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Appendix A. Search Strategy

Search 1: Major orthopedic surgery

Medline and Cochrane Central Register of Controlled Trials (OVID)

1. arthroplasty, replacement, knee/
2. knee.mp AND arthroplasty/
3. total knee replacement.mp
4. knee arthroplasty.mp
5. TKR.mp
6. knee prosthesis/
7. knee prosthesis.mp
8. knee joint.mp
9. arthroplasty, replacement, hip/
10. hip.mp AND arthroplasty/
11. total hip replacement.mp
12. hip arthroplasty.mp
13. THR.mp
14. hip prosthesis/
15. hip prosthesis.mp
16. hip fracture surgery.mp
17. HFS.mp
18. hip.mp AND fracture fixation, internal/
19. or/1-18
20. pulmonary embolism/
21. pulmonary embol*.mp
22. pulmonary thromboembol*.mp
23. PE.mp
24. deep vein thrombos*.mp
25. deep venous thrombos*.mp
26. deep venous thromboembol*.mp
27. deep vein thromboembol*.mp
28. DVT.mp
29. venous thromboembolism/
30. venous thromboembol*.mp
31. VTE.mp
32. venous thrombosis/
33. venous thrombos*.mp
34. clot.mp
35. or/20-34
36. anticoagulants/
37. aspirin/
38. aspirin.mp
39. clopidogrel.mp
40. ticlopidine.mp

41. prasugrel.mp
42. heparin/
43. heparinoids/
44. heparin.mp
45. UFH.mp
46. heparin, low-molecular weight/
47. low molecular weight heparin.mp
48. LMWH.mp
49. enoxaparin.mp
50. dalteparin.mp
51. nadroparin.mp
52. ardeparin.mp
53. bemiparin.mp
54. certoparin.mp
55. parnaparin.mp
56. reviparin.mp
57. tinzaparin.mp
58. danaparoid.mp
59. fondaparinux.mp
60. idraparinux.mp
61. rivaroxaban.mp
62. hirudins/
63. desirudin.mp
64. argatroban.mp
65. bivalirudin.mp
66. lepirudin.mp
67. dabigatran.mp
68. warfarin/
69. 4-Hydroxycoumarins/
70. warfarin.mp
71. acenocoumarol.mp
72. dicoumarol.mp
73. dextran sulfate/
74. dextran sulfate.mp
75. or/36-74
76. stockings, compression/
77. compression stocking.mp
78. compression stockings.mp
79. compression boot.mp
80. graduated compression stocking.mp
81. graduated compression stockings.mp
82. elastic stocking.mp
83. elastic stockings.mp
84. graduated compression stocking.mp
85. graduated compression stockings.mp
86. GCS.mp

87. venous foot pump.mp
88. VFP.mp
89. intermittent pneumatic compression devices/
90. intermittent pneumatic compression.mp
91. pneumatic compression stocking.mp
92. pneumatic compression stockings.mp
93. pneumatic hose.mp
94. pneumatic compression hose.mp
95. IPC.mp
96. or/76-95
97. vena cava filters/
98. vena cava filter.mp
99. vena cava filters.mp
100. IVC.mp
101. or/97-100
102. 75 or 96 or 101
103. 19 and 35 and 102

Scopus

((((ALL(anticoagulants OR aspirin OR clopidogrel OR ticlopidine OR prasugrel OR heparin OR heparinoids OR ufh OR low-molecular weight heparin OR low molecular weight heparin OR lmwh OR enoxaparin OR dalteparin OR nadroparin OR ardeparin OR bemiparin OR certoparin OR parnaparin OR reviparin OR tinzaparin OR danaparoid OR fondaparinux OR idraparinux OR rivaroxaban OR hirudin OR desirudin OR argatroban OR bivalirudin OR lepirudin OR dabigatran OR warfarin OR 4-hydroxycoumarin OR acenocoumarol OR dicoumarol OR dextran sulfate)) OR (ALL(vena cava filters OR vena cava filter OR ivc)) OR (((((ALL(compression stocking$)) OR (ALL(graduated compression stocking$)) OR (ALL(elastic stocking$)) OR (ALL(venous foot pump)) OR (ALL(intermittent pneumatic compression)))) OR (ALL(pneumatic compression)))))) AND (((((ALL(deep vein thrombos*)) OR (ALL(deep venous thrombos*)) OR (ALL(venous thromboembol*)) OR (ALL(deep vein thrombos*)) OR (ALL(deep venous thrombos*)))) OR (((ALL(venous thromboembol*)) OR (ALL(pulmonary thromboembol*)) OR (ALL(pulmonary embol*)) OR (ALL(venous thrombos*)))))) AND (((ALL(knee replacement)) OR (ALL(knee arthroplasty)) OR (ALL(hip arthroplasty)) OR (ALL(hip replacement)) OR (ALL(hip fracture surgery)))))

