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The Risk of Venous Thromboembolism with Aspirin Compared to Anticoagulants after Hip and Knee Arthroplasty

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Abstract

Background—Recent guidelines include aspirin as an option to prevent venous thromboembolism (VTE) in selected patients undergoing hip or knee replacement surgery. However, the efficacy of aspirin after arthroplasty has not been well-defined, particularly in more contemporary patient populations. We compared rates of post-operative VTE between patients who received aspirin-only versus anticoagulants after hip or knee arthroplasty, using data from a large US-based administrative database.

Materials and Methods—We conducted a retrospective cohort study of 231,780 adults who underwent total knee arthroplasty and 110,621 who underwent total hip arthroplasty in 2009–2012 and who received pharmacologic VTE prophylaxis (aspirin or anticoagulant) within the first 7 days after surgery. We compared the risk of post-operative VTE between patients receiving aspirin-only vs. anticoagulants, controlling for clinical and hospital characteristics using multivariable logistic regression with propensity score adjustment.

Results—Aspirin-only prophylaxis was administered to 7.5% of patients after knee arthroplasty and 8.0% after hip arthroplasty. Post-operative VTE was diagnosed in 2,217 (0.96%) patients after knee arthroplasty and 454 (0.41%) after hip arthroplasty. Compared to anticoagulants, aspirin was not associated with a higher risk for post-operative VTE either after knee arthroplasty (adjusted odds ratio and 95% confidence interval [OR] 0.34 [0.24–0.48]) or hip arthroplasty (OR 0.82 [0.45–1.51]).

Conclusions—Aspirin was uncommonly administered as the sole prophylactic agent after hip or knee arthroplasty in this study. However, patients who received aspirin-only had similar rates of post-operative VTE compared to patients who received anticoagulants. Further research should

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Authorship

J. Chu contributed to the study concept and design, interpretation of the data, and writing and revising of the manuscript.
A. Auerbach contributed to the study concept and design, interpretation of the data, and revising and reviewing the manuscript for intellectual content.
J. Maselli contributed to the statistical analysis and interpretation of the data and reviewed the manuscript for intellectual content.
M. Fang contributed to the study concept and design, interpretation of the data, revising and reviewing the manuscript for intellectual content.

focus on distinguishing which patients benefit more from anticoagulants versus aspirin after arthroplasty.

Keywords

anticoagulants; arthroplasty; aspirin; prevention; venous thromboembolism

Background

Post-operative venous thromboembolism (VTE), primarily deep vein thrombosis (DVT) or pulmonary embolism (PE), are well-documented and potentially preventable complications of major orthopedic surgery[1, 2]. Anticoagulants such as low-molecular-weight heparins (LMWH), warfarin, fondaparinux, and direct oral anticoagulants have been shown to reduce the risk of post-operative VTE after hip or knee arthroplasty[3]. However, the benefits of using anticoagulants to prevent VTE must be weighed against an increased risk of hemorrhage[1].

National guidelines, including from the American Association of Orthopedic Surgeons (AAOS) and the American College of Chest Physicians (ACCP) recommend the administration of pharmacologic agents or mechanical compressive methods to prevent VTE in patients undergoing elective hip and knee arthroplasty [4, 5]. Although warfarin and LMWHs are the most widely used agents for VTE prophylaxis after arthroplasty, guidelines recently included aspirin as an option for VTE prophylaxis after joint arthroplasty, particularly for patients who are at increased risk for adverse bleeding events [4, 5]. Aspirin is an appealing alternative to anticoagulants because of its lower cost and ease of administration. However, the evidence base supporting the efficacy and safety of aspirin after arthroplasty is only weak to moderate in quality, with few randomized clinical trials addressing the topic in more contemporary patient populations [6–11]. In the absence of high quality clinical trial evidence, observational studies can provide important insights in trends in medication utilization and outcomes.

Our study used a large administrative database to describe rates of aspirin use in patients undergoing elective hip or knee arthroplasty and compared their rates of post-operative VTE to patients who received anticoagulants.

Methodology

We conducted a retrospective cohort study using data from the Perspective (Premier, Inc.) database, an ongoing database representing >700 mostly small to mid-size hospitals in the US serving a largely urban patient population. Developed to measure health care quality and utilization, the Perspective database contains hospital discharge file data, date-stamped records of charges for devices, materials, medications, and procedures, hospital level data (including number of beds and region), and de-identified patient level data (including demographics, admission type, and discharge diagnosis)[12].

