



## Massive Transfusion in Trauma: A Retrospective analysis of MTP utilization and Futility Across Sociodemographic Groups

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### Abstract

**Background:** Blood shortages are a national crisis, creating dangerous scenarios for patients requiring massive transfusion protocol (MTP) in the trauma setting. Judicious use of blood products is critical to rescue salvageable patients while avoiding unnecessary MTP to preserve precious resources.

**Methods:** This retrospective study analyzed ED trauma activations from a database of an urban Level I Trauma Center were analyzed from January 1, 2017, to June 30, 2022, inclusive. In-ED mortality, RBC transfusion volumes during initial resuscitation, patient sociodemographic factors, and trauma event factors were analyzed. The primary outcomes were MTP activation and MTP transfusion. Univariable analyses and multivariable logistic regressions were conducted, applying class balancing sensitivities to the multivariable regressions to address data imbalance. Statistical significance was set at  $P < 0.05$ .

**Results:** Among the 8,670 trauma activations, the in-ED mortality rate was 0.3%. MTP activation and MTP transfusion were associated with higher in-ED mortality rates (3.8% and 15.4%, respectively, compared to 0.2% without MTP). Younger patients, males, and Medicaid recipients were more likely to undergo MTP activation, whereas Medicare patients were less likely. Penetrating trauma significantly increased the likelihood of both MTP activation (OR 5.81) and transfusion (OR 3.63). The logistic regression models identified penetrating trauma, lower probability of survival, and age as the most important covariates. The models demonstrated high discriminatory value (AUROC 0.876 for MTP activation, 0.935 for MTP transfusion) and precision (0.974 for activation, 0.994 for transfusion), with class balancing further enhancing model performance and precision scores.

**Conclusions:** These findings underscore the need for equitable assessment of MTP futility and suggest that future transfusion guidelines should consider the likelihood of patient survival, irrespective of age and trauma mechanism.

**Level of Evidence:** Level IV, original research, case-control

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**Citation:** Monique Arnold, Bharti Sharma, Matthew Conn, Kate Twelker, Navin D Bhatia, George Agriantonis, Sittha Cheerasarn, Jasmine Dave, Juan Mestre, Zahra Shafae, Jennifer Whittington. Massive Transfusion in Trauma: A Retrospective analysis of MTP utilization and futility across sociodemographic groups. *Journal of Surgery and Research*. 7 (2024): 408-416

**Received:** August 13, 2024

**Accepted:** August 26, 2024

**Published:** September 09, 2024

**Keywords:** Transfusion; Trauma; Emergency

### Background

Blood shortages create significant challenges for healthcare facilities when treating patients and safely performing life-sustaining interventions

[1]. Massive Transfusion Protocol (MTP) typically involves transfusing at least 5 units of blood products in fixed ratios (usually 1:1:1 packed red blood cells (pRBC): fresh frozen plasma (FFP): platelets) within an hour to manage hemorrhagic shock; the optimal ratio of blood products remains debatable<sup>2,3</sup>. The decision to activate MTP is at the institution's and the physicians' discretion during trauma resuscitation.<sup>1,4,5</sup> Utilization of MTP dramatically affects blood inventory and availability—although only up to 5% of traumas require massive transfusions, they consume up to 70% of all blood transfused at trauma centers [1,3,6,7].

Despite the development of markers of injury severity such as Injury Severity Score (ISS), Probability of Survival (Ps), and scoring systems for bleeding in trauma such as the Traumatic Bleeding Severity Score (TBSS) and Trauma-Associated Severe Hemorrhage (TASH), there are currently no clear, universally accepted criteria for when to activate MTP in severely injured trauma patients [7-13].

Patient mortality despite receiving MTP may indicate the futility of transfusion. Several factors may contribute to mortality in patients receiving MTP, including age, mechanism of trauma, initial Glasgow Coma Scale Score (GCS), and total amount of blood transfused at 4 hours and 24 hours [7]. These factors should form the basis of an algorithm to determine when massive transfusion should be continued or stopped.

Race, ethnicity, and insurance status independently predict outcome disparities after trauma—specifically, data from a study of almost 430,000 trauma patients shows that African American and Hispanic patients were more likely to be uninsured and to sustain penetrating trauma than White patients, and that African American patients, Hispanic patients, and uninsured patients have worse outcomes during traumas [14]. Insurance status had the strongest association with mortality after trauma, with results showing that uninsured patients were almost 50% more likely to die as a result of trauma [14]. Our study supports the need for equitable assessment of MTP futility and suggests that future transfusion guidelines should consider salvageability in cases with a low probability of survival, regardless of age and trauma mechanism.

