#### THE COMMUNITY OF TRAUMA CARE: PARTNERING WITH STAKEHOLDERS TO IMPROVE INJURY OUTCOMES

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**Introduction**: Engaging trauma survivors/caregivers results in research findings that are more relevant to patients' needs and priorities. As such, their perspectives increase research significance; however, the underlying presumption is a lack of consensus. We aimed to describe stakeholder perspectives to assure research is meaningful, respectful, and relevant to the injured patient and their caregivers. **Methods**: A multiphase, inductive exploratory qualitative study was performed, the first phase of which is described here. Virtual focus groups to elicit stakeholder perspectives and preferences were conducted across 19 trauma centers in the United States during 2022. Discussion topics were chosen to identify patients' motivation to join research studies, preferences regarding outcomes, efficacy, and exception from informed consent. The focus groups were audio recorded, transcribed, coded, and analyzed to identify the range of perspectives and common themes.

**Results**: Ten 90-minute focus groups included patients/caregivers (n=21/1) and researchers (n=14). Data analysis identified common themes emerging across groups (Table 1). The importance of trust and pre-existing relationships with the clinical care team pervaded the data across all groups.

**Conclusion**: Our findings reveal common themes in preferences, motivations, and best practices to increase participation in trauma research. The next phases will involve a vignette based survey to establish broad stakeholder consensus, followed by education and dissemination to share strategies to increase research engagement and relevance for patients, and form a panel of patients to support future research endeavors.

Table 1.	
Topics of Discussion	Themes
Motivation to Participate	Altruism, New knowledge/perspective, Health status, Recognition of benefits of giving back
Informed Consent Best	Timing, Researcher's approach/characteristics,
Practices	Focus on altruistic nature, Trust/respect

Tabla 1

## ANTIBIOTICS AND SURGICALLY TREATED ACUTE APPENDICITIS, WHEN WHERE AND WHY?

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**Introduction**: Antibiotics within an hour of incision reduces the incidence of surgical site infection (SSI) in clean-contaminated abdominal surgery. Patients who undergo emergency surgery are often receiving treatment antibiotics and may not benefit from additional antibiotics immediately prior to skin incision though hospital protocols may recommend them. We hypothesized that additional prophylactic antibiotic coverage does not decrease incidence of SSI in emergency appendectomy patients. Methods: We evaluated outcomes of patients after a policy change recommending pre-incision antibiotics regardless of ongoing antimicrobial therapy. We reviewed all adult patients at a single institution that underwent emergency appendectomies for acute appendicitis between 2013 and 2020. Variables included age, sex, perforation, body mass index (BMI), Elixhauser comorbidity index (ECI), surgical approach, emergency department antibiotics (EDA), and preoperative antibiotics. EDA were further subclassified into none, narrow and broad spectrum. The primary outcomes were superficial/deep and organ-space SSIs. Bivariable and multivariable logistic regression models were created to assess the independent impact of each strategy. Multivariable models compared those receiving pre-incision cefazolin to those receiving no pre-incision antibiotics.

**Results**: Patients (n= 1328) with a mean age (SD) of 39.5 (17.0) years (40% female) were reviewed. Age, sex, perforated appendicitis, EDA, ECI and BMI all were predictive of infection (table). Pre-incision antibiotics were not predictive of SSI (p= 0.632). After adjustment for age, sex, perforation, EDA, ECI and BMI only perforation [OR 17.08 95% CI (6.97 – 51.43)] and male sex [OR 2.75 95% CI (1.29 – 6.43)] were associated with organ-space infection while pre-incision cefazolin was not [OR 0.83 95% CI (0.38 – 1.97)]. ED broad spectrum antibiotics were associated with lower incidence of superficial/deep infection [OR 0.06 95% CI (0.00 – 0.68)] however pre-incision cefazolin was not [OR 0.71 95% CI (0.08 – 15.34)].

**Conclusion**: For patients undergoing emergency appendectomies who have received broad spectrum antibiotic treatment, additional pre-incision cefazolin does not reduce the incidence of superficial/deep or organ-space SSI.

# ANTIHISTAMINES VS. RESUSCITATION AND COMPLICATIONS IN BURN INJURIES: A RETROSPECTIVE STUDY

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**Introduction**: In theory, management of vascular permeability after thermal injuries via antihistamines may reduce the histamine-mediated synthesis of reactive oxygen species, inflammation, and edema. Antihistamine use to target microvascular endothelial barrier dysfunction following thermal injuries in humans is not well known. The therapeutic application of histamine receptor antagonists may reduce resuscitation requirements and ultimately improve outcomes in thermal injuries.

