A CLINICAL DECISION-MAKING RULE FOR MILD HEAD INJURY IN CHILDREN LESS THAN THREE YEARS OLD

by

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Public Health Significance: The objective of this study is to establish a clinical decision-making rule for mild head injury in young children, an extremely common type of injury seen in emergency departments. These children appear to respond differently to mild head injuries and face different developmental issues than do older children and management guidelines remain unclear.

Methods: Subjects were 97 children less than three years old with mild head injury (ICD9 codes 800-804 and 850-854) and an initial Glasgow Coma Scale score of 14 or 15, consecutively evaluated at a Level 1 Pediatric Emergency Department. Demographic, injury, symptom and treatment characteristics were abstracted from the medical records.

A classification and regression tree (CART) program was used to identify characteristics that were correlated with intracranial injury (ICI) among children in the study. The information garnered from the tree was used to construct a clinical decision-making rule for the evaluation of very young children with mild head injuries. A cost analysis was done to determine potential cost savings from the new decision-making rule.

Results: Forty-six percent of the children were less than 12 months, 24% were 12-23 months and 30% were 24-35 months old at the time of injury. Three-quarters of all injuries occurred from falls. Almost 25% of the children had evidence of an ICI on the CT scan; more than two-thirds of the ICIs occurred in children less than 12 months old ($p=0.03$).

We examined multiple CART models to assess the impact of different misclassification penalties and missing data. The main parent node on the final CART model was the presence of vision changes; splits also occurred with the presence of scalp lacerations, vomiting, the child being inconsolable, sex and area of residence.

Minor changes in the way children without ICIs are treated could result in cost savings of as much as $90,000 per year.

Conclusion: While similarity exists between decision-making rules for older children and that found for this cohort, very young children have unique characteristics that merit further study and may require a separate decision-making process.

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PREFACE

It is impossible to undertake, and complete, a project such as this one without the assistance and support of many people. I would first like to thank my advisor, Dr. Thomas Songer, for his encouragement and advice. He was always available to assist with logistical and technical issues and kept me motivated and moving forward. I would also like to thank my committee members: Dr. Henri Ford, who provided not only the impetus for this study but also his wisdom and support throughout; Dr. Evelyn Talbott, who provided helpful input throughout this process but especially in the data collection phase; Dr. Stephen Wisniewski, who offered his statistical expertise and insight and who was always was able to get to crux of the problem; Dr. Laura Cassidy, who was an invaluable member of my committee, sharing her knowledge about pediatric injury and passion for children, as well as providing a welcome and much needed respite from this dissertation.

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1.0 INTRODUCTION

Head injuries are a significant public health issue. Most people have some type of head injury at least once in their lives, but rarely do they require a hospital visit. However, each year about two million people suffer from a more serious head injury, and up to 750,000 of them are severe enough to require hospitalization [1]. Traumatic brain injury (TBI) is a major cause of death and life-long disability in the United States and one of the primary causes of death in children, accounting for more than 3,000 deaths annually [2].

Head injuries vary in degree of severity. Some head injuries will only require care at home while others result in weeks- or months-long hospital stays. Children with head injuries are seen in disproportionate numbers at hospitals when compared to adults with head injuries, as more than 50% of the emergency department (ED) patients and 25% of the hospitalizations for head injuries are in children. The highest rate of ED visits is for children 0 - 14, and male rates are higher than female for all age groups [3]. However, 91.5% of children who sustain a head injury are treated and released from the ED [4]. These figures illustrate the tremendous amount of resources that it takes to treat head injuries among children annually.

Treatment guidelines are well-defined for children with severe injury and moderate head injury. The general practice is that these children get x-ray or CT imaging to determine the type and severity of damage to the brain and are admitted to the hospital for either observation or, if

needed, other diagnostic or surgical procedures. While mild head injuries constitute the majority of head injuries seen, physicians are unsure about the most appropriate way in which to treat them. Approximately 3% of mild head injury patients who initially present with normal levels of consciousness and functioning will develop an intracranial injury (ICI) within 24 hours of the initial injury, which can require surgery or lead to the death of the patient [5]. The fear among physicians is that they will miss this possible development and, if the patient is discharged home and subsequently develops an ICI, the prognosis will be more adverse than if this was detected while the patient was staying in the hospital.

One conservative approach for treating children with mild head injuries is to use diagnostic x-ray or CT imaging and an overnight in-hospital observation, similar to what is done with moderate head injuries, to ensure that no ICI is missed. However, because only 3% of mild injuries will deteriorate and develop an ICI, this results in a large overuse of resources. In an era of cost containment, there is a strong need to find a better approach for treating children with mild head injuries. There is a need to better identify which 3% of the children with mild head injuries will develop an ICI.

Efforts recently have been undertaken to determine which patients might deteriorate. Several clinical criteria have been identified that may help predict which symptoms are indicative of subsequent subacute ICI. However, the results of these efforts are not consistent nor are they specific enough to warrant a wide spread change in current decision-making. In particular, management guidelines for children less than three years old remain unclear. These children appear to be different than older children both with respect to presenting symptoms, because they are not able to verbalize many symptoms used to determine the severity of injury in older children and adults, and the rate of deterioration to ICI, which is the highest of any age

group. Thus, younger children may require different management guidelines. To date, no formal guidelines have been issued for this age group due to a lack of definitive results in the literature. Thus, current perspectives on the treatment of mild head injury recommend further study on predictive symptoms and evaluations of the cost effectiveness of new clinical decision-making rules.

The long-term effects of TBI in children differ in several ways from the effects in an injured adult because a TBI may alter the course of development of the brain and its functions. However, even children who suffer milder head injuries may face life-long disabilities. Recent studies have indicated that the incidence of moderate and severe disability in young people and adults one year after mild head injury is similar to that seen in survivors of moderate and severe head injury [6]. Previously learned information, which provides important building blocks for subsequent learning, is retained and used in adults sustaining a TBI, however, in very young children, these building blocks are relatively few, handicapping them as learners in comparison to similarly brain-injured older children or adults, who have larger foundations of intact information.

The effects of the TBI on the child may not be seen directly after injury, but only become apparent later in the child's life when the affected skills are needed. Because of this lag, the TBI may not be identified as the source of the problem and frequently such problems are dealt with as if they are due to learning disabilities or emotional causes rather than the TBI [7]. This highlights the importance not only of appropriately treating these children but also conducting follow-up for long-term effects.

This study used information on the injury characteristics and presenting symptoms of a cohort of children with mild head injuries treated at Children's Hospital of Pittsburgh, with

emphasis on those children less than three years old, to determine if a clinical-decision making rule could be developed which minimized the use of resources but identified correctly children whose injuries may deteriorate. Variables on patient and injury characteristics and presenting symptoms were abstracted anonymously from patient charts. A follow-up survey with the parents of these children was also conducted. This survey ensured that children with late-deteriorating injuries were not missed and also provided valuable information on the long-term effects of mild head injury in this cohort. As a final step, a comparison was done to evaluate the potential cost savings of using the new decision-making rule versus the usual standard of care.

2.0 EPIDEMIOLOGY OF INJURIES

To understand the public health significance of mild head injuries in children, it is helpful to look first at the wider spectrum of injury, then more specifically at head injuries, finally focusing on mild head injuries.

All injuries can be characterized as the abnormal transfer of energy. Injuries to the human body result from extreme levels of energy transfer to the body, in excess of the physiological threshold that can be tolerated. Injuries can be due to different types of energy transfer: mechanical, such as moving objects, thermal, electrical, radiation or chemical. If the injury energy is localized then the resultant injury is likely to be penetrating, such as a gunshot wound; if the injury energy is more diffuse then the resultant injury will likely be a non-penetrating or blunt injury, such as that sustained in a motor vehicle crash. Mechanical energy injuries are the most common, accounting for approximately three-quarters of all injuries [8].

2.1 PUBLIC HEALTH SIGNIFICANCE OF INJURIES

Injuries, including those to the head, typically fall in to two major categories: unintentional and intentional. Unintentional injuries are involuntarily caused by motor vehicle collisions, drownings, falls, burns or accidental poisonings. Intentional injuries result from deliberate actions, such as child abuse, family violence, suicide or homicide.

Blunt and penetrating injuries, often termed trauma, kill more people between the ages of one and 44 than any other disease or illness. As shown in Figure 1, which uses data from the National Center for Health Statistics, trauma deaths, including unintentional injuries and homicides, vary by age but are significant among children and young adults.

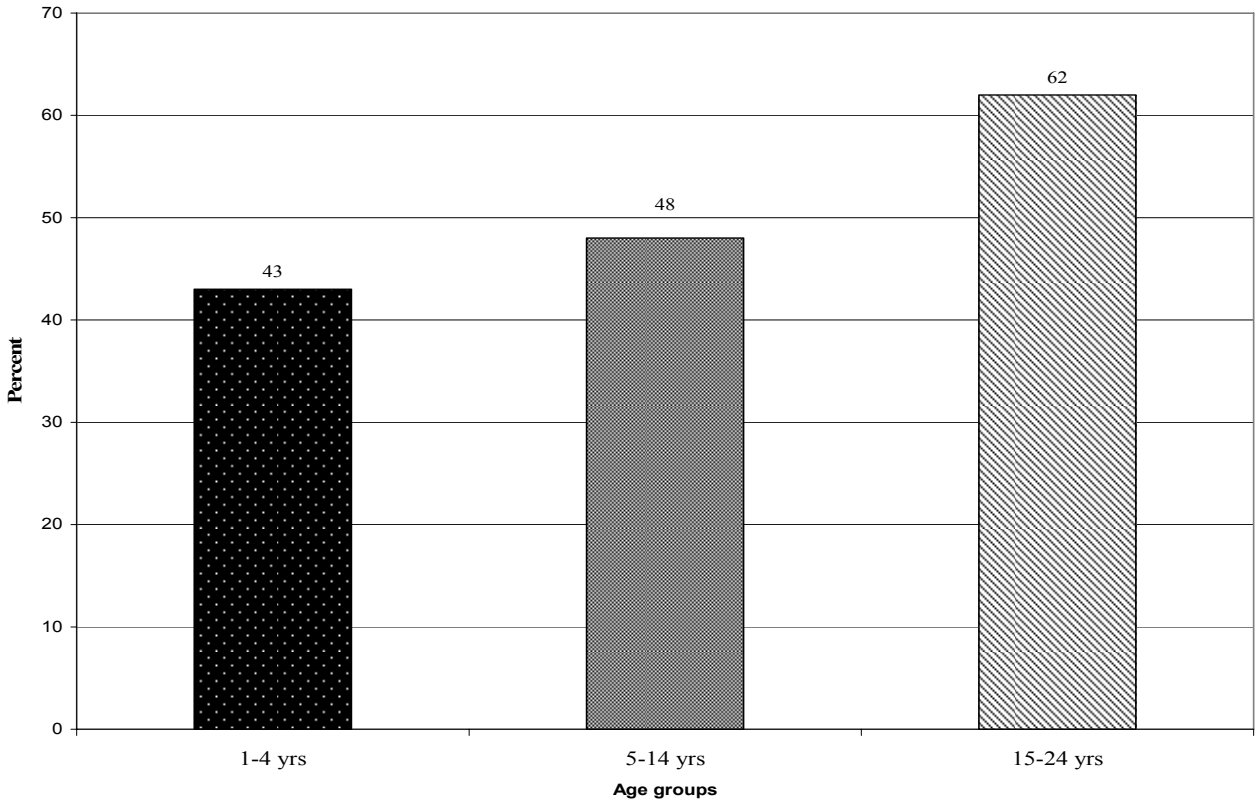
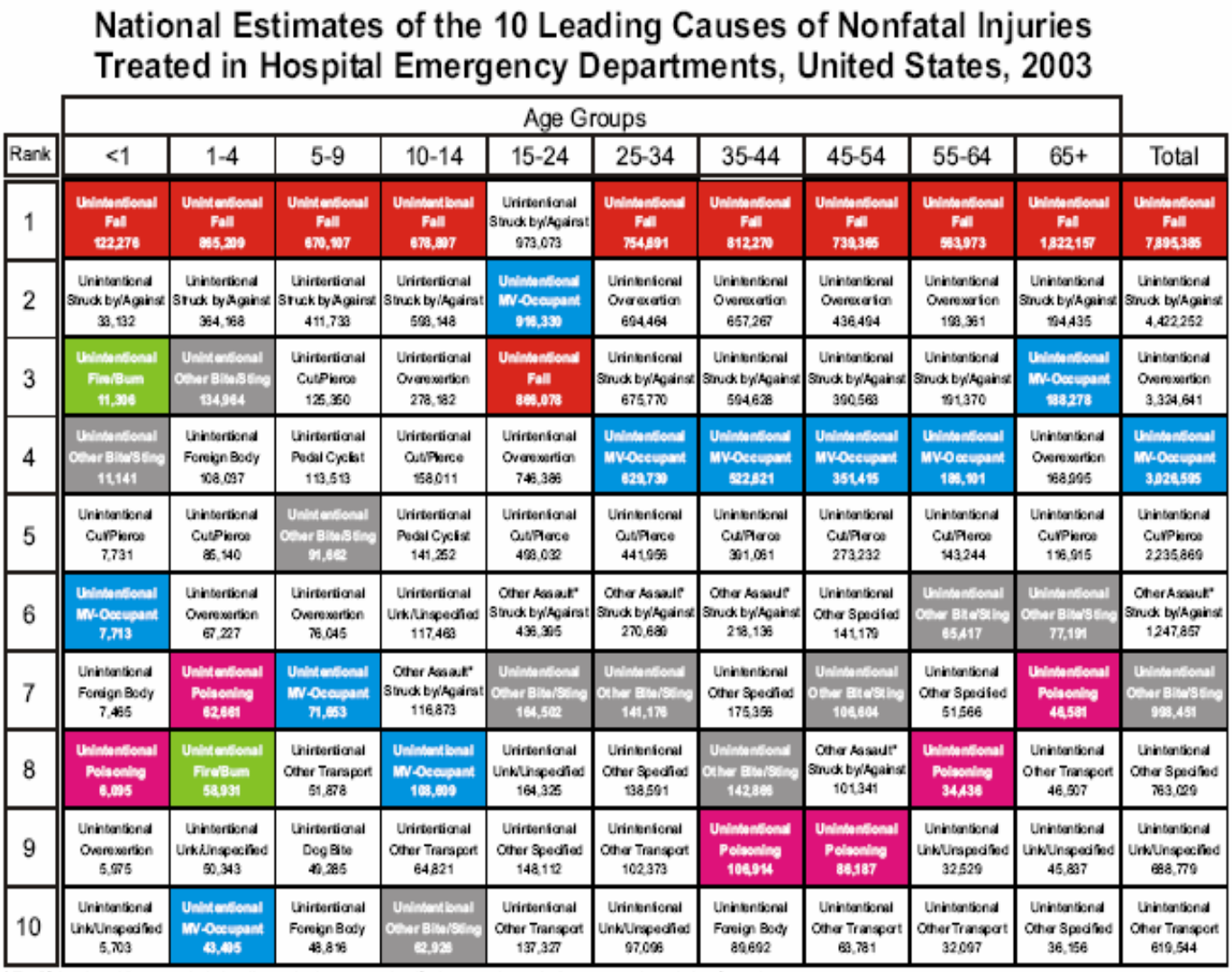


Figure 1. Percent of Deaths Due to Injury by Age

Unintentional injuries are a leading cause of death for Americans of all ages, regardless of gender, race, or socioeconomic status. In 1999, they were the leading cause of death for persons ages one to 34 years and the fifth leading cause of death overall. Nearly 98,000 people died in 1999 as a result of unintentional injuries, including such causes as motor vehicle crashes, falls, poisonings, drownings, fires, bicycle crashes, suffocation, or pedestrians being struck by motor vehicles [9]. Motor vehicle accidents are the leading cause of injury deaths [10].

In addition to death, millions of Americans experience nonfatal injuries each year. In 2000, one in 10 people experienced a nonfatal injury serious enough to require a visit to an emergency department [9], while one in four experienced any injury [10]. Falls are the leading cause of non-fatal injury, and in 2000, over 7 million people were injured by falls [11]. The second most common cause of non-fatal injury in 2000 for all people was unintentionally being struck by or against an object, followed by being involved in a motor vehicle crash and unintentional overexertion, such as lifting, pushing or pulling [11]. Serious injuries have a substantial impact on the lives of those injured, their families, and society. The physical and emotional effects of injuries can be extensive and wide-ranging, and in the case of disabling injuries, they can last a lifetime.

As shown in Figure 2, unintentional fall is the most common cause of non-fatal injury for all age groups, except 15-24 year olds among whom it ranks third. For children less than 15 years old, being unintentionally struck by or against an object is the second leading cause of injury. The third leading cause varies by age and includes unintentional fire/burns, unintentional bites/stings, unintentional cuts/pierce and unintentional overexertion.



National Estimates of the 10 Leading Causes of Nonfatal Injuries Treated in Hospital Emergency Departments, United States, 2003

	Age Groups										
Rank	<1	1-4	5-9	10-14	15-24	25-34	35-44	45-54	55-64	65+	Total
1	Unintentional Fall 122,276	Unintentional Fall 865,209	Unintentional Fall 670,107	Unintentional Fall 678,897	Unintentional Struck by/Against 973,073	Unintentional Fall 754,891	Unintentional Fall 812,270	Unintentional Fall 739,365	Unintentional Fall 563,973	Unintentional Fall 1,822,157	Unintentional Fall 7,895,385
2	Unintentional Struck by/Against 33,132	Unintentional Struck by/Against 364,168	Unintentional Struck by/Against 411,733	Unintentional Struck by/Against 598,148	Unintentional MV-Occupant 916,330	Unintentional Overexertion 694,464	Unintentional Overexertion 657,267	Unintentional Overexertion 436,494	Unintentional Overexertion 198,361	Unintentional Struck by/Against 194,435	Unintentional Struck by/Against 4,422,252
3	Unintentional Fire/Burn 11,306	Unintentional Other Bite/Sting 134,964	Unintentional Cut/Pierce 125,350	Unintentional Overexertion 278,182	Unintentional Fall 886,078	Unintentional Struck by/Against 675,770	Unintentional Struck by/Against 594,628	Unintentional Struck by/Against 390,563	Unintentional Struck by/Against 191,370	Unintentional MV-Occupant 188,278	Unintentional Overexertion 3,334,641
4	Unintentional Other Bite/Sting 11,141	Unintentional Foreign Body 108,097	Unintentional Pedal Cyclist 113,513	Unintentional Cut/Pierce 158,011	Unintentional Overexertion 746,386	Unintentional MV-Occupant 629,730	Unintentional MV-Occupant 522,821	Unintentional MV-Occupant 351,415	Unintentional MV-Occupant 186,101	Unintentional Overexertion 168,995	Unintentional MV-Occupant 3,026,595
5	Unintentional Cut/Pierce 7,731	Unintentional Cut/Pierce 85,140	Unintentional Other Bite/Sting 91,662	Unintentional Pedal Cyclist 141,252	Unintentional Cut/Pierce 499,032	Unintentional Cut/Pierce 441,956	Unintentional Cut/Pierce 391,061	Unintentional Cut/Pierce 273,232	Unintentional Cut/Pierce 143,244	Unintentional Cut/Pierce 116,915	Unintentional Cut/Pierce 2,235,869
6	Unintentional MV-Occupant 7,713	Unintentional Overexertion 67,227	Unintentional Overexertion 76,045	Unintentional Unk/Unspecified 117,463	Other Assault* Struck by/Against 436,395	Other Assault* Struck by/Against 270,680	Other Assault* Struck by/Against 218,136	Unintentional Other Specified 141,179	Unintentional Other Bite/Sting 65,417	Unintentional Other Bite/Sting 77,191	Other Assault* Struck by/Against 1,247,857
7	Unintentional Foreign Body 7,465	Unintentional Poisoning 62,661	Unintentional MV-Occupant 71,653	Other Assault* Struck by/Against 116,873	Unintentional Other Bite/Sting 164,502	Unintentional Other Bite/Sting 141,176	Unintentional Other Specified 175,356	Unintentional Other Bite/Sting 106,604	Unintentional Other Specified 51,566	Unintentional Poisoning 46,581	Unintentional Other Bite/Sting 998,451
8	Unintentional Poisoning 6,095	Unintentional Fire/Burn 58,931	Unintentional Other Transport 51,878	Unintentional MV-Occupant 108,809	Unintentional Unk/Unspecified 164,325	Unintentional Other Specified 138,591	Unintentional Other Bite/Sting 142,866	Other Assault* Struck by/Against 101,341	Unintentional Poisoning 34,436	Unintentional Other Transport 46,507	Unintentional Other Specified 763,029
9	Unintentional Overexertion 5,975	Unintentional Unk/Unspecified 50,343	Unintentional Dog Bite 49,285	Unintentional Other Transport 64,821	Unintentional Other Specified 148,112	Unintentional Other Transport 102,373	Unintentional Poisoning 106,914	Unintentional Poisoning 86,187	Unintentional Unk/Unspecified 32,529	Unintentional Unk/Unspecified 45,837	Unintentional Unk/Unspecified 688,779
10	Unintentional Unk/Unspecified 5,703	Unintentional MV-Occupant 43,495	Unintentional Foreign Body 48,816	Unintentional Other Bite/Sting 62,926	Unintentional Other Transport 137,327	Unintentional Unk/Unspecified 97,096	Unintentional Foreign Body 89,692	Unintentional Other Transport 63,781	Unintentional Other Transport 32,097	Unintentional Other Specified 36,156	Unintentional Other Transport 619,544

* The "Other Assault" category includes all assaults that are not classified as sexual assault. It represents the majority of assaults.

Source: National Electronic Injury Surveillance System—All Injury Program operated by the U. S. Consumer Product Safety Commission.

Produced by: Office of Statistics and Programming, National Center for Injury Prevention and Control, CDC.

Figure 2. Leading Causes of Nonfatal Injuries by Age from the National Electronic Injury Surveillance System, 2003

2.2 COST OF INJURIES

In addition to being widespread and common, injuries are also very costly. In 2000 dollars, injury costs were estimated at $406 billion [12]. These costs include direct medical care, rehabilitation, lost wages and lost productivity. The federal government pays approximately $12.6 billion annually in injury-related medical costs and approximately $18.4 billion in death and disability benefits. Insurance companies and other private sources pay approximately $161 billion in injury-related claims [13].

According to Rice et al [10], there are three types of cost related to injuries: direct, morbidity and mortality. Direct costs include the amount spent for personal health care, including hospital and nursing home care, physician visits, prescription drugs, physical therapy, ambulance and helicopter services, attendant care, and other expenses such as wheel chairs and appliances for injured people. Non-medical direct costs include expenditures for home modifications, vocational rehabilitation, and overhead and administrative costs for automobile and health insurance. Direct expenditures for medical and non-medical care amount to $80.2 billion, or 29 percent of the total lifetime cost of injury [12].

Morbidity cost is the value of goods and services not produced because of injury-related illness and disability. To the degree that injury prevents or deters people from producing goods and services in the marketplace, in the public sector, or in their homes, the value of morbidity losses is a cost borne by the society. Estimates of morbidity cost involve applying average earnings to work years lost and imputing a dollar value to housekeeping services for those unable to perform them. Morbidity cost is valued at $166.5 billion, or 41 percent of the total [12].

Mortality cost is the value of the lifetime earnings lost by all who are fatally injured and die prematurely. This cost is the product of the number of injury deaths and the expected value of future earnings with gender and age taken into account. This method takes into consideration life expectancy at the age of death, changing patterns of earnings at successive ages, varying labor force participation rates, imputed value for housekeeping services, and a six percent discount rate to convert aggregate earnings over a lifetime to present worth. This is a large component of injury because of the high degree of premature mortality associated with injury. Mortality cost amounts to $121.8 billion, or 30 percent of the total [12].

Injuries to children 0 to four years old account for 4% of the total expenditures or $16.2 billion, while injuries to children five to 14 years old account for 9% of the total or $36.5 billion. Because a childhood-injury related death deprives the world of the child's potential earnings, 77% of the total lifetime costs are due to productivity losses.

These estimates are based on the human capital approach to cost-of-illness measurement. This method takes into account all the medical care and related resources used for care, treatment, and rehabilitation of injured persons. Also included is the value of medical care resources used and earnings forgone because of illness, disability, and premature death due to injury. Included is an imputed value for housekeeping services. However, several important injury effects are not measured, such as pain and suffering, reduced productivity of family members and caregivers, and the value of volunteer services. Legal and court costs and property damage are also not included in this method [10].

2.3 INJURIES IN ADULTS

Some groups in the population are at higher risk for unintentional injuries. For example at any age, nearly twice as many males as females die of unintentional injuries each year. For some types of unintentional injury deaths, such as those related to residential fires, low-income groups are at increased risk. [9]

Overall, the risk of injury is highest among males; they sustain 57 percent of the injuries but account for 68 percent of the cost. Almost three in ten males living in the United States incur an injury in a year [10]. Males age 65 and older have the highest suicide rate and more than three-quarters of school homicide and suicide victims are male [13]. They are also higher risk than females for motor vehicle crashes, falls, drownings and homicide. In contrast, females are more likely to attempt suicide and more likely to be victims of rape or physical assault by a partner. They are also more likely to be murdered by an intimate partner. Women are also more likely to sustain hip fractures during a fall than are men [13].

Differences exist by race as well. The injury rate for African Americans is higher than any other racial group. African Americans between 15 and 19 years old die more from homicide than any other cause. African Americans are also most at risk from injury from residential fire and are more than twice as likely as whites to be injured in pedestrian accidents. The injury rate for Hispanics is lower than for non-Hispanics except for pedestrian fatalities and injuries resulting from violence among Hispanic youth [13]. American Indians/Alaska Natives have the

highest unintentional injury death rate [9]. American Indian/Native American women are more likely than any other racial group to report being raped or physically assaulted. Teens and young adults in this group are at increased risk for suicide [13].

More injuries occur among adults aged 25-44 than in any other age group, and the lifetime cost is highest at $164 billion, 40 percent of the total cost. Injury to persons aged 15-24 ranks second, accounting for 20 percent of total cost [12]. The morbidity loss for persons disabled because of injury amount to 86 percent of the total economic cost lost, valued at $141 billion [12]. The pedestrian death rate for people 65 or older is higher than any other age group [13]. Falls are the leading cause of injury among this age group; hip fractures are among the most serious type of injury resulting from a fall. Older adults have had the highest rate of suicide since 1933 when such data keeping began, accounting for nearly 20 percent of all suicides [13].

2.4 INJURIES IN CHILDREN

Infants and young children are at risk for many injuries, due in part to characteristics typical of all children, including curiosity and limited physical coordination and cognitive skills. In 2000, a study of the incidence of injury among children was published using data from the National Health Interview Survey from 1987 to 1994 [14]. The investigators found that 20.6 million children in the United States were injured each year or approximately 25 injuries per

100 children. This translates to 56,000 nonfatal injury episodes each day that require medical attention or limit children's activity. For fatal injuries, the rate was 38 children per 100,000. Danseco et al. [14] also found that the nonfatal injury rate for males was higher than the rate for females, the fatal injury rate for males was more than twice that of females, and that injury rates increased with age.

Motor vehicle injuries are the leading cause of death among children one to four years old and children five to 14 years old [13]. Nearly half of all children under four who died in motor vehicle accidents were riding unrestrained; only 6% of children four to eight years old ride in booster seats as recommended. Nearly two-thirds of children 15 years old and younger who died in alcohol-related motor vehicle crashes were riding with the drinking driver.

Children under five years old account for more than half of the accidental poisonings and are among those most at risk to be injured in residential fires. They also account for more than 75% of the maltreatment fatalities [15]. During 2003, approximately 906,000 children were determined to be victims of child abuse or neglect by the child protective services agencies [15]. Head trauma, often due to violent shaking by caretakers, is the leading cause of death and disability among abused children and infants. In 2003, an estimated 1,500 children died from maltreatment [15]. Drowning is the second leading cause of death among children five to 14 years old; also nearly, one-third of bicyclists killed in traffic crashes are in this age group. For children ages 10 to 14 years old, suicide is the third leading cause of death; the suicide rate for children 10 to 14 increased 109% between 1980 and 1997. [13]

Teens and young adults are affected by injuries, both intentional and unintentional more than any other age group. Homicide rates are highest at this age. Motor vehicle-related injuries and deaths are also significant. In 1998, 21% of drivers ages 15 to 20 years old who died in motor vehicle crashes had blood alcohol concentrations of at least 0.10% [13].

Another major cause of injuries among both children and young adults is sports. Using data from the 1997 and 1998 National Hospital Ambulatory Medical Care Survey, there were an average annual estimated 2.6 million emergency visits for sports-related injuries by persons between the ages of five and 24 years [16]. As a proportion of all kinds of injuries presenting to the ED, sports-related injuries accounted for more than one fifth of the visits by persons five to 24 years old. The sports-related injury visit rate for male patients was more than double the rate for female.

Visits from sports-related activities for this age group were more frequent for basketball and cycling compared with other categories (e.g., baseball, skateboarding, and gymnastics). Compared with non sports-related injuries for this age group, sports-related injuries were more likely to be to the brain or skull and upper and lower extremities. Patients with sports-related injuries were more likely to have a diagnosis of fracture and sprain or strain and less likely to have an open wound. They were also more likely to need diagnostic and therapeutic services, especially orthopedic care [16].

3.0 HEAD INJURIES

To better understand the significance of injuries to the head, it is helpful to understand the definition, clinical factors and natural history of head injuries. A traumatic brain injury (TBI) is defined as a blow or jolt to the head or a penetrating head injury that disrupts the function of the brain. Not all blows or jolts to the head result in a TBI. The severity of such an injury may range from mild, or a brief change in mental status or consciousness, to severe, with an extended period of unconsciousness or amnesia after the injury.

The Centers for Disease Control and Prevention have defined traumatic brain injury as "an occurrence of injury to the head that is documented in a medical record, with one or more of the following conditions attributed to the head injury:

- observed or self-reported decreased level of consciousness,
- amnesia,
- skull fracture,
- objective neurological or neuropsychological abnormality, or
- diagnosed intracranial lesion;

or as an occurrence of death resulting from trauma, with head injury listed on the death certificate, autopsy report, or medical examiner's report in the sequence of conditions that

resulted in death". [17] This definition encompasses a broad range of head injuries in terms of severity and mechanism.

3.1 BIOLOGY OF HEAD INJURIES

The brain floats within the cerebrospinal fluid in the skull, which is a rigid container. This means that, when the head is subjected to significant forces, the brain can be injured by the skull. As with other injuries, there are two main types of traumatic brain injury (TBI), penetrating and blunt, or closed head, injury. A penetrating injury, such as a gunshot wound to the head, results from an object breaching the skull and entering the brain. A blunt injury is one without any penetrating injury to the brain. It can result from a direct blow to the head or from a moving head being rapidly stopped, such as when a person's head hits a windshield in a car accident. The kind of injury the brain receives in a closed head injury is determined by whether or not the head was unrestrained upon impact and the direction, force, and velocity of the blow. If the head is resting on impact, the maximum damage will be found at the impact site. A moving head will cause a "contrecoup injury" where the brain damage occurs on the side opposite the point of impact, because of the brain slamming into that side of the skull.

A closed head injury also may occur without the head being struck, such as when a person experiences whiplash. This type of injury occurs because the brain is a different density than the skull, and can be injured when brain tissues hit against the rough inner surface of the

skull. Both blunt and penetrating head injuries can cause swirling movements throughout the brain, tearing nerve fibers and causing widespread bleeding or a blood clot in or around the brain. Swelling may raise pressure within the skull and may block the flow of oxygen to the brain. [1]

Both blunt and penetrating injuries result from significant forces acting on the brain [1] and can cause injury by direct mechanical effects on the cellular components of the brain or by shear-type forces on axons. The brain can experience significant rotational forces, which may also lead to shearing injuries [1]. The shearing forces disrupt fragile structures in the brain, primarily axons and small vessels. These injuries cause transport failures in the axon, leading to swelling or death of the axon [18]. Vascular injury can disrupt small veins, causing hemorrhaging or edema [19].

3.2 SECONDARY BRAIN INJURIES

While much damage is caused by the initial injury to the brain, or the primary injury, the brain may also be damaged by what are referred to as secondary injuries. The initial structural injury caused by the impact on the brain may include fractures, hematomas, contusions, lacerations or axonal injury, however, secondary brain injury occurs in the hours or days following the trauma and includes swelling, increased intracranial pressure or hematoma. Because these secondary

injuries may cause as much, if not more, damage than the primary injury, patients with head injuries are closely monitored for such changes.

Bleeding inside the skull may accompany a head injury and cause such additional damage. If the clot is located between the bones of the skull and the covering of the brain, or dura, it is called an epidural hematoma; between the dura and the brain tissue itself, it is called a subdural hematoma. In other cases, bleeding may occur deeper inside the brain; this is called an intracerebral hemorrhage or intracerebral contusion. These types of intracranial injuries (ICIs) can occur if a blood vessel between the skull and the brain ruptures, pressing against brain tissue and causing symptoms from a few hours to a few weeks after the injury. If the hematoma is apparent within 48 hours on the initial injury, it is called subacute; if it appears within two weeks of the injury it is called chronic. Subacute and, especially, chronic intracranial injuries are a major concern when treating head injuries, because the patient is often discharged from the hospital during this crucial period. Patients could deteriorate at home and only return for care after the intracranial injury has resulted in additional brain damage.

3.3 SEVERITY OF HEAD INJURIES

The distribution by severity of head injuries in the population is often characterized by a pyramid. Severe, fatal injuries are relatively few in number and are therefore at the top of the pyramid. Hospitalizations from injury occur in greater numbers than fatal injuries and make up the next level in the pyramid. Injuries that require medical attention are an even more frequently occurring type of injury but are less severe than the two previous levels. The final, bottom layer of the pyramid are injuries that can be treated at home or those not requiring treatment; this type of injury is the most common and least severe of all injury types. There is also a reverse pyramid, or inverted pyramid of injury reporting. This pyramid indicates that while we have very good mechanisms in place to capture severe or fatal injuries or even injuries requiring hospitalizations, we are less likely to capture injuries requiring only medical attention or those requiring home care. This same pyramid is true when considering head injuries. As shown in the Figure 3, 1.4 million head injuries occur each year and most that require health care result in a visit to the Emergency Department (ED), indicating that these are generally milder head injuries [4].

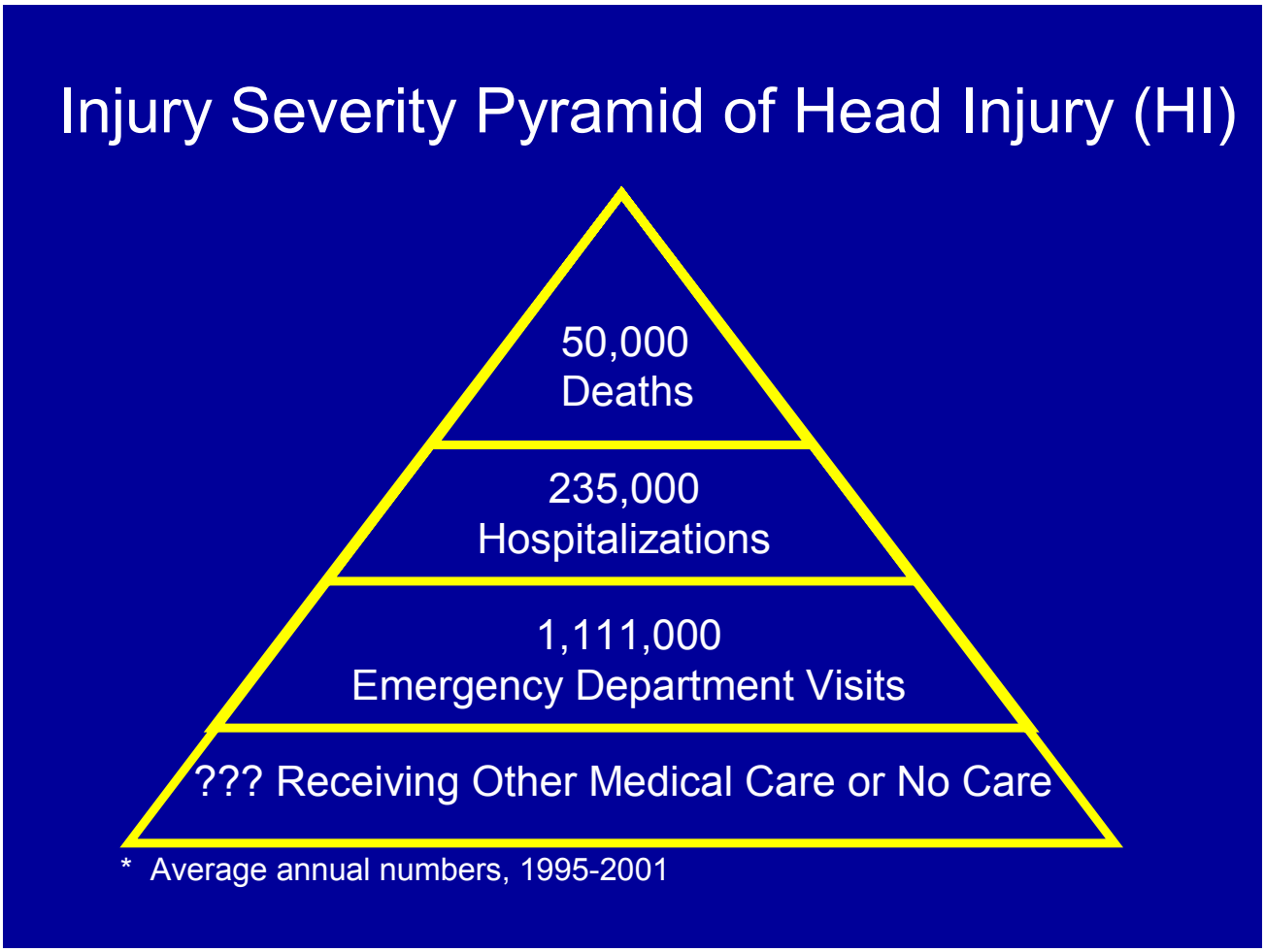


Figure 3. Injury Severity Pyramid of Traumatic Brain Injuries in the United States [4]

The severity of TBI is primarily defined by the acute injury characteristics rather than the severity of symptoms at points after the trauma [18]. Historically, clinicians and investigators have classified traumatic brain injury as mild, moderate, and severe using the Glasgow Coma Scale (GCS), a scoring system which was designed to assess coma and impaired consciousness [20-22]. Currently, there are no more biologically objective measures of severity of head injury than GCS score, loss of consciousness [23] and post-traumatic amnesia (PTA) [18]. However, the GCS has been validated in many studies and is used as a predictor in injury severity scores as well as a predictor of outcome [24]. The GCS is used to rate three aspects of functioning: eye opening, motor response and verbal response, as shown below.

Table 1. Glasgow Coma Scale Scoring System

Eye Opening Response	Spontaneous--open with blinking at baseline	4 points
	Opens to verbal command, speech, or shout	3 points
	Opens to pain, not applied to face	2 points
	None	1 point
Verbal Response	Oriented	5 points
	Confused conversation, but able to answer questions	4 points
	Inappropriate responses, words discernible	3 points
	Incomprehensible speech	2 points
	None	1 point
Motor Response	Obeys commands for movement	6 points
	Purposeful movement to painful stimulus	5 points
	Withdraws from pain	4 points
	Flexion to pain	3 points
	Extension to pain	2 points
	None	1 point

Clinicians evaluate patients on these three aspects of functioning and add the components together for a final GCS score. These scores are used as a guide of injury severity and types of treatment required. A GCS score of 3 indicates the most severe injury, describing a person who is totally unresponsive or comatose; a GCS score of 15 indicates no impairment in functioning using this scale. Severity of injury is typically categorized into three levels: mild (or minor), moderate and severe. Patients with scores of 8 or less are classified as severe; scores of 9 to 12 are moderate; and scores of 13 to 15 are mild [24].

