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Risk-stratified thromboprophylaxis effects of aspirin versus low-molecular-weight heparin in orthopaedic trauma patients: a secondary analysis of the PREVENT CLOT trial

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Media Summary: Among trauma patients with a fracture, thromboembolic outcomes were similar with aspirin or enoxaparin, even among patients at highest risk of VTE. Aspirin was favored if patient medication satisfaction was also considered.

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ABSTRACT

Background

The PREVENT CLOT trial concluded that thromboprophylaxis with aspirin was noninferior to low-molecular-weight heparin (LMWH) in preventing death after orthopaedic trauma. However, it was unclear if these results applied to patients at highest risk of thrombosis. Therefore, we assessed if the effect of aspirin versus LMWH differed based on patients' baseline risk of venous thromboembolism (VTE).

Methods

The PREVENT CLOT trial enrolled 12,211 adult patients with fractures. This secondary analysis stratified the study population into VTE risk quartiles: low (<1%) to high (>10%) using the Caprini Score. We assessed stratum-specific treatment effects using the win ratio method, in which each patient assigned to aspirin was paired with each assigned to LMWH. In each pair, we compared outcomes hierarchically, starting with death, then pulmonary embolism, deep vein thrombosis, and bleeding. The secondary outcome added patients' medication satisfaction as a fifth composite component.

Results

In the high risk quartile (n=3052), 80% had femur fracture, pelvic, or acetabular fractures. Thoracic (47%) and head (37%) injuries were also common. In the low risk quartile (n=3053), most patients had a tibia fracture (67%), 5% had a thoracic injury, and less than 1% had head or spinal injuries. Among high risk patients, thromboembolic events did not differ statistically between aspirin and LMWH (win ratio, 0.94; 95% CI, 0.82–1.08, p=0.42). This result was

consistent in the low (win ratio, 1.15; 95% CI, 0.90–1.47, p=0.27), low-medium (win ratio, 1.05; 95% CI, 0.85–1.29, p=0.68), and medium-high risk quartiles (win ratio, 0.94; 95% CI, 0.80–1.11, p=0.48). When medication satisfaction was considered, favorable outcomes were 68% more likely with aspirin (win ratio, 1.68; 95% CI, 1.60–1.77; p<0.001).

Conclusion

Thromboembolic outcomes were similar with aspirin or LMWH, even among patients at highest risk of VTE. Aspirin was favored if medication satisfaction was also considered.

Level of Evidence: Level I, (therapeutic/care management)

Key Words: Thromboprophylaxis; Aspirin; Low-Molecular-Weight Heparin; Trauma

BACKGROUND

Orthopaedic trauma is a known risk factor for venous thromboembolism (VTE) because of the initial injury, surgical intervention, and postoperative immobilization.[1,2] Current thromboprophylaxis guidelines recommend low-molecular-weight heparin (LMWH) in this patient population.[3–6] The PREVENT CLOT trial recently concluded that thromboprophylaxis with aspirin was non-inferior to LMWH in preventing fatal events after orthopaedic trauma.[7]

Selecting the best treatment for a given patient is very different from determining the best treatment on average. As such, clinicians and patients are naturally interested in understanding if the PREVENT CLOT findings are likely to apply to various types of patients with variable risks for VTE. In particular, it is important to assess if the PREVENT CLOT's main findings also apply to patients at increased risk of VTE. Furthermore, little work has been done to incorporate patient satisfaction with treatments into more traditional clinical results.

This paper uses robust approaches for a patient-centered secondary analysis of the PREVENT CLOT trial data to guide patients' and healthcare providers' thromboprophylaxis decision-making.[8–10] Our primary aim was to evaluate if the global assessment of treatment effects varied based on patients' baseline risk of venous thromboembolism. Specifically, this secondary analysis sought to determine if the PREVENT CLOT results apply to patients at highest risk of thrombosis. Our secondary aim added medication satisfaction to the risk-stratified global assessment of treatment effects.

METHODS

Study Design

This study was a secondary analysis of data from the PREVENT CLOT trial.[7,11] PREVENT CLOT was an open-label, pragmatic, randomized clinical trial performed at 21 trauma centers in the United States and Canada. The trial was co-led by the University of Maryland School of Medicine and the Major Extremity Trauma Research Consortium at the Johns Hopkins University Bloomberg School of Public Health. The study was approved by the institutional review boards at all participating sites and the data coordinating center. The CONSORT guidelines were used to ensure proper reporting of methods, results, and discussion (Supplemental Digital Content 1, http://links.lww.com/TA/D453).

Study Participants

We included adult patients who had an indication for thromboprophylaxis and had an operatively treated fracture of the extremities or a pelvic or acetabular fracture treated either operatively or nonoperatively. We excluded patients who presented to the hospital more than 48 hours after injury, were taking long-term blood thinners before their injury, or had a thromboembolic event in the 6 months before the injury. We did not exclude patients due to other traumatic injuries. The protocol allowed patients to receive up to 2 doses of low-molecular-weight heparin as the standard of care for thromboprophylaxis before randomization.[11]

Study Interventions

We randomly assigned patients to aspirin or LMWH with a 1:1 ratio using a computer-generated randomization scheme. Aspirin was to be prescribed at an 81mg dose twice daily per oral (PO)

or per rectal if strict NPO. LMWH was to be prescribed at a 30mg subcutaneous dose twice daily and could be weight-based adjusted according to participating site protocols. The initiation and duration of thromboprophylaxis were based on the existing hospital guidelines at each site. The trial protocol instructed clinicians to be consistent in their indications and prescription duration regardless of treatment assignment. We monitored treatment adherence daily during the index hospital admission and at discharge, and these results have been published.[7] The patient, treating clinicians, and site study coordinators were aware of the treatment allocation. However, the treatment assignment was masked during data monitoring and adjudication.

Study Outcome

The primary outcome of this study was a composite of all-cause mortality, pulmonary embolism (PE), deep vein thrombosis (DVT), and bleeding events within 90 days of randomization. The components were ranked in the aforementioned order based on patients' stated preferences.[12] VTE screening was not required, as per the trial protocol. We defined bleeding events based on previously used definitions as symptomatic bleeding into a critical area or organ, bleeding causing a drop in hemoglobin level of 2g/dL or more within a 24-hour period leading to a transfusion of 2 or more units of whole blood or red cells, or bleeding requiring reoperation.[13,14]

The secondary outcome added medication satisfaction assessed 90 days after randomization as a fifth and final component to the composite outcome. We measured patient satisfaction with their thromboprophylaxis medication using a modified version of the Treatment Satisfaction Questionnaire for Medication (TSQM).[15] We modified the TSQM based on feedback from our patient stakeholder committee and input from the developers. For this trial, we captured overall

satisfaction with the medication on a single item from the larger instrument. The 7-point ordinal item used a Likert scale ranging from "extremely dissatisfied" to "extremely satisfied."

We ascertained study outcomes through an interview with the patient by our clinical research team performed during a clinical appointment or by phone. For patients who ceased clinical follow-up before 90 days or were non-responsive to phone contact, clinical research staff reviewed the patient's medical records to obtain evidence that the patient was alive at 90 days post-randomization or had a study event within the time window. In addition, we queried LexisNexis Accurint, which included access to the Limited Access Death Master File, for mortality information on patients with an unknown status at 90 days post-randomization and to obtain additional contact information from public records. Finally, we used a centralized call center to call each available phone number at least three times for all patients with unknown outcome information.

