

## The pragmatic randomized optimal platelet and plasma ratios trial: what does it mean for remote damage control resuscitation?

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*This article is a counterpoint to: Maegele M. Coagulation factor concentrate-based therapy for remote damage control resuscitation (RDCR): a reasonable alternative? Transfusion 2016;56 (Suppl 2):S157-S165.*

**BACKGROUND:** Implications from the pragmatic, randomize, optimal platelet and plasma ratios (PROPPR) trial are critical for remote damage control resuscitation (DCR). Utilizing DCR principals in remote settings can combat early mortality from hemorrhage. Identifying the appropriate transfusion strategy is mandatory prior to adopting prehospital hemostatic resuscitation strategies.

**STUDY DESIGN AND METHODS:** The PROPPR study was examined in relation to the following questions: 1) Why is it important to have blood products in the prehospital setting?; 2) Which products should be investigated for prehospital hemostatic resuscitation?; 3) What is the appropriate ratio of blood product transfusion?; and 4) What are the appropriate indications for hemostatic resuscitation?

**RESULTS:** PROPPR demonstrates that early and balanced blood product transfusion ratios reduced mortality in all patients at 3 hours and death from exsanguination at 24 hours ( $p = 0.03$ ). The median time to death from exsanguination was 2.3 hours, highlighting the need for point-of-injury DCR capabilities. A 1:1:1 transfusion ratio of plasma:platelets:packed red blood cells increased the percentage of patients achieving anatomic hemostasis ( $p = 0.006$ ). PROPPR used the assessment of blood consumption score to identify patients likely to require ongoing hemostatic resuscitation. The critical administration threshold predicted patient mortality and identified patients likely to require ongoing hemostatic resuscitation.

**CONCLUSION:** A balanced resuscitation strategy demonstrates an early survival benefit, decreased death from exsanguination at 24 hours and a greater likelihood of achieving hemostasis in critically injured patients receiving a 1:1:1 ratio of plasma:platelets:PRBCs. This finding highlights the need to import DCR principals to remote locations.

### INTRODUCTION

In June of 2015, the THOR network convened in Bergen, Norway for the fifth annual remote damage control resuscitation (RDCR) symposium. Previously, this conference delineated the goals, challenges, and future applications of RDCR.<sup>1</sup> In February of 2015 the pragmatic, randomized, optimal platelet, and plasma ratios (PROPPR) trial was published by the PROPPR Study Group.<sup>2</sup> This publication has critical implications for RDCR. Here we review the potential influences, outcomes, and questions still lingering as the body of literature supporting early hemostatic resuscitation expands. However, to understand the impacts of PROPPR on RDCR it is important to briefly review the impact of damage control surgery (DCS) and damage control resuscitation (DCR) on RDCR.

DCS, cited originally in 1976 by Lucas and Ledgerwood,<sup>3</sup> was brought to the clinical forefront by Stone in 1983.<sup>4</sup> Stone et al. described the immediate surgical control of hemorrhage using intra-abdominal packing, control of gross contamination, temporary abdominal closure, and limited initial operative time.<sup>4</sup> Of 31 patients studied, 14 had traditional emergent operations and 17 had DCS. One patient survived in the traditional group

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**TABLE 1. Principals of damage control resuscitation**

1. Compressible hemorrhage control
2. Hypotensive resuscitation
3. Rapid surgical control of bleeding
4. Avoidance of the overuse of crystalloids and colloids
5. Prevention or correction of acidosis, hypothermia, and hypocalcemia
6. Hemostatic resuscitation

compared with 11 patients in the DCS group.<sup>4</sup> The logical expansion of these concepts included the perioperative period, termed: Damage Control Resuscitation.<sup>5</sup> DCR subsequently migrated into emergency room protocols for the management of hemorrhaging patients. DCR, like its parent DCS, demands readily available blood components to achieve the clinical end points of hemostasis and resuscitation. The principals of DCR as defined by Dr. Holcomb and formally listed at the THOR conference are shown in Table 1.<sup>1,6</sup>

### CRYSTALLOID RESUSCITATION

Modern hemostatic resuscitation arose following the demonstration of the deleterious effects of crystalloid and colloid resuscitation. Coined initially as De Nang lung in Vietnam and later termed Acute Lung Injury,<sup>7</sup> the inflammatory effects of these fluids have plagued resuscitation strategies for decades. In 1998, Rhee et al. used a swine hemorrhage model to demonstrate increased neutrophil activation when resuscitation was carried out with lactated Ringers (LR).<sup>8</sup> This effect was mirrored in swine undergoing sham hemorrhage and receiving LR infusion alone.<sup>8</sup>