This paper examines whether insurance status affects the likelihood of activating and receiving MTP, and how this interacts with other socioeconomic variables and markers of futility. Understanding the futility of MTP is crucial for improving future transfusion guidelines while addressing these disparities. This study is the first large-scale analysis focusing on the association of these factors with MTP utilization and mortality in trauma, independent of blood supply constraints.

## Methods

### Data collection

Institutional Review Board approval with informed consent exemption was obtained, and we conducted a retrospective cohort study of all ED trauma activations at our urban Level I Trauma Center within a large US healthcare system in a major US city from January 2017 to June 2022 inclusive. Patients 18 years of age and older who arrived as a full trauma activation were included. Patients who arrived dead (no discernible blood pressure, pulseless, apneic) were excluded.

Patients for whom MTP was activated ('MTP activations') and who received massive transfusions (determined by the number of pRBCs transfused in the ED, termed 'MTP transfusions') were compared to patients for whom MTP was not activated or transfused. MTP was defined as the transfusion of more than 5 units of blood product within the first 6 hours of ED stay, consistent with the literature (Ang et al., 2023). Recorded data included RBC transfusion volume during initial resuscitation, patient demographics, trauma event characteristics, payer status, and standardized markers of futility such as ISS and Ps. Records missing data for age, sex, race, ethnicity, or payer status were excluded.

### Univariable analyses

Generally, between-group medians were compared using the non-parametric Wilcoxon rank sum test for comparing the median values of two groups and the non-parametric Kruskal-Wallis rank sum test for comparing the median values of three or more groups. Pearson's correlation coefficient was employed to assess the linear relationship between variables ISS and Ps.

Univariable regression analyses were conducted for a priori-determined variables (age, sex, race, ethnicity, Medicaid or Medicare insurance status, trauma type, ISS, and Ps). For numeric variables, the Wilcoxon rank-sum test or Kruskal-Wallis rank-sum test was used. Categorical variables were checked with the  $\chi^2$  test or Fisher's exact test if the number of observations was < 20. Odds ratios (OR), confidence intervals (CI), and p-values for the association of each variable with MTP activation and MTP transfusion were determined.

### Multivariable analyses

Multivariable logistic regression models were constructed to analyze the relationship between the sociodemographic and trauma variables with MTP activation and MTP transfusion. ORs, 95% CIs, and p-values for each covariate in the regression models were determined. MTP activation and transfusion were rare events in the dataset, leading to class imbalances in the data. To avoid biases due to class imbalances, we performed additional regression sensitivities in which we tested six class balancing techniques as below.<sup>15-18</sup>

1. *Weighting using inverse class frequencies*—balancing by scaling the weight of each class to the inverse of its frequency, thereby assigning higher weights to the minority class and lower weights to the majority class;
2. *Weighting using means*—balancing by scaling the weight of each class to the inverse of its frequency, similarly assigning higher weights to the minority class and lower weights to the majority class;
3. *Downsampling (undersampling)*—randomly subsetting (removing or reducing) the majority classes in the training set so that their class frequency matches the minority class;
4. *Upsampling (oversampling)*—randomly subsetting (and replacing with artificial or duplicate data points) the minority classes in the training set so that their class frequency matches the majority class;
5. *Synthetic Minority Over-sampling Technique (SMOTE)*—a hybrid method that downsamples the majority class and synthesizes new data of the minority class using the k-nearest neighbor algorithm;
6. *Random Oversampling Examples (ROSE)*—a hybrid method that utilizes majority downsampling and minority upsampling to synthesize new data of both classes.

**Performance evaluation**

The assessments of the models include Area Under the

Curve (AUC) of the Receiver Operating Characteristic Curve (ROC) and Precision scores (Area Under the Precision-Recall curves (AUPRC)). AUROC was calculated to assess the discriminatory power of the original models and the model sensitivities. AUC is a proxy for accuracy in predicting a binary outcome, with AUCs closer to 1 being more predictive. 95% CI for the AUC for each model was also noted. Precision scores were calculated to measure the overall precision of the models in predicting positive cases. Precision scores quantify the proportion of accurately predicted positive instances among all instances predicted as positive.

