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Douglas Fraser, *Western University*

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Identification of adverse events in pediatric severe traumatic brain injury patients to target evidence-based prevention for increased performance improvement and patient safety ☆

Tanyak Charyk Stewart[a,b,*], Kyle Luong[a,b], Ibrahim Alharfi[a,b], Brianna McKelvie[a,b], Douglas D. Fraser[a,b,c,d,e,f]

[a] Department of Paediatrics, Schulich School of Medicine & Dentistry, University of Western Ontario, London, ON, Canada
[b] Children's Hospital at London Health Sciences Centre, London, ON, Canada
[c] Translational Research Centre, London, ON, Canada
[d] Children's Health Research Institute, London, ON, Canada
[e] Physiology and Pharmacology, Western University, London, ON, Canada
[f] Clinical Neurological Sciences, Western University, London, ON, Canada

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ABSTRACT

Introduction: Trauma centres are required to continuously measure, evaluate and improve care. Severe traumatic brain injury (sTBI) patients are highly susceptible to adverse events (AE; unintended, potentially harmful events resulting from health care) due to their unstable condition requiring high risk interventions, multiple medications and invasive monitoring. Objectives were to describe: (1) a process for identifying AE in pediatric sTBI patients to identify safety risks, target and implement evidence-based prevention strategies; and (2) a tertiary care PICU's sTBI AE experience.

Methods: Merging databases, Trauma Registry with Adverse Events Management System, identified AE in patients. Details on the event location, type and severity of harm were combined with patient demographics, injury data, costs and outcomes in a cohort of 193 PICU sTBI patients (2000-15). Descriptive statistics and multivariate logistic regression were undertaken to describe AE, and their association with risk factors and outcomes.

Results: 103/193 sTBI patients (53%) suffered at least one AE. 238 AE occurred (1.23 AE/patient), with 30% of patients having 2+ AE. Most resulted in no harm (54%) with decubitus ulcers (15%) the most common AE. AE patients were more likely to be monitored for elevated ICP ($p<0.001$), with fewer ventilator-free days ($p=0.015$), longer LOS for PICU (11 vs. 3.5 days; $p<0.001$) and in-hospital (31 vs. 11 days; $p<0.001$) with higher median costs ($121,234 vs. $53,341; $p=0.031$). AE patients required a higher level of care on discharge ($p=0.035$).

Conclusions: Merging databases is an effective practice to identify AE and safety risks in trauma populations. Utilizing this method, a PICU AE rate of 1.23 events per patient was found with TBI severity the most important factor to increase the odds of AE. AE represent performance improvement events, opportunities to optimize care, decrease costs, as well as improve outcomes, to ultimately improve patient safety in this vulnerable population.

Introduction

According to the American College of Surgeon's (ACS) *Resources for the Optimal Care of the Injured Patient* [1], trauma centres are required to continuously measure, evaluate and improve care to ensure it is safe, efficient and effective care for injured patients. As part of this process, unnecessary variation in patient care should be reduced as much as possible and adverse events (AE) prevented.

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* Corresponding author at: Research Park, University of Western Ontario, Rm LL02, 999 Collip Circle, London N6G 0J3, ON, Canada.
E-mail addresses: tanya.charykstewart@lhsc.on.ca (T. Charyk Stewart), kluong2016@meds.uwo.ca (K. Luong), Ibrahim.alharfi@gmail.com (I. Alharfi), brianna.mckelvie@lhsc.on.ca (B. McKelvie), douglas.fraser@lhsc.on.ca (D.D. Fraser).

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Despite concerted effort, AE still occur. It has been estimated that approximately 400,000 hospitalized patients annually experience a preventable AE, with costs totaling $4 to $20 billion each year [2,3]. AE are unintended, unexpected, potentially harmful events resulting from healthcare management that occur independent of patient's injury or underlying condition [4]. They are important performance improvement (PI) events that should be monitored for trauma patients to identify improvement opportunities in patient care and safety.

Severe traumatic brain injury (sTBI) is a significant cause of morbidity and mortality in the pediatric population [5,6], and outcomes are highly dependent on patient management [7,8]. Patients with sTBI are admitted to pediatric intensive care units (PICU) where AE potentially add another layer of complexity to their care [9]. The high rate of AE in critically ill patients is likely multifactorial; their underlying condition is severe and unstable and they frequently require high-risk interventions, multiple medications, continuous invasive monitoring and prolonged immobility [10,11]. As well, their management is fast-paced, complex and requires urgent, high-risk decision making. These factors may lead to higher rates of medical error compared to hospital patients without critical illness. This risk may be further increased for PICU patients due to their significant variability in age, size, comorbidities and diagnoses [9,12]. As a result, children and adolescents with sTBI treated within a PICU are highly susceptible to AE and are more likely to experience AE there than in any other hospital unit [12].

