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# Type O Whole Blood Prehospital Resuscitation For Trauma And Hemorrhage

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A full list of the TOWAR study group is listed in the Supplementary Appendix

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## Abstract

**Background:** The prehospital blood transfusion reduces mortality from traumatic hemorrhage and shock. The benefit of whole blood over component transfusion, and the effect of its storage age, is not certain.

**Methods:** In a pragmatic, multicenter, cluster-randomized, phase-3 trial of trauma patients requiring prehospital transfusion, 44 air medical bases were randomized (2:1) to 1-month blocks of transfusing up to 2 units of whole blood or as needed plasma or red blood cell components. The primary outcome was 30-day mortality. An observational sub-study assessed outcomes according to blood storage age.

**Results:** 715 patients were transported via air bases assigned to the whole blood group and 305 to the component group; 695 and 298, respectively, were included in the primary analysis. Mortality at 30 days was 25.9% in the whole blood group and 20.5% in the component group (adjusted odds ratio 1.24, 95% CI, 0.87 to 1.76; P=0.24). There were no differences in adverse events. In the observational sub-study, 30-day mortality was 26.4% among 443 patients receiving whole blood with storage age 1-14 days and 27.1% among 210 patients with storage age 15-21 days (adjusted odds ratio 0.99, 95% CI, 0.74 to 1.32).

**Conclusions:** In injured patients with hemorrhagic shock, prehospital whole blood did not result in a lower 30-day mortality compared to component blood transfusion.

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## Introduction

Contemporary management of the severely injured patient focuses on the early transfusion of blood products.[1-3] Despite advances in resuscitation, hemorrhage remains a leading cause of preventable death.[4] The transfusion of blood components (red blood cells and/or plasma) in the prehospital environment prior to arrival to definitive care, is associated with improve survival.[2,3]

Treatment with low-titer group O whole blood is increasingly used in both military and civilian settings due to its simplified transfusion logistics and broad donor availability.[5,6] Whole blood can provide rapid, balanced volume resuscitation and concomitant coagulopathy reversal. Multiple observational studies demonstrate that whole blood resuscitation is safe and associated with improved outcomes as compared to component blood resuscitation.[5,7] Despite benefits in the early hospital setting, high-level evidence is limited regarding the efficacy and safety of whole blood in the prehospital phase of care. Knowledge regarding any diminution of hemostatic potential during whole blood storage remains limited.[8-11]

The Type O Whole Blood and assessment of Age during prehospital Resuscitation (TOWAR) trial was designed to determine the safety and efficacy of prehospital low-titer

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group O whole blood as compared to component blood transfusion and to characterize outcome differences attributable to the storage age of whole blood in severely injured patients at risk of hemorrhagic shock requiring transfusion. We hypothesized that prehospital low-titer group O whole blood would reduce 30-day mortality.

## Methods

### Trial Design

The TOWAR trial was a pragmatic, multicenter, cluster-randomized, phase 3 clinical trial comparing whole blood and component transfusion in injured patients at risk of hemorrhagic shock who require blood transfusion prior to definitive care. We compared outcomes for patients administered up to two units of low-titer group O whole blood (low anti-A and anti-B antibody titers; whole blood group) compared to those who received red cells and/or plasma (component group) during prehospital resuscitation. Other than the blood product administered, no other aspect of care was altered during the prehospital phase or after hospital arrival.

Drs. Sperry, Guyette, and Wisniewski designed the study, gathered the data, performed the analyses and vouch for them, wrote the manuscript, and had final responsibility to submit it for publication. There were no agreements between the sponsor and the authors that restricted access to the data, limited the authors' ability to analyze the data independently, or constrained the preparation or submission of the manuscript

### Trial Oversight

The US FDA (Investigational New Drug 26968), the Office of Human Research Oversight of the US Department of Defense, and the Human Research Protection Office at the University of Pittsburgh approved the clinical trial. An external data and safety monitoring board oversaw the trial. The single Institutional Review Board (IRB) at the University of Pittsburgh, with review and acknowledgment from local site IRBs, approved an exception from informed consent to enroll participants. This approval included community consultation and public disclosure. We notified enrolled participants and/or their legally authorized representative as soon as feasible and obtained consent for continued participation. The data are reported according to the CONSORT guidelines. [12]

### Patient Population

Patients transferred from the scene of injury or a referring emergency department to a participating trauma center were eligible for enrollment in the TOWAR trial if they had at least one episode of hypotension (systolic blood pressure ≤ 90mmHg) and tachycardia (defined as a heart rate ≥ 108 beats per minute) or if they had severe hypotension (systolic blood pressure ≤ 70 mmHg) without tachycardia. Eligible patients were enrolled and randomized during transport to the participating trauma center regardless of whether transfer originated at the trauma scene or a referring emergency department. Exclusions included age < 18 or >90 years, isolated falls, drowning, hanging, burns, pregnancy, legal detention, traumatic arrest, penetrating brain injury, inability to obtain intravenous or intraosseous

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access, subject or family member objection or if they were wearing an ‘opt out’ bracelet (Additional exclusions noted in Table S1 in the Supplementary Appendix).

