OI)	23		23	CBCL	Int. and Ext.
Mrazik, 2016	371 (OI & TD)	256			BASC-2	Int. and Ext.
O'Conner, 2012	31 (OI)	134		26	PHQ-9	Int.
Taylor, 2015	90 (OI)	176			CBCL	Int. and Ext.
Wade, 2011	71 (OI)		42	16	CBCL	Int. and Ext.
Walz, 2011	85 (OI)		43	19	CBCL	Int. and Ext.

Note: TD = Typically Developing; OI = Orthopedic Injury; BASC-2 = Behavior Assessment System for Children, 2nd Edition; CBCL = Child Behavioral Checklist; CDI = Child Depression Inventory; ECBI-Parent = Eyberg Child Behavior Inventory; ERC = Emotion Regulation Checklist; PHQ9 = The Patient Health Questionnaire (9), Depression Module; SCARED-R = Screen for Child Anxiety Related Disorders, Revised; Int.=Internalizing; Ext.=Externalizing

Meta-Analyses

Internalizing Problems Across Group Severity. Overall, internalizing problems based on parent-report measures had an effect size of -0.560 (95% CI [-0.874, -0.246]; $p < 0.001$). The confidence interval for the effect size is small, thus providing a tight range for the actual effect size. Publication bias for internalizing symptom severity was investigated using a funnel plot (see Figure 2). A funnel plot is generally symmetrical, with guidelines suggesting 95% of studies should fall within the outer limits represented by the triangle (Sterne et al., 2011). Four of the studies included in this meta-analysis fall outside this range, indicating a risk for publication bias. A classic fail-safe N test was then used to further investigate the risk of publication bias, which revealed an additional 443 studies with non-significant results would be needed to bring *p*-values for the parent-reported measures above 0.05. A *Q*-test analysis revealed that there were significant effect-size differences between severity groups $Q = 140.025$, $p < 0.001$. These results are summarized and presented in Figure 3.

Figure 2. Funnel plot for all studies included in analyses of internalizing symptoms.



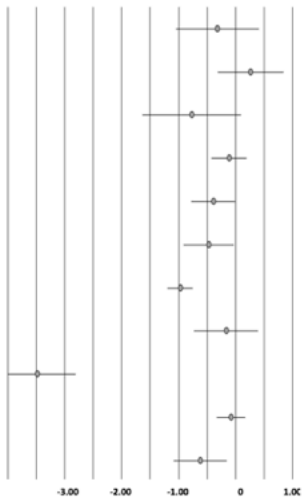
Study Name	Point Estimate	Standard Error	Variance	Lower Limit	Upper Limit	Z-Value	p-Value
Antshel 2007	-0.318	0.372	0.138	-1.047	0.411	-0.855	0.393
Barker-Collo 2007	-0.047	0.208	0.043	-0.456	0.361	-0.227	0.821
Catroppa 2012	-0.601	0.211	0.045	-1.016	-0.187	-2.844	0.004
Juranek 2012	0.436	0.31	0.096	-0.172	1.044	1.407	0.16
Karver 2012	-0.35	0.13	0.017	-0.604	-0.096	-2.703	0.007
Kirkwood 2000	-0.609	0.157	0.025	-0.917	-0.301	-3.877	0.000
Konigs 2016	-0.523	0.145	0.021	-0.807	-0.238	-3.603	0.000
Liu 2013	-0.973	0.113	0.013	-1.195	-0.752	-8.604	0.000
Max 1998	-0.439	0.206	0.042	-0.843	-0.036	-2.133	0.033
O'Conner 2012	-2.852	0.24	0.058	-3.323	-2.381	-11.862	0.000
Taylor 2015	-0.08	0.129	0.017	-0.333	0.173	-0.619	0.536
Wade 2011	-0.359	0.14	0.02	-0.634	-0.084	-2.56	0.010
Walz 2011	-0.509	0.152	0.023	-0.806	-0.211	-3.354	0.001
	-0.56	0.16	0.026	-0.874	-0.246	-3.494	0.000

Figure 3. Overall internalizing symptoms across group severity.

Internalizing Problems by Group Severity. Analysis of the mild TBI condition included ten studies that reported internalizing symptoms. The overall effect size for this group was -0.624 (95% CI [-1.090, -.158]; p = 0.009). Only four studies included measures for the moderate severity TBI group, which had an effect size of -.238 (95% CI [-.452, -.024]; p = 0.029). Ten studies provided information for the severe TBI group, which had an effect size of -.923 (95% CI [-1.341, -.504]; p < 0.001). These results are presented in Figure 4.

