Title
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Permalink
https://escholarship.org/uc/item/5vj0p771

Journal
Transfusion, 60(5)

ISSN
0041-1132

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Publication Date
2020-05-01

DOI
10.1111/trf.15784

Peer reviewed

Cost-effectiveness evaluation of the PROPPR trial transfusion protocols

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CONFLICTS OF INTEREST

The authors have disclosed no conflicts of interest.

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Abstract

BACKGROUND: There have been no prior investigations of the cost effectiveness of transfusion strategies for trauma resuscitation. The Pragmatic, Randomized, Optimal Platelet and Plasma Ratios (PROPPR) study was a Phase III multisite, randomized trial in 680 subjects comparing the efficacy of 1:1:1 transfusion ratios of plasma and platelets to red blood cells with the 1:1:2 ratio. We hypothesized that 1:1:1 transfusion results in an acceptable incremental cost-effectiveness ratio, when estimated using patients' Age-specific life expectancy and cost of care during the 30-day PROPPR trial period.

STUDY DESIGN AND METHODS: International Classification of Diseases, Ninth Revision codes were prospectively collected, and subjects were matched 1:2 to subjects in the Healthcare Utilization Program State Inpatient Data to estimate cost weights. We used a decision tree analysis, combined with standard costs and estimated years of expected survival to determine the cost effectiveness of the two treatments.

RESULTS: The 1:1:1 group had higher overall costs for the blood products but were more likely to achieve hemostasis and decreased hemorrhagic death by 24 hours (p = 0.006). For every 100 patients treated in the 1:1:1 group, eight more achieved hemostasis than in the 1:1:2 group. At 30 days, the total hospital cost per 100 patients was $5.6 million in the 1:1:1 group compared with $5.0 million in the 1:1:2 group. For each 100 patients, the 1:1:1 group had 218.5 more years of life expectancy. This was at a cost of $2994 per year gained.

CONCLUSION: The 1:1:1 transfusion ratio in severely injured hemorrhaging trauma patients is a very cost-effective strategy for increasing hemostasis and decreasing trauma deaths.

Trauma is the leading cause of death of those aged 1 to 44 years old.[1] It is estimated to be the sixth most costly health care condition in the United States[2] resulting in between $168 billion to over $400 billion dollars in total yearly costs[2,3] including $38 billion to $80 billion in direct costs. The vast majority of the total variation in expenditures reflects the difficulty in quantifying indirect expenditures including costs associated with loss of life expectancy.[3–5]

The largest loss of life from preventable causes of death is attributed to hemorrhage, and most of these deaths happen early in hospitalization.[6–8] Although most of these deaths occur within 6 hours, the care of these patients is extraordinarily resource intensive, including highly trained personnel, equipment, consuming precious blood products, and costing significant fiscal dollars.

Strategies aimed at improving outcome from hemorrhagic death have included balanced deployment of plasma and platelet-rich blood transfusion practices.[9,10] Retrospective and prospective observational data have suggested that trauma patients suffering hemorrhagic injury benefit from receiving blood product resuscitation that aims to achieve equal ratios of red blood cells (RBCs) and plasma.[9–11] No prior investigations of the cost effectiveness of these strategies exist in the literature. The optimal transfusion protocol would improve hemostasis, decrease trauma deaths, and prevent organ damage without increasing overall hospital costs.[12,13]

The Pragmatic, Randomized, Optimal Platelet and Plasma Ratios (PROPPR) study[6] was a Phase III multisite, randomized trial in 680 subjects comparing the efficacy and safety of 1:1:1 transfusion ratios of plasma and platelets to RBCs with the 1:1:2 ratio. The co-primary outcomes of 24-hour and 30-day mortality were previously reported.[3] In parallel with the primary endpoints was a planned prospective economic analysis to quantify costs associated with the two transfusion strategies. We hypothesized, a priori, that 1:1:1 transfusion results in an acceptable incremental cost-effectiveness ratio (ICER), when estimated using patients' age-specific life expectancy and cost of care during the 30-day PROPPR trial period.