Because young children may not have the ability to give a proper verbal response to cues or commands, for children under five the verbal response criteria are adjusted as follows:

Table 2. Revised Glasgow Coma Scale Scoring for Children (Verbal Component)

SCORE	2 to 5 Years	0 to 23 Months
5	Appropriate words or phrases	Smiles or coos appropriately
4	Inappropriate words	Cries and consolable
3	Persistent cries and/or screams	Persistent inappropriate crying &/or screaming
2	Grunts	Grunts or is agitated or restless
1	No response	No response

While there has been some debate over the usefulness of the pediatric GCS, recent studies have indicated that the score compared favorably when used in children two years old or younger as when used in older children for the evaluation of blunt head trauma [25]. In 2005, Holmes et al. [26] published a study which evaluated the performance of the pediatric GCS in preverbal children with blunt head injury. They prospectively enrolled 2,043 children under 18 years old; 327 of whom were less than three years old. They found that the area under the ROC curve for predicting traumatic brain injury on CT scan by the GCS score was 0.72 in children less than three years old and 0.82 in older children. They also found that the area under the ROC curve was 0.97 in children less than three years old and 0.87 in older children when predicting those injuries in need of acute intervention. The authors concluded that the pediatric GCS score compares favorably with the standard GCS in evaluating children with blunt head trauma and is particularly accurate for predicting those children in need of acute intervention.

The Infant Face Scale (IFS) was developed to overcome the limitations of the GCS in pre-verbal children [27]. It further modifies the verbal component of the GCS to include different types of crying interspersed with periods of wakefulness and modifies the motor component to be more appropriate for infants. While these changes may improve the usefulness of such a scale in very young children, the IFS has not yet been standardized.

3.4 CLINICAL BACKGROUND OF MILD HEAD INJURIES

Mild traumatic brain injury (MTBI) is commonly referred to in the literature as concussion, minor head injury, minor brain injury, minor head trauma, or minor TBI [21, 28, 29]. Mild TBI is one of the most common neurological disorders [30] [31]. The causes of mild TBI are the same as severe TBI [18]. The strength of the force acting on the brain, though, is usually lower. Compared to severe injuries from high levels of force applied to the head, mild head injuries result from a lower level of force and are likely to result in a brief alteration of mental status, such as confusion or disorientation, loss of memory for events immediately before or after the injury, or brief loss of consciousness. The definition of a mild head injury has been the subject of debate and controversy [32, 33]. Typically loss of consciousness and post-traumatic amnesia are features [18]. However, they do not have to be present to define MTBI. Headache, nausea and vomiting are also frequently associated with mild head injury [31].

In 1993, the Mild TBI Committee was convened by the American Congress of Rehabilitation Medicine to determine a working definition [33] and established the following: A patient with mild traumatic brain injury is a person who has had a traumatically induced physiological disruption of brain function as manifested by at least one of the following:

any period of loss of consciousness;

any loss of memory for events immediately before or after the accident;

any alteration in mental state at the time of the accident (e.g., feeling dazed, disoriented, or confused);

and focal neurological deficit(s) that may or may not be transient but where the severity of the injury does not exceed the following: loss of consciousness of

approximately 30 minutes or less; after 30 minutes, an initial Glasgow Coma Scale (GCS) of 13-15; and posttraumatic amnesia (PTA) not greater than 24 hours.

As defined by the committee, loss of consciousness is not required to fulfill the definition of a mild TBI. Mechanisms of injury like whiplash and assault are more common in mild TBI than in severe TBI because they rarely generate the amount of force necessary for a severe injury.

When compared to the definition of traumatic brain injury as proposed by the CDC, it is apparent that the definition of mild head injury proposed by the MTBI Committee is more inclusive. This definition allows head injuries that occur without loss of consciousness whereas the CDC definition seems to preclude those types of injuries.

4.0 EPIDEMIOLOGY OF HEAD INJURIES

Head injuries account for a substantial proportion of all injuries. For example, head injuries account for one-third of all injury related deaths [34] and for two-thirds of the trauma deaths in hospitals [35]. Each year, more than 2 million Americans sustain a TBI, or eight times the number of people diagnosed with breast cancer and 34 times the number of new cases of HIV/AIDS each year [13]. Seventy to ninety percent of TBIs are mild cases [36], and the majority of these are among people who present to the hospital but are not admitted, a very common occurrence in mild head injuries [35]. A review by Bazarian et al of the National Hospital Ambulatory Medical Care Survey (NHAMCS) from 1998-2000 found that the incidence of isolated mild TBI cases presenting to EDs was estimated at 153,296 per year or 56.4/100,000 [36]. These patients use a tremendous amount of hospital resources, as shown in the study, where 44.3% of the patients received CT scans and 23.9% received x-rays [36].

4.1 PUBLIC HEALTH SIGNIFANCE OF HEAD INJURIES

Head injuries are an important public health problem in the United States. Because the problems that result from TBI, such as those of thinking and memory, are often not visible, and because awareness about TBI among the general public is limited, it is frequently referred to as the "silent epidemic" [4].

Most people have had some type of head injury at least once in their lives, but rarely do they require a hospital visit. However, each year about two million people suffer from a more serious head injury, and up to 750,000 of them are severe enough to require hospitalization [1]. Injuries to the head can be caused by traffic accidents, sports, falls, workplace accidents, assaults, or bullets, among others. Brain injury is most likely to occur in males between ages 15 and 24, usually because of car and motorcycle accidents. About 70% of all accidental deaths are due to head injuries, as are most of the disabilities that occur after trauma.

These figures indicate that head injuries place a tremendous burden on healthcare and personal resources. Millions of families are affected by a head injury each year; even if the injury is not severe, the effects of the injury can influence personal relationships, finances and work.

4.2 COST OF HEAD INJURIES

Max and colleagues [37] analyzed U.S. incidence and cost data for all TBIs that resulted in hospitalization or death in 1985. MTBI accounted for $16.5 billion or 44% of the estimated total lifetime cost ($37.8 billion) of TBIs that year. The CDC updated these estimates using incidence data from 1995 and adjusting for inflation to yield an estimated total cost of $56 billion, $16.7 billion of which was for MTBI [38].

For several reasons, this figure underestimates the economic burden MTBI poses on the United States. First, it does not include injuries treated in EDs; this omission is significant, given the decreasing trend to hospitalize persons with TBI. Additionally, it excludes injured persons treated in other, non-hospital medical care settings, such as private physicians' offices. The costs of lost productivity and lost quality of life; and indirect costs borne by family members and friends who care for persons with MTBI. Because our knowledge about the current cost to society from TBI and MTBI is limited [38], these additional costs need to be quantified and need to be studied to address the impact of the changes in health care practices that shifted the care of less severe forms of TBI from inpatient care to ED and outpatient treatment and follow-up [39]. Unfortunately, there is currently no population based outcome information available to document the amount of disability that is sustained by children with mild TBIs.

4.3 HEAD INJURIES IN ADULTS

Traumatic brain injury (TBI) is a major cause of death and life-long disability in the United States. The annual incidence of TBI in the United States has been estimated to be 180-220 cases per 100,000 population [1]. Table 1 shows the average annual number of emergency department visits, hospitalizations and deaths for traumatic brain injury by age group. The table indicates that rate of ED visits for the very young are almost double that of other age groups and that the highest rates of hospitalization and death are among 15-19 and 20-24 years olds and those greater than 75 years old.

Table 3. Average Annual Numbers, Rates, and Percentages of Traumatic Brain Injury-Related Emergency Department Visits, Hospitalizations, and Deaths, by Age Group, United States, 1995–2001[4]

Age (yrs)	Emergency Department Visits*			Hospitalizations†			Deaths		
	Number	Rate§	Row %	Number	Rate§	Row %	Number	Rate§	Row %
00-4	200,000	1,035.0	92.4	15,000	79.9	7.1	1,099	5.7	0.5
5-9	122,000	603.3	91.5	11,000	53.0	8.0	628	3.1	0.5
10-14	113,000	567.0	90.2	11,000	56.9	9.0	957	4.8	0.8
15-19	129,000	661.1	81.2	25,000	129.1	15.9	4,756	24.3	3.0
20-24	79,000	429.3	77.3	18,000	98.7	17.8	5,092	27.5	5.0
25-34	146,000	357.6	79.4	30,000	76.3	16.4	7,720	18.9	4.2
35-44	129,000	291.0	77.7	29,000	66.5	17.7	7,619	17.2	4.6
45-54	75,000	211.3	74.1	20,000	57.6	20.2	5,776	16.4	5.7
55-64	35,000	150.9	65.7	14,000	61.6	26.9	3,927	17.0	7.4
65-74	29,000	158.1	59.1	16,000	86.8	32.5	4,188	22.5	8.4
>75	54,000	336.4	51.0	44,000	272.1	41.3	8,095	50.6	7.7
Total	1,100,000	403.1	79.6	235,000	85.2	16.8	49,900	18.1	3.6

* Persons who were hospitalized, died, transferred to another facility, or who had an unknown disposition were excluded.
† Persons who died while being hospitalized were excluded.
‡ Numbers, rates, and percentages may not sum to totals due to rounding.
§ Average annual rate per 100,000 population.

When the patterns of care for TBI are evaluated, the incidence of mild traumatic brain injury (MTBI) seen in emergency departments (EDs) appears to have increased, almost doubling from 216 per 100,000 in 1991 [34] to 392 per 100,000 in 1996[3]. In contrast, MTBI hospitalizations appear to have declined from 130 per 100,000 to 51 per 100,000 between 1980 and 1994 [39]. Of those who were hospitalized, 146,000 stayed in the hospital for only one night [34]. These findings may reflect changes in hospital practices that shift the care of persons with less severe forms of TBI from hospital inpatient care to ED and outpatient treatment. Such changes indicate a growing need to document and study MTBIs treated in EDs and outpatient settings. Cases not admitted to the hospital account for approximately 80% of all head injuries and about half of all disability days [35].

Of the persons sustaining a head injury each year, an anticipated 80,000 to 90,000 will have a long-term disability [40]. In 1999, an estimated 5.3 million Americans were living with a permanent TBI-related disability [40]. Approximately one in four adults with TBI are unable to return to work within one year of the injury [13]. Disabilities following a TBI are often called an invisible epidemic because they are not always readily apparent; they can however impact the patients' cognitive, emotional, sensory and motor abilities, as well as affecting vocational, social and familial relationships [40].

According to a 1999 publication based on 1980-1995 National Hospital Discharge Survey data, the risk of a TBI is highest among the very young (<5 years), the very old (>75 years) and adolescents [39]. Males are almost two times as likely as females to sustain a head injury [39]. In general, 50% to 60% of all brain injuries result from motor vehicle-related incidents [41], both for occupants and pedestrians/bicyclists [42]. Motor vehicle accidents are also the leading cause of hospitalization for TBI; other causes include falls, sports or recreational

activities and inflicted injuries [43]. In children age two years or younger, physical abuse is the most common cause of serious head injury. In children age three years and older, falls and motor vehicle, bicycle, and pedestrian accidents are responsible for most traumatic brain injuries.

4.4 HEAD INJURIES IN CHILDREN

Different considerations must be taken into account when examining children with head injuries rather than adults. Children have unique developmental, anatomic and physiologic factors that create a unique response to a head injury [44]. They have a larger head-to-body ratio, thinner skull and weaker neck muscles than do adults; their skeletal structure may allow traumatic forces to extend more deeply which can create injury without fracture. Skull fractures occur in 10%-20% of children with mild head injuries [44].

Brain trauma is one of the primary causes of death in children, accounting for more than 3,000 deaths annually [2]. Children between 15 and 19 years old have the highest fatality rate [39]. Data from the National Hospital Ambulatory Medical Care Survey from 1995-96 indicate that the overall incidence rate for ED visits for TBI was 392/100000 or over 1 million ED visits per year [3]. The highest rate of ED visits was for children 0-14, again male rates were higher than female [3]. Among children less than 14, 37,000 children are hospitalized and 435,000 are seen in emergency departments annually [2]. These numbers indicate that head injury in

children has tremendous public health significance, yet controversy exists regarding the evaluation and treatment of these children.

For children and young adults, TBI is the type of injury most often associated with death from unintentional injury. Existing data indicate that the rates of hospital admissions and emergency department visits for head injuries are several times higher among children than the general adult population [35], with the highest rates among children under age five [45] and among children in lower socioeconomic groups [46]. Approximately 80% of the hospital admissions for head injuries are for mild head injuries.

In 2003, Hawley and colleagues [47] published a population-based prevalence report on traumatic brain injury in children in the UK. Participants were children admitted for 24 hours or more with a TBI; severity was assessed using the British Society of Rehabilitation Medicine Classification of Medicine. Minor injury was defined as unconscious for less than 15 minutes and a GCS 13-15; moderate injury was unconsciousness for more than 15 minutes and a GCS 9-12 and severe injury was unconsciousness for 6 hours or more and a GCS 3-8.

They found that 2/3 of head injury victims were male, that injuries were most prevalent among children whose families live in deprived areas and that the most common mechanism was falls, followed by motor vehicle accidents. Their findings indicate that 280/100,000 children per year are admitted for 24 hour observation with a TBI, of these, 84% are mild, 9% moderate and 7% severe. One to two year olds were the most commonly admitted age group and children under two accounted for 18.5% of the injuries. The authors concluded that these statistics should help in future planning for health resources and studies for mild cases [35].

Long-term impact studies have indicated that the incidence of moderate and severe disability in young people and adults one year after mild head injury is similar to that seen in

survivors of moderate and severe head injury [6]. This raises the possibility that cognitive and motor function continues to deteriorate for months and possibly years after the initial injury in long-term survivors of head injury [48]. Although the largest group of TBI survivors are young adults in their prime working years, many survivors, particularly those with a severe TBI, do not return to work. Estimates vary widely, ranging from a low of 12.5% to as high as 80% who do not return to work; the ability to return to work is highly correlated to the post-acute functional limitations of the survivor [48], [49]. In a national survey in Canada, 66% of TBI survivors living in the community reported an ongoing need for assistance with some activities of daily living,75% were not working, and 90% reported limitations or dissatisfaction with social integration [48].

The CDC estimates that more than 10,000 children become disabled from a brain injury each year. Children who suffer a severe brain injury may lose part(s) of muscle, speech, vision, hearing, or taste function depending on the area of brain damage. Long- or short-term changes in personality or behavior may also occur. These children require life-long medical and rehabilitative (physical, occupational, or speech therapy) management.

Children tend to have more diffuse injuries than adults, and traumatic intracerebral hematomas are less common in children than in adults. In addition, early posttraumatic seizures are more common in children than in adults. Overall, children have much lower morbidity and mortality rates from traumatic head injury compared to adults [1].

TBI may also alter the course of development of the brain and its functions. It had been previously thought that the plasticity of the child's brain offered hope that damaged tissue and areas of deficit would be bypassed in the child's brain by other parts taking over for the areas

that no longer work as well, known as the Kennard Principle [50]. Recent research suggests that this may not be the case [51] [7].

Previously learned information, which provides important building blocks for subsequent learning, is retained and used in adults sustaining a TBI, however, in very young children, these building blocks are relatively few, handicapping them as learners in comparison to similarly brain-injured older children or adults, who have larger foundations of intact information. The effects of the TBI on the child may not be seen directly after injury, but only become apparent in the child's life when, during the course of the child's development, the affected skills are needed. Because of this lag in the emergence of problems, TBI may not be recognized as the cause of the problem. Frequently, such problems are dealt with as if they are due to learning disabilities or emotional causes rather than the TBI.

While typically expected to clear within days, the deficits incurred from a mild head injury can take 6 to 12 weeks to clear completely [18]. For injuries that are moderate or severe, recovery may take several months or years or, in some instances, may never totally resolve back to levels of functioning prior to the injury [18].

5.0 CLINICAL DIAGNOSIS AND MANAGEMENT OF HEAD INJURIES

Because head trauma is common among children and adults, it results in a significant number of visits to physicians' offices, emergency departments and hospitals. While most patients have mild to moderate trauma, appropriate evaluation requires considerable clinical judgment and is one of the most challenging problems confronting pediatricians and emergency physicians.

As stated earlier, when treating patients with head injuries it is crucial not only to treat the effects of the primary injury but also to manage patients in such a way as to eliminate or minimize secondary injury. The determination of the severity of the head injury is based primarily on the GCS score; GCS scores of 3-8 are severe, 9-12 are moderate and 13-15 are mild. Each of these types are treated differently both for primary and secondary injuries.

5.1 PATIENTS WITH MODERATE OR SEVERE HEAD INJURY

Patients with severe head injuries have life threatening injuries and acute treatment is critical. Severely head injured patients are often in need of urgent anesthetic assessment as airway compromise and/or reduced lung ventilation is likely [52]. They are routinely hospitalized and require intensive care. Treatment measures include intravenous fluids, elevation of the head, sedation, intracranial pressure monitoring or surgery if required [52]. Neurosurgeons recognize that all of the brain damage does not occur at the moment of impact but continues during the next hours or days and much of the treatment is designed to minimize these delayed insults. The Brain Trauma Foundation, as part of their guidelines for the management of severe traumatic brain injury, recommends monitoring intracranial pressure to prevent intracranial hypertension [53]. While some guidelines for the treatment of severe traumatic brain injury are still controversial, including the optimal level of cerebral perfusion pressure, patients with severe head injuries are routinely admitted to the hospital and referred to the trauma team. When patients have a moderate head injury, their condition is not as life-threatening as with a severe injury. Treatments are often the same, though, and designed to minimize secondary brain damage. Because the existing controversies regarding the treatment of severe and moderate head injuries are more clinical in nature, they will not be discussed further here.

5.2 PATIENTS WITH MODERATE TO MILD HEAD INJURIES

In the past, physicians believed that patients with mild head injury (GCS scores of 13-15) were at very low risk of deterioration or severe intracranial injury [54]. As summarized below, the results of these studies have indicated that patients with GCS score of 13 or 14, while typically classified as having mild head injuries, have a different risk for secondary injury compared to patients with a GCS score of 15 and, for example, should routinely get a CT scan. Thus, many clinicians will argue that studies of treatment protocols should not include GCS 13 or 14 patients with GCS 15 patients.

Stein et al [54] found, in a study of 658 patients with mild head injury defined as GCS 13-15 and brief LOC or amnesia, that patients with a GCS score of 13 due to a head injury so commonly have abnormal CT scans that these injuries should be classified as moderate rather than mild. In 2000, Wang et al [55] published the results of a prospective, population-based study including 13 trauma centers and 94 receiving hospitals of all children with head injuries to determine the incidence of intracranial lesions in children with a GCS score of 13 or 14 and closed head injuries. Their population included 8488 children less than 15 years old who were transported to designated centers that were participating in the study; 209 had field GCS 13 or 14, 86% of these had CT scans, 27.4% (44) had abnormal results and 68% (30) of these had ICI. The investigators did not find any significant differences in the injury profile of patients with GCS scores of 13 or 14. They also attempted to use symptoms as predictors of intracranial injury but found that deteriorating mental status, LOC, cranial fracture and external fractures all had poor positive (range 0.173-0.500) and negative predictive values (range 0.809-0.875). They

concluded that all children with GCS 13 or 14 should undergo CT scanning because of the poor predictive values of clinical criteria, the higher frequency of ICI and the severe implications of missing a child with an ICI.

In 2001, the Emergency Medical Journal published a best evidence topic report reviewing the evidence for the use of CT scans in children with mild head injury [56]. The review searched and analyzed the current literature to determine the relevance of using CT scanning on children with mild head injuries. After reviewing the literature, the authors concluded that ICI occurs with normal GCS and focal neurology. They recommended that all head injured children with GCS score <15 undergo CT scanning as well as asymptomatic infants with head injury and scalp hematoma.

While formally considered part of "mild" head injuries, GCS scores of 13 or 14 are now often considered moderate, and the management guidelines are different than those for persons with a GCS score of 15. While there is no consensus statement for this group, they typically are given a CT scan and may be admitted for observation [57]. There is considerable debate, though, about the appropriate management guidelines for subjects with GCS scores of 15. The current study will focus on children with GCS scores of 15 to help answer this debate.

5.3 PATIENTS WITH MILD HEAD INJURY (GCS SCORE OF 15)

There has been much discussion about the need to redefine mild TBI from a clinical and management perspective. Even when mild head injury is limited to patients with a GCS score of 15, researchers and clinicians cannot agree on the homogeneity, diagnosis or treatment of this group.

In 1997, Hsiang attempted to refine the definition of mild head injury, traditionally defined as a GCS score of 13-15, with a prospective study of 1360 patients with head-injury (age 11-92) and GCS 13 -15 [58]. Results showed that patients with lower GCS had more serious injury; there was a statistically significant trend across GCS for positive radiographic findings, neurosurgical interventions and poor outcome. The authors then divided all of the patients into low and high-risk groups. Mild head injury (low risk) was defined as GCS 15 without radiographical abnormalities; high risk was GCS 13, 14, or 15 with abnormalities. The authors concluded that this simple definition should be in wider use to avoid confusion regarding mild injuries.

A follow-up letter to the editor [59] refuted this definition as too simplistic and noted that using radiographic imaging only would result in missed abnormalities in this cohort as well as many other published studies. Stein noted that loss of consciousness appeared to be a more reliable predictor of the need for CT scan than radiographic abnormalities both in terms of safety and cost-effectiveness.

Homer and Kleinman [60] conducted a literature review to find articles on the best approach for identifying mild head injury in children. A total of 108 articles were abstracted, however, variations in the definitions used for mild head injury in the studies precluded pooling.

The authors found that the prevalence of ICI ranged from 0-7%. Their analysis revealed that children with no clinical symptoms are at lower risk than those with symptoms but that the magnitude is inconsistent. The authors noted that CT scan is the most sensitive and specific tool for detection of intracranial abnormalities, especially when compared to skull radiographs. However, they concluded that the existing literature does not provide enough evidence to publish any evidence-based recommendations.

In 2002, Batchelor et al published the results of a meta analysis of literature to look for case-control studies on both adult and child patients with GCS scores of 15 [61]. The authors hypothesized that GCS score is an insensitive way of defining a heterogeneous group of injuries and they attempted to develop an extended GCS 15 category. They identified three studies that fit their entrance criteria, which were full papers, using a case-control design and including documentation of symptoms. The meta analysis indicated that the symptoms of severe headache, nausea and vomiting were most likely to indicate CT abnormality with GCS 15. Dizziness and blurred vision were not predictive of abnormal CT. The authors concluded that the results of this study provide a framework on which GCS 15 patients can be stratified according to risk. However, the restrictions of the entrance criteria and the small number of studies included make these results difficult to generalize and have not led to widespread utilization.

5.4 DIAGNOSTIC TOOLS FOR HEAD INJURIES

Because the time frame for treating head injuries is so critical and the results of poor or delayed care can be so devastating, it is important that head injuries are quickly and accurately diagnosed. With moderate or severe traumatic brain injury (TBI), the diagnosis is often self evident because of the severity of the incapacitation. Unfortunately, if physicians are not vigilant, mild traumatic brain injury may not be diagnosed until the individual begins to have problems in what were once easy tasks or social situations.

Several evaluations can be done that allow physicians to make a determination of the severity of the head injury and the most appropriate treatment. When the patient is unconscious, the duration or length of coma [23] may be used to assess the severity of TBI and predict outcome. The longer the length of coma, the more severe the injury is. An LOC of longer than about 6 hours after admission reflects severe injury; between 20 minutes and 6 hours suggests moderate injury; between about and 20 minutes reflects a mild-moderate brain injury and LOC of less than about one minute reflects mild injury. Also, a neurological examination may show signs indicating the severity of injury such as increased reflexes and muscle tone (spasticity), abnormal movements (tremors), difficulty swallowing, or slurring of speech, all of which may indicate a moderate to severe head injury. Patients with mild head injury often have very minor or no neurological deficits.

Various imaging tools have been used to assist in the identification and diagnosis of head injuries. Neuroradiological tests using computer-assisted brain scans help visualize damage to the brain. The most common of these is computerized tomography, or CT scan, an x-ray

technique that produces a cross-sectional image of the brain. CT scans can detect physical changes in the brain such as hematomas and swelling, which may require immediate treatment. The procedure is painless and takes 15 to 45 minutes, during which the patient must lie completely still.

The literature review below helps to assess the effectiveness of various types of evaluations and imaging techniques in the diagnosis of mild head injury.

5.4.1 Skull Radiographs

Originally, studies documenting the most effective way to diagnose mild head trauma focused on using skull radiographs, or skull x-rays, as the imaging mode of choice. In 1987, Masters et al. [62] described the results from a multidisciplinary panel of experts convened to review evidence regarding use of skull radiographs for head trauma. Seventy-five peer-reviewed published articles were included in the review; the authors then used these articles to identify high and low risk groups of head injuries. The review found that high risk was for patients who had a severe open or closed-head injury with clinically obvious findings; the authors recommended that these patients be referred for emergency CT scan, neurological consultation or both. Low risk patients were defined as asymptomatic or having one or more of the following: headache, dizziness, scalp hematoma, laceration, contusion or abrasion; radiographic imaging is not recommended for this group. A medium-risk group, which the authors had trouble defining specifically, may benefit from skull radiographs.

The management strategy designed by the review was validated in a prospective study of 7035 patients with head trauma in 31 participating EDs. The investigators collected data from the emergency room and from a three-month follow-up evaluation. Skull x-rays were obtained for 58% of the cohort; 21.5% of the high, 4.2% of the moderate and 0.4% of the low-risk groups had skull fractures. The medical records of the patients were then reviewed for indications of intracranial injury. No ICIs were discovered in low-risk patients, 4% of the moderate and 29% of the high-risk patients had indications of intracranial injury. Intracranial injury occurred in the absence of a skull fracture but the presence of a fracture had a higher association of ICI. The authors concluded that the management strategy is valid and that physicians can use this strategy both to identify patients who do not require imaging and those in need of urgent neurological consultation, CT scanning or both.

Other studies were also conducted to determine the validity of skull radiographs as an imaging tool for head injury. Rosenthal et al. [63] published a retrospective study of 459 children with normal neurological exam after head injury with LOC; they considered this level of injury as moderate for this study. Of the 459 children in the study, 358 had skull radiographs taken and 14% were found to have fractures. The investigators found intracranial complications in six children (1.3%); all of these children had skull fractures. The authors concluded that with the absence of a skull fracture, alert children can be safely discharged home from the ED with a competent adult. This study did not validate their findings with CT scans.

In 1990, Teasdale [64] conducted a prospective study of risk factors in 8406 children and adults with head injury, and 1007 who had had an operation for acute intracranial hematoma following a head injury, to determine factors influencing the risk of intracranial hematoma. Children comprised 28.3% of the head injured patients (2380/8406) and 11.8% of the surgical

patients (119/1007) who were defined as 14 years old or younger. The groups were stratified according to their level of consciousness: oriented and alert (equivalent to GCS 15), impaired consciousness (GCS 9-14) and comatose (GCS 3-8). Results indicated that children overall were at less risk than adults for intracranial abnormalities and analyses were kept separate for the two groups. The presence of a skull fracture and changes in consciousness identified groups at differing degrees of risk; the highest risk in children were those in a coma with a skull fracture, the highest risk for adults were those with skull fractures. The authors concluded that while children appear to be at lower overall risk of intracranial hematoma than adults, their patterns and indicators of risk are the same. They recommended that the guidelines for managing head injury in adults be applied to children; they also recommended revising guidelines to include earlier scanning as more CT facilities become available.

While authors during this period recognized the importance of imaging as a screening tool for head injuries, many also realized that the current modality, skull radiographs, lacked specificity and better methods were needed [65] [66] [67]. The results of these studies are difficult to interpret in the diagnosis of mild head injury as defined here because they included patients with GCS scores of 13, 14 and 15. However, clearly from these results even patients with GCS scores of 15 had injuries that deteriorated and required more careful observation and management to prevent significant secondary injury. In 2005, Reed et al. [68] examined the effect on the detection of intracranial injuries in children aged one to 14 years old with head injury of an institutional policy change that had eliminated the use of skull x-rays to assess these patients. They found that the effect of this policy change was a slight increase in the use of CT scans, no change in the rate of positive CT scans and no change in the admission rate. They

concluded that skull x-rays can be safely abandoned as a scanning modality in children with head injuries with no significant adverse effects.

5.4.2 CT Scans

Cranial computed tomography (CT) is an imaging technique that uses special x-ray equipment to obtain images from different angles and then join them together to show a cross-section of body tissues and organs. CT scanning provides more detailed information on head injuries and other brain diseases than do regular radiographs and can show bone, soft tissues and blood vessels in the same images. This is an obvious advantage over radiographs by allowing physicians to better determine if a head injury may have led to any internal injuries, such as hematomas.

Many of the studies involving the evaluation of CT scan as a tool to identify significant mild head injury used mixed populations of children and adults and had patients with GCS scores of 13, 14 and 15 [69]. While these studies typically found that CT scan use was warranted in patients with mild head injury [70] [71] [72] [73] [74] [75] [69], it was difficult to determine if the same results would be found if only children with GCS scores of 15 had been included.

Several studies, using children with GCS scores of 15 and mild head injuries, found that when these children had normal CT scans they could be discharged home safely rather than admitted to the hospital [76] [77] [78] [79] [80]. Mandera [81] furthered this recommendation by suggesting that CT scans be given to all children with MTBI because of the high occurrence of ICI and the likelihood of missing an injury using symptoms only.

Determining which children can be discharged rather than admitted is a priority in the treatment of mild head injury. The high volume of these types of injuries and the costs associated with admitting and observing them are often an unnecessary burden on the healthcare system. CT scans were also studied to determine if their use could effectively separate which patients would require admission and observation and which could be discharged [82] [83] [84].

The cost of CT scans for all patients must also be a consideration. Stein et al [85] reviewed the records of 658 consecutively admitted patients age 3-74 with mild head injury to calculate the hypothetical costs of different courses of treatment. They compared 3 hypothetical situations: 1) if all patients were given skull radiographs and admitted for observation, 2) if all patients were given CT and those identified as having ICI were admitted, and 3) if all patients were given skull radiographs and only those with fractures were given CT scans. The authors concluded that every patient with LOC or amnesia should be given a CT scan; if the scan is normal, then the patient can safely be discharged home. Using this protocol, physicians would be able to discharge safely more than 85% of patients presenting in the ED with mild head injury. In addition, using the CT scan as a triage device was considerably less expensive than admitting all patients for observation. The authors recommended that this treatment protocol be considered optimal care and noted that it was cost-effective.

The identification and treatment of mild head injuries in children is recognized as a problem both nationally and internationally. In 1999, results of an international pilot study of mild head injury were published [86]. The authors found that , in their cohort of 2478 patients age 0 to 15, 56.4% of head injuries were mild but that these children underwent the most skull x-rays and admissions yet had the lowest incidence of brain damage (1.6%) of any of the 3 groups of head injuries (mild, moderate, severe). They concluded that mandatory admission for head

injured children with no negative findings on CT is not warranted and that new guidelines for the treatment of mild head injury need to be developed.

In 2001, Murgio et al published a follow up to their study, which included 4690 children age 0 to 15 with head injuries [87]. In this update, they found that 79.1% of the injuries were mild. CT scans were performed on 14.3% of children and 236, or 35%, of these were abnormal. Of these, 23.3% of the abnormal CT scans were on children with mild injuries (GCS 14-15) and positive scans were more common in children 3-9.

Another important issue to consider is physicians' willingness to use CT scans as an imaging modality for mild head injuries. To address the growing use of CT scan for mild head injury, Graham [88] anonymously surveyed a cross-section of emergency physicians in Canada. They had three main interests: (1) to assess their use of and attitudes toward radiographic clinical decision rules (2) to determine the use of CT head and cervical spine radiography and (3) to determine the potential for acceptance of a new rule for CT scanning in mild head injury patients.

The results indicated that more than 95% of responding physicians, 81% of those surveyed, use an existing clinical decision-making rule and would consider using a new rule. They found that 85% of the respondents did not agree that all patients with mild head injury should get CT scan and that only 3.5% refer these patients for a CT scan. They also found that 97% would be willing to consider using a well-validated CT scan rule for mild head injury; however, 52% said that a new rule should be 100% sensitive.

The availability of CT has improved in recent years and has led to both a lower threshold for obtaining CT and the publication of more studies involving the use of CT to investigate head trauma. However, CT scans do involve radiation exposure and, in fact, are a relatively high-dose

procedure [23]. In an examination of the institutional rates of CT scans, Mettler et al. [23] found that the rate of CT scans had increased from 6.1% to 11.1% of all radiology procedures during the 1990's. They also found that 11.2% of the scans were performed on children 0-15 years of age. They caution that this rate is probably higher than previously thought and higher than that found in previous studies (4%), potentially indicating an increase in the number of children referred for CT scans.

While CT scans account for approximately 1/10 of the total number of radiological procedures, they contribute 2/3 of the collective radiation dose [89]. As shown in cohorts of atomic bomb survivors, children are more sensitive to the effects of radiation than are adults [90]. This appears to be due to two main reasons: children have more time to express the cancer than do adults and children have more dividing cells and radiation acts on those cells. Brenner estimated that the lifetime attributable cancer mortality risk following a single 200 mAs dose head CT scan was 0.05%, or 1 in 2,000, in children less than one year old at the time of the scan; this rate dropped to 0.01% (1 in 10,000) in children 15 years old [89]. As might be expected, brain and thyroid cancer risks are the highest.

The difficulty with these data is that the individual benefit of a CT scan almost always outweighs the individual risk. On a more widespread basis, recent concern about possible exposure to radiation, especially among children, has resulted in recommendations to limit exposure [91] [92] [93]. Researchers have found, however, that more targeted scanning or lower dose CT scanning can reduce the impact of the radiation exposure in young children [159]. These concerns, as well as concerns about the high cost of CT scans, led researchers to look at clinical symptoms as a way to identify head injuries that may deteriorate.

5.4.3 Clinical Symptoms

While the use of CT scans for mild head injury is becoming more commonplace, there is also interest in determining if significant head injuries can be predicted from the patients' presenting or clinical symptoms. Some early studies used mixed populations of children and adults or adults only. These studies identified many different symptoms, common with mild head injuries, which appeared to be associated with ICI (Table 4).

Table 4. Clinical symptoms found to be predictive of intracranial injury

Predictive Symptom	Study Population	
	Adults and Children	Children Only
Patient unresponsive	Reinus et al 1993 [94]	None
Focal neurologic deficit	Reinus et al 1993 [94] Borczuk et al 1995 [95]	Davis et al 1994 [96] Rivara et al 1987 [97] Quayle et al 1997 [98]
Depressed sensorium	Reinus et al 1993[94]	None
GCS score	Harad et al 1992 [99] Mikhail et al 1992 [100]	Dietrich et al 1993 [101] Klassen et al 2000 [102] Rivara et al 1987 [97]
Age	Borczuk et al 1995 [95] Jeret et al 1993 [103] Mikhail et a1 992 [100]	None
LOC	Moran et al 1994 [104] Harad et al 1992 [99]	Dietrich et al 1993 [101] Klassen et al 2000 [102] Rivara et al 1987 [97] Quayle et al 1997 [98]
Amnesia	Harad et al 1992 [99]	Dietrich et al 1993 [101]
Tissue injury	Borczuk et al 1995 [95]	None
Mechanism of injury	Harad et al 1992 [99] Jeret et al 1993 [103]	Klassen et al 2000 [102] Davis et al 1994 [96]
Nausea	Miller et al 1997 [105]	None
Vomiting	Miller et al 1997 [105]	None
Skull fracture	Moran et al 1994 [104] Borczuk et al 1995 [95] Jeret et al 1993 [103] Miller et al 1997 [105]	Simon et al 2001 [106] Quayle et al 1997 [98]
Headache	Mikhail et al 1992 [100]	None
No symptoms were predictive	Falimirski et al 2003 [107] Vilke et al 2000 [108]	Adams et al 2001 [79] Schunk et al 1996 [109] Roddy et al 1998 [110] Simon et al 2001 [106]

As shown in Table 4, many symptoms, alone or in combination, have been found to predict ICI. However, no one symptom has universally been shown to be predictive and some studies found that no symptoms were predictive. The authors of many of the above studies noted that ICI may occur with no signs or symptoms, especially in children less than one and that ICI in neurologically normal children needs further study.

Other authors determined that a normal head CT, where no ICI is found, could predict which children could be safely discharged home [111] [112] [113]. However, these studies included children with GCS scores of 13-15 and had small sample sizes (n=62, n=55 and n=401, respectively). When larger, more homogeneous populations were investigated, results indicated two important results: that some clinical factors may be predictive of ICI and that children with GCS scores of 15 still had ICIs. However, other studies could not identify any predictive factors and emphasized the need for all children with mild head injuries to have CT scans; these studies recommended prospective patient enrollment to understand better the relationship between mild head injury, clinical symptoms and ICI.

In 1995, Ramundo et al published the results of a prospective study of 300 children age 0-18 years (mean 9 years) with closed-head injury and CT scans to identify clinical features that were highly positively or negatively predictive of abnormalities [114]. Eighteen percent of the children had abnormal CT scans. Suspected abuse, focal motor deficit and papillary asymmetry were each more than 50% positively predictive of abnormalities in all age groups; LOC more than 5 minutes was positively predictive in children older than two. The only patients to undergo surgical interventions were those with CT scan abnormalities. The authors concluded that no single factor can predict abnormalities with certainty but those children suspected of having been abused, with focal motor deficits or pupillary asymmetry should be imaged. The authors also

noted that judicious use of CT scans ultimately reduces unforeseen morbidity and minimizes resultant intensive care costs.

Quayle et al [115] published an article that reviewed the existing literature and found that symptoms were not predictive of ICI because, although they are common in children with ICI, they are also found in children without ICI. They also reviewed the toddler and infant literature and found that the presence of scalp hematomas indicates the possibility of skull fractures and those children less than two years old cannot be evaluated using the same criteria as older children. The literature on head injuries due to child abuse showed that it is more common in children under two; 25%-65% of head injuries in this age were presumed inflicted. Their final recommendations for children with mild head injury included careful physical examination and history taking; physicians should obtain CT scans for children with altered mental status, focal neurological deficits, basal skull fracture, seizures or depressed skull fracture. Skull radiographs were not recommended. The authors concluded that children with normal CT and neurological exams could be safely discharged home without admitting for observation.

Dunning et al [116] also reviewed the literature on the predictive value of clinical symptoms in a meta-analysis. They identified 16 articles that met their criteria: control or nested case-control studies of children with head injury who had skull radiographs, recording of symptoms and CT scans. Skull fracture, focal neurology, LOC and GSC score <15 were statistically significant predictors of ICI; headache, vomiting and seizures were not statistically significant and, in fact, vomiting had an inverse relationship with ICI. Kupperman [117] noted in a commentary to the Dunning article that the results may not translate well in to clinical practice because of the variation in the definition of mild head injury and the use of univariate analyses in the studies pooled.

To derive and validate a set of clinical criteria that could be used to identify patients with minor head injury who did not need a CT scan, Haydel et al conducted a two-phase study [118]. Phase one consisted of 520 patients age 3-90 (average age 36) with minor head injury, defined as brief LOC, GCS score of 15 and normal neurological exam; all patients had a CT scan (per institutional policy) and were evaluated for the following clinical symptoms: age, headache, vomiting, drug/alcohol intoxication, short-term memory deficits, post-traumatic seizure, history of coagulopathy and evidence of trauma above clavicles. Patients with abnormal and normal CT scans were compared using recursive partitioning; the sensitivity and specificity of the models were then computed. Univariate analyses in Phase 1 identified three clinical findings positively associated with abnormal CT scan: deficits in short-term memory, drug/alcohol intoxication and physical evidence of trauma above clavicles. The authors calculated that using these three criteria to eliminate patients who did not need scanned would have reduced the number of scans by 31% in Phase one, although two abnormalities would have been missed (94% sensitivity). Recursive partitioning identified a set of seven criteria: headache, vomiting, age over 60, seizure and the previously identified three signs that could have been used to differentiate patients with abnormal scans from those with normal scans.

