Clinical Policy: Critical Issues in the Evaluation of Adult Patients Presenting to the Emergency Department with Acute Blunt Trauma

This DRAFT is EMBARGOED – Not for Distribution

From the American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Blunt Trauma

Charles J. Gerardo, MD, MHS, FACEP (Subcommittee Chair)
Michelle Blanda, MD, FACEP
Nidhi Garg, MD, FACEP
Kaushal H. Shah, MD, FACEP
Richard Byyny, MD, MSc, FACEP (Methodologist)
Stephen J. Wolf, MD (Committee Co-Chair)
Deborah B. Diercks, MD, MSc (Committee Co-Chair)

Members of the American College of Emergency Physicians Clinical Policies Committee (Oversight Committee):

Stephen J. Wolf, MD (Chair 2018 – 2020, Co-Chair, 2021-2022)
Deborah B. Diercks, MD, MSc (Committee Co-Chair, 2021-2022, Chair 2023-2024)
John Anderson, MD
Richard Byyny, MD, MSc (Methodologist)
Christopher R. Carpenter, MD, FACEP
John T. Finnell, MD
Benjamin W. Friedman, MD (Methodologist)
Seth R. Gemme, MD
Charles J. Gerardo, MD, MHS
Steven A. Godwin, MD
Sigrid A. Hahn, MD, MPH
Benjamin W. Hatten, MD, MPH
Jason S. Haukoos, MD, MSc (Methodologist)
Amy Kaji, MD, MPH, PhD (Methodologist)
Heemun Kwok, MD, MS (Methodologist)
Bruce M. Lo, MD, MBA, RDMS
Sharon E. Mace, MD, FACEP, FAAP
Maggie Moran, MD (EMRA Representative)
Susan B. Promes, MD, MBA, FACEP
Kaushal H. Shah, MD, FACEP
Richard D. Shih, MD, FACEP
Scott M. Silvers, MD, FACEP
Andrea Slivinski, RN, DNP (ENA Representative)
Michael D. Smith, MD, MBA, FACEP
Molly E. W. Thiessen, MD
Christian A. Tomaszewski, MD, MS, MBA, FACEP
Stacy A. Trent, MD, MPH (Methodologist)
Jonathan H. Valente, MD, FACEP
Stephen P. Wall, MD, MSc, MAEd (Methodologist)
Lauren M. Westafer, DO
Yanling Yu, PhD (Advocate for Patient Safety)
Stephen V. Cantrill, MD, FACEP (Liaison with Quality and Patient Safety Committee)
Travis Schulz, MLS, AHIP, Staff Liaison, Clinical Policies Committee
Kaeli Vandertulip, MBA, MSLS, AHIP, Staff Liaison, Clinical Policies Committee and Subcommittee on Blunt Trauma

DRAFT

ABSTRACT

This clinical policy from the American College of Emergency Physicians is a revision of the 2018 "Clinical Policy: Critical Issues in the Evaluation of Adult Patients Presenting to the Emergency Department with Acute Blunt Abdominal Trauma".[1] A writing subcommittee conducted a systematic review of the literature to derive evidence-based recommendations to answer the following clinical questions: 1) In adult patients presenting to the emergency department with blunt trauma, does whole-body CT improve clinically important outcomes in hemodynamically stable patients? 2) In geriatric patients presenting to the emergency department with blunt trauma, does age-based, differential trauma triage reduce morbidity and/or mortality? 3) In adult patients presenting to the emergency department with blunt trauma, what is the ideal blood product ratio to reduce morbidity and /or mortality in patients requiring transfusion? 4) In adult patients presenting to the emergency department with blunt trauma, does resuscitative endovascular balloon occlusion of the aorta (REBOA) reduce morbidity and/or mortality in arrested or peri-arrest patients compared to ED thoracotomy? Evidence was graded and recommendations were made based on the strength of the available data.

INTRODUCTION

Trauma is a leading cause of death in the United States and contributes to more years of potential life lost compared to any other cause of death.[2,3] Blunt trauma is the most common mechanism of injury. The triage, evaluation, and treatment of these patients is a routine element of the practice of emergency medicine.[4] Consequently, there is substantial opportunity in the emergency department (ED) to minimize preventable morbidity and mortality due to blunt trauma. This policy is an update of the 2018 American College of Emergency Physicians' (ACEP) clinical policy on acute blunt abdominal trauma[1] which is now expanded to address acute blunt trauma not limited to the abdomen.

Despite the high prevalence of patients with blunt trauma, care of these patients is constantly evolving and continues to present a clinical challenge. For example, occult injury remains common as physical examination has limited accuracy in patients with altered mental status, intoxication, other distracting injuries or even in asymptomatic patients with a normal sensorium.[5,6] This fact, combined

DRAFT

with technical advances in CT, have resulted in changes to cross-sectional imaging protocols since the last clinical policy update. Our understanding of the response of the geriatric population to blunt trauma has also evolved and this has resulted in the variable incorporation of age into trauma triage. Lastly, lessons learned from military trauma care, such as resuscitation with changing blood product ratios and incorporation of advanced invasive techniques for managing non-compressible torso hemorrhage, have been applied and studied in civilian blunt trauma.

This policy will address current challenges in the diagnosis and treatment of adult patients with blunt trauma in the era of evolving cross sectional imaging approaches, differential trauma triage incorporating age, blood product resuscitation ratios, and resuscitative endovascular balloon aortic occlusion (REBOA).

METHODOLOGY

This ACEP clinical policy was developed by emergency physicians with input from medical librarians and a patient safety advocate. It is based on a systematic review and critical, descriptive analysis of the medical literature and is reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[7]

Search and Study Selection

This clinical policy is based on a systematic review with a critical analysis of the medical literature meeting the inclusion criteria. Searches of PubMed, SCOPUS, Embase, Web of Science, and the Cochrane Database of Systematic Reviews were performed by a librarian. Search terms and strategies were peer reviewed by a second librarian. All searches were limited to human studies published in English. Specific key words/phrases, years used in the searches, dates of searches, and study selection are identified under each critical question. In addition, relevant articles from the bibliographies of included studies and more recent articles identified by committee members and reviewers were included.

DRAFT

Two subcommittee members independently read the identified abstracts to assess them for possible inclusion. Of those identified for potential inclusion, each full-length text was reviewed for eligibility. Those identified as eligible were subsequently forwarded to the committee's methodology group (emergency physicians with specific research methodological expertise) for methodological grading using a Class of Evidence framework (Appendix A.).

Assessment of Risk of Bias and Determination of Classes of Evidence

Each study identified as eligible by the subcommittee was independently graded by 2 methodologists. Grading was done with respect to the specific critical questions; thus, the Class of Evidence for any one study may vary according to the question for which it is being considered. For example, an article that is graded an "X" because of "inapplicability" for one critical question may be considered perfectly relevant for another question and graded I to III. As such, it was possible for a single article to receive a different Class of Evidence grade when addressing a different critical question.

Design 1 represents the strongest possible study design to answer the critical question, which relates to whether the focus was therapeutic, diagnostic, prognostic, or meta-analysis. Subsequent design types (ie, design 2 and design 3) represent weaker study designs, respectively. Articles are then graded on dimensions related to the study's methodological features and execution, including but not limited to randomization processes, blinding, allocation concealment, methods of data collection, outcome measures and their assessment, selection and misclassification biases, sample size, generalizability, data management, analyses, congruence of results and conclusions, and potential for conflicts of interest.

Using a predetermined process that combines the study's design, methodological quality, and applicability to the critical question, 2 methodologists independently assigned a preliminary Class of Evidence grade for each article. Articles with concordant grades from both methodologists received that grade as their final grade. Any discordance in the preliminary grades was adjudicated through discussion, which involved at least 1 additional methodologist, resulting in a final Class of Evidence

DRAFT

assignment (ie, class I, class II, class III, or class X) (Appendix B). Studies identified with significant methodologic limitations and/or ultimately determined to not be applicable to the critical question received a Class of Evidence grade "X" and were not used in formulating recommendations for this policy. However, the content in these articles may have been used to formulate the background and to inform expert consensus in the absence of evidence. Question-specific Classes of Evidence grading may be found in the Evidentiary Table included at the end of this policy.

Translation of Classes of Evidence to Recommendation Levels

Based on the strength of evidence for each critical question, the subcommittee drafted the recommendations and supporting text, synthesizing the evidence using the following guidelines:

Level A recommendations. Generally accepted principles for patient care that reflect a high degree of scientific certainty (eg, based on evidence from 1 or more Class of Evidence I, or multiple Class of Evidence II studies that demonstrate consistent effects or estimates).

Level B recommendations. Recommendations for patient care that may identify a particular strategy or range of strategies that reflect moderate scientific certainty (eg, based on evidence from 1 or more Class of Evidence II studies or multiple Class of Evidence III studies that demonstrate consistent effects or estimates).

Level C recommendations. Recommendations for patient care that are based on evidence from Class of Evidence III studies or, in the absence of adequate published literature, based on expert consensus. In instances where consensus recommendations are made, "consensus" is placed in parentheses at the end of the recommendation.

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as consistency of results, the uncertainty of effect magnitude, and publication bias, among others, might lead to a downgrading of recommendations. When possible, clinically oriented statistics (eg, likelihood ratios [LRs], number needed to treat) are presented to help the reader better understand how the results

DRAFT

may be applied to the individual patient. This can assist the clinician in applying the recommendations to most patients but allow adjustment when applying to patients with extremes of risk (Appendix C).

Evaluation and Review of Recommendations

Once drafted, the policy was distributed for internal review (by members of the entire committee), followed by an external expert review and an open comment period for all ACEP membership. Comments were received during a 60-day open comment period, with notices of the comment period sent electronically to ACEP members, published in *EM Today*, posted on the ACEP website, and sent to other pertinent physician organizations. The responses were used to further refine and enhance this clinical policy, although responses did not imply endorsement. Clinical policies are scheduled for revision every 3 years; however, interim reviews are conducted when technology, methodology, or the practice environment changes significantly.

Application of the Policy

This policy is not intended to be a complete manual on the evaluation and management of patients with suspected appendicitis but rather a focused examination of critical questions that have particular relevance to the current practice of emergency medicine. The potential benefits and harms of implementing recommendations are briefly summarized within each critical question.

It is the goal of the Clinical Policies Committee to provide evidence-based recommendations when the scientific literature provides sufficient quality information to inform recommendations for a critical question. When the medical literature does not contain adequate empirical data to inform a critical question, the members of the Clinical Policies Committee believe that it is equally important to alert emergency physicians to this fact.

This clinical policy is not intended to represent a legal standard of care for emergency physicians. Recommendations offered in this policy are not intended to represent the only diagnostic or management options available to the emergency physician. ACEP recognizes the importance of the

DRAFT

individual physician's judgment and patient preferences. This guideline provides clinical strategies based on medical literature to inform the critical questions addressed in this policy. ACEP funded this clinical policy.

Scope of Application. This guideline is intended for physicians working in EDs.

Inclusion Criteria. This guideline is intended for non-pregnant adult blunt trauma patients.

Exclusion Criteria. This guideline is not intended for pediatric, pregnant, or penetrating trauma patients.

CRITICAL QUESTIONS

1. In adult patients presenting to the emergency department with blunt trauma, does whole-body CT improve clinically important outcomes in hemodynamically stable patients?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. Due to the lack of quality evidence, use clinical judgement and hospital-specific protocols to decide between selective CT and whole-body CT imaging in hemodynamically stable, adult, blunt trauma patients. [Consensus]

Potential Benefit of Implementing the Recommendations:

The spectrum of trauma patients arriving at the emergency department is very broad. Given the equipoise in risks and benefits of whole-body CT among hemodynamically stable trauma patients, using clinical judgment will likely lead to the appropriate resource utilization, minimal radiation exposure, and the best outcome for a given patient.

Potential Harm of Implementing the Recommendations:

DRAFT

Without clear decision-rules, over-use and under-use of whole-body CT in trauma is possible. Over-use would result in additional cost, unnecessary radiation exposure, and potentially false positive findings that require further evaluation and unnecessary risks. Under-use could result in missed diagnoses and delays in diagnosis.

Key words/phrases for literature searches: nonpenetrating wounds, nonpenetrating injuries, blunt trauma, blunt injuries, contusions, bruise, beating injuries, whole-body scan, pan scan, computed tomography, CT, whole-body imaging, x-ray computed tomography, hemodynamics, stable hemodynamics, hemodynamically stable, trauma centers, emergency departments, emergency wards, emergency rooms, emergency services and variations and combinations of the key words/phrases. Searches included January 2003 to the search dates of July 6, 2020, and May 20, 2021.

