Original Article

Characterizing the burden of complications in traumatic brain injury: a retrospective study

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Background: Previous research has demonstrated that complications are associated with poorer outcomes after traumatic brain injury (TBI). Here we characterize the burden of 12 complications on discharge disposition and hospital length of stay (LOS) for patients with isolated TBI.

Methods: We identified all TBI admissions from the 2012–2016 National Trauma Data Bank and utilized multivariate regression analyses to assess the impact of each complication on discharge disposition (home *vs.* care facility/rehab) and hospital LOS. Secondary subtype analysis investigated severe, moderate, mild, pediatric, and adult TBI groups separately. We quantified burden on discharge disposition as the risk difference upon exposure to a complication and LOS burden as a ratio of extra-to-total hospital days. Complications included acute kidney injury (AKI), acute respiratory distress syndrome (ARDS), cardiac arrest, deep vein thrombosis (DVT), myocardial infarction (MI), pneumonia, pulmonary embolism, sepsis, stroke, urinary tract infection (UTI), organ surgical site infection (SSI), and superficial SSI. Analyses adjusted for age, gender, race, GCS score, ISS score, payment method, comorbidities, unplanned intubation, hospital teaching status, region and TBI volume. Statistical significance was assessed at $P<0.05$.

Results: There were 103,668 isolated TBI admissions during the study period. Following multivariate adjustment, pneumonia was associated with the greatest risk of worse discharge disposition [odds ratio (OR) =4.605, 95% CI, 3.858, 5.496, $P<0.001$]. UTI (OR =3.923, 3.352, 4.591, $P<0.001$) and DVT (OR =3.117, 2.411, 4.029, $P<0.001$) also significantly impacted the likelihood of returning home. Among patients with isolated TBI, these complications were associated with the highest burden on short-term outcomes, in terms of population attributable risk (PNA =0.052, UTI =0.037, DVT =0.011). In addition, pneumonia (+10.8 days), UTIs (+7.7 days), DVT (+7.8 days), and SSIs (organ space SSI: +18.9 days; superficial SSI: +18.4 days) dramatically increased LOS across groups ($P<0.001$ for all LOS associations). Similar results were seen across all TBI subtypes.

Conclusions: Across TBI subtypes, pneumonia, UTI, and DVT present the greatest complication burden, highlighting areas of focus for TBI care. Wide inter-institutional variability in complication rates also suggests places for optimization of care processes to influence TBI outcomes.

Keywords: Traumatic brain injury (TBI); TBI outcomes; TBI complications; neurotrauma; National Trauma Data Bank

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Introduction

Traumatic brain injury (TBI) is one of the leading causes of hospitalization, death, or disability worldwide, with between 64–74 million global incidences of TBI annually (1,2). Previously, pediatric TBI alone has contributed more than $1 billion to hospital charges each year (3,4). As the incidence of TBI across all age groups continues to rise, the significant public health concern and financial burden of this "silent epidemic" necessitates the study of factors that may impact outcomes (1,5). Previous research has suggested that complications can increase in-hospital mortality, length of stay, and costs for trauma patients (6-10). Additional research has also attempted to use complication rates as an indicator of trauma care performance (11). However, the influence of complications on TBI outcomes specifically, remains unclear.

Prior research has focused on characterizing the epidemiology of TBI and various factors impacting mortality and injury severity, including associated injuries, blood loss, and mechanism of injury (12-15). To our knowledge, no group has focused on characterizing the burden of complications on TBI outcomes. Therefore, the primary goal of our study was to analyze the burden of twelve distinct complications on discharge disposition and total hospital length of stay (LOS) for isolated TBI patients. We hypothesized that among survivors, the occurrence of a complication would increase the duration of hospital stay and the percentage of TBI patients who require care post-discharge. We focused primarily on patients with isolated TBI to minimize the likelihood that complications were associated with systemic trauma, rather than with the post-injury management of TBI. Nonetheless, we also examined whether trends across isolated and all TBI populations were similar. We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/jeccm-21-53).

Methods

Study population

This study was conducted using data from the 2012–2016 National Trauma Data Bank (NTDB). The NTDB is managed and compiled by the American College of Surgeons (ACS) Committee on Trauma (16). Although more recent years of the NTDB are available, these files do not contain important clinical and facility-related confounding variables, precluding their use in this investigation. The study population consisted of traumatic brain injury patients between ages 0 and 89. TBI patients were identified using the following International Classification of Diseases, 9th Revision Clinical Modification (ICD-9-CM) and International Classification of Diseases, 10th Revision Clinical Modification (ICD-10-CM) codes for intracranial injury: 850.0–854.1 (ICD-9-CM) and codes in the S06 category (ICD-10-CM). Isolated TBI was defined as having only ICD-9-CM or ICD-10-CM codes corresponding with TBI. Patients with missing age information were excluded. To identify and remove patients with a low chance of survival, we followed a similar method as Watson *et al.* (17), eliminating patients who exhibited no signs of life (admission systolic blood pressure =0 and pulse rate =0) and no neurological activity (GCS =3) upon admission to the ED (*Figure 1*).

Demographic and clinical data including gender, age, race, primary payment method, Injury Severity Score derived from hospital-submitted Abbreviated Injury Scores (ISSAIS score), total Glasgow Coma Scale (GCS) score, comorbidities present, injury type (blunt *vs.* penetrating *vs.* other/unspecified), mortality, total length of stay (LOS) in the hospital, the occurrence of unplanned intubation, and hospital discharge disposition were isolated for each patient. Only comorbidities present in at least 1% of the patient population were investigated, in order to reduce the risk of model overfitting. These included hypertension requiring medication (33.3%), bleeding disorder (10.0%), congestive heart failure (4.2%), history of stroke or cerebrovascular accident (4.0%), diabetes (14.7%), respiratory disease (7.5%), and history of myocardial infarction (1.8%). Patients with missing GCS or hospital LOS information were removed. To determine the impact of specific complications on TBI outcomes, we identified the occurrence of the following complications based on the native NTDB complications variable: organ space surgical site infection (SSI), superficial SSI, acute respiratory distress syndrome (ARDS), deep vein thrombosis (DVT), myocardial infarction (MI), pneumonia (PNA), pulmonary embolism, stroke or cerebrovascular accident (CVA), cardiac arrest, urinary tract infection (UTI), acute kidney injury (AKI), and sepsis. Only patients who developed a condition after initial presentation were counted as having the complication. For each patient, facility data including hospital teaching status (community or university), region of the hospital, and TBI volume were also obtained from the NTDB.