Patients were included in our analysis if they were aged 18 years or older and hospitalized during the time period January 1, 2009 and March 31, 2012 with a principal diagnosis of

primary total hip arthroplasty or total knee arthroplasty (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9] diagnosis codes 81.51 or 81.54). Only hospitals with 12 months or more of data were included. We next restricted the analysis to patients who received a charge for a medication used for VTE prevention after surgery, specifically, aspirin or anticoagulants. Patients who were admitted from emergency departments or as transfers from other acute care facilities were excluded because our focus was on elective hip or knee arthroplasty.

We obtained data on patient demographic data, including patient age, gender, race/ethnicity, primary health insurance payer, as well as hospital data, including geographic region, bed size, and teaching status. We also searched for secondary ICD-9 discharge diagnosis codes for specific medical diagnoses considered risk factors for VTE, such as malignancy, congestive heart failure, chronic obstructive pulmonary disease (COPD), and myocardial infarction[13] as well as for clinical factors comprising the validated VTE risk score developed by Caprini et al., which has been previously validated in other surgical settings [14, 15]. ICD-9 codes were also used to calculate an Elixhauser comorbidity risk score, a validated measure of hospital comorbidity[16].

Pharmacologic Prophylaxis for VTE

The primary predictor of the analysis was type of pharmacologic VTE prophylaxis administered after surgery. We searched for itemized charges for specific antithrombotic agents used for VTE prophylaxis administered at any time within the first seven days after the index hip or knee surgery. VTE prophylaxis was considered any of the following anticoagulant medications: warfarin sodium (any dose); injectable heparin sodium at doses between 5,000 and 7,500 units; prophylactic doses of LMWH (enoxaparin at doses of 30mg or 40mg, dalteparin at doses of 2,500 or 5,000 units, or tinzaparin at doses of 3,500 or 4,500 units); fondaparinux at a dose of 2.5mg; or prophylactic doses of direct oral anticoagulants (dabigatran at doses of 75mg or 150mg, rivaroxaban at a dose of 10mg, or apixaban at a dose of 2.5mg). Receipt of aspirin for VTE prophylaxis was defined as a charge for aspirin (at any dose) in non-combination formulations.

Patients were grouped into three separate categories: 1) patients who received aspirin-only after surgery; 2) patients who received anticoagulants alone; and 3) patients who received both aspirin and anticoagulants.

Post-operative VTE and Hemorrhagic Outcomes

The primary outcome of the study was VTE that occurred during the index hospitalization or within 30 days of the index surgery, ascertained through a combination of ICD-9 and “present-on-admission” codes[17]. VTE events that occurred during the index hospitalization were identified by searching for discharge diagnosis codes for lower extremity DVT or PE during the index hospitalization (ICD-9 codes: 415.11, 415.19, 451.11, 451.19, 451.2, 451.81, 451.9, 453.40, 453.41, 453.42, 453.8, 453.9) combined with a present-on-admission code of “no”[17]. VTE events that occurred after discharge and within 30 days were identified as a readmission to a hospital participating in the Premier consortium with a principal diagnosis code of DVT or PE.

We also examined as a secondary clinical outcome the rate of post-operative bleeding complications, defined using ICD-9 codes 998.1, 998.11, 998.12, 998.13, 852.4, 432.0, 578.9, 39.98, 39.99, 83.14, 83.19, 83.39, 83.44, 83.49, 578.xx, 86.04, 86.22, 86.28, 96.58, 96.59, 97.15, 97.16, in combination with a present-on-admission code of “no”[10]. These codes encompassed gastrointestinal and extradural hemorrhages; wound hemorrhage/hematoma/or seromas; and procedures related to management of wound complications such as fasciotomy, incision/drainage, debridement, or wound packing.

Statistical analysis

We first described the distribution of antithrombotic prophylaxis (aspirin-only, anticoagulants-only, and aspirin plus anticoagulants) used after surgery in our study population, stratified by hip and knee arthroplasty. Using bivariable analysis, we tested the association of individual risk factors, including demographics, hospital factors, and medical conditions, with the primary clinical outcome of post-operative VTE using Chi-squared tests for categorical variables and t-tests for continuous variables.

In order to account for the potential risk of allocation bias in this observational study where patients were not randomly assigned VTE prophylaxis strategies, we developed propensity scores to model the likelihood of a patient receiving aspirin-only therapy[18]. Using all available baseline clinical and hospital variables, we developed a propensity score for patients undergoing hip arthroplasty and a separate score for knee arthroplasty. The initial development step involved testing bivariable associations between individual risk factors and the likelihood of receiving aspirin-only. Variables were retained in the final propensity score if the bivariate association was significant at a p of < 0.1. Then, each cohort (hip or knee) was stratified by quintiles of propensity score and the distribution of covariates between aspirin-only and anticoagulant groups was examined to determine whether they were more equally distributed.