Study Selection:

Eight hundred and thirteen articles were identified in the searches. Forty-two articles were identified from the search results for further review. After grading for methodologic rigor, 0 Class I studies, 0 Class II studies, and 0 Class III studies were included for this question.

Main Text

There were 42 articles identified to help answer the question, however they were all deemed to be either low relevance regarding this critical question or low quality as assessed by the methodologists. No articles were graded as level 3 or higher. Nevertheless, there are insights that may be relevant to emergency physicians.

Whole-body CT has become commonplace in the evaluation of trauma patients.[8] There are several meta-analyses that demonstrate a mortality benefit for patients who meet "trauma activation criteria" or the need for a trauma team evaluation.[9-11] In addition, multiple studies also report the benefit of identifying unexpected findings and change in management.[12,13] Within this cohort that meet trauma

DRAFT

activation criteria, the injury severity can vary tremendously and it is possible that the benefits are driven by the select cohort of more severely injured patients, whereas this question focuses on whole-body CT in the hemodynamically stable patient population.

REACT-2, a large, multicenter randomized trial by Sierink et al[14]concluded that whole-body CT compared to selective imaging did not demonstrate a difference in mortality. This widely cited study was excluded from consideration because it provided only indirect evidence to answer our question and had important methodologic limitations. We considered this study indirect evidence as it studied a mixed population of hemodynamically unstable and stable patients. The important methodologic limitations resulting in additional downgrading of this study to an X included: randomization without concealment, inability to blind physicians and patients, and approximately 15% of the patients were excluded after randomization without a clearly reported reason.

The additional studies evaluated and graded X did not contribute substantially to our recommendation.[15-17] All demonstrated that injuries of uncertain clinical significance were found by whole-body CT. Some authors concluded that these injuries were not impactful, while others concluded that that they were important.[15-17]

Brief Summary

In summary, the yield of clinically important outcomes from whole-body CT among hemodynamically stable trauma patients is low. However, unexpected significant injuries and emergency interventions are occasionally identified. Whether early identification and intervention for these injuries results in improved clinically important outcomes remains unclear. Consequently, we recommend using clinical judgement and local protocols in the use of whole-body CT versus selective CT in hemodynamically stable blunt trauma patients.

Future Research

A large high quality randomized trial comparing whole-body CT to selective CT for hemodynamically stable trauma patients with a reliable exam using a clear, widely accepted definition

DRAFT

of a clinically important injury, is necessary to answer this question and help guide emergency physicians on best practices in CT imaging of trauma patients.

2. In geriatric patients presenting to the emergency department with blunt trauma, does age-based, differential trauma triage reduce morbidity and/or mortality?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations.

Emergency physicians should factor age (greater than 65 years) into triage of older adult trauma patients as they have increased morbidity and mortality, compared with similarly injured adults.

Level C recommendations. None specified.

Potential Benefit of Implementing the Recommendations

Incorporating age into trauma triage for older adult blunt trauma patients would enhance early identification of at-risk patients. This could lead to more timely diagnostic evaluation and therapeutic interventions in this time-dependent disease with resultant improved outcomes.

Potential Harm of Implementing the Recommendations

Incorporating age into trauma triage for older adult blunt trauma patients may decrease the specificity and increase resource utilization without consequent improvement of morbidity and mortality. Additionally, unnecessary diagnostic evaluation and treatment may occur when an older patient is incorrectly triaged to be high risk.

<u>Key words/phrases for literature searches:</u>

nonpenetrating wounds, nonpenetrating injuries, blunt trauma, blunt injuries, contusions, bruise, beating injuries, geriatric, aged, older adult, elder, elderly, gerontology, triage, differential triage, age-

DRAFT

based triage, morbidity, mortality, death, trauma centers, emergency departments, emergency wards, emergency rooms, emergency services and variations and combinations of the key words/phrases. Searches included January 2003 to the search dates of July 6, 2020 and May 20, 2021.

Study Selection:

Eight hundred and sixteen articles were identified in the searches. Seventy-four articles were identified from the search results for further review. After grading for methodologic rigor, 0 Class I studies, 0 Class II studies, and 6 Class III studies were included for this question.

Main Text

Age is a risk factor for mortality in trauma patients.[18-20]The older population has decreased physiologic reserve compared with their younger counterparts. Additionally, immune function is impaired, and older adults have unique alterations in pulmonary function and cardiovascular response to injury and shock. Polypharmacy is common, and many older patients are on anticoagulation. Early identification of an at-risk population is the goal of trauma triage as there is evidence that improved outcomes occur when early intensive monitoring and aggressive fluid resuscitation is performed.[21,22]

The National Guidelines for the Field Triage of Injured patients in 2021: Recommendations of the National Expert Panel on Field Triage[23] uses a criterion of age greater than 65 years with a systolic blood pressure (SBP) less than 110 mmHg or HR greater than SBP for recommending medical care in a specialized trauma centers. This is changed from prior guidelines in which age was considered but there were the same recommendations for SBP as there were for all adults. For older adults, the benefit of specialized tertiary trauma centers is less clear than for children or other adult patients.

The effectiveness of field triage is commonly looked at by the degree of over- and under-triage. Under-triage has been shown to be the highest in older adults and half of seriously injured adults are treated in non-trauma centers in the United States.[24-27] This under-triage suggests that the older adult is not consistently being taken to hospitals best equipped to meet their needs. This is not unique to the United States. Destination non-compliance led to poorer outcomes for older trauma patients. It has been

DRAFT

shown that not only were older adults under triaged compared to their younger counterparts, but a larger proportion of the in-hospital deaths occur in centers with no major trauma services compared to major trauma centers.[28]

In a Class III, retrospective cohort study by Lim et al,[29] the mortality of older adult, even when risk stratified, was increased by 2.7% for each year of life. Additionally, in a Class III study by Ahmed[19], the authors evaluated patients 65 years and older who look normal after a fall from ground level at home. In this study of 40,800 patients 938 (2.3%) patients died in the hospital. and logistic regression showed older age was associated with a higher risk of in-hospital mortality.

The additional Class III studies included for review here are also retrospective reviews of trauma databases.[30-33] They look at modifying the criteria, for adult trauma triage based on age to determine either the effects on morbidity and mortality or the criteria's ability to predict morbidity and mortality. As we know that early intervention in severely injured trauma improves morbidity and mortality, these studies can provide only indirect evidence of benefit or harm.

The Class III study by Ichwan[30] defined patients aged 70 years or older as "geriatric." Based on age, this study modified multiple elements of the trauma triage criteria to assess a revised older adult trauma triage. Of 101,577 patients, 33,379 (33%) were aged ≥ 70 years old. This cohort of older adults were less severely injured, with only 13% having an Injury Severity Score (ISS) greater than 15 indicating moderate to severe injury, compared with 29% of younger adults. They were also less likely to have an ICU stay (17%versus 28%) and an operating room procedure within 48 hours (13% versus 29%). Interestingly, despite the older group being less injured (lower ISS, fewer ICU and OR admissions) the mortality between the 2 groups was similar with 6.8% of older adults and 9.3% of younger adults dying in the ED or hospital. Modification of the adult trauma triage as described improved sensitivity from 61% (95% CI 60%, 62%) to 93% (95% CI 92%, 94%). There was a concomitant modest decrease in specificity from 61% (95% CI 61%, 62%) to 49% (95% CI 48%, 49%). The improvement in the test performance of this proposed "geriatric" trauma triage compared to non-age-based criteria is demonstrated in the change in likelihood ratios, which were calculated based on the

DRAFT

study's data. With age-based triage the positive likelihood ratio improved from 1.6 to 1.8 and the negative likelihood ratio improved more dramatically from 0.8 to 0.1. This suggests the geriatric criteria improve our ability to identify older patients with serious injuries, need for operative or ICU care, or death.

In another Class III study, Brown[31] evaluated the performance of substituting an SBP of less than 110 mm Hg for the current SBP of less than 90 mm Hg criterion. The primary outcome was under- and over-triage as defined by the ISS, which is an established surrogate for clinical outcome for trauma activation criteria. In this 12-year study 428,828 older adults were identified, they found that substituting an SBP of less than 110 mm Hg for the current SBP of less than 90 mm Hg in older patients achieves a reduction in 4.4% under-triage with a 4.3 % increase in over-triage. Regarding mortality, the older patients with SBP of 90 mm Hg to 109 mm Hg had an odds of mortality similar to older patients with SBP of less than 90 mm Hg (adjusted odds ratio, 1.03; 95% confidence interval, 0.88–1.20; $p = 0.71$).

Anantha et al[32] evaluated whether a geriatric-specific (age $\geq$ 65 years) triage protocol appropriately identified severely injured (ISS>15) trauma patients. The modified criteria for trauma activation included: SBP less than 110 mm Hg (rather than 90 mm Hg), HR less than 50 or greater than 100 bpm, any MVC or fall from any height. They report that 61% of the severely injured older patients were under-triaged despite the geriatric-specific trauma triage protocol. Fortunately, mortality in the under-triaged group was 5% vs the 31% in the correctly identified group. They concluded that despite geriatric triage protocols, older adults remain under-triaged as measured by ISS, but that age-based protocols do capture the highest risk patients.

In 2018, Hung et al[33] published the performance of the activation criteria for the trauma system in Hong Kong where the trauma team activation (TTA) criteria have been specifically modified for older adults and included risk factors such as rib fractures. In this 10-year cohort study (2006 to 2015), 2218 patients over the age of 55 were identified. The 30-day mortality was 7.5% for those aged 55–70 and 17.7% for those above 70 years of age. The under-triage rate was 59% for age 55–70, and 69.1% for those aged above 70. The sensitivity of TTA in identifying severe outcomes decreases as the age

DRAFT

increases. This study reinforces that age is an important triage criteria and possibly specific criteria should be developed for patients older than 70 years of age.

Brief Summary

With advancing age in adult blunt trauma patients, standard trauma triage criteria under perform in predicting severity of illness and outcomes. Age based trauma triage improves the criteria's ability to prevent under-triage and limit over-triage. As there is evidence of under- and over-triage's impact on morbidity and mortality, there is indirect evidence supporting age-based trauma triage to improve patient outcomes.

Future Research

The definition of geriatric is still variable in research (ranging from an age cutoff of 55 years to 70 years). Future research should focus on an acceptable definition of the older trauma patient and determine subpopulations who will benefit from triage to major trauma centers., The direct effect on morbidity, mortality, resource utilization, and the effectiveness of trauma system implementation should be prospectively assessed.

Further work incorporating both quantitative and qualitative methods will be required to better understand factors to address how to manage the older trauma patient and identify appropriate remedies and their implementation. This should focus on geographic differences, patient preferences, EMS provider training and preferences, structure of the EMS system, and local facility factors.

3. In adult patients presenting to the emergency department with blunt trauma, what is the ideal blood product ratio to reduce morbidity and /or mortality in patients requiring transfusion?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations

DRAFT

In adult patients presenting to the emergency department with blunt trauma, use a fresh frozen plasma (FFP): platelet: packed red blood cells (PRBC) ratio from1:1:1 to1:1:1.5 to reduce 24-hour mortality without increasing morbidity.

Level C recommendations. None specified.

Potential Benefit of Implementing the Recommendations

- Administration of recommended blood product ratios within 6 hours of resuscitation may decrease 24-hour mortality, exsanguination and hypothermia.
- The identification of optimal goal of blood product ratio will allow trauma centers and blood banks to protocolize massive transfusion protocols (MTP) to improve consistency of high-quality care.

Potential Harm of Implementing the Recommendations

Increased FFP and platelet ratios may create new needs and stress on the existing limited blood product supply.

Key words/phrases for literature searches:

nonpenetrating wounds, nonpenetrating injuries, blunt trauma, blunt injuries, contusions, bruise, beating injuries, blood transfusion, blood product, blood product ratio, leukocyte transfusion, blood platelet transfusion, massive transfusion protocol, autologous blood transfusion, erythrocyte transfusion, morbidity, mortality, death, trauma centers, emergency departments, emergency wards, emergency rooms, emergency services and variations and combinations of the key words/phrases. Searches included January 2003 to the search dates of July 6, 2020 and May 20, 2021.

Study Selection:

DRAFT

Eight hundred and six were identified in the searches. Two-hundred and ninety articles were identified from the search results for further review. After grading for methodologic rigor, 0 Class I studies, 0 Class II studies, and 5 Class III studies were included for this question.

