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Trends in imaging findings, interventions, and outcomes among children with isolated head trauma

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Abstract

Objective—Analyze the impact of decreased head CT imaging on detection of abnormalities and outcomes for children with isolated head trauma.

Methods—Multicenter retrospective cohort of patients <19 years old presenting for isolated head trauma to emergency departments in the Pediatric Health Information System database from 2003–2015. Patients directly admitted or transferred to another facility and those with a discharge diagnosis code for child maltreatment were excluded. Outcomes were ascertained from administrative and billing data. Trends were tested using mixed effects logistic regression, accounting for clustering within hospitals and adjusted for age, gender, insurance type, race, presence of a complex chronic condition, and hospital-level case mix index.

Results—Between 2003–2015, 306,041 children presented for isolated head trauma. The proportion of children receiving head CT imaging was increasing until 2008, peaking at just under 40%, before declining to 25% by 2015. During the recent period of decreased head CT imaging, the detection of skull fractures (Odds Ratio (OR)/year 0.96, 95% CI 0.95–0.97) and intracranial bleeds (OR/year 0.96, 95% CI 0.94–0.97), hospitalization (OR/year 0.96, 95% CI 0.95–0.96), neurosurgery (OR/year 0.91, 95% CI 0.87–0.95), and re-visit (OR/year 0.98, 95% CI 0.96–1.00) also decreased, without significant changes in mortality (OR/year 0.93, 95% CI 0.84–1.04) or persistent neurologic impairment (OR/year 1.03, 95% CI 0.92–1.15).

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Contributors' Statement:

ERC designed the study, wrote the statistical analysis plan, cleaned and analyzed the data, and drafted and revised the paper. TBN wrote the statistical analysis plan, analyzed the data, and revised the paper. MH wrote the statistical analysis plan and revised the paper. JW cleaned and analyzed the data and revised the paper. SLB designed the study and revised the paper. ARS designed the study, wrote the statistical analysis plan, and drafted and revised the paper.

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Conclusions—The recent decline in CT scanning in children with isolated head trauma was associated with a reduction in detection of intracranial abnormalities, and a concomitant decrease in interventions, without measurable patient harm.

Introduction

Head trauma is common, with overall incidence estimates in high-income countries of 47 to 618 per 100,000 person-years, the majority of which affect children and young adults.¹ Mortality and disability from head trauma are high,^{2,3} making rapid assessment and neurosurgery critical for severe cases. Computed tomography (CT) scans are the gold standard to identify skull fractures and intracranial hemorrhages, but are also a non-trivial source of radiation.⁴ Associations between CT radiation exposure and subsequent malignancies^{5–7} have generated campaigns,⁸ algorithms,⁹ and proposals^{10,11} to reduce overreliance on CT imaging. These interventions are showing success, with head CT imaging declining in United States (US) children's hospitals,^{12–14} but it is unknown if this decline has impacted detection of intracranial abnormalities and patient outcomes.

Comparing trends in the detection of abnormalities to trends in outcomes as reliance on diagnostic technology changes provides a means to assess the value of diagnosis. For example, screening for phenylketonuria led to increased detection and decreased morbidity,¹⁵ demonstrating the importance of early detection for this condition. On the other hand, increased use of CT pulmonary angiography resulted in more pulmonary emboli diagnoses (and anticoagulation complications) but no change in mortality, suggesting overdiagnosis.¹⁶ Both increases and decreases in testing and detection of abnormalities represent opportunities to assess the value of diagnosis. In the present study, we analyze the impact of reduced head CT imaging on detection of intracranial abnormalities and patient outcomes for children with isolated head trauma.

Methods

Study Design and Setting

We identified a retrospective cohort of children receiving care at hospitals participating in the Pediatric Health Information System (PHIS) database. This database provides de-identified information detailing hospital and patient demographic data, administrative data such as discharge diagnosis and procedure coding, and detailed billing information for patients cared for at 49 US tertiary care children's hospitals, representing approximately 20% of all US pediatric hospitalizations. PHIS is operated by the Children's Hospital Association (Lenexa, KS). We used a de-identified PHIS dataset, which the University of Utah IRB determined qualifies as non-human subject research (IRB 00074483).