AE can be detrimental to patients in various ways, from adversely affecting care and their patient experience to resulting in negative health outcomes, including death.[13] AE also negatively impact the healthcare system, contributing substantially to increased healthcare costs. Reporting of AE are essential to identify system-level targets to improve patient safety. Implementing best practice to identify these events, followed by knowledge translation of results from the review of AE allows for improvement in the safety of medical care of our patients [14]. Evidence-based practice (EBP) is not possible if AE are not reported. Patient benefits must be weighed against harms and AE, along with an examination of quality of evidence, costs, resource use and feasibility within the context of patients' values and preferences when assessing patient treatment options and outcomes [15,16]. It is, therefore, vital for trauma centres to review the types and frequencies of AE occurring within their injured population for the identification of safety risks, to mitigate these risks in healthcare delivery for future patients. This is particularly important for the vulnerable PICU sTBI population.

To date, there have only been a few reports on the AE rates and composition in the PICU, but these studies did not specifically address pediatric sTBI patients [9,17–22]. As well, here is no 'gold standard' in the determination and reporting of AE in this patient population, with each methodology having its own limitations. Chart audits can be resource intensive in time and money; observational data are not always effective in identifying and quantifying harm; underutilization of incident reporting systems may occur due to time and funding constraints, institutional culture and engagement of physicians; and electronic trigger tools can be costly with manual tools highly labour intensive requiring training and time to review the chart [22–24].

Therefore, the objectives of this study were to describe: 1) a process for identifying AE in pediatric sTBI patients to identify safety risks, target and implement evidence-based prevention strategies; and 2) a tertiary care PICU's sTBI AE experience. This included an examination of the epidemiology of AE in the PICU for a cohort of well-described pediatric sTBI patients [25–31], to determine their incidence and association with various risk factors and outcomes. Our aims of this PI and patient safety (PIPS) project were to develop an efficient process to be used by pediatric trauma centres to identify AE, as well as provide insight into the burden of AE for sTBI patients. This will allow for the determination of specific areas of focus for education and evidence-based prevention strategies to reduce AE and optimize sTBI patient safety, the patient experience and outcomes, including healthcare expenditures.

Materials and methods

Study design and setting

This study was approved by the Health Sciences Research Board at Western University. All pediatric trauma patients (<18 years) with an Injury Severity Score (ISS) ≥ 12 treated in the PICU were screened over a 15-year period (2000-15; n=342). This retrospective cohort study included all patients with sTBI identified by a pre-sedation Glasgow coma scale (GCS) ≤ 8 and a head Maximum Abbreviated Injury Scale (MAIS) ≥ 4, no exclusions, that were admitted within 12 hours of their injury and treated in the PICU of Children's Hospital at London Health Sciences Centre (CH-LHSC), the Regional Pediatric Level 1 Trauma Centre for Southwestern Ontario. CH-LHSC has a catchment area of 190,000 km^2 with a pediatric population of greater than 50,000. Last year, our PICU treated 824 pediatric patients, with a 3% mortality rate and median [quartile 1 (Q1) – quartile 3 (Q3)] LOS, PRISM and PIM2 scores of 2 (1-3) days, 1 (0 - 5) and -4.62 (-5.51 – 2.22), respectively.

Data sources

Trauma registry data

CH-LHSC's trauma registry was utilized to identify pediatric patients satisfying the inclusion criteria, to form our cohort of sTBI PICU patients [25–31]. To ensure no patients were missed, eligible patients were cross-referenced with written and electronic PICU admission records. CH-LHSC's trauma registry is part of the Ontario Trauma Registry's (OTR) Comprehensive Data Set (CDS) which contains detailed injury, clinical and outcome data on severely injured patients treated at one of eleven trauma centres in the province. The OTR is a provincially mandated registry used to identify, describe and quantify trauma cases and injuries in Ontario. It is funded by the Ministry of Health and Long Term Care and managed by the Canadian Institute of Health Information (CIHI) [32]. To ensure a high quality of reliable injury data, data analysts at each trauma center are trained in data abstraction and ISS scoring, and the OTR is required to meet the targets set in CIHI's information quality framework [33]. Data utilized for this study included demographics, injury data, results of neuroimaging studies, interventions, and outcomes. Physiological data included pre-sedation GCS, pupillary light response (on CH-LHSC arrival) and initial laboratory tests.