Text

Hemorrhage is a leading cause of death in blunt trauma. Massive Transfusion Protocols (MTPs) have been utilized to prevent mortality from hemorrhage. Massive transfusion is defined as >10 units of packed red cells over 24 hours.[34-45] Massive transfusion is an independent risk factor for mortality and morbidity and is associated with acute coagulopathy and severe immunologic responses[46-49] leading to Multiorgan Failure (MOF) and Acute Respiratory Distress Syndrome (ARDS).[50-55] Acute coagulopathy is also a complication in 2% to 34% of blunt trauma patients receiving MTP, and is an independent factor associated with mortality.[47,56,57] Ratios of blood product, specifically ratios of fresh frozen plasma (FFP) and platelets to packed red blood cells (PRBC) (FFP: platelets: PRBC), administration in MTP has evolved over time. Additionally, damage control surgery has changed the utilization of blood products and in recent times, FFP: platelet: PRBC ratios of 1:1:1 are frequently employed in clinical practice based on US military experience.[58-60] Given the complex nature of MTPs, the proportion of FFP: platelets: PRBC is a topic of interest and varying ratios are employed and recommended by different societies.[61] We performed a comprehensive review of the medical literature comparing adult trauma patients requiring transfusions in blunt trauma patients. The literature review yielded 806 publications. Articles were excluded due to poor study design, incorrect population, incorrect intervention, or incorrect outcomes. Of the 25 remaining publications, 20 were deemed to be low relevance with regard to the critical question or low methodologic as assessed by the methodologists and 5 level III studies are included in this policy.[62-66]

In order to understand the methods and findings of these studies, a point of mathematical nomenclature used in this literature must be clarified. When discussing ratios of units of FFP or platelets to PRBC, a ratio of 1:1 is greater than 1:2, just as 1 divided by1 is greater than 1 divided by 2. This

DRAFT

applies to the nomenclature for multiple ratios as well. Hence a ratio of FFP: platelet: PRBC of 1:1:1 is greater than 1:1:1.5 which is greater than 1:1:2.

The first study by Brown et al[62] in 2012 was a multicenter prospective cohort study. In this study, a high FFP/PRBC (≥1:1.5) ratio was analyzed as a time dependent variable and at 6 hours was independently associated with reduction in 6, 12 and 24-hour mortality and a high FFP/PRBC (≥1:1.5) ratio at 12 hours was independently associated with a mortality reduction at 12 hours and 24 hours, and a high ratio at 24 hours was associated with a decline in mortality at 24 hours. Similarly, high platelet/PRBC (≥1:1.5) ratio was associated with an independent reduction in mortality.

A high ratio of FFP/PRBC or platelet/PRBC at 6 and 12 hours did not increase the risk of developing MOF, nosocomial infection (NI), or ARDS during admission. This study showed that early resuscitation using high FFP/PRBC and platelet/PRBC ratios leads to reduced mortality at 6 hours and throughout the first 24 hours from injury. When time-dependent analysis was performed, an increasing FFP/PRBC and platelet/PRBC ratio prevents early death from hemorrhage.[62]

The study by Reynolds et al[63] was also a multicenter prospective cohort study of 1961 patients and it suggests that even in those patients requiring massive transfusions who received a high FFP/PRBC transfusion ratio, a temperature lower than 34 C^{o} was not a significant independent risk factor for mortality (OR, 1.8; 95% CI, 0.9, 33.5) as opposed to low FFP/PRBC ratio group with more than a two-fold higher risk of mortality (OR, 2.2; 95% CI, 1.1±4.2). Hypothermia is common in temperature induced coagulopathy (TIC) patients and is associated with a greater independent risk of mortality of more than 85% in patients requiring MTP. This study suggests that effect of hypothermia can be controlled by the means of adequate resuscitation with high FFP/RBC ratio and may be the underlying mechanism behind mortality benefit in high ratio group.

Hagiwara et al[64] conducted a retrospective observational study across 15 sites in Japan with 189 blunt trauma patients and propensity score matching was performed to compare the two groups (FFP: PRBC ratio ≥1 within the first 6 h and FFP: PRBC ratio <1 within the first 6 h). Patients with an FFP:

DRAFT

PRBC ratio ≥1 within the first 6h had significantly better survival, with an unadjusted hazard ratio of 0.44 and an adjusted hazard ratio of 0.29. Blunt trauma patients transfused with an FFP: RBC ratio ≥ 1 within the first 6 h after admission had an unadjusted hazard ratio of about 0.4 (95% CI 0.25, 0.74) and an adjusted hazard ratio of 0.29 (95% CI 0.14, 0.62). This study suggested a benefit to an early administration of FFP in severe blunt trauma patients requiring blood transfusion.

Holcomb et al[65] conducted the Pragmatic Randomized Optimal Platelet and Plasma Ratios (PROPPR) Randomized Clinical Trial which was a pragmatic, phase 3, multisite, randomized clinical trial of 680 severely injured patients across 12 level I trauma centers. In this trial, administration of FFP, platelets, PRBC in a 1:1:1 ratio compared with a 1:1:2 ratio had no significant differences in 24 hours mortality and 30-day mortality. However, higher rate of hemostasis in the 1:1:1 group and fewer deaths in 24 hours due to exsanguination.

The last study that met inclusion was Sperry et al,[66] which was a multicenter prospective cohort study evaluating clinical outcomes in blunt injured adults with hemorrhagic shock patients who received an FFP: PRBC transfusion ratio ≥1:1.5 compared to patients who received <1: 1.5. Patient receiving greater ratios of FFP to PRBC had a significant lower risk of in-hospital mortality following massive transfusion which was most pertinent for mortality within the first 48 hours. Cox proportional hazard regression revealed that receiving a high ratio of FFP: PRBC was independently associated with lower mortality when adjusted for likely confounders, HR 0.48, 95% CI 0.3, 0.8). This study showed a dose-response relationship for mortality such that as FFP: PRBC ratio became smaller (less FFP relative to PRBCs) the patients who received minimal or no FFP had the highest early 24-hour mortality.

In adult patients presenting to the emergency department with blunt trauma, an FFP: platelet: PRBC ratio between 1:1:1 and 1:1:1.5 is ideal to reduce 24-hour mortality. This ratio also decreases exsanguination and FFP: PRBC ratios ≥1:1.5 reduces risk of death by hypothermia in the first 24 hours of resuscitation. FFP should be given within first 6 hours of resuscitation with goal of FFP: RBC ≥1:1.5.

DRAFT

Brief Summary

Literature has recently supported use of 1:1:1 FFP: platelet: PRBC ratio. There is no significant difference in morbidity in either 1:1:1 or 1:1:1.5 group.

Future Research

Laboratory guided resuscitation has been shown to have equivocal results with 1:1:1 FFP: Platelet: RBC ratio with less of utilization of non PRBC blood products, which may not universally available. Future trials to be designed with ≥1:1:1.5 FFP: Platelet: RBC ratio, whole-blood, and laboratory guided resuscitation.

4. In adult patients presenting to the emergency department with blunt trauma, does resuscitative endovascular balloon occlusion of the aorta (REBOA) reduce morbidity and/or mortality in arrested or peri-arrest patients compared to ED thoracotomy?

Patient Management Recommendations

Level A recommendations. None specified.

Level B recommendations.

In arrested or peri-arrest adult, blunt trauma patients, do not routinely use REBOA over ED thoracotomy.

Level C recommendations. None specified.

Potential Benefit of Implementing the Recommendations

Prevention of potential harms of REBOA if no benefit

Potential Harm of Implementing the Recommendations

DRAFT

Select, as of yet undefined, populations may benefit from REBOA.

Key words/phrases for literature searches:

nonpenetrating wounds, nonpenetrating injuries, blunt trauma, blunt injuries, contusions, bruise, beating injuries, REBOA, Resuscitative endovascular balloon occlusion of the aorta, Cardiac Arrest, Thoracotomy, cardiopulmonary arrest, asystoles, morbidity, mortality, death, trauma centers, emergency departments, emergency wards, emergency rooms, emergency services and variations and combinations of the key words/phrases. Searches included January 2003 to the search dates of July 6, 2020 and May 20, 2021.

Study Selection:

Eight hundred articles were identified in the searches. One hundred and sixty-eight articles were identified from the search results for further review; 30 articles were sent to the methodologists for grading. After grading for methodologic rigor, 0 Class I studies, 0 Class II studies, and 2 Class III studies were included for this question.

Text

Traumatic arrest from non-compressible torso hemorrhage due to blunt trauma has a high mortality.[67,68]Hemorrhage control using ED resuscitative thoracotomy (RT) results in low survival rates in arrested or peri-arrest blunt trauma patients.[69] Resuscitative endovascular balloon occlusion of the aorta (REBOA) has been proposed as an alternative to RT. This technique serves as a method of temporary hemorrhage control as a bridge to definitive treatment. It has seen application in both military and civilian trauma care.[70]The procedure uses common femoral artery catheter access to inflate an occlusive balloon at different zones of the aorta. The aorta can be divided into three zones; zone 1 is from the left subclavian artery to the celiac trunk, zone 2 is below the celiac and suprarenal, and zone 3

DRAFT

is infrarenal to the aortic bifurcation. REBOA is deployed in zone 1 for severe intra-abdominal or retroperitoneal hemorrhage, whereas zone 3 is used for pelvic hemorrhage.[71]

In the early observational evaluation of REBOA in trauma, its use was associated with improved mortality.[69,72-86] However, these studies' design and execution commonly suffered survival bias and bias by indication, as the patients undergoing RT typically had cardiac arrest in these cohorts.[70] These studies often also included penetrating and blunt trauma patients, making the determination of value suspect in blunt trauma patients specifically. Due to these confounders, it is unclear if these non-randomized, observational studies compared two similar populations and were ultimately graded X in our evaluation.

We performed a comprehensive review of the medical literature comparing REBOA to RT in arrested and peri-arrest blunt trauma patients. The literature review yielded 800 publications. Articles were excluded due to poor study design, incorrect population, incorrect intervention, or incorrect outcomes. Of the 32 remaining publications, 30 were excluded using our systematic grading criteria and 2 level III studies are included in this policy.[67,68]

In the first study by Aso et al,[68] the investigators performed a retrospective review of the National Inpatient Database in Japan from 2010 – 2014. Two hundred and fifty-nine trauma patients, aged >15 years old, with uncontrolled hemorrhagic shock were included in their analysis. Penetrating thoracic trauma patients were excluded. Importantly, the authors used propensity scoring to address the potential biases of prior observational studies. The primary outcome was mortality and secondary outcomes included ventilator-free days, total hospitalization costs, total amount of fluid resuscitation and total transfusion within day 1. Using the propensity score-adjusted analysis, this study found no benefit with REBOA versus RT in the primary outcome (hazard ratio 0.94; 95% CI, 0.60-1.48), nor in the secondary outcomes. The author's concluded that in-hospital outcomes were not significantly different between REBOA and RT in trauma patients with uncontrolled hemorrhage.[68]

DRAFT

The second study graded level III, by Joseph et al,[67] was conducted in the US. The authors performed a case-control retrospective analysis of the 2015-2016 American College of Surgeons Trauma Quality Improvement Program (ACS-TQIP) dataset using an advanced propensity score matching process. This larger study evaluated 420 total patients, of which 140 REBOA patients (cases) were matched 1:2 with 280 non-REBOA patients (controls). The outcome measures were rates of mortality and complications. The mortality was higher in the REBOA group (35.7% vs 18.9%, $p = 0.01$) and specific complications, acute kidney injury and lower extremity amputation, were also higher, (10.7% vs 3.2%, $p = 0.02$) and (3.6% vs 0.7%, $p = 0.04$) respectively. Application of this study is limited by the fact that it included penetrating trauma, albeit 92.1% were blunt trauma patients. The authors concluded that REBOA was associated with higher mortality, acute kidney injury and lower leg amputation rates.[67]

In addition to the level III evidence that does not show a benefit from REBOA in this patient population, REBOA requires a multi-disciplinary team with structured protocols, policies, education and quality assessments. The vast majority of trauma centers in the US do not have REBOA capabilities, much less the majority of EDs.[70] Given that there is no demonstrated benefit, and may be harm, it is unlikely to be cost effective to stand up these programs for use in this broadly defined blunt trauma population of patients. There are existing REBOA programs that will continue to refine a potential patient population that benefits from this intervention. Our recommendations do not apply to a military setting or to penetrating trauma patients.

<u>Summary</u>

There are limitations, such as the inclusion of some penetrating trauma patients, to the highest quality literature available to determine if there is benefit of REBOA versus RT. The best available evidence concludes that REBOA is associated with no benefit and potential harm.[67,68] Consequently, we do not recommend its routine use in arrested and peri-arrest adult blunt trauma patients.