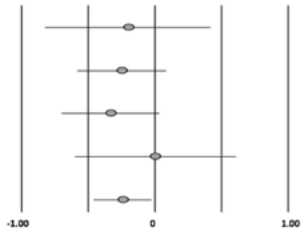
Mild

Study Name	Point Estimate	Standard Error	Variance	Lower Limit	Upper Limit	Z-Value	p-Value
Antshel 2007	-0.318	0.372	0.138	-1.047	0.411	-0.855	0.393
Barker-Collo 2007	0.265	0.298	0.087	-0.313	0.842	0.897	0.369
Catroppa 2012	-0.772	0.441	0.194	-1.637	0.093	-1.749	0.080
Karver 2012	-0.113	0.156	0.024	-0.419	0.193	-0.724	0.469
Kirkwood 2000	-0.392	0.196	0.038	-0.776	-0.008	-2.000	0.046
Konigs 2016	-0.471	0.224	0.050	-0.910	-0.032	-2.103	0.035
Liu 2013	-0.973	0.113	0.013	-1.195	-0.752	-8.604	0.000
Max 1998	-0.167	0.286	0.082	-0.728	0.394	-0.584	0.559
O'Conner 2012	-3.487	0.344	0.118	-4.161	-2.813	-10.137	0.000
Taylor 2015	-0.080	0.129	0.017	-0.333	0.173	-0.619	0.536
	-0.624	0.238	0.056	-1.090	-0.158	-2.627	0.009



Moderate

Study Name	Point Estimate	Standard Error	Variance	Lower Limit	Upper Limit	Z-Value	p-Value
Catroppa 2012	-0.200	0.315	0.099	-0.817	0.417	-0.635	0.525
Barker-Collo 2007	-0.246	0.169	0.029	-0.578	0.086	-1.451	0.147
Wade 2011	-0.333	0.187	0.035	-0.700	0.034	-1.777	0.076
Walz 2011	0.006	0.308	0.095	-0.597	0.609	-0.020	0.984
	-0.238	0.109	0.012	-0.452	-0.024	-2.183	0.029



Severe

Study Name	Point Estimate	Standard Error	Variance	Lower Limit	Upper Limit	Z-Value	p-Value
Catroppa 2012	-1.047	0.374	0.140	-1.781	-0.313	-2.796	0.005
Barker-Collo 2007	-4.452	1.030	1.061	-6.471	-2.434	-4.323	0.000
Juranek 2012	0.436	0.310	0.096	-0.172	1.044	1.407	0.160
Karver 2012	-0.880	0.233	0.054	-1.337	-0.423	-3.777	0.000
Kirkwood 2000	-0.682	0.216	0.047	-1.105	-0.259	-3.157	0.002
Konigs 2016	-0.742	0.220	0.049	-1.175	-0.311	-3.370	0.001
Max 1998	-0.733	0.297	0.088	-1.315	-0.151	-2.468	0.014
O'Conner 2012	-2.246	0.336	0.113	-2.905	-1.587	-6.680	0.000
Wade 2011	-0.605	0.250	0.063	-1.095	-0.115	-2.421	0.015
Walz 2011	-0.844	0.259	0.067	-1.351	-0.337	-3.264	0.001
	-0.923	0.214	0.046	-1.341	-0.504	-4.320	0.000

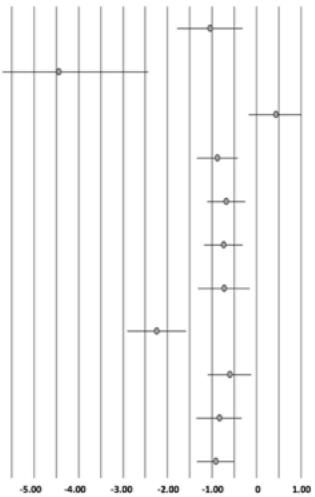


Figure 4. Summary of internalizing symptoms by group severity.

Externalizing Problems Across Group Severity. Overall externalizing problems based on parent-report measures had an effect size of -0.520 (95% CI [-.729, -.311]; $p < 0.001$). As with internalizing disorders, the effect size confidence interval is small, thus providing a tight range for the actual effect size. A funnel plot (Figure 5) revealed two of the included studies fell outside of the triangle range, which indicates potential publication bias or statistical outliers. Again, a fails-safe N test was used and showed that an additional 351 studies with non-significant results would be needed to bring *p*-values for the parent-reported measures above 0.05. A *Q*-test analysis revealed that there were significant effect-size differences between severity groups $Q = 51.769$, $p < 0.001$. See Figure 6 for a summary of these results.