Risk Stratification

We used the Caprini Score to calculate our study participants' baseline VTE risk.[16] The Caprini Score was first developed in 1991 and assigns points based on the presence of numerous known risk factors for venous thromboembolism.[16] More points indicate a higher baseline risk. The Caprini Score was the VTE risk assessment model recommended by the 2012 Chest guidelines for VTE prevention and has been validated in the orthopaedic trauma and critically ill surgical populations.[17–19] The points assigned based on our measured covariates are described in **Table 1**. We summed the points for each patient to determine their baseline risk (**Figure 1**).

Statistical Analysis

With 12,221 enrolled patients, we had 95% power to detect a 10% relative benefit in at least 2 of the composite outcome components, assuming no difference in the other components with an alpha of 5%.[21] In addition, each quartile in our heterogeneity of treatment effects (HTE) analysis had 90% power to detect a 15% relative benefit in 2 or more components of the composite outcome with an alpha of 5%.

We performed all analyses according to the intention to treat principle. Using the win ratio method, all patients assigned to the aspirin arm were paired with those assigned to LMWH. The pairwise comparison proceeded hierarchically, starting with all-cause mortality, followed by PE, DVT, then bleeding events when the patients could not be differentiated on an outcome of greater importance. The win ratio was then calculated as the total number of wins in the aspirin arm divided by the total number of wins in the LMWH arm. Given the paired hierarchical testing, the win rates can differ from the event rates reported in the primary publication as they assess the probability of avoiding the study outcome by treatment arm after adjusting for the competing risk of a more severe outcome.[7] We obtained 95% confidence intervals using methods described by Bebu and Lachin.[22] Our secondary outcome added patient medication satisfaction using an ordinal scale as the final component to further differentiate patients who did not incur a study event.

To assess the HTE, we assigned each patient Caprini Score risk points and then stratified the sample based on their cumulative points into quartiles. Next, we compared the frequency of each risk factor between risk quartiles using chi-square or Wilcoxon rank-sums tests, depending on

the data type. We then applied the win ratio technique to evaluate the primary and secondary outcomes within each risk stratum.

We imputed missing covariates required for the Caprini Score and missing patient medication satisfaction data using multiple imputations.[23] If the 90-day status was unknown for the other outcomes, we censored patients at their last observation. Our level of significance was set to 0.05. We did not adjust the confidence interval of our secondary outcome or HTE analysis for multiple testing. All statistical analyses were performed using R Version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria) using the *WinRatio* package.

RESULTS

Full Sample

The trial included 12,211 patients from April 2017 through February 2022. Of these, 6101 patients were randomly allocated to receive aspirin, and 6110 were assigned to LMWH (**Figure 2; Table 2**). The median age of the study population was 43 years (interquartile range, 29 to 59), and 62% were male. Nearly half (48%) had a femur, pelvic, or acetabular fracture, and 14% (n=1701) had an Injury Severity Score (ISS) of 16 or more. Forty percent (n=4913) of enrolled patients had a traumatic injury in addition to one or more eligible fractures. Less than 1% (n=89) had a history of VTE. We ascertained a final clinical status at 90 days post-randomization for 92% of the patients.

Our primary win ratio analysis found no statistical difference in the hierarchically assessed primary outcome (win ratio, 0.99; 95% CI, 0.91–1.09; p=0.90) (**Figure 3**). This result was based

on over 37 million pairwise comparisons. The aspirin group won 0.7% of the comparisons by protecting against death and another 14.2% of the comparisons by protecting against PE (1.4%), DVT (1.3%), and bleeding events (11.5%). In contrast, the LMWH group won 0.8% of the comparisons by protecting against death. The LMWH group won another 14.3% of the comparisons due to protection against PE (1.4%), DVT (1.9%), and bleeding events (11.0%). Over 27 million of the comparisons did not favor either medication.

When we added patients' satisfaction with their thromboprophylaxis medication as the fifth and final component to our composite outcome, an overall benefit was 68% more likely when assigned to aspirin than LMWH (win ratio, 1.68; 95% CI, 1.60–1.77; p<0.001) (**Figure 3**). This difference resulted from aspirin winning an additional 35.0% of the comparisons due to increased medication satisfaction. The LMWH group won with higher medication satisfaction in 14.7% of the comparisons. Once the fifth component was added to the composite, less than 8 million comparisons did not favor either treatment.

Risk Stratified Sample

Using the Caprini Score, we stratified the sample into 4 VTE risk quartiles (**Table 2**). The lowest risk quartile commonly featured patients 40 years of age or less (66%), ISS of less than 16 (99%), and a tibia fracture (67%). Patients in the high-risk quartile were distinguished as having a femur fracture (51%) or pelvis or acetabulum fracture (40%), as well as injuries to the abdomen (33%) or head (37%). The high-risk quartile also has the highest proportion of patients with previous diagnoses of cancer (6%) or VTE (2%).

In our win ratio analysis of the clinical outcomes, the 2 medications were statistically indistinguishable in any risk strata (**Figure 4**). When we added the medication satisfaction component to the outcome, aspirin was favored in all 4 risk quartiles. However, the magnitude of the benefit reduced sequentially from the low-risk quartile (win ratio, 2.18; 95% CI, 1.95–2.44; p<0.001) to the high-risk quartile (win ratio, 1.35; 95% CI, 1.23–1.49; p<0.001). The diminishing benefit in the highest risk groups is due to higher rates of clinical outcomes, including death, pulmonary embolism, deep vein thrombosis, or bleeding events, and, therefore, fewer pairs distinguished by the satisfaction component.

DISCUSSION

In our hierarchical global assessment of thromboembolic outcomes, we found no significant difference between aspirin or LMWH thromboprophylaxis among orthopaedic trauma patients. However, when we added medication satisfaction to the evaluation, favorable outcomes measured by the win ratio assessment were significantly more likely in patients assigned to aspirin. These results remained consistent regardless of patients' baseline risk of VTE as calculated by the Caprini Score.

The results of this study support the conclusion of the initial PREVENT CLOT analysis that thromboprophylaxis with aspirin is non-inferior to LMWH among orthopaedic trauma patients with respect to clinical outcomes.[7] In addition, taking a more patient-centered approach, our application of novel methods provides a single measure to infer the total benefits and harms between these treatments. The secondary outcome, which includes medication satisfaction, offers further evidence of patients' preference for aspirin. Medication satisfaction drives this observed

global benefit of aspirin in this patient population as most patients avoid a thromboembolic event after injury.

While our global assessment suggests overall clinical outcomes will be similar with either thromboprophylaxis agent, evaluating the component outcomes helps explain this result. A modest protection against DVT with LMWH is offset by aspirin's greater protection against the more frequent bleeding events. This marginal effect is observed in the full sample and within most risk strata, and it is consistent with a recent trial performed in patients undergoing hip and knee replacement surgery.[24]

The PREVENT CLOT trial's primary analysis used the traditional approach of assessing between-group differences for specific clinical efficacy and safety endpoints. As endpoints are often correlated,[25] this approach is suboptimal for evaluating the totality of the effect on patients.[26] Recent methodological techniques, such as the win ratio, have been developed to use outcomes to analyze patients rather than patients to analyze outcomes to improve the assessment of individual therapies.[8,26] The win ratio uses a composite outcome with ordinally ranked components to define the worst state reached by each patient under observation. Patients and clinicians are interested in multiple outcomes after treatment, but those endpoints often differ in their clinical severity or relative importance. This pragmatic technique better aligns with the patient and clinician experience of having to evaluate treatment options globally.