<u>Future Research</u>

DRAFT

At the time of this writing, there are ongoing trials of REBOA in other disease states including post-partem hemorrhage and non-traumatic out-of-hospital cardiac arrest. These studies combined with further insights from sub-groups of blunt trauma patients may give insight into a blunt trauma population that may benefit. A randomized clinical trial of REBOA in a sub-population of arrested and peri-arrest adult blunt trauma patients would be necessary to recommend its routine use.

REFERENCES

1. Diercks DB, Mehrotra A, Nazarian DJ, et al. Clinical policy: critical issues in the evaluation of adult patients presenting to the emergency department with acute blunt abdominal trauma. *Ann Emerg Med*. 2011;57(4):387-404. doi:10.1016/j.annemergmed.2011.01.013
2. US Centers for Disease Control and Prevention. Web-based Injury Statistics Query and Reporting System (WISQARS). 2017. Available at: https://www.cdc.gov/injury/wisqars/index.html. Accessed September 9, 2019.
3. Rhee P, Joseph B, Pandit V, Aziz H, Vercruysse G, Kulvatunyou N, et al. Increasing trauma deaths in the United States. *Ann Surg*. 2014;260(1):13-21.
4. Beeson MS, Ankel F, Bhat R, et al. The 2019 Model of the Clinical Practice of Emergency Medicine. *J Emerg Med*. 2020;59(1):96-120. doi:10.1016/j.jemermed.2020.03.018
5. Leenellett E, Rieves A. Occult Abdominal Trauma. *Emerg Med Clin North Am*. 2021;39(4):795-806. doi:10.1016/j.emc.2021.07.009
6. Roberts GJ, Jacobson LE, Amaral MM, et al. Cross-sectional imaging of the torso reveals occult injuries in asymptomatic blunt trauma patients. *World J Emerg Surg*. 2020;15:5. Published 2020 Jan 9. doi:10.1186/s13017-019-0287-5
7. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
8. Jeffrey Y. Shyu, MD, MPHa
   Shyu JY, Khurana B, Soto JA, et al. Major blunt trauma. ACR Appropriateness Criteria, 2019. Accessed January 18, 2024. https://acsearch.acr.org/docs/3102405/Narrative/
9. Arruzza E, Chau M, Dizon J. Systematic review and meta-analysis of whole-body computed tomography compared to conventional radiological procedures of trauma patients. *Eur J Radiol*. 2020;129:109099. doi:10.1016/j.ejrad.2020.109099
10. Chidambaram S, Goh EL, Khan MA. A meta-analysis of the efficacy of whole-body computed tomography imaging in the management of trauma and injury. *Injury*. 2017;48(8):1784-1793. doi:10.1016/j.injury.2017.06.003
11. Gunn ML, Kool DR, Lehnert BE. Improving Outcomes in the Patient with Polytrauma: A Review of the Role of Whole-Body Computed Tomography. *Radiol Clin North Am*. 2015;53(4):639-vii. doi:10.1016/j.rcl.2015.02.006
12. Self ML, Blake AM, Whitley M, Nadalo L, Dunn E. The benefit of routine thoracic, abdominal, and pelvic computed tomography to evaluate trauma patients with closed head injuries. *Am J Surg*. 2003;186(6):609-614. doi:10.1016/j.amjsurg.2003.08.003
13. Salim A, Sangthong B, Martin M, Brown C, Plurad D, Demetriades D. Whole body imaging in blunt multisystem trauma patients without obvious signs of injury: results

DRAFT

of a prospective study. *Arch Surg*. 2006;141(5):468-475. doi:10.1001/archsurg.141.5.468
14. Sierink JC, Treskes K, Edwards MJ, et al. Immediate total-body CT scanning versus conventional imaging and selective CT scanning in patients with severe trauma (REACT-2): a randomised controlled trial. *Lancet*. 2016;388(10045):673-683. doi:10.1016/S0140-6736(16)30932-1
15. Moussavi N, Ghani H, Davoodabadi A, et al. Routine versus selective chest and abdominopelvic CT-scan in conscious blunt trauma patients: a randomized controlled study. *Eur J Trauma Emerg Surg*. 2018;44(1):9-14. doi:10.1007/s00068-017-0842-2
16. Roberts J, Watts S, Klim S, Ritchie P, Kelly AM. Yield of serious axial injury from pan scans after blunt trauma in haemodynamically stable low-risk trauma patients. *Emerg Med Australas*. 2019;31(3):399-404. doi:10.1111/1742-6723.13174
17. Sampson MA, Colquhoun KB, Hennessy NL. Computed tomography whole body imaging in multi-trauma: 7 years experience. *Clin Radiol*. 2006;61(4):365-369. doi:10.1016/j.crad.2005.12.009
18. Keller JM, Sciadini MF, Sinclair E, O'Toole RV. Geriatric trauma: demographics, injuries, and mortality. *J Orthop Trauma*. 2012;26(9):e161-e165. doi:10.1097/BOT.0b013e3182324460
19. Ahmed N, Greenberg P. Early risk stratification of in hospital mortality following a ground level fall in geriatric patients with normal physiological parameters. *Am J Emerg Med*. 2020;38(12):2531-2535. doi:10.1016/j.ajem.2019.12.031
20. Meldon SW, Reilly M, Drew BL, Mancuso C, Fallon W Jr. Trauma in the very elderly: a community-based study of outcomes at trauma and nontrauma centers. *J Trauma*. 2002;52(1):79-84. doi:10.1097/00005373-200201000-00014
21. Demetriades D, Karaiskakis M, Velmahos G, et al. Effect on outcome of early intensive management of geriatric trauma patients. *Br J Surg*. 2002;89(10):1319-1322. doi:10.1046/j.1365-2168.2002.02210.x
22. Caterino JM, Valasek T, Werman HA. Identification of an age cutoff for increased mortality in patients with elderly trauma. *Am J Emerg Med*. 2010;28(2):151-158. doi:10.1016/j.ajem.2008.10.027
23. Newgard CD, Fischer PE, Gestring M, et al. National guideline for the field triage of injured patients: Recommendations of the National Expert Panel on Field Triage, 2021. *J Trauma Acute Care Surg*. 2022;93(2):e49-e60. doi:10.1097/TA.0000000000003627
24. Newgard CD Zive D Holmes JF Bulger EM Staudenmayer K Liao M, et al. A multisite assessment of the American College of Surgeons Committee on Trauma field triage decision scheme for identifying seriously injured children and adults. *J Am Coll Surg*. 2011;213(6):709–721.
25. Newgard CD Fu R Zive D Rea T Malveau S Daya M, et al. Prospective validation of the national field triage guidelines for identifying seriously injured persons. *J Am Coll Surg*. 2016;222(2):146–158.
26. Garwe T Stewart K Stoner J Newgard CD Scott M Zhang Y, et al. . Out-of-hospital and inter-hospital under-triage to designated tertiary trauma centers among injured older adults: a 10-year statewide geospatial-adjusted analysis. *Prehosp Emerg Care*. 2017;21(6):734–743.
27. Uribe-Leitz T Jarman MP Sturgeon DJ Harlow AF Lipsitz SR Cooper Z, et al. National study of triage and access to trauma centers for older adults. *Ann Emerg Med.* 2020;75(2):125–135.
28. Cox S, Morrison C, Cameron P, Smith K. Advancing age and trauma: triage destination compliance and mortality in Victoria, Australia. *Injury*. 2014;45(9):1312-1319. doi:10.1016/j.injury.2014.02.028

29. Lim YD, Lee DH, Lee BK, Cho YS, Choi G. Validity of the Korean Triage and Acuity Scale for predicting 30-day mortality due to severe trauma: a retrospective single-center study. *Eur J Trauma Emerg Surg*. 2020;46(4):895-901. doi:10.1007/s00068-018-1048-y

30. Ichwan B, Darbha S, Shah MN, et al. Geriatric-specific triage criteria are more sensitive than standard adult criteria in identifying need for trauma center care in injured older adults. *Ann Emerg Med*. 2015;65(1):92-100.e3. doi:10.1016/j.annemergmed.2014.04.019
31. Brown JB, Gestring ML, Forsythe RM, et al. Systolic blood pressure criteria in the National Trauma Triage Protocol for geriatric trauma: 110 is the new 90. *J Trauma Acute Care Surg*. 2015;78(2):352-359. doi:10.1097/TA.0000000000000523
32. Anantha RV, Painter MD, Diaz-Garelli F, et al. Undertriage Despite Use of Geriatric-Specific Trauma Team Activation Guidelines: Who Are We Missing?. *Am Surg*. 2021;87(3):419-426. doi:10.1177/0003134820951450
33. Hung KK, Yeung JHH, Cheung CSK, et al. Trauma team activation criteria and outcomes of geriatric trauma: 10 year single centre cohort study. *Am J Emerg Med*. 2019;37(3):450-456. doi:10.1016/j.ajem.2018.06.011
34. Barbosa RR, Rowell SE, Sambasivan CN, et al. A predictive model for mortality in massively transfused trauma patients. *J Trauma*. 2011;71(2 Suppl 3):S370-S374. doi:10.1097/TA.0b013e318227f18f
35. Chang R, Kerby JD, Kalkwarf KJ, et al. Earlier time to hemostasis is associated with decreased mortality and rate of complications: Results from the Pragmatic Randomized Optimal Platelet and Plasma Ratio trial. *J Trauma Acute Care Surg*. 2019;87(2):342-349. doi:10.1097/TA.0000000000002263
36. Falcone RE, Fried SJ, Zeeb P, Satiani B. Rapid volume replacement with warmed blood and fluids. *Angiology*. 1989;40(11):964-969. doi:10.1177/000331978904001105
37. Faringer PD, Mullins RJ, Johnson RL, Trunkey DD. Blood component supplementation during massive transfusion of AS-1 red cells in trauma patients. *J Trauma*. 1993;34(4):481-487. doi:10.1097/00005373-199304000-00002
38. Farion KJ, McLellan BA, Boulanger BR, Szalai JP. Changes in red cell transfusion practice among adult trauma victims. *J Trauma*. 1998;44(4):583-587. doi:10.1097/00005373-199804000-00004
39. Givergis R, Munnangi S, Fayaz M Fomani K, Boutin A, Zapata LC, Angus LG. Evaluation of massive transfusion protocol practices by type of trauma at a level I trauma center. *Chin J Traumatol*. 2018;21(5):261-266. doi:10.1016/j.cjtee.2018.01.005
40. Murry JS, Zaw AA, Hoang DM, et al. Activation of Massive Transfusion for Elderly Trauma Patients. *Am Surg*. 2015;81(10):945-949.
41. Riskin DJ, Tsai TC, Riskin L, et al. Massive transfusion protocols: the role of aggressive resuscitation versus product ratio in mortality reduction. *J Am Coll Surg*. 2009;209(2):198-205. doi:10.1016/j.jamcollsurg.2009.04.016
42. Sisak K, Manolis M, Hardy BM, Enninghorst N, Bendinelli C, Balogh ZJ. Acute transfusion practice during trauma resuscitation: who, when, where and why?. *Injury*. 2013;44(5):581-586. doi:10.1016/j.injury.2012.08.031
43. Sisak K, Manolis M, Hardy BM, Enninghorst N, Balogh ZJ. Epidemiology of acute transfusions in major orthopaedic trauma. *J Orthop Trauma*. 2013;27(7):413-418. doi:10.1097/BOT.0b013e31827d7f30
44. Stevens WT, Morse BC, Bernard A, et al. Incompatible type A plasma transfusion in patients requiring massive transfusion protocol: Outcomes of an Eastern Association