METHODS

PROPPR trial description

This economic analysis uses data from the PROPPR Phase III multisite trial conducted for safety and efficacy.[6] Details of the enrollment, primary outcomes (24 hr and 30 days mortality), and protocol have been previously published.[6,14] In summary, this was the largest randomized, prospective trial of differing blood product transfusion ratios for use in traumatic hemorrhage to date. Patients were enrolled if they were a highest-level trauma activation with severe injury at one of 12 North American Level 1 trauma centers. Patients were randomized within each site to receive either a 1:1:1 transfusion ratio or a ratio of 1:1:2 of blood products. The two groups differed in the amount of plasma that was received, with the 1:1:1 group receiving equal packed RBCs to plasma to platelets and the 1:1:2 group receiving a lower quantity of plasma compared with RBCs (one-half as much plasma). The blood products were transfused in a prespecified order depending upon the assigned treatment group to ensure that the ratios were correct. The trial also included real-time recording of predetermined complications of interest using standard definitions, including but not limited to infectious, transfusion, pulmonary, cardiac, renal, and multiorgan failure. [6,14] Patients were followed until 30 days or until death if occurring before 30 days.

Design

The economic analysis focuses on the estimated total hospital costs of the first 30 days of care. A decision tree design was used to examine the economic cost and consequences of using the two specific (1:1:1 vs. 1:1:2) transfusion protocols in the PROPPR study.[15] The tree organizes the clinical trial data to reflect the original trial results for two standard populations of 100 patients (Fig. 1). We used a decision tree populated by the prespecified trial outcomes, combined with standard costs and estimated years of expected survival from

public health statistical reports[16] to structure the data for comparison of the cost effectiveness of the two treatments.[10]

The economic analysis used a decision tree design with an assumption of 100 patients randomized on each arm of the tree. The economically enriched clinical study data were analyzed to provide the proportions and parameters for populating the decision tree. Figure 1 shows the distribution of study patients among the tree branches. The upper part of the tree reflects outcomes for the 338 patients randomized to receive 1:1:1 protocol transfusions, and the lower branch shows the distribution of the 342 patients who were randomized to receive 1:1:1 protocol transfusions. The tree captures the 86.1 and 78.1% hemostasis rates reported in the clinical paper and shows the survival rates for each group based on hemostasis. The column "Population" shows the number of patients out of 100 per treatment who were recorded for each branch at the end of the study, 30 days from randomization. Thus, the tree organizes the clinical trial data to reflect the trial results for two standard populations of 100 patients.

Each branch of the tree has a number of "twigs" that capture the population observed in the study with the specific outcomes. Mean cost of blood and hospital care, and the mean number of years of life expectancy were calculated for each twig. The parameters were then used to calculate costs and outcomes for each twig and summed for the two branches that reflect the treatment groups.

Analyses were performed with computer software (SAS version 9.4, SAS Institute). Multivariable models with a log-link transformation were used to control for any differential effects of age, race, and study site when costs were compared by treatment group.

Estimating overall cost of care

The standard approach used for economic studies in clinical trials that are performed in many sites is to collect data on the treatment resources used and apply "standard" cost weight to the resource counts.[1,8,9] This approach is chosen because neither charges nor estimated costs may be assumed to be similar across the sites. Thus, we collected data only on resource use during the hospital admission, and use the International Classification of Diseases, Ninth Revision (ICD-9) diagnosis and procedure codes to estimate costs per hospital day from a US database that contain all-payer hospital cost data. The effect of this approach was examined in a sensitivity analysis. Hospital length of stay (LOS), including days in the intensive care unit, was recorded, as was the time on ventilator and adverse events (complications) that may impact cost of care and/or LOS.