To investigate the impact of complications on discharge

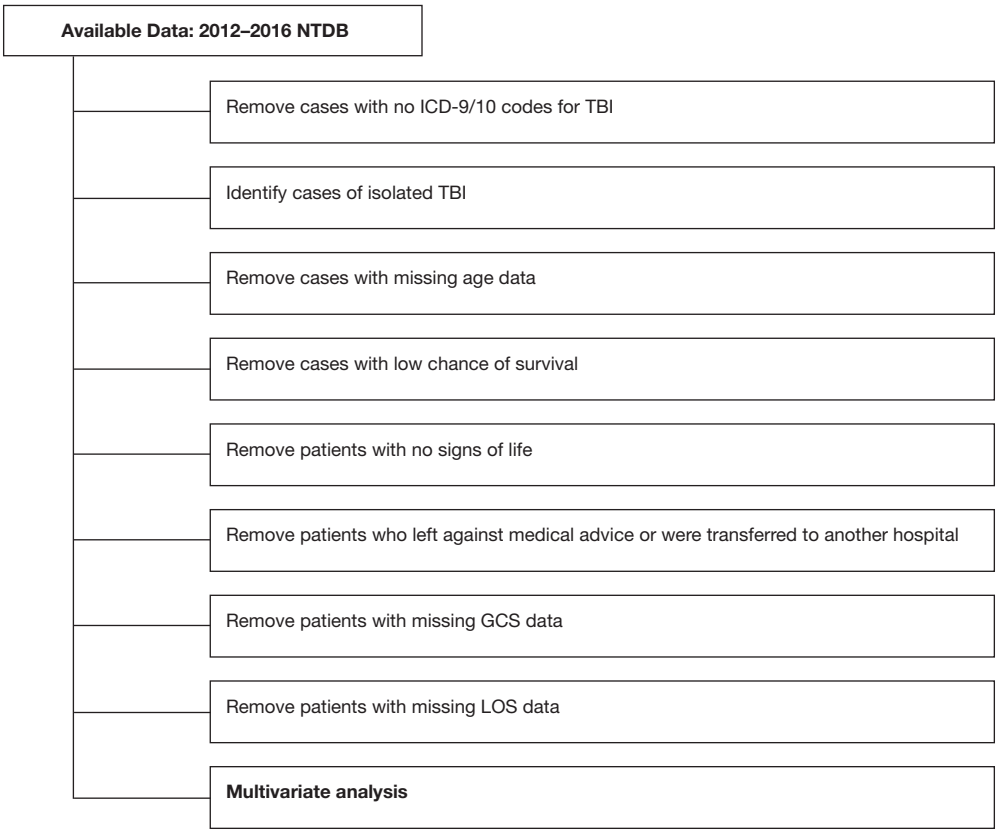

Figure 1 Study population exclusion criteria. Data reduction steps using data from the 2012–2016 National Trauma Data Bank. Isolated TBI population subset: n=103,668; Total TBI population: n=968,909.

disposition, the native hospital discharge disposition outcomes within the NTDB were grouped as home (discharged home without home services, discharged home under care of organized home service, routine discharge), care facilities (transfer to a long-term care facility, transfer to an intermediate care facility, transfer to a skilled nursing facility, transferred to rehab), or terminal (death or hospice). Patients who left against medical advice, who were transferred to a different hospital for care, or whose outcomes were unknown were excluded. We quantified burden on discharge disposition as the risk difference upon exposure to a complication using the equation for population attributable risk (PAR) for a variable with a single level of exposure (complication *vs.* no complication). This metric takes into account both the proportion (p) of patients with a complication and relative risk (RR) of that complication for determining a poorer outcome Eq. [1].

$$PAR = \frac{p(RR-1)}{1+p(RR-1)} \quad [1]$$

LOS burden was calculated as a ratio of number of extra hospital days attributable to a complication divided by the mean LOS.

Statistical analysis

To determine the impact of each complication on isolated TBI outcomes, we performed multivariate regression analysis using the total study population. Analyses controlled for age, sex, race, primary method of payment, region of hospital, hospital teaching status, hospital TBI volume, comorbidities, GCS score, ISS score, and unplanned intubation. The primary outcomes investigated included total hospital LOS and whether the patient was discharged home or to a care facility. Statistical significance was assessed at $P<0.05$. All analyses were performed using Stata Version 16.1 (StataCorp, College Station, TX, USA).

We also conducted a secondary set of analyses to investigate whether the trends we observed in the isolated TBI population persisted in TBI with polytrauma and

across TBI subtypes. Two duplicate sets of analyses were performed using the following TBI populations: isolated TBI and all TBI (including isolated TBI and TBI with polytrauma). For both groups, we separately divided the study population into subcategories based on GCS (severe, moderate, mild) or age (pediatric *vs.* adult) for analysis. Following earlier research and guidelines (18), patients in the severe, moderate and mild TBI groups were defined as having a total GCS score of 3–8, 9–12 and 13–15, respectively, upon admission to the hospital. Age categories were defined as pediatric (0–18 years) or adult (18–89 years). We controlled for the same variables as in the primary analysis.

Ethics

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was exempt from Institutional Board Review due to the publicly available and de-identified nature of the data in the NTDB. The National Trauma Data Bank is available to researchers in all partner institutions that contribute data to the dataset. Ethical review and approval were not required for this study on human participants in accordance with the local legislation and institutional requirements.

Results

Study population

After applying the exclusion criteria, there were 103,668 isolated TBI admissions to 857 distinct institutions in the 2012–2016 NTDB. 83,735 (80.8%) patients were adults, with a mean age of 49.5 years old [standard deviation (SD) =27.1, range, 1–89]. 19,933 (19.2%) patients constituted the pediatric population. The majority of the total cases were white (72.2%) and male (59.3%), and injuries were most commonly blunt (73.9%). Patients were also more likely to be treated at a university hospital (45.8%) than a community (40.0%) or non-teaching institution (14.2%; *Table 1*). Within TBI subtypes, there were 9,590 severe TBI patients (mean severe TBI GCS =4.2±1.8), 4,594 moderate TBI patients (mean moderate TBI GCS =10.7±1.1), and 89,484 mild TBI patients (mean mild TBI GCS =14.8±0.5; *Table 1*). The secondary analysis dataset, which included all types of TBI (non-isolated and isolated) contained 968,909 TBI patients (Table S1).

Prevalence of complications

Pneumonia was one of the most prevalent complications in the isolated TBI population (1.5%), followed by UTI (1.3%; *Table 1*). Similar trends were also observed in the expanded dataset that included all TBI patients (PNA =3.4%, UTI =1.8%; Table S1) and across all TBI subtypes (Table S2). Over the study period, the yearly incidence of pneumonia decreased from 1.6% to 1.1%. Analysis of prevalence by TBI subtype revealed that severe TBI patients, specifically, experienced higher rates of ARDS (Isolated Severe TBI =2.3%, All Severe TBI =4.1%) and cardiac arrest (Isolated Severe TBI =1.8%, All Severe TBI =4.0%; Table S2) compared to patients in the less severe TBI groups (Table S2). Interestingly, investigation of prevalence by facility demonstrated wide inter-hospital variability in complication rates, particularly for pneumonia (Range: Isolated TBI =0–28.5%; All TBI =0–50.0%), UTI (Range: Isolated TBI =0–25.0%; All TBI =0–19.4%) and MI (Range: Isolated TBI =0–33.3%; All TBI =0–12.5%; Figure S1).