To further complicate the patient and clinician experience, individual patients have many characteristics that might affect the likelihood of 1 or more outcomes or a worse health state.

Thus, selecting the best treatment for a given patient is very different from determining the best treatment on average. As outcomes tend to correlate, so do baseline factors that can modify treatment effects.[27] The conventional approach to analyzing if treatment effects vary across patients is to stratify patients on single characteristics. This subgroup analysis technique disregards that patients have an indefinite number of attributes and therefore belong to an indefinite number of subgroup strata. Low statistical power and multiplicity also limit the 'one-variable-at-a-time' method. The risk modeling approach suggested by Kent et al.[9,10] overcomes these limitations by stratifying patients according to their multivariate baseline risk of the outcome.

In brief, the design of this secondary analysis offers several strengths not present in the previous literature.[7] The win ratio method provides a single measure to estimate a difference in the totality of benefits and harms between treatments. The method also protects against competing risks. The pairwise comparisons overcome challenges with correlated outcomes. Furthermore, this unique approach overcomes issues pertaining to statistical power and multiple testing that plague most subgroup comparisons.[9,10] Finally, we observed a clear difference in the outcome risk after stratifying the study population with the Caprini Score, confirming its suitability to risk stratify this patient population.[17]

The study has several limitations. Due to anticipated enrollment challenges at the initial hospital admission, the protocol allowed study participants to receive up to 2 doses of low-molecular-weight heparin before randomization. However, given the short half-life of low-molecular-weight heparin and the small percentage of before-consent doses relative to the total number of

doses received, we suspect this design feature had a negligible impact on the findings. The outcome hierarchy can be debated but is supported by robust stated preference research.[12] Furthermore, our composite outcome is likely not exhaustive, and other outcomes might influence the thromboprophylaxis preferences of patients and healthcare providers. Multiple VTE risk scoring systems are relevant to this patient population.[28,29] Many factors included in other scoring systems were not available within our data, such as ventilator duration and the Glasgow Coma Score.[28,29] Given the consistent result across the tested risk strata, we expect that other risk scores would yield a similar result.

The results of this study suggest that thromboembolic outcomes will be similar with either aspirin or LMWH in patients who sustained orthopaedic trauma. This holds true even for patients at highest risk of VTE. Aspirin is heavily favored if patient medication satisfaction is considered in addition to the clinical outcomes. The treatment effects on our global clinical outcomes assessment did not vary based on patient's baseline risk of VTE.

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Legends

Figure 1. Distribution of Caprini Risk Scores for the study population. Patients were grouped into risk quartiles, including low risk (0–4 points), low-medium risk (5–7 points), medium-high risk (8–10 points), and high risk (11 points or more).

Figure 2. CONSORT diagram.

Figure 3. Win ratio analysis for the primary and secondary outcome with the full sample. The left column reports the percentage of wins for each treatment arm decided at each component outcome. The right column reports the win ratio for the primary outcome, which included only clinical outcomes, and the secondary outcome, which added medication satisfaction as the final component of the composite outcome.

Figure 4. Win ratio analysis of primary and secondary outcomes stratified by venous thromboembolism risk quartile. The left column reports the percentage of wins for each treatment arm decided at each component outcome. The right column reports the win ratio for the primary outcome, which included only clinical outcomes, and the secondary outcome, which added medication satisfaction as the final component of the composite outcome.