## Randomization and Masking

We employed a single-stage cluster randomization scheme in which air medical bases followed fixed 1-month blocks with a 2:1 allocation to the use of whole blood or component therapy for transfusion; the starting assignment within each block was randomly determined. This randomization scheme was chosen to minimize blood waste, simplify delivery logistics and ensure adequate power for a whole blood observational sub-study. The intervention assignment was open label allowing required regulatory procedures. Assignments were blinded to personnel assessing trial outcomes. There were two participating sites that employed whole blood as their standard prehospital practice at the initiation of the trial. These sites followed the appropriate randomization assignment.

## Intervention Assignment

Blood products were collected using site blood banking protocols and stored at air medical bases following existing procedures. Air medical bases assigned to whole blood for a given month were stocked with two units (group O, anti-A and anti-B titers <256; shelf life up to 21 days). Eligible patients received up to two units of whole blood, with administration of the second unit guided by clinical status and site protocols (available at nejm.org). Bases assigned to the component arm were stocked with red cells and/or plasma; eligible patients received component therapy per standard transfusion practices without protocol-defined minimums or limits. Air medical bases were not limited to carrying only investigational blood products during whole blood assignment months. All additional care, including that received upon arrival at the receiving hospital, was determined by the treating clinicians without further study requirements.

## Trial Outcomes

The primary outcome for the trial was 30-day mortality. Additional prespecified secondary outcomes included 3, 6, and 24-hour mortality, in-hospital mortality, mortality attributable to hemorrhage or brain injury, 24-hour blood transfusion requirements, incidence of multiple organ failure, nosocomial infection, acute respiratory distress syndrome, allergic/transfusion reactions, time to hemostasis, and coagulation measurements. Platelet function was assessed in a convenience sample of patients at 3 sites with measurement capabilities. We analyzed the effect of treatment in prespecified subgroups (Table S2).

**Observational Sub-Study:** To assess the potential association between whole blood age and trial outcomes , we prespecified an observational sub-study limited to patients in the whole blood group in which the 30-day mortality and secondary outcomes were assessed according to whole-blood age of 15–21 vs. 1–14 days since donation.

## Statistical Analysis

Baseline characteristics are summarized by treatment group. The primary outcome, 30-day mortality, was compared using a two-sided Donner–Klar test for proportions. A mixed-

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effects logistic regression model was used to estimate the association between whole blood and 30-day mortality, with a random intercept for service provider and adjustment for study month plus variables imbalanced at baseline prespecified as those with P<0.1 (traumatic brain injury and prehospital intubation).

Prespecified subgroup analyses assessed heterogeneity of the treatment effect using models consistent with the primary analysis, including a treatment-by-subgroup interaction term.

The analysis of secondary outcomes varied according to outcome distribution and otherwise followed the primary analysis. Binary outcomes were analyzed with mixed-effects logistic regression, continuous outcomes with mixed-effects linear regression, and count outcomes with negative binomial regression. Time to death within 30 days was assessed with Kaplan–Meier curves, whereas time to hemostasis was analyzed with a Cox proportional-hazards frailty model to estimate hazard ratios.

Baseline demographic and clinical characteristics were stratified by age of whole blood among patients assigned to the whole-blood group with available storage-age data. When two units of whole blood were transfused, the average age was utilized for analyses. A generalized boosted regression model was used to estimate propensity scores for receipt of older whole blood (15–21 days), incorporating pre-randomization variables known to be associated with the primary outcome. A mixed-effects log-binomial regression model with inverse probability weighting based on the propensity score was used to estimate the association between whole-blood storage age and 30-day mortality. Prespecified subgroup analyses included interaction terms between age and subgroup. Analyses of other outcomes followed the same distribution-based approaches described above.

Sensitivity analyses were performed under multiple assumptions for missing 30-day survival status, including assigning all patients as alive, excluding those with missing outcomes, and assigning all as deceased.