The propensity scores for receiving aspirin-only were then included in the multivariable logistic regression models testing the association of VTE with aspirin-only exposure. Variables corresponding to patient demographics, hospital characteristics, Elixhauser comorbidity, and the Caprini VTE risk score were included in the model as potential adjustors. PROC GENMOD was used to account for potential effects of clustering at the individual hospital level. All analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC). This study was approved by the institutional review board of the University of California, San Francisco.

Results

We identified 399,696 elective primary total hip and knee arthroplasty procedures performed between January 1, 2009 and March 31, 2012 at 323 and 327 hospitals, respectively. Pharmacologic VTE prophylaxis, either aspirin-only, anticoagulant-only, or anticoagulants plus aspirin, was administered to 342,401 (85.7%) of hospitalized patients within the first 7 days after surgery; this constituted our analytic cohort. Among the 231,780 patients undergoing knee arthroplasty, most received anticoagulants-only (79.7%), while 7.5% received aspirin only, and 12.8% received both anticoagulants and aspirin. Among the

110,621 patients undergoing hip arthroplasty, most received anticoagulants only (79.9%), while 8.0% received aspirin only, and 12.1% received both anticoagulants and aspirin. The most common antithrombotic medication prescribed post-operatively was warfarin only, given to 29.6% of patients undergoing knee arthroplasty and 30.8% undergoing hip arthroplasty. Enoxaparin only was the next most common, administered to 28.3% after knee arthroplasty and 26.2% after hip arthroplasty. Other anticoagulants, including fondaparinux, dalteparin, dabigatran, and rivaroxaban, were uncommonly used (each <6% prevalence).

Table 1 and Table 2 present the clinical characteristics of patients undergoing knee and hip arthroplasty, stratified by type of VTE prophylaxis administered. Due to the large cohort size, comparisons of the frequency of individual variables were often statistically significantly different, but the absolute differences were generally small. Patients who received both anticoagulants and aspirin had somewhat higher Caprini VTE risk score, longer lengths of stay, and a higher number of comorbidities.

Overall, we identified 2,217 (0.96%) patients with a diagnosis of DVT and/or PE occurring during the index hospitalization or within 30 days in patients undergoing knee arthroplasty, and 454 (0.41%) in patients undergoing hip arthroplasty. Table 3 presents the unadjusted rates of VTE as well as the rate of post-operative hemorrhagic complications. A total of 1131 (0.49%) of patients with knee arthroplasty and 769 (0.70%) of patients with hip arthroplasty had codes for gastrointestinal hemorrhage or hemorrhage/hematoma/or seroma complicating a procedure; we did not find any patients who received a code for the other categories of post-operative wound complications. For both knee and hip arthroplasty, unadjusted rates of VTE and hemorrhage were lowest in patients who received aspirin-only, followed by those who received anticoagulants-only, and highest in patients who received both anticoagulants and aspirin.

Table 4 shows the adjusted odds of post-operative VTE associated with receiving aspirin-only after surgery, adjusted for other clinical factors and controlling for the propensity score of receiving aspirin-only therapy. Patients who underwent knee arthroplasty and received aspirin-only had a lower risk of post-operative VTE, with an adjusted odds ratio and 95% confidence interval [OR] of 0.34 [0.24–0.48]. For patients undergoing hip arthroplasty, VTE risk was not statistically different between aspirin only and anticoagulant-based prophylaxis (OR 0.82 [0.45–1.51]).

Discussion

In this large observational cohort of patients undergoing elective primary total hip or knee arthroplasty, aspirin was used as the sole antithrombotic agent in approximately 8% of patients who received thromboprophylaxis. Patients who received aspirin only did not have a higher risk of subsequent VTE than did patients who received anticoagulants.

Our study contributes to the increasing body of evidence that aspirin may be a reasonable option for preventing VTE after knee and hip arthroplasty. Systematic reviews and meta-analyses of randomized studies that compared aspirin to anticoagulants for VTE prevention did not find significant differences in VTE rates between aspirin and anticoagulant groups,

although the majority of these studies were conducted during the 1980s or 1990s and used screening ultrasounds to detect VTE[7, 10]. Subsequent studies in more contemporaneous populations, both in observational cohorts as well as studies of multimodal interventions to prevent VTE after arthroplasty, have found aspirin to be a reasonable choice in some patients[19–22].

At present, anticoagulants continue to remain the most common form of VTE prevention used in the United States, despite updated national guidelines that allow for the use of aspirin[4, 5, 23, 24]. In part, this may be due to the challenges in being able to accurately risk-stratify patients undergoing arthroplasty according to VTE risk. Risk-stratification schemes such as the one developed by Caprini et al.[22] categorize all patients undergoing arthroplasty as having high VTE risk. There may also be financial disincentives to incurring an increased risk of post-operative complications in settings where payment is linked to defined episodes of care, such as in joint replacement[25]. Nevertheless, our study and others show that selected patients undergoing arthroplasty who receive aspirin only can have favorable outcomes, and the main challenge now is how to distinguish between low-risk patients in whom aspirin is sufficient, and higher-risk patients who may benefit from anticoagulants[26]. At present, there is not yet a widely adopted risk stratification system that has been shown to effectively guide thromboprophylaxis strategies after arthroplasty. However, efforts to develop and test such risk stratification tools are underway[27].