All data were analyzed using R version 4.3.1 (version "Beagle Scouts", released June 6, 2016) and RStudio Version 2023.09.1+494. Statistical significance was defined as  $p < 0.05$  for significance at the 95% CI,  $p < 0.01$  at the 99% CI, and  $p < 0.001$  at the 99.99% CI.

There were 8,670 trauma activations. Table 1 shows the socio-demographic and trauma characteristics of the patient sample segregated by MTP activation and MTP transfusion. 90% were traumas due to blunt force and 10% to penetrating trauma. 66% of the sample was male, with a mean age of 53.7 years. Only 3% (n=265) of traumas saw an MTP activation; of those, there were 213 traumas for which MTP was activated but < 5 units of pRBCs were given. As such, only 0.5% of traumas saw an actual MTP transfusion. The median amount of pRBC for those with MTP activations was 2 units and for those with MTP transfusions was 5 units, a statistically significant difference ( $p < 0.01$ ).

**Table 1:** Patient Characteristics

Characteristic	Overall, N = 8,670 <sup>1</sup>	MTP Activated?		MTP Transfused?	
		NO, N= 8405 <sup>1</sup>	YES, N= 265 <sup>1</sup>	NO, N= 8618 <sup>1</sup>	YES, N= 52 <sup>1</sup>
AGE	53.05 (24.23)	53.64 (24.30)	38.60 (19.43)	53.11 (24.26)	43.81 (17.22)
SEX					
Female	2,909 (34%)	2,851 (34%)	58 (22%)	2,896 (34%)	13 (25%)
Male	5,761 (66%)	5,554 (66%)	207 (78%)	5,722 (66%)	39 (75%)
RACE					
American Indian	5 (<0.1%)	5 (<0.1%)	0 (0%)	5 (<0.1%)	0 (0%)
Asian	1,138 (13%)	1,109 (13%)	29 (11%)	1,131 (13%)	7 (13%)
Black	809 (9.3%)	780 (9.3%)	29 (11%)	805 (9.3%)	4 (7.7%)
Native Hawaiian or Other Pacific Islander	7 (<0.1%)	6 (<0.1%)	1 (0.4%)	7 (<0.1%)	0 (0%)
Other	4,843 (56%)	4,681 (56%)	162 (61%)	4,811 (56%)	32 (62%)
White	1,868 (22%)	1,824 (22%)	44 (17%)	1,859 (22%)	9 (17%)
ETHNICITY					
Hispanic Origin	3,154 (36%)	3,041 (36%)	113 (43%)	3,133 (36%)	21 (40%)
Non-Hispanic Origin	5,516 (64%)	5,364 (64%)	152 (57%)	5,485 (64%)	31 (60%)
INSURANCE STATUS					
Medicaid	2,818 (33%)	2,717 (32%)	101 (38%)	2,797 (32%)	21 (40%)
Medicare	2,338 (27%)	2,309 (27%)	29 (11%)	2,334 (27%)	4 (7.7%)
No Charge	889 (10%)	847 (10%)	42 (16%)	879 (10%)	10 (19%)

Other	1,059 (12%)	1,022 (12%)	37 (14%)	1,054 (12%)	5 (9.6%)
Private	1,566 (18%)	1,510 (18%)	56 (21%)	1,554 (18%)	12 (23%)
<b>TRAUMA TYPE</b>					
Blunt	7,789 (90%)	7,623 (91%)	166 (63%)	7,752 (90%)	37 (71%)
Penetrating	881 (10%)	782 (9.3%)	99 (37%)	866 (10%)	15 (29%)
<b>PROBABILITY OF SURVIVAL</b>					
ISS	4.00 (6.92)	4.00 (6.27)	17.00 (13.25)	4.00 (6.71)	25.50 (13.23)
PRBC	0.00 (0.67)	0.00 (0.16)	2.00 (2.66)	0.00 (0.38)	5.00 (2.93)
<b>IN-ED MORTALITY</b>					
N	8,647 (100%)	8,392 (100%)	255 (96%)	8,603 (100%)	44 (85%)
Y	23 (0.3%)	13 (0.2%)	10 (3.8%)	15 (0.2%)	8 (15%)
MTP TRANSFUSED?	52 (0.6%)	0 (0%)	52 (20%)		
MTP ACTIVATION?				213 (2.5%)	52 (100%)

<sup>1</sup>Median (SD); n (%)