Search 2: Other orthopedic surgery

Medline and Cochrane Central Register of Controlled Trials (OVID)

1. knee arthroscop*
2. arthroscop* adj knee
3. meniscectomy ADJ arthroscop*
4. synovectomy ADJ arthroscop*
5. cruciate ligament AND (arthroscop* OR repair)
6. casts, surgical/ OR casts, surgical.mp
7. plaster cast.mp
8. splint*.mp OR splints/

9. Achilles ADJ tendon
10. tibial plateau fracture.mp
11. distal ADJ femur fracture.mp
12. lumbar ADJ laminectomy.mp
13. lumbar ADJ diskectomy.mp
14. lumbar ADJ spinal fusion.mp
15. (fracture fixation, internal/ OR fracture fixation, intramedullary/) AND (femur OR femor* OR tibia* OR ankle OR foot)
16. osteotomy.mp AND (femur OR femor* OR tibia*)
17. or/1-16
18. anticoagulants/
19. aspirin/
20. aspirin.mp
21. clopidogrel.mp
22. ticlopidine.mp
23. prasugrel.mp
24. heparin/
25. heparinoids/
26. heparin.mp
27. UFH.mp
28. heparin, low-molecular weight/
29. low molecular weight heparin.mp
30. LMWH.mp
31. enoxaparin.mp
32. dalteparin.mp
33. nadroparin.mp
34. ardeparin.mp
35. bemiparin.mp
36. certoparin.mp
37. parnaparin.mp
38. reviparin.mp
39. tinzaparin.mp
40. danaparoid.mp
41. fondaparinux.mp
42. idraparinux.mp
43. rivaroxaban.mp
44. hirudins/
45. desirudin.mp
46. argatroban.mp
47. bivalirudin.mp
48. lepirudin.mp
49. dabigatran.mp
50. warfarin/
51. 4-Hydroxycoumarins/
52. warfarin.mp
53. acenocoumarol.mp

54. dicoumarol.mp
55. dextran sulfate/
56. dextran sulfate.mp
57. or/18-56
58. stockings, compression/
59. compression stocking.mp
60. compression stockings.mp
61. compression boot.mp
62. graduated compression stocking.mp
63. graduated compression stockings.mp
64. elastic stocking.mp
65. elastic stockings.mp
66. graduated compression stocking.mp
67. graduated compression stockings.mp
68. GCS.mp
69. venous foot pump.mp
70. VFP.mp
71. intermittent pneumatic compression devices/
72. intermittent pneumatic compression.mp
73. pneumatic compression stocking.mp
74. pneumatic compression stockings.mp
75. pneumatic hose.mp
76. pneumatic compression hose.mp
77. IPC.mp
78. or/58-77
79. pulmonary embolism/
80. pulmonary embol*.mp
81. pulmonary thromboembol*.mp
82. PE.mp
83. deep vein thrombos*.mp
84. deep venous thrombos*.mp
85. deep venous thromboembol*.mp
86. deep vein thromboembol*.mp
87. DVT
88. venous thromboembolism/
89. venous thromboembol*.mp
90. VTE
91. venous thrombosis/
92. venous thrombos*.mp
93. clot.mp
94. or/79-93
95. 57 or 78
96. 17 and 94 and 95