There are several limitations to our analysis. As an observational study of clinical care, patients were not randomly assigned to aspirin or anticoagulants. Thus, it is probable that patients who were considered at lower risk for VTE were more likely to receive aspirin, while higher risk patients received anticoagulants. Although we attempted to control for this non-randomized treatment allocation through the use of propensity scores, selection bias may still be present. Our study was not able to determine the daily dosage of aspirin received by patients, and the optimal dosing of aspirin after arthroplasty is still not clear. Our study relied on ICD-9 codes from the index admission and subsequent hospitalizations to calculate the risk scores, such as the Caprini et al. VTE risk score, and to identify post-operative VTE and hemorrhagic outcomes. Reliance on diagnosis codes may lead to misclassification or inaccurate estimation of true event rates[28]. Caution should be used in interpreting the calculated Caprini score in our study with other investigations using prospective methods. We did not have details about whether screening ultrasounds were used or not, nor about the type or adherence to post-discharge thromboprophylaxis strategies, which could have contributed to differences in VTE rates. Finally, we may have underestimated the true rate of VTE since we did not have information on VTE events that were diagnosed and treated in non-hospital settings.

Our study of more than 300 hospitals in the United States shows that aspirin may be a viable option to prevent VTE for selected patients undergoing total joint replacement surgery. The main questions now are how best to distinguish those patients who will gain the most benefit from anticoagulants, highlighting the importance of conducting more contemporary randomized clinical trials to address the efficacy and suitability of aspirin after arthroplasty.

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Appendix. Caprini et al. Risk Stratification Scoring System for Estimating Venous Thromboembolism Risk [15]

1 point	2 points	3 points	5 points
• Age 41–60 years • Minor surgery • Prior major surgery within 1 month • Pregnancy or postpartum within 1 month • Varicose veins • Inflammatory bowel disease • Swelling of legs • Obesity (BMI>25) • Oral contraceptives, patch, or hormone replacement therapy	• Age > 60 years • Malignancy or current chemo/ radiation therapy • Major surgery (>45 min) • Laparoscopic surgery (>45 min) • Confined to bed >72 h • Immobilizing cast < 1 month • Central venous access <1 month • Tourniquet time >45 min	• Age > 75 years • Prior DVT or PE • Family history of thrombosis • Factor V Leiden • Medical patient with risk factors of MI, CHF, COPD • Congenital or acquired thrombophilia	• Major, elective lower-extremity arthroplasty • TKR, THR • Hip, pelvis, or leg fracture within 1 month • Stroke within 1 month • Multiple traumas within 1 month • Acute spinal cord injury with paralysis within 1 month

Highlights

- Guidelines recommend using aspirin or anticoagulants after arthroplasty to prevent venous thromboembolism (VTE), but relatively few high-quality data exist describing aspirin use and outcomes after arthroplasty
- This observational study of 231,780 adults undergoing knee arthroplasty and 110,621 undergoing total hip arthroplasty compared VTE rates by type of antithrombotic prophylaxis used after surgery
- Aspirin was used as the sole pharmacoprophylactic agent in 7.5% of patients after knee arthroplasty and 8.0% after hip arthroplasty
- Post-operative VTE risk was not higher in patients who received aspirin alone compared to those who received anticoagulants after knee or hip arthroplasty

Table 1

Clinical characteristics of patients who underwent elective knee arthroplasty (n=231,780), stratified by type of post-operative VTE prophylaxis.

