

# Impact of critical care–trained flight paramedics on casualty survival during helicopter evacuation in the current war in Afghanistan

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| <b>BACKGROUND:</b>        | The US Army pioneered medical evacuation (MEDEVAC) by helicopter, yet its system remains essentially unchanged since the Vietnam era. Care is provided by a single combat medic credentialed at the Emergency Medical Technician – Basic level. Treatment protocols, documentation, medical direction, and quality improvement processes are not standardized and vary significantly across US Army helicopter evacuation units. This is in contrast to helicopter emergency medical services that operate within the United States. Current civilian helicopter evacuation platforms are routinely staffed by critical care–trained flight paramedics (CCFP) or comparably trained flight nurses who operate under trained EMS physician medical direction using formalized protocols, standardized patient care documentation, and rigorous quality improvement processes. This study compares mortality of patients with injury from trauma between the US Army's standard helicopter evacuation system staffed with medics at the Emergency Medical Technician – Basic level (standard MEDEVAC) and one staffed with experienced CCFP using adopted civilian helicopter emergency medical services practices. |
| <b>METHODS:</b>           | This is a retrospective study of a natural experiment. Using data from the Joint Theater Trauma Registry, 48-hour mortality for severely injured patients (injury severity score $\geq 16$ ) was compared between patients transported by standard MEDEVAC units and CCFP air ambulance units.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| <b>RESULTS:</b>           | The 48-hour mortality for the CCFP-treated patients was 8% compared to 15% for the standard MEDEVAC patients. After adjustment for covariates, the CCFP system was associated with a 66% lower estimated risk of 48-hour mortality compared to the standard MEDEVAC system.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| <b>CONCLUSIONS:</b>       | These findings demonstrate that using an air ambulance system based on modern civilian helicopter EMS practice was associated with a lower estimated risk of 48-hour mortality among severely injured patients in a combat setting. ( <i>J Trauma Acute Care Surg.</i> 2012;73: S32–S37. Copyright © 2012 by Lippincott Williams & Wilkins)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
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Rapid evacuation and early treatment of the severely wounded are paramount to saving lives. Evacuation by helicopter was popularized during the Korean War and revolutionized during the Vietnam War.<sup>1–3</sup> Although the US Army pioneered medical evacuation by helicopter, its system remains essentially unchanged since the Vietnam era.<sup>4</sup> Care is provided by a single combat medic credentialed at the Emergency Medical Technician – Basic level (EMT-B). Treatment protocols, documentation, medical direction, and quality improvement processes are not standardized and vary significantly across US Army helicopter evacuation units. This is in contrast to helicopter emergency medical services (HEMS) that operate within the United States.

Current civilian helicopter evacuation platforms are routinely staffed by critical care–trained flight paramedics (CCFP) or comparably trained flight nurses who operate under trained EMS physician medical direction using formalized protocols, standardized patient care documentation, and rigorous quality improvement processes.

Although it seems intuitive that medical aircrews with a greater scope of practice would yield better patient outcomes, findings and opinions in the civilian literature have been mixed.<sup>5–11</sup> Although numerous studies of HEMS have been performed, Level I evidence supporting or refuting the benefit of HEMS systems is lacking. Studies on HEMS often focus on cost-effectiveness of civilian HEMS systems in the context of civilian injury patterns (primarily blunt vehicular trauma) and often reflect the authors' biases.<sup>5,10–13</sup> These studies are not necessarily transferable to the battlefield setting where penetrating and explosion-related injuries predominate and transport times are often much longer. However, in the setting of conditions common in the military setting, such as multiple injuries, head injury, airway compromise, ventilatory insufficiency, or prolonged evacuation time, there is literature to support the use of advanced practice providers as part of a HEMS system.<sup>10,14–25</sup>

Helicopter evacuation is the principal method of moving patients from the point of injury to an advanced care facility in

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the current conflict in Afghanistan, yet there are currently no data evaluating clinical outcomes of patients transported by US Army medical evacuation (MEDEVAC) helicopters in a combat environment, even after a decade of war. Data are needed to determine the necessary skills, training, and system improvements needed to optimize outcomes during prehospital care.

This review sought to take advantage of a “natural experiment” where mortality of patients with severe injuries caused by combat in Afghanistan transported by the conventional US Army medical evacuation system was compared with the mortality of those transported by an Army National Guard system staffed by clinically active civilian CCFP using current civilian HEMS practices.