Participants

We included patients <19 years old receiving emergency department (ED) or inpatient care at a PHIS hospital between January 2003 and September 2015 with any of the following *International Classification of Diseases, Ninth Revision* (ICD-9) discharge diagnosis codes for head trauma (any position, not just primary diagnosis): 800–801.XX, 803–804.XX, 850–854.XX, and 959.01. Various combinations of these ICD-9 codes have been used

by prior investigators to study pediatric head trauma^{14,17,18} and our codes represent the most inclusive set, to our knowledge. We did not include encounters after implementation of ICD-10 coding in September 2015 due to threats to data validity that occurred when we attempted to crosswalk the ICD-10 to ICD-9 codes. We excluded patients admitted to a PHIS hospital without going through the PHIS hospital's ED and patients transferred out of the PHIS hospital. We excluded patients with an ICD-9 discharge diagnosis code for neurological impairment¹⁹ or procedure code for neurosurgery (01.XX Incision and excision of skull, brain, and cerebral meninges; 02.XX Other operations on skull, brain, and cerebral meninges; 04.XX Operations on cranial and peripheral nerves) on a visit within the year preceding their index head trauma visit, as well as patients seen during the first year that a given hospital began to contribute data to PHIS. We excluded patients with an ICD-9 discharge diagnosis code during their head trauma visit suggesting child maltreatment^{20,21} (Appendix 1). Finally, to focus on the population most targeted by campaigns and algorithms to limit head CT exposure, we limited the cohort to children with isolated head trauma, excluding patients receiving a procedure or imaging of a body part besides the head (other than a chest x-ray) during their index encounter or a discharge diagnosis code for an injury of a body part besides the head. However, we also performed an additional analysis of these children with poly-trauma.

Variables

We restricted head imaging studies to initial head CT, skull x-ray, and brain MRI, performed on the first or second day of an encounter because the hour of care is not specified in the PHIS database. This method ensured that a patient presenting in the evening of day 1 with an imaging study in the early morning of day 2 would have that imaging attributed to the initial presentation. Quantified abnormalities were intracranial bleed (Appendix 2) and skull fracture (Appendix 3), occurring during a patient's index encounter. Further subdivisions by type of fracture or bleed (i.e. subdural vs epidural) were not possible because ICD-9 codes do not distinguish this level of granularity. We measured re-visits as any ED or inpatient visits to the same PHIS hospital with an included head trauma code within 7 days of the initial encounter. Neurosurgery outcomes included the ICD-9 procedure codes 01.XX (Incision and excision of skull, brain, and cerebral meninges) and 02.XX (Other operations on skull, brain, and cerebral meninges). We assigned persistent neurologic impairment to patients with a new (not present during any PHIS encounter in the prior year) diagnosis of a brain injury without return to pre-existing conscious level, coma, anoxic brain damage, or paralysis; or the placement of a gastric tube or tracheostomy during an included head trauma encounter (Appendix 4). Only neurosurgery, mortality, and persistent neurologic impairment outcomes experienced during the index visit or re-visit were included.

Statistical Analysis

Categorical variables were summarized with frequencies and percentages, while continuous variables were summarized with medians and interquartile ranges (IQR). Annual trends in dependent variables were tested using mixed effects logistic regression, allowing for different intercepts across hospitals and accounting for clustering within hospitals. We adjusted for age (with restricted cubic splines to account for nonlinear effects), gender, insurance (government, private, or other), race, presence of a complex chronic condition,

and hospital-level case mix index. Complex chronic conditions are defined by ICD-9 codes and derived from hospitalization patterns of children with costly illnesses and congenital defects.²² PHIS case mix is determined as the average cost weight after each discharge in PHIS is assigned an All-Patient-Refined Diagnosis Related Group (APR-DRG; 3M) and severity level. Annual trends were analyzed before and after 2008, the year in which head CT scanning began declining in our dataset. To obtain adjusted hospital-level variation for head CT use in 2015, we used the predicted values from a linear regression model, adjusted for the above covariates. The trend in the annual proportion of head trauma and child maltreatment encounters in the cohort relative to all encounters in PHIS was tested with univariate linear regression.