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((((((lumbar PRE/1 spinal fusion) OR (lumbar PRE/1 diskectomy) OR (lumbar PRE/1 laminectomy) OR (open reduction internal fixation PRE/1 ankle) OR (open reduction internal fixation PRE/1 foot))) OR (((open reduction internal fixation PRE/1 tibia*) OR (open reduction internal fixation PRE/1 femur*) OR (osteotomy PRE/1 femur*) OR (osteotomy PRE/1 tibia*) OR (distal PRE/1 femur* fracture) OR (tibial plateau fracture) OR (intermedullary fixation))))) AND (((((ALL(deep vein thrombos*)) OR (ALL(deep venous thrombos*)) OR (ALL(venous thromboembol*)) OR (ALL(deep vein thrombos*)) OR (ALL(deep venous thrombos*)))) OR (((ALL(venous thromboembol*)) OR (ALL(pulmonary thromboembol*)) OR (ALL(pulmonary embol*)) OR (ALL(venous thrombos*)))))

Appendix B. Data Extraction Form

VTE Prophylaxis in Orthopedic Surgery CER Key Questions 1, 3-9

STUDY IDENTIFICATION

Unique ID:	**First author's name, publication year:**	**Study acronym (if applicable):**	**Publication format:** ❑ Full text manuscript ❑ Abstract ❑ Other (specify):

Funding Source (specify): ☐ Industry ☐ Government/Foundation ☐ Academia ☐ Other/Unknown	**Geographic location:**	**Number of Centers:**	**Total N randomized (N randomized in arms we use):**

STUDY DESIGN AND QUALITY CHARACTERISTICS

(Select either RCT or observational and complete corresponding section, if you answer N report why)

❑ Randomized controlled trial	
Were the groups similar baseline in terms of baseline characteristics? Y ☐ N ☐ Partially ☐ Can't tell ☐	Were outcomes assessed using a valid methodology and criteria? Y ☐ N ☐ Partially ☐ Can't tell ☐
Were subjects and providers blind to intervention status of participants? Y ☐ N ☐ Partially ☐ Can't tell ☐	Were outcome assessors blind to intervention status? Y ☐ N ☐ Partially ☐ Can't tell ☐
Randomization technique described:	Outcome assessment described:
Was intention to treat analysis used? Y ☐ N ☐	
Were methods used for randomization adequate? Y ☐ N ☐ Partially ☐ Can't tell ☐	Was incomplete data adequately addressed? Y ☐ N ☐ Partially ☐ Can't tell ☐
Was allocation concealment adequate? Y ☐ N ☐	Conflicts of interest reported and insignificant? Y ☐ N ☐

Partially ☐ Can't tell ☐	Partially ☐ Can't tell ☐
Was the differential loss to followup between groups <10%? Y ☐ N ☐	Was the overall loss to followup <20%? Y ☐ N ☐
Duration of followup (longest):	Followup % for the primary outcome: Intervention Comparator
Overall quality score (use protocol for criteria): good☐ fair☐ poor☐	

❑ **Controlled observational study (specify design in detail):**			
Unbiased selection of cohort: Y ☐ N ☐ Partially ☐ Can't tell ☐	Selection minimizes baseline differences: Y ☐ N ☐ Partially ☐ Can't tell ☐	Blinded outcome assessment: Y ☐ N ☐ Partially ☐ Can't tell ☐	Outcome assessment described:
Sample size calculated: Y ☐ N ☐ Partially ☐ Can't tell ☐	Adequate description of cohort: Y ☐ N ☐ Partially ☐ Can't tell ☐	Validated method to ascertain exposure: Y ☐ N ☐ Partially ☐ Can't tell ☐	Validated method to ascertain outcomes: Y ☐ N ☐ Partially ☐ Can't tell ☐
Adequate followup period: Y ☐ N ☐ Partially ☐ Can't tell ☐	Completeness of followup: Y ☐ N ☐ Partially ☐ Can't tell ☐	Adequate analysis to control for confounding: Y ☐ N ☐ Partially ☐ Can't tell ☐	Covariates/potential confounders adjusted for:
Overall quality score (use protocol for criteria): good☐ fair☐ poor☐			

Diagnosis of DVT and PE
(describe protocol including diagnostic tests, timing, if symptoms were required for screening)

