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ANTITHROMBOTIC THERAPY AND PREVENTION OF THROMBOSIS, 9TH ED: ACCP GUIDELINES

Prevention of VTE in Nonorthopedic Surgical Patients

Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Michael K. Gould, MD, FCCP; David A. Garcia, MD; Sherry M. Wren, MD; Paul J. Karanicolas, MD, PhD; Juan I. Arcelus, MD, PhD; John A. Heit, MD; and Charles M. Samama, MD, PhD, FCCP

Background: **VTE is a common cause of preventable death in surgical patients.**
Methods: **We developed recommendations for thromboprophylaxis in nonorthopedic surgical patients by using systematic methods as described in Methodology for the Development of Antithrombotic Therapy and Prevention of Thrombosis Guidelines. Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines in this supplement.**
Results: **We describe several alternatives for stratifying the risk of VTE in general and abdominal-pelvic surgical patients. When the risk for VTE is very low (< 0.5%), we recommend that no specific pharmacologic (Grade 1B) or mechanical (Grade 2C) prophylaxis be used other than early ambulation. For patients at low risk for VTE (~1.5%), we suggest mechanical prophylaxis, preferably with intermittent pneumatic compression (IPC), over no prophylaxis (Grade 2C). For patients at moderate risk for VTE (~3%) who are not at high risk for major bleeding complications, we suggest low-molecular-weight heparin (LMWH) (Grade 2B), low-dose unfractionated heparin (Grade 2B), or mechanical prophylaxis with IPC (Grade 2C) over no prophylaxis. For patients at high risk for VTE (~6%) who are not at high risk for major bleeding complications, we recommend pharmacologic prophylaxis with LMWH (Grade 1B) or low-dose unfractionated heparin (Grade 1B) over no prophylaxis. In these patients, we suggest adding mechanical prophylaxis with elastic stockings or IPC to pharmacologic prophylaxis (Grade 2C). For patients at high risk for VTE undergoing abdominal or pelvic surgery for cancer, we recommend extended-duration, postoperative, pharmacologic prophylaxis (4 weeks) with LMWH over limited-duration prophylaxis (Grade 1B). For patients at moderate to high risk for VTE who are at high risk for major bleeding complications or those in whom the consequences of bleeding are believed to be particularly severe, we suggest use of mechanical prophylaxis, preferably with IPC, over no prophylaxis until the risk of bleeding diminishes and pharmacologic prophylaxis may be initiated (Grade 2C). For patients in all risk groups, we suggest that an inferior vena cava filter not be used for primary VTE prevention (Grade 2C) and that surveillance with venous compression ultrasonography should not be performed (Grade 2C). We developed similar recommendations for other nonorthopedic surgical populations.**
Conclusions: **Optimal thromboprophylaxis in nonorthopedic surgical patients will consider the risks of VTE and bleeding complications as well as the values and preferences of individual patients.**
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Abbreviations: CABG = coronary artery bypass graft; ES = elastic stockings; ICH = intracranial hemorrhage; IPC = intermittent pneumatic compression; IVC = inferior vena cava; LDUH = low-dose unfractionated heparin; LMWH = low-molecular-weight heparin; PE = pulmonary embolism; QALY = quality-adjusted life year; RR = risk ratio; VCU = venous compression ultrasonography

Summary of Recommendations

Note on Shaded Text: Throughout this guideline, shading is used within the summary of recommendations sections to indicate recommendations that are newly added or have been changed since the publication of Antithrombotic and Thrombolytic Therapy: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Recommendations that remain unchanged are not shaded.

3.6.1. For general and abdominal-pelvic surgery patients at very low risk for VTE (< 0.5%; Rogers score, < 7; Caprini score, 0), we recommend that no specific pharmaclogic (Grade 1B) **or mechanical** (Grade 2C) **prophylaxis be used other than early ambulation.**

3.6.2. For general and abdominal-pelvic surgery patients at low risk for VTE (~1.5%; Rogers score, 7-10; Caprini score, 1-2), we suggest mechanical prophylaxis, preferably with intermittent pneumatic compression (IPC), over no prophylaxis (Grade 2C)**.**

3.6.3. For general and abdominal-pelvic surgery patients at moderate risk for VTE (~3.0%; Rogers score, > 10; Caprini score, 3-4) who are not at high risk for major bleeding complications, we suggest low-molecular-weight heparin (LMWH) (Grade 2B)**, low-dose unfractionated heparin (LDUH)** (Grade 2B)**, or mechanical prophylaxis, preferably with IPC** (Grade 2C)**, over no prophylaxis.**

Remarks: Three of the seven authors favored a strong (Grade 1B) recommendation in favor of LMWH or LDUH over no prophylaxis in this group.

3.6.4. For general and abdominal-pelvic surgery patients at moderate risk for VTE (3.0%; Rogers score, > 10; Caprini score, 3-4) who are at high risk for major bleeding complications or those in whom the consequences of bleeding are thought to be particularly severe, we suggest mechanical prophylaxis, preferably with IPC, over no prophylaxis (Grade 2C)**.**

3.6.5. For general and abdominal-pelvic surgery patients at high risk for VTE (~6.0%; Caprini score, ≥ 5) who are not at high risk for major bleeding complications, we recommend pharmacologic prophylaxis with LMWH (Grade 1B) **or LDUH** (Grade 1B) **over no prophylaxis. We suggest that mechanical prophylaxis with elastic stockings (ES) or IPC should be added to pharmacologic prophylaxis** (Grade 2C)**.**

3.6.6. For high-VTE-risk patients undergoing abdominal or pelvic surgery for cancer who are not otherwise at high risk for major bleeding complications, we recommend extended-duration pharmacologic prophylaxis (4 weeks) with LMWH over limited-duration prophylaxis (Grade 1B)**.**

Remarks: Patients who place a high value on minimizing out-of-pocket health-care costs might prefer limited-duration over extended-duration prophylaxis in settings where the cost of extended-duration prophylaxis is borne by the patient.

3.6.7. For high-VTE-risk general and abdominal-pelvic surgery patients who are at high risk for major bleeding complications or those in whom the consequences of bleeding are thought to be particularly severe, we suggest use of mechanical prophylaxis, preferably with IPC, over no prophylaxis until the risk of bleeding diminishes and pharmacologic prophylaxis may be initiated (Grade 2C)**.**

3.6.8. For general and abdominal-pelvic surgery patients at high risk for VTE (6%; Caprini score, ≥ 5) in whom both LMWH and unfractionated heparin are contraindicated or unavailable and who are not at high risk for major

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Affiliations: From the Keck School of Medicine (Dr Gould), University of Southern California, Los Angeles, CA; University of New Mexico School of Medicine (Dr Garcia), Albuquerque, NM; Stanford School of Medicine (Dr Wren), Stanford, CA; Surgical Oncology (Dr Karanicolas), Sunnybrook Health Sciences Centre, Toronto, ON, Canada; University of Granada Medical School (Dr Arcelus), Granada, Spain; College of Medicine (Dr Heit), Mayo Clinic, Rochester, MN; and Department of Anaesthesiology and Intensive Care (Dr Samama), Hotel-Dieu University Hospital, Paris, France.
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Correspondence to: Michael K. Gould, MD, FCCP, Department of Research and Evaluation, 100 S Los Robles, Pasadena, CA 91101; e-mail: michael.k.gould@kp.org

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bleeding complications, we suggest low-dose aspirin (Grade 2C)**, fondaparinux** (Grade 2C)**, or mechanical prophylaxis, preferably with IPC** (Grade 2C)**, over no prophylaxis.**

3.6.9. For general and abdominal-pelvic surgery patients, we suggest that an inferior vena cava (IVC) filter should not be used for primary VTE prevention (Grade 2C)**.**

3.6.10. For general and abdominal-pelvic surgery patients, we suggest that periodic surveillance with venous compression ultrasound (VCU) should not be performed (Grade 2C)**.**

4.4.1. For cardiac surgery patients with an uncomplicated postoperative course, we suggest use of mechanical prophylaxis, preferably with optimally applied IPC, over either no prophylaxis (Grade 2C) **or pharmacologic prophylaxis** (Grade 2C)**.**

4.4.2. For cardiac surgery patients whose hospital course is prolonged by one or more nonhemorrhagic surgical complications, we suggest adding pharmacologic prophylaxis with LDUH or LMWH to mechanical prophylaxis (Grade 2C)**.**

5.4.1. For thoracic surgery patients at moderate risk for VTE who are not at high risk for perioperative bleeding, we suggest LDUH (Grade 2B)**, LMWH** (Grade 2B)**, or mechanical prophylaxis with optimally applied IPC** (Grade 2C) **over no prophylaxis.**

Remarks: Three of the seven authors favored a strong (Grade 1B) recommendation in favor of LMWH or LDUH over no prophylaxis in this group.

5.4.2. For thoracic surgery patients at high risk for VTE who are not at high risk for perioperative bleeding, we suggest LDUH (Grade 1B) **or LMWH** (Grade 1B) **over no prophylaxis. In addition, we suggest that mechanical prophylaxis with ES or IPC should be added to pharmacologic prophylaxis** (Grade 2C)**.**

5.4.3. For thoracic surgery patients who are at high risk for major bleeding, we suggest use of mechanical prophylaxis, preferably with optimally applied IPC, over no prophylaxis until the risk of bleeding diminishes and pharmacologic prophylaxis may be initiated (Grade 2C)**.**

6.4.1. For craniotomy patients, we suggest that mechanical prophylaxis, preferably with IPC, be used over no prophylaxis (Grade 2C) **or pharmacologic prophylaxis** (Grade 2C)**.**

6.4.2. For craniotomy patients at very high risk for VTE (eg, those undergoing craniotomy for malignant disease), we suggest adding pharmacologic prophylaxis to mechanical prophylaxis once adequate hemostasis is established and the risk of bleeding decreases (Grade 2C)**.**

7.4.1. For patients undergoing spinal surgery, we suggest mechanical prophylaxis, preferably with IPC, over no prophylaxis (Grade 2C)**, unfractionated heparin** (Grade 2C)**, or LMWH** (Grade 2C)**.**

7.4.2. For patients undergoing spinal surgery at high risk for VTE (including those with malignant disease or those undergoing surgery with a combined anterior-posterior approach), we suggest adding pharmacologic prophylaxis to mechanical prophylaxis once adequate hemostasis is established and the risk of bleeding decreases (Grade 2C)**.**

8.4.1. For major trauma patients, we suggest use of LDUH (Grade 2C)**, LMWH** (Grade 2C)**, or mechanical prophylaxis, preferably with IPC** (Grade 2C)**, over no prophylaxis.**

8.4.2. For major trauma patients at high risk for VTE (including those with acute spinal cord injury, traumatic brain injury, and spinal surgery for trauma), we suggest adding mechanical prophylaxis to pharmacologic prophylaxis (Grade 2C) **when not contraindicated by lower-extremity injury.**

8.4.3. For major trauma patients in whom LMWH and LDUH are contraindicated, we suggest mechanical prophylaxis, preferably with IPC, over no prophylaxis (Grade 2C) **when not contraindicated by lower-extremity injury. We suggest adding pharmacologic prophylaxis with either LMWH or LDUH when the risk of bleeding diminishes or the contraindication to heparin resolves** (Grade 2C)**.**

8.4.4. For major trauma patients, we suggest that an IVC filter should not be used for primary VTE prevention (Grade 2C)**.**

8.4.5. For major trauma patients, we suggest that periodic surveillance with VCU should not be performed (Grade 2C)**.**

VTE is a common cause of preventable death in hospitalized patients. Approximately one-third of the 150,000 to 200,000 VTE-related deaths per year in the United States occur following surgery.[1] The

high incidence of postoperative VTE and the availability of effective methods of prevention mandate that thromboprophylaxis should be considered in every surgical patient. In this article, we review the literature pertaining to thromboprophylaxis in nonorthopedic surgical patients and make recommendations for VTE prevention after explicitly weighing the trade-offs between the potential benefits and harms of alternative strategies for prophylaxis.

1.0 Methods

To develop recommendations for thromboprophylaxis among patients undergoing nonorthopedic surgery, we first used the population, intervention, comparator, outcome format to generate a list of questions (Table 1). Through the evidence review, we attempted to identify all relevant studies that compared one or more interventions for thromboprophylaxis with any alternative (including placebo or no treatment) among nonorthopedic surgical patients. We favored studies or systematic reviews that limited inclusion to the target populations and considered indirect evidence from other populations when direct evidence was limited in quantity or quality.

Preferred outcomes included death from any cause, fatal pulmonary embolism (PE); objectively confirmed, nonfatal, symptomatic PE and DVT; fatal bleeding; bleeding requiring reoperation; and other major bleeding. We accepted the definition of major bleeding used in each study, recognizing that there would be substantial heterogeneity in definitions across studies. When symptomatic VTE events were few in number or not reported, we used information about asymptomatic, proximal DVT, preferably when detected or confirmed by ultrasonography or venography. In some cases in which better-quality evidence was not available, we used information about asymptomatic DVT detected by radioactive fibrinogen uptake, recognizing that the sensitivity and specificity of this test are poor.

The Oregon Evidence-Based Practice Center updated the literature review from the prior edition of these guidelines by searching Medline, the Cochrane Controlled Trials Register, and the Cochrane Database of Systematic Reviews for all randomized trials, observational studies, and systematic reviews of thromboprophylaxis in surgical patients published between January 1, 2005, and November 4, 2009 (Table S1). (Tables and figures that contain an "S" before the number and any appendices denote supplementary information not contained in the body of the article and available instead in an online data supplement. See the "Acknowledgments" for more information.) We performed additional searches through December 31, 2010. In addition, we searched other online resources, including Trial Results Center[2]; retrieved original reports from articles that were included in prior systematic reviews, scanned reference lists of retrieved articles, and shared articles from our personal files with one another and with authors of other prevention topic articles in this supplement.

We abstracted relevant information from each study regarding study characteristics, risk of bias, and results. When available, we collected this information from published systematic reviews. When desired information was not available in a published systematic review, we used data from individual studies or pooled data across studies using random-effects models and RevMan statistical software (Cochrane Information Management System), as appropriate.

When formulating recommendations, we considered trade-offs between desirable and undesirable patient-important outcomes by comparing the absolute numbers of expected events. To estimate absolute numbers of expected events, we used relative risk estimates from randomized trials or systematic reviews of randomized trials. We applied these estimates of relative risk to estimates of the baseline risk of symptomatic events that we obtained from observational studies.[3] For example, if prophylaxis reduces the risk of VTE by 50%, and the baseline risk of symptomatic VTE in the absence of prophylaxis in a given population is 20 per 1,000 (2%), then the absolute number of VTE events prevented is 10 per 1,000 patients treated.

When weighing absolute numbers of desirable and undesirable events, we used explicit information about values and preferences for specific outcomes based on results of a survey of Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines panel members.[3] To facilitate weighing trade-offs between thrombotic events and bleeding complications, we frequently elected to combine estimates of nonfatal PE and symptomatic DVT when estimating baseline and relative risks.

To estimate baseline risks of VTE and bleeding events, we sought large, population-based, observational studies with few exclusions or losses to follow-up that measured objectively confirmed, patient-important outcomes over a sufficiently long time horizon (1-3 months). Many studies of baseline VTE risk were limited by small samples, referral center bias, retrospective design, short time horizons, and missing or incomplete information about prophylaxis received. To estimate the expected baseline risk of VTE in the absence of prophylaxis, we adjusted for prophylaxis received by dividing the observed risk of VTE by the relative risk of VTE associated with prophylaxis. For example, in a retrospective study of 1,126 plastic and reconstructive surgery patients, the observed that the risk of symptomatic VTE within 60 days of surgery was 1.27% among patients at moderate risk for VTE, all of whom received mechanical prophylaxis with intermittent pneumatic compression (IPC).[4] Assuming that the relative risk of VTE in patients who receive IPC compared with no prophylaxis is 0.48, the estimated baseline risk of VTE in the absence of prophylaxis is 2.6%.

Studies of bleeding risk were few in number and limited by small samples and heterogeneous definitions of major bleeding. When necessary, we used pooled estimates of bleeding risk from the control groups of randomized controlled trials.

Like other topic articles in these guidelines, we used the Grades of Recommendations, Assessment, Development, and Evaluation system to assess the quality of evidence and describe the strength of recommendations.[5-7] Accordingly, we noted when randomized trials were limited by unclear allocation concealment, incomplete blinding (especially for "subjective" outcomes), measurement of surrogate outcomes (eg, asymptomatic DVT), large (or differential) losses to follow-up, failure to adhere to an intention-to-treat analysis, stopping early for benefit, and failure to report outcomes.

2.0 Safety and Effectiveness of Interventions for Thromboprophylaxis

Alternative interventions for thromboprophylaxis that have been evaluated in studies of nonorthopedic surgical patients include elastic stockings (ES), IPC devices, low-dose unfractionated heparin (LDUH), low-molecular-weight heparin (LMWH), fondaparinux, aspirin, inferior vena cava (IVC) filters, and surveillance with venous compression ultrasonography (VCU) as summarized in Tables 2-4. Characteristics and risk of bias in individual trials are summarized in Tables S2 and S3. Additional details are provided in Appendix S1.

Table 1—*Structured Clinical Questions*

Sections	PICO Question					Methods
	Informal Questions	Population	Intervention	Comparator	Outcome	
3.1. General and abdominal-pelvic surgery, including GI, GU, and Gyn surgery 3.2. Bariatric surgery 3.3. Vascular surgery 3.4. Plastic and reconstructive surgery 4. Cardiac surgery 5. Thoracic surgery 6. Craniotomy 7. Spinal surgery 8. Trauma	Type, timing, dose, frequency, and duration of prophylaxis	Specific surgical population, stratified by risk of VTE	Mechanical prophylaxis (ES, IPC, IVC filter) and pharmacologic prophylaxis (LDUH, LMWH, fondaparinux, aspirin)	No treatment, mechanical prophylaxis and pharmacologic prophylaxis	Asymptomatic proximal DVT, symptomatic DVT, symptomatic PE, fatal PE, bleeding requiring reoperation, fatal bleeding, intracranial bleeding, death	RCTs
All nonorthopedic surgery	Prognostic factors associated with risk of VTE	All	Any or none		Asymptomatic proximal DVT, symptomatic DVT, PE, fatal PE	Case control, retrospective and prospective cohort studies, RCTs
All nonorthopedic surgery	Prognostic factors associated with risk of bleeding complications	All	Any pharmacologic prophylaxis (LDUH, LMWH, fondaparinux, aspirin)		Major bleeding, bleeding requiring reoperation, fatal bleeding, intracranial bleeding	Case control, retrospective and prospective cohort studies, RCTs
All nonorthopedic surgery	Screening with ultrasonography for asymptomatic VTE	All	Any or none		Asymptomatic DVT, symptomatic DVT, PE, fatal PE	Case control, retrospective and prospective cohort studies, RCTs

ES = elastic stockings; GU = urological; Gyn = gynecologic; IPC = intermittent pneumatic compression; IVC = inferior vena cava; LDUH = low-dose unfractionated heparin; LMWH = low-molecular-weight heparin; PE = pulmonary embolism; PICO = population, intervention, comparator, outcome; RCT = randomized controlled trial.

Table 2—*Relative Risk Estimates From Published Systematic Reviews and Selected Randomized Trials of Pharmacologic Prophylaxis*

Study/Year and Population	Death From Any Cause	Fatal PE	Nonfatal PE	Symptomatic DVT or VTE	Any DVT or VTE (Including Asymptomatic)	Proximal DVT (Including Asymptomatic)	Fatal Bleeding	Nonfatal Major Bleeding	Bleeding Requiring Reoperation
LDUH vs no prophylaxis									
IMT[8]/1975 General surgery[a]	0.81 (0.61-1.10)	0.13 (0.02-0.55)	NA	0.35 (0.18-0.69)	0.31 (0.23-0.42)	0.11(0.04-0.27)	0.81 (0.21-3.0)	1.37[b] (1.09-1.73)	NA
Collins et al[9]/1988 Mixed surgery[c]	0.82 (0.69-0.99)	0.53 (0.31-0.91)	0.59 (0.41-0.84)	NA	NA	NA	1.14 (0.41-3.15)	1.57 (1.32-1.87)	NA
Collins et al[9]/1988 General surgery[c]	0.82 (0.68-0.99)	0.50 (0.20-1.30)	0.44 (0.31-0.63)	NA	NA	NA	1.01 (0.35-2.97)	1.56 (1.29-1.88)	NA
Collen et al[10]/2008 Neurosurgery	NA	NA	0.96 (0.10-9.06)	NA	0.50 (0.11-2.38)	NA	NA	NA	NA
LMWH vs no prophylaxis									
Pezzuoli et al[11]/1989 Abdominal surgery[a]	0.44 (0.22-0.89)	0.50 (0.12-2.08)	NA	0.33 (0.09-1.23)	NA	NA	None	3.11[d] (1.84-5.28)	2.24 (1.46-3.43)
Iorio and Agnelli[12]/2000 Neurosurgery	1.74 (0.94-3.22)	NA	NA	NA	0.54 (0.38-0.77)	0.48 (0.28-0.83)	NA	1.68 (0.62-4.52)	NA
Mismetti et al[13]/2001 General surgery	0.54 (0.27-1.10)	NA	0.25 (0.08-0.79)	0.29 (0.11-0.73) 0.31[e] (0.12-0.81)	0.28 (0.14-0.54)	NA	NA	2.03 (1.37-3.01)	NA
LMWH vs LDUH									
Geerts et al[14]/1996 Major trauma[a]	NA	None	1 (LMWH)	2 DVT with HIT (LDUH)	0.70 (0.50-0.96)	0.42 (0.13-0.88)	None	5.27 (0.62-44.5)	1 (LMWH)
Mismetti et al[13]/2001 General surgery	1.04 (0.89-1.20)	NA	0.88 (0.64-1.20)	0.71 (0.51-0.99)	0.90 (0.79-1.02)	NA	NA	0.89 (0.75-1.05)	NA
Akl et al[15]/2008 Cancer surgery	0.88 (0.65-1.19)	NA	0.60 (0.22-1.64)	0.73 (0.23-2.28)	NA	NA	NA	0.95 (0.51-1.77)	NA
Collen et al[10]/2008 Neurosurgery	NA	NA	0.43 (0.08-2.41)	NA	1.46 (0.61-3.51)	NA	1.78[f] (0.37-8.50)	1.00 (0.18-5.74)	NA
Extended- vs limited-duration LMWH									
Akl et al[15]/2008 Cancer surgery	1.23 (0.70-2.15) (1 y)	NA	NA	NA	0.21 (0.05-0.94)	NA	NA	2.94 (0.12-71.8)	NA
Bottaro et al[16]/2008 Abdominal surgery	NA	NA	NA	NA	0.46 (0.29-0.74)	0.24 (0.09-0.67)	NA	0.83 (0.22-3.12)	NA
Rasmussen et al[17]/2009 Abdominal/pelvic surgery	1.12 (0.65-1.93)	NA	NA	0.22 (0.06-0.80)	0.41 (0.26-0.63)	0.27 (0.13-0.57)	NA	1.11 (0.62-1.97)	NA
Kakkar et al[18]/2010 Abdominal and pelvic cancer surgery[a]	1.29 (0.45-3.66)	0.32[g] (0.03-3.07)	None	NA	0.63 (0.37-1.10)	0.12 (0.02-0.96)	None	1.97 (0.18-21.6)	NA
Fondaparinux plus IPC vs IPC alone									
Turpie et al[19]/2007 Abdominal surgery[a]	1.64 (0.54-4.98)	1.02 (0.06-16.3)	1.01 (0.06-16.2)	1.01 (0.06-16.2)	0.31 (0.14-0.73)	0.14 (0.02-1.14)	None	10.2 (1.31-79.7)	4/635 vs0/650
Fondapariunx vs LMWH									
Agnelli et al[20]/2005 Abdominal surgery[a]	0.75 (0.38-1.45)	1.0 (0.20-4.94)	2/1,465 vs 0/1,462	1.20 (0.37-3.92)	0.75 (0.52-1.09)	1.00 (0.29-3.45)	0.99 (0.14-7.05)	1.43 (0.93-2.21)	1.57 (0.77-3.23)

(Continued)

Table 2—*Continued*

Study/Year and Population	Death From Any Cause	Fatal PE	Nonfatal PE	Symptomatic DVT or VTE	Any DVT or VTE (Including Asymptomatic)	Proximal DVT (Including Asymptomatic)	Fatal Bleeding	Nonfatal Major Bleeding	Bleeding Requiring Reoperation
Low-dose aspirin vs no prophylaxis									
PEP trial[21]/2000 Hip fracture, hip or knee replacement[a]	0.96 (0.85-1.09)	0.42 (0.25-0.72)	0.78 (0.51-1.21)	0.72 (0.53-0.96)	NA	NA	0.87 (0.41-1.82)	1.12 (0.94-1.34)	0.97 (0.63-1.51)
Higher-dose aspirin vs no prophylaxis									
APT[22]/1994 Mixed surgery	NA	NA	0.33 (0.03-0.63)	NA	0.77 (0.57-0.97)	NA	NA	1.87 (1.00-3.50)	NA
APT[22]/1994 General surgery	NA	NA	0.29 (0.01-0.57)	NA	0.63 (0.47-0.79)	NA	NA	1.39 (1.12-1.74)	NA

Data are presented as relative risks or OR (95% CI). APT = Antiplatelet Trialists' Collaboration; HIT = heparin-induced thrombocytopenia; IMT = International Multicenter Trial, IPC = intermittent pneumatic compression; NA = not available; PEP = Pulmonary Embolism Prevention; SCITI = Spinal Cord Injury Thromboprophylaxis Investigators. See Table 1 legend for expansion of other abbreviations.

[a]RCTs.

[b]Wound hematoma.

[c]Reanalysis of data using random-effects models.

[d]Postoperative bleeding requiring treatment discontinuation.

[e]Reanalysis of data to reflect reclassification of miscoded events from study by Pezzuoli et al.[11]

[f]Intracranial bleeding.

[g]VTE-related death.

Table 3—*Relative Risk Estimates From Published Systematic Reviews and Selected Randomized Trials of Mechanical Prophylaxis*

Study/Year and Population	PE	Symptomatic DVT	Asymptomatic DVT (Any)	Asymptomatic Proximal DVT
		IPC vs no prophylaxis		
Vanek[23]/1998 Mixed surgery	0.89 ($P = .82$)	NA	0.38 ($P < .001$)	0.43 ($P < .001$)
Roderick et al[24]/2005 Mixed medicine/surgery	NS	NA	0.34 (0.20-0.48)	0.48 (0.22-0.74)
Urbankova et al[25]/2005 Mixed surgery	1.12 (0.53-2.35)	NA	0.40 (0.29-0.56)	NA
Collen et al[10]/2008 Neurosurgery	0.37 (0.03-4.06)	NA	0.41 (0.21-0.78)	NA
		ES vs no prophylaxis		
Roderick et al[24]/2005 Mixed medicine/surgery	NS	NA	0.34 (0.14-0.54)	0.36 (0-1.30)
CLOTS1[26]/2009 Acute stroke	0.65 (0.32-1.31)	0.90 (0.62-1.31)	0.90 (0.73-1.11)	1.01 (0.74-1.36)
Sachdeva et al[27]/2010 Mixed surgical	0.13 (0-6.68)	NA	0.35 (0.26-0.47)	NA
		IPC vs ES		
Vanek[23]/1998 Mixed surgery	1.47 ($P = .71$)	NA	0.53 ($P = .04$)	0.74 ($P = .56$)
Collen et al[10]/2008 Neurosurgery	0.49 (0.08-2.85)	NA	0.81 (0.32-1.78)	NA
		Add ES to pharmacologic prophylaxis		
Sachdeva et al[27]/2010 Mixed medicine and surgery	0.36 (0.13-0.99)	NA	0.25 (0.17-0.36)	NA
Reanalysis of data from Roderick, Sachdeva, Kakkar et al[18]	0.43 (0.16-1.18)	NA	0.40 (0.25-0.65)	0.28 (0.09-0.87)
		Add IPC to pharmacologic prophylaxis		
Reanalysis of data from Roderick, Sachdeva, Kakkar	0.57 (0.16-2.0)	NA	0.45 (0.20-1.03)	1.04 (0.29-3.79)
		Add any mechanical prophylaxis to pharmacologic prophylaxis		
Reanalysis of data from Roderick, Sachdeva, Kakkar	0.48 (0.22-1.05)	NA	0.41 (0.27-0.62)	0.50 (0.21-1.16)

Data are presented as relative risk (95% CI), unless otherwise indicated. CLOTS1 = Clots in Legs or Stockings after Stroke; NS = not significant. See Table 1 and 2 legends for expansion of other abbreviations.

2.1 ES vs No Prophylaxis

A Cochrane review summarized results of eight older trials of ES vs no prophylaxis, including four trials in general surgery and one trial each in orthopedic, cardiac, gynecologic, and neurosurgery.[27] The studies had many limitations, including small samples, incomplete blinding, uncertain concealment of treatment allocation, and use of fibrinogen leg scanning to identify asymptomatic DVT. Across all trials, ES reduced the odds of DVT (including distal and asymptomatic DVT) by 65%. A previous meta-analysis reported similar results for all DVT, but reductions in proximal DVT and PE were neither confirmed nor excluded.[24]

More recently, a large, multicenter, randomized controlled trial in patients with acute stroke provided additional, indirect evidence by comparing thigh-length ES plus routine care with routine care alone (including the use of heparin, warfarin, or alteplase in 12% of participants). Reductions in the risk of fatal or nonfatal PE (OR, 0.65; 95% CI, 0.32-1.31) and symptomatic proximal DVT (OR, 0.84; 95% CI, 0.53-1.31) were neither confirmed nor excluded, but use of ES was associated with a fourfold increase in the risk of skin complications (5.1% vs 1.3%), including breaks, ulcers, blisters, and necrosis.[26] A subsequently published trial of thigh-length stockings vs calf-length stockings found that thigh-length stockings reduced the risk of symptomatic or asymptomatic proximal DVT by 31%, an absolute difference of 2.5 percentage points.[29] In this study, skin complications were observed in 3.9% of patients in the thigh-length ES group. The incidence of skin complications with ES in nonorthopedic surgical patients is likely to be lower than that observed in these trials of elderly patients with stroke who wore stockings for up to 30 days.

2.2 IPC vs No Prophylaxis

Several meta-analyses have compared IPC and no prophylaxis in mixed surgical populations.[23-25]

Table 4—*Relative Risk Estimates From Published Systematic Reviews of Studies Comparing Pharmacologic and Mechanical Prophylaxis*

Study/Year and Population	PE	Asymptomatic DVT (Any)	Asymptomatic Proximal DVT	Nonfatal Major Bleeding	ICH	Death From Any Cause
LDUH vs nonpharmacologic						
Collen et al[10]/2008 Neurosurgery	NA	NA	NA	0.85 (0.12-5.99)	2.11 (0.39-11.3)	0.97 (0.13-7.37)
LMWH vs nonpharmacologic						
Collen et al[10]/2008 Neurosurgery	NA	NA	NA	0.95 (0.18-5.09)	1.97 (0.64-6.09)	0.96 (0.47-1.96)
LMWH vs IPC						
Collen et al[10]/2008 Neurosurgery	1.62 (0.35-7.46)	0.79 (0.30-2.12)	NA	NA	NA	NA
LMWH vs ES						
Collen et al[10]/2008 Neurosurgery	0.29 (0.05-1.85)	0.60 (0.44-0.81)	NA	NA	NA	NA
Any mechanical vs LDUH or LMWH						
Eppsteiner et al[28]/2010 Mixed surgery	1.03 (0.48-2.22)	1.07 (0.72-1.61)	NA	0.43 (0.19-0.98)	NA	NA
Any mechanical vs LDUH						
Eppsteiner et al[28]/2010 Mixed surgery	NA	0.71 (0.42-1.19)	NA	NA	NA	NA
Any mechanical vs LMWH						
Eppsteiner et al[28]/2010 Mixed surgery	NA	1.80 (1.16-2.79)	NA	NA	NA	NA
IPC vs heparin						
Vanek[23]/1998 Mixed surgery	1.04 ($P = 1.0$)	0.52 ($P = .01$)	0.43 ($P = .06$)	NA	NA	NA

ICH = intracranial hemorrhage. See Table 1 and 2 legends for expansion of other abbreviations.

Urbankova et al[25] identified 15 trials, including five in orthopedics, four in general surgery, three in oncologic surgery, three in neurosurgery, and one in urology. Roderick et al[24] identified 19 trials, including five in general surgery, five in orthopedics, five in neurosurgery, two in gynecology, one in urology, and one in trauma. Many studies were limited by small samples, lack of blinding, unclear concealment of allocation sequence, and use of fibrinogen leg scanning (or less commonly, ultrasound or venography) to identify asymptomatic DVT, although DVT was subsequently confirmed by venography in most of the studies that used fibrinogen scanning. Both analyses found that compared with no prophylaxis, IPC reduced the risk of DVT (including asymptomatic and distal DVT) by 60%. In the analysis that examined proximal DVT, IPC reduced the odds by 50%.[24] Results failed to demonstrate or to exclude an effect on PE.[25] Other outcomes (fatal PE, skin complications) were not reported.

Adherence with IPC often is less than optimal. However, in one randomized trial of patients with acute spinal cord injury, 90% of participants were noted to use IPC for at least 75% of the recommended 22 h per day.[30] In another study, adherence with IPC was assessed at six times over a 24-h period in 227 nonambulatory trauma patients.[31] Although full adherence was noted in only 19% of patients, overall adherence across all six measurements was 53%.

2.3 Unfractionated Heparin vs No Prophylaxis

Low doses (10,000-15,000 units/d) of subcutaneously administered unfractionated heparin have been evaluated in numerous randomized controlled studies in heterogeneous surgical populations. Moderate- to high-quality evidence comes from a meta-analysis that analyzed data from 69 studies of LDUH prophylaxis in general surgery, urological surgery, and orthopedic surgery.[9] Many of the studies were limited by lack of blinding, unclear concealment of treatment allocation, and use of fibrinogen leg scanning to identify asymptomatic DVT. However, results were consistent with those from the International Multicenter Trial, a large randomized controlled trial with a low risk of bias.[8] In our reanalysis of data from this meta-analysis, we found that LDUH was associated with an 18% reduction in the odds of death from any cause, a 47% reduction in the odds of fatal PE, and a 41% reduction in the odds of nonfatal PE, along with a 57% increase in the odds of nonfatal major bleeding (Figs S1-S5).

2.4 LMWH vs No Prophylaxis

A meta-analysis summarized data from eight trials of five different preparations of LMWH vs no prophylaxis in general or abdominal surgery.[13] Two of eight studies were open label, and of three studies that reported symptomatic VTE, only one was potentially biased by the routine use of fibrinogen leg scanning to identify asymptomatic DVT. In the control groups, the pooled (baseline) risks of clinical PE, clinical VTE, and death were 0.5%, 0.9%, and 0.9%, respectively. Compared with no prophylaxis, LMWH reduced the risk of clinical PE and clinical VTE by ~70%. In addition, LMWH was associated with a possible reduction in the risk of death from any cause (risk ratio [RR], 0.54; 95% CI, 0.27-1.10). LMWH led to an approximate doubling of the risks of major bleeding (RR, 2.03; 95% CI, 1.37-3.01) and wound hematoma (RR, 1.88; 95% CI, 1.54-2.28). Similar results were reported in the more recent meta-analysis by the British National Collaborating Centre for Acute Care, which included studies of GI, gynecologic, urological, and thoracic surgery.[32]

2.5 LMWH vs LDUH

A meta-analysis of 51 randomized controlled trials compared LMWH and LDUH in >48,000 general and abdominal surgery patients.[13] About one-third of the studies were open label, and a majority used fibrinogen uptake scanning (with or without confirmatory venography) to identify asymptomatic DVT. In most studies, follow-up was for either 7 days or 1 month. Across all studies that reported clinical VTE events, the risk was ~30% lower in the LMWH groups. However, this difference was not apparent when the analysis was restricted to blinded, placebo-controlled trials. In addition, results failed to demonstrate or to exclude a beneficial effect of LMWH vs LDUH on clinical PE, death from any cause, major bleeding, and wound hematoma. Similar results were reported in the meta-analysis by the British National Collaborating Centre for Acute Care.[32]

2.6 Extended- vs Limited-Duration LMWH

The risk of VTE remains elevated for at least 12 weeks following surgery. A population-based, prospective study from the United Kingdom reported that compared with no surgery, the risk of VTE remained 10 to 50 times higher in weeks 7 to 12 following inpatient surgery.[33] In another study, the median time to postoperative VTE was 65 days.[34] Several studies compared extended-duration prophylaxis with LMWH (typically for 4 weeks) with limited-duration prophylaxis. Three systematic reviews summarized the results of these studies.[15-17] Study limitations include an open-label design in two studies and measurement of asymptomatic DVT by venography as a surrogate outcome. All three analyses concluded that extended-duration prophylaxis reduced

the risk of symptomatic or asymptomatic DVT by at least 50%, and two reported that proximal DVT was reduced by 75%. Results failed to demonstrate or exclude differences between groups in other outcomes, including major bleeding and death.

More recently, a multicenter, randomized, blinded, placebo-controlled trial compared an additional 3 weeks of pharmacoprophylaxis with bemiparin with no additional prophylaxis in 626 patients who underwent abdominal or pelvic surgery for cancer, all of whom received ~1 week of prophylaxis with once-daily bemiparin.[18] Surveillance venography was performed after 3 weeks, and patients were followed for clinical events for as long as 3 months. Approximately 20% of patients were excluded from assessment of the primary end point because venography was inadequate or not performed. The primary outcome was a composite of any DVT (including asymptomatic and distal events), nonfatal PE, and death from any cause. Although the risk of the composite outcome was 24% lower and the risk of proximal DVT was 88% lower in the extended-duration prophylaxis group, there were no symptomatic, nonfatal VTE events in either group. Although results failed to demonstrate or exclude a difference in bleeding, major bleeding was very uncommon, suggesting that any true underlying absolute differences will be small.

2.7 Fondaparinux vs LMWH

Fondaparinux was compared with the LMWH dalteparin in a blinded, randomized controlled trial of 2,927 patients at high risk for VTE who underwent abdominal (primarily GI) surgery.[20] Fondaparinux was associated with a possible reduction in asymptomatic or symptomatic DVT (RR, 0.75; 95% CI, 0.52-1.09), but results failed to demonstrate or exclude differences in the risks of fatal PE and nonfatal symptomatic VTE. There was a possible increase in the risk of nonfatal major bleeding with fondaparinux (RR, 1.43; 95% CI, 0.93-2.21), but differences in the risks of fatal bleeding and bleeding requiring reoperation were neither confirmed nor excluded.

Moderate-quality evidence from studies of patients undergoing elective hip replacement, elective knee replacement, and hip fracture surgery, when pooled with results of the previous study[20] in abdominal surgery, suggests that when compared with LMWH, fondaparinux does not reduce patient-important VTE events but leads to more major bleeding events.[35]

2.8 Fondaparinux Plus IPC vs IPC Alone

Another placebo-controlled study compared fondaparinux plus IPC with IPC alone in 1,309 patients who underwent major GI, gynecologic, urological, or other abdominal surgery.[19] In this study, the risk of any VTE (including asymptomatic DVT) was 69% lower in the fondaparinux group, and fondaparinux was associated with a possible reduction in the risk of proximal DVT (RR, 0.14; 95% CI, 0.02-1.14), but there was only one case of symptomatic VTE in each of the treatment groups. Major bleeding was more common among those who received fondaparinux (RR, 10.2; 95% CI, 1.31-79.7), but differences between the groups in fatal bleeding and bleeding requiring reoperation were neither confirmed nor excluded.

2.9 Low-Dose Aspirin (160 mg) vs No Prophylaxis

Perioperative use of low-dose aspirin was studied in orthopedic surgical patients in the PEP (Pulmonary Embolism Prevention) trial, a blinded, placebo-controlled study of > 13,000 patients undergoing hip fracture surgery and almost 4,100 patients undergoing elective arthoplasty.[21] The treatment group received aspirin 160 mg/d for 35 days, with the first dose chewed prior to surgery. In our reanalysis of data from both hip fracture and elective arthroscopy patients (Figs S6-S11), benefits included a 28% reduction in the risk of nonfatal symptomatic DVT (RR, 0.72; 95% CI, 0.53-0.96) and a 58% reduction in the risk of fatal PE (RR, 0.42; 95% CI, 0.25-0.72), whereas harms included a possible increase in the risk of nonfatal myocardial infarction (RR, 1.59; 95% CI, 0.98-2.57). Differences between aspirin and placebo were neither confirmed nor excluded for other outcomes.

Strengths of the PEP trial include the very large sample, adequate blinding of patients and outcome adjudicators, adequate concealment of the allocation sequence, complete follow-up, and reporting of well-defined clinically important outcomes. However, although several types of nonfatal bleeding complications were reported, it is somewhat difficult to assess their severity. A potentially more important limitation is uncertainty about whether the results are applicable to nonorthopedic surgical patients. There have been no studies of low-dose aspirin in nonorthopedic surgical patients, and we consider higher doses of aspirin to be a distinct intervention with uncertain risks and benefits (Figs S12-S23). Because of concerns about indirectness, attendees at the AT9 final conference voted that low-dose aspirin should not be an alternative for pharmacologic prophylaxis in most nonorthopedic surgical patients. Our recommendations for low-dose aspirin, therefore, apply only in circumstances in which LDUH and LMWH are contraindicated or not available.

2.10 Mechanical vs Pharmacologic Prophylaxis

A meta-analysis identified 16 studies that compared mechanical prophylaxis with either LDUH or

LMWH, including seven studies in general or abdominal-pelvic surgery, six in orthopedics, and three in trauma.[28] Studies compared heparin with IPC (nine studies), foot pump (four studies), or ES (three studies). Sample sizes ranged from 51 to >2,000 participants. Patients and treating physicians were not blinded to treatment assignment, and radiologists were blinded in only six studies. Follow-up ranged between 3 and 6 weeks in most studies. When results from all studies were pooled, a difference in the risk of DVT (including asymptomatic and distal DVT) was neither confirmed nor excluded (RR, 1.07; 95% CI, 0.72-1.61). However, when the analysis was restricted to eight studies that compared mechanical prophylaxis with LMWH, the risk of DVT was 80% higher in the mechanical prophylaxis group (RR, 1.80; 95% CI, 1.16-2.79). The risk of major bleeding complications was 57% lower in those who received mechanical prophylaxis, with no difference in the relative risk of bleeding between studies of LDUH and LMWH.

2.11 Mechanical Prophylaxis Plus Pharmacologic Prophylaxis vs Pharmacologic Prophylaxis Alone

Ten studies compared ES plus pharmacologic prophylaxis with pharmacologic prophylaxis alone, including six in general or abdominal surgery[36-41] and four in orthopedics.[42-45] Background (pharmacologic) prophylaxis included LDUH in five studies, dextran in three studies, LMWH in one study, and aspirin in one study. Many of the studies were limited by small samples, incomplete blinding, uncertain concealment of the allocation sequence, and measurement of surrogate outcomes (Table S4). Pooling the results of these studies, we found that the addition of ES resulted in a 60% reduction in DVT (including asymptomatic and distal DVT) and a 72% reduction in proximal DVT, but a difference in the risk of PE was neither confirmed nor excluded (OR, 0.43; 95% CI, 0.16-1.18) (Figs S24-S27).

Five studies compared IPC plus pharmacologic prophylaxis with pharmacologic prophylaxis alone, including four studies in orthopedics and one study in general surgery.[46-50] Background prophylaxis included LMWH (two studies), LDUH (one study), dextran (one study), and aspirin (one study). Once again, most studies were limited by small samples, incomplete blinding, unclear concealment of the allocation sequence, and measurement of surrogate outcomes. Pooled results across all five studies revealed a possible reduction in symptomatic or asymptomatic DVT (OR, 0.45; 95% CI, 0.20-1.03), but differences in proximal DVT or PE were neither confirmed nor excluded (Figs S24-S27).

For studies of both ES and IPC, reductions in symptomatic or asymptomatic DVT were similar across subgroups defined by surgical population (general and abdominal vs orthopedic), background agent used for pharmacoprophylaxis, whether the allocation sequence was adequately concealed, and whether there was blinded assessment of outcomes. Reductions in symptomatic or asymptomatic DVT differed depending on the test or tests used to identify and confirm DVT, with greater magnitudes of benefit observed in studies that used ultrasound (with or without confirmatory venography) or fibrinogen uptake with confirmatory venography than in those that used fibrinogen uptake or venography alone (Figs S28-S47).

2.12 IVC Filter vs No IVC Filter

The highest-quality evidence regarding the effectiveness of IVC filters is indirect, coming from a randomized controlled trial that compared IVC filter placement to no filter placement in patients with objectively confirmed, symptomatic, proximal DVT. In this study, filter placement was associated with a 78% reduction in the odds of symptomatic or asymptomatic PE at day 12, but after 2 years, there was an 87% increase in the odds of DVT, and a difference in PE was neither confirmed nor excluded.[51] After 8 years of follow-up, a 9% absolute reduction in the risk of PE was offset by a 10% absolute increase in the risk of DVT.[52]

More direct, but lower-quality evidence comes from a large, prospective cohort study that used propensity scoring methods to compare VTE outcomes among bariatric surgery patients with and without IVC filters.[53] Before propensity adjustment, patients with IVC filters had higher rates of postoperative VTE and death or serious disability. Following propensity adjustment, the difference in postoperative VTE was no longer statistically significant, but the risk of death or serious disability remained 2.5 times higher in the filter group.

A systematic review of seven nonrandomized studies in trauma reported that the pooled odds of PE were 79% lower (OR, 0.21; 95% CI, 0.09-0.49) among patients who received an IVC filter compared with historical control subjects who were variably matched for type of injury, age, sex, injury severity, and VTE risk.[54] A previous systematic review of 16 case series reported the following pooled risks after IVC filter placement: PE, 0.6%; DVT, 9.3%; insertion site thrombosis, 2%; IVC occlusion or thrombosis, 1.6%; placement complications, 1.4%; and filter migration, 0.4%.[55] Thus, although placement of an IVC filter probably reduces the risk of PE over the short term, complications appear to be frequent, and long-term benefits are unclear. Although retrievable filters have the potential to reduce long-term complications, they often are not removed.

2.13 VCU vs No VCU

Most studies of surveillance VCU have been performed in trauma patients. These patients often have contraindications to pharmacologic and mechanical prophylaxis, and the risk of VTE may be high even when prophylaxis is used.[56-59] However, it is not clear that using VCU to detect and treat asymptomatic DVT reduces the risk of PE or fatal PE. Some studies have demonstrated that PE can occur even when VCU is negative.[60,61] A large retrospective study from a single center reported that over a 6-year period ending in 2000, the frequency of surveillance VCU decreased from 32% to 3.4%, with no increase in the incidence of PE.[61] Furthermore, compared with venography, >50% of the apparently positive findings on surveillance VCU may be false positives,[30] and the potential risks associated with treating false-positive findings are substantial.

2.14 Economic Evaluations of Interventions for Thromboprophylaxis

At least seven studies have examined economic outcomes associated with thromboprophylaxis in nonorthopedic surgical patients (Tables S5, S6). Most used a decision analysis approach and assumed a societal perspective in which all costs were considered. None of the results met prespecified criteria for upgrading or downgrading recommendations on the basis of resource use considerations.[3]

One study compared ES, IPC, LDUH, and no prophylaxis. Compared with no prophylaxis, ES saved 28 lives and reduced costs by $335,000 per 10,000 patients treated. Compared with ES, IPC saved six additional lives and cost an additional $413,000 per 10,000 patients treated, whereas LDUH saved seven additional lives and cost an additional $568,000 per 10,000 patients treated.[62]

Four studies compared LMWH with LDUH in different surgical populations (colorectal, general, gynecologic, and abdominal surgery) within different health-care systems (Ontario, Canada; Germany; US Medicare).[63-66] In two of these studies,[63,65] total costs associated with LMWH treatment were marginally higher than those for LDUH. In contrast, in a study of general surgical patients in Germany,[64] LMWH was more effective than LDUH by 0.01 quality-adjusted life years (QALYs) and was less expensive by $160 per patient treated. In another study in abdominal surgery patients that used Medicare reimbursement as a proxy for costs,[66] LMWH prophylaxis with dalteparin 5,000 units/d cost $21,800 per QALY gained relative to LDUH. One study compared LMWH plus IPC with IPC alone in gynecologic surgery patients and found that LMWH plus IPC cost between $7,200 and $20,000 per QALY gained.[67] Finally, one study compared enoxaparin and fondaparinux and reported that total hospital charges were higher for patients treated with enoxaparin.[68]

3.0 Risk Stratification, Rationale for Prophylaxis, and Recommendations in General, Abdominal-Pelvic, Bariatric, Vascular, and Plastic and Reconstructive Surgery

We divide the remainder of the article into sections based on surgical specialty and body region. We discuss relevant information about risk factors and risk stratification for thrombosis and bleeding, provide recommendations, and explain their rationale. Additional details are provided in the Appendix S1 and Tables S7 and S8.

3.1 Target Population: General and Abdominal-Pelvic Surgery, Including GI Surgery, Gynecologic Surgery, and Urological Surgery

This section covers general and abdominal-pelvic surgery. This group includes patients undergoing GI, urological, and gynecologic surgery as well as other general surgery patients (including those having operations on the breast and thyroid and parathyroid glands).

3.1.1 Baseline Risk, Risk Factors, and Risk Stratification for VTE: In patients undergoing general and abdominal-pelvic surgery, the risk of VTE varies depending on both patient-specific and procedure-specific factors. Examples of relatively low-risk procedures include laparoscopic cholecystectomy, appendectomy, transurethral prostatectomy, inguinal herniorrhaphy, and unilateral or bilateral mastectomy.[69-76] Open-abdominal and open-pelvic procedures are associated with a higher risk of VTE.[75,77] VTE risk appears to be highest for patients undergoing abdominal or pelvic surgery for cancer.[71,75,78,79] A comprehensive list of population-based, procedure-specific estimates of the 91-day risk of clinically diagnosed VTE has been compiled from the California Patient Discharge Data Set.[76]

Patient-specific factors also determine the risk of VTE, as demonstrated in several relatively large studies of VTE in mixed surgical populations. Independent risk factors in these studies include age >60 years, prior VTE, and cancer[80]; age ≥60 years, prior VTE, anesthesia ≥2 h, and bed rest ≥4 days[78]; older age, male sex, longer length of hospital stay, and higher Charlson comorbidity score[34]; and sepsis, pregnancy or postpartum state, central venous access, malignancy, prior VTE, and inpatient hospital stay >2 days.[81] In another study, most of the moderate to strong

independent risk factors for VTE were surgical complications, including urinary tract infection, acute renal insufficiency, postoperative transfusion, perioperative myocardial infarction, and pneumonia.[77]

Risk stratification for VTE is challenging but essential and requires consideration of both patient- and procedure-specific risk factors. Although several models for risk stratification exist, all have important limitations. In the absence of rigorously developed and extensively validated risk assessment models, clinicians should consider the following options as a guide for decision making that should be adapted to individual patient circumstances. Table 5 summarizes the findings of two risk assessment models in three different surgical populations and provides rough estimates for the baseline risk of VTE (in the absence of prophylaxis) in very-low-, low-, moderate-, and high-risk patients.

One rigorously developed model used data from 183,069 patients in the Patient Safety in Surgery Study who underwent general, vascular, and thoracic procedures at one of 128 Veterans Administration medical centers or 14 private sector hospitals between 2002 and 2004.[82] This model assigned points (the Rogers score) to variables that were found to be independent predictors of VTE risk, including type of operation, work relative value units, patient characteristics, and laboratory values (Table 6). Using this model, the risk of symptomatic VTE varied from very low (0.1%) to low (~0.5%) to moderate (~1.5%) in both development and validation samples (Table 5). Unfortunately, this model is somewhat cumbersome to use and has not been externally validated. In addition, information was not provided about how many patients received prophylaxis. It is likely that at least some patients received mechanical prophylaxis, pharmacologic prophylaxis, or both, which may help to explain the relatively low observed risk of VTE.

Another model (the Caprini score) estimates VTE risk by adding points for various VTE risk factors, as shown in Table 7.[83,84] In our adaptation of this model, VTE risk is categorized as being very low (0-1 point), low (2 points), moderate (3-4 points), or high (≥5 points). Although this model was not developed using rigorous statistical methods, and includes some variables that were later found not to be associated with VTE risk,[81] it is relatively easy to use and appears to discriminate reasonably well among patients at low, moderate, and high risk for VTE.

The Caprini score was validated in a large retrospective study in a sample of general, vascular, and urological surgery patients.[81] This study included a representative sample of surgical patients, avoided exclusions, minimized losses to follow-up and was therefore judged to have a low risk of bias. In addition, the investigators collected information about prophylaxis received, which enabled us to adjust for this and estimate what the baseline risk of VTE would have been in the absence of prophylaxis (Table 5). The Caprini score has also been validated in a sample of plastic and reconstructive surgery patients.[4] Although neither the Caprini score nor the Rogers score has yet been validated specifically in gynecologic surgery patients, we believe that these patients are sufficiently similar to other abdominal and pelvic surgery patients to permit generalization.

To derive estimates of the baseline risk of VTE across risk groups, we used the observed risks of VTE reported in the validation study by Bahl et al[81] and adjusted for prophylaxis received. As shown in Table 5, the estimated baseline risks of VTE were < 0.5%, 1.5%, 3.0%, and 6.0% in patients at very low, low, moderate, and high risk for VTE, respectively (after adjusting for prophylaxis received). To estimate the baseline risk of fatal PE, we assumed that the ratio of fatal PE to nonfatal PE was ~20%[9] and further assumed that this ratio did not vary across low-, moderate-, and high-VTE risk categories.

3.1.2 Baseline Risk, Risk Factors, and Risk Stratification for Major Bleeding Complications: Relatively little research has attempted to identify risk factors for thromboprophylaxis-related bleeding in general or abdominal-pelvic surgery, although a few studies have identified risk factors in patients undergoing gastric cancer surgery,[85] pancreaticoduodenectomy,[86] partial hepatic resection,[87] and mixed abdominal surgery (Table 8).[88]

In the absence of data from large, prospective, population-based observational studies, the baseline risk of bleeding can be derived from the control (placebo or no pharmacologic prophylaxis) groups in randomized trials. However, most randomized controlled trials of pharmacoprophylaxis exclude patients who are believed to be at increased risk for bleeding. With that limitation in mind, we estimated the average baseline risk of major bleeding in the absence of prophylaxis by using the pooled risk from the control groups in seven randomized trials of LMWH as reported in a meta-analysis.[13] In our reanalysis of these data, the pooled (random effects) risk of major bleeding in the control groups was 1.2% (95% CI, 0.9%-1.7%). Another meta-analysis reported that the mean risk of wound hematoma and bleeding requiring reoperation in the control groups of randomized trials of thromboprophyaxis with LDUH or LMWH were 0.8% and 0.7%, respectively.[95] When making trade-offs between benefits and harms of pharmacologic prophylaxis, we estimated that the baseline risk of major bleeding is 1.8 times greater in high-risk patients based on data from Cohen et al.[96]

Table 5—*Risk Stratification for VTE in General, Abdominal-Pelvic, Bariatric, Vascular, and Plastic and Reconstructive Surgery*

	Patient Population							
	Patients Undergoing Major General, Thoracic, or Vascular Surgery		Patients Undergoing General Surgery, Including GI, Urological, Vascular, Breast, and Thyroid Procedures		Patients Undergoing Plastic and Reconstructive Surgery			
AT9 VTE Risk Category	Rogers Score	Observed Risk of Symptomatic VTE, %	Caprini Score	Observed Risk of Symptomatic VTE, %	Caprini Score	Observed Risk of VTE, %	Other Surgical Populations in Risk Category	Estimated Baseline Risk in the Absence of Pharmacologic or Mechanical Prophylaxis, %
Very low	< 7	0.1	0	0	0-2	NA	Most outpatient or same-day surgery	< 0.5
Low	7-10	0.4	1-2	0.7	3-4	0.6	Spinal surgery for nonmalignant disease	1.5
Moderate	> 10	1.5	3-4	1.0	5-6	1.3	Gynecologic noncancer surgery Cardiac surgery Most thoracic surgery Spinal surgery for malignant disease	3.0
High	NA	NA	≥ 5	1.9	7-8	2.7	Bariatric surgery Gynecologic cancer surgery Pneumonectomy Craniotomy Traumatic brain injury Spinal cord injury Other major trauma	6.0

AT9 = Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines.

Table 6—*Risk Assessment Model From the Patient Safety in Surgery Study*

Risk Factor	Risk Score Points
Operation type other than endocrine	
Respiratory and hernic	9
Thoracoabdominal aneurysm, embolectomy/thrombectomy, venous reconstruction, and endovascular repair	7
Aneurysm	4
Mouth, palate	4
Stomach, intestines	4
Integument	3
Hernia	2
ASA physical status classification	
3, 4, or 5	2
2	1
Female sex	1
Work RVU	
> 17	3
10-17	2
Two points for each of these conditions	2
Disseminated cancer	
Chemotherapy for malignancy within 30 d of operation	
Preoperative serum sodium > 145 mmol/L	
Transfusion > 4 units packed RBCs in 72 h before operation	
Ventilator dependant	
One point for each of the conditions	1
Wound class (clean/contaminated)	
Preoperative hematocrit level ≤ 38%	
Preoperative bilirubin level > 1.0 mg/dL	
Dyspnea	
Albumin level ≤ 3.5 mg/dL	
Emergency	
Zero points for each of these conditions	0
ASA physical status class 1	
Work RVU < 10	
Male sex	

ASA = American Society of Anesthesiologists; RVU = relative value unit. Republished with permission from Rogers et al.[82]

3.2 *Target Population: Bariatric Surgery*

Despite the explosion in the number of bariatric surgical procedures over the past 2 decades, few randomized controlled trials have evaluated interventions for VTE prophylaxis in these patients. Low-quality evidence comes from a number of uncontrolled and nonrandomized controlled studies (Table S9). We elected to apply higher-quality evidence about relative risks from randomized controlled trials in patients undergoing abdominal and pelvic surgery (section 3.1.2) when making recommendations for bariatric surgery patients, most of whom are at high risk for VTE.

3.2.1 Baseline Risk, Risk Factors, and Risk Stratification for VTE and Major Bleeding Complications: Obesity and perioperative stasis and hypercoagulability place most bariatric surgery patients at high risk for VTE. A systematic review of 37 studies of varying design concluded that obesity is a risk factor for VTE in both medical and bariatric surgical patients.[89] Across 11 studies of bariatric surgery patients, the median incidence of symptomatic VTE and fatal PE were 2.4% and 0.3%, respectively. In most studies, patients received some form of prophylaxis, most often a combination of mechanical and pharmacologic methods, so the baseline risk is almost certainly higher. In the International Bariatric Surgery Registry, PE was the most common cause of postoperative death, accounting for 30% of all mortal events.[97] Reported risk factors for postoperative VTE following bariatric surgery include higher BMI,[97-104] older age,[53,105,106] male sex,[98,103,104] obstructive sleep apnea or obesity hypoventilation syndrome,[98,102,103,107] and a history of VTE.[100,102,103,108] Although these characteristics may help to identify bariatric surgery patients who are at especially high risk, virtually all bariatric surgery patients will have a Caprini score of at least 4 and, therefore, be at least at moderate risk for VTE, and many will have an even higher score that places them in the high-risk category. Although we did not identify studies that specifically addressed the risk of bleeding complications following bariatric surgery, we provide a list of potential risk factors as a guide (Table 8).

3.3 *Target Population: Vascular Surgery*

Eight small randomized controlled trials of thromboprophylaxis have been performed in vascular surgery (Tables S2, S3).[109-116] Most enrolled patients undergoing diverse vascular procedures, but two studied patients undergoing aortic surgery,[109,115] and one enrolled patients undergoing lower-extremity amputation.[116] Three studies compared LDUH (with or without IPC) to no prophylaxis, one compared aspirin to no prophylaxis, and three compared LDUH to LMWH. One study compared LDUH, LDUH plus ergotamine, and dextran.[112] Studies were limited by small samples, incomplete blinding, unclear concealment of treatment allocation, and inconclusive results (Figs S48-S51). Because of these limitations, we apply more-precise estimates of relative risk from higher-quality studies in general and abdominal-pelvic surgery when making recommendations for vascular surgery patients.

3.3.1 Baseline Risk, Risk Factors, and Risk Stratification for VTE: In vascular surgery, inflammation, stasis, and hypercoagulability are at least partially mitigated by intraoperative anticoagulation and early postoperative mobilization. Other unique considerations include a relative contraindication to mechanical prophylaxis in some vascular patients who undergo lower-limb bypass procedures. Although numerous observational studies have examined VTE risk in

Table 7—*Caprini Risk Assessment Model*

1 Point	2 Points	3 Points	5 Points
Age 41-60 y	Age 61-74 y	Age ≥ 75 y	Stroke (< 1 mo)
Minor surgery	Arthroscopic surgery	History of VTE	Elective arthroplasty
BMI > 25 kg/m^2	Major open surgery (> 45 min)	Family history of VTE	Hip, pelvis, or leg fracture
Swollen legs	Laparoscopic surgery (> 45 min)	Factor V Leiden	Acute spinal cord injury (< 1 mo)
Varicose veins	Malignancy	Prothrombin 20210A	
Pregnancy or postpartum	Confined to bed (> 72 h)	Lupus anticoagulant	
History of unexplained or recurrent spontaneous abortion	Immobilizing plaster cast	Anticardiolipin antibodies	
Oral contraceptives or hormone replacement	Central venous access	Elevated serum homocysteine	
Sepsis (< 1 mo)		Heparin-induced thrombocytopenia	
Serious lung disease, including pneumonia (< 1 mo)		Other congenital or acquired thrombophilia	
Abnormal pulmonary function			
Acute myocardial infarction			
Congestive heart failure (< 1 mo)			
History of inflammatory bowel disease			
Medical patient at bed rest			

vascular surgery patients (Appendix S1), most were limited by small samples, incomplete information about use of prophylaxis, and measurement of surrogate outcomes (asymptomatic DVT).

Data from the British Million Women Study showed that the risk of symptomatic VTE in the 12 weeks following inpatient surgery is almost as high in vascular surgery patients (one in 115) as it is in those who have surgery for cancer (one in 85).[33] Another study that used data from the California Discharge Data Set reported that the risk of symptomatic VTE within 91 days of vascular surgery was ~1.7% for all the following vascular procedures: peripheral vascular shunt or bypass, resection and replacement of abdominal aorta, above-knee amputation, aortoilliofemoral bypass or femoral-popliteal aneurysm resection with graft, and ligation and stripping of varicose veins.[75] The risk was slightly lower for patients who underwent below-knee amputation and arteriovenous fistula placement (0.5%-0.9%), and it was lowest for carotid endarterectomy (0.2%). Use of prophylaxis was not described in either of these studies, so the risk of symptomatic VTE in the absence of prophylaxis is likely to be higher.

Risk factors for VTE in vascular surgery are not well established, although several studies have attempted to identify risk factors in this population, with little success.[117-119] However, vascular surgery patients comprised 16% of the retrospective cohort in a validation study of the Caprini model (V. Bahl, DMD, MPP, personal communication, November 29, 2010). Likewise, vascular patients comprised 18% of the sample in the Patient Safety in Surgery Study,[82] supporting the generalizability of both models to vascular surgery patients.

3.3.2 Baseline Risk, Risk Factors, and Risk Stratification for Major Bleeding Complications: Few studies have examined the risk of bleeding in vascular surgery. Across three randomized trials of thromboprophylaxis,[109,111,115] the pooled weighted risk of major bleeding in the control (no prophylaxis) groups was 0.3% (95% CI, 0.2%-2.4%). However, an observational study reported that the incidence of life-threatening hemorrhage among 973 patients undergoing complex major vascular procedures was 1.8%, with most episodes of bleeding occurring intraoperatively and only 0.4% of patients experiencing severe bleeding postoperatively.[120] Because the baseline risk of bleeding is difficult to pinpoint in vascular surgery, we use the baseline risk from studies of general and abdominal-pelvic surgery (1.2%) and provide a list of risk factors as a guide (Table 8).

3.4 Target Population: Plastic and Reconstructive Surgery

Because there have been no randomized controlled trials of thromboprophylaxis in plastic and reconstructive surgery, we applied indirect evidence about relative risks from trials in general and mixed surgical patients when making recommendations.

3.4.1 Baseline Risk, Risk Factors, and Risk Stratification for VTE: A retrospective study examined the 60-day risk of postoperative VTE in 1,126 patients who were at least at moderate risk for VTE (Caprini score, 3-4) and underwent plastic and reconstructive surgery at one of five tertiary-care facilities in the United States between 2006 and 2009.[4] All patients received mechanical prophylaxis with IPC.

Table 8—*Risk Factors for Major Bleeding Complications*

General risk factors
Active bleeding
Previous major bleeding
Known, untreated bleeding disorder
Severe renal or hepatic failure
Thrombocytopenia
Acute stroke
Uncontrolled systemic hypertension
Lumbar puncture, epidural, or spinal anesthesia within previous 4 h or next 12 h
Concomitant use of anticoagulants, antiplatelet therapy, or thrombolytic drugs
Procedure-specific risk factors
Abdominal surgery
Male sex, preoperative hemoglobin level < 13 g/dL, malignancy, and complex surgery defined as two or more procedures, difficult dissection, or more than one anastamosis[89]
Pancreaticoduodenectomy
Sepsis, pancreatic leak, sentinel bleed[87]
Hepatic resection
Number of segments, concomitant extrahepatic organ resection, primary liver malignancy, lower preoperative hemoglobin level, and platelet counts[88]
Cardiac surgery
Use of aspirin[90]
Use of clopidogrel within 3 d before surgery[91]
BMI > 25 kg/m^2, nonelective surgery, placement of five or more grafts, older age[92]
Older age, renal insufficiency, operation other than CABG, longer bypass time[93]
Thoracic surgery
Pneumonectomy or extended resection[94]
Procedures in which bleeding complications may have especially severe consequences
Craniotomy
Spinal surgery
Spinal trauma
Reconstructive procedures involving free flap

CABG = coronary artery bypass graft.

The observed risks of symptomatic VTE, stratified by Caprini score, were 0.6% among those with a score of 3 to 4, 1.3% among those with a score of 5 to 6, 2.7% among those with a score of 7 to 8, and 11.3% among those with a score > 8 (Table 5). Of note, these scores in plastic and reconstructive surgery patients correspond to lower risks of VTE than would be expected in patients undergoing general or abdominal-pelvic surgery.

3.4.2 Baseline Risk, Risk Factors, and Risk Stratification for Major Bleeding Complications: Across three observational studies of patients who underwent plastic and reconstructive procedures, the baseline risk of wound hematoma (in the absence of pharmacologic prophylaxis) ranged from 0.5% to 1.8%.[121-123] Based on this limited evidence, we consider most plastic and reconstructive surgery patients to be at average risk for bleeding complications, recognizing that the consequences of wound hematoma in patients with free flaps can be dire.

3.5 Explanation of Evidence Profiles and Rationale for Recommendations

We believe that the risk stratification scheme described in Table 5 is appropriate for use in general, GI, urological, gynecologic, bariatric, and vascular surgery patients. In addition, the Caprini score can be used in plastic and reconstructive surgery patients, although the baseline risk of VTE appears to be lower among these patients with any given Caprini score (Table 5). For example, although a Caprini score of 3 to 4 is associated with a moderate risk of VTE (~3.0%) in general or abdominal-pelvic surgery, this same score is associated with a low risk of VTE (~1.5%) in plastic and reconstructive surgery.

Information presented in the Table 8 can be used as a guide to help to identify patients in whom the risk of bleeding is high or the consequences of bleeding are especially severe. Statements about the quality of evidence refer to recommendations for patients undergoing general or abdominal-pelvic surgery. Because of indirectness, the quality of evidence should be rated down in other surgical populations.

Among patients with a very low risk of symptomatic VTE (< 0.5%), there is moderate-quality evidence that the harms of pharmacologic prophylaxis with LDUH or LMWH outweigh the benefits. Compared with no prophylaxis, one can expect zero to three fewer nonfatal VTE events and four to 10 more nonfatal major bleeding complications per 1,000 patients treated with LDUH. Trade-offs are similar for LMWH and no prophylaxis. There is low-quality evidence that compared with no prophylaxis, mechanical prophylaxis with IPC or ES can also be expected to prevent zero to three nonfatal VTE events at the expense of inconvenience, cost, and an uncertain number of skin complications, including breaks, blisters, ulcers, and necrosis, suggesting that the harms of mechanical prophylaxis probably outweigh the benefits in this very-low-risk group.

Among patients with a low risk of VTE (~1.5%), moderate-quality evidence suggests that, compared with no prophylaxis, pharmacologic prophylaxis with either LDUH (Table 9) or LMWH (Table 10) can be expected to result in similar numbers of nonfatal VTE events prevented and nonfatal major bleeding events caused, and there is no important reduction in fatal PE. Low-quality evidence suggests that mechanical prophylaxis with either IPC (Table 11) or ES (Table 12) can be expected to prevent about eight to 10 nonfatal VTE events per 1,000 patients treated at the expense of an uncertain number of skin complications. Although direct high-quality evidence

Table 9—*Summary of Findings: Unfractionated Heparin Compared With No Prophylaxis for VTE Prevention in Surgical Patients*

Patient or population: patients with VTE, prevention in surgical patients
Settings: hospital
Intervention: unfractionated heparin
Comparison: no prophylaxis

Outcomes	Illustrative Comparative Risks[a] (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Quality of the Evidence (GRADE)
	Assumed Risk No Prophylaxis	Corresponding Risk Unfractionated Heparin			
Fatal PE (autopsy)	Low-risk population[b]		OR 0.53 (0.31-0.91)	13,492 (20 studies[c])	High[d]
	3 per 1,000	2 per 1,000 (1-3)			
	Medium-risk population[b]				
	6 per 1,000	3 per 1,000 (2-5)			
	High-risk population[b]				
	12 per 1,000	6 per 1,000 (4-11)			
Fatal bleeding (autopsy)	Study population[e]		OR 1.14 (0.41-3.15)	13,280 (7 studies[c])	Moderate[f]
	1 per 1,000	1 per 1,000 (0-3)			
	Low-risk population[e]				
	1 per 1,000	1 per 1,000 (0-3)			
	Medium-risk population[e]				
	2 per 1,000	2 per 1,000 (1-6)			
Nonfatal symptomatic VTE inferred from nonfatal PE (clinical diagnosis)	Low-risk population[g]		OR 0.44 (0.31-0.63)	12,698 (22 studies[c])	Moderate[h,i,j]
	15 per 1,000	7 per 1,000 (5-10)[k]			
	Medium-risk population[g]				
	30 per 1,000	13 per 1,000 (9-19)[k]			
	High-risk population[g]				
	60 per 1,000	27 per 1,000 (19-39)[k]			

(Continued)

Table 9—*Continued*

Patient or population: patients with VTE, prevention in surgical patients
Settings: hospital
Intervention: unfractionated heparin
Comparison: no prophylaxis

Outcomes	Illustrative Comparative Risks[a] (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Quality of the Evidence (GRADE)
	Assumed Risk No Prophylaxis	Corresponding Risk Unfractionated Heparin			
Nonfatal major bleeding inferred from excessive intraoperative bleeding or need for transfusion (clinical diagnosis)	Low-risk population[l]		OR 1.57 (1.32-1.87)	12,929 (44 studies)	Moderate[h,m]
	12 per 1,000	19 per 1,000 (16-22)[n]			
	Medium-risk population[l]				
	22 per 1,000	34 per 1,000 (29-40)[n]			

GRADE Working Group grades of evidence: high quality, further research is very unlikely to change our confidence in the estimate of effect; moderate quality, further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality, further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and very low quality, we are very uncertain about the estimate. GRADE = Grades of Recommendations, Assessment, Development, and Evaluation. See Table 1 legend for expansion of other abbreviations.

[a]The basis for the assumed risk (eg, the median control group risk across studies) is provided in the following footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

[b]Pooled risk of fatal PE was 55 of 6,683 (0.8%) in the control groups. Risk of fatal PE in low-, moderate-, and high-risk groups calculated under the assumption that the ratio of PE to fatal PE did not vary across risk categories.

[c]Relative risk estimates based on reanalysis of data reported in meta-analysis by Collins et al,[9] using a random-effects statistical model. Duration of follow-up varied, but usually to hospital discharge.

[d]Mild to moderate unexplained heterogeneity across 10 studies of general surgery; no significant heterogeneity between surgical populations or across all 20 studies.

[e]Pooled risk of fatal bleeding was six of 6,577 (0.1%) in the control groups. Risk of fatal bleeding in low- and high-risk groups calculated under the assumption that the ratio of clinically important bleeding to fatal bleeding did not vary across risk categories.

[f]Pooled effect includes possibility of both substantial benefit and serious harm.

[g]Baseline risk of VTE in moderate-, high-, and very-high-risk patients, after adjustment for prophylaxis received. Data from Bahl et al.[81] In low-risk patients, rate of symptomatic VTE was 0%.

[h]Many studies were not blinded, and allocation concealment was not adequately described.

[i]There was mild heterogeneity across surgical specialties. OR for nonfatal PE was 0.44 (95% CI, 0.31-0.63) in 22 trials of general surgery, 0.29 (95% CI, 0.03-2.24) in two trials of urological surgery and 4.66 (95% CI, 0.53-40.8) in two trials of orthopedic trauma.

[j]Relative risk of symptomatic VTE assumed to be identical to that for nonfatal PE.

[k]Overall incidence of VTE within 30 d of surgery in a large prospective study of patients undergoing general, urological, or vascular surgery (Bahl et al[81]) prior to adjustment for prophylaxis.

[l]In seven studies of LMWH vs no prophylaxis in abdominal surgery (Mismetti et al[13]), the weighted pooled (random-effects model) risk of major bleeding in the control groups was 1.2%. In 36 studies of LMWH vs unfractionated heparin in abdominal surgery, the pooled risk of major bleeding in the unfractionated heparain groups was 3.2%, including 2.7% of patients without cancer and 8.1% of patients with cancer. After adjustment for prophylaxis, the risks for noncancer and cancer surgery were 1.7% and 5.1%, respectively. In a more-recent comparison of LMWH vs fondaparinux, the risk of bleeding requiring reoperation or intervention was 1.0% in the LMWH group (Agnelli et al[20]). In a secondary analysis of RCT data (Cohen et al[90]), the odds of major bleeding were 1.8 times greater in patients with cancer.

[m]Surrogate outcome: major bleeding defined as excessive intraoperative bleeding or need for transfusion.

[n]Pooled observed risk of clinically important bleeding in unfractionated heparin groups, not adjusted for prophylaxis.

Table 10—*Summary of Findings: LMWH Compared With No Prophylaxis for VTE Prevention in Surgical Patients*

Patient or population: patients with VTE, prevention in surgical patients
Settings: hospital
Intervention: LMWH
Comparison: no prophylaxis

Outcomes	Illustrative Comparative Risks[a] (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Quality of the Evidence (GRADE)
	Assumed Risk No Prophylaxis	Corresponding Risk LMWH			
Fatal PE inferred from all-cause mortality Follow-up: 7-270 d	Low-risk population[b]		RR 0.54 (0.27-1.1)	5,142 (5 studies)	Moderate[c]
	3 per 1,000	2 per 1,000 (1-3)			
	Medium-risk population[b]				
	6 per 1,000	3 per 1,000 (2-7)			
	High-risk population[b]				
	12 per 1,000	6 per 1,000 (3-13)			
Fatal bleeding Follow-up: 21-270 d	Study population		No events reported	5,078 (4 studies)	Moderate
	See comment	See comment			
	Low-risk population				
	1 per 1,000	0 per 1,000 (0-0)			
	Medium-risk population				
	2 per 1,000	0 per 1,000 (0-0)			
Nonfatal symptomatic VTE Follow-up: 21-270 d	Low-risk population[d]		RR 0.31 (0.12-0.81)	4,890 (3 studies)	Moderate[e]
	15 per 1,000	5 per 1,000 (2-12)			
	Medium-risk population[d]				
	30 per 1000	9 per 1000 (4-24)			
	High-risk population[d]				
	60 per 1,000	19 per 1,000 (7-49)			
Nonfatal major bleeding (clinical diagnosis) Follow-up: 7-270 d	Low-risk population[f]		RR 2.03 (1.37-3.01)	5,457 (7 studies)	High[g]
	12 per 1,000	24 per 1,000 (16 to 36)			
	Medium-risk population[f]				
	22 per 1,000	45 per 1,000 (30 to 66)			

GRADE Working Group grades of evidence: high quality, further research is very unlikely to change our confidence in the estimate of effect; moderate quality, further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality, further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and very low quality, we are very uncertain about the estimate. RR = risk ratio. See Table 1 and 9 legends for expansion of other abbreviations.

[a]The basis for the assumed risk (eg, the median control group risk across studies) is provided in the following footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

[b]Pooled risk of death from any cause was 24 of 2,589 (0.9%) in the control groups. Risk of fatal PE in low-, moderate-, and high-VTE risk groups was calculated under the assumption that the ratio of death from any cause to symptomatic VTE did not vary across risk categories.

[c]The 95% CI includes the possibility of both no effect and substantial benefit.

[d]Baseline risk of VTE in moderate-, high-, and very-high-risk patients after adjustment for prophylaxis received. Data from Bahl et al.[81] In low-risk patients, rate of symptomatic VTE was 0%.

[e]One study was not blinded, and one study had unclear concealment of allocation sequence; nonfatal symptomatic VTE was not objectively confirmed in one large study.

[f]In seven studies of LMWH vs no prophylaxis in abdominal surgery (Mismetti et al[13]), the weighted pooled (random-effects model) risk of major bleeding in the control groups was 1.2%. In 36 studies of LMWH vs unfractionated heparin in abdominal surgery, the pooled risk of major bleeding in the unfractionated heparin groups was 3.2% but was only 2.7% in noncancer surgery and 8.1% in cancer surgery. After adjustment for prophylaxis, the risks for noncancer and cancer surgery were 1.7% and 5.1%, respectively. In a more-recent comparison of LMWH vs fondaparinux, the risk of bleeding requiring reoperation or intervention was 1.0% in the LMWH group. In a secondary analysis of RCT data (Cohen et al[90]), the odds of major bleeding were 1.8 times greater in patients with cancer.