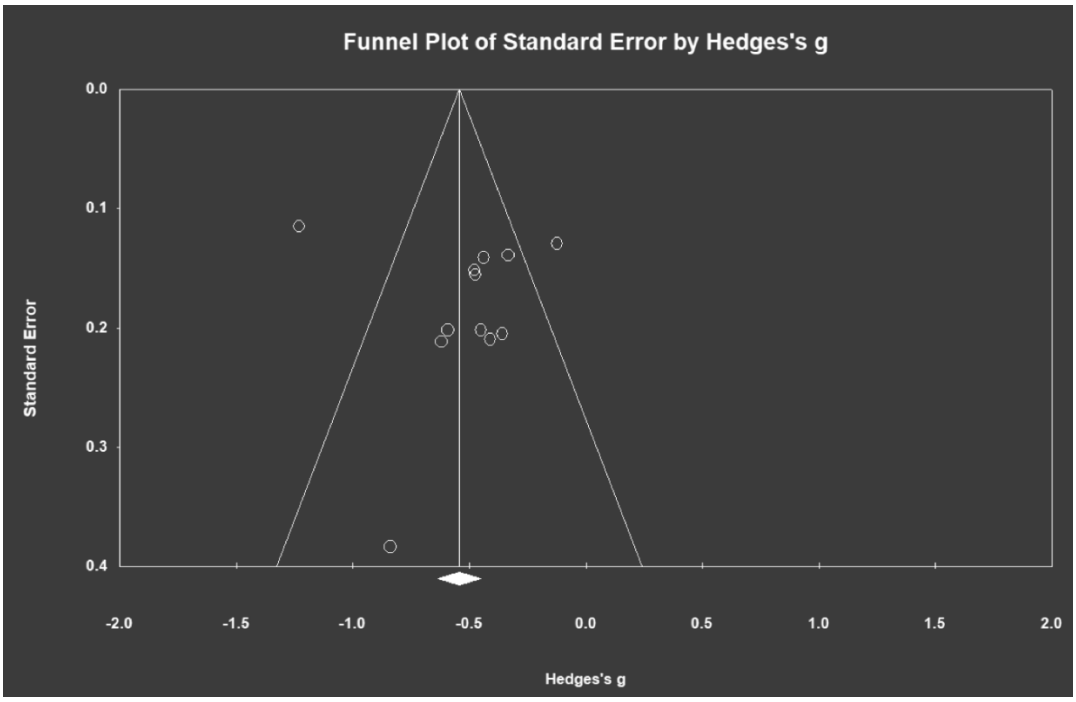
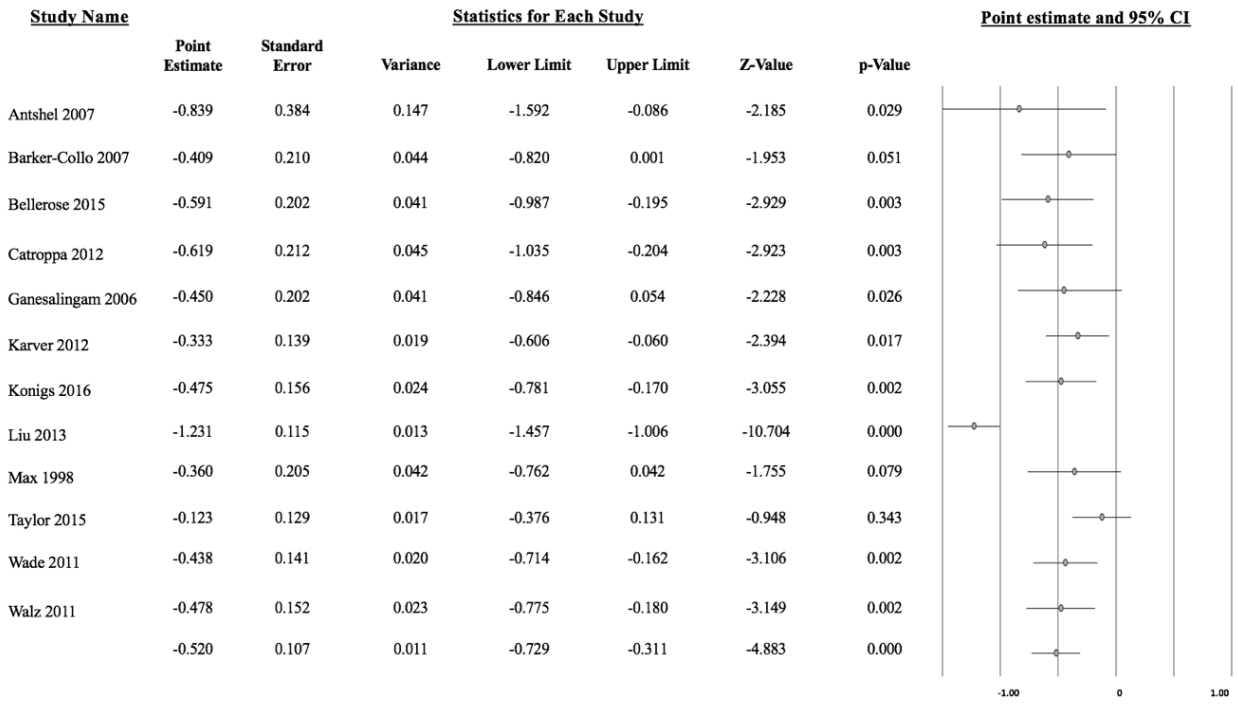


Figure 5. Funnel plot for all studies included in the analysis of externalizing symptoms.