Sample size calculations were carried out prior to the start of the study. A difference in 30-day mortality of 26% versus 16%[3] was able to be detected, assuming 80% power, a two-sided type I error rate of 0.05, 40 service providers, an intraclass correlation coefficient of 0.02[3], a 2:1 random allocation, 340 participants in the component arm and 680 in the whole blood arm (total sample size was 1020).

## Results

From May 2022 to June 2025, a total of 9554 patients who were transported by 44 prehospital bases to 11 trauma centers were assessed for eligibility. A total of 1098 patients were eligible for enrollment. Of those patients, 715 were transported via air bases randomly assigned to the whole blood group, and 305 assigned to the component blood group. A total of 1020 patients met all inclusion and no exclusion criteria comprising the modified intention-to-treat cohort (Figure 1).

Most patients were male (73.0%) and suffered blunt mechanism of injury, with a median injury severity of 25 (interquartile range 14 to 34, score range 0 to 75; score of >15

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indicating major trauma). Traumatic brain injury was present in 405 patients (39.7%) while prehospital intubation occurred in 536 patients (52.5%). Operative intervention was required during the first 24 hours in 634 patients (62.2%). Most patients were transported from the scene (70.8%) with the remaining from a referring emergency department (Table S3). The enrolled patient cohorts were similar across demographics, injury characteristics and prehospital vital signs (Table 1).

## Protocol Adherence

Prehospital teams administered the assigned type of blood transfusion in 964 of 1020 enrolled patients (94.5%). In the whole blood group, 343 patients (48.0%) received 1 unit of whole blood, 326 patients (45.6%) received 2 units of whole blood, and 45 patients received no whole blood. Additional component blood products were transfused in 31.6% of patients randomized to whole blood.

In the component group, 136 patients (44.6%) received 1 unit of red cells, 129 patients (42.3%) received 2 units of red cells, 117 patients (38.6%) received 1 unit of plasma and 93 patients (30.7%) received 2 units of plasma. There were 175 component group patients (59.1%) who received both red cells and plasma. Among component patients, 15 (5.0%) received 1 unit of whole blood while 11 (3.6%) received 2 units of whole blood.

## Primary Outcome

Data on the primary outcome of 30-day mortality was available for 972 patients (95.3%), with 13 patients in the whole blood group and 8 patients in the component blood group having primary outcome data imputed. For the primary analysis, 695 patients in the whole blood group and 298 patients in the component group were analyzed. At 30 days following randomization, overall mortality was 24.3%, with 180 deaths in the whole blood group and 61 deaths in the component blood group. In the intention-to-treat analysis, 30-day mortality was 25.9% in the whole blood group and 20.5% in the component blood group after imputation and adjustment for clustering and imbalance (adjusted odds ratio, 1.24; 95% CI, 0.87–1.76; P=0.24; Table 2). The intraclass correlation coefficient was 0.01 (95% CI, −0.017 to 0.043), indicating negligible clustering and no statistically meaningful site-level variation. The Donner–Klar test showed a between-group difference of 0.082 (P=0.08), indicating no significant difference after accounting for clustering. The results of sensitivity analyses addressing missing 30-day vital status and were similar (Table S4). The Kaplan-Meier survival curves were similar across randomized groups (log-rank chi-square test, 2.18; P=0.13) (Figure 2A). There did not appear to be any differences in 30-day mortality in the 7 prespecified subgroups (Figure 2B).

A per-protocol analysis of patients who received prehospital whole blood or component blood alone is shown in Tables S5 and S6.

## Secondary Outcomes

Mortality at 3, 6, 24 hours and in-hospital mortality appeared to be similar between whole blood and component blood groups. No apparent differences between groups were noted with respect to transfusion requirements, the incidence of multiple organ failure, nosocomial

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infection or acute respiratory distress syndrome. (Table 2). Coagulation measurements and a convenience sample of platelet function measures are shown in Table S7.

**Observational Study of Whole Blood Storage Age:** Of the 668 patients who in the prehospital whole blood group with storage age of whole blood transfused available, 452 patients (67.7%) received whole blood with a storage age of 1 through 14 days since donation while 216 patients (32.3%) received whole blood with a storage age between 15 and 21 days (Figure S1 and Table S8 in the Supplementary Appendix). The storage age of whole blood did not appear to be associated with differences in 30-day mortality (27.1% vs 26.4%, adjusted odds ratio 0.99, 95% CI, 0.74 to 1.32) or other secondary outcomes. (Table S9). The Kaplan-Meier survival curves appeared similar across whole blood age groups (log-rank chi-square test, 0.01; Figure 3A). The results of the 30-day mortality analysis in the 7 prespecified subgroups according to the age of the whole blood suggested no apparent differences. (Figure 3B).