[g]Variable definition of major bleeding across studies.

Table 11—*Summary of Findings: IPC Compared With No Prophylaxis for VTE Prevention in Surgical Patients*

Patient or population: patients with VTE, prevention in surgical patients
Settings: hospital
Intervention: IPC
Comparison: no prophylaxis

Outcomes	Illustrative Comparative Risks[a] (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Quality of the Evidence (GRADE)
	Assumed Risk No Prophylaxis	Corresponding Risk IPC			
Symptomatic VTE, inferred from proximal DVT (FUT ± IPG ± venography or DUS + venography)	Low-risk population		OR 0.48 (0.22-0.74)	1,534 (9 studies)	Low
	15 per 1,000	7 per 1,000 (3-11)			
	Medium-risk population				
	30 per 1,000	15 per 1,000 (7-22)			
	High-risk population				
	60 per 1,000	30 per 1,000 (14-45)			
Skin breaks, blisters, ulcers, necrosis	No evidence				

GRADE Working Group grades of evidence: high quality, further research is very unlikely to change our confidence in the estimate of effect; moderate quality, further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality, further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and very low quality, we are very uncertain about the estimate. DUS = Doppler ultrasound; FUT = fibrinogen uptake test; IPG = impedence plethysmography. See Table 1 and 9 legends for expansion of other abbreviations.
[a]The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

is lacking, we favor IPC over ES primarily on basis of indirect evidence from the Clots in Legs or Stockings after Stroke (CLOTS1) trial in patients with stroke that ES increased the risk of skin complications without reducing the risk of VTE.[26] Low-quality evidence favors mechanical prophylaxis over pharmacologic prophylaxis with either LMWH (Table 13) or LDUH (Table 14) in this group of patients.

Among patients with a moderate risk of VTE (~3.0%) who are not at high risk for major bleeding complications, moderate-quality evidence indicates that compared with no prophylaxis, pharmacologic prophylaxis with either LDUH (Table 9) or LMWH (Table 10) will result in approximately twice as many nonfatal VTE events prevented as nonfatal major bleeding events caused. In addition, one can expect zero to three fewer deaths from PE per 1,000 patients treated. Low-quality evidence suggests that mechanical prophylaxis with either IPC (Table 11) or ES (Table 12) can be expected to prevent 13 to 17 nonfatal VTE events per 1,000 patients treated at the expense of an uncertain number of skin complications. Although low-quality evidence for the direct comparisons between mechanical prophylaxis and LMWH (Table 13) or LDUH (Table 14) seems to favor mechanical prophylaxis in this group of patients, three of the seven authors of this article placed more value on the higher-quality evidence favoring pharmacologic prophylaxis and, therefore, preferred pharmacologic prophylaxis over mechanical prophylaxis in this group. There is moderate-quality evidence that LMWH is at least as safe and effective as LDUH (Table 15).

Among patients with a moderate risk of VTE (~3.0%) who are at high risk for major bleeding complications, moderate-quality evidence indicates that compared with no prophylaxis, pharmacologic prophylaxis with either LDUH (Table 9) or LMWH (Table 10) can be expected to result in similar numbers of nonfatal bleeding events caused and nonfatal VTE events averted. Although the quality of the evidence is low, the balance between desirable and undesirable outcomes appears to be more favorable with mechanical prophylaxis (Tables 11, 12), particularly IPC, which is expected to result in seven to 20 fewer nonfatal VTE events per 1,000 patients at the expense of an uncertain number of skin complications.

Among patients who are at high risk for VTE (~6.0%) but not at high risk for major bleeding complications, there is high-quality evidence that compared with no prophylaxis, LDUH will result in one to eight fewer deaths from PE (Table 9), and there is moderate-quality evidence that LMWH prophylaxis may result in six fewer (95% CI, nine fewer to one more) deaths from PE (Table 10). In addition, there

Table 12—*Summary of Findings: ES Compared With No Prophylaxis for VTE Prevention in Surgical Patients*

Patient or population: for VTE prevention in surgical patients
Settings: hospital
Intervention: ES
Comparison: no prophylaxis

Outcomes	Illustrative Comparative Risks[a] (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Quality of the Evidence (GRADE)
	Assumed Risk No Prophylaxis	Corresponding Risk ES			
Symptomatic VTE inferred from distal or proximal DVT (venography or FUT or IPG ± venography) Follow-up: usually to hospital discharge[b]	Low-risk population[c]		OR 0.35 (0.26-0.47)[d]	1,239 (8 studies[e,f])	Low[g,h]
	15 per 1,000	5 per 1,000 (4-7)[i]			
	Medium-risk population[c]				
	30 per 1,000	11 per 1,000 (8-14)[i]			
	High-risk population[c]				
	60 per 1,000	22 per 1,000 (16-29)[i]			
Skin breaks, blisters, ulcers, necrosis case note review Follow-up: 1-30 d	13 per 1,000	52 per 1,000 (31-87)	OR 4.18 (2.4-7.27)	2,518 (1 study)	Low[j,k]

GRADE Working Group grades of evidence: high quality, further research is very unlikely to change our confidence in the estimate of effect; moderate quality, further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality, further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and very low quality, we are very uncertain about the estimate. See Table 1, 3, 9, and 11 legends for expansion of abbreviations.

[a]The basis for the assumed risk (eg, the median control group risk across studies) is provided in the following footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

[b]Duration of follow-up varied, but usually to hospital discharge.

[c]Baseline risk of VTE in moderate-, high-, and very-high-risk patients after adjustment for prophylaxis received. Data from large, retrospective, observational study by Bahl et al.[81] In low-risk patients, rate of symptomatic VTE was 0%.

[d]The OR for PE (one study) was 0.13 (95% CI, 0-6.7). In a separate meta-analysis by Roderick et al,[24] the pooled OR for proximal DVT was 0.36 (95% CI, 0-1.30).

[e]Data for other critical outcomes (eg, fatal PE) not available; bleeding complications not relevant.

[f]Meta-analysis by Sachdeva et al[27] included eight studies of ES in mixed surgical populations.

[g]Unblinded assessment of outcomes and unclear concealment of allocation sequence in many studies.

[h]Relative risk of symptomatic VTE inferred from surrogate outcome (proximal or distal DVT).

[i]Pooled observed risk of proximal or distal DVT in ES groups across eight studies.

[j]Unblinded ascertainment based on case note review.

[k]Based on data from the CLOTS1 study in patients with stroke.

Table 13—*Summary of Findings: Mechanical Prophylaxis Compared With LMWH for VTE Prevention in Surgical Patients*

Patient or population: patients with VTE, prevention in surgical patients
Settings: hospital
Intervention: mechanical prophylaxis
Comparison: LMWH

Outcomes	Illustrative Comparative Risks[a] (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Quality of the Evidence (GRADE)
	Assumed Risk LMWH	Corresponding Risk Mechanical Prophylaxis			
Symptomatic VTE inferred from proximal or distal DVT	Low-risk population		RR 1.80 (1.16-2.79)	3,134 (8 studies[c])	Low
	5 per 1,000	9 per 1,000 (6-14)[b]			
	Medium-risk population				
	9 per 1,000	16 per 1,000 (10-25)[b]			
	High-risk population				
	19 per 1,000	34 per 1,000 (22-53)[b]			
Major bleeding	Low-risk population[d]		RR 0.51 (0.4-0.64)	5,457 (7 studies)	High
	24 per 1,000	12 per 1,000 (10-15)			
	Medium-risk population[d]				
	45 per 1,000	23 per 1,000 (18-29)			
Skin breaks, ulcers, blisters, necrosis	51 per 1,000	13 per 1,000 (7-22)	RR 0.25 (0.14-0.43)	2,518 (1 study)	Low[e,f]

GRADE Working Group grades of evidence: high quality, further research is very unlikely to change our confidence in the estimate of effect; moderate quality, further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality, further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and very low quality, we are very uncertain about the estimate. See Table 1, 3, 9, and 10 legends for expansion of abbreviations.

[a]The basis for the assumed risk (eg, the median control group risk across studies) is provided in the following footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

[b]Numbers of events in control group were not reported. Estimated number at risk, assuming equal numbers in intervention and control groups.

[c]Data for other critical outcomes (eg, fatal PE) were not available.

[d]Baseline risk of bleeding estimated from control groups in trials of LMWH vs no prophylaxis adjusted to reflect use of LMWH in all patients.

[e]Unblinded assessment based on case note review.

[f]Data from CLOTS1 study in patients with stroke; applies specifically to prophylaxis with graduated compression stockings and not IPC.

Table 14—*Summary of Findings: Mechanical Prophylaxis Compared With Unfractionated Heparin for VTE Prevention in Surgical Patients*

Patient or population: patients with VTE, prevention in surgical patients
Intervention: mechanical prophylaxis
Comparison: unfractionated heparin

Outcomes	Illustrative Comparative Risks[a] (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Quality of the Evidence (GRADE)
	Assumed Risk Unfractionated Heparin	Corresponding Risk Mechanical Prophylaxis			
Symptomatic VTE inferred from any DVT Follow-up: variable	Low-risk population[b]		RR 0.71 (0.42-1.19)[c]	1,269 (8 studies[d])	Low[e]
	7 per 1,000	5 per 1,000 (3-8)[f]			
	Medium-risk population[b]				
	13 per 1,000	9 per 1,000 (5-15)[f]			
	High-risk population[b]				
	26 per 1,000	18 per 1,000 (11-31)[f]			
Major bleeding, defined as excessive intraoperative bleeding or need for transfusion	Low-risk population[g]		OR 0.47 (0.32-0.7)	12,929 (44 studies)	Low[h,i]
	19 per 1,000	9 per 1,000 (6-13)			
	Medium-risk population[f]				
	35 per 1,000	17 per 1,000 (11-25)			
Skin breaks, ulcers, blisters, necrosis	51 per 1,000	13 per 1,000 (7-22)	RR 0.25 (0.14-0.43)	2,518 (1 study)	Low[j,k]

GRADE Working Group grades of evidence: high quality, further research is very unlikely to change our confidence in the estimate of effect; moderate quality, further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality, further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and very low quality, we are very uncertain about the estimate. See Table 1, 3, 9, and 10 legends for expansion of abbreviations.

[a]The basis for the assumed risk (eg, the median control group risk across studies) is provided in the following footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

[b]Baseline risk of VTE in moderate-, high-, and very-high-risk patients after adjustment for prophylaxis received. Data from Bahl et al.[S1] In low-risk patients, rate of symptomatic VTE was 0%.

[c]Pooled OR for PE across 15 studies was 1.03 (95% CI, 0.48-2.22). Pooled OR for any DVT for comparison of LMWH vs mechanical across eight studies was 0.71 (95% CI, 0.42-1.19), and pooled OR for any DVT for comparison of unfractionated heparin vs mechanical across eight studies was 1.80 (95% CI, 1.16-2.79).

[d]Data for other critical outcomes (eg, fatal PE) not available.

[e]95% CI includes possibility of both substantial benefit and no effect.

[f]Numbers of events in control group were not reported. Estimated number at risk, assuming equal numbers in intervention and control groups.

[g]Baseline risk of bleeding estimated from control groups in trials of LMWH vs no prophylaxis, adjusted to reflect use of unfractionated heparin in all patients.

[h]Lack of blinding, incomplete details about concealment of allocation sequence, measurement of surrogate outcome.

[i]Data from studies of general, urological, and elective orthopedic surgery and trauma (Collins et al[9]).

[j]Unblinded assessment based on case note review.

[k]Data from CLOTS1 study in stroke patients; applies specifically to prophylaxis with graduated compression stockings and not IPC.

Table 15—*Summary of Findings: LMWH Compared With LDUH for VTE Prevention in Surgical Patients*

Patient or population: patients with VTE, prevention in surgical patients
Settings: hospital
Intervention: LMWH
Comparison: LDUH

Outcomes	Illustrative Comparative Risks[a] (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Quality of the Evidence (GRADE)
	Assumed Risk LDUH	Corresponding Risk LMWH			
Fatal PE inferred from all-cause mortality	Low-risk population[b]		RR 1.04 (0.89-1.2)	41,386 (30 studies)	High
Follow-up: 7-10 d in most studies	3 per 1,000	3 per 1,000 (3-4)[c]			
	Medium-risk population[b]				
	6 per 1,000	6 per 1,000 (5-7)[c]			
	High-risk population[b]				
	12 per 1,000	12 per 1,000 (11-14)[c]			
Symptomatic VTE (objectively confirmed)	Low-risk population[d]		RR 0.71 (0.51-0.99)[e]	13,776 (23 studies)	Moderate[f]
Follow-up: 7-10 d in most studies	7 per 1,000	5 per 1,000 (4-7)[c]			
	Medium-risk population[d]				
	13 per 1,000	9 per 1,000 (7-13)[c]			
	High-risk population[d]				
	26 per 1,000	18 per 1,000 (13-26)[c]			
Major bleeding clinical diagnosis	Medium-risk population[g]		RR 0.89 (0.75-1.05)	18,555 (36 studies)	Moderate[f,h]
Follow-up: 7-10 d in most studies	19 per 1,000	17 per 1,000 (14-20)[c]			
	High-risk population[g]				
	35 per 1,000	31 per 1,000 (26-37)[c]			

GRADE Working Group grades of evidence: high quality, further research is very unlikely to change our confidence in the estimate of effect; moderate quality, further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality, further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and very low quality, we are very uncertain about the estimate. See Table 1, 9, and 10 legends for expansion of abbreviations.

[a]The basis for the assumed risk (eg, the median control group risk across studies) is provided in the following footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

[b]Pooled risk of death in unfractionated heparin groups was higher in patients with cancer (4.8% ± 0.8%) than in patients without cancer (1.5% ± 0.1%).

[c]Estimated number of events and patients at risk, assuming equal numbers of patients at risk in unfractionated heparin and LMWH groups.

[d]Baseline risk of symptomatic VTE was higher in patients with cancer (1.8%) than in patients without cancer (1.2%). High-risk estimate from Bahl et al,[81] adjusted to control for prophylaxis given.

[e]Indirect OR is 0.52 (95% CI, 0.18-1.45) based on indirect comparison of LMWH vs unfractionated heparin from studies of LMWH vs placebo and unfractionated heparin vs placebo or no prophylaxis.

[f]About one-half of studies were unblinded; allocation procedures were not described; and, most importantly, trends favoring LMWH for all outcomes disappeared when only double-blinded studies were analyzed.

[g]Baseline risk of major bleeding was higher in patients with cancer (8.1% ± 1.0%) vs patients without cancer (2.7% ± 0.2%).

[h]Definition of major bleeding varied across studies.

is moderate-quality evidence that both LDUH and LMWH will result in substantially more nonfatal VTE events prevented than nonfatal major bleeding events caused. Only low-quality evidence supports the use of mechanical prophylaxis with IPC or ES, which can be expected to result in 30 to 40 fewer nonfatal VTE events per 1,000 patients and an uncertain number of skin complications (Tables 11, 12). However, there is low-quality evidence that in this group of patients, use of mechanical prophylaxis compared with LMWH results in a similar number of major bleeding events averted and VTE events not prevented (Table 13). Nevertheless, we favor LDUH or LMWH over mechanical methods in this group because of the higher quality of evidence and the expected reductions in fatal PE.

Among patients with a high risk of VTE (~6.0%) who are at high risk for major bleeding complications, moderate-quality evidence indicates that the trade-offs still favor pharmacologic prophylaxis with either LDUH (six fewer fatal PE, 33 fewer nonfatal VTE events, and 12 more nonfatal major bleeding events per 1,000 patients) or LMWH (six fewer deaths from any cause, 41 fewer nonfatal VTE events, and 23 more nonfatal major bleeding events per 1,000 patients) over no prophylaxis (Tables 9, 10). However, as the baseline risk of major bleeding approaches 4%, the harms of pharmacologic prophylaxis begin to outweigh the benefits, suggesting that mechanical prophylaxis with IPC (Table 11) or ES (Table 13) should be chosen when the risk of bleeding is judged to be very high or the consequences of major bleeding are believed to be particularly severe.

Among high-VTE risk patients, there is low-quality evidence (Tables 16, 17) that the absolute number of nonfatal VTE events can be further reduced by the addition of either IPC (10 fewer events per 1,000) or ES (11 fewer events per 1,000) to pharmacologic prophylaxis at the expense of an uncertain number of skin complications. The additional reduction in VTE applies to lower-risk groups as well, but the absolute number of events prevented is fewer.

Among patients at high risk for VTE undergoing abdominal surgery for cancer, there is moderate-quality evidence that compared with limited-duration prophylaxis (1 week), extended-duration prophylaxis (4 weeks) with LMWH provides additional protection from nonfatal VTE (13 fewer events per 1,000), without an important increase in the risk of nonfatal major bleeding complications (Table 18). The additional reduction in VTE applies to lower-risk groups as well, but the absolute number of events prevented is smaller. In addition, the quality of evidence is lower in noncancer surgery patients and patients at lower risk for VTE because of indirectness.

Some patients who would otherwise benefit from anticoagulant prophylaxis are not eligible to receive LDUH or LMWH primarily because of heparin allergy or a history of heparin-induced thrombocytopenia. Among such patients who are at high risk for VTE but not at increased risk for perioperative bleeding complications, low-quality evidence supports the use of either fondaparinux (Table 19), low-dose aspirin (Table 20), or mechanical prophylaxis (Tables 11, 12) over no prophylaxis. Among such patients at high risk for VTE who are at high risk for major bleeding, trade-offs favor mechanical prophylaxis. Because of the very low quality of the evidence and the availability of preferable alternatives, we do not recommend the use of high-dose aspirin for VTE prevention in any group of patients (Table 21).

For patients at high risk for VTE who are not candidates for either mechanical or pharmacologic prophylaxis, very-low-quality evidence suggests that IVC filter placement will probably cause at least as many DVT events as PE events prevented and that additional serious complications may occur in as many as 5% of patients (Table 22). Likewise, it is not clear that using VCU to detect and treat asymptomatic DVT reduces the risk of PE or fatal PE in patients at high risk for VTE. Furthermore, false-positive findings are common, and the potential risks associated with treating false-positive findings are substantial.

3.6 Recommendations

The following recommendations apply to patients undergoing general surgery, GI surgery, urological surgery, gynecologic surgery, bariatric surgery, vascular surgery, and plastic and reconstructive surgery (Table 23).

3.6.1. For general and abdominal-pelvic surgery patients at very low risk for VTE (< 0.5%; Rogers score, < 7; Caprini score, 0), we recommend that no specific pharmacologic (Grade 1B) **or mechanical** (Grade 2C) **prophylaxis be used other than early ambulation.**

3.6.2. For general and abdominal-pelvic surgery patients at low risk for VTE (~1.5%; Rogers score, 7-10; Caprini score, 1-2), we suggest mechanical prophylaxis, preferably with IPC, over no prophylaxis (Grade 2C)**.**

3.6.3. For general and abdominal-pelvic surgery patients at moderate risk for VTE (~3.0%; Rogers score, > 10; Caprini score, 3-4) who are not at high risk for major bleeding complications, we suggest LMWH (Grade 2B)**, LDUH** (Grade 2B)**, or mechanical prophylaxis, preferably with IPC** (Grade 2C)**, over no prophylaxis.**

Table 16—*Summary of Findings: Combined Therapy With IPC and Pharmacologic Prophylaxis Compared With Pharmacologic Prophylaxis Alone for VTE Prevention in Surgical Patients*

Patient or population: patients with VTE, prevention in surgical patients
Settings: hospital
Intervention: combined therapy with IPC and pharmacologic prophylaxis
Comparison: pharmacologic prophylaxis alone

Outcomes	Illustrative Comparative Risks[a] (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Quality of the Evidence (GRADE)
	Assumed Risk Pharmacologic Prophylaxis Alone	Corresponding Risk Combined Therapy With IPC and Pharmacologic Prophylaxis			
Symptomatic VTE inferred from any DVT (Venography [2], ultrasound [2], and FUT [1]) Follow-up: usually to hospital discharge	Low-risk population[b]		OR 0.45 (0.2-1.03)[c]	2,429 (5 studies[d])	Very low[e,f,g]
	5 per 1,000	2 per 1,000 (1-5)			
	Medium-risk population[b]				
	9 per 1,000	4 per 1,000 (2-9)			
	High-risk population[b]				
	19 per 1,000	9 per 1,000 (4-20)			
Skin breaks, blisters, ulcers, necrosis	No evidence				

GRADE Working Group grades of evidence: high quality, further research is very unlikely to change our confidence in the estimate of effect; moderate quality, further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality, further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and very low quality, we are very uncertain about the estimate. See Table 1, 9, and 11 legends for expansion of abbreviations.

[a]The basis for the assumed risk (eg, the median control group risk across studies) is provided in the following footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

[b]Baseline risk of VTE in moderate-, high-, and very-high-risk patients was adjusted to assume that all patients received background prophylaxis with LMWH. Data from Bahl et al.[91] In low-risk patients, the rate of symptomatic VTE was 0%.

[c]Reanalysis of data from Roderick et al[24] and Kakkar et al.[18] Pooled risks of proximal DVT and PE were 1.04 (95% CI, 0.29-3.79) and 0.57 (95% CI, 0.16-2.00), respectively.

[d]Data for other critical outcomes (eg, fatal PE) not available; bleeding complications were not relevant.

[e]Unblinded assessment of VTE, unclear concealment of allocation sequence, and measurement of surrogate outcome (asymptomatic DVT).

[f]Data from studies of orthopedic surgery (four) and general surgery (one). Background agents included dextran, unfractionated heparin, LMWH, LMWH plus ES, and aspirin plus ES plus hypotensive epidural anesthesia.

[g]The 95% CI includes the possibility of both substantial benefit and no effect.

Table 17—*Summary of Findings: Combined Therapy With ES and Pharmacologic Prophylaxis Compared With Pharmacologic Prophylaxis Alone for VTE Prevention in Surgical Patients*

Patient or population: patients with VTE, prevention in surgical patients
Settings: hospital
Intervention: combined therapy with ES and pharmacologic prophylaxis
Comparison: pharmacologic prophylaxis alone

Outcomes	Illustrative Comparative Risks[a] (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Quality of the Evidence (GRADE)
	Assumed Risk Pharmacologic Prophylaxis Alone	Corresponding Risk Combined Therapy With ES and Pharmacologic Prophylaxis			
Symptomatic VTE inferred from any DVT Follow-up: to hospital discharge	Low-risk population[b]		OR 0.40 (0.25-0.65)[c]	1,089 (10 studies[d])	Low[e,f,g]
	5 per 1,000	2 per 1,000 (1-3)[h]			
	Medium-risk population[b]				
	9 per 1,000	4 per 1,000 (2-6)[h]			
	High-risk population[b]				
	19 per 1,000	8 per 1,000 (5-12)[h]			
Skin breaks, blisters, ulcers, necrosis (Case note review) Follow-up: 1-30 d	13 per 1,000	54 per 1,000 (31-95)	RR 4.18 (2.4-7.27)	2,518 (1 study)	Low[i,j]

GRADE Working Group grades of evidence: high quality, further research is very unlikely to change our confidence in the estimate of effect; moderate quality, further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality, further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and very low quality, we are very uncertain about the estimate. See Table 1, 3, 9, and 10 legends for expansion of abbreviations.

[a]The basis for the assumed risk (eg, the median control group risk across studies) is provided in the following footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

[b]Baseline risk of VTE in moderate-, high-, and very-high-risk patients was adjusted to assume that all patients received background prophylaxis with LMWH. Data from Bahl et al.[81] In low-risk patients, rate of symptomatic VTE was 0%.

[c]OR for proximal DVT and PE were 0.28 (95% CI, 0.09-0.87) and 0.43 (95% CI, 0.16-1.18), respectively.

[d]Data for other critical outcomes (eg, fatal PE) not available; bleeding complications not relevant.

[e]Unclear concealment of allocation sequence and unclear blinding and measurement of surrogate otucomes in most or all studies.

[f]Mild to moderate unexplained heterogeneity across studies.

[g]Data from studies of general and abdominal (six) and orthopedic (four) surgery. Background prophylaxis included unfractionated heparin (five), dextran (three), LMWH (one), and aspirin (one).

[h]Pooled risk of any DVT in the combined therapy treatment groups.

[i]Unblinded ascertainment based on case note review.

[j]Based on data from CLOTS1 study in patients with stroke.

Table 18—*Summary of Findings: Extended-Duration Prophylaxis Compared With Limited-Duration Prophylaxis for VTE Prevention in Surgical Patients at High Risk for VTE*

Patient or population: patients with VTE, prevention in high-VTE risk surgical patients
Settings: hospital and postdischarge
Intervention: extended-duration prophylaxis
Comparison: limited-duration prophylaxis

Outcomes	Illustrative Comparative Risks[a] (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Quality of the Evidence (GRADE)
	Assumed Risk Limited-Duration Prophylaxis	Corresponding Risk Extended-Duration Prophylaxis			
All-cause mortality Follow-up: 3 mo	54 per 1,000	60 per 1,000 (36-99)	OR 1.12 (0.65-1.93)	1,021 (4 studies)	Moderate[b]
Nonfatal symptomatic VTE Follow-up: 3 mo	Low-risk population		OR 0.22 (0.06-0.8)	901 (4 studies)	Low[c,d]
	5 per 1,000	1 per 1,000 (0-4)			
	Medium-risk population				
	8 per 1,000	2 per 1,000 (0-6)			
	High-risk population				
	17 per 1,000	4 per 1,000 (1-14)			
Major bleeding Follow-up: 3 mo	Low-risk population		OR 1.11 (0.62-1.97)	1,242 (4 studies)	Low[b,c]
	12 per 1,000	13 per 1,000 (7-23)			

GRADE Working Group grades of evidence: high quality, further research is very unlikely to change our confidence in the estimate of effect; moderate quality, further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality, further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and very low quality, we are very uncertain about the estimate. See Table 1 and 9 legends for expansion of abbreviations.

[a]The basis for the assumed risk (eg, the median control group risk across studies) is provided in the following footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

[b]The 95% CI around the estimate includes the possibility of both substantial benefit and serious harm.

[c]Incomplete blinding and incomplete details about concealment of allocation sequence.

[d]Bias introduced by measurement of surrogate outcome (venographic assessment of asymptomatic DVT).

Table 19—*Summary of Findings: Fondaparinux Compared With No Prophylaxis for VTE Prevention in Surgical Patients*

Patient or population: patients with VTE, prevention in surgical patients
Settings: hospital
Intervention: fondaparinux
Comparison: no prophylaxis

Outcomes	Illustrative Comparative Risks[a] (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Quality of the Evidence (GRADE)
	Assumed Risk No Prophylaxis	Corresponding Risk Fondaparinux			
Fatal PE inferred from death from any cause	Low-risk population[b]		RR 0.41 (0.15-1.07)	1,433 (6 studies)	Low[c,d]
	3 per 1,000[e]	1 per 1,000 (0-3)[f]			
	Medium-risk population[b]				
	6 per 1,000[e]	2 per 1,000 (1-6)[f]			
	High-risk population[b]				
	12 per 1,000[e]	5 per 1,000 (2-13)[f]			
Nonfatal symptomatic VTE	Low-risk population[g]		RR 0.39 (0.13-1.18)	1,465 (4 studies)	Very low[c,d,h]
	15 per 1,000	6 per 1,000 (2-18)[f]			
	Medium-risk population[g]				
	30 per 1,000	12 per 1,000 (4-35)[f]			
	High-risk population[g]				
	60 per 1,000	23 per 1,000 (8-71)[f]			
Nonfatal major bleeding	Low-risk population[i]		RR 2.92 (1.62-5.25)	1,433 (8 studies)	Low[c,h]
	12 per 1,000	35 per 1,000 (19-63)[f]			
	High-risk population[i]				
	22 per 1,000	64 per 1,000 (36-116)[f]			

GRADE Working Group grades of evidence: high quality, further research is very unlikely to change our confidence in the estimate of effect; moderate quality, further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality, further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and very low quality, we are very uncertain about the estimate. See Table 1, 9, and 10 legends for expansion of abbreviations.

[a]The basis for the assumed risk (eg, the median control group risk across studies) is provided in the following footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

[b]Risk of death from any cause was 20 of 1,429 (1.4%) in the LMWH (control) group, which was higher than the risk of death in treatment groups in studies of LMWH vs no prophylaxis (0.4%). For overall baseline risk, we used pooled risk from control groups in studies of LMWH vs no prophylaxis (0.9%). Risk of death from any cause in low-, moderate-, and high-risk groups was calculated under the assumption that ratio of death from any cause to symptomatic VTE did not vary across risk categories.

[c]ORs calculated based on indirect comparison from large RCT of fondaparinux vs LMWH and meta-analysis of five studies of LMWH vs placebo, all in patients undergoing abdominal surgery.

[d]The 95% CI includes the possibility of both substantial benefit and no effect.

[e]Pooled risk of death in control groups from studies of LMWH vs placebo or no prophylaxis (Mismetti et al[13]).

[f]Absolute risks in fondaparinux group taken from Agnelli et al.[20]

[g]Baseline risk of VTE in moderate-, high-, and very-high-risk patients after adjustment for prophylaxis received. Data from Bahl et al.[81] In low-risk patients, rate of symptomatic VTE was 0%.

[h]In a large RCT comparing fondaparinux and LMWH, generation and concealment of allocation sequence were not described; measurement of patient-important outcomes (symptomatic VTE) was potentially confounded by surveillance for asymptomatic events.

[i]In seven studies of LMWH vs no prophylaxis in abdominal surgery (Mismetti et al[13]), the weighted pooled (random-effects model) risk of major bleeding in the control groups was 1.2%. In a more-recent comparison of LMWH vs fondaparinux, the risk of bleeding requiring reoperation or intervention was 1.0% in the LMWH group. After adjustment for prophylaxis, the risk was 0.5%. In a secondary analysis of RCT data (Cohen et al[90]), the odds of major bleeding were 1.8 times greater in patients with cancer.

Table 20—*Summary of Findings: Low-Dose Aspirin Compared With No Prophylaxis for VTE Prevention in Nonorthopedic Surgical Patients*

Patient or population: patients with VTE, prevention in nonorthopedic surgical patients
Settings: hospital
Intervention: low-dose aspirin
Comparison: no prophylaxis

Outcomes	Illustrative Comparative Risks[a] (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Quality of the Evidence (GRADE)
	Assumed Risk No Prophylaxis	Corresponding Risk Low-Dose Aspirin			
Fatal PE inferred from death from any cause Follow-up: 35 d	Low-risk population[b]		RR 0.97 (0.85-1.1)	13,356 (1 study)	Moderate[c]
	3 per 1,000	3 per 1,000 (3-3)			
	Medium-risk population[b]				
	6 per 1,000	6 per 1,000 (5-7)			
	High-risk population[b]				
	12 per 1,000	12 per 1,000 (10-13)			
Nonfatal symptomatic VTE (objectively confirmed with venography, ultrasound, lung scan, or pulmonary angiogram) Follow-up: 35 d	Low-risk population[d]		RR 0.71 (0.54-0.94)	13,356 (1 study)	Low[c,e]
	15 per 1,000	11 per 1,000 (8-14)			
	Medium-risk population[d]				
	30 per 1,000	21 per 1,000 (16-28)			
	High-risk population[d]				
	60 per 1,000	43 per 1,000 (32-56)			
Nonfatal major bleeding inferred from all reported nonfatal bleeding complications, including hematemesis, melena, hematoma, bleeding from wound, and other bleeding requiring transfusion Follow-up: 35 d	Low-risk population[f]		RR 1.32 (1.17-1.48)[g]	13,356 (1 study)	Moderate[c]
	12 per 1,000	16 per 1,000 (14-18)			
	Medium-risk population[f]				
	22 per 1,000	29 per 1,000 (26-33)			
	High-risk population[f]				
	40 per 1,000	53 per 1,000 (47-59)			
Nonfatal myocardial infarction (Two or more of the following: typical chest pain, ECG changes, or enzyme changes) Follow-up: 35 d	3 per 1,000	5 per 1,000 (3-8)	RR 1.57 (0.93-2.65)	13,356 (1 study)	Low[e,h]

(Continued)

Table 20—*Continued*

Patient or population: patients with VTE, prevention in nonorthopedic surgical patients
Settings: hospital
Intervention: low-dose aspirin
Comparison: no prophylaxis

Outcomes	Illustrative Comparative Risks[a] (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Quality of the Evidence (GRADE)
	Assumed Risk No Prophylaxis	Corresponding Risk Low-Dose Aspirin			
Nonfatal stroke (Rapid development of cerebral dysfunction lasting at least 24 h) Follow-up: 35 d	4 per 1,000	5 per 1,000 (3-7)	RR 1.13 (0.69-1.85)	13,356 (1 study)	Moderate[c]

GRADE Working Group grades of evidence: high quality, further research is very unlikely to change our confidence in the estimate of effect; moderate quality, further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality, further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and very low quality, we are very uncertain about the estimate. See Table 1, 2, 9, and 10 legends for expansion of abbreviations.

[a]The basis for the assumed risk (eg, the median control group risk across studies) is provided in the following footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

[b]Pooled risk of death from any cause was 24/2,589 (0.9%) in the control groups in studies of LMWH vs no prophylaxis. Risk of death in low-, moderate-, and high-VTE risk groups was calculated under the assumption that the ratio of death from any cause to symptomatic VTE did not vary across risk categories.

[c]PEP study performed in orthopedic surgery patients; results were taken from patients with hip fractures. Approximately 44% of patients also received prophylaxis with LMWH or unfractionated heparin and ~30% received mechanical prophylaxis with ES, evenly distributed between the treatment groups.

[d]Baseline risk of VTE in moderate-, high-, and very-high-risk patients after adjustment for prophylaxis received. Data from Bahl et al.[81] In low-risk patients, rate of symptomatic VTE was 0%.

[e]Among patients at high risk for VTE , the lower limit of the 95% CI for absolute number of events overlaps with the upper limit for absolute number of major bleeding complications.

[f]In seven studies of LMWH vs no prophylaxis in abdominal surgery (Mismetti et al[13]), the weighted pooled (random-effects model) risk of major bleeding in the control groups was 1.2%. In 36 studies of LMWH vs unfractionated heparin in abdominal surgery, the pooled risk of major bleeding in the unfractionated heparin group was 3.2% but was only 2.7% in noncancer surgery and 8.1% in cancer surgery groups. After adjustment for prophylaxis, the risks for the noncancer and cancer surgery groups were 1.7% and 5.1%, respectively. In a secondary analysis of RCT data (Cohen et al[90]), the odds of major bleeding were 1.8 times greater in patients with cancer.

[g]In PEP, risk of hematoma requiring evacuation was 24 of 6,679 (0.4%) in the aspirin group and 33 of 6,677 in the control group (0.5%). The relative risk was 0.73 (95% CI, 0.43-1.23).

[h]The 95% CI includes the possibility of both serious harm and no effect.

Table 21—*Summary of Findings: High-Dose Aspirin (600-1,500 mg/d) Compared With No Prophylaxis for VTE Prevention in Nonorthopedic Surgical Patients*

Patient or population: patients with VTE, prevention in nonorthopedic surgical patients
Settings: hospital
Intervention: high-dose aspirin (600-1,500 mg/d)
Comparison: no prophylaxis

Outcomes	Illustrative Comparative Risks[a] (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Quality of the Evidence (GRADE)
	Assumed Risk No Prophylaxis	Corresponding Risk High-Dose Aspirin (600-1,500 mg/d)			
Fatal PE inferred from all-cause mortality Follow-up: hospital discharge	Low-risk population[b]		OR 0.45 (0.14-1.49)	1,102 (2 studies)	Low[c,d]
	3 per 1,000	1 per 1,000 (0-4)			
	Medium-risk population[b]				
	6 per 1,000	3 per 1,000 (1-9)			
	High-risk population[b]				
	12 per 1,000	5 per 1,000 (2-18)			
Nonfatal symptomatic VTE inferred from any DVT (FUT ± venography or venography) Follow-up: usually to hospital discharge	Low-risk population[e]		RR 0.52 (0.32-0.83)[f]	3,173 (8 studies)	Low[g,h]
	15 per 1,000	8 per 1,000 (5-12)			
	Medium-risk population[e]				
	30 per 1,000	16 per 1,000 (10-25)			
	High-risk population[e]				
	60 per 1,000	31 per 1,000 (19-50)			
Major bleeding inferred from excessive intraoperative or other bleeding Follow-up: to hospital discharge	Low-risk population[i]		OR 1.61 (1-2.6)	1,645 (2 studies)	Low[j,k]
	12 per 1,000	19 per 1,000 (12-31)			
	High-risk population[i]				
	22 per 1,000	35 per 1,000 (22-55)			

GRADE Working Group grades of evidence: high quality, further research is very unlikely to change our confidence in the estimate of effect; moderate quality, further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality, further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and very low quality, we are very uncertain about the estimate. See Table 1, 9, and 11 legends for expansion of abbreviations.

[a]The basis for the assumed risk (eg, the median control group risk across studies) is provided in the following footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

[b]Pooled risk of death from any cause was 24 of 2,589 (0.9%) in the control groups in studies of LMWH vs no prophylaxis. Risk of death in low-, moderate-, and high-VTE risk groups was calculated under the assumption that ratio of death from any cause to symptomatic VTE did not vary across risk categories.

[c]Exclusion of patients after randomization (two of eight).

[d]The 95% CI includes the possibility of both substantial benefit and no effect.

[e]Baseline risk of VTE in moderate-, high-, and very-high-risk patients after adjustment for prophylaxis received. Data from Bahl et al.[81] In low-risk patients, rate of symptomatic VTE was 0%.

[f]Relative risk of proximal DVT in four trials was 0.41 (95% CI, 0.10-1.68), and relative risk of any PE in six trials (with mild heterogeneity across trials) was 0.43 (95% CI, 0.20-0.92), whereas the risk of symptomatic DVT in three trials was 0.90 (95% CI, 0.46-1.75).

[g]Unclear concealment of allocation sequence (seven of eight); measurement of surrogate outcomes (six of eight); exclusion of patients after randomization (two of eight); unclear or absent blinding (two of eight).

[h]Moderate unexplained heterogeneity across trials.

[i]In seven studies of LMWH vs no prophylaxis in abdominal surgery (Mismetti et al[13]), the weighted pooled (random-effects model) risk of major bleeding in the control groups was 1.2%. In 36 studies of LMWH vs unfractionated heparin in abdominal surgery, the pooled risk of major bleeding in the unfractionate heparin group was 3.2% but was only 2.7% in noncancer surgery and 8.1% in cancer surgery groups. After adjustment for prophylaxis, the risks for noncancer and cancer surgery were 1.7% and 5.1%, respectively. In a secondary analysis of RCT data (Cohen et al[90]), the odds of major bleeding were 1.8 times greater in patients with cancer.

[j]Unclear concealment of allocation sequence (seven of eight); measurement of surrogate outcomes (six of eight); exclusion of patients after randomization (two of eight); unclear or absent blinding (two of eight).

[k]The 95% CI includes the possibity of both serious harm and no effect.

Table 22—*Summary of Findings: IVC Filters Compared With No Filter for VTE Prevention in High-VTE Risk Patients With Trauma*

Patient or population: patients with VTE, prevention in high VTE-risk trauma patients
Settings: hospital
Intervention: IVC filters
Comparison: no filter

Outcomes	Illustrative Comparative Risks[a] (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Quality of the Evidence (GRADE)
	Assumed Risk No Filter	Corresponding Risk IVC Filters			
Fatal or nonfatal PE	Low-risk population[b]		OR 0.21 (0.09-0.49)	1,900 (7 studies)	Low[c]
	5 per 1,000	1 per 1,000 (0-2)			
	Medium-risk population[b]				
	10 per 1,000	2 per 1,000 (1-5)			
	High-risk population[b]				
	20 per 1,000	4 per 1,000 (2-10)			
Symptomatic DVT	Low-risk population[b]		RR 1.60 (0.76-3.37)	232 (2 studies)	Very low[c,d,e]
	10 per 1,000	16 per 1,000 (8-34)			
	Medium-risk population[b]				
	20 per 1,000	32 per 1,000 (15-67)			
	High-risk population[b]				
	40 per 1,000	64 per 1,000 (30-135)			
Complications, including insertion site thrombosis (5), IVC thrombosis (8), hematoma (1), tilting filter (1), and migration to RV (1)			RR 0 (0 to 0)	375 (5 studies)	Low

GRADE Working Group grades of evidence: high quality, further research is very unlikely to change our confidence in the estimate of effect; moderate quality, further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality, further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and very low quality, we are very uncertain about the estimate. RV = right ventricle. See Table 1, 9, 10 legends for expansion of other abbreviations.

[a]The basis for the assumed risk (eg, the median control group risk across studies) is provided in the following footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

[b]Baseline risk of VTE in moderate-, high-, and very-high-risk patients after adjustment for prophylaxis received. Data from Bahl et al.[81] In low-risk patients, rate of symptomatic VTE was 0%. Distribution of PE and DVT assumes that roughly one-third of all VTE events are PE.

[c]Comparison with historical control subjects, variably matched for age, severity, and diagnosis.

[d]Severe unexplained heterogeneity in study results.

[e]The 95% CI includes the possibility of both serious harm and no effect.

Table 23—*Recommendations for Thromboprophylaxis in Various Risk Groups*

Risk of Symptomatic VTE	Risk and Consequences of Major Bleeding Complications	
	Average Risk (~1%)	High Risk (~2%) or Severe Consequences
Very low (< 0.5%)	No specific prophylaxis	
Low (~1.5%)	Mechanical prophylaxis, preferably with IPC	
Moderate (~3.0%)	LDUH, LMWH, *or* mechanical prophylaxis, preferably with IPC	Mechanical prophylaxis, preferably with IPC
High (~6.0%)	LDUH *or* LMWH *plus* mechanical prophylaxis with ES *or* IPC	Mechanical prophylaxis, preferably with IPC, until risk of bleeding diminishes and pharmacologic prophylaxis can be added
High-risk cancer surgery	LDUH *or* LMWH *plus* mechanical prophylaxis with ES *or* IPC *and* extended-duration prophylaxis with LMWH postdischarge	Mechanical prophylaxis, preferably with IPC, until risk of bleeding diminishes and pharmacologic prophylaxis can be added
High risk, LDUH and LMWH contraindicated or not available	Fondaparinux *or* low-dose aspirin (160 mg); mechanical prophylaxis, preferably with IPC; or both	Mechanical prophylaxis, preferably with IPC, until risk of bleeding diminishes and pharmacologic prophylaxis can be added

See Table 1 for expansion of abbreviations. See Table 5 for details about risk stratification for VTE; see Table 8 for information about risk factors for major bleeding.

Remarks: Three of the seven authors favored a strong (Grade 1B) recommendation in favor of LMWH or LDUH over no prophylaxis in this group.

3.6.4. For general and abdominal-pelvic surgery patients at moderate risk for VTE (~3.0%; Rogers score, > 10; Caprini score, 3-4) who are at high risk for major bleeding complications or those in whom the consequences of bleeding are thought to be particularly severe, we suggest mechanical prophylaxis, preferably with IPC, over no prophylaxis (Grade 2C)**.**

3.6.5. For general and abdominal-pelvic surgery patients at high risk for VTE (~6.0%; Caprini score, ≥ 5) who are not at high risk for major bleeding complications, we recommend pharmacologic prophylaxis with LMWH (Grade 1B) **or LDUH** (Grade 1B) **over no prophylaxis. We suggest that mechanical prophylaxis with ES or IPC should be added to pharmacologic prophylaxis** (Grade 2C)**.**

3.6.6. For high-VTE-risk patients undergoing abdominal or pelvic surgery for cancer who are not otherwise at high risk for major bleeding complications, we recommend extended-duration pharmacologic prophylaxis (4 weeks) with LMWH over limited-duration prophylaxis (Grade 1B)**.**

Remarks: Patients who place a high value on minimizing out-of-pocket health-care costs might prefer limited-duration over extended-duration prophylaxis in settings where the cost of extended-duration prophylaxis is borne by the patient.

3.6.7. For high-VTE-risk general and abdominal-pelvic surgery patients who are at high risk for major bleeding complications or those in whom the consequences of bleeding are thought to be particularly severe, we suggest use of mechanical prophylaxis, preferably with IPC, over no prophylaxis until the risk of bleeding diminishes and pharmacologic prophylaxis may be initiated (Grade 2C)**.**

3.6.8. For general and abdominal-pelvic surgery patients at high risk for VTE (~6%; Caprini score, ≥ 5) in whom both LMWH and unfractionated heparin are contraindicated or unavailable and who are not at high risk for major bleeding complications, we suggest low-dose aspirin (Grade 2C)**, fondaparinux** (Grade 2C)**, or mechanical prophylaxis, preferably with IPC** (Grade 2C)**, over no prophylaxis.**

3.6.9. For general and abdominal-pelvic surgery patients, we suggest that an IVC filter should not be used for primary VTE prevention (Grade 2C)**.**

3.6.10. For general and abdominal-pelvic surgery patients, we suggest that periodic surveillance with VCU should not be performed (Grade 2C)**.**

4.0 Target Population: Cardiac Surgery

Of two randomized controlled trials of VTE prophylaxis in cardiac surgery patients (Appendix S1), one compared ES alone with ES plus IPC,[124] and the other compared LDUH plus IPC with LDUH alone in patients who underwent cardiac surgery at a single center over a period of 10 years.[125] Because direct evidence about the safety and effectiveness of prophylaxis in patients undergoing cardiac surgery is limited, we applied indirect evidence about relative risks from studies of mixed surgical patients when making recommendations. Risk stratification is discussed next.

4.1 Baseline Risk, Risk Factors, and Risk Stratification for VTE

The risk of VTE following cardiac surgery is uncertain. Predisposing factors include perioperative stasis, inflammation, and activation of the coagulation system, but these are mitigated by early mobilization and use of anticoagulants, aspirin, and other antiplatelet drugs.

Relatively precise, but possibly dated estimates of the risk of VTE following cardiac surgery come from the California Patient Discharge Data Set for the years 1992 to 1996.[75] In this large data set, the risks of VTE in the 91 days after coronary artery bypass graft (CABG) and valve replacement surgery were 1.1% and 0.5%, respectively. Similarly, in an analysis of registry data from New York State in 1999, 133 of 16,325 (0.8%) patients were readmitted for VTE within 30 days after CABG.[126] Unfortunately, information about the use of prophylaxis was not reported in either study.

Based on results of these and other studies, we believe that most cardiac surgery patients are at moderate risk for VTE.[127-131] Possible factors that increase the risk of VTE in cardiac surgery include older age,[130] postoperative complications,[127,130] prolonged preoperative hospitalization or postoperative recovery,[128,129] CABG surgery compared with valve surgery,[129] and off-pump CABG compared with cardiopulmonary bypass.[132]

4.2 Baseline Risk, Risk Factors, and Risk Stratification for Major Bleeding Complications

A systematic review of English-language studies of surgical bleeding complications published between 1997 and 2007 identified six studies in cardiac surgery patients, including four retrospective cohort studies and two randomized trials.[133] In five studies, major bleeding was defined as bleeding requiring reexploration[90-92,134]; across these studies, the risk of major bleeding was remarkably consistent, with a median risk of 4.7% (range, 3.1%-5.9%). Thus, we classify most cardiac surgery patients as being at high risk for anticoagulant prophylaxis-related bleeding.

Risk factors for bleeding following cardiac surgery varied across studies (Table 8). One study found that the risk of bleeding was similar for on-pump compared with off-pump CABG.[135] Two others reported that the risk of bleeding was approximately twice as high in patients treated with aspirin[90] or clopidogrel, at least when given within 3 days of surgery.[91] In one series of 2,898 consecutive patients undergoing CABG, independent risk factors for bleeding requiring reexploration included BMI $\geq$ 25 kg/m^2, nonelective surgery, placement of five or more grafts, and older age.[92] In an earlier study of 6,015 patients undergoing cardiopulmonary bypass between 1986 and 1993, independent risk factors for bleeding included older age, renal insufficiency, operation other than CABG, and longer bypass time.[93]

4.3 Explanation of Evidence Profiles and Rationale for Recommendations in Cardiac Surgery

We classify most patients undergoing cardiac surgery as being at moderate risk for VTE and at high risk for major bleeding complications. In these patients, low-quality evidence (moderate-quality evidence downgraded for indirectness) suggests that the benefits of pharmacologic prophylaxis with either LDUH (Table 9) or LMWH (Table 10) are probably outweighed by the potential harms. In contrast, low-quality evidence suggests that the balance between desirable and undesirable outcomes is more favorable with mechanical prophylaxis (Tables 11, 12), which is expected to result in 15 to 20 fewer nonfatal VTE events at the expense of an uncertain number of skin complications.

When additional risk factors for VTE are present and the baseline risk of VTE is high, the trade-offs still appear to favor mechanical prophylaxis over both no prophylaxis (Tables 11, 12) and pharmacologic prophylaxis (Tables 13, 14). However, the relatively high risk of postoperative bleeding almost surely decreases over time in patients whose hospital course is prolonged by one or more nonhemorrhagic surgical complications. We classify such patients as being at high risk for VTE and low (or average) risk for bleeding, and these patients may benefit from the addition of pharmacologic prophylaxis to mechanical prophylaxis, although the trade-offs only slightly favor combined prophylaxis over mechanical prophylaxis alone (Table 24).

4.4 Recommendations for Cardiac Surgery

4.4.1. For cardiac surgery patients with an uncomplicated postoperative course, we suggest use of mechanical prophylaxis, preferably with optimally applied IPC, over either no prophylaxis (Grade 2C) **or pharmacologic prophylaxis** (Grade 2C)**.**

4.4.2. For cardiac surgery patients whose hospital course is prolonged by one or more nonhemorrhagic surgical complications, we suggest adding pharmacologic prophylaxis with LDUH or LMWH to mechanical prophylaxis (Grade 2C)**.**

5.0 Target Population: Thoracic Surgery

Of two small trials in thoracic surgery, one compared LDUH 5,000 bid with LDUH 7,500 bid,[136]

Table 24—*Summary of Findings: Combined Therapy With Pharmacologic Plus Mechanical Prophylaxis Compared With Mechanical Prophylaxis Alone for VTE Prevention in Surgical Patients*

Patient or population: patients with VTE, prevention in surgical patients
Settings: hospital
Intervention: combined therapy with pharmacologic plus mechanical prophylaxis
Comparison: mechanical prophylaxis alone

Outcomes	Illustrative Comparative Risks[a] (95% CI)		Relative Effect (95% CI)	No. of Participants (studies)	Quality of the Evidence (GRADE)
	Assumed Risk Mechanical Prophylaxis Alone	Corresponding Risk Combined Therapy With Pharmacologic Plus Mechanical Prophylaxis			
Symptomatic VTE inferred from PE (objectively confirmed events) Follow-up: until hospital discharge or 30 d after discharge	Low-risk population		RR 0.39 (0.24-0.64)	3,978 (3 studies)	Moderate
	7 per 1,000	3 per 1,000 (2-4)			
	Medium-risk population				
	14 per 1,000	5 per 1,000 (3-9)			
	High-risk population				
	29 per 1,000	11 per 1,000 (7-19)			
Major bleeding (clinical diagnosis) Follow-up: 7 to 270 d	Low-risk population		RR 2.03 (1.37-3.01)	5,457 (7 studies)	Moderate
	12 per 1,000	24 per 1,000 (16-36)			
	High-risk population				
	22 per 1,000	45 per 1,000 (30-66)			

GRADE Working Group grades of evidence: high quality, further research is very unlikely to change our confidence in the estimate of effect; moderate quality, further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality, further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and very low quality, we are very uncertain about the estimate. See Table 1, 9, and 10 legends for expansion of abbreviations.
[a]The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

whereas the other compared fixed-dose with weight-adjusted-dose nadroparin (Appendix S1).[137] Although direct evidence about the safety and effectiveness of prophylaxis in patients undergoing thoracic surgery is limited, we believe that evidence about relative risks from studies of patients undergoing general or abdominal-pelvic surgery can be applied to thoracic surgery patients without downgrading for indirectness. Baseline risk and risk stratification is discussed next.

5.1 Baseline Risk, Risk Factors, and Risk Stratification for VTE

Based on results of observational studies and our clinical judgment, we consider most thoracic surgery patients to be at least at moderate risk for VTE. Three relatively large retrospective studies reported the risk of symptomatic VTE events. In one study of 693 thoracotomies for lung cancer, symptomatic VTE was observed in 1.7% of patients, including PE in 1.3%, despite routine use of prophylaxis with LDUH or LMWH. In another analysis of 1,735 lung resections for malignancy, autopsy-confirmed fatal PE occurred in 1.2% of patients, despite ongoing heparin prophylaxis in most of them.[138] Another study of 706 thoracic surgery patients reported objectively confirmed PE in 20 of 344 (7%) patients who did not receive prophylaxis, but there were no episodes of PE among 362 patients who wore IPC.[139] Finally, the 91-day risk of clinically detected VTE for almost 13,000 patients undergoing major lung resection for malignant disease was 1.6% in the California Patient Discharge Data Set.[75]

Thoracic surgery patients undergoing extended pulmonary resection, pneumonectomy, extrapleural pneumonectomy, or esophagectomy are probably at higher risk for VTE. In a prospective study of 336 patients undergoing pneumonectomy for malignancy, the risk of symptomatic VTE was 7.4%.[140] Similarly, in a study of 496 patients undergoing extrapleural pneumonectomy for malignant mesothelioma, DVT occurred in 6.4% of patients, and fatal PE was observed in 1.2%.[141] Other risk factors for VTE in thoracic surgery have not been rigorously evaluated, although individual studies have implicated malignancy, larger tumors, and pack-years of smoking as possible risk factors.[140,142-144] In another study, age, sex, BMI, operation time, time to ambulation, operative method, and malignancy were not associated with VTE.[139]

5.2 Baseline Risk, Risk Factors, and Risk Stratification for Major Bleeding Complications

A review of complication rates from 14 studies of patients undergoing major lung resections for cancer distinguished between standard resection and pneumonectomy or extended resection.[94] Across nine studies of almost 17,000 patients who underwent standard resection, bleeding requiring reoperation was reported in 1%. However, in five studies of 1,223 patients who underwent pneumonectomy or extended resection, ~5% of patients required reexploration for bleeding. In a more-recent retrospective analysis of 1,100 patients who underwent video-assisted thoroscopic lobectomy at a single center, intraoperative bleeding required conversion to thoracotomy in six (5.5%) patients, and 45 (41%) patients required postoperative red cell transfusion, but there were no episodes of fatal bleeding or bleeding requiring reoperation.[145]

5.3 Explanation of Evidence Profiles and Rationale for Recommendations in Thoracic Surgery

Most thoracic surgery patients are at moderate risk for VTE. In these patients, moderate-quality evidence suggests that compared with no prophylaxis, pharmacologic prophylaxis with either LDUH or LMWH will result in more cases of VTE events prevented than bleeding episodes caused (Tables 9, 10). Low-quality evidence supports the use of mechanical prophylaxis over no prophylaxis, preferably with IPC (Tables 11, 12). The addition of mechanical prophylaxis with either ES (Table 16) or IPC (Table 17) to pharmacologic prophylaxis will prevent a few additional VTE events at the expense of skin complications, added cost, comfort, and convenience.

For thoracic surgery patients at high risk for VTE (including those undergoing extended pulmonary resection, pneumonectomy, extrapleural pneumonectomy, and esophagectomy), moderate-quality evidence suggests that when compared with no prophylaxis, the benefits of pharmacologic prophylaxis with LDUH (Table 9) or LMWH (Table 10) outweigh the harms. Because the risk of bleeding requiring reexploration appears to be elevated in patients who require pneumonectomy or extended-lung resection, prudence dictates that mechanical prophylaxis should be used until adequate hemostasis has been established and the risk of bleeding diminishes.

5.4 Recommendations for Thoracic Surgery

5.4.1. For thoracic surgery patients at moderate risk for VTE who are not at high risk for major bleeding, we suggest LDUH (Grade 2B)**, LMWH** (Grade 2B)**, or mechanical prophylaxis with optimally applied IPC** (Grade 2C) **over no prophylaxis.**

Remarks: Three of the seven authors favored a strong (Grade 1B) recommendation in favor of LMWH or LDUH over no prophylaxis in this group.

5.4.2. For thoracic surgery patients at high risk for VTE who are not at high risk for major bleeding, we suggest LDUH (Grade 1B) **or LMWH** (Grade 1B) **over no prophylaxis. In addition, we suggest that mechanical prophylaxis with ES or IPC should be added to pharmacologic prophylaxis** (Grade 2C)**.**

5.4.3. For thoracic surgery patients who are at high risk for major bleeding, we suggest use of mechanical prophylaxis, preferably with optimally applied IPC, over no prophylaxis until the risk of bleeding diminishes and pharmacologic prophylaxis may be initiated (Grade 2C)**.**

6.0 Target Population: Craniotomy

Two published meta-analyses summarized the results of randomized controlled trials of pharmacologic and mechanical prophylaxis in neurosurgery, including patients undergoing craniotomy and spinal surgery.[12,10] Many of the studies were limited by small samples; open-label design; incomplete follow-up; and use of ultrasound, venography, or fibrinogen uptake scanning to identify asymptomatic DVT.

One meta-analysis summarized the results of three trials in mixed neurosurgical patients that compared LMWH with placebo with or without adjunctive use of ES in both treatment groups.[12] In these studies, LMWH reduced the risk of any VTE (including asympotomatic DVT) by 46% and venographically confirmed proximal DVT by 52%. Consistent with results of studies in general and abdominal surgery, LMWH increased the risk of nonfatal major bleeding complications (mostly intracranial) by 68%. In addition, there was a possible increase in the risk of death from any cause (OR, 1.74; 95% CI, 0.94-3.22).

Another meta-analysis made several comparisons, including IPC vs no prophylaxis, LDUH vs no prophylaxis, LDUH vs LMWH, and IPC vs LMWH.[10] In two trials that compared IPC and no prophylaxis in mixed neurosurgery patients,[146,147] IPC reduced the risk of asymptomatic DVT by 59% and PE by 63%. For the other comparisons, differences in the risk of DVT, PE, or intracranial hemorrhage (ICH) were neither confirmed nor excluded. Accordingly, for these comparisons, we applied indirect but higher-quality evidence about relative risks from studies of general or mixed surgical patients in our evidence profiles.

6.1 Baseline Risk, Risk Factors, and Risk Stratification for VTE

Although no VTE risk stratification scheme has been validated for patients undergoing craniotomy, data from published observational studies suggest that cancer, advanced age, longer duration of surgery, and paresis are associated with an increased risk of VTE.[148-150] To estimate the baseline risks of nonfatal PE and symptomatic VTE in the absence of prophylaxis, we used data from an observational study of almost 2,400 neurosurgical admissions[151] and a structured literature review that pooled results from numerous smaller studies of patients undergoing craniotomy.[152] In the study by Chan et al,[151] the risk of clinically diagnosed VTE within 30 days after discharge was 3.9% among all patients, and it was especially high for patients undergoing craniotomy for primary malignancy (7.5%) or metastasis (19%). In this study, pharmacologic and mechanical prophylaxis was used in 67% of patients with cancer and 84% of patients without cancer. Smaller studies of malignant glioma patients reported risks of symptomatic, postoperative DVT that ranged between 3% and 25%.[153] In the analysis by Danish et al,[152] the pooled risk of symptomatic VTE was 2.1% across 13 studies that included almost 3,000 patients who received prophylaxis with IPC alone, whereas it was 2.2% in five studies that included $>3,500$ patients who received combined prophylaxis with unfractionated heparin and IPC. Accordingly, we classify craniotomy patients as being at high risk for VTE, especially those who undergo craniotomy for malignancy.

6.2 Baseline Risk, Risk Factors, and Risk Stratification for ICH

In craniotomy patients, we focus on ICH rather than on the more generic major bleeding outcome because ICH is a potentially devastating complication of craniotomy and because pharmacologic VTE prophylaxis increases the risk of operative site bleeding. Although the risk of ICH probably varies depending on patient- and procedure-specific factors, we found no validated bleeding risk stratification system for craniotomy patients. Data from a structured literature review that included 20 different studies and $>31,000$ patients who underwent craniotomy without pharmacologic prophylaxis indicate that the baseline risk of ICH is $\sim$1.1% (95% CI, 0.9%-1.4%).[152] We favor this relatively precise estimate of baseline risk, although we recognize that it is higher than those reported in the meta-analysis by Collen et al,[10] in which the pooled risks of intracranial hemorrhage were 0.04% (95% CI, 0%-3.7%) among those who did not receive pharmacologic prophylaxis, 0.35% (95% CI, 0%-7.4%) among those who received LDUH, and 1.5% (95% CI, 1.1%-1.9%) among those who received LMWH.

6.3 Explanation of Evidence Profiles

We classify patients undergoing craniotomy for nonmalignant disease as being at high risk for VTE

(~5%) and those with malignant disease as being at very high risk (≥ 10%). Although the baseline risk of bleeding (ICH) is probably ~1%, the consequences of ICH are likely to be very severe.

For craniotomy patients at high risk for VTE (~5%), such as those undergoing craniotomy for vascular disease, there is low-quality evidence that mechanical prophylaxis with IPC is beneficial. Compared with no prophylaxis, one can expect 11 to 40 fewer symptomatic VTE events per 1,000 patients treated with IPC (Table S10). As mentioned previously (Table S11), we favor IPC over ES primarily on the basis of indirect evidence from the CLOTS1 trial in stroke patients that ES increased the risk of skin complications without reducing the risk of VTE,[29] although differences between IPC and ES were neither demonstrated nor excluded in the meta-analysis of studies in neurosurgery.

In this group, there is moderate-quality evidence that compared with no prophylaxis, the benefits of pharmacologic prophylaxis with low-dose LMWH are probably outweighed by the harms (Table S12). First of all, LMWH was associated with a possible increase in the risk of death from any cause. In addition, although LMWH can be expected to prevent between eight and 36 VTE events, this comes at a cost of four to 22 additional intracranial bleeds. Based on the assumption that the disutility of intracranial hemorrhage is approximately two to three times greater than that associated with an average VTE event, the trade-offs favor no prophylaxis over LMWH. Although the trade-offs appear to be somewhat more favorable for LDUH compared with no prophylaxis (Table S13), the evidence is low in quality and sufficiently indirect to cast doubt on its relevance to craniotomy patients. Low-quality evidence for the comparison between LMWH and IPC suggests that the trade-offs favor IPC over pharmacologic prophylaxis in this group (Table S14).

For craniotomy patients at very high risk for symptomatic VTE (~10%), such as those with cancer, low-quality evidence favors IPC, LDUH, and (possibly) LMWH over no prophylaxis (Tables S10, S12, S13). Trade-offs for the comparison between LMWH and IPC probably favor IPC, with six to 26 more nonfatal VTE events per 1,000 patients treated but four to 22 fewer episodes of nonfatal ICH (Table S14).

A more difficult question is whether and when to add pharmacologic prophylaxis to mechanical prophylaxis in the very-high-risk craniotomy patient. Indirect evidence from studies in patients undergoing abdominal or elective orthopedic surgery suggests that the addition of fondaparinux or warfarin to mechanical prophylaxis further reduces DVT or PE by ~60%. Assuming that the risk of symptomatic VTE is 4.1% in those who receive IPC alone, low-quality evidence suggests that adding pharmacologic prophylaxis to IPC will prevent 23 additional VTE events per 1,000 patients treated (95% CI, 34 fewer to three more) at the expense of 11 more intracranial bleeds (95% CI, four more to 22 more) (Table S15). Because most ICH occur in the first 12 to 24 h after craniotomy, whereas approximately one-half of VTE events occur after the first week,[150] it is advisable to delay adding LMWH or LDUH until adequate hemostasis is established and the risk of bleeding is judged not to be excessively high.

6.4 Recommendations for Craniotomy

6.4.1. For craniotomy patients, we suggest that mechanical prophylaxis, preferably with IPC, be used over no prophylaxis (Grade 2C) **or pharmacologic prophylaxis** (Grade 2C)**.**

6.4.2. For craniotomy patients at very high risk for VTE (eg, those undergoing craniotomy for malignant disease), we suggest adding pharmacologic prophylaxis to mechanical prophylaxis once adequate hemostasis is established and the risk of bleeding decreases (Grade 2C)**.**

7.0 Target Population: Spinal Surgery

Six randomized trials examined interventions to prevent VTE in spinal surgery patients, most limited by small samples, unclear concealment of treatment allocation, incomplete blinding, and measurement of asymptomatic DVT (Tables S2-S4). One compared pharmacologic prophylaxis with placebo,[154] one compared unfractionated heparin with LMWH,[155] and three compared different methods of mechanical prophylaxis with or without pharmacologic prophylaxis.[156-158] A meta-analysis summarized results of these and several other trials that enrolled mixed neurosurgical patients.[10] The authors found that IPC reduced the risk of DVT by 59% compared with no prophylaxis (RR, 0.41; 95% CI, 0.21-0.78). However, for comparisons of IPC with ES (RR, 0.81; 95% CI, 0.32-1.78) and LMWH with IPC (RR, 0.79; 95% CI, 0.30-2.12), differences in the risk of DVT were neither confirmed nor excluded. Because studies of mixed surgical patients provide higher-quality evidence and more-precise estimates of treatment effect, we used indirect evidence from these studies to estimate the relative risk of symptomatic VTE for these comparisons.

7.1 Baseline Risk, Risk Factors, and Risk Stratification for VTE

Three systematic reviews described in Appendix S1 have examined the baseline risk of VTE in spinal

surgery.[159-161] Most of the studies were limited by small sample sizes and the measurement of asymptomatic DVT, although one large retrospective study reported a very low risk of symptomatic DVT (0.05%) among 1,919 patients who received heparin prophylaxis and did not undergo routine surveillance for DVT.[162]

Risk factors for VTE in spinal surgery patients likely include a combined anterior-posterior approach; multiple operative levels; and patient-related factors, such as older age, prior VTE, and malignancy.[163,164] In a population-based retrospective analysis of discharges from California hospitals in 1992 to 1996, the risk of symptomatic VTE within 91 days of surgery was 0.5% (95% CI, 0.4%-0.5%) among 34,355 patients who underwent spinal surgery for nonmalignant disease, whereas the risk of VTE was 2.0% (95% CI, 1.4%-2.6%) among 1,545 who underwent spinal surgery for malignant disease.[75] Accordingly, we classify the baseline risk of VTE in spinal surgery as low for most patients with nonmalignant disease and moderate for those with malignancy.

7.2 Baseline Risk, Risk Factors, and Risk Stratification for Major Bleeding Complications

In a large retrospective study of spinal surgery patients treated with nadroparin,[162] major bleeding (defined as hemorrhage associated with a mass effect on postoperative spinal MRI and neurologic deterioration or a large-wound hematoma with intractable pain) was observed in 13 of 1,954 (0.7%) patients. In another observational study, 720 noncranial neurosurgical patients who were not at high risk for bleeding received twice-daily prophylaxis with LDUH. Two patients (0.3%) developed epidural hematomas that required reoperation.[165] In a small randomized trial of LDUH vs placebo, deep hematomas were noted in two patients in the placebo group and no patients in the heparin group.[154] In another trial comparing LMWH plus dihydroergotamine vs LDUH plus dihydroergotamine, there were no hematomas in either group, although increased intraoperative bleeding was noted to be more common in the LDUH group.[155] Based on these data, we believe that the baseline risk of major bleeding in spinal surgery is probably $< 0.5\%$, but the consequences are potentially very severe.

7.3 Explanation of Evidence Profiles

Among spinal surgery patients at low risk for VTE, including those with nonmalignant disease, we estimate that compared with no prophylaxis, there will be similar reductions in the numbers of symptomatic VTE events when prophylaxis is given with IPC (five per 1,000), ES (six per 1,000), LDUH (five per 1,000), and LMWH (six per 1,000) (Tables S16-S19). These modest reductions are offset by similar increases in the absolute numbers of major bleeding complications with LDUH (three per 1,000) and LMWH (five per 1,000). Likewise, the benefits of IPC and ES are offset by an uncertain number of skin complications. Comparisons of IPC vs ES (Table S20), IPC vs LDUH (Table S21), and IPC vs LMWH (Table S22) suggest that the balance of desirable and undesirable outcomes favors IPC in these patients.

Among spinal surgery patients at moderate risk for VTE, including those with malignant disease and those undergoing surgery with a combined anterior-posterior approach, even greater reductions in symptomatic VTE events are anticipated with IPC (29 per 1,000), ES (31 per 1,000), LDUH (27 per 1,000), and LMWH (33 per 1,000), all compared with no prophylaxis (Tables S16-S19). Although the balance between benefits and harms favors either pharmacologic or mechanical methods over no prophylaxis, the tradeoffs involved in the comparison between pharmacologic prophylaxis and mechanical prophylaxis with IPC are not as clear cut (Tables S21, S22). IPC may still be preferred over LMWH if the consequences of a nonfatal major bleeding event are believed to be at least two times more severe than those of nonfatal VTE.

7.4 Recommendations for Spinal Surgery

7.4.1. For patients undergoing spinal surgery, we suggest mechanical prophylaxis, preferably with IPC, over no prophylaxis (Grade 2C)**, unfractionated heparin** (Grade 2C)**, or LMWH** (Grade 2C)**.**

7.4.2. For patients undergoing spinal surgery at high risk for VTE (including those with malignant disease and those undergoing surgery with a combined anterior-posterior approach), we suggest adding pharmacologic prophylaxis to mechanical prophylaxis once adequate hemostasis is established and the risk of bleeding decreases (Grade 2C)**.**

8.0 Target Population: Major Trauma, Including Traumatic Brain Injury, Acute Spinal Cord Injury, and Traumatic Spine Surgery

Decision making about thromboprophylaxis in trauma patients poses numerous challenges. Although traumatic inflammation, fractures, immobilization, and surgical intervention contribute to the high risk of VTE, both the risk and, potentially, the dire consequences of bleeding complications weigh heavily, especially in cases of visceral, spinal, and head injury.

Seven randomized controlled trials of LMWH thromboprophylaxis in trauma limited enrollment to patients with isolated lower-extremity injuries; results of these trials and accompanying recommendations are described by Falck-Ytter et al[35] in this supplement. Nineteen other trials enrolled diverse groups of moderately to severely injured patients, including eight trials in patients with spinal cord injury[30,166-172] and four studies in patients with orthopedic injuries.[173-176] Studies evaluated both mechanical (eg, IPC, myostimulation, continuous passive motion) and pharmacologic (eg, LDUH, LMWH) interventions, but no randomized trials examined IVC filter placement or use of surveillance ultrasound. Study limitations included small samples, incomplete or absent blinding, unclear concealment of treatment allocation, use of surrogate outcomes, exclusion of large numbers of randomized patients from primary outcome assessment, and imprecise results (Appendix S1). Accordingly, there is little moderate- or high-quality direct evidence to support the use of one or more interventions for thromboprophylaxis in trauma. Therefore, when making recommendations, we used estimates of relative risk from studies in other populations that suffered from less risk of bias and that were more precise.

8.1 Baseline Risk, Risk Factors, and Risk Stratification for VTE

Numerous studies have examined the risk of VTE in trauma (Appendix S1). Across four studies of patients with mixed trauma, the risk of symptomatic VTE ranged from > 1% to 7.6%.[61,177-179] The risk is probably highest among patients with spinal trauma (2.2% despite near-universal prophylaxis), acute spinal cord injury (5%-6%), or traumatic brain injury (3%-5% among those who received pharmacologic prophylaxis within 24 to 48 h; up to 15% when initiation of pharmacologic prophylaxis was delayed beyond 48 h).[180-185] A systematic review identified patients with spinal fractures (OR, 2.3; 95% CI, 1.4-3.6) or spinal cord injury (OR, 3.0; 95% CI, 1.8-5.4) as having a higher risk of VTE than other patients with trauma.[186] Older age has also been implicated as a risk factor for VTE in a number of studies.[177,178,187]

Other independent risk factors for VTE, inconsistent across studies, included blood transfusion, surgery, femoral or tibial fracture, and spinal cord injury[177]; head injury, major operation, lower-extremity fracture, venous injury, and (especially) > 3 days of mechanical ventilation[178]; and male sex, black race, complete paraplegia (vs tetraplegia), and multiple comorbidities.[181] Based on results of these studies, we believe that the baseline risk of VTE in most patients with major trauma is at least 3% to 5% and that the risk is even higher (8%-10%) among patients with traumatic brain or spinal cord injury and among those who require spinal surgery.

8.2 Baseline Risk, Risk Factors, and Risk Stratification for Major Bleeding Complications

Few studies have examined bleeding complications associated with thromboprophylaxis in trauma. In a prospective study of 525 patients with traumatic brain injury who were judged to be eligible to receive LMWH prophylaxis within 48 h of admission, progressive hemorrhagic changes were seen on head CT scan in 18 patients (3.4%), including in six (1.1%) in whom there was a change in management or outcome.[188] In a retrospective study of nosocomial complications in 525 adult patients with trauma, the reported risk of bleeding requiring red cell transfusion of > 4 units was 4.7%.[179]

Another source of data to estimate the baseline risk of major bleeding complications comes from patients who were assigned to receive nonpharmacologic management in randomized trials of thromboprophylaxis. Unfortunately, only three trials in patients with trauma reported major bleeding complications in four groups that did not receive pharmacologic prophylaxis.[189-191] In these groups, the pooled (random-effects) risk of major bleeding was 0.7% (95% CI, 0.2%-1.7%). This is likely to represent a lower boundary for the baseline risk of bleeding because patients judged to be at increased risk for bleeding were excluded from most trials of thromboprophylaxis. Relative contraindications to pharmacologic prophylaxis in trauma include severe head injuries, nonoperatively managed liver or spleen injuries, renal failure, spinal column fracture with epidural hematoma, severe thrombocytopenia, and coagulopathy.[192]

8.3 Explanation of Evidence Profiles

For patients with major trauma who are at average risk for VTE and average risk for major bleeding, low-quality evidence suggests that pharmacologic prophylaxis with LDUH or LMWH can be expected to prevent approximately four times as many nonfatal VTE events as nonfatal bleeding complications caused (Tables S23, S24). Low-quality evidence suggests that mechanical prophylaxis with ES or IPC can be expected to prevent a similar number of nonfatal VTE events (Tables S25, S26) at a cost of an uncertain number of skin complications.

For patients with major trauma who are at especially high risk for VTE and average risk for bleeding complications (eg, acute spinal cord injury, spinal surgery for trauma), low-quality evidence suggests that pharmacologic prophylaxis with LDUH or LMWH can be expected to prevent almost 10 times as many nonfatal VTE events as nonfatal bleeding complications

caused (Tables S23,S24). Moderate-quality evidence suggests that both LDUH and LMWH can also be expected to prevent four deaths from PE per 1,000 patients treated. The addition of mechanical prophylaxis can be expected to prevent 15 additional nonfatal VTE events per 1,000 patients treated (Table S27) at a cost of an uncertain number of skin complications.

For patients with major trauma at high risk for major bleeding (including those with traumatic brain injury), low-quality evidence suggests that the numbers of nonfatal VTE events prevented by pharmacologic methods are only slightly larger than the numbers of nonfatal major bleeding complications caused (Tables S23, S24). In these patients, mechanical prophylaxis with ES or IPC prevents sizable numbers of nonfatal VTE events at the expense of skin complications but without increasing the risk of bleeding (Tables S25,S26).

Few studies address the optimal duration of prophylaxis for patients with acute spinal cord injury. However, in a retrospective study of > 16,000 patients discharged from California hospitals between 1991 and 2001, > 90% of all thromboembolic events reported within 1 year after injury occurred in the first 91 days.[178] Pending further evidence, we agree with others[193] that 3 months is a reasonable time for VTE prophylaxis in most patients with acute spinal cord injury. Shorter durations may be appropriate for patients who regain purposeful movement of the lower extremities before 3 months, but further study is needed. For information about the use of IVC filters and DVT surveillance with VCU in trauma patients, please see sections 2.12, 2.13 and 3.5, and Table 22.

8.4 Recommendations for Patients With Trauma

Recommendations for patients with isolated lower-extremity injuries are provided by Falck-Ytter et al[35] in this supplement.

8.4.1. For major trauma patients, we suggest use of LDUH (Grade 2C)**, LMWH** (Grade 2C)**, or mechanical prophylaxis, preferably with IPC** (Grade 2C)**, over no prophylaxis.**

8.4.2. For major trauma patients at high risk for VTE (including those with acute spinal cord injury, traumatic brain injury, and spinal surgery for trauma), we suggest adding mechanical prophylaxis to pharmacologic prophylaxis (Grade 2C) **when not contraindicated by lower-extremity injury.**

8.4.3. For major trauma patients in whom LMWH and LDUH are contraindicated, we suggest mechanical prophylaxis, preferably with IPC, over no prophylaxis (Grade 2C) **when not contraindicated by lower-extremity injury. We suggest adding pharmacologic prophylaxis with either LMWH or LDUH when the risk of bleeding diminishes or the contraindication to heparin resolves** (Grade 2C)**.**

8.4.4. For major trauma patients, we suggest that an IVC filter should not be used for primary VTE prevention (Grade 2C)**.**

8.4.5. For major trauma patients, we suggest that periodic surveillance with VCU should not be performed (Grade 2C)**.**

9.0 Suggestions for Good Clinical Practice

The following general considerations for good clinical practice apply to thromboprophylaxis in all surgical groups:

- It may be advisable for every institution to have a formal, written policy for preventing VTE in surgical patients.
- Adherence with IPC often is less than optimal and, therefore, should be monitored actively. Portable, battery-powered devices capable of recording and reporting proper wear time may facilitate monitoring. Efforts should be made to achieve at least 18 h of use daily.
- Proper fit and adherence with ES is necessary to ensure efficacy. The correct pressure at the ankle level for primary prophylaxis is 18 to 23 mm Hg, which is lower than for therapeutic stockings used to treat postthrombotic syndrome (30-40 mm Hg). Based on indirect evidence from patients with stroke,[29] we favor thigh-high elastic stockings over calf-high stockings.
- Relative contraindications to IPC and ES include dermatitis, skin breakdown, or ulceration; peripheral vascular disease; lower-extremity bypass procedure; and lower-extremity trauma with plaster cast. Unilateral compression in an unaffected limb should not be used as the sole means of prophylaxis.
- In the overwhelming majority of trials that demonstrated efficacy, LDUH and LMWH were given 2 h preoperatively, although LMWH appears to be effective and is possibly associated with a lower risk of bleeding when the first dose is given 12 h preoperatively.[194,195]
- When using pharmacologic prophylaxis, we suggest following the manufacturer's recommendations for dosing. It may be prudent to consult with a pharmacist regarding dosing in

bariatric surgery patients and other patients who are obese who may require higher doses of LDUH or LMWH.