Study Name	Point Estimate	Standard Error	Variance	Lower Limit	Upper Limit	Z-Value	p-Value
Antshel 2007	-0.839	0.384	0.147	-1.592	-0.086	-2.185	0.029
Barker-Collo 2007	-0.409	0.210	0.044	-0.820	0.001	-1.953	0.051
Bellerose 2015	-0.591	0.202	0.041	-0.987	-0.195	-2.929	0.003
Catroppa 2012	-0.619	0.212	0.045	-1.035	-0.204	-2.923	0.003
Ganesalingam 2006	-0.450	0.202	0.041	-0.846	0.054	-2.228	0.026
Karver 2012	-0.333	0.139	0.019	-0.606	-0.060	-2.394	0.017
Konigs 2016	-0.475	0.156	0.024	-0.781	-0.170	-3.055	0.002
Liu 2013	-1.231	0.115	0.013	-1.457	-1.006	-10.704	0.000
Max 1998	-0.360	0.205	0.042	-0.762	0.042	-1.755	0.079
Taylor 2015	-0.123	0.129	0.017	-0.376	0.131	-0.948	0.343
Wade 2011	-0.438	0.141	0.020	-0.714	-0.162	-3.106	0.002
Walz 2011	-0.478	0.152	0.023	-0.775	-0.180	-3.149	0.002
	-0.520	0.107	0.011	-0.729	-0.311	-4.883	0.000

Figure 6. Overall externalizing symptoms across group severity.

Externalizing Problems by Group Severity. Analysis of the mild TBI condition included nine studies that reported externalizing symptoms. The overall effect size for this group was -0.531 (95% CI [-.882, -.180]; $p = 0.003$). Five studies included measures for the moderate severity group, which had an effect size of -0.257 (95% CI [-.445, -0.069]; $p = 0.007$). Seven studies provided information for the severe TBI group, with an effect size of -0.909 (95% CI [-1.312, -0.506]; $p < 0.001$). Results are summarized in Figure 7.