Figure 1

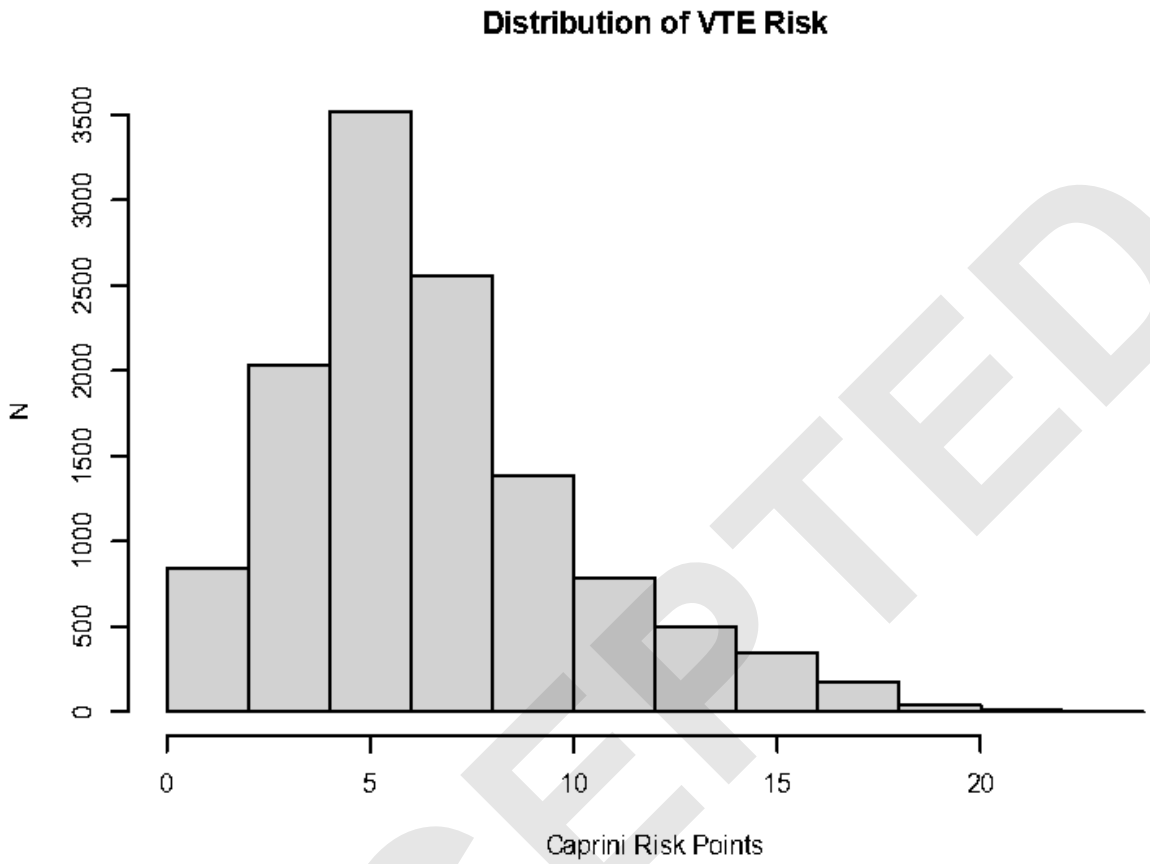

Figure 2

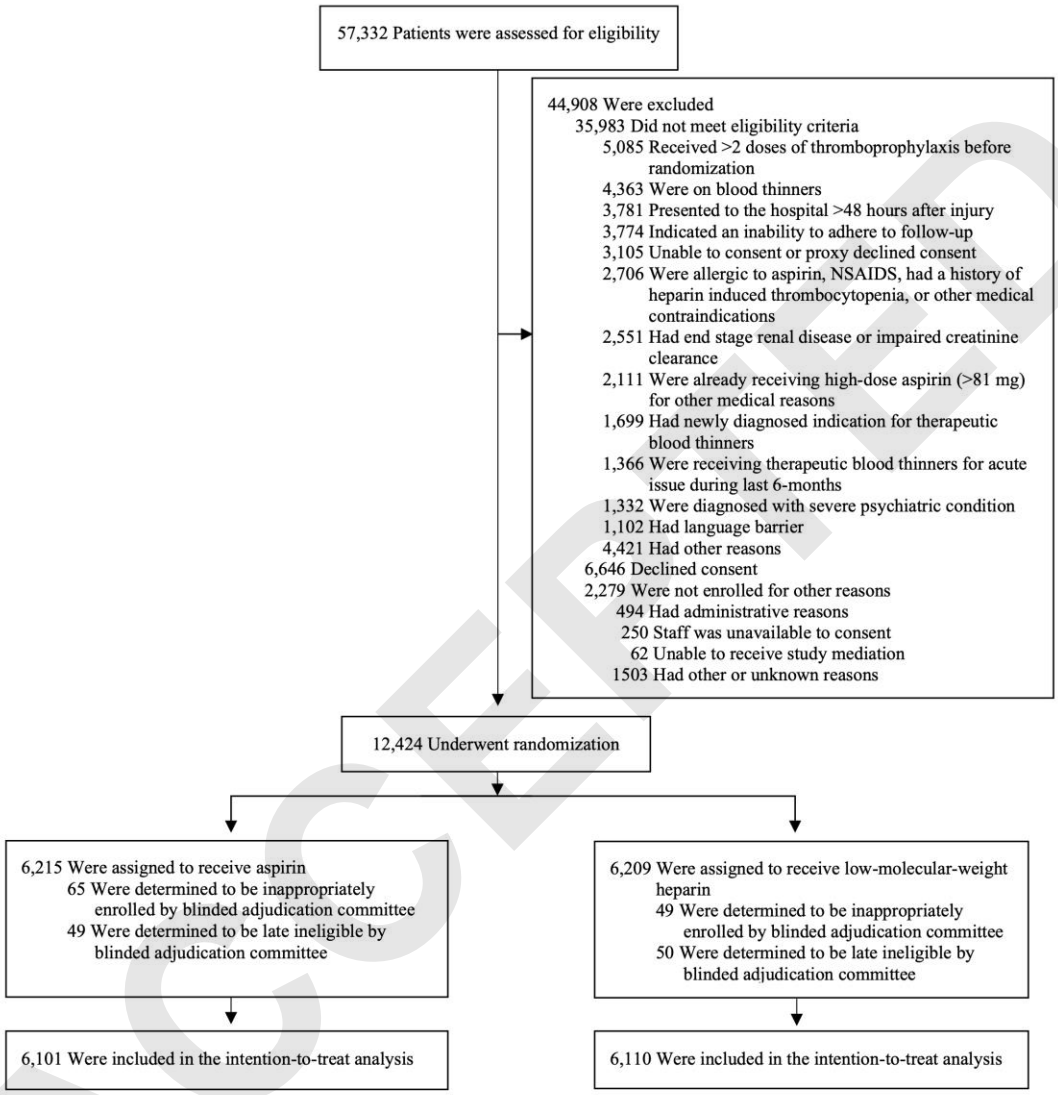

Figure 3

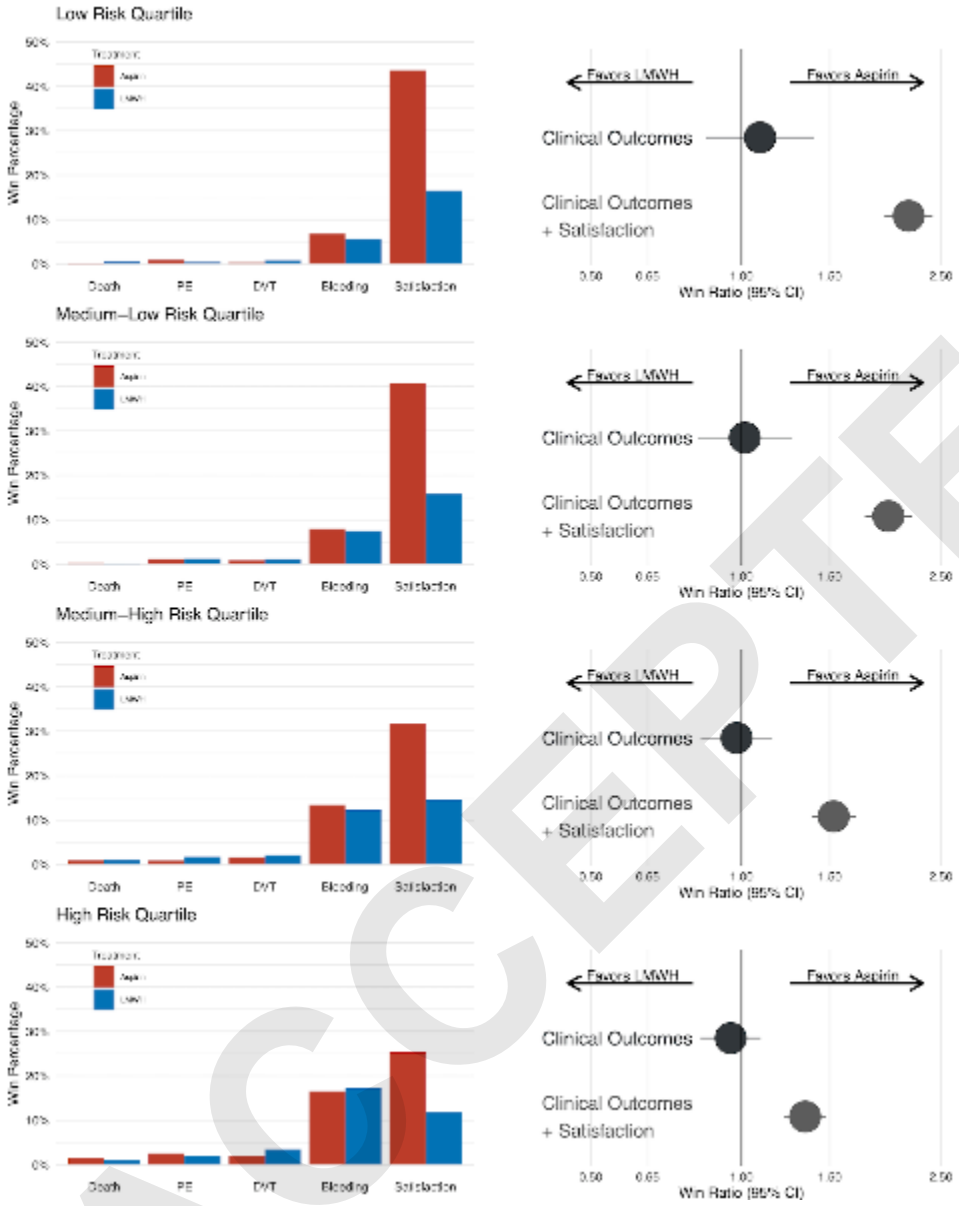

Figure 4

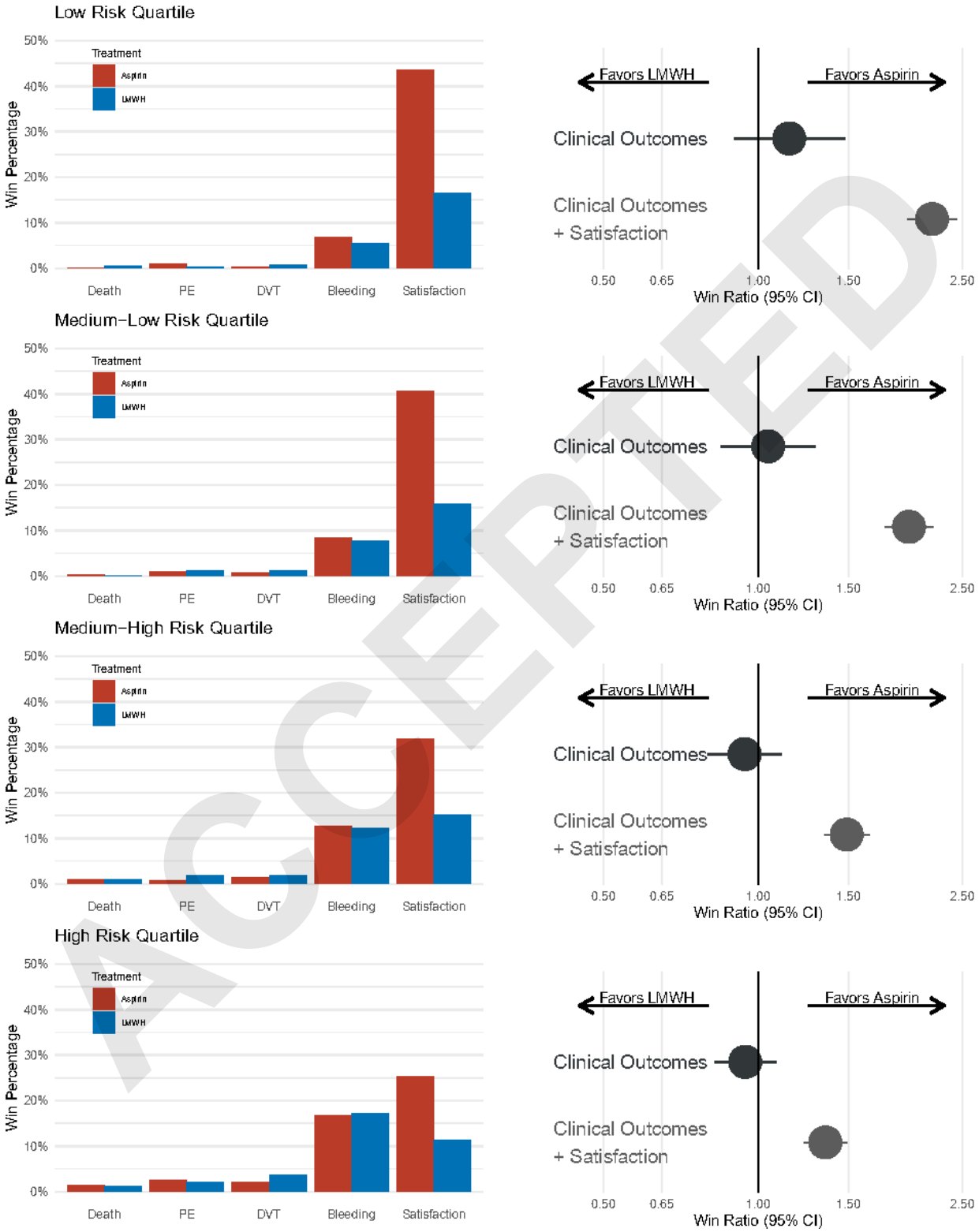

Table 1. Covariates Used to Risk Stratify the Study Population and the Points Assigned for Venous Thromboembolism Risk for Each Covariate

Caprini Score Value	Risk Factor
1 point	Age 41–60 years Body mass index >30 kg/m^2 History of myocardial infarction Congestive heart failure Cerebrovascular disease Diabetes Oral contraceptives or hormone replacement therapy Abdominal injury Thoracic injury
2 points	Age 61–74 years Prior cancer diagnosis Immobilization due to restricted weight bearing Fracture of the tibia Head injury
3 points	Age ≥75 years Previous venous thromboembolism
5 points	Multi-trauma (Injury Severity Score ≥16)[20] Fracture of the femur, pelvis, or acetabulum Spinal cord injury

Note: Abdominal, thoracic, and head injuries were indicated by Abbreviated Injury Scale values of 1 or more in the abdomen, chest, and head categories, respectively. Spinal cord injuries were determined based on qualifying Abbreviated Injury Scale codes.

Table 2. Patient Characteristics at Baseline Stratified by Risk Quartile

Characteristic	Overall (N = 12,211)	Low Risk, (N = 3053)	Low-Medium Risk, (N = 3053)	Medium-High Risk, (N = 3053)	High Risk, (N = 3052)	P-Value
Age, years						<0.001
40 or less	5,689 (47%)	2,024 (66%)	1,488 (49%)	1,004 (33%)	1,173 (38%)	
41–60	3,918 (32%)	790 (26%)	1,220 (40%)	906 (30%)	1,002 (33%)	
61–74	2,001 (16%)	225 (7.4%)	299 (9.8%)	877 (29%)	600 (20%)	
75 or more	603 (4.9%)	14 (0.5%)	46 (1.5%)	266 (8.7%)	277 (9.1%)	