## MATERIALS AND METHODS

This study was conducted under a protocol reviewed and approved by the US Army Medical Research and Materiel Command Institutional Review Board and in accordance with the approved protocol.

The study population included all military and civilian patients with an injury severity score (ISS) of 16 or higher transported by air ambulance to military hospitals in southern and eastern Afghanistan between December 2007 and March 2010. These two regions had the greatest volume of combat casualties during the study period and were the regions in which the two different HEMS systems both operated. This study used the natural convenience sample provided by the normal 8- to 12-month rotation of MEDEVAC units into Afghanistan. We compared the mortality of patients transported by the Army's standard helicopter evacuation system (standard MEDEVAC) to those transported by a system staffed with experienced US Army National Guard CCFP who adopted civilian HEMS practices.

Demographics, type of battlefield injury, critical treatment information, and outcome data were obtained from the Joint Theater Trauma Registry (JTTR) database.<sup>26</sup> The JTTR, maintained at the US Army Institute of Surgical Research and modeled after civilian trauma registries, is the largest known combat trauma registry in existence. It includes more than 60,000 combat trauma cases from Iraq and Afghanistan since 2001. Variables examined for this review included age, hospital location (eastern Afghanistan or southern Afghanistan), patient category (US military, North Atlantic Treaty Organization [NATO] military, Afghani military, Afghani civilians), ISS, arrival systolic blood pressure (at the receiving medical facility), injury cause (explosion/blast, gunshot wound, burn, or other/unknown), mechanism of injury (blunt, penetrating, or burn), season of the year, evacuation system (standard MEDEVAC or CCFP), and 48-hour mortality. For much of the analysis, US and NATO military groups were combined because the medical assets, equipment, and treatment protocols in the field are similar. Patients were excluded from the analysis if 48-hour mortality was unknown. Although most trauma system studies examine outcomes at 1 month, most patients transported during this period were Afghani; no mechanism is currently in place to obtain outcomes data from the Afghan facilities. Forty-eight-hour mortality was chosen as an adequate period to identify early deaths related to con-

ditions that might possibly benefit from advanced prehospital or in-flight interventions: hemorrhage, loss of an airway, inability to adequately ventilate or oxygenate, or secondary brain injury.

Standard contingency table analysis was used for categorical data, with significance defined as  $p < 0.05$ . When univariate analysis suggested an association between prespecified variables ( $p < 0.1$ ), they were entered into a multivariate logistic regression model to evaluate their effect on the estimated risk of 48-hour mortality. The standard  $c$  statistic was used to evaluate the predictive accuracy of the overall model, and the Hosmer-Lemeshow test was used for calibration. All data were analyzed with the Statistics Predictive Analytics Software (version 18.0.1; IBM SPSS, Somers, NY).

## RESULTS

Of the 26,000 patients in the JTTR from Operation Enduring Freedom–Afghanistan, 788 patients met initial inclusion criteria. Of those, 117 were excluded because 48-hour mortality information was unavailable. Excluded patients were not significantly different from those included in the study with regard to age, ISS, and distribution of injury cause. The remaining 671 patients comprised the final study population.

Table 1 shows the patient characteristics by evacuation system. A total of 469 patients (70%) were transported by standard MEDEVAC and 202 (30%) were transported by CCFP. Standard MEDEVAC-treated patients were relatively evenly distributed between the eastern and the southern regions of Afghanistan, whereas 84% of CCFP-treated patients were in the eastern region. The distribution of injury causes across groups was similar, with explosives/blast causing most of all injuries treated in both groups followed by gunshot wounds. The 48-hour mortality of the CCFP-treated group was 8% compared with 15% in the standard MEDEVAC-treated group ( $p = 0.011$ ).

Table 2 shows the results of the logistic regression analysis. After adjusting for covariates including an observed interaction between evacuation system and patient category, the odds ratio (OR) for the association between evacuation system and mortality was lower for those transported by CCFP compared with standard MEDEVAC (OR, 0.34; 95% confidence interval [CI], 0.14–0.88). Further, in similar models stratified by patient category, the OR for the association between CCFP and mortality was lowest among the Afghani patients (OR, 0.24; 95% CI, 0.10–0.56).