10.0 Recommendations for Research

Most of the recommendations in this guideline are based on low-quality evidence. Many older randomized controlled trials were limited by small samples, incomplete blinding, unclear concealment of treatment allocation, and measurement of surrogate outcomes. Future randomized trials should enroll representative samples (ideally in community settings) and be adequately powered to show differences in patient-important outcomes, including objectively confirmed, symptomatic VTE events and clearly defined bleeding complications. Reporting of bleeding outcomes in trials involving surgical patients should be standardized to include fatal bleeding, bleeding requiring reoperation, critical organ bleeding, and other consequential bleeding as recommended by the Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis.[196-198]

One high-priority target for randomized controlled trials is a comparison of pharmacologic prophylaxis (preferably with LMWH) with mechanical prophylaxis (preferably with IPC) in nonorthopedic surgical patients at moderate risk for VTE. Other priorities include a trial of IPC plus pharmacologic prophylaxis vs pharmacologic prophylaxis alone in patients at high risk for VTE and a trial of retrievable IVC filter placement vs no IVC filter placement in high-VTE-risk patients who are not candidates for pharmacologic prophylaxis.

The VTE risk assessment models cited in this article have important limitations. Rigorously developed and extensively validated models of VTE risk in well-defined surgical populations are urgently needed. There is a similar need for validated models that stratify the risk of bleeding complications in specific groups of surgical patients.

Relatively few studies have examined methods for implementing thromboprophylaxis guidelines in hospital settings. Although passive dissemination alone appears to be inadequate, the relative effectiveness of electronic reminders, clinical champions, audit and feedback, and decision support requires further study.[199]

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Dr Garcia: contributed as deputy editor.
Dr Wren: contributed as frontline clinician.
Dr Karanicolas: contributed as panelist.
Dr Arcelus: contributed as panelist.
Dr Heit: contributed as panelist.
Dr Samama: contributed as panelist.
Financial/nonfinancial disclosures: The authors of this guideline provided detailed conflict of interest information related to each individual recommendation made in this article. A grid of these disclosures is available online at http://chestjournal.chestpubs.org/content/141/2_suppl/e227S/suppl/DC1. In summary, the authors have reported to *CHEST* the following conflicts of interest: Dr Arcelus participated as an invited speaker in three lectures in Australia in March 2010 sponsored by Sanofi-Aventis LLC. Dr Samama reports serving as co-investigator for two observational studies of VTE prophylaxis in surgical patients with cancer, sponsored by Sanofi-Aventis. Dr Samama has also received consulting honoraria from companies that manufacture hemostatic agents (LFB, Octapharma, CSL, and Behring) and from companies that manufacture anticoagulants (Boehringer Ingelheim, Bayer, and Daichii Sankyo), though most of the funds have gone to his institution. Dr Samama's travel expenses to two recent conferences were paid by Bayer. Drs Gould, Garcia, Heit, Karanicolas, and Wren have reported that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.
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CHEST Online Data Supplement

Prevention of VTE in Nonorthopedic Surgical Patients

Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Michael K. Gould, MD, FCCP; David A. Garcia, MD; Sherry M. Wren, MD; Paul J. Karanicolas, MD, PhD; Juan I. Arcelus, MD, PhD; John A. Heit, MD; and Charles M. Samama, MD, PhD, FCCP

Appendix S1

In this section, we provide additional details about selected trials of thromboprophylaxis and studies of baseline risk.

1.0 Randomized Controlled Trials in General and Abdominal-Pelvic Surgery

1.1 Low-Dose Unfractionated Heparin vs No Prophylaxis

The International Multicentre Trial (IMT) was an open-label study of prophylaxis in 4,121 adults who underwent major elective surgery at one of 28 centers in Europe, Australia, and South Africa in the early 1970s.[1] Participants were randomly assigned to receive either no prophylaxis or low-dose unfractionated heparin (LDUH) 5,000 units, with the first dose given 2 h before surgery and subsequent doses administered every 8 h for 7 days. In this study, LDUH prophylaxis was associated with statistically significant reductions in autopsy-confirmed fatal pulmonary embolism (PE) (87%), clinically suspected DVT (51%), clinically suspected and objectively confirmed DVT (65%), DVT detected by fibrinogen leg scanning (69%), and proximal DVT detected by fibrinogen uptake testing (89%). Wound hematoma and excessive intraoperative bleeding were more commonly noted in the LDUH group, but risks of fatal bleeding and red cell transfusion were similar.

1.2 Low-Molecular-Weight Heparin vs No Prophylaxis

A large, randomized, blinded, placebo-controlled, Italian multicenter study examined prophylaxis with the low-molecular-weight heparin (LMWH) CY216 (nadroparin) given once daily (first dose given 2 h before surgery) in patients undergoing abdominal (65%), thoracic (10%), pelvic (2%), or other surgery.[2,3] In this study, treatment with nadroparin reduced all-cause mortality by 56% and vascular mortality by 75%. However, reductions in clinically symptomatic, nonfatal DVT (0.33; 95% CI, 0.09-1.23) and fatal PE (0.50; 95% CI, 0.12-2.08) were neither confirmed nor excluded.

1.3 Aspirin vs No Prophylaxis

Data from studies of VTE prophylaxis with relatively high doses of aspirin and other antiplatelet drugs have been summarized in a meta-analysis by the Antiplatelet Trialists Collaborative.[4] In its subgroup analysis of studies performed in general surgery patients, any antiplatelet therapy reduced the risk of asymptomatic distal or proximal DVT (compared with no treatment or other treatment) by 37% in 22 trials (risk ratio [RR], 0.63; 95% CI, 0.47-0.79) accompanied by a 71% reduction in the risk of clinical PE in 26 trials (RR, 0.29; 95% CI, 0.01-0.57) and a 39% increase in the risk of bleeding requiring reoperation, hematoma formation, or wound infection in 25 trials (RR, 1.39; 95% CI, 1.12-1.74). Similarly, in a subgroup analysis of studies comparing aspirin prophylaxis alone to no prophylaxis in either general or orthopedic surgery, the risk of asymptomatic DVT was reduced by 23% in 10 trials (RR, 0.77; 95% CI, 0.57-0.97) accompanied by a 67% reduction in clinical PE in 21 trials (RR, 0.33; 95% CI, 0.03-0.63) and an 87% increase in the need for blood transfusion in 45 trials (RR, 1.87; 95% CI, 1.00-3.50).

Our reanalysis of data from the eight studies of general or abdominal surgery patients in which aspirin alone was compared with no prophylaxis showed

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that aspirin reduced the risk of asymptomatic distal or proximal DVT by 48%, proximal DVT by 59%, and PE by 57%, although there was mild to moderate heterogeneity in results across studies for each of these outcomes (Figs S12-S23). Differences in the risks of symptomatic DVT (RR, 0.90; 95% CI, 0.46-1.75) and death from any cause were neither confirmed nor excluded. In the two studies that reported bleeding complications, the risk of bleeding was 61% greater among those who received aspirin. Important limitations of these studies include unclear concealment of allocation sequence in seven studies, exclusion of patients after randomization in two studies, and unclear or absent blinding in two studies; inconsistency across studies for VTE outcomes; and imprecision in the relative risk of bleeding complications. In addition, six studies used fibrinogen uptake scanning for surveillance of asymptomatic DVT.

2.0 Uncontrolled and Nonrandomized Studies in Bariatric Surgery

2.1 Low-Dose Unfractionated Heparin

Several uncontrolled studies reported patient-important outcomes among bariatric surgery patients treated with LDUH (Table S6).[5-12] Typical daily doses ranged between 10,000 and 15,000 units, and many patients received adjunctive prophylaxis with elastic stockings (ES), intermittent pneumatic compression (IPC), and inferior vena cava (IVC) filters. Across studies, the risk of PE ranged from 0% to 0.85% (median, 0.24%), and the risk of major bleeding complications varied from 0% to 2.4% (median, 1.2%).

2.2 Standard- vs High-Dose LMWH

Three studies compared standard doses of LMWH with a higher dose of the same LMWH preparation and reported patient-important outcomes in bariatric surgery patients, including one randomized controlled trial and two nonrandomized controlled trials.[13-15] A small, open-label randomized controlled trial compared nadroparin 5,700 International Units/d with nadroparin 9,500 International Units/d in 60 patients undergoing Roux-en-Y gastric bypass.[13] There were no symptomatic or asymptomatic VTE events in either group, but there were two major bleeding complications in the high-dose group and no bleeding complications in the usual-dose group. In another prospective study of 40 patients who underwent laparoscopic gastric bypass or banding and received either enoxaparin 40 mg/d or enoxaparin 60 mg/d, there were no symptomatic VTE events in either group.[15] After the third dose of enoxaparin, 44% of patients in the low-dose group but none in the high-dose group had serum anti-Xa levels below the authors' therapeutic range. However, supratherapeutic levels were seen in 57% of patients in the high-dose group. Finally, in a retrospective analysis of 481 consecutive patients undergoing bariatric procedures, 92 patients received enoxaparin 30 mg bid, and 389 patients received 40 mg bid. There were five (5.4%) symptomatic VTE events in the low-dose group and two (0.6%) symptomatic VTE events in the high-dose group along with one major bleeding complication in each group.

The relationship between BMI and anti-Xa levels following administration of LMWH is uncertain, with at least one study showing a strong negative correlation[16] and another showing no correlation.[17] A small, open-label randomized controlled trial measured anti-Xa levels in 66 bariatric surgery patients, including 36 patients who were assigned to receive standard doses of parnaparin (median, 4,250 International Units) and 30 who received higher doses (median, 6,400 International Units), both for 7 to 11 days beginning 12 h before surgery.[18] In this study, 98% of those in low-dose group were within the therapeutic range, whereas 63% of those in the high-dose group were supratherapeutic. However, another nonrandomized study found therapeutic anti-Xa levels after the third dose of enoxaparin in 42% of the high-dose group (40 mg bid) but in only 9% of the lower-dose group (30 mg bid).[19]

2.3 LMWH vs LDUH

In a nonrandomized prospective comparison of patients undergoing laparoscopic gastric bypass, 238 received enoxaparin 40 mg bid preoperatively and until discharge, whereas 238 patients received LDUH 5,000 units tid preoperatively and until discharge.[20] All patients were treated with sequential compression devices and early ambulation. There was one PE in the LDUH group. Fourteen patients (6%) in the enoxaparin group required postoperative transfusions compared with three (1%) in the heparin group ($P = .01$). Four patients (1.7%) in the enoxaparin cohort required reexploration for bleeding compared with none in the LDUH cohort.

2.4 Extended- vs Limited-Duration LMWH

In another prospective cohort study of 308 bariatric surgery patients, 90% of whom underwent laparoscopic Roux-en-Y gastric bypass, all patients received enoxaparin 30 mg bid until discharge, whereas 176 patients also received a 10-day course of enoxaparin 40 mg once daily at home after discharge.[21] The risk of VTE was lower (0%) in the extended-duration group than in the limited-duration group (4.5%), and two-thirds of VTE events occurred after discharge in patients who had negative findings on

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ultrasound at the time of discharge. Bleeding complications were similar in the two groups.

3.0 Randomized Controlled Trials in Cardiac Surgery

We identified two randomized controlled trials of VTE prophylaxis in cardiac surgery patients. An unblinded trial in 330 patients undergoing coronary artery bypass graft (CABG) surgery compared ES alone with ES plus IPC.[22] Asymptomatic proximal DVT was seen in five of 164 (3.0%) patients in the combination therapy group and six of 166 (3.6%) patients who received ES alone, and there was one PE in each group, including one fatal PE in the combination group.

Another large, unblinded trial compared LDUH plus IPC with LDUH alone in patients who underwent cardiac surgery at a single center over a period of 10 years.[23] In this study, clinically suspected, objectively confirmed PE was observed in 21 of 1,355 (1.5%) patients in the combination group and 48 of 1,196 (4.0%) patients in the LDUH group.

4.0 Randomized Controlled Trials in Thoracic Surgery

In a small, double-blind randomized controlled trial, Cade et al[24] compared LDUH 5,000 units bid with LDUH 7,500 units bid in 100 patients undergoing diverse major thoracic procedures. DVT by daily fibrinogen uptake was seen in 16 of 49 (33%) patients in the low-dose group vs 11 of 51 (22%) patients in the higher-dose group, but most DVT were distal. Two episodes of popliteal DVT were seen in the low-dose group. Excessive postoperative bleeding was not observed in either group.

One other study compared fixed-dose with weight-adjusted dose nadroparin in 148 patients undergoing thoracic operations for cancer. In this unblinded study, there were no episodes of symptomatic VTE and no ultrasound evidence of asymptomatic DVT on postoperative day 8 in either group, but major bleeding was three times more frequent in the adjusted-dose group (9% vs 3%).[25]

5.0 Randomized Controlled Trials in Craniotomy Patients

A meta-analysis made several comparisons, including IPC vs no prophylaxis, LDUH vs no prophylaxis, LDUH vs LMWH, and IPC vs LMWH.[26] In two trials that compared IPC and no prophylaxis in mixed neurosurgery patients,[27,28] IPC reduced the risk of any DVT (including asymptomatic and distal DVT) by 59% and PE by 63%. However, in three studies that compared LDUH and no prophylaxis,[29-31] four studies that compared LDUH and LMWH[32-35] and two trials that compared IPC with LMWH,[36,37] differences in the risk of DVT or PE were neither documented nor excluded. In four studies that compared LMWH and nonpharmacologic management[36-39] and three studies that compared LDUH and nonpharmacologic management,[29,30,40] an increased risk of intracranial hemorrhage was neither confirmed nor excluded.

6.0 Randomized Controlled Trials in Major Trauma

Numerous different interventions were studied: three compared mechanical methods with no prophylaxis,[41-43] one compared different mechanical methods,[44] one compared LDUH with IPC and no prophylaxis,[43] two compared LMWH with mechanical methods,[45,46] two compared LMWH with LDUH,[47,48] one compared combination therapy with LDUH and continuous passive motion against LDUH alone,[49] one compared fixed-dose with adjusted-dose LMWH, and one compared early initiation of enoxaparin (within 24-48 h after injury) with foot pump plus delayed initiation of enoxaparin (5 d after injury).[50] There were no randomized trials of IVC filter placement or ultrasound surveillance.

In one study that compared IPC with no prophylaxis in patients with orthopedic injuries,[42] there was a possible 65% reduction in proximal DVT, but results failed to demonstrate or exclude an effect on symptomatic VTE (Figs S52-S54). Pooled results from this study and two others of mixed trauma surgical patients (one of which compared myostimulation to no prophylaxis) failed to demonstrate or exclude an effect on either outcome. An underpowered study of adult patients with trauma compared LDUH with no prophylaxis and similarly failed to demonstrate or exclude an effect on symptomatic VTE or proximal DVT.[43] In another study that compared foot pumps with IPC, the overall risk of proximal DVT was 20%, but results neither confirmed nor excluded a difference between the two treatment groups.[44] Pooled results from three studies that compared pharmacologic with mechanical prophylaxis did not confirm or exclude differences in symptomatic VTE or major bleeding, but there was an (imprecise) 89% reduction in the risk of proximal DVT (OR, 0.11; 95% CI, 0.01-0.92).

Three studies compared LMWH and LDUH in patients with moderate to severe trauma[47,48] or acute spinal cord injury.[51] Symptomatic VTE was uncommon, and differences between groups were neither confirmed nor excluded (Figs S52-S54). In one study, the

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risk of proximal DVT was 62% lower in the LMWH group, but the risk of major bleeding was more than five times higher.[48] Pooled results across these three studies and one other study that compared LDUH plus IPC with LMWH[52] failed to demonstrate or exclude an effect on major bleeding.

In another study performed in patients with orthopedic trauma, the risk of proximal DVT was 90% lower in those who received LDUH plus continuous passive motion compared with LDUH alone.[49] Finally, in a study of hospitalized patients with blunt skeletal trauma that compared early initiation of LMWH with delayed initiation plus use of a foot pump, results failed to demonstrate or exclude an effect on the risk of symptomatic VTE or major bleeding complications.[50]

In summary, low-quality but direct evidence from studies in patients with trauma suggests that the risk of asymptomatic proximal DVT is reduced by 89% with pharmacologic prophylaxis (compared with mechanical methods), by 58% with LMWH (compared with LDUH), and by 90% with combined LDUH plus continuous passive motion (compared with LDUH alone). However, pooled results from fixed-effects models failed to demonstrate or exclude a beneficial effect of any intervention on symptomatic VTE and major bleeding outcomes (Figs S52-S54).

7.0 Studies of Baseline Risk, Risk Factors, and Risk Stratification for VTE

7.1 Baseline Risk, Risk Factors, and Risk Stratification for VTE in General and Abdominal-Pelvic Surgical Patients

In a prospective registry of 2,373 consecutive patients who underwent abdominal, urologic, gynecologic, or thoracic surgery for cancer (82% of whom received prophylaxis, including LMWH in 74%), the overall risk of postoperative VTE was 2.1%, and VTE risk factors included age $\geq$ 60 years, prior VTE, anesthesia $\geq$ 2 h, and bed rest $\geq$ 4 days.[53] Similarly, in a retrospective review of 1,862 patients undergoing gynecologic surgery (all of whom received IPC prophylaxis), independent risk factors included age $>$ 60 years, prior VTE, and cancer.[54] The risk of VTE was more than five times higher among patients who had two or three risk factors (3.2%) than it was among those who had zero or one risk factor (0.6%).[55]

A study of 2,208 patients who underwent radical or partial nephrectomy reported that the incidence of VTE was 1.5% (95% CI, 1.1%-2.1%), despite use of mechanical prophylaxis with IPC in all patients. In bivariate analyses, greater intraoperative blood loss, longer hospital stay, and a history of arrhythmia were associated with an increased risk of VTE.

In another retrospective study of 8,216 general, vascular, and urologic surgery patients, most of whom received either mechanical or pharmacologic prophylaxis, the observed risk of clinically suspected and objectively confirmed VTE up to 30 days after surgery was 1.4%.[56] Independent risk factors for VTE included sepsis, pregnancy or postpartum state, central venous access, malignancy, prior VTE, and (especially) inpatient hospital stay longer than 2 days. Another retrospective review of abdominal surgical discharges from a national managed-care database reported that only 2% of 131,181 patients received pharmacologic prophylaxis; symptomatic VTE occurred in 3% of patients.[57] VTE risk factors in this study included older age, male sex, longer length of hospital stay, and higher Charlson comorbidity score.

In a large prospective study of 75,771 veterans who underwent one of eight common surgical procedures, the 30-day risk of VTE was 0.7%; use of VTE prophylaxis was not described.[58] In this study, most of the moderate to strong independent risk factors for VTE were surgical complications, including urinary tract infection, acute renal insufficiency, postoperative transfusion, perioperative myocardial infarction, and pneumonia. Somewhat surprisingly, hemodialysis, diabetes, and higher preoperative albumin levels were associated with a reduced risk of VTE.

Finally, among 183,069 patients from the Patient Safety in Surgery Study who underwent general, vascular, and thoracic procedures at one of 128 Veterans Administration medical centers or 14 private-sector hospitals between 2002 and 2004, the 30-day risk of VTE was only 0.6%; once again, use of prophylaxis was not reported.[59] Independent predictors of VTE included patient factors (female sex, higher American Society of Anesthesiologists class, ventilator dependence, preoperative dyspnea, disseminated cancer, chemotherapy within 30 days, and $>$4 units red cell transfusion) and preoperative laboratory values (albumin level, $<$3.5 mg/dL; bilirubin level, $>$1.0 mg/dL; sodium level, $>$145 mmol/L; hematocrit level, $<$38%).

7.2 Baseline Risk, Risk Factors, and Risk Stratification for VTE in Vascular Surgery

In studies of patients who underwent open-abdominal vascular procedures for aneurysm or occlusive arterial disease,[60-66] the median risk of asymptomatic proximal DVT was 3% (range, 0%-9%), and the median risk of symptomatic VTE was 0.5% (range, 0%-1.5%), despite documented use of pharmacologic or combined prophylaxis in two of the studies. In one study of patients who did not receive prophylaxis, asymptomatic

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proximal DVT was reported in 9% of patients who underwent abdominal procedures. In three small studies of patients undergoing endovascular aortic repair, the median risk of symptomatic VTE was 1%.[66-68] The risk was 0% in a study that used combination prophylaxis in all patients,[66] whereas it was 6% in a study in which < 20% of patients received LDUH.[68]

In studies of patients who underwent peripheral vascular surgery, the median risk of asymptomatic proximal DVT was 6% (range, 0%-23%), although there were no symptomatic episodes of DVT or PE.[63,65,69-72] Data from seven studies of patients undergoing lower-extremity amputation suggest that the risks of asymptomatic proximal DVT (median, 14.3%) and symptomatic VTE (median, 2.9%) are moderate in this group, although some of these studies were performed > 30 years ago.[63,73-78]

Risk factors for VTE in vascular surgery are not well established, although several studies have attempted to identify risk factors with little success. In a prospective study of 193 patients undergoing abdominal aortic aneurysm repair, there was no association between VTE and numerous potential risk factors, including age, BMI, cardiovascular disease, prior VTE, aneurysm diameter, preoperative use of antiplatelet or anticoagulant therapy, duration of surgery, or laboratory variables.[66] In another prospective study of 72 patients undergoing lower-extremity amputation, there was no association between VTE and age, diabetes, malignancy, prior amputation, lower-extremity vascular surgery, or dialysis.[76] In yet another prospective study of 50 consecutive aortic surgery patients, there was no association between VTE and clamp time, intraoperative heparin dose, blood loss, transfusion, or use of protamine.[79]

7.3 Baseline Risk, Risk Factors, and Risk Stratification for VTE in Cardiac Surgery

Relatively precise but possibly dated estimates of the risk of VTE following cardiac surgery come from the California Patient Discharge Data Set for the years 1992 to 1996.[80] In this large data set, the risks of VTE in the 91 days after CABG and valve replacement were 1.1% and 0.5%, respectively. Similarly, in an analysis of registry data from New York State in 1999, 133 of 16,325 (0.8%) patients were readmitted for VTE within 30 days following CABG.[81] Unfortunately, information about use of prophylaxis was not reported in either of these studies.

Additional, albeit conflicting, evidence comes from three even older retrospective studies.[82-84] One reported a relatively high risk of PE (3.2%), whereas the others reported lower risks of VTE (0.7%) and PE (0.6%). More recently, in a smaller prospective study of 270 CABG surgery patients, the risk of (asymptomatic) proximal DVT was 2.6%, despite the use of prophylaxis in almost 90% of the patients. Another recent study of both cardiac and thoracic surgery patients reported that the risk of VTE was reduced after implementation of a locally developed VTE prevention guideline (0% vs 0.4%).

7.4 Baseline Risk, Risk Factors, and Risk Stratification for VTE in Thoracic Surgery

Several small, prospective studies measured asymptomatic VTE by using fibrinogen uptake,[85,86] compression ultrasound,[87,88] or CT pulmonary angiography.[89] Two early studies in thoracic surgery used fibrinogen uptake to identify DVT in 51% of patients and proximal DVT in 9%.[85,86] In two other studies, the risk of asymptomatic DVT by ultrasound was 4% to 19%.[87,88] A more recent study identified PE by CT pulmonary angiography in seven patients (14%), but only two patients had symptoms.[89]

Other estimates of baseline VTE risk in thoracic surgery come from retrospective studies. These studies have the advantage of reporting clinically suspected rather than surveillance-detected events. In one retrospective study of 179 consecutive patients with stage I non-small cell lung cancer undergoing video-assisted thoracoscopic lobectomy, PE was observed in 1.1% of patients.[90] In another retrospective study of 149 patients undergoing thoracoscopic lobectomy, fatal PE occurred in one patient with a history of recurrent PE, despite use of full anticoagulation.[91] Two larger studies reported relatively high rates of PE. In one study of 693 thoracotomies for lung cancer, symptomatic VTE was observed in 1.7% of patients, including PE in 1.3% despite routine use of prophylaxis with LDUH or LMWH. In another analysis of 1,735 lung resections for malignancy, autopsy-confirmed fatal PE occurred in 1.2% of patients despite ongoing heparin prophylaxis in most of them.[92] Another study of 706 thoracic surgery patients reported objectively confirmed PE in 20 of 344 patients (7%) who did not receive any prophylaxis but zero of 362 (0%) who wore IPC.[93] Finally, the 91-day risk of clinically detected VTE for almost 13,000 patients undergoing major lung resection for malignant disease was 1.6% in the California Patient Discharge Data Set.[80]

7.5 Baseline Risk, Risk Factors, and Risk Stratification for VTE in Spinal Surgery

Several uncontrolled studies, most of them prospective, have examined the risk of VTE in spinal

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surgery patients. In a recent systematic review of 14 studies, the pooled risks of DVT and PE (variably defined) were 1.09% (95% CI, 0.54%-1.64%) and 0.06% (95% CI, 0.01%-0.12%), respectively.[94] In this analysis, operative level and underlying diagnosis did not appear to influence the risk of DVT. Another systematic review reported that the pooled risk of DVT in the absence of pharmacologic prophylaxis appeared to be slightly higher among patients who underwent surgery for trauma (6.0%) or deformity (5.3%) than for those who underwent surgery for degenerative conditions (2.3%).[95] Most studies were limited by small samples and the measurement of asymptomatic DVT detected by ultrasound surveillance, although one large retrospective study reported a very low risk of symptomatic DVT (0.05%) among 1,919 patients who received heparin prophylaxis and did not undergo surveillance.[96] An older review of 15 studies calculated that the mean risk of VTE across studies was 7.1%, but this varied from 0% to 56% and depended on the definition of VTE and methods used for prophylaxis and surveillance.[97]

Risk factors for VTE in spinal surgery patients likely include a combined anterior-posterior approach, multiple operative levels, and patient-related factors such as older age, prior VTE, and malignancy.[98,99] In a population-based, retrospective analysis of discharges from California hospitals in 1992 to 1996, the risk of symptomatic VTE within 91 days of surgery was 0.5% (95% CI, 0.4%-0.5%) among 34,355 patients who underwent spinal surgery for nonmalignant disease, whereas the risk of VTE was 2.0% (95% CI, 1.4%-2.6%) among 1,545 patients who underwent spinal surgery for malignant disease.[80]

7.6 Baseline Risk, Risk Factors, and Risk Stratification for VTE in Trauma

A prospective study of 716 consecutive patients with major trauma and an injury severity score ≥ 9, of whom none received any form of prophylaxis, demonstrated a substantial risk of asymptomatic VTE.[100] In this study, 58% of 349 patients who underwent venography had evidence of DVT 14 to 21 days after admission, 18% had proximal DVT, and 2.5% had symptomatic VTE before venography could be performed. Independent risk factors for VTE included older age, blood transfusion, surgery, femoral or tibial fracture, and spinal cord injury.

A retrospective analysis of $>10{,}000$ admissions to the trauma service at a single institution between 1995 and 2000 reported that the risk of symptomatic DVT, PE, and any VTE was $\sim 0.6\%$, 0.3%, and 2.8%, respectively.[101] During the study period, most patients received at least one form of prophylaxis in accordance with an evolving protocol, and ultrasound surveillance was used selectively in $\sim 10\%$ of patients.

A study from roughly the same time period that included 450,000 patients who received care at one of 131 trauma centers that contributed data to the National Trauma Data Bank of the American College of Surgeons[102] reported risks of VTE and PE of 0.36% and 0.13%, respectively, although neither outcome was specifically defined and use of prophylaxis was not reported. Independent risk factors for VTE, in order of increasing magnitude, included head injury with acute injury score ≥ 3, major operation, lower-extremity fracture with acute injury score ≥ 3, age ≥ 40 years, venous injury, and (especially) >3 days of mechanical ventilation. In a more recent retrospective study of nosocomial complications in 525 adult patients with trauma at a single tertiary-care center, the risk of clinically diagnosed VTE was 7.6%.[103] In a more narrowly defined sample of 978 patients who underwent spinal surgery for trauma over the 25-year period ending in 2004, symptomatic, objectively confirmed VTE was observed in 22 (2.2%) despite near-universal use of prophylaxis, including pharmacologic or combined prophylaxis in 97% of patients.[104]

Observational studies have addressed the risk of symptomatic VTE in patients with acute spinal cord injury.[105] In a cohort of 716 patients with major trauma who received neither pharmacologic nor mechanical prophylaxis, spinal cord injury was the strongest of five independent risk factors for DVT.[100] In this study, 21 of 26 (81%) patients with acute spinal cord injury had venographic evidence of DVT, although most events were probably asymptomatic. In a retrospective review of 16,240 patients with acute spinal cord injury in California from 1991 to 2001, the 91-day incidence of symptomatic VTE was 5.4%.[106] The risk remains elevated from the time of acute injury through rehabilitation. Among patients with spinal cord injury from the National Spinal Cord Injury Statistical Center database, the risk of symptomatic VTE during the rehabilitation phase decreased from 15.1% in 1996 to 6.1% in 1998.[107]

In the large retrospective study by Jones et al,[106] risk factors for VTE included male sex, black race, complete paraplegia (vs tetraplegia), and multiple comorbidities. In another study of 243 patients with acute spinal cord injury who were admitted for rehabilitation, 51 developed objectively confirmed VTE. Groups at highest risk included men and women aged >35 years with cancer, women between the ages of 36 and 58 years without cancer, and cancer-free men with flaccid paralysis.[108] A systematic review of observational studies in trauma reported that spinal fractures and spinal cord injury were associated with an increased risk of VTE, whereas sex, long-bone fracture, pelvic fracture, and head injury were not.[109]

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More recent evidence suggests that the risk of VTE may indeed be elevated following head injury.[110] In a retrospective study of 500 patients with traumatic brain injury, the risk of clinically suspected, objectively confirmed VTE was 3.8%, despite the use of combined pharmacologic and mechanical prophylaxis in all patients.[111] In another study of > 18,000 patients with trauma, the risk of DVT was especially high in those with traumatic brain injury and appeared to increase as the time to initiation of prophylaxis increased.[112] More specifically, among patients with brain injury, the risk of clinically suspected and objectively confirmed DVT increased from 3.6% among 2,098 patients who received pharmacologic prophylaxis within 24 h, to 15.4% among 1,307 patients in whom prophylaxis was withheld for 48 h. Among patients without brain injury, the risks were 0.7% and 5.2% for the early and delayed prophylaxis groups, respectively. Likewise, another study of patients with hemorrhagic shock following injury reported that although the risk of objectively confirmed VTE over up to 28 days was 5% among those who received prophylaxis within 48 h of injury, it was three times higher among those who did not receive prophylaxis until after day 4.[113]

8.0 Studies of Baseline Risk, Risk Factors, and Risk Stratification for Major Bleeding

8.1 Baseline Risk, Risk Factors, and Risk Stratification for Major Bleeding in Abdominal and Pelvic Surgery

In a nonrandomized comparison of LMWH plus ES vs ES alone in patients undergoing gastric cancer surgery,[114] the risk of postoperative bleeding was not associated with age, sex, BMI, comorbidity, history of abdominal surgery, combined resection, open vs laparoscopic procedure, type of lymph node dissection, or operating time. In a study of 362 patients who underwent pancreaticoduodenecomy,[115] risk factors for major bleeding included sepsis, pancreatic leak, and sentinel bleed. In a study of 1,759 patients who underwent partial hepatic resection at a tertiary-care center, independent risk factors for red cell transfusion included the number of segments resected, concomitant extrahepatic organ resection, primary liver malignancy, and lower preoperative hemoglobin levels and platelet counts.[116]

In a secondary analysis of data from a large randomized controlled trial of LMWH vs LDUH in abdominal surgery,[117] independent predictors of major bleeding (defined as that requiring discontinuation of prophylaxis, transfusion, reoperation, or evacuation or that attributed to the study drug) included male sex, preoperative hemoglobin level < 13 g/dL, malignancy, and complex surgery defined as two or more procedures, difficult dissection, or more than one anastamosis.[118] The magnitude of increased risk was greatest for malignancy (OR, 1.8) and complex surgery (OR, 3.5). Across this and 35 other trials of LMWH vs LDUH prophylaxis,[119] the pooled risk of major bleeding in the LDUH group was three times higher among patients undergoing surgery for cancer (8.1%) than those undergoing noncancer surgery (2.7%).

8.2 Baseline Risk, Risk Factors, and Risk Stratification for Major Bleeding in Vascular Surgery

An analysis of data from a registry of 4,587 patients who underwent carotid endarterectomy in northern New England from 2003 to 2008 suggested that the risk of bleeding requiring reoperation was lower among those who received protamine (0.6%) than those who did not (1.7%).[120] According to information from four statewide administrative databases for the years 1998 to 2003, bleeding complications (defined as anemia due to acute blood loss or postoperative hemorrhage, hematoma, or seroma) were less common following endovascular than open surgery for aortic aneurysm repair (8% vs 17.1%) and lower-extremity revascularization (7.3% vs 11.1%), but bleeding was more common following endovascular than open carotid surgery (5.3% vs 3.9%).[121]

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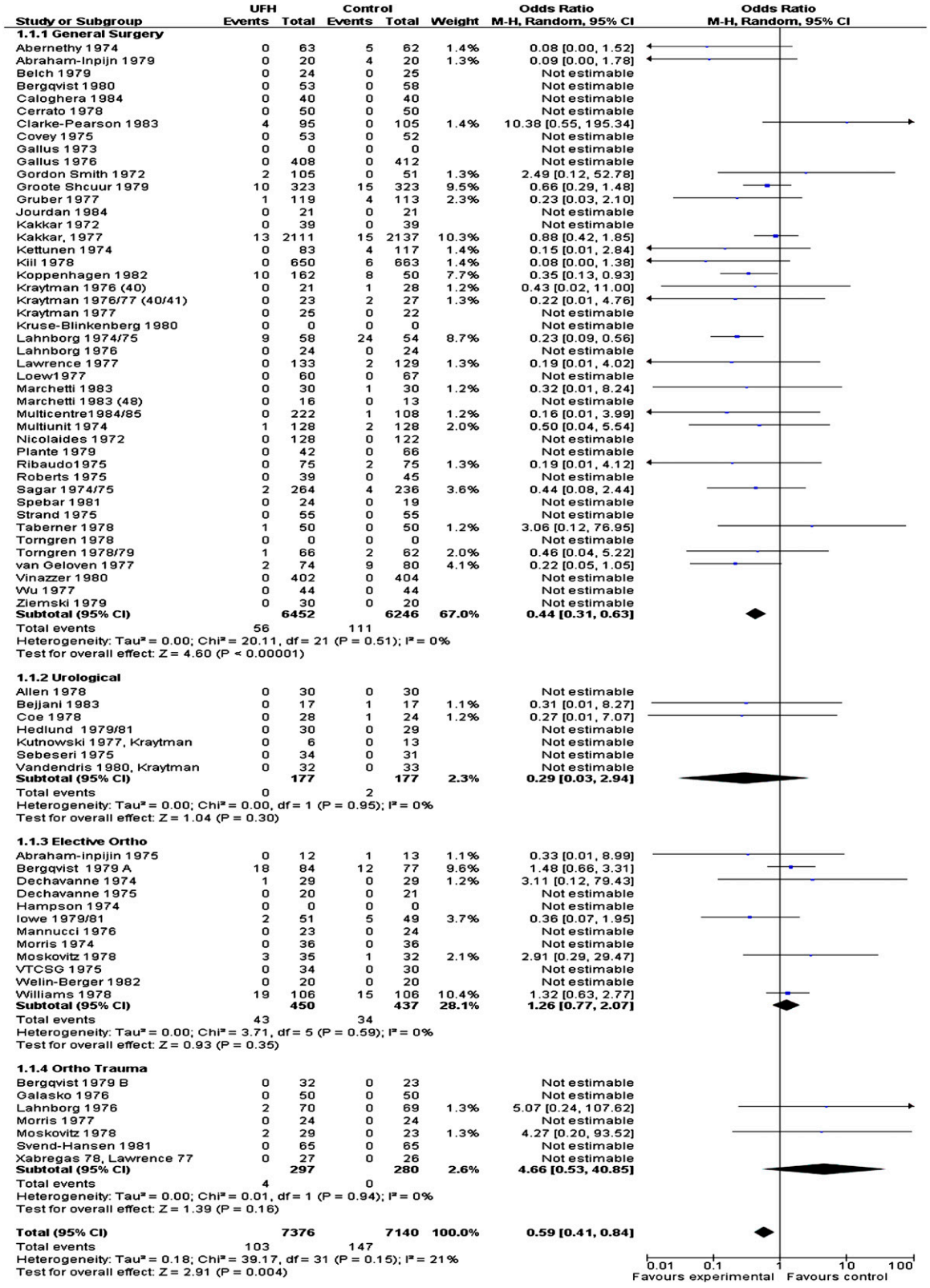


FIGURE S1. UFH vs no prophylaxis: nonfatal pulmonary embolism. *df* = degrees of freedom; M-H = Mantel-Haenszel; UFH = unfractionated heparin.

 DOI: 10.1378/chest.11-2287

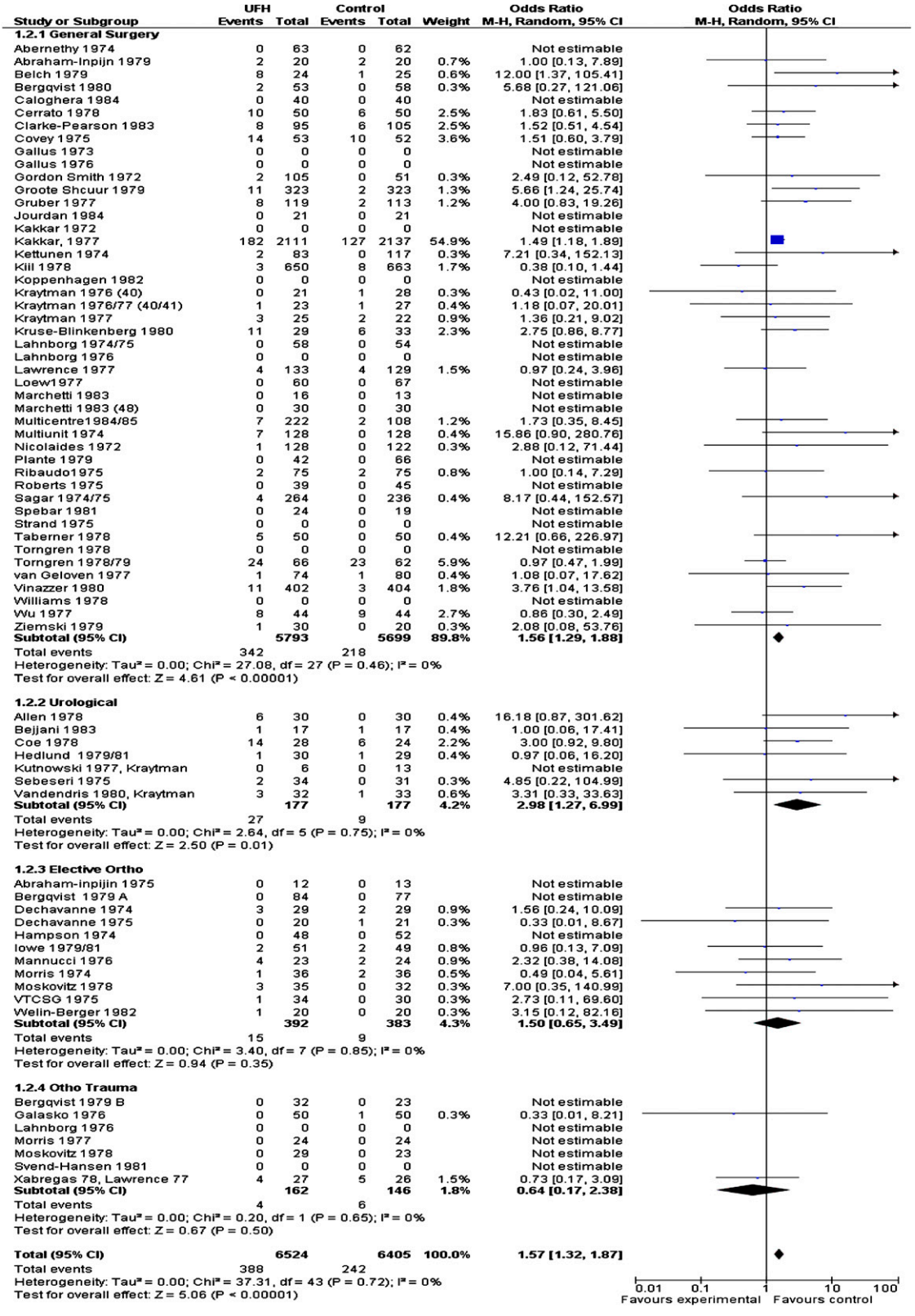


FIGURE S2. UFH vs no prophylaxis: nonfatal bleeding. See Figure S1 legend for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

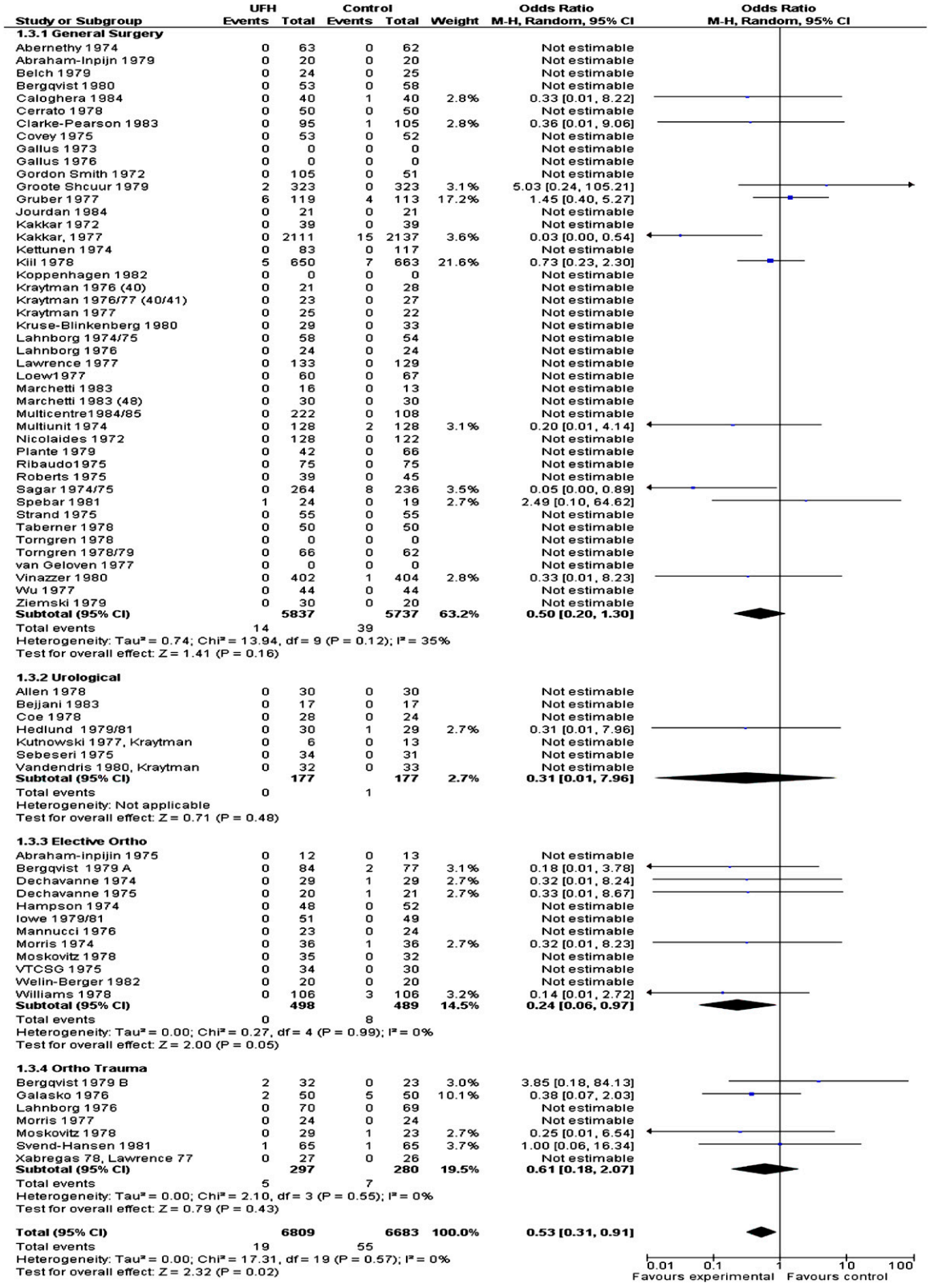


FIGURE S3. UFH vs no prophylaxis: fatal pulmonary embolism. See Figure S1 legend for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

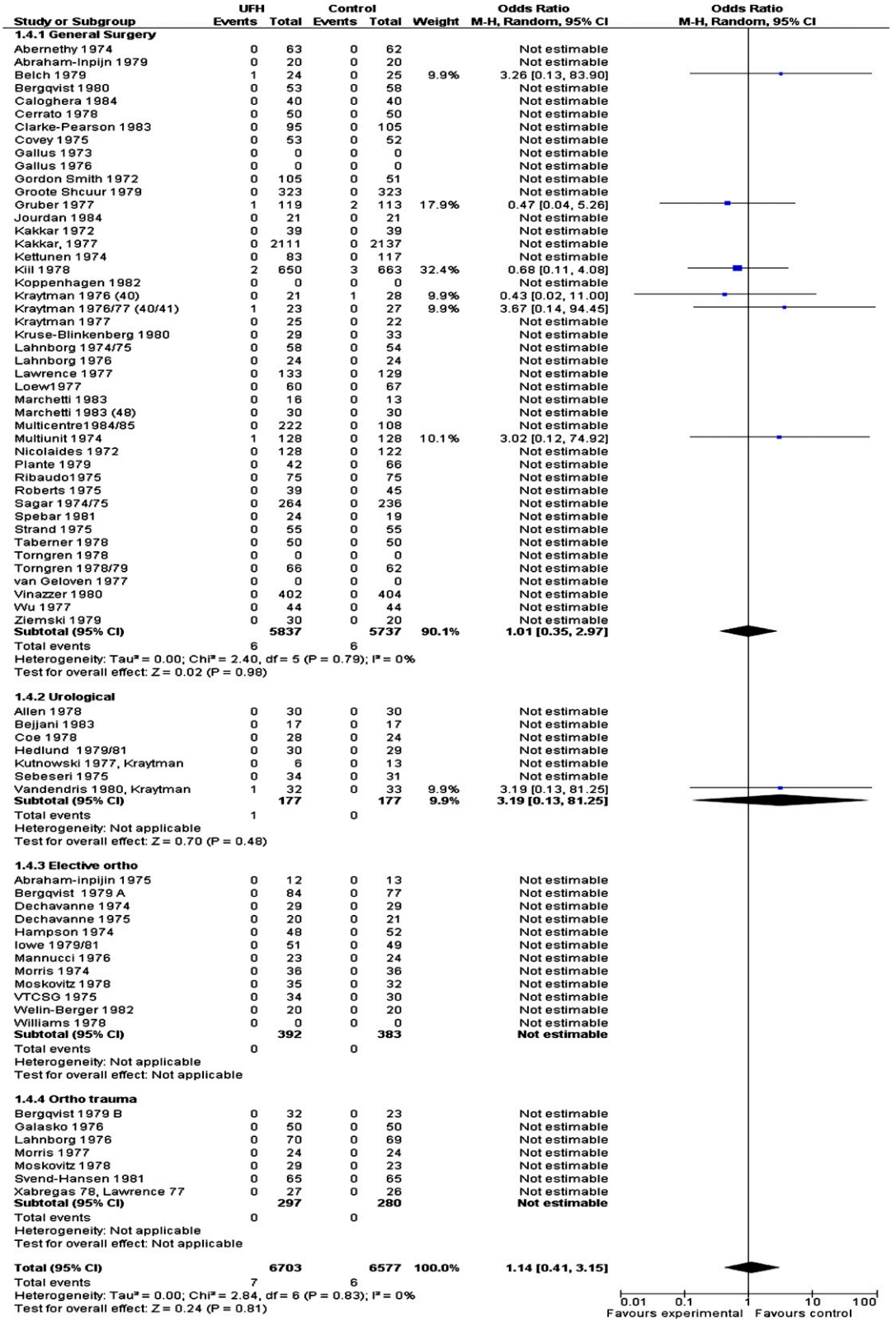


FIGURE S4. UFH vs no prophylaxis: fatal bleeding. See Figure S1 legend for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

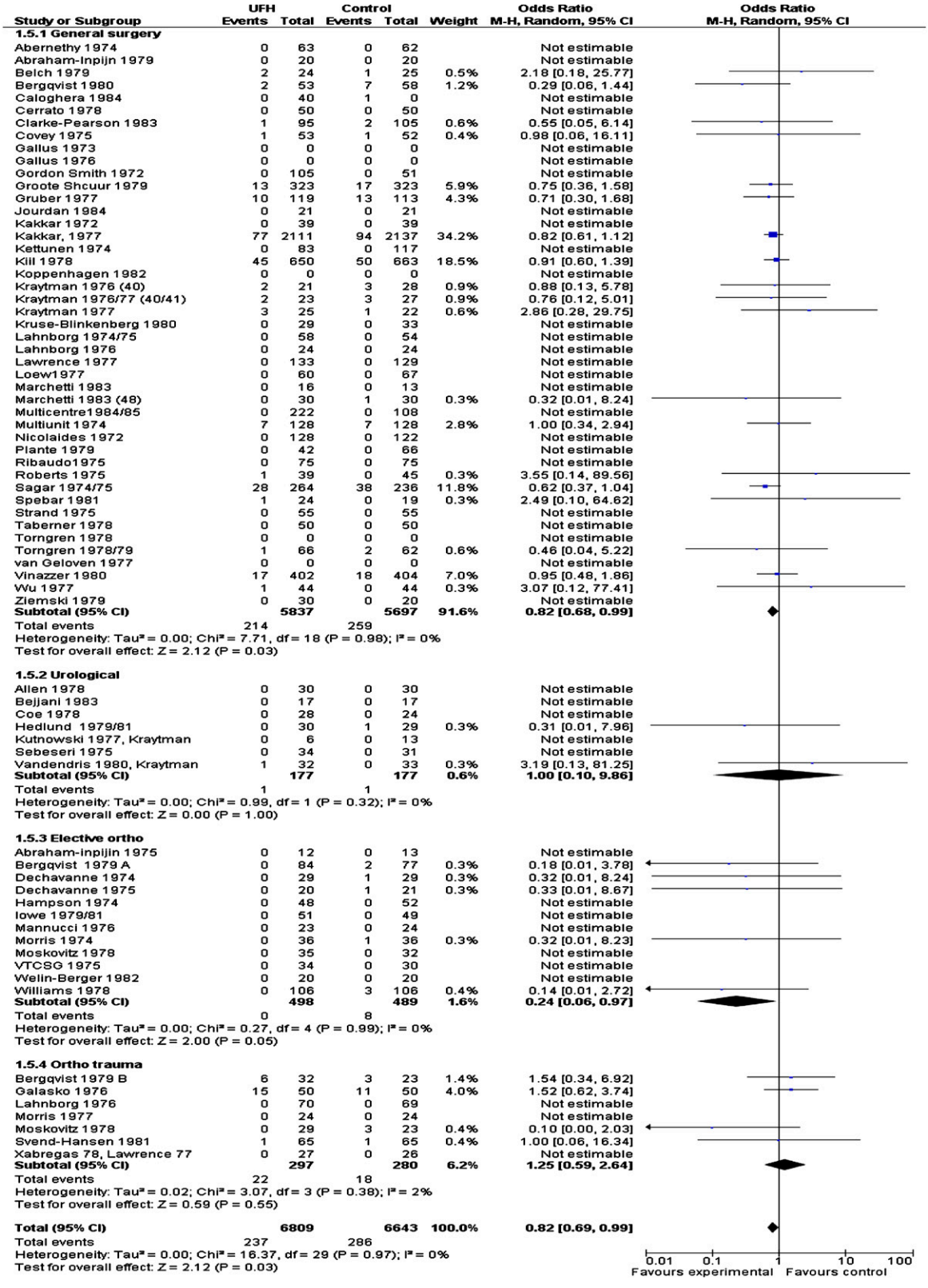


FIGURE S5. UFH vs no prophylaxis: Death from any cause. See Figure S1 legend for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

2.2 Non-fatal PE

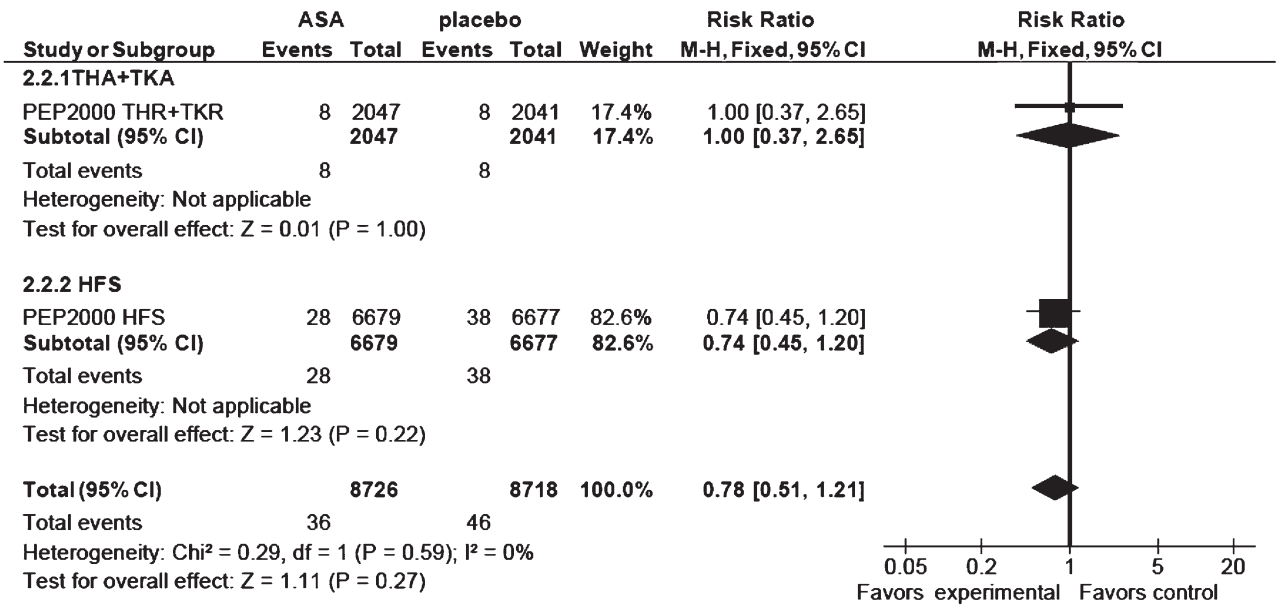


FIGURE S6. Low-dose ASA 160 mg vs placebo: nonfatal PE. ASA = aspirin; HFS = hip fracture surgery; PE = pulmonary embolism; PEP = Pulmonary Embolism Prevention trial; THR = total hip replacement; TKR = total knee replacement. See Figure S1 legend for expansion of other abbreviations.

2.3 Symptomatic DVT

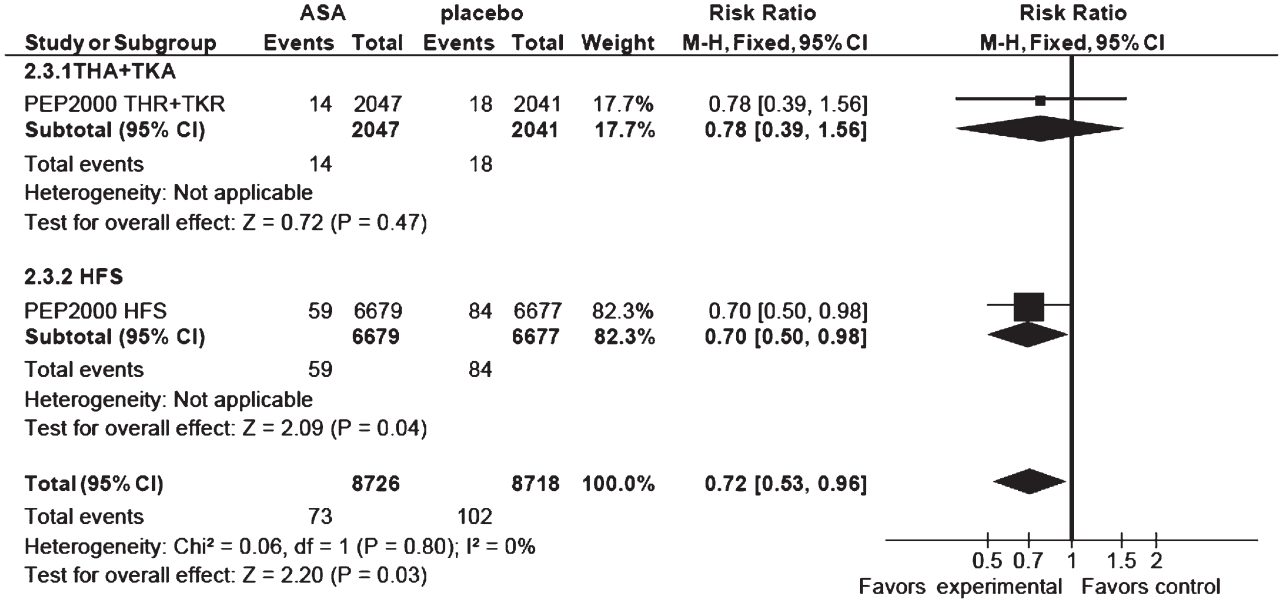


FIGURE S7. Low-dose ASA 160 mg vs placebo: symptomatic DVT. See Figure S1 and S6 legends for expansion of abbreviations.

 DOI: 10.1378/chest.11-2297

2.6 Bleeding req re-op

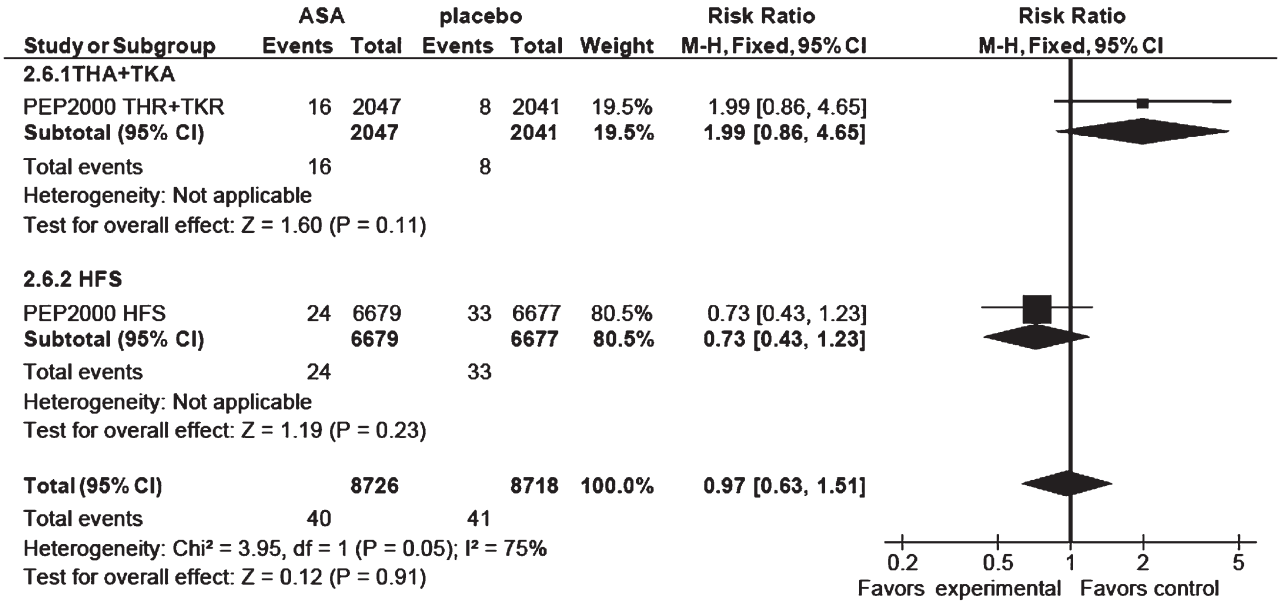


FIGURE S8. Low-dose ASA 160 mg vs placebo: bleeding requiring reoperation. See Figure S1 and S6 legends for expansion of abbreviations.

2.7 Major non-fatal bleeding

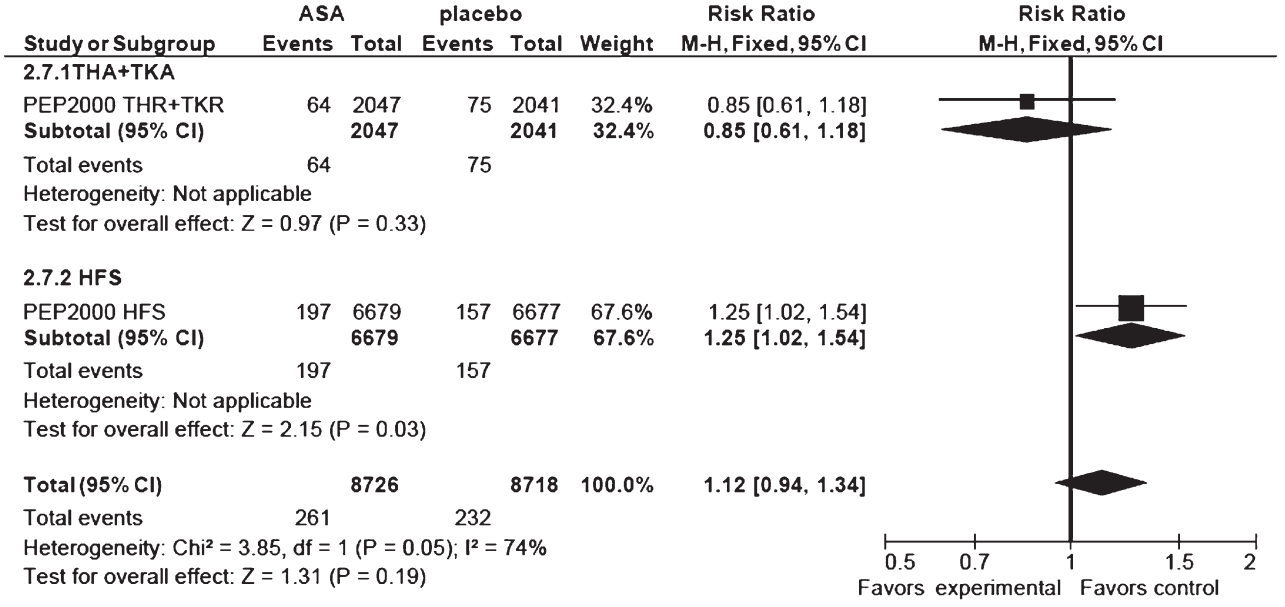


FIGURE S9. Low-dose ASA 160 mg vs placebo: major nonfatal bleeding. See Figure S1 and S6 legends for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

2.4 Non-fatal MI

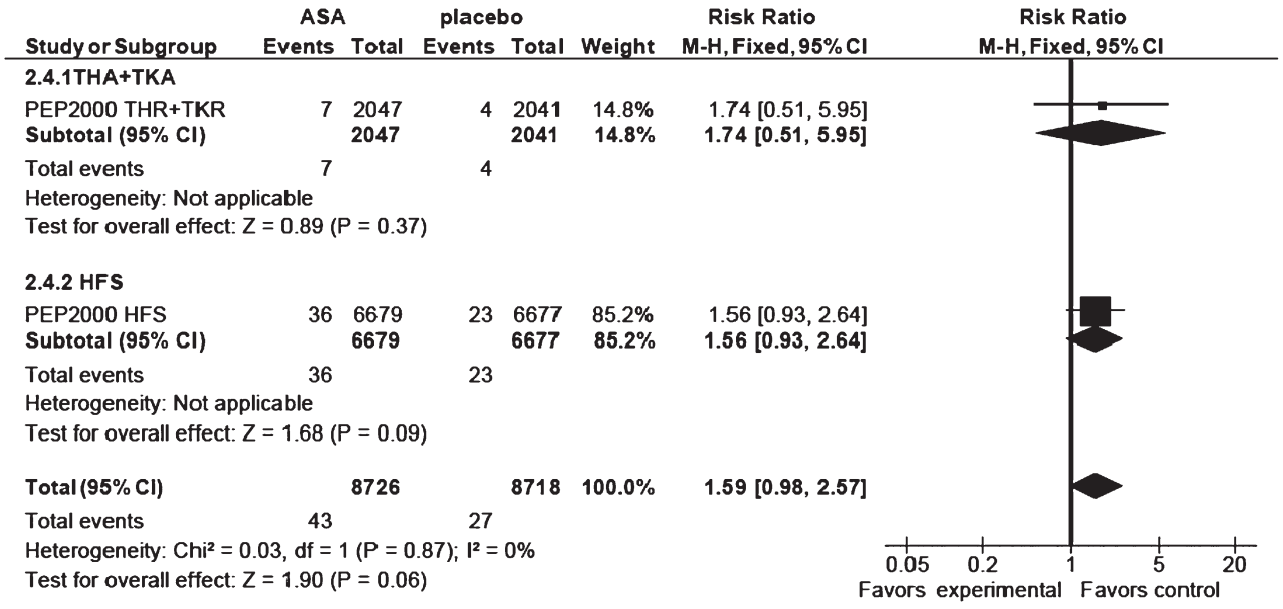


FIGURE S10. Low-dose ASA 160 mg vs placebo: nonfatal MI. MI = myocardial infarction. See Figure S1 and S6 legends for expansion of other abbreviations.

2.5 Total mortality

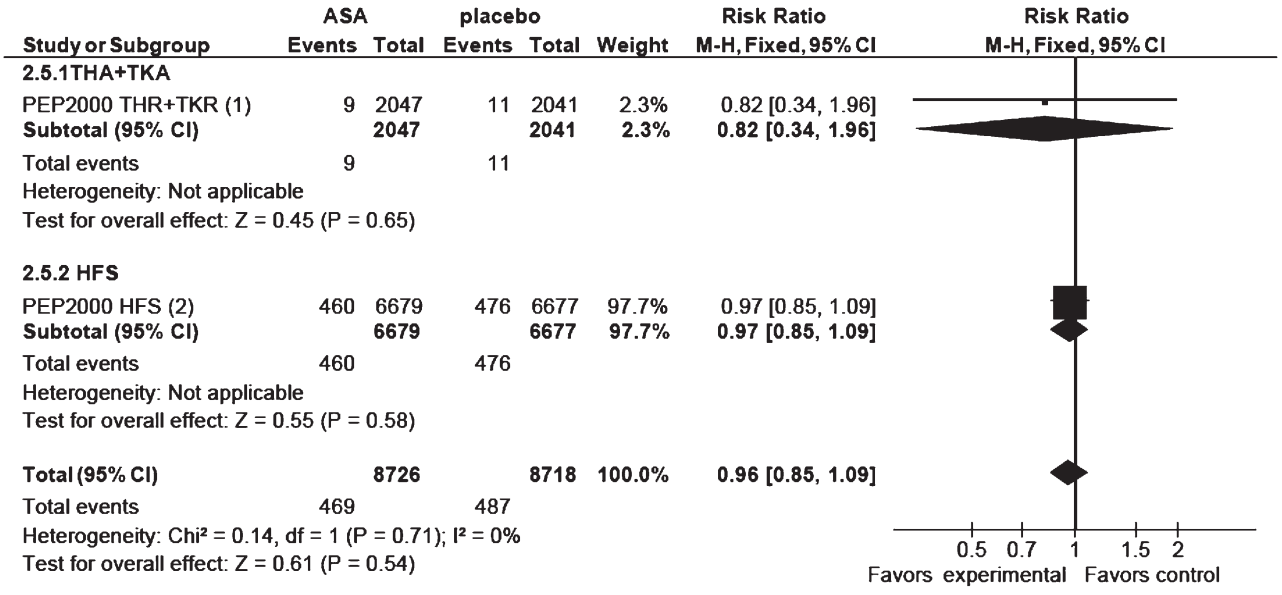


FIGURE S11. Low-dose ASA 160 mg vs placebo: total mortality. See Figure S1 and S6 legends for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

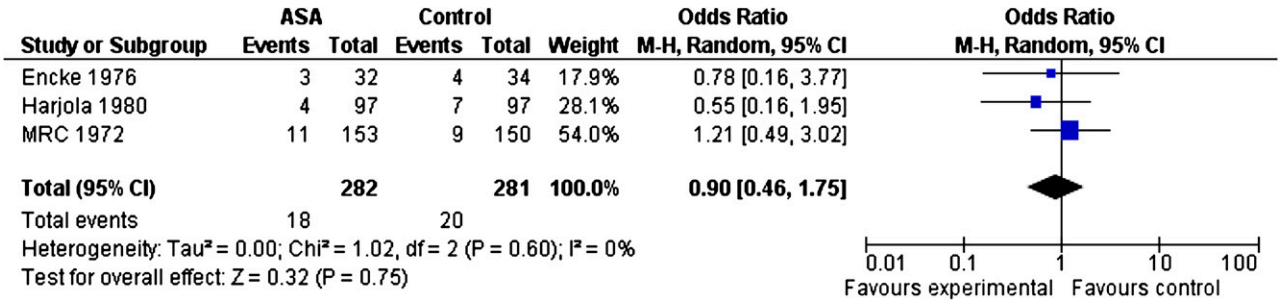


FIGURE S12. High-dose ASA vs no prophylaxis: symptomatic DVT. See Figure S1 and S6 legends for expansion of abbreviations.

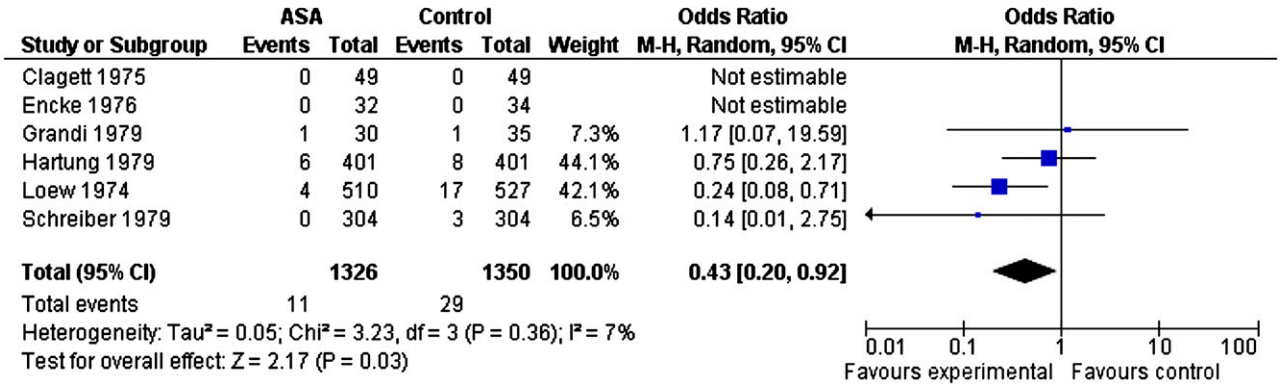


FIGURE S13. High-dose ASA vs no prophylaxis: pulmonary embolism. See Figure S1 and S6 legends for expansion of abbreviations.

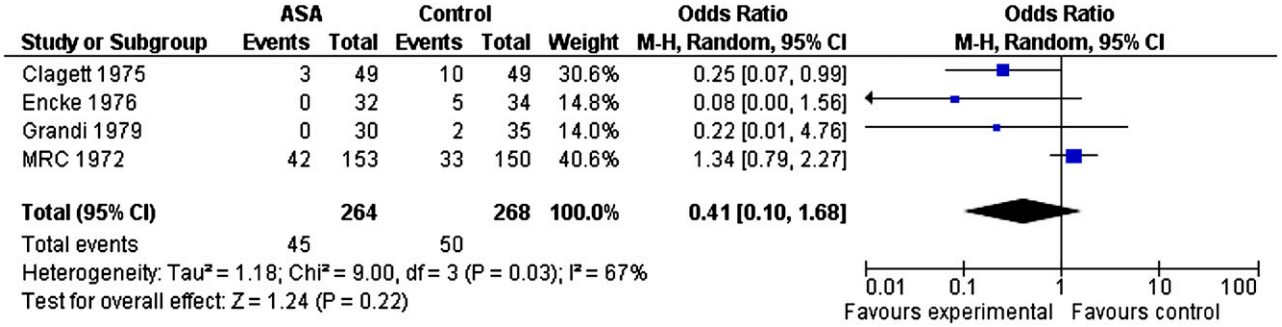


FIGURE S14. High-dose ASA vs no prophylaxis: proximal DVT. See Figure S1 and S6 legends for expansion of abbreviations.

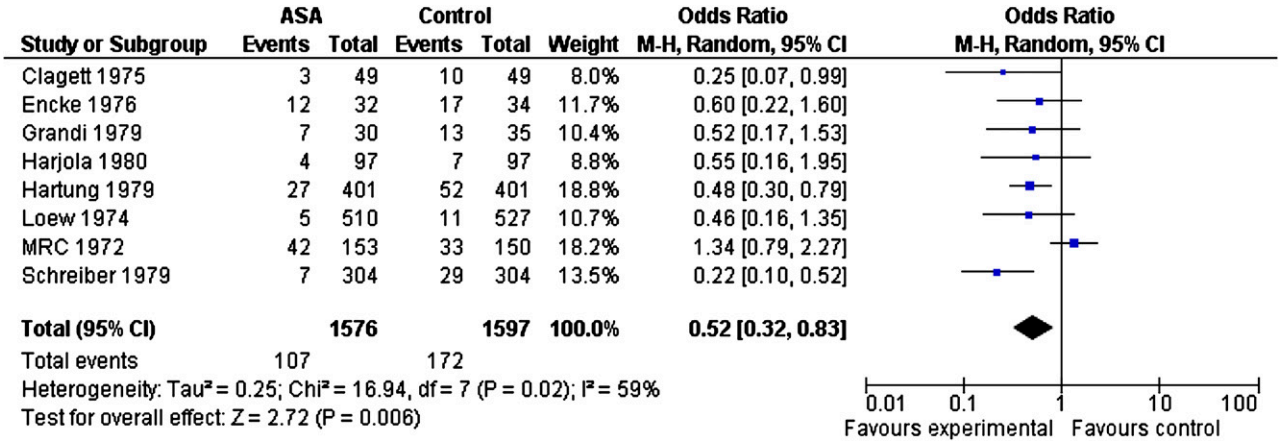


FIGURE S15. High-dose ASA vs no prophylaxis: any DVT. See Figure S1 and S6 legends for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

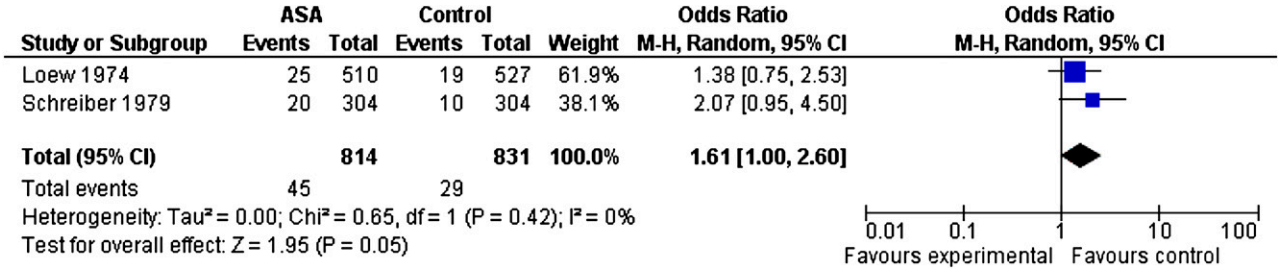


FIGURE S16. High-dose ASA vs no prophylaxis: bleeding (excessive intraoperative or other). See Figure S1 and S6 legends for expansion of abbreviations.

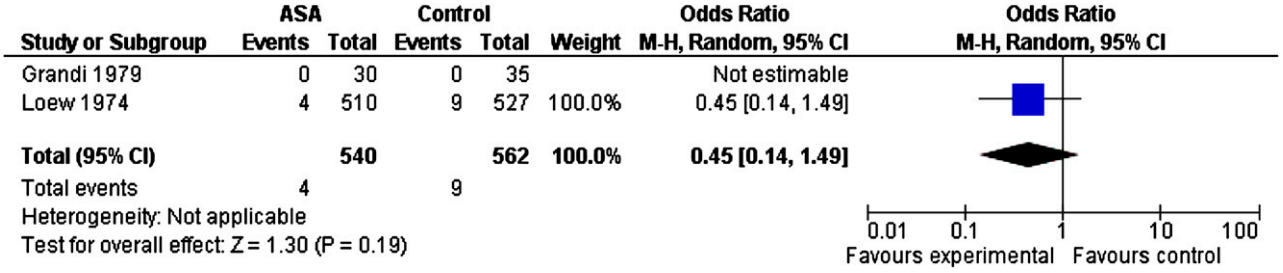


FIGURE S17. High-dose ASA vs no prophylaxis: death. See Figure S1 and S6 legends for expansion of abbreviations.