To validate the findings of Phase one, 909 patients age 3-94, with an average age of 36, were entered into Phase 2. These patients were separated in to two groups, those with at least one of the criteria identified in Phase 1 and those with none. Sensitivity, specificity and negative predictive value were then calculated. All patients with positive CT scans had at least one of the criteria (sensitivity 100% CI 95-100, negative predictive value 100% CI 99-100, and specificity 25% CI 22-28). Also, 23.3% patients had none of the seven clinical criteria and all of these had normal CT scans. The authors concluded that patients with mild head injury who may not need

CT scans can be identified based on the presence or absence of one or more clinical criteria but that the results of this study should be validated at other centers.

In 2005, Berger and Adelson reviewed the current literature on the predictive value of clinical symptoms in their state-of-the-art paper. They found that LOC, scalp hematoma, facial injury, abnormal neurologic exam and amnesia were more common with ICI but none had strong predictive values. Emesis, seizures and headache were neither predictive nor associated with ICI.

5.5 LONG-TERM EFFECTS OF MILD HEAD INJURY

The evidence of the long-term effects of mild head injury in adults is compelling [119], often resulting in memory and concentration problems and slower information processing. However, there has been debate about the effects in children. Rutter et al first published studies that indicated that severe head injury in children had significant long-term effects but that mild head injury did not [120]. However, subsequent reviews of these studies pointed out problems with control groups and testing procedures [121] and led Beers to conclude that, although the problems seen following a mild head injury in children are not as common nor as disabling as those following a severe head injury, they are important because of the high incidence of mild head injury in children.

The effects of age at time of injury are also poorly understood. Early researchers agreed with the Kennard Principle [50], that injuries among very young children could be overcome because much learning had yet to occur and the brain would work around existing limitations as new skills were learned. However, more recent research indicates that mild head injury in children disrupts the learning process and these limitations are not easily overcome [122] [123] [124]. Some studies have found that although children with mild head injuries may not necessarily show an initial deficit in functioning that recovered over time, they do show a deficit that emerged over time [125] [126] [127]. However, not all studies of mild head injury in children have found deficits in functioning [128]. In fact, in 1997 Satz et al [129] published a review of the research of mild head injury in children from 1970-1995 and concluded that there were no adverse effects on academic or psychosocial outcomes across the spectrum of mild head injuries. They also noted that the majority of the more rigorously conducted studies reported null outcomes. The authors cautioned though that many of the studies considered had very small sample sizes which may preclude identifying small subgroups of children with more long-term effects.

One prospective, longitudinal study of mild head injury in young children, age three to seven years old at time of injury, found few differences in function among children with head injury and those without [130]. Investigators prospectively enrolled 52 children with mild head injury and 35 healthy controls in to a study to determine the outcome following these types of injuries. Children were evaluated for previous head injuries and pre-existing physical, neurological, psychiatric or developmental disorders and given a battery of evaluations at the time of injury and at 12 and 30 months post injury. They found that up to 30 months post injury, children maintained their performance within a normal range on most measures, including

behavioral functioning and adaptive skills. However, deficits were found in Story Recall and Verbal Fluency tasks. The researchers suggested that these results indicate that children suffering mild head injuries in preschool years may have complications with high-level language based skills; however, the study is limited by its small sample size.

Studies by Ponsford et al also found deficits in some children following a mild head injury [131] [132]. They compared 130 children with mild head injury to 96 children with other minor injuries to identify any factors associated with persisting problems. They gave children a battery of tests at one week and three months post injury to determine if any significant deficits existed. They found that children with mild head injuries experienced headaches, dizziness and fatigue for at least the first week following the injury. No other significant differences were found between the two groups. At three months post injury, symptom differences had resolved and no evidence of cognitive impairment was found. However, they did note that the parents of 17% of the children reported behavioral problems; these children were more likely to have a history of previous head injury, learning difficulties or neurological or psychological problems. The authors concluded that children with preexisting conditions may be at higher risk for persistent problems following a mild head injury and that these children should be identified at admission for more careful assessment and monitoring.

5.6 HEAD INJURY DIFFERENCES BY AGE

Early studies and case reports seemed to indicate that children less than three years old might have different injury characteristics and outcomes than older children. Pietrzak [133] published a case report of a 13-month-old girl brought to the ED for evaluation of an asymptomatic scalp hematoma. Skull radiographs and CT scans indicated parietal skull fracture and subdural hematoma respectively. The authors noted that this case is indicative of the high frequency of complications following minor head injuries in children this age. They recommend a low threshold for imaging for children younger than two to avoid missing an injury with the potential to deteriorate.

The results of a retrospective study of 102 infants less than 13 months old with acute skull fractures were published in 1997 to determine if there were clinical predictors of ICI that may improve management [134]. Lethargy and temporal bone fracture were both predictive of ICI. Presence of any sign or symptom was 100% sensitive but only 35% specific. The authors noted that a high prevalence of fracture characteristics often associated with intentional injury are also associated with accidental injury, as in this cohort where almost all infants had accidental injuries. They concluded that several clinical predictors might be useful in predicting ICI in infants; however, prospective studies were recommended for validation.

Greenes and Schutzman [135] refuted these findings in a retrospective review of 101 infants with acute ICI. Their results indicated that ICI occurs in infants who are clinically occult and they caution that physicians cannot depend on the absence of symptoms to rule out ICI. Gruskin and Schutzman [136] furthered these conclusions by finding, in a case series of 278 children less than two years old evaluated for head injury, that clinical signs and symptoms were

insensitive predictors of ICI. They found that skull fracture and ICI were more common in children younger than 12 months than those 12-23 months and that injuries resulted from minor falls and occurred in children who were alert and neurologically normal. They noted, however, that a subset of children with falls from low heights (<3 feet), no history of neurological symptoms and a normal scalp examination were at low risk for complications.

6.0 DECISION-MAKING RULES AND GUIDELINES FOR HEAD INJURY

The next logical step after identifying symptoms that have the potential to differentiate significant and non-significant mild head injuries is to organize this information into clinically meaningful guidelines for physicians. Several studies have been conducted to create clinical decision-making rules for the management of head injuries. However, as discussed below, these rules have one of the same problems as do the studies of clinical criteria, using mixed populations of children and adults or using children of all ages.

6.1 CLINICAL DECISION-MAKING RULES FOR HEAD INJURIES

At first, decision-making rules were developed with and for use on adult populations with mild head injury. Stiell et al [137] published a multi-center prospective study of 3121 patients, age 16-99, who presented with acute minor head injury, defined as having all of the following: loss of consciousness, amnesia or disorientation, GCS scores of 13-15 and injury within 24 hours, to assess 1) the need for neurological intervention and 2) clinically important brain injury. In their

cohort, 67% had CT scans and the remaining 33% had a structured telephone interview about their symptoms (per the protocol). They found that 1% of the subjects required neurological intervention, 8% had clinically important ICI, and 4% had clinically unimportant lesions. The investigators used logistic regression and recursive partitioning to come up with five high-risk factors: failure to reach GCS score of 15 within two hours, suspected open skull fracture, any sign of basal skull fracture, two or more episodes of vomiting or age 65 years or older, and two medium risk factors: amnesia before impact and dangerous mechanism. The high-risk factors were 100% sensitive for predicting the need for neurological intervention and using these factors to triage patients would require CT scans on only 32% of patients. The medium risk factors were 98.4% sensitive and 49.6% specific and would require that 54% of the patients receive CT scans. The authors concluded that the use of a decision rule would improve and standardize patient care and lead to cost-savings through better utilization of resources.

Haydel et al designed a study to test whether a clinical decision rule on how to manage minor head injury that was developed in adults could be applied to children five years or older [138]. They prospectively enrolled 175 children aged 5 to 17 with nontrivial head injury; GCS score of 15 and loss of consciousness form an inner city Level 1 trauma center. The study questionnaire, which collected symptom data that had been validated in an adult population (headache, vomiting, drug/alcohol intoxication, short-term memory deficits, posttraumatic seizure and physical evidence of trauma above clavicles), was completed prior to CT scan. Patients were not followed upon discharge. In this population, 8% of the children had intracranial injury and 1% required surgical intervention. Results using the decision rule indicated that these criteria were 100% sensitive in identifying patients with intracranial injury and with skull fracture in all age groups; the specificity of the symptoms was between 23% and

29%. The authors concluded that use of the decision rule in this population would have reduced the need for CT scan by 23%.

Recently, Palchak et al published a decision rule for children at low risk for brain injuries after head trauma [139]. The investigators enrolled children with non-trivial blunt head trauma, which excluded falls from ground level and scalp lacerations, at a pediatric trauma center to evaluate the clinical predictors of traumatic brain injury on CT and traumatic brain injury requiring acute intervention. Traumatic brain injury was defined as the presence of intracranial hemorrhage, hematoma or cerebral edema; acute intervention was defined as a neurosurgical procedure, ongoing antiepileptic pharmacotherapy beyond seven days, presence of neurological deficit that persisted until discharge or two or more nights of hospitalization due to the head injury. Data were collected prospectively using a tool designed specifically to evaluate the variables of interest: amnesia, loss of consciousness, headache, seizure, clinical signs of skull fracture, focal neurological deficit, abnormal mental status and scalp hematoma in children less than three years old. These nine predictors were used in recursive partitioning analyses for both traumatic brain injury and for TBI requiring surgical intervention. Follow-up telephone calls within one week of evaluation were conducted to determine if additional visits to a physician were needed and to ascertain that there were no missed head trauma diagnoses.

Their population was 2043 children with a mean age of 8.3 years; 16% were two or younger, 65% were male and 36% had LOC. The most common mechanism of injury was falls, followed by motor vehicle crashes. They were able to follow 88% of the children; county morgue records and the hospital trauma registry were searched for those who were not contacted by telephone. Sixty-two percent of the children had a CT scan; of these, approximately 8% had positive CT scans and 8% required intervention. Binary recursive partitioning was used to manufacture decision trees and, using a conservation decision rule which combined TBI and surgical intervention trees, five variables were identified as important for identifying children at low risk for brain injuries after head trauma: abnormal mental status, skull fracture, headache, scalp hematoma in children less than two years old and history of vomiting, as shown in Figure 4 below.

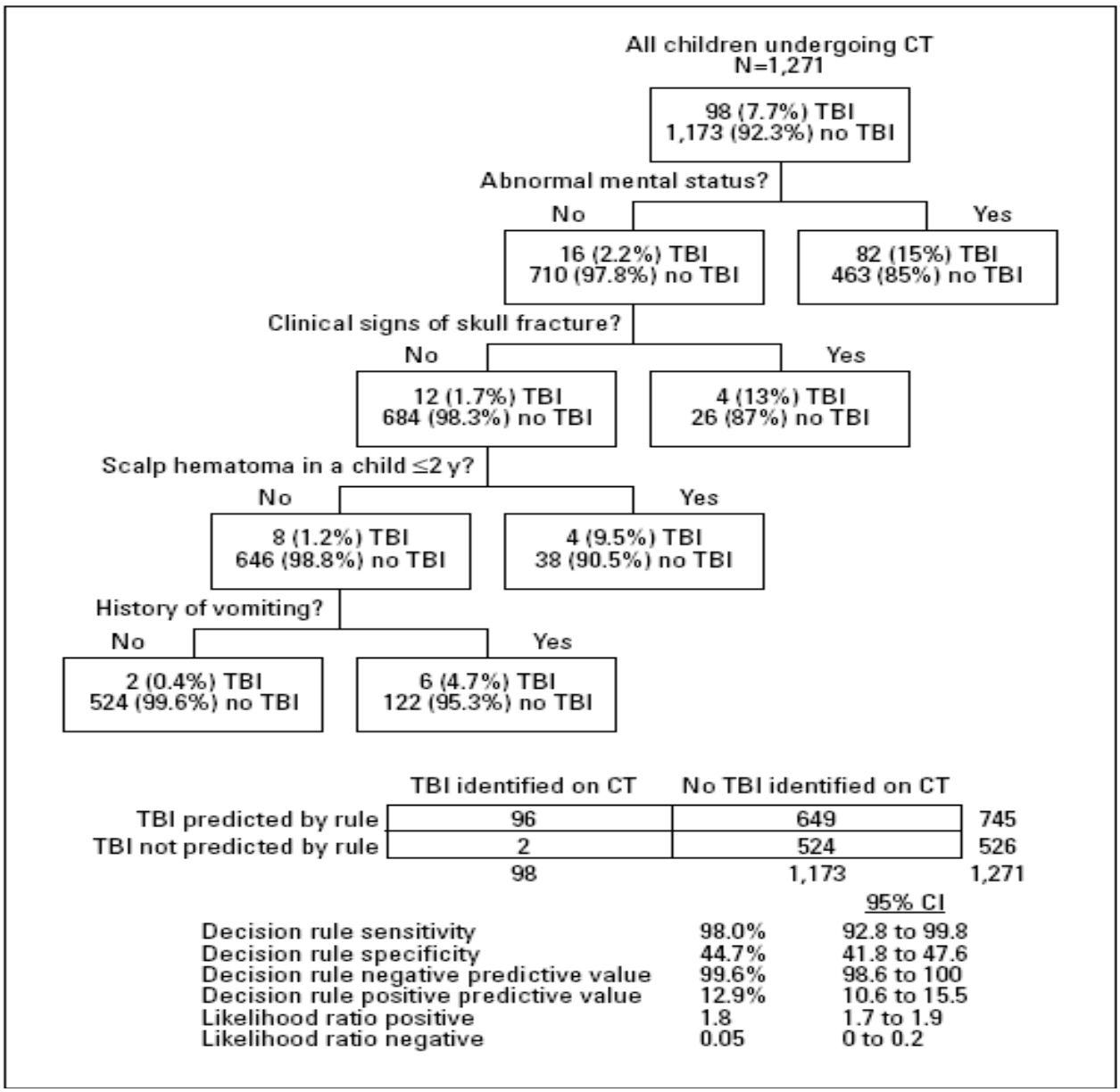


Figure 4. Palchak et al (2003) Decision tree for predicting children with traumatic brain injury on CT scan (Figure 1)

This rule correctly identified 98% of children with TBI identified on CT scan and 100% of children requiring surgical intervention; the absence of all five correctly predicted 99.7% of those without TBI on CT. Subgroup trees were developed for GCS scores of 14 or 15 and children less than three years old. The tree for GCS 14 or 15 included the same variables as in the TBI tree but in a different order. The tree for children less than three years old included scalp hematoma and abnormal mental status. Because in this study they did not image all children and only followed up with telephone interviews to parents within one week, they may have missed children who had clinically silent but radiographically visible TBIs.

In a follow-up to this study, Palchak et al [140] evaluated the association between an isolated LOC and/or amnesia and TBI. None of the children who had a CT scan and whose LOC and/or amnesia status was known had a TBI. Follow-up was conducted in 88% and none of these patients deteriorated. The authors concluded that LOC and/or amnesia can be ruled out as clinical symptoms predictive of ICI in mild head injuries and that by eliminating CT scans for patients with only these symptoms, CT scan use can be decreased.

6.2 MANAGEMENT GUIDELINES FOR HEAD INJURIES

The results of clinical symptom and decision-making rule studies enabled researchers and clinical groups to develop some management strategies for children with mild head injuries. It is inappropriate to generalize the treatment of head injury in adults to children because of the differences in anatomy and physiologic response to cerebral trauma [141]. Children are more predisposed than adults to head injury because their head to body ratio is greater, their brains are less myelinated and thus more prone to injury, and their cranial bones are thinner. In addition, children may lose relatively large amounts of blood from scalp lacerations and hematomas and present in hemorrhagic shock [141].

Two of the most essential parts of the successful management of children are a proper clinical assessment of the primary injury and an appreciation of the potential for intracranial complications. As with all injuries, the clinical assessment of head trauma should begin with an evaluation of the ABCs (airway, breathing and circulation) [57]. A detailed history, including a recounting of the incident and symptoms, and physical examination should follow. After these evaluations are completed, management should continue in one of three ways, based on the characteristics of the injury and child [57]: 1) severe head injury [142], 2) mild head injury in children three years old or greater [143] and 3) head injury in children less than three years old [144]. Of note is the split by age in the way children are managed.

As discussed below, research indicates that very young children have different injury characteristics and outcomes than older children and their head injuries cannot be managed the same.

6.2.1 Children Three Years Old or Greater

Current recommendations on the treatment of children with mild head injury vary and the most recently published practice guidelines and state-of-the-art care recommendations highlight some of the existing controversies. Schutzman et al [145] reviewed the current literature and practices regarding mild head injury in children and found that the available literature indicates that few children with mild head injury require surgery but many physicians fear missing the one injury that will deteriorate. Also, because so few children who deteriorate are included in the studies, it is impossible to prove that children with ICI have benign outcomes. No study has identified one or even a set of criteria that can identify children with ICIs, and, in fact, symptoms have poor sensitivity and specificity. Therefore, clinicians typically recommend imaging for any child with any symptom versus no imaging for a child with no symptoms. The authors also note that the true incidence of brain injury in asymptomatic children is unknown and that children under two present

special problems due to a higher risk of skull fracture and ICI after minor injury. The authors recommend future studies comparing different clinical guidelines and the cost effectiveness of each.

Also in 2001, the EAST Practice Management Guidelines Work Group [146], a group of trauma surgeons, reviewed the existing literature on mild TBI to make recommendations regarding the definition, diagnosis, testing, management and outcome. The committee reviewed 75 peer reviewed published articles and made the following recommendations:

- CT scan is the gold standard diagnostics imaging technique and should be performed on all patients with disturbance of neurological function,
- A subset of patients with MTBI will develop persistent symptoms in the absence of anatomic findings,
- Patients with isolated MTBI diagnosis following complete evaluation may be discharged home in responsible situations,
- Postconcussive symptoms including headache, dizziness, and memory problems may be indicative of subsequent increased risk for prolonged cognitive deficits

The authors recommended further studies on each of these issues.

In 2003, the Nursing Forum published practice guidelines for emergency departments and hospitalized patients regarding the management of mild TBI in children [147]. They defined MTBI in children as: eighteen years old or younger with a history of impact to the head, GCS score of 14 or 15, and no focal neurological deficits. They excluded patients with intentional injury, multiple trauma, cervical injury or presence of drugs or alcohol. The forum recommended

a relatively low threshold for CT scanning until large, prospective, multicenter studies are conducted which can define clear clinical criteria that would be predictive. The article includes the Children's Hospital of Philadelphia algorithm for management of mild TBI, which differentiates between children two or less years old (high risk, intermediate and low risk groups identified) and children greater than two years old, who are considered at risk if they have abnormal mental status, abnormal neurological exam or physical evidence of skull fracture; also strongly considered if LOC, amnesia or previous TBI. They note that skull radiographs may add important information to the diagnosis for children less than three years old but not if CT scans are going to be performed; the decision to x-ray should be left up to the individual physician. Discharge is appropriate for children if they have a normal neurological exam, are free of significant extracranial injury and in a responsible situation. They recommend further research into the clinical significance of individual symptoms and an investigation of prognostic factors and guidelines.

In 2005, Berger and Adelson published a review of the evaluation and management of pediatric head trauma [57]. In their review, they noted that the consensus statements focused on two clinical decisions: whether to perform cranial imaging and whether to admit. Two current position statements [144] [143] differ depending on the age of the child. Children less than three years old are treated more conservatively than older children because of the higher rate of ICI [144]. However, Berger and Adelson note that the literature for which the consensus statement of younger children is based is much weaker and less complete than that for older children.

6.2.2 Children Less Than Three Years Old

Early studies and case reports seemed to indicate that children less than three years old might have different injury characteristics and outcomes than older children. In a landmark study, Greenes et al [5] published the results of a prospective cohort study of all (n=422) asymptomatic head injured infants (0-24 months) seen in the ED to identify the clinical features which might indicate a high risk of skull fracture and to develop a clinical decision rule to determine which infants need head imaging. Asymptomatic head injuries were defined as no clinical signs of brain injury and no signs of depressed or basilar skull fracture. Among these children, 11% of the children were diagnosed with skull fracture and 3% had ICI. A trend was found toward higher rates of skull fracture in younger infants. Large scalp hematomas and parietal hematomas were associated with ICI. The investigators developed a clinical scoring system to determine the necessity of imaging which involved adding the child's age + hematoma size + hematoma location to yield a final score would give a ranking of the likelihood of skull fracture. Using this rule, 35% of the children would have been imaged and the rule had a sensitivity =.98 and specificity =.45 for skull fractures in this cohort; it detected all cases of ICI. The authors caution that the decision rule should be validated in other populations before widespread use.

Schutzman et al also reviewed the literature for relevant studies on mild head injury and a panel of experts reviewed the results to recommend guidelines for imaging in children two or less years old with MHI [144]. For their review, ICI was defined as intracranial hematoma, cerebral

contusion and/or cerebral edema. The authors devised four categories of risk: (1) high (always get CT) - symptoms would include depressed mental status, focal neurological findings, depressed/basilar skull fracture, skull fracture by physical exam, irritability or bulging fontanel, (2) symptomatic with some risk (usually get CT) - symptoms would include 3-4 episodes of vomiting, transient LOC, resolved lethargy or irritability, non-acute skull fracture, (3) asymptomatic with some risk (observe and/or get CT)- symptoms would include higher force mechanism, falls, scalp hematomas, unwitnessed trauma, (4) low risk (no CT) - low energy mechanisms, no symptoms. The authors noted that the younger the child, the lower the threshold for imaging; also, the greater the number of symptoms, the lower the threshold. They indicated that there is some role for skull radiographs in this age group, although they are not used in older children, because these young children are at higher risk for skull fracture that can be picked up by skull radiograph and is predictive of ICI. They conclude by recommending testing these guidelines in other studies.

7.0 SUMMATION OF LITERATURE

Treatment guidelines are well-defined for children with severe injury and even for moderate injury. These children require intensive monitoring, evaluation and even surgery. However, the majority of head injuries seen in Emergency Departments are mild. These head injuries do not require the same use of resources as do moderate or severe head injuries but there is still the risk of deterioration so it may not be safe to send these children home. Physicians are still unsure about the best way in which to treat these individuals.

CT scans may be more economically efficient than hospital admission and observation [148]. However, a mounting concern about radiation exposure and resource allocation makes physicians cautious about scanning all children with mild head injuries. Uncertainty remains about which children will deteriorate and should be scanned. Several clinical criteria have been identified that may help predict which symptoms are indicative of deterioration or ICI, but results are not consistent, nor are they specific enough to initiate wide-spread use of decision-making rules.

In a review of the epidemiology, pathophysiology and complications of mild head injury, Savitsky et al discuss the current neuroimaging controversy in mild head injury [149]. They recount that the presence of some symptoms, including LOC, post-trauma amnesia, headache,

vomiting, motor weakness and lethargy, increases the relative risk of brain injury, but no one symptom, alone or in combination, has been identified as adequately sensitive to identify ICI [149]. The authors note that GCS scores of 13 and 14 are different from GCS scores of 15; these patients have higher rates of ICI and warrant immediate CT scan. The reported incidence of ICI in GCS 15 patients varies widely, from 0-7%, and studies are limited by small sample sizes, wide confidence intervals and lack of uniform criteria for CT scanning. They also note that although ICI was ruled out in patients with a GCS score of 15 but no symptoms in a study by Dietrich [101], the confidence intervals for the study were very wide and the exact incidence of injuries requiring surgery in this group was unknown. The authors conclude that hospitalization of all children with MTBI is not warranted and that the neuroimaging criteria for children less than three years old remain unknown.

The discussion above gives a clear indication of the direction in which research on mild head injury in children needs to go. The AAP guidelines recommend no imaging unless there is a history of LOC but as Palchak et al [140], and Schutzman and Greenes [145] have shown in their research, LOC is not always predictive of deterioration. While much research has been conducted regarding the characteristics of children with mild head injury, we still do not have a reliable clinical scoring system, which can separate those children with mild head injuries who will or will not deteriorate to ICI. The low specificity in studies indicates high false positive rate and overuse of resources.

Gaps in the literature indicate that further study on predictive symptoms and the cost effectiveness of clinical decision-making rules is warranted, particularly for children less than three years old. These children appear to be different than older children and may require different management guidelines.

8.0 PROPOSAL

8.1 STATEMENT OF PROBLEM

A major problem in the study of mild head injuries is the inability of current mild head injury decision rules to accurately identify the best method for treatment, and therefore, there has been an overuse of resources. As described, physicians and researchers are still debating the need to hospitalize or provide CT scans as the means to best allocate resources for the hospital and minimize the burden for children and their families. This study was designed to advance research in to clinical decision-making rules for mild head injury in children less than three years old. The work sought to examine how readily available information on signs and symptoms could be used to reliably distinguish children with mild head injuries who will face longer term health issues from those who will not. Further, this study examined the potential costs related to these rules and compared the costs to those incurred under present practice. Thus, the main aim of the present study was to determine the most efficient method for treating children (less than three years old) with mild head injuries.

8.2 SPECIFIC AIMS OF PROPOSAL

1) To utilize clinical and long-term follow-up data to develop a clinical decision rule for young children with mild head trauma. The goal of this aim was to develop an algorithm, using CART (classification and regression trees), to evaluate the effectiveness of using symptoms and clinical criteria to direct the management of mild pediatric head injury. Assessments of the sensitivity, and specificity of the proposed decision-making rule were used to examine the accuracy of using patient symptoms and clinical criteria to determine whether intracranial injury was present and likelihood of deteriorating injury after release from the hospital compared with the "gold standard" CT scan among pediatric patients with mild head injuries;

2) To identify the long-term implications of mild head trauma, including new or recurring symptoms, and late effects and indirect costs of the injury. This portion of the study followed a sample of patients recovering from a mild head injury to determine if any complications related to the mild head injury occurred; and

3) To investigate the direct and indirect costs of different courses of treatment for mild head injury. This aim evaluated the direct costs related to the management of pediatric head injury, including emergency department (ED), admission and rehabilitation (if applicable) costs,

and the family's costs associated with the injury, including lost work time before and after the injury. It also evaluated the anticipated savings of using the algorithm developed in the first aim to manage mild pediatric head injuries and compared these costs with those of the current standard practice.

8.3 PUBLIC HEALTH SIGNIFICANCE OF PROPOSAL

This study presented a unique opportunity to investigate the significant problem of mild head injuries in children and the allocation and use of resources associated with these injuries. In a September 2003 survey of Level I trauma centers [150], less than half of the trauma program managers indicated that they had a formal protocol for evaluating mild traumatic brain injury. Hospitals have no consistent practice for determining which patients are evaluated, who performs the evaluations or which tools should be used. The authors concluded that there currently are no standard practices for defining, evaluating or managing mild TBI and that a consistent definition and management protocol could facilitate data collection, analysis and comparison.

Children are susceptible to potential long-term consequences following a mild head injury, emphasizing the importance of both giving children the best and most appropriate care for their injury while balancing the utilization and cost of resources required for this care. While CT scans have been used as the "gold standard" for determining the existence and severity of intracranial

injury, they have the associated risk of exposing children to relatively high doses of radiation at a time in their lives when they are most susceptible to radiation-induced cancers from such procedures. Also, some facilities do not have CT scans readily accessible to image children with mild head injuries and still other facilities feel both CT scan imaging and overnight observation is the best, although most conservative, way to assess children with mild head injuries.

This study investigated and identified the clinical characteristics that maximize care and minimizes costs for these resource intensive, yet minor, injuries. The public health significance of this study was that 1) a decision rule using clinical criteria could influence pediatric head injury management strategies and 2) developing a decision rule, which maintained high sensitivity to capture children who may develop ICI but increased specificity, helped to minimize the use of resources, including CT scans, in this population.

8.4 STUDY DESIGN

This study used information from two sources: 1) a retrospective review of medical records to obtain anonymous information on patient and injury characteristics and presenting symptoms and 2) a parent questionnaire and consent for the release of medical records. The medical records

review involved data abstraction from electronic patient medical records at Children's Hospital of Pittsburgh (CHP). The questionnaire was completed by parents of children who had a mild head injury and included questions regarding symptoms the child experienced before and after the hospital visit as well as information about indirect costs experienced by the family. The study results from each source were combined and were used to examine the reliability of a clinical decision-making rule for children who present at the hospital with mild head injury and to examine the costs associated with using the rule.

CHP is the only Level 1 Pediatric Trauma Center in Southwestern Pennsylvania and one of only three Pediatric Regional Resource Trauma Centers in the state accredited by the Pennsylvania Trauma Systems Foundation and 17 in the country. Each day, more than 150 children are seen in the Emergency Department or approximately 60,000 ED visits per year; 2,000 of those are for closed head injuries. Approximately 750 children are admitted to the Benedum Pediatric Trauma Program each year for head injuries. CHP is one of the first pediatric hospitals in the nation where physicians use an information management system for virtually all inpatient care orders, from blood tests to medications to treatments, which eliminates handwritten and verbal orders and allows hospital personnel and researchers access to the patient's complete record in one place. Because it is the only dedicated children's hospital in the area and because of the electronic records system, collaboration with CHP allows the opportunity to efficiently capture and abstract data from medical records of children which represents those types on injuries seen in the area.

8.5 SAMPLE SIZE

The overall goal of the study was to be able to use a systematic sample of children with mild head injuries to make valid and precise statistical inferences about the characteristics of their injuries that could be used to develop a clinical decision-making rule for practitioners. The required number of abstracted medical records to adequately address this goal was determined by the appropriate sample size calculation.

Sample size was calculated using the equation below:

$$n = (TP + FN) / p$$

Where $TP + FN = \text{Z}^2 * ((Sens(1 - Sens)) / B^2)$

In the formula, Sens was the sensitivity of the diagnostic test (CT scan), estimated here at 99%, B was the bound on the error of estimation (or ½ the width of the desired confidence interval), and z was the standard normal distribution value for the desired level of confidence (here, 95%, z=1.96). This allowed population values to be estimated with 95% confidence and an error bound (B) of 0.05.

The third determinant of the sample size was the estimated overall proportion of the characteristic of interest in the general population, or "p". For this sample, p, or the proportion of

children who develop intracranial injury (ICI) following a mild head injury, was taken from the most current literature on mild head injuries in children and estimated at p=0.15 for children younger than three years old.

The information for the sample size was based on the available number of children less than three years old seen in the Emergency Department from 1/1/2005-12/31/2005 for mild head injuries (ICD codes 800-804 and 850-854); 122 children in the database met these criteria.

Using the equation and limits above resulted in a target sample of 101 children less than 3 years old. Because we did not expect all parents to respond to the mailed survey, the "working" sample size estimate was found by inflating the "required" sample size by factor of 1/0.70 or 1.43 to account for a projected overall 70% response rate. After inflating the target sample size for non-response, the final sample size for the survey phase of the study was 145. The target sample for the abstraction phase remained 101 as there were no response issues associated with that portion of the study.

8.6 DATA COLLECTION

8.6.1 Data sources

Data collection occurred in two phases, using different data sources. For part one, medical records data were abstracted retrospectively from the Emergency Department (ED) and trauma databases at CHP using records from 2005, to eliminate recall bias and facilitate locating the families, and included injuries with ICD codes 800-804 and 850-854 (mild head injuries).

For part two, Ms. Buchanich, through Dr. Noel Zuckerbraun at the CHP Emergency Department, contacted the families of eligible children, explaining the follow-up study and requesting consent for the release of medical records related to the mild head injury and that the child's parent complete and return the enclosed questionnaire or agree to a telephone interview.

The questionnaire was brief and contained questions regarding the child's symptoms, care and behavior following the injury, and any missed school or work time due to the injury. This information was important to the decision rule, as it provided data on the characteristics of children with acute or subacute ICI, namely those whose injuries deteriorate within 48 hours (acute) or two weeks (subacute); information about deterioration may not be available from the CHP record if the child was taken to a different hospital for the deteriorating injury.

8.6.2 Inclusion and exclusion criteria

The inclusion criteria for this study were as follows: children age less than 3 years old with mild head injury (ICD 800-804, 850-854) treated at CHP between 1/1/2005 and 12/31/2005 with an initial Glasgow Coma Scale (GCS) score of 14 or 15 when seen in the Emergency Department. The exclusion criteria were: children with penetrating injuries, children with depressed skull fractures requiring surgery, children with injuries suspected to be intentional and children who had their initial CT scan >24 hours after the injury occurred. For this study, intracranial injury was defined as: intracranial hematoma, intracranial hemorrhage, cerebral contusion and/or cerebral edema.

The current institutional recommendations at CHP for CT scans are that CT scans should be given to children with blunt force trauma to the head with a GCS score of 14 or 15 and loss of consciousness and/or amnesia. That means that based on the entrance criteria for this study, most, if not all, of the subjects were likely to have CT scans as part of their standard of care. One issue that occurred is that, regardless of the institutional recommendations, CT scans were ultimately at discretion of the treating physician and children who did not meet the institutional recommendations may have had scans. Because physicians err on the side of caution when treating children with mild head injuries, we did not anticipate enrolling children who were eligible for a CT scan but did not receive one.

8.6.3 Data collection methods

For part one, Ms. Buchanich and Dr. Zuckerbraun abstracted the variables of interest from the electronic medical record files held by CHP. These data were recorded anonymously in accordance with HIPAA standards. As shown in Appendix A, the IRB protocol for part one, the variables that were collected were: age in years, race, gender, zip code, admission month, injury type, severity and mechanism, presenting symptoms, co-morbidities, procedure and diagnostics codes, history of other underlying medical disorders, charges, payer and discharge/disposition status. This part of the protocol was approved by the University of Pittsburgh IRB under their rules governing exempt studies (Appendix B).

Part two was submitted separately to the University of Pittsburgh for expedited review (protocol Appendix C; approval Appendix D). For part two, Dr. Zuckerbraun sent out an introductory letter (Appendix E) with the consent form (Appendix F) and questionnaire (Appendix G) to eligible participants. The letter explained the study and requested informed consent for the release of medical records related to the mild head injury and also for a brief interview regarding the child's behavior and care following the injury and the costs associated with work and school time missed due to the injury.

Family members agreeing to participate returned the signed consent form and completed questionnaire in an enclosed postage-paid envelope. Families who returned a signed consent form, but not a completed questionnaire, were called for an interview (Appendix H); families who did

not respond were called to assess their willingness to participate and sent another mailing if requested (Appendix I).

The questionnaire was brief (approximately 15 minutes) and contained questions regarding the child's symptoms upon being injured, care and behavior following the injury and any missed school or work time due to the injury. Because of a poor response rate to the initial questionnaire, an abbreviated version of the survey was also created (Appendix J), along with a modified approach letter (Appendix K) and consent form (Appendix L) and approved by the IRB (Appendix M). This questionnaire was re-sent to the families of children who had not responded to the long form and for whom we had a valid address; a packet of stickers was included in the abbreviated survey mailing as an incentive for participation.

8.7 DATA ANALYSIS

The statistical analysis for the study occurred in several phases. A classification and regression tree (CART) program was used to identify symptoms that may be relevant to intracranial injury and poorer outcomes among children in the study. After developing a final classification tree, the predictors of importance from the tree were entered into a logistic regression model to confirm the

overall fit; this allowed a more familiar and conventional depiction of the CART model. The third and final part of the analysis was a cost simulation and analysis. Analyses were performed using CART [151], SAS v8.02 [152], Minitab Release 14.12.0 [153] and TreeAge Pro 2007 v6.0 [154].

8.7.1 Classification and Regression Trees (CART)

Classification and regression tree diagramming (CART), or binary recursive partitioning, is a statistical procedure introduced in 1984 to analyze either categorical or continuous data, using classification or regression respectively [155]. It is ideally suited to the generation of decision-making rules because it can easily handle large numbers of predictor variables, even those which are not normally distributed, it can identify complex interactions or patterns within the data and it is simpler to interpret than a multiple logistic regression model, making it more likely to be used in a clinical setting.

CART requires four basic pieces of information for each analysis: an outcome variable, predictor variables, a learning dataset on which to base the tree, and a test dataset on which to test the tree; the test dataset does not have to be separate from the learning dataset, as described below.

Further, a decision problem requires two additional components: the prior probability of the outcome, or the probability of randomly-selected patient will have the outcome of interest, and a misclassification cost matrix, which is the penalty associated with misclassifying a future patient.

The CART analysis applied in this study involved four steps. The first step was tree building, during which the tree was built by recursive splitting. The grown tree showed the target (predicted) variable's probability at the initial, or parent node, and then at each secondary, or child node, split. In these models the target variable was the presence of intracranial injury (ICI). The second step was stopping the tree growing process, which grew until the maximal tree was built; this tree typically overfit the data and needed to be pruned, which was the third step in the process. Pruning removed the nodes that provided the least amount of information about the target variable, creating simpler and simpler trees. The final step was selecting the optimal tree, the one which provided the best fit for the data but did not overfit them.

The tree building step evaluated all possible splits for all variables included in the model. It used binary partitioning with two and only two possible answers at each point to classify objects in to terminal nodes. The results were always in the form of an inverted tree, beginning with a root node and ending with terminal nodes, or final classifications [151].

CART analysis, in general, continues drilling down until it is not possible to create any more splits, either because there is only one observation in the child nodes or each observation in the child node has an identical distribution of predictor variables, making further splitting impossible. This maximal tree can then be examined to determine if selective pruning should be used to create a smaller tree by eliminating unnecessary or unhelpful nodes [151]. Each CART run

produces multiple trees including one the program denotes as optimal, typically the one with the lowest misclassification cost. A CART run will always perform with higher accuracy on the original dataset than on subsequent test datasets, because it can fit a tree exactly to any idiosyncrasies in the original dataset. The optimal tree should be pruned to eliminate idiosyncratic nodes which will allow the tree to perform well on future datasets and not just the original dataset. This is particularly important, as in this study, when creating a decision-making rule for general clinical use.

Another important factor in CART analysis is considering the effects of misclassifying the target variable. When creating a tree for a medical decision-making rule, often misclassifying one outcome is worse than misclassifying another; in this case, it may be worse to discharge a child with the potential to deteriorate than to conservatively treat a child who will not deteriorate. CART has adjustable misclassification penalties, allowing investigators to vary the way in which different outcomes are handled. In this analysis, different misclassification penalties for incorrectly classifying a child whose head injury deteriorated were examined to ensure that the decision-making rule is as accurate as possible while still predictive on other datasets.

CART is adept at handling missing data. Rather than discarding those observations for which variable information is missing, CART instead searches for a surrogate splitting variable. Surrogates are variables which have distribution patterns within the dataset similar to those of the missing variable, relative to the predicted variable. This allows the CART program to fully utilize the available information and allows more observations to be used, rather than discard observations with missing information.

CART validates the tree that is created by classifying another dataset. If data are unavailable from a separate test sample, CART has the ability to cross-validate the model using data from the original sample. To do so, CART first determines the optimal tree using the entire sample. Then, the sample is divided into approximately ten equal parts; each of these parts will be used to generate an independent decision tree and compared to the other 9/10 of the sample. The results from all ten mini-trees are combined to form error rates; the error rates are then applied to the optimal tree that was formed using the entire original sample. This information is provided with the optimal tree and allows the investigator to consider how useful the tree will be with different datasets, even if the initial dataset is small. Ten-fold cross-validation was used here to validate the tree.