Discharge disposition

Unadjusted comparison of changes in discharge disposition after the occurrence of each complication demonstrated dramatic shifts in the number of patients discharged home versus a care facility for isolated TBI patients (*Figure 2A*). Presence of a complication was also associated with a greater shift towards poor outcomes when present in the all TBI population compared to the isolated TBI population (*Figure 2A,B*). Subsequent controlled multivariate analysis in the isolated TBI dataset showed that developing pneumonia had a significant negative impact on discharge outcome [odds ratio (OR) =4.605, 95% CI, 3.858–5.496, P<0.001] and presented the greatest burden on discharge disposition (PAR =0.052; *Table 2*, *Figure 3*). DVT (OR =3.117, 2.411–4.029, P<0.001), UTI (OR =3.923, 3.352–4.591, P<0.001), and stroke (OR =6.288, 3.937–10.043) also decreased the likelihood that patients returned home, with burdens of 0.011, 0.037 and 0.015, respectively (*Table 2*, *Figure 3*). Sensitivity analysis of the impact of complications on discharge disposition in the population expanded to include non-isolated TBI supported these trends, with similar values for burden on discharge disposition for these complications (PNA =0.070, UTI =0.035, DVT =0.020, Stroke =0.011; Table S3, *Figure 3*).

Table 1 Characteristics of isolated TBI admissions in the 2012–2016 NTDB

Variable	Number of admissions (%)
Age, in years	
Pediatric	19,933 (19.2)
Adult	83,735 (80.8)
Mean ± standard deviation	49.5±27.1
Sex	
Male	61,507 (59.3)
Female	42,133 (40.6)
Other/unknown	28 (<0.1)
Race	
White	74,685 (72.0)
African American	13,656 (13.2)
Asian	2,266 (2.2)
American Indian	807 (0.8)
Native Hawaiian/Pacific Islander	225 (0.2)
Other/unknown	12,029 (11.6)
Hospital teaching status	
Community	41,465 (40.0)
University	47,486 (45.8)
Non-teaching	14,717 (14.2)
Hospital region	
Northeast	16,390 (15.8)
Midwest	32,380 (31.2)
South	34,755 (33.5)
West	20,143 (19.4)
Injury type	
Blunt	76,616 (73.9)
Penetrating	8 (<0.1)
Other	27,044 (26.1)
GCS admission score	
Severe	9,590 (9.3)
Moderate	4,594 (4.4)
Mild	89,484 (86.3)
Mean ± standard deviation	13.6±3.2
Complications	
Acute kidney injury	386 (0.4)
Acute respiratory distress syndrome	473 (0.5)
Cardiac arrest	374 (0.4)
Deep vein thrombosis	550 (0.5)
Myocardial infarction	234 (0.2)
Organ space SSI	22 (<0.1)
Pneumonia[+]	1,536 (1.5)
Pulmonary embolism	112 (0.1)
Sepsis	236 (0.2)
Stroke	305 (0.3)
Superficial SSI	45 (<0.1)
Urinary tract infection[+]	1,312 (1.3)
Comorbidities present	
Hypertension requiring medication	34,498 (33.3)
Bleeding disorder	10,324 (10.0)
Congestive heart failure	4,394 (4.2)
Stroke/CVA	4,112 (4.0)
Diabetes	15,263 (14.7)
Respiratory disease	7,737 (7.5)
Myocardial infarction	1,829 (1.8)
ISS (mean ± standard deviation)	9.2±7.6

Percentages reported in parentheses may not add up to 100% due to rounding or missing data. [+]Complication information for pneumonia and urinary tract infection were not present in the 2016 NTDB. Prevalence and analysis based on 2012–2015 data only.

Hospital LOS

Multivariate analysis of the burden of each complication on total hospital LOS also demonstrated highly significant relationships for isolated TBI patients. In particular, the occurrence of an organ space SSI (+18.9 days, P<0.001) or superficial SSI (+18.4 days, P<0.001; *Figure 4*) was correlated with a dramatic increase in the duration of in-hospital treatment. Additionally, SSIs were associated with the greatest LOS burden (Organ space SSI: 4.53,