Thus, all ICD-9 code diagnosis and procedure data reported were prospectively collected on the 680 patients enrolled in the study.[6] We used the Healthcare Cost and Utilization Program (HCUP) State Inpatient Data (SID)[17] set for the estimation of the study cost weights. Patients were matched in a 2:1 ratio of HCUP patients to PROPPR study patients matched upon ICD-9 codes for primary diagnosis. Patients were also matched for LOS, death, intensive care stay, ventilator status, and use of blood. Matching was successful for over 95% of the cohort (1296 controls from HCUP for 680 PROPPR patients). The mean cost per

hospital day was estimated from the matched trauma cases admitted in New York during 2012 and 2013. PROPPR was conducted from August 2012 to December 2013.[3]

The data from New York contained detailed revenue information including unit numbers and charges for any blood components. This level of detail was needed to allow separation of the blood product charges from the total charges. Blood product data were not universally available in the other state SID. Standard daily cost weights were calculated from the extracted New York discharge records for patient subgroups defined by LOS and survival. The cost weights used in the study reflected the mean cost per day of care for trauma patients in the states represented in the study. The derived cost weights were then used to calculate the cost per admission for the PROPPR trial patients based on their survival status and recorded LOS. The cost weights used in the model are provided in Table 1. A sensitivity analysis of the study estimates was performed using state-specific (Kentucky, New Jersey, Florida, Washington, Arizona, Texas) cost weights from the 2011 National Inpatient Sample (NIS) for a matched sample.

Estimating the cost of transfusions

Transfusion cost was assessed separately to evaluate the direct marginal cost of each intervention. Cost of blood was calculated for each patient from the transfusion records in the trial. We used a cost per unit of $230 for RBCs; $65 for plasma, $575 for platelets, and $55 for cryoprecipitate, which were the mean costs reported across the PROPPR sites. We examined the mean blood unit costs calculated from the New York SID billing data in 2012 and 2013 and found very similar mean cost values. Cannon and colleagues[30] report that in a survey of 213 blood banks, the mean purchase cost per unit from a supplier was $211 for RBCs, $61 for plasma, and $533 for platelets.

Incremental cost-effectiveness ratio and sensitivity analysis

The probability of different outcomes observed in the trial, combined with life expectancy for trial patients, were used together with the standard cost data to estimate the ICER of the interventions. Because the cost weights were based on mean values, this estimate exhibits less variation than would be expected if using individual cost and survival data for trial patients. To examine the potential effects of changes in the model parameters, we used a Monte Carlo estimation statistical approach (Excel, Microsoft; Crystal Ball, Oracle), which demonstrates the effect that random variation would be expected to have on the ICER.[18]

This approach reestimates the model results using randomly drawn data points from the critical modeling parameters. We used the calculations of the ICER for total cost per additional year of life expectancy for the sensitivity analysis because this estimate included three important measures used together: 1) blood use, 2) hospital cost, and 3) life expectancy. A total of 1000 simulations were performed to show the effects of variations in the blood and hospital cost and life expectancy parameters on the cost-effectiveness estimates of the main decision model. The results were graphed in a scatter plot to show the effect of the variability of the trial data on the economic estimate. Figure 2 shows how the 1000 estimates were distributed. The horizontal axis shows the difference in cost per patient on protocol 1:1:1 versus protocol 1:1:2. The vertical axis shows the difference in life

expectancy achieved for a patient on protocol 1:1:1 versus protocol 1:1:2. All estimates above the horizontal axis show that protocol 1:1:1 patients had better life expectancy, and estimates below the horizontal axis show that patients on protocol 1:1:2 had better life expectancy. The units are differences in the cost per patient.

RESULTS

Direct cost of blood products and outcomes between treatment arms

The original study outcomes have been reported previously.[6] In summary, the 1:1:1 treatment group (n = 338 patients) and the 1:1:2 group (n = 342 patients) were similar with regard to all baseline characteristics including age, race, and injury severity (injury severity score, 26.5 vs. 26; p = NS; Table 2). Overall blood products used in the first 24 hours were 25.5 units in the 1:1:1 group compared with 19 units in the 1:1:2 group.[6] In considering only the cost attributable to the blood products, the 1:1:1 group had higher overall costs for the blood products but were more likely to achieve hemostasis and decreased hemorrhagic death by 24 hours p = 0.006; (Table 2).