### Safety

Adverse events, including serious adverse events were similar across randomized intention-to-treat groups (Table S10). Adverse events were also similar across whole blood age groups in the observational sub-study (Table S11)

## Discussion

Prehospital blood transfusion for patients at risk of hemorrhagic shock is increasingly common and is associated with improved survival.[1-3,13-15] Whole blood resuscitation is now widely adopted in military and civilian trauma centers because of its logistical and potential hemostatic benefits.[16-21] Despite these changes, high-level evidence demonstrating benefit of prehospital whole blood relative to component resuscitation remains limited.[22,23] Among 1,020 prehospital-enrolled patients, 30-day survival did not differ between groups, nor were apparent differences observed in secondary outcomes including 24-hour transfusion requirements, multiple organ failure, nosocomial infection, acute respiratory distress syndrome, coagulation parameters and platelet function measurements. These results have important implications for both civilian prehospital resuscitation and military blood supply planning.

Hemostatic resuscitation using component blood products in austere, far-forward military settings may not be feasible.[16-18] Whole blood combines the benefits of all three blood components, has a long shelf life, and reduces the need to monitor multiple units of blood product outside the blood bank.[24] The current observational sub-study results represent essential data on patient outcomes and hemostatic function across the storage age of whole blood.

Prehospital care for the severely injured has evolved over time. In a prior prehospital transfusion trial in patients at risk of hemorrhagic shock, which enrolled nearly a decade ago, the standard care arm overall mortality was 33.0%.[3] For the current trial, in a similar patient population, the overall mortality rate for all enrolled patients was 24.3%. A recent prehospital whole blood randomized trial demonstrated similar 30-day mortality

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rates.[23] Improvements including reduced crystalloid resuscitation, early blood transfusion and emphasis on hemorrhage control and resuscitation adjuncts may contribute to lower mortality.[1-3,25-29]

The strengths of the current trial are the pragmatic design with generalizability, pragmatic inclusion criteria, and large sample size. The randomization block design (2:1; whole blood group: component blood group) allowed for a robust observational whole blood sub-study.

Limitations of the trial include the cluster randomized design which was essential due to the logistics of prehospital care. Several variables may have increased the potential risk of type II error for the primary analysis. Blood product crossover occurred across randomized groups. Blood transfusion prior to randomization was not a trial exclusion criteria potentially limiting differences across the randomized groups. The overall transfusion volume provided in the prehospital phase of care was low compared to products provided in-hospital. A proportion of patients in the component blood arm received both plasma and red cells which may have resulted in similar resuscitation characteristics across the randomized groups. Similarly, a proportion of patients in the whole blood arm concomitantly received additional component blood transfusion. The number of blood product units transfused in the prehospital environment was not protocolized. The intervention could not be masked with the potential for treatment bias. Coagulation and platelet functional measurements were limited by missingness and potential spectrum bias. The primary and secondary outcome analyses could be limited by unmeasured or unknown confounders.

In conclusion, in patients requiring prehospital blood transfusion at risk of hemorrhagic shock, whole blood did not result in a lower 30-day mortality. The storage age of whole blood through 21 days from donation was not associated with apparent differences in outcomes.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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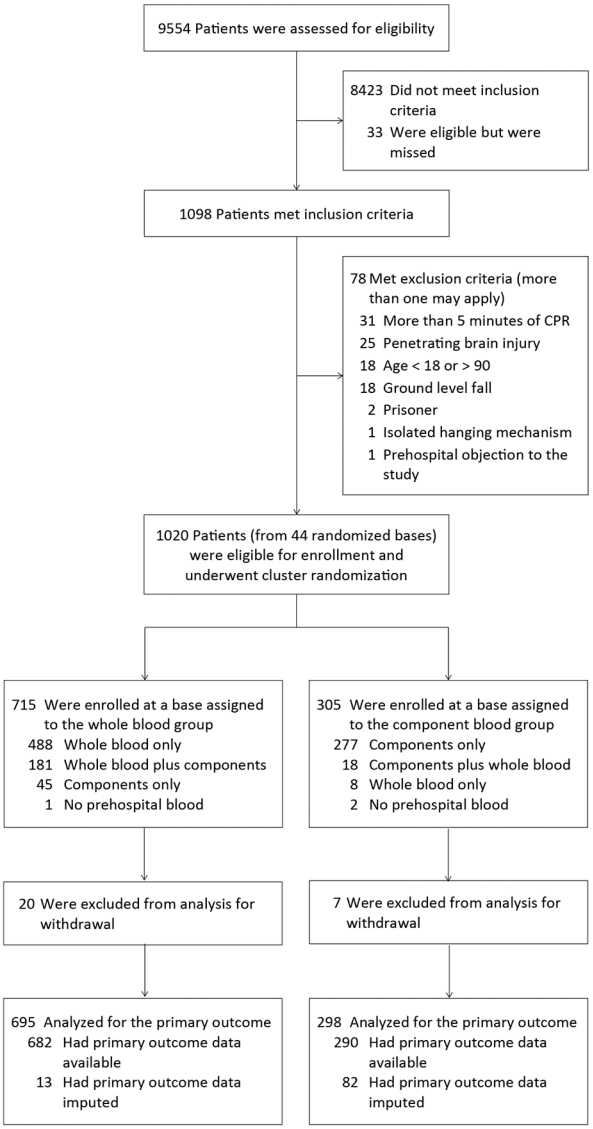