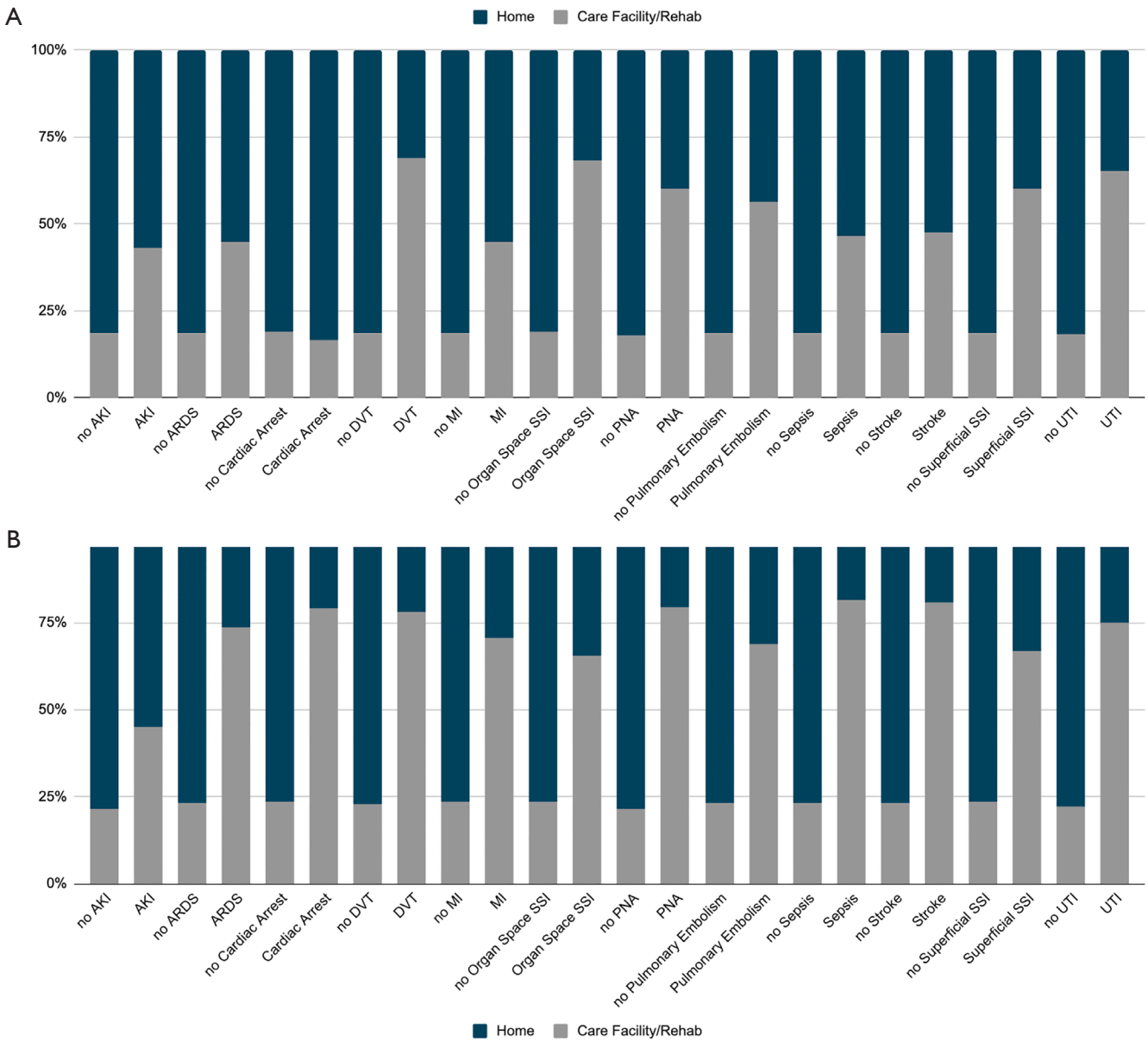

Figure 2 Impact of each complication on the proportion of patients discharged home *vs.* care facility/rehabilitation center. Unadjusted secondary comparison of discharge disposition (home *vs.* care facility or rehab) based on the presence of each complication. (A) Study population = Isolated TBI. (B) Study population = All TBI (isolated and non-isolated). AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; DVT, deep vein thrombosis; MI, myocardial infarction; SSI, surgical site infection; PNA, pneumonia; UTI, urinary tract infection.

Superficial SSI: 4.42; *Table 2*). Developing pneumonia (+10.8 days), DVT (+7.8 days), and UTI (+7.7 days, P<0.001 for all complications; *Figure 4*) also resulted in significant extensions in LOS, with corresponding high values of burden (*Table 2*). Cardiac arrest decreased time spent in the hospital by 1.6 days (*Figure 4*), likely due to increased in-hospital mortality associated with this event. Secondary subtype analyses further supported these findings, demonstrating the same trends across TBI subtypes (Tables S4,S5, Figure S2).

Table 2 Burden of each complication on isolated TBI care based on adjusted multivariate analysis

Complication	Burden discharge disposition	Odds ratio, [95% CI]	Discharge disposition, P value	Burden LOS
AKI	0.004	2.037, [1.473, 2817]	<0.001	0.82
ARDS	0.009	2.946, [2.057, 4.221]	<0.001	0.71
Cardiac arrest	0.006	2.766, [1.491, 5.170]	0.001	–0.39
DVT	0.011	3.117, [2.411, 4.029]	<0.001	1.87
MI	0.002	1.895, [1.273, 2.821]	0.001	0.49
Organ space SSI	<0.001	2.932, [0.710, 12.108]	0.137	4.53
Pneumonia	0.052	4.605, [3.858, 5.496]	<0.001	2.59
Pulmonary embolism	0.001	2.149, [1.199, 3.851]	0.010	1.68
Sepsis	0.003	2.110, [1.250, 3.563]	0.005	1.28
Stroke	0.015	6.288, [3.937, 10.043]	<0.001	0.91
Superficial SSI	<0.001	1.975, [0.848, 4.596]	0.114	4.42
UTI	0.037	3.923, [3.352, 4.591]	<0.001	1.83

All results are reported for an interval of +1 patients. 95% confidence intervals are listed. Odds ratio >1 indicates more likely to be discharged to a care or rehab facility than home. Discharge Disposition Burden represents the proportion of patients with a worse discharge disposition attributable to the complication. LOS burden represents the proportional change in LOS attributable to the complication in days.

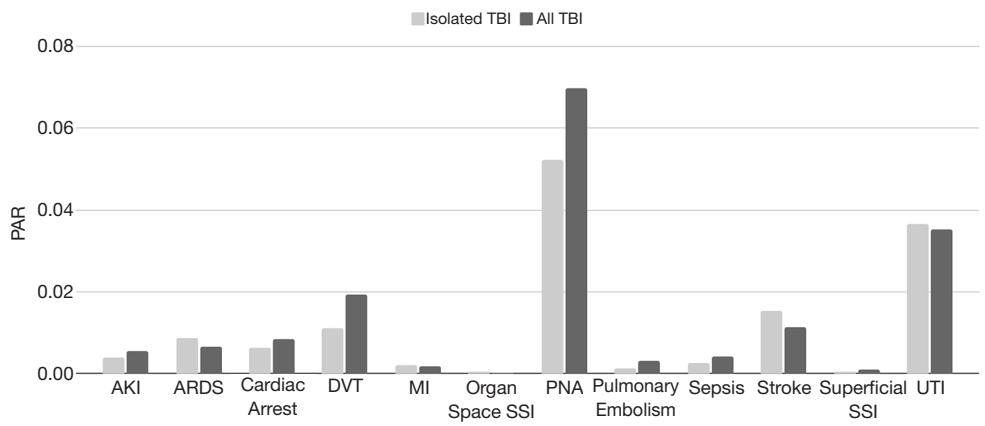

Figure 3 Burden associated with each complication by TBI type. Adjusted PAR associated with the occurrence of a complication in the isolated TBI and all-TBI population. Isolated TBI, light gray bars. All TBI = dark gray bars. AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; DVT, deep vein thrombosis; MI, myocardial infarction; SSI, surgical site infection; PNA, pneumonia; UTI, urinary tract infection.

Discussion

In this study, we found that pneumonia, UTI, and DVT presented the greatest burden on isolated TBI outcomes (*Table 2*, *Figure 3*, Table S5, Figure S2A). SSIs also contributed significantly to total LOS (*Figure 4*, *Table 2*). Previous trauma research has established that complications can negatively impact patient outcomes (9,10). TBI-focused studies have also found that associated injuries and mechanism of injury can influence hospital course and mortality (12-15). Due to the paucity of information on