DVT	☐ Venography ☐ Ultrasound ☐ Other:
PE	☐ Angiography ☐ CT scan ☐ Other: ☐ VQ Scan plus [❑ PIOPED ❑ Biello et al. ❑ Clinical suspicion]

PATIENT POPULATION

Surgical procedure (If more than 1 of the three surgeries please indicate n/N (%) for each surgery):
❑ Total hip replacement ❑ Total knee replacement ❑ Hip fracture surgery

Surgical procedure (If more than 1 of the three surgeries please indicate n/N (%) for each surgery):
❑ Knee arthroscopy
Specify types of surgeries included:
❑ Elective spine surgery
Specify types of surgeries included:

❑ Surgical repair of lower extremity injury distal to the hip Specify types of surgeries included:	
Inclusion criteria:	**Exclusion criteria:**

STUDY INTERVENTION

❑ Pharmacologic agent versus placebo ❑ Mechanical agent versus placebo
❑ Pharmacologic agent versus pharmacologic agent ❑ Mechanical agent versus mechanical agent
❑ Pharmacologic agent versus mechanical agent ❑ Mechanical agent versus IVC filter
❑ Pharmacologic agent versus pharmacological + mechanical agents (or vice versa)* ❑ Others (SPECIFY) ❑ Prolonged versus standard duration pharmacological prophylaxis

*When combination therapy is compared to a mono-therapy, indicate in the box below which interventions are working as a combination therapy.

Please specify the intervention(s) below:

Intervention 1	Intervention 2	Intervention 3	Intervention 4
	Placebo ❑	Placebo ❑	Placebo ❑
Pharmacologic Class:	Pharmacologic Class:	Pharmacologic Class:	Pharmacologic Class:
Drug name:	Drug name:	Drug name:	Drug name:
Dose:	Dose:	Dose:	Dose:
Route:	Route:	Route:	Route:
Frequency:	Frequency:	Frequency:	Frequency:
Timing of first dose:	Timing of first dose:	Timing of first dose:	Timing of first dose:
Duration of therapy (no. days):	Duration of therapy (no. days):	Duration of therapy (no. days):	Duration of therapy (no. days):
Other (ex. INR goals):	Other (ex. INR goals):	Other (ex. INR goals):	Other (ex. INR goals):
Mechanical Intervention Product name:	Mechanical Intervention Product name	Mechanical Intervention Product name:	Mechanical Intervention Product name:

Initiation relative to surgery:	Initiation relative to surgery:	Initiation relative to surgery:	Initiation relative to surgery:
Duration applied /d:	Duration applied /d:	Duration applied /d:	Duration applied /d:
Total duration of therapy:	Total duration of therapy:	Total duration of therapy:	Total duration of therapy:
Inferior vena cava filter intervention Device name:	Inferior vena cava filter intervention Device name:	Inferior vena cava filter intervention Device name:	Inferior vena cava filter intervention Device name:

CONCURRENT STANDARD THERAPIES / INTERVENTIONS
(therapies which were given to all patients regardless of arm to which they were randomized)

Concurrent mechanical (e.g. stockings):	**Mobilization regimen:**	**Concurrent medications:**
Other:		

PATIENT CHARACTERISTICS

Characteristic	**Intervention 1**	**Intervention 2**	**Intervention 3**	**Intervention 4**
Number of participants (N)				
Age (mean±SD, median IQR)				
Females n/N (%)				
Race n/N (%) • White				
• Black				
• Hispanic				
• Asian				
• Other				
Weight (mean ± SD, range)				
BMI (mean ± SD, range)				
Smoker n/N (%)				

Characteristic	Intervention 1	Intervention 2	Intervention 3	Intervention 4
Obesity n/N (%)				
History of VTE n/N (%)				
Varicosity n/N (%)				
Estrogen intake n/N (%)				
Diabetes n/N (%)				
Cancer n/N (%)				
CHF n/N (%)				
COPD n/N (%)				
CVD n/N (%)				
Previous orthopedic surgery n/N (%)				
Multiple risk factors present (3+ or specify) n/N (%)				