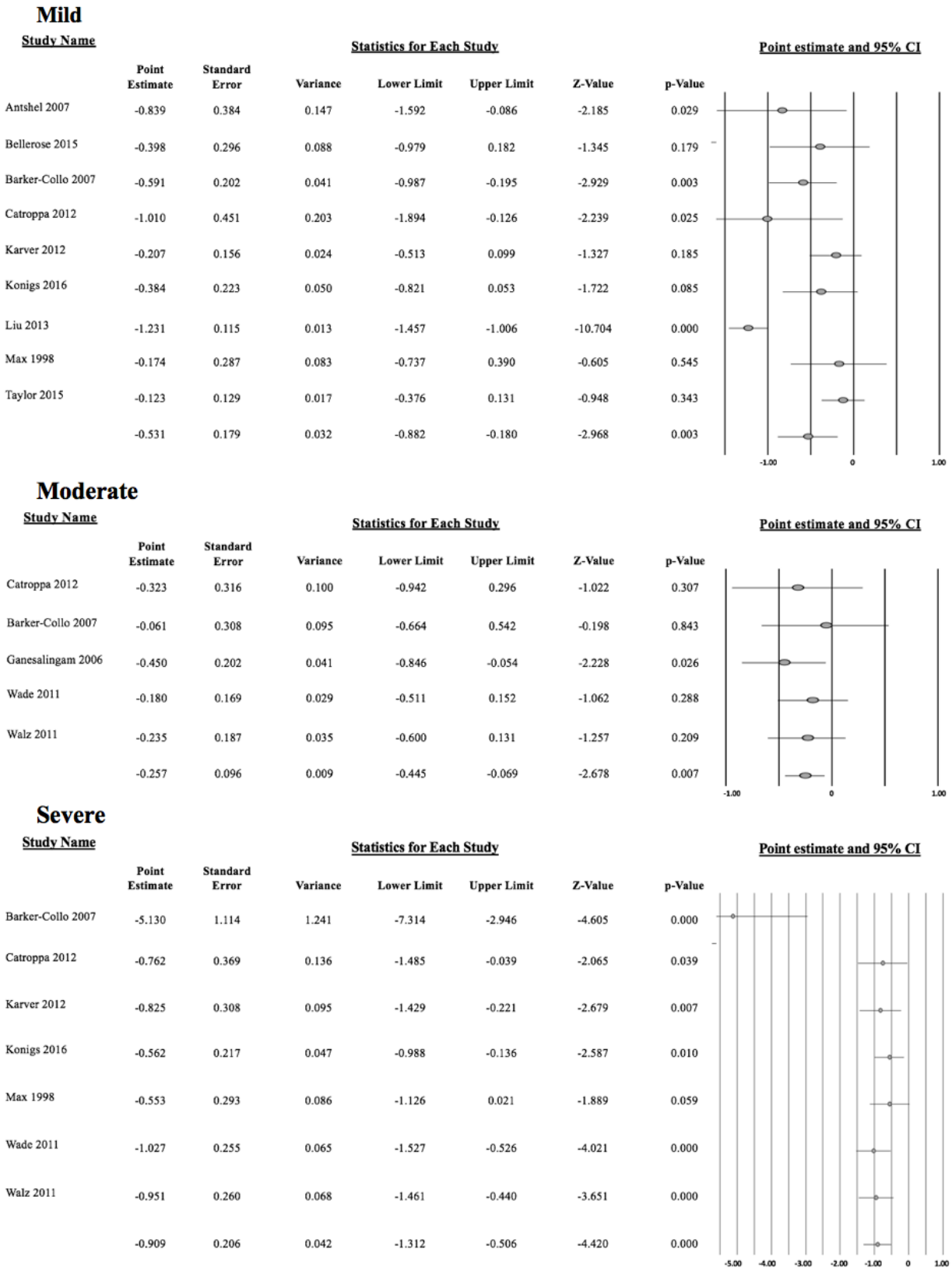


Figure 7. Summary of externalizing symptoms by group severity

Meta-Regressions

Effect of Time Since Injury. In order to address the effects of time since injury on the severity of internalizing problems, a random effects meta-regression was conducted. The Hedge's *g* of 17 samples was regressed on time since injury and severity of injury was controlled for by including the GCS score as a covariate. Overall, the model was nonsignificant (Q = 3.66, p = 0.160). Goodness of fit analyses revealed that a significant, non-zero proportion of variance (Q = 38.93, p = 0.0004). The calculated R^2 analog was 0.11. The coefficients and confidence intervals are included reported in Table 2.

Table 2
Results Of Meta-Regression Investigating The Effects Of Time Since Injury On The Effect Size Of Internalizing Problems With GCS As An Ovariate

Covariate	β	Standard Error	95% CI Lower	95% CI Upper	p
Time Since Injury	-0.04	0.03	-0.1	0.03	0.29
GCS	0.04	0.02	-0.01	0.09	0.09
Intercept	-0.66	0.25	-1.15	0.17	0.01

Similarly, the Hedge's *g* of externalizing symptoms was regressed on time since injury with GCS included as a covariate in a random effects meta-regression to determine the impact on time since injury on externalizing symptoms. The overall model was nonsignificant (Q = 4.31, p = 0.116). Goodness of fit analyses revealed that the model accounted for a significant, non-zero proportion of variance (Q = 26.04, p = 0.011, R^2 analog = 0.22). Only GCS had a significant

coefficient $\beta = 0.0533$, $p = 0.0421$. All coefficients and confidence intervals are included in **Table 3.**

Table 3
Results Of Meta-Regression Investigating The Effects Of Time Since Injury On The Effect Size Of Externalizing Problems With GCS As A Covariate.

Covariate	β	Standard Error	95% CI Lower	95% CI Upper	p
Time Since Injury	0.0	0.03	-0.06	0.07	0.89
GCS	0.05	0.03	0.0	0.1	0.04
Intercept	-1.1	0.35	-1.8	-0.41	0.0

Effect of Age at Injury. A random effects meta-regression was conducted to determine the effect of age at injury on Hedge's *g* for internalizing symptoms, with GCS included as a covariate. The overall model was nonsignificant $Q = 5.24$, $p = 0.0729$. Goodness of fit indices indicated that the model explained a significant non-zero proportion of variance $Q = 29.56$, $p = 0.0054$ with R^2 analog explaining the proportion of between-study variance by the model at 0.25. The coefficient for GCS was significant, $\beta = 0.0502$, $p = 0.0230$. Age at injury was not a significant predictor of internalizing symptom severity, $\beta = 0.0164$, $p = 0.7534$. See Table 4 for confidence intervals.

Table 4
Results Of Meta-Regression Investigating The Effects Of Age At Injury On The Effect Size Of Internalizing Symptoms With GCS As A Covariate.

Covariate	β	Standard Error	95% CI Lower	95% CI Upper	p
Age at Injury	0.02	0.05	-0.09	0.12	0.75
GCS	0.05	0.02	0.01	0.09	0.02
Intercept	-1.04	0.47	-1.96	-0.13	0.03

Finally, a random effects meta-regression was conducted to evaluate the relationship between age at injury and Hedge's *g* of externalizing symptoms. Overall, the model was nonsignificant, $Q = 0.0947$. Goodness of fit analyses indicated that the model explained a significant non-zero proportion of variance $Q = 24.74$, $p = 0.0184$. The R^2 analog for this meta-regression was 0.27, indicating the model accounted for 27% of the between-study variance. GCS was a significant predictor of Hedge's *g*, $\beta = 0.0519$, $p = 0.03$. The coefficient for age at injury was not significant, $\beta = 0.0087$, $p = 0.870$. See **Table 5** for coefficient, standard error, and confidence interval information.

Table 5
Results Of Meta-Regression Investigating The Effects Of Age At Injury On The Effect Size Of Externalizing Symptoms With GCS As A Covariate.

Covariate	β	Standard Error	95% CI Lower	95% CI Upper	p
Age at Injury	0.01	0.05	-0.09	0.11	0.87
GCS	0.05	0.02	0.01	0.1	0.03
Intercept	-1.11	0.43	-1.95	-0.27	0.01

Discussion

In this meta-analysis, we found that parents of children with a traumatic brain injury reported more severe internalizing and externalizing symptoms than parents of children without a brain injury. And that this finding was consistent across mild, moderate and severe injury groups. Children with a TBI exhibited more internalizing symptoms than children with an orthopedic injury or no injury at all. Based on the results of the meta-analysis, the severe TBI group experienced the most severe internalizing problems, moderate TBI the least, and mild TBI falling between the two groups with a moderate overall effect size.