The mean blood cost for patients on protocol 1:1:1 who achieved hemostasis and survived 30 days were $7662, compared to $4530 for those on protocol 1:1:2 (Table 2). For those patients who did not survive, blood costs were higher if they were in the 1:1:1 group. Specifically, if a patient died before achieving hemostasis, mean blood costs were $16,023 versus $9132 (Table 2).

Direct overall hospital costs and life expectancy between treatment arms

The two treatment arms resulted in differing mean hospital costs that reflect the expected economic "penalty" for survival. In PROPPR, at 30 days, difference in survival was 3.7% higher in the 1:1:1 group.[6] For patients who survived after achieving hemostasis, protocol 1:1:1 was more expensive compared with 1:1:2 ($56,131 vs. $54,590; Table 2). In contrast, hospital costs for patients who initially achieved hemostasis on the protocol but ultimately did not survive were lower ($19,431 vs. $25,255). If hemostasis was never achieved resulting in death, the hospital costs were the lowest ($11,009 vs. $10,830).

ICER of 1:1:1 compared with 1:1:2 treatment arm

The ICER of each intervention is presented in Table 3. For total blood costs per 100 patients, the cost was $934,883 for protocol 1:1:1 and $584,744 for protocol 1:1:2. For every 100 patients treated in the 1:1:1 group, 8 more achieved hemostasis than in the 1:1:2 group. The ICER for these additional patients achieving hemostasis was $43,634, which is the difference in cost divided by the difference in the benefit achieved by the two approaches.

At 30 days, the total hospital cost per 100 patients was approximately $5.6 million in the 1:1:1 group compared with $5.0 million in the 1:1:2 group (Table 3). For each additional survivor in the 1:1:1 treatment arm, the ICER was $91,324. Although this group was more expensive, there were 218.5 more years of life expectancy gained. Thus, the ICER per year of life expectancy gained from 1:1:1 transfusion was $2994 when estimated using patients' age-specific life expectancy and cost of care during the 30-day trial period.

Sensitivity analysis

To evaluate the effect of selecting New York cost data for our estimates, we performed a sensitivity analysis for the calculation of the ICER per year of life expectancy. No centers enrolling patients in PROPRR were located in New York. Therefore, we used the 2011 NIS state-specific costs for mean cost per day for matched trauma patients from the states enrolling patients in PROPPR. This resulted in an increase in the ICER from $2994 to $3258 (9% difference).

A Monte Carlo sensitivity analysis was performed to show the effects of variations in the blood and hospital cost and life expectancy parameters on the cost-effectiveness estimates of the main decision model. The results are shown in Fig. 2. The simulation found that protocol 1:1:1 resulted in better life expectancy and lower cost in 30% of the simulations, and better life expectancy and higher cost in 48% of the simulations. Thus, in 860 of the 1000 simulations that used randomly drawn data points from the study data, the model estimated that protocol 1:1:1 achieved better outcome, and 380 of the 1000 simulations also estimated cost savings. Thus, random variation in the data demonstrated minimal effect on the ICER estimates.

ICER for subgroups of interest

The effects of the treatment arms were examined for subgroups including penetrating trauma, initial altered mental status (Glasgow Coma Scale [GCS] score < 9), and structural confirmation of significant traumatic brain injury (TBI) as measured by Abbreviated Injury Scale (AIS) Head score greater than 2 (Table 4). The ICER for blood cost per additional hemostasis was slightly improved over the base estimate for the penetrating trauma subgroup, and greatly improved for those with a GCS score less than 9 at baseline ($19,472 vs. $43,634), and for patients with an AIS Head score greater than 2 at baseline ($24,480 vs. $43,634). The ICER for total cost per additional year of life expectancy improved to $2243 for the penetrating injury subgroup and $1196 for the subgroup with AIS Head score greater than 2 at baseline.