**Figure 1. Screening, Randomization, and Analysis**

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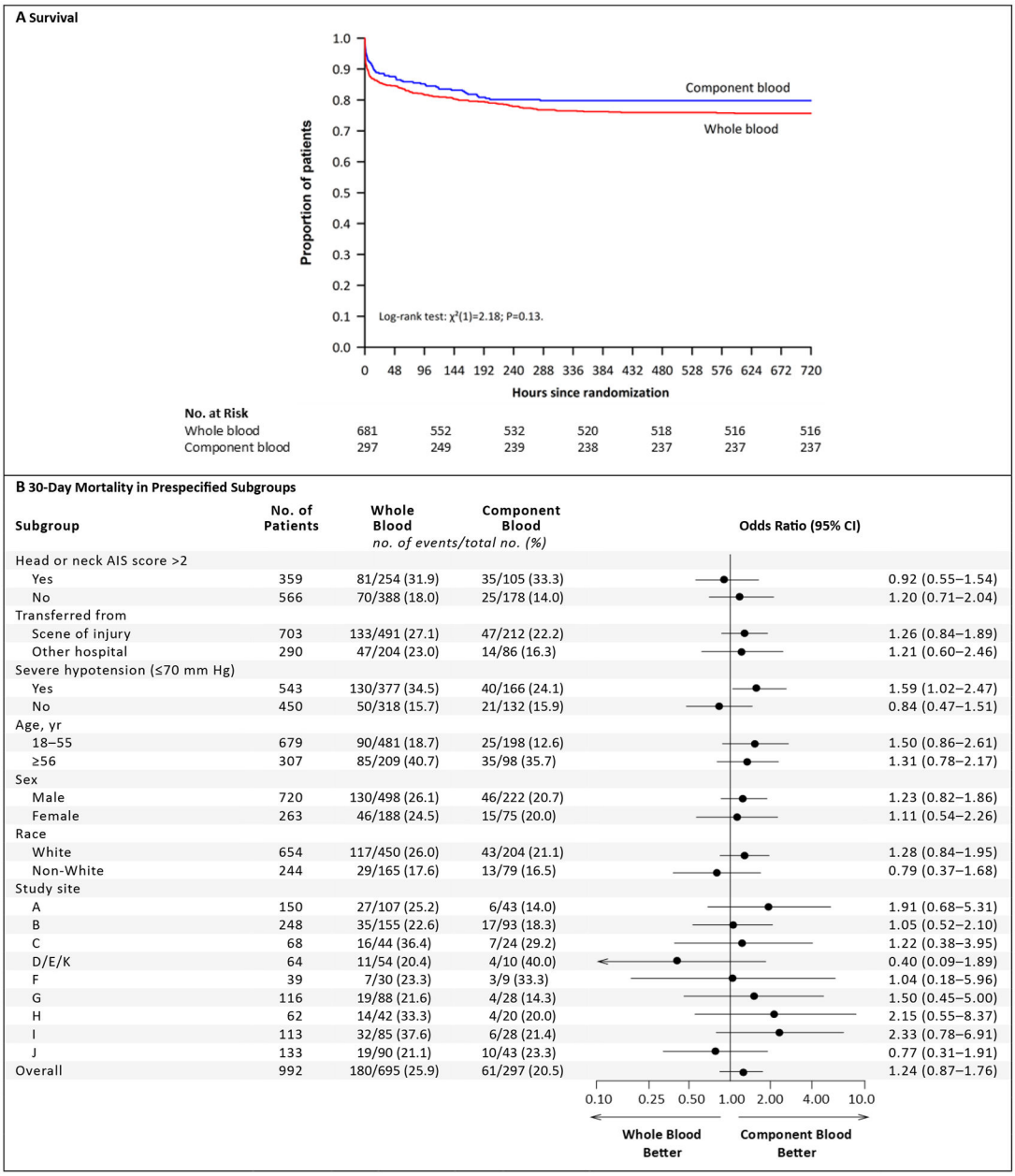