Consistent with prior research, parents of children with a TBI reported more severe psychiatric symptoms than parents of children who had not sustained a head injury. Previous studies often looked at the diagnosis of a novel psychiatric disorder following injury. One such study by Max and colleagues (2012) followed a cohort of children to determine what percentage of the children developed a novel psychiatric disorder following a TBI compared to those who sustained an orthopedic injury. In their sample, the TBI groups consistently had a higher percentage of participants qualifying for a novel psychiatric diagnosis. The results of this meta-analysis are consistent with these findings as both highlight the increased frequency of psychiatric symptoms following injury. Additionally, Max's results suggest the difference between TBI and control groups was equivocal for both internalizing and externalizing symptoms. This suggests children who experience a TBI are equally likely to experience increases in both types of symptoms, but does not indicate symptom severity is equivalent across internalizing and externalizing symptoms. Rather, both internalizing and externalizing symptoms are reportedly more severe for children with a TBI than for those with no injury or an orthopedic injury. While the current meta-analysis did not seek to establish whether children met criteria for

a psychiatric disorder, other studies have demonstrated the most common psychiatric conditions following TBI are personality changes, depressive disorders, and ADHD (Bloom et al., 2001). The average age of the sample recruited by Bloom and colleagues was similar to those included in this meta-analysis (9 years), suggesting convergence between Bloom's findings and the results of this meta-analysis.

One goal of the current study was to determine the effect of time-since-injury and age-at-injury on the severity of internalizing and externalizing symptoms in children with traumatic brain injury. Results of the meta-regression models testing this aim were null, indicating that age-at-injury and time-since-injury were not significant predictors of the effect size differences in the samples. However, severity was included as a covariate, and found a significant predictor for both internalizing and externalizing symptoms. This may indicate that severity is more closely tied to psychiatric symptoms following a TBI than time-since-injury or age-at-injury. Previous research has indicated age-at-injury may affect the expression of psychiatric symptoms, with younger children exhibiting more internalizing symptoms and externalizing problems increasing with age (Bloom et al., 2001). The younger the age at injury, the higher the risk of developing long-term deficits, especially for those with a severe TBI (Anderson et al., 2005). Thus, it may be that the largest risk for developing psychiatric symptoms after a TBI is closely linked to the severity of the TBI. The weighted average age at injury included in this meta-analysis was 8.96 with a range of 3-16. So, the majority of the cases in this meta-regression were pre-adolescent. Additionally, the average time since injury was 2.15 years post-injury with a range of 2 months to 10 years. It is likely that due to the scarcity of longitudinal studies no effect was detected for time since injury.

Other factors, such as family support, may play a factor in predicting outcome and recovery from a pediatric TBI. For example, Taylor and colleagues found that child behavior and family stress interacted with time post-injury such that a bi-directional effect was found between family distress and child behavioral problems (Taylor et al., 2000). Age at injury appears to be most closely related to cognitive problems, while the family and home environment are most closely tied to behavioral and functional outcomes (Yeates, Taylor, Walz, Stancin, & Wade, 2010).

It is possible that children who sustain a TBI are more likely to demonstrate internalizing and externalizing symptoms prior to injury. Most studies include an orthopedic injury control group to account for pre-injury behavioral characteristics such as hyperactivity and impulsivity (Mathias et al., 2013). Some studies indicate that while TBI and OI groups do not differ on family history of psychiatric illness, the TBI group continue to show larger effect sizes indicating more severe symptomatology or greater numbers of individuals diagnosed with a novel psychiatric disorder (Max et al., 1998; Max et al., 2012).

The results of this meta-analysis indicate that children who have acquired any severity of TBI may have more severe psychiatric symptoms than those who have not. Healthcare providers, especially those involved in the rehabilitation process, should be aware of this increased severity of psychiatric symptoms. These providers can then incorporate screening tools when working with these children and their families. Incorporating specific interventions, such as therapy and parent management training, may facilitate the rehabilitation process.

This meta-analysis has several limitations. First, as in all meta-analyses, there is inherent risk of publication bias. Publication bias is the possibility that only those studies that found significant effects were published. The inference is many other studies with nonsignificant

findings between TBI and control groups were never published, thus, not included in this meta-analysis. We attempted to address this issue by including results from the classic fail-safe N test, which estimates the number of null studies required to make the results nonsignificant. Second, due to the stringent inclusion criteria, only a small number of studies (n=16) were included in the meta-analysis, leaving it susceptible to publication bias and the results of findings from additional studies. This is likely to be especially true for the moderate TBI group, which had the least amount of studies representing this group. Third, all of the studies included in the meta-analysis approximated behavioral performance through parent report. There are challenges and limitations with such an approach, such as poor reliability and source bias. However, Babcock and colleagues found that adolescents reported more severe symptoms than their parents (Babcock et al., 2013), and concluded an adolescent report was likely more accurate relative to younger children given their ability to better articulate their symptoms. Another prospective cohort study found inconsistency in parent's ratings dependent on the child's age. Parents of younger children reported more severe symptoms than the children's reports, while parents of older children and adolescents reported less severe symptoms than the children's report (Barlow, Crawford, Brooks, Turley, & Mikrogianakis, 2015). Future studies should include multi-method models of assessing behavior in children, such as including teacher and self-report. Finally, the results of this meta-analysis are contingent upon the methodologies used in the source studies and acknowledge these potential limitations in our study.