	Aspirin Only N=17,443	Anticoagulant Only N=184,790	Both Anticoagulant & Aspirin N=29,547	P value
	N (%)			
Age				<0.001
18–64	7185 (41.2)	81661 (44.2)	10047 (34.0)	
65–69	3323 (19.1)	34634 (18.7)	5667 (19.2)	
70–74	2868 (16.4)	28890 (15.6)	5440 (18.4)	
75–79	2264 (13.0)	22260 (12.1)	4581 (15.5)	
≥80	1803 (10.3)	17345 (9.4)	3812 (12.9)	
Male	6783 (38.9)	66002 (35.7)	12789 (43.3)	<0.001
Race/ethnicity				<0.001
White	13848 (79.4)	138006 (74.7)	23119 (78.2)	
Black	1069 (6.1)	14807 (8.0)	2058 (7.0)	
Hispanic	363 (2.1)	3026 (1.6)	399 (1.4)	
Other	2163 (12.4)	28951 (15.7)	3971 (13.4)	
Primary payer				<0.001
Uninsured	57 (0.3)	670 (0.4)	75 (0.3)	
Indemnity	1826 (10.5)	19557 (10.6)	2510 (8.5)	
Managed care	5087 (29.2)	54,300 (29.4)	6997 (23.7)	
Medicaid	337 (1.9)	4850 (2.6)	619 (2.1)	
Medicare	9902 (56.8)	103313 (55.9)	19046 (64.5)	
Other	234 (1.3)	2100 (1.1)	300 (1.0)	
Comorbidities				
Heart failure	243 (1.4)	3992 (2.2)	1349 (4.6)	<0.001
Valvular disease	639 (3.7)	6816 (3.7)	1601 (5.4)	<0.001
Pulmonary circulation disease	70 (0.4)	1801 (1.0)	581 (2.0)	<0.001
Peripheral vascular disease	271 (1.6)	3327 (1.8)	1060 (3.6)	<0.001
Hypertension	11467 (65.7)	125491 (67.9)	22952 (77.7)	<0.001
Paralysis	30 (0.2)	409 (0.2)	120 (0.4)	<0.001
Other neurological disease	593 (3.4)	7411 (4.0)	1301 (4.4)	<0.001
Chronic pulmonary disease	2309 (13.2)	28237 (15.3)	4633 (15.7)	<0.0001
Diabetes	3274 (18.8)	39009 (21.1)	8450 (28.6)	
Hypothyroidism	2773 (15.9)	29644 (16.0)	4781 (16.2)	0.70
Renal failure	585 (3.4)	6941 (3.8)	1828 (6.2)	<0.001
Liver disease	114 (0.7)	1461 (0.8)	224 (0.8)	0.13
Peptic ulcer disease	2 (0.01)	24 (0.01)	7 (0.02)	0.34
AIDS	5 (0.03)	36 (0.02)	2 (0.01)	0.20

	Aspirin Only N=17,443	Anticoagulant Only N=184,790	Both Anticoagulant & Aspirin N=29,547	P value
	N (%)			
Cancer	131 (0.8)	1654 (0.9)	257 (0.9)	0.15
Rheumatoid arthritis/collagen vascular disease	622 (3.6)	7404 (4.0)	1026 (3.5)	<0.001
Coagulopathy	461 (2.6)	4192 (2.3)	767 (2.6)	<0.001
Obesity	3756 (21.5)	41649 (22.5)	6598 (22.3)	0.005
Weight loss	112 (0.6)	473 (0.3)	143 (0.5)	<0.001
Chronic blood loss anemia	198 (1.1)	2966 (1.6)	485 (1.6)	<0.001
Fluid & electrolyte disorders	1299 (7.5)	16240 (8.8)	3252 (11.0)	<0.001
Iron deficiency anemia	2273 (13.0)	27082 (14.7)	4548 (15.4)	<0.001
Drug/alcohol abuse	164 (0.9)	2448 (1.3)	367 (1.2)	<0.001
Psychoses	272 (1.6)	3531 (1.9)	537 (1.8)	0.003
Depression	2052 (11.8)	25023 (13.5)	3593 (12.2)	<0.001
Length of stay				
Mean (SD)	2.8 (1.1)	3.2 (1.4)	3.6 (2.0)	<0.001
Caprini VTE risk score[15]				
Mean (SD)	11.2 (0.8)	11.2 (0.9)	11.4 (0.9)	<0.001
Elixhauser Comorbidity Score[16]				
Mean (SD)	−0.17 (4.33)	−0.06 (4.61)	0.67 (5.33)	<0.001
≥ 3 comorbidities	5261 (30.2)	63682 (34.5)	12298 (41.6)	
Characteristics of Hospitals				
Location				<0.001
Rural	936 (5.4)	22012 (11.9)	3216 (10.9)	
Urban	16507 (94.6)	162778 (88.1)	26331 (89.1)	
Region				<0.001
Midwest	1538 (8.8)	322227 (17.4)	5770 (19.5)	
Northeast	4875 (28.0)	32373 (17.5)	7070 (23.9)	
South	5860 (33.6)	80635 (43.6)	12419 (42.0)	
West	5170 (29.6)	39555 (21.4)	4288 (14.5)	
Number of beds				<0.001
0–99	1014 (5.8)	6097 (3.3)	762 (2.6)	
100–199	2710 (15.5)	24283 (13.1)	5653 (19.1)	
200–299	2889 (16.6)	37086 (20.1)	6036 (20.4)	
300–399	5727 (32.8)	42276 (22.9)	5541 (18.8)	
400–499	2372 (13.6)	29507 (16.0)	3313 (11.2)	
≥ 500	2731 (15.7)	45541 (24.6)	8242 (27.9)	
Teaching hospital	8450 (48.4)	64256 (34.8)	12273 (41.5)	<0.001
Hospital annual volume of surgeries				
Mean (SD)	150 (146)	354 (264)	127 (175)	<0.001