Subsequently, in 2004 Hasan et al. used a swine hemorrhage model to demonstrate not only increased neutrophil activation with both colloid and LR resuscitation ( $p < 0.05$ ), but also no significant neutrophil activation when whole blood was used for resuscitation.<sup>9</sup> The upregulation of inflammatory receptors, including Toll-like receptors, has been demonstrated in rat hemorrhage models following LR resuscitation.<sup>10</sup> These investigations, in association with others demonstrating increased inflammation, hyperchloremic acidosis, artificial elevation of the blood pressure, and fluid overload highlight the dangers of aggressive crystalloid and colloid resuscitation.<sup>11-16</sup>

Over the past decade, the acute coagulopathy of trauma (ACoT) has been extensively described.<sup>16-19</sup> ACoT is an endogenous process demonstrated to be present prior to the initiation of fluid resuscitation.<sup>7,17,20</sup> Disruption of the endothelial matrix contributes to ACoT and is described as the 'endotheliopathy of trauma' (EoT).<sup>21,22</sup> EoT results in increased vascular permeability, edema, and inflammation; this effect is reversed with plasma resuscitation following hemorrhage.<sup>21,22</sup> Distinct from ACoT, is the exogenous process known as trauma-induced

coagulopathy (TIC). TIC is related to the infusion of crystalloids during resuscitation and compounds the adverse effects of ACoT.<sup>23</sup> Plasma therapy is critical for avoiding TIC and correcting ACoT.<sup>6,22-25</sup>

### HEMOSTATIC RESUSCITATION

Borgman et al. reviewed the experience of 246 patients undergoing massive transfusion at a Combat Support Hospital (CSH) in 2007.<sup>26</sup> They demonstrated that a ratio approaching 1:1 transfusion of plasma:RBCs (red blood cells) was associated with increased survival ( $p < 0.001$ ).<sup>26</sup> Additionally, Duchesne et al. reported an increased survival in massively transfused patients with a plasma:RBC transfusion ratio approaching 1:1 compared with a 1:4 ratio (26% vs 87%  $p = 0.001$ ).<sup>27</sup> In 2008, Spinella and colleagues first demonstrated the independent association between fresh frozen plasma (FFP) transfusion and increased survival in trauma patients at a CSH (OR 1.16 [1.05-1.28]  $p = 0.003$ ).<sup>28</sup>

Platelet resuscitation reviews, from the military and civilian experience, have demonstrated a survival advantage with higher transfusion ratios.<sup>29,30</sup> In 2009 Perkins et al. published a review from 3 years of massive transfusion data with apheresed platelets at a military hospital in Baghdad. The authors noted an independent association between improved survival and a high (>1:8) aPlatelet:RBC transfusion ratio at 24 hours and 30 days.<sup>29</sup>

The CSH, where the aforementioned data were generated, is a fully functional mobile medical unit. These units have surgical capabilities and can be deployed in austere environments. Although this study was not intended to test the potential for prehospital platelet transfusions, it suggests that having platelets closer to the point of injury is associated with a survival benefit in severely injured patients. Furthermore, all patient groups in this study had an initial platelet count  $> 200$  ( $1000/\text{mm}^3$ ), advocating for a trauma induced platelet dysfunction not appropriately identified by current coagulation metrics, and possibly mitigated by the early and balanced administration of platelets.<sup>29</sup>

Additionally, as commented by Dr. Cotton, an interesting analysis would have been to compare outcomes in patients receiving fresh whole blood transfusions to the population receiving a higher aPlatelet:RBC transfusion ratio. Patients receiving whole blood transfusions were excluded from the analysis.<sup>29</sup>

Holcomb et al. reviewed 466 civilian patients who received massive transfusions, demonstrating a reduction in mortality at 6 hours, 24 hours, and 30 days when a transfusion ratio of 1:1 for both plasma:RBC and platelets:RBCs was approached ( $p < 0.05$ ).<sup>31</sup> The retrospective nature and influence of survival bias from these investigations has caused controversy within the trauma community.<sup>15,32,33</sup> Scalea et al. published a prospective cohort

study demonstrating no significant reduction in mortality for massively transfused trauma patients over 24 hours when a FFP:RBC transfusion ratio between 0.9 and 1.1 was attained.<sup>33</sup>