**Table 2:** Comparison of In-ED mortality with MTP Activation and Transfusion

In-ED Mortality			
	NO	YES	p-value <sup>1</sup>
<b>MTP Activation?</b>			<0.001
NO	8,392 (99.8%)	13 (0.2%)	
YES	255 (96.2%)	10 (3.8%)	
<b>Total</b>	8,647 (99.7%)	23 (0.3%)	
<b>MTP Transfusion?</b>			<0.001
NO	8,603 (99.8%)	15 (0.2%)	
YES	44 (84.6%)	8 (15.4%)	
<b>Total</b>	8,647 (99.7%)	23 (0.3%)	

<sup>1</sup>Fisher's exact test

The in-ED mortality rate was 0.3% (Table 2). As expected, in-ED mortality was higher with higher ISS and with lower Ps. The median ISS for those who died in the ED was 30 versus 4 for those who did not; this result was statistically significant ( $p < 0.001$ ). The median Ps for those who died in the ED was 0.191 versus 0.983 for those who did not; this result was also statistically significant ( $p < 0.001$ ). MTP activation and MTP transfusion were associated with in-ED mortality—those with MTP activations had a higher rate of in-ED mortality than those without (3.8% vs. 0.2%,  $p < 0.001$ ). Similarly, those receiving MTP transfusions had a higher rate of in-ED mortality than those without (15.4% vs. 0.2%,  $p < 0.001$ ). The discriminatory value of MTP activation on in-ED mortality was high at 0.703 (95% CI 0.599–0.806), while the discriminatory value of MTP transfusion was slightly lower at 0.671 (95% CI 0.572–0.771).

From the univariable analyses shown in table 3, it is evident that younger patients were more likely to have MTP activated and transfused—median age of patients with MTP activation in trauma was 38.60 years vs. 53.64

years for those whom MTP was not activated ( $p < 0.001$ ); similarly, median age of patients with MTP transfusion was 43.81 years vs. 53.11 years for those whom MTP was not transfused ( $p < 0.05$ ). Interestingly, men were almost twice as likely to have MTP activated (OR 1.83, 95% CI 1.37–2.48,  $p < 0.001$ ) but there was no statistically significant difference for sex for MTP transfusion (OR 1.52, 95% CI 0.83–2.96,  $p = 0.18$ ). Though non-Hispanic patients were slightly less likely to have MTP activated (OR 0.76, 95% CI 0.60–0.98,  $p < 0.05$ ), there was no statistically significant difference for MTP transfusion (OR 0.84, 95% CI 0.49–1.49,  $p = 0.55$ ). Likewise, there was no statistically significant difference of MTP activation or MTP transfusion based on race ( $p > 0.05$ ). Patients on Medicare were much less likely to have MTP activated (OR 0.32, 95% CI 0.22–0.47,  $p < 0.001$ ) or have MTP transfused (OR 0.22, 95% CI 0.07–0.55,  $p < 0.001$ ). Patients on Medicaid were more likely to have MTP activated (OR 1.30, 95% CI 1.00–1.66,  $p < 0.05$ ) but there was no statistically significant difference in MTP transfusion (OR 1.42, 95% CI 0.80–2.46,  $p = 0.22$ ).

MTP activation and transfusion also varied with trauma characteristics. Specifically, patients with penetrating trauma were almost 6 times more likely to have MTP activated (OR = 5.81, 95% CI 4.47–7.52,  $p < 0.001$ ) and almost 4 times more likely to have MTP transfused (OR 3.63, 95% CI 1.93–6.50,  $p < 0.001$ ). Trauma type had the largest effects (largest ORs) of all the variables tested. ISS was significantly higher in patients with MTP activations ( $p < 0.001$ ) and MTP transfusions ( $p < 0.001$ ). Median Ps was significantly lower in MTP activations ( $p < 0.001$ ) and MTP transfusions ( $p < 0.001$ ). ISS and Ps were negatively correlated ( $\tau = 0.520, p < 0.001$ ).