Several of the covariates were associated with higher mortality. Specifically, patients injured in the southern region were more than 3.5 times more likely to die during the first 48 hours compared with their counterparts in the eastern region. Patients evacuated during the winter months (December, January, and February) were twice as likely to die compared with those transported during the fall months (September, October, and November) and even significantly higher than the other 6 months as well. A higher ISS was also associated with a slightly increased mortality across all groups (OR, 1.03; 95% CI, 1.00–1.05).

To further evaluate the interaction between evacuation system and patient category, separate models by patient category were calculated. Within the subgroup of US/NATO

**TABLE 1.** Characteristics of the Study Population

| Risk Factors                                   | CCFP<br>(n = 202) | Standard MEDEVAC<br>(n = 469) |
|------------------------------------------------|-------------------|-------------------------------|
| Age, mean (SD), y                              | 25.2 (13.1)       | 29.4 (20.4)                   |
| Military treatment facility location,<br>n (%) |                   |                               |
| East                                           | 170 (84)          | 228 (49)                      |
| South                                          | 32 (16)           | 241 (51)                      |
| Patient category, n (%)                        |                   |                               |
| US military                                    | 63 (31)           | 120 (26)                      |
| NATO military                                  | 5 (2)             | 27 (6)                        |
| Afghani military                               | 78 (39)           | 148 (31)                      |
| Afghani civilians                              | 56 (28)           | 174 (37)                      |
| ISS, mean (SD)                                 | 25.4 (8.9)        | 24.8 (9.7)                    |
| Systolic blood pressure, mean<br>(SD), mm Hg   | 122.0 (63.7)      | 115.7 (32.6)                  |
| Cause of injury, n (%)                         |                   |                               |
| Explosive/blast                                | 118 (58)          | 253 (54)                      |
| Gunshot                                        | 61 (30)           | 128 (27)                      |
| Burn                                           | 0 (0)             | 2 (<1)                        |
| Other blunt                                    | 18 (9)            | 60 (13)                       |
| Other penetrating                              | 1 (<1)            | 1 (<1)                        |
| Other unspecified                              | 3 (2)             | 14 (3)                        |
| Unknown/not documented                         | 1 (<1)            | 11 (2)                        |
| 48-h outcome, n (%)                            |                   |                               |
| Lived                                          | 186 (92)          | 398 (85)                      |
| Died                                           | 16 (8)            | 71 (15)                       |

military patients, the OR for the association between evacuation system and mortality was not statistically significant (OR, 1.32; 95% CI, 0.57–3.06). However, within the Afghani subgroup, the OR for the association between CCFP and mortality was lower than that in the overall model (OR, 0.24; 95% CI, 0.10–0.56; data not shown).

Table 3 shows injury severity characteristics stratified by evacuation system and patient category. Within the Afghani patient categories, a marked difference in 48-hour mortality rates is observed between the CCFP-treated and standard MEDEVAC-treated groups. There was no statistical difference between the groups in the US/NATO category.

US/NATO deaths by evacuation system are compared in Table 4. The US/NATO 48-hour mortality was slightly higher in the CCFP group than in the standard MEDEVAC-treated group (15% vs. 12%, respectively), but this difference was not statistically significant. However, US/NATO patients who died were more severely injured than those who died in the standard MEDEVAC-treated group (average ISS, 36 vs. 22, respectively). This finding was also not statistically significant ( $p = 0.075$ ). Specifically, of the 10 deaths in the in the CCFP group, 2 were catastrophically injured with an ISS of 75: 1 with multiple injuries and massive burns and 1 with a devastating blunt head injury (Abbreviated Injury Score [AIS], 6). Five others had significant head injuries (AIS, 4–5). In the standard MEDEVAC-treated group, two patients had an ISS of 75 as in the CCFP group but neither died before 48 hours. One had an isolated gunshot wound to the head and died after 48 hours, whereas another had multiple injuries from a blast injury with

a severe chest wound (AIS, 6) and survived. Seven patients who died in the standard MEDEVAC-treated group had severe head injuries (AIS, 5), but 8 (47%) of 17 who died in the conventional MEDEVAC-treated group had an ISS lower than 20. Patients in the standard MEDEVAC-treated group were also more likely to be hypotensive on arrival to the hospital compared with the CCFP patients, although this also was not statistically significant.