DISCUSSION

Trauma is the leading cause of death worldwide[3,19] and in the United States in those aged 1 to 44 years old.[4] Hemorrhage is the leading cause of potentially preventable death. The economic burden is tremendous, with it ranking first in the number of productive life years lost,[9] but the actual cost of care has been sparsely investigated. Expenditures are estimated between $168 and $400 billion per year,[2,3] including $38 to $80 billion in direct costs.[3–5] Although massively bleeding patients represent a small percentage of overall trauma patients, they are the most resource intensive to care for and have substantially more direct cost attributable to them.[19,20]

In recent years, there has been great interest in defining the optimum transfusion strategy for these bleeding patients. Those resuscitated with more balanced ratios of plasma:platelets:RBCs have shown an improved mortality compared with the historic strategies that were plasma and platelet poor.[10,21,22] Recently, in PROPPR, a randomized

controlled trial of differing transfusion ratios, a small survival advantage for those suffering exsanguinating hemorrhage was found in those receiving a 1:1:1 ratio.[6] More patients in the 1:1:1 arm also achieved hemostasis compared with the 1:1:2 arm.[6] Based on these results, the American College of Surgeons Trauma Quality Improvement Program, the Eastern Association for the Surgery of Trauma and the United Kingdom's National Health Service have promulgated guidelines endorsing a balanced transfusion approach[13,23,24] as the standard of care.

The standard approach used for economic studies in multicenter clinical trials is to collect data on the treatment resources used and apply "standard" costs to each resource.[1,4,5] This addresses variation in charges or costs across sites when determining ICERs. The strength of this study includes the a priori decision to investigate the economic impact of the two treatment arms. This allowed prospective, high-fidelity data collection of economically meaningful variables (ICD-9 codes). Thus, all data necessary to calculate cost weights that are relevant to real practice were available. As expected, those receiving the 1:1:1 strategy had higher direct blood costs. This reflects the study design, whereby this group would receive more plasma and platelets. Likewise, the total hospital costs were higher compared with the 1:1:2 group, but there were substantial gains in life expectancy (218.5 years) for this added cost.

Our estimates of hospitalization costs are similar to the only other US study including trauma patients that examined blood costs. Costs were $46,033 per hospitalization using 2010 to 2012 figures.[20] This is nearly identical to our cost found in patients with penetrating trauma who survived. However, the Zbrozek study also included cardiac surgery patients and did not account for years of life gained for the transfusions or differences in transfusion strategies. In contrast, in the current study we were able to determine the ICER for additional years of life gained by the 1:1:1 approach, which was only $2994. This number is very low compared with accepted cost-effectiveness benchmarks in the literature that range from $20,000 to $100,000 per quality-adjusted life year.[25] Thus, our data support that the 1:1:1 ratio is a cost-effective use of scarce medical resource.

In a sensitivity analysis, the 1:1:1 ratio resulted in increased life expectancy in 86% of the simulations. We used the calculations of the ICER for total cost per additional year of life expectancy for the sensitivity analysis by accounting for the most important determinants: blood use, hospital cost, and life expectancy. This approach is important because improved transfusion protocols are expected to decrease early deaths from trauma, but they may have economic implications, over and above the cost of the blood products used. The results of the study show the importance of collecting data for an economic analysis alongside a clinical trial for patients with costly conditions where the "economic penalty" for even small differences in increased survival is especially heavy. The cost of care can reflect the length of time a patient survives. Those who die of hemorrhage within hours of presentation will appear much less expensive if life expectancy is not considered, whereas those who survive an initial hemorrhagic insult may be extremely costly due to increased length of stay. Thus, it is important to consider ICERs for this study that are derived from more than just blood products used. These analyses are particularly important to slow or halt the diffusion of interventions that do not deliver good value for our health care dollars.[4]

The usefulness of the 1:1:1 ratio was further demonstrated by the decreased ICER for subgroups of particular interest including TBI and those suffering penetrating trauma. The fiscal dollars spent on TBI care are staggering, with the lifetime costs for severe TBI eclipsing $1.8 million per case.[26] The cost effectiveness of plasma and platelet-rich resuscitation in patients presenting with concomitant TBI and hemorrhage has not been previously reported. The ICER was only $1196 for those with an AIS Head score greater than 2 supporting 1:1:1 as an especially beneficial and cost-effective strategy in TBI patients.