Obese, BMI >30 kg/m^2	4,238 (35%)	719 (24%)	1,084 (36%)	1,174 (38%)	1,261 (41%)	<0.001
Diabetes	1,002 (8.2%)	60 (2.0%)	160 (5.2%)	351 (11%)	431 (14%)	<0.001
History of VTE	89 (0.7%)	1 (<0.1%)	1 (<0.1%)	18 (0.6%)	69 (2.3%)	<0.001
History of cancer	306 (2.5%)	5 (0.2%)	27 (0.9%)	97 (3.2%)	177 (5.8%)	<0.001
History of MI	98 (0.8%)	3 (<0.1%)	11 (0.4%)	36 (1.2%)	48 (1.6%)	<0.001
History of CHF	88 (0.7%)	3 (<0.1%)	5 (0.2%)	21 (0.7%)	59 (1.9%)	<0.001
History of CVD	96 (0.8%)	4 (0.1%)	5 (0.2%)	32 (1.0%)	55 (1.8%)	<0.001
Estrogen medication	219 (1.8%)	36 (1.2%)	58 (1.9%)	61 (2.0%)	64 (2.1%)	0.029
Discharge weightbearing status						<0.001
As tolerated	4,512 (37%)	1,111 (36%)	947 (31%)	1,244 (41%)	1,210 (40%)	
Protected	535 (4.4%)	163 (5.3%)	85 (2.8%)	130 (4.3%)	157 (5.1%)	
Non-weightbearing	5,455 (45%)	1,390 (46%)	1,501 (49%)	1,196 (39%)	1,368 (45%)	
Touchdown	1,709 (14%)	389 (13%)	520 (17%)	483 (16%)	317 (10%)	
Injury Severity Score†	9 (4 to 10)	4 (4 to 9)	5 (4 to 9)	9 (5 to 9)	16 (9 to 22)	<0.001
Humerus fracture	1,132 (9.3%)	362 (12%)	154 (5.0%)	203 (6.6%)	413 (14%)	<0.001
Radius or ulna fracture	1,618 (13%)	591 (19%)	242 (7.9%)	286 (9.4%)	499 (16%)	<0.001
Femur fracture	3,915 (32%)	44 (1.4%)	835 (27%)	1,481 (49%)	1,555 (51%)	<0.001
Tibia fracture	5,934 (49%)	2,034 (67%)	1,671 (55%)	1,036 (34%)	1,193 (39%)	<0.001
Pelvis or acetabulum fracture	2,610 (21%)	28 (0.9%)	527 (17%)	829 (27%)	1,226 (40%)	<0.001
Foot fracture	1,292 (11%)	507 (17%)	266 (8.7%)	203 (6.6%)	316 (10%)	<0.001
Head injury	1,567 (13%)	28 (0.9%)	112 (3.7%)	302 (9.9%)	1,125 (37%)	<0.001
Spinal injury‡	1,267 (10%)	107 (3.5%)	168 (5.5%)	221 (7.2%)	771 (25%)	<0.001
Thorax injury	2,255 (18%)	172 (5.6%)	216 (7.1%)	445 (15%)	1,422 (47%)	<0.001