for the Surgery of Trauma multicenter study. *J Trauma Acute Care Surg*. 2017;83(1):25-29. doi:10.1097/TA.0000000000001532
45. Weinberg JA, McGwin G Jr, Marques MB, et al. Transfusions in the less severely injured: does age of transfused blood affect outcomes?. *J Trauma*. 2008;65(4):794-798. doi:10.1097/TA.0b013e318184aa11
46. Bochicchio GV, Napolitano L, Joshi M, Bochicchio K, Meyer W, Scalea TM. Outcome analysis of blood product transfusion in trauma patients: a prospective, risk-adjusted study. *World J Surg*. 2008;32(10):2185-2189. doi:10.1007/s00268-008-9655-0
47. Akbari E, Safari S, Hatamabadi H. The effect of fibrinogen concentrate and fresh frozen plasma on the outcome of patients with acute traumatic coagulopathy: A quasi-experimental study. *Am J Emerg Med*. 2018;36(11):1947-1950. doi:10.1016/j.ajem.2018.02.018
48. Dunne JR, Malone DL, Tracy JK, Napolitano LM. Allogenic blood transfusion in the first 24 hours after trauma is associated with increased systemic inflammatory response syndrome (SIRS) and death. *Surg Infect (Larchmt)*. 2004;5(4):395-404. doi:10.1089/sur.2004.5.395
49. Powell EK, Hinckley WR, Gottula A, Hart KW, Lindsell CJ, McMullan JT. Shorter times to packed red blood cell transfusion are associated with decreased risk of death in traumatically injured patients. *J Trauma Acute Care Surg*. 2016;81(3):458-462. doi:10.1097/TA.0000000000001078
50. Charles A, Shaikh AA, Walters M, Huehl S, Pomerantz R. Blood transfusion is an independent predictor of mortality after blunt trauma. *Am Surg*. 2007;73(1):1-5. doi:10.1177/000313480707300101
51. Croce MA, Tolley EA, Claridge JA, Fabian TC. Transfusions result in pulmonary morbidity and death after a moderate degree of injury. *J Trauma*. 2005;59(1):19-24. doi:10.1097/01.ta.0000171459.21450.dc
52. Mahambrey TD, Fowler RA, Pinto R, et al. Early massive transfusion in trauma patients: Canadian single-centre retrospective cohort study. *Can J Anaesth*. 2009;56(10):740-750. doi:10.1007/s12630-009-9151-5
53. Robinson WP 3rd, Ahn J, Stiffler A, et al. Blood transfusion is an independent predictor of increased mortality in nonoperatively managed blunt hepatic and splenic injuries. *J Trauma*. 2005;58(3):437-445. doi:10.1097/01.ta.0000153935.18997.14
54. Wudel JH, Morris JA Jr, Yates K, Wilson A, Bass SM. Massive transfusion: outcome in blunt trauma patients. *J Trauma*. 1991;31(1):1-7.
55. Kivioja A, Myllynen P, Rokkanen P. Survival after massive transfusions exceeding four blood volumes in patients with blunt injuries. *Am Surg*. 1991;57(6):398-401.
56. MacLeod JB, Winkler AM, McCoy CC, Hillyer CD, Shaz BH. Early trauma induced coagulopathy (ETIC): prevalence across the injury spectrum. *Injury*. 2014;45(5):910-915. doi:10.1016/j.injury.2013.11.004
57. Mitra B, Mori A, Cameron PA, Fitzgerald M, Paul E, Street A. Fresh frozen plasma (FFP) use during massive blood transfusion in trauma resuscitation. *Injury*. 2010;41(1):35-39. doi:10.1016/j.injury.2009.09.029
58. Cap AP, Spinella PC, Borgman MA, Blackbourne LH, Perkins JG. Timing and location of blood product transfusion and outcomes in massively transfused combat casualties. *J Trauma Acute Care Surg*. 2012;73(2 Suppl 1):S89-S94. doi:10.1097/TA.0b013e318260625a
59. Riha GM, Schreiber MA. Update and new developments in the management of the exsanguinating patient. *J Intensive Care Med*. 2013;28(1):46-57. doi:10.1177/0885066611403273

60. Teixeira PG, Oncel D, Demetriades D, et al. Blood transfusions in trauma: six-year analysis of the transfusion practices at a Level I trauma center. *Am Surg*. 2008;74(10):953-957.
61. Dzik WH, Blajchman MA, Fergusson D, et al. Clinical review: Canadian National Advisory Committee on Blood and Blood Products--Massive transfusion consensus conference 2011: report of the panel. *Crit Care*. 2011;15(6):242. doi:10.1186/cc10498
62. Brown JB, Cohen MJ, Minei JP, et al. Debunking the survival bias myth: characterization of mortality during the initial 24 hours for patients requiring massive transfusion. *J Trauma Acute Care Surg*. 2012;73(2):358-364. doi:10.1097/TA.0b013e31825889ba
63. Reynolds BR, Forsythe RM, Harbrecht BG, et al. Hypothermia in massive transfusion: have we been paying enough attention to it?. *J Trauma Acute Care Surg*. 2012;73(2):486-491.
64. Hagiwara A, Kushimoto S, Kato H, et al. Can Early Aggressive Administration of Fresh Frozen Plasma Improve Outcomes in Patients with Severe Blunt Trauma?--A Report by the Japanese Association for the Surgery of Trauma. *Shock*. 2016;45(5):495-501. doi:10.1097/SHK.0000000000000536
65. Holcomb JB, Tilley BC, Baraniuk S, et al. Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs a 1:1:2 ratio and mortality in patients with severe trauma: the PROPPR randomized clinical trial. *JAMA*. 2015;313(5):471-482. doi:10.1001/jama.2015.12
66. Sperry JL, Ochoa JB, Gunn SR, et al. An FFP:PRBC transfusion ratio >/=1:1.5 is associated with a lower risk of mortality after massive transfusion. *J Trauma*. 2008;65(5):986-993. doi:10.1097/TA.0b013e3181878028
67. Joseph B, Zeeshan M, Sakran JV, et al. Nationwide Analysis of Resuscitative Endovascular Balloon Occlusion of the Aorta in Civilian Trauma. *JAMA Surg*. 2019;154(6):500-508. doi:10.1001/jamasurg.2019.0096
68. Aso S, Matsui H, Fushimi K, Yasunaga H. Resuscitative endovascular balloon occlusion of the aorta or resuscitative thoracotomy with aortic clamping for noncompressible torso hemorrhage: A retrospective nationwide study. *J Trauma Acute Care Surg*. 2017;82(5):910-914. doi:10.1097/TA.0000000000001345
69. Abe T, Uchida M, Nagata I, Saitoh D, Tamiya N. Resuscitative endovascular balloon occlusion of the aorta versus aortic cross clamping among patients with critical trauma: a nationwide cohort study in Japan [published correction appears in Crit Care. 2017 Feb 22;21(1):41]. *Crit Care*. 2016;20(1):400. Published 2016 Dec 15. doi:10.1186/s13054-016-1577-x
70. Bulger EM, Perina DG, Qasim Z, et al. Clinical use of resuscitative endovascular balloon occlusion of the aorta (REBOA) in civilian trauma systems in the USA, 2019: a joint statement from the American College of Surgeons Committee on Trauma, the American College of Emergency Physicians, the National Association of Emergency Medical Services Physicians and the National Association of Emergency Medical Technicians. *Trauma Surg Acute Care Open*. 2019;4(1):e000376. Published 2019 Sep 20. doi:10.1136/tsaco-2019-000376
71. Brenner ML, Moore LJ, DuBose JJ, et al. A clinical series of resuscitative endovascular balloon occlusion of the aorta for hemorrhage control and resuscitation. *J Trauma Acute Care Surg*. 2013;75(3):506-511. doi:10.1097/TA.0b013e31829e5416
72. Saito N, Matsumoto H, Yagi T, et al. Evaluation of the safety and feasibility of resuscitative endovascular balloon occlusion of the aorta. *J Trauma Acute Care Surg*. 2015;78(5):897-904. doi:10.1097/TA.0000000000000614
73. Moore LJ, Brenner M, Kozar RA, et al. Implementation of resuscitative endovascular balloon occlusion of the aorta as an alternative to resuscitative thoracotomy for

noncompressible truncal hemorrhage. *J Trauma Acute Care Surg*. 2015;79(4):523-532. doi:10.1097/TA.0000000000000809
74. Moore HB, Moore EE, Burlew CC, et al. Establishing Benchmarks for Resuscitation of Traumatic Circulatory Arrest: Success-to-Rescue and Survival among 1,708 Patients. *J Am Coll Surg*. 2016;223(1):42-50. doi:10.1016/j.jamcollsurg.2016.04.013
75. DuBose JJ, Scalea TM, Brenner M, et al. The AAST prospective Aortic Occlusion for Resuscitation in Trauma and Acute Care Surgery (AORTA) registry: Data on contemporary utilization and outcomes of aortic occlusion and resuscitative balloon occlusion of the aorta (REBOA). *J Trauma Acute Care Surg*. 2016;81(3):409-419. doi:10.1097/TA.0000000000001079
76. Inoue J, Shiraishi A, Yoshiyuki A, Haruta K, Matsui H, Otomo Y. Resuscitative endovascular balloon occlusion of the aorta might be dangerous in patients with severe torso trauma: A propensity score analysis. *J Trauma Acute Care Surg*. 2016;80(4):559-567. doi:10.1097/TA.0000000000000968
77. Manzano Nunez R, Naranjo MP, Foianini E, et al. A meta-analysis of resuscitative endovascular balloon occlusion of the aorta (REBOA) or open aortic cross-clamping by resuscitative thoracotomy in non-compressible torso hemorrhage patients. *World J Emerg Surg*. 2017;12:30. Published 2017 Jul 14. doi:10.1186/s13017-017-0142-5
78. Brenner M, Bulger EM, Perina DG, et al. Joint statement from the American College of Surgeons Committee on Trauma (ACS COT) and the American College of Emergency Physicians (ACEP) regarding the clinical use of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA). *Trauma Surg Acute Care Open*. 2018;3(1):e000154. Published 2018 Jan 13. doi:10.1136/tsaco-2017-000154
79. Otsuka H, Sato T, Sakurai K, et al. Effect of resuscitative endovascular balloon occlusion of the aorta in hemodynamically unstable patients with multiple severe torso trauma: a retrospective study. *World J Emerg Surg*. 2018;13:49. Published 2018 Oct 25. doi:10.1186/s13017-018-0210-5
80. Pieper A, Thony F, Brun J, et al. Resuscitative endovascular balloon occlusion of the aorta for pelvic blunt trauma and life-threatening hemorrhage: A 20-year experience in a Level I trauma center. *J Trauma Acute Care Surg*. 2018;84(3):449-453. doi:10.1097/TA.0000000000001794
81. Sadeghi M, Nilsson KF, Larzon T, et al. The use of aortic balloon occlusion in traumatic shock: first report from the ABO trauma registry. *Eur J Trauma Emerg Surg*. 2018;44(4):491-501. doi:10.1007/s00068-017-0813-7
82. Sato R, Kuriyama A, Takaesu R, et al. Resuscitative endovascular balloon occlusion of the aorta performed by emergency physicians for traumatic hemorrhagic shock: a case series from Japanese emergency rooms. *Crit Care*. 2018;22(1):103. Published 2018 Apr 21. doi:10.1186/s13054-018-2032-y
83. Teeter WA, Bradley MJ, Romagnoli A, et al. Treatment Effect or Effective Treatment? Cardiac Compression Fraction and End-tidal Carbon Dioxide Are Higher in Patients Resuscitative Endovascular Balloon Occlusion of the Aorta Compared with Resuscitative Thoracotomy and Open-Chest Cardiac Massage. *Am Surg*. 2018;84(10):1691-1695.
84. Yamamoto R, Cestero RF, Suzuki M, Funabiki T, Sasaki J. Resuscitative endovascular balloon occlusion of the aorta (REBOA) is associated with improved survival in severely injured patients: A propensity score matching analysis. *Am J Surg*. 2019;218(6):1162-1168. doi:10.1016/j.amjsurg.2019.09.007
85. Yamamoto R, Cestero RF, Muir MT, et al. Delays in Surgical Intervention and Temporary Hemostasis Using Resuscitative Endovascular Balloon Occlusion of the aorta (REBOA): Influence of Time to Operating Room on Mortality. *Am J Surg*. 2020;220(6):1485-1491. doi:10.1016/j.amjsurg.2020.07.017

86. Hilbert-Carius P, McGreevy DT, Abu-Zidan FM, Hörer TM; the ABOTrauma Registry research group. Pre-hospital CPR and early REBOA in trauma patients - results from the ABOTrauma Registry. *World J Emerg Surg*. 2020;15(1):23. Published 2020 Mar 30. doi:10.1186/s13017-020-00301-8

Appendix A. Literature classification schema.*

Design/ Class	**Therapy**†	**Diagnosis**‡	**Prognosis**§
1	Randomized, controlled trial or meta-analysis of randomized trials	Prospective cohort using a criterion standard or meta-analysis of prospective studies	Population prospective cohort or meta-analysis of prospective studies
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
3	Case series	Case series	Case series

*Some designs (eg, surveys) will not fit this schema and should be assessed individually.
†Objective is to measure therapeutic efficacy comparing interventions.
‡Objective is to determine the sensitivity and specificity of diagnostic tests.
§Objective is to predict outcome, including mortality and morbidity.

Appendix B. Approach to downgrading strength of evidence.