The CART program outputs a great deal of information about each model to help with the interpretation and assessment of fit. The main output shows the optimal tree with the receiver operating characteristic (ROC) curve probability for the original and test datasets. The optimal tree maximizes the probability for each of the ROCs. It also provides a table describing the level at which each node split and the observation count going left and right. There is also a report about the importance of each variable, which includes variables not show in the tree if they were important as surrogates. Finally, information is provided about the misclassification rates on the original and test datasets and the overall prediction success of the tree for the original and test datasets.

The advantages of using CART, in general, are that it is able to handle complex data sets, is robust with respect to outliers, can use combinations of categorical and continuous variables, can

discover dependent relationships and interactions and can handle variables with missing values. Specifically in this study, CART created a decision tree in a form that was easily understandable and informative to clinicians. The ten-fold cross validation also allowed the decision making rule to be evaluated on original and test datasets, which provided some indication of how the rule would perform on other data.

8.7.2 Logistic Regression

Logistic regression is part of a category of statistical models called generalized linear models. Logistic regression is a form of regression which is used when the dependent variable is dichotomous, such as the presence or absence of an ICI. The independent variables can be any type so can be used to predict a dependent variable on the basis of continuous and/or categorical independents. Logistic regression can also determine the percent of variance in the dependent variable explained by the independent variables, rank the relative importance of independent variables and assess interaction effects [156]. In those ways it is similar to the models developed by CART but in a more conventional format.

Logistic regression allows investigators to assess both the fit of the overall model and the importance of individual model parameters [156]. The likelihood ratio test is based on -2LL (deviance) and tests the significance of the difference between the likelihood ratio (-2LL) for the

final model minus the likelihood ratio for a reduced model. Here the reduced model will be the baseline model with the constant only and the likelihood ratio test will test the significance of the final model as a whole. A well-fitting model is significant at the .05 level or better, meaning the final model is significantly different from the one with the constant only. The likelihood ratio test assesses the overall logistic model but does not tell us if particular independent variables are more important than others. This can be done, however, by comparing the difference in -2LL for the overall model with a nested model which drops one of the independent variables. We can use the likelihood ratio test to drop one variable from the model to create a nested reduced model. In this situation, the likelihood ratio test tests if the logistic regression coefficient for the dropped variable can be treated as 0, thereby justifying dropping the variable from the model. A non-significant likelihood ratio test indicates no difference between the full and the reduced models, hence justifying dropping the given variable so as to have a more parsimonious model that works just as well.

The variables at the node splits from the final CART tree were forced in to a logistic regression equation and the results of the final CART model were validated. The fit of the decision-tree was then assessed using this more standard methodology. Both the fit of the overall model, using the likelihood ratio test of the final tree compared with the baseline, and the significance of the node-split variables, using the likelihood ratio test as each variable was removed from the model, was investigated. While the CART model remained as the final model for the decision-making rule, it was interesting to assess how similar or different the results would have been using the standard logistic regression.

Because the result of the CART analysis, and the confirmation using logistic regression, was a decision-making rule, it was appropriate to use a receiver operating characteristics (ROC) curve to assess its predictive power. An ROC is a plot of the true positive rate against the false positive rate for the different possible cutpoints of a diagnostic test [157]. The accuracy of the test depends on how well it separates the sample into those with and without the characteristic in question, which here was intracranial injury. The accuracy of the decision-making rule was measured by examining the area under the ROC curve. An area of 1.0 represents a perfect test; an area of 0.5 represents a worthless test. For this study, we attempted to achieve an area of 0.8 (good) or higher.

8.7.3 Cost Analysis

As the third part of the analysis, a cost analysis was performed. Formal economic analysis represents a means to both qualitatively and quantitatively compare the financial implications of competing plans, in which the costs and consequences of actions much be considered [158]. Here, we assessed the cost effectiveness of the CART model and the recommended changes to the current practice. The costs and benefits of following a treatment guideline based on these findings were compared to the costs observed with the current protocol for head injury treatment.

The cost analyses for the two treatment practices were represented through the use of decision trees, using TreeAge Pro 2007. A decision tree maps the path that the treated subject followed in the course of their clinical care and this decision tree can be used as both a visual and an analytic tool. Treatment and outcome probabilities are applied at each branch of the tree to calculate the expected value of competing alternatives.

The cost analysis considered direct and indirect costs. Direct healthcare costs include the cost of hospitalization, emergency room services, hospital procedures and home healthcare services (if applicable). Indirect costs relate to productivity costs and loss of time from paid and unpaid work. While, ideally, measures of cost would be used for the evaluation, they are not always readily available from institutions. In this case, they were not and charges were used. Costs take into account the quantity and value of resources used to produce something or to provide a service. Charges, however, may or may not reflect true cost. Charges reflect what institutions get reimbursed for goods or services and may be influenced by market conditions.

A tree was produced for both the current and proposed practices, using charges supplied by a Midwest children's hospital similar in demographics to the one under study. The probability of each outcome, generated from the dataset, was used to assign a final charge to each branch of the decision tree and the total treatment charges for the current and proposed practices were then compared.

Finally, the charge implications of using the recommended practice were examined in the context of each incorrect decision made. This type of analysis is a summary measure of unit of charge per outcome. In this case, the ratio analyzed was the unit of charge per incorrect clinical decision made regarding the treatment of each child.

9.0 RESULTS

9.1 PARTICIPANT ELIGIBILITY

The target sample size for this study, based upon the sensitivity of the CT scan as a diagnostic test and the incidence of ICI in the general population, was 101. In this report, 122 children were identified as potential participants (Figure 5). However, 25 were excluded after examination of their medical records. The most common reason for a child to be excluded was suspected non-accidental trauma (n=12). Thus, a total of 97 research subjects met the eligibility criteria for the study and are the basis for the evaluation of the specific aims outlined prior. While this is four less than the targeted size, the population prevalence of ICI was estimated in the sample size calculations as 15%; as discussed below in more detail, the rate found here was 22%. Had 22% been used in the initial sample size calculations, the target sample size would have been 76 children. The 97 children identified for this study, therefore, were adequate to address the main goal of the study, using symptom information to create a clinical decision-making rule in very young children.

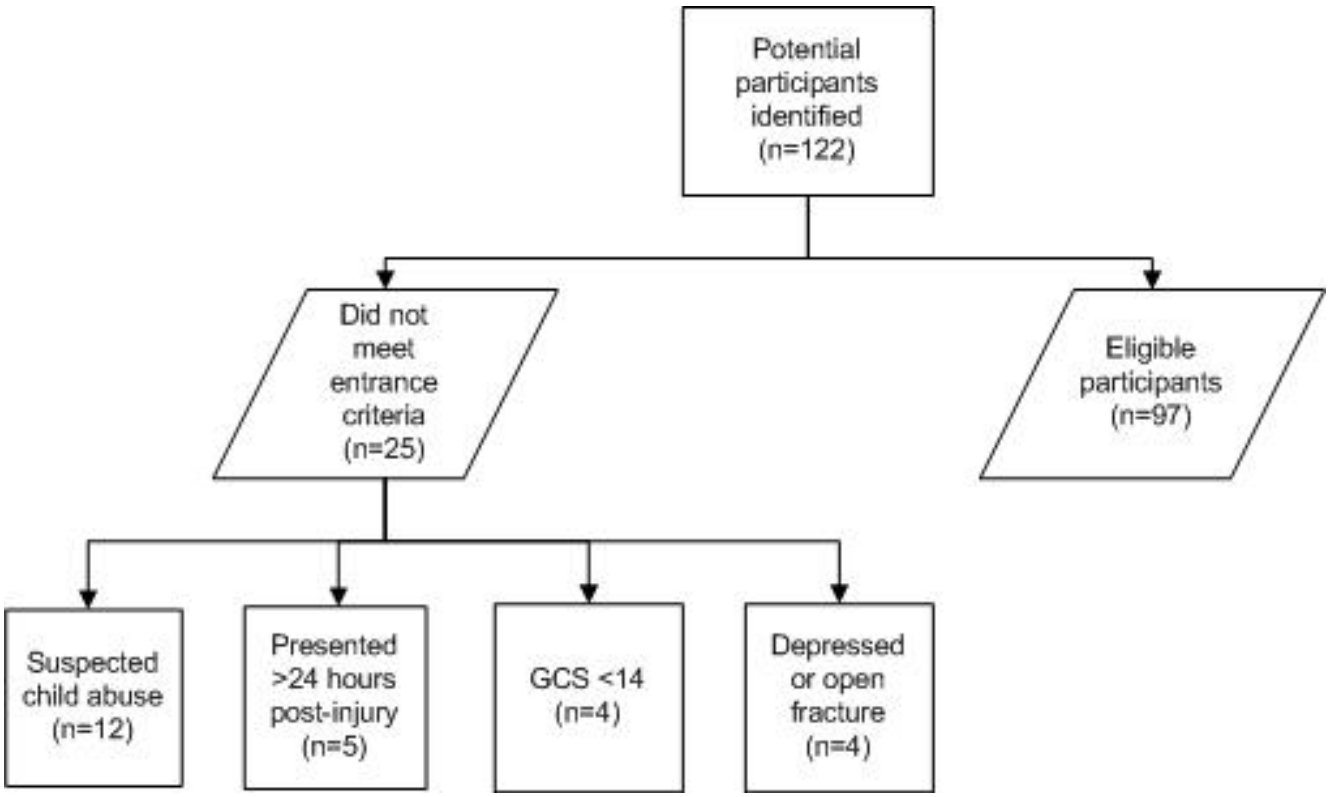


Figure 5. Reasons for Participant Exclusions

As shown in the tables below, the mean age of the children who were and were not eligible was not statistically significantly different (Table 5) and neither was the proportion of each group by sex (Table 6, Fisher's exact p=0.26).

Table 5. Age in months of eligible and non-eligible children

	Number	Age (Months)		
		Mean	St. Dev	P-value
Eligible	97	15.2	11.4	0.93
Not Eligible	25	15.5	10.6	

Table 6. Sex distribution of eligible and non-eligible children

	Sex		Total (%)
	Male (%)	Female (%)	
Eligible	52 (84)	45 (75)	97 (80)
Not Eligible	10 (16)	15 (25)	25 (20)
Total	62 (100)	60 (100)	122 (100)

9.2 MEDICAL RECORDS ABSTRACTION

Demographic, symptom, injury and treatment information was abstracted from the medical records of the 97 eligible children. Demographic information, including race, sex and age, was found in all of the medical records. At least one symptom was specified in every chart and each medical record had detailed information about the cause of injury, whether a head CT scan was performed and the result of the scan and the length and disposition of the ED visit.

Four variables were recoded or aggregated to allow for larger sizes in the groups and more meaningful comparisons. Age in months was grouped by year (< 12 months, 12-23 months, 24-35 months). Forty-six percent of the children were less than 12 months old at the time of injury. Over 75% of the children were white so race was recoded to white and other/unknown (n=15 and 9, respectively). Because month of admission was captured to look for temporal trends, it was recoded to winter (December, January, February), spring (March, April, May), summer (June, July, August) and fall (September, October, November). The first three digits of the zip code were recoded by area: city of Pittsburgh (152XX), Allegheny County (150XX and 151XX), outside of Allegheny County (all other).

9.2.1 Demographic Characteristics

Before entering the abstracted demographic, symptom and injury information into a clinical decision-making model, it was important to explore the characteristics of the dataset to evaluate the relationships between the predictor variables and also the relationship between the predictor and target variable. The initial data analyses evaluated these types of interactions. Because the facility being studied is a tertiary care institution it was also important to consider those effects on the population being studied. For that reason, area of residence and transfer status were included in these initial analyses.

Boys accounted for 54% (n=52) and girls 46% (n=45) of the injuries in this sample (p=0.50). The distribution of age group was statistically significant (p=0.02); 46% of the children were less than 12 months old at the time of their visit. Children 12-23 months accounted for 24% and children between 24 and 35 months accounted for 30% of the visits. Neither the distribution of sex by age group nor grouped race by age group were statistically significantly different (p=0.52 and p=0.64 respectively).

Approximately 30% of the injuries occurred each in the summer and fall, although this was not statistically significantly different from the winter and spring (p=0.29). The distribution by season was also not statistically significantly different by age group (p=0.26) or cause of injury (p=0.61).

More than one-half of the children came to CHP from outside of Allegheny County (p<0.001). Table 7 shows the area in which the children resided by age group. While this

distribution is not statistically significant (p=0.48), it does show that 53% of all children were from outside of the county and 62% of the children 24-35 months old.

Table 7. Area of residence by age group

Area of Residence	Age (Months)			Total (%)
	<12 (%)	12-23 (%)	24-35 (%)	
Pittsburgh	12 (27)	3 (13)	4 (14)	19 (19)
Allegheny County	12 (27)	8 (35)	7 (24)	27 (28)
Other	21 (46)	12 (52)	18 (62)	51 (53)
Total	45 (100)	23 (100)	29 (100)	97 (100)

9.2.2 Head Injury Symptom Characteristics

Information on head injury symptoms was abstracted from the electronic medical records for all eligible children. This information was typically gathered from the triage and presenting history portion of the medical record. A symptom was recorded as present ("yes'), symptom absent ("no") or symptom not mentioned ("unknown") based on its availability in the medical record. The symptoms scalp hematoma and scalp lacerations were considered separately and also combined as scalp abnormality to be consistent with the literature [136]. Table 8 shows the distribution of symptoms abstracted from the medical records, ordered by the percent of records with the symptom present.

The most commonly recorded variable was loss of consciousness (94%) followed by vomiting (73%); all other variables were not recorded in at least 50% of the records. The least commonly recorded variables were changes in vision and seizures. The most common symptom present was the combination scalp abnormality (36%), then cuts on the head or face present in 35% of the children. The other symptoms mentioned in the medical records were headache (n=2), lethargy (n=3) and irritability (n=5).

Table 8. Symptom information abstracted from medical records

Symptom	Present (%)	Absent (%)	Unknown (%)
Scalp abnormality*	36 (37)	9 (9)	52 (54)
Cuts on head or face	34 (35)	13 (13)	50 (52)
Scalp hematoma	33 (34)	9 (9)	55 (57)
Alert	27 (28)	3 (3)	67 (69)
Loss of consciousness	23 (24)	68 (70)	6 (6)
Skull fracture	20 (21)	10 (10)	67 (69)
Vomiting	18 (19)	53 (55)	26 (27)
Drowsiness	13 (13)	17 (18)	67 (69)
Other	10 (10)	0 (0)	87 (90)
Seizures	7 (7)	3 (3)	87 (90)
Not consolable	5 (5)	28 (29)	64 (66)
Scalp lacerations	5 (5)	15 (15)	77 (79)
Focal neurological deficits	3 (3)	27 (28)	67 (69)

Table 8. continued			
Symptom	**Present (%)**	**Absent (%)**	**Unknown (%)**
Vision changes	(2)	9 (9)	86 (89)
Gait changes	0 (0)	18 (19)	79 (81)
Sleeping more than usual	0 (0)	18 (19)	79 (81)

*The combined symptoms of scalp hematoma and scalp laceration

9.2.3 Treatment and Injury Characteristics

Co-morbidities, defined here as ICD9-CM codes not related to the head injury but specified on the discharge form, were present in one-fifth of the children seen for mild head injuries (n=21). However, the presence of other co-morbidities was not significant by age group (p=0.63) nor by area of residence (p=0.55) (data not shown). Twenty-five percent of the children (n=24) had other injuries associated with their head injury. Not surprisingly, the most common of these (n=16) was facial contusions and abrasions. The next most common injury was leg fractures (n=4); two of

these occurred from falls from a heights of five or more feet and the other two occurred when the child was struck by an object. Three-quarters of the children had isolated head injuries.

Reported falls accounted for 73% of all injuries, as shown in Table 9, but the cause of injury was not different among the age groups (p=0.60). Only 4% of the children were injured by motor vehicle accidents.

Table 9. Cause of injury by age group

Cause of injury	Age (Months)			Total (%)
	<12 (%)	12-23 (%)	24-35 (%)	
Falls	35 (78)	17 (74)	19 (66)	71 (73)
Struck by/against	8 (18)	6 (26)	8 (27)	22 (23)
Motor vehicle accidents	2 (4)	0 (0)	2 (7)	4 (4)
Total	45 (100)	23 (100)	29 (100)	97 (100)

To further evaluate the effect of falling, falls were categorized by type: free (off of an object), drop (similar to free but from a hold), stairs (down a certain number of stairs) and stumble (fall from child's height). Table 10 shows the breakdown of mechanism of fall by age group, which was statistically significant (p=0.02); of the 71 children who were injured by falling, one-half were due to a free fall where the child fell off or from an object. Unsurprisingly, children less than 12 months were more likely to be dropped or to free fall while children 12-23 months were the most likely to fall down stairs and the oldest group was most likely to suffer injury due to stumbling. The height of the fall was not statistically significantly different by age group either as continuous height (p=0.22) nor grouped in to less than or equal to or greater than three feet (p=0.37) (data not shown).

Table 10. Mechanism of fall by age group

Mechanism of fall	Age (Months)			Total (%)
	<12 (%)	12-23 (%)	24-35 (%)	
Drop	9 (26)	1 (6)	2 (11)	12 (17)
Free	19 (54)	7 (41)	9 (47)	35 (49)
Stairs	7 (20)	8 (47)	4 (21)	19 (27)
Stumble	0 (0)	1 (6)	4 (21)	5 (7)
Total	35 (100)	17 (100)	19 (100)	71 (100)

Ninety-six of the ninety-seven children in this study received CT scans during their initial ED visit (99%), while only 6% had x-rays. More than two-thirds of the CT scans (69%) were flagged as abnormal due to an intracranial injury (ICI) or skull fracture. Almost 25% (n=22) of the children suffered an ICI following their head injury. None of the children with ICIs required surgical intervention.

The one child who did not receive an initial CT scan was a nine month old from the city who was injured after crawling to and falling down 12 concrete steps. The child was treated and released from the ED and returned to the ED seven days later because of a worsening scalp hematoma. A CT scan was done during the return visit and they child was found, at that time, to have an ICI. Two other children also returned to the ED following their initial visits. One child with an initial positive scan was found to have a worsening bleed three days after the initial visit. One five month old child, injured after falling out of an infant swing, had an initial negative CT scan. The family returned to the hospital five days later because of a worsening scalp hematoma and, with a repeat scan, the child was found to have an ICI.

Table 11 shows the distribution of ICI by age group. One-third of the children who were less than 12 months old at the time of injury had an ICI ($p=0.03$), compared to only 7% of the children aged 24-35 months. The mean and median ages for children with an ICI were 10.77 months and 8.00 months, respectively. The mean and median ages for children without an ICI were 16.51 months and 16.00 months, respectively.

Table 11. Intracranial injury by age group

Intracranial Injury	Age (Months)			Total (%)
	<12 (%)	12-23 (%)	24-35 (%)	
Yes	15 (33)	5 (22)	2 (7)	22 (23)
No	30 (67)	18 (78)	27 (93)	75 (77)
Total	45 (100)	23 (100)	29 (100)	97 (100)

Children with an ICI were less likely to be boys than girls, although the difference was not statistically significant (OR 0.65, 95%CI 0.25, 1.70 p=0.38). White children were also slightly more likely to have an ICI than non-white children (OR 1.15, 95%CI 0.37, 3.55 p=0.80).

The most common symptom among children with an ICI was the presence of a scalp hematoma (45%). Vomiting was the next most common symptom, found in 27% of the ICI cases. Loss of consciousness was only noted in the medical records of four of the twenty-two children (18%). Two of the twenty-two children with ICIs were asymptomatic (9%). Both of these children were less than six months old at the time of injury and both were injured after free falls (one fell from a caretaker's arms and one fell from an infant swing).

None of the symptoms shown in Table 8 alone were univariately statistically significant predictors of ICI. The presence of scalp hematoma (p=0.23) and the child not being consolable when crying (p=0.16) approached borderline significance. The combination variable scalp abnormality was also of borderline significance (p=0.15). Not surprisingly, children with an ICI were two times as likely to have a scalp abnormality as those without an ICI (OR=2.00, 95%CI 0.76, 5.24). The association of scalp abnormalities with skull fractures was even more striking. Children with a skull fracture were more than five times as likely to have a scalp abnormality (OR=5.40, 95%CI 2.11, 13.80).

To investigate the effects of the missing or not recorded symptom information, the distribution of each variable with ICI was rerun with unknown variables excluded. No additional variables were identified as statistically or nearly statistically significant and, when missing values were excluded, the p-value for the presence of scalp hematoma approached one. However, when missing values were excluded whether the child was consolable remained a predictor of borderline statistical significance (p=0.15).

Fifty-two children (54%) had a skull fracture detected by the CT scan. Table 12 shows the distribution of ICI by skull fracture as determined by the CT scan. While not statistically significant (p=0.56), the odds ratio of the association was 1.33, indicating a slightly higher risk of ICI with the presence of skull fracture. However, only 41% of the ICIs occurred without a skull fracture and 52% of the skull fractures occurred without an ICI. Two-thirds of all skull fractures

occurred in children younger than 12 months (n=35) while 83% (n=24) of the children 24-35 months old did not have skull fractures. The distribution of skull fracture by age group was statistically significant ($p<0.001$).

Table 12. Intracranial injury by skull fracture

Intracranial Injury	Skull Fracture		Total (%)
	Yes	No	
Yes	13 (25)	9 (20)	22 (23)
No	39 (75)	36 (80)	75 (77)
Total	52 (100)	45 (100)	97 (100)

As shown in Table 13, the distribution of ICI did not differ significantly by cause of injury ($p=0.41$). Children injured by motor vehicle accident were slightly more likely than children injured by falls or being struck but the number of children involved in MVAs was small (n=4).

The distribution by ICI also did not differ when considered by type or height of fall (p=0.62 and p=0.90, respectively, data not shown).

Table 13. Intracranial injury by cause of injury

Intracranial Injury	Cause of Injury			Total (%)
	Fall	MVA	Struck by/ Against	
Yes	15 (21)	2 (50)	5 (23)	22 (23)
No	56 (79)	2 (50)	17 (77)	75 (77)
Total	71 (100)	4 (100)	22 (100)	97 (100)

The presence of other co-morbidities or of other injuries were also not related to ICI (p=0.30 and p=0.75, respectively). As might be expected, the odds ratio for the association between ICI and co-morbidities was reduced (OR=0.50, 95%CI 0.13, 1.89) since, by definition, these were conditions present but unrelated to the head injury. The odds ratio for the association

between the presence of other injuries and ICI, however, was a not statistically significant 1.19 (95%CI 0.40, 3.49).

The season in which the visit occurred was statistically related to ICI (p=0.04) as shown in Table 14; 50% of the injuries with ICIs happened in the fall (September, October or November). More specifically, six children with ICIs were seen in October and four more in November. Of these children, seven were injured by falls (three drop, three free and one stairs) and three were injured when struck on the head by or against an object.

Table 14. Intracranial injury by season

Intracranial Injury	Season				Total (%)
	Winter	Spring	Summer	Fall	
Yes	5 (23)	4 (18)	2 (9)	11 (50)	22 (23)
No	14 (19)	16 (21)	27 (36)	18 (24)	75 (77)
Total	19 (19)	20 (21)	29 (30)	29 (30)	97 (100)

9.2.4 Transfer Status

The area in which the child resided, within the city limits, within the county of the hospital or outside of the county of the hospital, was not associated with ICI (p=0.49). However, an effort was made to determine if area of residence was a surrogate for transfer status (whether the children came to the hospital from an outside facility or whether they presented directly to the hospital). Forty-five percent of the children seen at the hospital in this study transferred from other facilities. This includes 76% of the children who resided outside of the county where the hospital was situated. In contrast, 89% of the children in the two closer areas (city or county of hospital) presented directly to the hospital. Pertinent demographic and injury characteristics were compared to transfer status to investigate any differences between the two groups.

There were no associations between transfer status and the sex, race or age of the children (p= 0.81, 0.60 and 0.57, respectively), although white children had an associated odds ratio of transfer of 0.78 (95%CI 0.31, 1.96) compared to non-white children. The distribution by cause of injury was also unremarkable; slightly more children injured by falling presented directly to the hospital (56%) but motor vehicle accidents and struck by/against were evenly split (50% each, p=0.86 data not shown).

Table 15 shows the distribution of transfer status by intracranial injury. While there is not a statistically significant association between the two (p=0.14), there is an elevated odds ratio of 2.05 (95%CI 0.78, 5.39) for intracranial injury when the child transferred to the hospital. There

was also a slightly elevated odds ratio for the association between transfer status and skull fracture. The odds ratio was 1.27 (95%CI 0.57, 2.83 p=0.56) indicating that children with skull fractures were also more likely to transfer in rather than present directly to the hospital.

Table 15. Transfer status by intracranial injury

Transfer Status	Intracranial Injury		Total (%)
	Yes	No	
Yes	13 (59)	31 (41)	44 (45)
No	9 (41)	44 (59)	53 (55)
Total	22 (100)	75 (100)	97 (100)

When controlling for transfer status, an interesting finding emerged with regard to age and intracranial injury. The age distribution among children transferring in to the hospital was not statistically significantly associated with the presence of ICI (p=0.22), although 91% of the

children age 24-35 months who transferred in did not have an ICI compared to approximately two-thirds in the two younger age groups. The age distribution among those presenting directly to the hospital was of borderline statistical significance (p=0.09). Of the nine children who presented directly to the hospital with an ICI, seven (78%) were less than 12 months old, one (11%) was between 12 and 23 months and one (11%) was 24 to 35 months old.

Also striking were the findings regarding ICI and skull fracture. Sixteen percent of the children who transferred in to the hospital had both ICI and skull fracture, 14% had isolated ICI, 41% had isolated skull fracture and 30% had neither, resulting in a not statistically significant p-value of 0.79 and an odds ratio of 0.84 (95%CI 0.23, 3.10) for the association; 46% of the ICIs occurred without a skull fracture. However, when considering those children who presented directly to the hospital with head injuries, 11% had both ICI and skull fracture, 5% had isolated ICI, 40% had isolated skull fracture and 43% had neither, resulting in an elevated odds ratio of 2.19 (95%CI 0.49, 9.88 p=0.30) for the association; 67% of the ICIs occurred without a skull fracture.

9.2.5 Disposition

Thirty-six (37%) of the children were admitted to CHP from the ED for their head injury; 36% were observed for 23 hours and then released and 27% were treated and released from the ED.

The distribution of ED disposition did not differ by age group, presence of co-morbidities or presence of other injuries (data not shown). The ED disposition, however, was of borderline statistical significance regarding its association with ICI, as shown in Table 16 (p= 0.14). Not unexpectedly, children with an ICI were more likely to be admitted and, conversely, children without an ICI were more likely to be treated and released. However, more than 80% of the children without ICIs were either observed for 23 hours or overnight. Of those admitted to the hospital, the median length of the hospital stay for children both with and without an ICI was two days, with a range of 1-8 days for those with and 1-7 days for those without an ICI. The child without an ICI admitted for seven days had complications unrelated to the head injury.

Table 16. Intracranial injury by ED disposition

Intracranial Injury	ED Disposition			Total (%)
	Admitted	23 hr observation	Treated and released	
Yes	12 (33)	5 (14)	5 (19)	22 (23)
No	24 (67)	30 (86)	21 (81)	75 (77)
Total	36 (100)	35 (100)	26 (100)	97 (100)

9.3 FOLLOW-UP SURVEY RESPONSE

Figure 6 depicts the efforts to obtain valid mailing addresses, consent and completed original surveys from the parents of the eligible children whose medical records were abstracted. Valid mailing addresses were found for 91% of the families. Of these, only 11% (n=10) of the parents returned their completed consent forms and surveys without telephone follow-up. With additional telephone calls, another four families with a valid phone number (n=67) returned their consent forms and completed surveys. Three of the families were found to be ineligible because the child was currently living with a guardian and not a parent. Three of the parents refused to participate (3%) and the remainder of the families did not respond at all. Thus, the overall participation rate for the original follow-up survey was 14% (14/97).

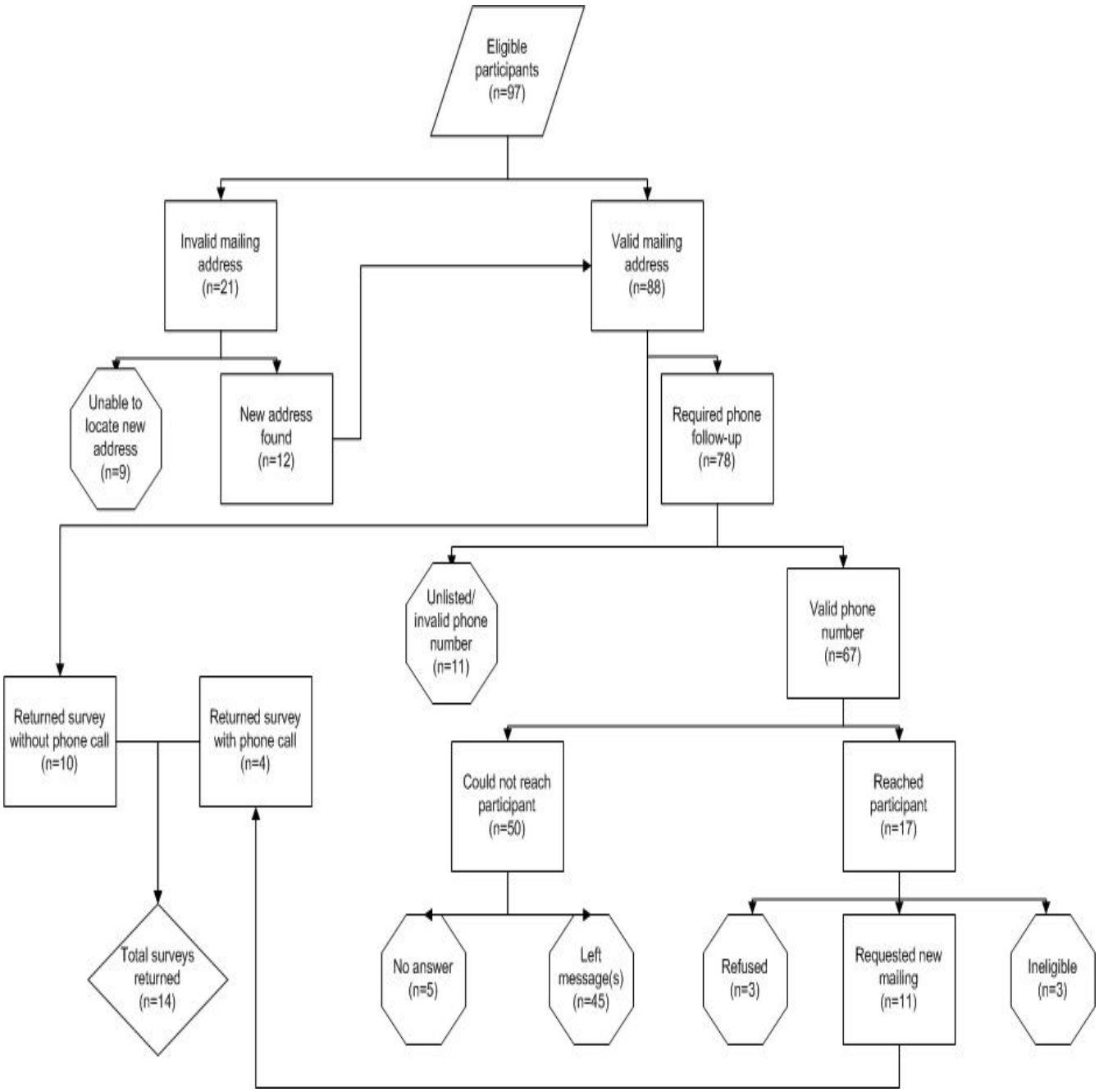


Figure 6. Participation in follow-up survey

Table 17 shows the parental report of their child's symptoms present at the time of the injury for those that responded to the original survey. The symptoms are in descending order by reported presence and, within percent, by ascending order of percent unsure. As show in the table, parents responding to the survey reported irritability and loss of consciousness most often (25%), with the least amount of uncertainty (8%). Seven symptoms were not reported by any parents and 75% of the parents were unsure whether their child experienced numbness as a result of the injury, the highest proportion of unsure responses. Headache and amnesia also had at least 50% unsure responses.

Table 17. Symptom information at the time of the injury from the original survey

Symptom	Present (%)	Absent (%)	Unsure (%)
Irritability	3 (25)	8 (67)	1 (8)
Loss of consciousness	3 (25)	8 (67)	1 (8)
Drowsiness	3 (25)	7 (58)	2 (17)
Vomiting	2 (17)	9 (75)	1 (8)
Nausea	2 (17)	5 (42)	5 (42)
Headache	2 (17)	2 (17)	8 (67)
Sleeping more than usual	1 (8)	10 (83)	1 (8)
Trouble falling asleep	1 (8)	10 (83)	1 (8)
Sadness	1 (8)	8 (67)	3 (25)
Balance problems	1 (8)	6 (50)	5 (42)
Dizziness	1 (8)	2 (17)	9 (75)
Seizures	0 (0)	11 (92)	1 (8)
More emotional than usual	0 (0)	10 (83)	2 (17)
Sensitivity to noise	0 (0)	9 (75)	3 (25)
Sensitivity to light	0 (0)	8 (67)	4 (33)
Feeling slowed down	0 (0)	8 (67)	4 (33)
Amnesia	0 (0)	6 (50)	6 (50)
Numbness	0 (0)	3 (25)	9 (75)

As discussed in the methods, the poor response rate of the original survey led to the development of an abbreviated survey and another mailing. The abbreviated survey was mailed to 68 families four to nine months after the original survey mailing (Figure 7). In that time, seven of the families moved and, additionally, 17 families had their telephone numbers disconnected. Three families returned completed surveys before the telephone calls began and seven families returned a completed survey after the telephone calls began for a participation rate in the abbreviated survey of 15% (10/68); two families refused to participate in the abbreviated survey (3%).

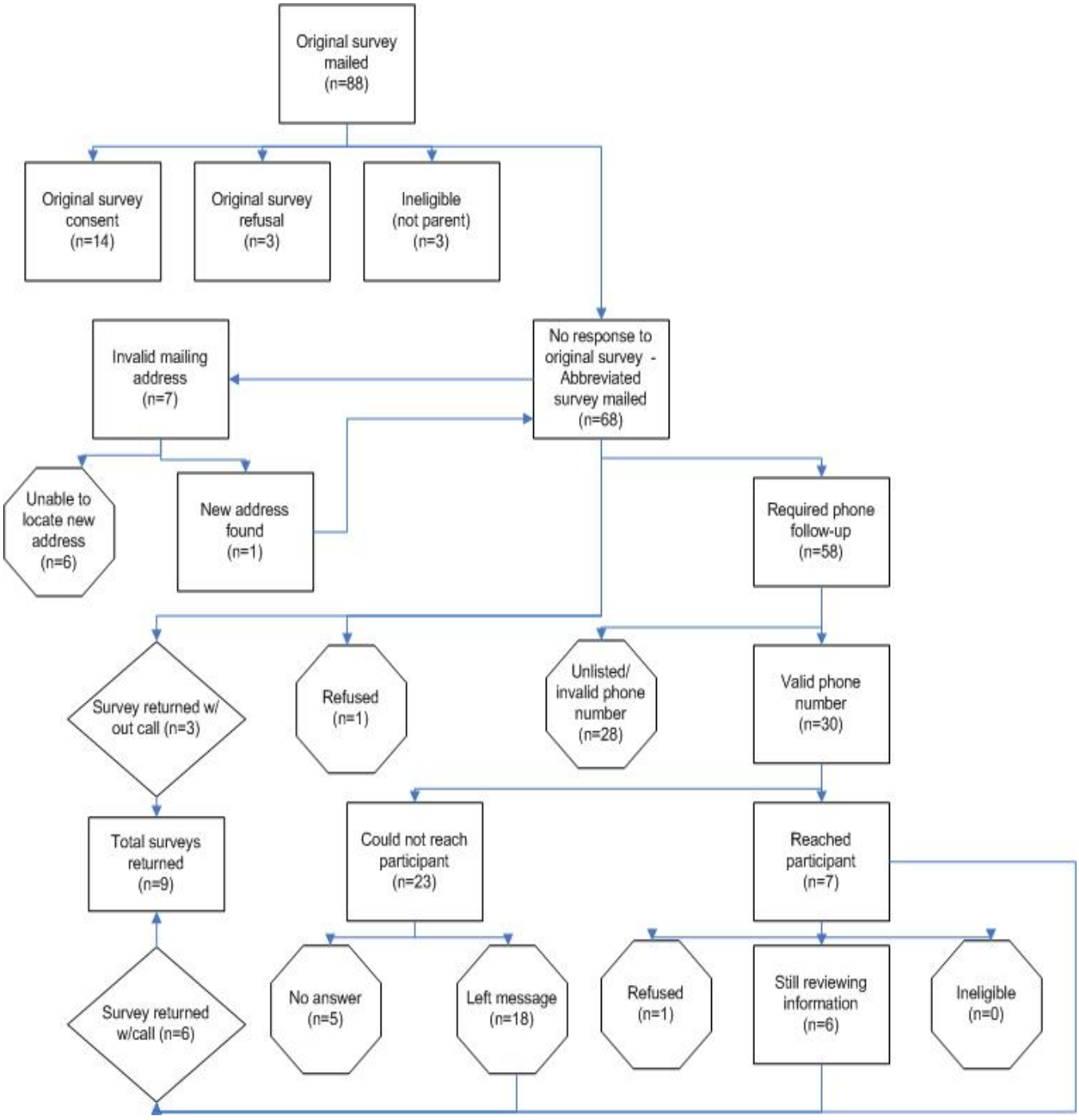


Figure 7. Response to abbreviated survey mailing

In total there were 24 survey responses (25%), 14 to the original survey and 10 to the abbreviated survey. The responses to both surveys were pooled together because the respondents did not vary by age group of the child (p=0.99), presence of ICI (p=0.35), sex of the child (p=0.56) or cause of injury (p=0.40). Area of residence was of borderline statistical significance when considered by response to the original or abbreviated survey (p=0.05); 43% of the respondents to the original survey resided outside of Allegheny County (n=6) but 90% of the respondents to the abbreviated survey were from outside the county (n=9) (data not shown). However, when any survey response was compared to no survey response, there was no association with area of residence (p=0.36).

Table 18 indicates that the rate of response to the combined surveys did not vary by age group (p=0.76) when compared to the total cohort. However, the rate of response was of borderline statistical significance when considered with the presence of ICI (Table 19, p=0.17). Three parents of children with ICIs responded to the survey, one to the original survey and two to the abbreviated survey. All three of these children were less than one year old at the time of injury and transferred to the hospital. One was injured from being dropped, one was struck in the head and one was injured as a restrained rear passenger in a motor vehicle accident.

Table 18. All survey responses by age group

Survey response	Age (Months)			Total (%)
	<12 (%)	12-23 (%)	24-35 (%)	
Yes	10 (22)	7 (30)	7 (24)	24 (25)
No	35 (78)	16 (70)	22 (76)	73 (75)
Total	45 (100)	23 (100)	29 (100)	97 (100)

Table 19. All survey responses by intracranial injury

Survey response	Intracranial injury		Total (%)
	Yes	No	
Yes	3 (14)	21 (28)	24 (25)
No	19 (86)	54 (72)	73 (75)
Total	22 (100)	75 (100)	97 (100)

The abbreviated survey only had five symptom questions, mainly to facilitate keeping the form limited to one page. The symptoms that were included were those in the original survey most likely to be known to the parents through observation, since most of these children were pre-verbal and unable to express symptom information. They were also the symptoms more likely to be present in the post-injury period, which was more important for the follow-up since the symptoms present at the time of injury were recorded in the medical record. For instance, loss of consciousness was not included on the abbreviated survey since it was not likely to manifest in the post-injury period, but irritability was included. Table 20 shows the parental responses to those five questions, from both the original and abbreviated surveys, for the period following the injury. Three families whose child had an ICI responded to the surveys, however, none of the families reported any positive symptom information. Therefore, symptoms are not broken out by ICI here. As shown, the most commonly reported post-injury symptoms were irritability, reported in 21% of the children, and sleeping more than usual, present in 17% of the children. Post-injury seizures were not reported by any parents.