In this study the authors analyzed three groups of patients admitted to the ICU: 1) RBC transfusion alone; 2) PRBC and FFP transfusion; and 3) no transfusion.<sup>33</sup> The former two groups were identified by requiring a transfusion within 24 hours of admission; however, the indication(s) for not transfusing FFP with PRBCs was not reported. The study reports the mean PRBC:FFP ratio as 1.35, which when analyzed as a continuous variable did not demonstrate a significant predictive probability for 30 day mortality.<sup>33</sup> The authors then used a 1:1 ratio as a binary outcome, and again did not show an association with mortality.<sup>33</sup> Based on the observed mortality rate of 4% at 24 hours, notably lower than the rate reported by other multi-institution studies, the authors acknowledge the possibility of different patient populations, potentially influencing the generalizability of the outcomes.<sup>33</sup>

Within the 1:1 group and the non-1:1 group, there was a significant reduction in the number of PRBCs transfused (6.5 units vs. 9.3 units;  $p = 0.02$ ).<sup>33</sup> This suggests that hemostasis may have been achieved earlier when FFP was administered in a 1:1 fashion as compared with a lower ratio.

Overall, this is an interesting study; however, the selection of patient groups based on the need for a single transfusion of either PRBCs or FFP within 24 hours likely dilutes the population of interest. This potentially masks the true benefit an early balanced hemostatic resuscitation strategy imparts to patients likely to die from early trauma induced hemorrhage.

Funded by the US DoD, Holcomb et al. developed a protocol to prospectively address survival bias and further define the optimal transfusion ratio for hemorrhaging patients.<sup>34</sup> The prospective, observational, multicenter massive transfusion trial (PROMMTT), published in 2013, redemonstrated the fact that mortality for actively bleeding patients occurs within the first 24 hours (94%), and a significant number of those patients die within the first 3 hours (60%).<sup>34</sup> The median time to death from admission was 2.6 hours.<sup>34</sup> The PROMMTT investigators demonstrated a reduction in mortality associated with early (less than 24 hr from admission) and increased plasma:RBC and platelet:RBC ratios. Of note, these ratios were independently associated with decreased 6-hour mortality (odds ratios 0.31 and 0.55 consecutively).<sup>34</sup> These data highlight the critical time to administration and initiation of hemostatic resuscitation. In an effort to limit survival bias, PROMMTT investigators used real time data collection and shifted from an enrollment strategy limited by 24-hour transfusion totals to a more rapid inclusion criterion of "1 unit of RBCs in the first 6 hours following admission."<sup>34</sup> PROMMTT, and the previous stated reviews,

served as the foundation for the development of PROPPR by identifying inconsistent transfusion ratios employed during hemorrhagic resuscitation.

The evolution of DCR theory from the highly regulated environment of the operating room, progressing through the structured milieu of the ICU and ER, is now being tested in the largely uncontrolled prehospital environment. It is the charge of the THOR conference to further expand the principals learned from DCR investigations to forward, remote, and austere environments.

## REMOTE DCR

The prehospital arenas influenced by RDCR were outlined by the 2013 THOR conference.<sup>1</sup> These definitions are further buttressed by the time to evacuation of the patient to a DCS capable facility, defined as delayed (>60 min) or prolonged (> 6 hr).<sup>1</sup>

As shown in PROMMTT, the median time to death from hemorrhage is approximately 3 hours from admission,<sup>34</sup> well within the time span of a prolonged evacuation. Eliminating potentially preventable hemorrhagic deaths in the field demands investigators to push the techniques of DCR to the RDCR arena. In 2015, investigators from Bergen, Norway published their experience with placing two units of PRBCs and AB freeze dried plasma (FDP) on rotor wing ambulances.<sup>35</sup> Flight personnel included a "prehospital anesthesiologist" capable of determining the need for transfusion and a systolic blood pressure < 90 mmHg or minimal response to initial fluid resuscitation was utilized as a trigger to give blood products. The administration of all studied FDP products preceded the introduction of prehospital RBC transfusions. No transfusion reactions or deaths were documented.<sup>35</sup> The authors demonstrated a median crystalloid infusion of 0 mL in the prehospital setting, consistent with a blood product first resuscitation strategy.<sup>35</sup> At the time of publication only four patients had received RBC transfusions, limiting statistical analysis; however, demonstrating the practicality of point-of-injury plasma and RBC transfusion.