Abdominal injury	1,573 (13%)	108 (3.5%)	143 (4.7%)	319 (10%)	1,003 (33%)	<0.001

BMI, body mass index; VTE, venous thromboembolism; MI, myocardial infarction; CHF, congestive heart failure; CVD, cardiovascular disease.

† median (interquartile range)

‡ None of these were spinal cord injuries.

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CONSORT CHECKLIST

Table. CONSORT 2010 Checklist of Information to Include When Reporting a Randomized Trial[a]

Section and Topic	Item No.	Checklist Item	Reported on Page No.
Title and abstract			
	1a	Identification as a randomized trial in the title	Title pa
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	Abstrac
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	1
	2b	Specific objectives or hypotheses	1
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	2
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	NA
Participants	4a	Eligibility criteria for participants	2
	4b	Settings and locations where the data were collected	2
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	2
Outcomes	6a	Completely defined prespecified primary and secondary outcome measures, including how and when they were assessed	3
	6b	Any changes to trial outcomes after the trial commenced, with reasons	3
Sample size	7a	How sample size was determined	4
	7b	When applicable, explanation of any interim analyses and stopping guidelines	NA
Randomization Sequence generation	8a	Method used to generate the random allocation sequence	2
	8b	Type of randomization; details of any restriction (such as blocking and block size)	2
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	2
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	2
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	2
	11b	If relevant, description of the similarity of interventions	2
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	4-5
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	5
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome	Fig 1
	13b	For each group, losses and exclusions after randomization, together with reasons	Fig 1
Recruitment	14a	Dates defining the periods of recruitment and follow-up	5
	14b	Why the trial ended or was stopped	NA
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 1
Numbers analyzed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Fig 1
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	6
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	6
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing prespecified from exploratory	6-7
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	6-7
Comment			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	9-10
Generalizability	21	Generalizability (external validity, applicability) of the trial findings	10
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	10
Other information			
Registration	23	Registration number and name of trial registry	Title Pa
Protocol	24	Where the full trial protocol can be accessed, if available	Primary
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	Title

[a]We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomized trials, noninferiority and equivalence trials, nonpharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up-to-date references relevant to this checklist, see http://www.consort-statement.org.

The Journal of Trauma and Acute Care Surgery

CONFLICT OF DISCLOSURE FORM

Based on ICMJE Form

Date: 7/27/2021

Your Name: Deborah M. Stein

Manuscript Title: Risk-Stratified Thromboprophylaxis Effects of Aspirin Versus Low-Molecular-Weight Heparin in Orthopaedic Trauma Patients: A Secondary Analysis of the PREVENT CLOT Trial

Manuscript Number (if known): Click or tap here to enter text.

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related or unrelated to the content of your manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

Participants of an accredited activity must disclose all personal **financial and non-financial relationships**, over the previous 36 months with an **ineligible company** (formerly defined as a commercial interest). **Financial relationships** are those relationships in which the individual benefits by receiving a salary, royalty, consulting fee, honoraria, ownership interest (e.g., stocks, stock options or other ownership interest), or other financial benefits, and may affect activity content relevant to products or services of an **ineligible company**, defined as an entity whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

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The author's relationships/activities/interests should be defined broadly and not only related to the manuscript in question. For example, if your manuscript pertains to the epidemiology of shock, you should declare all relationships with manufacturers of treatments used in shock, even if that form of treatment is not mentioned in the manuscript.

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		Air Force Office of Scientific Research - grant	National Highway Traffic Safety Administration (NHTSA) - grant
		Coalition for National Trauma Research/Department of Defense- grant	
3	Royalties or licenses	☒ None	
4	Consulting fees	☐ None	
		CSL Behring, LLC – participation in DSMB	
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☐ None	
		Austin Trauma & Critical Care Conference	University of Texas Southwest/Parkland
		University of Cincinnati	
		University of Arizona	
6	Payment for expert testimony	☒ None	
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		Method and Apparatus or Monitoring Collection of Physiological Patient Data - US Patent Number: 15/976,409	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☐ None	
		CSL Behring, LLC – participation in DSMB	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☐ None	
		Past President of Eastern Association for the Surgery of Trauma	Program Committee member and Algorithm Chair, Western Trauma Association
		Board member, Eastern Association for the Surgery of Trauma	Vice Chair, Trauma, Burns, and Surgical Critical Care Board, American Board of Surgery
		Examiner, American Board of Surgery	Geriatric Content Lead, American College of Surgeons Advanced Life Support (ATLS) 11th Edition
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Date: 7/26/2022

Your Name: A. Britton Christmas, MD, MBA, FACS

Manuscript Title: Risk-Stratified Thromboprophylaxis Effects of Aspirin Versus Low-Molecular-Weight Heparin in Orthopaedic Trauma Patients: A Secondary Analysis of the PREVENT CLOT Trial

Manuscript Number (if known): Click or tap here to enter text.

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Your Name: Joseph Cuschieri

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7	Support for attending meetings and/or travel	☒ **None**	

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10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ None	
11	Stock or stock options	☒ None	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ None	
13	Other financial or non-financial interests	☒ None	
14	Family Disclosure. Disclose any financial associations involving a spouse, partner, or children	☒ None	

Please place an "X" next to the following statement to indicate your agreement:

☒ I certify that I have answered every question and have not altered the wording of any of the questions on this form.

The Journal of Trauma and Acute Care Surgery

CONFLICT OF DISCLOSURE FORM

Based on ICMJE Form

Date: 7/25/2023

Your Name: Debra Marvel, MA

Manuscript Title: Risk-Stratified Thromboprophylaxis Effects of Aspirin Versus Low-Molecular-Weight Heparin in Orthopaedic Trauma Patients: A Secondary Analysis of the PREVENT CLOT Trial

Manuscript Number (if known): Click or tap here to enter text.

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related or unrelated to the content of your manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

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Time frame: Since the initial planning of the work			
1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing,	☒ None	
			Click the tab key to add additional rows.