	Aspirin Only N=17,443	Anticoagulant Only N=184,790	Both Anticoagulant & Aspirin N=29,547	P value
	N (%)			
Compression stockings post-surgery	9052 (51.9)	94095 (50.9)	15051 (50.9)	0.047
Hospital length of stay				
≤7 days	17356 (99.5)	182408 (98.7)	28665 (97.0)	<0.001
>7 days	87 (0.5)	2382 (1.3)	882 (3.0)	
Disposition				<0.001
Home/home health	12630 (72.4)	119585 (64.7)	17530 (59.3)	
Transfer to another acute care facility	240 (1.4)	2545 (1.4)	550 (1.9)	
Skilled nursing facility/Rehab	4557 (26.1)	62529 (33.8)	11420 (38.7)	
Died	10 (0.06)	89 (0.05)	37 (0.13)	
Other	6 (0.03)	42 (0.23)	10 (0.03)	

Table 2

Clinical characteristics of patients who underwent elective hip arthroplasty (n=110,621), stratified by type of post-operative VTE prophylaxis

	Aspirin Only N=8,853	Anticoagulant Only N=88,349	Both Anticoagulant & Aspirin N=13,419	P value
	N(%)			
Age				<0.001
18–64	4421 (49.9)	42997 (48.7)	4495 (33.5)	
65–69	1484 (16.8)	13586 (15.4)	2326 (17.3)	
70–74	1114 (12.6)	11485 (13.0)	2191 (16.3)	
75–79	883 (10.0)	9761 (11.1)	2032 (15.1)	
>=80	951 (10.7)	10520 (11.9)	2375 (17.7)	
Male	3982 (45.0)	37562 (42.5)	6553 (48.8)	<0.001
Race/ethnicity				<0.001
White	7457 (84.2)	67904 (76.9)	10891 (81.2)	
Black	508 (5.7)	6569 (7.4)	733 (5.5)	
Hispanic	82 (0.9)	813 (0.9)	106 (0.8)	
Other	806 (9.1)	13063 (14.8)	1689 (12.6)	
Primary payer				<0.001
Uninsured	102 (1.2)	784 (0.9)	64 (0.5)	
Indemnity	705 (8.0)	9464 (10.7)	1042 (7.8)	
Managed care	3586 (40.5)	28142 (31.9)	3256 (24.3)	
Medicaid	114 (1.3)	2914 (3.3)	249 (1.9)	
Medicare	4268 (48.2)	46124 (52.2)	8676 (64.7)	
Other	78 (0.9)	921 (1.0)	132 (1.0)	
Comorbidities				
Heart failure	102 (1.2)	2007 (2.3)	670 (5.0)	<0.001
Valvular disease	316 (3.6)	3467 (3.9)	797 (5.9)	<0.001
Pulmonary circulation disease	29 (0.3)	723 (0.8)	184 (1.4)	<0.001
Peripheral vascular disease	151 (1.7)	1829 (2.1)	568 (4.2)	<0.001
Hypertension	4620 (52.2)	51939 (58.8)	9710 (72.4)	<0.001
Paralysis	19 (0.3)	260 (0.3)	84 (0.6)	<0.001
Other neurological disease	244 (2.8)	3180 (3.6)	547 (4.1)	<0.001
Chronic pulmonary disease	958 (10.8)	12841 (14.5)	1989 (14.8)	<0.001
Diabetes	927 (10.5)	12265 (13.9)	2759 (13692)	<0.001
Hypothyroidism	1167 (13.2)	11928 (13.5)	1964 (14.6)	<0.001
Renal failure	211 (2.4)	3226 (3.7)	851 (6.3)	<0.001
Liver disease	75 (0.9)	851 (1.0)	101 (0.8)	0.043
Peptic ulcer disease	0	18 (0.02)	1 (0.01)	0.25
AIDS	7 (0.08)	82 (0.09)	12 (0.09)	0.92