**Methods**: A retrospective analysis was conducted using the EMR records at the University Medical Center in Lubbock, TX. We checked if the burn patients from July 2015 to July 2021 (N=199) had a previous prescription for antihistamines prior to the hospital visit and/or a 24-hour Medical Administration Record (MAR) of antihistamines during the hospital stay. The patients were grouped into three categories: control (no antihistamine usage), patients using H1 blockers, and patients using H2 blockers. Outcomes were assessed on infection rates, sepsis development, graft loss  $\geq$  20%, hospital LOS, acute kidney injury, amount of resuscitation fluid used, urine output, and mortality.

**Results**: Out of the participants, 39.7% used H2 blockers, and 7.7% used H1 blockers. Chi square analysis was used. When compared to the control group, there were no significant differences in outcomes relating to graft loss of over 20% or infection rates in patients using H1 or H2 blockers. However, only H2 blockers were found to significantly decrease mortality rates (p=0.018) in burn patients in comparison to the control group. **Conclusion**: H2 blocker usage prior to or within 24 hours of a burn injury can potentially decrease mortality rates. The antagonistic mechanism of H2 blockers on histamine-mediated processes in a burn injury may contribute to improved vascular permeability management and, thus, decreased damage

from burn-induced reactive oxygen species and edema.

## DEVELOPMENT AND VALIDATION OF A PREDICTIVE MODEL FOR ACUTE RESPIRATORY DISTRESS SYNDROME AFTER TRAUMA

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**Introduction:** ARDS is a well-known complication after trauma associated with increased morbidity and mortality. Little is known about factors predisposing injury victims to develop ARDS. With the current project we aim to develop a predictive model for ARDS development after trauma.

**Methods:** The TQIP database (2013-2020) was queried. Patients  $\geq$ 15 years with a hospital stay  $\geq$ 48h were examined. Data were split into training and testing subsets at a 4:1 ratio. Uni- & multi-variable logistic regression models were fitted, and subsequently ten-fold cross-validated with a logistic LASSO model to select optimal penalization for AUC maximization. Variable selection cut-offs were determined with Yudens J-statistic.

**Results:** A total of 4,045,541 patients were analyzed. The selected LASSO model reduced the variable pool from 58 considered to 35, without sacrificing performance (all-models AUC 0.83). Male gender [O.R. 1.48 95% C.I. (1.43-1.53)], and BMI [1.01 (1.01-1.01)], as well as history of diabetes [1.13 (1.08-1.17)], bleeding disorders [1.94 (1.83-2.05)], COPD (but not smoking) [1.59 (1.52-1.67)], hypertension [1.16 (1.12-1.20)], prior MI [1.94 (1.76-2.14)], CHF [1.28 (1.20-1.37)], alcoholism [1.66 (1.59-1.73)] & cirrhosis [1.68 (1.53-1.85)] all predisposed for ARDS. Penetrating (and specifically firearm) injuries [6.44 (2.87-14.41)], as well as burns [3.01 (2.71-3.34)], motor-vehicle crashes [1.6 (1.54-1.67)] and struck pedestrians [1.58 (1.48-1.69)] also independently increased risk for ARDS, as did lower pressure [0.997 (0.997-0.998)], temperature [0.84 (0.82-0.86)], O2 [0.989 (0.987-0.99)], and GCS [0.87 (0.87-0.87)] in the ED. Patients with rib [1.56 (1.51-1.61)] (and especially flail chest [2.31 (2.16-2.47)]) and pelvic [1.19 (1.14-1.24)] (but not lower extremity) fractures, pulmonary contusions [1.94 (1.86-2.01)], and those requiring thoracotomy [2.04 (1.83-2.27)], or cranial decompression [2.30 (2.12-2.49)] had increased risk for ARDS. Contrast to published data, age and race were not predictors, and neither were plasma, platelet and cryoprecipitate transfusions. Red blood cells were [1.06 (1.05-1.07)].

**Conclusion:** Our validated model may be used as an online tool to determine patients at risk for ARDS development, so critical care admission and appropriate strategies and resources can be allocated.

