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Abstract

Mild traumatic brain injuries (mTBI) put children and adolescents at risk for short and long-term health risks. The purpose of this study was to evaluate sex differences in post-acute outcomes among children and adolescents presenting to the Emergency Department (ED) for mTBI. The study is a secondary analysis of a de-identified dataset which was drawn from a concurrent cohort, prospective, and longitudinal study design that included 8 to 16 year-old children with mTBI and a comparison group of children with mild orthopedic injuries (OI) not involving the head. Participants were recruited and completed an initial assessment during their initial visit to the ED. They returned for a post-acute assessment within two weeks of injury. Outcomes of interest included parent and child ratings of somatic and cognitive symptoms, and standardized tests of neurocognitive functioning and balance. Girls reported a significantly larger increase in somatic symptoms post-mTBI than boys, using OI as a comparison group. In contrast, no significant sex differences were found for child ratings of cognitive symptoms, parent ratings of somatic or cognitive symptoms, neurocognitive functioning, or balance. The results suggest only limited sex differences in post-acute outcomes of mTBI in a pediatric ED population. The findings have potential implications for clinical and public health which include being used to guide implementation of policies related to pediatric injury prevention. Future research is needed to examine how rule and equipment changes can improve the sex differences found in somatic symptoms after mTBI.

Keywords: mild traumatic brain injury, children, adolescents, emergency department, sex

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A concussion is a type of mild traumatic brain injury (mTBI) that involves a change in the normal functioning of the brain caused by a mechanical blow directly to the head or to the body with an impulsive force transmitted to the head (McCrory et al., 2018). Concussions in children and adolescents are particularly worrisome due to the vulnerability of the developing brain. A brain injury sustained during the developing years can lead to impaired neuroplasticity, or the ability of the brain to adapt to changes (Giza & Hovda, 2001). Furthermore, several studies illustrate persistent neurocognitive deficits after pediatric mTBI (Moser & Schatz, 2002; Moser, Schatz, & Jordan, 2005; Giza & Hovda, 2001; Dean & Sterr, 2013; Anderson et al., 2017).

Traumatic brain injury (TBI) is a leading cause of emergency department (ED) visits, hospitalizations, and mortality in the United States (US). An estimated 1.7 million people sustain a TBI in the US annually, with an associated 1.4 million ED visits, 275,000 hospitalizations, and 52,000 deaths (Faul, Xu, Wald, Coronado, & Dellinger, 2010). In the US in 2013, among children younger than 15 years old, TBI accounted for 1,500 deaths, 18,000 hospitalizations, and more than 640,000 ED visits (Taylor, Bell, Breiding, & Xu, 2017). Still, these numbers are an underestimation of the true burden of mTBI, because they do not account for untreated mTBIs or mTBIs that are treated in non-ED settings (Arbogast et al., 2016).

Among all age groups, children aged 0 to 4 years and adolescents aged 15 to 19 years are especially likely to sustain a TBI (Faul et al., 2010). Nearly half a million TBI-related ED visits involved children aged 0 to 4 annually (Faul et al., 2010). Importantly, persons aged 0 to 24 years had the highest rates of TBI-related ED visits, hospitalizations, and deaths due to being struck by or against an object (Taylor et al., 2017). Sport and recreational related injuries likely account for most injuries sustained via this mechanism, especially among persons over the age of four, when sport participation begins (Taylor et al., 2017).

In fact, sport activities account for over 50% of all mTBIs among children and adolescents (Gordon, Dooley, & Wood, 2006). Among children aged 6 to 16 years, mTBI is six times more likely to happen in organized sport activity than any other activity (Browne & Lam, 2006). To address the high prevalence of sport-induced pediatric mTBI and the risks associated with such injuries, legislation has been enacted in all fifty states (Harvey, 2013). The legislation solely focuses on secondary prevention and includes removal from play, evaluation by a healthcare worker, and education for parents and coaches on signs and symptoms of concussion (Harvey, 2013). However, to receive effective care for concussion, young athletes must first report symptoms. Several studies suggest that over 50% of athletes who sustain a concussion fail to report symptoms (McCrea, Hammeke, Olsen, Leo, & Guskiewicz, 2004; Register-Mihalik et al., 2013; Delaney, Lamfookon, Bloom, Al-Kashmiri, & Correa, 2015).

Furthermore, rates of pediatric TBI are increasing (Chen et al., 2017). Between 2006 and 2013, pediatric TBI patients increased by 34.1% in US EDs (Chen et al., 2017). In children under 17 years, approximately 51,000 TBI associated hospitalizations occurred in the US in 2000 alone (Chen et al., 2017). An increase in visits for concussions and unspecific head injuries explained the 34.1% increase in pediatric TBI ED visits (Chen et al., 2017). The rising trend of pediatric TBI-related ED visits has been attributed to growing public awareness and youth sport concussion laws (Chen et al., 2017).

Given the high prevalence and increasing rate of pediatric TBI and the main mechanisms by which TBIs occur in this age range, evaluating the epidemiology of sport-related concussion becomes critical. Annually in the US, an estimated 44 million children and adolescents participate in sports, and the number of participants is increasing every year (National Council on Youth Sports, 2008). Researchers estimate 1.6 to 3.8 million sport and recreational related TBIs occur annually in the US (Langlois, Rutland-Brown, & Wald, 2006). While the majority of sport-related concussions result from football, researchers also discovered that boys' lacrosse and girls' soccer had the next highest sport-related concussion rates among 27 high school sports (Daneshvar, Nowinski, McKee, & Cantu, 2011; O'Connor et al., 2017).

Historically, sport-related concussion research has focused on males. However, since the establishment of Title IX, growing number of females have begun participating in youth sports (National Council of Youth Sports, 2008). Given the increasing trend for female participation in youth sports, an evaluation of sex differences in the epidemiology of concussion is warranted. Faul, Xu, Wald, Coronado, and Dellinger (2010) and Taylor, Bell, Breiding, and Xu (2017) showed that across all age groups, TBI numbers were higher for males than females. However, despite a larger number of males sustaining concussions, research illustrates that female athletes experience higher absolute injury rates for concussion after equating for exposure and sport. Collegiate female athletes had a 1.4 times higher overall concussion injury rate than male athletes in sex-comparable sports including softball, basketball, ice hockey, and soccer (Covassin Moran, & Elbin, 2016). Other studies have presented similar findings, showing high school female athletes suffered a higher incidence of concussions than males (Marar, McIlvain, Fields, & Comstock, 2012; Lincoln et al., 2011). Since these findings suggest that females are more susceptible to sustaining concussions, an evaluation of sex differences in post-concussion outcomes also becomes increasingly important.

Despite growing recognition of the public health burden posed by pediatric concussion and the possibility of sex differences in outcomes, significant barriers remain in addressing this concern. The majority of research on sex differences in sport-related concussion and mTBI has been conducted on young adults, leaving a major gap in our understanding of sex differences among children.

Statement of Purpose

The purpose of the current study is to evaluate sex differences in acute outcomes among children and adolescents presenting to the ED for mTBI to determine how these differences might impact public health policy and clinical management.

Literature Review

In 1966, the Congress of Neurological Surgeons defined concussion as “a clinical syndrome characterized by immediate and transient impairment of neural functions, such as alteration of consciousness, disturbance of vision, equilibrium, etc. due to mechanical forces” (Committee on Head Injury Nomenclature of the Congress of Neurological Surgeons, 1966, p. 388).

Since 1966, multiple organizations have provided definitions of concussion as outlined in Table 1 (Mild Traumatic Brain Injury Committee, American Congress of Rehabilitation Medicine (ACoRM), 1993; Committee on Quality Improvement, 1999; Carroll, Cassidy, Holm, Kraus, & Coronado, 2004). All of these attempts by professional organizations to define concussion led to an emphasis on four important criteria: loss of consciousness (LOC), posttraumatic amnesia, alteration in mental status, and neurological signs (Bodin, Yeates, & Klamar, 2012). Despite some similarities shared between definitions, all of them vary significantly.