Children's hospitals can contribute data to PHIS from satellite centers, and observations from these affiliated centers are not consistently flagged in the database. The introduction of data from satellite centers with lower acuity could bias observed trends. In preliminary analyses, new satellite contributions showed up as a disproportionately large contribution of ED visits relative to inpatient visits from one year to the next. To limit this potential bias, we measured the annual percentage changes in ED and inpatient visits at the individual hospital level. Outlier bounds for the percent difference between ED and inpatient annual rates of change at each hospital were calculated using Tukey's outlier criteria: values $< P25 - 1.5 * IQR$ and values $> P75 + 1.5 * IQR$, where P25 and P75 are the 25th and 75th percentiles of the data, respectively.²³ At the individual hospital level, all years prior to a year in which the difference between ED and inpatient annual change met outlier criteria were excluded (thereby preventing analysis of discontinuous data). To be included, a PHIS center had to have >2 consecutive qualifying years of data. Only years when hospitals contributed both inpatient and ED encounters were included.

To obtain estimates of the causal effect of initial CT scanning on neurosurgery and mortality among the patients in whom it was discretionary, i.e., those in whom it would have been done in hospitals and years when more, rather than fewer CT scans were done (the so-called complier average causal effect²⁴), we used instrumental variable analyses. For the instrument, we used the proportion of children who received initial CT scans in the year and hospital in which the child was seen (not counting that child), entered as a restricted cubic spline in bivariate probit regression models. We did sensitivity analyses using the instrument as a single continuous variable and dichotomizing at 0.30 (the median) and using 2-stage least squares instead of bivariate probit regression models. All analyses were performed using STATA version 14 (Stata-Corp, College Station, TX, USA).

Results

Study Population

We identified 795,310 pediatric visits for head trauma. After applying exclusion criteria, 309,188 visits for isolated head trauma at 34 US children's hospitals remained (Figure 1), among 306,041 children. The majority of children were male and one third of the sample was under 2 years of age (Table 1). The most common diagnoses for which children were included in the sample were "head injury unspecified" (72%) and concussion (24%).

Head Trauma Encounter Trend

Our cohort was responsible for 1.46% (95% CI 1.46 to 1.47%) of all PHIS ED encounters, a proportion that increased (absolute percent change/year, 0.031%; 95% CI 0.030 to 0.033%) over the study period.

Head Imaging and Findings

Figure 2 displays trends in head imaging and the detection of intracranial abnormalities. The trend in the proportion of children exposed to head CT imaging was increasing up to 2008, peaking at just below 40%, but demonstrated a significant decline thereafter to 25% in 2015. Skull x-rays were less often performed and declined more consistently. An increase in brain MRIs after 2008 may reflect the adoption of fast MR protocols in the trauma setting, but MRI remained a rarely used test (<1% of patients). When combining all three imaging modalities, an overall decline in head imaging was found after 2008. The decline in head CT occurred for all age groups, but was most pronounced among children older than 10 years (Table 2). There remained substantial variation across children's hospitals for use of head CT imaging in 2015 (adjusted range 11–56%, standard deviation 12%).

An intracranial abnormality was detected in 17,056 (5.6%) patients as follows: skull fracture in 10,542 patients, intracranial bleed in 2,635 patients, and concomitant skull fracture and intracranial bleed in 3,879 patients. After 2008, the trend in diagnoses of skull fractures and intracranial bleeds was declining (Figure 2) and independent of age (Table 2). Among the various types of intracranial bleeds, decreased detection of cerebral lacerations and contusions contributed most to the decline.

Interventions and Patient Outcomes

Patients were infrequently hospitalized (n=15,549, 5.1% of cohort) and rarely experienced neurosurgical intervention (n=656, 0.2% of cohort, 5 patients with >1 neurosurgery), hospital re-visit (n=2,754 patients, 0.9% of cohort), mortality (n=104 patients, 0.03% of cohort), or persistent neurologic impairment (n=74 patients, 0.02% of cohort). While rates of hospitalization, neurosurgery, and re-visit declined after 2008, the trends of mortality and persistent neurologic impairment were each statistically unchanged over the same time period (Figure 3). Intervention and outcome trends were similar across age groups, with a notably larger decline in neurosurgery among children <2 years old (Table 2). Fewer craniotomies and procedures to elevate skull fractures were most responsible for the decline in neurosurgical procedures.