Table 20. Symptom information after the injury from both surveys

Symptom	Present (%)	Absent (%)	Unsure (%)
Irritability	5 (21)	18 (75)	1 (4)
Sleeping more than usual	4 (17)	19 (79)	1 (4)
Trouble falling/staying asleep	2 (8)	20 (83)	2 (8)
More emotional than usual	2 (8)	20 (83)	2 (8)
Seizures	0 (0)	23 (96)	1 (4)

Three of the parents (13%) reported behavior changes following the injury, described as increased irritability, clinginess and crying. More than two-thirds (n=17) of the parents took their child back to their PCP for follow-up care after being released from the hospital; two of these parents also had their child seen at the UPMC Center for Sports Medicine. None of the children needed an urgent care visit or a return trip to the hospital for their head injuries.

Family members for more than half (n=14) of the children missed work to take their child to the hospital. Of those, one family had a member who missed one-half to one day of work, five

missed one day of work and eight missed more than one day. Eight of the families (33%) also had a family member miss work to care for their child following the release from the hospital. Figure 8 depicts the amount of work time that parents missed following the injury and indicates one-quarter of the parents who missed work missed one day and more than half missed three or more days.

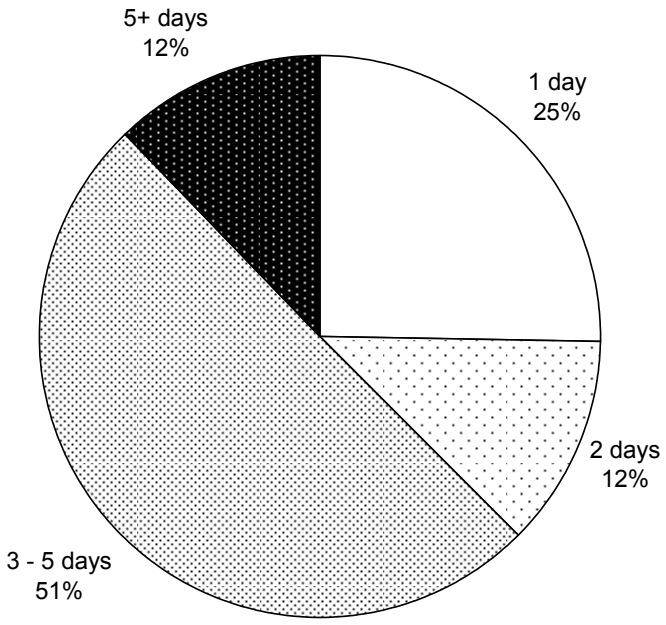


Figure 8. Amount of work time missed following the injury

9.4 CLASSIFICATION AND REGRESSION TREE (CART) ANALYSIS

Demographic, injury and symptom variables abstracted from the medical record were included in a CART analysis to identify important factors related to the presence of ICI on the CT scan. Twenty-two variables were included in all of the models: age, race, sex, area of residence, cause of injury, presence of co-morbidities, other injuries, loss of consciousness, vomiting, drowsiness, sleeping more than usual, focal neurologic deficits, gait changes, vision changes, scalp lacerations, scalp hematomas, cuts on the face, seizures, skull fracture by examination, whether the child was alert and whether the child was consolable.

The combination variable, scalp abnormalities, was also evaluated in the models but resulted in uniformly less predictive models than when scalp lacerations and scalp hematomas were considered separately; therefore, only the separate information is shown here. The effect of transfer status was also evaluated but, again, resulted in less predictive models than when area of residence was included independently; therefore area of residence was used in all models rather than transfer status. While month of admission, or season, was obtained in the abstraction phase and was a significant predictor of ICI in this cohort, it was not included in the CART analyses. It

does not make sense clinically to evaluate children based on month of admission and its significance is most likely an anomaly with this dataset. Models were also evaluated comparing falls as the cause of injury to all other causes. These models produced only one parent node split, on age, with no child nodes. These models, therefore, were deemed uninformative.

The analysis was handled systematically to investigate the potential differences in resulting CART models related to missing data, misclassification and splitting rules. The misclassification penalty, which is adjustable, allows investigators to specify the importance of correctly classifying the target variable. Setting it to one gives the same weight to correctly classifying the target as it does to incorrectly classifying it. Increasing the misclassification penalty makes it more important to correctly classify the target variable and influences the split decisions.

As mentioned earlier, one of the primary goals of the CART analysis is to produce a model which maximizes sensitivity, identifying those children with ICIs (true positives), and minimizes specificity, identifying those children without ICIs (true negatives), for its predictions. This will be evaluated here by examining the receiver operator characteristics (ROC) curve associated with each model. The ROC curve is a graph of the sensitivity versus 1-specificity of the model. The area under the ROC curve is a representation of the accuracy of the model, with values over 0.70 representing fair to good accuracy; the accuracy increases as the value approaches one.

All of the models shown below follow the same general pattern. The top node shows the entire cohort with the total number of children with and without ICIs. The subsequent nodes show the split criteria for each branch. Within each child node is the total number of children, plus the count and percent of children with and without ICIs. The terminal nodes are shown with thinner

blue or thicker red outlines. The thinner blue outline indicates that the terminal node was classified for children not having ICI and the thicker red outlines is for terminal nodes classifying children with ICI.

In the first set of CART analyses, unknown data from the medical record abstraction were coded as nine. First, the misclassification penalty was set to one. This resulted in a model with only one parent node, age, and no child nodes. The model had an ROC curve statistic of 0.63 in the original dataset and 0.61 in the test (10-fold cross validation) dataset. Next, the misclassification penalty was set to two. The model generated is shown in Figure 9, using the default splitting rule, gini. The next common splitting rule, twoing, produced the same model. As shown, a tree was generated with grouped age as the parent node. However, handling missing data this way resulted in CART creating splits based on unknown categories. The model has child nodes using cut points of nine, including splitting on unknown focal neurological deficit status and unknown gait changes. It had an ROC curve statistic of 0.70 in the original dataset and 0.55 in the test (10-fold cross validation) dataset. However, since basing decisions on unknown characteristics is not valid for clinical purposes, unknown values were not handled this way in subsequent models.

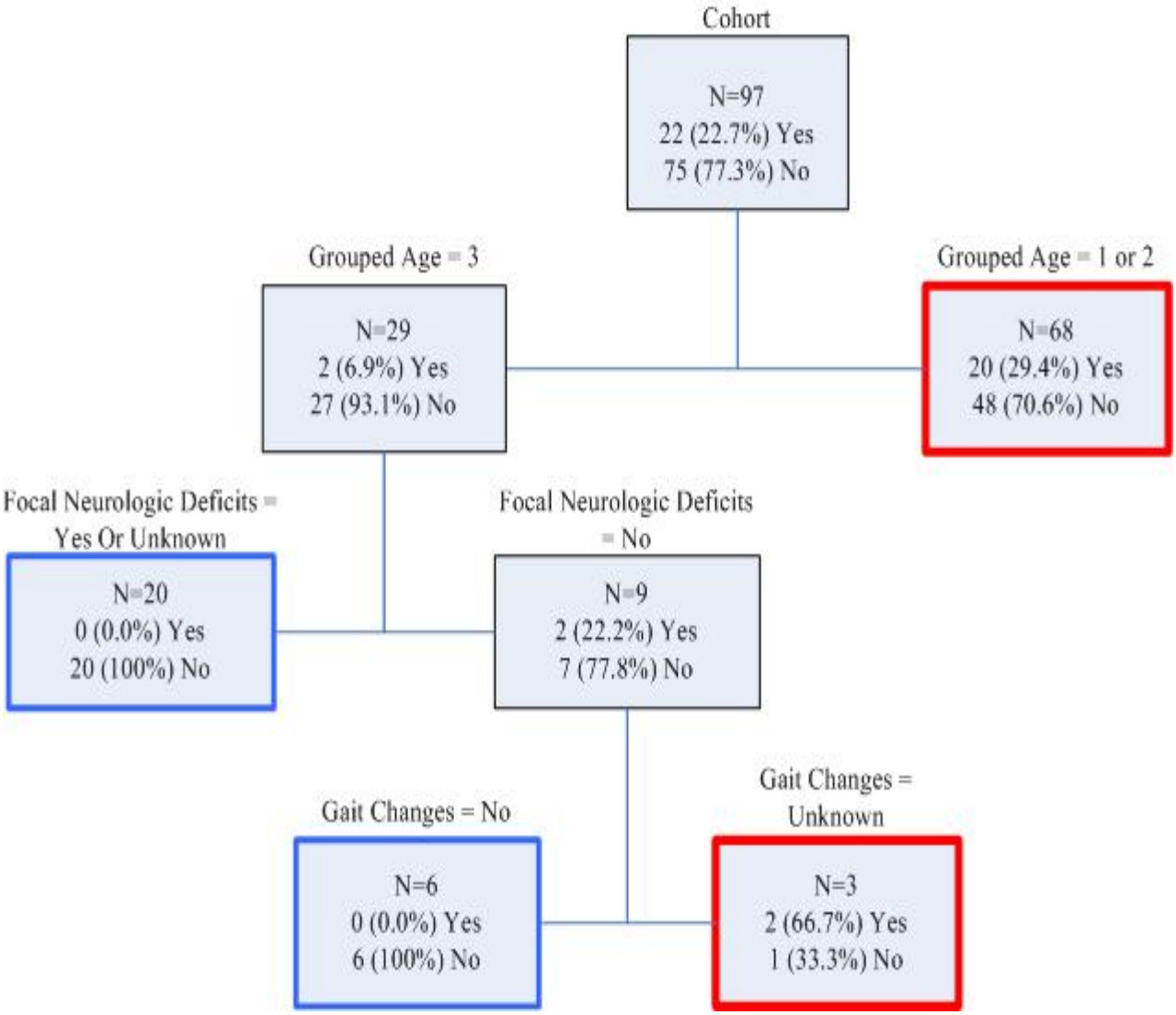


Figure 9. CART model: missing treated as unknown, misclassification penalty = 2, grouped age

In the next set of analyses, models were created with missing data treated as no. This should be a clinically valid assumption because treating physicians typically note the presence of symptoms but not necessarily the absence of symptoms, leading to missing symptom information. Unfortunately, using a misclassification penalty of one or two resulted in a tree with only one split, a parent node based on grouped age. Increasing the misclassification penalty to five, ten or twenty only resulted in one additional child node being produced, for falls as the cause of injury (data not shown).

Finally, missing data was treated as null in the modeling process. As described earlier, when CART encounters missing data, it searches for splits on surrogate variables to allow observations with missing data to be included in the modeling. For the model shown in Figures 10 and 11, the default splitting rule, gini, was again used. The models did not differ when twoing was used as the splitting rule. In Figure 10, the misclassification penalty was set to one, indicating no difference between correctly or incorrectly classifying ICI. In Figure 11, the misclassification penalty was set to two indicating that it was twice as bad to miss an ICI as it was to conservatively treat a child without an ICI. Grouped age was used in both of these models.

When the misclassification penalty is set to one (Figure 10), the parent node is whether the child is consolable. Child nodes are then produced for age, seizures, skull fractures and scalp lacerations. This model correctly classified the presence of an ICI 73% of the time (16/22) and the absence of an ICI 68% of the time (51/75). This model has an ROC curve statistic of 0.73 using the original dataset and 0.54 in the test (10-fold cross validation) dataset.

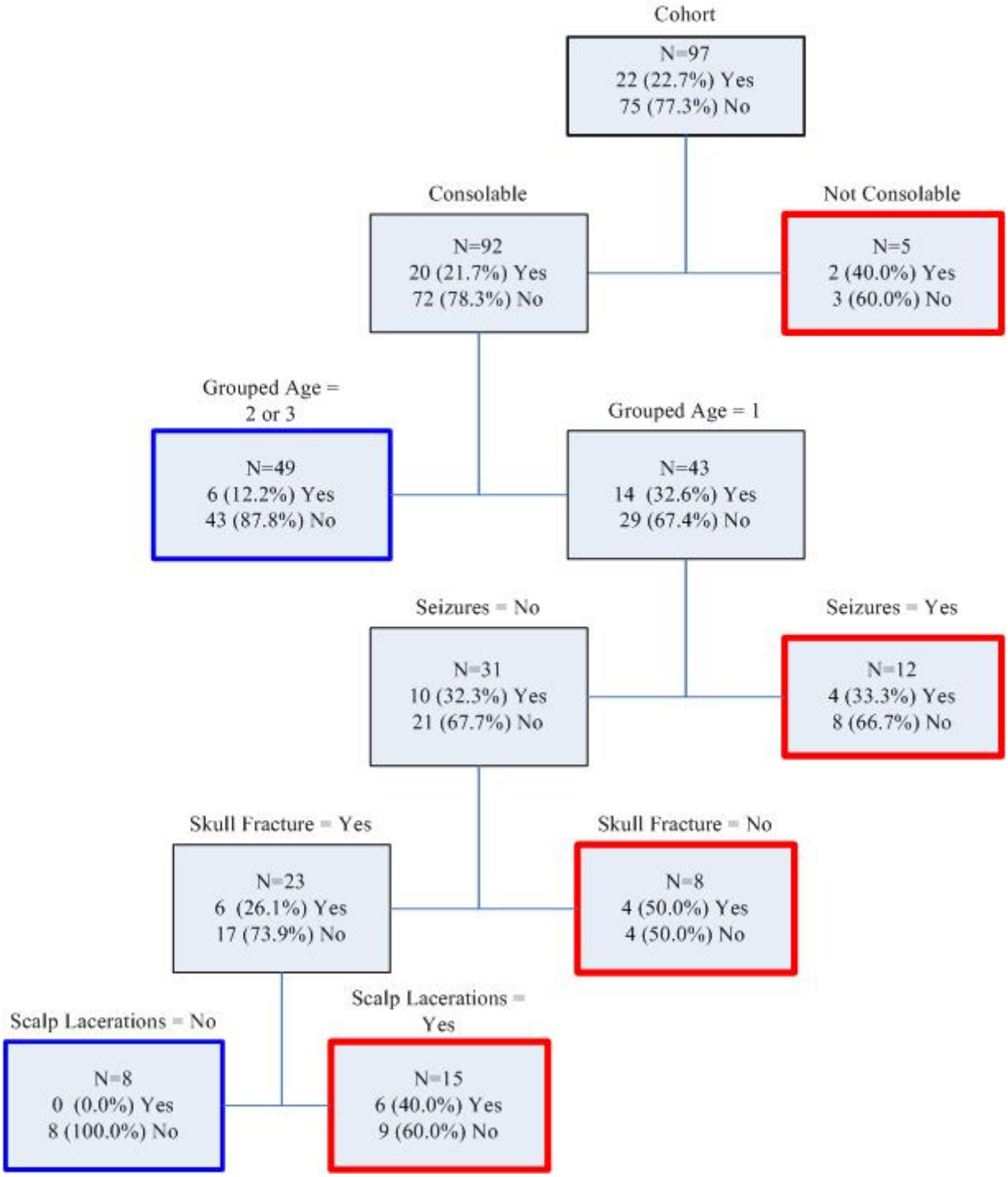


Figure 10. CART model: missing treated as null, misclassification = 1, grouped age

The model shown in Figure 11 has a misclassification penalty of two and treats missing data as null. The parent node split is whether the child experienced vision changes. Child splits occurred whether the child is consolable, has scalp lacerations, vomiting, by sex and by area of residence. There was no split based on age in this model. The model shown in Figure 11 correctly classified the presence of an ICI 100% of the time but the absence of an ICI only 40% of the time (30/75), reflecting the effect of the misclassification penalty. This model had an ROC curve statistic of 0.75 using the original dataset and 0.61 in the test (10-fold cross validation) dataset. Increasing the misclassification penalty to five or ten did not change the model (data not shown).

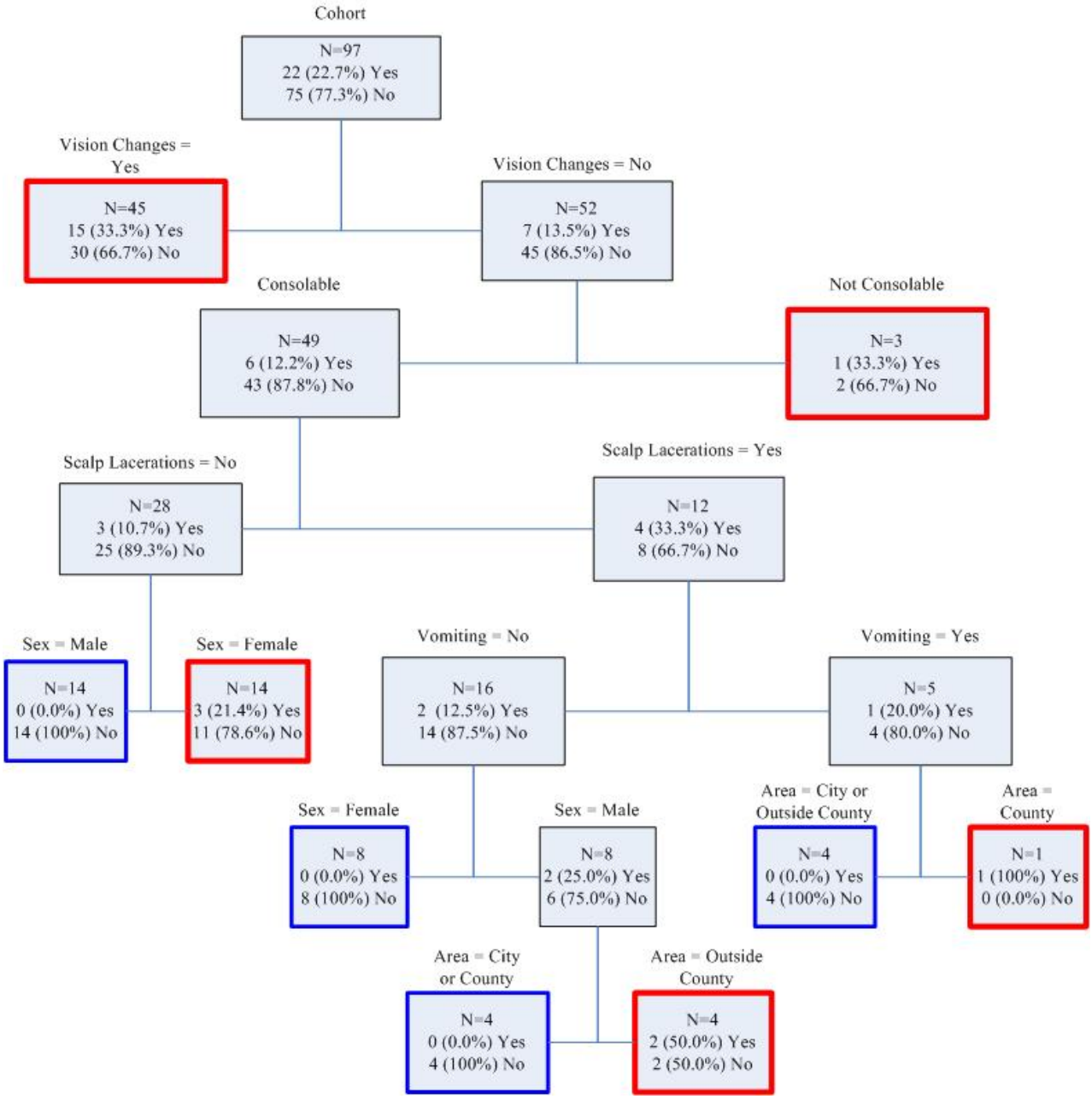


Figure 11. CART model: missing treated as null, misclassification penalty = 2, grouped age

Because using grouped age may miss an important split within an age group, the models with missing data treated as null were re-run using age as a continuous variable. When the misclassification penalty was set to one, a tree was produced with a parent node of whether the child was consolable and one child node of age less than 301 days (data not shown).

When the misclassification penalty was again set to two, it resulted in a larger tree (Figure 12). The parent node was still vision changes with whether the child was consolable as the first child split, as in Figure 11. Subsequently, there were some different child nodes from the model in which age was grouped, including the presence both of cuts on the head and face and drowsiness. Age in days was the split in four different terminal nodes, splitting at 342 days, 688 days, 721 days and 1015 days old. In this model, the presence of an ICI was correctly classified 100% of the time and the absence of an ICI was correctly classified 53% of the time, both improvements over the previous model. The model shown in Figure 12 has an ROC curve statistic for the original dataset of 0.82, higher than that using grouped age; the ROC curve statistic for the test dataset, 0.45, is lower than with grouped age though.

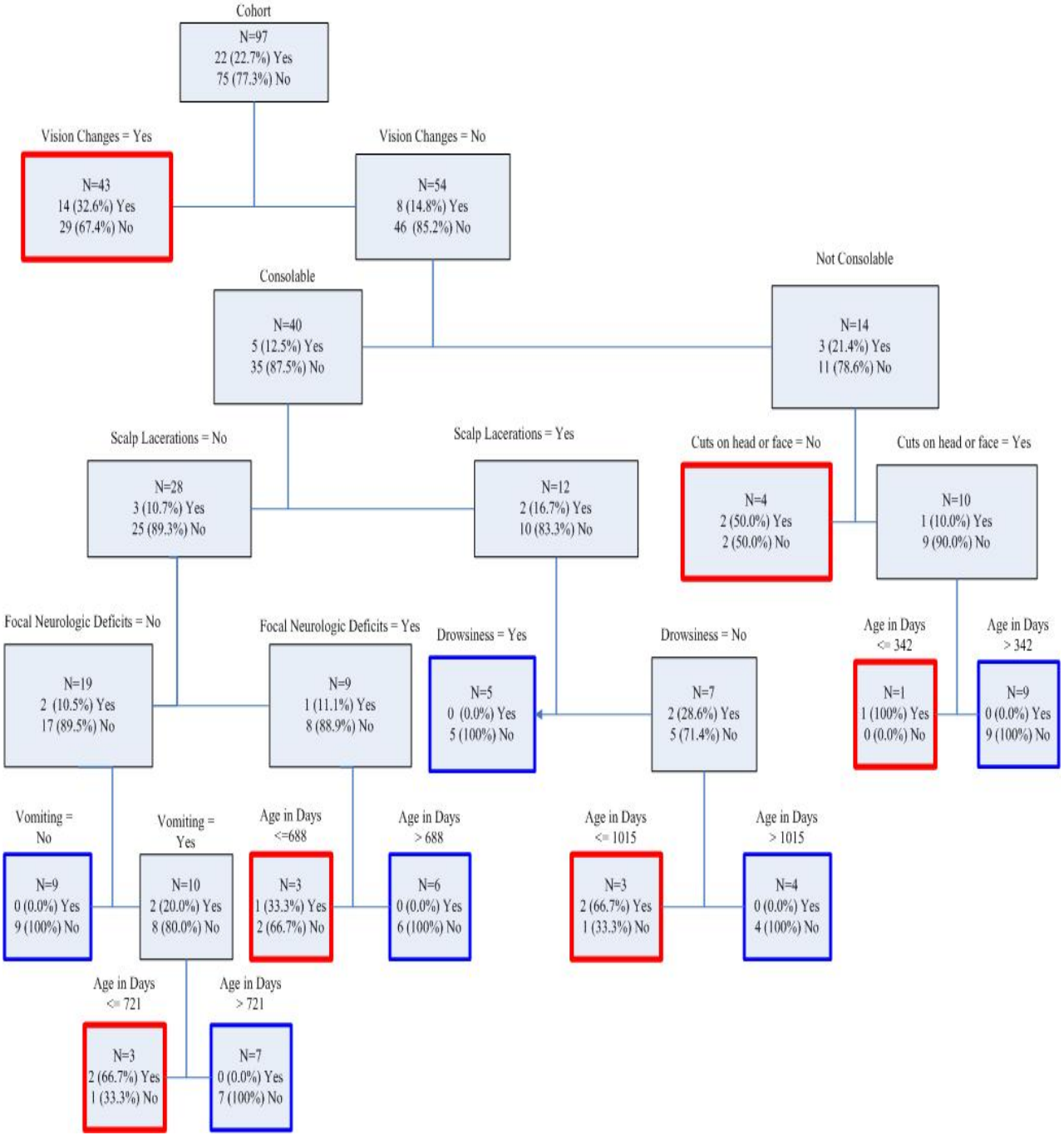


Figure 12. CART model: missing treated as null, misclassification = 2, continuous age (days)

To make a decision-rule that is as useful and helpful as possible, it should not require calculations by physicians. The model in Figure 12 highlights a problem with using age in days, namely that it does not lend itself easily to determining age in the more conventional months or years. To increase the usefulness of the rule, the models were re-run using continuous age in months rather than days. Using a misclassification penalty of one resulted in a model with a parent node of whether the child was consolable and one child node, age split at 11.5 months (data not shown).

Increasing the misclassification penalty to two with continuous age in months resulted in the model shown in Figure 13. The parent node was still vision changes and whether the child was consolable was the first child split, as in Figures 11 and 12. After that, some differences emerged. Cuts on the head or face was dropped and skull fracture was included. Two of the four age nodes were eliminated altogether and two age splits remained, at 23 and 24 months. In this model, the presence of an ICI was still correctly classified 100% of the time but the absence of an ICI was correctly classified only 37% of the time (28/75), a decline from the model in Figure 12. This model has an ROC curve statistic for the original dataset of 0.75, similar to that using grouped age but lower than continuous age in days. The ROC curve statistic for the test dataset is 0.54, lower than that with grouped age but higher than continuous age in days.

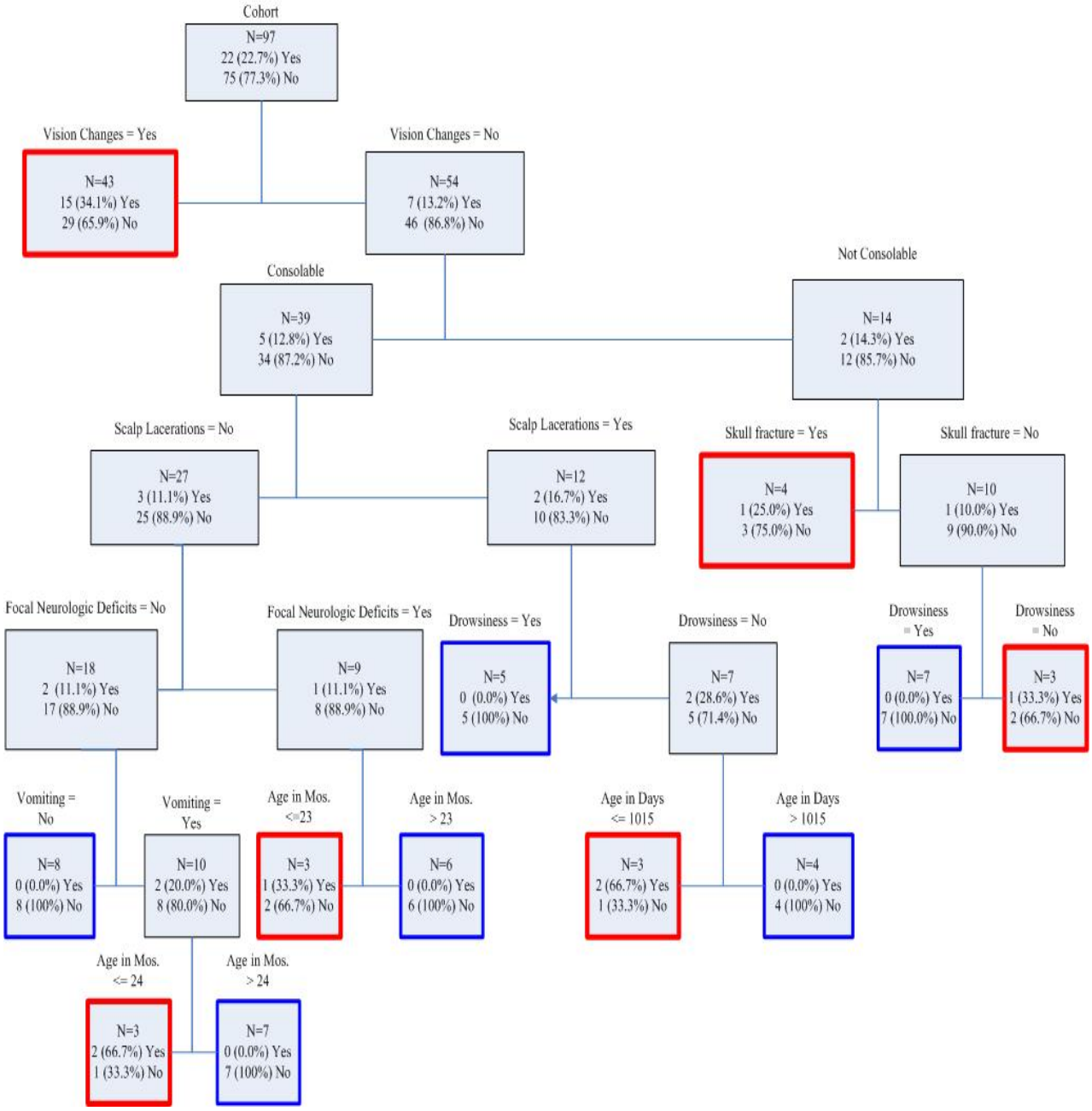


Figure 13. CART model: missing treated as null, misclassification = 2, continuous age (months)

A decision-making rule must balance high predictive power with ease of use. While the model using age in days was most predictive in the original dataset, the 10-fold cross validation showed it to be much less predictive on other potential datasets (0.82 and 0.45, respectively). It was also difficult to interpret. Using age in months improved the interpretability of the model, however, it lowered the predictive power of the model in the original dataset and increased it in the test dataset (0.75 and 0.54, respectively). Therefore, the final model chosen was the one shown in Figure 11, using grouped age and a misclassification penalty of two. This model maintained the same predictive power of the model using continuous age in months (0.75) but also had high predictive power in the test dataset (0.59), an improvement over both the models with age in months or days.

Because the final model chosen in Figure 11 may still be too complex to use in clinical practice, a simplified model was evaluated which included only the main parent split of vision changes and the first child split with whether the child was consolable. This model (data not shown) had both lower predictive power in the original dataset (0.67) and in the test dataset (0.50). It also only correctly specified 20 of the 22 children with ICIs, a sensitivity of 91%, even with a misclassification penalty of two. So while this model may be easier for clinicians to interpret, the decreases in predictive power and classification ability render it uninformative and not recommended for clinical purposes. Therefore, the final model remains as shown in Figure 11.

The model shown in Figure 11 classified the children as shown in Table 21. According to this classification, the sensitivity of the decision-making rule is TP/TP+FN or 22/22 (100%). The specificity is TN/FP+TN or 30/75 (40%). The positive predictive value is TP/TP+FP or 22/67 (33%) and the negative predictive value is TN/FN+TN or 30/30 (100%).

Table 21. Classification of children using the final decision-making rule

Result of Decision-Making Rule	Result of CT Scan		Total
	Positive	Negative	
Positive	22 (TP)	45 (FP)	67 (TP + FP)
Negative	0 (FN)	30 (TN)	30 (FN + TN)
Total	22 (TP + FN)	75 (FP + TN)	97

9.5 LOGISTIC REGRESSION ANALYSIS

The CART analysis resulted in a series of ten models, depending upon how missing data were treated, the misclassification penalty that was used and whether grouped or continuous age was included. As described in the analysis plan, the variables identified as node splits in the CART models were evaluated with logistic regression. These variables were forced in to the logistic regression models and the ROC curve statistic for the logistic regression was compared to that of the CART model.

As with the CART models, the first logistic regression models treated missing data as unknown. Two separate logistic regression models were run using the node variables from the CART models with misclassification penalties of one and two. In the first logistic regression model only age in years was used and was a statistically significant predictor of ICI. The odds ratio (OR) for ICI with age less than 12 months compared to age 24 to 35 months was 6.3 (95%CI 1.3-30.0); the OR comparing age 12 to 23 months to age 24 to 35 months was 3.1 (95%CI 0.5-17.8). The model had an ROC curve statistic of 0.67. In the second model, age in years, gait changes and focal neurological deficits were entered in to a logistic regression model (Figure 9). Of the three, only age was a significant parameter in the model, again specifically age less than 12 months. The model had an ROC curve statistic of 0.68. However, the likelihood ratio test for the model was not significant ($p=0.11$), indicating that the additional parameters did not significantly improve the fit of the model.

Next, missing data was treated as no in the logistic regression models. In the first logistic regression model only age in years was used, which was a statistically significant predictor and had similar ORs as in the previous models. The ROC curve statistic was again 0.67. Second, to coincide with CART model using a misclassification penalty of two, age in years and cause of injury were included in the logistic regression model. This resulted in an ROC curve statistic of 0.70. In this case, though, the likelihood ratio test for the model was significant (p=0.03), indicating that adding cause of injury did significantly improve the fit of the model.

Because SAS cannot handle observations with missing values, instead of being treated as null as was done in the third set of CART models, they were left as unknown (9) in the logistic regression models. Grouped age and the variables identified as splits with misclassification penalties of one and two were included in the logistic regression equation. First, a model was run using age in years, whether the child was consolable, seizures, skull fractures and scalp lacerations (Figure 10). Age in years, whether the child was consolable and seizures were statistically significant predictors in the model. The model had a significant likelihood ratio test (p=0.001) and an ROC curve statistic of 0.83.

Then, logistic regression models were run to compare to the other, non-final CART models. The CART model using continuous age in days and a misclassification penalty of one converged in SAS. The only parameters in the model were age and whether the child was consolable. The logistic regression model had an ROC curve statistic of 0.71 and a likelihood ratio test of p=0.02, indicating a good fit. The logistic regression model equivalent to the CART model using continuous age in days with a misclassification penalty of two (Figure 12) did not

converge in SAS. To overcome the convergence problems, which may have occurred due to estimating parameters with the small sample sizes, LogXact 5.0 was used to produce a model using exact logistic regression. The variables vision changes, whether the child was consolable, scalp lacerations, cuts on the face, focal neurologic deficits, drowsiness and age in days were entered into LogXact. Both age in days and scalp lacerations were statistically significant predictors in the model (exact p=0.003 and p=0.04, respectively). Drowsiness and whether the child was consolable were of borderline statistical significance (both exact p=0.09).

Finally, logistic regression was done to model exactly the final CART model (Figure 11). The variables vision changes, whether the child was consolable, scalp lacerations, sex, vomiting and area were entered in to a logistic regression model to parallel the CART model with grouped age and a misclassification penalty of two. These variables produced a model with only quasi-convergence so the modeling was done using LogXact.

Exact logistic regression produced a model with a significant likelihood ratio statistic ($p<0.001$). Scalp lacerations was the only statistically significant predictor in the model (exact p=0.02), although whether the child was consolable was of borderline statistical significance (exact p=0.06). Complete information on the parameter coefficients from logistic regression is shown in Table 22. As shown, in the logistic regression model, scalp lacerations was the best predictor of ICI, with an inverse relationship (OR=0.81). That variable was the second most important predictor in the CART model. The most important predictor in the CART model was whether the child was consolable, the second best predictor in the logistic regression model. While the inverse relationships between scalp lacerations and vomiting, respectively, and ICI may seem inconsistent

with the CART model, CART does not specify the strength of the relationship between the variables and both the presence and the absence of scalp lacerations and vomiting are used as split criteria. The first-order interaction terms for all parameters were also entered in to the model but none were significant (data not shown).

Table 22. Comparison of regression and CART parameters

Parameter	Beta	OR	OR 95%CI	P-value	CART node type	CART rank of variable importance
Area	0.37	1.45	0.70, 3.00	0.32	child	3
Not consolable	0.17	1.18	0.99, 1.41	0.06	child	1
Scalp lacerations	-0.21	0.81	0.67, 0.97	0.02	child	2
Sex	0.60	1.83	0.66, 5.07	0.24	child	4
Vision changes	0.14	1.16	0.89, 1.50	0.27	parent	5
Vomiting	-0.02	0.97	0.85, 1.11	0.70	child	6

Directly comparing models produced by logistic regression and CART is extremely difficult given the ways in which the two methods differ. Logistic regression cannot handle observations with missing variable information, while CART can. In this study, logistic regression was run with the variable information included as unknown instead of eliminating many observations without known symptom information. CART used nested splits, representing complex interactions. These interactions were extremely difficult to reproduce in logistic regression. Therefore, caution must be used when comparing the results of the logistic regression model to those found from the CART model.

The results of the model building process to develop a decision-making rule for mild head injury in children indicate that the most predictive model was developed when missing values were treated as null. Using grouped age provided a model that had better predictive value in the test datasets than did using continuous age in either months or days. Using CART's adjustable misclassification penalty allowed a model to develop that gave higher priority to correctly classifying children with ICIs as opposed to incorrectly classifying children without ICIs. The final model (Figure 11) correctly identified 100% of the children with ICIs in the original dataset and 77% in the test dataset.

9.6 COST ANALYSIS

The final phase of the analysis was to investigate the costs associated with the current and proposed practices. Cost, or charge as is used here, is often an important consideration in decision-making and an evaluation of charges can provide concrete figures for a charge comparison between two treatment guidelines. It can also provide some guidance to practitioners about potential charge savings within the current treatment protocol.

The approach to calculating the charge savings was done as follows. First, each distinct outcome was outlined in a decision tree. Each child was categorized by the following factors: the ED visit, incurred by all of the children; whether or not a child had a CT scan; the child's disposition from the ED; and, finally, the child's outcome upon being discharged. The disposition from the ED had three decision points: treated and released, 23 hour observation or overnight observation. The child's final outcome was whether the child required a return visit to the hospital for the head injury or was released with no other effects requiring follow-up care.

The goal of the analysis was to compare the charges associated with the current practice to those associated with the proposed practices. Therefore, three sets of probabilities were used. First, to calculate the charge of the current practice, the probability of each outcome was assigned based on the actual outcomes of the children in the cohort. For example, in this cohort 21 of 96 children had a positive CT scan during their initial hospital visit; that branch was assigned a probability of 0.22.

Second, to calculate the charge of the proposed practice, the probabilities were based upon the disposition of each child had the recommendations garnered from this study been in place. These recommendations are two-fold: every child receives a CT scan and all children a negative CT scan (without an ICI) are treated and released from the ED. The third simulation combined the results from the CART analysis with the recommendations above. As shown in Table 21, 30 children without ICIs were categorized as such in the model (true negatives). These children could have been identified based upon their symptom patterns according to the final model and treated and released from the emergency department without a CT scan. The final simulation combined releasing those children directly from the ED without a scan with the recommendation of also treating and releasing children with a negative CT scan.

The total charge for each outcome was summed across all procedures done to the children in that branch. An example would be adding together the charge of an ED visit plus the charge of a CT scan plus the charge of one overnight admission. A sensitivity analysis was performed, inflating the actual charges by 20% and 50%, to determine if varying the charge assumptions would change the decision-making process. The end point of each branch shows the total charge and probability associated with that branch. At each node, the figure shown represents the charge of treating the children when the probability of each outcome was considered.

The charges associated with the treatment were unavailable from the hospital under study and had to be obtained from a different facility. While the facility providing the charge estimates is also a dedicated children's hospital, it is not located in the immediate area of the hospital in this study. There could be some regional or institutional-specific differences in the actual charges from

those used here. However, both institutions are in similar size cities, both are teaching institutions and both have a wide cachement area so charge differences should be minimal.