Outcomes for sTBI patients included in-hospital mortality, hospital and PICU lengths of stay (LOS), ventilator-free days (i.e., unventilated days in the first 28 days of admission), and discharge destination (i.e., chronic rehabilitation hospital, acute care hospital, or home, with or without support services). Where available, total inpatient costs, including costs directly related to patient care activities (i.e., nursing labour, supply costs, pharmaceuticals, etc.) and indirect healthcare costs including costs allocated from overhead functional centres (i.e., plant operations, information technology, finance, health records, etc.) were examined for sTBI patients.

Adverse events

Consistent with a previous PICU study [9], AE were defined as "any injury, large or small, caused by the use (including non-use) of a drug, test, or treatment identified during the PICU stay".

Table 1
Definitions of adverse event (AE) categories.

Adverse Event categories	Definition
Drug-related events	Included an adverse drug reaction (ADR), drug error, or unspecified drug event if no further detail could be discerned from Adverse Events Management System (AEMS) or the patient chart.
Treatment-related events	Procedure-related events included any unintended event as a result of a procedure or misadministration of a procedure, having the potential to harm the patient. Medical device instrument (MDI) or machine malfunctions were events where any medical device or instrument failed to carry out its intended purpose independent of other factors. Any unintended event related to a laboratory or other test, ICP monitor/EVD or any other 'treatment' not classified elsewhere.
Surgery	Any unintended event resulting from surgery.
Line/Tube-related events	Unintended line and tube removals were defined as any unplanned removal of lines or tubing. Line and tube removals enacted by both patients and healthcare staff were recorded. If the line or tube was not pulled out, but an adverse event or complication was associated with that line or tube, then it is recorded based on the type of line or tube involved in the event (i.e., NG/OG/G/J tube, arterial line, central/venous line or peripheral IV-related AE).
Airway-related	This category includes any unintended, potentially harmful event related to the airway, including self-extubation, as well as any AE associated with intubation, a tracheostomy or chest tube.
Fall	Any AE relate to an in-hospital fall.
Other	This category includes all other potentially harmful events that occurred during the patient's PICU stay that did not fit under any event category of AEMS, but was nonetheless determined to be an AE by healthcare staff and reported at the time of its occurrence. This includes administrative events, eating/nutrition and all other in-hospital events.

Legend: ICP = Intracranial pressure; EVD = External ventricular drain; NG = Nasogastric; OG = Orogastric; G = Gastric; J = Jejunal; IV = Intravenous.

Events also had to be outside the standard of care. As such, generally accepted mechanical and technical complications such as multiple attempts for vascular access were omitted. Only events that occurred during PICU admission were included in this study. Infections were excluded, as these data were previously described for this sTBI cohort [25].

AE were identified by querying the Adverse Events Management System (AEMS) for all sTBI patients identified from the trauma registry. AEMS is an electronic, web-based documentation system for collecting, tracking and managing data on patient safety risks, events, findings, recommendations and actions. Incident reporting is the cornerstone of the patient safety culture at CH-LHSC. It is the responsibility of all staff and physicians, who observe, are involved in, or made aware of an AE or near miss to ensure it is reported in AEMS. Once an AE was identified, AE were reviewed from progress notes to include only AE occurring during the patient's PICU stay. Events were retrospectively rated on the AEMS severity of harm scale: Level 1, no injury/harm with assessment required; Level 2, no injury/harm with intervention/monitoring required; Level 3, minor to moderate injury/harm; Level 4, serious injury/harm/disability; Level 5, death. Events were left unrated if the severity of harm could not be discerned from AEMS or PICU progress notes. The AE listed were the standard AEMS categories, with similar events grouped (i.e., NG/OG/G/J tube-related) to make up the 20 specific AE categories. These were further collapsed into 8 categories, as defined in Table 1.

Statistical analysis

All data were screened for normality and skewed data points were presented as medians with Interquartile Range (IQR). Two cohorts of patients were compared: those with a PICU AE and those without. Pearson's Chi Square test was used to analyse categorical variables, and the non-parametric Mann Whitney U test was used to analyse continuous variables. A sub-analysis of hospital LOS, PICU LOS, post discharge destination and costs were assessed for survivors only. For all analyses, a p value of < 0.05 was considered statistically significant.

Multivariable logistic regression modeling was performed with PICU AE as the outcome variable in order to determine the association of patient's demographics, physiologic variables, neuroimaging abnormalities, intervention and injury severity on sustaining a PICU AE, while controlling for possible confounding effects of these variables on the relationships. Possible confounders were identified *a priori*. Variables found to be significant in univariate analyses at the 0.25 level were then entered in the model. These variables included age (years), weight (kg), MAIS of the head, thorax and face, bilateral fixed pupils, hypotension, subarachnoid hemorrhage, cerebral herniation, midline shift, cerebral contusion, fracture of the vault of the skull, and interventions including use of mannitol, hypertonic saline, ICP monitor, blood transfusion, desmopressin, vasopressin, a decompressive craniectomy and PICU LOS (days).