Of the 2,754 patients who re-visited the hospital within 7 days, 1,674 (61%) had not received head imaging during the first 2 days of their index encounter- none of these patients were ultimately diagnosed with persistent neurologic impairment or suffered mortality. Of the 104 patients who died, 87 (84%) did not receive any head imaging. The patients who died without any head imaging had very short lengths of stay (median 1 day, IQR 1–1 days) and none received neurosurgery, suggesting that they presented too injured (e.g. in full cardiac arrest) to warrant scanning.

The instrumental variable analyses found that a head CT scan on initial presentation (among patients for whom it was discretionary) was associated with a 0.88% (95% CI 0.31 to 1.46%) absolute increased probability of receiving neurosurgery. Results were unchanged regardless of how the instrument was coded, and similar (0.80% increased risk, 95% CI 0.47 to 1.13%) using 2-stage least squares regression. Head CT was not associated with mortality in any of the instrumental variable analyses (bivariate probit model 0.02% decrease, 95% CI -0.21 to +0.16%). All instruments used were strongly ($P < 0.0001$) associated with exposure (e.g., $F(4,33) = 5520$, for two-stage least squares regression), but tests of endogeneity were of borderline significance (and $P = 0.037$ for bivariate probit regression and $P = 0.044$ for two-stage least squares models), indicating relatively weak evidence for unmeasured confounding variables.

Additional Analyses

A sensitivity analysis including patients with a child maltreatment diagnosis did not change any of the trend directions or statistical significance found in the primary analysis. The proportion of patients receiving a diagnosis of child maltreatment increased over the study period (absolute percent change/year, 0.0006%; 95% CI, 0.0004 to 0.0009%). An analysis of the 99,599 children excluded from the primary analysis because of evidence of poly-trauma between 2008–2015 demonstrated a decline in head imaging (OR/year 0.93, 95% CI 0.92–0.94), hospitalization (OR/year 0.98, 95% CI 0.98–0.99), and neurosurgery (OR/year 0.95, 95% CI 0.92–0.97), but no statistically significant changes in the detection of skull fractures (OR/year 1.00, 95% CI 0.99–1.01) and intracranial bleeds (OR/year 0.99, 95% CI 0.98–1.00), re-visit (OR/year 0.98, 95% CI 0.95–1.02), mortality (OR/year 0.98, 95% CI 0.94–1.02), or persistent neurologic impairment (OR/year 1.00, 95% CI 0.96–1.04).

Discussion

In this analysis of isolated head trauma visits to 34 US children's hospitals, we demonstrate a decrease in head imaging starting in 2008 accompanied by a decline in diagnosis of intracranial bleeds and skull fractures. In turn, the reduction in these diagnoses was associated with fewer interventions, including hospitalization and neurosurgical procedures, without measurable increase in mortality or persistent neurologic impairment. Trends in imaging, findings, interventions, and outcomes were consistent across age groups.

The Pediatric Emergency Care Applied Research Network (PECARN) landmark publication in 2009 of a validated predictive algorithm, identifying head injured children in whom a CT scan could be avoided, may have influenced these observed trends, as well as two nuances in our results. First, the decline in detection of intracranial abnormalities is less pronounced than the decline in imaging, suggesting that providers' decreased reliance on head CT was not arbitrary, but rather informed by the PECARN algorithm, which is designed to decrease imaging among only patients with the lowest risk of having an intracranial abnormality. Similarly, the decrease in detection of intracranial abnormalities and exposure to interventions was most pronounced among children with isolated head trauma, a population presumably more impacted by the PECARN algorithm compared to children with poly-trauma. However, despite the apparent success of the PECARN

algorithm, considerable inter-hospital variability in the proportion of children exposed to head CT scans in 2015 implies that some degree of unnecessary scanning persists.

One inference from the observed trends is that skull fractures and intracranial bleeds may have been previously overdiagnosed and overtreated. Analyzing the impact of changing rates of technology on disease detection and outcomes is a conventional approach utilized to study overdiagnosis,^{25,26} which is commonly defined as the accurate detection of an abnormality from which a patient does not receive net benefit.²⁷ Therefore, unlike misdiagnosis and false positives, overdiagnosis occurs when a patient truly has the condition in question. Previous reports have found that increased detection of accurate abnormalities (e.g. adults with pulmonary embolus¹⁶ and thyroid cancer²⁸ and children with hypoxemia in bronchiolitis²⁹) was associated with costly and potentially harmful interventions without any evidence of benefit to patients. While these investigations examined how increases in technology use drove overdiagnosis, our investigation demonstrates that reduced technology use may mitigate overdiagnosis. When an intracranial abnormality is detected, even if the clinical appearance is reassuring, clinicians may feel obliged to intervene. The majority of children with minor skull fractures, for example, are hospitalized, even though these hospitalizations provide no measurable benefit.³⁰ The present study found that receiving a discretionary CT scan was associated with a small increased probability of receiving neurosurgery. It is likely that as imaging has decreased, more children with skull fractures and/or bleeds are going undiagnosed and being discharged home from EDs. While some clinicians might fear the consequences of “missing” these diagnoses, our findings suggest that such non-detection may help children avoid unnecessary medical intervention.