The original multivariable logistic regression models were a priori constructed to include age, sex, race, ethnicity, Medicaid or Medicare status, trauma type, ISS, and Ps, as

**Table 3:** Univariable Analysis of Predictors of MTP Activation and MTP Transfusion in Trauma Patients

Characteristic	MTP Activation				MTP Transfusion			
	OR <sup>1</sup>	SE <sup>1</sup>	95% CI <sup>1</sup>	p-value <sup>2</sup>	OR <sup>1</sup>	SE <sup>1</sup>	95% CI <sup>1</sup>	p-value <sup>2</sup>
<b>Age</b>	0.98	0.003	0.98, 0.99	<0.001***	0.99	0.006	0.98, 1.00	0.042*
<b>Race = White</b>				0.14				0.96
White	—	—	—		—	—	—	
American Indian	0	239			0	1,073		
Asian	1.08	0.242	0.67, 1.73		1.28	0.505	0.46, 3.44	
Black	1.54	0.243	0.95, 2.47		1.03	0.602	0.28, 3.16	
Native Hawaiian or Other Pacific Islander	6.91	1.09	0.36, 41.6		0	907		
Other	1.43	0.172	1.03, 2.03		1.37	0.378	0.68, 3.06	
<b>Sex = Male</b>	1.83	0.15	1.37, 2.48	<0.001***	1.52	0.321	0.83, 2.96	0.18
<b>Ethnicity = Non-Hispanic Origin</b>	0.76	0.126	0.60, 0.98	0.033*	0.84	0.284	0.49, 1.49	0.55
<b>Mechanism = Penetrating Trauma</b>	5.81	0.132	4.47, 7.52	<0.001***	3.63	0.308	1.93, 6.50	<0.001***
<b>ISS</b>	1.13	0.006	1.12, 1.15	<0.001***	1.12	0.01	1.10, 1.15	<0.001***
<b>Ps</b>	0.01	0.256	0.01, 0.02	<0.001***	0.01	0.364	0.00, 0.02	<0.001***
<b>Medicare</b>	0.32	0.198	0.22, 0.47	<0.001***	0.22	0.521	0.07, 0.55	<0.001***
<b>Medicaid</b>	1.3	0.129	1.00, 1.66	0.046*	1.42	0.284	0.80, 2.46	0.22

<sup>1</sup>OR = Odds Ratio, SE = Standard Error, CI = Confidence Interval

**Table 4:** Multivariable analysis of predictors of MTP Activation and MTP Transfusion in trauma patients

Characteristic	MTP Activation				MTP Transfusion			
	OR <sup>1</sup>	SE <sup>1</sup>	95% CI <sup>1</sup>	p-value <sup>2</sup>	OR <sup>1</sup>	SE <sup>1</sup>	95% CI <sup>1</sup>	p-value <sup>2</sup>
<b>(Intercept)</b>	2.72	0.75	0.62, 11.8	0.18	0.26	1.16	0.03, 2.48	0.24
<b>Age</b>	0.99	0.004	0.98, 1.00	0.006**	1	0.009	0.98, 1.02	0.94
<b>Race = White</b>								
White	—	—	—		—	—	—	
American Indian	0	387		0.98	0	1,048		>0.99
Asian	0.84	0.269	0.49, 1.41	0.51	0.82	0.537	0.27, 2.34	0.71
Black	0.89	0.284	0.50, 1.54	0.68	0.68	0.654	0.17, 2.31	0.55
Native Hawaiian or Other Pacific Islander	2.51	1.39	0.09, 25.2	0.51	0	788		0.99
Other	0.76	0.233	0.48, 1.20	0.23	0.81	0.488	0.31, 2.15	0.66
<b>Gender = Male</b>	0.84	0.179	0.60, 1.20	0.34	0.8	0.365	0.40, 1.69	0.55
<b>Ethnicity = Non-Hispanic Origin</b>	0.87	0.189	0.60, 1.25	0.45	1.14	0.4	0.51, 2.47	0.74
<b>Medicaid</b>	0.9	0.156	0.66, 1.22	0.5	1.38	0.326	0.72, 2.61	0.33
<b>Medicare</b>	0.69	0.266	0.41, 1.16	0.17	0.37	0.621	0.10, 1.18	0.11
<b>Mechanism = Penetrating</b>	9.79	0.183	6.86, 14.0	<0.001***	3.92	0.391	1.79, 8.36	<0.001***
<b>ISS</b>	0.98	0.017	0.95, 1.01	0.27	0.99	0.02	0.95, 1.03	0.69
<b>PS</b>	0	0.646	0.00, 0.01	<0.001***	0	0.871	0.00, 0.01	<0.001***
<b>ISS * PS</b>	1.19	0.019	1.15, 1.24	<0.001***	1.19	0.028	1.13, 1.26	<0.001***