The charge for each emergency department and hospital procedure considered in the analysis is shown in Table 23. Because the figures shown here are being used as surrogate charges for those actually used by the treating facility, also shown are the charges inflated by 20% and 50%.

Table 23. Itemized emergency department and hospital charges

Item	Actual Charge	20% Inflated Charge	50% Inflated Charge
Emergency department treatment	$145	$174	$218
23 hour observation*	$350	$422	$529
Overnight observation (Bed day)	$368	$441	$552
Head CT scan	$885	$1062	$1328

*Prorated from one hospital bed day

Table 24 summarizes the charge data that will be shown in Figures 14-18 to facilitate interpreting the information in the diagrams. The figures are discussed in more detail below. However, there are some things to note from the summary. In actual practice, the charge of treating any child and the charge of treating children who receive CT scans are slightly different because one child did not receive an initial CT scan; in the recommended practice, these charges are the same because all children will receive a CT scan. In the recommended practice, each child with a negative CT scan will be discharged home so those charges are the same. Likewise, no child with a negative CT scan will be admitted for over night observation in the recommended practice so that information is not applicable.

Table 24. Summary of charges generated by the decision models by type of treatment protocol

Charge	Actual (Fig 14)	Actual +50% bed (Fig 15)	Recommended (Fig 16)	Rec + 50% bed (Fig 17)	Rec w/CART (Fig 18)
Avg charge per child	$1478	$1626	$1176	$1228	$915
Avg charge per child w/CT scan	$1484	$1630	$1176	$1228	$1227
Avg charge per child w/ positive CT (ICI)	$1651	$1880	$1655	$1884	$1880
Avg charge per child w/negative CT (No ICI)	$1437	$1560	$1041	$1043	$1043
Avg charge per child w//negative CT with discharge	$1142	$1160	$1041	$1043	$1043
Avg charge per child w/negative CT with overnight obs	$1766	$2134	NA	NA	NA

Figure 14 shows a simulation of the charges associated with each treatment and outcome node, based upon the actual experience of the children in the current study (current practice). Only one child was discharged home without a CT scan; this was, of course, the child who returned later with an ICI deterioration. However, this child did not require surgery upon being readmitted, only observation. The charge associated with not imaging a child with a CT scan, even if that child has an ICI, is $881. Because only one child in this sample did not receive a CT scan, these figures must be interpreted with caution.

One of the most striking pieces of information available from the figure is that there is only a $214 difference in the average charges associated with the treatment of children with ICI ($1651) and those without ($1437). Another interesting observation is that the charge of treating a child without an ICI who is then discharged home is $1142 but the charge of admitting a child without an ICI is $1766, a difference of $624. Charge simulations were also conducted using the 20% and 50% inflated charges (data not shown). As might be expected, the differences between the treatments increased accordingly. With charges inflated 50%, the difference between the charge of treating a child with an ICI and without an ICI is $320.

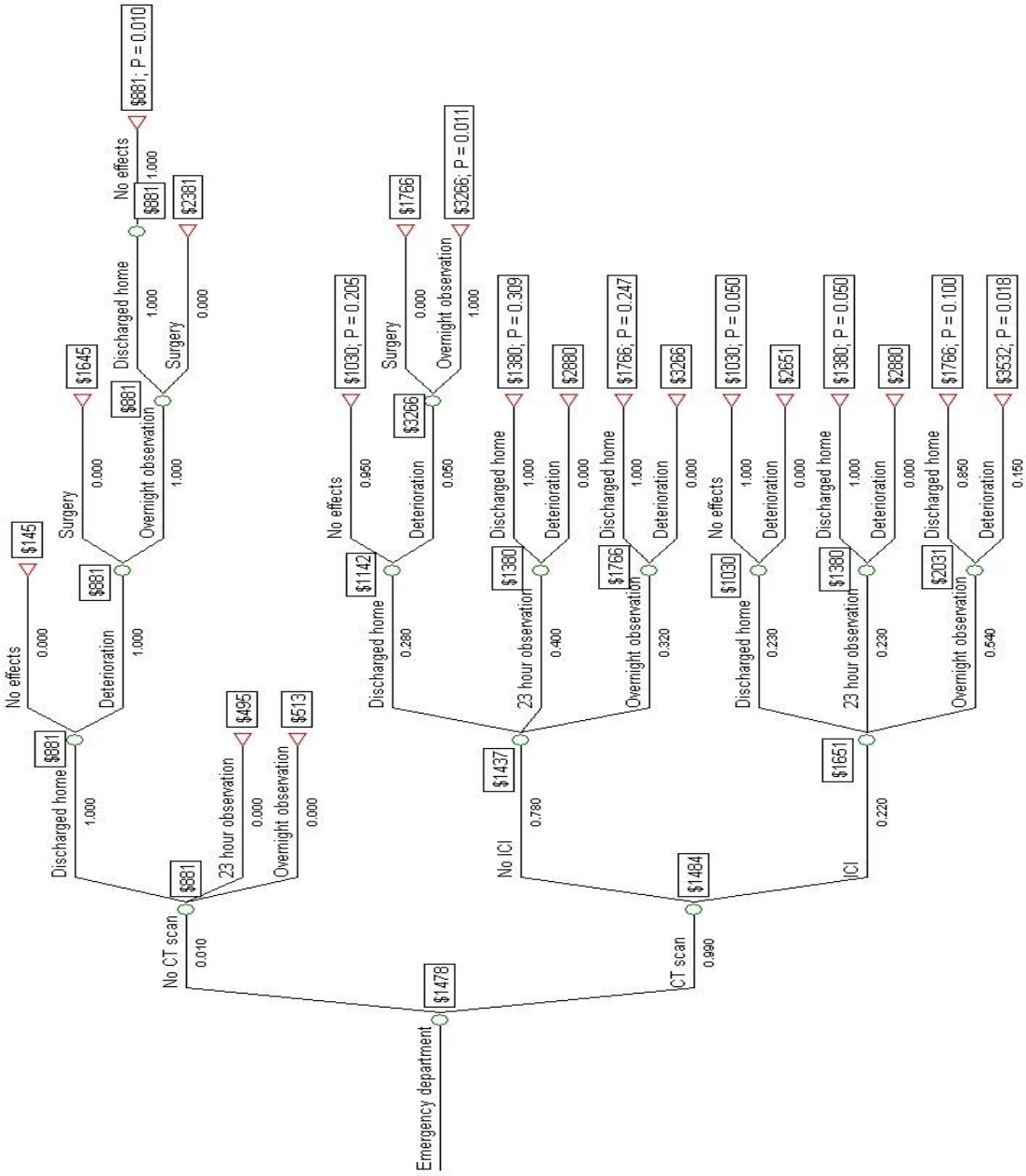


Figure 14. Actual charge simulation (current treatment protocol)

Because the charge associated with one bed day appeared to be low, the simulation was conducted with only that charge inflated. Figure 15 shows those results. Several differences are immediately obvious. One is that the charge associated with not imaging a child is $1249, much closer than in Figure 14 to the average charge of giving a child a CT scan ($1630). Another difference is that the charge difference associated with discharging a child without an ICI rather than admitting that child for overnight observation is now nearly $1000. Finally, the difference between the average charge of treating a child with and without an ICI, after doing a CT scan, is $380. This emphasizes the high use of resources to treat children with mild head injuries but without ICIs. It appears that substantial charge reductions are possible within that treatment arm.

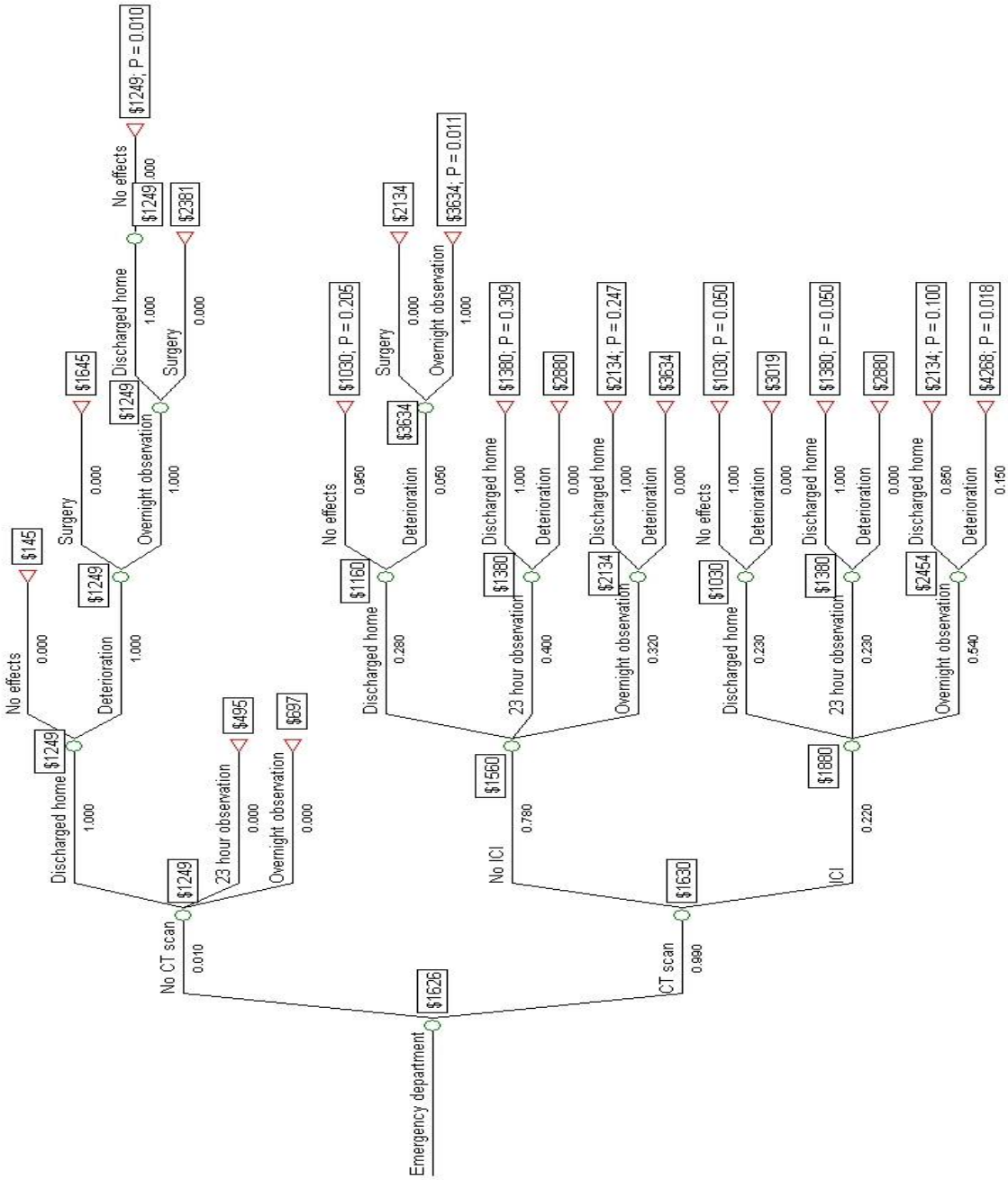


Figure 15. 50% inflated bed day charge simulation (current treatment protocol)

The second charge simulation conducted considered the charges associated with each treatment and outcome decision based upon making the clinical disposition changes suggested by this study. The results of making a strategy change to 1) give a CT scan to every child and 2) automatically discharge every child with a negative result are shown in Figure 16. Implementing these new strategies leaves the average charge of treating a child with an ICI basically unchanged at $1655. However, the average charge of treating a child without an ICI is now $1041. This results in an average charge savings of more than $500 per child without an ICI compared to the usual practice (Figure 14). If it were to be assumed that each child with a positive CT scan went on to be admitted for overnight observation, the difference between the charge to treat a child without an ICI compared to a child with an ICI is nearly $1000, or $2031 compared to $1041.

Seventy-five children in this cohort had negative CT scans (no ICI). Of these, only 21 were discharged home; 30 children were admitted for 23-hour observation and 24 children were admitted for overnight observation. Based upon the findings of this study, those observations were unnecessary because they did not and would not have detected any deterioration in the conditions of the children. Making the two recommended changes to the way in which children are treated after their CT scan would result in the following savings:

30 children x ($1380 - $1041) = $10,170

24 children x ($1766 - $1041) = $17,400

Total savings = $10,170 + $17,400 = $27,570

Figure 17 shows the simulation assuming a 50% inflation in the bed day charge. The average charge of treating a child with an ICI is $1884 (similar to that in Figure 15). However, the average charge of treating a child without an ICI is $1043. Therefore the charge savings that could be realized if the true bed day charge is underrepresented in these figures would be:

30 children x ($1380 - $1043) = $10,110

24 children x ($2134 - $1043) = $26,184

Total savings = $10,110 + $26,184 = $36,294

The total charge savings could also be affected by a 20% or 50% inflation of all charges. In those cases the savings would be $33,084 and $41,355, respectively.

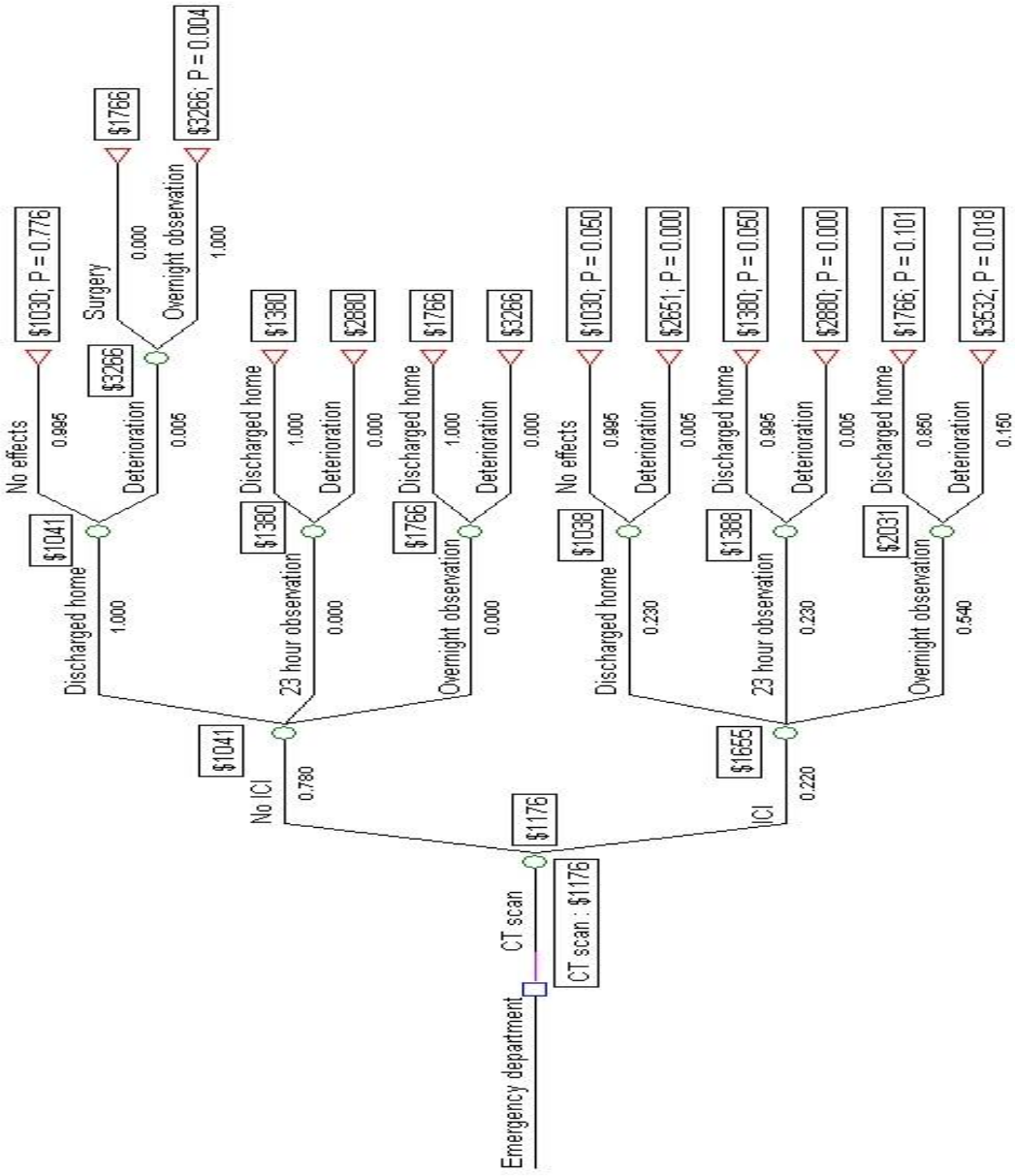


Figure 16. Actual charge simulation (recommended treatment protocol)

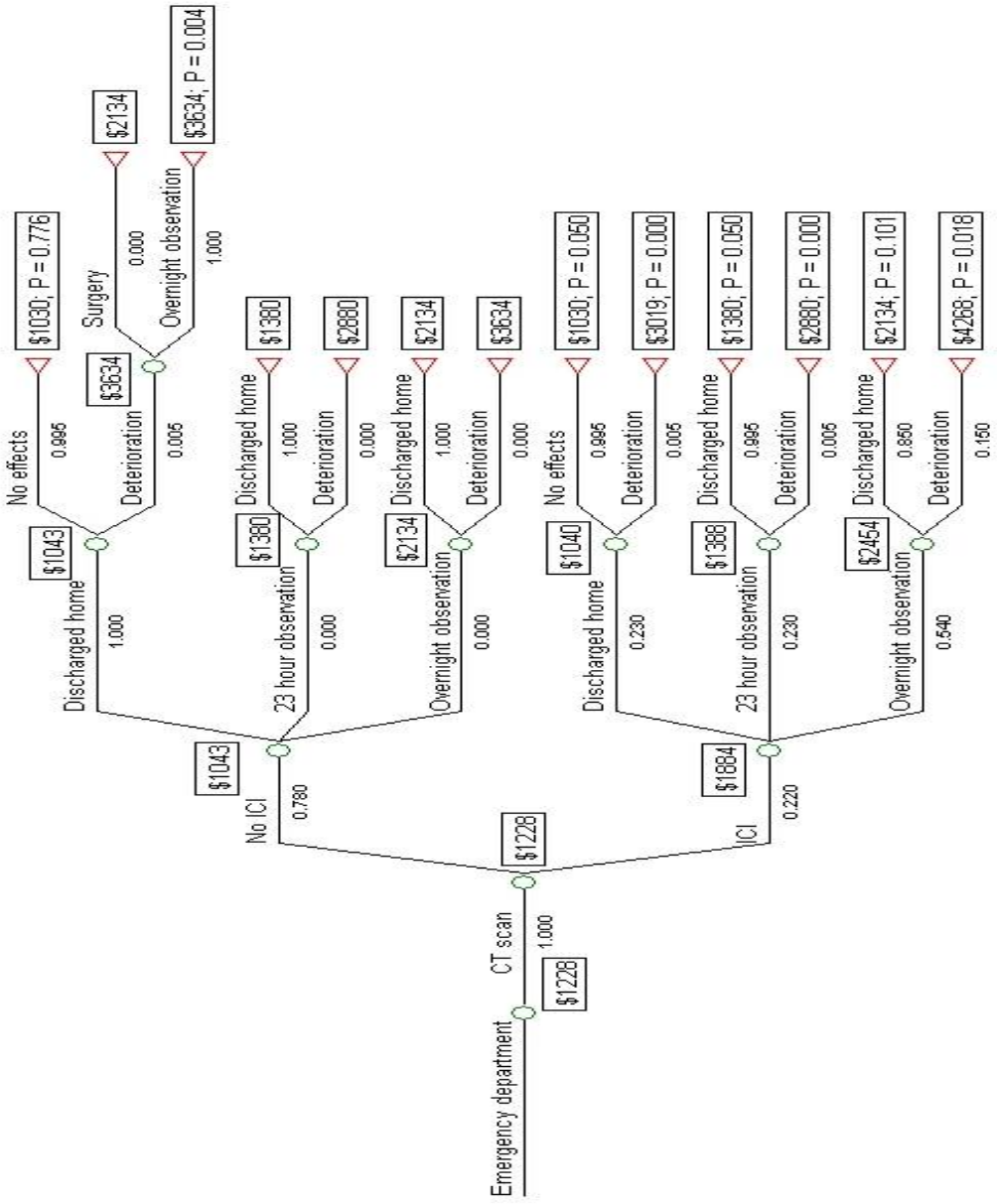


Figure 17. 50% inflated bed day charge simulation (recommended treatment protocol)

Figure 18 shows the third, and most extreme, case of savings possible, shown with a 50% inflated bed day figure. The simulation in Figure 18 combines the reduction in the number of CT scans necessary based on the number of children categorized in the negative terminal nodes in the CART model with the recommended changes in a child's disposition following a negative CT scan. Based on the CART model, 29% of the children could be safely discharged home without a CT scan. The average charge of treating those children would be $151 instead of $1560 as in the current practice. The average charge of treating a child with a CT scan remains as shown in Figure 17. However, instead of 54 of these children, as in the previous simulations, there are now only 24. For this simulation, the proportion undergoing 23-hour and overnight admissions was kept the same as in the actual practice, 45% and 55% respectively. The charge savings that could be realized by both eliminating some CT scans, per the CART model, and following the recommended discharge practices would be:

30 children x ($1560 - $151) = $42,270

11 children x ($1380 - $1043) = $3,707

13 children x ($2134 - $1043) = $14,183

Total savings = $42,270 + $3,707 + $14,183 = $60,160

These figures could also be affected by an overall inflation of the charges shown in Table 24 which would increase the total savings to between $71,000 (20%) and $89,000 (50%).

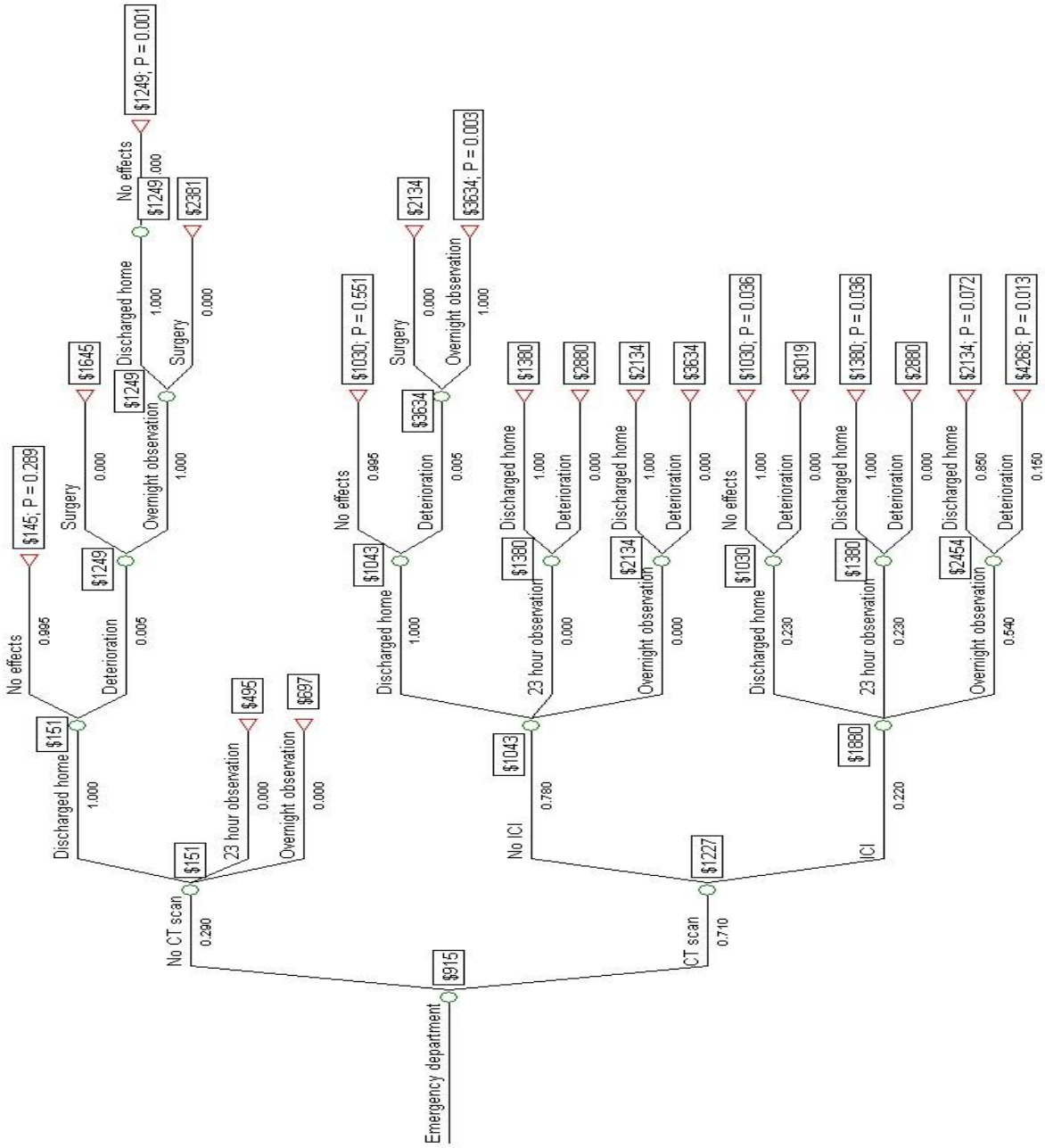


Figure 18. 50% inflated bed day charge simulation (combined recommended practice)

The charge savings in the way children less than three years old with mild head injuries are managed if some or all of the recommendations of this study were to be applied ranges from $27,000 to $89,000 per year.

The indirect charge associated with the injury was calculated as the amount of time that a parent missed work to either take their child to the hospital for the injury or to care for their child afterward. Parents responding to the survey missed an average of seven hours of work to take their child to the hospital for the initial injury (calculated as the total amount of time missed divided by the total number of respondents). Parents also missed an average of 10 hours of work to care for their child following the injury. The average week wage in 2005 for residents of the Pittsburgh metropolitan area was $871 [159]; the average hourly rate would be $21.78 assuming a work week of 40 hours. That indicates that, on average, parents lost $152 in wages to take their child to the hospital and $217 to care for their child after the injury.

Finally, the charge implications of using the recommended practice were examined in the context of each incorrect decision made. The charge savings that could have been realized by treating and releasing children with negative CT scans is $36,294 (assuming the bed day charge is low). Fifty-four of 75 children without ICIs were admitted for 23 hour or overnight observation; these children are considered to be incorrectly managed.

The charge effectiveness ratio per incorrect decision is:

$$\frac{\$36,394}{54} = \$673.96$$

The charge analyses indicate that there is substantial room for savings with only minor modifications made to the way in which children less than three years old with mild head injuries are managed. These savings can be safely incurred without any detriment to the quality of care that the children receive or the outcome following their injury. This is evidenced in particular by the fact that there was only one long term complication among the children in this study.

10.0 DISCUSSION

This study had three specific goals at the outset: to develop a clinical decision-making rule for very young children with mild head injuries; to identify long-term implications and costs associated with the mild head injury; and to investigate the costs associated with the current and proposed practices, including identifying areas in which resources could be better utilized. Each of these goals was met as part of a two phase data collection protocol which enabled information on symptom and injury characteristics to be gathered from multiple sources.

This study examined the characteristics of children less than three years old with mild head injury to determine if a decision-making rule could be developed to categorize children with intracranial injuries from those without. It was designed to make valid and precise statistical inferences about the characteristics of their injuries that could be used to develop a clinical decision-making rule for practitioners. This is an important problem currently facing hospitals because mild head injuries are one of the most common reasons children are treated at hospitals; the incidence of mild head injury peaks at 1115/100,000 population in children less than five years old [36]. However, the available literature does not currently provide any clear guidance regarding the most efficient way to treat most of the children in this age group. The current guidelines

published by the American Academy of Pediatrics (AAP) are only for children from ages two to 20; children less than two years old are excluded from the guidelines [143]. Therefore, this study provides very important and previously unavailable information regarding the development and utility of a clinical decision-making rule for these children.

While having a CT scan was not part of the inclusion criteria for this study, 99% (96/97) received a CT scan during their initial emergency department (ED) visit. The guidelines for CT scanning in this population are ill-defined and are, therefore, subjective by both institution and practitioner [160]. The findings of this study emphasize the liberal use of CT scan in very young children, used to determine whether the child should be admitted for observation or discharged home. While certain characteristics, such as abnormal examination findings, give clear indication that a CT scan should be done, CT scans are also common when the child has a normal GCS score and there are no structural abnormalities to the skull [160], as with the children in this study.

An alternative, preferred by some institutions and practitioners is to admit these children directly to the hospital for overnight observation instead of obtaining a head CT scan. However at the institution in this study, which is the only pediatric Level 1 facility in a large metropolitan area, there is pressure for hospital beds and an attempt is made to admit only those children with significant head injury. Also, this facility has the resources necessary to provide CT scans to children.

These considerations help to explain the high rate of CT scans found in this study; however, the rate of admissions also emphasizes that physicians treat this group of patients very conservatively and do not necessarily feel comfortable discharging a child with a negative CT scan

without some period of observation. While some controversy remains over exposing such young children to radiation, researchers have found that more targeted scanning or lower dose CT scanning can reduce the impact of the radiation exposure [159]. As this research progresses, physicians may feel more comfortable scanning and discharging children, which is one of the recommendations made by this study. However, because CT scans remain a costly and resource-intensive procedure, reductions in the amount of radiation that the children receive will not eliminate efforts to find a set of clinical criteria that can be used to identify patients with mild head injury who can be safely discharged without CT scans.

10.1 INJURY CHARACTERISTICS

In one calendar year, 122 children less than three years old were seen at the local Level 1 Pediatric facility ED for mild head injury complaints. Ninety-seven children were eligible for the current study based upon the *a priori* exclusion criteria. This group of children represents a substantial use of resources because of a high rate of CT scans and because of their disposition from the ED. Thirty-seven percent of these children were admitted to the hospital from the ED. An additional

36% were observed from 23 hours and then released. Only 27% of the children in this study were treated and released from the ED.

The causes of injury and types of falls found in this study are almost identical to those in the Gruskin and Schutzman [136] study of head trauma in children less than two years old. The leading cause of injury in each study was by falling (85% [136] vs. 71% here) and the most common type of fall was a free fall off of an object, such as a counter (53% [136] vs. 49% here). The published literature suggests rates of skull fracture between 60%-100% of the patients with mild head injuries [5] [109] [98] [101]. In this study, 59% of the children with ICI also had skull fractures. These findings provide additional emphasis to the recommendation that skull radiographs not be used to detect brain injury if CT scans are available [160]. However, in the absence of CT scans, radiographs may provide useful screening information [144].

While the incidence rate of ICI among the children in this study, 22%, is approaching the high end among recent studies of mild head injury (5% [102] to 25% [109]), it is not that unusual. In fact, studies of children less than two years old have found a wider range of incidence rates (3.4% [136] to 30% [161]) than studies of all ages. Greenes and Schutzman's [5] study of children younger than two with mild head injury found that 28% of the children with head injuries had ICIs and, of these, 19% had occult, or asymptomatic, ICIs. Their incidence rate, with a similar population, is very close to the incidence rate of this study. Here, two of the twenty-two children with ICIs were asymptomatic (9%); both were less than six months old.

Unlike three previously published studies including 261 patients [109] [5] [145] [98], this study found one case of late deterioration in a child with an initial negative CT scan. While this

indicates an incidence rate of approximately 0.3%, this type of deterioration can be devastating without vigilant caretakers. This type of deterioration is one of the primary reasons that children are treated so conservatively. However, the child in this study returned to the ED five days after the initial negative head CT scan so even overnight observation would not have caught the change.

As found in other studies [144], the age of the child was associated with the presence of ICIs. Sixty-eight percent (n=15) of the 22 ICIs in this study occurred in children less than 12 months old. One-third of the children in this age group had an ICI (15/45). Five of the 23 children 12 to 23 months old (22%) and only 7% of the children 24 to 35 months old (2/29) had an ICI.

This study confirmed the findings of many previous studies in that no single symptom was predictive of ICI [101] [143] [135]. In the Batchelor et al [61] meta analysis of studies of adults and children with mild head injury, they found that headache, nausea and vomiting were most likely to indicate the presence of an ICI while dizziness and blurred vision were not predictive. Here, vomiting was present in 27% of the ICI cases but was not univariately predictive of ICI. The most commonly reported symptom among children with ICIs was the presence of a scalp hematoma (45%). The two most predictive symptoms of ICI were whether the child was consolable and the presence of scalp abnormalities (scalp lacerations or scalp hematomas). Children with a scalp abnormality were two times as likely to have an ICI as those without an abnormality.

Gruskin and Schutzman [136] found that the presence of a scalp abnormality, along with age younger than 12 months and a fall from greater than three feet, was the combination of variables most predictive of ICI. However, Schutzman et al recommend that a head CT scan be

performed on children less than two years old with any of these symptoms: depressed mental status, focal neurological deficits, depressed or basilar skull fracture, irritability/not easily consoled, bulging fontanel, seizure, more than five episodes of vomiting or loss of consciousness for one or more minutes [144].

Similar to the findings of Palchak et al [140], there were no children in this study with an ICI whose only symptom was loss of consciousness. This emphasizes the difficulty with using loss of consciousness as an indicator for intracranial injury of mild head injuries in very young children. Some studies [101] [102] [97] [98] have found a limited relationship between the two. In this study, there were actually slightly more children without an ICI who had a reported loss of consciousness (25%) than children with an ICI and a reported loss of consciousness (18%).

It may also be possible to identify a subgroup of children who do not require imaging and can be safely discharged home. Only two of 29 children between 24 and 35 months old had ICIs and both had somewhat extenuating circumstances to their injuries which would have put them into a higher risk group. One was a restrained rear passenger in a motor vehicle accident with documented loss of conscious and multiple abrasions and the other was hit in the head with a stick and suffered seizures following the injury. Schutzman et al [144] identified a low risk subgroup of children with mild head injury, characterized by low energy mechanisms, such as falls from heights less than three feet, no signs or symptoms two or more hours after the injury and age greater than 12 months. For this group, observation is recommended; imaging is felt to be unnecessary.

In order to determine if a set of characteristics or pattern of symptoms could identify children with ICIs, a series of classification and regression tree (CART) models was run. This process was designed to integrate the symptom and injury information abstracted from the medical records into a clinical decision-making rule.

10.2 CLINICAL DECISION-MAKING RULE

CART [155] is ideally suited to the generation of decision-making rules because it can easily handle large numbers of predictor variables and can identify complex interactions or patterns within the data. It is also simpler to interpret than a multiple logistic regression model, making it more likely to be used in a clinical setting. As CART [155] allows the user to specify a misclassification penalty, different penalties for missing a child with an ICI as opposed to classifying a child without an ICI as having an ICI were investigated here.

The final model chosen from all of the CART runs was the model using grouped age and a misclassification penalty of two. This tree, shown in Figure 11, correctly classified children with ICIs 100% of the time. It also performed well in the test dataset, classifying 73% of the ICIs

correctly. The specificity of the rule, 40%, was as good or better than previously published clinical decision-making rules of mild head injury in children [139] [138].

The final model produced in this study provides a relatively simple way to categorize children with mild head injuries who can safely be treated and released rather than admitted to the hospital for 23-hour or overnight observation. While the model includes six predictor variables, which might make it somewhat unwieldy in clinical practice, pruning back the model to increase its simplicity severely limited its predictive power and classification ability. This model, while possibly needing some refinement, does provide physicians with some definite demographic characteristics and symptom information to guide clinical decision-making. It also gives clinicians some valuable new information about the importance of specific mild head injury symptoms in children less three years old.

The decision-making rule shown in Figure 11 first splits children with respect to vision changes. This immediately classified two-thirds of the children with ICIs. Next, whether the child was consolable was used to classify one more child with ICI. The remaining six children with ICI moved on in the tree. One half of these were classified as females with no scalp lacerations (two node splits), two others were classified as females, no vomiting and the final child was classified by the presence of vomiting and residence in the county of the hospital.

Vision changes is an unusual variable on which to base the decision tree, compared to other decision-making rules published about mild head injury. Palchak et al [139] identified abnormal mental status as the primary split in their decision tree. Haydel et al [138], in their study of older children (5-17 years old), found that a combination of six variables accurately predicted the

presence of ICI; changes in vision was not one of the predictive variables. In this model, vision changes is being used primarily as a surrogate for grouped age, which displayed a strong univariate relationship with ICI. However, whether the child was consolable and the presence of scalp lacerations were also part of the surrogate relationship.

The ability to use surrogate variables is both an advantage and disadvantage to CART [155]. One advantage is that not only can CART handle observations with missing values but, by analyzing the response patterns of all variables, it can identify heretofore unknown relationships among variables and between predictor and target variables. In this case, vision changes was identified as the primary split for the model. This could indicate that physicians should give more emphasis to determining if vision changes have occurred in children with mild head injury.

However, the use of vision changes as a surrogate could also indicate that the pattern of variables identified as a surrogate, or surrogates, for visions changes would have been given more emphasis in a different cohort. In this case, grouped age was the top surrogate for vision changes and whether the child was consolable was the second best surrogate. Grouped age was not used as a splitter in the model shown in Figure 11, although age has been considered in other clinical decision-making models [139] [138]. This could indicate that vision changes itself is a weak predictor of ICI and that grouped age is a better predictor, but CART's use of surrogates forced vision changes into the model. Whether the child was consolable appeared in the model as the first child split, rather than the main parent node split. Its appearance in the model could indicate that the consolability of the child is an important consideration when evaluating children in this age group, who are largely pre-verbal. Physicians may need to evaluate and rely on such cues rather

than those symptoms that can be directly expressed by older children or adults, such as amnesia or nausea. The presence of scalp lacerations may also play an important role in mild head injuries in children less than three years old. The presence of scalp hematomas has been given emphasis in clinical decision-making rules for mild head injury [138] [162] but scalp lacerations have not. It could be that these types of abrasions are more important in younger children, where lower force mechanisms may cause ICIs, than in older children or adults.

While the logistic regression analysis confirmed some of what the CART modeling produced, the information presented in Table 22 highlighted some of the difficulties directly comparing logistic regression to CART. Directly comparing models produced by logistic regression and CART is extremely difficult, and perhaps impossible, given the ways in which the two methods differ. Logistic regression cannot handle observations with missing variable information, while CART can. In this study, logistic regression was run with the variable information included as unknown instead of eliminating many observations without known symptom information. Immediately, then, the two models that were produced used different variable information for their estimates.

Also, CART did not output parameter estimates, which made a direct comparison with logistic regression very difficult. Additionally, CART used nested splits, representing complex interactions. These interactions were extremely difficult to reproduce in logistic regression. Therefore, while using logistic regression to confirm the fit of the CART model was an interesting exercise, it did not add any information of importance to the main aim of this study, producing and evaluating a clinical decision-making rule in children less than three years old.

For this study, then, the use of CART was a logical and important analysis tool. One of the major advantages of using CART to develop a clinical decision-making rule is that symptom information and patient characteristics do not occur in isolation. Physicians make decisions based on characteristics and symptoms occurring simultaneously. CART is an extremely powerful analytic tool and is able to capture and categorize these complex relationships.

While this model provides some new and important guidance for treating physicians, it does have some limitations. One limitation with the model shown in Figure 11 was that it grouped 15 of the 22 children with ICIs in to a child-node split following a positive response for vision changes (the left side of the model) but was unable to produce any further splits. This means that approximately two-thirds of the ICIs could not be characterized any more clearly than by vision changes, or perhaps by its surrogate, grouped age. Having a surrogate variable in the model may prevent it from wide use among clinicians. They may feel that until more research is done about the exact meaning of vision changes in this model that it should not be used. The surrogate variable may represent other, more powerful predictors, like age, that would have been more important in another cohort or if less symptom information had been missing from the medical records.