An additional contributor to our findings may be that head injuries evaluated at EDs have become less severe over time, a theory for which we considered two potential drivers. First, education and policy interventions aimed at reducing the burden of traumatic head injuries abound and it is possible that campaigns to increase seatbelt or bicycle helmet use, for example, have resulted in a recent reduction in head trauma severity among children.³¹ Second, a heightened emphasis on the importance of medical evaluation for head trauma could drive increased numbers of ED visits for minor injuries that are unlikely to prompt imaging, hospitalization, or neurosurgery. In the present cohort, we did find a statistically significant increase in the annual proportion of head trauma encounters relative to all ED encounters in PHIS and several recent investigations demonstrate that medical visits for concussions are increasing.^{32–34} However, with one notable exception,³⁵ the increased visits in these prior investigations are largely occurring in the primary care setting. The possibility that policy interventions or heightened awareness are diluting the denominator of head injuries presenting to EDs with less severe cases is tempered by the fact that we did not observe a decrease in the rates of mortality and persistent neurologic impairment. Furthermore, the trends we observed were consistent across age groups. If, for example, heightened concerns for concussion were diluting the cohort over time with less severe head trauma cases, one would not expect trends among children <2 years old to be affected because concerns for concussion have focused on older children. Lastly, the decrease in CT scanning in children’s hospitals has been observed for multiple other conditions as well^{12,36} and therefore is more likely to reflect conscientious efforts to limit unnecessary studies and radiation exposure than a dilution effect.

This study has important limitations. Our findings may not be generalizable to community hospitals, where head imaging patterns may differ.³⁷ The discharge diagnosis codes we used to identify head trauma are validated and have been shown to have a high specificity but low sensitivity,³⁸ though a low sensitivity that is consistent over time represents a low risk of bias to our analysis. Indeed, there were no substantial changes over the study period to the ICD-9 codes used. We could not adjust for other covariates that influence the decision to image but are not present in the PHIS database, like a patient's Glasgow Coma Scale score. Additionally, the number of participating hospitals and the number of visits per hospital in PHIS varies over time. Although we excluded outlier hospital years where the ratio of ED to inpatient visits increased disproportionately, this may not have been sufficient to control for temporal changes in case mix. Such temporal changes in case mix would violate the ("exclusion restriction") assumption that the instrumental variables are associated with outcomes only through their effect on initial CT scanning. It is possible that more judicious imaging and decreased detection of intracranial abnormalities might miss cases of child maltreatment, though we found that diagnoses of child maltreatment were actually increasing over the study period. Similarly, we examined only the most severe, acute outcomes after head trauma and decreased detection and intervention for intracranial abnormalities could be associated with worsened subtle, long term neurocognitive outcomes. Lastly, there is potential for outcome ascertainment bias, given that mortality, hospital re-visits, and neurosurgical care occurring outside of the index PHIS hospital would not be captured.