Table 1

Components of Three Organization's Definitions of Concussion

	ACoRM (1993)	American Academy of Pediatrics (1999)	World Health Organization (2004)
Loss of consciousness (LOC)	Yes	<1 min	<30 min
Post-traumatic amnesia	Retrograde or Anterograde	N/A	<24 hours
Alteration in mental state	Present at the time of accident	Normal at time of examination	Confusion or disorientation
Focal neurological deficits	May or may not be transient	None	Transient
Evidence of other injuries	N/A	No evidence of skull fracture	Not due to other injuries or treatment for other injuries caused by other problems or caused by penetrating craniocerebral injury
Extra comments	N/A	Can include seizures, emesis, headache, and lethargy	Glasgow Coma Scale (GCS) 13-15 after 30 min injury or presenting to healthcare, not due to drugs, alcohol, medications

In 2016, the International Conference on Concussion in Sport was held in Berlin, and the Concussion in Sport Group (CISG) defined a sport-related concussion (SRC) as "a traumatic brain injury induced by biomechanical forces" (McCrory et al., 2018, p. 839). The CISG definition noted that an SRC does not necessarily require a direct blow to the head but can occur when a hit to another body region causes an impulsive force to the head. The CISG further defined SRC to involve spontaneously resolving and transient impairment of neurologic function. The CISG mentioned that some variation in time of symptom onset is permitted, as some neurologic manifestations evolve over minutes to hours. The CISG stated that concussion is largely a functional disturbance and not a structural injury, as no changes can be seen on standard neuroimaging studies. Additionally, they pointed out that concussions may be accompanied by a wide range of symptoms that resolve in a sequential order and do not need to include LOC. Similarly to the WHO (World Health Organization), the CISG also excluded symptoms better explained by drugs, alcohol, medications, or other injuries or comorbidities (McCrory et al., 2018). Most importantly, the CISG definition does not emphasize LOC or post-traumatic amnesia, but instead focuses on the acute functional changes that follow concussion.

Despite advances in scientific knowledge about concussion over the past decade, no consensus regarding its definition has been reached (Bodin et al., 2012). The lack of consensus leads to misperceptions concerning the seriousness of the injury among parents and children, as well as confusion about how to properly diagnose and manage the injury among health care providers (Bodin et al., 2012). The term ‘concussion’, which is the preferred terminology among sports medicine specialists, is frequently used interchangeably with the terms ‘minor closed health injury’, ‘mild closed health injury’, and ‘mild traumatic brain injury (mTBI)’ by other medical specialists (Bodin et al., 2012). The use of different terms to describe the same pathological process leads to misunderstanding whether or not a concussion is a brain injury (Bodin et al., 2012). In fact, researchers discovered that only 34.3% of athletes, coaches, and parents identified concussion as a brain injury (Nanos, Franco, Larson, Mara, & Laskowski, 2017). Despite a call to action to phase out the term concussion and use mTBI in its place, no changes have been made within the clinical or research communities to address this issue (Bodin et al., 2012). Furthermore, no agreement exists whether a distinction exists between concussion and mTBI (Bodin et al., 2012).

In addition to a lack of consensus regarding the definition of concussion, confusion continues regarding the classification of concussion, grading of concussion, and differentiating the management of concussion in children versus adults (Bodin et al., 2012). Because most past concussion research has focused on young adults, a large gap exists in our understanding of pediatric concussion (Bodin et al., 2012). Traditionally, concussion assessments use adult measures, rely on verbal and motor components that may not be appropriate for children, and rely on the accuracy of parents' recall, which may not be reliable or valid (Bodin et al., 2012). Finally, pediatric concussion grading systems do not exist, and no differences exist in classification schemes for pediatric versus adult concussions (Bodin et al., 2012).

Concussion Diagnosis and Management in Children

In an attempt to summarize 25 years of research on pediatric concussion, Lumba-Brown et al. (2018) published a systematic review on the diagnosis and management of mTBI in children under the age of 18. With regard to diagnostic assessments, the authors concluded with moderate confidence that a combination of computerized cognitive testing and validated postconcussion symptom rating scales should be used to distinguish children with and without mTBI (Lumba-Brown et al., 2018). While no risk factors for sequelae greater than one year post-mTBI were identified with high confidence, risk factors for ongoing impairment, more severe symptoms, or delayed recovery (less than 1-year postinjury) identified with high confidence included Hispanic ethnicity; premorbid factors such as neurologic or psychiatric problems, learning difficulties, behavioral problems, and post-concussion like symptoms; lower socioeconomic status; and apolipoprotein E ε4 allele (Lumba-Brown et al., 2018). Importantly, the only consistent sex difference reported less than one-year post-injury was females experiencing more headaches than males (Lumba-Brown et al., 2018). Sex of the child was not found to be associated with post-injury symptoms after one week; academic, social, and physical problems after three months; neurocognitive change from baseline; or neurologic deterioration after a lucid interval (Lumba-Brown et al., 2018). However, confidence in the evidence for these associations was low. Insufficient evidence was available to support any treatment modalities for improving mTBI-related outcomes (Lumba-Brown et al., 2018). While this systematic review helps identify diagnostic modalities appropriated for pediatric mTBI and risk factors for short-term poorer outcomes, it also highlights key gaps in major components of clinical practice in the management of pediatric mTBI (Lumba-Brown et al., 2018).

Post-concussion Outcomes

Several studies illustrate persistent neurocognitive deficits after pediatric mTBI (Moser & Schatz, 2002; Moser et al., 2005; Giza & Hovda, 2001; Dean & Sterr, 2013; Anderson et al., 2017). These studies show that children who sustained concussions demonstrated significantly lower performances on measures of general cognitive ability, attention span, mental speed, working memory, and cognitive flexibility (Moser & Schatz, 2002; Moser et al., 2005; Giza & Hovda, 2001; Dean & Sterr, 2013; Anderson et al., 2017). Furthermore, about a quarter of children who sustain a mTBI will develop a symptom complex consisting of persistent somatic, cognitive, sleep, and affective symptoms, termed postconcussion syndrome, lasting at least one month after their injury (Barlow, 2014). Risk factors for prolonged recovery and postconcussion syndrome include injury factors like amnesia, admission to hospital, magnitude of acute symptoms, and the presence of other injuries (Barlow, 2014). Other risk factors include premorbid problems such as learning and school difficulties, impaired coping strategies, adverse life events, parental anxiety, and lower IQ (Barlow, 2014). The role that sex plays in post-concussion outcomes remains controversial in the absence of strong evidence.

Sex Differences

As mentioned previously, research on sex differences in post-mTBI outcomes among children and adolescents is limited. Therefore, studies that focus on adults will be included in this review.

One of the few studies that evaluated sex differences in pediatric concussion outcomes was conducted by Ledoux et al. (2018), and evaluated symptom change and recovery in patients aged 5 to 18 years with concussion. The results indicated that female adolescents had a protracted recovery post-mTBI relative to male adolescents, with more than half failing to recover by week 12 post-injury (Ledoux et al., 2018). Additionally, across all age groups (5 to 18 years old), females were more symptomatic than boys (Ledoux et al., 2018). This study suggests that while females report more subjective symptoms across all age groups, only female adolescents experience clearly extended recovery times (Ledoux et al., 2018).

Bazarian, Blyth, Mookerjee, He, and McDermott (2010) evaluated mTBI patients over the age of three years at three months post-injury on three outcomes, including post-concussive symptoms (PCS), number of days to return to normal activity, and number of days of work missed. Three months post mTBI, females had significantly higher odds of a higher PCS score, and this association was most prominent during the ages of 14-56 (Bazarian, Blyth, Mookerjee, He, & McDermott, 2010). The researchers speculated that the observed pattern of females experiencing worse symptoms during child-bearing years is due to a disruption in hormone production (Bazarian et al., 2010). Interestingly, the study found no sex difference in number of days to return to normal activity or number of days of work missed (Bazarian et al., 2010). While this study does not focus on the pediatric population, the findings suggest that the sex differences in post-mTBI outcome may be more physiological than sociological (Bazarian et al., 2010). Importantly, however, a higher PCS score, which is inherently subjective, did not translate into a less-subjective measure of longer recovery time and more days of missed work (Bazarian et al., 2010).

Broshek et al. (2005) evaluated high school and collegiate athletes before and after concussion to examine sex differences in the subjective experience of symptoms and the magnitude of cognitive change from baseline. Importantly, baseline cognitive performances on the neurocognitive assessment tool did not differ according to sex (Broshek et al., 2005). The results showed that females demonstrated significantly greater declines in simple and complex reaction times and reported greater number of postconcussion symptoms than their male counterparts (Broshek et al., 2005). Furthermore, females were 1.7 times more likely to be cognitively impaired than males (Broshek et al., 2005). The differences remained significant after the researchers controlled for the use of helmets (Broshek et al., 2005). Interestingly, the researchers also discovered that females were not followed-up as quickly as males (Broshek et al., 2005). Even though females waited a longer time before their post-concussion evaluation, they still demonstrated poorer objective and subjective outcomes (Broshek et al., 2005).

Brown, Elsass, Miller, Reed, and Reneker (2015) conducted a systematic review and meta-analysis to evaluate sex differences in symptom reporting at baseline and after a sport-related concussion among high school and collegiate athletes. The researchers discovered that females were 43% more likely than males to report any symptom associated with concussion at baseline, including headache/migraine, difficulty concentrating, energy/sleep disturbances, emotional disturbances, and vision/hearing problems (Brown, Elsass, Miller, Reed, & Reneker, 2015). However, while females had higher total symptom scores at baseline and post-concussion, these findings were found to be clinically insignificant (Brown et al., 2015). The researchers suggested that the symptoms that females were more likely to report than males at baseline and post-concussion were also symptoms associated with premenstrual syndrome (Brown et al., 2015). The researchers recommended that future research focus on analyzing the difference between baseline symptom reporting pre-menstruation and during menstruation (Brown et al., 2015). The study illustrates that while females report more symptoms at baseline and post-concussion, the symptoms may be due to other biological processes and are not clinically relevant to mTBI (Brown et al., 2015).