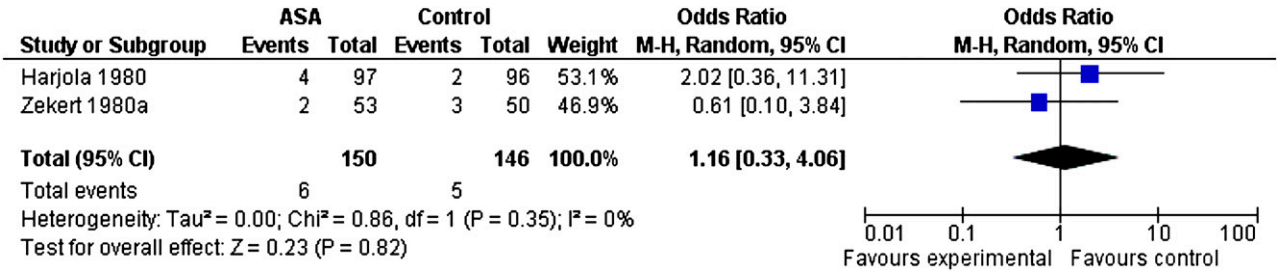


FIGURE S18. High-dose ASA vs other prophylaxis: symptomatic DVT. See Figure S1 and S6 legends for expansion of abbreviations.

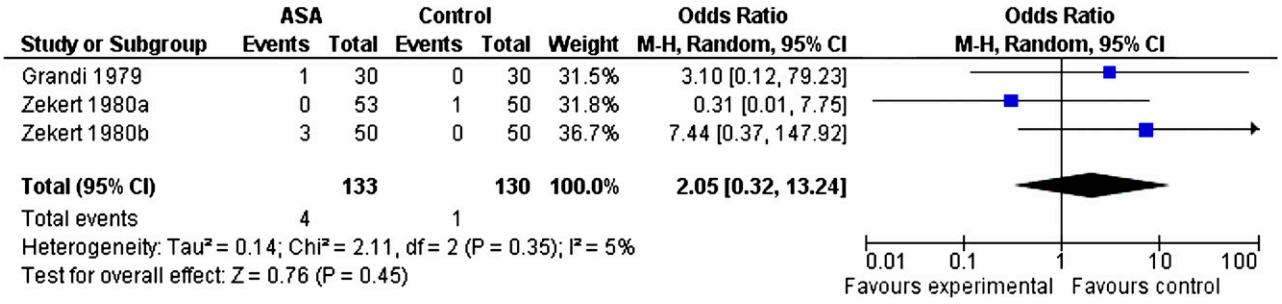


FIGURE S19. High-dose ASA vs other prophylaxis: pulmonary embolism. See Figure S1 and S6 legends for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

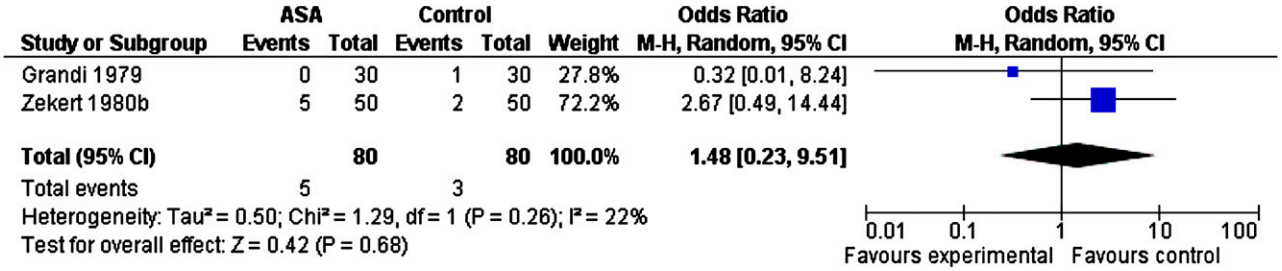


FIGURE S20. High-dose ASA vs other prophylaxis: proximal DVT. See Figure S1 and S6 legends for expansion of abbreviations.

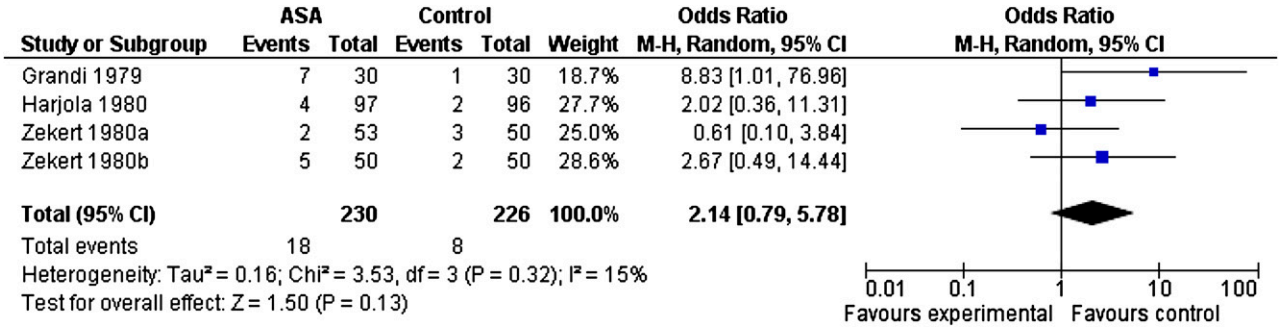


FIGURE S21. High-dose ASA vs other prophylaxis: any DVT. See Figure S1 and S6 legends for expansion of abbreviations.

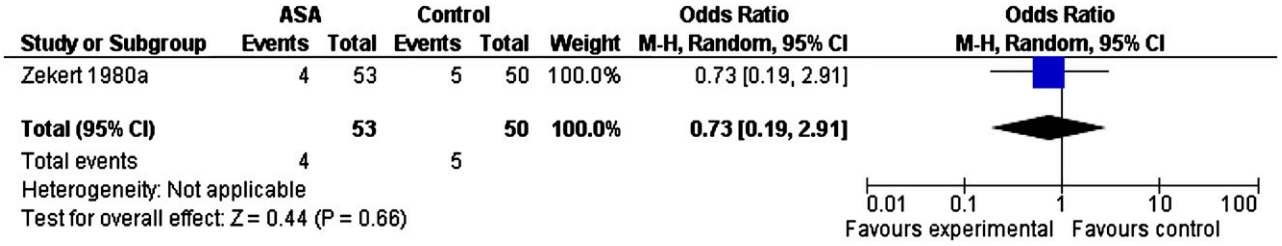


FIGURE S22. High-dose ASA vs other prophylaxis: major bleeding. See Figure S1 and S6 legends for expansion of abbreviations.

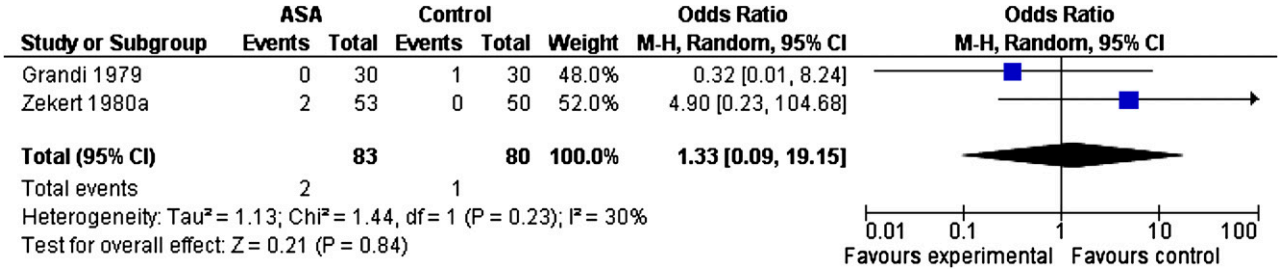


FIGURE S23. High-dose ASA vs other prophylaxis: death. See Figure S1 and S6 legends for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

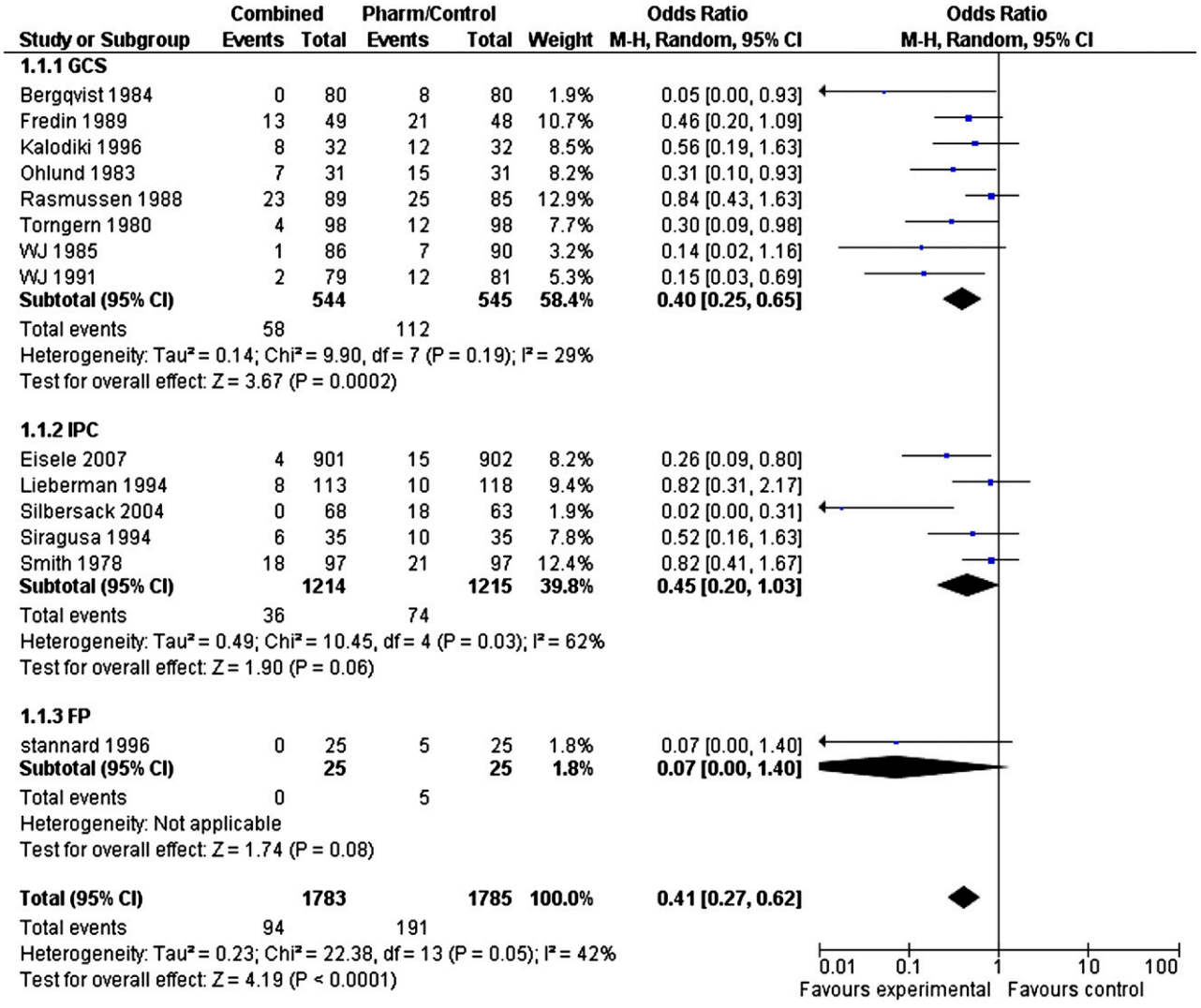


FIGURE S24. Combination vs pharmacologic prophylaxis: any DVT. Between-subgroup heterogeneity: $\chi^2 = 2.03$, $df = 2$, $P = .36$. FP = foot pump; GCS = graduated compression stockings; IPC = intermittent pneumatic compression. See Figure S1 legend for expansion of other abbreviation.

 DOI: 10.1378/chest.11-2287

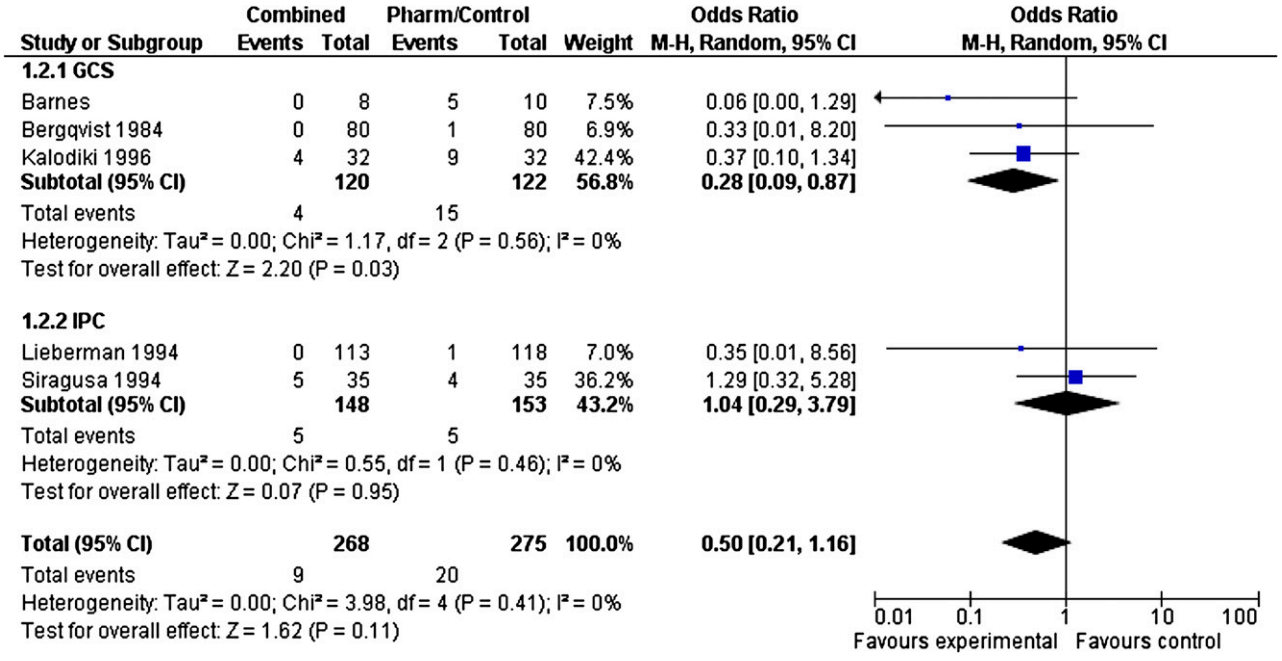


FIGURE S25. Combination vs pharmacologic prophylaxis: proximal DVT. Between-subgroup heterogeneity: $\chi^2 = 2.26$, $df = 1$, $P = .13$. See Figure S1 and S24 legends for expansion of abbreviations.

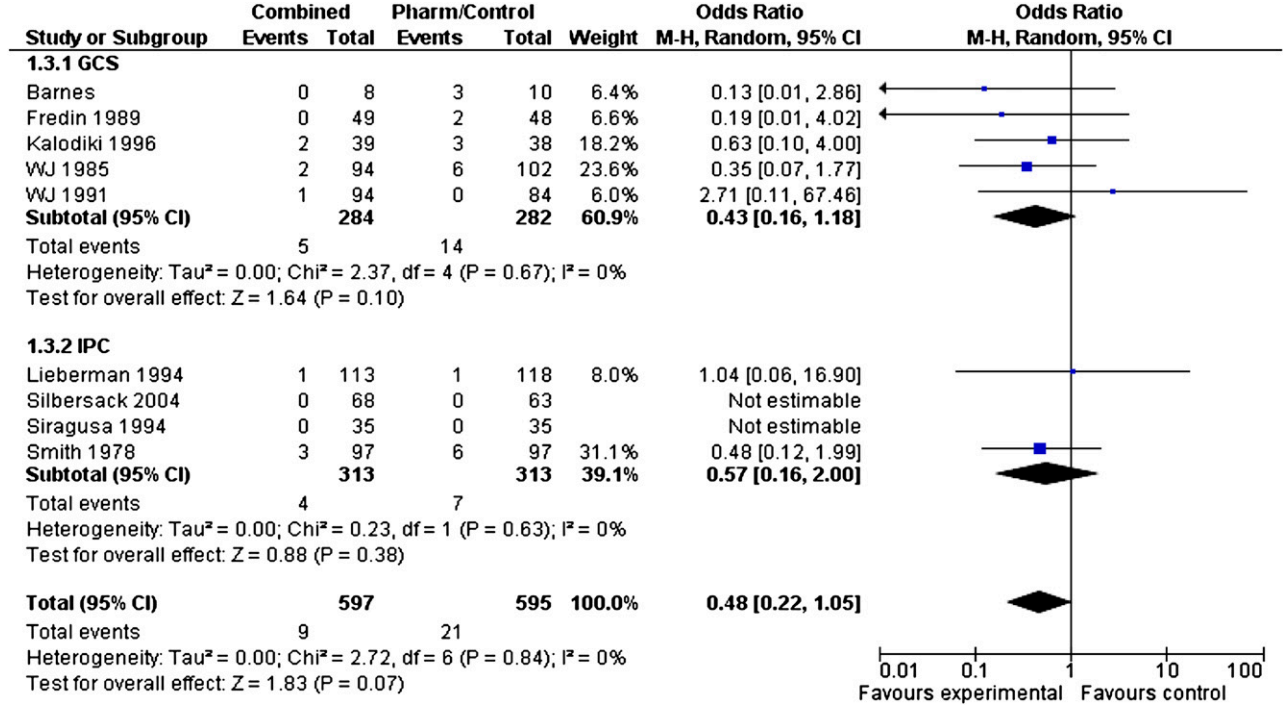


FIGURE S26. Combination vs pharmacologic prophylaxis: pulmonary embolism. Between-subgroup heterogeneity: $\chi^2 = 0.12$, $df = 1$, $P = .73$. See Figure S1 and S24 legends for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

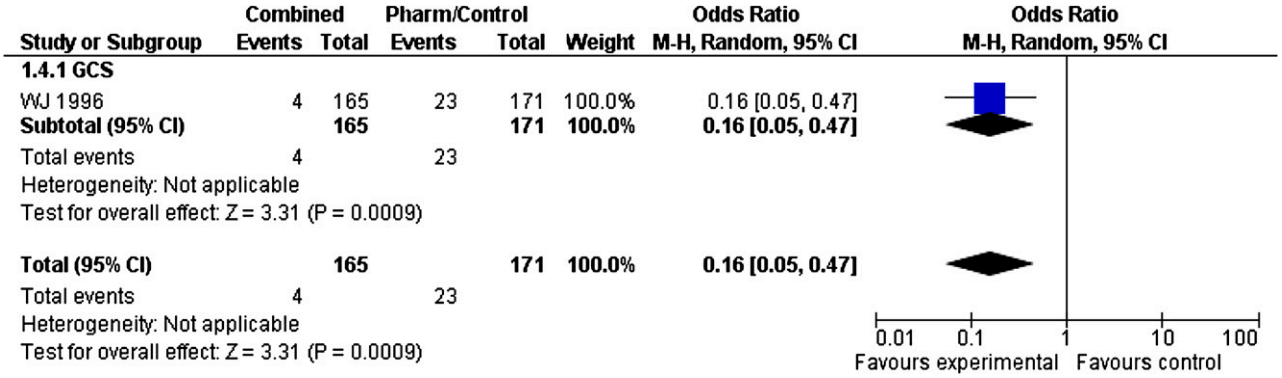


FIGURE S27. Combination vs pharmacologic prophylaxis: any VTE. See Figure S1 and S24 legends for expansion of abbreviations.

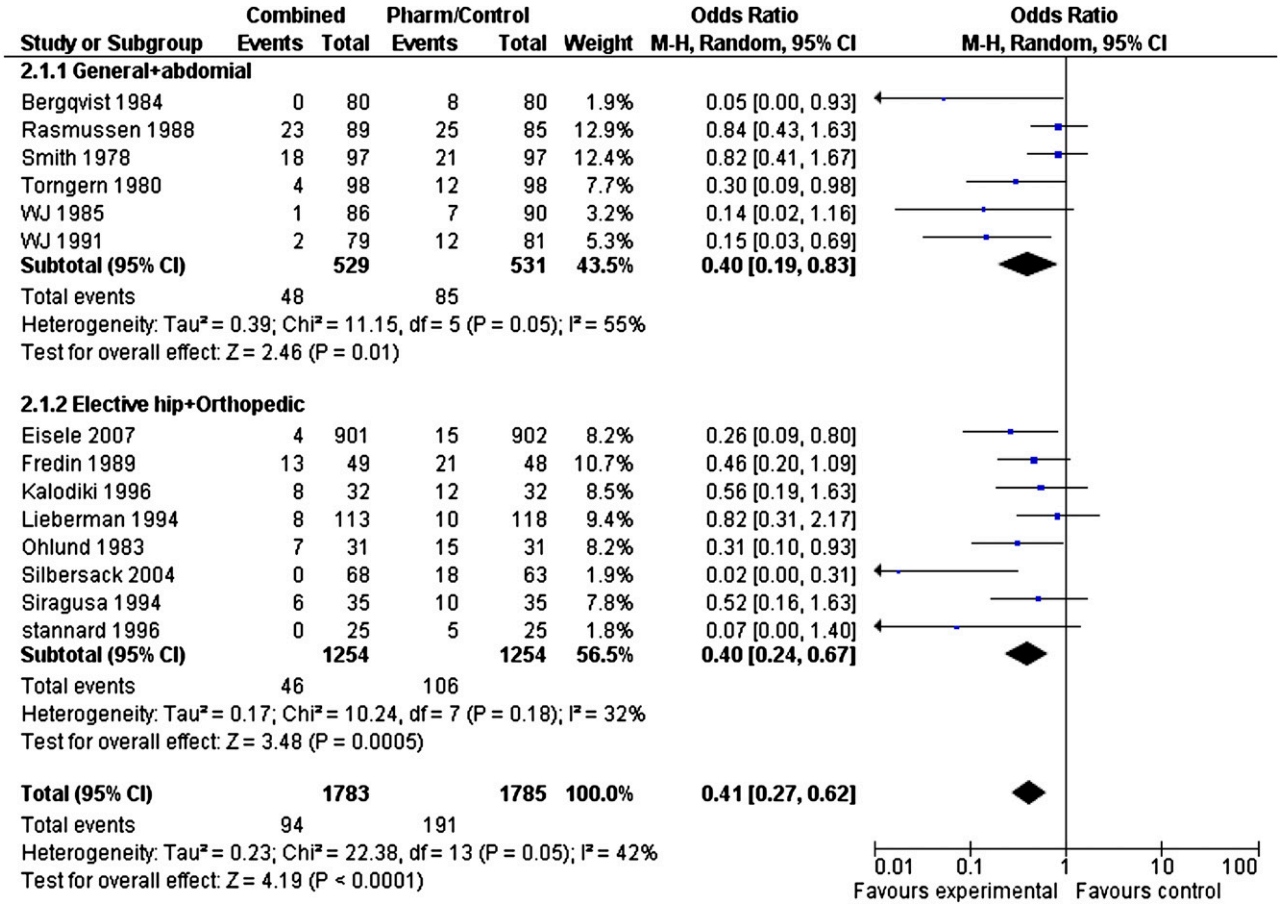


FIGURE S28. Combination vs pharmacologic prophylaxis: any DVT (stratified by surgical population). Between-subgroup heterogeneity: $\chi^2 = 0.99$, $df = 1$, $P = .32$. See Figure 1 legend for expansion of abbreviation.

 DOI: 10.1378/chest.11-2287

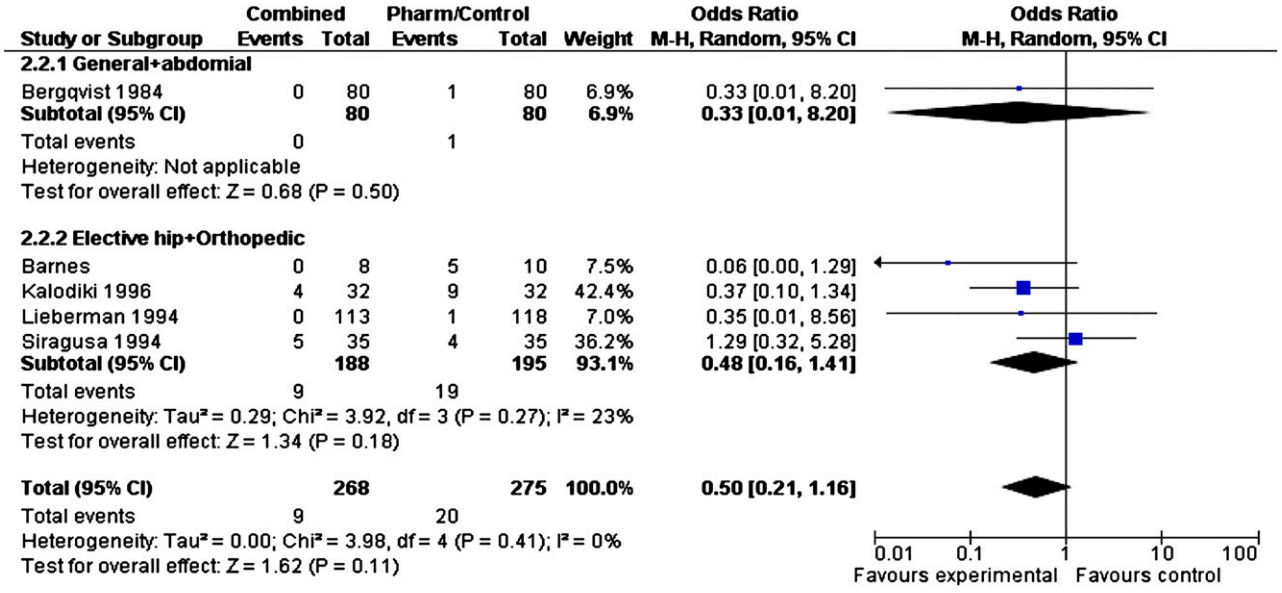


FIGURE S29. Combination vs pharmacologic prophylaxis: proximal DVT (stratified by surgical population). Between-subgroup heterogeneity: $\chi^2 = 0.06$, $df = 1$, $P = .81$. See Figure 1 legend for expansion of abbreviation.

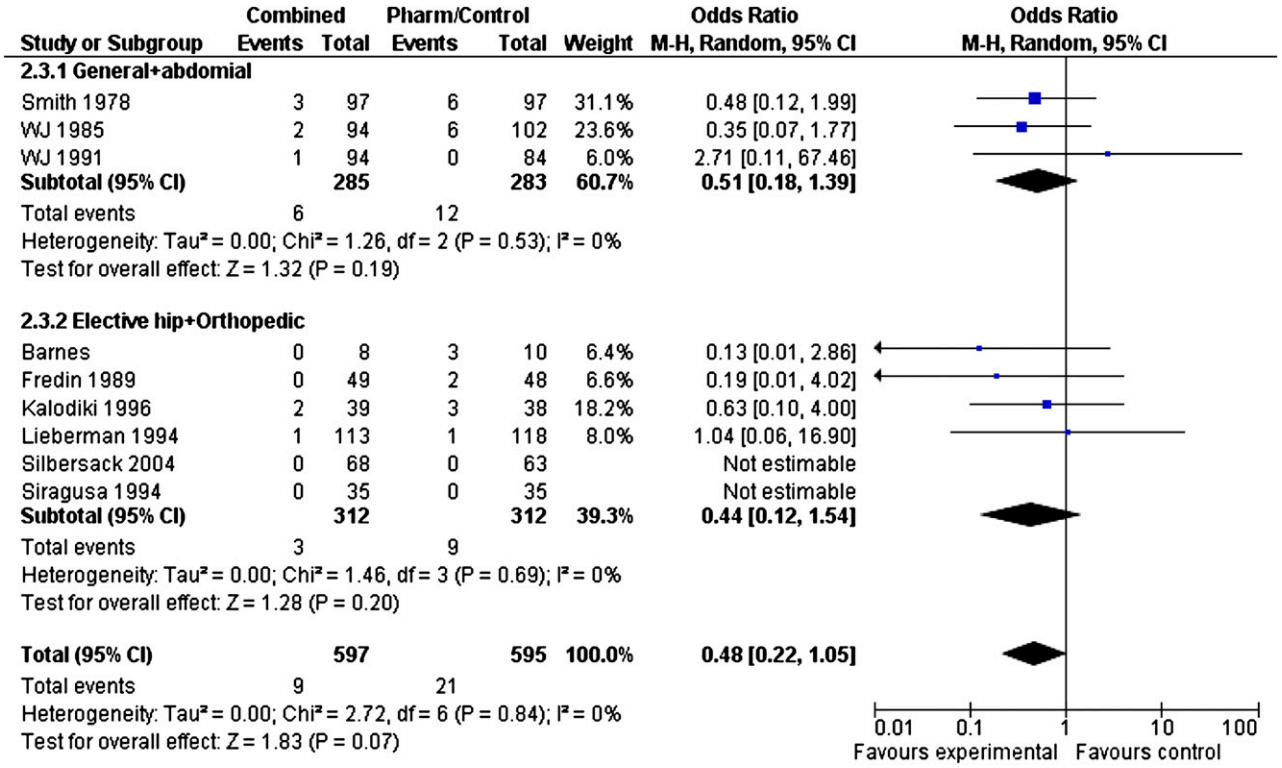


FIGURE S30. Combination vs pharmacologic prophylaxis: pulmonary embolism (stratified by surgical population). Between-subgroup heterogeneity: $\chi^2 = 0$, $df = 1$, $P = 1.00$. See Figure 1 legend for expansion of abbreviation.

 DOI: 10.1378/chest.11-2287

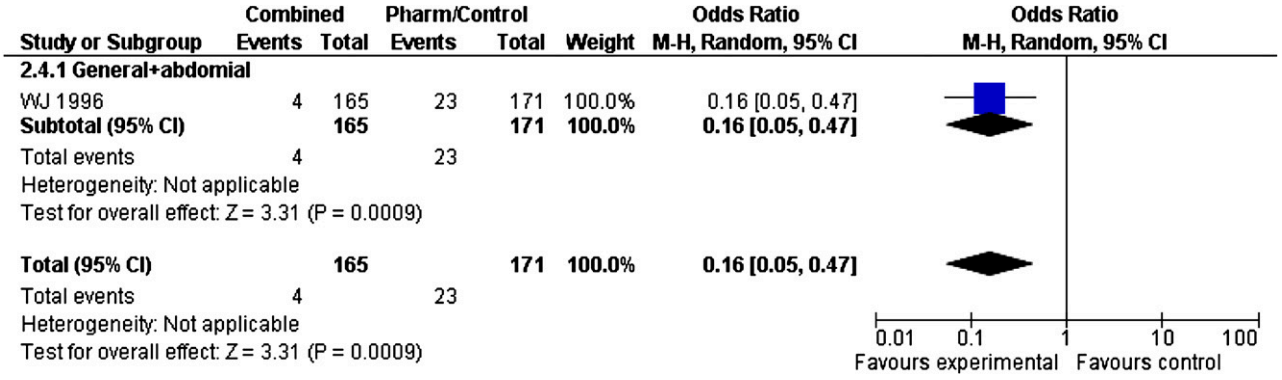


FIGURE S31. Combination vs pharmacologic prophylaxis: any VTE (stratified by surgical population). See Figure 1 legend for expansion of abbreviation.

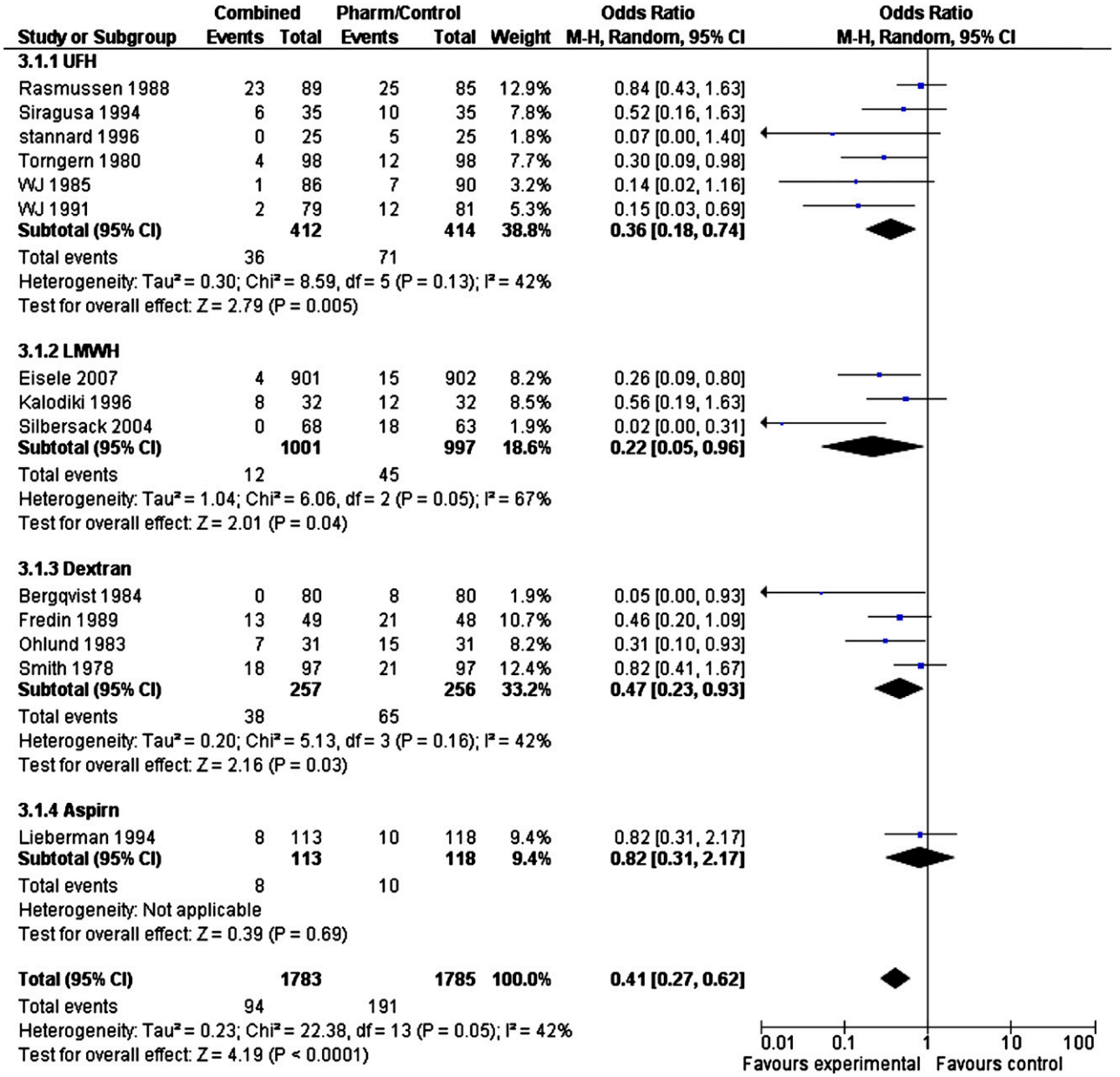


FIGURE S32. Combination vs pharmacologic prophylaxis: any DVT (stratified by background agent). Between-subgroup heterogeneity: $\chi^2 = 2.60$, $df = 3$, $P = .46$. LMWH = low-molecular-weight heparin. See Figure 1 legend for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

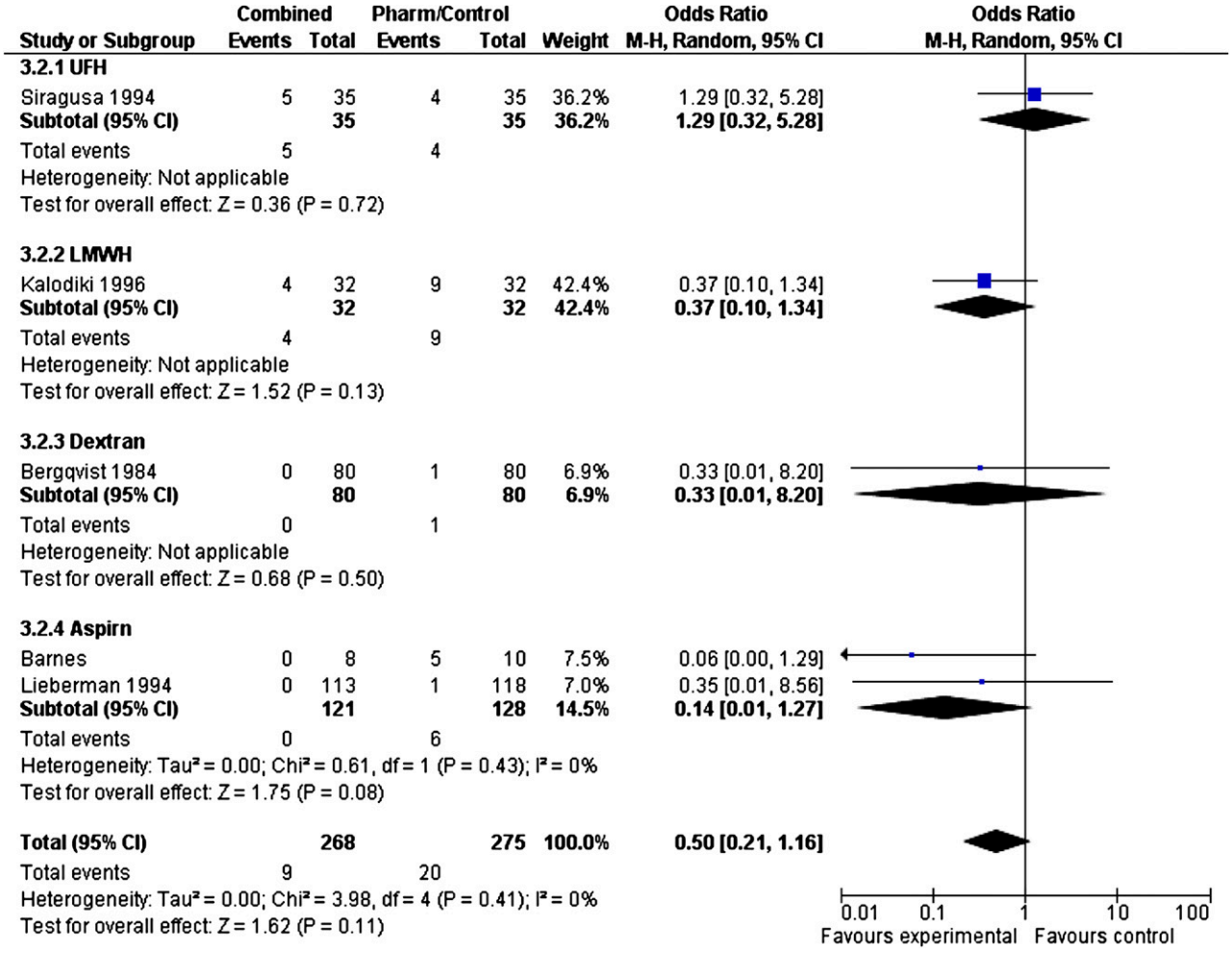


FIGURE S33. Combination vs pharmacologic prophylaxis: proximal DVT (stratified by background agent). Between-subgroup heterogeneity: $\chi^2 = 3.37$, $df = 3$, $P = .34$. See Figure S1 and S32 legends for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

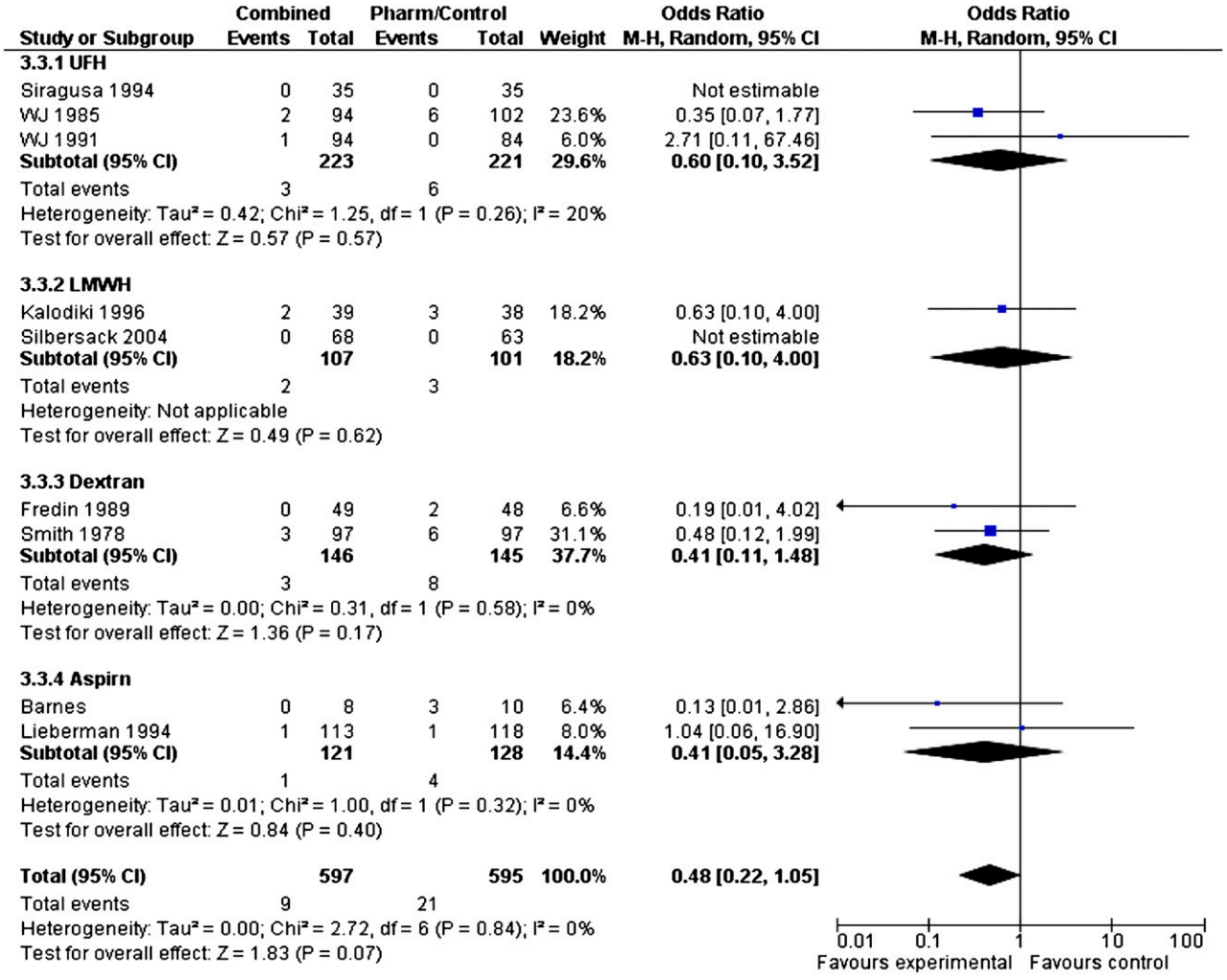


FIGURE S34. Combination vs pharmacologic prophylaxis: pulmonary embolism (stratified by background agent). Between-subgroup heterogeneity: $\chi^2 = 0.16$, $df = 3$, $P = .98$. See Figure S1 and S32 legends for expansion of abbreviations.

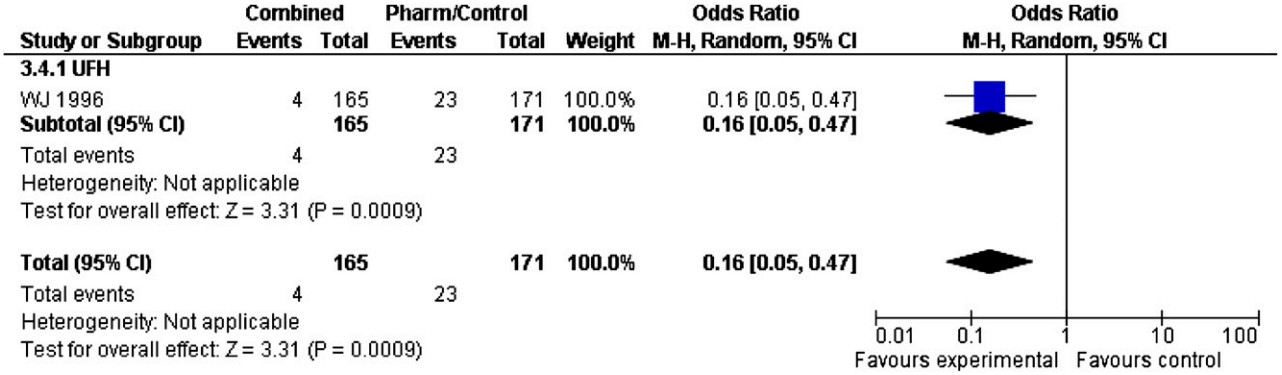


FIGURE S35. Combination vs pharmacologic prophylaxis: any VTE (stratified by background agent). See Figure S1 legend for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

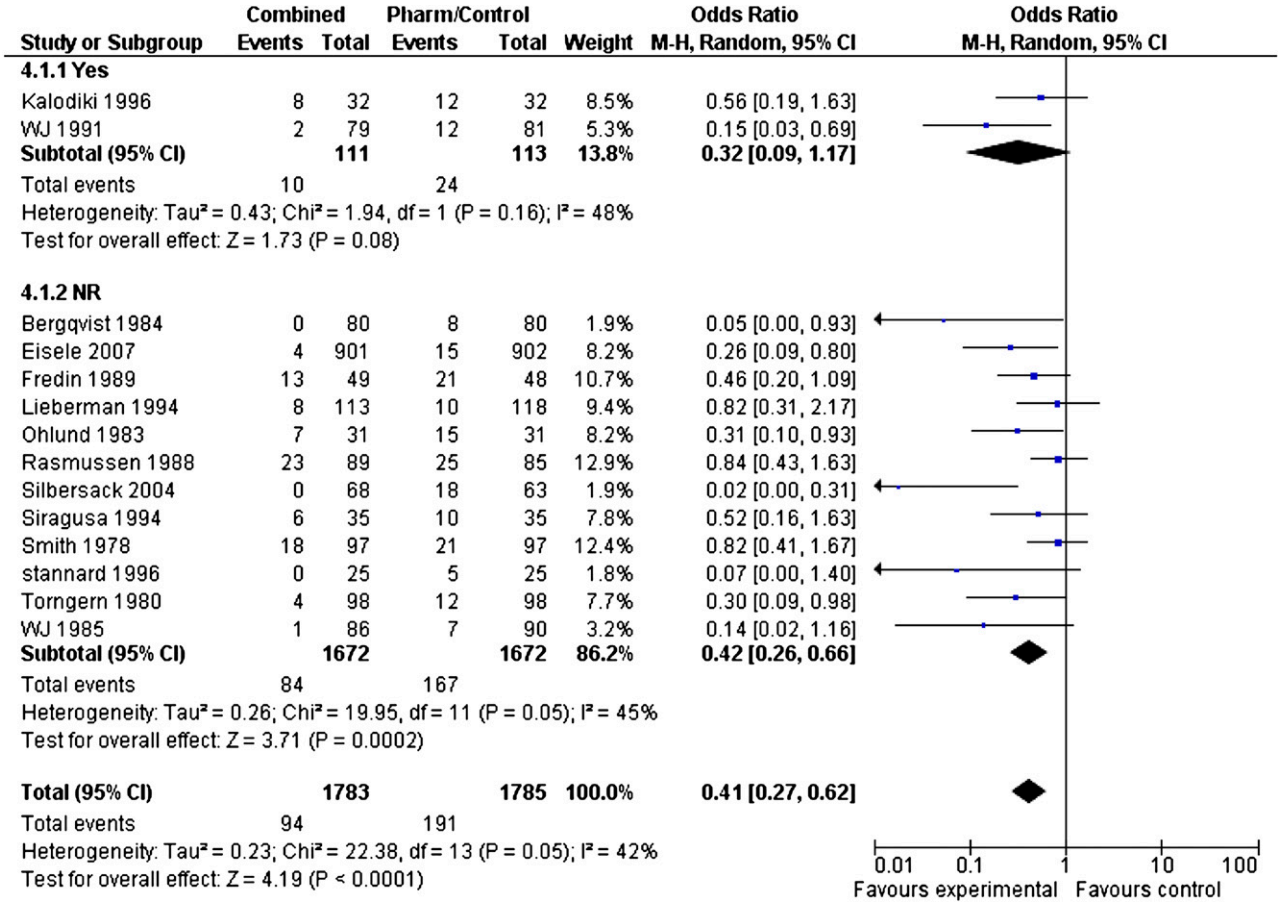


FIGURE S36. Combination vs pharmacologic prophylaxis: any DVT (stratified by allocation concealment). Between-subgroup heterogeneity: $\chi^2 = 0.49$, $df = 1$, $P = .48$. See Figure S1 legend for expansion of other abbreviation.

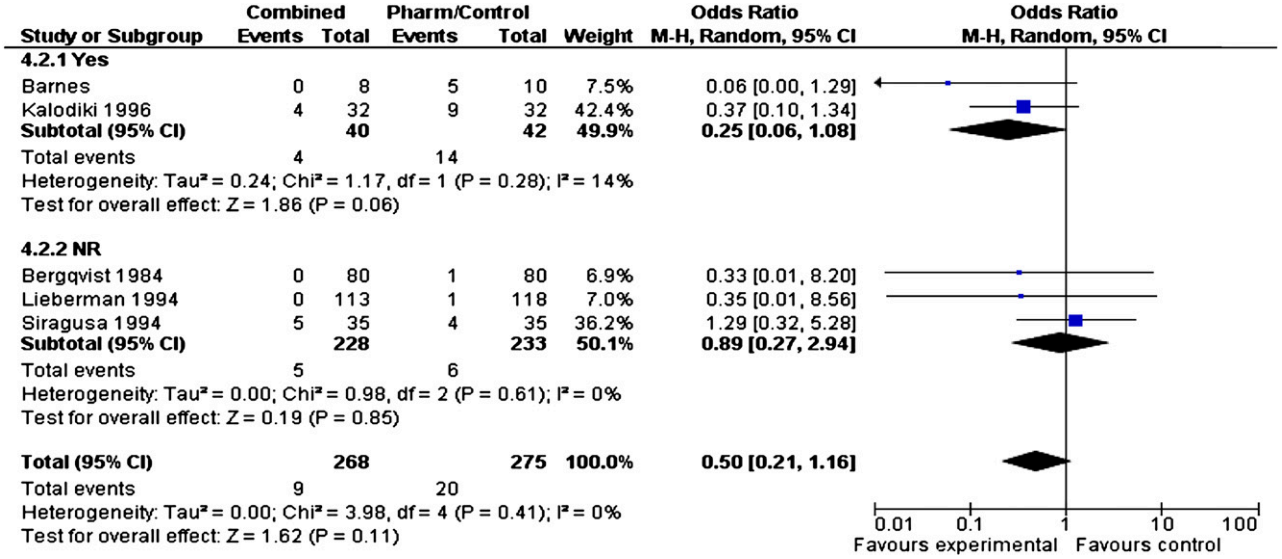


FIGURE S37. Combination vs pharmacologic prophylaxis: proximal DVT (stratified by allocation concealment). Between-subgroup heterogeneity: $\chi^2 = 1.83$, $df = 1$, $P = .18$. See Figure S1 and S36 legends for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

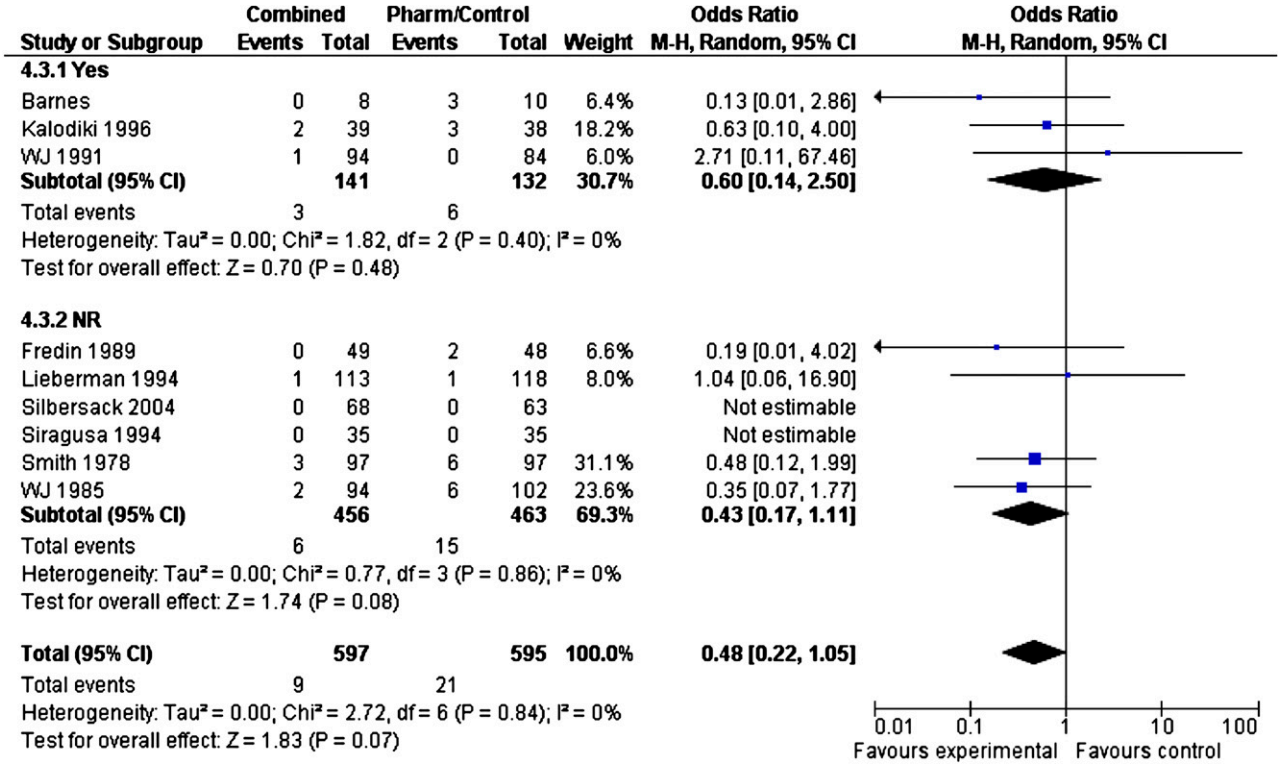


FIGURE S38. Combination vs pharmacologic prophylaxis: pulmonary embolism (stratified by allocation concealment). Between-subgroup heterogeneity: $\chi^2 = 0.13$, $df = 1$, $P = .72$. See Figure S1 and S36 legends for expansion of abbreviations.

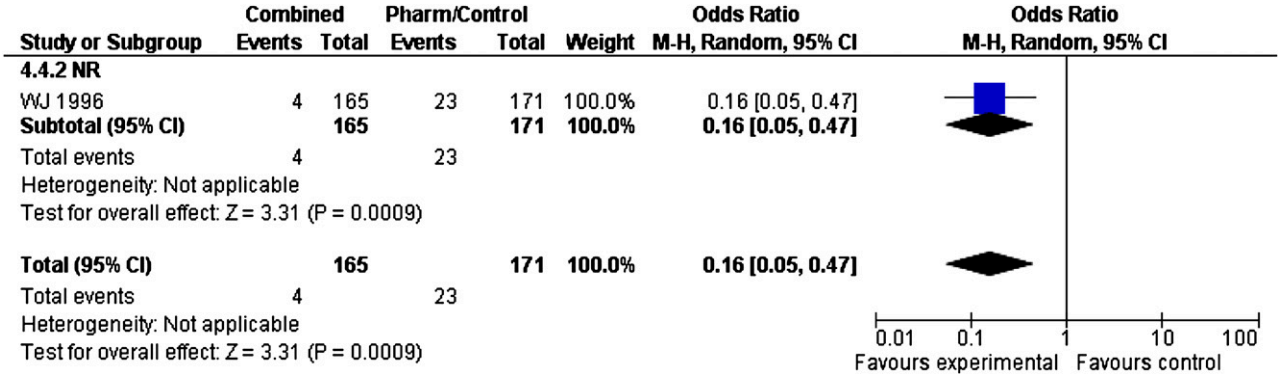


FIGURE S39. Combination vs pharmacologic prophylaxis: any VTE (stratified by allocation concealment). See Figure S1 and S36 legends for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

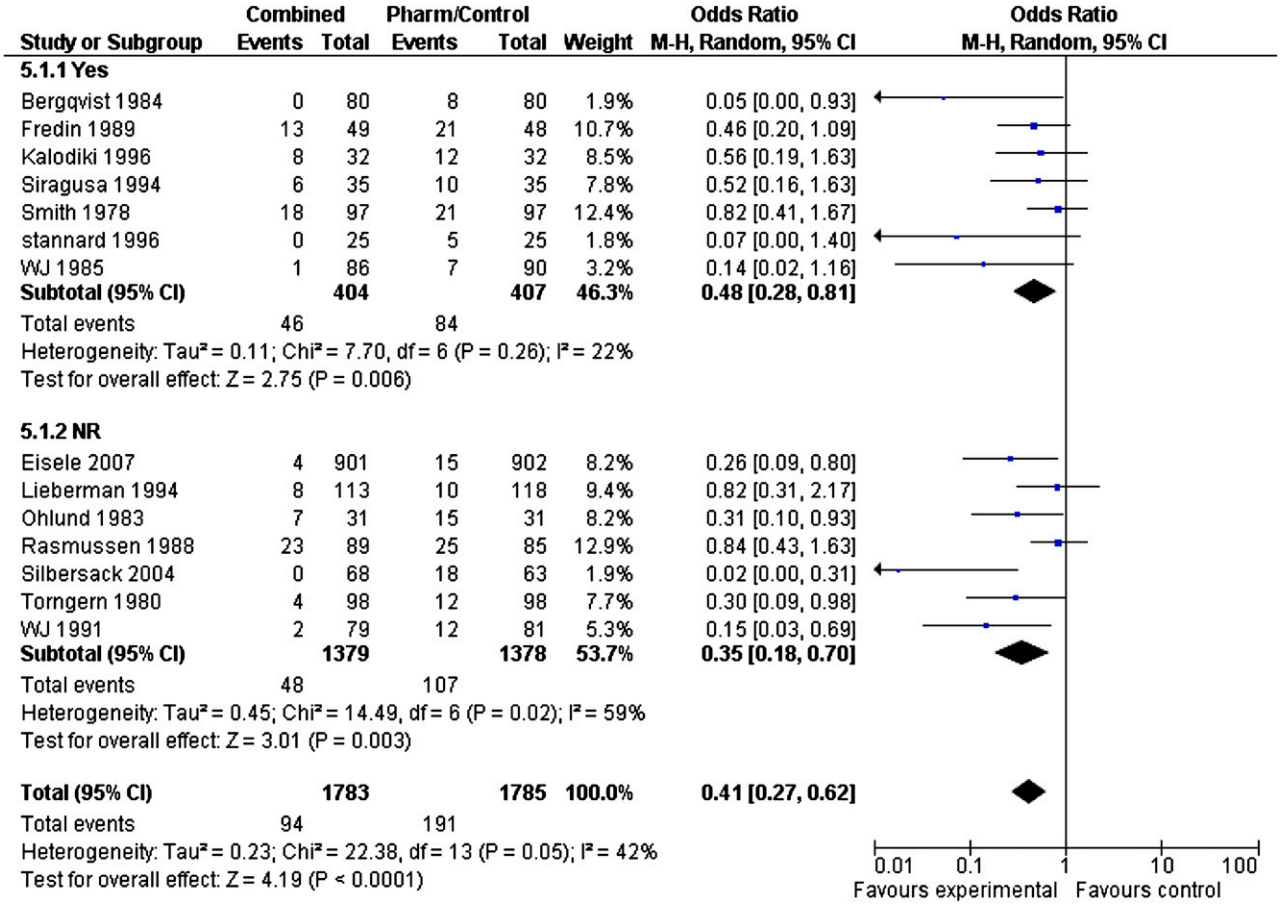


FIGURE S40. Combination vs pharmacologic prophylaxis: any DVT (stratified by blinding of outcome assessment). Between-subgroup heterogeneity: $\chi^2 = 0.19$, $df = 1$, $P = .66$. See Figure S1 and S36 legends for expansion of abbreviations.

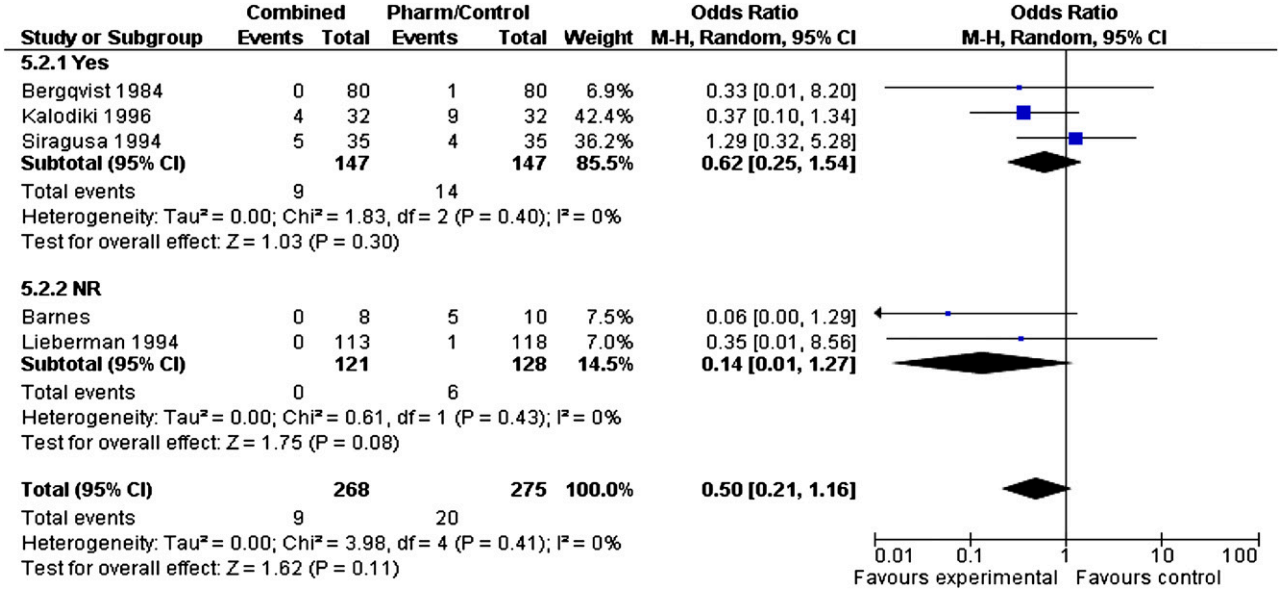


FIGURE S41. Combination vs pharmacologic prophylaxis: proximal DVT (stratified by blinding of outcome assessment). Between-subgroup heterogeneity: $\chi^2 = 1.54$, $df = 1$, $P = .21$. See Figure S1 and S36 legends for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

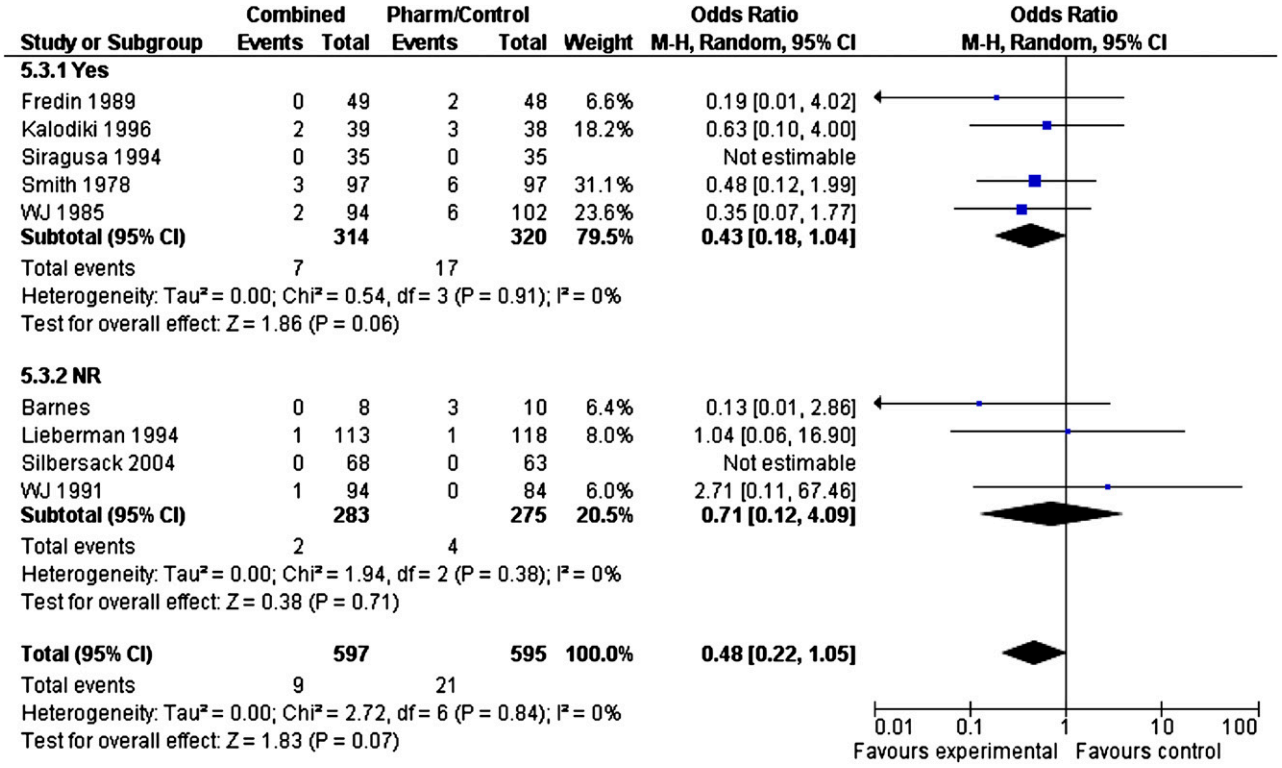


FIGURE S42. Combination vs pharmacologic prophylaxis: pulmonary embolism (stratified by blinding of outcome assessment). Between-subgroup heterogeneity: $\chi^2 = 0.24$, $df = 1$, $P = .62$. See Figure S1 and S36 legends for expansion of abbreviations.

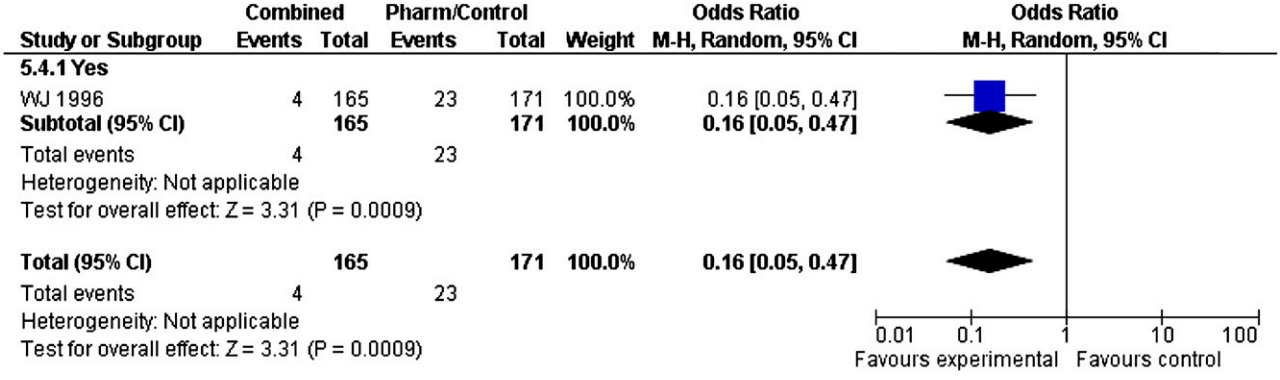


FIGURE S43. Combination vs pharmacologic prophylaxis: any VTE (stratified by blinding of outcome assessment). See Figure 1 legend for expansion of abbreviation.

 DOI: 10.1378/chest.11-2287

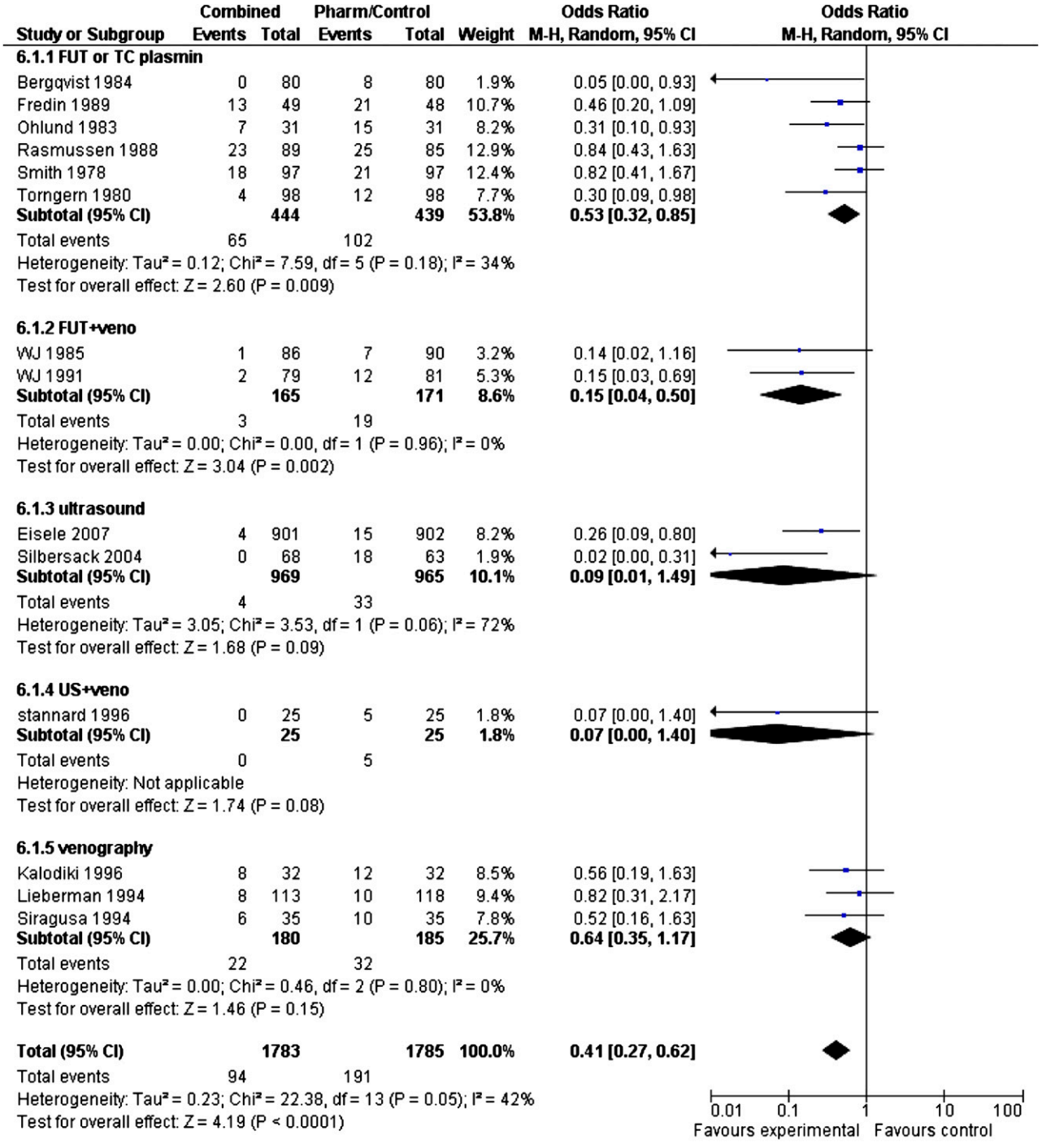


FIGURE S44. Combination vs pharmacologic prophylaxis: any DVT (stratified by diagnostic method). Between-subgroup heterogeneity: $\chi^2 = 10.8$, $df = 4$, $P = .03$. FUT = fibrinogen uptake test; TC = technetium; veno = venography; US = ultrasound. See Figure S1 legend for expansion of other abbreviation.

 DOI: 10.1378/chest.11-2287

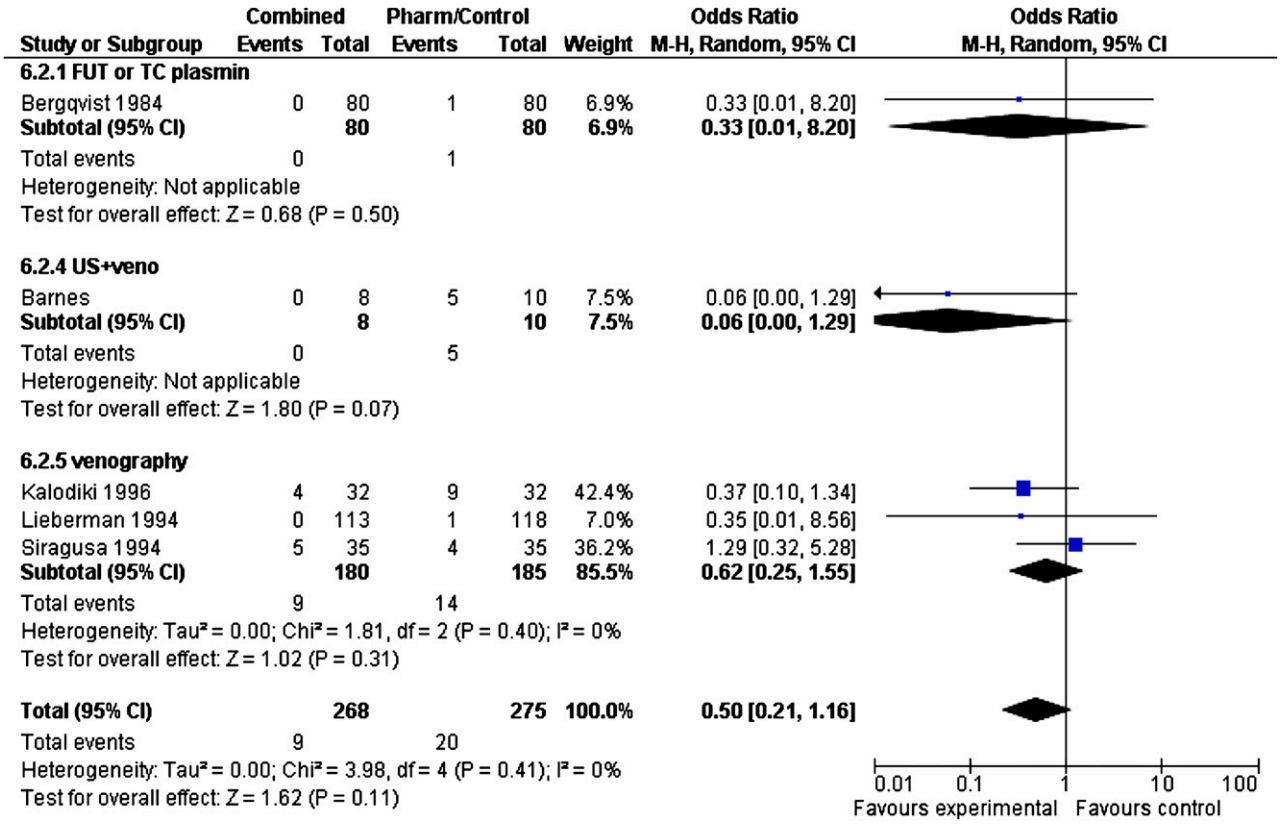


FIGURE S45. Combination vs pharmacologic prophylaxis: proximal DVT (stratified by diagnostic method). Between-subgroup heterogeneity: $\chi^2 = 2.17$, $df = 2$, $P = .34$. See Figure S1 and S44 legends for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

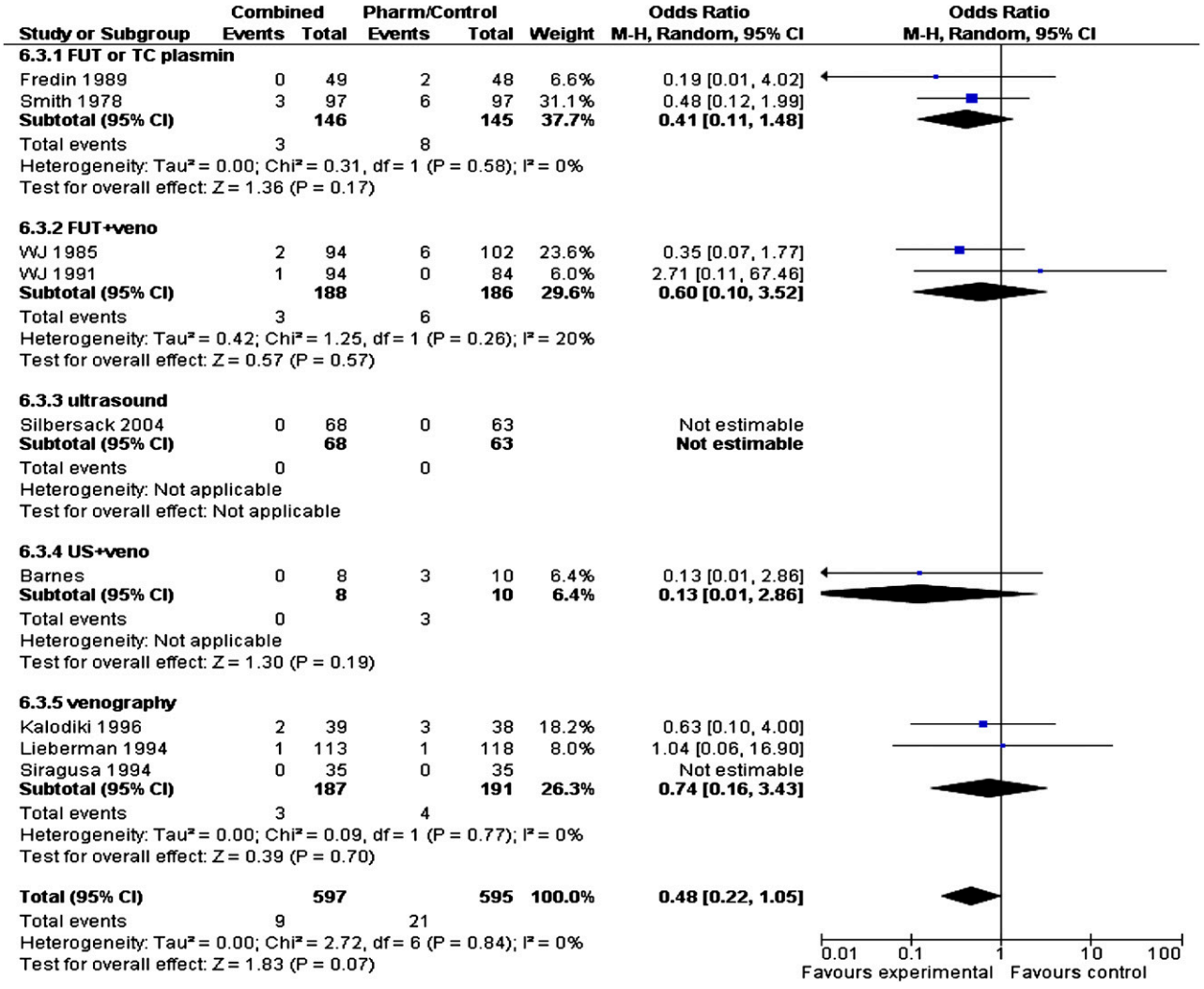


FIGURE S46. Combination vs pharmacologic prophylaxis: pulmonary embolism (stratified by diagnostic method). Between-subgroup heterogeneity: $\chi^2 = 1.07$, $df = 3$ ($P = .78$). See Figure S1 and S44 legends for expansion of abbreviations.