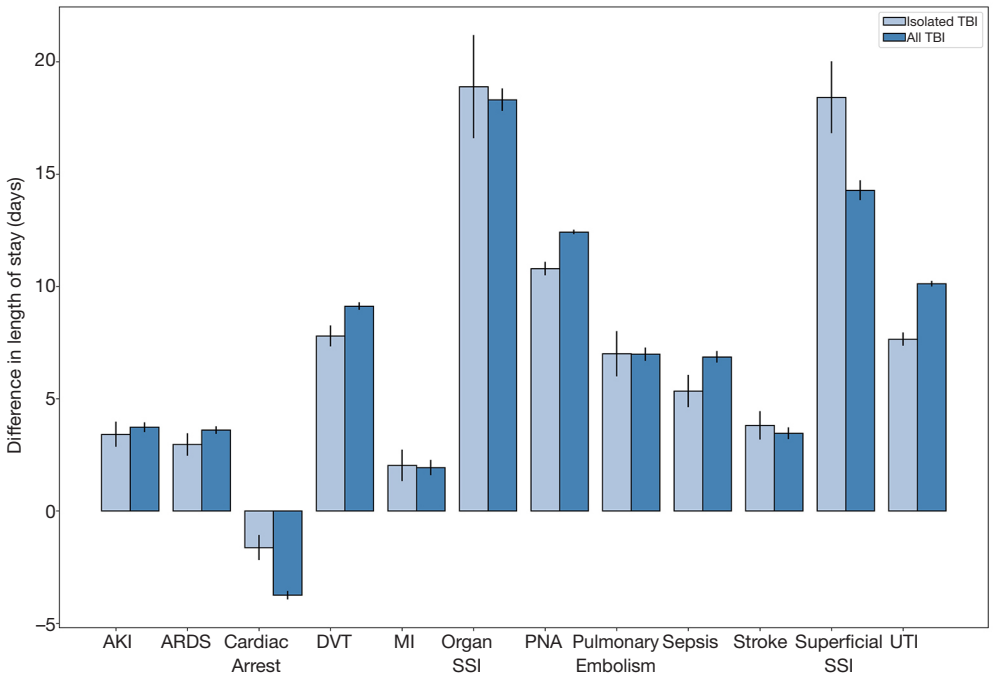

Figure 4 Adjusted difference in LOS attributable to each complication. All results are reported for an interval of +1 patients after multivariate analysis controlling for demographic, clinical, and facility variables. Error bars show 95% confidence intervals. Differences in LOS for isolated TBI patients (light blue). Differences in LOS including non-isolated TBI (dark blue). AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; DVT, deep vein thrombosis; MI, myocardial infarction; SSI, surgical site infection; PNA, pneumonia; UTI, urinary tract infection.

the burden of complications for TBI patients specifically, the present study aimed to characterize the impact of 12 complications on TBI outcomes.

Pneumonia was associated with worse TBI outcomes

With some of the highest incidences of all investigated complications (*Table 1*), pneumonia presented the greatest burden for discharge disposition (*Table 2*, *Figure 3*). Unadjusted comparison of the impact of pneumonia on discharge disposition in the isolated *vs.* all TBI population showed that complications had a greater effect in the dataset that included all TBI patients (*Figure 3*). These results were supported by controlled analysis, which demonstrated greater odds ratios and PAR values for the inclusive dataset (Table S3, *Figure 3*). One possible explanation is that complications in the setting of multi-system injuries elicit a cascade effect where one complication leads to another. Alternatively, complications in the polytrauma context may more directly reflect the presence of injury to other organ systems. For example, pulmonary complications such as pneumonia have been shown to trigger hypoxic or hypercapnic respiratory failure in TBI patients, and the management of comorbid TBI and respiratory complications is difficult due to the competing effects of ventilator strategies on intracranial pressure (19,20). Given that pulmonary complications can increase the burden of initial TBI, preventative measures against pneumonia development are crucial, particularly in more severe TBI cases where diminished protective airway reflexes leave patients more susceptible to aspiration (19).

In the isolated TBI population, where polytrauma is unlikely to bias the onset of respiratory complications, the occurrence of pneumonia was associated with a change in LOS of 10.8 additional days (*Figure 4*) and high LOS burden (*Table 2*). These findings align with prior research, which showed that ventilator associated pneumonia was associated with longer hospital LOS (21). Furthermore, these effects were consistent in an identical sensitivity analysis that included non-isolated TBI patients (*Figure 4*, Table S3). Taken together, these data highlight pneumonia prevention as a potential critical node for improvement

of TBI care. Analysis of prevalence by facility revealed great inter-institutional variability in pneumonia rates (Figure S1), suggesting this may be a modifiable factor related to local TBI management strategies.

UTI and DVT were correlated with worse TBI outcomes

Multivariate analysis also demonstrated that the development of a UTI or DVT during treatment were associated with poorer discharge disposition, longer LOS, and greater burden (*Table 2*, *Figure 4*). Studies investigating the connection between TBI and DVT have found that TBI is independently associated with the development of DVT, regardless of when prophylactic treatment is initiated (22). The safest and most effective timing for chemoprophylaxis after DVT also remains controversial, particularly for patients with intracranial hemorrhage (23). Given our present findings that DVT is associated with worse discharge disposition and longer LOS, further development of measures to mitigate the risk of DVT development may benefit TBI outcomes and decrease the cost associated with treatment of these patients.

Previous research has also highlighted TBI-induced immunosuppression as a potential contributor to high rates of post-trauma infectious complications, particularly the development of UTIs, pneumonia, and intracranial infections (24,25). The mechanisms underlying immunosuppression after TBI that provide a permissive environment for infectious complications remain an area of active research (24). Future efforts that aim to understand the susceptibility of the immune system to TBI-related dysregulation may inform preventative strategies for nosocomial infections.

Complications were associated with longer hospital LOS

Our analyses also demonstrated that with the exception of cardiac arrest, all complications were highly associated with an extended LOS (*Table 2*, *Figure 4*). In particular, organ space and superficial SSIs, contributed significantly to time spent in the hospital, increasing the LOS by as much as 450% (*Table 2*). Evidence from prior critical care research has demonstrated a significant cost associated with an increase in LOS (6-8). Therefore, identifying methods of reducing complication rates may be one strategy to lower costs for both the patient and institution, as well as decrease the burden on physicians and hospital staff. Interestingly, however, when secondary analyses were performed based on TBI subtype, only pneumonia, DVT, UTI, and superficial SSIs remained significant across severe, moderate and mild, as well as pediatric and adult isolated TBI categories (Figure S2A). Although these differences from the total study population results may be influenced by a smaller sample size, the results underscore the burden of these specific complications on TBI outcomes. Further research into the causes of the variation between groups is needed.

Analysis of complication prevalence by institution demonstrated wide inter-hospital variability across all complications, but particularly for pneumonia, UTI, and MI. Differences in hospital status (i.e., university *vs.* community) may explain these variations. however, because our analysis accounted for center specific variables such as teaching status and TBI volume, these disparities were unlikely to have significantly affected the present results. Regardless, this inter-institution variability in prevalence suggests an area for optimization of TBI outcomes. Another possible explanation for differing complication rates is hospital-specific strategies for managing TBI and related complications. Thus, standardization of treatment practices and systematic training may benefit TBI care through minimization of complications. Future research on the best standards for managing each complication in the context of TBI is necessary.

Limitations

Certain limitations of this study that may restrict the generalizability of the results. The NTDB contains data voluntarily submitted by hospitals and may not be a fully complete representation of true trauma burden and care. However, this database was the best resource for this study because it is the largest trauma registry in the United States. Data on pupillary response, ICP, and volume of intracranial hemorrhage for each patient was not available, so confounding due to differences in case severity may still exist. As with any database, the potential for recording inaccuracies is also present. However, the NTDB implements several quality assurance measures to reduce the frequency of these inaccuracies (26). Because only initial admission data are included in the NTDB, the short-term outcomes assessed here may not precisely reflect the ultimate functional outcomes of the investigated TBI subpopulations. Finally, the data presented here represent associations between complications and outcomes. Information on timing of complication onset was also not available. Future research will be necessary to identify causal

effects and impacts of complication timing on outcomes.