Variables were removed from the model at the 0.15 level in a backwards elimination strategy. Sensitivity analyses were performed using different modeling methods (i.e., forward stepwise logistic regression). The Hosmer-Lemeshow statistic was calculated to evaluate model fit and the C statistic was calculated to evaluate the predictive accuracy of our model. Multi-collinearity was assessed with a correlation coefficient analysis. In the final multivariate logistic regression model, each estimated coefficient provides an estimate of the log odds (OR) of PICU adverse events, adjusting for or controlling for the confounding effects of all other variables included in the model. All analyses were performed using IBM® SPSS® Statistics Version 26 (IBM Corporation, Armonk, NY).

Results

Adverse events

A total of 193 sTBI PICU patients were identified that met study inclusion, comprising 56% of the 342 severely injured (ISS≥12) PICU patients. AE were identified in 53% of sTBI patients (n=103/193), with 30% of all sTBI patients (n=57/193) experiencing more than one AE while cared for in the PICU, for a total of 238 individual AE (Fig. 1) with an AE rate of 1.23 per patient and 15.6 per 100 patient days. The most common AE was a decubitus ulcer at 15.1% (n=36/238), an incidence rate of 18.7% (n=36/193 patients) in this sTBI population. Fig. 2 depicts the broader categories of AE with treatment-related AE, including ICP monitoring, laboratory tests and medical device failures, as the most common category at 26% (n=63/238).

As depicted in Table 2, the majority of these events (54%) were rated 'no harm/injury' as Level 1 (assessment required; 13%) or

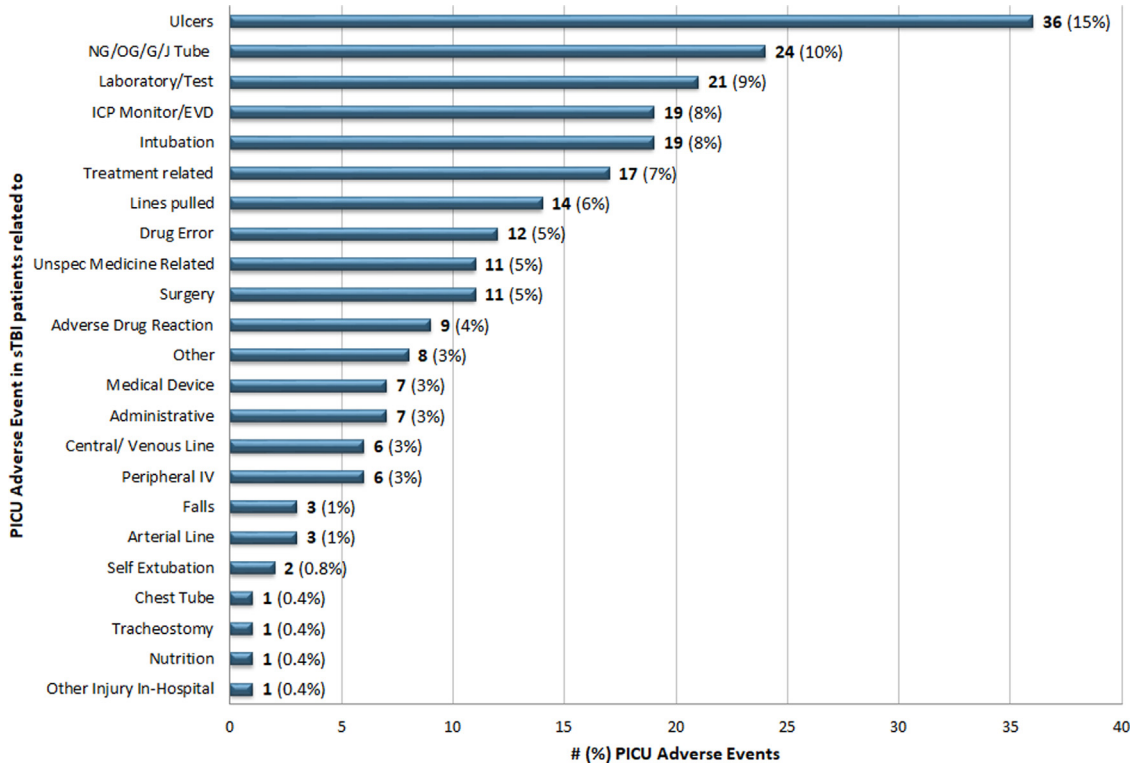

Fig. 1. Number of Pediatric Intensive Care Unit (PICU) adverse events (AE), n=238 PICU AE, in 193 pediatric severe traumatic brain injury patients, 2000-15. Legend: NG = Nasogastric; OG = Orogastric; G = Gastric; J = Jejunal; ICP = Intracranial pressure; EVD = External ventricular drain; IV = Intravenous.