Covassin, Harris, Parker, and Kontos (2012) evaluated sex differences in symptom reporting, neurocognitive performance, and postural stability in high school and collegiate athletes after concussion. The results showed that females performed worse on visual memory tests and reported more symptoms after concussion in comparison to males (Covassin, Harris, Parker, & Kontos, 2012). However, high school male athletes scored worse on dynamic postural stability than high school female athletes, and college female athletes scored worse than college male athletes (Covassin et al., 2012). The results reflect sex differences in subjective and objective measures across both high school and college, whereas the postural stability findings suggest an interaction of age and sex (Covassin et al., 2012).

Iverson et al. (2017) conducted a systematic review to determine predictors of clinical recovery from concussion. While the researchers admit that controversy continues regarding sex differences in recovery time and persistent symptoms, the researchers concluded that the literature, overall, indicates that females have longer recovery times and more persistent symptoms in comparison to males (Iverson et al., 2017). They suggested that the evidence shows that the increased risk for persistent symptoms among females climaxes during the teenage years (Iverson et al., 2017). This systematic review again highlights female adolescence as a risk factor for poorer outcomes post-concussion (Iverson et al., 2017). Similarly, Dougan, Horswill, and Geffeen (2014) conducted a meta-analysis to determine what factors impact neuropsychological functioning after a sports-related concussion. They discovered that females and adolescents demonstrated greater neuropsychological impairment than males and adults (Dougan et al., 2014).

Kostyun and Hafeez (2015) conducted a retrospective chart review of children and adolescents aged 11 to 18 who sustained a mTBI and were being seen in an outpatient adolescent sports medicine concussion clinic to determine if sex played a role in concussion management. The researchers discovered that female adolescent athletes required more treatment interventions and had a longer recovery time compared to their male counterparts (Kostyun & Hafeez, 2015). Additionally, female athletes were more likely than males to require medication, vestibular therapy, and academic accommodations (Kostyun & Hafeez, 2015). These findings suggest that females may require additional and longer treatment interventions because they suffer poorer concussion outcomes (Kostyun & Hafeez, 2015).

In 2018, Sicard, Moore, and Ellemberg conducted a study to evaluate sex differences amongst college athletes on long-term cognitive outcomes following concussion. All participants were assessed using the Cogstate computerized battery, which measures four cognitive domains: executive function (N-back task), visual learning (One Card Learning task), attention (Identification task), and processing speed (Detectoin task) (Sicard, Moore, & Ellemberg, 2018). The researchers added an additional measure that required a high level of executive functioning (Sicard et al., 2018). The N-back Task analysis revealed that females with a history of concussion performed slower on the 2-Back condition than males (Sicard et al., 2018). Because the 2-Back condition of the N-back Task was the test to show a group difference, the researchers suggested that tests that assess higher level executive functioning are needed to ensure that differences between sexes are detected (Sicard et al., 2018).

Mechanisms Explaining Sex Differences

Sex differences in the severity of mTBI outcomes has been attributed to a range of cultural, hormonal, and physical characteristics that differ between males and females. As noted earlier, females report more symptoms at baseline and post-concussion compared to males. Researchers propose that sex differences in subjective symptom reporting can be attributed to cultural differences. Beginning in childhood, men and women undergo different socialization processes that teach them what is socially acceptable according to their sex (Barsky, Peekna, & Borus, 2001). Males are taught to refrain from disclosing distress and discomfort, while females are taught that openly sharing that information is socially acceptable (Barsky et al., 2001). Researcher suggest that this socialization process leads to females being more willing to disclose or overreport/dramatize concussion symptoms in comparison to males (Barsky et al., 2001). However, one study showed that men and women generally report their symptoms accurately and women's higher symptom reporting is a reflection of true disability (Merrill, Seeman, Kasl, & Berkman, 1997). Another study failed to support the idea that females somaticize more than males (Piccinelli & Simon, 1997). Interestingly, research suggests that conformity to traditional masculine norms, such as winning at all costs, may play a larger role than sex in reporting concussion symptoms. For example, in 2017, Kroshus, Baugh, Stein, Austin, and Calzo conducted research to investigate how sex and self-reported conformity to masculinity norms impact intention to report concussion symptoms. While females scored higher on intention to report concussion symptoms, high conformity with traditional masculine norms was associated with lower reporting intention regardless of sex (Kroshus, Baugh, Stein, Austin, & Calzo, 2017). Therefore, the socialization process that occurs within sport culture may play a larger role in determining concussion symptom reporting than the sex-typed social roles to which children are exposed. Nevertheless, cultural differences cannot explain sex differences on objective tests of cognitive functioning post-concussion, as they are not self-reported.

Biological differences, which include physiological, metabolic, and neuroanatomical differences, are another potential mechanism to explain why females fare worse than males after concussion. Sex-based differences in response to injurious stimuli have been documented in neuroanatomy, cerebrovascular organization, and cellular response (Cheng et al., 2009; Esposito, Van Horn, Weinberger, & Berman, 1996; Roof & Hall, 2000; Andreason, Zametkin, Guo, Baldwin, & Cohen, 1994). Because females having greater cerebral blood flow rates and basal rates of glucose metabolism, they may experience greater impairments post-mTBI because brain injury exacerbates the demands placed on the brain by decreasing cerebral blood flow.

In addition to neuroanatomical differences, males and females have different levels of sex hormones circulating in their bodies and those levels change throughout life. Therefore, researchers are investigating whether sex hormones modulate response to mTBI. Multiple studies have evaluated the effect of estrogen and progesterone on the brain post mTBI. Djebali, Guo, Pettus, Hoffman, and Stein (2005) discovered that progesterone and its metabolite, allopregnanolone, have anti-apoptotic and anti-astrogliotic effects post TBI in male rats, leading to improved outcomes when either neurosteroid is administered post-injury. Roof, Duvdevanj, Braswell, and Stein (1994) found that progesterone reduced neuronal degeneration and edema and improved cognitive recovery in male rats. Furthermore, clinical trials have shown improved outcomes post TBI in patients treated with progesterone (Wright et al., 2007; Xiao, Wei, Yan, Wang, & Lu, 2008). Given these findings, sex hormones may be neuroprotective.

Thus, women of childbearing age, with the highest levels of naturally circulating hormones, might be expected to have better outcomes. However, women of child bearing age actually experience worse outcomes post-mTBI compared to premenarchal and postmenopausal women and men (Berry et al., 2009; Davis 2006; Bazarian et al., 2010). When evaluating risk factors for injuries in female youth ice hockey players ages 9 to 17, Decloe, Meeuwisse, Hagel, and Emery (2014) discovered that among players at the PeeWee level, female athletes who had begun menstruating before the beginning of the season were four times more likely to incur an injury in comparison to premenarchal females. Another study examined how the phase of a female's menstrual cycle at the time of the mTBI impacted 1-month outcomes (Wunderle, Hoeger, Wasserman, & Bazarian, 2014). The results showed that women who sustained a mTBI during the luteal phase of their menstrual cycle, when progesterone concentration is at its highest, performed worse on quality of life and symptom measures than women who sustained a mTBI during the follicular phase of their menstrual cycle or who were taking oral contraceptives (Wunderle et al., 2014). Given that sex hormones appear to be neuroprotective and women of childbearing age experience worse outcomes post TBI, the researchers propose a 'withdrawal hypothesis', such that people who have a higher concentration of circulating sex hormones at the time of injury experience worse outcomes because mTBI causes a sudden decrease in sex hormone concentration (Wunderle et al., 2014).

Finally, researchers propose that females experience poorer outcomes post-mTBI based on sex differences in neck strength and injury biomechanics. Studies show that females have smaller and weaker necks than males, and that athletes are at a greater risk of concussion if they have smaller neck circumferences, smaller neck to head circumference ratios, and weaker neck strength (Eckner, Oh, Joshi, Richardson, & Ashton-Miller, 2014; Collins et al., 2014). Additionally, greater neck strength and anticipatory cervical muscle activation reduces the magnitude of a head's response to impulsive loads in each anatomic plane and may reduce the risk of sport-related concussion (Eckner et al., 2014). Tierney et al. (2005) discovered that females showed greater head-neck segment peak angular acceleration and displacement in comparison to males, and attributed this to females exhibiting less isometric strength, neck girth, and head mass. Additionally, the mechanisms by which females sustain concussions differ from males (Dick, 2009). Male athletes are more likely to suffer a concussion due to player contact while females are more likely to suffer a concussion due to surface or ball contact (Dick, 2009). These findings suggest that females may be at higher risk for concussion and experience worse outcomes post-concussion because of sex differences in head-neck kinematics and injury biomechanics.