Conclusions

Across TBI subtypes, pneumonia, UTIs, and DVT complications presented the greatest burden on isolated TBI care. The occurrence of SSIs also significantly impacted a patient's likelihood of returning home and increased LOS. These trends suggest targets for optimization of TBI management.

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Footnote

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Data Sharing Statement: Available at https://dx.doi.org/10.21037/jeccm-21-53

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/jeccm-21-53). Ms. ARK reports serving as a Director for Cress Health (unpaid) and owns shares of NeuroPace, outside the submitted work. Dr. WFA reports grants from Vivonics Inc., grants from Biogen Inc., outside the submitted work. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was exempt from Institutional Board Review due to the publicly available and de-identified nature of the data in the NTDB. Ethical review and approval were not required for this study on human participants in accordance with the local legislation and institutional requirements.

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Supplementary

Table S1 Characteristics of All TBI Admissions in the 2012-2016 NTDB

Variable	Number of Admissions (%)
Age, in years	
Pediatric	135,841 (14.0)
Adult	833,068 (86.0)
Mean ± standard deviation	46.8±24.4
Sex	
Male	624,416 (64.4)
Female	344,191 (35.5)
Other	2 (<0.1)
Race	
White	699,779 (72.2)
African American	120,435 (12.4)
Asian	21,355 (2.2)
American Indian	7,998 (<0.1)
Native Hawaiian/Pacific Islander	2,387 (<0.1)
Other/unknown	116,955 (12.1)
Hospital teaching status	
Community	380,081 (39.2)
University	460,968 (47.6)
Non-teaching	127,860 (13.2)
Hospital region	
Northeast	168,156 (17.4)
Midwest	237,964 (24.6)
South	350,122 (36.1)
West	212,667 (21.9)
Injury type	613,381 (63.3)
Blunt	289 (<0.1)
Penetrating	355,239 (36.7)
Other	
GCS admission score	125,826 (13.0)
Severe	43,439 (4.5)
Moderate	799,644 (82.5)
Mild	13.2 ± 3.7
Mean ± Standard Deviation	
Complications	6,061 (0.6)
Acute Kidney Injury	9,498 (1.0)
Acute Respiratory Distress Syndrome	8,156 (0.8)
Cardiac Arrest	10,308 (1.1)
Deep Vein Thrombosis	2,221 (0.2)
Myocardial Infarction	1,019 (0.1)
Organ Space SSI	25,756 (3.4)
Pneumonia [+]	3,158 (3.3)
Pulmonary Embolism	4,258 (0.4)
Sepsis	4,103 (0.4)
Stroke	1,364 (0.1)
Superficial SSI	14,043 (1.8)
Urinary Tract Infection[+]	
Comorbidities Present	268,140 (27.7)
Hypertension Requiring Medication	72,188 (7.5)
Bleeding Disorder	27,541 (2.8)
Congestive Heart Failure	25,815 (2.7)
Stroke/CVA	110,519 (11.4)
Diabetes	60,136 (6.2)
Respiratory Disease	12,131 (1.3)
Myocardial Infarction	
ISS (Mean ± Standard Deviation)	12.9 ± 9.9

*Percentages may not add up to 100% due to rounding or missing data. [+] Complication information for pneumonia and urinary tract infection were not present in the 2016 NTDB. Prevalence and analysis based on 2012-2015 data only.

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Table S2 Prevalence of Complications by TBI Subgroup

Variable	Severe TBI (n=9,590)	Moderate TBI (n=4,594)	Mild TBI (n=89,484)	Pediatric TBI (n=19,933)	Adult TBI (n=83,735)
Complications: Isolated TBI					
AKI	86 (0.9)	47 (1.0)	253 (0.3)	2 (<0.1)	384 (0.5)
ARDS	225 (2.3)	42 (0.9)	206 (0.2)	19 (0.1)	454 (0.5)
Cardiac Arrest	168 (1.8)	27 (0.6)	179 (0.2)	24 (0.1)	350 (0.4)
DVT	155 (1.6)	64 (1.4)	331 (0.4)	13 (0.1)	537 (0.6)
MI	53 (0.5)	19 (0.4)	162 (0.1)	0	234 (0.3)
Organ Space SSI	11 (0.1)	2 (<0.1)	9 (<0.1)	4 (<0.1)	18 (<0.1)
Pneumonia[+]	652 (7.0)	182 (4.1)	702 (0.8)	57 (0.3)	1,479 (1.8)
Pulmonary Embolism	24 (2.5)	18 (0.4)	70 (0.1)	0	112 (0.1)
Sepsis	72 (0.8)	30 (0.7)	134 (0.1)	4 (<0.1)	232 (0.3)
Stroke	108 (1.1)	25 (0.5)	172 (0.2)	15 (0.1)	290 (0.3)
Superficial SSI	10 (0.1)	7 (0.2)	28 (<0.1)	2 (<0.1)	43 (0.1)
UTI[+]	252 (2.7)	124 (2.8)	936 (1.1)	21 (0.1)	1,291 (1.6)
GCS (Mean + SD)	4.2 ± 1.8	10.7 ± 1.1	14.8 ± 0.5	14.1 ± 2.5	13.5 ± 3.3
ISS (Mean + SD)	16.6 ± 9.5	11.0 ± 8.4	8.3 ± 6.9	4.9 ± 5.2	10.2 ± 7.8
Subgroup size (n)	9,590	4,594	89,484	19,933	83,735
Complications: All TBI					
AKI	2,050 (1.6)	486 (1.1)	3,525 (0.4)	157 (0.1)	5,904 (0.1)
ARDS	5,162 (4.1)	872 (2.0)	3,464 (0.4)	771 (5.7)	8,727 (1.0)
Cardiac Arrest	5,045 (4.0)	487 (1.1)	2,624 (0.3)	739 (5.4)	7,417 (0.9)
DVT	4,336 (3.4)	871 (2.0)	5,101 (0.6)	427 (3.1)	9,881 (1.2)
MI	458 (3.6)	176 (0.4)	1,587 (0.2)	7 (<0.1)	2,214 (0.3)
Organ Space SSI	456 (3.6)	85 (0.2)	478 (0.1)	96 (0.1)	923 (0.1)
Pneumonia[+]	13,970 (14.3)	2,571 (7.6)	9,215 (1.5)	1,698 (1.6)	24,058 (3.7)
Pulmonary Embolism	1,068 (0.8)	240 (0.6)	1,850 (0.2)	81 (0.1)	3,077 (0.4)
Sepsis	1,831 (1.5)	399 (0.9)	2,028 (0.3)	147 (0.1)	4,111 (0.5)
Stroke	1,727 (1.4)	361 (0.8)	2,015 (0.3)	228 (0.2)	3,875 (0.5)
Superficial SSI	584 (0.5)	114 (0.3)	666 (0.1)	113 (0.1)	1,251 (0.2)
UTI[+]	4,235 (4.3)	1,276 (3.8)	8,532 (1.4)	589 (0.5)	13,545 (2.1)
GCS (Mean + SD)	4.1 ± 1.7	10.7 ± 1.1	14.8 ± 0.5	13.3 ± 3.6	13.2 ± 3.7
ISS (Mean + SD)	24.1 ± 13.1	15.8 ± 10.5	11.0 ± 7.8	10.3 ± 9.8	13.4 ± 9.8
Subgroup size (n)	125,826	43,439	799,644	135,841	833,068

* Prevalence is reported as a percentage in parenthesis [+] Complication information for PNA and UTI not present in the 2016 NTDB. Prevalence and analysis based on 2012-2015 data only.