Table 2
The Adverse Events Management System (AEMS) level of severity rating for adverse events (AE) in the Pediatric Intensive Care Unit for severe traumatic brain injury patients (n=103).

AEMS severity scale	Number of documented AE n=238
Level 1: No injury/harm with assessment required	30 (12.6%)
Level 2: No injury/harm with intervention/monitoring required	98 (41.2%)
Level 3: Minor to moderate injury/harm	86 (36.1%)
Level 4: Serious injury/harm/disability	3
1 each of Arterial line, Intubation and Surgery-related AE	(1.3%)
Level 5: Death	2
1 each of Adverse Drug Reaction and Treatment-related AE, both resulting in arrhythmia.	(0.83%)
Unable to Rate Severity	19
All 11 (100%) Unspecified Medicine-related; 5/17 (29%) Treatment-related; 3/8 (38%) Other AE severity could not be rated.	(8.0%)

Level 2 (intervention or monitoring required; 41%), and 36% were Level 3 (minor to moderate injury/harm) on the AEMS severity of harm scale. In two cases, the AE was associated with a patient death; both patients died of arrhythmia during either re-intubation for pulmonary atelectasis or inter-facility transport with inadequate monitoring. An additional three events caused serious injury and disability to the patients, including arterial line, intubation and surgery-related AE. There were 19 cases that were unable to have their severity rated due to insufficient information: all unspecified medicine-related AE, 5/17 (29%) treatment-related AE and 3/8 (38%) AE classified as "Other". In total, 52% (n=54) of the AE cohort experienced 2 or more events, with certain patients experiencing up to 8 different categories of AE during their PICU admission.

Cohort characteristics

A comparison of patient and injury demographics is presented in Table 3 for the 103 (53%) pediatric sTBI patients who sustained a PICU AE and for the cohort of patients (n=90; 47%) that did not. The two cohorts were similar with respect to patient demographics, etiology, injury severity, and clinical admission criteria. There were no statistically significant differences except the PICU AE cohort had slightly more severe facial injuries. The PICU AE cohort had statistically significantly higher use of ICP interventions, except for blood transfusions (Table 3). Any variable with a statistical difference between the two groups was entered into the logistic regression model to control for the effects of these potentially confounding factors on sustaining a PICU AE.

Patient outcomes

A comparison of outcomes found that the PICU AE cohort had significantly fewer ventilator free days (median 19 vs. 24 days in the cohort without PICU AE; p=0.015) (Table 3). For survivors, the PICU AE cohort had approximately triple the LOS, both in PICU and overall hospital stay [11 vs. 3.5 days (p<0.001) and 31 vs. 11 days (p<0.001), respectively]. In the PICU AE cohort, there was a

Table 3
Patient admission demographics, injuries and clinical criteria; interventions; and outcomes by presence or absence of a Pediatric Intensive Care Unit (PICU) adverse event (AE) for pediatric severe traumatic brain injury patients.

Variable[a]	PICU AE *n*=103 (53.4%)	No PICU AE *n*=90 (46.6%)	*p* value
Age (years)	14.0 (10)	11.0 (12)	0.370
Weight (kg)	55.0 (48.0)	40.5 (48.5)	0.175
Male (%)	69 (67.0%)	62 (68.9%)	0.778
Etiology			0.786
MVC	75 (72.8%)	62 (68.9%)	
Fall	9 (8.7%)	8 (8.9%)	
Assault/Abuse	10 (9.7%)	13 (14.4%)	
Other	9 (8.7%)	7 (7.8%)	
Injury Severity Score	33 (12)	31 (12)	0.606
Injury Profile			
MAIS Head	5 (0)	5 (0)	0.088
MAIS Face	2 (1)	1 (1)	**0.015**
MAIS Neck	3 (2)	2 (0)	1.000
MAIS Thorax	3 (1)	3 (1)	0.082
MAIS Abdomen	2 (1)	2 (0)	0.282
MAIS Spine	2 (0)	2 (1)	0.675
MAIS Upper Extremity	2 (0)	2 (1)	0.495
MAIS Lower Extremity	2 (1)	3 (1)	0.697
MAIS External	1 (0)	1 (0)	0.367
Pre-sedation GCS	5 (4)	4 (4)	0.971
Pre-sedation GCS Motor Component	2 (3)	2 (3)	0.595
Fixed Pupil(s)	66 (61.1%)	49 (54.4%)	0.174
Hypotension	20 (19.4%)	25 (27.8%)	0.171
Intervention	**PICU AE**	**No PICU AE**	**p value**
Intracranial Pressure Monitor	59 (57.3%)	18 (20.0%)	**<0.001**
3% Saline	52 (50.5%)	19 (21.1%)	**<0.001**
Mannitol	62 (60.2%)	30 (33.3%)	**<0.001**
Decompressive Craniectomy	24 (23.3%)	8 (8.9%)	**0.007**
Therapeutic Hypothermia	13 (12.6%)	2 (2.2%)	**0.007**
Thiopental infusion	18 (17.5%)	6 (6.7%)	**0.023**
Blood Transfusion	53 (51.5%)	37 (41.1%)	0.151
Outcome[a]	**PICU AE**	**No PICU AE**	**p value**
Mortality	23 (22.3%)	32 (35.6%)	**0.042**
Ventilator Free Days median (IQR)	19 (18)	24 (27)	**0.015**
Survivors	80 (77.7%)	58 (64.4%)	**0.042**
Hospital LOS (days)	31 (31)	11 (16)	**<0.001**
PICU LOS (days)	11 (9)	3.5 (4)	**<0.001**
Discharge Destination for Survivors[b]			**0.049**
Home with support services	43 (53.8%)	43 (74.1%)	
Another Acute Care Facility	9 (11.3%)	3 (5.2%)	
Rehabilitation Facility	28 (35.0%)	12 (20.7%)	