SURGICAL CHARACTERISTICS

Characteristic	Intervention 1	Intervention 2	Intervention 3	Intervention 4
Primary surgery n/N (%)				
Revision surgery n/N (%)				
Cemented fixation n/N (%)				
Tourniquet use n/N (%)				
Anterolateral approach n/N (%)				
Posteriolateral approach n/N (%)				
Autologous blood transfusion n/N (%)				
Duration of surgery in min (mean ± SD, range)				
Duration of anesthesia in min (mean ± SD, range)				
General anesthesia n/N (%)				
Regional				

Characteristic	Intervention 1	Intervention 2	Intervention 3	Intervention 4
anesthesia n/N (%)				
General and regional anesthesia n/N (%)				
Hospital LOS Mean (SD)				

FINAL HEALTH OUTCOMES (report both n/N (%) and hazard ratios when available for all outcomes)

Outcome	Definition	Time point	Intervention 1	Intervention 2	Intervention 3	Intervention 4
Symptomatic objectively confirmed VTE						
Major VTE (proximal DVT, non-fatal PE, or VTE related mortality)						
Fatal PE						
Non-fatal PE						
PE not otherwise specified (fatal or not)						
Post-thrombotic syndrome						
Mortality due to bleeding						
Total Mortality						
Health related QOL Scale:						

INTERMEDIATE HEALTH OUTCOMES (report both n/N (%) and hazard ratios when available for all outcomes)

Outcome	Definition	Time point	Intervention 1	Intervention 2	Intervention 3	Intervention 4
Total DVT (asymptomatic, symptomatic, distal, or proximal)						
Asymptomatic DVT						
Symptomatic DVT						

Outcome	Definition	Time point	Intervention 1	Intervention 2	Intervention 3	Intervention 4
Proximal DVT						
Distal DVT						

ADVERSE OUTCOMES (report both n/N (%) and hazard ratios when available for all outcomes)

Outcome	Definition	Time point	Intervention 1	Intervention 2	Intervention 3	Intervention 4
Major bleeding						
Minor bleeding						
Major bleeding leading to re-operation						
Surgical site bleeding						
Bleeding leading to infection						
Bleeding leading to transfusion						
Heparin-induced thrombocytopenia						
Discomfort						
Re-admission						
Re-operation						
IVC filter placement-associated insertion site thrombosis						

Does This trial or study have sub group analysis looking at age, gender and ethnicity? ☐ Yes ☐ No If yes, report data:

Does this trial or study have information that might be used to answer
KQ2?
KQ1?
KQ3?
If yes, please print a copy of the article and put into the correct pile for KQ1, 2 or 3.