Overall, the research supports increasing female participation in youth sports, females being more susceptible to sustaining concussions than males, females reporting more symptoms post-concussion than males, and females experiencing poorer objective outcomes post-concussion than males. Despite these findings, major gaps in the literature remains regarding sex differences in post-concussion outcomes among the pediatric population. The study aims to fill in that gap by examining sex differences within a pediatric population presenting to the ED for mTBI in regard to post-concussion acute subjective and objective outcomes.

Methods

The study is a secondary analysis of a pre-existing, de-identified dataset that was collected as part of grant number R01HD076885, entitled Predicting Outcomes in Children with

Mild Traumatic Brain Injury, with permission of Dr. Keith Yeates. The funding agency is National Institute of Child Health and Human Development. Due to the nature of the dataset, the study was determined to be exempt from IRB oversight based on Wright State University's IRB's decision flowchart (Appendix A).

Participants and Recruitment

The study involved a concurrent cohort, prospective, and longitudinal design that included 8 to 16 year-old children with mTBI and a comparison group of children with mild orthopedic injuries (OI) not involving the head. Participants were recruited during their initial visits to the EDs at Nationwide Children's Hospital (NCH) in Columbus, Ohio or Rainbow Babies and Children's Hospital (RBCH) in Cleveland, Ohio. Recruitment occurred from 8:00 am to 10:00 pm, seven days a week, and lasted 42 to 48 months. All recruitment decisions regarding inclusion and exclusion criteria were reviewed by an attending physician at each site. Prior to any involvement in the study, parents provided written informed consent and children provided written assent.

The mTBI group included children who sustained a blunt head trauma that resulted in at least one of the following three criteria: (1) an observed loss of consciousness (LOC), (2) a Glasgow Coma Scale (GCS) score of 13 or 14, or (3) at least two acute signs or symptoms of concussion as noted by ED medical personnel on a standard case report form (i.e., post-traumatic amnesia, focal neurological deficits, skull fracture, post-traumatic seizure, vomiting, headache, dizziness, other mental status changes) (Teasdale & Jennett, 1974). Exclusion criteria included delayed neurological deterioration, neurosurgical intervention, LOC > 30 minutes, and GCS <13. Children were not excluded if they were hospitalized or intracranial lesions or skull fractures were found on CT scan. Children were not required to have undergone a CT scan to be eligible for the study, but if CT scans were completed, then they were available for the purpose of injury classification.

The OI group included children who sustained upper or lower extremity fractures associated with Abbreviated Injury Scale (AIS) scores of 4 or less (American Association for Automotive Medicine, 1990). Exclusion criteria for the OI group included any head trauma or symptoms of concussion, as well as any injury requiring surgery or the administration of sedative medication.

Children were not excluded from either group if they were administered analgesic medication, including narcotics, but the administration of pain medication was tracked. Additional exclusion criteria for both groups included: (a) any other severe injury as defined by an AIS score greater than four; (b) any associated injury likely to interfere with neuropsychological testing (e.g., fracture of preferred upper extremity); (c) hypoxia, hypotension, or shock during or following the injury; (d) alcohol or drug ingestion involved with the injury; (e) history of previous TBI requiring hospitalization; (f) premorbid neurological disorder or mental retardation; (g) injury resulting from child abuse or assault; (h) history of severe psychiatric disorder requiring hospitalization; or (i) medical contraindication to MRI.

The first set of assessments occurred at the time of recruitment during a participant's initial visit to the ED. Then, each participant and their families were assessed within two weeks of injury (post-acutely). Although the children were assessed weekly by email and in face-to-face assessments at three- and six-months post-injury, only the post-acute visit data are included in this study's analysis.

Measures

Table 2 summarizes the measures that were assessed at the initial ED visit and at the post-acute assessment that will be included in the current analyses. All measures have demonstrated satisfactory reliability and validity.

Table 2

Measures Collected at Initial Emergency Department Visit and at Post-acute Visit

Domain measures	Source/ reporter	ED (day of injury)	Post-acute (w/i 14 days)
Acute signs and symptoms			
Injury case report form	RA	X	
Balance			
Balance Error Scoring System	C	X	X
Neuropsychological functioning			
NIH Toolbox cognitive test battery	C		X
Post-concussive symptoms			
Health and Behavior Inventory	C & P	X[a]	X
Premorbid functioning			
Wechsler Abbreviated Scale of Intelligence	C		X

[a]Retrospective ratings by parents at post-acute assessment to assess premorbid functioning.
NOTE: ED= Emergency Department; P = parent; C = child; RA = research assistant.

Predictors.

Acute signs/symptoms. A standardized injury case report form was used to elicit details regarding the injury and acute signs and symptoms of concussion including LOC, GCS scores, mechanisms of injury, neurological status, reports of retrograde or anterograde amnesia, emesis, and other clinical factors. The information was gathered from medical records and medical personnel by recruiters and verified by attending physicians. These variables were selected because they have been shown to be associated with either increased or decreased risk of significant intracranial injury after mTBI (Dunning et al., 2004; Dunning et al., 2007; Kuppermann et al., 2009).

Balance. The Balance Error Scoring System (BESS) was used to assess three stances (narrow double leg stance, single leg stance, and tandem stance) and two footing surfaces (firm surface/floor vs. medium density foam) held for 20 seconds with hands on hips and eyes closed. Error points (up to 10 per trial) were given for opening eyes, lifting hands off hips, and stepping, stumbling, or falling. The BESS has shown satisfactory reliability in children and adolescents (McLeod, Barr, McCrea, & Guskiewicz, 2006). In the current study, the administration of the BESS was videotaped, and approximately 10% of the assessments were scored twice by independent raters. The total BESS score showed excellent reliability as assessed using Krippendorf's alpha (.953), with satisfactory reliability on each of the six trials (alpha = .64-.86).

Neuropsychological functioning. The NIH Toolbox computerized cognitive test battery was used to assess cognitive abilities. The battery consists of seven individual subtests that assess cognitive flexibility, visual attention and inhibitory control, processing speed, episodic memory, working memory, vocabulary knowledge, and reading. Standard scores that correct for age, sex, race, ethnicity, and parental education are derived for individual subtests and for fluid and crystallized cognitive composites.

Outcomes.

***Post-concussive symptoms*.** PCS were assessed using the Health and Behavior Inventory (HBI) (Ayr, Yeates, Taylor, & Brown, 2009; Mittenberg, Wittner, & Miller, 1997). The HBI includes parent and child forms. Additionally, the HBI is a core measure in the Common Data Elements for Pediatric Traumatic Brain Injury and yields separate scores for cognitive and somatic symptom scales (McCauley et al., 2012). The HBI has shown reliability and validity (Janusz, Sady, & Gioia, 2012; Yeates et al., 2012).

Potential confounds.

Premorbid child functioning. The two-subtest version of the Wechsler Abbreviated Scale of Intelligence (WASI) was used to assess children's general intellectual functioning (The Psychological Corporation, 1999).

Data Analysis

The statistical software packages, RStudio 1.1.442 and SPSS Version 25, were used to perform all analyses (RStudio, 2019; IBM Corp, 2017).

Contingency tables were constructed to compare the counts for two different categorical variables (e.g., Consented/Refused versus Sex). When appropriate, the two-proportion test, which is equivalent to a chi-square test, was used to compare proportions for the two different groups. Student's *t*-test was used to compare means for quantitative variables (e.g., census tract income for consented and refused groups). Test statistics, *p*-values, and 95% confidence intervals are reported.

When the response variable did not follow a normal distribution (e.g., family income), a Mann-Whitney U nonparametric test was used two compare the medians for two groups. This test procedure is not influenced by outliers.

Linear models were fit for the parental and child ratings of cognitive and somatic symptoms, and for the measures of cognitive abilities (i.e., Fluid and Crystallized Cognition Composites) and balance. For each response variable, a fixed effects linear model, including interaction, was fit with sex and group as explanatory factors. The models also included age at injury as a covariate to account for age-related variation in the outcomes, except for the two cognitive abilities measures, which are already adjusted for age. For cognitive and somatic symptoms ratings, another covariate representing pre-injury ratings was included. For measures of cognitive abilities, socioeconomic status also was included as a covariate.

ANOVA tables with degrees of freedom, mean sum of squares, test statistics, and *p*-values are reported. For any response variable for which a group by sex interaction was significant, interaction plots were created by plotting the cell means for the response variable of interest against group and profiling by sex.