Design/Class

DRAFT

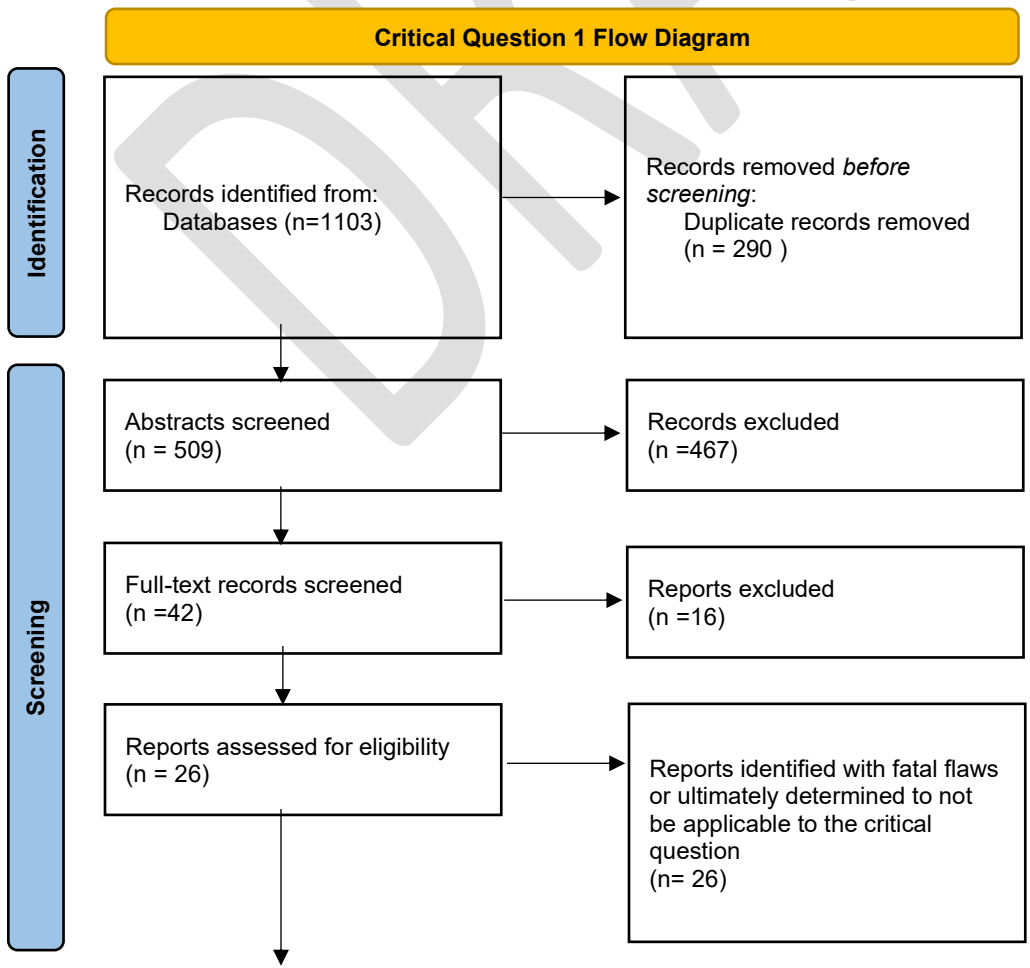
Downgrading	1	2	3
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X

Appendix C. Likelihood ratios and number needed to treat.*

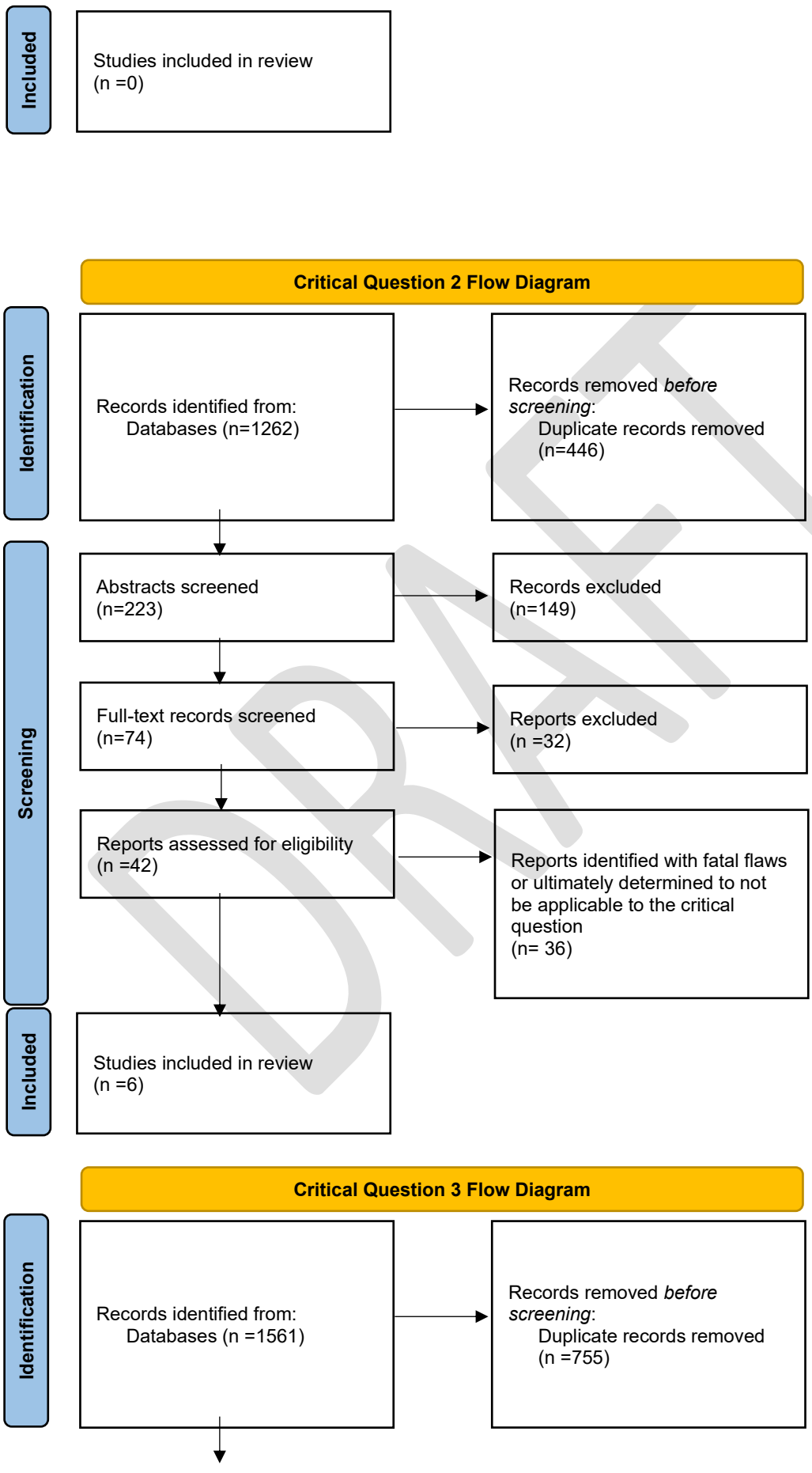
LR (+)	LR (–)	
1.0	1.0	Does not change pretest probability
1–5	0.5–1	Minimally changes pretest probability
10	0.1	May be diagnostic if the result is concordant with pretest probability
20	0.05	Usually diagnostic
100	0.01	Almost always diagnostic even in the setting of low or high pretest probability

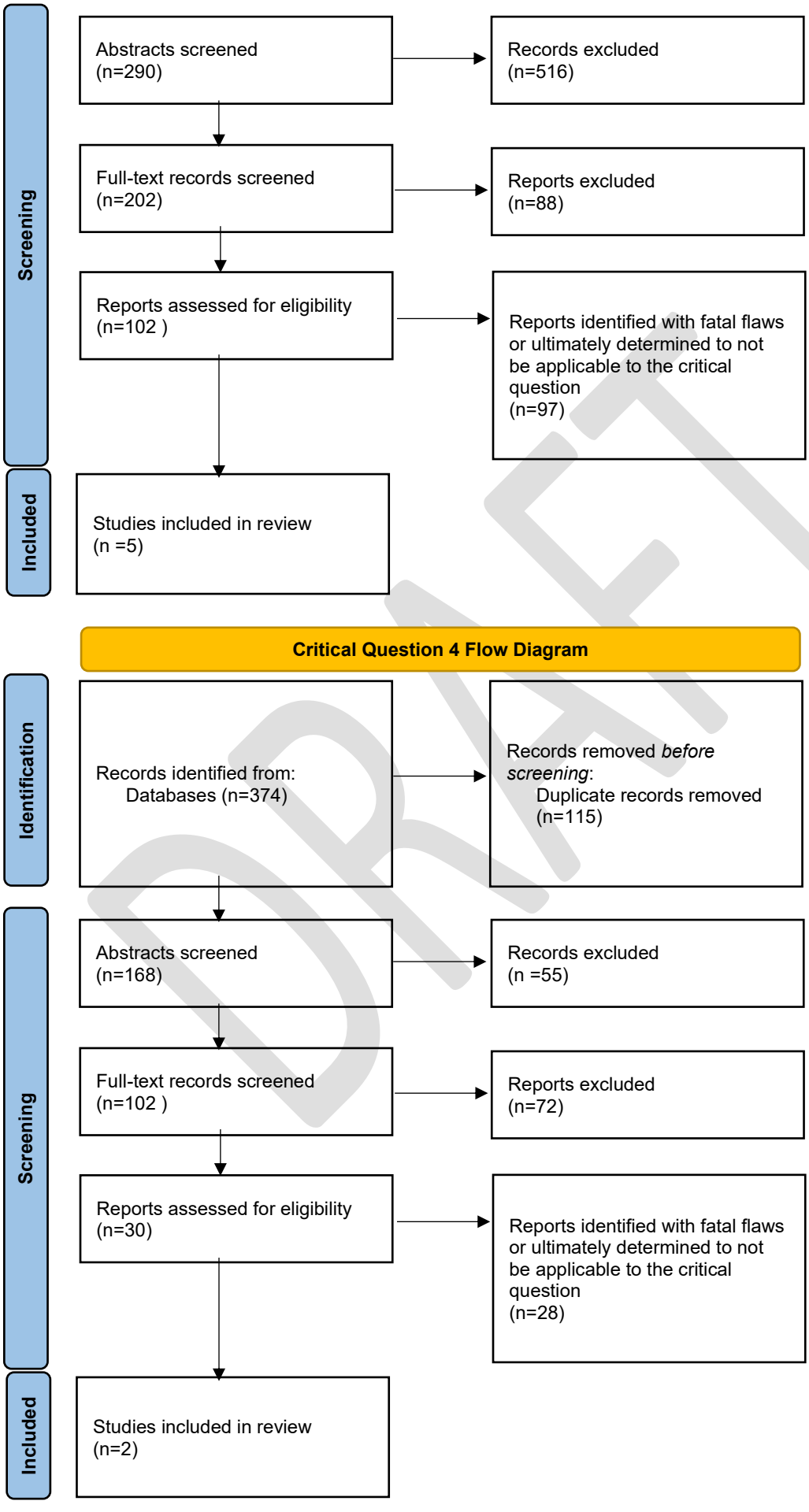
LR, likelihood ratio.
*Number needed to treat (NNT): number of patients who need to be treated to achieve 1 additional good outcome; NNT=1/absolute risk reduction×100, where absolute risk reduction is the risk difference between 2 event rates (ie, experimental and control groups).

Appendix D. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagrams.[7]



DRAFT


Included
Studies included in review
(n =0)
Critical Question 2 Flow Diagram
Identification
Records identified from:
Databases (n=1262)
Records removed *before screening*:
Duplicate records removed
(n=446)
Screening
Abstracts screened
(n=223)
Records excluded
(n=149)
Full-text records screened
(n=74)
Reports excluded
(n =32)
Reports assessed for eligibility
(n =42)
Reports identified with fatal flaws or ultimately determined to not be applicable to the critical question
(n= 36)
Included
Studies included in review
(n =6)
Critical Question 3 Flow Diagram
Identification
Records identified from:
Databases (n =1561)
Records removed *before screening*:
Duplicate records removed
(n =755)
DRAFT


Screening
Abstracts screened
(n=290)
Records excluded
(n=516)
Full-text records screened
(n=202)
Reports excluded
(n=88)
Reports assessed for eligibility
(n=102)
Reports identified with fatal flaws or ultimately determined to not be applicable to the critical question
(n=97)
Included
Studies included in review
(n =5)
Critical Question 4 Flow Diagram
Identification
Records identified from:
Databases (n=374)
Records removed *before screening*:
Duplicate records removed
(n=115)
Screening
Abstracts screened
(n=168)
Records excluded
(n =55)
Full-text records screened
(n=102)
Reports excluded
(n=72)
Reports assessed for eligibility
(n=30)
Reports identified with fatal flaws or ultimately determined to not be applicable to the critical question
(n=28)
Included
Studies included in review
(n=2)

DRAFT

794
795

DRAFT

Evidentiary Table.