Conclusion

Regardless of TBI severity and in the context of the study's limitations, the results of this meta-analysis indicate that parents of children who sustain a TBI report more severe symptomatology than parents of children who were not head injured. The effect size for

internalizing and externalizing symptoms was large for severe TBI, medium for mild TBI, and small for moderate TBI with a medium effect size across TBI severity. Age at injury at time since injury did not appear to be significant predictors of psychiatric symptoms following head injury.

References

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.

Anderson, V., Catroppa, C., Morse, S., Haritou, F., & Rosenfeld, J. (2005). Functional plasticity or vulnerability after early brain injury? *Pediatrics, 116*(6), 1374-1382.

Anderson, V., Catroppa, C., Morse, S., Haritou, F., & Rosenfeld, J. (2000). Recovery of intellectual ability following traumatic brain injury in childhood: Impact of injury severity and age at injury. *Pediatric Neurosurgery; Basel, 32*(6), 282-90. Retrieved from http://search.proquest.com/docview/224152197/abstract/4E3D3A13E09B4B78PQ/1

Babcock, L., Byczkowski, T., Wade, S. L., Ho, M., Mookerjee, S., & Bazarian, J. J. (2013). Predicting postconcussion syndrome after mild traumatic brain injury in children and adolescents who present to the emergency department. *JAMA Pediatrics, 167*(2), 156-161. doi:10.1001/jamapediatrics.2013.434

Babikian, T., Merkley, T., Savage, R. C., Giza, C. C., & Levin, H. (2015). Chronic aspects of pediatric traumatic brain injury: Review of the literature. *Journal of Neurotrauma, 32*(23), 1849-1860. doi:10.1089/neu.2015.3971

Barlow, K. M., Crawford, S., Brooks, B. L., Turley, B., & Mikrogianakis, A. (2015). The incidence of postconcussion syndrome remains stable following mild traumatic brain injury in children. *Pediatric Neurology, 53*(6), 491-497. doi:10.1016/j.pediatrneurol.2015.04.011

Beauchamp, M.H., & Anderson, V. (2013). Cognitive and psychopathological sequelae of pediatric traumatic brain injury. In O. Dulac, M. Lassonde, & H.B. Sarnat (Eds.), *Handbook*

of clinical neurology, vol. 112 (3rd series) pediatric neurology part II (pp. 913-920). Amsterdam, Netherlands: El Sevier.

Bijur, P., Golding, J., Haslum, M., & Kurzon, M. (1988). Behavioral predictors of injury in school-age children. *American Journal of Diseases of Children (1960), 142*(12), 1307-1312.

Bloom, D. R., Levin, H. S., Ewing-Cobbs, L., Saunders, A. E., Song, J., Fletcher, J. M., & Kowatch, R. A. (2001). Lifetime and novel psychiatric disorders after pediatric traumatic brain injury. *Journal of the American Academy of Child & Adolescent Psychiatry, 40*(5), 572-579. doi:10.1097/00004583-200105000-00017

Brown, G., Chadwick, O., Shaffer, D., Rutter, M., & Traub, M. (1981). A prospective study of children with head injuries: III. psychiatric sequelae. *Psychological Medicine, 11*(1), 63-78.

Bruns, J., & Hauser, W. A. (2003). The epidemiology of traumatic brain injury: A review. *Epilepsia, 44*, 2-10. doi:10.1046/j.1528-1157.44.s10.3.x

Doyle, A., & Ostrander, R. (1997). Convergent and criterion-related validity of the behavior assessment system for children-parent rating scale. *Journal of Clinical Child Psychology, 26*(3), 276.

Emery, C. A., Barlow, K. M., Brooks, B. L., Max, J. E., Villavicencio-Requis, A., Gnanakumar, V., . . . Yeates, K. O. (2016). A systematic review of psychiatric, psychological, and behavioural outcomes following mild traumatic brain injury in children and adolescents. *The Canadian Journal of Psychiatry, 61*(5), 259-269. doi:10.1177/0706743716643741

Gerring, J. P., Brady, K. D., Chen, A., Vasa, R., Grados, M., Bandeen-Roche, K. J., . . . Denckla, M. B. (1998). Premorbid prevalence of ADHD and development of secondary ADHD after

closed head injury. *Journal of the American Academy of Child and Adolescent Psychiatry, 37*(6), 647-654. doi:10.1097/00004583-199806000-00015

Ghajar, J. (2000). Traumatic brain injury. *The Lancet, 356*(9233), 923-929. doi:10.1016/S0140-6736(00)02689-1

Jones, C. (1979). Glasgow coma scale. *The American Journal of Nursing, 79*(9), 1551-1553. doi:10.2307/3424679

Mathias, J.L., Dennington, V., Bowden, S.C., & Bigler, E.D. (2013). Community versus orthopaedic controls in traumatic brain injury research: How comparable are they? *Brain Injury, 27*(7-8), 887-895. doi:10.3109/02699052.2013.793398.