Results

Demographic Variables

As illustrated in Figure 1, of the 588 eligible participants who were approached to participate in the study, 315 consented and 273 refused. Of the 315 participants who consented to participate in the study, 98 were seen only at the initial ED visit and 217 returned for the post-acute visit. Initial comparisons were conducted between those who refused and consented, and between those who were only seen at the initial ED visit and those who returned for the post-acute visit, to identify any participation bias. Variables of interest included group, sex, age, race, and socioeconomic status (SES).

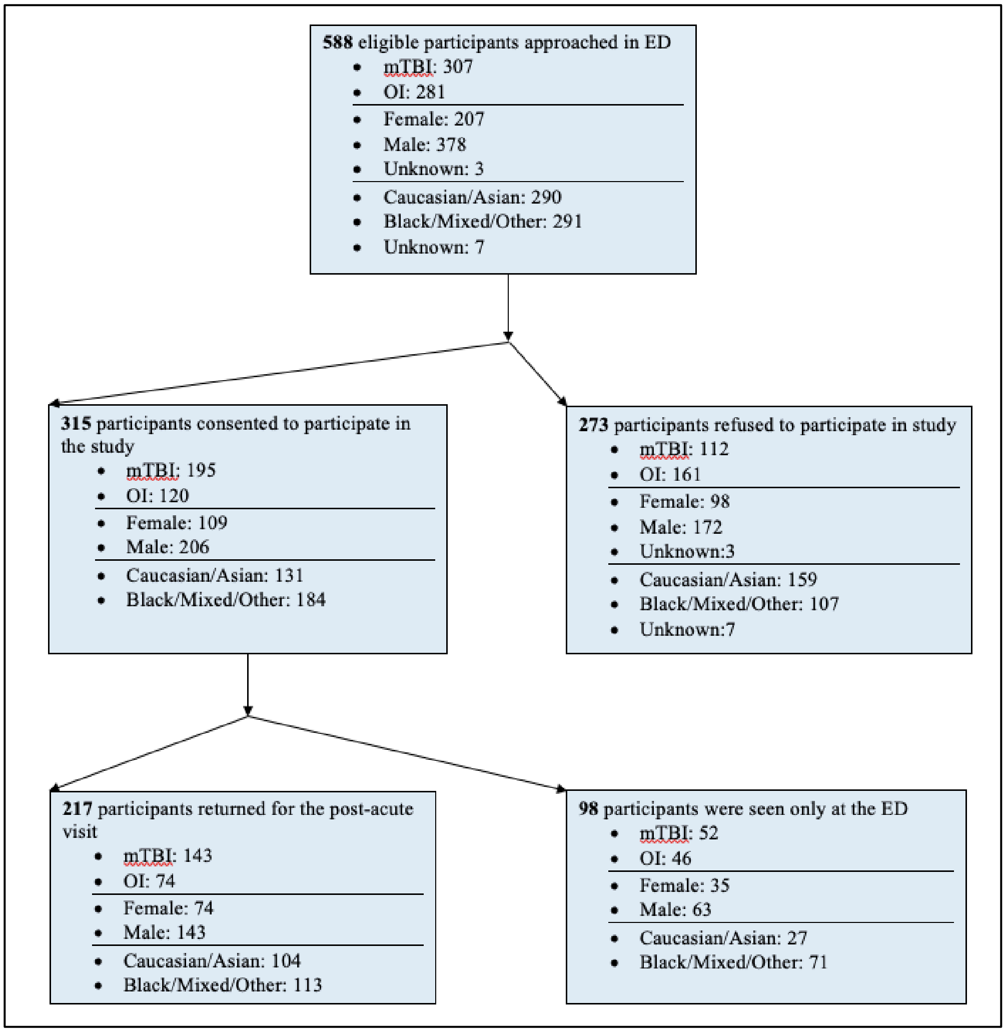

Figure 1. Flow of participants through study.

Among those approached, those who consented versus those who refused did not differ based on sex, $\chi^2(1)=0.182$, $p=0.367$, or age, $\chi^2(581)=0.119$, $p=0.905$. With 95% confidence, 12.6 to 29.1% more participants consented for the mTBI group than the OI group, $\chi^2(1) =24.772$, $p <$ .001. Additionally, with 95% confidence, 9.7 to 26.4% more Black/Mixed/Other participants consented than Caucasian/Asian participants, $\chi^2(1)=18.361$, $p < .001$. Because median family income, percentage of minorities, and percentage of residents below the poverty line (all determined based on participants' census tract) were not normally distributed, a Mann-Whitney U nonparametric test was used to compare medians. In conjunction with the above finding about race and consent, those who consented lived in census tracts with significantly lower median family income, and higher percentage of minorities and residents below the poverty line, than those who refused, p = .001, .000, .004 respectively.

Among those who consented, those who were seen only at the ED and those who returned for the post-acute visit did not differ based on sex, $\chi^2(1)$= 0.078, p = 0.438, or age, $\chi^2(313)$=-0.245, p = 0.807. With 95% confidence, 0.3 to 23.0% more mTBI participants returned for the post-acute visit than OI participants, $\chi^2(1)$=4.1891, p = .041. With 95% confidence, 7.5 to 28.5% more Caucasian/Asian participants returned for the post-acute visit than Black/Mixed/Other participants, $\chi^2(1)$=10.714, p = .001. Because median family income, percentage of minorities, and percentage of residents below the poverty line were not normally distributed, a Mann-Whitney U Test nonparametric test was used to compare medians. In conjunction with the above finding about race and return for the post-acute visit, those who returned for the post-acute visit resided in census tracts with higher median family income, and lower percentages of minorities and residents below the poverty line, than those who were seen only in the ED, p = .003, .000, .028 respectively.

While a higher proportion of Black/Mixed/Other participants consented for the study, a higher proportion of Caucasian/Asian returned for the post-acute visit; as a result, participants who returned for the post-acute visit were not significantly different in race from the combined group of participants who refused to participate in the study or were seen only in the ED, $\chi^2(1)$=.547, p = 0.257. This suggests limited systematic bias in the race of who was seen for the post-acute visit. Among those who consented, the overall retention rate for the post-acute visit was 68.9%.

As illustrated in Table 3, among the participants who returned for the post-acute visit, the mTBI and OI groups did not differ based on sex, age at injury, or full-scale IQ at initial assessment. With 95% confidence, the mTBI and OI groups did differ based on race, with the mTBI group having 0.4 to 27.1% more Caucasians/Asians participants than the OI group, $\chi^2(1) = 4.579$, df=1, $p = .023$. Additionally, the mTBI and OI groups differed based on SES, t(215)=2.794, $p = .006$, 95% CI=.116-.672, which was higher in the mTBI group.

Table 3

Demographic and Clinical Characteristics of Post-Acute Visit Participants

Variable	OI	Mild TBI
Sample size	74	143
Male, No. (%)	48 (64.9)	95 (66.4)
Female, No. (%)	26 (35.1)	48 (33.6)
Age at injury, y, mean (SD)	12.35 (2.37)	12.56 (2.61168)
Caucasian/Asian, No. (%)	28 (37.8)	76 (53.1)
Socioeconomic status, mean (SD)	-0.26 (0.90)	0.13 (1.03)
Full-scale IQ at initial assessment, mean (SD)	97.89 (15.54)	98.71 (15.05)
Loss of consciousness, No. (%)	NA	38 (27.1)

Linear Models

Table 4 shows the estimated marginal means for each dependent variable broken down by sex and group.

Table 4

Estimated Marginal Means for Dependent Variables

	OI		Mild TBI	
	74		*143*	
Outcome measures	Female	Male	Female	Male
Parent ratings of cognitive symptoms, M (std. error)	10.469 (1.395)	9.096 (.986)	13.775 (.989)	11.770 (.714)
Parent ratings of somatic symptoms, M (std. error)	4.377 (.960)	2.824 (.682)	8.323 (.681)	6.934 (.489)
Child ratings of cognitive symptoms, M (std. error)	8.769 (1.615)	10.542 (1.188)	15.229 (1.188)	13.266 (.849)
Child ratings of somatic symptoms, M (std. error)	3.949 (1.094)	5.539 (.794)	10.744 (.793)	8.624 (.564)
Age standardized Cognitive Fluid Composite Score, M (std. error)	93.755 (3.747)	101.633 (2.289)	91.750 (2.797)	93.068 (1.924)
Age standardized Cognitive Crystallized Composite Score, M (std. error)	96.064 (2.657)	102.906 (1.946)	99.720 (2.004)	100.554 (1.386)
BESS Total Score, M (std. error)	23.128 (2.566)	27.579 (1.727)	24.147 (1.333)	23.646 (.955)

As shown in Table 5 and Figure 2, the group by sex interaction was significant for child ratings of somatic symptoms. Figure 2 shows a larger group (mild TBI vs. OI) difference in somatic symptoms for females than males. In contrast and as illustrated in Tables 6 through 8, the group by sex interaction was not significant for child ratings of cognitive symptoms or parent ratings of somatic and cognitive symptoms.