The clinical decision-making rule developed in this study is the first developed specifically for children with mild head injuries who are less than three years old. This rule had only the presence of vomiting in common with other published decision-making rules in children [139] [138]. The presence of vision changes, whether the child was consolable, and the presence of scalp lacerations are all new variables to consider when evaluating these children for ICIs.

Currently, the NEXUS group [162] is analyzing the data from a large multi-center prospective trial on mild head injury. They identified six symptoms highly predictive of ICI in children: evidence of significant skull fracture, altered level of alertness, neurologic deficit, persistent vomiting, presence of scalp hematoma, abnormal behavior, and coagulopathy. However, the goal of their study was to identify what they called "clinically important ICI" or those requiring neurosurgical intervention or that were likely to be associated with significant long-term neurologic impairment. The problem with this definition is two-fold. First, as shown clearly in this study, the overuse of resources occurs not with children requiring neurosurgical intervention but with those who do not. While such a decision-making rule may be helpful for some neurosurgeons, it does not help most physicians who are treating children whose head injuries will never require surgery but need to be able to effectively manage the children while minimizing the use of resources. Second, as discussed earlier, it is extremely difficult to foresee the long-term complications of mild head injuries in very young children. The evidence suggests that there may be some children more susceptible to negative long-term consequences. These children require careful follow-up and it may not be possible to identify such children with clinical symptoms only.

As noted in the Berger and Adelson review [60], the literature on which to form a consensus statement regarding the treatment of children less than three years old is weak. This study provides some new and important evidence on the two areas in which mild head injury consensus statements are based: whether to perform cranial imaging and whether to admit. As evidenced by this study, children with mild head injuries who are less than three years old should

undergo CT scanning because of the high rate of asymptomatic ICIs found in this population. For children with negative CT scans, there does not seem to be evidence necessitating overnight admission for observation.

This study may provide physicians some insight in to characteristics that are important to identifying children with ICIs. Only additional studies will be able to determine if the criteria identified here will be applicable to populations beyond the one included in this study. Also, additional studies could elucidate some characteristics that could be used to further split the ICIs grouped by the presence of vision changes but not on any other characteristics.

10.3 SURVEY RESPONSE

The follow-up survey was designed to provide information about the symptoms that children may have experienced upon their release from the hospital, their follow-up care, behavioral changes and the amount of time parents missed work to care for the child. The information garnered from the survey elucidated the use of resources for these types of injuries, indirect costs associated with such injuries and the potential long-term effects.

For purposes of sample size calculations, the projected survey response rate was 70%. This original survey had a response rate of 14% (14/97). Even after a simplified survey was developed, a small incentive was included and multiple telephone calls were made to the participants, only ten additional responses were received. The total response rate was 25% (24/97). Only three families of children with an ICI chose to participate, leading to a borderline statistically significant difference in the rate of response among families whose child had an ICI and those who did not. The refusal rate for this study was very low; only 5% of the parents refused to participate. The majority of the families simply never responded at all.

The responses to both surveys were pooled together because the respondents did not vary by age group of the child, presence of ICI, sex of the child or cause of injury. However, nine of the ten respondents to the abbreviated survey resided outside of Allegheny County. The reasons for such a response differential are unclear; it could be that, for families who had to travel a greater distance for treatment, the experience was more profound and they felt some obligation to respond upon receiving the one-page survey and stickers. It could also be that families from outside of the county were better off financially or had a higher SES and were therefore more likely to respond. Three parents of children with ICIs responded, one to the original survey and two to the abbreviated survey. All of these children were less than one year old at the time of injury and all transferred to the hospital from outside of the county.

Recent research has found a decline in survey response rates over the past several decades [163]. This decline is attributed to concerns with privacy, confidentiality and the exploitation of personal information [163]. However even given lower response rates in recent years to surveys in general, the response rate to this survey is exceptionally low.

Some of the specific characteristics of this population have been associated with very low response rates, including urban residence and young age [164]. One study attempting to assess the hospital experience of inner-city patients [165] found that obtaining accurate data was difficult due to changing addresses, variable access to telephones and a higher prevalence of illiteracy than in many other populations. Similar factors were identified in this study in which 30% of the participants had moved since the hospital visit and new addresses could not be located for half of those. In fact, almost 10% of the families moved between the original and abbreviated survey mailings. Additionally, 40% of the families had unlisted or disconnected telephone numbers, including 17 families who had their telephone numbers disconnected between the mailings for the two surveys. However, no direct measures of socioeconomic status (SES) were available from the medical records beyond zip code of residence so no inferences regarding parental education or income are possible here.

The effects of the child's injury on the parents may have also contributed to the low response rate. Nearly all of the accidents were witnessed by a caretaker and parents were directly involved in all of the drop type of injuries. A study of the association between parental posttraumatic stress disorder (PTSD) symptoms following a child's injury found that 20% of mothers and 11% of fathers met the clinical diagnostic criteria for the disorder [166]. The authors

concluded that "parents are directly and indirectly affected by the illness or accidents of their children: They are traumatized by their own experiences (e.g., feelings of guilt) and they are exposed as witnesses to traumatic experiences of their beloved children." [166]

However, even with the limited response rate some interesting findings emerged, especially regarding the indirect costs to families. While discharge instructions recommended follow-up care with the child's primary care physician (PCP), 30% of the parents responding to the survey did not do so. Also 58% of the families had one parent miss at least part of one work day either at the time of the accident or after the child's discharge. The majority of families had someone miss two or more days of work. The data presented here must be interpreted very cautiously due to the low response rate but it does provide some information regarding the amount of time and money being spent by families on even the most minor of mild head injuries in very young children.

10.4 LONG TERM OUTCOMES

The short- and long-term consequences of mild head injuries in children are not well understood. This study attempted to investigate new or recurring symptoms in the children following their mild

head injury through the use of the follow-up survey. The survey also gathered information regarding the late effects of the initial injury and any post-injury treatment that was required.

A group of symptoms, known as post-concussive syndrome, includes headache, dizziness, blurriness, irritability, anxiety and concentration and memory problems can occur after mild head injuries. The most commonly reported post-injury symptoms from the survey responses were irritability, reported in 21% of the children, and sleeping more than usual, present in 16% of the children. The risks of these symptoms following mild head injury have been studied in children. In one study [167], parents of 28% of the children reported that their child's personality had changed following their mild head injury. Likewise, Ponsford et al [131] found that 17% of parents continued to report symptoms and behavioral problems more than three months following the injury. In the current study, 13% of the parents responding to the survey reported behavior changes in their children, including increased clinginess, crying and irritability.

The long-term effects of a child's mild head injury continue to be controversial. Of the 40 studies considered in the Satz et al [129] review, 13 reported adverse, 18 reported null and 9 reported indeterminate findings. They concluded that the stronger studies were generally associated with the null findings and that mild head injury may result in transitory alterations in functioning. McKinlay et al [168], however, found that children who experienced a mild head injury severe enough to warrant hospitalization were more likely to exhibit hyperactivity, inattention and conduct disorders between ages 10 and 13, especially if the injury occurred before the child was five years old. Children seen as outpatients for their mild head injuries were comparable to the non-injured control group. The children in this study would be in the high risk

group for developing problems as they grow older. However, the current study was not designed to address behavioral or psychosocial outcomes from the mild head injury beyond one point of contact at approximately one year following the injury. Even in the short-term, though, these children exhibited some behavioral changes that parents attributed to the mild head injury.

Because mild head injuries occur so often in children, understanding both the short- and long-term outcomes of these injuries is crucial. Prospective studies need to continue, especially to identify a threshold at which a child with a mild head injury could have long-term repercussions. Also, physicians need to be able to inform parents of the potential consequences of a mild head injury in children. Discussing short- and long-term consequences should be part of the routine discharge information provided to caretakers. Parents, families and teachers need to be prepared to deal with any symptoms or behavioral problems that remain or develop following a mild head injury.

10.5 COST

The cost, or charge, analysis conducted here indicates that substantial charge and resource savings can be realized by some minor changes in the treating practices at the study institution. Namely,

the combination of both CT scan and overnight observation can be eliminated for children with negative CT scans. One child had a deterioration following an initial negative CT scan. However, this deterioration occurred five days after the initial visit and would not have been detected during an overnight observation. This finding emphasizes the fact that the recommendations proposed for the charge analysis could be safely implemented without jeopardizing the health of the children.

Using the information garnered from this study, it was presumed that children with an initial negative CT scan can be safely discharged home under the care of responsible parents or guardians with appropriate guidelines for monitoring and returning to the hospital if new symptoms develop or existing symptoms worsen. This alone would eliminate 66% of the hospital admissions and 86% of the 23 hour observations for mild head injury in children less than three years old. The associated charge savings would be $36,294 per year. Using the clinical decision-making rule would result in a charge savings of between $20,000 and $30,000 compared to the usual practice. The most extreme case of savings, combining the two practices, would result in savings of between $60,000 and $90,000 annually. This represents substantial savings potential, especially considering that the cohort on which these findings are based only consisted of 97 children. The changes in practice could save almost $1000 per child if employed completely.

One other published study was identified that investigated the costs associated with treating mild head injuries [80] [148]. While that study was based upon healthcare data from four studies in two countries (one Norway and three US), their conclusions regarding the most cost-effective method of treatment were remarkably similar to those found here. The investigators compared the costs associated with overnight observation of mild head injury compared to the strategy of using

CT scan and discharging patients with negative scans. They found that costs were one-third lower with the CT strategy compared to the observation strategy. As shown in Figure 15, this study also found a 33% reduction in costs if children with negative CT scans were to be discharged rather than admitted for observation.

The results of this study confirm that there is currently an overuse of resources to treat children less than three years old with mild head injury. Depending upon the comfort level of the physician, moderate to large resource and charge savings could be realized from small changes in the way these children are treated. If the results of the CART analysis were put in to practice, approximately 30% of the children could potentially be discharged from the ED without undergoing a CT scan. Even if the decision-making rule is not put in to use immediately, changes in the way children with negative CT scans are treated would allow a better use of resources. It appears that these children could be safely discharged from the ED with extremely low risk of any negative consequences.

10.6 STRENGTHS OF THE STUDY

This study is one of the first designed specifically to generate a clinical decision-making rule for the treatment of mild head injury in children less than three years old. The results of the decision

rule indicate that it is possible to identify children with ICIs in this age group with a high degree of accuracy. The decision rule also indicates that there is the potential to identify a group of children at low to no risk of deterioration that could be treated less conservatively. Overall, the results indicate that there is an overuse of resources in treating such children and substantial cost and resource savings could be possible by implementing small changes in their disposition. The total savings, in a relatively small cohort of 97 children, could be as such as $90,000 per year.

This study had many strengths. First, unlike many studies of this type which rely on convenience samples, this study was designed to make valid and precise statistical inferences about the characteristics of the injuries of children less than three years old that could be used to develop a clinical decision-making rule for practitioners. For that, sample size calculations were done using the sensitivity of the CT scan to detect ICIs. While the target sample size was 101 and only 97 children met the eligibility criteria for the study, the proportion of children estimated to have ICIs, based on the current literature, actually underestimated the proportion found here. Thus, this study had an adequate sample size to detect meaningful differences between children with and without ICIs.

Also, the study was designed to include consecutively admitted children with mild head injuries from one major Level 1 Pediatric hospital. The sample captured all eligible children from one calendar year and thus provides a representative picture of both the types and characteristics of the children less than three years old being treated at the institution with mild head injuries. Also the treating hospital has completely computerized medical records, enabling researchers to easily

and readily locate both an individual file and the necessary symptom, injury and treatment information.

The data abstracted from the medical records was included in a clinical decision-making rule, designed to distinguish children who could be safely treated and released from the hospital from those requiring more care. The rule that was produced was predictive, simple and clinically useful. It identified not only with 100% accuracy those children with ICIs, but also identified a group of children at low risk for deterioration; these children could potentially be treated less conservatively.

The addition of the follow-up survey provided data on symptoms following the injury that was not otherwise available. It also provided information on the types of follow-up care that the children received and some of the indirect costs to the families that were associated with the injury. This information helps to present a clearer picture of the amount of care that these children with mild head injuries require and the types of resources being utilized in these instances.

Finally, the inclusion of a cost analysis provides clear cut guidance to both physicians and hospital administrators regarding the areas in which potential charge savings could be realized. Traditionally, children with mild head injuries are treated very conservatively so as not to miss any deteriorations. The guidelines proposed here offer minor suggestions that maintain careful and thorough treatment protocols but also allow for a more judicious use of resources.

10.7 LIMITATIONS OF THE STUDY

While this study had many important strengths, it also had some notable limitations. Many of these were inherent to the study design. This study was a retrospective record review and was thus limited to the symptom, injury and treatment information abstracted from the medical record. There were no opportunities to clarify or obtain any missing data. Because of that, some assumptions had to be made regarding the symptoms reported at the time of injury. It was unclear whether a symptom not noted in the medical record was truly unknown or simply not recorded because of its absence; missing symptom information was, therefore, considered both ways in this study. Also, while GCS score during the CHP ED visit was noted in the medical records, it was possible that children who transferred had a GCS score lower than 14 at the initial institution that improved by the time they presented to CHP.

It is possible that these results would not be replicated in a different cohort, especially those of from the CART model. The characteristics and injury symptoms of the children in this cohort could be unique and a CART model run on children on the same age might not produce the same symptom nodes. This could also be true of the charge simulation, which would be influenced by the number and characteristics of children with ICIs, although to a lesser extent that then CART model would be. These results, based upon one year of data from one institution, need to be interpreted as such and the results cannot be over-generalized.

The low response rate to the follow-up survey was also a limitation. The lack of information from 75% of the eligible participants severely limits the generalizability of the survey results. However, the response rate of this study highlights many of the problems found with other studies of similar populations, including a transient population [164] and potential effects of the child's accident on the parents [166].

As with any retrospective survey, there was a potential for recall bias in the parents' responses. However, that does not seem to be a great issue here. The study was designed to take advantage of the first complete year of available data from the hospital (2005) specifically to minimize the amount of time since the injury had occurred. Also, the symptom information that could be compared from the parental survey and from the medical records was in agreement.

It might also be argued that the parents of children who experienced ICIs would be more likely not to respond, given the literature discussed above. That could account for the differential response rate found between families of children with ICI and those without. The three families who responded to the survey whose children had ICIs did not report any behavioral changes or post-injury symptoms.

Another potential limitation involves misclassification bias. Children with intentional injuries were intended to be excluded from the study. However, it is possible that some of these cases were intentional injury and either were not identified in the medical record or were followed up on at a time when that information did not get entered in to the medical chart. Thus, it is possible that some of the injuries examined here were intentional. It is also possible that inaccuracies in the medical record regarding time of injury versus time of admission led to children

being excluded who had actually presented to the hospital within 24 hours of their injury. Finally, potential participants were identified from the hospital discharge database using ICD9-CM codes and age at time of injury. If there were incomplete or inaccurate, eligible participants may have been missed.

As with any study, there are also some potential threats to the external validity of this work. The specific components of this study population require careful consideration about the populations to whom these results can be extrapolated. The data presented here was from one Pediatric Level 1 hospital in a major metropolitan area. The physicians at this facility had readily accessible access to CT scanning, as evidenced by 99% of the children receiving CT scans during their initial visit. A facility with more limited access to CT scans may want to observe children for longer periods of time to rule out the intracranial injuries found here by CT scan. More than half of the children seen for the mild injuries investigated in this study were transferred from outside facilities. Hospitals who treat the majority of presenting patients themselves may find that the decision-making rule is not as applicable to their populations. Also, the specific age, race, sex and cause of injury characteristics of these children may not be generalizable to other groups, although these children had very similar characteristics to other published studies of mild head injury in very young children.

10.8 RECOMMENDATIONS FOR FUTURE STUDIES

This study has provided an important foundation for studying mild head injury in children less than three years old but there is still more work to be done. One essential component to any future study would be a prospective design with data on symptoms captured at the time of admission using one standardized form with clear symptom and variable definitions. This would enable physicians to capture the relevant symptom information completely and would eliminate the disadvantages associated with a retrospective record review.

One important consideration for any future study of mild head injury in very young children would be to obtain parental consent for medical record review and, potentially, follow-up at the time of admission. The follow-up survey in this study was limited by lack of consent; problematic were both an inability to locate the families and parents being notified and not responding. Emphasizing the importance of such studies as this one at the time of the injury may improve these rates. It might also get parents invested in such studies at a time when they were most interested in the outcome of the study (at the time of injury), rather than waiting, as done here, when they could be too busy or unwilling to recall the events surrounding the injury.

It would also be helpful to have a shorter follow-up period, with follow-up contact made one week, several weeks and several months after the injury. This would allow a more accurate portrayal of the child's recovery, would eliminate recall bias and would also enable researchers to keep up-to-date with contact information in what appears to be, in this study at least, a rather

transient population. The need for longer term follow-up, including social, behavioral and school performance evaluations, is also vital.

Finally, one hospital alone cannot produce the necessary number of patients nor the generalizability to develop a clinical decision-making rule that would be widely implemented by physicians. Data on patient symptoms and injury characteristics from different hospitals would enable researchers to have the sample size necessary to make detailed comparisons. An intriguing hypothesis not fully able to be answered on this somewhat limited study population is that two year olds, especially older ones, may be more similar to older children than to infants. This type of refinement would only be possible with a larger sample size. Data from multiple centers would also allow researchers to investigate decision-making rules based on different population demographics. While the NEXUS group [162] has many of these recommendations in place for their ongoing study of mild head injury, they have limited their decision-making rule to predicting which patients will require neurosurgical intervention, rather than investigating ICI more broadly. This restriction and the fact that their study was not designed specifically to make inferences to children less than three years old limits generalizing their results to predicting the incidence of ICI in very young children. Future studies need to consider this age group specifically and more research needs to be done to determine exactly which injuries have a lasting impact on the health and long-term future of children.

11.0 CONCLUSION

The objective of this study was to establish a clinical decision-making rule for mild head injury in young children, an extremely common type of injury seen in emergency departments. These children appear to respond differently to mild head injuries and face different developmental issues than do older children and management guidelines remain unclear. The findings of this study corroborate those of other studies of mild head injury in children, especially regarding the demographic and injury characteristics of these populations.

A CART model was developed that correctly identified all of the children with ICI in this sample and also had good reproducibility in a test sample. This work now needs to be replicated and expanded upon in other populations. While similarity exists between decision-making rules for older children and that found for this cohort, very young children have unique characteristics that merit further study and may require a separate decision-making process. A prospective, multi-center study with standardized CT scanning and treatment protocols, using standardized data abstraction forms, and requesting parental consent at the time of injury, would be the ideal situation in which to continue this important work.

Finally, it appears that substantial cost saving could be realized by discharging children with mild head injuries and negative head CT scans rather than admitting them for observation.

APPENDIX A

MEDICAL RECORDS ABSTRACTION EXEMPT IRB SUBMISSION

IRB COVER SHEET: REQUEST FOR EXEMPT REVIEW
AND WAIVER OF HIPAA AUTHORIZATION
(Medical Record Review by Investigator with Patient Care Responsibilities)

☒ **NEW SUBMISSION** ☐ **RESPONSE TO COMMENTS** **§46.101b(4)** ☐**; §46.102(f)** v. 042505	**To be completed by IRB staff**: IRB # __ __ __ __ __ __ __ **Date Received**: **By**:

Title of Study: A Clinical Decision-Making Rule for Mild Head Injury in Children: Record Review

Principal Investigator: Last name: **Zuckerbraun** First name: **Noel**

Title: Assistant Professor Department: **Pediatrics**

Pitt Faculty ☒; Pitt/UPMC staff ☐; Pitt student ☐; Other:

School: Arts & Sciences; ☐ Business ☐; Dental ☐; Educ ☐; Heath & Rehab Sci ☐; Info Sci ☐; Medicine ☒; Nursing ☐; Pharmacy ☐; Pub Health ☐; Social Work ☐; LRDC ☐; Other (specify):

Office Address: 3705 Fifth Avenue, Suite 200 SB; Pittsburgh, PA 15213

Phone number: 412-692-7692 **Fax number**: 412-692-7464 E-mail address: **zuckns@chp.edu**

Co-Investigators: **Tom Songer PhD, Jeanine Buchanich, MPH and Barbara A Gaines MD**

If PI or Co-Investigator is student, list name of **faculty sponsor** *or* **mentor** *who will take responsibility for the oversight of this research, and has signed the attached Faculty/Mentor assurance*:

Name:

To whom should IRB correspondence be sent: PI? Yes ☒ No ☐; Other Name? **Jeanine Buchanich Other Fax**: 412-624-9969 Other E-mail: **jeanine@pitt.edu**

Where will study take place? University of Pittsburgh ☐; UPMC Oakland Campus ☐; CHP ☒; Magee ☐; Other UPMC Hospitals ☐ (specify): ; Other (specify): – U.S. ☐; foreign ☐.
*****Is documentation attached authorizing conduct of research at non-Pitt/UPMC site? No ☐ Yes ☐

Estimated duration of entire study: 2 years

Source of Financial Support: Federal (e.g., NIH, NSF, CDC) ☐ (name of agency):
Commercial Sponsor ☐ (name): ; Other ☐ (name): ; None ☒

Does any research team member have a financial conflict of interest: No ☒ Yes ☐: **If yes**,
(a) do they have an equity interest in the commercial sponsor that exceeds 5% or $10,000? No ☐ Yes ☐
(b) do they receive payments from the commercial sponsor that are expected to exceed $10,000/year? No ☐ Yes ☐
(c) do they possess a licensing agreement that may lead to revenue sharing from developing technology? No ☐ Yes ☐

Are all records currently available for study? No ☐ Yes ☒

The PI of this study must (a) be a UPMC staff member and/or have UPMC-privileges, *and* (b) provide related care (i.e., related to the information desired), or is in the position to provide related care (including treatment and/or diagnostic services), to the types of patients whose medical records will be studied in this investigation. Please describe how the PI meets *both* of those criteria.
The PI is a member of the Children's Hospital of Pittsburgh medical staff who routinely provides medical care to patients with traumatic emergencies who are evaluated first in the pediatric emergency department. She has legitimate access to the medical records of the types of patients whose records will be studied as a part of this retrospective medical record review.

IRB Protocol

1. **Study Aims**

(a)**What is this research intended to accomplish**? The main aim of the present study is to determine the most efficient method for treating children (<17 year old) with mild head injuries. This study intends to utilize clinical data to develop a decision making rule for patients with mild head trauma. It will investigate the sensitivity, specificity and positive and negative predictive values of patients' symptoms versus the results of a CT scan. It will also develop an algorithm, using CART (classification and regression trees) to evaluate the effectiveness of using symptoms or clinical criteria to direct the management of mild pediatric head injury. The goal of the study is to evaluate whether patient symptoms can be used to determine the severity of injury and likelihood of adverse outcomes compared with the "gold standard" CT scan among pediatric patients with mild head injuries.

2. **Background and Significance**

(a) **What observations or prior scientific findings serve as the basis for this study**? Traumatic brain injury (TBI) is a major cause of death and life-long disability in the United States. The annual incidence of TBI in the United States has been estimated to be 180-220 cases per 100,000 population (Sumas & Narayan, 1999). In the United States, with a population of almost 300 million, approximately 600,000 new TBIs occur per year. As many as 10% of these injuries

are fatal, resulting in almost 550,000 persons hospitalized annually in the United States with head injuries. The incidence of mild traumatic brain injury (MTBI), or mild head injury, in emergency departments (EDs) appears to have increased, almost doubling from 216 per 100,000 in 1991 (Sosin et al., 1996) to 392 per 100,000 in 1996 (Guerrero et al., 2000). In contrast, MTBI hospitalizations appear to have declined from 130 per 100,000 to 51 per 100,000 between 1980 and 1994 (Thurman & Guerrero, 1999). Existing data indicate that the rates of hospital admissions and emergency department visits for head injuries are several times higher among children than the general adult population (Jennett, 1996), with the highest rates among children under age five (Beattie, 1997) and among children in lower socioeconomic groups (Adelson & Kochanek, 1998). Approximately 80% of the hospital admissions for head injuries are for mild head injuries.

(b)**Why is it important to conduct this research**? Children are susceptible to potential long-term consequences following a mild head injury, emphasizing the importance of both giving children the best and most appropriate care for their injury and balancing the utilization and cost of resources required for this care. This study intends to investigate and identify the clinical characteristics that maximize care and minimize costs for these resource intensive, yet minor, injuries. The public health significance of this study is that 1) a decision rule using clinical criteria could influence pediatric head injury management strategies and 2) developing a decision rule which maintains high sensitivity to capture children who may develop intracranial injury (ICI) but increases specificity will help to minimize the use of resources in this population.

3. **Medical Records to be studied**

(a) **At which hospital(s) will medical records will be studied?** Medical records will come from Children's Hospital of Pittsburgh.

(b) **Specify the inclusion/exclusion criteria for the selection of medical records requested for this study.** Inclusion criteria for this study are as follows: children age less than three years old with mild head injury (ICD 800-804, 850-854) treated at CHP between 1/1/2005 and 12/31/2005 and an initial Glasgow Coma Scale (GCS) score of 15 when seen in the Emergency Department. Exclusion criteria will include: children with penetrating injuries, children with depressed skull fractures requiring surgery, children with injuries suspected to be intentional and children who had their initial CT scan >24 hours after the injury occurred.

(c) **Specify the approximate number of individual patient medical records that will be requested for the purpose of this study.** 2,000

(d) **Describe or list the specific data elements that will be extracted from these medical records for the purpose of this study.** The specific data that we will be extracting includes: Age, gender, sex, race, zip code, admission month, injury type, severity and mechanism, presenting symptoms, co-morbidities, procedure and diagnostics codes, history of other underlying medical disorders, charges, payor and discharge/disposition status. The data set will be completely anonymous.

NOTE: Under NO circumstances can identifiers (i.e., names, social security numbers, phone numbers, medical record numbers, street addresses, etc.) be recorded with the data. The dataset must be completely anonymous. For that reason, once the information has been extracted from the medical record, it will not be possible for the investigator to go back to that same medical record and add other patient-specific information to this research dataset.

4. **Data Analysis**

(a) How will the medical record information be analyzed to determine that the objectives aims of this study have been met? For the statistical analysis of this study, we will construct a classification and regression tree (CART) which will be used to identify symptoms that may be relevant to intracranial injury and poorer outcomes among children in the study. CART is a decision tree tool which evaluates all possible splits for all variables included in the model. It uses binary partitioning with two and only two possible answers at each point to classify objects, in this case patients, in to terminal nodes which maximize the differences between the groups based on the variables included in the model. During the CART analysis, 1/2 of the cohort will be used to get an appropriate fit to the model and 1/2 will be used to validate the model. The sensitivity, specificity, positive and negative predictive values and positive and negative likelihood ratios will be performed on the regression tree to further measure the fit of the model and determine any

misclassification error. Upon developing a classification tree, the predictors of importance from the tree can be used in the logistic regression model to confirm the overall fit of the final tree.

5. **Summarize the qualifications and experience of the Principal Investigator that are relevant to conduct this research study:** Dr. Zuckerbraun is an Assistant Professor and physician in the Department of Pediatrics, Division of Pediatric Emergency Medicine. She has a Master's degree of Public Health from the University of Pittsburgh. Dr. Zuckerbraun has conducted and is currently involved in many clinical research studies, several of which involve the study of pediatric injury.

6. **Additional Information, Clarification, or Comments for the IRB Reviewer**:

Request for Waiver of HIPAA Authorization

Because medical records will be accessed as part of this research study, the investigator must request a waiver of HIPAA authorization. This request requires investigators to address the following three criteria: (1) The use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals, based on an adequate plan to protect the identifiers from improper use and disclosure, (2) the research could not practicably be conducted without the waiver, and (3) the research could not practicably be conducted without access to and use of the protected health information. Please address each of the following issues completely:

1. **How will the privacy of medical record information be protected during the conduct of this study?** The medical information will be recorded without patient identifiers (e.g., names, phone numbers, addresses, etc.) or linkage codes (e.g., social security numbers, medical record numbers, etc.). Thus, there is no collection of protected health information (i.e., identifiable medical record information) or any possibility of subsequent disclosure of protected health information. Furthermore, and consistent with this waiver request, the investigators who will access the protected health information also provide related care, or are in the position to provide that care, to these patients, thus minimizing privacy and confidentiality concerns.

2. **Why is in not practicable to conduct this research without the waiver?** The patients

whose protected health information will be accessed under this waiver request have not previously provided informed consent for this retrospective research activity and it is impractical to obtain consent from these individuals because they are no longer in the hospital and contacting them is precluded by the researcher's inability to use patients' identifiable contact information without their prior consent. Thus, obtaining the HIPAA authorization of these patients for the research use of their health information is impractical.

3. **Why is it not practicable to conduct this research without access to and use of the protected health information?** The overall scientific design of the study focuses on identifying and/or evaluating inter-relationships among various medical variables, and that could not be accomplished without access to the protected health information in the medical record. Consistent with the "minimum necessary standard" of the HIPAA privacy rule, we will access and collect only the specific health information necessary to complete this research study.

APPENDIX B

ABSTRACTION IRB APPROVAL

University of Pittsburgh
Institutional Review Board

Exempt and Expedited Reviews

University of Pittsburgh FWA: 00006790
University of Pittsburgh Medical Center: FWA 00006735
Children's Hospital of Pittsburgh: FWA 00000600

3500 Fifth Avenue
Suite 100
Pittsburgh, PA 15213
Phone: 412.383.1480
Fax: 412.383.1508

TO: Noel Zuckerbraun, M.D.

FROM: Sue R. Beers, Ph.D., Vice Chair

DATE: January 26, 2006

PROTOCOL: A Clinical Decision-Making Rule for Mild Head Injury in Children: Record Review

IRB Number: 0601086

The above-referenced protocol has been reviewed by the University of Pittsburgh Institutional Review Board. Based on the information provided in the IRB protocol, this project meets all the necessary criteria for an exemption, and is hereby designated as "exempt" under section 45 CFR 46.101(b)(4).

The IRB has approved a waiver of HIPAA authorization to access protected health information/patient medical record information for a retrospective research study.

The regulations of the University of Pittsburgh IRB require that exempt protocols be re-reviewed every three years. If you wish to continue the research after that time, a new application must be submitted.

- If any modifications are made to this project, please submit an 'exempt modification' form to the IRB.
- Please advise the IRB when your project has been completed so that it may be officially terminated in the IRB database.
- This research study may be audited by the University of Pittsburgh Research Conduct and Compliance Office.

Approval Date: January 26, 2006
Expiration Date: January 26, 2009

SRB: kh

APPENDIX C

FOLLOW-UP SURVEY IRB PROTOCOL

Protocol for A Clinical Decision-Making Rule for Mild Head Injury in Children: Follow-Up

1.0 Specific Aims

This protocol is part of a larger project designed to determine the most efficient method for treating children (<3 years old) with mild head injuries. The specific aim of this study is: to investigate the symptoms, late effects and indirect costs of injury. This study will contact a sample of patients recovering from a mild head injury to determine if any late effects or post-hospital complications related to the injury occurred within three months post-injury. The other aims of the larger study will be evaluated in a separate protocol (A Clinical Decision-Making Rule for Mild Head Injury in Children: Record Review IRB#0601086).

2.0 Background and Significance

2.1 Background

Traumatic brain injury (TBI) is a major cause of death and life-long disability in the United States. The annual incidence of TBI in the United States has been estimated to be 180-220 cases per 100,000 population (Sumas & Narayan, 1999). In the United States, with a population of

almost 300 million, approximately 600,000 new TBIs occur per year. As many as 10% of these injuries are fatal, resulting in almost 550,000 persons hospitalized annually in the United States with head injuries.

The incidence of mild traumatic brain injury (MTBI), or mild head injury, in emergency departments (EDs) appears to have increased, almost doubling from 216 per 100,000 in 1991 (Sosin et al., 1996) to 392 per 100,000 in 1996 (Guerrero et al., 2000). In contrast, MTBI hospitalizations appear to have declined from 130 per 100,000 to 51 per 100,000 between 1980 and 1994 (Thurman & Guerrero, 1999).

Existing data indicate that the rates of hospital admissions and emergency department visits for head injuries are several times higher among children than the general adult population (Jennett, 1996), with the highest rates among children under age five (Beattie, 1997) and among children in lower socioeconomic groups (Adelson & Kochanek, 1998). Approximately 80% of the hospital admissions for head injuries are for mild head injuries.

These findings may reflect changes in hospital practices that shift the care of persons with less severe forms of TBI from hospital inpatient care to ED or outpatient treatment. Such changes indicate a growing need to document and study MTBIs treated in EDs and outpatient settings, especially in children.

2.2 Significance

This study presents a unique opportunity to investigate the significant problem of mild head injuries in children and the allocation and use of resources associated with these injuries. In a September 2003 survey of Level I trauma centers (Blostein & Jones, 2003), less than half of the trauma program managers indicated that they had a formal protocol for evaluating mild traumatic brain injury. Hospitals have no consistent practice for determining which patients are evaluated, who performs the evaluations or which tools should be used.

Children are susceptible to potential long-term consequences following a mild head injury, emphasizing the importance of both giving children the best and most appropriate care for their injury and balancing the utilization and cost of resources required for this care. However, only limited information on the long-term effects of head injuries in very young children is documented

in the literature on the subject. The public health significance of this study is that 1) it may help identify characteristics in children with mild head injuries that indicate deteriorating injuries and 2) by concentrating on very young children, it will add valuable information to the otherwise limited literature.

3.0 Research Design and Methods

3.1 Drug/Device Information

Not applicable.

3.2 Research Design and Methods

This study is an investigation designed to investigate symptoms and late-effects of mild head injuries in children that will ultimately be used to create a clinical decision-making rule for mild head injury in children. The Principal Investigator, Jeanine M. Buchanich, M.Ed., M.P.H. will oversee all aspects of the study in conjunction with Barbara A. Gaines, M.D. Assistant Professor of Surgery at CHP, Noel Zuckerbraun, M.D., Assistant Professor of Pediatrics, Emergency Medicine at CHP and Thomas Songer, Ph.D., Assistant Professor of Epidemiology, Graduate School of Public Health.

This study will include an interview with one of the injured child's parents (we are requesting that the mother participate, if she lives with the child, and will refer to the parent throughout as "mother"; if the mother does not live with the child, then we are requesting that the father participate. If the child does not live with either parent, then that child is not eligible to participate) regarding care and behavior following the injury as well as costs associated with missed time at work and school after the injury.

3.3 Data Collection and Statistical Considerations

This study will collect data directly from the mothers of children seen with a mild head injury at the emergency department (ED) at Children's Hospital of Pittsburgh (CHP) in 2005, to eliminate recall bias and facilitate locating the families, and will include injuries with ICD codes 800-804 and 850-854 (mild head injuries). Dr. Zuckerbraun at CHP, will contact the families of

eligible children, explaining the study and requesting consent for the release of medical records related to the mild head injury and an interview with the child's mother. We estimate that 170 families will need to be contacted to get a representative sample of children less than three years old at the time of injury.

Dr. Zuckerbraun will send out an introductory letter with the consent form and questionnaire to potential participants (see attached letter, consent and questionnaire). Mothers agreeing to participate will return the signed consent form for her and her child's participation and completed questionnaire in an enclosed postage-paid envelope. This procedure is detailed in the approach letter for the mothers.

Mothers who return a signed consent form but not a completed questionnaire will be called for an interview. Mothers who do not respond will be called to assess their willingness to participate and sent another mailing if requested. These phone calls will occur within the two month period after the letters are sent by Dr. Zuckerbraun.

The questionnaire is brief and contains questions regarding the child's symptoms, care and behavior following the injury, and any missed school or work time due to the injury. The questionnaire or interview should take approximately 10-15 minutes to complete. The information garnered from the questionnaire is critical to the decision rule, as it provides data on the characteristics of children with subacute or chronic ICI, namely those whose injuries disintegrate after 48 hours (subacute) or 2 weeks (chronic).

The statistical analysis for the study will occur in several phases. Initially, a classification and regression tree (CART) program will be used to identify symptoms that may be relevant to intracranial injury and poorer outcomes among children in the study. CART is a decision tree tool which evaluates all possible splits for all variables included in the model. It uses binary partitioning with two and only two possible answers at each point to classify objects, in this case patients, in to terminal nodes which maximize the differences between the groups based on the variables included in the model.

The sensitivity, specificity, positive and negative predictive values and positive and negative likelihood ratios will be performed on the regression tree to further measure the fit of the

model and determine any misclassification error. The developed tree will serve as a decision-making rule for children presenting to CHP with mild head injury with the nodes as the classification points.

4.0 Human Subjects

4.1 General Characteristics

The study population will include approximately 170 children seen at CHP with mild head injury in 2005. The racial, gender and ethnic characteristics of the study population reflect the demographics of the area surrounding CHP and the patients seen there. No exclusion criteria will be based on race, ethnicity, gender or HIV status.

4.2 Inclusion/Exclusion Criteria

Inclusion criteria for this study are as follows: children age less than three years old at the time of injury with mild head injury (ICD 800-804, 850-854) treated at CHP in 2005 and an initial Glasgow Coma Scale (GCS) score of 15 (normal) when seen in the Emergency Department. Exclusion criteria are: children with penetrating injuries, children with depressed skull fractures requiring surgery, children with injuries suspected to be intentional and children who had their initial CT scan >24 hours after the injury occurred.

Because this study includes children, we are providing the additional information below to specifically address their inclusion in this study.

1) provide a rationale for the specific age ranges of children to be included. Because the literature on mild head injuries is much more limited in children less than 3 years old, this study is designed to look at that age group exclusively. Children less than 3 years old have a higher rate of intracranial injury following a mild head injury than do older children; therefore a clinical-decision making rule designed for or with an older population of children can not be applied to very young children. Any rule for very young children must be based upon a sample of children in that age group and is expected to have different significant predictors than a rule for older children.

2) describe the expertise of the investigative team for dealing with children of the specified age ranges. Ms. Buchanich has several years experience in research studies involving children.

Drs. Zuckerbraun and Gaines are physicians who treat injured children, in the ED and trauma program, on a daily basis.

3) describe the adequacy of the research facilities to accommodate children of the specified age ranges. Children and their mothers will be approached to participate through the mail and will be called for an interview if a completed questionnaire is not returned. Children will not be treated or seen at any research facilities.

4) provide information about inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose of the study. The sample size for this study was based on an equation that accounts for both the desired sensitivity of the decision-making rule (99%), the estimated prevalence of intracranial injury in children less than 3 years old (15%) and participant non-response (60% response rate). The target sample size is 101 children and their mothers; the inflated sample size is 169.

This study satisfies Criterion 1 (45 CFR 46.404) that the research presents no greater than minimal risk to the children. The study involves the release of medical records and a brief questionnaire to be completed by the child's mother. The children are only at risk of a breach of confidentiality from participating in this study.

4.3 Recruitment Procedures

Subjects are a random sample of approximately 170 patients less than 3 years old treated for a mild head injury at CHP Emergency Medicine in 2005. Mothers of eligible children will be mailed a packet of information for the study containing an introductory letter from Dr. Zuckerbraun at CHP, two copies of the consent form and a copy of the questionnaire. The letter will explain the study, request informed consent for the release of medical records related to the mild head injury and request a brief interview regarding the child's behavior and care following the injury and costs associated with work and school time missed due to the injury. One parent (the mother, if living with the child; otherwise, the father) will be asked to sign and return one copy of the consent form; she may also complete the questionnaire and mail it back with the signed consent form.

We are requesting a waiver of informed consent to use personal health information (PHI) to identify potential participants (8.3.1.1). Dr. Zuckerbraun is an ED physician at CHP and was involved in the care of these children when they were brought to the hospital for their head injury. Therefore, she was the personal physician for the children during that time and can have access to their medical records for the purpose of identifying children for this study; there is no potential breach of privacy or confidentiality since she already has access to these records. This waiver is only to identify children for participation and is not a waiver of informed consent for participants.