## DISCUSSION

This retrospective study of severely injured patients in a combat setting demonstrated that a US Army air ambulance model based on current civilian air ambulance standards was associated with a 66% lower estimated risk of mortality when compared with standard US Army air ambulance units.

Several differences between the CCFP and the standard MEDEVAC systems likely account for the reduced mortality. First, and perhaps most importantly, are the differences in training and experience of the flight medics. Nearly two thirds (14 of 23) of the medics in the CCFP group were EMT paramedics with an average of 9 years of experience and extensive critical care training before deployment. In contrast, under current standards, only 1 year of experience as an EMT-B is required to become an Army flight medic. Moreover, under the current training model, there is no requirement for preceptor-supervised patient care in a clinical or field setting. Army flight medics may deploy to combat without ever participating in the care of a seriously ill or injured patient in the course of their initial or flight medic training.

The CCFP group adopted the common civilian helicopter transport model using two care providers to transport all but the most routine cases.<sup>27</sup> Those flight medics assigned to the CCFP unit who were certified at the EMT-B or EMT-I level flew only as a second medical crewmember under the supervision of

**TABLE 2.** Logistic Regression Analysis: Evaluation of Risk Factors for 48-Hour Mortality\*

| Risk Factor                                   | OR (95% CI)†     | <i>p</i> |
|-----------------------------------------------|------------------|----------|
| Evacuation system                             |                  |          |
| CCFP                                          | 0.34 (0.14 0.88) | 0.024    |
| MEDEVAC <sub>ref</sub>                        | 1.00             |          |
| ISS                                           | 1.03 (1.00 1.05) | 0.024    |
| Location                                      |                  |          |
| South                                         | 3.66 (1.98 6.78) | 0.000    |
| East <sub>ref</sub>                           | 1.00             |          |
| Season                                        |                  |          |
| Winter                                        | 2.29 (1.01 5.20) | 0.048    |
| Spring                                        | 1.17 (0.48 2.86) | 0.723    |
| Summer                                        | 1.03 (0.48 2.21) | 0.934    |
| Fall <sub>ref</sub>                           | 1.00             |          |
| Patient category                              |                  |          |
| US/NATO military                              | 0.51 (0.26 1.02) | 0.055    |
| Afghan (military and civilian) <sub>ref</sub> | 1.00             |          |

\*Hosmer-Lemeshow statistic 1.47,  $p = 0.99$ ,  $df = 8$ .

†Adjusted for age and (patient category)  $\times$  (evacuation system).

**TABLE 3.** Injury Severity Characteristics Stratified by Evacuation System and Patient Category

| Injury Severity Characteristics    | CCFP-Treated Patients         |                             |                              | MEDEVAC-Treated Patients       |                              |                               |
|------------------------------------|-------------------------------|-----------------------------|------------------------------|--------------------------------|------------------------------|-------------------------------|
|                                    | US /NATO Military<br>(n = 68) | Afghan Military<br>(n = 78) | Afghan Civilians<br>(n = 56) | US /NATO Military<br>(n = 147) | Afghan Military<br>(n = 148) | Afghan Civilians<br>(n = 174) |
| Patients with penetrating injuries | 41                            | 58                          | 44                           | 84                             | 95                           | 119                           |
| Patients with blunt injuries       | 22                            | 18                          | 10                           | 46                             | 38                           | 44                            |
| Patients with ISS of 16–24, n (%)  | 35 (51)                       | 44 (56)                     | 26 (46)                      | 92 (63)                        | 69 (47)                      | 88 (51)                       |
| Patients with ISS ≥25, n (%)       | 32 (47)                       | 34 (44)                     | 30 (54)                      | 55 (37)                        | 79 (53)                      | 86 (49)                       |
| Patients with ISS ≥75, n (%)       | 2 (3)                         | 0                           | 0                            | 2 (1)                          | 1 (≈ 1)                      | 3 (2)                         |
| 48-h mortality rate, %             | 15                            | 4                           | 5                            | 12                             | 18                           | 16                            |
| ISS, mean (SD)                     | 26.0 (11.6)                   | 24.5 (7.2)                  | 26.3 (9.3)                   | 23.9 (9.1)                     | 24.4 (8.3)                   | 26.0 (10.8)                   |

an experienced CCFP. In contrast, standard MEDEVAC helicopters are typically staffed with a single EMT-B flight medic who often treats patients with multiple critical injuries.