Author & Year Published	Class of Evidence	Setting & Study Design	Methods & Outcome Measures	Results	Limitations & Comments
Ahmed et al[19] (2020)	III for Q 2	Retrospective review of NTDB Also - multivariate logistic regression model on clinical variables related to patient mortality - ROC curve was fit and area under the curve (AUC) with sensitivity analysis	Patients ground level from home, ≥65 years with normal (SBP) [Ref 90 –160 mm Hg], heart rate (HR) [Ref: 60-100,GCS 15 Other variables: sex, race and ethnicity, respiratory rate (RR), injury severity score (ISS), existing comorbidities including: smoking, chronic kidney disease (CKD), cerebrovascular accident/neurologic deficit (CVA), DM, HTN Objective: to determine incidence of in-hospital mortality and develop validated risk model to identify high risk	40,800 patients; 938 (2.3%) patients died in the hospital; 39,862 (97.7%) survived Significant difference based on: **Age** (median [IQR]) (82.0 [77.0, 86.0], vs. 80.0 [73.0, 85.0], P <.001) **Sex** (male: 49.8% vs. 30.6%, P <.001) **ISS** (median [IQR]: 9.0 [9.0, 14.0] vs 9.0 [4.0, 9.0], P <.001) Sensitivity analysis showed higher rate of comorbidities, including chronic kidney disease (CKD) and HTN), (7.5% vs. 2.8%, and 67.3% vs. 62.5%, all P <.05). Tested model for higher LOC (trauma center designation I & II) versus lower level and impact on mortality; none were found.	Brain injury-most frequent injury found (21.86% vs 21.48%) Higher brain hemorrhage and cervical spine injury in group that died Femoral neck or intertrochanteric fractures - no difference between groups Normal physiological measures at the scene do not eliminate the risk of in-hospital mortality in geriatric patients who fell from a ground level height at home 2.3% incidence of in-hospital mortality Older age, male sex, lower SBP, higher HR, and RR, ISS, and a history of CKD, DM, and HTN requiring medications were associated with a higher risk of in-hospital mortality

DRAFT

Anantha et al[32] (2021)	III for Q 2	Single-center retrospective Multivariable logistic regression analysis done to identify predictors of appropriate triage and variables independently associated with appropriate triage	Included all (ISS >15), ≥65 years (between1/14 and 9/17). Undertriage: lack of TTA despite presence of severe injuries. Primary outcome: in-hospital mortality; secondary outcomes: mortality within 48 hours of admission and urgent hemorrhage control or shock(need for transfusion, or lactate being ≥ 4.0 mmol/L .	1039 patients, 628 (61%) did not undergo TTA. Undertriaged patients were older, had more comorbidities (stroke, dementia and bleeding disorders) In-hospital mortality was 5% vs 31% (P <.0001) 1% of undertriaged patients needed urgent hemorrhage control, vs to 6% appropriately triaged group (P < .0001) 1% undertriaged patients died within 48 hours vs 19% appropriately triaged group (P < .0001) Predictors of appropriate triage: GCS, heart rate, systolic blood pressure, lactic acid, ISS, shock, and absence of dementia, stroke, or alcoholism	Utility of ISS Retrospectively collected variable may not useful for triage
Brown et al[31] (2015)	III for Q 2	Retrospective review- Data extraction National trauma data bank	Used SBP of 110 mm Hg instead of 90 mm Hg to determine if geriatric pts (greater then 65) have mortality rates similar to those with lower BP Used physiologic (prehospital VS, GCS) and anatomic criteria (from ICD 9 codes) to determine placement into trauma center Trauma center need based on ISS greater then 15, ICU	438,828 geriatric pts Geriatric patients newly triaged with SBP 90 to 109 mm Hg odds of mortality same as those with SBP less the 90 mm Hg (Adjusted OR 1.03 ;95% CI) Also had similar discrimination and better goodness of fit using SBP <110 and those with SBP range (90 -109 mm Hg) had odds of mortality similar to those with SBP < 90 (Adjusted OR1.02 95CI%) Using SBP of less then 110 mm Hg for trauma center improves undertriage in geriatric pts but not in adults. It improves sensitivity at the expense of specificity.	Majority of patients were adults, not geriatric; however still large number of geriatric patients. Conclusion that older people with BP of 109 - 90 have same mortality as those with Bp of 90 mm Hg suggests they warrant trauma center care

DRAFT

<table>
<tr>
<td></td>
<td></td>
<td></td>
<td>admission, urgent surgery and death as primary outcome. Mortality was secondary outcome</td>
<td>
<table>
<tr><th>Characteristics of the Geriatric and Adult Cohorts</th><th>Geriatric Cohort n = 438,828</th><th>Adult Cohort n = 1,117,116</th><th>P</th></tr>
<tr><td>Age, median (IQR), y</td><td>80 (73–86)</td><td>37 (25–50)</td><td><0.01</td></tr>
<tr><td>Sex, male, %</td><td>39</td><td>71</td><td><0.01</td></tr>
<tr><td>Blunt injury, %</td><td>99</td><td>85</td><td><0.01</td></tr>
<tr><td>Prehospital time, median (IQR)</td><td>48 (37–70)</td><td>44 (32–67)</td><td><0.01</td></tr>
<tr><td>Prehospital SBP, median (IQR)</td><td>144 (128–164)</td><td>131 (118–146)</td><td><0.01</td></tr>
<tr><td>Prehospital SBP < 90 mm Hg, %</td><td>2.7</td><td>5.3</td><td><0.01</td></tr>
<tr><td>Prehospital SBP < 110 mm Hg, %</td><td>9.0</td><td>15.5</td><td><0.01</td></tr>
<tr><td>ISS, median (IQR)</td><td>9 (4–10)</td><td>6 (4–13)</td><td><0.01</td></tr>
<tr><td>TCN, %</td><td>32</td><td>40</td><td><0.01</td></tr>
<tr><td>Mortality, %</td><td>4.4</td><td>3.8</td><td><0.01</td></tr>
</table>
</td>
<td></td>
</tr>
<tr>
<td>Hung et al[33] (2018)</td>
<td>III for Q2</td>
<td>10 year single center cohort study – retrospective review trauma registry in Hong Kong 2006 to 2015</td>
<td>Patients ≥55 years in trauma registry
Separated ages 55-70, and >70years.
Outcomes: death within 30 days; the need for surgery;
or the need for ICU care</td>
<td>2218 patients 30-day mortality was 7.5% for aged 55-70 years and 17.7% for above 70 years.
The under-triage rate was 59% for age 55 –70 years, and 69.1% for those aged above 70 years.</td>
<td>TTA is tiered. First tier: 2 EM physicians. Second tier: 2 general surgeons, an orthopaedic surgeon, and an ICU physician.

Sensitivity of TTA criteria decreases as age increases- Justifies need</td>
</tr>
</table>

DRAFT

					for specific criteria for pts 70 years and older.
Ichwan et al[30] (2015)	III for Q 2	Retrospective review of Ohio trauma registry	Used greater than 70 years of age to define geriatrics Triage criteria predicted need for trauma care	Geriatric triage criteria applied increased sensitivity but not specificity Mortality was similar between 2 groups 6.8 (adult) vs 9.3 (geriatric Appeared geriatric patients were less severely injured (lower ISS, lower ICU care) but mortality rate 6.8 in geriatrics vs 9.3 in adults Increased geriatric trauma from 42 to 57% Sensitivity increased (61 to 93%) but specificity decreased (61 to 49%) have CI	Use of geriatric trauma criteria improved sensitivity of identifying need for trauma center
Lim et al[29] (2020)	III for Q2	Retrospective cohort from 1/2016 to 12/ 2017	All patients > 18 years with injury severity score ≥16) Goal was to validate Korean Trauma Activation (KTAS) Score which has 4 levels and to analyze the prognostic performances of KTAS in 30-day	827 patients, 30-day mortality observed in 14.9% (n=123). Patients in the survivor group were younger and had higher values of both ISS and shock index. Survivors (n=704) Age (years) 59.1 (46.1–72.0) Non-survivors (n=123) Age (years) 69.1 (57.0–76.1)	Mortality of older adult was increased by 2.7 % for each year of life
Brown et al[62] (2012)	III for Q 3	multicenter prospective cohort study of adults , 7 institutions during a 8-year period (2003 to 2010)	Inclusion criteria: blunt trauma, presence of prehospital or emergency department hypotension (systolic blood pressure [SBP] <90 mm Hg) or an elevated base deficit (BD) (>6 mEq/L),	Of the 1,961 subjects in the cohort, 604 met MT inclu- sion criteria and constituted the study cohort. For the entire cohort, the 6-, 12-, and 24-hour mortality was 8.6%, 12.1%, and 13.1%, respectively. These subjects required a median of 16.3 U (IQR, 12.5±25.7) of PRBC, 8.3 U (4.3±13.4) of FFP, and 1.5 U (0.67±2.5) of PLT during the first 24 hours. Overall,	Despite similar degrees of early shock and coagulopathy, high FFP/PRBC and PLT/PRBC ratios are associated with a survival benefit as early as 6 hours and throughout the first 24

DRAFT

			blood transfusion requirement within the first 12 hours, and any body region exclusive of the brain with an AIS of 2 or higher, allowing exclusion of patients with isolated traumatic brain injury. Patients younger than 18 years or older than 90 years and those with cervical spinal cord injury were also excluded from enrollment. High FFP/PRBC (≥1:1.5) and PLT/PRBC (≥1:9) ratios at 6, 12, and 24 hours were compared with low ratio groups. MOD was outcome	55.3% developed MOF, 48.2% developed NI, and 29.8% developed ARDS. A high FFP/PRBC ratio at 6 hours was associated with an independent mortality reduction at 6, 12, and 24 hours .Similarly, a high FFP/PRBC ratio at 12 hours was associated with an independent mortality reduction at 12 hours and 24 hours, and a high ratio at 24 hours was associated with a mortality benefit at 24 hours When FFP/PRBC ratio was analyzed as a time-dependent covariate, a higher ratio was associated with an independent reduction in mortality (Table 3). Similarly, when PLT/PRBC ratio was analyzed as a time-dependent covariate, a higher ratio was associated with an independent reduction in mort A high ratio of FFP/PRBC or PLT/PRBC at 6 hours was not independently associated with the risk of developing MOF, NI, or ARDS during admission. Similarly, a high FFP/ PRBC or PLT/PRBC ratio at 12 hours or 24 hours was not associated with any complication outcome studied ($p < 0.05$	hours. Moreover, this held true at all time points at which ratio groups were determined. Most importantly, when FFP and PLT to PRBC ratios were analyzed as time-dependent variables, an increasing ratio was independently associated with a mortality reduction during the first 24 hours from injury. early resuscitation using high FFP/PRBC and PLT/PRBC ratios results in reduced mortality at 6 hours and throughout the first 24 hours from injury. When time-dependent effects of early component transfusion are accounted for, an increasing FFP/PRBC and PLT/PRBC ratio remains protective against early death from hemorrhage.
Reynolds et al[63] (2012)	III for Q 3	multicenter prospective cohort study of	Inclusion criteria :blunt trauma, presence of prehospital or	Of the 1961 patients with blunt injury enrolled during the study period, 604 (31%) required 10 U or more of PRBCs in	this analysis verifies that hypothermia, nadir temperatures lower than