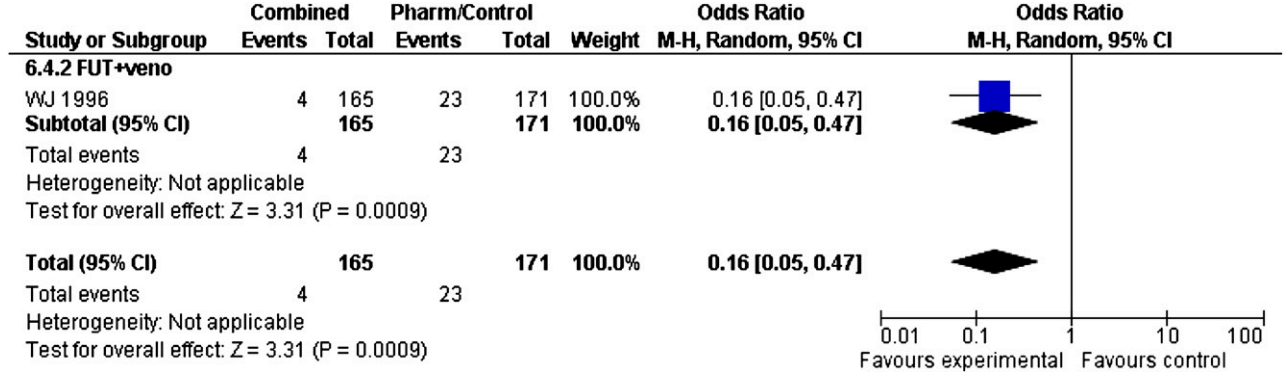
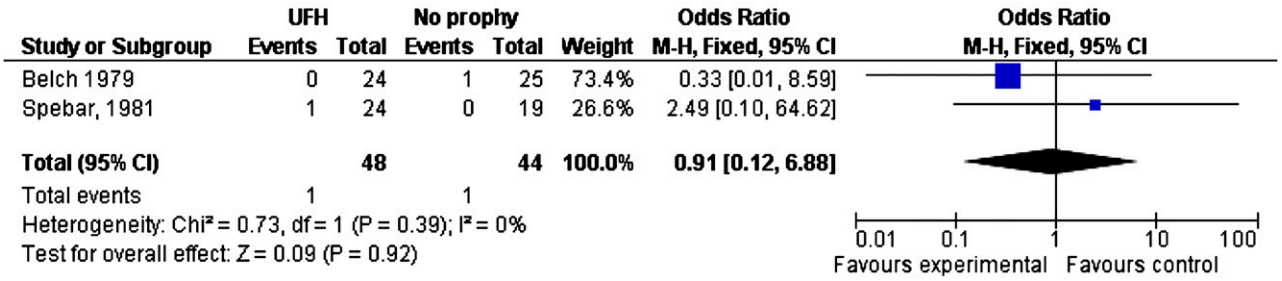


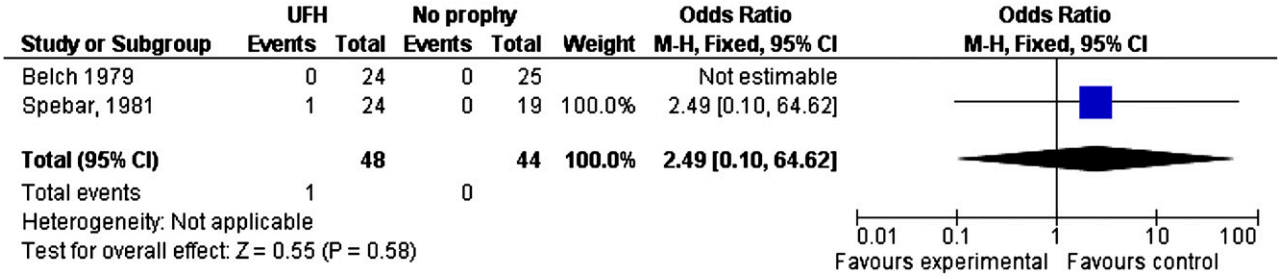
FIGURE S47. Combination vs pharmacologic prophylaxis: any VTE (stratified by diagnostic method). See Figure S1 and S44 legends for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

1 **Asymptomatic, proximal DVT, symptomatic DVT or PE**



2 **Symptomatic DVT or PE**



3 **Major bleeding**

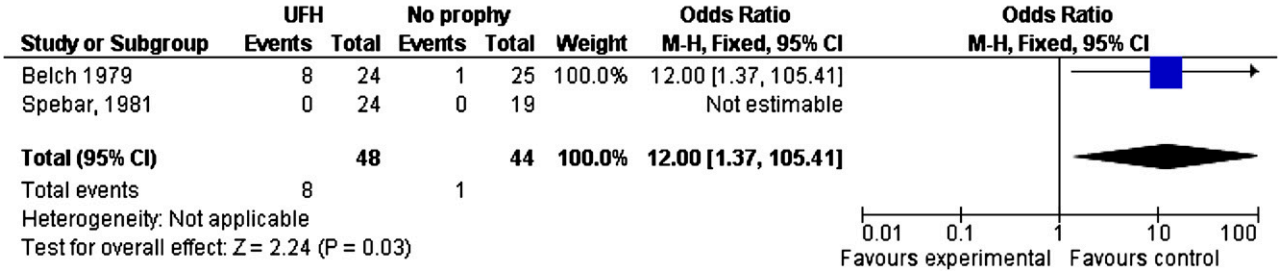


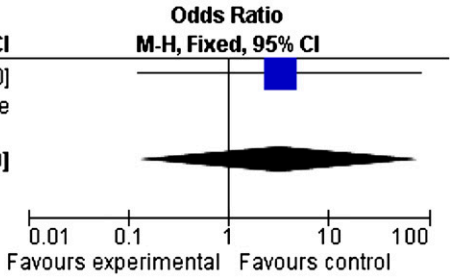
FIGURE S48. Vascular surgery, UFH vs no prophylaxis. 48.1, Asymptomatic, proximal DVT, symptomatic DVT or pulmonary embolism. 48.2, Symptomatic DVT or pulmonary embolism. 48.3, Major bleeding. 48.4, Bleeding requiring reoperation. 48.5, Death. 48.6, Fatal bleeding. See Figure S1 legend for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

4 **Bleeding requiring reoperation**

Study or Subgroup	UFH Events	Total	No prophy Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Belch 1979	1	24	0	25	100.0%	3.26 [0.13, 83.90]
Spebar, 1981	0	24	0	19		Not estimable
Total (95% CI)		**48**		**44**	**100.0%**	**3.26 [0.13, 83.90]**
Total events	1		0			

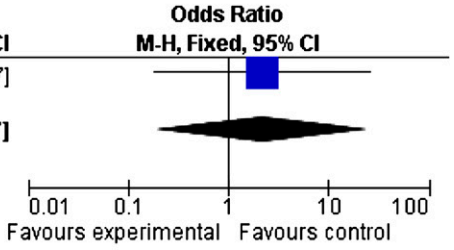
Heterogeneity: Not applicable
Test for overall effect: Z = 0.71 (P = 0.48)



5 **Death**

Study or Subgroup	UFH Events	Total	No prophy Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Belch 1979	2	24	1	25	100.0%	2.18 [0.18, 25.77]
Total (95% CI)		**24**		**25**	**100.0%**	**2.18 [0.18, 25.77]**
Total events	2		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.62 (P = 0.54)



6 **Fatal bleeding**

Study or Subgroup	UFH Events	Total	No prophy Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Belch 1979	1	24	0	25	100.0%	3.26 [0.13, 83.90]
Spebar, 1981	0	24	0	19		Not estimable
Total (95% CI)		**48**		**44**	**100.0%**	**3.26 [0.13, 83.90]**
Total events	1		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.71 (P = 0.48)

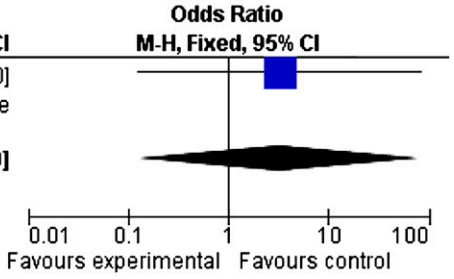


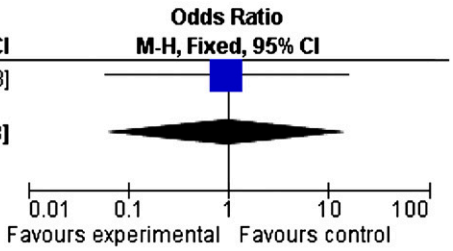
FIGURE S48. Continued

 DOI: 10.1378/chest.11-2287

1 **Asymptomatic, proximal DVT, symptomatic DVT or PE**

Study or Subgroup	UFH+IPC Events	Total	No prophy Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Killewich, 1997	1	50	1	48	100.0%	0.96 [0.06, 15.78]
Total (95% CI)		**50**		**48**	**100.0%**	**0.96 [0.06, 15.78]**
Total events	1		1			

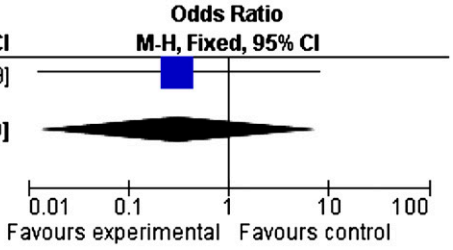
Heterogeneity: Not applicable
Test for overall effect: Z = 0.03 (P = 0.98)



2 **Symptomatic DVT or PE**

Study or Subgroup	UFH +IPC Events	Total	No prophy Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Killewich, 1997	0	50	1	48	100.0%	0.31 [0.01, 7.89]
Total (95% CI)		**50**		**48**	**100.0%**	**0.31 [0.01, 7.89]**
Total events	0		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.70 (P = 0.48)



3 **Major bleeding**

Study or Subgroup	UFH+IPC Events	Total	No prophy Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Killewich, 1997	0	50	0	48		Not estimable
Total (95% CI)		**50**		**48**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable

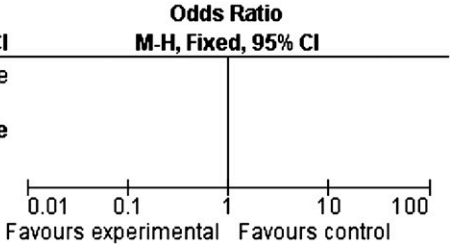
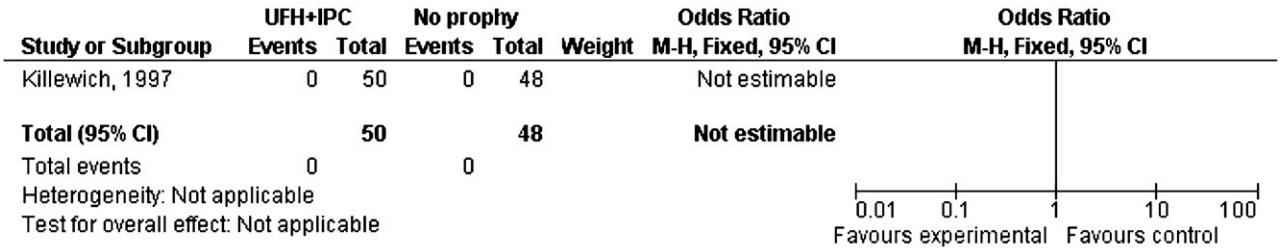


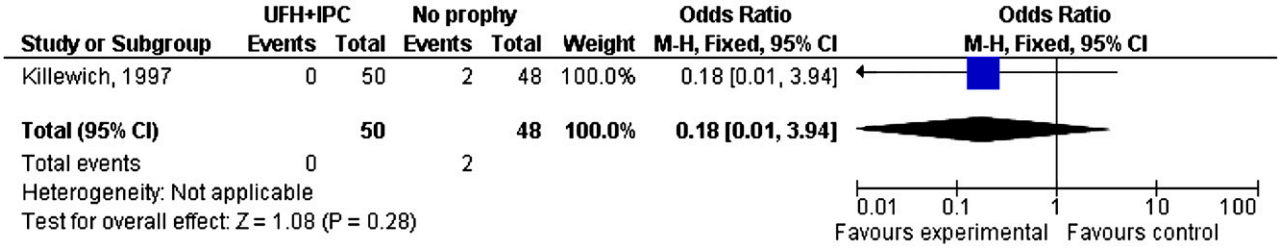
FIGURE S49. Vascular surgery, UFH plus IPC vs no prophylaxis. 49.1, Asymptomatic, proximal DVT, symptomatic DVT, or pulmonary embolism. 49.2, Symptomatic DVT or pulmonary embolism. 49.3, Major bleeding. 49.4, Bleeding requiring reoperation. 49.5, Death. 49.6, Fatal bleeding. See Figure S1 and S24 legends for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

4 **Bleeding requiring reoperation**



5 **Death**



6 **Fatal bleeding**

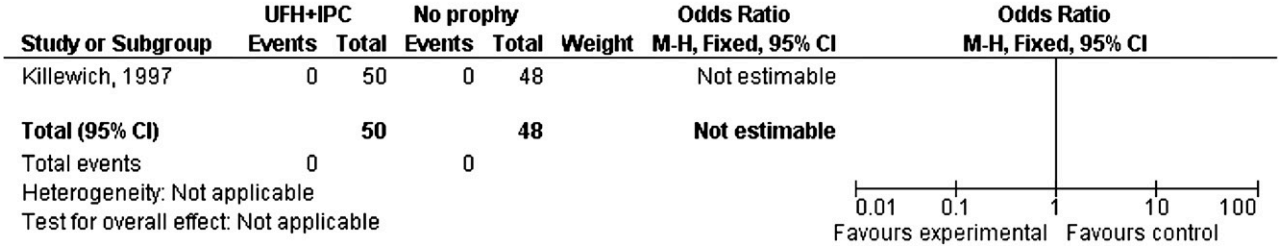
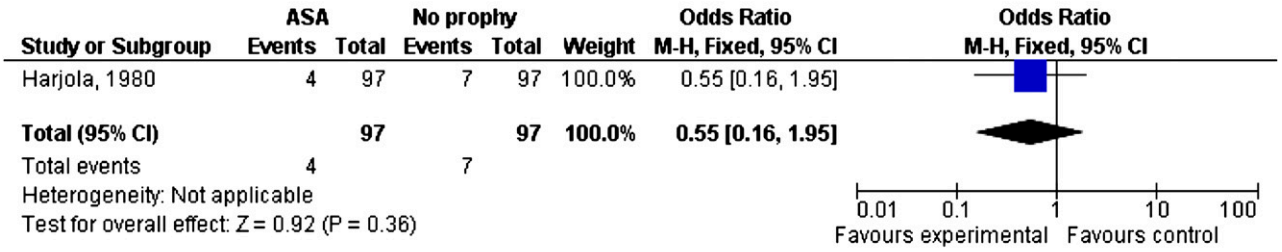


FIGURE S49. Continued

 DOI: 10.1378/chest.11-2297

1 **Asymptomatic, proximal DVT, symptomatic DVT or PE**



2 **Symptomatic DVT or PE**

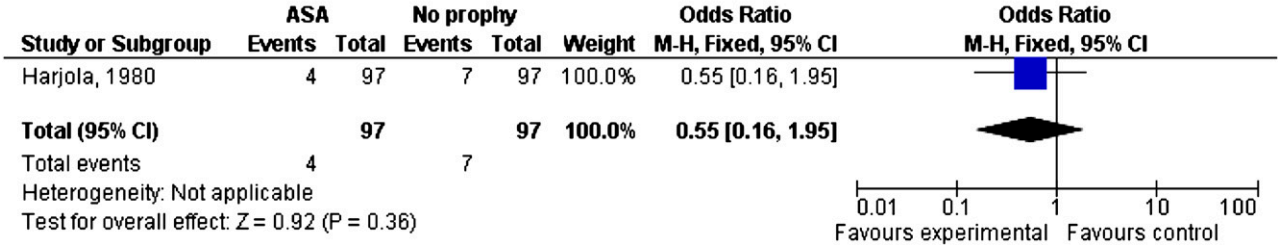


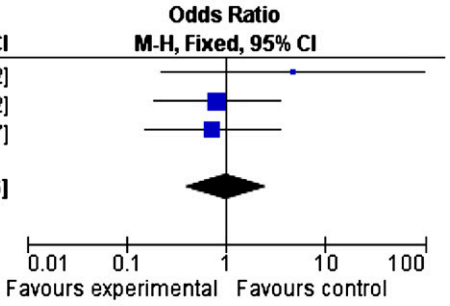
FIGURE S50. Vascular surgery: ASA vs no prophylaxis. 50.1, Asymptomatic, proximal DVT, symptomatic DVT, or pulmonary embolism. 50.2, Symptomatic DVT or pulmonary embolism. See Figure S1 and S6 for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

1 **Asymptomatic, proximal DVT, symptomatic DVT or PE**

Study or Subgroup	LMWH Events	LMWH Total	UFH(Control) Events	UFH(Control) Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Farkas, 1993	2	122	0	111	6.3%	4.63 [0.22, 97.42]
Lastoria, 2006	4	41	4	34	48.1%	0.81 [0.19, 3.52]
Speziale, 1988	3	46	4	46	45.6%	0.73 [0.15, 3.47]
Total (95% CI)		**209**		**191**	**100.0%**	**1.01 [0.39, 2.66]**
Total events	9		8			

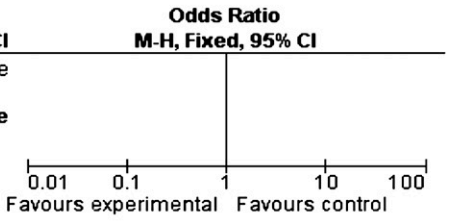
Heterogeneity: Chi² = 1.21, df = 2 (P = 0.55); I² = 0%
Test for overall effect: Z = 0.03 (P = 0.98)



2 **Symptomatic DVT or PE**

Study or Subgroup	LMWH Events	LMWH Total	UFH(Control) Events	UFH(Control) Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Farkas, 1993	0	122	0	111		Not estimable
Total (95% CI)		**122**		**111**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable



3 **Major bleeding**

Study or Subgroup	LMWH Events	LMWH Total	UFH(Control) Events	UFH(Control) Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Farkas, 1993	3	122	3	111	100.0%	0.91 [0.18, 4.59]
Lastoria, 2006	0	41	0	34		Not estimable
Total (95% CI)		**163**		**145**	**100.0%**	**0.91 [0.18, 4.59]**
Total events	3		3			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.12 (P = 0.91)

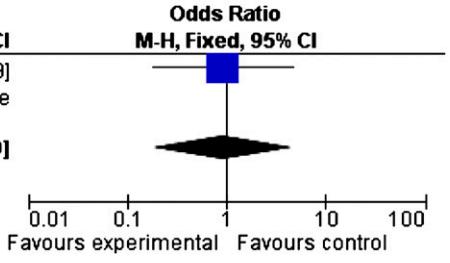


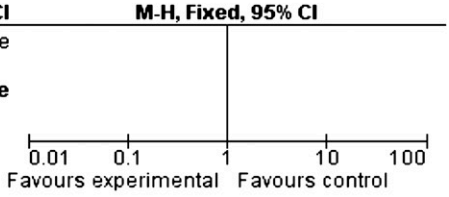
FIGURE S51. Vascular surgery: LMWH vs UFH. 51.1, Asymptomatic, proximal DVT, symptomatic DVT, or pulmonary embolism. 51.2, Symptomatic DVT or pulmonary embolism. 51.3, Major bleeding. 51.4, Bleeding requiring reoperation. 51.5, Death. 51.6, Fatal bleeding. See Figure S1 and S32 legends for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

4 **Bleeding requiring reoperation**

Study or Subgroup	LMWH Events	LMWH Total	UFH(Control) Events	UFH(Control) Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Lastoria, 2006	0	41	0	34		Not estimable
Total (95% CI)		**41**		**34**		**Not estimable**
Total events	0		0			

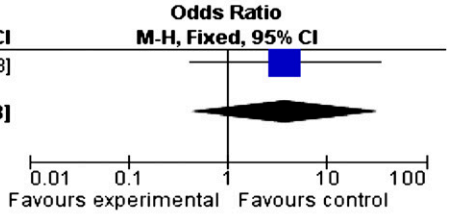
Heterogeneity: Not applicable
Test for overall effect: Not applicable



5 **Death**

Study or Subgroup	LMWH Events	LMWH Total	UFH(Control) Events	UFH(Control) Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Farkas, 1993	4	122	1	111	100.0%	3.73 [0.41, 33.88]
Total (95% CI)		**122**		**111**	**100.0%**	**3.73 [0.41, 33.88]**
Total events	4		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.17 (P = 0.24)



6 **Fatal bleeding**

Study or Subgroup	LMWH Events	LMWH Total	UFH(Control) Events	UFH(Control) Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Farkas, 1993	0	122	0	111		Not estimable
Lastoria, 2006	0	41	0	34		Not estimable
Total (95% CI)		**163**		**145**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable

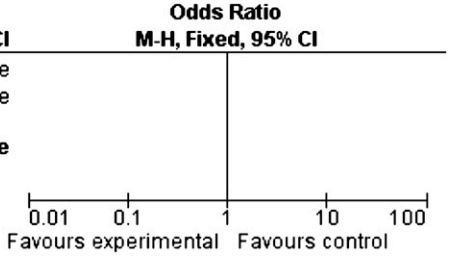
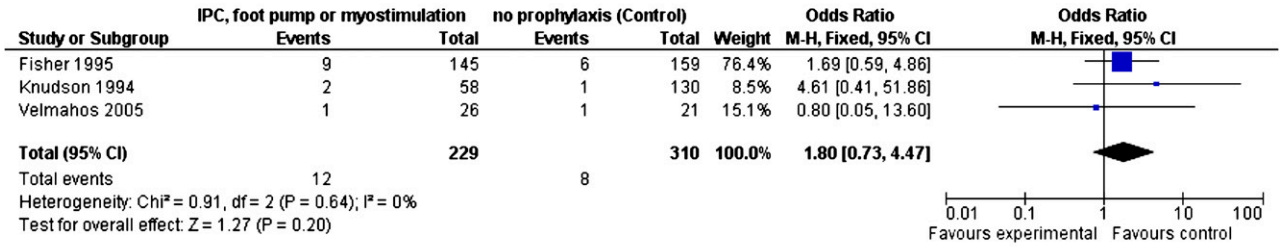


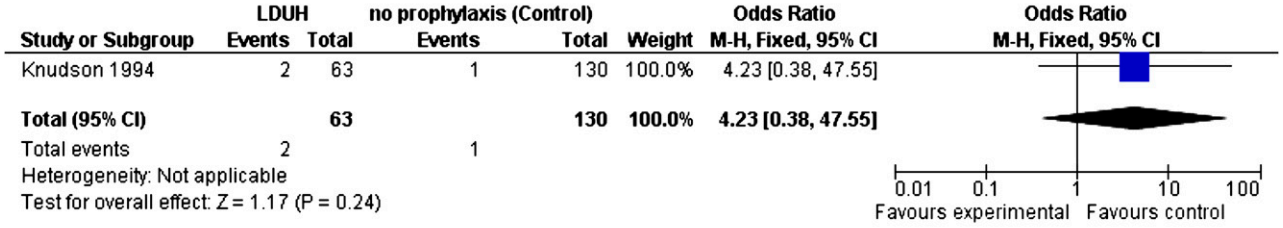
FIGURE S51. Continued

 DOI: 10.1378/chest.11-2287

1 IPC, foot pump or myostimulation versus no prophylaxis



2 LDUH versus no prophylaxis



3 FP versus IPC

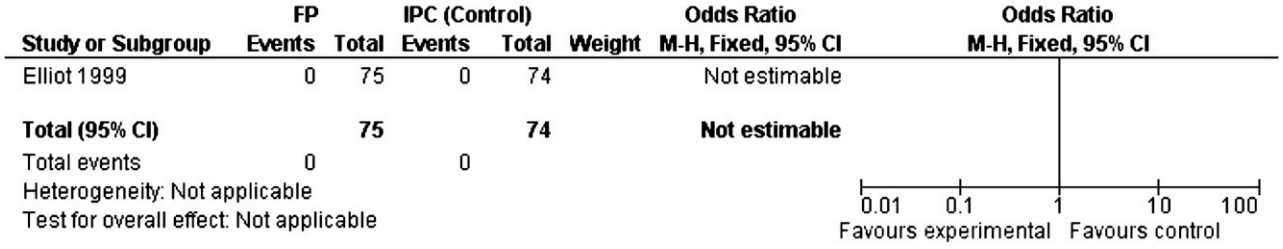
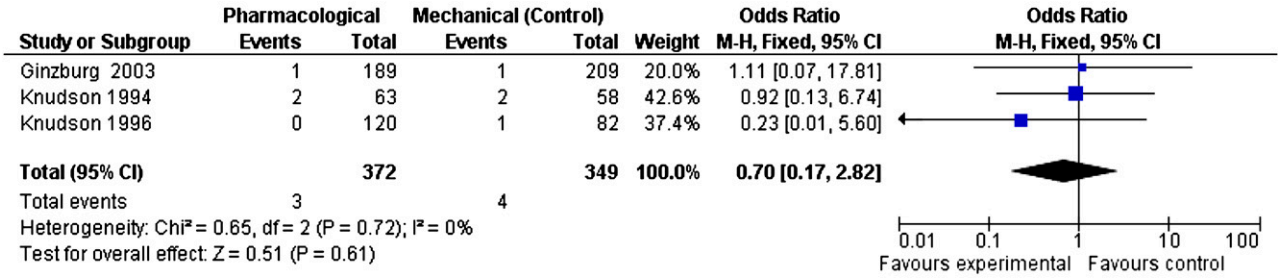


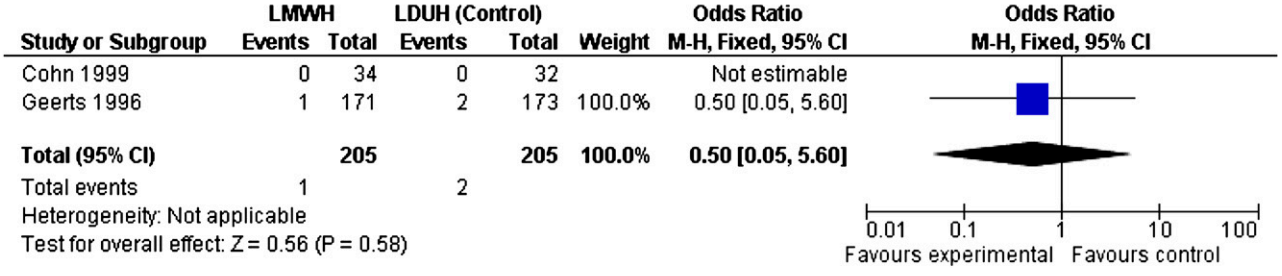
FIGURE S52. Major trauma: symptomatic VTE. 52.1, IPC, FP, or myostimulation vs no prophylaxis. 52.2, LDUH vs no prophylaxis. 52.3, FP vs IPC. 52.4, Pharmacologic vs mechanical. 52.5, LMWH vs LDUH. 52.6, Combined (LDUH plus CPM) vs LDUH. 52.7, Delayed vs early LMWH. CPM = continuous passive motion; LDUH = low-dose unfractionated heparin. See Figure S1, S24, and S32 legends for expansion of other abbreviations.

 DOI: 10.1378/chest.11-2287

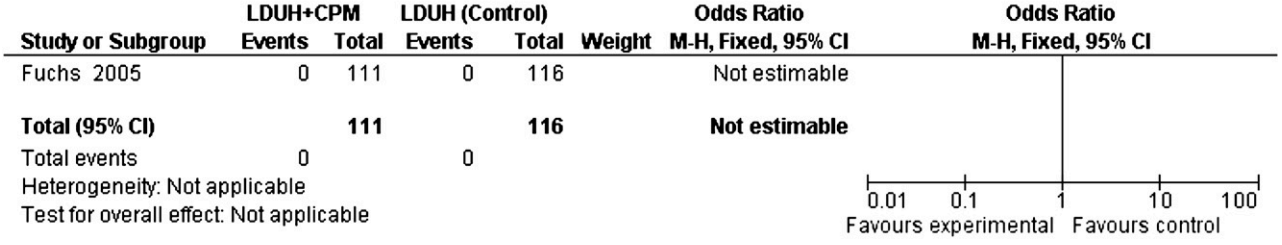
4 Pharmacological versus mechanical



5 LMWH versus LDUH



6 Combined (LDUH plus CPM) versus LDUH



7 Delayed versus early LMWH

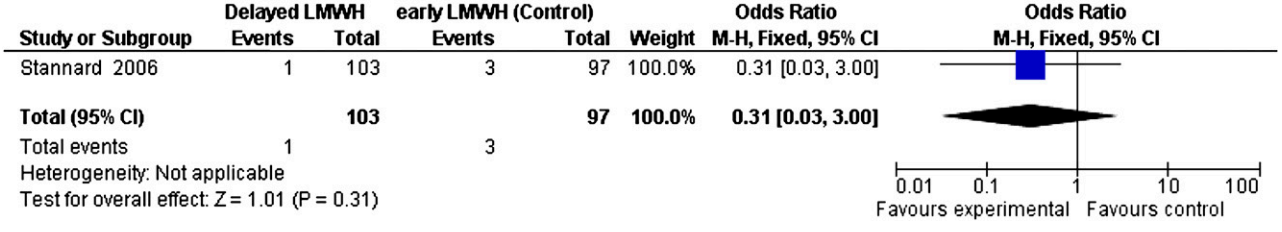
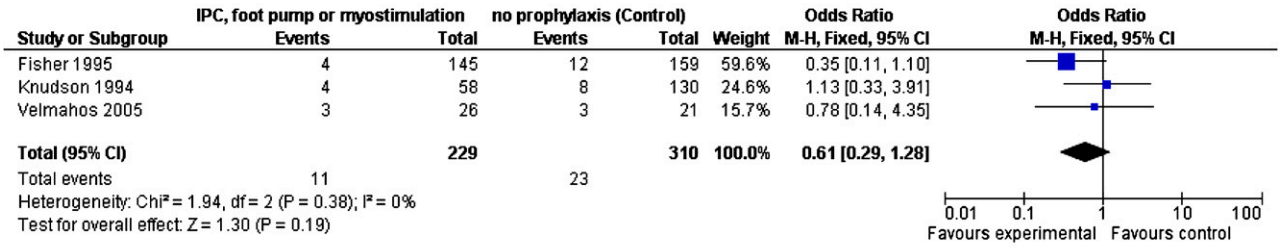
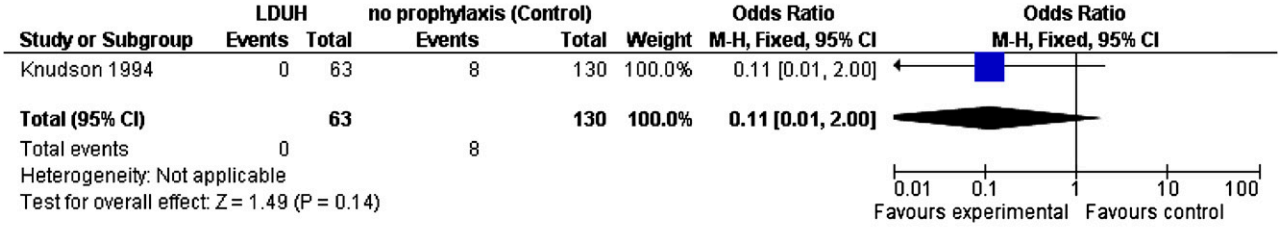


FIGURE S52. Continued

1 **IPC, foot pump or myostimulation versus no prophylaxis**



2 **LDUH versus no prophylaxis**



3 **FP versus IPC**

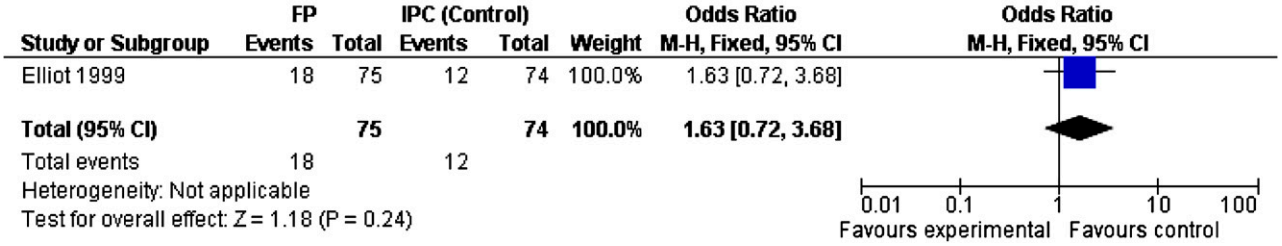
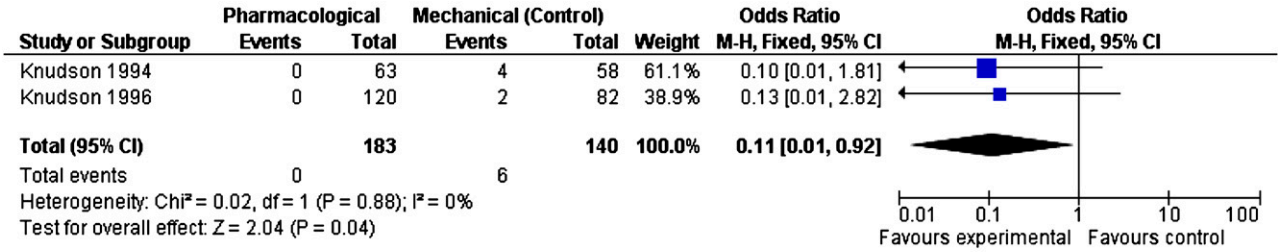


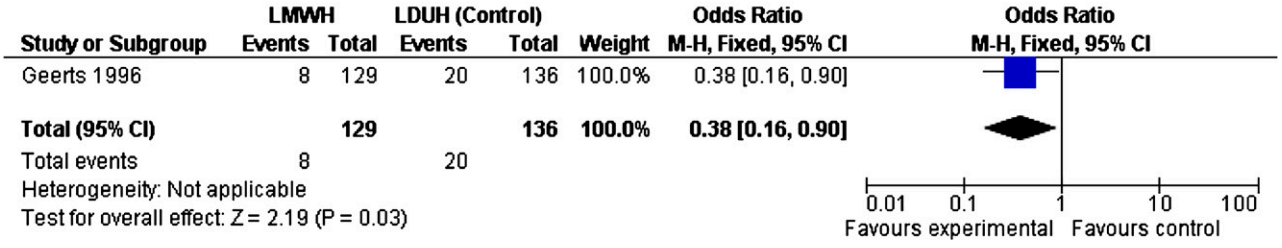
FIGURE S53. Major trauma: proximal DVT. 53.1, IPC, FP, or myostimulation vs no prophylaxis. 53.2, LDUH vs no prophylaxis. 53.3, FP vs IPC. 53.4, Pharmacologic vs mechanical. 53.5, LMWH vs LDUH. 53.6, Combined (LDUH plus CPM) vs LDUH. See Figure S1, S24, S32 and S52 legends for expansion of abbreviations.

 DOI: 10.1378/chest.11-2287

4 Pharmacological versus mechanical



5 LMWH versus LDUH



6 Combined (LDUH plus CPM) versus LDUH

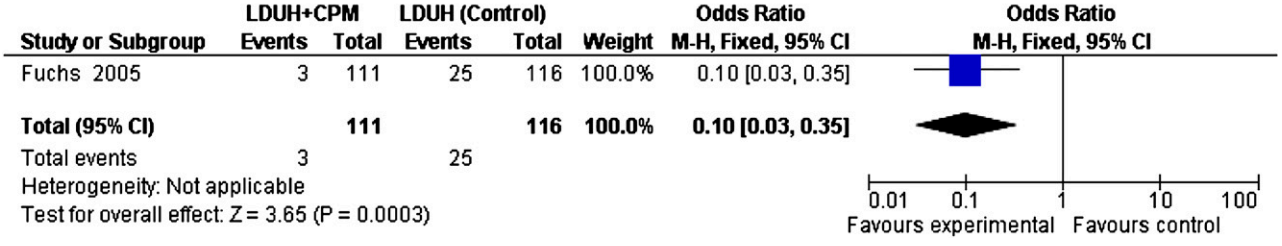


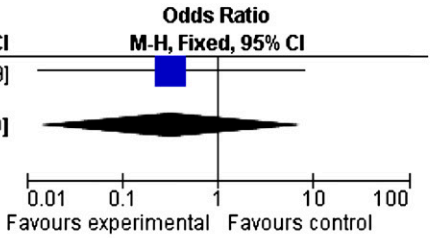
FIGURE S53. Continued

 DOI: 10.1378/chest.11-2297

1 **FP versus IPC**

Study or Subgroup	FP Events	FP Total	IPC (Control) Events	IPC (Control) Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Elliot 1999	0	75	1	74	100.0%	0.32 [0.01, 8.09]
Total (95% CI)		**75**		**74**	**100.0%**	**0.32 [0.01, 8.09]**
Total events	0		1			

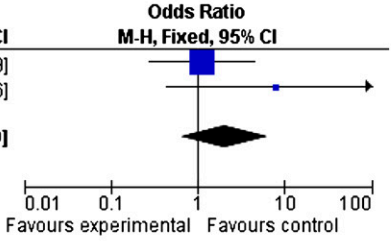
Heterogeneity: Not applicable
Test for overall effect: Z = 0.69 (P = 0.49)



2 **Pharmacological versus mechanical**

Study or Subgroup	Pharmacological Events	Pharmacological Total	Mechanical (Control) Events	Mechanical (Control) Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Ginzburg 2003	4	189	4	209	86.8%	1.11 [0.27, 4.49]
Knudson 1996	5	120	0	82	13.2%	7.86 [0.43, 144.06]
Total (95% CI)		**309**		**291**	**100.0%**	**2.00 [0.63, 6.39]**
Total events	9		4			

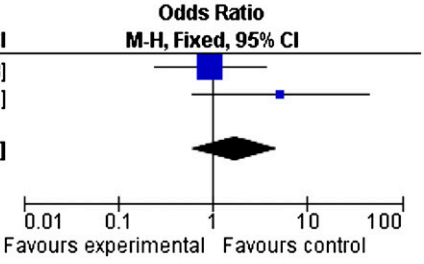
Heterogeneity: Chi² = 1.53, df = 1 (P = 0.22); I² = 35%
Test for overall effect: Z = 1.17 (P = 0.24)



3 **LMWH versus LDUH**

Study or Subgroup	LMWH Events	LMWH Total	LDUH (Control) Events	LDUH (Control) Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Cohn 1999	5	34	5	32	82.0%	0.93 [0.24, 3.58]
Geerts 1996	5	171	1	173	18.0%	5.18 [0.60, 44.81]
Total (95% CI)		**205**		**205**	**100.0%**	**1.70 [0.58, 4.94]**
Total events	10		6			

Heterogeneity: Chi² = 1.79, df = 1 (P = 0.18); I² = 44%
Test for overall effect: Z = 0.97 (P = 0.33)



4 **Delayed versus early LMWH**

Study or Subgroup	Delayed LMWH Events	Delayed LMWH Total	early LMWH (Control) Events	early LMWH (Control) Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Stannard 2006	19	103	18	97	100.0%	0.99 [0.49, 2.03]
Total (95% CI)		**103**		**97**	**100.0%**	**0.99 [0.49, 2.03]**
Total events	19		18			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.02 (P = 0.98)

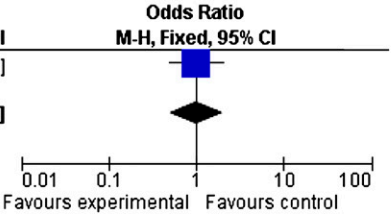


FIGURE S54. Major trauma: major bleeding. 54.1, FP vs IPC. 54.2, Pharmacologic vs mechanical. 54.3, LMWH vs LDUH. 54.4, Delayed vs early LMWH. See Figure S1, S24, S32 and S52 legends for expansion of abbreviations.

Table S1—*Medline Search Strategy*

Prevention in nonorthopedic surgery patients
Executed November 4, 2009
1. embolism/ or thromboembolism/ or venous thrombosis/ or thrombophlebitis/
2. exp Bariatric Surgery/
3. colorectal surgery/ or general surgery/ or gynecology/ or neurosurgery/ or otolaryngology/ or surgery, plastic/ or thoracic surgery/ or traumatology/ or urology/
4. exp "wounds and injuries"/ or exp abdominal injuries/ or amputation, traumatic/ or exp arm injuries/ or asphyxia/ or athletic injuries/ or exp back injuries/ or exp barotrauma/ or exp burns/ or exp craniocerebral trauma/ or exp dislocations/ or exp drowning/ or exp electric injuries/ or esophageal perforation/ or exp fractures, bone/ or exp fractures, cartilage/ or exp hip injuries/ or lacerations/ or exp leg injuries/ or multiple trauma/ or exp neck injuries/ or exp radiation injuries/ or retropneumoperitoneum/ or exp rupture/ or shock, traumatic/ or soft tissue injuries/ or spinal cord injuries/ or exp spinal injuries/ or exp thoracic injuries/ or exp trauma, nervous system/ or exp wounds, nonpenetrating/ or exp wounds, penetrating/
5. exp Cardiovascular Surgical Procedures/
6. prophylax$.mp.
7. Primary Prevention/
8. Secondary Prevention/
9. prevent$.mp. [mp = title, original title, abstract, name of substance word, subject heading word, unique identifier]
10. 4 or 3 or 2 or 5
11. 8 or 6 or 7 or 9
12. 11 and 1 and 10
13. limit 12 to (English language and humans and yr = "2005-Current")

 DOI: 10.1378/chest.11-2287

Table S2—*Characteristics of Randomized Controlled Trials of Thromboprophylaxis*

First Author, Year	Specific Population	Interventions	No. in Each Intervention	Outcomes	Comments
		General, mixed, and abdominal-pelvic surgery			
Agnelli,[122] 2005	High-risk abdominal surgery	Fondaparinux 2.5 mg vs dalteparin 5,000 or 2,500 unit	1,465 1,462	Symptomatic DVT PE Fatal PE Bleeding requiring reoperation Fatal bleeding Death from any cause	
Bergqvist,[123] 1986	Abdominal surgery (gastric, biliary, colonic, rectal, pancreatic)	LMWH 5,000 International Units preoperative and 5,000 daily and placebo daily vs Low-dose heparin 5,000 International Units SC preoperative and 5,000 SC bid for 5-7 d	215 217	30 d of follow-up Asymptomatic DVT	Placebo given in evening to LMWH group to observe same injection schedule as low-dose group
Bergqvist,[124] 1988	Abdominal surgery (gastric, biliary, colonic, rectal, pancreatic)	LMWH 5,000 International Units SC preoperative and daily and placebo daily vs low-dose heparin 5,000 International Units SC preoperative and bid (first dose was placebo)	505 497	30 d of follow-up Asymptomatic DVT (proximal, distal)	Patients given first injection SC at 10 PM on evening of the day before surgery and second injection 2 h before surgery
Bergqvist,[125] 1995	Abdominal surgery (gastric, biliary, colonic, rectal, pancreatic)	LMWH 5,000 International Units SC daily vs LMWH 2,500 International Units SC daily	1,036 1,034	30 d of follow-up Asymptomatic DVT Bleeding Death	First dose given night before surgery then daily thereafter
Bergqvist,[126] 1997	Age >40 y Open GI, urologic, gynecologic cancer	1. UFH 5,000 units -2 h; tid day 10 ± 2 2. Enoxaparin 40 mg -2 h; day 10 ± 2	1. 319 2. 312	VTE by venogram Symptomatic VTE PE Bleeding DeathVTE <3 mo Bleeding <3 mo	ENOXACAN study

(Continued)

Table S2—*Continued*

First Author, Year	Specific Population	Interventions	No. in Each Intervention	Outcomes	Comments
Bergqvist,[127] 2002	Curative open surgery for abdominal or pelvic cancer	Enoxaparin 40 mg SC daily postoperatively vs placebo	253 248	Asymptomatic DVT Symptomatic DVT PE Death Bleeding	All patients received enoxaparin 40 mg SC, 10-14 h preoperatively, and daily for 6-10 d, then randomized
Bounameaux,[128] 1997	Laparoscopic cholecystectomy	1. Dalteparin 2,500 units preoperative PM; qhs postoperative until venogram 6-10 d 2. Placebo	1. 15 2. 25	Asymptomatic DVT Major bleed VTE > 4 wk	
Enocke,[129] 1988	Age > 40 y	1. Fraxiparin 7,500 units SC daily -2 h; < 7 d 2. Heparin 5,000 units SC tid -2 h; < 7 d	1. 960 2. 936	Asymptomatic DVT Major bleed Minor bleed PE	European Fraxiparin study
Fricker,[130] 1988	Age > 40 y Cancer	1. Fragmin 2,500 units, -2 h; 12 h after first; 5,000 units every AM for 10 d 2. Heparin 5,000 units, -2 h; q8h for 10 d	1. 40 2. 40	Fibrinogen daily < 4 d Every other day < 10 d Position confirmed by venogram PE confirmed by V̇/Q̇ scan Bleeding	75% gynecologic cancer
Gallus,[131] 1976	Abdominothoracic surgery	Aqueous heparin sodium 5,000 units SC 2 h preoperatively, and then tid postoperatively vs no prophylaxis	408 412	Asymptomatic DVT (proximal, distal) Bleeding	
Haas,[132] 2005	Surgery	LMWH (certoparin) 3,000 International Units SC daily vs UFH 5,000 International Units SC tid	11,542 11,536	Fatal PE Death Bleeding	First dose given preoperatively Placebo given to certoparin group to conform to 2X blind design
Heilmann,[133] 1998	Breast and pelvic cancer surgery	UFH 5,000 International Units SC tid vs LMWH: 3,000 International Units SC daily	164 160	Asymptomatic DVT (proximal, distal) Bleeding PE death	Treatment started 2-5 h preoperatively then 7 d LMWH also received placebo injection bid

(Continued)

Table S2—*Continued*

First Author, Year	Specific Population	Interventions	No. in Each Intervention	Outcomes	Comments
International Multicentre Trial,[1] 1975	Major surgery	Heparin 5,000 units SC tid vs control	2,045 2,076	Asymptomatic DVT Symptomatic DVT Death PE	Treatment group received 5,000 units 2 h preoperatively
Kakkar,[134] 1985	GI, gynecologic, urologic, other miscellaneous surgery	LMWH 1,850 aPTT units daily and placebo daily vs UFH 5,000 aPTT units bid	196 199	Asymptomatic DVT (proximal, distal)	First dose given 2 h preoperatively and then for 7 d postoperatively Open study also conducted
Kakkar,[117] 1993	Age > 40 y	1. Fragmin 2,500 units daily + 1 placebo injection; > 5 d 2. Heparin 5,000 units bid; > 5 d	1. 1,894 2. 1,915	Symptomatic DVT Proximal DVT Distal DVT PE Minor bleeding Major bleeding Death	
Kakkar,[135] 1997	Abdominal surgery (general, gynecologic)	LMWH 1,750 International Units SC daily and placebo daily vs UFH 5,000 International Units SC bid	648 663	Asymptomatic DVT PE Bleeding (including hematoma)	First dose 2 h preoperatively Second dose 8 h postoperatively for at least 5 d (longer if confined to bed)
Lausen,[136] 1998	Abdominal Noncardiac thoracic	1. TED + tinzaparin 3,500 units daily < 7 d 2. TED + tinzaparin 3,500 units daily < 28 d	1. 89 2. 87	Asymptomatic DVT Symptomatic DVT PE	
McLeod,[137] 2001	Colorectal	1. Heparin 5,000 units SC q8h; < 10 d 2. Enoxaparin 40 mg SC every AM + placebo; < 10 d	1. 675 2. 674	Asymptomatic DVT Symptomatic DVT Proximal DVT Distal DVT Minor bleeding Major bleeding PE	Risk factors analyzed
Nurmohamed,[138] 1995	Age > 40 y > 45 min	1. Heparin 5,000 units SC tid < 10 d 2. Enoxaparin 20 mg SC every AM < 10 d + placebo	1. 709 2. 718	Fibrinogen uptake Asymptomatic DVT Symptomatic DVT PE	

(Continued)

Table S2—*Continued*

First Author, Year	Specific Population	Interventions	No. in Each Intervention	Outcomes	Comments
Pezzuoli,[2] 1989	Age > 40 y > 7 d hospitalization	1. CY216 0.30 mL (7,500 units equiv) 2. Placebo	1. 2,247 2. 2,251	PE Death	Not commercial drug No VTE surveillance
Rasmussen,[139] 2006	Major abdominal surgery	No further treatment after day 7 (short-term thromboprophylaxis) vs dalteparin 5,000 International Units SC for a further 21 d (prolonged thromboprophylaxis)	222 205	SDVT PE Fatal PE HIT Fatal bleeding Death from any cause	All patients received dalteparin 5,000 International Units SC daily and wore GCS for 7 d
Rasmussen,[139] 2006	Age > 18 y Surgery > 1 h Not laparoscopic	1. 7-d group: dalteparin 5,000 units SC daily; 5,000 units -hs or 2,500 units -2 h and hs; GCS < 7 d 2. 28-d group: dalteparin 5,000 units SC daily; 5,000 units -hs or 2,500 units -2 h and hs; GCS < 728	1. 178 2. 165	VTE Distal DVT Proximal DVT PE Death Major bleeding	Prophylaxis duration study
Sagar,[140] 1975	Major surgery (thoracic, gastric, biliary, intestinal, laparotomy, urologic, prostactectomy, hiatus hernia)	Heparin sodium 5,000 International Units SC 2 h preoperatively and bid for 5 d vs control	264 236	Fatal PE Bleeding	Control was no prophylaxis administered
Samama,[141] 1988	General surgery	LMWH 60 mg/40 mg/20 mg vs UFH 5,000 units SC tid	157 (60 mg) 124 (40 mg) 167 (20 mg) 147 (UFH) 123 (UFH) 167 (UFH)	Asymptomatic DVT PE	LMWH given 2 h preoperatively UFH given SC 8 h preoperatively Both for 7 d postoperatively
Schaepkens van Riempst,[142] 2002	Laparoscopic cholecystectomy	1. Nadroparin 0.30 mL -2 h daily 2. Placebo	1. 105 2. 133	Asymptomatic DVT	Only asymptomatic events
Schulz,[143] 2005	Surgery	LMWH 20 mg (< 30 BMI) or 30 mg (40 > BMI) SC daily + GCS (24 h/d) vs LMWH	2,393 2,272	Symptomatic DVT (proximal, distal)PE	
Scurr,[144] 1987	General surgery	GCS + IPC vs IPC both applied to either right or left leg	78 78	Asymptomatic DVT (proximal, distal)	Patients served as control and intervention (each leg)

(Continued)

Table S2—*Continued*

First Author, Year	Specific Population	Interventions	No. in Each Intervention	Outcomes	Comments
Simonneau,[145] 2006	Colorectal surgery for cancer	Nadroparin 2,850 International Units vs enoxaparin 4,000 International Units	65 635	Symptomatic DVT PE Fatal PE HIT Fatal bleeding Death from any cause	
Tincani,[146] 2005	Laparoscopic appendectomy Low risk for DVT	Stockings Early ambulation	53	Symptomatic DVT PE	Not randomized
Turpie,[147] 2007	Age >40 y	1. Fondaparinux 2.5 mg 6-8 h postoperative 2. Placebo	1. 650 2. 659	Asymptomatic DVT Symptomatic DVT PE Major bleeding	
Wiig,[148] 1995	Age >40 y Cancer	1. Enoxaparin 20 mg SC daily -2 h < 10 d + placebo inf to match 2. Dextran 70 500 mL postoperatively + 0, +hs, + 1 d, + 3 d, + 5 d; placebo SC to match	1. 128 2. 134	Proximal DVT Distal DVT Asymptomatic DVT Symptomatic DVT PE Major bleeding Death	Part 1 of 2 consider dextran data as baseline for patients with cancer
Wiig,[148] 1995	Age >40 y Cancer	1. Enoxaparin 40 mg SC daily -2 h < 10 d + placebo inf to match 2. Dextran 70 500 mL postoperatively + 0, +hs, + 1 d, + 3 d, + 5 d; placebo SC to match	1. 49 2. 39 (case controls)	Proximal DVT Distal DVT Asymptomatic DVT Symptomatic DVT PE Major bleeding Death	Part 2 of 2 consider dextran data as baseline for patients with cancer
Wille-Jørgensen,[149] 1995	Age >40 y	1. Heparin 5000 U SC bid 2. LDH as above + TED	1. 171 2. 165	VTE	

(Continued)

Table S2—*Continued*

First Author, Year	Specific Population	Interventions	No. in Each Intervention	Outcomes	Comments
		Urologic surgery			
Coe,[150] 1978	All adult patients undergoing urological operations	Heparin 5,000 units SC 2 h preoperatively then q12h postoperatively until discharge vs external pneumatic compression of calves from start of operation until discharge vs control (neither)	28 29 24	DVT PE	
Hendolin,[151] 1981	Retropubic prostatectomy for BPH	Epidural anesthesia vs general anesthesia	17 21	DVT	Outcomes of venographically confirmed DVT are not reported for each group; therefore, no useful data available from this trial.
Soderdahl,[152] 1997	Major urologic surgery	Calf-length vs thigh length pneumatic compression, both placed at beginning of operation until ambulatory	43 47	DVT	
		Gynecologic surgery			
Baykal,[153] 2001	Nonsmokers undergoing gynecologic cancer surgery with pelvic and paraaortic lymphadenectomy	Enoxaparin 2,500 units 2 h preoperatively and daily postoperative vs heparin 5,000 2 h preoperatively and tid postoperatively	47 55	Blood loss, drainage, transfusion requirement, hemoglobin, hematoma, clinical DVT	
Clarke-Pearson,[154] 1983	Patients undergoing major operation for known or presumed gynecologic malignancy	Low-dose heparin 5,000 SC 2 h preoperatively, q12h postoperatively for 7 d vs control (no prophylaxis)	88 97	Venous thromboembolic complication, proximal DVT, calf vein thrombosis, PE	
Clarke-Pearson,[155] 1990	Patients aged >40 y undergoing major gynecologic surgery for known or presumed malignancy	1. No prophylaxis 2. Heparin 5,000 units SC 2 h preoperatively, q8h postoperatively (regimen I) 3. Heparin 5,000 units SC q8h preoperatively and q8h postoperatively (regimen II)	1. 103 2. 104 3. 97	1. Asymptomatic VTE, fibrinogen scan, exclude 2. Symptomatic DVT, impedance plethysmography, contrast venography 3. Symptomatic PE, $\dot{V}/\dot{Q}$ scan, pulmonary arteriography 4. Bleeding complications	
Clarke-Pearson,[156] 1993	Patients undergoing surgery for gynecologic malignancy	Low-dose (5,000 units) heparin q8h starting day before surgery until discharge, postoperative day 7, or ambulatory vs calf IPC for 5 d postoperatively	107 101	DVT Bleeding complications	

(Continued)

Table S2—*Continued*

First Author, Year	Specific Population	Interventions	No. in Each Intervention	Outcomes	Comments
Maxwell,[157] 2001	Patients aged >40 y undergoing major operation for gynecologic malignancy	LMWH (dalteparin) 2,500 units SC 1-2 h preoperatively, 2,500 12 h postoperatively, then 5,000 units SC q24h for 5 d or until discharge vs extended pneumatic compression placed in operating room and kept for 5 d	105 106	Asymptomatic DVT Symptomatic DVT PE	
Ward,[158] 1998	Major gynecologic surgery	LMWH (fragmin) 5,000 units SC daily starting 12 h preoperatively until 5 d postoperatively vs heparin 5,000 units SC bid starting 12 h preoperatively until 5 d postoperatively	280 286	Thromboembolic events Bleeding up to 6 wk postoperatively	
		Bariatric surgery			
Imberti,[18] 2009	Bariatric surgery	Parnaparin 4,250 International Units (median BMI, 46.7 kg/m^2; range, 36.5-58.8) vs 6,400 International Units) median BMI, 43.7 kg/m^2; range, 36.1-64.1) for 7-11 d	36 30	Anti-Xa on day 0, 4, 6, (before and 4 h after injection)	Start 12 h preoperatively
Kalfarentzos[13] 2001	RYGBP	Nadroparin 5,700 International Units vs nadroparin 9,500 International Units SC once preoperatively and once daily postoperatively until the day of discharge	30 30	Asymptomatic DVT (proximal, distal) Major bleeding	
Nguyen,[159] 2001		ORYGBP vs LRYGBP	34 36	Primary end point of the study was the change in molecular coagulation activity Secondary end points were clinical evidence of postoperative DVT and PE	Thigh-length pneumatic sequential compression sleeves and thigh-length antiembolic stockings were placed on both lower extremities for DVT prophylaxis in both groups before the induction of anesthesia. The SCD and TED were continued postoperatively on the ward until patients were discharged.

(Continued)

Table S2—*Continued*

First Author, Year	Specific Population	Interventions	No. in Each Intervention	Outcomes	Comments
			Vascular surgery		
Belch,[160] 1979	Aortic bifurcation graft surgery	Heparin calcium 2,500 International Units preoperatively and 5,000 bid vs placebo	24 25	Asymptomatic DVT (proximal, distal) Bleeding Wound complications Death	All patients given 3,000 units Ca heparin intraoperatively
Farkas,[161] 1993	Aortic or aortoiliac aneurysm repair, aortofemoral, femoropopliteal bypass, or femorodistal bypass	UFH 5,000 preoperatively and 7,500 daily for 7 d vs enoxaparin 20 mg preoperatively and 40 mg/d for 7 d	111 122	Asymptomatic DVT (proximal, distal) Major bleeding Death	All patients given heparin 50 International Units/kg intraoperatively
Harjola,[162] 1980	400 consecutive vascular (reconstructive arterial) surgery patients	Dipyridamole 150 tid, ASA 0.5 g tid, or both, preoperative day 1 or 2 to discharge vs no prophylaxis	99 (dipyridamole + ASA) 96 (dipyridamole) 97 (ASA) 97 (control)	Symptomatic DVT PE	
Killewich,[163] 1997	Aortic surgery: aneurismal (75) or occlusive (25)	UFH 5,000 bid plus calf-length IPC vs no prophylaxis	50 48	Symptomatic DVT PE Symptomatic VTE + asymptomatic DVT (proximal)	All patients given heparin 70 units/kg intraoperatively
Lastoria,[164] 2006	Lower-extremity amputation (above-knee or below-knee amputation)	UFH 5,000 tid vs enoxaparin 40 mg/d	34 41	DVT not otherwise specified	
Spebar,[165] 1981	Vascular surgery: aortic or carotid reconstruction, leg revascularization, pseudoaneurysm repair, lumbar sympathectomy, repair of arteriovenous fistula	UFH 5,000 2 h preoperatively and bid vs no prophylaxis	24 19	Asymptomatic DVT (all, proximal) PE	
Speziale,[166] 1988	92 vascular surgery patients (abdominal aortic aneurysm or aortoiliofemoral bypass)	LMWH (fluxum) 15,000 anti-XA units SC preoperatively and daily for 7 d vs heparin 5,000 International Units SC preoperatively and bid for 7 d	46 (LMWH) 46 (heparin)	Asymptomatic DVT	
Urbanyi,[167] 1982	130 vascular surgery patients (carotid, aortic, proximal lower extremity)	Heparin 5,000 SC tid vs heparin 5,000 SC bid plus DHE 0.5 mg SC vs dextran 60 500 mL daily for 6 d	43 (heparin) 41 (heparin + DHE) 46 (dextran 60)	Clinical signs of DVT or asymptomatic DVT	Prophylaxis begun preoperatively Not clear whether heparin groups received prophylaxis after postoperative day 1

(Continued)

Table S2—*Continued*

First Author, Year	Specific Population	Interventions	No. in Each Intervention	Outcomes	Comments
		Cardiac and thoracic surgery			
Azorin,[25] 1997	Thoracic surgery for cancer	Nadroparin 3,075 International Units anti-Xa (fixed dose) vs nadroparin 4,100 or 6,150 International Units anti-Xa (dose adjusted for body weight only) over a period of 8 d started 12 h preoperatively	74 74	DVT PE	Multicenter, open randomized trial
Cade,[24] 1983	Thoracic surgery (46 lobectomies, 21 pneumonectomies, 27 gastroesophageal, 6 thoracic only)	UFH 5,000 International Units × 2 vs 7,500 International Units U × 2 commenced 1-2 h preoperatively and continued until the patient was fully ambulatory	49	Calf	Daily leg scanning postoperatively following the IV injection of ~100 iiCi 1,251 fibrinogen
		All patients in addition received electrical calf muscle stimulation during surgery	51	Popliteal DVT	
Goldhaber,[168] 1995	Coronary artery bypass graft	GCS vs GCS + IPC	166 164	Proximal DVT Distal DVT PE	All patients received aspirin Before discharge, patients underwent ultrasonography on or after postoperative day 4 Both legs were examined from the groin distally, including calves
Ramos,[23] 1996	Cardiac surgery	UFH 5,000 bid plus IPC vs UFH 5,000 bid alone	1,355 1,196	Clinically suspected PE, confirmed by high-probability lung scan, pulmonary angiography, or autopsy	Single center, 1984-1994
		Craniotomy			
Constantini,[40] 2001	Craniotomy for brain tumor	Heparin 5,000 units q12h (including 2 h preoperative dose) vs placebo	55 48	Bleeding only (blood loss, no. of transfusions, surgeon assessment)	No efficacy assessment
Dickinson,[36] 1998	Craniotomy for brain tumor	SCD vs enoxaparin 30 mg q12h (first dose preoperatively) vs SCD + enoxaparin 30 mg q12h	22 21	Symptomatic VTE + asymptomatic DVT (by ultrasound)	Cranial base neoplasms and pituitary adenomas excluding all patients given TED hose.
			23	Clinical bleeding	Stopped early because of ICHs (4) in patients receiving enoxaparin

(Continued)

Table S2—*Continued*

First Author, Year	Specific Population	Interventions	No. in Each Intervention	Outcomes	Comments
Goldhaber,[34] 2002	Craniotomy for brain tumor	Enoxaparin 40 mg/d vs UFH 5,000 units bid	75 75	Asymptomatic DVT by ultrasound (all, proximal) Clinical bleeding	GCS and IPC in all patients
Iorio,[169] 2000	Meta-analysis of four randomized controlled trials on various neurosurgery populations	Heparin or LMWH ± GCS vs placebo ± GCS	410 417	All VTE (proximal, distal) All bleeding Major bleeding Composite of death, PE, major bleeding	Three studies LMWH (enoxaparin 40 mg/d, enoxaparin 20 mg/d, nadroparin 7,500 units daily) One study UFH 5,000 units tid
Macdonald,[35] 2003	Craniotomy (various indications)	Dalteparin 2,500 units daily vs UFH 5,000 units bid (both started in the operating room)	51 49	All VTE (asymptomatic or symptomatic) Bleeding (ICH, blood loss, surgeon assessment)	IPC in all patients
Lacut,[170] 2005	Acute ICH (traumatic or spontaneous)	IPC + ES vs ES alone	74 77	All VTE (asymptomatic by ultrasound or symptomatic)	Proximal and distal DVT reported separately
Wautrecht,[171] 1995	Craniotomy for brain tumor	IPC + ES vs ES alone	25 10	All VTE (including asymptomatic by venogram)	Proximal and distal DVT reported separately
			Spinal surgery		
Gruber,[30] 1984	Lumbar disc surgery	Placebo UFH + DHE	25 25	Bleeding Symptomatic DVT PE	Nine patients enrolled despite meeting exclusion criteria
Voth,[33] 1992	Lumbar disc surgery	LMWH + DHE UFH + DHE	87 92	DVT PE Bleeding	
Macouillard,[172] 1995 (abstract)	Lumbar spinal surgery with at least two patient-related risk factors for VTE	Enoxaparin 40 mg/d Enoxaparin 20 mg/d	30 30	Asymptomatic DVT PE Bleeding complications	

(Continued)

Table S2—*Continued*

First Author, Year	Specific Population	Interventions	No. in Each Intervention	Outcomes	Comments
Rokito,[173] 1995	Major reconstructive spinal surgery	ES alone ES + IPC ES + low-dose warfarin (target prothrombin time 1.3-1.5 of control)	42 33 35	All VTE (CUS on both legs in all patients day 6 ± 1)	110 of 329 patients randomized; others failed to meet inclusion criteria or declined
Nelson,[174] 1996	Posterior lumbar decompression with fusion and fixation for degenerative disease or spondylolisthesis	ES + ASA ES + ASA + IPC	60 57	Symptomatic VTE Asymptomatic proximal DVT by DUS	
Wood,[175] 1997	Anterior or posterior thoracic, thoracolumbar, or lumbar multilevel decompressions and/or spinal fusions	ES + foot pneumatic wrap (Plexipulse compression device) ES + IPC	75 59	DVT PE Local complications Comfort	
		Spinal cord injury			
Chiou-Tan,[176] 2003	100 patients with acute, complete, or incomplete SCI, (within 3 mo of the date of injury)	Enoxaparin 30 mg SC bid Dalteparin 5,000 International Units daily	36 36	Symptomatic DVT PE DeathBleeding	Majority of patients enrolled more than 2 wk after SCI; most patients treated (and followed) for 1.5-3 mo
Frisbie,[177] 1981	32 patients with acute SCI	LDUH 5,000 bid No prophylaxis	15 17	Asymptomatic DVT Symptomatic DVT	Prophylaxis given for 60 d
Green,[178] 1982	27 patients with acute SCI and complete lower-limb paralysis	EPCC EPCC + ASA 300 mg bid + dipyridamole 75 mg tid No prophylaxis	15 12 37	DVT PE Bleeding	Prophylaxis given for 4 wk Untreated patients were not studied concurrently with prophylaxis patients, but methods and procedures were identical
Green,[179] 1988	75 patients with complete motor SCI	LDUH 5,000 units bid Adjusted-dose UFH (on average 1.5 times higher dose)	29 29	DVT Bleeding PE	Prophylaxis given for 12 wk
Green,[180] 1990	41 patients with SCI and complete motor paralysis	UFH 5,000 units tid vs LMWH 3,500 anti-Xa units daily	21 20	Asymptomatic DVT Symptomatic DVT PE Bleeding requiring discontinuation of heparin	Prophylaxis started 24 h after injury
Lohmann,[181] 2001	166 patients	LDUH 7,500 units bid Dalteparin 5,000 International Units daily	80 86		Prophylaxis given for about 6 wk

(Continued)

Table S2—*Continued*

First Author, Year	Specific Population	Interventions	No. in Each Intervention	Outcomes	Comments
Merli,[182] 1992	48 patients with acute SCI	Placebo LDUH 5,000 units SC bid + gradient ES + EPC	19 15	DVT PE	Prophylaxis given for 4 wk Control group was from previous study
SCI Thromboprophylaxis Investigators,[52] 2003	107 patients (from multiple centers) with acute SCI (enrolled within 72 h)	UFH q8h (+ IPC) Enoxaparin 30 mg SC q12h	49 58	All VTE Asymptomatic DVT (proximal) PE Symptomatic DVT	476 patients randomized, but only 107 deemed assessable Separate analysis for 181 patients who had adequate proximal (but not distal) vein imaging
		Major trauma (excluding isolated lower extremity or other orthopedic injuries)			
Cohn,[47] 1999	Moderately injured patients (excluded brain or severe visceral injuries) Average ISS, 12	1. UFH 5,000 units bid until patients were fully ambulatory or discharged 2. Enoxaparin 30 mg bid until patients were fully ambulatory or discharged	1. 32 2. 34	Symptomatic DVT Bleeding complications Pulmonary embolism	Randomized double-blind single-center study
Elliot,[44] 1999	Nonlower-extremity major trauma	1. Thigh-length pneumatic compression (SCD) 2. Plantar pump	1. 62 (79) 2. 62 (70)	Asymptomatic DVT and proximal detected by bilateral duplex 8 d after randomization Major bleeding Death	Anticoagulants or antiplatelets not allowed Not double blind
Fisher,[42] 1995	Patients operated for hip and pelvic fractures	1. Intermittent compression with SCD, starting postoperatively and until full ambulation 2. Control without prophylaxis	1. 145 2. 159	Asymptomatic DVT Proximal DVT PE	Randomized single-center open study
Fuchs,[49] 2005	Trauma to the spine, pelvis, femur, tibia, or ankle or total hip replacement following fracture of the femoral neck	Arthroflow device (CPM) vs no Arthroflow	111 116	DVT (symptoms not specified) Proximal DVT PE Death from any cause	All patients received UFH 5,000 units SC tid Open RCT
Geerts,[48] 1996	Trauma patients with ISS > 8	1. LDUH 5,000 units bid starting within 36 h of injury and up to 14 d 2. Enoxaparin 30 mg starting within 36 h of injury and up to 14 d	1. 136/173 2. 129/171	Asymptomatic DVT and proximal detected by bilateral venography 10-14 d after randomization Major bleeding Death	Randomized double-blind No mechanical methods allowed

(Continued)

Table S2—*Continued*

First Author, Year	Specific Population	Interventions	No. in Each Intervention	Outcomes	Comments
Ginzburg,[46] 2003	Trauma patients with ISS > 8	1. Calf-length IPC	1. 209/224	Asymptomatic DVT detected by routine duplex	Not blinded
		2. Enoxaparin 30 mg bid starting within 24 h of trauma	2. 189/218	PE Major and minor bleeding Death HIT	
Haentjens,[183] 1996	Trauma patients with spinal, pelvic, or lower-extremity fractures receiving surgical treatment	1. Fixed-dose nadroparin 3,075 International Units for 24 h starting within 8 h of injury and lasting 6 wk	1. 142 for ITT analysis 2. 141 for ITT analysis	Asymptomatic total DVT	Not blinded
		2. Weigh-adjusted nadroparin (depending on weight < 50, 50-70, or > 70 kg) (40-60 International Units/kg) and with an increase in dose on the fourth postoperative day	1. 106 for per protocol efficacy analysis at 10 d and 76 at 6 wk 2. 109 for per protocol efficacy analysis at 10 d and 74 at 6 wk	PE Mortality Major bleeding HIT Death	
Knudson,[43] 1994	Adult trauma patients admitted to a trauma service	1. UFH 5,000 units/12 h 2. SCD 3. Control without prophylaxis	1. 63 2. 58 3. 130	Asymptomatic DVT Proximal DVT Symptomatic DVT PE	Randomization to UFH, SCD and/or no prophylaxis within 3 different groups, including any treatment, LE fracture, and anticoagulation contraindicated
Knudson,[45] 1996	Trauma patients with different types of bone and visceral injuries	1. LMWH (enoxaparin 30 mg bid) initiated within 24 h 2. Compression methods: SCD 3. Arterial venous impulse (FP)	1. 120 2. 199 3. 53	Asymptomatic DVT Proximal DVT	Randomized open study
Stannard,[184] 2005	Blunt trauma and at least one of the following findings: abbreviated injury score of ≥ 3 and a long-bone fracture, multiple long-bone fractures, or age of 55 y and a long-bone fracture	Enoxaparin 30 mg SC beginning 24-48 h after trauma vs Plexipulse FP + enoxaparin 30 mg SC beginning 5 d after admission	97 103	DVT (symptoms not specified) Fatal PE (no deaths) PE ICH Fatal bleeding (no deaths) Death from any cause (no deaths	

(Continued)

Table S2—*Continued*

First Author, Year	Specific Population	Interventions	No. in Each Intervention	Outcomes	Comments
Velmahos,[41] 2005	Major trauma (ISS >9) and contraindications for receiving prophylactic heparin	Muscle electrostimulation vs standard care	30 30	DVT (symptoms not specified) PE Fatal PE HIT (no complications) Bleeding requiring reoperation (no complications) Fatal bleeding (no complications) Death from any cause	All patients were allowed to have standard prophylaxis by SC heparin when contraindication for its use was no longer present and by SCDs if the extremities were not injured at the site of placement.
		Same-day surgery			
Baca,[185] 1997	Laparoscopic cholecystectomy and other types of minimally invasive surgery	LMWH (reviparin SC daily) + graduated ES vs graduated ES	359 359	Asymptomatic DVT PE Bleeding	Manuscript in German
		Aspirin			
Clagett,[186] 1975	Middle-aged and elderly patients postoperative (Gyn, urologic, general)	ASA 650 mg 2-6 h postoperatively until ambulatory or discharged vs no prophylaxis	49 49	Asymptomatic DVT Platelet survival	Those who could not take orally were administered a suppository
Encke,[187] 1988	Abdominal surgery	Placebo ASA 330 mg tid Dipyridamole 75 + ASA 330 mg tid	34 32 30	DVT	
Harjola,[162] 1980	Peripheral vascular reconstructive surgery	ASA 0.5 g tid + dipyridamole 150 mg tid vs dipyridamole 150 mg tid only vs ASA 0.5 g tid only vs no prophylaxis	100 100 100 100	Symptomatic DVT PE	Treatment started orally on first or second postoperative day
Hartung,[188] 1979	Age >30 y GI, urologic Hip fracture	ASA 1,500 mg/d Placebo	401 401	DVT PE Fatal PE	Prospective randomized with matched cohorts 49 excluded because of no match
Loew,[189] 1974	Mixed surgical	ASA Placebo	510 527	PE	Background use of compression stockings in approximately equal numbers in two groups
Medical Research Council,[190] 1972	Elective surgery	ASA 600 mg 24 h preoperatively and then daily for 5 d vs placebo 600 mg 24 h preoperatively and then daily for 5 d	153 150	Asymptomatic DVT	

(Continued)

Table S2—*Continued*

First Author, Year	Specific Population	Interventions	No. in Each Intervention	Outcomes	Comments
Schreiber,[191] 1979	General surgery	ASA 1,500 mg/d Placebo	304 304	DVT PE GI bleeding	
Zekert,[192] 1980	Major abdominal surgery	ASA + DHE vs ASA (1 g/d) only vs DHE (0.5 mg bid) only Treatment started on day of surgery and stopped upon discharge	50 50 50	Asymptomatic DVT Symptomatic DVT PE	If VTE or PE occurred, prophylaxis replaced by heparin Dose for orally fed was DHE (2.5 mg) and ASA (0.5 g)
Zekert,[192] 1980	Abdominal surgery, women	LDUH 5,000 units SC bid Heparin + ASA 1.5 g (500 mg tid)ASA 1.5 g (500 mg tid)	49 50 53	Clinical VTE Superficial VT DVT PE Suspected and confirmed bleeding during operation Death 14 d	First dose before surgery

-2 = 2 hours before surgery; +0 = at time of surgery; +hs = at night; aPTT = activated partial thromboplastin time; ASA = aspirin; BPH = benign prostatic hyperplasia; CPM = continuous passive motion; CUS = compression ultrasound; DHE = dihydroergotamine; DUS = duplex or doppler ultrasound; ENOXACAN = Enoxaparin and Cancer study; EPCC = external pneumatic calf compression; FP = foot pump; GCS = graduated compression stockings; HIT = heparin-induced thrombocytopenia; ICH = intracranial hemorrhage; inf = in frequency; IPC = intermittent pneumatic compression; ISS = injury severity score; ITT = intention to treat; LDUH = low-dose unfractionated heparin; LMWH = low-molecular-weight heparin; LRYGBP = laparscopic Roux-en-Y gastric bypass; ORYGBP = open Roux-en-Y gastric bypass; PE = pulmonary embolism; qhs = every night at bedtime; RYGBP = Roux-en-Y gastric bypass; SC = subcutaneous; SCD = sequential compression device; SCI = spinal cord injury; TED = thromboembolic deterrent; UFH = unfractionated heparin; $\dot{V}/\dot{Q}$ = ventilation/perfusion.