**Figure 2. Survival and Subgroup Analyses of Mortality at 30 Days by Treatment Group.**

Panel A shows Kaplan–Meier estimates of survival among patients who were assigned to whole blood resuscitation or component blood resuscitation in the prehospital setting. Time zero was defined as arrival at a participating TOWAR site. Panel B shows the odds ratio of 30-day mortality across seven prespecified subgroups. The solid vertical line represents an odds ratio of 1.0, indicating no difference in mortality between the whole-blood group and the component-therapy group. Estimates are derived from logistic regression models with 30-day mortality as the outcome, including treatment-by-subgroup interaction terms. All models were adjusted for traumatic brain injury, prehospital intubation, and month of enrollment as fixed effects, with random intercepts and random slopes for air-medical base. Non-White race included Asian, Black or African American, American Indian or Alaska

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Native, and Other. Owing to small numbers of patients and/or events and model convergence limitations, some study sites were combined.

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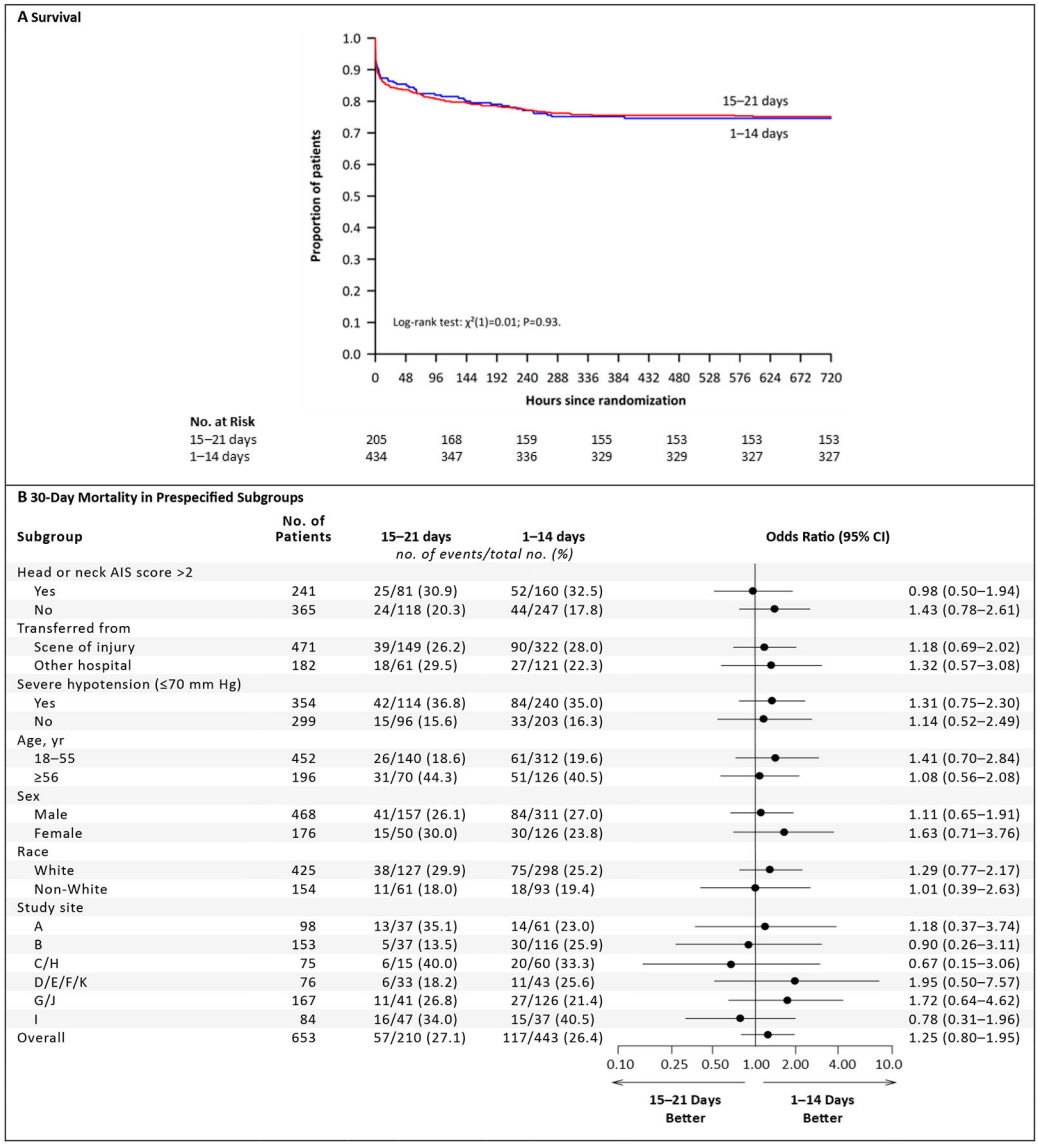