DRAFT

		adults with blunt injury with hemorrhagic shock 7 institutions during a 6-year period (December 2003 -January 2010)	emergency department systolic hypotension (<90 mm Hg) or an elevated base deficit (<6 mEq/L), blood transfusion requirement within the first 12 hours, and any region of the body excluding the brain with an Abbreviated Injury Scale score of 2 or higher, allowing the exclusion of patients with isolated traumatic brain injury. Patients younger than 16 years or older than 90 years and those with cervical spinal cord injury were also excluded from enrolment. For the current secondary data analysis, only patients requiring MT, defined as 10 U or more of packed red blood cells (PRBCs) in the first 24 hours after injury, were selected for analysis. Our primary outcomes for the analysis were in-hospital mortality,	the first 24 hours after injury and constituted the primary study population. Regression analysis revealed that temperature in an MT co- hort (lowest 24-hour measurement as a continuous variable) was associated with a significantly greater independent risk of mortality after controlling for differences in demographics, injury severity, shock parameters, and transfusion and resus-citation confounders (OR, 0.82; 95% CI, 0.7Y0.9; p = 0.013). An interpretation of this OR suggests that a greater indepen-dent risk of mortality of more than 18% is associated with every decrease in the temperature level (-C) of a patient requiring MT in the first 24 hours after injury. When stratified by the period of enrollment, a tem- perature lower than 34-C remained a significant independent predictor of mortality with more than a twofold higher risk of mortality in the early period (OR, 2.24; 95% CI, 1.2Y4.1; p = 0.012, When stratified by the attainment of a high FFP/PRBC transfusion ratio (>1:2) in the first 24 hours versus a low FFP/ PRBC transfusion ratio (<1:2), a temperature lower than 34-C remained a significant independent predictor of mortality in the low FFP/PRBC ratio group with more than a twofold higher risk of mortality (OR,	34-C in the first 24 hours, is common and independently associated with a greater independent risk of mortality of more than 85% on patients requiring MT. These associations were most robust on patients who received a low FFP/PRBC transfusion ratio and were negated in the recent enrollment period (2007-2010) in which a more aggressive blood component resuscitation strategy has been previously documented. These data suggest that the clinical significance of hypothermia may be affected by the way a patient is resuscitated and may be as important as addressing the early coagulopathy in these patients

DRAFT

			MOF development, and nosocomial infection (NI).	2.2; 95% CI, 1.1±4.2; p = 0.021, In those patients requiring MT who received a high FFP/PRBC transfusion ratio, a temperature lower than 34-C was no longer a significant independent risk factor for mortality (OR, 1.8; 95% CI, 0.933.5; p = 0.100).	
Hagiwara et al[64] (2016)	III for Q 3	Retrospective observational study, Fifteen medical institutions participated from Japan, subgroup study from the Japanese Observational Study for Coagulation and Thrombolysis in Early Trauma (J-OCTET) January and December 2012	189 blunt trauma patients ≥ 18 years with ISS ≥16 requiring RBC transfusions within the first 24 h. cut-off values of the FFP/RBC ratio for outcome. cut-off values of the FFP/RBC ratio for outcome.	A total of 139 blunt trauma patients survived and were discharged alive, and 62 blunt trauma patients died FFP/RBC ratio at 6 h for survivor 1.0 [0.5, 1.3] vs 0.8[0.6,1.0], P = 0.066 FFP/RBC ratio at 24 h for survivor 1.0 [0.6, 1.3] vs 0.83[0.6,1.1], P = 0.177 Cox proportional hazards analysis of time to death FFP/RBC ratio ≥ 1 within 6 h 0.29 (0.14 – 0.62) P =0.001 FFP/RBC ratio ≥ 1 within 24 h 1.27 (0.59 – 2.74) P=0.540	Blunt trauma patients transfused with an FFP/RBC ratio ≥ 1 within the first 6 h after admission had a hazard ratio of about 0.4. In other words, their risk of death was reduced by about 60%. Transfusion of an FFP/RBC ratio □1 within the first 6 h was associated with the outcome of severe blunt trauma patients with ISS ≥ 16 and needed a transfusion within 24 h. The present results suggest that early aggressive administration of FFP may be crucial for resuscitation in patients with severe blunt trauma

DRAFT

				PSM was performed to compare the two groups (FFP/RBC ratio □1 within the first 6 h and FFP/RBC ratio <1 within the first 6 h). The propensity score was created from the following 13 covariates: age, fluid therapy before admission, use of anticoagulant/antiplatelet drugs, ISS, use of tranexamic acid, HR, SBP, RR, WBC, Hb, PLT, CPK, and BE. Patients with an FFP/ RBC ratio □1 within the first 6h had significantly better survival, with an unadjusted hazard ratio of 0.44 and an adjusted hazard ratio of 0.29 (adjusted by all variables in Table 2).	requiring blood transfusion

DRAFT

Holcomb et al[65] (2015)	III for Q 3	Pragmatic, phase 3, multisite, randomized clinical trial at 12 level I trauma centers in North America August 2012 and December 2013	Inclusion criteria: patient having at least 1 U of any blood component transfused prior to hospital arrival or within 1 hour of admission and prediction by an Assessment of Blood Consumption score of 2 or greater or by physician judgment of the need for a massive transfusion (defined as =10 U of RBCs within 24 hours Exclusion: Received a lifesaving intervention from an outside hospital or health care facility, Had devastating injuries and expected to die within 1 hour of admission (eg, lethal traumatic brain injury), Directly admitted from a correctional facility, Required a thoracotomy prior to	No significant differences in mortality were detected at 24 hours (12.7% in the 1:1:1 group vs 17.0% in the 1:1:2 group; difference, −4.2% [95% CI, −9.6% to 1.1%) or at 30 days (22.4% vs 26.1%, respectively; difference, −3.7% [95% CI, −10.2% to 2.7%) range of intent-to-treat P values computed for all possible combinations of 30-day outcomes for the 4 patients with missing values did not change these results. Exsanguination, the predominant cause of death within the first 24 hours, was decreased in the 1:1:1 group (9.2%) vs the 1:1:2 group (14.6%) (difference, −5.4% [95% CI, −10.4% to −0.5%], P= .03); the median time to death due to exsanguination was 106 minutes (interquartile range [IQR], 54 to 198 minutes) and 96 minutes (IQR, 43 to 194 minutes), respectively. From 24 hours through 30 days, the numbers of additional all-cause deaths were similar (32 for the 1:1:1 group vs 31 for the 1:1:2 group). Over 30 days, deaths due to exsanguination occurred in 10.7% of patients in the 1:1:1 group vs 14.7% in the 1:1:2 group, whereas deaths due to traumatic brain injury were 8.1% vs	Transfusing patients based on an empirical ratio rather than guided solely by laboratory data (goal-directed) is considered controversial by some researchers. This trial was not designed to study this question. However, after the controlled, ratio-driven intervention was completed, clinicians treated patients based on local laboratory-guided standard-of-care practice. It appears that laboratory-directed catching up occurred in the 1:1:2 group with plasma and platelets approaching a cumulative ratio of 1:1:1. Other studies have shown similar results with laboratory-directed resuscitation. This catching up after the completion of randomized blood

DRAFT

			receiving randomized blood products in the emergency department, Younger than 15 years or weighed less than 50 kg if age unknown, Known pregnancy in the emergency department, Had burns covering greater than 20% total body surface area Suspected inhalation injury, Received greater than 5 consecutive minutes of cardiopulmonary resuscitation (with chest compressions) prior to arriving at the hospital or within the emergency department, Known do-not-resuscitate order prior to randomization, Enrolled in a concurrent, ongoing, interventional, randomized clinical trial, Activated the opt-out process for the PROPPR trial (usually by wearing a bracelet given out at a community consent presentation), More	10.3%, respectively. Additional causes of death were infrequent More patients achieved anatomic hemostasis in the 1:1:1 group (86.1% vs 78.1% in the 1:1:2 group, P= .006) with a median time of 105 minutes (IQR, 64 to 179 minutes) vs 100 minutes (IQR, 56 to 181 minutes), respectively (P= .44) in those who achieved anatomic hemostasis During the intervention, patients received median ratios of plasma to RBCs of 1.0 in the 1:1:1 group and 0.5 in the 1:1:2 group. The median ratios of platelets to RBCs during the intervention were 1.5 for the 1:1:1 group and 0.4 for the 1:1:2 group.	product transfusion may have decreased the ability to detect differences in mortality at 24 hours and 30 days or in the prespecified ancillary outcomes Limitations include power to detect differences smaller than the effect size we considered to be both clinically meaningful and affordable to study when we designed the trial.

DRAFT

			than 3 U of red blood cells given before randomization primary outcome: 24 hour and 30 day mortality		
Sperry et al[66] (2008)	III for Q 3	**multicenter prospective cohort study evaluating clinical outcomes in blunt injured adults with hemorrhagic shock** seven US institutions, during a 3.5-year period (November 2003–March 2007)	Included :blunt mechanism of injury, presence of prehos-pital or emergency department systolic hypotension (<90 mm Hg) or an elevated base deficit (≥6 meq/L), blood transfusion requirement within the first 12 hours, and any body region exclusive of the brain with an abbreviated injury score (AIS) ≥2, allowing exclusion of patients with isolated traumatic brain injury. Patients younger than 16 years or older than 90 years and those with cervical spinal cord injury were excluded. For the current study,	high F:P ratio , n-102, low F:P ratio , n= 313. Of the 1,036 blunt injured patients enrolled during the study period, 415 patients had a blood transfusion requirement of ≥8 units within the initial 12 hours after injury, and constituted the study population. In this cohort, 39 patients received no FFP within the first 12 hours from injury (FFP: PRBC ratio = 0) despite having a ≥8 unit blood transfusion requirement. The overall mortality for the study population was 33.5%, whereas the overall complication rates for MOF, NI, and ARDS were 56.4%, 46.5%, and 29.6%, respectively. Those who received a high F:P ratio had higher ISS score and extremity AIS scores, higher APACHE II scores, lower GCS scores, and had lower nadir core body temperature measurements in the first 24 hours postinjury. They also had greater length of stay, ICU, and ventilator requirements; however, these comparisons would be inaccurate if an early mortality	patients who received an FFP:PRBC transfusion ratio ≥1:1.5, relative to patients who received <1:1.51 FFP:PRBC ratio, had a significant lower risk of in-hospital mortality following massive transfusion after controlling for important confounders. This protective effect was most pertinent for mortality within the first 48 hours after injury and was independent of the blood transfusion requirement each individual patient received. Although crude mortality differences between the high F:P and low F:P groups did not reach statistical significance, the significant difference in early (24 hour)

DRAFT

			only patients who required ≥8 units of PRBCs within the first 12 hours from injury were included in the analysis. The FFP:PRBC variable, specifically the low F:P group, was then categorized as 1:2 (1:1.51–1:2.50, n = 105), 1:3 to 4 (1:2.51–1:4:50, n = 111), and ≤1:5 (≤1:4.51, n = 97) groups , MOF and mortality were outcomes	difference existed between the two groups. Hospital free days, ICU free days, and ventilator free days were compared with adjust for any such difference and confirmed that high F:P ratio patients had fewer hospital, ICU, and ventilator free days. Although the survival curves overall were not statistically different (log- rank: p = 0.119), the mortality rate at day 1 postinjury was significantly lower in the high F:P group (3.9% vs. 12.8%, p □ 0.012). Although underpowered to be statistically different, when the FFP:PRBC variable was stratified into groups(highF:P,1:2,1:3–4,and≤1:5),similar findings with early separation of the survival curves are apparent at day 1 postinjury, with a dose response being demonstrated, based on the transfused FFP:PRBC ratio high F:P ratio, relative to patients who received a low F:P ratio, was independently associated with a 52% lower risk of mortality (HR 0.48, p = 0.002, 95% CI 0.3– 0.8), after controlling for important confounders. The hazard ratio for high F:P ratio patients remained significant with the protective effect for mortality being unaltered (HR 0.57, p = 0.026, 95% CI 0.35– 0.93).	mortality was likely responsible for this overall mortality risk reduction. As the FFP:PRBC ratio became smaller (less FFP relative to PRBCs) a dose-response relationship was demonstrated for mortality, with those patients who received minimal or no FFP having the highest early mortality.

DRAFT

				However, a high F:P ratio was associated with almost a twofold higher risk of ARDS, after controlling for important confounders study is a secondary analysis of a prospective cohort study looking at the genomic and proteomic response after severe injury and hemorrhagic shock	
Aso et al[68] (2017)	III for Q 4	Retrospective Cohort of national Inpatient Database (Japan) 2010-2014.	Trauma patients with uncontrolled hemorrhagic shock. Excluded penetrating thoracic trauma. > 15 years old. Propensity score adjusted Outcome: Mortality 2ndary ventilator-free days, total amount of fluid within 1 day, total transfusion within 1	259 patients total • 191 REBOA, 68 Resuscitative Thoracotomy (RT) Propensity score adjusted Cox Regression: Hazards ratio = 0.94 (95% CI 0.60, 1.48) No difference in secondary outcomes	Retrospective Registry Study. But propensity score adjusted.

DRAFT

			day, total hospitalization costs.		
Joseph et al[67] 2019	III for Q 4	Case Control US single center	Case-control Study using ACS TQIP	420 REBOA cases matched 280 controls 50/240 = 35.7% 53/180 = 18.9%	

DRAFT