## DIVING DEEPER INTO POST-INJURY SEPSIS: EPIDEMIOLOGY OF CULTURE NEGATIVE AND RECURRENT SEPSIS

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Introduction: While critically injured trauma patients are known to be at high-risk for subsequent infection, patterns of negative microbiologic culture and recurrent sepsis events remain poorly understood. Methods: We performed a retrospective analysis of 3,194 critically ill trauma patients admitted to our Level 1 Trauma Center between 2012-2020 requiring mechanical ventilation  $\geq 3$  days. Sepsis events were identified by a novel, automated method based on clinical data from the electronic health record, consistent with Sepsis-3 definitions. Culture results and recurrent sepsis episodes were determined and linked to clinical outcomes. **Results:** The overall incidence rate of sepsis in this severely injured (median ISS 30, IQR 25-43) population was 24% (n=747/3194). The median time to onset of 1<sup>st</sup> sepsis episode was 8 days (IQR 6-11). Half of all initial sepsis events (n=372, 49%) occurred within the first 7 days, while only 12% (n=93) developed late, after day 14. Pre-existing organ dysfunction was common prior to sepsis onset (SOFA 3, IQR 2-6). While microbiologically confirmed pneumonia was the leading source of infection (n=342, 46%), one-third (n=249, 33%) of initial sepsis events were culture negative. More than one-third of septic patients (n=257, 34%) developed 1 or more additional sepsis episodes during their hospitalization. Compared to isolated septic episodes, a trajectory of recurrent sepsis was independently associated with baseline characteristics of shock on arrival, advancing age, and penetrating mechanism. Additionally, the incidence of chronic critical illness (61% vs 36%), as well as ventilator, ICU & hospital days, were all significantly greater in patients with recurrent sepsis events (all p<0.001). Conclusion: A high rate of negative microbiologic cultures and pre-existing organ dysfunction are likely contributors to the challenges of timely and accurate diagnosis of sepsis among critically ill trauma patients. Recurrent sepsis episodes are associated with a clinical trajectory of chronic critical illness, which has been linked with an endotype of persistent inflammation and immunosuppression, and poor long-term outcomes.

# EFFECT OF VOLUME RESUSCITATION ON CEFAZOLIN PHARMACOKINETICS IN TRAUMA PATIENTS

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**Introduction:** Cefazolin is regularly used as prophylaxis in trauma patients to avoid infection. However, evidence-based antibiotic dosing guidelines are lacking among patients receiving massive transfusion. We hypothesized that an association between volume resuscitation and cefazolin pharmacokinetics (PK) exists.

**Methods:** We conducted a prospective study to develop a population PK model using remnant blood samples of fifteen trauma patients meeting indications for cefazolin and initiation of massive transfusion protocol. Individual Bayesian estimates for cefazolin clearance (CL) and volume of the central compartment ( $V_c$ ) were derived from the model. Linear regression was performed to evaluate associations between these PK parameters and various volume resuscitations received including whole blood, packed red blood cells (PRBCs), fresh frozen plasma (FFP), and crystalloids.

**Results:** Patients received between 525-2100ml of whole blood, 350-9223ml of PRBCs, 0-5265ml of FFP, and 1400-6025ml of crystalloid. The median cefazolin CL and V<sub>c</sub> were 4.6 L/h (range 1.6-10.3 L/h) and 4.4 L (range 2.3-25.2 L), respectively. The p-value (P) and R<sup>2</sup> for the association between resuscitation type and cefazolin CL and V<sub>c</sub> are listed in the table below.

Resuscitation type	CL	Vc
Whole blood	$P=0.08, R^2=0.2$	
PRBCs	$P=0.9, R^2=0.0004$	
FFP	$P=0.9, R^2=0.002$	$P=0.2, R^2=0.1$
Total blood products	$P=0.9, R^2=0.001$	
Crystalloids	$P=0.7, R^2=0.008$	
Total volume resuscitation	$P=0.83, R^2=0.004$	$P=0.2, R^2=0.1$

**Conclusions:** In this prospective pilot study, there was no statistically significant association between cefazolin PK parameters and the amount of volume resuscitation received. These data suggest that re-dosing of cefazolin should be conducted independent of the volume of blood products or crystalloid administered.