**Figure 3. Survival and Subgroup Analyses of Mortality at 30 Days by Age of Whole Blood.**

Panel A shows Kaplan–Meier estimates of survival among patients who were assigned to whole blood resuscitation or component blood resuscitation in the prehospital setting. Time zero was defined as arrival at a participating TOWAR site. Panel B shows the odds ratio of 30-day mortality across seven prespecified subgroups. The solid vertical line represents an odds ratio of 1.0, indicating no difference in mortality between the whole-blood group and the component-therapy group. Estimates are derived from logistic regression models with 30-day mortality as the outcome, including treatment-by-subgroup interaction terms. All models were adjusted for month of enrollment (fixed effect), air-medical base (random effect to account for clustering), and inverse probability of treatment weighting (IPTW). Non-White race included Asian, Black or African American, American Indian or Alaska Native, and Other. Owing to small numbers of patients and/or events and model convergence limitations, some study sites were combined.

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**Table 1.**

Characteristics of the Patients at Baseline.*

| Characteristic | Whole Blood (N = 715) | Component Blood (N = 305) |
|---|---|---|
| Mean age — yr | 44.8±18.9 | 45.5±19.3 |
| Female sex — no. (%) | 193 (27.3) | 77 (25.3) |
| Non-white race — no. (%) | 168 (26.6) | 80 (27.7) |
| Hispanic ethnicity — no. (%) | 65 (10.6) | 31 (11.8) |
| Injury type — no. (%) | | |
| Blunt | 564 (79.8) | 233 (76.4) |
| Penetrating | 143 (20.2) | 72 (23.6) |
| Injury mechanism — no. (%)† | | |
| Fall | 53 (7.5) | 28 (9.2) |
| Machinery | 6 (0.8) | 3 (1.0) |
| Motor vehicle collision | 478 (67.6) | 190 (62.3) |
| Struck by or against | 16 (2.3) | 5 (1.6) |
| Firearm | 107 (15.1) | 51 (16.7) |
| Impalement | 2 (0.3) | 1 (0.3) |
| Stabbing | 27 (3.8) | 16 (5.2) |
| Other | 45 (6.4) | 19 (6.2) |
| Abbreviated Injury Scale — no. (%)‡ | | |
| Head/Neck >2 | 260 (39.3) | 106 (36.6) |
| Face >2 | 26 (3.9) | 16 (5.5) |
| Chest >2 | 386 (58.4) | 155 (53.4) |
| Abdomen >2 | 222 (33.6) | 112 (38.6) |
| Extremity >2 | 268 (40.5) | 120 (41.4) |
| External >2 | 11 (1.7) | 3 (1.0) |
| Injury Severity Score — median (IQR)§ | 25.0 (16.0–34.0) | 23.0 (14.0–34.0) |
| Qualifying Glasgow Coma Scale — median (IQR) | 11.0 (3.0–15.0) | 13.0 (3.0–15.0) |
| Traumatic brain injury — no. (%) | 296 (41.4) | 109 (35.7) |
| Transferred from — no. (%) | | |
| Scene of injury | 507 (70.9) | 215 (70.5) |
| Other hospital | 208 (29.1) | 90 (29.5) |
| Prehospital interventions — no. (%) | | |
| Intubation | 389 (54.4) | 147 (48.4) |
| CPR | 74 (10.4) | 22 (7.3) |
| Defibrillation | 12 (1.7) | 3 (1.0) |
| Tourniquet | 94 (13.1) | 49 (16.1) |
| Pelvic binder | 155 (21.7) | 67 (22.0) |
| Tranexamic acid | 298 (41.8) | 114 (37.5) |

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| Characteristic | Whole Blood (N = 715) | Component Blood (N = 305) |
|---|---|---|
| Crystalloids/colloids | 446 (62.6) | 192 (63.4) |

[*] Plus–minus values are mean±SD.