Conclusion

The benefits of limiting unnecessary head CTs may extend beyond avoidance of the costs and radiation associated with the test itself, to include prevention of overdiagnosis and overtreatment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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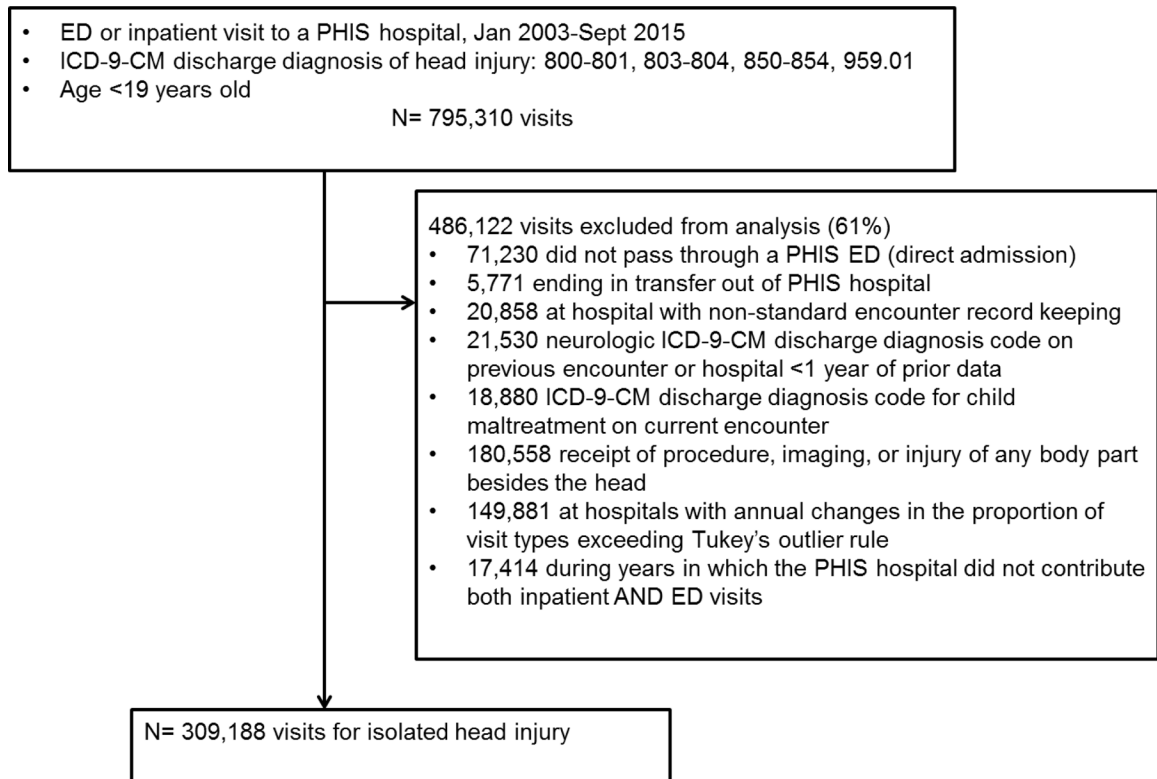
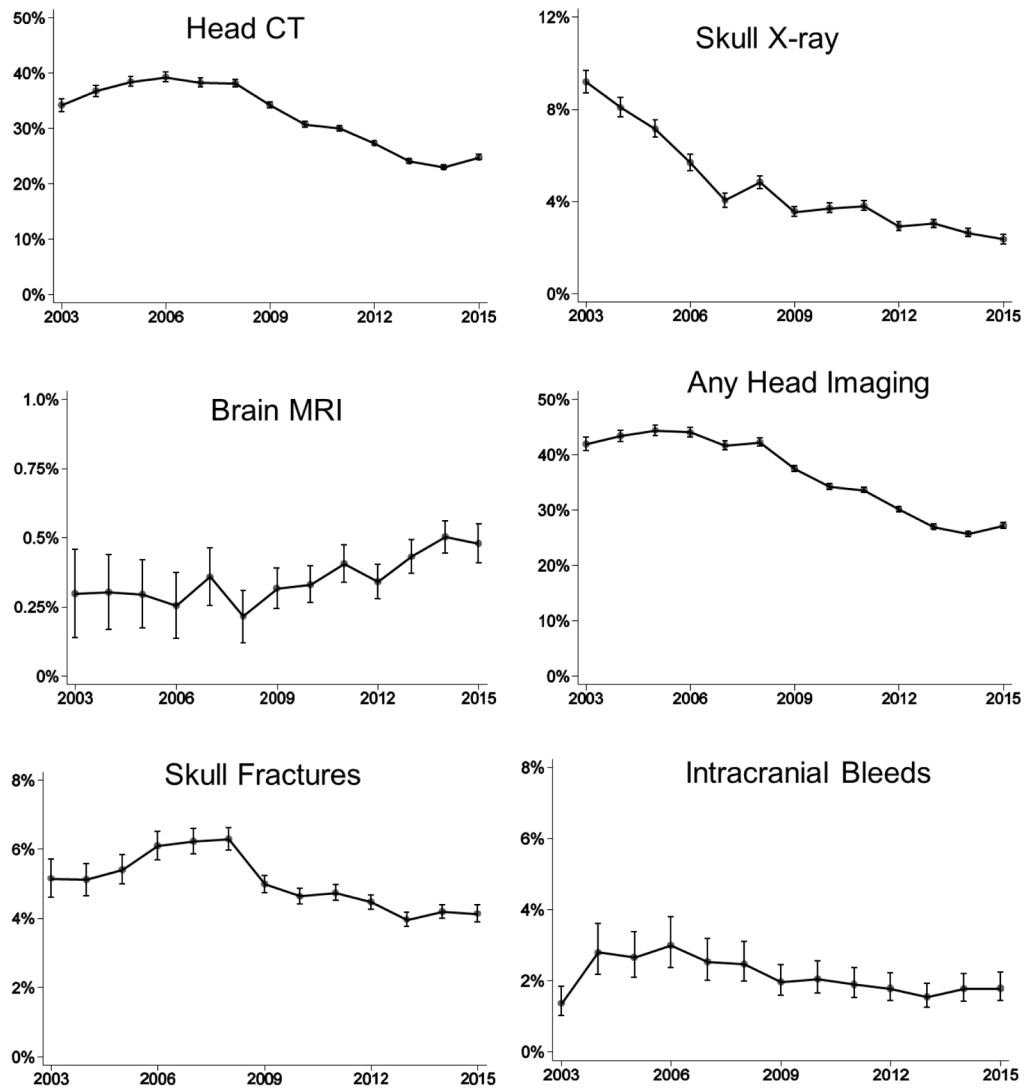
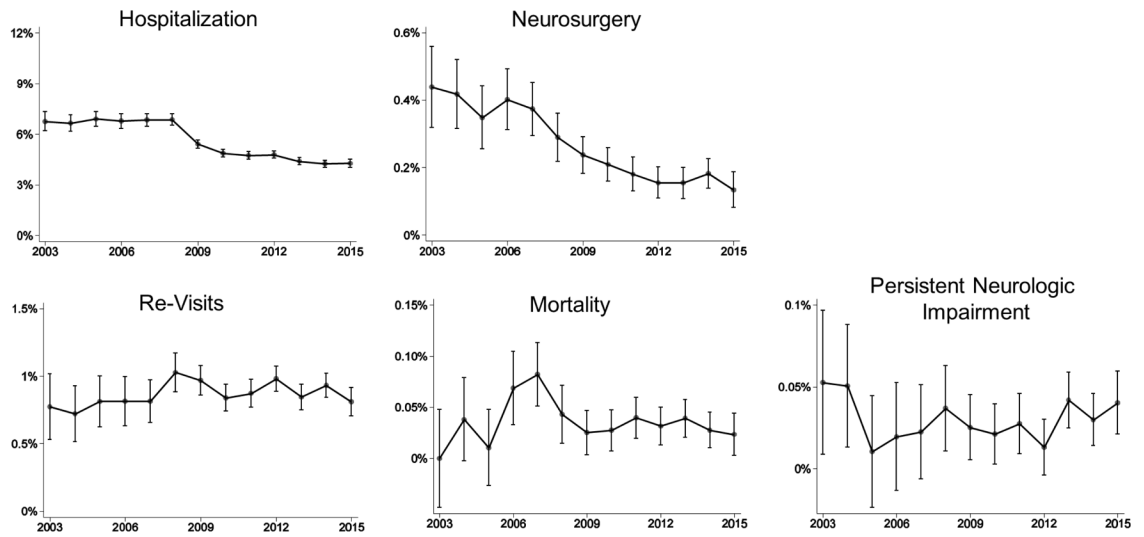