# FACTORS ASSOCIATED WITH ANXIETY AND DEPRESSION AT ONE-YEAR POST-MAJOR TRAUMA: A MULTI CENTRE STUDY

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**Introduction**: Longer term recovery following trauma is impacted by physical and psychological factors. The presence and impact of anxiety and depression on longer term recovery in severely injured patients is unknown. This multi-site study investigated the prevalence of anxiety and depression at one year after trauma critical care admission.

Methods: Adult trauma patients admitted to four Level 1 Critical Care Units were enrolled over 18 months. Survivors were followed-up at one year post injury using EQ-5D-5L questionnaires (n=990). Patient responses were dichotomized into those with or without reported anxiety or depression. **Results**: 295 questionnaires were completed (30% response rate). Two thirds (63%) reported anxiety or depression (AoD) at one year following injury, and this was associated with a worse overall health state (p < 0.0001). Those with AoD were younger (53 years vs. 60 years, p=0.03) and more likely to have experienced psychological problems (16% vs. 5%, p<0.01). Injury severity was the same for both groups (median 25), but penetrating injury was more common (9% vs. 2%, p=0.01) in those with AoD. Anxiety and depression were associated with longer critical care (11 vs. 8 days, p=0.04) and hospital stays (32 vs. 24 days, p<0.01). All physical EQ-5D problems were worse in the presence of AoD, especially pain (severe/extreme pain 53% vs. 23%, p<0.001). In multivariable analysis, factors associated with anxiety and depression at one year were: younger age (OR 0.97 [95% CI 0.96-0.99] p=0.008), a previous psychological diagnosis (OR 3.2 [95% CI 1.4-7.3] p=0.005), penetrating injury (OR 10.6 [95% CI 1.9 – 57.7] p=0.006) and pain at follow up (OR 1.7 [95% CI 1.2-2.4] p=0.002).

**Conclusion**: Longer term anxiety and depression following significant trauma was common in those with previous psychological problems. Clinical assessment in hospital should include screening to identify those at risk. Improved longer term pain management may also enhance psychological recovery after injury.

# FRAILTY SCORE AND INCENTIVE SPIROMETRY PREDICT ICU LENGTH OF STAY IN PATIENTS WITH RIB FRACTURES

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**Introduction**: Guidelines suggest mandatory Intensive Care Unit (ICU) stay for geriatric patients with rib fractures may improve outcomes. However, not all geriatric patients have the same degree of frailty. The Clinical Frailty Scale (CFS), a measure of physiologic condition, independently predicts adverse patient outcomes among geriatric patients. Incentive spirometry (IS) values are associated with the physiologic quality of the respiratory system. CFS and intake IS are values that can be quickly collected during patient triage. The objective of this study is to determine if CFS and intake IS are independently associated with ICU length of stay and discharge disposition in patients of age  $\geq$  45 with rib fractures.

**Methods**: Medical records from patients greater than 45 years-old with rib fractures admitted to a Level 1 trauma center from 2016 to 2019 were reviewed. Primary outcome was ICU length of stay  $\geq$ 2 days, with a primary predictor of CFS. This was assessed using logistic regression and controlled for the following covariates: age, sex, ISS, chest AIS, GCS, Charlson score, IS (<500, 500-999, 1000-1499, 1500+, or missing), number of fractures, and bilateral rib fractures. Area under the curve (AUC) was calculated for this multivariable logistic regression model as well as for age, CFS, and IS independently. Mean CFS among the discharge disposition groups (home, facilities, death, or other) was assessed using linear regression.

**Results**: 883 patients were included. 361 patients (40.9%) had an ICU LOS  $\geq 2$  days. Higher CSF was significantly associated with an ICU LOS  $\geq 2$  days (p=0.001; OR for a one-point increase in CFS: 1.28 [95% CI: 1.11, 1.47]). The full model had an AUC of 0.74 (95% CI: 0.71-0.78), indicating good discrimination between patients with and without longer ICU LOS. Age on its own did not successfully discriminate between the two groups (AUC 0.50 [95% CI: 0.47-0.54]). CFS and the IS categories performed better than age, but each alone provided weak discrimination between the groups (CFS: AUC 0.56 [95% CI: 0.52-0.60], IS: AUC 0.63 [95% CI: 0.59-0.66]). Mean CFS differed by discharge disposition (p<0.0001). Patients discharged to a facility also had a higher average CFS than those discharged home (0.41 points [95% CI: 0.24, 0.58]).