Table S3—*Risk of Bias in Randomized Controlled Trials of Thromboprophylaxis*

First Author, Year	Randomization Concealment	Outcome: Surveillance	Blinding	Lost to Follow-up	Analysis	Comments
			Generic, mixed, abdominal surgery			
Agnelli,[122] 2005	NR (were randomized, method NR)	All patients assessed with bilateral ascending contrast venography of the legs between days 5 and 10 postsurgery followed by ultrasound if DVT suspected PE confirmed by high-probability lung scan, pulmonary angiography, helical CT, or at autopsy	Patients: PY (double dummy, double blind) Caregivers: PY (double dummy, double blind) Data collectors: PY (double dummy, double blind) Outcome adjudicators: DY (adjudicated by a central independent committee that was unaware of the patients' treatment assignment and the local assessment) Data analysts: NR		Number of primary efficacy outcome analysis excluded, 879/2,927 (30%); 810 (28%) of excluded patients were not evaluable for primary analysis for unspecified reasons	
Bergqvist,[123] 1986	NS, block randomization/ every 10 patients	Fibrinogen leg scanning preoperatively, on first postoperative day, and every second day thereafter, except for an uptake increase where measurements were made daily	Patients: Y Caregivers: Y Data collectors: NS Outcome adjudicators: NS Data analysts: NS	0/432	ITT	Only 382 subjects received correct prophylaxis
Bergqvist,[124] 1988	NS, block randomization/ every 10 patients	Fibrinogen given day prior to surgery Measured once preoperatively and then for 7 postoperative days Positive FUT underwent phlebography when possible Symptomatic DVT verified by scintigraphy	Patients: Y Caregivers: Y Data collectors: NS Outcome adjudicators: NS Data analysts: NS	0/1,002	ITT	Correct prophylaxis was given to 826 patients (405 LDUH and 421 LMWH)

(Continued)

Table S3—*Continued*

First Author, Year	Randomization Concealment	Outcome: Surveillance	Blinding	Lost to Follow-up	Analysis	Comments
Bergqvist,[125] 1995	O, block randomization/ every 10 patients For every randomized patient, there was a box with eight syringes of each dose	Fibrinogen leg scanning day before surgery, preoperatively, and 7 d postoperatively Patients with positive FUT underwent phlebography when possible	Patients: Y Caregivers: Y Data collectors: NS Outcome adjudicators: NS Data analysts: NS	0/2,070	ITT	Correct prophylaxis provided to 1,732 patients Dextran or additional heparin Allowed after LMWH regimen complete
Bergqvist,[126] 1997	NS	Venogram < 1 d after last injection Upon symptoms If PE V̇/Q̇ and/or pulmonary angiography Major bleeding with definitions	Y	460 lost with explanation	TR	Four most common procedures were general surgical
Bergqvist,[127] 2002	NS	Venogram verified by a central committee (performed routinely days 25-31) PE confirmed by V̇/Q̇ lung scanning, angiography, or both	Patients: Y Caregivers: Y Data collectors: NS Outcome adjudicators: Y Data analysts: NS	I: 88/253 C: 81/248	ITT	
Bounameaux,[128] 1997	NS	Venography > 6 < 10 d VTE > 4 wk Major bleeding	Double	Intervention = 41 Placebo = 41 15 intervention received venography 26 placebo received venography Differential loss as above; reasons specified	TR	Small number

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Table S3—*Continued*

First Author, Year	Randomization Concealment	Outcome: Surveillance	Blinding	Lost to Follow-up	Analysis	Comments
Encke,[187] 1988	NS	Fibrinogen Confirmatory venography	Single	8/5 with explanation	TR	
Fricker,[130] 1988	None, open	Fibrinogen Confirmatory venogram Confirmatory $\dot{V}/\dot{Q}$	None, open	Fragmin intervention lost 1 with explanation	TR	Poor study; some patients temporarily withdrawn from treatment
Gallus,[131] 1976	O, allocation cards drawn from sealed, numbered envelopes	I-labeled fibrinogen leg scanning confirmed by phlebography	Patients: N Caregivers: N Data Collectors: NS Outcome adjudicators: NS Data analysts: NS	0/820	ITT	
Haas,[132] 2005	O, centralized computer-generated randomization list	O, autopsy	Patient: Y Caregivers: Y Data Collectors: NS Outcome adjudicators: NS Data analysts: NS	0/23,078	ITT	Study ended prematurely because would not be sufficiently powered to show superiority of certoparin over UFH
Heilmann,[133] 1998		Noninvasive testing with IPG on days 1, 3, 5, 7, and 10 If DVT suspected, confirmed with ascending venography	Patient: Y Caregivers: Y Data Collectors: NS Outcome adjudicators: NS Data analysts: NS	19/179: LMWH 15/175: UFH	TR	

(Continued)

Table S3—*Continued*

First Author, Year	Randomization Concealment	Outcome: Surveillance	Blinding	Lost to Follow-up	Analysis	Comments
International Multicentre Trial,[1] 1975	Sealed envelopes	FUT for 7 d (10 centers did this) and confirmed by phlebography PE confirmed by radiography and ECG	Patient: N Caregivers: N Data Collectors: NS Outcome adjudicators: NS Data analysts: NS	0/176 0/174	ITT	
Kakkar,[134] 1985	O, boxes with ampoules numbered in random order and one provided to each patient	FUT for 7 d If patient had inconsistent counts, phlebograms were performed.	Patients: Y Caregivers: Y Data collectors: NS Outcome adjudicators: NS Data analysts: NS	0/395	ITT	49 patients, about equally distributed between the two groups, did not receive a complete course of prophylaxis
Kakkar,[117] 1993	Labeled syringes	Confirmation by venography or V̇/Q̇	Double	Fragmin = 66; heparin = 63 Reasons provided	TR	No routine screening done
Kakkar,[135] 1997	NS	FUT daily, if 2 positive scans in 24 h patient, given phlebography when possible Symptomatic (PE) verified by V̇/Q̇ lung scanning, pulmonary angiography, or both Final DVT/PE diagnosis based on assessment of blinded expert committee	Patients: Y Caregivers: Y Data collectors: NS Outcome adjudicators: NS Data analysts: NS	0/1,351	ITT	Operation canceled for 9 patients; thus 665 LMWH and 677 UFH for perioperative hemorrhagic events Efficacy analysis comprised 648 patients taking LMWH and 663 patients taking UFH for whom conclusive diagnosis obtained by expert committee after review of all patient information

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Table S3—*Continued*

First Author, Year	Randomization Concealment	Outcome: Surveillance	Blinding	Lost to Follow-up	Analysis	Comments
Lausen,[136] 1998	SE	Confirmation by venography	Double	7-d arm = 29; 28-d arm = 29 with explanation	TR	Nearly one-third dropout
McLeod,[137] 2001	SE	Confirmation by venography	Double	Heparin = 32; enoxaparin = 21 with explanation	TR	DVT not tabulated; reported as %
Nurmohamed[138] 1995	SE	Fibrinogen uptake; confirmation by 8 venography	Double	10/7 with explanation	TR	
Pezzuoli,[2] 1989	NS	NS	Double	35/34 with partial explanation	TR	
Rasmussen,[139] 2006	Envelopes, other (computer-generated random allocation)	Asymptomatic and symptomatic DVT detected by venography Symptomatic PE verified by V̇/Q̇ scan or spiral CT DVT or PE verified at autopsy	Patients: DN (open label) Caregivers: DN (open label) Data collectors: NS DN (open label) Outcome adjudicators: DY (radiologists were unaware of the personal data of the patients, the randomization group, the clinical course, and the date of venography) Data analysts: DN (open label)		ITT	
Sagar,[140] 1975	NS, Cambridge tables	None	Patients: NS Caregivers: N Data collectors: NS Outcome adjudicators: NS Data analysts: NS	0/500	ITT (likely)	Twelve patients did not receive the full course of heparin

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Table S3—*Continued*

First Author, Year	Randomization Concealment	Outcome: Surveillance	Blinding	Lost to Follow-up	Analysis	Comments
Samama,[141] 1988	NS	FUT on first postoperative day and every second day thereafter, except when FUT increased in which measurements made daily	Patient: N Caregivers: N Data collectors: NS Outcome adjudicators: NS Data analysts: NS	0	ITT	
Schaepkens van Riempst,[142] 2002	NA	Ultrasound at 10 d	No		TR	Not randomized
Schulz,[143] 2005	NA	None	Patients: NS Caregivers: NS Data collectors: NS Outcome adjudicators: NS Data analysts: NS			Prophylaxis measures administered to patients who were not operated on if immobile for > 6 h during the day for > 2 d
Scurr,[144] 1987	NS	FUT, ultrasound, and plethysmography on days 1, 3, 5, and 7 and venography for confirmation	Patient: N Caregivers: N Data collectors: NS Outcome adjudicators: NS Data analysts: NS	0/78		
Simonneau,[145] 2006	Central randomization	All patients received a venography of the legs between days 8 and 12 Symptomatic PE was confirmed by pulmonary angiography	Patients: PY (double dummy, double blind) Caregivers: PY (double dummy, double blind) Data collectors: PY (double dummy, double blind) Outcome adjudicators: PY (double dummy, double blind) Data analysts: PN		No Exclusion of 338/1,288 (26%) patients, primarily due to missing or nonconclusive venograms	
Tincani,[146] 2005	NA	Clinical presentation	Open	None	TR	Low numbers
Turpie,[147] 2007	O, computer generated	Venography	Double	Fondaparinux = 212; placebo = 231 with explanation	TR	

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Table S3—*Continued*

First Author, Year	Randomization Concealment	Outcome: Surveillance	Blinding	Lost to Follow-up	Analysis	Comments
Wiig,[148] 1995	O, block by site and risk	Venography	Double	NR	TR	Stopped early due to high incidence of DVT
Wiig,[148] 1995	O, block by site and risk	Venography	Single with case-control placebo	NR	TR	
			Urologic surgery			
Coe,[150] 1978	NS, random number table	Fibrinogen scan daily, phlebography if positive scan on 2 consecutive days	Outcome assessors: blinded Patients, clinicians, data analysts: NS	Two patients in pneumatic compression group excluded after randomization because they received heparin	TR (excluded crossover patients)	
Hendolin,[151] 1981	NS, sealed envelopes	Fibrinogen scan postoperative day 0, 1, 2, 3, 5, and 7 confirmed with phlebography if positive for 2 consecutive days	NS	0	NA	Outcomes of venographically confirmed DVT are not reported for each group; therefore, no useful data available from this trial
Soderdahl,[152] 1997	NS, random number table	Duplex ultrasound postoperative day 3 or 4 and postoperative day 6 or 7	Outcome assessors blinded Patients, clinicians, data analysts: NS	101 eligible 90 completed the study	TR	
			Gynecologic surgery			
Baykal,[153] 2001	NS	Clinical follow-up If DVT suspected, duplex ± venography If PE suspected, V̇/Q̇ scan ± arteriography	Patients: NS Caregivers: Y Data collectors: Y Adjudicators: NS Data analysts: NS	NR	NR	

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Table S3—*Continued*

First Author, Year	Randomization Concealment	Outcome: Surveillance	Blinding	Lost to Follow-up	Analysis	Comments
Clarke-Pearson,[154] 1983	NS	FUT daily until discharge and impedance plethysmography every 2 days. Venography to confirm whether either test positive. Venography, V̇/Q̇ scan, or pulmonary arteriography if clinical suspicion	NS	15 patients excluded after randomization None lost to follow-up	NR	
Clarke-Pearson,[155] 1990	NS	FUT daily until hospital discharge If fibrinogen test is positive, ascending venography to confirm DVT Followed clinically for 30 d postoperatively Symptoms of DVT assessed with impedance plethysmography and venography if clinically indicated Symptoms of PE assessed w V̇/Q̇ scan and pulmonary arteriography Laboratory tests to assess bleeding daily	Not reported for any group	20 patients excluded from further analysis after randomization	NR	
Clarke-Pearson,[156] 1993	NS	FUT daily until discharge Confirmed with venography Symptoms of DVT evaluated with plethysmography, Doppler ultrasound, venography is indicated. Symptoms of PE investigated with V̇/Q̇ scan and arteriography.	NS	10 patients excluded after randomization because of cancelled surgery No patients lost to follow-up.	NR	

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Table S3—*Continued*

First Author, Year	Randomization Concealment	Outcome: Surveillance	Blinding	Lost to Follow-up	Analysis	Comments
Maxwell,[157] 2001	NS	DUS between days 3 and 5 Telephone interview 30 d postoperatively	Patients: NS Caregivers: NS Data collectors: NS Adjudicators: Y Data analysts: NS	17 patients excluded after randomization	ITT	
Ward,[158] 1998	O, stated as "concealed from surgeon until after the operation" but not reported how	Clinically suspected thromboembolic disease confirmed with VQ scan, Doppler ultrasound, venography depending on clinical situation	NS	14 patients excluded from analysis who did not undergo planned surgery	NR	
			Vascular surgery			
Belch,[160] 1979	O, prepacked syringes	Fibrinogen leg scanning, preoperatively and on postoperative days 1, 3, 5, 7, etc until discharge Positive scans confirmed by repeating scan on next day and then by venography if still positive	Double blind Patients: Y Caregivers: Y	0	ITT	Stopped early for harm (bleeding complications)
Farkas,[161] 1993	O, randomly numbered ampules	DUS for symptoms or on day 7-10 Positive scans confirmed by venography	Radiologists and echocardiography technicians: Y Patients: NS Data collectors: NS Adjudicators: NS Data analysts: NS	36/269 16 UFH 9 enoxaparin 11 NS Diff: NS Reason: yes	ITT	
Harjola,[162] 1980	NS	No surveillance DVT suspected clinically and confirmed by venography	Surgeons blinded to prophylaxis	11 excluded postrandomization (1, 4, 3, 3)	TR	

(Continued)

Table S3—*Continued*

First Author, Year	Randomization Concealment	Outcome: Surveillance	Blinding	Lost to Follow-up	Analysis	Comments
Killewich,[163] 1997	NS	DUS preoperatively and on postoperative days 1, 3, 7, and weekly thereafter	Patients: NS Caregivers: NS Data collectors: NS Adjudicators: NS Data analysts: NS	0 (I) 2 excluded after death due to MI and intestinal infarct (C) Diff: N Reason: Y	ITT	
Lastoria,[164] 2006	SE	DUS 5 to 8 d postoperatively Repeated when inconclusive	Ultrasonographers: Y Otherwise: open label	0	ITT	
Spebar,[165] 1981	NS	Fibrinogen leg scanning preoperatively and daily for 5-7 d	Patients: NS Caregivers: NS Data collectors: NS Adjudicators: NS Data analysts: NS	0	ITT	
Speziale,[166] 1988	NS	Fibrinogen leg scanning daily Positive findings confirmed by DUS	NS	0	ITT	
Urbanyi,[167] 1982	NS	Fibrinogen leg scanning daily, followed by venogram and V̇/Q̇ scan if positive	NS	0	ITT	
			Cardiac and thoracic surgery			
Azorin,[25] 1997	Sealed envelopes	Doppler ultrasonography at days 0 and 8, controlled by bilateral ascending venography when positive	N	N	ITT	Bleeding: perioperative blood loss and postoperative bleeding complications

(Continued)

Table S3—*Continued*

First Author, Year	Randomization Concealment	Outcome: Surveillance	Blinding	Lost to Follow-up	Analysis	Comments
Cade,[24] 1983	NS	FUT	Double blind	N	ITT	100 consecutive patients having thoracotomy for carcinoma of the lung or esophagus
Goldhaber,[168] 1995	NS	Compression ultrasound	N	N	ITT	
Ramos,[23] 1996	NS	None	NS	~10% excluded postrandomization	NS	
			Craniotomy			
Constantini,[40] 2001	NS	Bleeding only (blood loss, number of transfusions, surgeon assessment)	Double blind Patients: Y Caregivers: Y	0	NS	No efficacy assessment
Dickinson,[36] 1998	None	Ultrasound days 1, 3, 5-7, and 10-14 postoperatively	None	0	ITT	Stopped early for bleeding in enoxaparin patients (no safety end point defined in methods)
Goldhaber,[34] 2002	NS	Predischarge ultrasound	Double blind Patients: Y Caregivers: Y	0	ITT	No safety end point defined in methods
Iorio,[169] 2000	N/A	Three venographies One (UFH) FUT	Three double blind Patients: Y Caregivers: Y One open label (UFH)	NR	ITT	Meta-analysis of four studies In two studies, proximal DVT was reported and meta-analyzed
Macdonald,[35] 2003	SE	Ultrasound day 7 (8% in both groups had additional ultrasound days 12-21) (ICH, blood loss, surgeon assessment)	Double blind Patients: Y Caregivers: Y	0	NS	

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Table S3—*Continued*

First Author, Year	Randomization Concealment	Outcome: Surveillance	Blinding	Lost to Follow-up	Analysis	Comments
Lacut,[170] 2005	NS	Ultrasound on day 10	Only outcome assessors blinded	0 at 1 mo 2.6% at 3 mo	ITT	18 patients (8 in ES and 10 in ES + IPC) not analyzed because they did not have an ultrasound prior to discharge
Wautrecht,[171] 1995	SE	Venogram (days 8-10)	Only outcome assessors blinded	0	NS	23 of 35 enrolled underwent venogram
			Spinal surgery			
Gruber,[30] 1984	Closed envelopes	None	Double-blind	None	ITT	Protocol violations in placebo (1) and heparin (2) groups
Voth,[33] 1992	NS	FUT, immediately postoperatively and daily	Double-blind	None	ITT	
Macouillard,[172] 1995 (abstract)	NS	DUS on day 3 and venogram on day 8	NS	None	ITT	
Rokito,[173] 1995	None	Ultrasound on day 6 ± 1	Only outcome assessors blinded	None for primary end point	NS	All patients followed for 1 year No mention of loss to follow-up Any patient with prior VTE excluded
Nelson,[174] 1996	NS	DUS day 3-6	Only outcome assessors	3 patients excluded postrandomization	No	
Wood,[175] 1997	NS	DUS day 5-7	Unblinded	24 of 160 patients with insufficient data to be included Not clear whether excluded before or after randomization		

(Continued)

Table S3—*Continued*

First Author, Year	Randomization Concealment	Outcome: Surveillance	Blinding	Lost to Follow-up	Analysis	Comments
			Spinal cord injury			
Chiou-Tan,[176] 2003	N	N/A	None	NS	NS	Compliance rate 99% 5 patients excluded
Frisbie and Sahara,[177] 1981	Patients selected for the study were assigned alternately to a nonheparin or a heparin group	Surveyed weekly by impedance plethysmography until DVT detected or 60 d IPGs that were positive for 2 consecutive days assessed by large volume ascending venography	N	0	TR	
Green,[178] 1982	NS	FUT on admission and then every 3 d Confirmed by venography	N Laboratory was blinded	0	TR	1 of 13 patients randomized to receive ASA/ dipyridamole was transferred to another facility on day 14 of the trial and, therefore, was not included in the data analysis
Green,[179] 1988	Computer generated	Daily clinical examinations, serial impedance plethysmography, and Doppler flow Confirmed by venography, V̇/Q̇ scans, or pulmonary angiography	NS	0	TR	All DVT/bleeds occurred within first 7 wk when 58 patients (29/group) were receiving prophylaxis Analysis done on this group

(Continued)

Table S3—*Continued*

First Author, Year	Randomization Concealment	Outcome: Surveillance	Blinding	Lost to Follow-up	Analysis	Comments
Green,[180] 1990	Computer-generated, pharmacist-prepared vials	IPG and DUS 2 times/wk for 2 wk, 1 time/wk for 2 wk, biweekly for 4 wk	N	Two in each group lost to follow-up Two in LMWH group switched to UFH because of unavailability	ITT	Mechanical prophylaxis withheld during 8-wk course of trial; stopped early for benefit
Merli,[193] 1988	NS	FUT daily confirmed by venography	NS Venograms interpreted by blinded observer	0	TR	
SCI Thromboprophylaxis Investigators,[52] 2003	SE	Venography (CUS also done on all patients)	No	NS	NS	Many patients discontinued/ excluded from the efficacy analysis for protocol deviations, bleeding. and other adverse clinical events, thrombocytopenia, and other adverse laboratory findings, withdrawal of consent, intercurrent illness, inadequate diagnostic assessment

(Continued)

Table S3—*Continued*

First Author, Year	Randomization Concealment	Outcome: Surveillance	Blinding	Lost to Follow-up	Analysis	Comments
			Trauma			
Cohn,[47] 1999	NS	Weekly serial ultrasound	Radiologists and echocardiography technicians: Y Patients: Y Data collectors: NS Adjudicators: NS Data analysts: NS	38/104	TR	
Elliot,[44] 1999	Computer-generated random numbers kept in sealed envelopes	Routine bilateral duplex (CUS) on the 8th day after randomization	Blinded to technologists and physician	Eight in group 1 and seven in group 2 Provided reasons for loss	ITT	
Fisher[42] 1995	NS	Preoperative venous Doppler Postoperative DUS on postoperative days 3 and 5 $\dot{V}/\dot{Q}$ scan between 5 and 10 d after surgery	Radiologists and echocardiography technicians: Y Patients: N Data collectors: N Adjudicators: N Data analysts: N	41/345	TR	Not blinded
Fuchs,[49] 2005	Computer randomization	Weekly CUS and venous occlusion plethysmography Venography	Radiologists and echocardiography technicians: Y Patients: N Data collectors: N Adjudicators: N Data analysts: N	79 excluded Provided reasons but not separate data	ITT	Not blinded

(Continued)

Table S3—*Continued*

First Author, Year	Randomization Concealment	Outcome: Surveillance	Blinding	Lost to Follow-up	Analysis	Comments
Geerts,[48] 1996	Computer generated No reference to any concealment	Routine bilateral weekly duplex examination with a baseline examination	Radiologists and echocardiography technicians: Y Patients: N Data collectors: NS Adjudicators: NS Data analysts: NS	37/173 in group 1 42 in group 2 Difference: NS Reason: Y	ITT	Venographic Marder score calculated for the two groups
Ginzburg,[46] 2003	NS	Routine ultrasound preoperatively and on postoperative days 1, 3, 7, and weekly thereafter	Patients: NS Caregivers: NS Data collectors: NS Adjudicators: NS Data analysts: NS	15/224 in IPC 29/218 in enoxaparin Reason: Y	TR	
Haentjens,[183] 1996	NS	Routine bilateral ultrasound at 10 d and 6 wk after injury If positive, confirmatory venography	Patients: NS Caregivers: NS Data collectors: NS Adjudicators: NS Data analysts: NS	36/142 in group 1 for 10 d and 66/142 for 3 wk 32/142 in group 1 for the 10-d duplex and 67 for the 6-wk follow-up	ITT and TR	
Knudson,[43] 1994	NS	Baseline screening with CUS, and then repeated at 5- to 7-d intervals until discharge or at least 3 wk	Radiologists and echocardiography technicians: NS Patients: N Data collectors: N Adjudicators: N Data analysts: N	145/396	TR	Allocation based on contraindications to SCD or UFH and then randomization into SCD, UFH, or control

(Continued)

Table S3—*Continued*

First Author, Year	Randomization Concealment	Outcome: Surveillance	Blinding	Lost to Follow-up	Analysis	Comments
Knudson,[45] 1996	NS	Screening and weekly CUS until discharge	Radiologists and echocardiography technicians: N Patients: N Data collectors: N Adjudicators: N Data analysts: N	115/487	TR	Randomization after cases with contraindications to receive heparin were allocated into compression with SCD or AVI
Stannard,[50] 2006	NS (computer-generated randomization)	All patients received either duplex ultrasound or magnetic resonance venography 24 h before discharge from hospital or earlier if symptoms of VTE	Patients: PN (blinded study) Caregivers: PN (blinded study) Data collectors: PN (blinded study) Adjudicators: DY (radiologists blinded) Data analysts: PN (NR)		N Analysis only included 200/224 (89%)	
Velhamos,[194] 2005	NS (computer-generated randomization)	Duplex venous ultrasound and bilateral contrast venography between days 7 and 15 and within 48 h of discontinuation of treatment	Patients: PN (NR) Caregivers: PN (NR) Data collectors: PN (NR) Adjudicators: PN (NR) Data analysts: PN (NR)		N	Study discontinued because of lack of funding and lack of clinically important trends, not based on benefit
			Same-day surgery			
Baca,[185] 1997	?	Duplex ultrasound	?	?	?	Manuscript in German
			Aspirin			
Clagett,[186] 1975	NS	FUT daily until discharge Phlebography to confirm positive FUT	NS	0	TR	
Encke,[187] 1988	NS	FUT	Double blind	None	ITT	

(Continued)

Table S3—*Continued*

First Author, Year	Randomization Concealment	Outcome: Surveillance	Blinding	Lost to Follow-up	Analysis	Comments
Harjola,[162] 1980	NS	Phlebography to confirm	Surgeons: Y	1/100 4/100 3/100 3/100 11/400	TR	
Hartung,[188] 1979	NS	Clinical change then FUT Venography Lung scan	Double blind	None	ITT	More aggressive in patients with risk factors
Lowe,[189] 1974	NS	Publication reference 10	Double blind	344 excluded from analysis Unclear whether before or after randomization		
Medical Research Council,[190] 1972	Tablets were identified only by the randomly allocated code number	FUT daily	Staff and patients: Y	NS	ITT	
Schreiber,[191] 1979	NS	FUT confirmed using ultrasound, venography, and lung scan	Double blind	None		
Zekert,[192] 1980	Balanced cross-classification by treatment groups and sex	FUT and radiology	NS	NS	ITT	
Zekert,[192] 1989	Consecutively numbered sealed envelope	FUT for 14 d Venogram if positive or clinically suspicious	Double blind	None	ITT	

AVI = A-V Impulse System (AVI; Orthofix Ltd); DY = definitely yes; FUT = fibrinogen uptake test; IPG = impedance plethysmography; MI = myocardial infarction; N = no; N/A = not applicable; NR = not reported; NS = not specified; O; PN = probably no; PY = probably yes; TR; Y = yes. See Table S2 legend for expansion of other abbreviations.

Table S4—*Characteristics of Studies That Compared Mechanical Plus Pharmacologic Prophylaxis With Pharmacologic Prophylaxis Alone*

First Author, Year	Population	Mechanical Prophylaxis	Background Agent	Concealed Allocation	Blinded Outcome Assessment	Diagnostic Method	Comments
Barnes,[195] 1978	Hip surgery	GCS	ASA	Y	NR	Ultrasound + venography	Stopped early
Bergqvist,[196] 1984	Abdominal	GCS	Dextran	NR	Y	FUT	
Eisele,[197] 2007	Orthopedic	IPC	LMWH + GCS	NR	NR	Ultrasound	
Fredin,[198] 1989	Elective hip	GCS	Dextran	NR	Y	FUT	
Kalodiki,[199] 1996	Elective hip	GCS	LMWH	Y	Y	Venography	
Lieberman,[200] 1994	Orthopedic	IPC	ASA + epidural + GCS	NR	NR	Venography	
Ohlund,[201] 1983	Elective hip	GCS	Dextran	NR	NR	FUT	
Rasmussen,[202] 1988	GS	GCS	UFH	NR	NR	Technetium plasmin	
Silbersack,[203] 2004	Elective hip/knee	IPC	LMWH	NR	NR	Ultrasound	
Siragusa,[204] 1994	Elective hip	IPC	UFH	NR	Y	Venography	
Smith,[205] 1978	General surgical	IPC	Dextran	NR	Y	FUT	
Stannard,[206] 1996	Elective hip	FP	UFH, ASA	NR	Y	DUS + venography	
Torngern,[207] 1980	General surgical	GCS	UFH	NR	NR	FUT	
Wille-Jørgensen,[208] 1985	Abdominal	GCS	UFH	NR	Y	FUT + venography	
Wille-Jørgensen,[209] 1991	Abdominal	GCS	UFH	Y	NR	FUT + venography	
Wille-Jørgensen,[149] 1996	Abdominal	GCS	UFH	NR	Y	FUT + venography	

See Table S2 and S3 legends for expansion of abbreviations

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Table S5—*Risk of Bias in Economic Evaluations of Thromboprophylaxis in Nonorthopedic Surgical Patients*

First Author, Year	Design	Prespecified Protocol Followed	Sponsor	Analysis Independent From Sponsor	Perspective	Assumptions Consistent With Stated Perspective	Preferences Measured	Time Horizon	Discounting	Sensitivity Analysis
Oster,[210] 1988	Decision model	NS	None	Y	Societal	Y	None	Lifetime	N	Y
Etchells,[211] 1999	Decision model	NS	Industry	Y	Payer	Y	NS	Lifetime	Y	Y
Szucs,[212] 1999	Decision model	NS	NS	NS	Societal	Y	NS	Lifetime	N	Y
Maxwell,[213] 2000	Decision model	NS	NS	NS	Societal	Y	NS	Lifetime	Y	Y
Dainty,[214] 2004	Decision model	NS	NS	NS	Societal	Y	NS	Lifetime	Y	Y
Heerey,[215] 2005	Decision model	NS	None	Y	Payer	Y	Patient	15 y	Y	Y
Farias-Eisner,[216] 2009	Observational	NS	Industry	No	Hospital	Y	None	1 mo	N	N

See Table S3 legend for expansion of abbreviations.

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Table S6—*Characteristics and Results of Economic Evaluations of Thromboprophylaxis in Nonorthopedic Surgical Patients*

First Author, Year	Surgical Population	Interventions	Comparator	Data Sources	Unit Costs	Results
Oster,[210] 1988	General	LDUH, IPC, ES	No prophylaxis	20 trials	Cost-adjusted charges in Maryland	Compared with no prophylaxis, ES saved 28 lives and $335,000 per 10,000 patients treated. Compared with ES, IPC cost $62,000, and LDUH cost $215,000 per additional life saved.
Etchells,[217] 1999	Colorectal	Enoxaparin	LDUH	7 RCTs, 1 meta-analysis	Ontario Health Plan	Incremental cost for LMWH vs LDUH was $146 per patient.
Szucs,[212] 1999	General	LMWH	LDUH	Meta-analysis	German health-care system	LMWH was less costly (by $160) and more effective (by 0.01 QALYs) than LDUH.
Maxwell,[213] 2000	Gynecologic	Enoxaparin	LDUH	31 RCTs	Medicare	Incremental cost for LMWH vs LDUH was $15 to $26 per patient, depending on age and operation.
Dainty,[214] 2004	Gynecologic	Enoxaparin + IPC	IPC	31 RCTs	Medicare	Compared with IPC alone, LMWH plus IPC cost $7,200 to $20,000 per QALY gained, depending on age and operation.
Heerey,[215] 2005	Abdominal	Dalteparin 2,500 or 5,000 International Units	LDUH	5 RCTs, 2 meta-analyses	Medicare	Compared with LDUH, dalteparin 2,500 International Units daily cost $9,300 per QALY, and dalteparin 5,000 International Units daily cost $21,800 per QALY. Compared with dalteparin 2,500 International Units daily, dalteparin 5,000 International Units daily cost $23,800 per QALY.
Farias-Eisner,[216] 2009	Nonorthopedic	Enoxaparin	Fondaparinux	Chart review	Hospital charges	Total hospital charges were higher for enoxaparin by $2,600 per patient.

QALY = quality-adjusted life year; RCT = randomized controlled trial. See Table S2 legend for expansion of other abbreviations.

Table S7—*Risk of Bias in Observational Studies of VTE Risk*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
			General, mixed, and abdominal-pelvic surgery				
Agnelli,[53] 2006 @RISTOS	Prospective registry to estimate symptomatic DVT, PE, PE death at 30 ± days after surgery 81.7% received prophylaxis (74% LMWH)	31 Italian surgery departments, consecutive abdominal, thoracic, gynecologic, and urologic cancer patients (n = 2,373) 41 with prior VTE 21% endoscopic (61% urologic)	External adjudication committee reviewed all outcomes, including all clinical documents and imaging reports	N/A (not an RCT)	N/A	Not specified	40% of VTE events occurred > 21 d postoperatively Rates confounded by inadequate information of prophylaxis
Alcalay,[218] 2006	Case-control retrospective	Colorectal cancer California 1993, 1995, 1997-1999	ICD-9-CM codes	N	N	N/A	
Antiplatelet Trialists,[4] 1994	Overview of RCTs of antiplatelet DVT prophylaxis prior to March 1990	General and orthopedic surgery and high-risk medical patients	FUT or venography clinical PE confirmed by V̇/Q̇ scan or autopsy	N/A	N/A	N/A	Good data on PE relative and absolute risk reduction by antiplatelet prophylaxis, but again, FUT inadequate as efficacy outcome measure
Bahl,[56] 2010	Symptomatic, objectively confirmed DVT or PE	Age group OR = 1.2 Sepsis OR = 4.0 Pregnant/ postpartum OR = 8.3 Central venous catheter OR = 1.8 Cancer OR = 2.3 Prior VTE OR = 2.1 Factor V Leiden OR = 3.4 HIT OR = 3.4 Inpatient ≥ 2 d OR = 10.6	VTE incidence by risk score: 0-1 = 0% 2 = 0.7% 3-4 = 0.97% 5-6 = 1.33% 7-8 = 2.58% 9 + = 6.51%		ORs are not adjusted for presence, type, or duration of DVT prophylaxis.		

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Bergqvist,[123] 1986	RCT, double-blind	Aged ≥ 40 y Scheduled for major elective abdominal surgery > 30 min duration	FUT for 7 d Follow-up for deaths to 30 d	Y			Randomized to UFH 5,000 units SC started 2 h preoperatively and then q12h for 5-7 d vs LMWH 5,000 anti-Xa units SC started 2 h preoperatively and then daily for 5-7 d
Bergqvist,[124] 1988	RCT, double blind	Aged ≥ 40 y Scheduled for major elective abdominal surgery > 30 min duration and expected postoperative hospital stay ≥ 5 d	FUT for 7 d, followed by venography for positive FUT, if possible	Y			Randomized to UFH 5,000 units SC started 2 h preoperatively and then q12h for 5-8 d vs LMWH 5,000 units SC started evening prior to surgery and then daily for 5-8 d
Bergqvist,[125] 1995	RCT, double blind	Elective general surgery for malignant and benign abdominal disease	FUT?				Full text unavailable electronically
Bergqvist,[127] 2002 ENOXACAN	RCT Double blind Placebo controlled	Aged ≥ 40 y undergoing planned curative surgery for abdominal or pelvic cancer	Mandatory bilateral leg venography between postoperative days 25 and 31	Y	Y	88/253 assigned to enoxaparin, and 81/248 assigned to placebo not evaluable for efficacy	After open enoxaparin 40 mg/d for 6-10 d, patients randomized to continued enoxaparin or placebo for 19-21 d.
Blake,[219] 2001	Case-control retrospective	Routine laparoscopic cholecystectomy	NR	N	N		Poor-quality article
Bottaro,[220] 2008	Meta-analysis	General surgery	NR	N			Extended postoperative prophylaxis
Caprini,[221] 1991	Nonempirically derived VTE risk assessment score	See Bahl et al (2010) for better data					

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Catheline,[222] 2000	Cohort	2,384 patients undergoing laparoscopic surgery from 1992-1997	Symptomatic VTE diagnosed by "venous Doppler" (unable to discern whether Doppler or duplex; continuous wave Doppler provided no image)	N	N	Patients seen in follow-up between postoperative day 8-10	All received perioperative LMWH and antiembolism stockings LMWH started 2 h preoperative and continued until ambulatory Confirmed follow-up only to postoperative days 8-10
Clarke-Pearson,[54] 2003	Cohort, single institution (Duke)	1,862 gynecologic surgery patients, from 1996-1997 receiving perioperative IPC	Objectively confirmed symptomatic postoperative VTE at 30 d			Completeness of follow-up uncertain	Logistic regression analysis for potential VTE risk factors, but 10 postoperative deaths, so estimates of VTE incidence and risk factors may be incorrect
Enoch,[223] 2003	Case-control retrospective	Varicose veins hernia	NR	N	N		
Flordal,[224] 1996	Post hoc analysis of RCT	2,070 elective major abdominal surgery patients randomized to dalteparin 2,500 vs 5,000 International Units	FUT Symptomatic PE	NA	NA	NA	Only abstract available electronically FUT unreliable end point measure
Gallus,[225] 1973	RCT	Aged >40 y Elective surgery Emergent surgery for hip fracture Medical patients with suspected MI	Randomized separately to UFH or "untreated" Elective surgery: 5,000 units SC 2 h preoperatively then tid until ambulatory Hip fracture: 5,000 units SC within 12 h of admission then tid until surgery; same as for elective surgery postoperatively Medical: 5,000 units within 18 h of admission then tid until fully mobile	FUT, followed by venography if DVT was suspected in the femoral or popliteal veins			Neither abstract nor text available electronically
Gallus,[131] 1976	RCT	Major elective surgery	FUT				Full text unavailable electronically
Gallus,[226] 1997	Review						Neither abstract nor manuscript available electronically Manuscript requested from library

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Gangireddy,[58] 2007	Retrospective cohort	75,771 veterans treated at Veterans Administration Hospital (n = 120) whose preoperative and postoperative data were tracked by the NSQIP, 1996-2001	Y	N	N	NR	Surgeries included elective AAA repair, infrainguinal vascular reconstruction, carotid endarterectomy, colectomy, open or laparoscopic cholecystectomy, lobectomy/pneumonectomy, total hip replacement, amputation Outcome: symptomatic VTE ≤ 30 d after surgery Data on DVT prophylaxis not collected
Haas,[132] 2005	RCT Double blind	23,078 surgical patients randomized to LMWH vs UFH tid	Autopsy-proven fatal PE within 14 d postoperatively	N/A 70.2% autopsy rate		NR	Because death is a fairly hard end point no concern about loss to follow-up
Huber,[227] 1992	Single-center cohort study of abdominal surgery	28,953 patients admitted to Clinic of Digestive Surgery (University Hospital of Geneva) 19,161 operated and the 9,792 treated conservatively 98% received UFH prophylaxis	Medical record review for PE during hospital stay and readmission for PE within 30 d of hospital discharge PE objectively diagnosed	N	N	NR	Authors suggested that it would be unlikely for one of the patients to be readmitted to a different hospital within 30 d of dismissal from the hospital, but no data were presented to confirm this
International Multicentre Trial,[1] 1975	RCT	4,121 patients aged >40 y, elective major surgery	Y	N	N		72% of controls and 66% of UFH deaths had autopsy

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Kakkar,[134] 1985	RCT Double blind Open cohort	395 surgery patients randomized to LMWH vs UFH 1,007 consecutive patients given LMWH 2 h preoperatively and daily for 7 d	FUT, followed by venogram if FUT positive	N	N	Of 395, 10 died during postoperative period; none from PE	
Kakkar,[135] 1997	RCT Double blind	Aged > 40 y scheduled for general or gynecologic surgery expected to remain in hospital at least 5 d	FUT followed by venogram if positive	Y			
Koch,[228] 2001	Meta-analysis of LMWH vs UFH RCTs						See Table S3
Mommertz,[229] 2007	Prospective cohort	451 patients admitted for vascular, general, or trauma surgery	NR Hertfelder VTE risk assessment model	N	N	0	A: Low-dose of LMWH B: Therapeutic dose of LMWH C: No VTE prophylaxis Risk assessment model: unclear whether variables were adjusted within model
Mismetti,[230] 2001	Meta-analysis	General surgery	Y				
Nurmohamed,[231] 1992	LMWH vs UFH in general and orthopedic surgery; meta-analysis of RCTs 1984-1991	Abdominothoracic or gynecologic surgery Limited to RCTs comparing LMWH vs UFH in currently recommended doses	General surgical trials used FUT as end point	NA	Y	NR	Final analysis included 6,878 general surgery patients in 17 studies

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Sagar,[140] 1975	RCT	Aged >50 y undergoing major surgery	Fatal PE identified at necropsy	Pathologists blinded to prophylaxis assignment			
Schulz,[232] 2005	Sequential prophylaxis study (not RCT)	Surgical patients	Y (DUS of patients with symptoms of DVT)	N	N	NR	Sequential groups A. LMWH + TEDs B. LMWH alone
Sweetland,[233] 2009	Prospective cohort (Million Women Study)	947,454 middle-aged women in the United Kingdom recruited 1996-2001	N (based on ICD codes)	N/A	Y	NR	
Truitt,[234] 2005	Case-control study: three cases Number of controls NR	Any patient (aged 0-16 y) admitted over past 7 y reviewed for DVT and PE	Duplex ultrasound and $\dot{V}/\dot{Q}$ scan used in diagnosis of DVT and PE, respectively	N	N	0	
White,[80] 2003	Retrospective cohort study	Uses discharge diagnosis codes from California Patient Discharge Data Set to identify rehospitalization for VTE within 91 d of various surgical procedures (1992-1996)	N	N	N Stratified by cancer	NR	Probably gives best information on baseline VTE risk by surgical procedure type, but use of DVT prophylaxis unknown Difficult to separate incident from recurrent VTE

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
			Urological surgery				
Kibel,[235] 1997	Prospective cohort	Radical prostatectomy w bilateral obturator lymph node dissection	Duplex ultrasound when patients returned for follow-up (~3 wk postoperatively) Verbal contact with all patients at 2 mo	N	N	158 consented, 106 underwent ultrasound (52 patients did not complete follow-up)	All patients had prophylaxis with pneumatic compressions stockings Warfarin starting the night of surgery with target INR 1.5 during hospitalization
Koya,[236] 2005	Retrospective cohort	Radical prostatectomy	As clinically indicated	N	N	NS	All patients had TEDs SCDs until full ambulation No patients had prophylactic anticoagulation
Kundu,[237] 2004	Retrospective cohort	Radical prostatectomy	As clinically indicated	N	N	53/3,477	
Montgomery,[238] 2005	Retrospective cohort	Urological laparoscopy	As clinically indicated	N	N	NS	Patients nonrandomly received heparin or SCDs
Permpongkosol,[239] 2007	Retrospective cohort	Urological laparoscopy	As clinically indicated	N	N	NS	NS whether any prophylaxis used
Pettus,[240] 2006	Retrospective cohort	Partial or radical nephrectomy	As clinically indicated	N	N	NS	All patients had pneumatic compression devices, no heparin
			Gynecologic surgery				
Abu-Rustum,[241] 2005	Retrospective cohort	168 patients with stage IIIC-IV adnexal/peritoneal cancer undergoing exploratory surgery	Doppler or CT if symptomatic	N	N	0	All patients received VTE prophylaxis wit pneumatic compression ± SC heparin.
Ageno,[242] 2006	Prospective cohort	266 consecutive patients without malignancy undergoing gynecologic laparoscopy	CUS 7 and 14 d postoperatively Telephone contact 30 and 90 d postoperatively	N	N	19 patients without ultrasound 10 patients without clinical follow-up	No patients received prophylaxis

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Suzuki,[243] 2005	Retrospective case-control study: 42 cases, 929 controls	6,218 patients who underwent gynecologic surgeries (excluding obstetric, infertility related, and uterine cervical conization)	NR	N	Y	0	IPC
Querleu,[244] 2006	Retrospective cohort	1,000 patients with gynecologic cancer undergoing laparoscopic lymph node dissection	NR	N	N	None at 6 mo	NR what prophylaxis, if any, were used
			Bariatric surgery				
Birkmeyer,[245] 2010	Prospective cohort	6,376 RYGBP (LRYGBP and ORYGBP) among which 542 IVC filters (8.5%)	?	N	N	0	Pharmacologic VTE prophylaxis not described. Patients in the IVC filter group tended to be older, male, and heavier; to have problems with mobility (able to walk only with a cane, walker, or requiring a wheelchair or scooter); and to have a history of VTE. They were less likely to have private health insurance. IVC filter patients had a greater likelihood of obesity-related comorbidity, including significantly higher rates of lung and cardiovascular diseases, renal failure, diabetes, liver disorders, and sleep apnea. With regard to case characteristics, they were less likely to have their procedures performed laparoscopically, and their cases were more likely to have a duration of > 3 h.

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Borkgren-Okonek,[246] 2008	Prospective cohort	223 bariatric surgery patients (laparoscopy, 208)	Lower-extremity venous ultrasonography, helical chest CT, or V̇/Q̇ lung scanning Major bleeding was defined as overt bleeding, acute anemia associated with a 2 g/dL decrease in hemoglobin level from the preoperative value (excluding postoperative hemodilution), or bleeding requiring reoperation or transfusion	N	N	1	Enoxaparin 40 mg (BMI <50 kg/m^2, n = 124) or 60 mg (BMI >50 kg/m^2, n = 99) every 12 h during hospitalization and once daily for 10 d after discharge
Brasileiro,[247] 2008	Prospective cohort	136 patients ORYGBP-LRYGBP	Color Doppler ultrasound performed before surgery and 2 and 5 wk after surgery	N	N	10	Enoxaparin 40 mg 15 d, no IPC Only one symptomatic DVT (calf vein)

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Carmody,[248] 2006	Prospective cohort	3,861 patients (2,839 open procedures, 1,022 laparoscopic)	PE: CT scan, angiogram, V̇/Q̇ scan, autopsy, clinical	N	N	0	Between 1980 and 1992, thigh-length IPC device was used and ambulation initiated on the evening of operation. Since 1992, routine prophylaxis included the addition of routine anticoagulation by instituting a computerized pathway for patient care as follows: either UFH 5,000 units SC bid or every 8 h or LMWH (enoxaparin). Details, however, about choice of anticoagulation agent, dose, and administration schedule (eg, preoperative vs intraoperative vs postoperative initiation) were not available. In 1998, standardization for all patients to enoxaparin 40 mg SC preoperatively and repeated as a daily dose until hospital discharge. IVC filters were placed prophylactically in 145 patients undergoing bariatric surgery over the 24-y period of study. Despite the IVC filter, postoperative PE developed in three patients, and one died as a consequence of that PE.

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Caruana,[249] 2009	Prospective cohort	1,652 RYGBP (147 LRYGBP, 1,505 ORYGBP)	PE: chest CT scan, when possible	N	N	0	Standard-risk patients (n = 1,075) received preoperative LDUH, had IPC devices, and were ambulated within 2 h of operation (standard prophylaxis). Intermediate-risk patients (n = 429) received standard prophylaxis plus postdischarge LDUH 7,500 units SC every 12 h for 3 wk. High-risk patients (n = 148) had standard prophylaxis plus postdischarge LDUH plus a preoperative or predischarge IVC filter. LDUH was administered by the patient or a family member postdischarge.
Clements,[250] 2009	Prospective cohort	957 LRYGBP	Clinically evident DVT and PE	N	N	1	Calf-length PCDs placed before induction of anesthesia and remained in place unless the patient was ambulating. All patients were educated and encouraged to ambulate beginning the day of the operation. Nurses on the postoperative ward were specifically trained in the importance of the use of PCDs and early ambulation.
Cotter,[7] 2005	Retrospective chart review	107 patients (ORYGBP, LRYGBP)	Doppler ultrasound for one patient	N	N	0	UFH 5,000 International Units two times, external compression devices (99%), and early ambulation every 4 h while awake. Only one symptomatic DVT after discharge (day 16).

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Escalante-Tattersfield,[12] 2008	Prospective cohort	618 LRYGBP	On postoperative day 1, routine bilateral lower-extremity Venous compression ultrasound (VCU) performed in all patients Scanning of the iliac, femoral, popliteal, and calf veins Postoperative follow-up 2, 8, 12, 24, and 52 wk	N	N	0	Every patient received heparin 5,000 units SC (SQH) before the induction of anesthesia, with continued SQH administration every 8 h after surgery for the first 24 h. After 24 h, SQH switched to enoxaparin 40 mg SC q12h until discharge (mean, 4 d). SCDs applied to both legs were also used intraoperatively and continued until the patients were fully ambulatory. All patients were actively encouraged to ambulate within the first 24 h postoperation. An IVC filter was placed before surgery if a patient met any of the following criteria: previous DVT or PE, BMI ≥ 60 kg/m^2, limited mobility, documented coagulation factor disorders, significant obstructive sleep apnea, documented pulmonary hypertension, and significant lymphedema (n = 24 patients).
Fernandez,[251] 2004	Retrospective database analysis	1,431 0RYGBP 580 LRYGBP Single center	PE assessment not described	N	N	0	Prophylaxis unknown
Flum,[252] 2009 LABS1	Prospective cohort	4,476 patients (3,412 RYGBP, 437 open procedures, 2,975 laparoscopic, 1,198 laparoscopic gastric banding, 166 other procedures)	VTE assessment not described	N	N	0	Prophylaxis unknown

(Continued)

Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Frederiksen,[16] 2003	Prospective study	17 patients (colorectal, biliary, bariatric surgery [(n = 10/17]) and 2 healthy volunteers	Anti-Xa activity	N	N	0	Enoxaparin 40 mg SC at 8 PM the evening before surgery
Frezza,[253] 2006	Retrospective study	150 patients (LRYGBP, laparoscopic gastric banding)	As needed duplex scans of calf, femoral, and iliac veins PE, when suspected, excluded by a spiral CT scan	N	N	0	Calf compression intraoperatively for all Low risk: enoxaparin 1.5 mg/kg SC preoperatively and postoperatively once or heparin 7,000 units SC once for 5 d High-risk: IVC filter or IV UFH preoperatively; postoperatively, enoxaparin 2 mg/kg SC once for 15 d; warfarin for 3 mo Four major bleeding and transfusion for the first 20 patients, then 0/130
Gargiulo,[254] 2007	Retrospective study	193 patients ORYGBP 213 patients LRYGBP	Perioperative pulmonary angiography, spiral CT scanning, and $\dot{V}/\dot{Q}$ scan not performed unless the patients had clinical sequelae suggestive of PE	N	N	0	IVC filter if BMI >55 kg/m^2 (eight ORYGBP patients), SCDs, TEDs, and weight-adjusted heparin 50 units/kg SC preoperatively and every 12 h postoperatively until ambulating >4 h/d
Gargiulo,[254] 2007	Retrospective case-control study	A: ORYGBP B: LRYGBP	Spiral CT, $\dot{V}/\dot{Q}$ scan, autopsy	N	N	0	All patients with a history of DVT, PE, or pulmonary hypertension (mean pulmonary artery pressure, >40 mm Hg) had IVC filters placed at the time of surgery.

(Continued)

Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Gonzalez,[255] 2006	Prospective Study	660 patients RYGBP	Postoperative calf pain, Homan sign, swelling, unexplained fever, or erythema underwent duplex ultrasound. Cases of PE were confirmed by chest CT angiography scan, by V̇/Q̇ scan and at necropsy in one patient	N	Y Multivariate-adjusted analysis (variables NR)	0	Heparin SC and SCDs on call to the operating room. Patients with BMI >50 kg/m² received LMWH (enoxaparin) 40 mg SC daily until discharge from the hospital. Patients with BMI <50 kg/m² received enoxaparin 30 mg bid. Patients with BMI >60 kg/m² or with relative immobility were discharged home on extended prophylaxis for 10 to 14 d. Prophylactic IVC filters were reserved for patients with a history of DVT, PE, or hypercoagulability disease.
Gonzalez,[255] 2006	Prospective cohort with nested case-control study 23 cases, 637 controls	660 consecutive patients who underwent RYGBP	DVT: Duplex ultrasound PE: CT angiography (54%), V̇/Q̇ scan (23%), at necropsy (23%) PE: CT angiography (54%), V̇/Q̇ scan (23%), at necropsy (23%)	N	Y Multivariate-adjusted analysis (variables NR)	0	All patients received perioperative prophylaxis for VTE (heparin [enoxaparin] bid and SCDs)
Hamad,[256] 2005	Retrospective analysis	668 patients ORYGBP, LRYGBP	Clinically suspected symptomatic cases of VTE were confirmed with Doppler ultrasonography, V̇/Q̇ scan, chest CT	N	N	0	A (n = 100): 30 mg preoperatively, 30 mg/d postdischarge B (n = 124): 40 mg/d postoperatively 10 d C (n = 84): 40 mg/d postoperatively 12-120 h D (n = 180): 40 mg/d postoperatively† 12-24 h E (n = 180): 40 mg q12h postoperatively 12-36 h 12-36 h

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Heffline,[257] 2006	Retrospective analysis	455 patients LRYGBP		N	N		1. 4-h gastric bypass class preoperatively, which included discussion of VTE prevention, signs and symptoms of VTE, maintaining adequate hydration, and the use of warfarin postoperatively 2. ASA suppository (650 mg) in PACU 3. SCDs initiated in PACU 4. Early ambulation (beginning day of surgery) 5. UFH 5,000 units SC q12h 6. IVC filter if BMI > 50 kg/m², known hypercoagulability, history of right-side heart failure, history of VTE, patient request 7. Warfarin 1 mg beginning postoperative day 1 if upper GI study shows no leak
Inabnet,[258] 2010 LABS1	Prospective cohort	3,802 procedures (3,577 primary 203 revisions)	VTE assessment not described	N	N	0	Prophylaxis unknown
Kligman,[259] 2009	Retrospective analysis	423 patients LRYGBP	?	N	N	0	All patients received LMWH (enoxaparin) 40 mg SC 2 h preoperatively and had PCDs applied in the operating room. Enoxaparin postoperatively unknown

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Kothari,[20] 2007	Prospective analysis of 2 cohorts	238 + 238 patients LRYGBP	Spiral CT of the chest and duplex ultrasound were performed to rule out PE and DVT, respectively, based on the presence of clinical signs or symptoms	N	N	0	The initial cohort of patients received enoxaparin 40 mg SC preoperatively, 40 mg SC on the evening of postoperative day 0, and bid until discharge. The second cohort of patients received UFH 5,000 units SC preoperatively, nothing on the evening of postoperative day 0, and 5,000 units tid until discharge. All patients were treated with SCDs and early ambulation. Patients were encouraged to continue use of their SCDs when not ambulating.
McCarty,[260] 2005	Prospective cohort	2,000 LRYGBP	PE assessment not described	N	N	0	Prophylaxis unknown
Magee,[261] 2008	Prospective cohort	735 laparoscopic bariatric procedures	VTE assessment not described	N	N	0	Patients received dalteparin 2,500 International Units SC immediately before surgery, followed by 5,000 International Units daily for the first 7 d for laparoscopic-adjustable gastric banding or for 21 postoperative days for all other procedures. Early mobilization from the first postoperative day was mandatory. Whole-leg or calf compression stockings, PCDs, and low-pressure pneumoperitoneum were not used. Any patient with history of PE, one DVT episode, or thrombophilia underwent preoperative placement of an IVC filter in addition to the LMWH injections.

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Miller,[6] 2004	Retrospective cohort	250 LRYGBP	Clinical assessment confirmed by duplex ultrasonography and V̇/Q̇ scan or pulmonary angiogram	N	N	0	Initiation 2 h prior to surgery with heparin 5,000 units SC for those patients with a BMI <50 kg/m^2 and heparin 7,500 units for those with a BMI >50. Heparin administration was continued every 8 h throughout the hospitalization. In addition, knee-high SCDs were placed at the beginning of the operation and remained in place unless the patient was ambulating. Early ambulation (including the evening of surgery) was enforced in all patients
Ojo,[262] 2008	Retrospective chart review	127 ORYGBP discharged with LMWH among 338 patients	VTE assessment not described	N	N	0	Enoxaparin 40 or 60 mg bid for 2 wk (total). The LMWH dose used was at the discretion of the operating surgeon. Only patients at a high risk for DVT or PE were treated. Inclusion criteria: previous history of PE or DVT; BMI ≥ 60 kg/m^2; or BMI ≥ 50 kg/m^2 with any of the following three risk factors: venous stasis disease; obstructive sleep apnea, or severe ambulation limitation
Overby,[263] 2009	Retrospective cohort	180 bariatric surgery candidates, patients were morbidly obese	Thrombophilia screening included testing inherited thrombophilias	N	N	0	Patients offered selective preoperative prophylactic IVC filter placement

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Piano,[264] 2007	Prospective cohort	59 patients LRYGPB and laparoscopic duodenal switch	Through the remaining retrieval sheath, a cavagram was performed to evaluate vena cava integrity. Before filter retrieval, all patients underwent lower-extremity venous color-flow duplex scanning	N	N	0	All patients had SCDs placed before undergoing anesthesia. Heparin infusion at 500 units/h for a BMI <50 kg/m^2 or 750 units/h for a BMI >50 kg/m^2. The mean dwell time of the removable vena cava filters was 63 ± 30 d (range, 32-162 d); the primary filter retrieval success was 90% (49/54). All failures of retrieval were due to filter tilt.
Poulose,[314] 2005	Retrospective database analysis	69,072 bariatric surgery	PE assessment not described	N	N	0	Prophylaxis unknown
Prystowsky,[8] 2005	Prospective cohort	106 Patients ORYGBP, LRYGBP	Patients studied on postoperative day 2 after RYGBP and again between postoperative day 8 and 15. The common femoral, popliteal, and gastrocnemius veins were examined bilaterally using one of three color-flow duplex scanners	N	N	0	All patients received UFH 5,000 units SC $\sim$30 min before transport to the operating room. Heparin was given q12h for the remainder of their hospitalization. Intermittent SCDs were used in all patients and before the induction of general anesthesia and until ambulatory postoperatively. Patients with a history of VTE underwent placement of a temporary IVC filter before surgery. All patients were treated with filters that had been approved for temporary use (Optease; Cordis Endovascular) and with the intent to retrieve the device once the patient was fully ambulatory and when full systemic anticoagulation was deemed safe if its use were to become necessary.

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Prystowsky,[8] 2005	Prospective cohort	106 consecutive RYGBP patients	Duplex scans	N	N	0	No comparison group; statistical analysis was descriptive only. All patients received UFH 5,000 units SC 30 min before transport to the operating room. Patients with a history of VTE underwent placement of a temporary IVC filter preoperatively.
Quebbemann,[9] 2005	Prospective cohort	822 bariatric surgery (634 laparoscopic gastric bypass procedures, 188 laparoscopic band procedures, and 10 revisional operations)	All clinically evident thromboembolic events were recorded. No routine surveillance studies were performed.	N	N	0	All patients were started on continuous IV UFH 400 units/h, starting 1 h before surgery. No bolus was given, and dose was not adjusted for weight, prothrombin time, or anti-Xa levels. All patients had SCDs placed and started prior to the induction of general anesthesia. Heparin was routinely discontinued on the day of discharge. Heparin infusion was prematurely discontinued when, in the surgeon's judgment, the patient was at excessive risk for bleeding or had evidence of bleeding.

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Raftopoulos,[21] 2008	Prospective cohort	308 bariatric surgery (90% LRYBP)	All patients underwent routine screening bilateral lower-extremity venous Doppler studies the day of hospital discharge	N	N	0	Between September 2003 and December 2005, 132/308 (42.9%) patients (group A) received enoxaparin 30 mg SC 1 h prior to surgery followed by enoxaparin 30 mg SC bid starting 12 h after surgery for the remaining length of hospital stay. Calf-length IPC devices were used routinely in both groups. Between January 2006 and August 2007, 176/308 (57.1%) patients (group B) received enoxaparin 30 mg SC bid starting 12 h after surgery for the duration of hospital stay followed by a 10-d course of enoxaparin 40 mg SC once a day at home after hospital discharge. Preoperative enoxaparin was not administered.
Rondina,[17] 2010	Prospective study	28 obese medically ill patients	Plasma anti-Xa level	N	N	0	Enoxaparin 0.5 mg/kg SC once daily was administered, and peak anti-Xa levels were measured ~4-6 h after the enoxaparin dose
Rowan,[19] 2008	Prospective cohort, 2 consecutive groups	52 laparoscopic gastric bypass or banding patients	Anti-Xa levels obtained 4 h after the first and third doses Levels between 0.18-0.44 units/mL considered appropriate	N	N	0	Group 1: enoxaparin 30 mg q12h Group 2: enoxaparin 40 mg q12h

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Sapala,[265] 2003	Retrospective database analysis	5,554 bariatric procedures: Jejunoileal bypass, horizontal gastroplasty, RYGBP with a 30-mL pouch, modified biliopancreatic diversion, the Sapala-Wood Micropouch gastric bypass, laparoscopic band, and revisions	In six patients, the diagnosis of fatal PE based on clinical assessment (ie, stable patient, sudden onset, terminal event) In the other six patients, PE confirmed at autopsy		N	0	ES: 2 patients ES + LDUH: 2 patients IPC + LDUH: 5 patients IPC + LDUH + IVC: 1 patient IVC: 1 patient IPC + LMWH + IVC: 1 patient Two patients died following transfemoral implantation of a Bird's Nest vena cava filter
Scholten,[14] 2002	Retrospective database analysis	481 consecutive patients were evaluated in the two study groups: 92 received enoxaparin 30 mg q12h, and 389 patients received enoxaparin 40 mg q12h	Ultrasound or venogram or PE documented by spiral CT scan and bleeding complications defined as bleeding requiring operation or a change in therapy with transfusions	N	N	0	All patients were treated with early ambulation, GCS usually consisting of elastic wraps from the foot to the thigh, and IPC devices or SCDs (depending on hospital availability) plus twice-daily administration of LMWH. LMWH was administered 2 h prior to surgery and continued q12h until the patient was fully ambulatory or at hospital discharge.
Shepherd,[5] 2003	Prospective	700 patients undergoing LRYGBP	VTE: symptomatic; surveillance screening of asymptomatic patients was not performed. Major bleeding: blood transfusion or reoperation	N	N	0	The UFH q12h dose that achieved the goal antifactor-Xa level ranged from 3,000 to 19,000 units, with a median of 8,000 units. Prophylactic UFH was begun the evening of the day of operation and continued q12h until discharge. Mechanical prophylaxis (TED stockings or 6-in elastic bandages applied foot to thigh with sequential pneumatic compression boots) was used. No thromboprophylaxis was used postdischarge.

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Simone,[15] 2008	Prospective cohort	40 patients undergoing laparoscopic gastric bypass or banding	Anti-Xa levels obtained 4 h after the first and third doses Therapeutic range, 0.18–0.44 units/mL	N	N	0	The dose of enoxaparin administered depended on the surgeon. Surgeon B used only enoxaparin 40 mg compared with surgeon A, who used mainly enoxaparin 60 mg except for patients judged to be at a higher risk for bleeding, to whom 40 mg was administered. Prophylaxis was continued for the duration of the hospital stay.
Smith,[266] 2004	Retrospective database analysis	779 patients undergoing RYGBP (328 LRYGBP, 451 open RYGBP)	VTE assessment not described	N	N	0	Prophylaxis unknown
Stroh,[267] 2009	Prospective cohort	3,122 bariatric procedures performed at 38 German hospitals 2,869 primary operations and 253 revisions		N	N	0	Roughly 97.5% in 2006 and 90.6% of patients in 2007 received prophylaxis for thromboembolism with LMWH
Vaziri,[268] 2009	Prospective cohort	29 bariatric surgery patients Mean BMI, 49 ± 8 kg/m^2	Ultrasound on mean postoperative day 16 ± 18 Venogram postoperative day 16 ± 6 (n = 26)	N	N	1	UFH 5,000 units SC within 30 min before the procedure and q8h postoperatively for the duration of the hospitalization. PCDs were used and placed before going to the operating room. High-risk patients (those with a history of VTE) underwent concurrent placement of retrievable IVC filters in the infrarenal position after general anesthesia.
Vascular surgery							
AbuRahma,[71] 1990	Prospective cohort	72 consecutive patients undergoing femoropopliteal reconstruction	IPG and DUS within 2 wk, positive findings confirmed by venography; random sample of n = 10 with negative results also had venography	Blinded to treatment assignment (4 different types of operations)	N	0	Early mobilization on postoperative day 1 or 2

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Angelides,[60] 1977	Prospective cohort	88 patients with aortoiliac disease	FUT scanning daily for 2 d with venographic confirmation of popliteal or more proximal abnormalities	N	N	0	All given heparin 5,000 to 10,000 units intraoperatively, subsequently reversed with protamine; other prophylaxis NS
Barnes,[75] 1976	Retrospective (group 1) and prospective (group 2) cohort	52 patients/54 amputations (group 1) 35 patients/42 amputations (group 2)	Doppler velocity study preoperatively and daily postoperatively in group 2	N	N	0	Plaster dressing applied for 4 wk in random sample of 51 patients; in wheelchair on postoperative day 2 and ambulating with crutches on postoperative day 5
Bradham,[73] 1965	Retrospective cohort	149 patients who underwent 157 primary lower-extremity amputations	NS	N	N	0	No details about prophylaxis
Burke,[77] 2000	Prospective cohort	Eight patients with below-knee amputation	Weekly measurement of thigh circumference, with DUS at weeks 2 and 4	NS	NS	0	Prophylaxis not specified; cast applied to residual below-knee stump in all patients
Bush,[67] 2001	Prospective cohort	104 consecutive patients with AAA undergoing endovascular repair	NS	NS	No	Complications not described for five patients	Prophylaxis not specified
De Maistre,[66] 2009	Prospective cohort with nested case control: 17 cases with VTE and 51 randomly selected controls	193 consecutive patients with AAA repair	DUS preoperatively and once postoperatively or when clinically suspicious	N	N	0	All patients received bimodality prophylaxis with enoxaparin 40 mg/d (or UFH 5,000 bid in renal insufficiency), 1-5 d postoperatively (median, 1 d), and thigh-high bandages or stockings. All received UFH 50 International Units/kg intraoperatively, neutralized with protamine at end of operation.

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Eagleton,[68] 2002	Prospective cohort	50 consecutive patients undergoing endovascular AAA repair	DUS on postoperative day 1 and within 4 wk of discharge	N	N	0	Twenty-six patients were on antiplatelet therapy and nine were on warfarin before surgery. Warfarin discontinued 4 d preoperative and given UFH SC (dose not specified) after surgery. No additional prophylaxis given. Excluded patients with evidence of preoperative DVT by DUS
Flectcher,[269] 1997	Prospective cohort	142 patients with nonemergent AAA repair, lower-extremity revascularization or amputation	DUS preoperatively and days 7-10 postoperatively	N	N	0	All patients received UFH 5,000 units SC tid and SCDs intraoperatively.
Hamer,[69] 1972	Prospective cohort	22 consecutive patients with peripheral vascular disease undergoing femoropopliteal bypass	Venography on day 7	N	N	0	Prophylaxis not specified
Harper,[74] 1973	Prospective cohort	15 patients with mid-thigh amputations for peripheral vascular disease	Cannula phlebography over 5-10 d	N	N	0	Indwelling cannula placed in long saphenous vein during operation
Hollyoak,[65] 2001	Prospective cohort	50 consenting patients with elective abdominal or peripheral vascular surgery	DUS 1 d preoperatively and day of discharge	N	N	Three patients died following abdominal surgery	No prophylaxis given, but all received heparin intraoperatively
Moore,[64] 2001	Prospective cohort	653 patients with aortoiliac aneurysms	NS	NS	N	0	Prophylaxis not specified
Myhre,[70] 1974	Prospective cohort	25 patients with leg edema following femoropopliteal bypass (24) or aortoiliac disease (1)	Venography, day 16 postoperatively (average)	N	N	0	All given heparin 30 mg intraoperatively without protamine reversal; dextran 500 mL IV on postoperative days 0, 1, and sometimes 2; warfarin started on postoperative day 2

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Olin,[79] 1993	Prospective cohort	50 consecutive patients after AAA resection and aortoiliac or aortofemoral bypass	Venography 5 d postoperatively	N	N	0	No prophylaxis given, but all received intraoperative heparin
Passman,[72] 2000	Prospective cohort	74 patients undergoing infrainguinal bypass grafting	Bilateral DUS within 1 wk and 6 wk postoperatively; repeat DUS at week 2 if week-1 scan inconclusive	N	N	11 patients did not undergo repeat DUS at week 6	Excluded three patients with evidence of preoperative DVT by DUS All received intraoperative heparin 5,000 units before clamping and 1,000 units every hour. Routine prophylaxis not used, but 18/71 patients were fully anticoagulated for another indication
Reilly,[62] 1982	Prospective cohort	Aortoiliac reconstruction, including AAA (51) and occlusive disease (49)	FUT scan days 1-4 DUS days 1, 3, 5, with positive results confirmed by venography	N	N	0	All given heparin 5,000-10,000 units intraoperatively, subsequently reversed with protamine; any other prophylaxis NS
Rogers,[59] 2007	Prospective cohort	183,069 patients from 128 Veterans Administration and 14 private hospitals (2002-2004) with major general or vascular surgery	DVT confirmed by DUS, venogram, or CT and treated with anticoagulation and IVC filter; PE confirmed by high-probability V̇/Q̇, CT pulmonary angiography, or pulmonary arteriogram	N	Y	286 with missing data not included in prediction models	Large, prospective study that developed a multivariate risk model. Main limitation was that there was no information about use of VTE prophylaxis among patients in the cohort.
Rogers,[59] 2007	Prospective case-control study	1,162 patients undergoing vascular or general surgery developed a VTE from 183,069 surgeries	Duplex-, venogram-, or CT scan-confirmed DVT; V̇/Q̇ scan, pulmonary arteriogram, or CT angiogram for PE	N	Y Multivariate analysis (variable NR)	0	No intervention

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Satiani,[61] 1979	Prospective cohort	Abdominal aortic reconstruction	FUT scan preoperatively and once postoperatively (mean, day 7) and confirmed by venography and IPG	N	N	0	All given intraoperative heparin reversed by protamine
Satiani,[270] 1980	Prospective cohort	AAA (n = 30) Aortofemoral bypass (n = 39)	FUT scanning 3-10 d (mean, 6.5 d), IPG preoperatively (mean, 4 d) and postoperatively (mean, 7.3 d), venography when leg scan was positive	N	N	0	All given heparin 5,000 units intraoperatively subsequently reversed with protamine; any other prophylaxis NS
Williams,[78] 1975	Prospective cohort	Lower-extremity amputation	Lung scan, confirmed by pulmonary angiography in some but not all with positive results	N	N	0	24/70 patients received 10% LMWH (dextran) 500 mL on operation day and 6 d postoperatively
Yeager,[76] 1995	Prospective cohort	72 patients with peripheral vascular disease undergoing major lower-extremity amputation, including 31 above-knee and 41 below-knee amputations	DUS preoperatively (within 3 d) and postoperatively (before discharge)	NS	N	Two patients not screened postoperatively because of early postoperative death	No routine anticoagulant prophylaxis; nine of 63 patients without DVT were receiving warfarin preoperatively for another indication
			Cardiac and thoracic surgery				
Ambrosetti,[271] 2004	Prospective cohort	270 CABG surgery patients 4-19 d after surgery	Within 2 d after admission, ultrasonography (duplex and color Doppler) Both legs scanned from the groin distally, including calf veins. If the finding of initial ultrasonography was normal or inadequate for interpretation, testing was repeated 7 d later	N	N	0	
Cartier,[272] 2001	Retrospective cohort	500 off-pump CABG compared with 1,476 CPB	?	N	N	0	

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Daddi,[89] 2006	Prospective study	Thoracic surgery for cancer: 50 patients (36 lobectomies, 12 pneumonectomies, 2 wedge resection)	All patients underwent chest multislice CT scanning within 7-15 d from the time of the operation.	N	N	0	
DeLaria,[82] 1991	Retrospective cohort (1975-1988)	10,638 procedures open heart surgery (CABG + valves)	DVT: Venous Doppler, phleborheography and duplex scanning; contrast venography reserved for patients with equivocal or technically unsatisfactory results of noninvasive tests. PE: V̇/Q̇ scans; pulmonary angiography performed on patients with acute or chronic lung abnormalities	N	N	0	
Dentali,[273] 2008	Retrospective chart analysis	693 thoracotomies for lung cancer: 93 (13.5%) patients underwent pneumectomy, and 597 (86.5%) underwent lobectomy or wedge resection	?	N	N	0	
Egawa,[274] 2009	Retrospective and prospective	Thoracic and cardiovascular surgery in 1,467 (before the guideline) + 1,389 (after the guideline) patients Total 800 thoracic 1,100 cardiac procedures	Contrast CT preoperatively in all patients who had a history of VTE After hospitalization, lower-limb venous ultrasonography was performed in patients who had these risk factors.	N	N	0	

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Garaghozloo,[275] 2003	Retrospective chart analysis	179 consecutive patients with clinical stage I (T1N0, T2N0) non-small cell lung cancer undergoing video-assisted thoracic surgical lobectomy	?	N	N	0	
Gillinov,[83] 1992	Retrospective chart analysis	5,694 patients.	Reports from morbidity and mortality conferences, all pulmonary $\dot{V}/\dot{Q}$, all pulmonary angiograms, and all autopsies reviewed Criteria for PE: $\dot{V}/\dot{Q}$ scan read as high probability, positive angiogram, or autopsy findings of PE	N	N	0	
Hannan,[81] 2003	Prospective cohort	16,325 patients and 2,111 (12.9%) readmissions CABG	?	N	N	0	
Jackaman,[85] 1978	Prospective cohort	183 lateral thoracotomies	IV ^{125}I-labeled fibrinogen given on the day before surgery Measurements made immediately before operation and then daily for 7 consecutive days If abnormally high counts detected, measurements continued at less-frequent intervals up to 14 d	N	N	0	
Josa,[84] 1993	Retrospective chart analysis	1,033 consecutive patients (CABG, 819; valve replacement, 120; combined 94)	PE confirmed by $\dot{V}/\dot{Q}$ scan, or pulmonary angiogram, or both	N	N	0	

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Kalweit,[92] 1996	Retrospective chart analysis	1,735 lung resections for malignancy	PE confirmed by autopsy	N	N	0	
Ljungstrom,[86] 1985	Small prospective cohort	45 (esophageal or tracheal resection, pneumonectomy, bilobectomy, lobectomy, excision of chest wall tumor, exploratory thoracotomy)	^{125}I-labeled fibrinogen test External scanning, using a scintillation counter with a scaler performed according to Kakkar et al Both legs were scanned at eight different points at least every 2nd day during the first postoperative week If a fibrinogen test positive, scanning performed daily	N	N	1	
Mason,[276] 2006	Prospective cohort	336 pneumonectomies for malignancy	DVT confirmed by Doppler ultrasound; occasionally, venography performed PE: $\dot{V}/\dot{Q}$ scanning coupled with clinical suspicion, CT	N	N	0	
Nagahiro,[93] 2004	Retrospective cohort	706 general thoracic surgery patients from December 1995 to December 2000	Patients suspected of having PE: echocardiogram, chest CT scan, ultrasound of femoral veins, pulmonary perfusion scan, pulmonary angiography if necessary	N	N	0	
Patel,[277] 2009	Retrospective chart analysis	186 consecutive patients undergoing induction therapy for non-small cell lung cancer and malignant pleural mesothelioma	PE had to be documented by CT or $\dot{V}/\dot{Q}$ scan, and DVT had to be documented by Doppler ultrasonography.	N	N	0	

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Ramos,[23] 1996	Pseudorandomized study (?) over 10 y	From 1984-1994, a total of 2,786 patients underwent open heart surgery Patients randomly allocated to one of two treatment groups according to a table of random numbers	PE considered in all patients with unexplained dyspnea or significant hypoxia: V̇/Q̇ scans and pulmonary angiography.	N	N	?	
Reis,[278] 1991	Prospective study	29 CABG patients	High-resolution B-mode ultrasound with color Doppler imaging	N	N	1	
Saarinen,[88] 2001	Small prospective study	25 thoracotomies (16 malignancies)	DVT: bilateral CUS preoperative and on the second postoperative day.	N	N	0	
Sugarbaker,[279] 2004	Retrospective and prospective	496 extrapleural pneumonectomies and among them review of postoperative morbidity in a subset of 328 cases of mesothelioma	?	N	N	?	
Walker,[91] 1998	Retrospective chart analysis	150 video-assisted lobectomies in 149 patients	?	N	N	0	

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Ziomek,[87] 1993	Small prospective cohort	77 pulmonary resections (eight pneumonectomies, 41 lobectomies, 14 segmentectomies, 14 wedge resections)	Duplex scanning performed 1-2 d preoperative and then every other day for 2 wk Findings classified as either no evidence of thrombus or presence of thrombus in the calf to the common femoral vein; V̇/Q̇ scans performed preoperatively (0-13 d; mean, 2.6 d) and repeated postoperatively (2-18 d; mean, 4.9 d) Patients with intermediate or high-probability V̇/Q̇ scans and those with low-probability scans that changed postoperatively underwent pulmonary angiography	N	N	0	
			Neurosurgery				
Brandes,[280] 1997	Prospective study (single institution)	77 patients on adjuvant radiochemotherapy following surgery for high-grade gliomas	Symptomatic VTE	N	N	NS	
Chan,[281] 1999	Retrospective cohort (compared with patients without VTE; single institution)	2,366 patients who were admitted to neurosurgery service	Clinically overt VTE in hospital or < 30 d after discharge	N	N	NS	67% of patients with cancer received some prophylaxis 84% of patients without cancer received some prophylaxis
Kim,[111] 2009	Retrospective cohort	1,195 adult patients admitted to neurosurgical ICU with spontaneous or traumatic ICH	Duplex ultrasound or spiral chest CT for VTE	N	N	For analysis of risk factors, 9 records were incomplete and therefore excluded	All patients received LDUH or enoxaparin for 24 h

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Rokito,[173] 1995	Prospective study	219 patients undergoing major reconstructive spinal surgery	Symptomatic VTE	N	N	NS	All patients received either ES alone or ES + IPC. These were patients who declined or were disqualified from RCT by same author.
Ruff,[282] 1983	Retrospective study	385 patients undergoing craniotomy for malignant tumor (2 groups: 268 did not receive IPC; 117 did)	Symptomatic DVT	N	N	NS	
Simanek,[283] 2007	Prospective study (single institution)	63 consecutive patients undergoing neurosurgery for high-grade glioma	Symptomatic VTE	N	N	0	A prophylactic regimen of LMWH was given during the postoperative hospital stay, usually during the first 10 postoperative days; all patients wore GCS.
Wen,[284] 1998	Prospective safety study of UFH 5,000 bid	872 patients undergoing neurosurgical procedure	Major and minor bleeding	N	N	NS	78 patients excluded for various reasons (including failure to continue treatment after surgery) 152 craniotomy cases included
			Spinal cord injury				
Aito,[285] 2002	Single-center cohort study	275 consecutive patients with SCI split into 99 admitted within 72 h of injury vs 176 admitted between 8 and 28 d after injury	Doppler ultrasound of the lower limbs and pelvis were performed on admission, after 30 ± 45 d and whenever clinically requested	NS	N/A		SC LMWH plus early mobilization permanently dressed PGES and external sequential pneumatic compression of the lower limbs, applied during the rest 30 d after injury, were given to all patients
Chen,[107] 1999	Observational registry, multicenter	1,649 patients with new SCIs enrolled in the NSCISC database	Clinical diagnoses entered into database				No information about the proportion of patients on prophylaxis This includes redundant data (also reported by DeVivo); however, the DVT rate was not reported by DeVivo

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Deep,[286] 2001	Single-center 18-mo retrospective review of patients with acute spinal injury	276 (130 with and 146 without neurologic deficit) patients with SCI admitted to Queen Elizabeth National spinal injuries unit, Glasgow, Scotland	Clinical diagnosis of DVT or PE				All patients received enoxaparin 40 mg SC daily
DeVivo,[287] 1999	Observational registry, multicenter	28,239 persons with traumatic SCI injured between 1973 and 1998 and seen within 1 y of injury	Death due to PE				Information was extracted from NSCISC database Limited useful data for our purposes; however, 1-y risk for fatal PE well estimated No information about the proportion of patients on prophylaxis
Green,[108] 2003	Retrospective observational study (single center)	All 243 patients admitted between 1992 and 1995 for rehabilitation after SCI who had at least one ultrasound assessment for DVT (51 developed clinical VTE)	Clinical diagnosis of DVT or PE				Offers very little information about baseline risks because only charts of patients who had undergone ultrasound testing considered
Green,[288] 2005	Single-center retrospective	Charts for all 329 admissions to SCI unit of a rehabilitations institute from November 1999 to February 2000	Clinical VTE				> 97% patients on prophylaxis (82% LMWH, 15% UFH) Patients with IVC filter of VTE during acute hospital stay excluded

(Continued)

Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Harris,[289] 1996	Single-center observational study (retrospective)	105 patients with acute SCI admitted over a 6-mo period	Charts reviewed for evidence of DVT, PE, and bleeding	N/A			All patients received enoxaparin 30 mg q12h Autopsies were not performed in the five patients who died (but other clinical causes were evident in all cases)
Jones,[106] 2005	Retrospective cohort analysis of all SCI cases (16,240) in California from 1991-2001	Using ICD-9 codes, authors assembled a large cohort of SCI cases using the California Patient Discharge Data Set	ICD-9 codes for VTE were searched				Excluded patients hospitalized for >90 d (<1%) and patients given a prior diagnosis of VTE VTE cases were classified as likely or very likely No information about use of prophylaxis
Jones,[106] 2005	Retrospective cohort	16,240 admissions, patients with spinal cord injury	ICD-9-CM codes, categorized as very likely (coupled with codes for diagnostic tests including CUS, V̇/Q̇ lung scan, helical scan of chest, etc) or likely (secondary codes for VTE and length of stay of ≥ 3 d) Among cases diagnosed within 91 d, 45% classified as very likely and 55% as likely	N	Y See comments	0	Widespread use of LMWH during time of study. Adjusted for the clustering of observations within hospitals by using a generalized estimating equations approach, with robust sandwich estimators of variance and an independent within-group correlation structure assumed. Age was modeled as a discrete variable, using age 30-49 y as the referent. Hospital length of stay was not included because diagnosis of VTE likely leads to an increase in the length of hospitalization. To adjust for any secular trends in the incidence of VTE over time, we included calendar year in the models. To determine which specific chronic comorbid conditions were associated with the development of VTE, variables not significantly associated ($P > .05$) were removed by backward elimination.