This study was designed to focus on the cost attributable to the initial 30 days following enrollment in the trial. Within the first days, patients accrue almost all the acute care hospital costs that may be expected to be affected by difference in approaches to achieving hemostasis. The largest cost "driver" in a trauma episode in the first 30 days is nearly always hospital LOS and intensity of hospital care.[27] The data, however, are also limited by this short time horizon, and we cannot draw conclusions about the long-term indirect costs for survivors. Postdischarge data were not available for trial participants including functional and quality-of-life outcomes.

The charges used for this economic analysis were taken from the data collected for the PROPPR patients and matched controls from New York. We were limited to using only New York data as they were the only available SID that contained detailed revenue charge codes including unit numbers and charges for blood components. Ideally, one would use the SID from the states of the centers enrolling patients in PROPPR, but the individual SIDs did not contain the necessary data for the ICER calculations for transfusion.

To assess the applicability of these economic data, we performed a sensitivity analysis examining the overall ICER of each treatment using hospital costs available in the SID from the states enrolling patients in PROPPR. The daily cost weights were very similar compared to those using the NY data. For example, weights derived from New York were within 2% of those derived from Texas, the highest-enrolling state. When the cost weights used reflected the mean cost per day of care for trauma patients based on a state-specific analysis using NIS 2011, the ICER increased slightly, from $2994 to $3258. Thus, we believe our results to be reflective of the relative charges associated with transfusion and overall hospital charges for the study groups.

The methodology applied in this analysis is similar to that which is used in economic studies of multicenter clinical trials and uses "standard" cost weights.[18,28,29] This approach is an important strength of this study. The use of absolute charges or costs can result in erroneous estimates for ICER. These figures cannot be assumed to be similar across the sites and using them has a risk of introducing bias toward a cost that more predominantly reflects the highest-enrolling centers. Finally, this study uses a Monte Carlo simulation to estimate the effect of random variation in the data used in the model for ICER calculations. Standard statistical tests are not used in analyses that use decision trees to estimate an ICER. Instead, the stability of the model is determined using a Monte Carlo approach that reestimates the model results using randomly drawn data points from the critical modeling parameters.

CONCLUSIONS

Few studies have examined the economic penalty or benefit of a trauma intervention. The PROPPR study offered the opportunity to examine the question whether two different transfusion strategies were clinically and economically different. The 1:1:1 transfusion ratio in severely injured hemorrhaging trauma patients is a cost-effective strategy for increasing hemostasis and decreasing trauma deaths.

ACKNOWLEDGMENTS

ABBREVIATIONS:

|	
AIS	Abbreviated Injury Scale
GCS	Glasgow Coma Scale
HCUP	Healthcare Cost and Utilization Program
ICD-9	International Classification of Diseases, Ninth Revision
ICER	incremental cost-effectiveness ratio
LOS	length of stay
NIS	National Inpatient Sample
PROPPR	Pragmatic, Randomized, Optimal Platelet and Plasma Ratios
SID	State Inpatient Data
TBI	traumatic brain injury