Following a 2011 trauma task force, the Israeli defense forces (IDF) adopted an FDP-first approach to hemostatic resuscitation for hemorrhaging patients and published their experience in 2013.<sup>24</sup> The IDF indications for transfusion are similar to other groups and include traumatic mechanism of injury and clinical evidence of hemorrhagic shock. Of note, all the designated locations for initial FDP distribution had prior RBC transfusion capabilities, thus allowing for a 1:1 transfusion ratio. The authors reviewed 10 patients with two deaths, a median transfusion of 1.5 units of FDP per patient, and no reported transfusion reactions.<sup>24</sup> Current FDP resuscitation systems are in place at German,<sup>36</sup> French,<sup>37</sup> UK, South African, and Norwegian<sup>35</sup> facilities. Recently, the investigators at the

US Army Institute of Surgical Research described the three battlefield point-of-injury transport systems in Afghanistan: The UK MERT system and the US PEDRO and DUSTOFF systems.<sup>38</sup> Prehospital RBCs and FFP were available on all three platforms. Transfusion ratios and indications were not reported, but the authors demonstrated the efficacy of prehospital hemostatic resuscitation in the combat environment.<sup>38</sup> The current literature has not demonstrated a clinically significant difference in the ability of FDP and FFP to correct coagulopathy.<sup>25,36,39</sup> However, the logistical difficulties of utilizing FFP in the deployed setting further underline the benefits of FDP in the prehospital setting.

The US civilian experience with RDCR hemostatic resuscitation was highlighted by the Mayo Clinic, describing placement of 3 units of RBCs (O negative) and 2 units of FFP (group A) onboard their rotary wing ambulances.<sup>40</sup> Equipped with point-of-care blood testing, Helicopter emergency medical systems (EMS) providers expanded the transfusion criteria from clinical to quantitative data points, including lactate and base deficit.<sup>40</sup> From 2010 through 2014, the authors report over 300 units of RBC and 350 thawed plasma transfusions, demonstrating the potential influence of thawed plasma in the prehospital setting.<sup>40</sup> The authors note that the future of prehospital transfusion medicine will likely include freeze dried products and potentially whole blood. Ongoing US civilian investigations are focusing on prehospital hemostatic resuscitation.<sup>41</sup>

## IMPLICATIONS FROM PROPPR

PROPPR, published in 2015, set out to define the optimal hemostatic resuscitation ratio for severely injured patients by comparing plasma, platelet, and RBC transfusion ratios of 1:1:1 versus 1:1:2.<sup>2</sup> The trial included 12 North American level 1 trauma centers. Six hundred eighty patients were randomized, 338 to the 1:1:1 group and 342 to the 1:1:2 group.<sup>2</sup> All patients were  $\geq 15$  years of age, expected to survive at least 1 hour in the emergency department, and were predicted to receive a massive transfusion. The primary outcomes were mortality at 24 hours and 30 days. There was no significant difference in mortality between the treatments groups at 24 hours or 30 days; however, patients in the 1:1:1 group were significantly more likely to achieve hemostasis than patients in the 1:1:2 group (86% vs. 78%;  $p = 0.006$ ).<sup>2</sup> Twenty-three ancillary outcomes tested the theory that increasing the overall number of transfusions would significantly increase the incidence of inpatient complications. None of the 23 pre-specified outcomes were significantly different between groups, including incidence of sepsis, acute kidney injury, deep venous thrombosis, or acute respiratory distress syndrome (ARDS).<sup>2</sup> Although the primary outcomes of the trial were not different between groups, PROPPR does

**TABLE 2. Assessment of blood consumption score**

Criteria	Points*
Penetrating mechanism	Yes = 1; No = 0
ED systolic blood pressure $\leq 90$ mmHg	
ED HR $\geq 120$ beats/minute	
Positive ultrasound FAST exam	

\* Score  $\geq 2$  increases likelihood of requiring massive transfusion.

address the following questions relating to the RDCR community: 1) Why is it important to have blood products available in the prehospital setting?; 2) Which products should be investigated for prehospital resuscitation algorithms?; 3) What is the most appropriate ratio of transfusion for these products?; and 4) What are the most appropriate indications for hemostatic resuscitation?