**Conclusion**: Together, CFS and intake IS values may be useful in predicting ICU length of stay and discharge disposition for those with traumatic rib fractures. These results provide a simple assessment that may help to guide admission disposition and resource use for patients with rib fractures and varying degrees of frailty.

## POTASSIUM IS AN EARLY INDICATOR OF MORTALITY, COMPLICATIONS, AND LENGTH OF STAY IN ADULT TRAUMA PATIENTS

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Introduction: The average trauma patient has a considerable amount of data collected in their initial evaluation with unclear significance. We hypothesized that an elevated potassium level in the first 24 hours of admission was associated with increased mortality and complications. Methods: All adult trauma patients in our internal registry from 2016 to 2021 with laboratory results available from the electronic medical record were analyzed. The maximum and minimum serum potassium over the patient's first 24 hours after admission were determined and outcomes for mortality and complications were compared using risk-adjusted multivariable logistic regression. Linear regression compared differences in length of stay. For all tests, statistical significance was set as p < 0.05. **Results**: We analyzed 8,220 adult trauma patients with 24-hour laboratory data. In the risk-adjusted multivariable analyses, greater peak serum potassium (SP) in the first 24 hours was associated with increased mortality (OR=1.53, p < 0.001), acute kidney injury (AKI) (OR=2.53, p<0.001), hemorrhagic shock (OR=2.75, p<0.001), multi-system organ failure (MOF) (OR=2.76. p<0.001), myocardial infarction (MI) (OR=1.98, p<0.001), severe sepsis (OR=2.04, p<0.001), and increased length of stay. This association persisted in those with blunt trauma. Cut-point analysis found that a peak serum level of 4.6 mEq/L was 81% specific for mortality and 4.47mEq/L correlated with increased mortality (OR=1.73, p<0.001), AKI (OR=2.05, p<0.001), and hemorrhagic shock (OR=2.14, p=0.006). Conclusion: In the first 24 hours of admission, higher maximum SP levels were associated with increased mortality, AKI, hemorrhagic shock, MOF, MI, severe sepsis, unplanned extubation, ICU days, and hospital days in all trauma patients. A peak SP greater than 4.6 mEq/L was 81% specific for mortality and 4.47 mEq/L showed a correlation with mortality, AKI, and hemorrhagic shock, underscoring its possible use in acute care.

# THE IMPACT OF BALANCED TRANSFUSION ON POST-HEMOSTASIS RESUSCITATION IN TRAUMA

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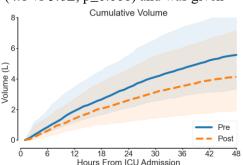
**Introduction:** Few interventions have changed the approach to trauma resuscitation as balanced blood product transfusion; yet, its impact on resuscitation after hemostasis remains unstudied. We sought to determine how post-hemostasis resuscitation has evolved after balanced transfusion and identify opportunities for further improvement.

**Methods:** We examined adult trauma patients transfused in the ED. Focusing on the post-hemostasis period after ICU arrival, we compared patient and injury characteristics, resuscitation over the first 48 hours of ICU admission, lab values, and outcomes pre- (2012-2015) and post-institutional implementation of balanced transfusion (2016-2019).

**Results:** The 2649 subjects were 70% male with blunt trauma (81%; ISS 27, IQR [17, 38]). Post-2015 (n=1472), patient and injury characteristics were similar apart from obesity (26% vs 10%, p $\leq$ 0.001), compared with pre-2015. On ICU arrival, pH (7.37 vs 7.35, p $\leq$ 0.001) and platelets (155 vs 149  $10^3/\mu$ L, p $\leq$ 0.001) were improved. In the ICU, more patients received blood (26% vs 13%, p $\leq$ 0.001) and vasopressors (17% vs 12%, p $\leq$ 0.001).

Crystalloid volume (IVF) decreased (4.1 vs 5.6L, p≤0.001) and was given

later in admission (Figure). Rate of INR >1.5 by 48 hours (43% vs 56%, p $\leq$ 0.001) decreased, while AKI rose (8% vs 5%, p=0.02). Mortality was similar at 16%. **Conclusion:** Post-2015, patients appear to be better resuscitated upon ICU arrival. In the ICU, resuscitation has shifted to embrace blood products and



vasopressors, and move away from IVF. While coagulopathy has improved, the incidence of AKI is higher, with the potential for poorer outcomes. There remains room for improvement, perhaps through earlier and more targeted IVF administration.