Figure 1.
Patient Selection



Figures display the unadjusted trend over time for each dependent variable, with a 95% confidence interval of the annual proportion.

Figure 2.
Trends of head imaging and findings among children with isolated head trauma



Figures display the unadjusted trend over time for each dependent variable, with a 95% confidence interval of the annual proportion.

Figure 3.
Trends of interventions and patient outcomes among children with isolated head trauma

Table 1

Cohort characteristics, N=306,041 patients presenting with isolated head trauma

	n (%)
Male, %	180,859 (59)
Age, years	
<2	105,253 (34)
2–10	134,887 (44)
11–18	65,901 (22)
Race, %	
Non-Hispanic white	152,559 (50)
Non-Hispanic black	64,983 (21)
Hispanic	37,706 (12)
Asian	5,456 (2)
Other	45,337 (15)
Insurance, %	
Government	136,953 (45)
Private	132,443 (43)
Other	36,645 (12)
Case mix index, median [IQR]	1.11 [1.03–1.19]
Complex chronic condition, %	4,151 (1)
Inclusion Codes, % *	
800 Fracture of vault of skull	7,391 (2)
801 Fracture of base of skull	5,434 (2)
803 Other and unqualified skull fractures	2,115 (1)
804 Multiple fractures involving skull or face with other bones	80 (0)
850 Concussion	72,048 (24)
851 Cerebral laceration and contusion	634 (0)
852 Subarachnoid subdural and extradural hemorrhage following injury	1,739 (1)
853 Other and unspecified intracranial hemorrhage following injury	368 (0)
854 Intracranial injury of other and unspecified nature	2,562(1)
959.01 Head injury, unspecified	219,452 (72)

IQR- interquartile range

* Percentages sum to more than 100 because patients could have more than 1 diagnosis

Table 2

Change in odds per year of imaging, findings, interventions, and outcomes among children with isolated head trauma since 2008, stratified by age

	Adjusted Odds Ratio (95% CI)
Head CT, all ages	0.89 (0.89–0.89)
<2 years	0.92 (0.91–0.93)
2–10 years	0.90 (0.90–0.91)
>10 years	0.83 (0.82–0.84)
Skull X-ray, all ages	0.94 (0.93–0.95)
<2 years	0.93 (0.92–0.95)
2–10 years	0.95 (0.93–0.97)
>10 years	0.90 (0.87–0.94)
Brain MRI, all ages	1.09 (1.06–1.13)
<2 years	1.06 (0.99–1.13)
2–10 years	1.09 (1.04–1.15)
>10 years	1.11 (1.06–1.17)
Any Head Imaging, all ages	0.89 (0.89–0.90)
<2 years	0.92 (0.91–0.92)
2–10 years	0.91 (0.90–0.91)
>10 years	0.83 (0.83–0.84)
Skull Fracture, all ages	0.96 (0.95–0.97)
<2 years	0.96 (0.95–0.98)
2–10 years	0.97 (0.95–0.98)
>10 years	.095 (0.92–0.98)
Intracranial Bleed, all ages	0.96 (0.94–0.97)
<2 years	0.97 (0.95–0.99)
2–10 years	0.96 (0.94–0.98)
>10 years	0.93 (0.91–0.96)
Re-presentation, all ages	0.98 (0.96–1.00)
2 years	0.96 (0.93–0.99)
2–10 years	0.99 (0.96–1.03)
>10 years	0.98 (0.94–1.02)
Mortality, all ages	0.93 (0.84–1.04)
<2 years	0.92 (0.73–1.16)
2–10 years	0.94 (0.81–1.08)
>10 years	0.92 (0.74–1.16)
Hospitalization, all ages	0.96 (0.95–0.96)
<2 years	0.95 (0.94–0.97)
2–10 years	0.96 (0.95–0.98)
>10 years	0.94 (0.92–0.96)
Neurosurgery, all ages	0.91 (0.87–0.95)
<2 years	0.87 (0.78–0.96)

	Adjusted Odds Ratio (95% CI)
2–10 years	0.92 (0.86–0.97)
>10 years	0.93 (0.85–1.03)
Neuro Impairment, all ages	1.03 (0.92–1.15)
<2 years	1.19 (0.91–1.56)
2–10 years	1.01 (0.85–1.20)
>10 years	0.97 (0.81–1.17)

CI- Confidence Interval

Displayed are adjusted odds ratios of the dependent variable per year over the period 2008–2015, with a 95% confidence interval, obtained from mixed effects logistic regression, accounting for clustering within hospitals and adjusted for gender, age, insurance type (government, private, or other), race (non-Hispanic white, non-Hispanic black, Hispanic, Asian, or Other), presence of a complex chronic condition, and hospital-level case mix index. The sub-analyses by age do not include the age variable in their regression calculation.

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