Death from exsanguination within the first 24 hours occurred in 31 (9.2%) patients in the 1:1:1 group and 50 (14.6%) patients in the 1:1:2 group ( $p = 0.03$ ).<sup>2</sup> The median time to death was 106 minutes and 96 minutes for the 1:1:1 and 1:1:2 groups, respectively.<sup>2</sup> The reported overall median time to death from exsanguination was 2.3 hours, again highlighting the need for point-of-injury DCR capabilities in RDCR arenas. Stemming from the PROMMTT outcomes, PROPPR demonstrates that early and balanced blood product transfusion ratios reduced mortality in all patients at 3 hours and death from exsanguination at 24 hours ( $p = 0.03$ ).<sup>2</sup> Additionally, a 1:1:1 transfusion ratio significantly increased the percentage of patients achieving anatomic hemostasis (86 vs. 78% in the 1:1:1 and 1:1:2 groups, respectively;  $p = 0.006$ ).<sup>2</sup> The early survival benefit seen in PROPPR has its greatest application in the prehospital setting and suggests that if a high transfusion ratio strategy can be achieved, the likelihood of delivering patients alive to receive definitive care is increased.

Interestingly, at 24 hours the units of RBCs transfused compared between the two groups were similar; however, there was a statistically significant increase in the amount of platelets and plasma transfused in the 1:1:1 group during this time frame.<sup>2</sup> This emphasizes the critical need for early platelet and plasma transfusion in severely injured patients, and suggests prehospital platelet and plasma availability are crucial for effective hemostatic resuscitation.

There are three critical aspects for pushing transfusion medicine into the prehospital arena: 1) appropriate identification of patients requiring a transfusion; 2) appropriate allocation of resources; and 3) a hospital based oversight program.<sup>40</sup>

Using the assessment of blood consumption (ABC, Table 2), PROPPR identified a strategy for early identification of this patient population.<sup>2</sup> The ABC score is an unweighted prediction model of four variables (hypotension, tachycardia, penetrating mechanism, and positive

**TABLE 3. Point-of-injury hemostatic resuscitation systems**

	Structure	Platform*	Offensive capabilities*	Patient capacity	Level provider	PRBCs	Plasma	Indications for transfusion
<b>UK Medical Emergency Response Team Enhanced (MERT—E)</b>	Military	CH-47 Chinook Helicopter	Yes	(8-9)	Anesthesia/Emergency room physician	x	x	Physician discretion
<b>US Air Force—PEDRO</b>	Military	HH-60 Pave Hawk	Yes	(2-3)	EMT-P/Pararescuemen	x	x	hemorrhagic shock
<b>US Army MEDEVAC—DUST OFF</b>	Military	UH-60A Blackhawk	No	(3-6)	EMT-Basic	x	x	Hemodynamic instability with traumatic mechanism SBP < 90, HR > 120, injury resulting in double, triple, or quadruple amputee
<b>Israeli Defense Forces Air platform</b>	Military	UH-60A Blackhawk	No	NA	ALS paramedic or physician	x	x	Hemorrhagic shock
<b>Ground Platform</b>	Military	NATO Role 1 Ground Medical Units	Yes	NA	ALS paramedic or physician	x†	x†	Hemorrhagic shock
<b>Norwegian Air Ambulance</b>	Civilian	EC-145, Augusta Westland 139 helicopters	No	2	Anesthesia/Emergency room physician	x	x†	SBP < 90 and minimal hemodynamic response to fluids, physician discretion
<b>Mayo Clinic Air Operations</b>	Civilian	EC-145 helicopter	No	(1-2)	ACLS/ALS paramedic or nurse	x	x	SBP < 90, HR ≥ 120, penetrating trauma, lactate ≥ 5, INR ≥ 1.5, base deficit ≥ 5, clinical judgment
<b>Houston Life Flight</b>	Civilian	EC-145 helicopter	No	2	ACLS/ALS paramedic or nurse	x	x	Assessment of Blood Consumption (ABC) score

\* Combat medical evacuations are routinely accompanied by additional fire support systems.

† Lyophilized plasma.

focused abdominal sonography in trauma exam (FAST) (Table 2).<sup>42,43</sup> A score  $\geq 2$  identified patients likely to require massive transfusion. The critical administration threshold (CAT) is defined as transfusion of  $\geq 3$  units of blood within 1 hour during the first 24 hours of admission. In the acute setting, the CAT is a better predictor of mortality and more sensitive indicator for identifying patients likely to require ongoing hemostatic resuscitation.<sup>44-46</sup> Extrapolating this definition into the prehospital setting is beneficial for identification of patients likely to require ongoing DCR. These tools antiquate prior strategies based on 24 hours transfusion totals and emphasize early identification, highlighting the increased mortality in this population prior to 24 hours.