Legend: MVC = Motor Vehicle Collision; MAIS = Maximum Abbreviated Injury Scale; GCS = Glasgow Coma Scale; IQR = Interquartile range; LOS = Length of stay; Bolded **p** values are statistically significant.

[a] Continuous variables are presented as median (IQR), and categorical variables as n (%).

[b] Statistically significant = more survivors were discharged to a rehabilitation facility vs. home with support services for patients with a PICU adverse event (p=0.035); the other pairwise comparisons between discharge destination were not statistically significant.

higher proportion of patients who were discharged to a rehabilitation facility (35% vs. 21%; p=0.035), signifying a higher level of care required on discharge. PICU AE patients were found to have higher median (Q1 – Q3) total inpatient costs of $121,234 ($67,596 – $232,524) compared to $53,341 ($17,642 - $113,568) for the PICU non-AE cohort (p=0.031). The median inpatient costs were higher for surviving PICU AE patients at $155,854 ($72,866 - $308,644) vs. $63,410 ($32,255 - $ 124,354) for patients without an AE, p=0.088.

Multivariate logistic regression modeling was conducted to examine the association between patient and injury variables and sustaining a PICU AE. Sensitivity analysis revealed the two identical models with both forward stepwise and backwards elimination, with no multi-collinearity of the variables evident in the model. The strength of association for all variables was the same in both models. For the model performance evaluation, a test of the full model against a constant only model was statistically significant, indicating that the predictor variables reliably distinguished between patients with or without PICU AE (Omnibus Test of model coefficients, $X_4 2$=28.30, p<0.001). There was no evidence of a lack of fit (Hosmer and Lemeshow $X_8 2$=4.72, p=0.788), with an overall classification success at 79% for the final model.

The C statistic was 0.887 (0.799-0.975); p<0.001), indicating a very good predictive accuracy of our model. Interpretation of the resulting model (Table 4) found that having bilateral fixed pupils increased the odds of sustaining a PICU AE by 5.2 times (p=0.043) and a 1-point increase in MAIS severity of injury in the face increased the odds of sustaining an AE in the PICU by 3.6 times (p=0.029), while controlling for the effect of the duration of stay

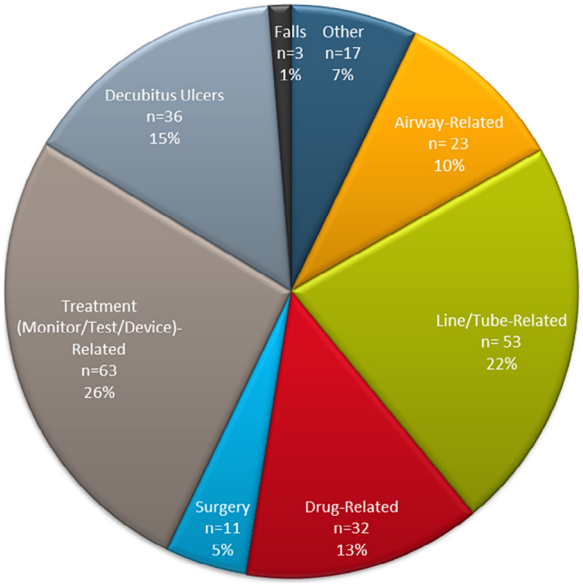

Fig. 2. Percentages of broad categories of Pediatric Intensive Care Unit (PICU) adverse events (AE), n=238 PICU AE, in 193 pediatric severe traumatic brain injury patients, 2000-15.