<sup>1</sup>OR = Odds Ratio, SE = Standard Error, CI = Confidence Interval

<sup>2</sup>\*p<0.05; \*\*p<0.01; \*\*\*p<0.001

well as an interaction variable between ISS and Ps (ISS\*Ps) given their high degree of correlation. Results are shown in table 4. Once again, penetrating trauma had the largest effect, with those with penetrating trauma being almost 10 times more likely to have MTP activated (OR 9.79, 95% CI 6.86–14.0,  $p < 0.001$ ) and almost 4 times more likely to have MTP transfused (OR 3.92, 95% CI 1.79–8.36). Age was a significant covariate for MTP activation (OR 0.99, 95% CI 0.98–1.00,  $p < 0.05$ ), however, it was not for MTP transfusion ( $p = 0.94$ ). AUROC for both models was high–0.876 (95% CI 0.850–0.902) for MTP activation model and 0.935 (95% CI 0.895–0.974) for MTP transfusion. Precision scores were also high–0.974 for MTP activation and 0.994 for MTP transfusion.

Table 5 shows the AUCs, their 95% CI, and Precision scores for the original models and each class balancing sensitivity. All models except the weighting using frequency model had higher AUCs and precision scores than the original regression. AUCs ranged from 0.875 to 0.881 for MTP activation and 0.933 to 0.946 for MTP transfusion across the models. Precision ranged from 0.970 to 0.992 for MTP activation and 0.994 to 1.000 for MTP transfusion across the different models.

## Discussion

This is the first study focusing on the variation in massive transfusion utilization with insurance status and how this interacts with other socioeconomic variables and markers of futility. Of the 8,670 trauma activations, 3.1% involved MTP activations, and 2.5% involved MTP transfusions. MTP activations were associated with higher in-ED mortality, higher ISS, and lower Ps. Patients on Medicare were less likely to have MTP activated, while patients on Medicaid were more likely. Additionally, men, younger patients, and those with penetrating trauma were more likely to have MTP activated; no significant difference was found concerning race. Penetrating trauma and Ps were the most important factors associated with MTP activation.

Univariable analyses indicated that younger age, male gender, and Medicaid recipients were more likely to undergo MTP activation, while those on Medicare were less likely. Penetrating trauma significantly increased the likelihood of both MTP activation (OR 5.81) and transfusion (OR 3.63). Multivariable logistic regression models, including age, sex, race, ethnicity, Medicaid or Medicare status, trauma type, ISS, and Ps, confirmed the substantial impact of penetrating trauma, making individuals almost 10 times more likely to have MTP activated and four times more likely to have MTP transfused. The models demonstrated high discriminatory values (AUROC 0.876 for activation, 0.935 for transfusion) and precision scores (0.974 for activation, 0.994 for transfusion). Class balancing sensitivity improved model performance across various models.

These findings underscore important trends in transfusion practice and raise critical questions about the use of MTP in patients with severe injuries. The decision to transfuse MTP must be judicious and restrictive, and MTP guidelines remain largely subjective. Patients who received MTP had higher ISS and lower Ps, indicating lower chances of survivability and possibly higher risks of futility of transfusion. However, it can be argued that for these patients, from the trauma providers’ perspectives, without MTP fatality is inevitable. This poses the question of how to balance the distribution of blood for those with urgent needs with those who are likely to most benefit when these do not substantially overlap.

## Age, transfusion, and mortality

Prior research shows that older patients are more likely to undergo RBC transfusions and MTP activation than younger patients [7,9,19,20]. Our data refute this, as younger patients were more likely to have MTP activated or transfused. Lim et al. (2018) showed that 32 out of 58 patients with hemorrhagic shock sustained from trauma received MT, with a mean age 11 years younger than those who did not, a statistically significant difference [21]. This large age difference may be explained by the fact that age is a predictor of mortality