[†] More than one may apply.

[‡] Abbreviated Injury Scale scores range from 1 to 6, with higher scores indicating more severe injury (1, minor; 2, moderate; 3, serious; 4, severe; 5, critical; and 6, maximal [untreatable]) and are assigned within each body region (e.g., head/neck, face, chest, abdomen, extremities, external).

[§] The Injury Severity Score (ISS) ranges from 1 to 75, with higher scores indicating more severe injury; it is calculated as the sum of the squares of the highest Abbreviated Injury Scale (AIS) scores in the three most severely injured body regions, with any AIS 6 injury assigned an ISS of 75.

[¶] The Glasgow Coma Scale ranges from 3 to 15, with lower scores indicating decreased level of consciousness; it is the sum of eye-opening (1–4), verbal response (1–5), and motor response (1–6) components

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**Table 2.**

Primary and Secondary Outcomes.*

| Outcome | Whole Blood (N = 695) | Component Blood (N = 298) | Effect Estimate OR / HR / IRR / β (95% CI) | P Value |
|---|---|---|---|---|
| **Primary** | | | | |
| 30-day mortality — no. (%) | 180 (25.9) | 61 (20.5) | 1.24 (0.87 to 1.76) | 0.24 |
| **Secondary** | | | | |
| 3-hour mortality — no. (%) | 64 (9.4) | 16 (5.4) | 1.72 (0.96 to 3.08) | |
| 6-hour mortality — no. (%) | 76 (11.2) | 21 (7.0) | 1.55 (0.92 to 2.62) | |
| 24-hour mortality — no. (%) | 98 (14.4) | 33 (11.1) | 1.25 (0.81 to 1.93) | |
| In-hospital mortality — no. (%) | 171 (24.8) | 58 (19.5) | 1.25 (0.87 to 1.78) | |
| Death by hemorrhage/exsanguination — no. (%)† | 61 (9.0) | 23 (7.8) | 1.08 (0.65 to 1.81) | |
| Death by TBI or herniation — no. (%)† | 61 (9.0) | 23 (7.8) | 0.98 (0.56 to 1.71) | |
| Units transfused within 24 h of arrival — median (IQR) | | | | |
| Whole | 0.0 (0.0–1.0) | 0.0 (0.0–1.0) | 0.91 (0.69 to 1.21) | |
| Plasma | 1.0 (0.0–4.0) | 1.0 (0.0–5.0) | 0.85 (0.66 to 1.11) | |
| Platelets | 0.0 (0.0–1.0) | 0.0 (0.0–1.0) | 0.86 (0.63 to 1.17) | |
| Red cells | 1.0 (0.0–4.0) | 2.0 (0.0–5.0) | 0.86 (0.67 to 1.09) | |
| Cryoprecipitate | 0.0 (0.0–0.0) | 0.0 (0.0–0.0) | 0.81 (0.49 to 1.32) | |
| Hemostasis — no. (%)‡ | 619 (89.2) | 277 (93.6) | 0.61 (0.35 to 1.04) | |
| Minutes to achievement — median (IQR) | 60.0 (60.0–78.0) | 60.0 (60.0–80.0) | 0.98 (0.88 to 1.09) | |
| Multiple organ failure — no. (%)§ | 98 (14.1) | 37 (12.4) | 1.12 (0.74 to 1.69) | |
| Nosocomial infection — no. (%) | 57 (8.2) | 26 (8.7) | 0.92 (0.55 to 1.54) | |
| Acute respiratory distress syndrome — no. (%)§ | 273 (39.3) | 121 (40.6) | 0.87 (0.66 to 1.17) | |
| INR >1.5 within 1 h of arrival — no. (%)¶ | 109 (20.3) | 57 (26.4) | 0.69 (0.46 to 1.02) | |
| PT within 1 h of arrival — median (IQR) | 14.2 (12.3–16.4) | 14.5 (12.2–16.5) | 0.05 (−0.68 to 0.78) | |

*All models were adjusted for traumatic brain injury, prehospital intubation, and month of enrollment as fixed effects, with random intercepts and random slopes for air-medical base. The widths of confidence intervals for secondary outcomes have not been adjusted for multiplicity and should not be used in place of hypothesis tests.

†Listed as ≥1 of up to 2 causes of death.

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[‡] No more than 1 unit of whole blood or red cells in any 60-min interval within 4 h of arrival.

[§] Among patients admitted to the ICU for 2–7 days.

[¶] Because the distribution was bimodal, the variable was dichotomized.