Table 4
Multivariate logistic regression model with Pediatric Intensive Care Unit adverse event as the outcome variable.

Variable	ß	SE	OR	95% CI	p value
Bilateral Fixed Pupils	1.64	0.81	5.15	1.06-25.11	**0.043**
MAIS Face	1.29	0.59	3.63	1.14-11.53	**0.029**
PICU LOS	0.22	0.07	1.24	1.07-1.43	**0.004**
MAIS Thorax	0.64	0.44	1.89	0.79-4.51	0.151

Constant ß=-6.28; SE=1.98
Legend: ß = Beta coefficients; SE = Standard error; OR = Odds ratio; CI = Confidence interval; LOS = Length of Stay; MAIS = Maximum abbreviated injury scale; PICU = Pediatric Intensive Care Unit.

in the PICU. For each day in the PICU, the odds of sustaining a PICU AE was increased by 1.2 times (p=0.004), after adjusting for the other variables in the model to control for any confounding.

Discussion

Pediatric trauma centres have a responsibility to keep their patients safe by delivering a focused, standardized approach to improving the quality, safety and consistency of care, while optimizing the patient experience and outcomes. Performance improvement and patient safety (PIPS) reviews at trauma centres rely on the trauma registry. These detailed clinical, demographic and outcome data collected at all trauma centres are pivotal to this important PIPS work [1]. Absent from most registries, yet vital to PIPS and EBP, is the identification and severity scoring of AE, potentially harmful events resulting from healthcare management [4]. It is only through analyzing these AE that lessons can be learned on how to mitigate contributing factions, prevent future errors and ultimately make patients safer [24]. Incident reporting systems have been implemented in organizations to track AE and document recommendations for actions [24].

In this PIPS project, our trauma registry was utilized to identify a vulnerable cohort of pediatric sTBI PICU patients, and then queried our institutional AEMS to identify any AE occurring during their PICU stay. Utilizing an administrative database, with data already collected and maintained, is an efficient, inexpensive method to use readily accessible data that does not interfere with the delivery of care, without the need to implement an additional tool, such as a trigger tool, which would require time and resources to train healthcare providers to collect additional data [34]. Utilizing an AE reporting system can only facilitate learning and improve patient safety if good quality data are collected [24]. Ways to improve AE reporting are to support a culture of safety at your trauma centre, engage staff and physicians, and importantly, couple the incident reporting with visible, sustainable actions, with true safety accountability and linkage of AE reporting to the electronic record, for a more automated system [24].

In our PICU, 53% of patients with sTBI experienced an AE and of these patients, 52% had more than one AE. After identifying the 238 AE in our 193 sTBI patients, descriptive and regression analysis was undertaken to define the burden of AE by AE classifications, occurrence, and severity of harm to allow for the identification of safety issues and determination of effective mitigation strategies.

Of the 238 AE, decubitus ulcers (15%) and feeding tube issues (10%) were the most common. Added together, catheter-related complications accounted for 13% of AE which is consistent with other PICU studies [9,22]. Most of the AE had low severity of harm with 54% rated at a Level 1 or 2 and only 1% was rated as serious harm, with 2 deaths. Both deaths were due to low cardiac output arrhythmias, and occurred at the time of either intubation or inadequate monitoring during inter-facility transportation. Our findings are in contrast to other PICU studies which found higher proportions of serious events at 3-10% [9,18–20].

Mortality rate was higher in patients not exposed to AE; however, as more than half of sTBI deaths occurred within the first few days of admission [26], they would be less likely to suffer AE. AE in sTBI survivors were associated with fewer ventilator-free days, greater LOS and a more dependent disposition on discharge. As another PICU study previously concluded [35], the significantly longer LOS may be a negative consequence of the AE, or alternatively, this longer exposure time may have contributed to increased probability for sustaining an AE. By including PICU LOS in our logistic regression analysis as a factor associated with the development of the outcome PICU AE, it was demonstrated that for each day in the PICU, the odds of sustaining an AE significantly increased by 1.24 (1.07-1.43; p=0.004), after adjusting for the effect of the other variables in the model including bilateral fixed pupils, face and thorax injuries. It allowed for an examination of the associations between these variables and the probability of sustaining a PICU AE, while controlling for any confounding effects the duration of stay in the PICU had on this outcome [39].