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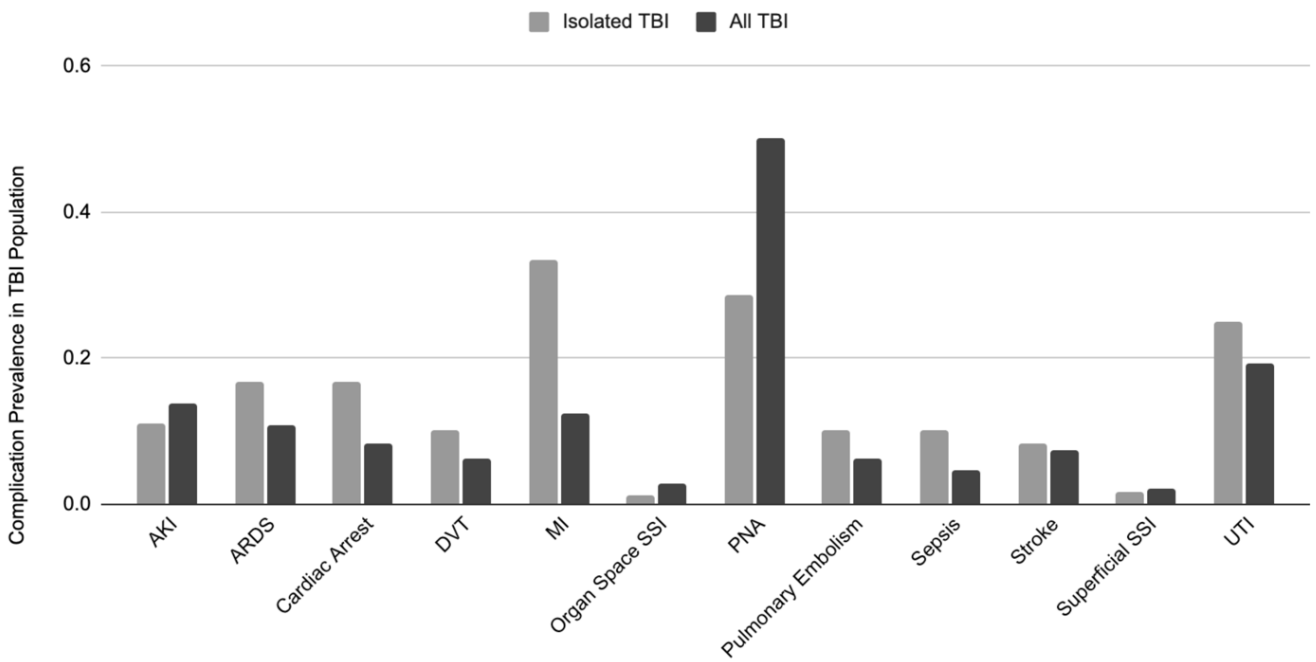

Figure S1 Range of Complication Prevalence in the TBI Population by Facility. Minimum and maximum proportion of patients who developed a complication across facilities. Prevalence of complications in the isolated TBI population shown in light gray and all TBI shown in dark gray. At least one facility had a prevalence = 0 for each complication. Abbreviations: ARDS = acute respiratory distress syndrome, DVT = deep vein thrombosis, MI = myocardial infarction, SSI = surgical site infection, PNA = pneumonia, UTI = urinary tract infection.

Table S3 Burden of Each Complication on All TBI Care Based on Adjusted Multivariate Analysis

Complication	Burden Discharge Disposition	Odds Ratio, [95% CI]	Discharge Disposition p-value	Burden LOS
AKI	0.006	1.899, [1.723, 2.094]	p<0.001	0.63
ARDS	0.007	1.683, [1.561, 1.814]	p<0.001	0.61
Cardiac Arrest	0.009	2.024, [1.724, 2.377]	p<0.001	–0.64
DVT	0.02	2.851, [2.665, 3.051]	p<0.001	1.55
MI	0.019	1.854, [1.614, 2.129]	p<0.001	0.33
Organ Space SSI	<0.001	1.316, [1.086, 1.595]	0.005	3.1
Pneumonia	0.07	3.221, [3.089, 3.358]	p<0.001	2.11
Pulmonary Embolism	0.003	2.004, [1.782, 2.254]	p<0.001	1.18
Sepsis	0.004	1.981, [1.742, 2.252]	p<0.001	1.16
Stroke	0.011	3.733, [3.275, 4.255]	p<0.001	0.59
Superficial SSI	0.001	1.646, [1.390, 1.949]	p<0.001	2.42
UTI	0.035	2.987, [2.845, 3.137]	p<0.001	1.71

All results are reported for an interval of +1 patients. 95% confidence intervals are listed. Odds ratio > 1 indicates more likely to be discharged to a care or rehab facility than home. Discharge Disposition Burden represents the proportion of patients with a worse discharge disposition attributable to the complication. LOS burden represents the proportional change in LOS attributable to the complication in days.

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Table S4 Adjusted Association of Each Complication with Likelihood of Discharge Home *vs.* Care or Rehab Facility by TBI Subtype for All TBI