	Aspirin Only N=8,853	Anticoagulant Only N=88,349	Both Anticoagulant & Aspirin N=13,419	P value
	N(%)			
Cancer	103 (1.2)	1187 (1.3)	200 (1.5)	0.11
Rheumatoid arthritis/collagen vascular disease	301 (3.4)	3580 (4.1)	456 (3.4)	<0.001
Coagulopathy	146 (1.7)	2239 (2.5)	492 (3.7)	<0.001
Obesity	999 (11.3)	13651 (15.5)	2095 (15.6)	0.005
Weight loss	32 (0.4)	473 (0.5)	77 (0.6)	0.07
Chronic blood loss anemia	86 (1.0)	1563 (1.8)	268 (2.0)	<0.001
Fluid & electrolyte disorders	459 (5.2)	8409 (9.5)	1683 (12.5)	<0.001
Iron deficiency anemia	813 (9.2)	13615 (15.4)	2335 (17.4)	<0.001
Drug/alcohol abuse	153 (1.7)	2209 (2.5)	273 (2.0)	<0.001
Psychoses	92 (1.0)	1455 (1.7)	190 (1.4)	<0.001
Depression	915 (10.3)	10551 (11.9)	1441 (10.7)	<0.001
Length of stay				
Mean (SD)	2.5 (1.3)	3.3 (1.7)	3.7 (2.3)	<0.001
Caprini VTE risk score[15]				
Mean (SD)	11.0 (0.9)	11.1 (1.0)	11.4 (1.0)	<0.001
Elixhauser Comorbidity Score[16]				
Mean (SD)	−0.04 (3.85)	0.45 (4.78)	1.29 (5.53)	<0.0001
≥ 3 comorbidities	1645 (18.6)	25041 (28.3)	5013 (37.4)	
Hospital Characteristics				
Location				
Rural	102 (1.2)	9531 (10.8)	1157 (8.6)	
Urban	8751 (98.9)	78818 (89.2)	12262 (91.4)	
Region				<0.001
Midwest	368 (4.2)	13525 (15.3)	2831 (21.1)	
Northeast	1705 (19.3)	20612 (23.3)	3972 (29.6)	
South	2928 (33.1)	33277 (37.7)	4514 (33.6)	
West	3852 (43.5)	20935 (23.7)	2102 (15.7)	
Number of beds				<0.001
0–99	420 (4.7)	2375 (2.7)	259 (1.9)	
100–199	1892 (21.4)	12286 (13.9)	2832 (21.1)	
200–299	2050 (23.2)	15843 (17.9)	2285 (17.0)	
300–399	1450 (16.4)	19703 (22.3)	2200 (16.4)	
400–499	1783 (20.1)	14152 (16.0)	1650 (12.3)	
≥ 500	1258 (14.2)	23990 (27.2)	4193 (31.3)	
Teaching hospital	3782 (42.7)	36152 (40.9)	6324 (47.1)	<0.001
Hospital annual volume of surgeries				
Mean (SD)	201 (180)	212 (225)	81 (125)	<0.001

	Aspirin Only N=8,853	Anticoagulant Only N=88,349	Both Anticoagulant & Aspirin N=13,419	P value
	N(%)			
Compression stockings post-surgery	5223 (59.0)	45823 (51.9)	6783 (50.6)	<0.001
Hospital length of stay				
≤ days	8785 (99.2)	86695 (98.1)	12853 (95.8)	<0.001
>7 days	68 (0.8)	1654 (1.9)	566 (4.2)	
Disposition				<0.001
Home/home health	7360 (83.3)	57090 (64.6)	7863 (58.6)	
Transfer to another acute care facility	62 (0.7)	1195 (1.4)	223 (1.7)	
Died	2 (0.02)	64 (0.07)	29 (0.22)	
Skilled nursing facility/Rehab	1428 (16.1)	29970 (33.9)	5294 (39.5)	
Other	1 (0.01)	30 (0.03)	10 (0.07)	

Table 3

Outcomes after primary knee and hip arthroplasty, stratified by post-operative VTE prophylaxis

	Knee Arthroplasty				Hip Arthroplasty			
	ASA only n=17443	**AC only n=184790**	**ASA + AC n=29547**	**Total n=231780**	**ASA only n=8853**	**AC only n=88349**	**ASA + AC n=13419**	**Total n=110621**
VTE during index hospitalization	10 (0.06%)	1357 (0.73%)	406 (1.37%)	1773 (0.76%)	6 (0.07%)	255 (0.29%)	56 (0.42%)	317 (0.29%)
PE only	0 (0%)	30 (0.02%)	12 (0.04%)	42 (0.02%)	0 (0%)	2 (0.002%)	4 (0.03%)	6 (0.005%)
DVT only	7 (0.04%)	591 (0.32%)	140 (0.47%)	738 (0.32%)	4 (0.05%)	100 (0.11%)	21 (0.16%)	125 (0.11%)
PE and DVT	3 (0.02%)	766 (0.41%)	266 (0.90%)	1035 (0.45%)	2 (0.02%)	155 (0.18%)	35 (0.26%)	192 (0.17%)
Readmitted within 30 days with primary diagnosis of VTE	30 (0.17%)	373 (0.20%)	41 (0.14%)	444 (0.19%)	8 (0.09%)	116 (0.13%)	13 (0.10%)	137 (0.12%)
PE	22 (0.13%)	236 (0.13%)	25 (0.03%)	283 (0.12%)	5 (0.06%)	72 (0.08%)	6 (0.04%)	83 (0.08%)
DVT	8 (0.05%)	137 (0.07%)	16 (0.05%)	161 (0.07%)	3 (0.03%)	44 (0.05%)	7 (0.05%)	54 (0.05%)
Overall VTE rate *	**40 (0.23%)**	**1730 (0.94%)**	**447 (1.51%)**	**2217 (0.96%)**	**14 (0.16%)**	**371 (0.42%)**	**69 (0.51%)**	**454 (0.41%)**
Post-operative gastrointestinal bleeding or hematoma/ hemorrhage /seroma complicating the procedure	115 (0.66%)	1611 (0.87%)	390 (1.32%)	2116 (0.91%)	67 (0.76%)	1092 (1.24%)	297 (2.21%)	1456 (1.32%)