**Table 5:** Performance Metrics of Logistic Regression Models.

Model Sensitivity	MTP Activation		MTP Transfusion	
	AUC (95% CI)	Precision	AUC (95% CI)	Precision
Original	0.876 (0.850–0.902)	0.974	0.935 (0.895–0.974)	0.994
Weighting Using Frequency	0.875 (0.848–0.901)	0.97	0.933 (0.893–0.973)	0.994
Weighting Using Means	0.881 (0.856–0.905)	0.992	0.946 (0.919–0.972)	0.999
Downsampling	0.876 (0.850–0.902)	0.992	0.939 (0.914–0.964)	1
Upsampling	0.880 (0.856–0.905)	0.992	0.945 (0.918–0.972)	0.999
SMOTE	0.881 (0.856–0.905)	0.992	0.945 (0.918–0.972)	0.999
ROSE	0.876 (0.852–0.901)	0.992	0.944 (0.914–0.974)	0.999

after trauma, with mortality increasing with age in massively transfused patients [22]. Another retrospective study showed that the association between plasma-to-RBC ratio and in-hospital mortality in non-geriatric patients was clearly shown; however, the relationship between plasma-to-RBC ratio with mortality among geriatric patients remained inconclusive in a trauma setting [23]. Based on these studies, there seems to be a statistically significant difference among ages in the outcome of MTP given in a traumatic setting.

### Sex, transfusion, and mortality

Numerous studies have shown that most patients receiving MTP are male; our results are consistent with this finding [24,25]. The secondary analysis of the Pragmatic Randomized Optimal Platelet and Plasma Ratios (PROPPR) trial, female patients received fewer units of total blood products than their male counterparts after hemostasis was achieved [26]. Specifically, women received lower volumes of all products, with a 38% reduction in FFP, 49% reduction in platelets, and 49% reduction in the volume of RBCs; however, there was no difference in transfusion requirement during active hemorrhage [26]. Finally, men have been shown to have improved outcomes after massive transfusion as compared to women. For example, in a retrospective study of 704 MTP-receiving patients at 23 Level I Trauma Centers, male patients receiving a high plasma-to-RBC ratio had lower 24-hour and 30-day mortality rates while women had no improvements in mortality rates [27].

### Age, ethnicity, race, and insurance status

Our data show that Medicaid patients were more likely to have MTP activated or transfused, while Medicare patients were less likely. Age, ethnicity, and race are intricately correlated with insurance status in the US. In 2010, when the Affordable Care Act (ACA) was passed, seventy percent of non-Hispanic Black nonelderly adults were more likely to be uninsured than non-Hispanic White adult patients.<sup>2</sup> Such disparities in insurance coverage result in poorer access to care leading to worse health outcomes [28-32]. As the number of Black and Hispanic beneficiaries has grown over time, Medicaid has played an increasingly vital role as a source of coverage for racial minorities [34]. Additionally, age is correlated with Medicare access, as, as of 2021, the majority of Medicare beneficiaries (86%) are ages 65 and older, with the remaining 14% qualifying for Medicare because of a long-term disability [33].

### Strengths

An important strength of this study is, as previously discussed, that it delineates MTP activation from MTP transfusion. The decision to activate MTP, as noted, is complex and discretionary. MTP transfusion is impacted by factors including, but not limited to, patient expiration before transfusion is complete or termination of ongoing MTP due

to perceived futility. Additionally, though patients for whom MTP was activated and transfused were a small proportion of the population, our use of class balancing techniques for adjusting for class imbalances reduces bias towards the majority class. These techniques are very popular in the scientific literature; for example, SMOTE is one of the most popular preprocessing techniques and is considered one of the standards in the framework of balancing imbalanced data [18]. The sensitivities had high AUC and precision for predicting MTP activation and transfusion.

### Limitations

Limitations of this study include the retrospective methodology, which comes with a high degree of incomplete and missing documentation. This limits the ability to use all available data in the analysis. Another limitation is our limited direct use of clinical factors affecting MTP activation. For example, vital signs, GCS on arrival, and prior resuscitation efforts have been shown to affect MTP activation in prior studies but were not directly assessed in our study. These factors, however, are incorporated in the calculations for ISS and Ps, so their effects are indirectly measured.

### Conclusions

Our institutional data demonstrate that while insurance status has some effect on MTP activation, penetrating trauma and Ps are the most important factors associated with MTP activation. These results are significant as assessing the futility of MTP should be equitable, and future transfusion guidelines should consider salvageability in cases with a low probability of survival despite age and mechanism.

### Author Contributions

Conceptualization- MA and BS; writing—original draft preparation- MA, BS, and, MC; writing—review and editing- BS, KT, NDB, GA, JD, JM, ZS, SC, and JW; figures and table, MA; supervision- BS and JW; project administration- BS and JW

**Acknowledgment:** Not Applicable

### Funding

There is no grant support or financial relationship for this manuscript.

### Institutional Review Board (IRB) Statement

This retrospective study has IRB approval

### Conflicts of interest

The authors have no competing interests to declare.

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