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
	article processing charges, etc.) No time limit for this item.		
		Time frame: past 36 months	
2	Grants or contracts from any entity (if not indicated in item #1 above).	☒ **None**	
3	Royalties or licenses	☒ **None**	
4	Consulting fees	☒ **None**	
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☐ **None**	
		University of Maryland/State of Maryland	Payments given to me in the year 2020 for my involvement to include participation in meetings and co-writing of manuscripts by providing input based on my experiences/perspectives as a patient/trauma survivor.
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
8	Patents planned, issued or pending	☒ None	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ None	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ None	
11	Stock or stock options	☒ None	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ None	
13	Other financial or non-financial interests	☒ None	
14	Family Disclosure. Disclose any financial associations involving a spouse, partner, or children	☒ None	

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The Journal of Trauma and Acute Care Surgery

CONFLICT OF DISCLOSURE FORM

Based on ICMJE Form

Date: 7/26/2023

Your Name: Greg Gaski, MD

Manuscript Title: Risk-Stratified Thromboprophylaxis Effects of Aspirin Versus Low-Molecular-Weight Heparin in Orthopaedic Trauma Patients: A Secondary Analysis of the PREVENT CLOT Trial

Manuscript Number (if known): Click or tap here to enter text.

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related or unrelated to the content of your manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

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Time frame: Since the initial planning of the work			
1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing,	[X] None	
			Click the tab key to add additional rows.

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
	article processing charges, etc.) No time limit for this item.		
	Time frame: past 36 months		
2	Grants or contracts from any entity (if not indicated in item #1 above).	☒ **None**	
3	Royalties or licenses	☐ **None**	
		Thieme Medical Publishing	Royalty <$500 annually as editor of a textbook
4	Consulting fees	☒ **None**	
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
8	Patents planned, issued or pending	☒ None	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ None	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ None	
11	Stock or stock options	☒ None	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ None	
13	Other financial or non-financial interests	☒ None	
14	Family Disclosure. Disclose any financial associations involving a spouse, partner, or children	☒ None	

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The Journal of Trauma and Acute Care Surgery

CONFLICT OF DISCLOSURE FORM

Based on ICMJE Form

Date: 7/27/2023

Your Name: Gerard P. Slobogean

Manuscript Title: Risk-Stratified Thromboprophylaxis Effects of Aspirin Versus Low-Molecular-Weight Heparin in Orthopaedic Trauma Patients: A Secondary Analysis of the PREVENT CLOT Trial

Manuscript Number (if known): Click or tap here to enter text.

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Time frame: Since the initial planning of the work			
1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing,	☐ None	
		PCORI	To institution
			Click the tab key to add additional rows.

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
	article processing charges, etc.) No time limit for this item.		
	Time frame: past 36 months		
2	Grants or contracts from any entity (if not indicated in item #1 above).	☐ None	
		National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health	Award Number K24AR076445
3	Royalties or licenses	☒ None	
4	Consulting fees	☐ None	
		Smith and Nephew	Unrelated to this work
		Zimmer	Unrelated to this work
		Tyber Medical	Unrelated to this work
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ None	
6	Payment for expert testimony	☒ None	
7	Support for attending meetings and/or travel	☒ None	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
8	Patents planned, issued or pending	☒ None	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ None	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ None	
11	Stock or stock options	☒ None	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ None	
13	Other financial or non-financial interests	☒ None	
14	Family Disclosure. Disclose any financial associations involving a spouse, partner, or children	☒ None	

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CONFLICT OF DISCLOSURE FORM

Based on ICMJE Form

Date: 7/26/2023

Your Name: Elliott R. Haut

Manuscript Title: Risk-Stratified Thromboprophylaxis Effects of Aspirin Versus Low-Molecular-Weight Heparin in Orthopaedic Trauma Patients: A Secondary Analysis of the PREVENT CLOT Trial

Manuscript Number (if known): Click or tap here to enter text.

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Time frame: Since the initial planning of the work			
1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing,	☐ None	
		PCORI	
			Click the tab key to add additional rows.

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
	article processing charges, etc.) No time limit for this item.		
	Time frame: past 36 months		
2	Grants or contracts from any entity (if not indicated in item #1 above).	☐ **None**	
		PCORI	
		AHRQ	
		NIH/NHLBI	
3	Royalties or licenses	☒ **None**	
4	Consulting fees	☒ **None**	
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
8	Patents planned, issued or pending	☒ None	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ None	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☐ None	
		Editor in Chief, TSACO (paid)	
		Coalition for National Trauma Research (CNTR) Board (unpaid)	
		National Blood Clot Alliance (NBCA) Board (unpaid)	
11	Stock or stock options	☒ None	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ None	
13	Other financial or non-financial interests	☒ None	
14	Family Disclosure. Disclose any financial associations involving a spouse, partner, or children	☒ None	

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The Journal of Trauma and Acute Care Surgery

CONFLICT OF DISCLOSURE FORM

Based on ICMJE Form

Date: 7/25/2023

Your Name: Katherine P. Frey

Manuscript Title: Risk-Stratified Thromboprophylaxis Effects of Aspirin Versus Low-Molecular-Weight Heparin in Orthopaedic Trauma Patients: A Secondary Analysis of the PREVENT CLOT Trial

Manuscript Number (if known): Click or tap here to enter text.

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Time frame: Since the initial planning of the work			
1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing,	☐ None	
		PCORI	Funding via subcontract to our institution
			Click the tab key to add additional rows.

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
	article processing charges, etc.) No time limit for this item.		
		Time frame: past 36 months	
2	Grants or contracts from any entity (if not indicated in item #1 above).	☐ **None**	
		PCORI	Funding via subcontract to our institution
3	Royalties or licenses	☒ **None**	
4	Consulting fees	☒ **None**	
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
8	Patents planned, issued or pending	☒ None	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ None	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ None	
11	Stock or stock options	☒ None	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ None	
13	Other financial or non-financial interests	☒ None	
14	Family Disclosure. Disclose any financial associations involving a spouse, partner, or children	☒ None	

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The Journal of Trauma and Acute Care Surgery

CONFLICT OF DISCLOSURE FORM

Based on ICMJE Form

Date: 7/24/2023

Your Name: William Obremskey

Manuscript Title: "Risk-Stratified Thromboprophylaxis Effects of Aspirin Versus Low-Molecular-Weight Heparin in Orthopaedic Trauma Patients: A Secondary Analysis of the PREVENT CLOT Trial"

Manuscript Number (if known): Click or tap here to enter text.

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Time frame: Since the initial planning of the work			
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		PCORI	
			Click the tab key to add additional rows.

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	article processing charges, etc.) No time limit for this item.		
	Time frame: past 36 months		
2	Grants or contracts from any entity (if not indicated in item #1 above).	☐ **None**	
		PCORI	
3	Royalties or licenses	☒ **None**	
4	Consulting fees	☒ **None**	
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
8	Patents planned, issued or pending	☒ None	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ None	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ None	
11	Stock or stock options	☒ None	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ None	
13	Other financial or non-financial interests	☒ None	
14	Family Disclosure. Disclose any financial associations involving a spouse, partner, or children	☒ None	

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The Journal of Trauma and Acute Care Surgery

CONFLICT OF DISCLOSURE FORM

Based on ICMJE Form

Date: 7/26/2023

Your Name: Reza Firoozabadi

Manuscript Title: Risk-Stratified Thromboprophylaxis Effects of Aspirin Versus Low-Molecular-Weight Heparin in Orthopaedic Trauma Patients: A Secondary Analysis of the PREVENT CLOT Trial

Manuscript Number (if known): Click or tap here to enter text.