ASA= aspirin, AC= anticoagulant

* VTE rate defined as PE and/or DVT during index hospitalization or readmitted within 30 days with primary diagnosis of VTE.

Table 4

Risk of venous thromboembolism after knee and hip arthroplasty, multivariable model results

	Adjusted Odds Ratio (95% Confidence Interval)	
	Knee arthroplasty	**Hip Arthroplasty**
Aspirin only (vs. Anticoagulant or Anticoagulant+Aspirin)	0.34 (0.24, 0.48)	0.82 (0.45, 1.51)
Female	1.15 (1.05, 1.26)	1.00 (0.82, 1.21)
Age		
18–64	Referent	Referent
65–69	1.28 (1.14, 1.43)	1.13 (0.82, 1.55)
70–74	1.20 (1.06, 1.36)	1.28 (0.93, 1.76)
75–79	1.16 (0.99, 1.36)	1.25 (0.89, 1.75)
≥80	0.84 (0.70, 1.00)	0.97 (0.68, 1.39)
Primary payer		
Uninsured	2.00 (1.24, 3.23)	1.98 (0.84, 4.69)
Indemnity	1.35 (1.17, 1.56)	1.00 (0.69, 1.44)
Managed care/capitated	0.97 (0.53, 1.78)	0.66 (0.19, 2.32)
Managed care/not capitated	1.16 (1.04, 1.29)	1.49 (1.11, 1.99)
Medicaid	0.75 (0.54, 1.03)	0.74 (0.39, 1.40)
Other	1.09 (0.79, 1.52)	1.44 (0.52, 3.97)
Medicare	Referent	Referent
Race/ethnicity		
White	Referent	Referent
Black	1.36 (0.95, 1.95)	1.12 (0.47, 2.69)
Hispanic	0.88 (0.69, 1.13)	0.81 (0.55, 1.19)
Other	1.14 (1.00, 1.29)	0.94 (0.66, 1.35)
Hospital location		
Rural	Referent	Referent
Urban	2.67 (1.96, 3.64)	3.88 (2.73, 5.51)
Hospital region		
Midwest	0.81 (0.59, 1.12)	0.59 (0.42, 0.83)
Northeast	1.62 (1.13, 2.32)	1.00 (0.73, 1.37)
South	Referent	Referent
West	1.36 (0.98, 1.89)	1.22 (0.86, 1.74)
Hospital bed size		
0–99	1.73 (1.00, 2.98)	2.82 (1.34, 5.94)
100–199	1.80 (1.12, 2.91)	1.73 (1.08, 2.77)
200–299	1.09 (0.70, 1.68)	1.66 (1.17, 2.37)
300–399	1.80 (1.20, 2.70)	1.84 (1.33, 2.55)
400–499	1.09 (0.73, 1.62)	2.03 (1.45, 2.83)

	Adjusted Odds Ratio (95% Confidence Interval)	
	Knee arthroplasty	**Hip Arthroplasty**
≥ 500	Referent	Referent
Teaching hospital status	1.89 (1.41, 2.52)	1.36 (1.04, 1.76)
Hospital volume	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
Compression stockings used	1.22 (1.08, 1.39)	1.23 (0.99, 1.53)
Elixhauser comorbidity score[16]	1.06 (1.05, 1.07)	1.05 (0.13, 1.06)
Caprini VTE risk score[15] (by points)	1.01 (0.97, 1.06)	1.14 (1.05, 1.24)
Length of stay (days)	2.12 (1.67, 2.68)	1.07 (1.04, 1.09)

* Multivariable models included all variables shown in the table as well as the propensity scores for aspirin-only treatment, and were controlled for clustering by individual hospital