Appendix C. Excluded Studies from Full-Text Review

Table 1. Excluded studies at the full text level from search one

Excluded as a duplicate publication (n=21)
Anders JO, Fuhrmann R, Roth A, et al. How can we deereose the number of thrombosis and pulmonary embolism in total hip replacement? Z Orthop Ihre 2004;142:328-32.
Banssillon V, Dejour H, Besson L, et al. Prevention of deep venous thromboses (DVT) in orthopaedic surgery for total hip replacement (THR). Randomised dose-ranging trial. ANN-CHIR 1987;41:377-85.
Bergqvist D, Breddin K, Ten Cate JW, et al. Thromboprophylaxis in hip fracture surgery: A pilot study comparing danaparoid, enoxaparin and dalteparin. Haemostasis 1999;29:310-7.
Camporese G, Bernardi E, Prandoni P, et al. Low-molecular-weight heparin versus compression stockings for thromboprophylaxis after knee arthroscopy: a randomized trial. Ann Intern Med 2008;149:73-82.
Enyart JJ, Jones RJ. Low-dose warfarin for prevention of symptomatic thromboembolism after orthopedic surgery. Ann Pharmacother 2005;39:1002-7.
Friksson BI, Ekman S, Lindbratt S, et al. Prevention of thromboembolism with use of recombinant hirudin. Results of a double-blind, multicenter trial comparing the efficacy of desirudin (revase) with Thai of unfractionated heparin in patients having a total hip replacement. Journal of Bone and Joint Surgery - Series A 1997;79:326-33.
Handoll HH, Farrar MJ, McBirnie J, et al. Heparin, low molecular weight heparin and physical methods for preventing deep vein thrombosis and pulmonary embolism following surgery for hip fractures. Cochrane database of systematic reviews (Online : Update Software) 2000.
Kakkar AK, Brenner B, Dahl OE, et al. Lancet 2008;372:31-9.
Kim YH, Choi IY, Park MR, et al. Deep vein thrombosis after uncemented total hip replacement. Bull Hosp Jt Dis 1997;56:133-9.
Lassen MR, Ageno W, Borris LC, et al. N Engl J Med 2008;358:2776-86.
Navarro-Quilis A, Castellet E, Rocha E, et al. Efficacy and safety of bemiparin compared with enoxaparin in the prevention of venous thromboembolism after total knee arthroplasty: a randomized, double-blind clinical trial. J Thromb Haemost 2003;1:425-32.
Paiement GD, Wessinger SJ, Walter AC, et al. Low dose warfarin versus external pneumatic compression against venous thromboembolism following total hip replacement. J Arthroplasty 1987;2:23-6.
Patel A, Couband D, Feron JM, et al. Prevention of deep venous thrombosis in arthroplastic surgery of the hip by the combination of heparinotherapy and the antithrombosis stocking. Presse medicale (Paris 1983;France.
Planes A, Vochelle N, Mazas F, et al. Enoxaparin versus standard heparin in the prophylaxis of deep vein thrombosis after total hip replacement: A double-blind randomized trial. Rev Med Interne 1988;9:327-33.
Rader CP, Kramer C, Hendrich C, et al. Experiences with an ankle joint moving device in thromboprophylaxis after total knee arthroplasty. Z Orthop Ihre 1998;136:467-70.
RE-MOBILIZE Writing C, Ginsberg JS, Davidson BL, et al. Oral thrombin inhibitor dabigatran etexilate vs North American enoxaparin regimen for prevention of venous thromboembolism after knee arthroplasty surgery. J Arthroplasty 2009;24:1-9.
Sevestre MA, Labarere J, Brin S, et al. Optimizing history taking for evaluating the risk of venous thromboembolism: The OPTIMEV study. J Mal Vasc 2005;30:217-27.
The German Hip Arthroplasty Trial,Group. Prevention of deep vein thrombosis with low molecular-weight heparin in patients undergoing total hip replacement. Arch Orthop Trauma Surg 1992;111:110-20.
Tian H, Song F, Zhang K, et al. Efficacy and safety of aspirin in prevention of venous thromboembolism after total joint arthroplasty. National Medical Journal of China 2007;87:3349-52.
Turpie AG, Lassen MR, Davidson BL, et al. Lancet 2009;373:1673-80.

Welin-Berger T, Bygdeman S, Mebius C. Deep vein thrombosis following hip surgery. Relation to activated factor X inhibitor activity: effect of heparin and dextran. Acta Orthop Scand 1982;53:937-45.

Excluded as a publication prior to 1980 (n=4)
Hull RD, Raskob GE, Gent M, et al. Effectiveness of intermittent pneumatic leg compression for preventing deep vein thrombosis after total hip replacement. J Am Med Assoc 1990;263:2313-7.
Lahnborg G. Effect of low-dose heparin and dihydroergotamine on frequency of postoperative deep-vein thrombosis in patients undergoing post-traumatic hip surgery. Acta Chir Scand 1980;146:319-22.
Paiement GD, Schutzer SF, Wessinger SJ, et al. Influence of prophylaxis on proximal venous thrombus formation after total hip arthroplasty. J Arthroplasty 1992;7:471-5.
Sarmiento A, Goswami AD. Thromboembolic prophylaxis with use of aspirin, exercise, and graded elastic stockings or intermittent compression devices in patients managed with total hip arthroplasty. J Bone Joint Surg Am 1999;81:339-46.