Max, J. E., Koele, S. L., Smith, W. L., Sato, Y., Lindgren, S. D., Robin, D. A., & Arndt, S. (1998). Psychiatric disorders in children and adolescents after severe traumatic brain injury: A controlled study. *Journal of the American Academy of Child and Adolescent Psychiatry, 37*(8), 832-840. doi:10.1097/00004583-199808000-00013

Max, J. E., Robin, D. A., Lindgren, S. D., Smith, W. L., Sato, Y., Mattheis, P. J., . . . Castillo, C. S. (1997). Traumatic brain injury in children and adolescents: Psychiatric disorders at two years. *Journal of the American Academy of Child and Adolescent Psychiatry, 36*(9), 1278-1285. doi:10.1097/00004583-199709000-00021

Max, J. E. (2014). Neuropsychiatry of pediatric traumatic brain injury. *The Psychiatric Clinics of North America, 37*(1), 125-140. doi:10.1016/j.psc.2013.11.003

Max, J. E., Koele, S. L., Castillo, C. C., Lindgren, S. D., Arndt, S., Bokura, H., . . . Sato, Y. (2000). Personality change disorder in children and adolescents following traumatic brain injury. *Journal of the International Neuropsychological Society, 6*(3), 279-289.

Max, J.E., Wilde, E.A., Bigler, E.D., MacLeod, M., Vasquez, A.C., Schmidt, A.T., Chapman, S.B., Hotz, G., Yang, T.T., & Levin, H.S. (2012). Psychiatric disorders after pediatric traumatic brain injury: A prospective, longitudinal, controlled study. *The Journal of Neuropsychiatry and Clinical Neurosciences, 24*(4), 427-436.

McKinlay, A., Grace, R. C., Horwood, L. J., Fergusson, D. M., Ridder, E. M., & MacFarlane, M. R. (2008). Prevalence of traumatic brain injury among children, adolescents and young adults: Prospective evidence from a birth cohort. *Brain Injury, 22*(2), 175-181. doi:10.1080/02699050801888824

McMahon, R. J. (1994). Diagnosis, assessment, and treatment of externalizing problems in children. *Journal of Consulting and Clinical Psychology, 62*(5), 901-917. doi:10.1037/0022-006X.62.5.901

Ollendick, T. H., & King, N. J. (1994). Diagnosis, assessment, and treatment of internalizing problems in children: The role of longitudinal data. *Journal of Consulting and Clinical Psychology, 62*(5), 918-927. doi:10.1037/0022-006X.62.5.918

Sterne, J.A.C., Sutton, A.J., Ioannidis, J.P.A., Terrin, N., Jones, D.R., Lau, J., . . . Higgins, J.P.T. (2011). Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomized controlled trials. *The BMJ, 343.* doi:https://doi.org/10.1136/bmj.d4002

Tan, C. S. (2007). Test review: Reynolds, C. R., & Kampaus, R.W. (2004). Behavior assessment system for children (2nd ed.). Circle Pines, MN: American guidance service. *Assessment for Effective Intervention, 32*(2), 121-124.

Taylor, H.G., Yeates, K.O., Wade, S.L., Drotar, D., Stancin, T., & Burant, C. (2000). Bidirectional child-family influences on outcome of traumatic brain injury in children. *Journal of the International Neuropsychological Society, 7,* 755-767.

Thurman, D. J. (2016). The epidemiology of traumatic brain injury in children and youths: A review of research since 1990. *Journal of Child Neurology, 31*(1), 20-27. doi:10.1177/0883073814544363

Viano, D. C., Casson, I. R., Pellman, E. J., Zhang, L., King, A. I., & Yang, K. H. (2005). Concussion in professional football: Brain responses by finite element analysis: Part 9. *Neurosurgery, 57*(5), 891-916. doi:10.1227/01.NEU.0000186950.54075.3B

Whiting, P. F., Rutjes, A. S., Westwood, M. E., Mallett, S., Deeks, J.J., … Bossuyt, P.M.M. (2011). Quadas-2: A revised tool for the quality assessment of diagnostic accuracy studies. *Annals of Internal Medicine, 155*(8), 529-536. doi:10.7326/0003-4819-155-8-201110180-00009

Yeates, K. O., Bigler, E. D., Abildskov, T., Dennis, M., Gerhardt, C. A., Vannatta, K., . . . Taylor, H. G. (2014). Social competence in pediatric traumatic brain injury: From brain to behavior. *Clinical Psychological Science, 2*(1), 97-107. doi:10.1177/2167702613499734

Yeates, K.O., Taylor, H.G., Walz, N.C., Stancin, T., & Wade, S.L. (2010). The family environment as a moderator of psychosocial outcomes following traumatic brain injury in young children. *Neuropsychology, 24*(3), 345-356.