(Continued)

Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Kadyan,[290] 2003							Excluded. On closer examination, this study tried to estimate DVT rate on admission using surveillance ultrasound.
Waring,[291] 1991	Data from NSCISC	1,419 subjects with SCI from October 1986 to June 1989 Data available for initial hospitalization (all) and 1-y follow-up (62.4%)	Clinical VTE				Information on use of prophylaxis not provided
			Major trauma				
Abelseth,[292] 1995	Prospective cohort study in patients with fractures of the lower limb distal to the hip	Patients undergoing operative fixation of the lower limb fractures	Venography on average 9 d after the operation	N	N	74/176	
Alejandro,[293] 2003	Retrospective study focusing on bleeding complications in patients receiving early (within 48 h) or late (> 48 h) LMWH prophylaxis	Patients with blunt splenic injuries treated nonoperatively	Bleeding complications	N	N	0	
Carlin,[294] 2002	Retrospective review comparing outcomes of patients receiving therapeutic filters vs prophylactic	Patients with blunt trauma undergoing IVC filter placement	Incidence of PE and mortality	N	N	0	

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Cipolle,[295] 2002	Retrospective review of a local registry	Patients admitted to a trauma center during a 5-yr period	Symptomatic and CUS DVT and PE	N	N	0	
Cornwell,[296] 2002	Prospective observational study	Nonambulatory trauma patients admitted to a noncritical-care setting	Compliance with the use of SCD	N	N	0	
Cyr,[297] 2006	Observational, single-group cohort, retrospective	11 severely injured children (age < 18 y, pediatric ICU or length of stay > 72 h) with a discharge diagnosis of VTE (per ICD-9 codes) selected from two trauma centers' patient registries (n = 3,291)	NR Categorized by ICD-9 codes	N	Y Multivariate analysis (variables NR)	0	
Denson,[110] 2007	Observational, single-group cohort, retrospective	88 patients with TBI who underwent lower-extremity surveillance color-flow Doppler imaging, and high-risk for VTE	Standardized venous duplex color-flow Doppler imaging	N	N	0	IGPC devices placed on all patients at time of admission and evaluated daily for initiation of prophylactic LMWH On diagnosis of DVT, patients started on LMWH (enoxaparin 1 mg/kg bid)
Geerts,[100] 1994	Prospective cohort study with routine venography	Patients admitted to a trauma unit	Venography (14-21 d after admission) and IPC	N	N	94/443 Inadequate or nonperformed venography	
Haas,[132] 2005	Prospective observational study on pharmacokinetics of enoxaparin	Multiple trauma patients	Determination of anti-Xa	N	N	4/25	Pharmacokinetics and pharmacodynamics of enoxaparin (30 mg SC bid) in nonedematous and edematous patients compared

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Hammers,[298] 1996	Prospective cohort study	Multiple high-risk trauma patients	Weekly CUS	N	N	0	
Haut,[298] 2007	Retrospective cohort study comparing the rate of VTE before and after implementation of a practice guideline	Patients admitted to a trauma service	Clinical- or DUS-detected VTE	N	N	0	The proportion of patients having a DUS increased from 20.9% before guidelines implementation to 81.5% afterward
Iskander,[299] 2006	Retrospective case-control study	698 trauma patients who underwent lower-extremity venous DUS scan during admission PE monitored with spiral CT in suspected cases	DUS using linear or curvilinear array scan heads and a pulsed Doppler frequency for DVT	N	N	0 All patients received mechanical prophylaxis.	All patients admitted to trauma services are candidates for chemical prophylaxis unless contraindicated by SCI or head injury or risk of major organ bleeding (these patients placed on chemical prophylaxis 3-7 d after admission).
Knudson,[102] 2004	Analysis of the NTDB of the American College of Surgeons for episodes of VTE	Trauma patients included in the NTDB	Confirmed clinical VTE	N	N	0	
Lu,[300] 2007	Prospective observational cohort study	547 consecutive trauma patients admitted to a single hospital with lower-limb fractures	DUS within 24 h of admission, on the 2nd postoperative day, and on the 7th postoperative day	N	N	0	
Macatangay,[301] 2008	Prospective cohort study	Patients admitted to the trauma services who received SCD	Compliance in the use of SCD before and after personnel education on VTE prevention	Y	N	0	

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Meissner,[302] 2003	Prospective cohort study	Injured patients with an ISS > 14	CUS at 1 and 3 d after admission, and then weekly until discharge (average follow-up, 12.4 d)	N	N	0	Most patients received prophylaxis
Nathens,[113] 2007	Prospective cohort study (secondary analysis)	Patients with hemorrhagic shock and injury admitted at least 7 d to ICU	Confirmed symptomatic VTE until hospital discharge or up to 28 d of admission	N	N	0	VTE rates stratified according to the initiation of prophylaxis: early (within 4 d from admission) or delayed (initiation beyond 4 d)
Nathens,[113] 2007	Secondary analysis of data from a prospective observational cohort study	Trauma patients with an ICU stay > 6 d	Confirmed clinical VTE	N	N	0	Rate of VTE as a function of timing of initiation of prophylaxis compared
Piotrowski,[303] 1996	Retrospective observational study	High-risk trauma patients	CUS within 48 h of admission and weekly	N	N	0	96% received prophylaxis with heparin, 74% with stockings, 81% with SCD
Platzer,[104] 2006	Retrospective chart review from a single-center prospective local registry on trauma	Patients operated for spinal injury	Confirmed symptomatic VTE (mean follow-up 17 d)	N	N	0	81% received LMWH, 16% combined LMWH and GCS. Prospective cohort
Proctor,[304] 2006	Prospective cohort	186 admissions to ICU, patients with multiple injuries (ISS score > 9)	Doppler examination	N	N	0	Pharmacologic or mechanical VTE prophylaxis

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Reiff,[112] 2009	Retrospective cohort	2,000 patients admitted to ICU with blunt or penetrating TBI	Ultrasound with spectral and color Doppler imaging	N	Y Other confounding factors DVT risk adjusted for age, race, BMI, ISS, mechanisms of injury, SCI, and lower-extremity fracture	0	Patients received pharmacologic DVT prophylaxis (LDUH or LMWH [enoxaparin]) Patients with DVT systematically anticoagulated
Riou,[305] 2006	Prospective multicenter observational cohort study	Patients with nonsurgical isolated lower-limb injuries with limb immobilization	Rate of VTE, including asymptomatic DVT detected by routine CUS after immobilization removal	N	N	937/3,698	61% received prophylaxis
Riou,[305] 2006	Prospective cohort	3,698 adult patients with nonsurgical isolated lower-limb injury below knee admitted to emergency department	Radiography (CUS) Final diagnosis determined by expert panel	N	Y The following variables were considered in the logistic model: age, sex, BMI, personal and family history of VTE, diseases increasing risk for VTE (including cancer), hormonal treatment, venous insufficiency, use of tobacco, injury severity, recommendation for walking, type of immobilization, duration of immobilization, and antithrombotic prophylaxis	937/3,698 (25%) An additional six patients were excluded from the final model because of missing values on various variables (6/2,761∝0.2%])	Prescribed antithrombotic prophylaxis: 1. High-risk dose 2. Moderate-risk dose 3. No prophylaxis

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Schuerer,[306] 2005	Case-control study comparing VTE rates before (historical control) and after (prospective arm) implementation on guidelines for VTE prophylaxis	Patients admitted to trauma services expected to stay for >48 h	Rates on confirmed VTE	N	N	0	
Schwarcz,[307] 2001	Retrospective chart review	Patients admitted to a trauma service and considered to be at high risk to develop VTE	CUS within 72 h of initiation of prophylaxis at admission and then weekly surveillance	N	N	0	All high-risk patients received enoxaparin 30 mg bid
Sems,[308] 2009	Prospective cohort study with routine CUS	Patients with complex lower extremities treated with external fixation	CUS 1-3 d before fixator removal	N	N	0	All patients received LMWH prophylaxis (enoxaparin 40 mg or dalteparin 5,000 units)
Steele,[309] 2005	Prospective cohort study with routine CUS	Patients operated for pelvic or acetabular fractures	CUS 10-14 d after surgery	N	N	3/103	Rate of DVT/PE in patients receiving enoxaparin 40 mg within 24 h of injury or those with delayed administration >24 h compared

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Table S7—*Continued*

First Author, Year	Design	Population	Outcome Confirmed	Blinded Outcome Assessment	Adjustment	Lost to Follow-up	Comments
Worley,[310] 2008	Retrospective cohort study	Patients admitted with acute SCI receiving either UFH or dalteparin	Confirmed clinical DVT or PE	N	N	90/189	Not blinded
			Same-day surgery				
Enoch,[223] 2003	Retrospective cohort	Hernia repair (n = 2,484) or varicose vein surgery (n = 2,186) lasting up to 30 min	Unclear	N	N	Unclear	
Riber,[311] 1996	Retrospective cohort	Hernia repair	Database Limited to admission within 30 d of surgery	N	Unclear		
			Plastic and reconstructive surgery				
Shermak,[312] 2007	Retrospective cohort	138 patients who had undergone body contouring operations	NR	N	N	0	Each patient received perioperative prophylaxis for VTE, including compression and heparin 5,000 units SC bid.

AAA = abdominal aortic aneurysm; CABG = coronary artery bypass graft; ICD-9-CM = *International Classification of Diseases, Ninth Edition, Clinical Modification*; IGPC = intermittent graded pneumatic compression; INR = international normalized ratio; IVC = inferior vena cava; LABS1 = Longitudinal Assessment of Bariatric Surgery-1; NSCISC = National Spinal Cord Injury Statistical Center; NSQIP = National Surgical Quality Improvement Program; PACU = postanesthesia care unit; PCD = pneumatic compression device; TBI = traumatic brain injury. See Tables S2, S3, and S6 for expansion of other abbreviations.

Table S8—*Results of Observational Studies of VTE Risk*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
			General, mixed, and abdominal-pelvic surgery		
Agnelli,[53] 2006 RISTOS	92 suspected events 50 adjudicated as VTE or PE death DVT: 10 (0.4%) Nonfatal PE: 21 (0.88%) PE death: 19 (0.82%)	Independent risk factors: Age ≥ 60 y, previous VTE, anesthesia ≥ 2 h, advanced stage, bed rest ≥ 4 d, but incorrect analysis for a cohort study (logistic regression) Bleeding: 9.9% (5% required transfusion); 11.4% with prophylaxis vs 3% without ($P < .001$), but *bleeding* not defined	Incidence: General surgery: 2.83% Gynecologic surgery: 2.0% Urologic surgery: 0.87%	N/A	N/A
Antiplatelet Trialists,[4] 1994	PE		Antiplatelet: 47/4,716 (1.0%) Control: 129/4,730 (2.7%)		
Bahl,[56] 2010	Symptomatic, objectively confirmed DVT or PE	Age group: OR = 1.2 Sepsis: OR = 4.0 Pregnant/postpartum: OR = 8.3 Central venous catheter: OR = 1.8 Cancer: OR = 2.3 Prior VTE: OR = 2.1 Factor V Leiden: OR = 3.4 HIT: OR = 3.4 Inpatient ≥ 2 d: OR = 10.6	VTE incidence by risk score: 0-1 = 0% 2 = 0.7% 3-4 = 0.97% 5-6 = 1.33% 7-8 = 2.58% 9 + = 6.51%		ORs not adjusted for presence, type, or duration of DVT prophylaxis

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Bergqvist,[123] 1986	Total: n = 432 UFH: n = 217 LWMH: n = 215 VTE: UFH: n = 9 (4.3%; 2.2%-7.9%) LMWH: n = 13 (6.4%; 3.8%-10.6%) *P* = NS Bleeding: UFH: n = 10 (4.6) LMWH: n = 25 (11.6) *P* = .007	No analysis of predictors Deaths: n = 10 (cancer n = 8) No PE-related deaths			
Bergqvist,[124] 1988	Analyzable patients: n = 1,002 Correct prophylaxis: n = 826 LMWH, n = 505 UFH, n = 497 VTE: LMWH, 5.5% (3.7%-8.0%) UFH, 8.7% (6.4%-11.6%) *P* = .05 Bleeding: LMWH, n = 30 (5.9%) UFH, n = 15 (3.0%) *P* = .03	No analysis of predictors Deaths within 30 d: n = 20 (10 in both groups), giving overall mortality = 2% Deaths with cancer: n = 13 Autopsy: n = 10 (one fatal PE in UFH group)			

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Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Bergqvist,[125] 1995	Overall Dalteparin 5,000: 6.8% Dalteparin 2,500: 13.1% ($P < .001$) ITT Dalteparin 5,000: 6.6% Dalteparin 2,500: 12.7% ($P < .001$) Cancer Dalteparin 5,000: 8.4% Dalteparin 2,500: 14.9%	No analysis of predictors			
Bergqvist,[127] 2002 ENOXACAN	All VTE Proximal DVT Distal DVT PE	No analysis of predictors	Placebo: 20/167 (12.0) Enoxaparin: 8/165 (4.8) Placebo: 3 (1.8) Enoxaparin: 1 (0.6) Placebo: 17 (10.2) Enoxaparin: 7 (4.2) Placebo: 1 (0.6)	60% risk reduction (12-82, $P = .02$)	
Blake,[219] 2001	Symptomatic VTE <4 wk PE <4 wk		0/587 0/587		
Bottaro,[220] 2008	VTE, DVT, proximal DVT, death, major bleed, minor bleed	Prophylaxis <4 wk Prophylaxis >4 wk	See Figures 2 and 3	See Figures 2 and 3	See Figures 2 and 3
Catheline,[222] 2000	Symptomatic DVT PE Deaths	8 (0.33%) 0 NR in abstract	Six cases had pneumoperitoneum >2 h, and two >3h Long operations and reverse Trendelenburg position suggested as risk factors for DVT No patients with cancer developed DVT	5 DVT/848 cholecystectomies (0.59%) 1 DVT/305 inguinal hernia repairs (0.33%) 1 DVT/45 colorectal resections (2.2%) 1 DVT/2 rectal prolapse surgery (50%)	

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Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Clarke-Pearson,[54] 2003	Symptomatic, objectively confirmed VTE	Overall = 1.3% TAH = 0.9% TAH/nodes = 4.1% Radical hysterectomy = 2.6% Debulking ovarian cancer = 1.6% Extended oncology surgery = 1.6% Sacral colpopexy = 0.6% Exploratory laparoscopy = 1.1% Radical vulvectomy = 0.2%	Risk factors Cancer: OR = 4.9 (1.7-14.5) Prior DVT: OR = 7.9 (1.7-35.6) Prior pelvic irradiation: OR = 3.5 (1.0-12) Hypertension: OR = 2.4 (1.1-18.7)		
Edmonds,[313] 2004	Meta-analysis of postoperative DVT risk factors	Prior VTE = 5.2 (3.2-8.5) Varicose veins = 2.4 (1.7-3.4) OCs = 2.4 (1.5-4.0) Cancer = 2.9 (2.0-4.3) General anesthesia = 2.9 (1.7-4.8) Others but no OR: Age, obesity (BMI > 30 kg/m^2), factor V Leiden, orthopedic surgery			No adjustment We do not know whether these are independent risk factors.
Enoch,[223] 2003	DVT < 3 mo	Varicose vein + heparin	3/1,283		
		Varicose vein – heparin	0/903		
		Hernia + heparin	1/1,854		
		Hernia – heparin	1/630		
	PE < 3 mo	Varicose vein + heparin	1/1,283		
		Varicose vein – heparin	0/903		
		Hernia + heparin	0/1,854		
		Hernia − heparin	0/630		

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Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Flordal,[224] 1996		Prior VTE, leg fracture or arthroplasty, present leg ulcer or cancer, OR time > 150 min, preoperative transfusion of ≥ 2, preoperative hospitalization of ≥ 6 d were independent VTE predictors			
Gallus,[225] 1973	DVT by FUT		6/169 UFH (3.6%) vs 39/181 untreated (21.5%) with DVT Among untreated: 4/118 (3.4%) elective surgery (9 hip replacement) 2/23 (8.7%) hip fracture 3/40 (7.5%) medical had femoral or popliteal DVT by venogram, but we do not know whether any were symptomatic		
Gallus,[131] 1976	Asymptomatic DVT through FUT	820 patients	Control: 16.0% UFH: 4.2%		
Gallus,[226] 1997	Prevention of postoperative DVT in patients with cancer				Unavailable electronically Requested from library
Haas,[132] 2005	Autopsy-proven fatal PE Overall mortality		Overall: 0.152% (0.10%-0.217%) Certoparin 3,000 IU daily: 0.147% (0.077%-0.217%) UFH 5000 tid: 0.156% (0.084%-0.228%) Certoparin: 1.44% UFH: 1.27%		

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Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Huber,[227] 1992	Objectively diagnosed PE In hospital		In-hospital symptomatic PE rate 0.31% (0.28%-0.38%) 30-d postdischarge PE rate 0.1% (0.07%-0.14%) Total PE incidence 0.41% (0.34%-0.49%)	Delayed PE more frequent after low-risk surgery	
International Multicentre Trial,[1] 1975	Deaths Autopsy-proven acute massive PE Autopsy-proven DVT		UFH: 80 Control: 100 UFH: 2 Control: 16 ($P < .005$) UFH: 6 Control: 11 ($P < .005$)		
Kakkar,[134] 1985	DVT Cohort (n = 910) receiving CY216 daily		CY216: 5/196 (2.5%) UFH: 15/199 (7.5%, $P < .05$) 30 (3.2%) postoperative deaths No PE found in those autopsied		
Kakkar,[135] 1997	Asymptomatic DVT PE		LMWH: 30/648 (4.6%) UFH: 28/663 (4.2%) LMWH: 1 (0.15%) UFH: 3 (0.45%)		
Koch,[228] 2001	PE All studies Orthopedic surgery General surgery General surgery with high-dose LMWH		LMWH: 0.8% UFH: 1.2% ($P = .05$) LMWH: 7.5% UFH: 10.6% ($P = .08$) LMWH: 0.4% UFH: 0.5% LMWH: 0.1% UFHL .7% ($P = .05$)		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Mismetti,[230] 2001	DVT by ultrasound, FUT, or venography PE, symptomatic VTE, death, major bleeding, hematoma, transfusion	LMWH UFH	See Table 4		See Table 5
Nurmohamed,[231] 1992	DVT		Unreliable because these were asymptomatic DVT by FUT		PE rates are potentially important because these would be symptomatic PE, but clinical diagnosis may be unreliable.
	PE (diagnosis accepted if found at autopsy, V̇/Q̇ scan, angiography, or clinical diagnosis)		LMWH: 9/2,888 (0.3%) UFH: 20/2,843 (0.7%) RR: 0.44 (0.21-0.95)		Very few fatal PE; not enough for meaningful analysis
Sagar,[140] 1975	Fatal PE	66 deaths; 60 autopsied The six patients not autopsied had terminal cancer (four in control group, two in UFH group)	Control: 8/236 (3.4%) UFH: 0/252 ($P < .01$)	See Table 2 for operative procedures	This is one of the best, if oldest, studies to give a fatal PE rate among major surgery patients not receiving prophylaxis. That said, does anyone really believe a fatal PE rate of 3.4% among today's patients?
Schulz,[143] 2005	DVT PE		LMWH/GCS: 3/2,393 LMWH: 2/2,272 One in each group		
Sweetland,[233] 2009	Followed by record linkage to (National Health Service) data on hospital admissions and deaths. 239,614 admitted for surgery during follow-up; 5,419 admitted for and 270 died of VTE	See Table 3 for estimated 3-mo cumulative incidence rates of VTE by surgery overall and by type of surgery			No information on perioperative DVT prophylaxis

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Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Truitt,[234] 2005	DVT/PE	All patients	3/3,637 (0.08%)	N/A	N/A
		Age ≥ 9y	NR	OR = 3.6	N/A
		GCS ≤ 8	NR	OR = 9.2	N/A
		CNS injury	NR	OR = 2.9	N/A
		ISS ≥ 25	NR	OR = 82	N/A
		Head injury, length of ICU stay, presence of spinal injury, and sex were not statistically significant factors for DVT/PE			
White,[80] 2003		See Tables 1 and 2 for estimated 91-d rehospitalization rates by type of surgery and cancer			
			Urologic surgery		
Kibel,[235] 1997	Symptomatic DVT	All patients	0/158		
	PE	All patients	1/158		
	All DVT	All patients	4/106		
Koya,[236] 2005	Lower-limb symptomatic DVT	All patients	2/1,373		
	PE	All patients	0/1,373		
Kundu,[237] 2004	Any VTE	All patients	45/3,477 (1.3%)		
Montgomery,[238] 2005	Symptomatic DVT	All patients	2/344		
		Heparin	2/172		
		SCD	1/172		
	PE	All patients	0/344		
		Heparin	0/172		
		SCD	2/172		
	Major bleeding	All patients	17/344		
		Heparin	12/172		
		SCD	5/172		
Permpongkosol,[239] 2007	Thrombophlebitis/ symptomatic DVT	All patients	8/2,775		
	PE		8/2,775		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Pettus,[240] 2006	Symptomatic DVT	All patients	14/2,208		
	PE	All patients	20/2,208		
	Any symptomatic VTE	All patients	33/2,208	ORs presented (95% CI)	No multivariable analysis presented
		Age (per y)		1.02 (1.0-1.1)	
		BMI (per kg/m^2)		1.0 (0.91-1.1)	
		EBL (per 100 mL)		1.02 (1.01-1.02)	
		OR time (per 10 min)		1.03 (1.0-1.1)	
		Length of stay		1.03 (1.0-1.1)	
		> T2		1.6 (0.71-3.4)	
		> N0		3.7 (0.7-13)	
		> M0		1.2 (0.23-3.9)	
		Malignant	26/1,855	0.77 (0.29-2.6)	
		Year of surgery		1.0 (0.96-1.2)	
		Arrhythmia	4/66	4.7 (1.12-14)	
		Cancer history	7/628	0.67 (0.25-1.6)	
		Clotting disorder	0/13	0 (0-23)	
		Coronary artery disease	3/135	2.2 (0.54-6.3)	
		CHF	0/12	0 (0-25)	
		COPD	1/40	1.7 (0-11)	
		Cerebrovascular accident	0/24	0 (0-11)	
		Diabetes	2/228	1.2 (0.3-3.5)	
		Previous DVT	1/6	14 (0.28-126)	
		Hypercholesterolemia	4/195	1.4 (0.36-4.1)	
		Hypertension	17/1,059	1.3 (0.63-2.9)	
		Smoking	19/1,068	1.3 (0.63-2.9)	
		Transient ischemic attack	1/13	5.6 (0.13-40)	

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Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
			Gynecologic surgery		
Abu-Rustum,[241] 2005	Symptomatic DVT or PE	All patients	8/168	NA	NR
		Intraoperative RBC transfusion vs not	$P = .49$	OR = 0.47	
		Postoperative RBC transfusion vs not	$P = .10$	OR = 3.32	
		Postoperative FFP transfusion vs no	3/16	OR = 6.78	
			5/152		
			$P = .01$		
		Postoperative any transfusion vs not	5/46	OR = 4.84	
			3/122		
			$P = .04$		
		Prophylactic heparin/LMWH	$P = .31$	OR = 2.33	
		No difference in age, BMI, stage, length of OR, EBL, ascites, residual disease			
Ageno,[242] 2006	Symptomatic VTE	All patients	0/256	N/A	N/A
	Asymptomatic proximal DVT	All patients	0/247		
Suzuki,[243] 2005	PE	All patients	42/6,218 (0.7%)	N/A	N/A
		All patients undergoing surgery for benign diseases	10/3,158 (0.32%)	N/A	N/A
		All patients undergoing surgery for malignant diseases	32/1,451 (2.21%)	N/A	N/A
		Age:			
		>40 y	39/42 (93%)	OR = 6.6, $P < .01$	RR = 2.6, NSD
		>50 y	29/42 (69%)	OR = 4.4, $P < .01$	RR = 3.4, NSD

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
		BMI:			
		>25 kg/m²	17/42 (40%)	OR = 3.7, $P < .01$	RR = 2.7, $P < .05$
		>28 kg/m²	7/42 (16%)	OR = 3.9, $P < .05$	RR = 3.9, $P < .05$
		Smoking	NR	OR = 0.8, NSD	RR = 1.03, NSD
		Hypertension	NR	OR = 3.0, $P < .01$	RR = 0.84, NSD
		Abnormal glucose tolerance	NR	OR = 6.3, $P < .05$	RR = 2.18, NSD
		Heart disease	NR	OR = 2.95, $P < .05$	RR = 1.15, NSD
		Collagen disease	NR	OR = 2.2, NSD	RR = 1.2, NSD
		Malignant tumor: endometrial cancer	32/42 (76%) 16/42 (38%)	OR = 8.3, $P < .01$	RR = 2.86, $P < .05$
		Benign disease	10/42 (24%)	NR	NR
		Blood transfusion	NR	OR = 7.2, $P < .01$	RR = 3.834, $P < .01$
		IPC: before vs after introduction	23/1,928 (1.2%) 14/3,525 (0.4%) $P < .01$	NR	RR = 0.396, $P < .05$
		Operative time:			
		≥4 h	26/42 (62%)	OR = 5.99, $P < .01$	NR
		≥6 h	15/42 (36%)	OR = 5.52, $P < .01$	NR
		Retroperitoneal lymph node dissection: alone vs pelvic + paraaorti	15/636 (2.4%) 13/211 (6.2%) $P < .01$	OR = 7.58, $P < .01$	NR
		Perioperative bleeding:			
		≥1,000 mL	19/42 (45%)	OR = 3.8, $P < .01$	NR
		≥2,000 mL	9/42 (21%)	OR = 4.2, $P < .01$	NR
Querleu,[244] 2006	DVT	All patients	3/1,000	N/A	N/A

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
			Bariatric surgery		
Birkmeyer,[245] 2010	VTE	Patients with mobility problems, BMI >50 kg/m², age >50 y, and patients undergoing open procedures	Before risk adjustment, patients with IVC filter had significantly higher rates of perioperative complications, including postoperative VTE (2.03% with IVC filters vs 0.53% without IVC filters, $P < .0001$), combined serious complications (7.56% vs 3.62%, $P < .0001$), and death/permanent disability (1.85% vs 0.51%, $P < .0001$). Prophylactic IVC filters for gastric bypass surgery do not reduce the risk of PE and may lead to additional complications.		Following propensity adjustment, patients receiving IVC filters remained at higher risk of postoperative VTE (OR, 1.28) and serious complications (OR, 1.40), although these differences were no longer statistically significant. IVC filter patient risks of death/permanent disability remained higher (OR, 2.49; 95% CI, 0.99-6.26; $P = .05$) following propensity adjustment. Of the 10 patients with IVC filters who died or experienced permanent disability, three experienced PE and two had complicaions directly related to the filter itself, including fatal IVC thrombosis and IVC filter migration to the heart.
Borkgren-Okonek,[246] 2008	Major bleeding Clinically evident VTE occurring ≤3 mo		Significant bleeding or anemia occurred in five (2.24%) patients, four (1.79%) of whom required transfusion and one who required reoperation. DVT and PE were diagnosed in one (0.45%) patient on postoperative day 37 by lower-extremity venous ultrasonography and chest CT.		
Brasileiro,[247] 2008	Total DVT		0.79% (1/136)		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Carmody,[248] 2006	Symptomatic PE	BMI = 50 kg/m^2 Primary (0.9% vs revision 0.5%) Venous stasis Hypoventilation syndrome Male sex	33 (0.85%) PE, among which four DVT Fatal PE 27% (0.2% total population) One-third after discharge		
Caruana,[249] 2009	Symptomatic PE Bleeding (transfusion > 1 unit)	BMI, sex, stasis, obstructive sleep apnea, VTE history	6/1,652 (0.36%) No death Bleeding: 1.2%		
Clements,[250] 2009	Symptomatic VTE		DVT: n = 3 (0.31%) PE: n = 1 (0.1%)		
Cotter,[7] 2005	Symptomatic DVT		0.94% (1/107)		
Escalante-Tattersfield,[12] 2008			Only one (0.16%) asymptomatic thrombosis of the right-side common femoral vein and proximal superficial femoral vein. No PE. Ten patients presented with postoperative bleeding; no patient developed clinically significant bleeding that warranted termination of the thromboprophylaxis.		
Fernandez,[251] 2004	PE	PE: independent predictor for death	ORYGBP: 1.2% (n = 17) LRYGBP: 1% (n = 6) NS		
Flum,[252] 2009 LABS1	DVT or VTE	History of VTE	0.4% (banding, 0.3%; LRYGBP, 0.4%; ORYGBP, 1.1%)		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Frederiksen,[16] 2003	Anti-Xa activity	Body weight	Strong negative correlation between body weight and anti-Xa activity after injection of LMWH		
Frezza,[253] 2006	Symptomatic VTE		0%		
Gargiulo,[254] 2007	Group ORYGBP, no IVC filter but BMI > 55 kg/m²: Three Fatal PE One nonfatal PE Group LRYGBP: One nonfatal PE + 1 femoral DVT (same patient, BMI < 55 kg/m²)	BMI > 55 kg/m² and ORYGBP			
Gargiulo,[254] 2007	PE	OGB vs LGB	4/193 (2.1%)	OR = 4.49	NR
			1/213 (0.5%)	(calculated)	
		OGB: BMI > 55 kg/m² vs BMI < 55 kg/m²	4/31 (13%)	RR = 10.2	NR
			0/162		
Gonzalez,[255] 2006	Symptomatic VTE Three fatal PE Eight nonfatal PE	30% after discharge Risk: age > 50 y, history of smoking, and previous DVT/PE and postoperative anastomotic leak	n = 23 (3.5%)		
Gonzalez,[255] 2006	VTE	All patients	23/660 (0.2%)	N/A	N/A
		Age > 50 y	12/23 (52%)	OR = 2.7	OR = 2.8
		VTE vs no VTE	185/637 (29%)	(calculated)	*P* = .04
			P = .04		
		Smoking	5/23 (22%)	OR = 3.6	OR = 6.7

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
			45/637 (7%)	(calculated)	$P < .01$
			$P < .01$		
		Previous DVT/PE	3/23 (14%)	OR = 7.2	OR = 13.1
			13/637 (2%)	(calculated)	$P < .001$
			$P = .02$		
		Open surgery	16/23 (68%)	OR = 2.1	OR = 2.59
			331/637 (52%)	(calculated)	$P = .16$
			$P = .03$		
		Revisional surgery	5/23 (22%)	OR = 2.8	OR = 0.71
			57/637 (9%)	(calculated)	$P = .67$
			$P = .02$		
		Anastomotic leak	7/23 (32%)	OR = 14.2	OR = 25
			19/637 (3%)	(calculated)	$P < .001$
			$P < .001$		
		No difference between VTE and non-VTE groups for sex, BMI, diabetes mellitus, obstructive sleep apnea, hypertension, mechanical arthropathy, coronary atherosclerosis			
	DVT	All patients	9/660 (1.4%)	N/A	N/A
	DVT+PE	All patients	7/660 (1.1%)	N/A	N/A
	PE	All patients	6/660 (0.9%)	N/A	N/A
	IVC thrombosis	All patients	1/660 (0.2%)	N/A	N/A
	Fatal PE	All patients	3/660 (0.4%)	N/A	N/A

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Hamad,[256] 2005	Symptomatic VTE: In addition to the death due to bleeding complications at center B, six severe bleeding complications (0.9%) were observed in centers D and E. These comprised of two cases of hematemesis (one at each center), two cases of GI bleeding (at center D), and two cases of vaginal bleeding (at center E).	Age > 40 y (five patients), followed by smoking (three patients), BMI > 60 kg/m² (two patients), oral contraceptive use (one patient), a history of VTE (one patient), and varicose veins (one patient).	Seven (1%) patients with a mean length of follow-up of 10.5 ± 7.1 mo (one [0.1%] patient had DVT, and six [0.9%] patient had PE)		
Heffline,[257] 2006	Symptomatic VTE		N = 6 (1.3%): five DVT, one PE, one death		
Inabnet,[258] 2010	DVT or PE	History of VTE Extreme BMI Inability to walk > 200 ft History of obstructive sleep apnea	DVT/PE within 30 d: revisional participants 1.8% vs 0.5% in the primary participants		
Kligman,[259] 2009	Symptomatic VTE		0		
	Hemorrhage		N = 15 (3.5%) Hematologic evaluation was completed in 10 patients: a markedly decreased number of dense granules per platelet was observed in all 10 patients.		
Kothari,[20] 2007	Symptomatic VTE		DVT 0% and 0%		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
			One PE in the UFH cohort		
	Bleeding: Fourteen (5.9%) patients in the enoxaparin cohort required postoperative transfusions compared with three patients (1.3%) in the heparin cohort ($P < .011$). Four (1.7%) patients in the enoxaparin cohort required reexploration for bleeding compared with none in the heparin cohort.				
McCarty,[260] 2005	PE		< 30 d: 0.1% (two patients)		
			> 30 d: 0.05%		
Magee,[261] 2008	Symptomatic DVT, PE		0 DVT 0 PE Three adverse events required repeat surgery, including two bleeding events		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Miller,[6] 2004	Symptomatic VTE		Six (2.4%) major hemorrhages (UFH + IV ketorolac) Three (1.2%) patients with symptomatic DVT/PE within 30 d of operation. All three had a PE confirmed by V̇/Q̇ scan or pulmonary angiogram, but only one demonstrated a lower-extremity DVT by ultrasound. Additionally, only one (0.4%) experienced a PE during hospitalization, and that patient's SC heparin had been discontinued secondary to hemorrhage. Two patients were at home and no longer receiving prophylaxis when they experienced their PEs (day 13 and 29).		
Ojo,[262] 2008	Major bleeding		0 vs 0 No VTE? One death (PE) after 1 mo despite IVC filter		
Overby,[263] 2009	VTE	Inherited plasma risk indicators:		NR	NR
		Antithrombin III	4/183 (2.19%)		
		Factor V Leiden	6/104 (5.77%)		
		Protein C activity	8/180 (4.44%)		
		Free protein S	5/174 (2.87%)		
		Protein S activity	8/183 (4.37%)		
		Fibrinogen	59/148 (39.86%)		
		Acquired plasma risk indicators:	17/177 (9.60%)	NR	NR
		Homocysteine	31/180 (17.22%)		
		DRVTT	24/180 (13.33%)		
		Lupus aPTT	1/163 (0.61%)		
		ACA IgG	2/163 (1.23%)		
		ACA IgM	47/151 (31.13%)		
		D-dimer	73/147 (49.66%)		
		Factor VIII	97/151 (64.24%)		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
		Factor IX			
		Factor XI	73/146 (50.00%)		
		Most plasma markers of both inherited and acquired thrombophilias were identified higher in the bariatric surgery group (obese patients) than the general population.			
Overby,[263] 2009	VTE	Inherited plasma risk indicators:		NR	NR
		Antithrombin III	4/183 (2.19%)		
		Factor V Leiden	6/104 (5.77%)		
		Protein C activity	8/180 (4.44%)		
		Free protein S	5/174 (2.87%)		
		Protein S activity	8/183 (4.37%)		
		Fibrinogen	59/148 (39.86%)		
		Acquired plasma risk indicators:		NR	NR
		Homocysteine	17/177 (9.60%)		
		DRVTT	31/180 (17.22%)		
		Lupus aPTT	24/180 (13.33%)		
		ACA IgG	1/163 (0.61%)		
		ACA IgM	2/163 (1.23%)		
		D-dimer	47/151 (31.13%)		
		Factor VIII	73/147 (49.66%)		
		Factor IX	97/151 (64.24%)		
		Factor XI	73/146 (50.00%)		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
		Most plasma markers of both inherited and acquire thrombophilias were identified higher in the bariatric surgery group (obese patients) than the general population			
Piano,[264] 2007	DVT (color ultrasound)	BMI = 55 kg/m², hypercoagulable state, severe immobility, venous stasis, or previous history of DVT or PE	DVT: 0%		
Poulose,[314] 2005	DVT/PE	Age group, 50-59 y	0.34%		
Prystowsky,[8] 2005	DVT (color ultrasound)		One (1%) patient with DVT after hospital discharge		
			Six patients who had a history of VTE underwent placement of a temporary IVC filter. Two of the six patients showed evidence of thrombus before filter removal. One patient had a positive duplex sonography for acute DVT diagnosed 14 d after operation. Both the preoperative and postoperative day 2 duplex sonography were negative in this patient. The other patient had thrombus on the filter as documented by the intraoperative venacavogram performed at the time of the anticipated filter removal.		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
	PE		0		
	Hemorrhage		2 patients; 1.9%		
Prystowsky,[8] 2005	VTE	All patients	4/106 (3.8%)	N/A	N/A
		History of VTE	2/6 (33%)	N/A	N/A
	PE	All patients	0/106 (0%)	N/A	N/A
Quebbemann,[9] 2005	PE		0.12% (1/822)		
Raftopoulos,[21] 2008	Incidence of VTE (DVT, PE, or both) during the first 30 d. The safety end point was the occurrence of significant post-operative bleeding during the first 30 d defined as (1) the need for reex-ploration, (2) the need for transfusion of blood products, or (3) a hemoglobin (Hb) level difference >2 g/dL between the first postoperative Hb level and last Hb drawn prior to hospital discharge.	A high RR of VTE was found in association with conversion (RR, 20.2) followed by length of stay >4 d (RR, 8.2), revision surgery (RR, 4.8), operative time >330 min (RR, 3.3), and BMI >60 kg/m^2 (RR, 3).	VTE: 1.9% (6/308) VTE occurred after hospital discharge in four of six (66.6%) patients, on postoperative days 12, 20, 26, and 30. Those four patients had negative ultrasounds prior to hospital discharge. Significant difference in VTE rates between the two groups (A, 6/132 [4.5%]; B, 0; $P = .006$). Transfusion of blood products, six (4.5%) vs zero. Reexploration rate for bleeding, mean Hb level difference, and frequency of Hb level difference (2 g/dL) were similar in the two groups.		
Rondina,[17] 2010			The average peak anti-Xa level was 0.25 units/mL (SD, ± 0.11 units/mL; range, 0.08-0.59 units/mL). Peak anti-Xa levels did not significantly correlate with weight or BMI.		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Rowan,[19] 2008	Anti-Xa level	There were no differences in BMI (51.2 vs 54.0 kg/m^2; P = NS)	In group 1, no patients had therapeutic levels after the first dose. In group 2, almost one-third of patients had a therapeutic level after the first dose. This difference was statistically significant (P = .01). For third-dose anti-Xa levels, a similar margin of increase was seen from 30 to 40 mg, but this difference was not statistically significant (P = .115). Percentage of appropriate anti-Xa levels at first dose differed 0% vs 30.8% (group 1 vs group 2; P = .01) and at third dose, 9.1% vs 41.7% (group 1 vs group 2; P = .155). Dose of 40 mg q12h may not be sufficient for bariatric surgery patients.		
Sapala,[265] 2003	Fatal PE	Severe venous stasis disease, BMI = 60 kg/m^2, truncal obesity, OHS/SAS	0.21% (12/5,554)		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Scholten,[14] 2002	VTE DVT PE Bleeding		Seven (1.4%) clinically evident VTE, one DVT, and four nonfatal PEs in group 1 (5/92, 5.4%) and two DVTs in group 2 (2/389, 0.6%, $P < .01$). Only one DVT and one PE in group 1 were clinically evident during the initial hospitalization; all other VTEs were after discharge. One bleeding complication in each group. A bleeding gastrojejunal anastomosis in one patient in group 1 required discontinuation of LMWH and transfusion. This patient subsequently developed a symptomatic DVT. One patient in group 2 developed bleeding from around her drain on postoperative day 2 and required reexploration. Operative findings revealed a large blood clot in the lesser sac, and no identifiable site of hemorrhage was found after clot evacuation. The LMWH was stopped.		
Shepherd,[5] 2003	Symptomatic VTE Bleeding		0 DVT 3 (0.4%) nonfatal PE Major bleeding rate: 1% Minor wound bleeding: 0.6%		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Simone,[15] 2008	Anti-Xa level		The first-dose mean anti-Xa concentration was 0.173 units/mL in the 40-mg group and 0.261 units/mL in the 60-mg group ($P < .005$) compared with the third-dose mean anti-Xa levels of 0.21 and 0.43 units/mL, respectively ($P < .001$). After the third dose of enoxaparin, the percentage of patients with anti-Xa concentrations who remained subtherapeutic showed a statistically significant difference: 44% in the 40-mg group vs 0% in the 60-mg group ($P = .02$). However, no supratherapeutic anti-Xa concentrations were observed in the 40-mg group, whereas 57% of the third-dose levels in the 60-mg group were supratherapeutic. Enoxaparin 60 mg q12h was superior to a dose of 40 mg q12h in achieving therapeutic anti-Xa concentrations and avoiding subtherapeutic anti-Xa levels.		
Smith,[266] 2004	Symptomatic VTE Bleeding		DVT: 1/328 (laparoscopic), 3/451 (open) PE: 0/328 (laparoscopic), 4/451 (open) GI hemorrhage: 11 Abdominal wall: 11 Hematoma: 5/328 (laparoscopic) 0/451 (open)		
Stroh,[267] 2009	DVT PE	Only male patients with a BMI > 50 kg/m^2 experienced PE.	PE was not observed during the hospital stay, whereas its frequency after discharge reached 0.06%.		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Vaziri,[268] 2009	VTE		21% incidence of recurrent DVT and 15% incidence of thrombus in the IVC filter, yet no PE occurred. IVC filters may be effective in preventing clinically significant PE by trapping venous emboli, but it does not provide protection of DVT and, in fact, may increase the incidence of DVT.		
			Vascular surgery		
AbuRahma,[71] 1990	DVT, not otherwise specified (although 40% of all patients had postoperative edema)	All patients	6/72 (8.3%)	N/A	N/A
Angelides,[60] 1977	Asymptomatic proximal DVT (during hospitalization)	All patients	18/88 had asymptomatic distal or proximal DVT, involving 24/176 limbs. DVT extended proximally in six limbs; overall incidence higher for AAA than for occlusive iliac disease.	N/A	N/A
Barnes,[75] 1976	Symptomatic DVT or PE	Group 1 patients	0/52	N/A	N/A
	Asymptomatic DVT	Group 2 patients	0/35		
	PE		1/35 (2.9%)		
Bradham,[73] 1965	PE	All patients	Three events among 149 patients and 157 procedures	N/A	N/A
Burke,[77] 2000	Asymptomatic, proximal DVT (2 wk)	All patients	4/8 (50%) (3/4 had deficiency of protein S, C, or both)	N/A	N/A
	Symptomatic DVT (2 wk)		2/4 (50%) DVT were symptomatic		
Bush,[67] 2001	Symptomatic DVT and/or PE	Endovascular AAA repair (all patients)	1/99 (1%), including 1/50 in low-risk group and 0/49 in high risk group, where high risk = comorbid heart, lung, liver disease or cancer	N/A	N/A
De Maistre,[66] 2009	Symptomatic DVT	All patients	0/193 (0%)	N/A	N/A
	Asymptomatic proximal DVT	All patients	2/193 (1%)	N/A	N/A
	PE	All patients	2/193 (1%)	N/A	N/A

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
	Asymptomatic DVT or PE	Open vs endovascular	14/137 (10.2%)	RR = 1.91	NR
			3/56 (5.3%)	(calculated)	
			P = .28		
		FFP vs no FFP	6/11 (54.5%)	OR = 5.04	NR
			11/57 (19.3%)		
			P = .02		
	No difference between VTE and non-VTE groups for age, BMI, cardiovascular disease, prior VTE, AAA diameter, preoperative antiplatelet treatment, anticoagulant treatment, duration of surgery or clamping, EBL, days in ICU, RBC transfusion, platelet concentration, Hgb level, platelets, and fibrinogen				
Eagleton,[68] 2002	Symptomatic DVT	All patients	3/50 (6%)	N/A	N/A
Fletcher,[269] 1997	Symptomatic DVT	All patients	0/142	N/A	N/A
	Asymptomatic proximal (fem-pop) DVT	All patients	9/142 (6.3%)		
		AAA	1/41 (2.4%)		
		Aortic occlusion	1/11 (9.1%)		
		Femorodistal bypass	4/54 (7.4%)		
		Miscellaneous	0/15		
		Amputation	3/21 (14.3%)		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
	PE	All patients	1/142 (0.7) (confirmed)		
			1/142 (0.7) (suspected)		
Hamer,[69] 1972	Asymptomatic proximal DVT (day 7)	All patients	9/22 with abnormal venography, including 4 with tibial clot, 3 with popliteal clot, and 2 with thrombosis of both tibial and popliteal 5/22 (23%) Any thrombosis more common with below-knee (7/12) than above-knee (2/7) anastamosis	N/A	N/A
Harper,[74] 1973	DVT	Control patients	10/15 (67%)	N/A	N/A
	PE		4/15 (27%)		
	DVT	500 mL 6% dextran 70 given immediately postoperatively and postoperative days 1, 3, and 5	1/6 (17%) and none with PE		
Hollyoak,[65] 2001	Symptomatic DVT	All patients	NS	N/A	N/A
	Asymptomatic proximal DVT	All patients	3/50 (6%)		
	PE	All patients	0/50		
	Asymptomatic proximal DVT	Abdominal vs peripheral surgery	2/22 (9.1%)	RR = 2.53 (calculated)	N/A
			1/28 (3.6%)		
Moore,[64] 2001	Symptomatic DVT or PE (30 d)	Aorto-uni-iliac graft	DVT = 2/121 (1.7%)	N/A	N/A
			PE = 1/121 (0.8%)		
		Tube repair	DVT = 1/153 (0.7%)		
			PE = 0		
		Bifurcated endograft	DVT = 3/268 (1.1%)		
			PE = 0		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
		Open repair	DVT = 1/111 (0.9%)		
			PE = 0		
Myhre,[70] 1974	Asymptomatic proximal DVT (on average, day 16)	All patients	2/25 with distal DVT	N/A	N/A
			0/25 with proximal DVT		
Olin,[79] 1993	Symptomatic DVT	All patients	0/50	N/A	N/A
	Asymptomatic proximal DVT		2/50 (4%)		
	PE		0/50		
	No difference between DVT and non-DVT groups for clamp time; intraoperative heparin dose; EBL; RBC, platelet, FFP transfusion; or use of protamine				
Passman,[72] 2000	Asymptomatic DVT	All patients	2/71 (2.8%)	N/A	N/A
	Asymptomatic proximal DVT		1/71 (1.4%)		
	Asymptomatic DVT	Hypercoagulable	1/22 (4.5%)	RR = 2.23 (calculated)	N/A
		Not hypercoagulable	1/49 (2.0%)		
Reilly,[62] 1982	Asymptomatic DVT, including distal	All patients	13/100 (13%)	N/A	N/A
	Asymptomatic DVT, proximal		3/100 (3%)		
	Symptomatic DVT, proximal and distal		5/100 (5%)		
	PE (overlaps with proximal DVT)		1/100 (1%)		
	Asymptomatic DVT, including distal	AAA vs aortoiliac	8/51 (16%) vs 5/49 (10%)		
Rogers,[59] 2007	Clinically diagnosed and treated VTE	Vascular patients (n = 29,810)	0.73%	N/A	N/A

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
		All patients	0.63%	N/A	N/A
		Low risk patients	0.10%	N/A	N/A
		Moderate risk patients	0.44%	N/A	N/A
		High risk patients	1.46%	N/A	N/A
		15 independent variables (Table 4)	See Tables 2 and 3		See Table 4
Rogers,[59] 2007	VTE	All patients	1,162/183,069 (0.63%)	N/A	N/A
		Work RVU: 10-17 vs < 10	NR	NR	OR = 2.239
					$P < .0001$
		Work RVU:	NR	NR	OR = 2.857
		> 17 vs < 10			$P < .0001$
		Ventilator dependent	NR	NR	OR = 1.856
					$P = .0036$
		Preoperative albumin level ≤ 3.5 vs > 3.5	NR	NR	OR = 1.214
					$P = .0609$
		Integument vs endocrine operation	NR	NR	OR = 3.248
					$P = .0261$
		Respiratory/hemic vs endocrine operation	NR	NR	OR = 9.369
					$P < .0001$
		Throacoabdominal vs endocrine operation	NR	NR	OR = 6.827
					$P = .0005$
		Aneurysm vs endocrine operation	NR	NR	OR = 3.724
					$P = .0111$

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
		Mouth/palate vs endocrine operation	NR	NR	OR = 4.001
					$P = .0209$
		Stomach/intestines vs endocrine operation	NR	NR	OR = 4.014
					$P = .0069$
		Hernia vs endocrine operation	NR	NR	OR = 1.856
					$P = .2603$
		Disseminated cancer	NR	NR	OR = 1.873
					$P < .0001$
		ASA class: 2 vs 1	NR	NR	OR = 1.328
					$P = .3948$
		ASA class: 3 vs 1	NR	NR	OR = 2.122
					$P = .0224$
		ASA class: 4-5 vs 1	NR	NR	OR = 2.378
					$P = .0122$
		Emergency	NR	NR	OR = 1.460
					$P = .0010$
		Preoperative hematocrit level < 38	NR	NR	OR = 1.320
					$P = .0044$
		Female vs male sex	NR	NR	OR = 1.370
					$P = .0024$
		Chemotherapy for malignancy in past 30 d	NR	NR	OR = 1.829

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
					$P = .0049$
		Preoperative bilirubin level > 1.0	NR	NR	OR = 1.298
					$P = .0155$
		RBC transfusion	NR	NR	OR = 1.609
					$P = .0366$
		Wound class: clean/ contaminated vs clean	NR	NR	OR = 1.401
					$P = .0053$
		Wound class: contaminated vs clean	NR	NR	OR = 1.167
					$P = .4106$
		Wound class: Infected vs clean	NR	NR	OR = 1.382
					$P = .0809$
		Preoperative serum sodium > 145 mmol/L	NR	NR	OR = 1.615
					$P =. 0410$
		Dyspnea vs none	NR	NR	OR = 1.223
					$P = .0476$

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
		Bivariate analysis showed differences between VTE and no-VTE groups for 30-d mortality rate, specialty code, race, sex, age, history of CHF, impaired CNS, ASA class, DNR status, dependent functional status, smoking status, hepatobiliary, preoperative laboratory characteristics, comorbidities, pre-operative processes, and postoperative complications (Tables 3 and 4) ($P < .0001$)		
Satiani,[61] 1979	Proximal DVT	All patients	0/22	N/A	N/A
Satiani,[270] 1980	Asymptomatic proximal DVT (during hospitalization)	All patients	0/69	N/A	N/A
			Positive leg scan in 17 limbs; 13/16 had normal venography; 2/16 had missing segments in calf veins and 1 small peroneal clot; 16/17 had normal postoperative IPG; and 1 borderline IPG was normal by venography		
Williams,[78] 1979	Asymptomatic or symptomatic PE by lung scan	All patients	41/70	N/A	N/A

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
	Asymptomatic or symptomatic PE confirmed by angiography		9/70 (13%)		
			(text says 10/70 but numbers do not add up)		
			17/41 had angiography		
			7/17 had PE confirmed		
			2/70 had fatal PE confirmed by autopsy		
	Symptomatic PE		5/70 (7%)		
			3 symptomatic		
			2 fatal		
Yeager,[76] 1995	Asymptomatic DVT, detected by DUS so likely proximal	All patients	3/72 (4%) with postoperative DVT by DUS, proximal in at least 2 of 3 patients	N/A	N/A
		Prior DVT or venous insufficiency vs none	3/9 (33%) with preoperative or postoperative DVT had prior venous disease	RR = 7.0 (calculated)	N/A
			3/63 (5%) without preoperative or postoperative DVT		
	No significant difference between patients with or without preoperative or postoperative DVT for the following: age, diabetes, malignancy, prior amputation, prior lower-extremity vascular surgery, dialysis, extensive ulceration, or infection				

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
			Cardiac and thoracic surgery		
Ambrosetti,[271] 2004	VTE	Age (> 65 y), female sex, and postoperative complications	DVT 47 patients (17.4%)		
			Proximal and isolated distal DVT was 2.6% (n = 7) and 14.8% (n = 40).		
			Two cases (0.7%) of symptomatic PE fatal in one case (0.4%).		
			43 (91%) DVT cases were diagnosed at admission, whereas serial ultrasound testing allowed diagnosis of an additional four distal DVT cases		
Cartier,[272] 2001	VTE	OPCAB: none	OPCAB: 2 iliofemoral DVT + 3 PE (1 fatal) = 5 (1%)		
		CPB: 4 patients HIT was suspected in one patient; a second patient had a perioperative cerebrovascular accident that resulted in right hemiplegia; a third patient was readmitted with a mediastinitis that required reexploration and prolonged hospitalization; and a fourth patient had an adrenal tumor	CPB: 4 infrapopliteal DVT; 1 ilifemoral + 3 PE = 8 (0.5%)		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Daddi,[89] 2006	PE	Male sex COPD vs no COPD Lobectomy Lower lobectomy, right side Tumor >3 cm	Seven (14%) patients showed PE at multislice CT scanning, five involving the central arteries (principal, lobar, and segmentary) and two involving the subsegmentary arteries. Only two of these patients were symptomatic. Only one patient had a clinically overt DVT confirmed by means of DUS.		
DeLaria,[82] 1991	VTE	Perioperative MI (16%), atrial fibrillation (41%), blood type A (70%), and CABG (98%).	Total VTE: 77 (0.7%) DVT without PE: 36 (0.3%) PE: 41 (0.4%) (16 DVT; in 11 (27%), the presentation was cardiac arrest)		
Dentali,[273] 2008	VTE		12 (1.7%) venous thromboembolic complications, of which 9 (1.3%) were PEs. All these complications occurred while patients were receiving antithrombotic prophylaxis with UFH or LMWH.		
Egawa,[274] 2009	VTE	The risk factors for perioperative PE were cancer, varicose veins, BMI >25 kg/m^2, a central venous catheter, and long periods of being bedridden.	Six (0.4%) patients in group A developed DVT or PE, whereas no patient in group B experienced thromboembolism.		
Garaghozloo,[315] 2003	PE		2/179 (1.1%)		
Gillinov,[83] 1992	PE	Bed rest, longer hospitalization before surgery, postoperative CHF	32/5,694 (0.56%) 12 deaths (34%)		
Hannan,[81] 2003	Complications after CABG		PE/DVT: 133 (6.3%) of readmissions Length of time until readmission 9 d (4-17)		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Jackaman,[85] 1978	^{125}I FUT (thrombosis) No definition of bleeding or blood loss	Unilateral thrombosis was found to be significantly more frequent in the leg opposite the side of the thoracotomy ($P < .005$).	No heparin: 32/63 (51%) Heparin: 33/120 (28%) without increasing postoperative blood loss		
Josa,[84] 1993	PE	Prolonged recovery, obesity, hyperlipemia, prior DVT and PE, HIT	33/10,033 (3.2%) (32/819 CABG [3.9%], 1/94 combined, 0/120 valves) Diagnosis within 7 d in 8 patients and within 2 wk in 23 Fatal PE: 0.73% (6/819)		
Kalweit,[92] 1996	PE		21 fatal PE/1,735 The time between the lung resection and the onset of symptoms, indicating the major bleeding or PE, was ≤ 48 h in 12 patients. In another eight cases, the event took place on the 3rd or 4th postoperative day. When the acute event occurred, 17 of the 23 cases were still under postoperative anticoagulation with heparin.		
Ljungstrom,[86] 1985	DVT	Blood of group B or AB History of VTE Most extensive operations	8/44 (18%) Two of the thrombi were femoral and two popliteal, and the remaining six were calf thrombi. One patient with unilateral calf thrombus had slight tenderness of the calf, but all the other thrombi were asymptomatic.		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Mason,[276] 2006	DVT PE	Higher pack-years of smoking was associated with increased risk as well as with earlier occurrence of VTE.	25/336 (7.4%) patients had postoperative VTE, with peak incidence 7 d postoperation; 17 (68%) DVT only, 5 (20%) PE only, and 3 (12%) both DVT and PE. The 20 cases of confirmed DVT occurred in 33 locations (14 upper extremity, 15 lower extremity, and 4 central [iliac and vena cava] cases). Patients with VTE had substantially lower survival than predicted from competing-risks analysis of survival without VTE (13% vs 60% at 18 mo), and this difference persisted after censoring for deaths directly attributable to VTE.		
Nagahiro,[93] 2004	PE No data on DVT	Age, sex, BMI, operative time, length of time until the patient became fully ambulatory, operative method (ie, open thoracotomy or video-assisted thoracic surgery), and disease character (ie, benign or malignant disease) did not correlate with the occurrence of symptomatic postoperative PE.	No prophylaxis: 20/344 (7%) IPC: 0/362 (0%) 6/7 patients with PE operated on in the right decubitus position, and the operative position and the prevalence of PE were significantly correlated.		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Patel,[277] 2009	Preoperative and postoperative VTE	The overall survival was similar between patients with or without VTE.	VTE developed in 23/186 (12.3%) patients undergoing induction therapy. VTE was diagnosed during induction therapy in 11 patients. PE was higher during induction therapy (9/11 patients), whereas DVT was observed predominantly postoperatively (7/12 patients). The rate of postoperative VTE ranged between 7% and 8%.		
Reis,[278] 1991	DVT	?	Fourteen (48.3%, 98% CI, 30.1-60.4%) had 20 documented leg vein thromboses Popliteal vein (proximal): 1 Muscular veins (soleus, sural, gastrocnemius): 14 Peroneal vein: 4 Posterior tibia1 vein: 1 Leg with DVT (compared with SVG harvest site) Ipsilateral: 10 Contralateral: 10		
Saarinen,[88] 2001	DVT	N/A	1/25 (4%) in a patient with lung fibrosis patient 0 cases of clinically manifest DVT of PE during 1-mo period postoperatively 2 asymptomatic preoperative DVTs		
Sugarbaker,[279] 2004	PE DVT	?	20 deaths/496 among which 6 fatal PE 5 PE/328 (1.5%) 21/328 (6.4%)		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Walker,[91] 1998	PE	?	1/149 (fatal) Patient with a history of recurrent severe PE Full anticoagulation before surgery		
Ziomek,[87] 1993	VTE	More frequent with bronchogenic carcinoma than with metastatic cancer or benign disease (15/59 [25%] vs 0/18 [0%]), adenocarcinoma compared with other types of carcinoma (11/25 [44%] vs 4/34 [12%]), large primary lung cancer (>3 cm in diameter) compared with smaller lesions (9/19 [47%] vs 6/40 [15%]), stage II compared with stage I (7/14 [50%] vs 7/34 [21%], $P < .04$), and pneumonectomy or lobectomy compared with segmentectomy and wedge resection (14/49 [29%] vs 1/28 [4%])	20/77 (26%) patients, 5/77 (6%) preoperatively and 15/77 (19%) postoperatively. Patient prevalence was less (16/77 [21%]) because four patients had both DVT and PE. DVT was located in the common femoral vein in seven patients, popliteal in four, and peroneal in four. PE was detected in five (6%) patients (one preoperatively, four postoperatively). One PE was fatal.		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
			Neurosurgery		
Brandes,[280] 1997	Clinically diagnosed DVT, PE		16/77 (20.8%), 1-y follow-up		
Chan,[281] 1999	Clinically diagnosed and treated VTE (PE + any leg DVT) PE Duration of follow-up not specified	All patients on neurosurgery service	92/2,366 (3.9%)	N/A	N/A
		Craniotomy for 1° tumor	32/429 (7.5%)		
		Craniotomy for metastatic diagnosis	13/68 (19.1%)		
		All patients undergoing surgery	73/1,985 (3.7%)		
		All patients (including those who did not undergo surgery)	16/2,366 (0.67%)		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
	No multivariate or comparative (case vs control) analysis of risk factors but Table 3 shows that (1) bed rest, (2) surgery, and (3) cancer are all very prevalent in the patients who developed VTE				
Kim,[111] 2009	Symptomatic VTE	All patients	46/1,195 (3.8%)	N/A	N/A
		SAH	12/179 (3.7%)	N/A	N/A
		ICH	15/516 (2.9%)	N/A	N/A
		TBI	19/500 (3.8%)	N/A	N/A
		Age > 40 y	8/10 (80%)	N/A	N/A
		SAH vs ICH vs TBI	10/11 (90.9%)		
			7/16 (43.8%)		
		Immobility > 72 h	10/10 (100%)	N/A	N/A
			11/11 (100%)		
			16/16 (100%)		
		Infection, presumed	10/10 (100%)	N/A	N/A
			8/11 (72.7%)		
			15/16 (93.8%)		
		Central venous catheter	10/10 (100%)	N/A	N/A
			6/11 (54.5%)		
			12/16 (75%)		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
		Frequency of risk factors for VTE were less commonly reported in the SAH, ICH, and TBI groups for obesity, smoking, history of MI or stroke, CHF, malignancy, hypercoagulable disease, prior VTE, and major surgery. *P* values were not calculated.			
Rokito,[173] 1995	Clinical DVT or PE	All patients	1/219 (0.4%)		
Ruff,[282] 1983	Clinically diagnosed DVT	All patients not wearing IPC	97/268 (36%), within 96 wk after surgery		
		All patients wearing IPC	12/117 (10%), within 36 wks after surgery		
		Age >60 y	62/117		
		Age <60 y	35/147		
	Paresis is mentioned as a risk factor, but no rates are given. Risk appears to be higher in first 6 wk after surgery than during subsequent periods.				
Simanek,[283] 2007	Clinically diagnosed DVT, PE	All patients	15/63 (24%) at 348 d		
		Patients with paresis	4/15 (27%)		
		Patients without paresis	7/48 (15%)		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
	Majority (56) of patients received combined radiation + chemotherapy after surgery. Majority (not specified further) of events occurred before 3 mo but after LMWH had been stopped.				
Wen,[284] 1998	Major and minor bleeding	All included neurosurgery patients	3/872 (0.34%) 2 epidural hematomas and 1 significant intraventricular hemorrhage		
		Craniotomy patients	1/151 (0.66%)		
	The study is limited by the fact that the treating physician could apparently opt out of pharmacologic thromboprophylaxis (and this happened in as many as 78 patients).				
			Spinal cord injury		
Aito,[285] 2002	DVT (not separated by symptomatic vs asymptomatic)	Admission < 72 h from trauma	2/99 (2%)		
		Admission > 8 d after trauma	46/176 (26%)		
	The incidence of DVT in late admitted patients was 26%. Of those, 60% were detected on admission, whereas the remaining 40% developed in a period not exceeding 6 wk of hospitalization; 65% of detected DVT did not show any evident clinical sign.				
Chen,[107] 1999	Clinical DVT		162/1,649 (9.8%)		
	Clinical PE		43/1,649 (2.6%)		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Deep,[286] 2001	Clinical PE	No neurologic deficit	1/146 (0.4%)		
		Yes neurologic deficit	1/130 (0.8%)		
	Clinical DVT	No neurologic deficit	0/146 (0%)		
		Yes neurologic deficit	6/130 (4.6%)		
	One case of intraspinal bleeding was reported (of 276 patients who received enoxaparin)				
DeVivo,[287] 1999	Fatal PE during first year after SCI	None listed	9.7% (highly variable, ranging from 2.0%-15.2% during different time periods)		
Green,[108] 2003	Cancer, spasticity, BMI > 30 kg/m^2, age > 35 y, female sex all were associated with VTE in univariate analysis.				
Green,[288] 2005	Clinical VTE during rehabilitation stay		6/76 (7.9%)		
Harris,[289] 1996	Clinical DVT/PE (60 patients with sign of neurologic impairment also underwent screening ultrasound)		0/105 (0%)		
	Bleeding (defined as decline in Hgb level of ≥ 2)		11/105 (10.5%) Only three cases of bleeding were attributed, at least in part, to use of enoxaparin.		
Jones,[106] 2005	Clinical DVT/PE during index hospital stay		774 (4.8%)		
	Clinical DVT/PE within 91 d		883 (5.4%) 45% very likely; 76% DVT + 24% PE		
	Clinical DVT/PE within 1 y		977 (6.0%)		
	Men (5.9%) vs women (4.1%), OR = 1.4; paraplegia (11%) vs tetraplegia (7.8%), OR = 1.8; presence of metastatic cancer vs not, OR = 2.5. Approximately one-half of all cases occurring within 91 d were diagnosed at the index hospital; 88% of all VTE diagnoses were made within 3 mo of injury.				

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Jones,[106] 2005	VTE at 91 d	All patients	883/16240 (5%)[b]	N/A	N/A
		Age: 8-13 y 14-19 y 20-29 y > 80 y	NR	NR	Referent = age 30-49 y OR = 0.2 OR = 0.7 OR = 0.7 OR = 0.6 $P < .05$
		Black	NR	NR	Referent = white OR = 1.6 $P < .01$
		Male sex	NR	NR	OR = 1.4 $P < .01$
		Elixhauser comorbidity index score > 3	NR	NR	Referent = Elixhauser Comorbidity Index Score = 0 OR = 1.6 $P \leq .01$
		Complete paraplegia vs tetraplegia	NR	NR	OR = 1.8 $P < .01$
		Medi-Cal insurance status	NR	NR	Referent = health maintenance organization OR = 1.3 $P < .05$
		Hospital size: 250–350 beds < 125 beds	NR	NR	Referent = University hospitals OR = 0.7 OR = 0.7 $P < .05$
		No significant difference between VTE and no-VTE groups for race (Hispanic, other), age 50-79 y, spinal fracture, and hospitalization.			
	DVT	All patients with VTE	742/977 (76%)	N/A	N/A
	PE	All patients with VTE	234/977 (24%)	N/A	N/A
Kadyan,[290] 2003	Excluded. On closer examination, this study tried to estimate DVT rate on admission using surveillance ultrasound.				

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Waring,[291] 1991	Clinical DVT during index hospitalization		14.5%		
		Paraplegia	15.9%		
		Quadriplegia	12.5%		
	Clinical PE during index hospitalization		4.6%		
		Paraplegia	4.3%		
		Quadriplegia	4.8%		
			Major trauma		
Abelseth,[292] 1996	DVT	All patients	29/102 (28%)	N/A	N/A
	Proximal DVT	All patients	4/102 (4%)	N/A	N/A
	PE	All patients	1/102 (1%)	N/A	N/A
	DVT	Fractured tibial plateau	12/28 (43%)	N/A	N/A
		Fractured femoral shaft	8/20 (40%)	N/A	N/A
		Fractured tibial shaft	12/54 (22%)	N/A	N/A
Alejandro,[293] 2003	Failure of nonoperative treatment (surgery required because of bleeding)	Early vs late LMWH	2/50 (4%) 4/64 (6%) *P* = .59	RR = 1.5	N/A
	Blood transfusions	Early vs late LMWH	25/50 (50%) 36/64 (56%) *P* = .50	RR = 1.2	N/A
	Number of transfusions (average)	Early vs late LMWH	3.2 3.0 *P* = .78	N/A	N/A
Carlin,[294] 2002	Mortality	Prophylactic vs therapeutic filters	2/78 (3%) 13/122 (11%) *P* = .07	RR = 3.6	N/A
Cipolle,[295] 2002	DVT	All patients	253/10,141 (2.5%)	N/A	N/A
	PE	All patients	30/10,141 (0.3%)	N/A	N/A

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
	Proximal DVT	All patients	141/10,141 (1.3%)	N/A	N/A
	Symptomatic DVT	All patients	58/10,141 (0.5%)	N/A	N/A
	Only five of 21 duplex scans were positive for DVT in patients with PE. The rate of DVT in high-risk patients with duplex scan was 16.7%				
Cornwell,[296] 2002	Compliance with the proper use of prescribed SCD (six observations per patient	Patients room visits	42/227 (19%)	N/A	N/A
			712/1,343 (53%)		
	Eighty-three percent of those patients who were not fully compliant with SCD use had risk factors for DVT.				
Cyr,[297] 2006	VTE	All patients	11/3,291 (0.3%)	N/A	N/A
		Age: 15-18 y vs 0-5 y	NR	OR = 19.5	NR
		ISS ≥ 9	NR	OR = 5.3	NR
		Injury:	NR	OR = 23.4	OR = 37.4
		Spinal		OR = 13.8	OR = 6.9 (chest)
		Thoracic		OR = 7.7	NR
		Abdominal			
		Procedures:	NR	OR = 54.8	NR
		Spine		OR = 29.8	NR
		Laparotomy		OR = 4.8	OR = 64.0
		Central venous catheter			

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
	DVT	All patients	8/3,291 (0.2%)	N/A	N/A
	PE	All patients	3/3,291 (0.1%)	N/A	N/A
Denson,[110] 2007	DVT	Patients with TBI	22/88 (25%)	N/A	N/A
		High-risk patients	NR (18%)	N/A	N/A
		All patients	NR (2%)	N/A	N/A
		Femoral access placement	5/9 (55.6%) $P < .04$	N/A	N/A
		Injury: IPH Subdural Subarachnoid Epidural Skull fracture Other TBI	12/24 (50%), $P < .001$ 11/36 (30%) 7/34 (20%) 1/8 (12%) 6/26 (23%) 2/14 (14%)	OR = 5.40 OR = 1.64 OR = 0.67 OR = 0.40 OR = 0.86 OR = 0.45 (calculated)	NR
		Length of stay in the ICU in days ($P = .006$) and days on the ventilator ($P = .014$) were significantly different between patients with and without DVT. No correlation of incidence of VTE was noted in age, hospital length of stay, ISS, abbreviated injury scale of the head, or GCS on admission			
	PE	Patients with TBI	1/88 (1.1%)	N/A	N/A
Geerts WH,[100] 1994	DVT	All patients	201/349 (57.6%)	N/A	N/A

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
	Proximal DVT	All patients	63/349 (18.1%)	N/A	N/A
	Bilateral DVT	All patients	51/285 (18%)	N/A	N/A
	Symptomatic DVT	All patients	3/349 (0.85%)	N/A	N/A
	PE	All patients	7/349 (2%)	N/A	N/A
	Fatal PE	All patients	3/349 (0.85%)	N/A	N/A
	DVT	Face, chest, or abdomen trauma	65/129 (50%)	N/A	N/A
		Head	49/91 (54%)	N/A	N/A
		Spine	41/66 (62%)	N/A	N/A
		Lower extremity	126/182 (69%)	N/A	N/A
	Proximal DVT	Face, chest, or abdomen	19/129 (14.7%)	N/A	N/A
		Head	18/91 (20%)	N/A	N/A
		Spine	18/66 (27%)	N/A	N/A
		Lower extremity	43/182 (23%)	N/A	N/A
Haas CE,[132] 2005	Proportion of patients with plasma anti-Xa activity >0.1 International Units/mL 4 h after injection	Nonedematous vs edematous	11/11 (100%) 4/10 (40%) *P* = .004		
	Proportion of patients with plasma anti-Xa activity >0.1 International Units/mL 8 h after injection	Nonedematous vs edematous	4/11 (36%) 1/10 (10%) *P* = .31		
	Proportion of patients with plasma anti-Xa activity >0.1 International Units/mL 12 h after injection	Nonedematous vs edematous	2/11 (18%) 0/10 (0) *P* = .48		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
	A significant lower drug exposure, as measured by the plasma anti-Xa activity area under the curve (0-12 h) was observed in the edematous patients. The authors conclude that the standard dose of enoxaparin recommended for VTE prevention in critically ill trauma patients provides highly variable and unreliable anti-Xa activity.				
Iskander,[299] 2006	DVT, infrageniculate	All patients	109/698 (15.7%)	N/A	N/A
		Suprageniculate propagation vs nonsuprageniculate propagation: age ≤ 62 y	12/14 (86%) 12/25 (48%)	NS	OR = 17.9 *P* = .0012
		Suprageniculate propagation vs nonsuprageniculate propagation: ISS > 35	7/14 (50%) 2/25 (8%)	NR, *P* = .0006	OR = 8.6 *P* = .0320

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
		Statistical difference between DVT propagation and no propagation groups for ICU admissions (P = .007), surgery (P = .0188), IVC filter (P = .0233), mean ISS (P = .004), ISS > 15 (P = .0060), ISS > 20 (P = .0076), ISS > 25 (P = .0068), and ISS > 30 (P = .0185). No difference (univariate analysis) between DVT propagation and no propagation groups for transfusion, age ≤ 62 y, GCS ISS > 35, and ISS > 40.			
Hammers,[298] 1996	DVT	All patients	19/136 (14%)		
	PE	All patients	3/136 (2.2%)		
Haut,[316] 2007	DVT in all patients	Before guidelines vs after guidelines implementation	1/1,389 (0.07%) 39/5,561 (0.7%) P = .0024	RR = 10	N/A
	PE in all patients	Before guidelines vs after guidelines implementation	1/1,389 (0.07%) 18/5,561 (0.32%) P = .15	RR = 4.57	N/A
Knudson,[102] 2004	VTE	All patients	1,602/450,375 (0.36%)		
	DVT	All patients	998/1,602 (0.22%)		
	PE Mortality in PE patients:18%	All patients	522/1,602 (0.11%)		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
	DVT and PE	All patients	82/1,602 (0.018%)		
	Independent risk factors for VTE (OR): Age > 40 y (2.01), lower-extremity fractures (1.92), abbreviated injury scale of the head > 2 (1.29), > 3 d on ventilator (8.08), venous injury (3.53), and major operative procedure (1.53)				
Lu,[300] 2007	DVT	All patients	68/547 (12.4%)	N/A	N/A
		Sex: Male vs female	13.6% 8.3% *P* = .12	NR	NR
		Smoker vs nonsmoker	NR	NR	OR = 2.34 *P* = .024
		Type of fracture:		NR	NR
		Femoral shaft	21/68 (30.6%)		
		Hip	11/68 (15.8%)		
		Knee	10/68 (14.5%)		
		Foot	8/68 (11.5%)		
		Tibia/fibula	7/68 (10.8%)		
		Upper arms	7/68 (9.9%)		
		Malleolus	5/68 (7.5%)		
		2-3 fractures vs 1 fracture	43/68 (63%) 7/68 (11%) (estimated from figure)	NR	NR

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
		Mechanism of injury:		NR	NR
		Fall	31/68 (46%)		
		Motor vehicle accident	20/68 (29%)		
		Industrial	9/68 (13%)		
		Pedestrial	3/68 (4%)		
		Bicycle/motor bike accident	1/68 (2%)		
		Other	4/68 (6%) (estimated from figure)		
Macatangay,[301] 2008	Compliance with the use of SCD (number of evaluations with SCD functioning properly/number of evaluations	All patients before vs after education	443/597 (74%) 385/502 (77%) $P = .38$	RR = 1.04	N/A
		Admitted to ICU before vs after education	293/344 (85%) 290/355 (82%) $P = .26$	RR = 1.04	N/A
		Admitted to surgical ward before vs after education	150/253 (59%) 95/147 (65%) $P = .34$	RR = 1.1	N/A
Meissner,[302] 2003	DVT	All patients	28/101 (27.7%)		
	Proximal DVT	All patients	7/101 (7%)		
	PE	All patients	2/101 (2%)		
	All VTE	Patients with prophylaxis on day 1 vs patients not receiving prophylaxis on day 1	23/69 (33%) 6/28 (21%) $P = .25$	RR = 1.57	
	Independent predictive risk factors: obesity and immobilization >3 d				

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
Nathens,[113] 2007	DVT	All patients	20/315 (6.3%)		
	PE	All patients	18/315 (5.7%)		
	VTE	Early pharmacologic prophylaxis vs delayed (> 4th day of admission)	5% 15%	RR = 3.0	
	Pharmacologic prophylaxis initiated within 48 h of ICU admission in 25% of patients. Another 25% went without prophylaxis for at least 7 d. Only 12% of patients had IVC filters during their admission. Independent factors associated with a delay (> 4 d) of pharmacologic prophylaxis were severe head injury, blood transfusion (> 6 units), no comorbidity, and severe lower-extremity injury.				
Nathens,[113] 2007	Total VTE	All patients	34/315 (11%)	N/A	N/A
	DVT	All patients	16/315 (5%)	N/A	N/A
	PE	All patients	14/315 (4.4%)	N/A	N/A
	DVT and PE	All patients	4/315 1.2%)	N/A	N/A
	VTE	Early prophylaxis	9/174 (5%)	RR = 3.0 (1.4-6.59)	N/A
		Delayed prophylaxis	20/137 (15%)		
Piotrowski,[303] 1996	DVT	All patients	20/343 (5.8%)		

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
	Proximal DVT	All patients	15/343 (4.3%)		
	Symptomatic DVT	All patients	3/343 (0.9%)		
	PE	All patients	3/343 (0.9%)		
	Fatal PE	All patients	2/343 (0.6%)		
	Logistic regression analysis identified age, length of stay, and ICU days as independent risk factors				
Platzer,[104] 2006	Total VTE	All patients	22/978 (2.2%)	N/A	N/A
		Symptomatic DVT	17/978 (1.7%)	N/A	N/A
		Symptomatic PE	9/978 (0.9%)	N/A	N/A
Reiff,[112] 2009	DVT (TBI vs no TBI)	Prophylaxis (time to initiation: 0-24 h, 24-48 h, > 48 h) vs no prophylaxis	Among those who received prophylaxis, increase in absolute DVT risk was seen with increase time to prophylaxis initiation	NR	RR = 4.83 RR = 3.80 RR = 2.67 RR = 2.59

(Continued)

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Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
		Univariate analysis of potential factors associated with TBI across prophylaxis groups identified age, race, injury mechanism, higher ISS and lower extremity fracture. Race was significantly different among the > 48 h and no prophylaxis groups ($P < .0001$). Injury mechanisms were significantly different among all patients with TBI.			
Riou,[305] 2007	All DVT	All patients	177/2,761 (6.4%)	N/A	N/A
	Proximal DVT	All patients	5 /2,761 (0.2%)	N/A	N/A
	Symptomatic DVT	All patients	27/2,761 (1%)	N/A	N/A
	PE	All patients	1 /2,761 (0.04%)	N/A	N/A
	Variables associated with increased VTE risk: age, severity of the injury, type of immobilization, and recommendation for walking.				
Riou,[305] 2007	DVT	All patients	177/2,749 (6.4%)	N/A	N/A
		Age > 50 y: VTE vs Non-VTE	101/177 (57%) 636/2,582 (25%) $P < .001$	OR = 4.1 (calculated)	OR = 3.14 $P < .0001$
		No weight bearing	120/177 (68%) 1,092/2,580 (42%) $P < .001$	OR = 2.9 (calculated)	OR = 4.11 $P = .0015$

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
		Severe injury	88/177 (50%) 517/2,584 (20%) $P < .001$	OR = 3.9 (calculated)	OR = 1.88 $P = .0002$
		Rigid immobilization	153/177 (86%) 1,336/2,580 (52%) $P < .001$	OR = 5.9 (calculated)	OR = 2.70 $P < .0001$
		Logistic model identified no significant colinearity between VTE and no-VTE groups for sex, BMI, personal or family history of VTE, diseases increasing risk of VTE, hormonal treatment, venous insufficiency, use of tobacco, recommendation for walking, and duration of immobilization.			
	Proximal DVT	All patients	5/2,749 (0.2%)	N/A	N/A
	Symptomatic DVT	All patients	27/2,749 (1.0%)	N/A	N/A
	PE	All patients	1/2,749 (0.04%)	N/A	N/A
Schuerer,[306] 2005	DVT	Before guidelines vs after guidelines implementation	24/1,347 (1.8%) 10/1,184 (0.84%) $P = .041$	RR = 0.46	N/A
	PE	Before guidelines vs after guidelines implementation	8/1,347 (0.6)	RR = 0.50	NA
			3/1,184 (0.3%)		
			$P = .19$		
	VTE in all patients	Before guidelines vs after guidelines implementation	26/1,347 (1.9%) 12/1,184 (1%) $P = .059$	RR = 0.52	N/A

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
	VTE in ICU patients	Before guidelines vs after guidelines implementation	21/419 (5%) 9/396 (2.3%) $P = .038$	RR = 0.46	N/A
Schwarcz,[307] 2001	DVT	Initial duplex scan	8/241 (3.2%)		
	DVT	Patients with initial negative scan	5/233 (3.34%)		
	DVT	Hospital admission	13/241 (5.4%)		
	DVT	After hospital discharge	6/228 (2.6%)		
	PE	During hospital admission	2/241 (0.8%)		
	PE	After hospital discharge	3/239 (0.8%)		
	Total VTE	Hospital admission and after discharge	19/241 (7.9%)		
	Bleeding	All patients	2/241 (0.8%)		
	HIT	All patients	1/241 (0.4%)		
Sems,[308] 2009	DVT	All patients	3/143 (2.1%)	N/A	N/A
Steele,[309] 2005	Proximal DVT	All patients	10/100 (10%)	N/A	N/A
	PE	All patients	5/100 (5%)	N/A	N/A
	Proximal DVT	Early LMWH (within 24 h) vs late LMWH (>24 h)	2/64 (3.1%) 8/36 (22%) $P < .01$	RR = 7.09	N/A
	PE (symptomatic) (one fatal)	Early LMWH (within 24 h) vs late LMWH (>24 h)	0/64 (0) 5/36 (14%) $P = .01$	N/A	N/A
Worley,[310] 2008	DVT	UFH vs dalteparin	1/47 (2.1%) 3/43 (7%) $P = .3$	RR = 3.3	
	Proximal DVT	UFH vs dalteparin	1/47 (2.1%) 2/43 (4.6%) $P = 1$	RR = 2.2	
	PE (no fatal cases)	UFH vs dalteparin	2/47 (4.2%) 2/43 (4.6%) $P = 1$	RR = 1.09	

(Continued)

Table S8—*Continued*

First Author, Year	Outcomes	Predictors	Unadjusted Risks (Absolute)	Unadjusted Risk (Relative) or OR	Adjusted Risk (Relative) or OR
	Major bleeding	UFH vs dalteparin	0/47 1/43 (2.3%) $P = 1$	NA	No HIT detected
	Death	UFH vs dalteparin	7/47 (14.8%) 2/43 (4.6%)	RR = 0.31	
			Same day surgery		
Enoch,[223] 2003 (varicose vein surgery)	DVT	Prophylaxis	3/1,283		
		No prophylaxis	0/903		
	PE	Prophylaxis	1/1,283		
		No prophylaxis	0/903		
Enoch,[223] 2003 (hernia repair)	DVT	Prophylaxis	1/1,854		
		No prophylaxis	1/630		
	PE	Prophylaxis	0/1,854		
		No prophylaxis	0/630		
Riber,[311] 1996	DVT	All patients	0/2,281		
	PE	All patients	1/2,281		
			Plastic and reconstructive surgery		
Shermak,[312] 2007	VTE	All patients	4/138 (3%)	N/A	N/A
		BMI ≥ 35 vs BMI < 35 kg/m²	4/45 (8.9%) 0/93 (0%) $P = .01$	N/A	N/A
		No relationship found among type of procedure, number of procedures, or blood transfusion			
	DVT	All patients	3/138 (2.2%)	N/A	N/A
	PE (fatal)	All patients	1/138 (0.7%)	N/A	N/A

ACA = anticardiolipin antibody; CHF = congestive heart failure; DRVTT = dilute Russell viper venom time; EBL = estimated blood loss; FFP = fresh frozen plasma; Hgb = hemoglobin; LGB = laparoscopic gastric bypass; NSD = no significant difference; OBCAB = off-pump coronary artery bypass; OBG = open gastric bypass; OC = oral contraceptive; OHS = obesity hypoventilation syndrome; RR = risk ratio; RVU = relative value unit; SAH = subarachnoid hemorrhage; SHS = supine hypotension syndrome; TAH = total abdominal hysterectomy. See Table S2, S3, and S6 legends for expansion of other abbreviations.