Given the longer LOS, it was expected that our PICU AE cohort would have significantly increased costs, with median inpatient costs more than double non-AE PICU patients ($121,234 vs. $53,341; p=0.031). This is the first study, to our knowledge, to report inpatient costs in this high acuity pediatric sTBI population. While no previous studies have reported inpatient costs in this specific cohort of PICU sTBI patients, what has been recently reported in other subpopulations of pediatric trauma has been much lower including median costs of $10,178 for high-grade abdominal injuries for pediatric patients treated mainly at non-children's hospitals [36]; median total cost of $27,571 for surgical patients treated at a Level 1 pediatric trauma centre [37]; and in abusive head trauma patients less than 5 years of age, an average inpatient cost (95% CI) of $31,901 ($29,266, $34,536) [38]. The complex care of our high injury severity cohort with multiple interventions and long LOS in the PICU, particularly with an AE, accounts for these increased, high costs of the inpatient visits in our study.

To further examine which factors put sTBI patients at risk for AE, logistic regression modeling was used to determine associations between specific variables and the probability of the occurrence of an PICU AE, after adjusting for a set of covariates to control for any possible confounding [39]. Given this was a retrospective study, logistic regression was the best method for determin-

ing the effect of multiple factors on sustaining PICU AE. The goal of this modeling was to statistically adjust the estimated effects of each variable for differences in the distributions of and associations among the other independent variables [40]. Based on this statistical technique, our results demonstrated that it is primarily the severity of the TBI, as represented by the presence of bilateral fixed pupils, along with duration of stay in the PICU and the associated injury profile that significantly increased the odds of sustaining a PICU AE. It is the effect of multiple injuries, specifically thoracic and facial injuries, not solely the sTBI that made patients more susceptible to AE. Thoracic injuries may contribute to increased AE rates by increased ventilation days secondary to pulmonary contusion. Facial trauma could potentially lead to difficulties with airway management and securement of endotracheal and gastric tubes. Indeed, 18% of documented AE were associated with intubation and gastric tubes. Increased awareness and training to educate PICU staff on the influence of polytrauma on these patients' care and outcome, together with better care strategies to lower the LOS in the PICU, may reduce the risk of AE in sTBI patients with concomitant facial and thoracic injuries and long PICU stays.

Consistent with other pediatric research [41], decubitus ulcers were found to be the most common AE in sTBI patients. Our incidence rate of 18.1% was slightly higher than the highest incidence (17.5%) of a 9-PICU study [42], but well below an older multisite study reporting a 27% PICU pressure injury incidence [43]. Lower rates in recent years are likely the result of the implementation of evidence-based prevention strategies to lower pressure injury incidence in the PICU [42,44,45]. Following our review, a pressure injury prevalence study and enhanced prevention program (including the development of a 'Solutions for Patient Safety' bundle for pressure injury) was implemented in our institution, resulting in decreased decubitus ulcers in the PICU for the past two years.

Five percent of our patients had a medication error, for which there is substantial evidence for an associated increase in mortality, LOS and hospital costs; with corresponding PI strategies to reduce the incidence of PICU medication errors [46]. In addition, *Protecting Canadians from Unsafe Drugs Act*, or Vanessa's Law, has recently introduced regulations that require mandatory reporting of serious adverse drug reactions and medical device incidents by hospitals to Health Canada, effective December 16th, 2019 which aims to increase compliance with reporting and attempts to prevent these AE by Canadian hospitals [47].

This study had several limitations. First, this is a retrospective, single center study. Despite this, we believe our results are relevant to other PICUs at Level 1 trauma centres, as we used strict sTBI inclusion criteria from trauma registry data, as well as a formalized AEMS that uses standardized coding and severity guidelines for the collection and management of AE data. Second, there is no gold standard for identifying AE, and therefore we may have underestimated the true incidence of AE in our sTBI population, but the safety culture at our institution supports AE reporting. Finally, we have demonstrated statistical associations, but cannot conclude cause-effect due to the limitations of our retrospective study design.

Conclusions

Merging databases is an effective practice to identify AE and patient safety risks in trauma populations. Utilizing this method, an AE rate of 1.23 events per patient was found with 53% of sTBI patients experiencing an AE during their PICU admission. TBI severity was the most important factor to increase the odds of an AE. AE represent PI events, opportunities to optimize the care and treatment protocols, decrease costs, as well as improve outcomes, to ultimately improve patient safety of this vulnerable population.

Author contribution

TCS undertook the data quality control, statistical analysis and interpretation of the data reports, along with performing literature searches, as well as drafting and revising the manuscript. KL undertook data collection for all adverse events and their classification, trauma injury data collection, literature search, and participated with the initial drafting of the manuscript. IA and BM participated in collection of trauma patient data, data interpretation and critical review of the manuscript. DD was the supervising author, developing study concept and design, interpreting the data results, as well as critical review and editing of the manuscript.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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