Table 5

ANOVA for Child Ratings of Somatic Symptoms

	df	*MS*	*F*	*p*	*ES*
Corrected Model	4	339.359	11.341	.000	.178
Intercept	1	4704.947	157.240	.000	.428
Parent ratings of pre-injury somatic symptoms	1	174.649	5.837	.017	.027
Group	1	1050.319	35.102	.000	.143
Sex	1	3.000	.100	.752	.000
Group*Sex	1	149.020	4.980	.027	.023

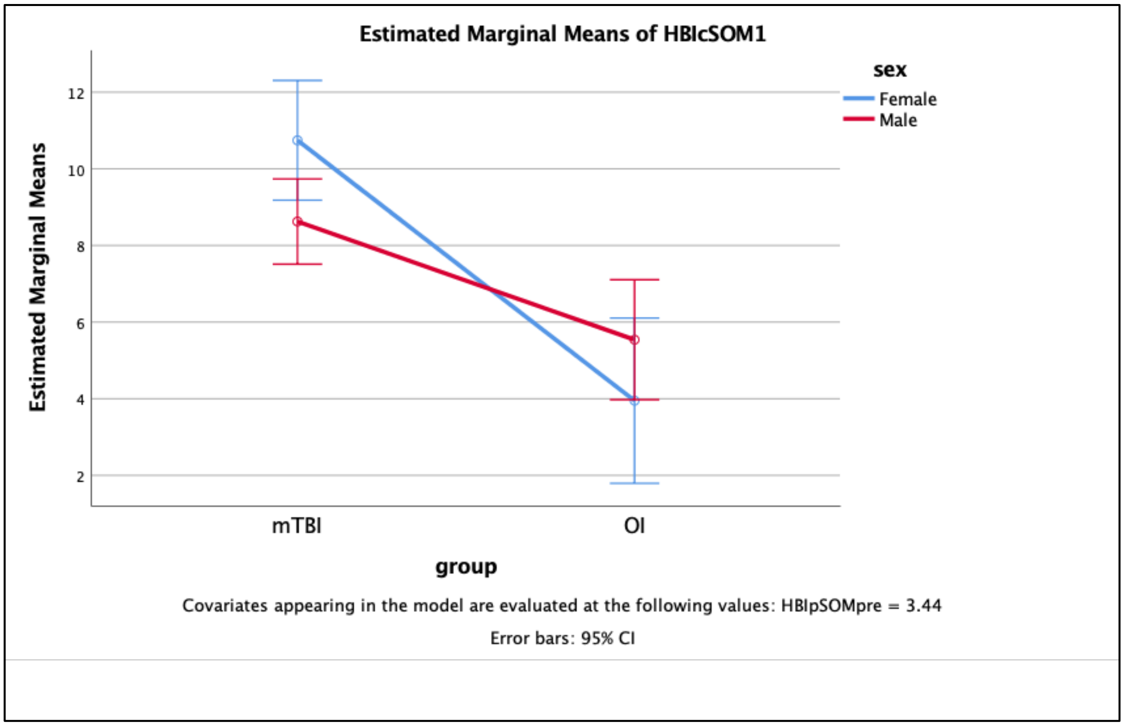

Figure 2. Interaction plot for child ratings of somatic symptoms.

The main effect for group was significant for all symptom ratings by parents and children, with the mild TBI group reporting more symptoms than the OI group in all cases (Tables 3 through 6). The main effect of sex was significant for parent ratings of somatic symptoms, such that parents reported more somatic symptoms for girls than boys, in both groups (Table 5). Premorbid symptom ratings were significant for all but children's rating of cognitive symptoms (Tables 3, 5, and 6).

Table 6

ANOVA for Child Ratings of Cognitive Symptoms

	df	*MS*	*F*	*p*	*ES*
Corrected Model	3	319.324	4.711	.003	.063
Intercept	1	25179.065	371.482	.000	.637
Group	1	929.308	13.711	.000	.061
Sex	1	.401	.006	.939	.000
Group*Sex	1	153.747	2.268	.134	.011

Table 7

ANOVA for Parent Ratings of Somatic Symptoms

	df	*MS*	*F*	*p*	*ES*
Corrected Model	5	337.380	15.319	.000	.271
Intercept	1	5.085	.231	.631	.001
Parent ratings of pre-injury somatic symptoms	1	412.945	18.750	.000	.083
Age of Injury	1	113.929	5.173	.024	.024
Group	1	682.893	31.007	.000	.131
Sex	1	90.747	4.120	.044	.020
Group*Sex	1	.287	.013	.909	.000

Table 8

ANOVA for Parent Ratings of Cognitive Symptoms

	df	*MS*	*F*	*p*	*ES*
Corrected Model	4	1800.838	38.584	.000	.427
Intercept	1	1134.003	24.296	.000	.105
Parent ratings of pre-injury cognitive symptoms	1	6672.020	142.951	.000	.408
Group	1	377.108	8.080	.005	.038
Sex	1	119.366	2.557	.111	.012
Group*Sex	1	3.965	0.085	.771	.000

As shown in Tables 9 and 10, the group by sex interaction was not significant for either the fluid or crystallized cognitive composites, nor were the group or sex main effects. SES was a significant covariate in both cases, with higher SES associated with better cognitive skills.

Table 9

ANOVA for Age Standardized Cognitive Fluid Composite Score

	df	*MS*	*F*	*p*	*ES*
Corrected Model	4	1258.030	3.653	.007	.066
Intercept	1	1546987.82	4492.458	.000	.956
SES	1	2652.723	7.704	.006	.036
Group	1	1136.444	3.300	.071	.016
Sex	1	903.120	2.623	.107	.013
Group*Sex	1	450.257	1.308	.254	.006

Table 10

ANOVA for Age Standardized Cognitive Crystallized Composite Score

	df	*MS*	*F*	*p*	*ES*
Corrected Model	4	2656.789	14.727	.000	.219
Intercept	1	1747627.78	9687.626	.000	.979
SES	1	9085.327	50.363	.000	.193
Group	1	17.716	.098	.754	.000
Sex	1	643.324	3.566	.060	.017
Group*Sex	1	386.521	2.143	.145	.010

As shown in Table 11, the group by sex interaction was not significant for balance testing, nor were the main effects for group or sex. Age was a significant covariate, with fewer errors shown by older children.

Table 11

ANOVA for Balance Error Scoring System (BESS) Total Score

	df	*MS*	*F*	*p*	*ES*
Corrected Model	4	341.732	4.410	.002	.098
Intercept	1	9268.452	119.610	.000	.425
Age of Injury	1	1009.376	13.026	.000	.074
Group	1	53.117	.685	.409	.004
Sex	1	99.505	1.284	.259	.008
Group*Sex	1	154.387	1.992	.160	.012

Discussion

Given the growing recognition of the public health burden posed by pediatric concussion and the possibility of sex differences in outcomes, the purpose of the study was to evaluate sex differences in acute outcomes among children and adolescents presenting to the ED for mTBI to determine how these differences might impact public health policy and clinical management.

Although girls were hypothesized to experience poorer outcomes post-mTBI relative to boys, the results do not fully support that hypothesis. Instead, the results indicate that though girls report a greater increase in self-reported somatic symptoms post-mTBI than boys (using OI as a comparison group), no significant sex differences were detected in self-reported cognitive symptoms or in objective outcomes (i.e., cognitive and balance testing). Additionally, although no hypothesis was offered regarding the influence of children's sex on parent ratings of children's symptoms, parents reported higher somatic symptoms for girls than boys, regardless of injury type. Thus, only self-report of somatic symptoms shows evidence of differential effects of mTBI by sex; no such differential effect was apparent for self-report of cognitive symptoms, parent symptom ratings, or objective outcomes.

While no study has directly examined how parent ratings of post-concussive symptoms are influenced by children's sex, one study found that adults were more likely to rate boys as experiencing higher levels of pain than girls despite the sexes reporting identical pain ratings (Earp et al. 2019). The researchers emphasize that while the adult raters were not parents of the target child and cannot emulate the parent-child relationship, healthcare providers need to be aware of potential gender biases in judgements concerning children's health experiences (Earp et al. 2019). Another study found only moderate agreement between child and parent ratings of both somatic and cognitive symptoms (Hajek et al., 2011). Correlations were higher for cognitive symptoms than somatic symptoms, and the researchers attribute this to somatic symptoms being less easily observed by parents (Hajek et al. 2011). Additionally, when comparing mean differences, children had significantly higher ratings of somatic symptoms than their parents (Hajek et al., 2011). These findings are relevant because they suggest that, despite moderate agreement between child and parent ratings, somatic symptoms may best be represented by the children's self-ratings.