Medical direction and oversight for the CCFPs were provided by physician medical directors with experience in trauma and EMS.<sup>28</sup> Standardized patient care protocols, based on those used in civilian EMS systems and adapted for combat, were used by the CCFP group to ensure a consistent standard of care. These protocols were established several years before deployment and allowed for training and evaluation of the CCFP group before their arriving in Afghanistan. While deployed in Afghanistan, the CCFPs received weekly case reports and peer- and medical-director review of standardized patient care reports or “run sheets” for adverse outcome/event analysis, which further ensured that their level of care met the standards of practice for CCFPs.

In contrast, oversight and professional development of the Army flight medic is delegated to the unit flight surgeon. In most cases, Army flight surgeons are primary care physicians, graduates of aerospace medicine residency programs (a preventive medicine subspecialty), or physicians who have completed an internship and are serving in the field while awaiting selection into a residency program. These physicians typically have little or no EMS medical direction, trauma, or critical care experience. The primary responsibility of most flight surgeons is to operate clinics that provide annual physical evaluations and basic urgent care services for Army personnel performing aircrew duties. Because of their obligation to clinic duties, flight surgeons may have limited interaction with their respective air ambulance units. This results in limited continuing medical education and professional development opportunities for the flight medic. Furthermore, treatment protocols, patient care documentation, and performance improvement vary across Army MEDEVAC units and the other military services such as the Navy and Air Force, which also transport patients by helicopter. The result is considerable variability in capability and proficiency across helicopter evacuation units.<sup>4,29–31</sup> It is the authors’ view that Army MEDEVAC medical direction must be systematized with standardized protocols and performance improvement and placed in the hands of experienced military EMS physicians operating in a cooperative role with MEDEVAC commanders.<sup>32</sup>

The lower mortality associated with CCFP transport of Afghani patients was an unanticipated finding. Because this study used trauma registry data that did not include detailed information about individual cases, explanation of these findings is speculative but likely attributable to several factors. First, when compared with US/NATO military personnel, Afghani civilian patients were more vulnerable, ranging in age from neonates to the very elderly and typically in fair to poor health. Many had underlying long-term medical conditions and malnutrition. Second, and probably the most contributory, is the lack of immediate on-scene care at the point of injury because no local EMS system exists. Afghan military and police units typically lack combat lifesavers or medics unless they are working with their US/NATO counterparts. Finally, these patients do not have the state-of-the-art protective gear (body armor, protective eyewear, helmets) that the US and NATO forces are issued. These factors, whether applied individually or collectively, create a patient who is in need of aggressive, advanced resuscitative interventions that take into account the age of the patient, the comorbidities, and the primary medical/trauma condition as soon as the aircraft arrives. Because the training of the standard

**TABLE 4.** Characteristics of US/NATO Military Fatalities Stratified by Evacuation System

| Risk Factors<br>(48-h Mortality)            | CCFP-Treated<br>Group<br>(n = 10, 15%) | Standard<br>MEDEVAC Treated<br>Group (n = 17, 12%) | p     |
|---------------------------------------------|----------------------------------------|----------------------------------------------------|-------|
| Age, mean (SD), y                           | 30.00 (13.16)                          | 31.5 (20.98)                                       | 0.849 |
| Military treatment facility location, n (%) |                                        |                                                    |       |
| East                                        | 9 (90)                                 | 4 (24)                                             | 0.001 |
| South                                       | 1 (10)                                 | 13 (76)                                            |       |
| Patient category, n (%)                     |                                        |                                                    |       |
| US military                                 | 7 (70)                                 | 10 (59)                                            | 0.561 |
| NATO military                               | 3 (30)                                 | 7 (41)                                             |       |
| ISS, mean (SD)                              | 36 (22.13)                             | 22 (4.59)                                          | 0.075 |
| Systolic blood pressure, mean (SD), mm Hg   | 112.3 (12.18)                          | 76.72 (20.90)                                      | 0.211 |

or conventional flight medic focuses primarily on the otherwise healthy combat soldier and does not address the broad age ranges and long-term medical conditions reflected in paramedic training, we hypothesize that these challenging patients benefited most from transport by the CCFP unit.