It is important to note that prehospital transfusion medicine is not intended for all EMS platforms. Placing RBCs and plasma on all EMS platforms is not logistically possible; however, allocating these resources to air ambulances and platforms dedicated to serving remote locations may be appropriate (Table 3). Furthermore, having dedicated training programs and defining specific indications for transfusion enables nonphysician, nonnurse providers the capability to use this resource.<sup>40</sup> The majority of international EMS systems employ prehospital physicians. The Australian<sup>47</sup> and Norwegian air ambulance systems,<sup>35</sup> in addition to the previously described UK MERT-E system,<sup>38</sup> each have an anesthesiologist or emergency room physician on all transports (Table 3). The US EMS system rarely deploys physicians in the prehospital arena, potentially exposing the US system to a higher rate of nontherapeutic or unindicated transfusions. However, as demonstrated by the successful implementation of civilian RDCR systems at the Mayo Clinic,<sup>40</sup> University of Texas,<sup>48</sup> Royal Caribbean cruise lines,<sup>40</sup> and from the nine institutions associated with the Inflammation and Host Response to Injury collaborative<sup>49</sup> prehospital systems led by nonphysician providers are capable of effectively instituting transfusion medicine.

A critical aspect to the implementation of any prehospital blood product transfusion platform is hospital system oversight. As demonstrated by all civilian RDCR programs, the hospital plays a vital role in reducing blood product waste and ensuring efficient use of this resource in the prehospital setting. If a blood product is not used in the prehospital setting, every institution cycles the product back to the inpatient setting for usage.<sup>40,48</sup> Modeling this highly efficient process, the University of Texas reported that out of 942 prehospital RBC and plasma transfusions, only 18 units (1.9%) were lost due to expiration.<sup>48</sup>

Every institution is responsible for training and ensuring prehospital providers are prepared to effectively use blood products in the prehospital setting. The contribution of these three principals highlights not only the chal-

lenges, but also the feasibility of transitioning hemostatic resuscitation to remote and austere settings.

## FUTURE DIRECTIONS

Improved early outcomes in the 1:1:1 group and the logistical difficulties associated with providing platelets and plasma in the prehospital setting, suggest that whole blood technology should re-emerge as an important therapeutic option. Whole blood transfusion has been a part of military resuscitation strategies for decades, and continues in the current conflicts as "walking blood banks."<sup>50,51</sup> Civilian usage fell from favor with the institution of blood component therapy; however, a recent investigation compared 24-hour transfusion totals between whole blood and component therapy.<sup>52</sup> After excluding patients with traumatic brain injury, a significant reduction in total transfusion requirements, without associated change in mortality, was noted for patients receiving whole blood transfusions ( $p = 0.02$ ).<sup>52</sup>

PROPPR does not address whole blood transfusion but it should spur further research into the design of prehospital whole blood resuscitation. Modifications, including lyophilization, have made the expansion of plasma resuscitation possible and prompt the question of expanding this technology to whole blood. Potentially, before freeze dried whole blood is a viable option, freeze dried alternatives for all three blood components would be acceptable.

Finally, the appropriate end points of resuscitation must be addressed. PROPPR used laboratory testing, angiographic evidence, and surgical control for determination of hemostasis.<sup>2</sup> The majority of these parameters, excluding some point of care testing, are not available in the prehospital environment, and absolutely absent in austere environments. However, expanding on the model of "controlled resuscitation" it appears appropriate to use hemodynamic parameters readily identified in any environment to determine the indications for initiation of a balanced transfusion. Using validated clinical parameters,<sup>53</sup> and point-of-care testing, one can imagine the future combat or civilian patient with an ABC score  $> 2$  receiving balanced hemostatic resuscitation in a 1:1:1 ratio in the field, until arrival at a DCR capable facility. Significant questions remain before this scenario is a reality. The THOR network is at the forefront of these issues, striving to reduce the leading cause of potentially preventable death after injury, uncontrolled hemorrhage.<sup>34,54,55</sup>

## CONCLUSION

The PROPPR study revealed an early survival benefit, decreased death from exsanguination at 24 hours, and a greater likelihood of achieving hemostasis in critically injured patients who received a 1:1:1 ratio of

plasma:platelets:PRBCs. This finding highlights the need to import damage control principles to remote locations. This work is the opinion of the authors, both of whom are affiliated with OHSU, which participated in the PROMMTT and PROPPR trials. Dr Schreiber is affiliated with the THOR network.

#### CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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