In most respects, our results appear to contradict previous studies regarding sex differences in concussion outcomes as outlined in the literature review. Several explanations may help account for the different findings. First, our analysis included a comparison or control group, which allowed us to assess the effect of concussion relative to other injuries. Other studies that have found sex differences after concussion did not include control groups, making it difficult to conclude that sex differences were attributable to concussion specifically (Ledoux et al., 2018; Bazarian et al., 2010; Kostyun & Hafeez, 2015). Second, our analysis focused on children and adolescents, whereas the majority of previous research has focused on adults (Bazarian et al., 2010; Broshek et al., 2005; Brown et al., 2015; Covassin et al., 2012; Sicard et al., 2018). Additionally, our study evaluated multiple outcome variables, including both subjective symptom ratings and objective measures of balance and cognition. By contrast, most previous studies have focused exclusively on symptoms (Ledoux et al., 2018; Brown et al., 2015). Our study also included a more racially diverse sample than previous studies of mTBI. Thus, our study embodies several methodological strengths relative to previous research.

Limitations

This research, however, is subject to several limitations. The first is that the study was conducted at two EDs in Ohio among children aged 8 to 16 years old. Therefore, the results cannot be generalized to children with mTBI who do not seek emergency care, or to children outside this age range. The second limitation concerns statistical power. While samples sizes for the female mTBI, male mTBI, and male OI groups ranged from 48 to 95, the female OI group had only 26 participants, limiting statistical power. Additionally, attrition leading to participant bias was a concern given the longitudinal study design. However, as outlined in the results section, analysis of the different groups suggested limited bias, because the children who completed post-acute assessments were similar to the combined group of children who either did not consent in the ED or who consented but did not return for post-acute assessments. Additionally, the observational study design precludes any definite conclusions about causality. However, our assumption is that group differences in outcomes, as well as any differential effects by sex, are related to the mTBI because the groups were similar demographically and also on retrospective ratings of pre-injury symptoms and functioning. Finally, the data reported here were collected at only one time point, which makes the design cross-sectional. While the data was derived from a longitudinal cohort study, the analyses were limited to the post-acute visit because the hypothesis did not concern effects over time and the effects of concussion are most apparent closer to the time of injury.

Clinical Implications

Despite these limitations, our findings may have implications for clinical practice. Although the results show no sex differences in the effects of concussion on objective measures, significant sex differences in subjective measures following concussion are still important because they reflect patients' direct experiences. Somatic symptoms are sources of distress and suffering for patients, and healthcare providers need to recognize those symptoms in order to form a therapeutic physician-patient relationship. Healthcare providers need to be aware of their own gender bias in clinical practice, and not conclude that girls are over-reporters who dramatize somatic symptoms or that boys are under-reporters who suppress those same symptoms. Simply put, healthcare providers need to be aware that girls' and boys' reporting styles may be different and symptom reporting is influenced by many factors, including sex. Additionally, girls' propensity to report more somatic symptoms than boys may mean they require more aggressive treatment. If girls report more somatic symptoms, they deserve to be treated as if those symptoms are real bodily sensations that are causing distress. Therefore, within the clinical realm, our findings have implications for general awareness, diagnosis, and management.

Public Health Implications

As stated earlier in the literature review, pediatric concussions pose a public health threat because they are a preventable pediatric injury that can cause negative short and long-term outcomes. Therefore, the results from this study are relevant to public health because they can be used to guide implementation of policies related to pediatric injury prevention. In fact, Healthy People 2020 presented multiple objectives related to concussion and mTBI. In broad terms, Healthy People 2020 aims to reduce fatal and nonfatal traumatic brain injuries, motor vehicle crash-related injuries, pedestrian injuries, and fall-related injuries, and increase usage of age-appropriate vehicle restraint systems, safety belts, and helmets (Office of Disease Prevention and Health Promotion, 2019). More specific to sport-related concussion, Healthy People 2020's injury and violence prevention objective 26 calls to decrease sports and recreation injuries (Office of Disease Prevention and Health Promotion, 2019). Additionally, the Surgeon General's National Prevention Strategy calls upon individuals and families to use safety belts, bicycle and motorcycle helmets, and protective sports gear, and teach and practice transportation safety to promote injury free living (U.S. Department of Health and Human Services, 2019). While pediatric mTBI have a multitude of causes (e.g., motor vehicle collisions), recreational and sport related concussion are the leading cause of mTBI among the age group targeted in this study and will be the focus of the public health implications.

Given the objectives and aims of national injury prevention strategies, the current results may suggest the need for equipment changes to provide additional protection for female athletes. Healthy People 2020 directly addresses the issue of sport equipment under injury and violence prevention objective 27, by calling upon public and private schools to require students to wear appropriate protective gear when engaged in school-sponsored physical activities (Office of

Disease Prevention and Health Promotion, 2019). The results of this study can be used to deem what protective gear is appropriate for each sex. In regard to all sport-related activity, lacrosse is one of the only sports that has sex-specific gear requirements (U. S. Lacrosse, n.d.). While males are required to wear padded shoulder pads, gloves, helmets, and mouthpieces, females are only required to wear a mouthpiece and eye protection, whereas close-fitting gloves and headgear are optional (U. S. Lacrosse, n.d.). Additionally, headgear was only recently adopted in 2017 as being an optional measure and differs significantly from the highly protective helmets that men are required to wear (Acabchuk & Johnson, 2017). Although female lacrosse players are not allowed to body check, they have the second highest rate of concussion following American football (Marshall, Guskiewicz, Shankar, McCrea, & Cantu, 2015). Given these findings and the results of this study, perhaps female lacrosse players require the same level of protective equipment as male lacrosse players. In addition to lacrosse, female soccer players disproportionately experience concussions in comparison to other sports and are not required to wear any protective headgear. When evaluating the effectiveness of reducing concussion in soccer by wearing headgear, Delaney, Al-Kashmiri, and Drummond (2008) discovered a relative risk of 2.65 of self-reported concussion symptoms in adolescent soccer players not wearing headgear relative to those wearing headgear. Additionally, Enniss et al. (2018) conducted a systematic review and supported a strong recommendation of head protective equipment in pediatric athletes. While males should also be protected from sport-related concussion, our results suggest that public health officials should consider whether female athletes need additional provisions to offset the additional symptoms they endure as a result of concussion.

In addition to equipment changes, rule changes may be warranted given the results of the study. While rule modifications have been invoked to reduce concussions for both sexes (e.g., moving the football kickoff line up five yards, and removing team members from the opposing court during volleyball hitting warm-ups), there are few differences in rules between males and females within the same sport. The prohibition of body checking is the one of the only rules that directly addresses sex and concussion prevention. Hockey and lacrosse are the two sports that prohibit body checking for females at all levels. However, as stated earlier, soccer is a leading cause of concussion among females and there is no rule regarding heading the ball, which is the main contributor of concussion in this sport because it leads to head-to-head collisions. Our results may suggest further research is needed to investigate whether the prohibition of heading in women's soccer below a certain age or level would lead to a decrease in concussion incidence among young girl soccer players.

Outside of rule and equipment changes, sport-related concussion prevention can be a relatively difficult task. Therefore, it is essential to look at changes that can be made after a concussion has occurred to prevent long-term sequalae. In this sense, the results may suggest that female athletes require more time off from play: because if girls suffer more somatic symptoms than boys, then they may experience a protracted recovery, a finding found by Ledoux et al. (2018). Currently, return to play guidelines are consistent between the sexes and rely on the discretion of the healthcare professional signing off to allow the athlete to return to play (Harvey, 2013). Therefore, aligned with clinical implications, healthcare professionals who are trained and allowed to sign off on return to play decisions need to be made aware of sex differences in concussion outcomes so they can make appropriate decisions.

Recommendations

Ultimately, the study reinforces the need for further studies examining sex differences in post-mTBI outcomes during childhood and adolescence. While this study builds upon limited previous research, future research could expand upon the current study by examining the interaction of concussion and sex over time, by involving more participants to provide greater statistical power, and by extending the outcomes studied to include neuroimaging and fluid biomarkers, to tease out potential mechanisms for the sex differences found in somatic symptoms after concussion.

Conclusion

In summary, this represents one of the first studies to evaluate sex differences in mTBI post-acute outcomes among a pediatric ED population. The study examined post-acute outcomes in terms of symptoms, cognitive abilities, and balance. The results showed a larger effect of concussion (relative to orthopedic injuries) for girls than boys only for self-reports of somatic symptoms. No differential effects by sex were found for self-reports of cognitive symptoms, parent ratings of cognitive or somatic symptoms, cognitive abilities, or balance. The findings suggest only limited sex differences in the outcomes of concussion in a pediatric ED population, but may nonetheless have implications for clinical and public health.