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			Click the tab key to add additional rows.

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
	article processing charges, etc.) No time limit for this item.		
		Time frame: past 36 months	
2	Grants or contracts from any entity (if not indicated in item #1 above).	☒ **None**	
3	Royalties or licenses	☐ **None**	
		Innomed	
4	Consulting fees	☐ **None**	
		Smith&Nephew	
		Depuy Synthes	
		Tyber Medical	
		SI-Bone	
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
8	Patents planned, issued or pending	☒ None	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ None	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ None	
11	Stock or stock options	☒ None	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ None	
13	Other financial or non-financial interests	☒ None	
14	Family Disclosure. Disclose any financial associations involving a spouse, partner, or children	☒ None	

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The Journal of Trauma and Acute Care Surgery

CONFLICT OF DISCLOSURE FORM

Based on ICMJE Form

Date: 7/26/2023

Your Name: Robert V. O'Toole

Manuscript Title: Risk-Stratified Thromboprophylaxis Effects of Aspirin Versus Low-Molecular-Weight Heparin in Orthopaedic Trauma Patients: A Secondary Analysis of the PREVENT CLOT Trial

Manuscript Number (if known): Click or tap here to enter text.

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3	Royalties or licenses	☐ **None**	
		Lincotek	Not related to this study
4	Consulting fees	☐ **None**	
		Stryker	Not related to this study
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	

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9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ None	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ None	
11	Stock or stock options	☐ None	
		Imagen	Not related to this study
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ None	
13	Other financial or non-financial interests	☒ None	
14	Family Disclosure. Disclose any financial associations involving a spouse, partner, or children	☒ None	

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The Journal of Trauma and Acute Care Surgery

CONFLICT OF DISCLOSURE FORM

Based on ICMJE Form

Date: 7/24/2023

Your Name: Nathan N. O'Hara

Manuscript Title: Risk-Stratified Thromboprophylaxis Effects of Aspirin Versus Low-Molecular-Weight Heparin in Orthopaedic Trauma Patients: A Secondary Analysis of the PREVENT CLOT Trial

Manuscript Number (if known): Click or tap here to enter text.

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Time frame: Since the initial planning of the work			
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		PCORI	To institution
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		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
	article processing charges, etc.) No time limit for this item.		
		Time frame: past 36 months	
2	Grants or contracts from any entity (if not indicated in item #1 above).	☒ **None**	
3	Royalties or licenses	☒ **None**	
4	Consulting fees	☒ **None**	
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
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9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ None	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ None	
11	Stock or stock options	☐ None	
		Arbutus Medical Inc	Personal stock options
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ None	
13	Other financial or non-financial interests	☒ None	
14	Family Disclosure. Disclose any financial associations involving a spouse, partner, or children	☒ None	

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CONFLICT OF DISCLOSURE FORM

Based on ICMJE Form

Date: 7/24/2023

Your Name: Anthony R. Carlini

Manuscript Title: Risk-Stratified Thromboprophylaxis Effects of Aspirin Versus Low-Molecular-Weight Heparin in Orthopaedic Trauma Patients: A Secondary Analysis of the PREVENT CLOT Trial

Manuscript Number (if known): Click or tap here to enter text.

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Time frame: Since the initial planning of the work			
1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing,	☐ None PCORI — To institution Click the tab key to add additional rows.	

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	article processing charges, etc.) No time limit for this item.		
		Time frame: past 36 months	
2	Grants or contracts from any entity (if not indicated in item #1 above).	☒ **None**	
3	Royalties or licenses	☒ **None**	
4	Consulting fees	☒ **None**	
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	

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8	Patents planned, issued or pending	☒ None	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ None	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ None	
11	Stock or stock options	☒ None	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ None	
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CONFLICT OF DISCLOSURE FORM

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Date: 7/28/2023

Your Name: Matthew E. Kutcher, MD MS

Manuscript Title: Risk-Stratified Thromboprophylaxis Effects of Aspirin Versus Low-Molecular-Weight Heparin in Orthopaedic Trauma Patients: A Secondary Analysis of the PREVENT CLOT Trial

Manuscript Number (if known): Click or tap here to enter text.

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2	Grants or contracts from any entity (if not indicated in item #1 above).	☒ **None**	
3	Royalties or licenses	☐ **None**	
		UpToDate, Inc.	Article royalties
4	Consulting fees	☐ **None**	
		General Information Dynamics Technology, Inc	Consulting fees for DoD grant review panels
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☐ **None**	
		Intuitive Surgical, Inc.	Travel/food/lodging

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
8	Patents planned, issued or pending	☒ None	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☐ None	
		University of Pittsburgh Medical Center	DSMB membership
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ None	
11	Stock or stock options	☒ None	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☐ None	
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Date: 7/28/2023

Your Name: Renan Castillo

Manuscript Title: Risk-Stratified Thromboprophylaxis Effects of Aspirin Versus Low-Molecular-Weight Heparin in Orthopaedic Trauma Patients: A Secondary Analysis of the PREVENT CLOT Trial

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		PCORI	
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	Time frame: past 36 months		
2	Grants or contracts from any entity (if not indicated in item #1 above).	☒ **None**	
3	Royalties or licenses	☒ **None**	
4	Consulting fees	☒ **None**	
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	

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9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ None	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ None	
11	Stock or stock options	☒ None	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ None	
13	Other financial or non-financial interests	☒ None	
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Risk-Stratified Thromboprophylaxis Effects of Aspirin vs Low-Molecular-Weight Heparin in Orthopaedic Trauma Patients

SECONDARY ANALYSIS OF PREVENT CLOT: A PRAGMATIC, RANDOMIZED CONTROLLED TRIAL

Study Population

12,211 adult patients with an orthopaedic injury enrolled at 21 trauma centers

Risk-Stratified with the Caprini Score for VTE Risk

	Risk Quartile			
	Low	Low-Medium	Medium-High	High
Age, IQR	26 – 47	29 – 55	34 – 65	31 – 62
Femur, pelvis, acetabulum	2%	40%	69%	80%
Thoracic injury	3%	5%	9%	34%
Spinal injury	<1%	<1%	3%	39%
Head injury	<1%	4%	12%	35%

Intervention

81mg aspirin, twice daily

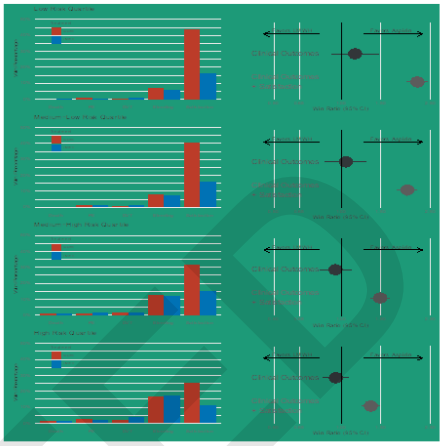
vs.

30mg low-molecular-weight heparin, twice daily

Outcomes

Primary Composite of Clinical Outcomes: Death, Pulmonary Embolism, Deep Vein Thrombosis, Bleeding Complication

Secondary Outcome: Clinical Outcome Composite + Medication Satisfaction



Stein DM et al. *Journal of Trauma and Acute Care Surgery*.
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