In requesting this waiver, we are noting the following:

1. The waiver applies specifically to the personal physician or a member of the personal physician's health care staff who is directly involved in the health care of the patient (Dr. Zuckerbraun) and not to any colleagues who are not involved directly in the care of the patient.

2. The "use" refers to recording only identifiable information necessary to accomplish the purpose of the waiver, to identify potential research subjects for recruitment (e.g., to develop a mass mailing).

3. The waiver is not intended to serve the purpose of performing a full review of the medical records to determined complete eligibility. The waiver is only to help in initial recruitment efforts.

We also are requesting this waiver based upon this study meeting the following Federal Policy Criteria (45 CFR46.116(d)):

1. Criterion: "The research [research activity] involves no more than minimal risk."

   Justification: The research activity for which this waiver of informed consent is being requested is limited to accessing and using patient medical record information for the purpose of identifying potential research subjects. There are no physical or psychological risks associated with this research activity.

   To ensure that the risk to the privacy and confidentiality of the involved patients remains minimal:

   (1) any identifiable health information recorded for the purpose of identifying patients for subsequent research study recruitment will be stored in a secure manner (e.g., locked file

cabinet, password protected database) accessible only to research study investigators who are also involved directly in the health care of the respective patients; and

(2) the recorded identifiable health information of any given patient will be destroyed immediately after (a) determining that the patient does not, in fact, qualify for participation in the research study; or (b) contacting the patient for discussion of the research study and his/her interest in study participation.

We hereby provide our assurance that any identifiable health information recorded for the purpose of identifying patients for subsequent research study recruitment will not be used by or disclosed to any research study investigator who is not also involved directly in the care of the involved patients. We also provide our assurance that this identifiable health information will not be reused or disclosed to any other person or entity, except as required by law or for authorized oversight of the research study.

2. Criterion: "The waiver will not adversely affect the rights and welfare of the subjects."

Justification: Consistent with this waiver request, access to, and the use of patient medical record information for the purpose of identifying potential research subjects will be limited to research study investigators who are also involved directly in the care of the respective patients. Since these investigators would already have knowledge of and access to the patients' identifiable medical record information, granting of this waiver will not adversely affect the privacy of the involved patients or the confidentiality of their medical record information.

3. Criterion: "The research [research activity] could not practicably be carried out without the waiver."

Justification: It is not possible to conduct this research study unless we are able to identify and recruit potential research subjects. If the identification and recruitment of patients who meet research study eligibility criteria must rely on waiting until such time that these individuals are seen for an injury at CHP, this will result in considerable delays in our ability to accrue study participants and likely result in the study's termination before our requirements for statistical significance are met. Research study recruitment efforts involving mass mailings directed at all patients seen in at CHP, the majority of whom would not meet study eligibility requirements, is not

only impractical but would impinge on the privacy of especially non-eligible patients. Thus, to practically conduct this research study requires that we be able to access and use patient medical record information to identify prospectively our patients who meet study eligibility criteria and to focus our recruitment efforts at these patients.

The mechanism recommended by the IRB and UPMC for the identification and recruitment of potential research subjects involves the use of an honest broker system/process to (1) perform an independent (i.e., independent of the research investigators) review of medical record information to identify patients who meet study eligibility criteria; and 2) to provide the names of these potentially eligible research subjects to their personal care givers for subsequent contact to introduce the research study and ascertain the patient's preliminary interest in study participation. The first of these steps (i.e., involvement of an honest broker system/process) is necessary so as to avoid a violation of the patients' privacy and medical record confidentiality by the research investigators. However, consistent with this waiver request, the research investigators who will access the patient medical record information to identify potential research subjects are also involved directly in the care of the patients, thus obviating the privacy and confidentiality concerns. The second of these steps (i.e., involvement of the patient's personal care givers in potential subject recruitment) is necessary so as to avoid "coldcalling" which is prohibited by the IRB. However, consistent with this waiver request, the honest broker would be providing the identities of the potential subjects to care givers who are also the research investigators. In so doing, the care giver-investigators would be obtaining identifiable private information about the patients for research purposes without the patients' consent; a violation of the Federal Policy regulations unless the IRB grants a waiver of the consent/authorization requirements for this research activity.

In summary, this research activity (i.e., use of patient medical record information to identify potential research subjects) could not practically be conducted without a waiver of the informed consent requirements.

4. Criterion: "Whenever appropriate, the subjects will be provided with additional pertinent information after participation."

Justification: Note that we are requesting a waiver of the requirements to obtain informed consent for the limited purpose of allowing research investigators to access and use patient medical record information to identify their patients who may be eligible for participation in this research study. The informed consent of these patients will be obtained for actual study participation/collection of their medical record information for study purposes.

4.4 Risk Benefit Ratio

Study members are subject to minimal risk as a result of this investigation, including risk from a breach of privacy or confidentiality. Confidentiality is maintained by individuals working with this project and by maintaining all study data in locked file cabinets at the Graduate School of Public Health. Data will be stored on properly protected cartridges accessible only to study personnel. We will protect participants' confidentiality by assigning a code to all data, keeping the participant's name and contact information separate from that data, and keeping the link between the two separate with restricted access (restricted to Dr. Zuckerbraun). Once participants have consented to the study, the link and name will be shared with Ms. Buchanich; no other investigators will have this information. Data will be published so that individuals cannot be identified.

There are no direct or guaranteed benefits to study participants. If, during the interview, a child is identified with a significant post-concussive syndrome, that family will be referred to Dr. Gaines at CHP for additional evaluation or treatment.

Data and Safety Monitoring Plan

Ms. Buchanich will meet with Drs. Zuckerbraun and Gaines quarterly to review the data collection progress and quality control of the study data. Because study subjects are at minimal risk by participating in this study, no changes in the risk-to-benefit ratio are anticipated, however, such possibilities will be discussed quarterly as well. The primary investigator regularly reviews related scientific literature and is abreast of current research considerations. Study guidelines regarding patient confidentiality are strictly enforced and will also be reviewed quarterly to determine potential improvements. Ms. Buchanich will report any serious or unexpected adverse

effect to the IRB office immediately and the information garnered from these quarterly reviews will be reported to the IRB office at the time of renewal.

5.0 Costs and Payments

5.1 Research Study Costs

There will be no support of the proposed research study.

5.2 Research Study Payments

No research subject will be charged nor paid to be a participant in this study.

6.0 Appendices

6.1 Qualifications of Investigators

The Principal Investigator of the study is Jeanine M. Buchanich, MPH, Research Specialist, who will be involved in all aspects of the study. Ms. Buchanich has been a senior-level staff member and project coordinator in the Department of Biostatistics at the University of Pittsburgh for almost 10 years and is getting her Ph.D. in Epidemiology. Ms. Buchanich has several years experience in injury research and is currently working on a project to develop a national trauma registry for children.

The co-investigator of the proposed project is Noel Zuckerbraun, M.D., Assistant Professor of Pediatrics at Children's Hospital of Pittsburgh. Dr. Zuckerbraun will have primary responsibility for obtaining the study file from CHP and sending out the approach letters introducing the study and Ms. Buchanich.

A second co-investigator of the study is Barbara A. Gaines, MD, Assistant Professor of Surgery at Children's Hospital of Pittsburgh. Dr. Gaines will provide input on the data analysis.

Thomas Songer, PhD, Assistant Professor of Epidemiology, Graduate School of Public Health will also act as a co-investigator. Dr. Songer is actively involved in both epidemiology and injury research. His research experience lies in investigating issues such as the role of medical factors in automobile crashes, surveillance systems for head injury, injury risks in wheelchair users, and the costs of child abuse. Dr Songer is the academic advisor to Ms. Buchanich and will provide oversight on the data collection, analysis of data, and preparation of publications.

6.2 Bibliography/References

Adelson PD, Kochanek PM. Head injury in children. *Journal of Child Neurology* 1998;13:2-15.

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Guerrero JL, Thurman DJ, Sniezek JE. Emergency department visits associated with traumatic brain injury: United States, 1995–1996. *Brain Injury* 2000;14:181-186.

Jennett B. Epidemiology of head injury. *Journal of Neurology, Neurosurgery & Psychiatry* 1996;60:362-369.

Sosin DM, Sniezek JE, Thurman DJ. Incidence of mild and moderate brain injury in the United States, 1991. *Brain Injury* 1996;10:47-54.

Sumas ME, Narayan RK. Head Injury. In: Grossman GR, Loftus CM (eds.) *Principles of Neurosurgery, 2nd edition*, Philadelphia, PA: Lippincott-Raven 1999;117-171.

Thurman D, Guerrero J. Trends in hospitalization associated with traumatic brain injury. *JAMA* 1999;282:954-957.

6.3 Multicenter Studies

Not applicable.

6.4 Investigator-Sponsored Investigational New Drug (IND) or Investigational Device (IDE) Studies

Not applicable.

APPENDIX D

FOLLOW-UP SURVEY IRB APPROVAL

University of Pittsburgh
Institutional Review Board

3500 Fifth Avenue
Ground Level
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)

MEMORANDUM

TO: Ms. Jeanine Buchanich

FROM: Christopher Ryan, Ph.D., Vice Chair

DATE: June 12, 2006

SUBJECT: IRB #0601105: A Clinical Decision-Making Rule for Mild Head Injury in Children: Follow-Up

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The above-referenced proposal has received expedited review and approval from the Institutional Review Board under 45 CFR 46.110 (5,7).

Please note that the waiver for the requirement to obtain informed consent to use medical record information to identify potential research subjects has been approved.

If applicable, please include the following information in the upper right-hand corner of all pages of the consent form:

Approval Date: June 12, 2006
Renewal Date: June 11, 2007
University of Pittsburgh
Institutional Review Board
IRB #0601105

Please note that it is the investigator's responsibility to report to the IRB any unanticipated problems involving risks to subjects or others [see 45 CFR 46.103(b)(5) and 21 CFR 56.108(b)]. The IRB Reference Manual (Chapter 3, Section 3.3) describes the reporting requirements for unanticipated problems which include, but are not limited to, adverse events. If you have any questions about this process, please contact the Adverse Events Coordinator at 412-383-1504.

The protocol and consent forms, along with a brief progress report must be resubmitted at least **one month prior** to the renewal date noted above as required by FWA00006790 (University of Pittsburgh), FWA00006735 (University of Pittsburgh Medical Center), FWA00000600 (Children's Hospital of Pittsburgh), FWA00003567 (Magee-Womens Health Corporation), FWA00003338 (University of Pittsburgh Medical Center Cancer Institute).

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

CR:kh

APPENDIX E

APPROACH LETTER

Date

Contact name

Address

Dear Contact:

We are writing to introduce you to a new research project that is investigating the impact of head injuries on children. We would like to request your participation in this because your child had a head injury and was seen in the Emergency Department of Children's Hospital of Pittsburgh in 2005. This study presents a unique opportunity to investigate the significant problem of head injuries in children and the distribution and use of resources associated with these injuries. Although you and your child may receive no direct benefit from participating in this study, the results may be used to improve the future treatment of children with head injuries. We are asking you to help in two ways: 1) by allowing researchers to review your child's medical records related to the head injury and 2) by answering some questions in a telephone interview or by completing

the enclosed questionnaire. The questionnaire should take about 10-15 minutes to complete, either by filling it out and returning it by mail, or on the telephone. It asks questions concerning the symptoms your child may have experienced when injured, other things that may have happened after your child's injury and things that may have cost your family money that were related to the head injury.

The Principal Investigator of the study is Jeanine M. Buchanich, MPH, Research Specialist, who will be involved in all aspects of the study. Ms. Buchanich is a staff member in the Department of Biostatistics at the University of Pittsburgh and is getting her Ph.D. in Epidemiology. Ms. Buchanich has several years experience in injury research and is currently working on a project to develop a national trauma registry for children.

If you wish to participate in this study, please sign, date and return one copy of the enclosed consent form in the postage-paid envelope to the University of Pittsburgh by January 26, 2007 and keep one copy of the consent form for your records. If you wish to participate, you must fill out and sign the section of the consent form entitled Voluntary Consent/Parental Certification.

You can also fill out and return the enclosed questionnaire. If you return a consent form but not a questionnaire, Ms. Buchanich will call you to complete the questionnaire. If we do not receive your consent form, I may call to determine your willingness to participate. All such calls will be made during the two months after you receive this letter. To be consistent among all study participants, we are requesting that the child's mother, if she lives with the child, sign the consent form and complete the questionnaire. If the child's mother is not living with the child, then we are requesting participation from the child's father. If neither parent is living with the child, then that

child is not eligible to participate.

Your participation in this study is voluntary. You have the right to refuse to participate in this study or to refuse to answer specific questions. Your decision whether or not to participate in this study or to answer questions will have no effect on any benefits to which you are entitled. The information that you provide to the researchers will not be used in any way that can identify any individual. Your help in this research is very important, and we look forward to your participation.

If you have any questions regarding your participation or about the study in general, you can contact Ms. Buchanich at 412-624-2423 or me at 412-692-7692. Please also feel free to contact one of us with any questions, comments or concerns about the consent form, the questionnaire or any other issues regarding this study.

Thank you for your cooperation.

Sincerely,

Noel S. Zuckerbraun, M.D.

Assistant Professor of Pediatric Emergency Medicine

Children's Hospital of Pittsburgh

APPENDIX F

FOLLOW-UP CONSENT FORM

University of Pittsburgh
Institutional Review Board
IRB # 0601105
Approval Date: June 12, 2006
Renewal Date: June 11, 2007

CONSENT TO PARTICIPATE IN AN OBSERVATIONAL STUDY

TITLE: A Clinical Decision-Making Rule for Head Injury in Children

PRINCIPAL INVESTIGATOR: Jeanine M. Buchanich
Research Specialist
Department of Biostatistics
Graduate School of Public Health
University of Pittsburgh
Pittsburgh, PA 15261
(412) 624-2423

CO-INVESTIGATOR: Barbara A. Gaines, M.D.
Assistant Professor of Surgery
Children's Hospital of Pittsburgh
Pittsburgh, PA 15261
(412) 692-8288

Noel S. Zuckerbraun, M.D.
Asst Professor of Pediatric Emergency Medicine
Children's Hospital of Pittsburgh
Pittsburgh, PA 15261
(412-692-7692

Thomas J. Songer, Ph.D.
Assistant Professor
Department of Epidemiology
Graduate School of Public Health
University of Pittsburgh
Pittsburgh, PA 15261
(412) 648-9296

SOURCE OF SUPPORT: None

DESCRIPTION OF STUDY: You and your child are being asked to participate in a research study because the Graduate School of Public Health at the University of Pittsburgh and Children's Hospital of Pittsburgh (CHP) are currently investigating the impact of head injuries on children. We would like to request you and your child's participation in this study because your child had a head injury and was seen at the Emergency Department of Children's Hospital of Pittsburgh in 2005.

The study includes both children and the mothers (if they are living with their child; otherwise, the child's father) of children who sustained head injuries. The information necessary for the study comes from two sources: your child's medical records from the 2005 injury and from talking to the mothers of the children. We estimate that 170 children less than 3 years old and who were treated for head injury in 2005 and their mothers will need to be contacted for the study.

This consent will allow University of Pittsburgh researchers to review your child's medical records from the head injury treated at CHP in 2005 and also to contact you for a telephone interview that will include questions on care following the injury, your child's behavior following the injury and any work or school time missed due to the injury. This interview should take 10-15 minutes. If you wish, you can also complete the enclosed questionnaire and return it in the postage-paid envelope with your consent form. If you return the completed questionnaire, you will not be called.

RISKS AND BENEFITS: Although every effort will be made to maintain confidentiality, you and your child are subject to the risk of a breach of confidentiality. This means that information provided by you or your child in this study may be viewed by persons outside of the study, despite investigators' efforts to maintain the confidentiality of your child's records and your responses. You and your child will likely receive no direct benefit from participation in this study, although society may benefit from increased knowledge about the treatment and health effects of head injuries in children.

NEW INFORMATION: You and your child will be promptly notified if any new information develops during the conduct of this research study that may cause you or your child to change your mind about continuing to participate.

COSTS AND PAYMENT: You and your child will not be charged nor will you

or your child be paid to take part in this study.

CONFIDENTIALITY: Any information about you or your child obtained from this research will be kept as confidential (private) as possible. All records related to you and your child's involvement in this research study will be stored in a locked file cabinet. We will protect participants' confidentiality by assigning a code to all data, keeping the participant's name and contact information separate from that data, and keeping the link between the two separate. You and your child will not be identified by name in any publication of research results unless you and your child sign a separate form giving your permission (release).

This research study will involve the recording of current medical information from your child's hospital records. The information that will be recorded will be limited to information concerning your child's head injury in 2005, including the mechanism of the injury, your child's symptoms, procedures undergone in the hospital, diagnoses, clinical and outcome variables and payment information. This information will be used to help develop a decision-making rule about the most effective way to treat children who come to the hospital with head injuries.

In addition to the investigators listed on the first page of this authorization (consent) form and their research staff, the following individuals will or may have access to identifiable information (which may include your child's identifiable medical record information) related to your and your child's participation in this research study:

> Authorized representatives of the University of Pittsburgh Research Conduct and Compliance Office may review your and your child's identifiable research information for the purpose of monitoring the appropriate conduct of this research study.
>
> In unusual cases, the investigators may be required to release identifiable information (which may include your child's identifiable medical information) related to your and your child's participation in this research study in response to an order from a court of law.

The investigators may continue to use and disclose, for the purposes described above, identifiable information (which may include your child's identifiable medical information), related to your and your child's participation in this research study for seven years following the final reporting of the information.

If the researchers learn that you or your child, or someone with whom you or your child is involved, is in serious danger or harm they will need to inform the appropriate agencies as required by Pennsylvania law.

RIGHT TO WITHDRAW: Your and your child's participation in this research study, to include the use and disclosure of your and your child's identifiable information for the purposes described above, is completely voluntary. (Note, however, that if you do not provide consent for the use and disclosure of identifiable information for the purposes described above, you and your child will not be allowed, in general, to participate in the research study.)

Your doctor may be involved as an investigator in this research study. As both your doctor and a research investigator, she is interested both in your child's medical care and the conduct of this research study. Before agreeing to participate in this research study, or at any time during your study participation, you or your child may discuss your child's care with another doctor who is not associated with this research study.

You and your child are not under any obligation to participate in any research study offered by your doctor.

You may withdraw, at any time, consent for participation in this research study, to include the use and disclosure of your or your child's information for the purposes described above. (Note, however, that if you withdraw consent for the use and disclosure of identifiable information for the purposes described above, you and your child will also be withdrawn, in general, from further participation in the research study.) Any identifiable information recorded for, or resulting from, your and your child's participation in this research study prior to the date that you formally withdraw consent may continue to be used and disclosed by the investigators for the purposes described above.

Your decision to withdraw consent for participation in this research study will have no effect on your or your child's current or future relationship with the University of Pittsburgh. Your decision to withdraw consent for participation in this research study will have no effect on your or your child's current or future medical care at a UPMC hospital or affiliated health care provider or your or your child's current or future relationship with a health care insurance provider. To formally withdraw consent for participation in this research study you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form.

VOLUNTARY CONSENT/ PARENTAL CERTIFICATION

All of the above has been explained to me and my child and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study, and that such future questions will be answered by the researchers listed on the first page of this form. Any questions I have about my rights or my child's rights as a research participant will be answered by the Human Subject Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668).

By signing this form, I agree to participate in this research study. A copy of this consent form will be given to me.

_____ _____
Parent Participant's Signature Date

_____
Printed Name of Child-Subject

"I understand that, as a minor (age less than 18 years), the above-named child is not permitted to participate in this research study without my consent. Therefore, by signing this form, I give my consent for his/her participation in this research study."

_____ _____
Parent's or Guardian's Name (Print) Relationship to Participant (Child)

_____ _____
Parent or Guardian Signature Date

_____ _____
Phone Number Best time to reach you

APPENDIX G

FOLLOW-UP SURVEY INSTRUMENT

Study of Long-Term Effects of Head Injury in Children

ID
— — —

A. Symptoms

I would like to ask you some questions about how your child reacted both before and after the hospital visit for the head injury.

A1. Did your child experience any of the following with the head injury? Please check all that apply.

		Yes	No	Unsure
a.	Headache……Before visit……	_____	_____	_____
	After visit ……	_____	_____	_____
b.	Nausea ……Before visit……	_____	_____	_____
	After visit ……	_____	_____	_____
c.	Vomiting…… Before visit……	_____	_____	_____
	After visit ……	_____	_____	_____
d.	Drowsiness/Sleepiness…… Before visit……	_____	_____	_____
	After visit ……	_____	_____	_____

e. Numbness or tingling…… Before visit……_____…….…….._____

After visit …… _____…….…….._____

f. Dizziness…… Before visit……_____…….…….._____

After visit …… _____…….…….._____

g. Balance problems……Before visit……_____…….…….._____

After visit …… _____…….…….._____

h. Sleeping more than usual……Before visit……_____…….…….._____

After visit……_____…….…….._____

i. Sensitivity to light……Before visit……_____…….…….._____

After visit …… _____…….…….._____

j. Sensitivity to noise…… Before visit……_____…….…….._____

After visit …… _____…….…….._____

k. Feeling slowed down……Before visit……_____…….…….._____

After visit …… _____…….…….._____

A1. Continued. Did your child experience any of the following with the head injury? Please check all that apply.

Yes No Unsure

l. Trouble falling asleep…… Before visit……_____…….…….._____

After visit …… _____…….…….._____

m. More emotional than usual…Before visit……_____…….…….._____

After visit …… _____…….…….._____

n. Irritability…… Before visit……_____…….…….._____

After visit …… _____…….…….._____

o. Sadness…… Before visit……_____…….…….._____

After visit …… _____…….…….._____

q. Amnesia (forgetting things)…Before visit……_____…….…….._____

After visit …… _____…….._____…….._____

r. Seizures……Before visit……_____…….._____…….._____

After visit …… _____…….._____…….._____

s. Loss of consciousness (black out) Before visit…_____…….._____……._____

After visit …… _____…….._____…….._____

t. Other……Before visit……_____…….._____…….._____

List_____

After visit …… _____…….._____…….._____

List_____

B. Injury Follow-up

I would like to ask you some questions about other things that may have happened after your child's visit to the hospital for the head injury.

B1. Did you notice any changes in your child's behavior following the injury?

1) Yes

If yes, how did it change_____

2) No

9) Unknown

B2. After your Emergency Department visit for this head injury, did he/she have any of the following health care visits for reasons related to the head injury?

a) Follow-up visit with Primary Care Physician (PCP) ____

1) Yes

2) No

9) Unsure

b) Follow-up visit with the Center for Sports Medicine ____

1) Yes
2) No

9) Unsure

c) Unplanned visit to urgent care center/clinic ____
1) Yes

2) No

9) Unsure

d) Return visit to hospital Emergency Department ____
1) Yes

Which hospital_____

Date _____

2) No

9) Unsure

e) Admission to hospital (Go to B4) ____
1) Yes

2) No

9) Unsure

B3. If he/she was admitted to the hospital, did he/she undergo any of the following procedures?

a) X-rays (X-rays are pictures of one part of the body, such as the skull or brain)
____

1) Yes

2) No

9) Unsure

b) CT scan (CT scans are done when you are lying on your back and a big donut-shaped machine that hums softly rotates slowly around your head)
____

1) Yes

2) No

9) Unsure

c) Surgery ____

1) Yes

2) No

9) Unsure

d) Other ____

1) Yes

If yes, what type _____

2) No

9) Unsure

B4. Before the injury from 2005, had your child had other head injuries?

1) Yes
   a. If yes, how many_____

   If yes, when (dates if possible)_____

2) No

9) Unsure

B5. Is your child involved in sports? ____

1) Yes

Which sports _____

2) No
9) Unknown

B6. Did this head injury occur during a sporting event? ____

1) Yes

If yes, which sport
_____

2) No

9) Unknown

C. Indirect Costs

Now I would like to ask you questions about things that happened regarding your child's injury that may have cost your family money.

C1. How did you get to the hospital for the initial injury? (Please check all that apply) ____

1) Private vehicle

   Your own _____

   Other _____

2) Public transportation

3) Emergency vehicle

4) Other _____

9) Unknown

C2. Did any member of your family have to miss work to take your child to the hospital for the initial injury?

1) Yes

2) No

9) Unknown

C3. If yes, how much work did they miss? ____

1) Less than ½ day

2) ½ to 1 day

3) 1 day

4) More than 1 day

9) Unknown

C4. Did any member of your family have to miss work to take care of your child after he/she came home from the hospital? ____

1) Yes

2) No

9) Unknown

C5. If yes, how much work did they miss (after the injury)? ____

1) Less than ½ day

2) ½ to 1 day

3) 1 day

4) 2 days

5) 3 – 5 days

6) More than 5 days

9) Unknown

C6. Did your child miss any school after he/she came home from the hospital? ____

1) Yes

2)No

9) Unknown

C7. If yes, how much time did they take off of school? ____

1) Less than ½ day

2) ½ to 1 day

3) 1 day

4) 2 days

5) 3 - 5 days

6) More than 5 days

9) Unknown

APPENDIX H

PHONE SCRIPT CONSENT

Interview Script for Mild Head Injury: Follow-Up – Consent Received

"Hello, I am with Children's Hospital of Pittsburgh. May I please speak to the mother of Child's name?"

[ONCE APPROPRIATE PERSON IS ON THE PHONE]

"We received your consent form to participate in the study of mild head injury in children. Do you have about 15 minutes to answer the questions from the survey that you received?"

If yes:

"Ok, great." Complete survey.

If no:

"Ok, I understand you don't have time now. Can you please let me know a better time to reach you?"

If yes:

"Great, I will call you on mm/dd at hh:mm. I look forward to talking to you then."

If no:

"If you do not want to complete the survey over the phone, would you be willing to complete the version that was mailed to you? Do you still have the survey from the packet?"

If yes:

"Thank you for your taking the time to complete the survey. I will send you another postage-paid envelope to return your completed survey. Do you have any questions about the survey?"

If no:

"I would be happy to mail another copy to you that you can complete and return to me at your convenience. "

APPENDIX I

PHONE SCRIPT NO CONSENT

Interview Script for Mild Head Injury: Follow-Up – No Consent Received

"Hello, I am with Children's Hospital of Pittsburgh. May I please speak to the mother of Child's name?"

[ONCE APPROPRIATE PERSON IS ON THE PHONE]

"I'm calling in regard to a packet of information you should have received regarding a study of mild head injury in children. Did you receive such information?

If yes:
"Ok, good. We haven't received a signed consent form from you. Are you interested in participating?

If yes:
"Great. We appreciate your help. You can either return both the signed consent form and completed survey or just the signed consent form by itself and I will call you back to complete the survey. Do you have any questions regarding the consent form or the study?"

If yes:
Answer questions

If no:
"I look forward to receiving your signed consent form and survey."

If no:

"Thank you for your time."

If no:

"Perhaps we have the wrong address. Would you be interested in receiving information about the study?"

If yes:
"Great, can you please give me your current address and I will send the information to you."

If no:
"Thank you for your time."

APPENDIX J

ABBREVIATED QUESTIONNAIRE

Study of Long-Term Effects of Head Injury in Children (Abbreviated Survey Form) ID ___

Thank you for taking the time to respond to our survey. Without your participation, this research would not be possible.

A. Did your child experience any of the following symptoms with the head injury?

		Yes	No	Unsure
1. Sleeping more than usual	Before ED	☐	☐	☐
	After ED	☐	☐	☐
2. Trouble falling/staying asleep	Before ED	☐	☐	☐
	After ED	☐	☐	☐
3. More emotional than usual	Before ED	☐	☐	☐
	After ED	☐	☐	☐
4. Irritability	Before ED	☐	☐	☐
	After ED	☐	☐	☐
5. Seizures	Before ED	☐	☐	☐
	After ED	☐	☐	☐

B1. Did you notice any changes in your child's behavior after the injury? ☐ ☐ ☐

If yes, how did it change_____

B2. After your Emergency Department visit for this head injury, did he/she have any of the following health care visits for reasons related to the head injury?

	Yes	No	Unsure
a) Follow-up visit with Primary Care Physician (PCP)	☐	☐	☐
b) Follow-up visit with the Center for Sports Medicine	☐	☐	☐
c) Unplanned visit to urgent care center/clinic	☐	☐	☐
d) Return visit to hospital Emergency Department	☐	☐	☐

C1. Did any member of your family have to miss work to take your child to the hospital for the initial injury? ☐ ☐ ☐

C1a. If yes, how much work did they miss at the time of the injury? _____

C2. Did any member of your family have to miss work to take care of your child after he/she came home from the hospital? ☐ ☐ ☐

C2a. If yes, how much work did they miss after the injury? _____

****

☐ **I do not wish to participate in this study**

APPENDIX K

APPROACH LETTER FOR ABBREVIATED SURVEY

Date

Contact name
Contact address

Dear Contact:

We are writing to you again to request your participation in a study investigating the impact of head injuries on children. We are requesting your participation in this study because your child had a head injury, and was seen in the Emergency Department of Children's Hospital of Pittsburgh in 2005, and we have not yet received a completed survey from you. We have revised and simplified the survey to make it easier to complete; we have also enclosed a small token of our appreciation for your child. Without your participation, this research would not be possible and we greatly appreciate the time you spend to complete the survey.

The questionnaire should take less than 5 minutes to complete, either by completing it and returning it by mail, or on the telephone. It asks questions concerning the symptoms your child may have experienced during or after the injury, care your child received and costs to your family that were related to the head injury.

The Principal Investigator of the study is Jeanine M. Buchanich, MPH, Research Specialist, who will be involved in all aspects of the study. Ms. Buchanich is a staff member in the Department of Biostatistics at the University of Pittsburgh and is getting her Ph.D. in Epidemiology. Ms. Buchanich has several years experience in injury research and is currently working on a project to develop a national trauma registry for children.

If you wish to participate in this study, please sign, date and return one copy of the enclosed consent form in the postage-paid envelope to the University of Pittsburgh by June 11, 2007 and keep one copy of the consent form for your records. If you wish to participate, you

must fill out and sign the section of the consent form entitled Voluntary Consent/Parental Certification.

If you do not wish to participate, please mark the bottom of the survey and return it in the postage-paid envelope.

You can also fill out and return the enclosed questionnaire in the postage-paid envelope. If you return a consent form but not a questionnaire, Ms. Buchanich will call you to complete the questionnaire. If we do not receive your consent form, I may call to determine your willingness to participate. All such calls will be made during the two months after you receive this letter.

To be consistent among all study participants, we are requesting that the child's mother, if she lives with the child, sign the consent form and complete the questionnaire. If the child's mother is not living with the child, then we are requesting participation from the child's father. If neither parent is living with the child, then that child is not eligible to participate.

Your participation in this study is voluntary. You have the right to refuse to participate in this study or to refuse to answer specific questions. Your decision whether or not to participate in this study or to answer questions will have no effect on any benefits to which you are entitled. The information that you provide to the researchers will not be used in any way that can identify any individual.

Your help in this research is very important, and we look forward to your participation. This research cannot be successful without your participation.

If you have any questions regarding your participation or about the study in general, you can contact Ms. Buchanich at 412-624-2423 or me at 412-692-7692. Please also feel free to contact one of us with any questions, comments or concerns about the consent form, the questionnaire or any other issues regarding this study.

Thank you for your cooperation.

Sincerely,

Noel S. Zuckerbraun, M.D.
Assistant Professor of Pediatric Emergency Medicine
Children's Hospital of Pittsburgh

APPENDIX L

CONSENT FORM FOR ABBREVIATED SURVEY

CONSENT TO PARTICIPATE IN AN OBSERVATIONAL STUDY

TITLE: A Clinical Decision-Making Rule for Head Injury in Children

PRINCIPAL INVESTIGATOR: Jeanine M. Buchanich
Research Specialist
Department of Biostatistics
Graduate School of Public Health
University of Pittsburgh
Pittsburgh, PA 15261
(412) 624-2423

CO-INVESTIGATOR: Barbara A. Gaines, M.D.
Assistant Professor of Surgery
Children's Hospital of Pittsburgh
Pittsburgh, PA 15261
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Noel S. Zuckerbraun, M.D.
Asst Professor of Pediatric Emergency Medicine
Children's Hospital of Pittsburgh
Pittsburgh, PA 15261
(412) 692-7692

Thomas J. Songer, Ph.D.
Assistant Professor
Department of Epidemiology
Graduate School of Public Health

University of Pittsburgh
Pittsburgh, PA 15261
(412) 648-9296

SOURCE OF SUPPORT: None

DESCRIPTION OF STUDY: You and your child are being asked to participate in a research study because the Graduate School of Public Health at the University of Pittsburgh and Children's Hospital of Pittsburgh (CHP) are currently investigating the impact of head injuries on children. We would like to request you and your child's participation in this study because your child had a head injury and was seen at the Emergency Department of Children's Hospital of Pittsburgh in 2005.

The study includes both children and the mothers (if they are living with their child; otherwise, the child's father) of children who sustained head injuries. The information necessary for the study comes from two sources: your child's medical records from the 2005 injury and from talking to the mothers of the children. We estimate that 170 children less than 3 years old and who were treated for head injury in 2005 and their mothers will need to be contacted for the study.

This consent will allow University of Pittsburgh researchers to review your child's medical records from the head injury treated at CHP in 2005 and also to contact you for a telephone interview that will include questions on care following the injury, your child's behavior following the injury and any work or school time missed due to the injury. This interview should take 5 minutes.

If you wish, you can also complete the enclosed questionnaire and return it in the postage-paid envelope with your consent form. If you return the completed questionnaire, you will not be called.

RISKS AND BENEFITS: Although every effort will be made to maintain confidentiality, you and your child are subject to the risk of a breach of confidentiality. This means that information provided by you or your child in this study may be viewed by persons outside of the study, despite investigators' efforts to maintain the confidentiality of your child's records and your responses. You and your child will likely receive no direct benefit from participation in this study, although society may benefit from increased knowledge about the treatment and health effects of head injuries in children.

NEW INFORMATION: You and your child will be promptly notified if any new information develops during the conduct of this research study that may cause you or your child to change your mind about continuing to participate.

COSTS AND PAYMENT: You and your child will not be charged nor will you or your child be paid to take part in this study. We have, however, enclosed a small token of our appreciation of the time spent on the survey for your child.

CONFIDENTIALITY: Any information about you or your child obtained from this research will be kept as confidential (private) as possible. All records related to you and your child's involvement in this research study will be stored in a locked file cabinet. We will protect participants' confidentiality by assigning a code to all data, keeping the participant's name and contact information separate from that data, and keeping the link between the two separate. You and your child will not be identified by name in any publication of research results unless you and your child sign a separate form giving your permission (release).

This research study will involve the recording of current medical information from your child's hospital records. The information that will be recorded will be limited to information concerning your child's head injury in 2005, including the mechanism of the injury, your child's symptoms, procedures undergone in the hospital, diagnoses, clinical and outcome variables and payment information. This information will be used to help develop a decision-making rule about the most effective way to treat children who come to the hospital with head injuries.

In addition to the investigators listed on the first page of this authorization (consent) form and their research staff, the following individuals will or may have access to identifiable information (which may include your child's identifiable medical record information) related to your and your child's participation in this research study:

Authorized representatives of the University of Pittsburgh Research Conduct and Compliance Office may review your and your child's identifiable research information for the purpose of monitoring the appropriate conduct of this research study.

In unusual cases, the investigators may be required to release identifiable information (which may include your child's identifiable medical information) related to your and your child's participation in this research study in response to an order from a court of law.

The investigators may continue to use and disclose, for the purposes described above, identifiable information (which may include your child's identifiable medical information), related to your and your child's participation in this research study for seven years following the final reporting of the information.

If the researchers learn that you or your child, or someone with whom you or your child is involved, is in serious danger or harm they will need to inform the appropriate agencies as required by Pennsylvania law.

RIGHT TO WITHDRAW: Your and your child's participation in this research study, to include the use and disclosure of your and your child's identifiable information for the purposes described above, is completely voluntary. (Note, however, that if you do not provide consent for the use and disclosure of identifiable information for the purposes described above, you and your child will not be allowed, in general, to participate in the research study.)

Your doctor may be involved as an investigator in this research study. As both your doctor and a research investigator, she is interested both in your child's medical care and the conduct of this research study. Before agreeing to participate in this research study, or at any time during your study participation, you or your child may discuss your child's care with another doctor who is not associated with this research study.

You and your child are not under any obligation to participate in any research study offered by your doctor.

You may withdraw, at any time, consent for participation in this research study, to include the use and disclosure of your or your child's information for the purposes described above. (Note, however, that if you withdraw consent for the use and disclosure of identifiable information for the purposes described above, you and your child will also be withdrawn, in general, from further participation in the research study.) Any identifiable information recorded for, or resulting from, your and your child's participation in this research study prior to the date that you formally withdraw consent

may continue to be used and disclosed by the investigators for the purposes described above.

Your decision to withdraw consent for participation in this research study will have no effect on your or your child's current or future relationship with the University of Pittsburgh. Your decision to withdraw consent for participation in this research study will have no effect on your or your child's current or future medical care at a UPMC hospital or affiliated health care provider or your or your child's current or future relationship with a health care insurance provider. To formally withdraw consent for participation in this research study you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form.

VOLUNTARY CONSENT/ PARENTAL CERTIFICATION

All of the above has been explained to me and my child and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study, and that such future questions will be answered by the researchers listed on the first page of this form. Any questions I have about my rights or my child's rights as a research participant will be answered by the Human Subject Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668).

By signing this form, I agree to participate in this research study. A copy of this consent form will be given to me.

_____ _____

Parent Participant's Signature Date

_____

Printed Name of Child-Subject

"I understand that, as a minor (age less than 18 years), the above-named child is not permitted to participate in this research study without my consent. Therefore, by signing this form, I give my consent for his/her participation in this research study."

_____ _____

Parent's or Guardian's Name (Print) Relationship to Participant (Child)

_____ _____

Parent or Guardian Signature Date

_____ _____

Phone Number Best time to reach you

APPENDIX M

ABBREVIATED SURVEY IRB APPROVAL

University of Pittsburgh
Institutional Review Board

3500 Fifth Avenue
Ground Level
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)

MEMORANDUM

TO: Ms. Jeanine Buchanich,

FROM: Christopher Ryan, PhD, Vice Chair

DATE: May 8, 2007

SUBJECT: IRB #0601105: A Clinical Decision-Making Rule for Mild Head Injury in Children: Follow-Up

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Your renewal of the above-referenced proposal has received expedited review and approval by the Institutional Review Board under 45 CFR 46.110 (5,7).

Please include the following information in the upper right-hand corner of all pages of the consent form:

Approval Date: May 7, 2007
Renewal Date: May 6, 2008
University of Pittsburgh
Institutional Review Board
IRB #0601105

Please note that it is the investigator's responsibility to report to the IRB any unanticipated problems involving risks to subjects or others [see 45 CFR 46.103(b)(5) and 21 CFR 56.108(b)]. The IRB Reference Manual (Chapter 3, Section 3.3) describes the reporting requirements for unanticipated problems which include, but are not limited to, adverse events. If you have any questions about this process, please contact the Adverse Event Coordinator at 412-383-1504.

The protocol and consent forms, along with a brief progress report must be resubmitted at least **one month prior** to the renewal date noted above as required by FWA00006790 (University of Pittsburgh), FWA00006735 (University of Pittsburgh Medical Center), FWA00000600 (Children's Hospital of Pittsburgh), FWA00003567 (Magee-Womens Health Corporation), FWA00003338 (University of Pittsburgh Medical Center Cancer Institute).

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

CR:kh

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