Excluded because citation was not a full text systematic review, study or trial (n=190)
Abdool-Carrim T, Adler H, Becker P, et al. The cost and benefit of prophylaxis against deep vein thrombosis in elective hip replacement. DVT/PE Prophylaxis Consensus Forum. SAMJ, S Afr med j 1997;87:594-600.
Adequate prophylaxis reduces deaths from venous thromboembolism. Drugs and Therapy Perspectives 1996;8:11-3.
Agnelli G, Cimminiello C. Prevention of venous thromboembolism in orthopedic surgery and traumatology. Recenti Prog Med 2007;98:25S-32S.
Agnelli G, Sonaglia F. Clinical status of direct thrombin inhibitors. Crit Rev Oncol 1999;31:97-117.
Agudelo JF, Morgan SJ, Smith WR. Venous thromboembolism in orthopedic trauma patients. Orthopedics 2005;28:1164-71.
Ahmed A. Prevention of deep vein thrombosis and pulmonary embolism in the perioperative period: A review. Journal of the Pakistan Medical Association 2005;55:343-7.
Alexander P, Giangola G. Deep venous thrombosis and pulmonary embolism: Diagnosis, prophylaxis, and treatment. Ann Vasc Surg 1999;13:318-27.
Alhenc-Gelas M. Heparin induced thrombocytopenia: Is it over? Revue Francophone des Laboratoires 2008;38:12-4.
Anbar M. Shifting from phenomenological thermography to pathophysiology based thermal imaging. IEEE Engineering in Medicine and Biology Magazine 1998;17:25-33.
Andreozzi GM, Mannucci P, Nuzzaci G, et al. Linee-guida per la diagnosi e il trattamento della trombosi venosa profonda. Minerva Cardioangiol 2000;48:201-75.
Annemans L, Minjoulat-Rey MC, De Knock M, et al. Cost consequence analysis of fondaparinux versus enoxaparin in the prevention of venous thromboembolism after major orthopaedic surgery in Belgium. Acta Clin Belg 2004;59:346-57.
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Ardeparin and danaparoid for prevention of deep vein thrombosis. Med Lett Drugs Ther 1997;39:94-5.
Arora VM, McGory ML, Fung CH. Quality indicators for hospitalization and surgery in vulnerable elders. J Am Geriatr Soc 2007;55.
Barrellier MT. Thromboprophylaxis and total hip replacement: A cost-efficacy study comparing duplex screening of asymptomatic venous thrombosis versus prolonged prophylaxis with low-molecular-weight heparins. Phlebology 2002;17:93-7.
Bauer KA, Eriksson BI, Lassen MR, et al. Influence of the duration of fondaparinux prophylaxis in preventing venous thromboembolism following hip fracture surgery. Blood 2002;100.
Berger R. Comparing options for preventing PE: Pneumatic compression vs anticoagulation. J Crit Illn 2001;16:9-11.
Bergqvist D. Inferior vena cava filters. World J Surg 2007;31:265-6.
Bergqvist D, Jonsson B. Cost-effectiveness of prolonged out-of-hospital prophylaxis with low-molecular-

weight heparin following total hip replacement. Haemostasis 2000;30:130-5.
Berry DJ. DVT prophylaxis after THA is safe and effective. Orthopedics 2000;23:1028-30.
Bjorvatn A, Kristiansen F. Fondaparinux sodium compared with enoxaparin sodium: a cost-effectiveness analysis. Am J Cardiovasc Drugs 2005;5:121-30.
Borris LC, Hauch O, Jorgensen LN, et al. Low molecular weight heparin (Enoxaparin) versus Dextran 70 in the prevention of postoperative deep vein thrombosis after total hip replacement: A Danish multicenter study [Abstract]. Acta Orthop Scand 1990;61:52.
Borris LC, Petersen MB, Lassen MR. Prevention of thrombosis in hip alloplasty. Ugeskr Laeger 2001;163:934-5.
Botteman MF, Caprini J, Stephens JM, et al. Results of an economic model to assess the cost-effectiveness of enoxaparin, a low-molecular-weight heparin, versus warfarin for the prophylaxis of deep vein thrombosis and associated long-term complications in total hip replacement surgery in the United States. Clin Ther 2002;24:1960-86.
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Brand RA. 50 Years ago in CORR: Postspinal anesthesia osteomyelitis of the lumbar spine P. L. Day MD and J. J. Hinchey MD CORR 1958;11:185-193. Clin Orthop 2008;466:1755-6.
Capri S, Ageno W, Imberti D, et al. Extended prophylaxis of venous thromboembolism with fondaparinux in patients undergoing major orthopaedic surgery in Italy: A cost-effectiveness analysis. Internal and Emergency Medicine 2010;5:33-40.
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Cohen AT, Hirst C, Sherrill B, et al. Meta-analysis of trials comparing ximelagatran with low molecular weight heparin for prevention of venous thromboembolism after major orthopaedic surgery. Br J Surg 2005;92:1335-44.
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Eriksson BI. A multicenter, randomized, placebo-controlled, double-blind study of fondaparinux for the prolonged prevention of venous thromboembolism in hip fracture surgery. Abstracts of the Sicot/Sirot XXII World Congress 2002;318p.
Eriksson BI, Dahl OE, van Dijk CN, et al. A New Oral Aniticoagulant, Dabigatran Etexilate, Is Effective and Safe in Preventing Venous Thromboembolism after Total Knee Replacement Surgery (The RE-MODEL Trial) [abstract]. Blood 2006;108:173.
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Table 2. Excluded studies at the full text level from search two