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Fig. 1.
Decision tree used to estimate trial cost-effectiveness ratios. Tran 1:1:1 denotes treatment group. No HS is proportion who did not reach hemostasis. Live 30D are patients surviving at end of study. Die are patients who died during the study period. Population are the estimated number of patients on each tree branch expected if 100 patients were enrolled in each trial arm. Numbers under each branch in the tree are the proportion of patients in the PROPPR trial with the outcome.
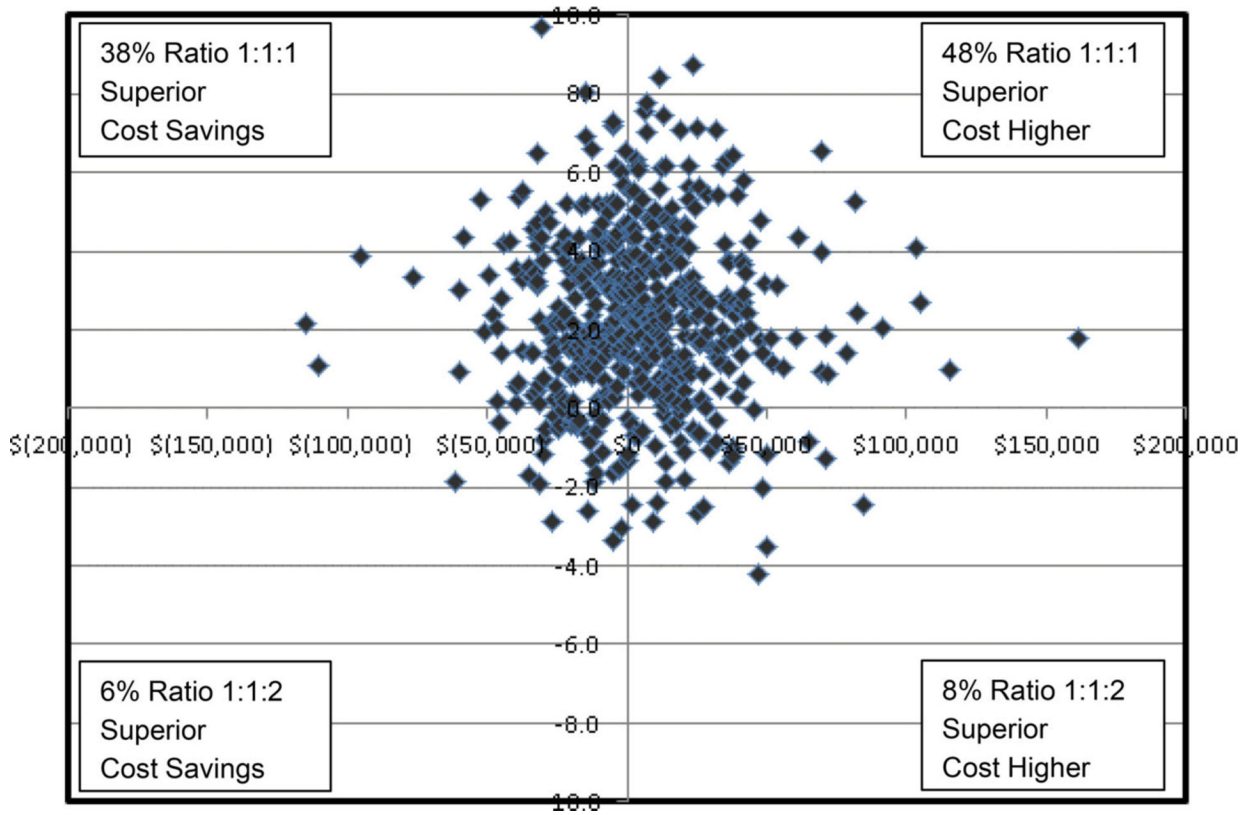
Fig. 2.
Sensitivity analysis of cost and life expectancy differences. Sensitivity analysis represents cost and life expectancy differences between treatments for 1000 Monte Carlo simulations of ICERs for model estimates for total costs per additional year of life expectancy with the percentage of simulations per quadrant.

TABLE 1.

Cost weights used to estimate model values

Type	Cost weight per unit or per day	Source
RBC/unit	$230	Study sites
Plasma/unit	$65	
Platelets/unit	$575	
Cryo/unit	$55	
Admission LOS <2, survivor	$4664	Matched HCUP SID data[*]
Admission LOS 2–5, survivor	$3116	
Admission LOS 6–10, survivor	$2793	
Admission LOS 11–20, survivor	$2634	
Admission LOS 21–29, survivor	$2558	
Admission LOS 30+, survivor	$3023	
Admission LOS <2, died	$9230	
Admission LOS 2–5, died	$4306	
Admission LOS 6–10, died	$3963	
Admission LOS 11–20, died	$3272	
Admission LOS 21–29, died	$2428	
Admission LOS 30+, died	$2994	

[*] Cost of blood excluded, cost calculated using HCUP cost-to-charge ratio data.