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Table S9—*Observed Risk of VTE in Studies of Bariatric Surgery*

First Author, Year (Procedure)	No.	Prospective	Screen	Prophylaxis	Outcome	Estimate
Mason,[317] 1997	14,641	N	NS	NS	Symptomatic VTE	0.3%
Scholten,[14] 2002	481	N	N	GCS, IPC, LMWH	Symptomatic VTE	7 (1.4%)
Sapala,[265] 2003	5,554	N	N	Varied by patient	Fatal PE	12 (0.2%)
Shepherd,[5] 2003 (LRYGBP)	700	Y	N	GCS, IPC, UFH	Symptomatic VTE	3 (0.4%)
White,[80] 2003	4,075	N	N	NS	Symptomatic VTE	42 (1.0%)
Fernandez,[251] 2004 (ORYGBP)	1,431	N	N	NS	PE	17 (1.2%)
Fernandez,[251] 2004 (LRYGBP)	580					6 (1%)
Miller,[6] 2004 (LRYGBP)	250	N	N	IPC, UFH		3 (1.2%)
Smith,[266] 2004 (ORYGBP)	451	N	N	NS	Symptomatic VTE	7 (1.6%)
Smith,[266] 2004 (LRYGBP)	328					1 (0.3%)
Cotter,[7] 2005 (RYGBP)	107	N	N	IPC, UFH	Symptomatic DVT	1 (0.9%)
Hamad,[256] 2005 (RYGBP)	668	N	N	LMWH	Symptomatic VTE	7 (1%)
McCarthy,[318] 2005 (LRYGBP)	2,000	Y	N	NS	PE	3 (0.2%)
Quebbemann,[9] 2005	822	Y	N	IPC, UFH	PE	1 (0.1%)
Poulose,[314] 2005	69,072	N	N	NS	Symptomatic VTE	0.3%
Prystowsky,[8] 2005 (RYGBP)	106	Y	Y	IPC, UFH ± IVCF	DVT (DUS)	1 (1%)
Carmody,[10] 2006	3,861	Y	N	Varied over time	PE	33 (0.9%)
Frezza,[253] 2006 (lap band, LRYGBP)	150	N	N	Heparin, IPC ± IVCF	Symptomatic VTE	0
Gonzalez,[255] 2006 (RYGBP)	660	Y	N	Heparin, IPC ± IVCF	Symptomatic VTE	23 (3.5%)
Hefline,[257] 2006 (LRYGBP)	455	N	N	ASA, IPC, UFH, warfarin ± IVCF	Symptomatic VTE	6 (1.3%)
Kothari,[20] 2007 (LRYGBP)	476	Y	N	IPC plus LMWH or UFH	Symptomatic VTE	1 (0.2%)
Borkgren-Okonek,[246] 2008	233	Y	N	LMWH		1 (0.5%)
Brasileiro,[247] 2008 (RYGBP)	136	Y	Y	LMWH	All DVT	1 (0.8%)
Escalente-Tattersfield,[12] 2008 (LRYGBP)	618	Y	Y	IPC, heparin ± IVCF	Symptomatic VTE	0
Magee,[261] 2008 (Lap)	735	Y	NS	LMWH ± IVCF	Symptomatic VTE	0
Raftopoulos,[21] 2008	308	Y	Y	IPC, LMWH	Symptomatic VTE	6 (1.9%)
Caruana,[249] 2009 (RYGBP)	1,652	Y	N	IPC, UFH ± IVCF, EP	PE	6 (0.4%)
Clements,[250] 2009 (LRYGBP)	957	Y	N	IPC	Symptomatic VTE	4 (0.4%)
Kligman,[259] 2009 (LRYGBP)	423	N	N	IPC, LMWH	Symptomatic VTE	0
Flum,[252] 2009 (ORYGBP)	437	Y	NS	NS	VTE	1.1%
Flum,[252] 2009 (LRYGBP)	2,975					0.4%
Flum,[252] 2009 (band)	1,198					0.3%
Stroh,[267] 2009					PE	0.1%
Inabnet,[258] 2010 (revision)	203	Y	NS	NS	Symptomatic VTE	1.8%
Inabnet,[258] 2010 (primary)	3,577					0.5%

EP = external pneumonic; IVCF = inferior vena cava filter. See Table S2 and S3 legends for expansion of other abbreviations.

Table S10—*[Section 6.3] Evidence Profile: Should IPC vs No Prophylaxis Be Used for VTE Prevention in Craniotomy Patients?*

Quality Assessment							Summary of Findings					
							No. of Patients		Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	IPC	No Prophylaxis	Relative (95% CI)	Absolute	Quality	Importance
Symptomatic VTE inferred from all DVT												
2	Randomized trials	Serious[a]	No serious inconsistency	Serious[b]	No serious imprecision	None	N/A	5.1%[c]	RR 0.41 (0.21-0.78)[d]	30 fewer per 1,000 (from 11 fewer to 40 fewer)	Low	Critical
								10%[c]		59 fewer per 1,000 (from 22 fewer to 79 fewer)		
Skin complications												
0	No evidence available					None	N/A	N/A	Not estimable	N/A		Important

Authors: David Garcia and Michael Gould. Date: December 16, 2010. Setting: hospital. Bibliography: Collen JF, Jackson JL, Shorr AF, Moores LK. Prevention of venous thromboembolism in neurosurgery: a metaanalysis. *Chest*. 2008;134(2):237-249. Danish SF, Burnett MG, Ong JG, Sonnad SS, Maloney-Wilensky E, Stein SC. Prophylaxis for deep venous thrombosis in craniotomy patients: a decision analysis. *Neurosurgery.* 2005;56(6):1286-1292, discussion 1292-1294. Chan AT, Atiemo A, Diran LK, et al. Venous thromboembolism occurs frequently in patients undergoing brain tumor surgery despite prophylaxis. *J Thromb Thrombolysis*. 1999;8(2):139-142. See Table S2, S3, and S8 legends for expansion of abbreviations.

[a] Lack of blinding; inclusion/exclusion not described; analysis includes studies that used asymptomatic distal DVT as an end point.

[b] Relative risk estimate based on surrogate outcome of uncertain relationship to symptomatic VTE.

[c] Medium risk estimate derived from pooled risk of symptomatic VTE from 13 studies of 2,949 mixed neurosurgical patients compiled by Danish et al (2005), adjusted to account for all receiving no prophylaxis rather than for mechanical prophylaxis with IPC. High-risk estimate derived from observational study of 2,366 neurosurgical patients by Chan (1995), among whom 84% underwent surgery and 67% had cancer. Estimate adjusted for prophylaxis received, including pharmacologic alone (15%), mechanical alone (4%), or both (53%). Of note, both the unadjusted and the adjusted risks of symptomatic VTE were similar in a recent retrospective study of 1,195 patients with spontaneous or traumatic intracranial hemorrhage (Chan, 2009).

[d] Relative risk of any DVT from meta-analysis by Collen, based on data from two studies of VTE prophylaxis in neurosurgery. Relative risk of PE was similar but imprecise (0.37; 95% CI, 0.03-4.06).

Table S11—*[Section 6.3] Evidence Profile: Should IPC vs GCS Be Used for VTE Prevention in Craniotomy Patients?*

Quality Assessment							Summary of Findings					
							No. of Patients		Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	IPC	GCS	Relative (95% CI)	Absolute	Quality	Importance
Symptomatic VTE inferred from all DVT												
3	Randomized trials	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	N/A	2.6%[c]	RR 0.81 (0.32-1.78)	5 fewer per 1,000 (from 18 fewer to 20 more)	Low	Critical
								5.1%[c]		10 fewer per 1,000 (from 35 fewer to 40 more)		
Skin breaks, ulcers, blisters, necrosis												
1	Randomized trials	Serious	No serious inconsistency	Serious	No serious imprecision	None	16/1,262 (1.3%)	64/1,256 (5.1%)	RR 0.25 (0.14-0.43)	38 fewer per 1,000 (from 29 fewer to 44 fewer)	Low	Important

Authors: David Garcia and Michael Gould. Date: December 16, 2010. Setting: hospital. Bibliography: Collen JF, Jackson JL, Shorr AF, Moores LK. Prevention of venous thromboembolism in neurosurgery: a metaanalysis. *Chest*. 2008;134(2):237-249. Danish SF, Burnett MG, Ong JG, Sonnad SS, Maloney-Wilensky E, Stein SC. Prophylaxis for deep venous thrombosis in craniotomy patients: a decision analysis. *Neurosurgery*. 2005;56(6):1286-1292, discussion 1292-1294. Chan AT, Atiemo A, Diran LK, et al. Venous thromboembolism occurs frequently in patients undergoing brain tumor surgery despite prophylaxis. *J Thromb Thrombolysis*. 1999;8(2):139-142. CLOTS Trials Collaboration; Dennis M, Sandercock PA, Reid J, et al. Effectiveness of thigh-length graduated compression stockings to reduce the risk of deep vein thrombosis after stroke (CLOTS trial 1): a multicentre, randomised controlled trial. *Lancet*. 2009;373(9679):1958-1965. See Table S2, S3, and S8 legends for expansion of abbreviations.

[a] Unblinded studies with incomplete follow-up and measurement of surrogate outcomes.

[b] CI includes possibility of both substantial benefit and no effect.

[c] Medium-risk estimate derived from pooled risk of symptomatic VTE from 13 studies of 2,949 mixed neurosurgical patients compiled by Danish et al (2005), adjusted to account for all receiving mechanical prophylaxis with GCS rather than IPC. High-risk estimate derived from observational study of 2,366 neurosurgical patients by Chan (1995), among whom 84% underwent surgery and 67% had cancer. Estimate adjusted to account for all receiving prophylaxis with GCS rather than actual prophylaxis received, including pharmacologic alone (15%), mechanical alone (4%), or both (53%).

Table S12—*[Section 6.3] Evidence Profile: Should LMWH vs No Prophylaxis Be Used for VTE Prevention in Craniotomy Patients?*

Quality Assessment							Summary of Findings: No. of Patients		Summary of Findings: Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	LMWH	No Prophylaxis	Relative (95% CI)	Absolute	Quality	Importance
Death from any cause (follow-up 30-56 d)												
3	Randomized trials	No serious limitations	No serious inconsistency	No serious indirectness	Serious[a]	None	27/461 (5.9%)	16/461 (3.5%)	OR 1.74 (0.94-3.22)	24 more per 1,000 (from 2 fewer to 69 more)	Moderate	Critical
Symptomatic VTE, inferred from proximal DVT (follow-up 30-56 d; surveillance venography or CUS confirmed by venography)												
2	Randomized trials	Serious[b]	No serious inconsistency	No serious indirectness	No serious imprecision	None	19/304 (6.3%)	5.1%[c]	OR 0.48 (0.28-0.83)	26 fewer per 1,000 (from 8 fewer to 36 fewer)	Moderate	Critical
								10%[c]		49 fewer per 1,000 (from 16 fewer to 70 fewer)		
ICH (follow-up 30-56 d)												
3	Randomized trials	No serious limitations	No serious inconsistency	Serious[d]	No serious imprecision	None	12/511 (2.3%)	7/511 (1.4%)	OR 2.03 (1.37-3.01)[f]	14 more per 1,000 (from 5 more to 26 more)	Moderate	Critical
								1.11%[e]		11 more per 1,000 (from 4 more to 22 more)		

Author: Michael Gould. Date: January 4, 2011. Setting: hospital. Bibliography: Iorio A, Agnelli G. Low-molecular-weight and unfractionated heparin for prevention of venous thromboembolism in neurosurgery: a meta-analysis. *Arch Intern Med*. 2000;160(15):2327-2332. Mismetti P, Laporte S, Darmon JY, Buchmüller A, Decousus H. Meta-analysis of low molecular weight heparin in the prevention of venous thromboembolism in general surgery. *Br J Surg*. 2001;88(7):913-930. Danish SF, Burnett MG, Ong JG, Sonnad SS, Maloney-Wilensky E, Stein SC. Prophylaxis for deep venous thrombosis in craniotomy patients: a decision analysis. *Neurosurgery*. 2005;56(6):1286-1292, discussion 1292-1294. Chan AT, Atiemo A, Diran LK, et al. Venous thromboembolism occurs frequently in patients undergoing brain tumor surgery despite prophylaxis. *J Thromb Thrombolysis*. 1999;8(2):139-142. See Table S1 and S2 legends for expansion of abbreviations.

[a] The 95% CI includes the possibility of both no effect and serious harm.

[b] Surrogate outcome.

[c] Medium-risk estimate derived from pooled risk of symptomatic VTE from 13 studies of 2,949 mixed neurosurgical patients compiled by Danish et al (2005), adjusted to account for all receiving no prophylaxis rather than mechanical prophylaxis with IPC. High-risk estimate derived from observational study of 2,366 neurosurgical patients by Chan (1995), among whom 84% underwent surgery and 67% had cancer. Estimate adjusted for prophylaxis received, including pharmacologic alone (15%), mechanical alone (4%), or both (53%). Of note, both the unadjusted and the adjusted risks of symptomatic VTE were similar in a recent retrospective study of 1,195 patients with spontaneous or traumatic intracranial hemorrhage (Chan, 2009).

[d] Relative risk estimate based on indirect evidence from studies of general and abdominal surgery.

[e] Pooled risk of ICH from 20 studies of almost 32,000 craniotomy patients who received IPC prophylaxis compiled by Danish et al (2005).

[f] Direct, but imprecise, evidence comes from two studies in neurosurgical patients, in which the OR for nonfatal major bleeding was 1.68 (95% CI, 0.62-4.52). Almost 90% of nonfatal major bleeding complications were ICH.

Table S13—*[Section 6.3] Evidence Profile: Should UFH vs No Prophylaxis Be Used for VTE Prevention in Craniotomy Patients?*

Quality Assessment							Summary of Findings					
							No. of Patients		Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	UFH	No Prophylaxis	Relative (95% CI)	Absolute	Quality	Importance
Nonfatal symptomatic VTE inferred from nonfatal PE												
22	Randomized trials	Serious[a]	No serious inconsistency	Serious[b]	No serious imprecision	None	0/0 (0%)	5.1%[c]	RR 0.44 (0.31-0.63)[d]	29 fewer per 1,000 (from 19 fewer to 35 fewer)	Low	Critical
								10%[c]		56 fewer per 1,000 (from 37 fewer to 69 fewer)		
Nonfatal ICH inferred from excessive intraoperative bleeding or requirement for transfusion												
44	Randomized trials	Serious[a,e]	No serious inconsistency	Serious[b]	No serious imprecision	None	0/0 (0%)	1.11%[f]	RR 1.57 (1.32-1.87)[g]	6 more per 1,000 (from 4 more to 10 more)	Low	Critical

Authors: David Garcia and Michael Gould. Date: December 16, 2010. Setting: hospital. Bibliography: Collins R, Scrimgeour A, Yusuf S, Peto R. Reduction in fatal pulmonary embolism and venous thrombosis by perioperative administration of subcutaneous heparin. Overview of results of randomized trials in general, orthopedic, and urologic surgery. *N Engl J Med*. 1988;318(18):1162-1173. International Multicentre Trial. Prevention of fatal postoperative pulmonary embolism by low doses of heparin. An international multicentre trial. *Lancet*. 1975;2(7924):45-51. Collen JF, Jackson JL, Shorr AF, Moores LK. Prevention of venous thromboembolism in neurosurgery: a metaanalysis. *Chest*. 2008;134(2):237-249. Danish SF, Burnett MG, Ong JG, Sonnad SS, Maloney-Wilensky E, Stein SC. Prophylaxis for deep venous thrombosis in craniotomy patients: a decision analysis. *Neurosurgery*. 2005;56(6):1286-1292, discussion 1292-1294. Chan AT, Atiemo A, Diran LK, et al. Venous thromboembolism occurs frequently in patients undergoing brain tumor surgery despite prophylaxis. *J Thromb Thrombolysis*. 1999;8(2):139-142. See Table S2, S3, and S8 legends for expansion of abbreviations.

[a] Many studies not blinded, and allocation concealment not adequately described.

[b] Relative risk estimate comes from studies in general, urological, and orthopedic surgery.

[c] Medium-risk estimate derived from pooled risk of symptomatic VTE from 13 studies of 2,949 mixed neurosurgical patients compiled by Danish et al (2005), adjusted to account for all receiving no prophylaxis rather than mechanical prophylaxis with IPC. High-risk estimate derived from observational study of 2,366 neurosurgical patients by Chan (1995), among whom 84% underwent surgery and 67% had cancer. Estimate adjusted for prophylaxis received, including pharmacologic alone (15%), mechanical alone (4%,) or both (53%)..

[d] Direct, but imprecise, evidence comes from three studies in neurosurgery in which the OR for any DVT was 0.50 (95% CI, 0.11-2.38).

[e] Surrogate outcome (excessive intraoperative bleeding or requirement for transfusion).

[f] Pooled risk of ICH from 20 studies of almost 32,000 craniotomy patients who received IPC prophylaxis compiled by Danish et al (2005).

[g] Direct, but imprecise, evidence comes from three studies in neurosurgery in which the OR for ICH was 2.11 (95% CI, 0.39-11.31).

Table S14—*[Section 6.3] Evidence Profile: Should LMWH vs IPC Be Used for VTE Prevention in Craniotomy Patients?*

Quality Assessment							Summary of Findings: No. of Patients		Summary of Findings: Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	LMWH	IPC	Relative (95% CI)	Absolute	Quality	Importance
Nonfatal symptomatic VTE inferred from all DVT												
8	Randomized trials	Serious[a]	No serious inconsistency	Serious[b]	No serious imprecision	None	0/0 (0%)	2.1%[c]	RR 0.56 (0.36-0.86)[d]	9 fewer per 1,000 (from 3 fewer to 13 fewer)	Low	Critical
								4.1%[c]		26 fewer per 1,000 (from 6 fewer to 26 fewer)		
Nonfatal ICH inferred from nonfatal major bleeding												
4	Randomized trials	Serious[e]	No serious inconsistency	Serious[f]	No serious imprecision	None	0/0 (0%)	1.11%[g]	RR 2.03 (1.37-3.01)[h]	11 more per 1,000 (from 4 more to 22 more)	Low	Critical

Authors: David Garcia and Michael Gould. Date: December 16, 2010. Setting: hospital. Bibliography: Eppsteiner RW, Shin JJ, Johnson J, van Dam RM. Mechanical compression versus subcutaneous heparin therapy in postoperative and posttrauma patients: a systematic review and meta-analysis. *World J Surg*. 2010;34(1):10-19. Collen JF, Jackson JL, Shorr AF, Moores LK. Prevention of venous thromboembolism in neurosurgery: a metaanalysis. *Chest*. 2008;134(2):237-249. Danish SF, Burnett MG, Ong JG, Sonnad SS, Maloney-Wilensky E, Stein SC. Prophylaxis for deep venous thrombosis in craniotomy patients: a decision analysis. *Neurosurgery.* 2005;56(6):1286-1292, discussion 1292-1294. Chan AT, Atiemo A, Diran LK, et al. Venous thromboembolism occurs frequently in patients undergoing brain tumor surgery despite prophylaxis. *J Thromb Thrombolysis*. 1999;8(2):139-142. See Table S2, S3, and S8 legends for expansion of abbreviations.

[a] Unblinded assessment of DVT in most studies; measurement of surrogate outcome (asymptomatic DVT) of uncertain relationship to patient-important outcome (symptomatic VTE).

[b] Relative risk estimate taken from eight studies of general and urological surgery, orthopedic surgery, trauma surgery, and gynecologic surgery.

[c] Medium-risk estimate derived from pooled risk of symptomatic VTE from 13 studies of 2,949 mixed neurosurgical patients compiled by Danish et al (2005). High-risk estimate derived from observational study of 2,366 neurosurgical patients by Chan (1995), among whom 84% underwent surgery and 67% had cancer. Estimate adjusted to account for assumption that all received IPC prophylaxis rather than actual prophylaxis received, including pharmacologic alone (15%), mechanical alone (4%), or both (53%).

[d] Direct, but imprecise, evidence comes from two studies in neurosurgical patients in which the OR for any DVT was 0.79 (95% CI, 0.30-2.12).

[e] Small studies with heterogeneous designs and patient populations.

[f] Relative risk estimate taken from seven studies of general and abdominal surgery.

[g] Pooled risk of ICH from 20 studies of almost 32,000 craniotomy patients who received IPC prophylaxis compiled by Danish et al (2005).

[h] Direct, but imprecise, evidence comes from four studies of LMWH vs nonpharmacologic management in neurosurgery in which the pooled relative risk for ICH was 1.97 (95% CI, 0.64-6.09).

Table S15—*[Section 6.3] Evidence Profile: Should Pharmacologic Prophylaxis Plus IPC vs IPC Alone Be Used for VTE Prevention in Craniotomy Patients?*

Quality Assessment							Summary of Findings					
							No. of Patients		Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	Pharmacologic Prophylaxis Plus IPC	IPC Alone	Relative (95% CI)	Absolute	Quality	Importance
Symptomatic VTE inferred from DVT (follow-up until hospital discharge or 30 d after discharge; objectively confirmed events)												
3	Randomized trials	Serious[a]	No serious inconsistency	Serious[b]	Serious[c]	None	23/2,060 (1.1%)	2.1%	RR 0.43 (0.17-1.08)[d]	12 fewer per 1,000 (from 17 fewer to 2 more)	Very Low	Critical
								4.1%		23 fewer per 1,000 (from 34 fewer to 3 more)		
Major bleeding (follow-up 7-270 d; clinical diagnosis)												
7	Randomized trials	No serious limitations	No serious inconsistency	Serious[e]	No serious imprecision	None	75/2,710 (2.8%)	37/2,747 (1.3%)	RR 2.03 (1.37-3.01)	14 more per 1,000 (from 5 more to 27 more)	Moderate	Critical
								1.11%		11 more per 1,000 (from 4 more to 22 more)		

Author: Michael Gould. Date: April 12, 2011. Setting: hospital. Bibliography: Kakkos SK, Caprini JA, Geroulakos G, Nicolaides AN, Stansby GP, Reddy DJ. Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients (Review) *Cochrane Library*. 2008;(4). Danish SF, Burnett MG, Ong JG, Sonnad SS, Maloney-Wilensky E, Stein SC. Prophylaxis for deep venous thrombosis in craniotomy patients: a decision analysis. *Neurosurgery.* 2005;56(6):1286-1292, discussion 1292-1294. Chan AT, Atiemo A, Diran LK, et al. Venous thromboembolism occurs frequently in patients undergoing brain tumor surgery despite prophylaxis. *J Thromb Thrombolysis*. 1999;8(2):139-142. Mismetti P, Laporte S, Darmon JY, Buchmüller A, Decousus H. Meta-analysis of low molecular weight heparin in the prevention of venous thromboembolism in general surgery. *Br J Surg*. 2001;88(7):913-930.See Table S1, S2, and S8 legends for expansion of abbreviations.

[a] One study was not blinded; the other study had large numbers of randomized patients excluded from assessment of primary outcome.

[b] Data for relative risk estimate taken from two studies in abdominal and elective orthopedic surgery; surrogate outcome. Pharmacologic prophylaxis included fondaparinux and warfarin in each study. Background mechanical prophylaxis included IPC without or without ES.

[c] The 95% CI includes the possibility of substantial benefit and essentially no effect.

[d] Relative risk recalculated by using a fixed-effects model after excluding the study by Ramos et al [Ramos R, Salem BI, De Pawlikowski MP, Coordes C, Eisenberg S, Leidenfrost R. The efficacy of pneumatic compression stockings in the prevention of pulmonary embolism after cardiac surgery. *Chest*. 1996;109(1):82-85], which examined IPC plus LDUH vs LDUH alone and is therefore not relevant to this comparison.

[e] Data for relative risk estimate taken from seven studies of LMWH vs no prophylaxis in general and abdominal surgery.

Table S16—*[Section 7.3] Evidence Profile: Should LDUH vs No Prophylaxis Be Used in VTE Prevention in Spinal Surgery?*

Quality Assessment							Summary of Findings					
							No. of Patients		Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	LDUH	No Prophylaxis	Relative (95% CI)	Absolute	Quality	Importance
Symptomatic VTE inferred from PE												
22	Randomized trials	Serious[a]	No serious inconsistency	Serious[b]	No serious imprecision	None	0/0 (0%)	0.9%[c]	RR 0.44 (0.31-0.63)	5 fewer per 1,000 (from 3 fewer to 6 fewer)	Low	Critical
								2.0%[c]		11 fewer per 1,000 (from 7 fewer to 14 fewer)		
								4.9%[c]		27 fewer per 1,000 (from 18 fewer to 34 fewer)		
Major bleeding (hemorrhage associated with a mass effect on postoperative spinal MRI or neurologic deterioration as well as a large-wound hematoma with intractable pain)												
36	Randomized trials	Serious[a]	No serious inconsistency	Serious[d]	No serious imprecision	None	0/0 (0%)	0.46%[e]	OR 1.57 (1.32-1.87)	3 more per 1,000 (from 1 more to 4 more)	Low	Critical

Authors: David Garcia and Michael Gould. Date: January 4, 2011. Setting: hospital. Bibliography: Collins R, Scrimgeour A, Yusuf S, Peto R. Reduction in fatal pulmonary embolism and venous thrombosis by perioperative administration of subcutaneous heparin. Overview of results of randomized trials in general, orthopedic, and urologic surgery. *N Engl J Med*. 1988;318(18):1162-1173. International Multicentre Trial. Prevention of fatal postoperative pulmonary embolism by low doses of heparin. An international multicentre trial. *Lancet*. 1975;2(7924):45-51. White RH, Zhou H, Romano PS. Incidence of symptomatic venous thromboembolism after different elective or urgent surgical procedures. *Thromb Haemost*. 2003;90(3):446-455. Cheng JS, Arnold PM, Anderson PA, Fischer D, Dettori JR. Anticoagulation risk in spine surgery. *Spine (Phila Pa 1976)*. 2010;35(9 Suppl):S117-S124. Sansone JM, del Rio AM, Anderson PA. The prevalence of and specific risk factors for venous thromboembolic disease following elective spine surgery. *J Bone Joint Surg Am*. 2010;92(2):304-313. Gerlach R, Scheuer T, Beck J, Woszczyk A, Seifert V, Raabe A. Risk of postoperative hemorrhage after intracranial surgery after early nadroparin administration: results of a prospective study. *Neurosurgery*. 2003;53(5):1028-1034. See Tables S2 and S8 legends for expansion of abbreviations.

[a] Many studies not blinded, with unclear concealment of allocation sequence.

[b] Estimate of relative risk derived from studies of general and abdominal surgery.

[c] Low-risk estimate derived from study of > 34,000 discharges following spinal surgery for nonmalignant disease in California from 1992 to 1996 (White, 2003). Observed risk of symptomatic VTE within 91 d was 0.5% (95% CI, 0.4%-0.5%). Assuming that 50% received mechanical prophylaxis, the adjusted risk of VTE in the absence of prophylaxis is 0.8%. High-risk estimate derived from data from the same study for 1,545 discharges following spinal surgery for malignant disease in California from 1992 to 1996 (White, 2003). Observed risk of symptomatic VTE within 91 d was 2.0% (95% CI, 1.4%-2.6%). Assuming that 100% received mechanical prophylaxis, the adjusted risk of VTE in the absence of prophylaxis is 4.5%. Moderate-risk estimate applies to patients with VTE risk factors undergoing nonhigh-risk procedure (Bahl V, Hu H, Henke PK, et al. A validation study of a retrospective venous thromboembolism risk scoring method . *Ann Surg*. 2010;251(2):344-350).

[d] Relative risk of major bleeding with UFH in spinal surgery patients not known; in the one small study by Gruber et al. *Eur Arch Psychiatr Neurol Sci*. 1984;234:157-161, the risk of deep wound hematoma was 0/25 among patients who received UFH and 2/25 among patients who received placebo; numbers with increased intraoperative bleeding and increased postoperative drainage were similar in the two groups; therefore, the estimate of relative risk is taken from studies of abdominal and pelvic surgery.

[e] Based on a retrospective study of 1,954 spinal procedures at different levels from 1999 to 2002 (Gerlach R, Raabe A, Beck J, Woszczyk A, Seifert V. Postoperative nadroparin administration for prophylaxis of thromboembolic events is not associated with an increased risk of hemorrhage after spinal surgery. *Eur Spine J*. 2004;13:9-13). All treated with nadroparin 2,850 anti-Xa units daily (within 24 h) plus ES (elastic stockings); ASA held for 7. Major postoperative hemorrhage defined as a hemorrhage associated with a mass effect on postoperative spinal MRI and neurologic deterioration as well as a large-wound hematoma with intractable pain. Major hemorrhage occurred in 13 of 1,954 (0.7%) patients, including five in whom bleeding occurred prior to nadroparin administration; after adjustment, baseline risk of major bleeding is calculated to be 0.46%.

Table S17—*[Section 7.3] Evidence Profile: Should LMWH vs No Prophylaxis Be Used for VTE Prevention in Spinal Surgery?*

Quality Assessment							Summary of Findings					
							No. of Patients		Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	LMWH	No Prophylaxis	Relative (95% CI)	Absolute	Quality	Importance
Symptomatic VTE (follow-up 30-56 d)												
3	Randomized trials	No serious limitations	No serious inconsistency	Serious[a]	No serious imprecision	None	0/0 (0%)	0.9%[b]	OR 0.31 (0.12-0.81)	6 fewer per 1,000 (from 2 fewer to 8 fewer)	Moderate	Critical
								2.0%[b]		14 fewer per 1,000 (from 4 fewer to 18 fewer)		
								4.9%[b]		33 fewer per 1000 (from 9 fewer to 43 fewer)		
Major bleeding												
7	Randomized trials	No serious limitations	No serious inconsistency	Serious[c]	No serious imprecision	None	0/0 (0%)	0.46%[d]	OR 2.03 (1.37-3.01)	5 more per 1,000 (from 2 more to 9 more)	Moderate	Critical

Author: Michael Gould. Date: January 4, 2011. Setting: hospital. Bibliography: Mismetti P, Laporte S, Darmon JY, Buchmüller A, Decousus H. Meta-analysis of low molecular weight heparin in the prevention of venous thromboembolism in general surgery. *Br J Surg*. 2001;88(7):913-930. White RH, Zhou H, Romano PS. Incidence of symptomatic venous thromboembolism after different elective or urgent surgical procedures. *Thromb Haemost*. 2003;90(3):446-455. Cheng JS, Arnold PM, Anderson PA, Fischer D, Dettori JR. Anticoagulation risk in spine surgery. *Spine (Phila Pa 1976)*. 2010;35(9 Suppl): S117-S124. Sansone JM, del Rio AM, Anderson PA. The prevalence of and specific risk factors for venous thromboembolic disease following elective spine surgery. *J Bone Joint Surg Am*. 2010;92(2): 304-313. See Table S2 legend for expansion of abbreviation.

[a] No studies of LMWH vs placebo in spinal surgery (two studies in neurosurgery included 1%-15% of spinal surgery patients); estimate of relative risk taken from studies of LMWH vs no prophylaxis in general and abdominal surgery.

[b] Low-risk estimate derived from study of >34,000 discharges following spinal surgery for nonmalignant disease in California from 1992 to 1996 (White, 2003). Observed risk of symptomatic VTE within 91 d was 0.5% (95% CI, 0.4%-0.5%). Assuming that 50% received mechanical prophylaxis, the adjusted risk of VTE in the absence of prophylaxis is 0.8%. High-risk estimate derived from data from the same study for 1,545 discharges following spinal surgery for malignant disease in California from 1992 to 1996 (White, 2003). Observed risk of symptomatic VTE within 91 d was 2.0% (95% CI, 1.4%-2.6%). Assuming that 100% received mechanical prophylaxis, the adjusted risk of VTE in the absence of prophylaxis is 4.5%. Moderate-risk estimate applies to patients with VTE risk factors undergoing nonhigh-risk procedure (Bahl V, Hu H, Henke PK, et al. A validation study of a retrospective venous thromboembolism risk scoring method . *Ann Surg*. 2010;251(2):344-350).

[c] Relative risk of major bleeding with LMWH in spinal surgery patients not known; estimate of relative risk taken from studies of abdominal and pelvic surgery.

[d] Based on a retrospective study of 1,954 spinal procedures at different levels from 1999 to 2002 (Gerlach R, Raabe A, Beck J, Woszczyk A, Seifert V. Postoperative nadroparin administration for prophylaxis of thromboembolic events is not associated with an increased risk of hemorrhage after spinal surgery. *Eur Spine J*. 2004;13:9-13); all treated with nadroparin 2,850 anti-Xa units daily (within 24 h) plus CS; ASA held for 7 d. Major postoperative hemorrhage defined as a hemorrhage associated with a mass effect on postoperative spinal MRI and neurologic deterioration as well as a large-wound hematoma with intractable pain. Major hemorrhage occurred in 13 of 1,954 (0.7%) patients, including five in whom bleeding occurred prior to nadroparin administration; after adjustment, baseline risk of major bleeding is calculated to be 0.46%.

Table S18—*[Section 7.3] Evidence Profile: Should IPC vs No Prophylaxis Be Used for VTE Prevention in Spinal Surgery?*

Quality Assessment							Summary of Findings					
							No. of Patients		Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	IPC	No Prophylaxis	Relative (95% CI)	Absolute	Quality	Importance
Symptomatic VTE inferred from all DVT												
2	Randomized trials	Serious[a]	No serious inconsistency	Serious[b]	No serious imprecision	None	0/0 (0%)	0.9%[c]	RR 0.41 (0.21-0.78)[d]	5 fewer per 1,000 (from 2 fewer to 7 fewer)	Low	Critical
								2.0%[c]		12 fewer per 1,000 (from 4 fewer to 16 fewer)		
								4.9%[c]		29 fewer per 1,000 (from 11 fewer to 39 fewer)		
Skin complications												
0	No evidence available					None	0/0 (0%)	0/0 (0%)	Not estimable	0 fewer per 1,000 (from 0 fewer to 0 fewer)		Important

Authors: David Garcia and Michael Gould. Date: January 4, 2011. Setting: hospital. Bibliography: Collen JF, Jackson JL, Shorr AF, Moores LK. Prevention of venous thromboembolism in neurosurgery: a metaanalysis. *Chest*. 2008;134(2):237-249. White RH, Zhou H, Romano PS. Incidence of symptomatic venous thromboembolism after different elective or urgent surgical procedures. *Thromb Haemost*. 2003;90(3):446-455. Cheng JS, Arnold PM, Anderson PA, Fischer D, Dettori JR. Anticoagulation risk in spine surgery. *Spine (Phila Pa 1976).* 2010;35(9 Suppl):S117-S124. Sansone JM, del Rio AM, Anderson PA. The prevalence of and specific risk factors for venous thromboembolic disease following elective spine surgery. *J Bone Joint Surg Am*. 2010;92(2):304-313. See Tables S2 and S8 legends for expansion of abbreviations.

[a] Data from two small, unblinded studies. Inclusion/exclusion were not described; 53% of patients underwent spine surgery in one study, whereas only 6% underwent spine surgery in the other study of primarily craniotomy patients. IPC used in combination with GCS in one study.

[b] Surrogate outcome (asymptomatic DVT).

[c] Low-risk estimate derived from study of >34,000 discharges following spinal surgery for nonmalignant disease in California from 1992 to 1996 (White, 2003). Observed risk of symptomatic VTE within 91 d was 0.5% (95% CI, 0.4%-0.5%). Assuming that 50% received mechanical prophylaxis, the adjusted risk of VTE in the absence of prophylaxis is 0.9%. High-risk estimate derived from same study for 1,545 discharges following spinal surgery for malignant disease in California from 1992 to 1996 (White, 2003). Observed risk of symptomatic VTE within 91 d was 2.0% (95% CI, 1.4%-2.6%). Assuming that 100% received mechanical prophylaxis, the adjusted risk of VTE in the absence of prophylaxis is 4.9%. Moderate-risk estimate applies to patients with VTE risk factors undergoing nonhigh-risk procedure (Bahl V, Hu H, Henke PK, et al. A validation study of a retrospective venous thromboembolism risk scoring method. *Ann Surg*. 2010;251(2):344-350).

[d] Relative risk of any DVT from meta-analysis by Collen et al (2008), based on data from two studies of VTE prophylaxis in neurosurgery. Relative risk of PE was similar but imprecise (0.37; 95% CI, 0.03-4.06).

Table S19—*[Section 7.3] Evidence Profile: Should ES vs No Prophylaxis Be Used for VTE Prevention in Spinal Surgery Patients?*

Quality Assessment							Summary of Findings					
							No. of Patients		Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	ES	No Prophylaxis	Relative (95% CI)	Absolute	Quality	Importance
Symptomatic VTE inferred from all DVT												
8	Randomized trials	Serious[a]	No serious inconsistency	Serious[b]	No serious imprecision	None	86/622 (13.8%)[c]	0.9%[d]	OR 0.35 (0.26-0.47)	6 fewer per 1,000 (from 5 fewer to 7 fewer)	Low	Critical
								2.0%[d]		13 fewer per 1,000 (from 10 fewer to 15 fewer)		
								4.9%[d]		31 fewer per 1,000 (from 25 fewer to 36 fewer)		
Skin breaks, ulcers, blisters, necrosis												
1	Randomized trials	Serious[e]	No serious inconsistency	Serious[f]	No serious imprecision	None	64/1,256 (5.1%)	16/1,262 (1.3%)	RR 4.18 (2.4-7.27)	40 more per 1,000 (from 18 more to 79 more)	Low	Important

Author: Michael Gould. Date: January 10, 2011. Setting: hospital. Bibliography: Sachdeva A, Dalton M, Amaragiri SV, Lees T. Elastic compression stockings for prevention of deep vein thrombosis. *Cochrane Database Syst Rev*. 2010;(7):CD001484. White RH, Zhou H, Romano PS. Incidence of symptomatic venous thromboembolism after different elective or urgent surgical procedures. *Thromb Haemost*. 2003;90(3):446-455. Cheng JS, Arnold PM, Anderson PA, Fischer D, Dettori JR. Anticoagulation risk in spine surgery. *Spine (Phila Pa 1976)*. 2010;35(9 Suppl):S117-S124. Sansone JM, del Rio AM, Anderson PA. The prevalence of and specific risk factors for venous thromboembolic disease following elective spine surgery. *J Bone Joint Surg Am*. 2010;92(2):304-313. CLOTS Trials Collaboration; Dennis M, Sandercock PA, Reid J, et al. Effectiveness of thigh-length graduated compression stockings to reduce the risk of deep vein thrombosis after stroke (CLOTS trial 1): a multicentre, randomised controlled trial. *Lancet*. 2009;373(9679):1958-1965. CLOTS1 = Clots in Legs Or sTockings after Stroke. See Table S2 and S8 legends for expansion of other abbreviations.

[a] Surrogate outcome (asymptomatic DVT); allocation concealment lacking or uncertain in six of eight studies; blinding incomplete or uncertain in five of eight studies; information about incomplete outcome data incomplete or uncertain in two of eight studies.

[b] Relative risk estimate based on studies of general surgery (four), cardiac surgery (one), gynecologic surgery (one), orthopedic surgery (one), and neurosurgery (one).

[c] Pooled risk of any DVT (including asymptomatic DVT) in GCS groups.

[d] Low-risk estimate derived from study of >34,000 discharges following spinal surgery for nonmalignant disease in California from 1992 to 1996 (White, 2003). Observed risk of symptomatic VTE within 91 d was 0.5% (95% CI, 0.4%-0.5%). Assuming that 50% received mechanical prophylaxis, the adjusted risk of VTE in the absence of prophylaxis is 0.8%. High-risk estimate derived from the same study for 1,545 discharges following spinal surgery for malignant disease in California from 1992 to 1996 (White, 2003). Observed risk of symptomatic VTE within 91 d was 2.0% (95% CI, 1.4%-2.6%). Assuming that 100% received mechanical prophylaxis, the adjusted risk of VTE in the absence of prophylaxis is 4.5%. Moderate-risk estimate applies to patients with VTE risk factors undergoing nonhigh-risk procedure (Bahl et al, 2010).

[e] Unblinded assessment based on case note review.

[f] Data from CLOTS1 trial in stroke patients.

Table S20—*[Section 7.3] Evidence Profile: Should IPC vs ES Be Used for VTE Prevention in Spinal Surgery?*

Quality Assessment							Summary of Findings					
							No. of Patients		Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	IPC	ES	Relative (95% CI)	Absolute	Quality	Importance
Symptomatic VTE inferred from all DVT												
3	Randomized trials	Serious[a]	No serious inconsistency	Serious[b]	Serious[c]	None	0/0 (0%)	0.3%[d]	RR 0.81 (0.32-1.78)	1 fewer per 1,000 (from 2 fewer to 2 more)	Very low	Critical
								0.7%[d]		1 fewer per 1,000 (from 5 fewer to 5 more)		
								1.7%[d]		3 fewer per 1,000 (from 12 fewer to 13 more)		
Skin breaks, ulcers, blisters, necrosis												
1	Randomized trials	Serious[e]	No serious inconsistency	Serious[f]	No serious imprecision	None	16/1,262 (1.3%)[g]	64/1,256 (5.1%)	RR 0.25 (0.14-0.43)	38 fewer per 1,000 (from 29 fewer to 44 fewer)	Low	Important

Authors: David Garcia and Michael Gould. Date: January 4, 2011. Setting: hospital. Bibliography: Collen JF, Jackson JL, Shorr AF, Moores LK. Prevention of venous thromboembolism in neurosurgery: a metaanalysis. *Chest*. 2008;134(2):237-249. White RH, Zhou H, Romano PS. Incidence of symptomatic venous thromboembolism after different elective or urgent surgical procedures. *Thromb Haemost*. 2003;90(3):446-455. Cheng JS, Arnold PM, Anderson PA, Fischer D, Dettori JR. Anticoagulation risk in spine surgery. *Spine (Phila Pa 1976).* 2010;35(9 Suppl):S117-S124. Sansone JM, del Rio AM, Anderson PA. The prevalence of and specific risk factors for venous thromboembolic disease following elective spine surgery. *J Bone Joint Surg Am*. 2010;92(2):304-313. CLOTS Trials Collaboration; Dennis M, Sandercock PA, Reid J, et al. Effectiveness of thigh-length graduated compression stockings to reduce the risk of deep vein thrombosis after stroke (CLOTS trial 1): a multicentre, randomised controlled trial. *Lancet*. 2009;373(9679):1958-1965. See Table S2, S8, and S19 legends for expansion of abbreviations.

[a] Unblinded studies with incomplete follow-up and measurement of surrogate outcome.

[b] One of three studies performed in spinal surgery patients; the others were performed in craniotomy patients.

[c] CI includes possibility of both substantial benefit and no effect.

[d] Low-risk estimate derived from study of >34,000 discharges following spinal surgery for nonmalignant disease in California from 1992 to 1996 (White, 2003). Observed risk of symptomatic VTE within 91 d was 0.5% (95% CI, 0.4%-0.5%). Assuming that 50% received mechanical prophylaxis, the adjusted risk of VTE in the setting of GCS prophylaxis is 0.3%. High-risk estimate derived from data from the same study for 1,545 discharges following spinal surgery for malignant disease in California from 1992 to 1996 (White, 2003). Observed risk of symptomatic VTE within 91 d was 2.0% (95% CI, 1.4%-2.6%); adjusted risk with ES is 1.7%. Moderate-risk estimate applies to patients with VTE risk factors undergoing nonhigh-risk procedure (Bahl et al, 2010), and is the same as for high-risk patients.

[e] Unblinded assessment based on case note review.

[f] Data from CLOTS1 study in stroke patients; applies specifically to prophylaxis with GCS and not IPC.

[g] Risk of skin complications with IPC assumed to be the same as for no mechanical prophylaxis in CLOTS1 trial.

Table S21—*[Section 7.3] Evidence Profile: Should LDUH vs IPC Be Used for VTE Prevention in Spinal Surgery Patients?*

Quality Assessment							Summary of Findings: No. of Patients		Summary of Findings: Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	LDUH	IPC	Relative (95% CI)	Absolute	Quality	Importance
Symptomatic VTE inferred from all DVT												
22[a]	Randomized trials	Serious[b]	No serious inconsistency	Serious[c]	Serious[d]	None	0/0 (0%)	0.4%[e]	RR 1.22 (0.23-6.49)	1 more per 1,000 (from 3 fewer to 22 more)	Very low	Critical
								0.8%[e]		2 more per 1,000 (from 6 fewer to 44 more)		
								2.0%[e]		4 more per 1,000 (from 15 fewer to 110 more)		
Major bleeding (hemorrhage associated with a mass effect on postoperative spinal MRI or neurologic deterioration as well as a large-wound hematoma with intractable pain)												
36	Randomized trials	Serious[f]	No serious inconsistency	Serious[g]	No serious imprecision	None	0/0 (0%)	0.46%[h]	OR 1.51 (1.13-2.02)	2 more per 1,000 (from 1 more to 5 more)	Low	Critical

Author: Michael Gould. Date: January 10, 2011. Setting: hospital. Bibliography: Collen JF, Jackson JL, Shorr AF, Moores LK. Prevention of venous thromboembolism in neurosurgery: a metaanalysis. *Chest*. 2008;134(2):237-249. Collins R, Scrimgeour A, Yusuf S, Peto R. Reduction in fatal pulmonary embolism and venous thrombosis by perioperative administration of subcutaneous heparin. Overview of results of randomized trials in general, orthopedic, and urologic surgery. *N Engl J Med*. 1988;318(18):1162-1173. International Multicentre Trial. Prevention of fatal postoperative pulmonary embolism by low doses of heparin. An international multicentre trial. *Lancet*. 1975;2(7924):45-51. White RH, Zhou H, Romano PS. Incidence of symptomatic venous thromboembolism after different elective or urgent surgical procedures. *Thromb Haemost*. 2003;90(3):446-455. Cheng JS, Arnold PM, Anderson PA, Fischer D, Dettori JR. Anticoagulation risk in spine surgery. *Spine (Phila Pa 1976)*. 2010;35(9 Suppl):S117-S124. Sansone JM, del Rio AM, Anderson PA. The prevalence of and specific risk factors for venous thromboembolic disease following elective spine surgery. *J Bone Joint Surg Am*. 2010;92(2):304-313. See Table S2 and S8 legends for expansion of abbreviations.

[a] Indirect statistical comparison based on 22 studies of UFH vs no prophylaxis in mixed surgical patients and two studies of IPC vs no prophylaxis in neurosurgical patients.

[b] Data for IPC from two small, unblinded studies. Inclusion/exclusion not described. Surrogate outcome reported; 53% of patients underwent spine surgery in one study, whereas only 6% underwent spine surgery in the other study of primarily craniotomy patients. IPC used in combination with GCS in one study. Data for UFH from 22 studies, many not blinded.

[c] Indirect statistical comparison using data from mixed surgical populations.

[d] The 95% CI includes the possibility of both serious harm and substantial benefit.

[e] Low-risk estimate derived from study of > 34,000 discharges following spinal surgery for nonmalignant disease in California from 1992 to 1996 (White, 2003). Observed risk of symptomatic VTE within 91 d was 0.5% (95% CI, 0.4%-0.5%). Assuming that 50% received mechanical prophylaxis, the adjusted risk of VTE in the setting of 100% IPC prophylaxis is 0.36%. High-risk estimate derived from data from the same study for 1,545 discharges following spinal surgery for malignant disease in California from 1992 to 1996 (White, 2003). Observed risk of symptomatic VTE within 91 d was 2.0% (95% CI, 1.4%-2.6%). Assuming that 100% received mechanical prophylaxis, this is the baseline risk in the setting of IPC prophylaxis. Moderate-risk estimate applies to patients with VTE risk factors undergoing nonhigh-risk procedures (Bahl et al, 2010) and is the same as for high-risk patients.

[f] Many studies not blinded.

[g] Relative risk of major bleeding with LDUH in spinal surgery patients not known; estimate of relative risk taken from studies of abdominal and pelvic surgery.

[h] Based on a retrospective study of 1,954 spinal procedures at different levels from 1999 to 2002 (Gerlach et al, 2004). All were treated with nadroparin 2,850 anti-Xa units daily (within 24 h) plus ES; ASA held for 7 d. Major postoperative hemorrhage defined as a hemorrhage associated with a mass effect on postoperative spinal MRI and neurologic deterioration as well as a large-wound hematoma with intractable pain. Major hemorrhage occurred in 13 of 1,954 (0.7%) patients, including five in whom bleeding occurred prior to nadroparin administration; after adjustment, baseline risk of major bleeding is calculated to be 0.46%.

Table S22—*[Section 7.3] Evidence Profile: Should LMWH vs IPC Be Used in VTE Prevention in Spinal Surgery?*

Quality Assessment							Summary of Findings: No. of Patients		Summary of Findings: Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	LMWH	IPC	Relative (95% CI)	Absolute	Quality	Importance
Symptomatic VTE inferred from all DVT												
2	Randomized trials	Serious[a]	No serious inconsistency	Serious[b]	Serious	None	0/0 (0%)	0.4%[c]	RR 0.56 (0.36-0.86)	2 fewer per 1,000 (from 1 fewer to 3 fewer)	Very low	Critical
								0.8%[c]		4 fewer per 1,000 (from 1 fewer to 5 fewer)		
								2.0%[c]		9 fewer per 1,000 (from 3 fewer to 13 fewer)		
Major bleeding												
7	Randomized trials	No serious limitations	No serious inconsistency	Serious[d]	No serious imprecision	None	0/0 (0%)	0.46%[e]	RR 2.03 (1.37-3.01)	5 more per 1,000 (from 2 more to 9 more)	Moderate	Critical

Authors: David Garcia and Michael Gould. Date: January 4, 2011. Setting: hospital. Bibliography: Eppsteiner RW, Shin JJ, Johnson J, van Dam RM. Mechanical compression versus subcutaneous heparin therapy in postoperative and posttrauma patients: a systematic review and meta-analysis. *World J Surg*. 2010;34(1):10-19. Mismetti P, Laporte S, Darmon JY, Buchmüller A, Decousus H. Meta-analysis of low molecular weight heparin in the prevention of venous thromboembolism in general surgery. *Br J Surg*. 2001;88(7):913-930. White RH, Zhou H, Romano PS. Incidence of symptomatic venous thromboembolism after different elective or urgent surgical procedures. *Thromb Haemost*. 2003;90(3):446-455. Gerlach R, Scheuer T, Beck J, Woszczyk A, Seifert V, Raabe A. Risk of postoperative hemorrhage after intracranial surgery after early nadroparin administration: results of a prospective study. *Neurosurgery*. 2003;53(5):1028-1034. See Table S2 and S8 legends for expansion of abbreviations.

[a] Data for IPC vs no prophylaxis from two small, unblinded studies. Inclusion/exclusion not described. Surrogate outcome reported; 53% of patients underwent spine surgery in one study, whereas only 6% underwent spine surgery in the other study of primarily craniotomy patients. IPC used in combination with GCS in one study.

[b] Estimate for relative risk based on formal statistical indirect comparison from studies of IPC vs no prophylaxis and LMWH vs no prophylaxis.

[c] Low-risk estimate derived from study of >34,000 discharges following spinal surgery for nonmalignant disease in California from 1992 to 1996 (White, 2003). Observed risk of symptomatic VTE within 91 d was 0.5% (95% CI, 0.4%-0.5%). Assuming that 50% received mechanical prophylaxis, the adjusted risk of VTE in the setting of 100% IPC prophylaxis is 0.36%. High-risk estimate derived from data from the same study for 1,545 discharges following spinal surgery for malignant disease in California from 1992 to 1996 (White, 2003). Observed risk of symptomatic VTE within 91 d was 2.0% (95% CI, 1.4%-2.6%). Assuming that 100% received mechanical prophylaxis, this is the baseline risk in the setting of IPC prophylaxis. Moderate-risk estimate applies to patients with VTE risk factors undergoing nonhigh-risk procedures (Bahl et al, 2010) and is the same as for high-risk patients.

[d] Relative risk of major bleeding with LMWH in spinal surgery patients not known; estimate of relative risk taken from studies of abdominal and pelvic surgery.

[e] Based on a retrospective study of 1,954 spinal procedures at different levels from 1999 to 2002 (Gerlach et al, 2004). All were treated with nadroparin 2,850 anti-Xa units daily (within 24 h) plus CS; ASA held for 7 d. Major postoperative hemorrhage defined as a hemorrhage associated with a mass effect on postoperative spinal MRI and neurologic deterioration as well as a large-wound hematoma with intractable pain. Major hemorrhage occurred in 13 of 1,954 (0.7%) patients, including five in whom bleeding occurred prior to nadroparin administration; after adjustment, baseline risk of major bleeding is calculated to be 0.46%.

Table S23—*[Section 8.3] Evidence Profile: Should LDUH vs No Prophylaxis Be Used for VTE Prevention in Patients With Trauma?*[a]

Quality Assessment							Summary of Findings					
							No. of Patients		Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	LDUH	No Prophylaxis	Relative (95% CI)	Absolute	Quality	Importance
Fatal PE												
20	Randomized trials	No serious limitations	No serious inconsistency	Serious[b]	No serious imprecision	None	19/6,809 (0.3%)	0.4%[c]	RR 0.53 (0.31-0.91)	2 fewer per 1,000 (from 0 fewer to 3 fewer)	Moderate	Critical
								0.9%[c]		4 fewer per 1,000 (from 1 fewer to 6 fewer)		
Fatal bleeding												
7	Randomized trials	No serious limitations	No serious inconsistency	Serious[b]	Serious[b]	None	7/6,703 (0.1%)	6/6,577 (0.1%)	RR 1.14 (0.41-3.15)	0 more per 1,000 (from 1 fewer to 2 more)	Low	Critical
Nonfatal symptomatic VTE												
22	Randomized trials	Serious[e]	No serious inconsistency[f]	Serious[b]	No serious imprecision	None	4/384 (1%)[g]	4.0%[h]	RR 0.59 (0.41-0.84)	16 fewer per 1,000 (from 6 fewer to 24 fewer)	Low	Critical
								9.0%[h]		37 fewer per 1,000 (from 14 fewer to 53 fewer)		

(Continued)

Table S23—*Continued*

Quality Assessment							Summary of Findings					
							No. of Patients		Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	LDUH	No Prophylaxis	Relative (95% CI)	Absolute	Quality	Importance
Nonfatal clinically important bleeding												
36	Randomized trials	Serious[e]	No serious inconsistency	Serious[b,i]	No serious imprecision	None	6/205 (2.9%)[j]	0.7%[k]	RR 1.57 (1.32-1.87)	4 more per 1,000 (from 2 more to 6 more)	Low	Critical

Author: Michael Gould. Date: March 29, 2011. Setting: hospital. Bibliography: Collins R, Scrimgeour A, Yusuf S, Peto R. Reduction in fatal pulmonary embolism and venous thrombosis by perioperative administration of subcutaneous heparin. Overview of results of randomized trials in general, orthopedic, and urologic surgery. *N Engl J Med*. 1988;318(18):1162-1173. Geerts WH, Code KI, Jay RM, Chen E, Szalai JP. A prospective study of venous thromboembolism after major trauma. *N Engl J Med*. 1994;331(24):1601-1606. Platzer P, Thalhammer G, Jaindl M, et al. Thromboembolic complications after spinal surgery in trauma patients. *Acta Orthop*. 2006;77(5):755-760. See Table S2, S7, and S8 legends for expansion of abbreviations.

[a] Duration of follow-up varied but usually to hospital discharge.

[b] Relative risk estimates derived using random-effects model and data from meta-analysis by Collins et al (1988), which included studies of general, urologic, and orthopedic surgery.

[c] In study by Geerts et al (1994), fatal PE occurred in 3 of 716 (0.4%) patients before venography could be performed; high-risk estimate assumes that risk of fatal PE is 10% of nonfatal VTE in high-risk patients.

[d] The 95% CI includes the possibility of both substantial benefit and serious harm.

[e] Many studies not blinded with unclear concealment of allocation sequence.

[f] Mild heterogeneity in results across studies.

[g] Simple pooling of risk of symptomatic VTE in UFH groups across four studies of VTE prophylaxis in major trauma.

[h] See text for explanation. High-risk refers to patients with TBI, acute SCI, or spinal injury requiring surgery. Lower-risk estimate applies to other major trauma patients.

[i] Surrogate outcome: relative risk of clinically important bleeding assumed to be identical to that for excessive intraoperative bleeding or need for transfusion

[j] Simple pooling of risk of major bleeding in UFH group in two studies of VTE prophylaxis in major trauma.

[k] See text for explanation.

Table S24—*[Section 8.3] Evidence Profile: Should LMWH vs No Prophylaxis Be Used for VTE Prevention in Patients With Trauma?*

Quality Assessment							Summary of Findings					
							No. of Patients		Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	LMWH	No Prophylaxis	Relative (95% CI)	Absolute	Quality	Importance
Fatal PE inferred from all-cause mortality												
5	Randomized trials	No serious limitations	No serious inconsistency	Serious[a]	No serious imprecision	None	11/2,553 (0.4%)	0.4%[b]	RR 0.54 (0.27-1.1)	2 fewer per 1,000 (from 3 fewer to 0 more)	Moderate	Critical
								0.9%[b]		4 fewer per 1,000 (from 7 fewer to 1 more)		
Fatal bleeding inferred from studies of LDUH												
7	Randomized trials	No serious limitations	No serious inconsistency	Serious[a]	Serious[c]	None	7/6,703 (0.1%)	6/6,577 (0.1%)	RR 1.14 (0.41-3.15)	0 more per 1,000 (from 1 fewer to 2 more)	Low	Critical
Nonfatal symptomatic VTE												
3	Randomized trials	Serious[d]	No serious inconsistency	Serious[a]	No serious imprecision	None	5/611 (0.8%)[e]	4.0%[f]	RR 0.31 (0.12-0.81)[g]	28 fewer per 1,000 (from 8 fewer to 35 fewer)	Low	Critical
								9.0%[f]		62 fewer per 1,000 (from 17 fewer to 79 fewer)		

(Continued)

Table S24—*Continued*

Quality Assessment							Summary of Findings					
							No. of Patients		Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	LMWH	No Prophylaxis	Relative (95% CI)	Absolute	Quality	Importance
Nonfatal major bleeding												
7	Randomized trials	No serious limitations	No serious inconsistency	Serious[a]	No serious imprecision	None	39/670 (5.8%)[h]	0.7%[i]	RR 2.03 (1.37-3.01)[j]	7 more per 1,000 (from 3 more to 14 more)	Moderate	Critical

Author: Michael Gould. Date: March 29, 2011. Setting: hospital. Bibliography: Geerts WH, Code KI, Jay RM, Chen E, Szalai JP. A prospective study of venous thromboembolism after major trauma. *N Engl J Med*. 1994;331(24):1601-1606. Platzer P, Thalhammer G, Jaindl M, et al. Thromboembolic complications after spinal surgery in trauma patients. *Acta Orthop*. 2006;77(5):755-760. Mismetti P, Laporte S, Darmon JY, Buchmüller A, Decousus H. Meta-analysis of low molecular weight heparin in the prevention of venous thromboembolism in general surgery. *Br J Surg*. 2001;88(7):913-930. Geerts WH, Jay RM, Code KI, et al. A comparison of low-dose heparin with low-molecular-weight heparin as prophylaxis against venous thromboembolism after major trauma. *N Engl J Med*. 1996;335(10):701-707. Knudson MM, Lewis FR, Clinton A, et al. Prevention of venous thromboembolism in trauma patients. *J Trauma*. 1994;37(3):480-487. Fisher CG, Blachut PA, Salvian AJ, Meek RN, O'Brien PJ. Effectiveness of pneumatic leg compression devices for the prevention of thromboembolic disease in orthopaedic trauma patients: a prospective, randomized study of compression alone versus no prophylaxis. *J Orthop Trauma*. 1995;9(1):1-7. Velmahos GC, Petrone P, Chan LS, et al. Electrostimulation for the prevention of deep venous thrombosis in patients with major trauma: a prospective randomized study. *Surgery*. 2005;137(5):493-498. Knudson MM, Morabito D, Paiement GD, Shackleford S. Use of low molecular weight heparin in preventing thromboembolism in trauma patients. *J Trauma*. 1996;41(3):446-459. Cohn SM, Moller BA, Feinstein AJ, et al. Prospective trial of low-molecular-weight heparin versus unfractionated heparin in moderately injured patients. *Vasc Surg*. 1999;33(X):219-223. Ginzburg E, Cohn SM, Lopez J, Jackowski J, Brown M, Hameed SM; Miami Deep Vein Thrombosis Study Group. Randomized clinical trial of intermittent pneumatic compression and low molecular weight heparin in trauma. *Br J Surg*. 2003;90(11):1338-1344. Kurtoglu M, Yanar H, Bilsel Y, et al. Venous thromboembolism prophylaxis after head and spinal trauma: intermittent pneumatic compression devices versus low molecular weight heparin. *World J Surg*. 2004;28(8):807-811. Stannard JP, Lopez-Ben RR, Volgas DA, et al. Prophylaxis against deep-vein thrombosis following trauma: a prospective, randomized comparison of mechanical and pharmacologic prophylaxis. *J Bone Joint Surg Am*. 2006;88(2):261-266. See Table S2, S6, S7, and S8 legends for expansion of abbreviations.

[a] Relative risk estimates taken from studies of LMWH in patients undergoing general or abdominal surgery.

[b] In study by Geerts et al (1994), fatal PE occurred in three of 716 (0.4%) patients before venography could be performed; high-risk estimate assumes that risk of fatal PE is 10% of nonfatal VTE in high-risk patients.

[c] The 95% CI includes the possibility of both substantial benefit and serious harm.

[d] One study not blinded and one study with unclear concealment of allocation sequence. Nonfatal symptomatic VTE not objectively confirmed in one large study.

[e] Simple pooling of risk of symptomatic VTE in LMWH groups across five studies of VTE prophylaxis in major trauma.

[f] See text for explanation. High risk refers to patients with TBI, acute SCI, or spinal injury requiring surgery. Lower-risk estimate applies to other major trauma patients.

[g] Data from Mismetti et al (2001). Pooled relative risk of symptomatic VTE with LMWH in three RCTs of VTE prophylaxis in abdominal surgery.

[h] Simple pooling of risk of major bleeding in LMWH groups across six studies of VTE prophylaxis in major trauma.

[i] See text for explanation.

[j] Data from Mismetti et al (2001). Pooled relative risk of major bleeding with LMWH in seven RCTs of VTE prophylaxis in abdominal surgery.

Table S25—*[Section 8.3] Evidence Profile: Should ES vs No Prophylaxis Be Used for VTE Prevention in Patients With Trauma?*

Quality Assessment							Summary of Findings					
							No. of Patients		Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	ES	No Prophylaxis	Relative (95% CI)	Absolute	Quality	Importance
Nonfatal symptomatic VTE												
8	Randomized trials[a-c]	Serious[d]	No serious inconsistency	Serious[e]	No serious imprecision	None	13/494 (2.6%)[f]	4.0%[g]	OR 0.35 (0.26-0.47)[h]	26 fewer per 1,000 (from 21 fewer to 29 fewer)	Low	Critical
								9.0%[g]		57 fewer per 1,000 (from 46 fewer to 65 fewer)		
Skin breaks, blisters, ulcers, necrosis (follow-up 1-30 d; case note review)												
1	Randomized trials	Serious[i]	No serious inconsistency	Serious[j]	No serious imprecision	None	64/1,256 (5.1%)	16/1,262 (1.3%)	RR 4.18 (2.4-7.27)	40 more per 1,000 (from 18 more to 79 more)	Low	Important

Author: Michael Gould. Date: March 29, 2011. Setting: hospital. Bibliography: Roderick P, Ferris G, Wilson K, et al. Towards evidence-based guidelines for the prevention of venous thromboembolism: systematic reviews of mechanical methods, oral anticoagulation, dextran and regional anaesthesia as thromboprophylaxis. *Health Technol Assess*. 2005;9(49):1-78. Sachdeva A, Dalton M, Amaragiri SV, Lees T. Elastic compression stockings for prevention of deep vein thrombosis. *Cochrane Database Syst Rev*. 2010;(7):CD001484. Bahl V, Hu HM, Henke PK, Wakefield TW, Campbell DA Jr, Caprini JA. A validation study of a retrospective venous thromboembolism risk scoring method. *Ann Surg*. 2010;251(2):344-350. CLOTS Trials Collaboration; Dennis M, Sandercock PA, Reid J, et al. Effectiveness of thigh-length graduated compression stockings to reduce the risk of deep vein thrombosis after stroke (CLOTS trial 1): a multicentre, randomised controlled trial. *Lancet*. 2009;373(9679):1958-1965. See Table S2, S8, and S19 legends for expansion of abbreviations.

[a] Data for other critical outcomes (eg, fatal PE) not available, bleeding complications not relevant.

[b] Duration of follow-up varied, but usually to hospital discharge.

[c] Meta-analysis by Sachdeva et al (2010) included eight studies of ES in mixed surgical populations, including four studies of general surgery, one of orthopedic surgery, one of cardiac surgery, one of gynecologic surgery, and one of elective or traumatic cranial or spinal surgery.

[d] Unblinded assessment of outcomes and unclear concealment of allocation sequence in many studies.

[e] Relative risk of symptomatic VTE inferred from surrogate outcome (proximal or distal DVT).

[f] Simple pooling of risk of symptomatic VTE in mechanical prophylaxis groups across three trials of VTE prophylaxis in patients with trauma.

[g] See text for explanation. High risk refers to patients with TBI, acute SCI, or spinal injury requiring surgery. Lower-risk estimate applies to other patients with major trauma.

[h] The OR for PE (one study) was 0.13 (95% CI, 0-6.7). In a separate meta-analysis by Roderick et al (2005), the pooled OR for proximal DVT was 0.36 (95% CI, 0-1.30).

[i] Unblinded assessment based on case note review.

[j] Data from CLOTS1 study in patients with stroke; applies specifically to prophylaxis with ES and not IPC.

Table S26—*[Section 8.30] Evidence Profile: Should IPC vs No Prophylaxis Be Used for VTE Prevention in Patients With Trauma?*

Quality Assessment							Summary of Findings					
							No. of Patients		Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	IPC	No Prophylaxis	Relative (95% CI)	Absolute	Quality	Importance
Symptomatic VTE inferred from proximal DVT (FUT ± IPG ± venography or DUS + venography)												
9	Randomized trials[a]	Serious[b]	No serious inconsistency	Serious[c]	No serious imprecision	None	45/755 (6%)[d]	4.0%[e]	OR 0.48 (0.22-0.74)	20 fewer per 1,000 (from 10 fewer to 31 fewer)	Low	Critical
								9.0%[e]		45 fewer per 1,000 (from 22 fewer to 69 fewer)		
Skin breaks, blisters, ulcers, necrosis												
0	No evidence available											

Date: March 30, 2011. Setting: hospital. See Table S2, S3, and S8 legends for expansion of abbreviations.

[a] Data for other critical outcomes (eg, fatal PE) not available; bleeding complications not relevant.

[b] Many studies limited by incomplete blinding and incompletely described methods for concealment of allocation sequence.

[c] Meta-analysis by Roderick et al (Roderick P, Ferris G, Wilson K, et al. Towards evidence based guidelines for the prevention of venous thromboembolism: systematic reviews of mechanical methods, oral anticoagulation, dextran and regional anaesthesia as thromboprophylaxis. *Health Technol Assess.* 2005;9(49):1-78) included nine trials of IPC (two gynecological, one urological, one neurosurgery, one trauma, one medical, and three orthopedic surgeries); proximal DVT reported as surrogate outcome.

[d] Pooled, observed risk of proximal DVT.

[e] See text for explanation. High risk refers to patients with TBI, acute SCI, or spinal injury requiring surgery. Lower-risk estimate applies to other patients with major trauma.

Table S27—*[Section 8.3] Evidence Profile: Should Combined Therapy With Mechanical and Pharmacologic Prophylaxis vs Pharmacologic Prophylaxis Alone Be Used for VTE Prevention in Patients With Trauma?*

Quality Assessment							Summary of Findings					
							No. of Patients		Effect			
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	Combined Therapy With Mechanical and Pharmacological Prophylaxis	Pharmacological Prophylaxis Alone	Relative (95% CI)	Absolute	Quality	Importance
Nonfatal symptomatic VTE inferred from proximal DVT												
9	Randomized trials[a]	Serious[b]	No serious inconsistency	Serious[c]	Serious[d]	None	3/111 (2.7%)	1.2%[e]	OR 0.45 (0.20-1.03)	7 fewer per 1,000 (from 10 fewer to 0 more)	Very low	
								2.8%[e]		15 fewer per 1,000 (from 22 fewer to 1 more)		
Skin complications												
0	No evidence available					None	0/0 (0%)	0/0 (0%)	RR 0 (0-0)	0 fewer per 1,000 (from 0 fewer to 0 fewer)		
								0%		0 fewer per 1,000 (from 0 fewer to 0 fewer)		

Author: Michael Gould. Date: March 29, 2011. Setting: hospital. Bibliography: Fuchs S, Heyse T, Rudofsky G, Gosheger G, Chylarecki C. Continuous passive motion in the prevention of deep-vein thrombosis: a randomised comparison in trauma patients. *J Bone Joint Surg Br.* 2005;87(8):1117-1122. See Table S2, S3, and S8 legends for expansion of abbreviations.

[a] Data for other critical outcomes (eg, fatal PE) not available; bleeding complications not relevant.

[b] Many studies limited by incomplete blinding and incompletely described methods for concealment of allocation sequence.

[c] Relative risk estimate taken from meta-analysis by Roderick et al (Roderick P, Ferris G, Wilson K, et al. Towards evidence based guidelines for the prevention of venous thromboembolism: systematic reviews of mechanical methods, oral anticoagulation, dextran and regional anaesthesia as thromboprophylaxis. *Health Technol Assess.* 2005;9(49):1-78), which included nine trials of IPC (two gynecological, one urological, one neurosurgery, one trauma, one medical, and three orthopedic surgeries); proximal DVT reported as surrogate outcome. In another study in orthopedic trauma, the addition of CPM to LDUH reduced the risk of proximal DVT by 87% (RR, 0.13; 95% CI, 0.04-0.40). In this study, there were no symptomatic VTE events in either group.

[d] The 95% CI includes the possibility of both substantial benefit and no effect.

[e] See text for explanation. High risk refers to patients with TBI, acute SCI, or spinal injury requiring surgery. Lower-risk estimate applies to other patients with major trauma. Estimates adjusted by a factor of 0.31 to reflect use of LMWH prophylaxis.

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