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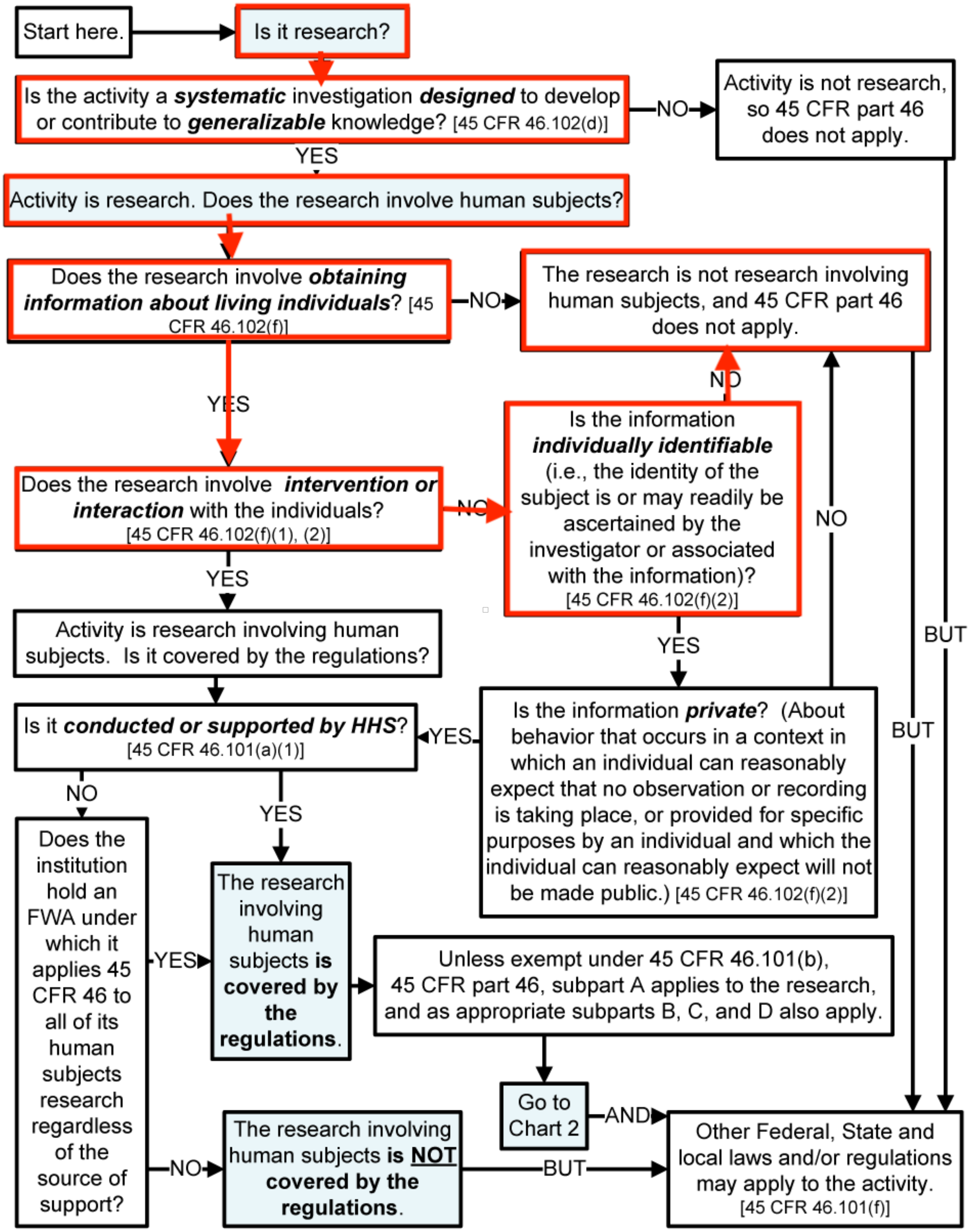
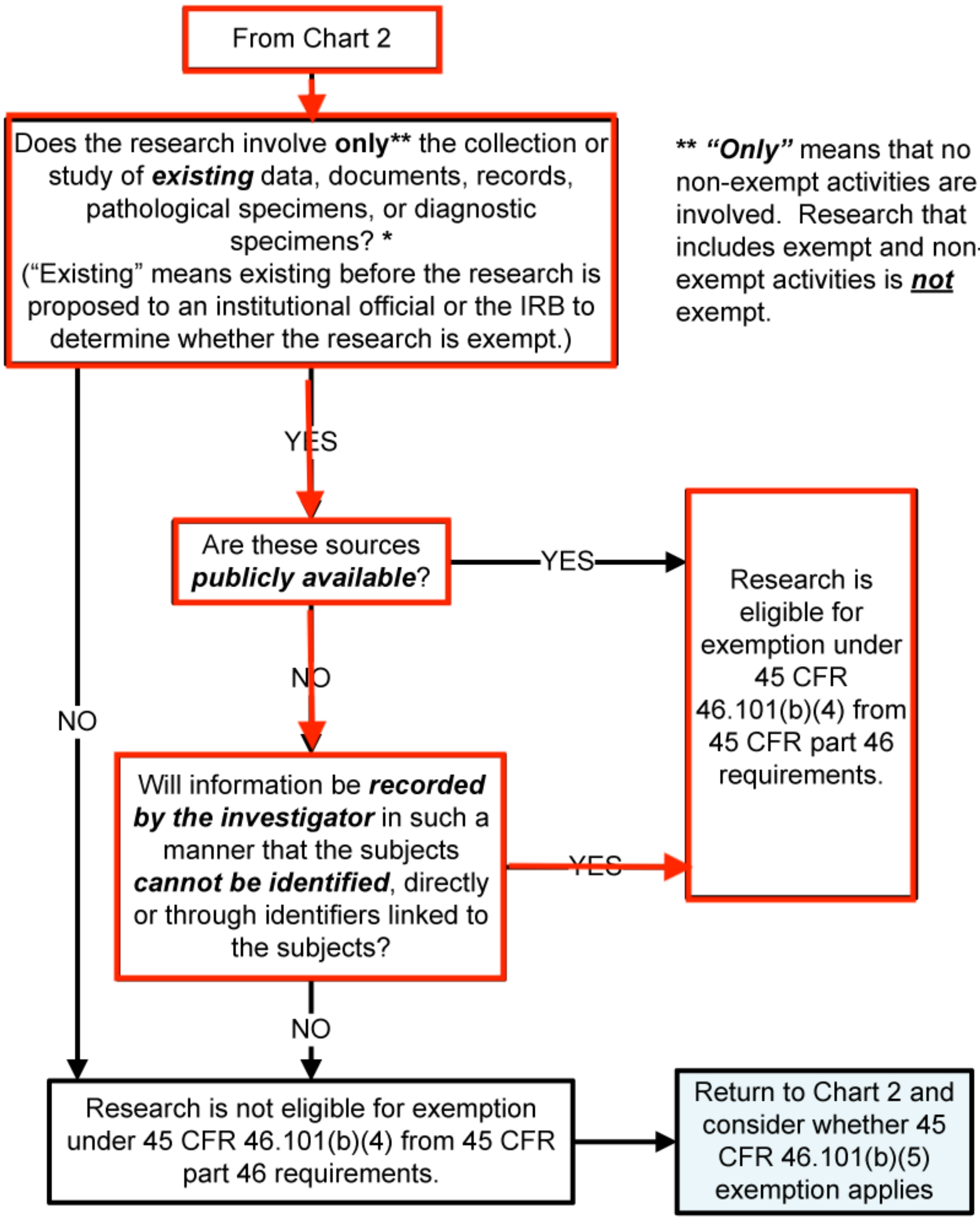
Appendix A: Human Subjects Regulations Decision Chart

Charts taken from https://www.hhs.gov/ohrp/regulations-and-policy/decision-charts/index.html





* Note: See **OHRP** guidance on research use of stored data or tissues and on stem cells at http://www.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-research-involving-stem-cells/index.html, and on coded data or specimens at http://www.hhs.gov/ohrp/regulations-and-policy/guidance/research-involving-coded-private-information/index.html for further information on those topics.

Appendix B: List of Competencies Met in Integrative Learning Experience

CEPH Foundational Competencies

Evidence-based Approaches to Public Health
1. Apply epidemiological methods to the breadth of settings and situations in public health practice
2. Select quantitative and qualitative data collection methods appropriate for a given public health context
3. Analyze quantitative and qualitative data using biostatistics, informatics, computer-based programming and software, as appropriate
4. Interpret results of data analysis for public health research, policy or practice
Communication
18. Select communication strategies for different audiences and sectors
19. Communicate audience-appropriate public health content, both in writing and through oral presentation
Interprofessional Practice
21. Perform effectively on interprofessional teams

WSU MPH Population Health Concentration Competencies

1. Use evidence based problem solving in the context of a particular population health challenge.
2. Demonstrate application of an advanced quantitative or qualitative research methodology.
3. Demonstrate the ability to contextualize and integrate knowledge of specific population health issues.