HCUP = Healthcare Cost and Utilization Program; LOS = length of stay; SID = State Inpatient Data.

TABLE 2.

Distribution of patients in the PROPPR trial and model parameters derived from the clinical trial and the linked economic data

Variable	Treatment group 1:1:1 N = 338	Treatment group 1:1:2 N = 342	p value
Age (SD)	39.0 (17.4)	38.4 (17.5)	0.66
Race, n (%)			0.35
White	210 (62.1)	224 (65.5)	
Black	93 (27.5)	93 (27.2)	
Other	35 (10.4)	25 (7.3)	
Hemostasis, n (%)	291 (86.1)	267 (78.1)	0.006
Died in study, n (%)	75 (22.4)	89 (26.1)	0.26
Time to death from exsanguination, median (IQR)	106 minutes (54–198)	96 minutes (43–194)	0.57
Blood cost *			
Hemostasis, survivor	7,662 (6,866–8,551)	4,530 (4,036–5084)	
Hemostasis, died	13,320 (9,761–18,177)	9,401 (6,788–13,019)	
No hemostasis, died	16,023 (12,187–21,066)	9,132 (7,249–11,505)	
Total hospital cost *			
Hemostasis, survivor	56,131 (52,434–60,088)	54,590 (50,834–58,624)	
Hemostasis, died	19,431 (16,990–23,613)	25,255 (20,632–30,914)	
No hemostasis, died	11,009 (9273–13,069)	10,830 (9386–12,496)	
Estimated life expectancy, mean (SD)	36.5 (23.1)	34.3 (23.8)	0.22

*
Mean and 95% confidence interval estimated controlling for patient age, race, and study site.

IQR = interquartile range; SD = standard deviation.

TABLE 3.

Decision tree model results: cost, benefits, and ICER for 100 patients for each treatment

Costs and benefits	Treatment group 1:1:1 N = 100	Treatment group 1:1:2 N = 100	Difference or ICER[*]
Base models:			
Total blood cost	$934,883	$584,744	$350,139
Total hemostasis	86.1	78.1	8.0
Cost per additional hemostasis achieved			$43,634
Total survivors at 30 days	77.8	74.0	3.8
Cost per additional survivor			$91,324
Total cost at 30 days	$5,659,725	$5,005,639	$654,086
Total expected life years	3,658.3	3,429.8	218.5
Cost per additional expected life year			$2994

[*]
Note: The calculation of the ICER uses the standard formula (CostT1:1:1 − CostT1:1:2) − (BenefitT1:1:1 − BenefitT1:1:2) = Cost/ Benefits.

ICER = incremental cost-effectiveness ratio.

TABLE 4.

Decision tree model results: base model and sub-group analyses estimates

Costs and benefits	Difference in costs	Difference in benefits	ICER
Base model: blood cost per additional hemostasis:	$350,139	8.0	$43,634
Penetrating trauma patients only	$326,156	7.6	$42,858
Severe brain injury patients only (GCS <9)	$350,411	18.0	$19,472
Severe head trauma patient AIS Head >2	$272,885	11.1	$24,480
Base model: blood cost per additional survivor	$350,139	3.8	$91,324
Penetrating trauma patients only	$326,156	4.5	$72,732
Severe brain injury patients only (GCS <9)	$350,411	12.1	$28,924
Severe head trauma patient AIS Head >2	$272,885	9.6	$28,370
Base model: hospital cost per additional year of life expectancy	$654,086	218.5	$2994
Penetrating trauma patients only	$390,271	174.0	$2243
Severe brain injury patients only (GCS <9)	$1,044,788	607.9	$1719
Severe head trauma patient AIS Head >2	$714,596	597.4	$1196

AIS = Abbreviated Injury Scale; GCS = Glasgow Coma Scale; ICER = incremental cost-effectiveness ratio.