The results of our study show that the Afghani patient group, which formed the largest segment of the study population, had the greatest improvement in 48-hour survival after transport by the CCFP system. This benefit was not as readily apparent within the US/NATO group. The latter may, in part, be because of the greater severity of injury, and thus the greater likelihood of dying, among the CCFP group compared with the standard MEDEVAC-treated group, within the US/NATO patients, although this difference was not statistically significant. Overall, US/NATO deaths were relatively few in number compared with the Afghani deaths, reducing the statistical power to detect subgroup differences.

Significant differences in mortality were seen between the southern and the eastern regions of Afghanistan. Standard MEDEVAC transports of almost all urgent and priority missions in eastern Afghanistan were typically augmented by a US Army flight surgeon. In contrast, most MEDEVAC missions occurring in southern Afghanistan did not have flight surgeons aboard, in part because that region had fewer available flight surgeons. Therefore, most critically ill patients in the eastern region were flown by a flight physician/flight medic team both before and after the CCFP group, whereas in the south, most of the patient transports were staffed by a single EMT-B flight medic.

Our study has several limitations. JTTR data, like civilian trauma registries, are not population based. Data are abstracted retrospectively from available patient medical records and the total population at risk is not known. However, the JTTR remains the most complete source of data for identifying modern combat-related injuries. This study neither accounted for differences in the number or intensity of tactical operations nor evaluated differences in the quality or availability of prehospital or field surgical care. In some instances, patients in the standard MEDEVAC-treated group were flown with a flight physician, physician assistant, or Air Force pararescuemen trained at the EMT paramedic level. It is also possible that some conventional flight medics obtained paramedic training on their own. Unfortunately, instances where a more advanced provider transferred patients in the standard MEDEVAC-treated group could not be identified because prehospital care documentation is absent from the medical records in most cases. Forward surgical capability, although doctrinally uniform, may have significant differences in the actual experience and capabilities of the providers. There was no way to evaluate or control for the differences in the care received. Transport times were not controlled for because these remain classified information. Although we are unable to present these times, multiple open-source media report that evacuation times in Afghanistan averaged 1.5 hours during the first half of the study period.<sup>33</sup> In January 2009, Secretary of Defense Robert Gates prioritized the need to decrease evacuation times to less than 1 hour. In December 2009, open-source media reported the average evacuation time in Afghanistan had been reduced from 100 to 42 minutes over the preceding year.<sup>34</sup> The CCFP group was deployed in the

middle of the study period from December 2008 to October 2009. It is reasonable to infer that evacuation times were trending downward during the latter half of the study period. Of note, most patients flown by standard MEDEVAC were from November 2009 to August 2010. If time played a significant role in improving outcomes, this benefit would have occurred mostly in the standard MEDEVAC-treated group.

Despite the numerous limitations and potential confounders cited here, this study provides unique and important information concerning the outcomes of patients in the prehospital military setting. Because of the challenges of conducting research in a combat theater, minimal data are available, even after a decade of war. This study was able to take advantage of a natural experiment and should allow military- and national-level policy makers to focus resources needed to improve casualty survival during combat operations.

## CONCLUSIONS

This is the first study to examine the effectiveness of the US Army's helicopter evacuation system in the care of combat casualties on the modern battlefield. This study demonstrates that a US Army National Guard air ambulance unit using CCFP and current EMS practices with a combat adaptation reduced 48-hour mortality in combat casualties with an ISS of 16 or higher by 66% compared with standard Army air ambulance units. This compelling finding warrants expeditious evaluation of a two-provider CCFP-based MEDEVAC aircrew model under professional EMS medical direction. Confirmation of this study's findings should drive aggressive innovation in US Army medical evacuation doctrine to close this capability gap and improve outcomes for those requiring emergency care in the deployed environment.

## AUTHORSHIP

W.C.D. designed this study, for which R.L.M. designed the protocol. All authors participated in analyzing the data. R.L.M. and J.P. prepared the manuscript, which R.T.G. and W.C.D. reviewed.

## DISCLOSURE

The authors have no financial or proprietary interest in the subject matter and no other identifiable conflict of interest. This work was conducted under a protocol approved by the institutional review board at the US Army Medical Research and Materiel Command, Fort Detrick, MD.

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