Complication	Severe TBI (n=125,826)	Moderate TBI (n=43,439)	Mild TBI (n=799,644)	Pediatric TBI (n=135,841)	Adult TBI (n=833,068)
AKI	1.279, [1.038, 1.575] *	1.220, [0.854, 1.745]	2.131, [1.901, 2.388] **	0.926, [0.442, 1.941]	1.933, [1.752, 2.133] **
ARDS	1.154, [1.046, 1.273] *	1.827, [1.451, 2.300] **	2.797, [2.475, 3.160] **	1.158, [0.906, 1.480]	1.753, [1.620, 1.897] **
Cardiac Arrest	1.474, [1.146, 1.897] *	1.089, [0.627, 1.892]	2.696, [2.175, 3.341] **	2.591, [1.401, 4.790] *	1.961, [1.661, 2.315] **
DVT	2.001, [1.146, 2.242] **	2.270, [1.790, 2.879] **	3.503, [5.311, 3.820] **	3.514, [2.494, 4.952] **	2.873, [2.681, 3.078] **
MI	1.344, [0.994, 1.968]	1.014, [0.588, 1.750]	1.978, [1.697, 2.307] **	1.009, [0.075, 13.553]	1.850, [1.611, 2.124] **
Organ Space SSI	0.818, [0.622, 1.074]	1.589, [0.838, 3.013]	1.940, [1.492, 2.522] **	0.672, [0.351, 1.288]	1.409, [1.152, 1.723] *
Pneumonia	2.891, [2.726, 3.066] **	2.584, [2.279, 2.931] **	3.726, [3.491, 3.977] **	4.083, [3.486, 4.783] **	3.206, [3.070, 3.348] **
Pulmonary Embolism	1.114, [0.905, 1.372]	1.391, [0.901, 2.148]	2.721, [2.358, 3.140] **	4.121, [1.921, 8.843] **	2.015, [1.789, 2.269] **
Sepsis	1.657, [1.365, 2.011] **	1.851, [1.216, 2.817] *	2.274, [1.901, 2.722] **	1.702, [0.575, 3.062]	2.016, [1.767, 2.299] **
Stroke	2.612, [2.069, 3.298] **	2.076, [1.373, 3.138] *	4.535, [3.840, 5.355] **	4.178, [2.532, 6.786] **	3.718, [3.243, 4.262] **
Superficial SSI	1.446, [1.106, 1.891] *	1.057, [0.615, 1.816]	1.950, [1.556, 2.443] **	2.161, [1.167, 4.002] *	1.628, [1.366, 1.940] **
UTI	1.803, [1.638, 1.985] **	1.863, [1.583, 2.193] **	3.557, [3.351, 3.775] **	2.904, [2.266, 3.722] **	3.001, [2.855, 3.155] **

All results are reported for an interval of +1 patients. 95% confidence intervals are listed. Odds ratio > 1 indicates more likely to be discharged to a care or rehab facility than home. * indicates $p<0.05$. ** indicates $p<0.001$.

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Table S5 Adjusted Association of Each Complication with Likelihood of Discharge Home *vs.* Care or Rehab Facility by TBI Subtype for Isolated TBI

Complication	Severe TBI (n=9,590)	Moderate TBI (n=4,594)	Mild TBI (n=89,484)	Pediatric TBI (n=19,933)	Adult TBI (n=83,735)
AKI	3.084, [1.127, 8.442] *	0.618, [0.225, 1.702]	2.203, [1.522, 3.188] **	0.248, [0.005, 11.904]	2.077, [1.498, 2.879] **
ARDS	1.490, [0.907, 2.448]	2.568, [0.829, 7.956]	7.293, [4.089, 13.007] **	4.863, [1.096, 21.583] *	2.911, [2.014, 4.209] **
Cardiac Arrest	3.179, [1.035, 9.767] *	1.091, [0.114, 10.411]	3.249, [1.500, 7.033] *	2.060, [0.001, 6533.637]	2.791, [1.492, 5.220] *
DVT	1.918, [1.149, 3.202] *	6.536, [2.362, 18.083] **	3.223, [2.369, 4.386] **	4.040, [0.923, 17.684]	3.038, [2.345, 3.936] **
MI	0.993, [0.349, 2.823]	1.141, [0.284, 4.576]	2.169, [1.375, 3.420] *	--	1.869, [1.255, 2.783] *
Organ Space SSI	1.541, [0.207, 11.491]	0.183, [0.006, 5.499]	11.628, [1.017 132.937] *	1.339, [0.012, 155.656]	3.033, [0.690, 13.339]
Pneumonia	3.835, [2.918, 5.041] **	3.950, [2.277, 6.855] **	5.084, [3.923, 6.588] **	3.730, [1.608, 8.653] *	4.739, [3.949, 5.687] **
Pulmonary Embolism	1.239, [0.371, 4.137]	0.721, [0.134, 3.886]	2.740, [1.323, 5.677] *	--	2.228, [1.240, 4.004] *
Sepsis	2.235, [0.843, 5.924]	0.292, [0.084, 1.013]	3.003, [1.496, 6.029] *	4.878, [0.342, 69.493]	2.106, [1.236, 3.589] *
Stroke	5.150, [1.667, 15.694] *	1.971, [0.357, 10.880]	6.848, [3.975, 11.798] **	17.981, [1.847, 52.670] *	5.915, [3.650, 9.585] **
Superficial SSI	1.895, [0.336, 10.701]	--	1.655, [0.563, 4.870]	12.018, [2.921, 49.451] **	2.264, [0.501, 5.490]
UTI	1.924, [1.255, 2.950] *	2.329, [1.351, 4.017] *	4.253, [3.556, 5.087] **	0.289, [0.006, 13.251]	3.869, [3.302, 4.534] **

All results are reported for an interval of +1 patients. 95% confidence intervals are listed. Odds ratio > 1 indicates more likely to be discharged to a care or rehab facility than home. * indicates p<0.05. ** indicates p<0.001.

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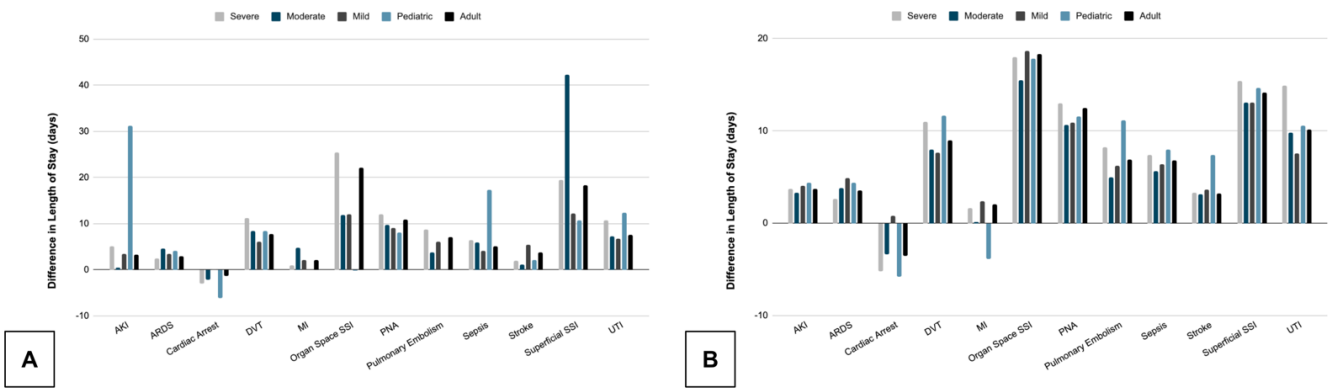

Figure S2 Adjusted Difference in LOS by Complication for Each TBI Subtype. All results are reported for an interval of +1 patients after multivariate analysis controlling for demographic, clinical, and facility variables. A. Differences in LOS for isolated TBI patients. B. Differences in LOS including non-isolated TBI. Abbreviations: AKI = acute kidney injury, ARDS = acute respiratory distress syndrome, DVT = deep vein thrombosis, MI = myocardial infarction, SSI = surgical site infection, PNA = pneumonia, UTI = urinary tract infection.

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