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Appendix D. Quality and characteristics of included trials and studies

Table 3. Quality and characteristics of randomized controlled trials in major orthopedic surgery

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Fuji, 2010	Publication type: Full text Geographic location: Japan Funding: Industry Number of centers: 38 Randomization and allocation concealment: Randomized into 4 treatment groups using a computer-generated scheme stratified by study center in block of 4 Outcome assessment: Diagnostic tests for VTE were evaluated centrally by an independent adjudication committee blinded to treatment allocation, two medical experts reviewed all cases of bleeding Total number randomized: 512 (379)	Inclusion criteria: Age ≥20y; weight ≥40kg; primary, unilateral elective TKA; signed, informed consent Exclusion criteria: Any bleeding diathesis; major surgery, trauma, uncontrolled HTN, MI in last 3m; clinically relevant bleeding, gastric/duodenal ulcer in last 6m; hx hemorrhagic stroke or acute intracranial bleeding; hx VTE or preexisting condition requiring anticoagulant therapy; severe liver disease or elevated AST or ALT >2xULN; significant renal disease; treatment with anticoagulants, antiplatelet agents, or NSAIDs with a half-life of >12h within 7d before TKA; anticipated requirement for IPC of lower limb; pregnancy, women of child-bearing potential; hx TCP; previous leg amputation; active malignant disease Intervention 1: Dabigatran 150mg po at least 2h after removing indwelling catheter + confirming absence of abnormal bleeding at drainage site, 150mg 8h+ after first dose then QD at 8AM for 11-14d postoperatively Intervention 2: Dabigatran 220mg po at least 2h after removing indwelling catheter and confirming absence of abnormal bleeding at drainage site, 220mg 8h or more after the first dose, then QD at 8AM for 11-14d postoperatively Comparator: Placebo capsules	Duration of followup: post-operative Followup: Dabigatran 150mg 82.54%; 220mg 74.42%; placebo 81.45% Final: Major VTE, PE, fatal PE, nonfatal PE, mortality, mortality due to bleeding (post-operative) Intermediate: DVT, asymptomatic DVT, symptomatic DVT, proximal DVT (post-operative) Adverse events: Major bleeding, minor bleeding, major bleeding leading to reoperation, bleeding leading to transfusion (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Partially 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? No 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Chin, 2009	Publication type: Full text Geographic location: Singapore Funding: NR Number of centers: 1 Randomization and allocation concealment: NR Outcome assessment: Bilateral DUS was carried out by ultrasonographers blinded to the prophylactic method used Total number randomized: 440 (220)	Inclusion criteria: Elective TKA; low-risk patients and those without predisposition to thromboembolism Exclusion criteria: Use of anticoagulants or aspirin; history of PE or DVT in the previous year; obesity; pre-operative prolonged immobilization or wheelchair bound; bleeding tendency or a history of GI bleeding; surgery in the previous 6m; CVA in the previous 3m; uncontrolled HTN; CHF; renal or liver impairment; allergy to heparin or HIT; varicose veins or CVI; PVD; skin ulcers; dermatitis or wounds; malignancy Intervention: Enoxaparin 40mg/d SQ started postoperatively until 5-7d or if DVT or PE suspected Comparator: Control	Duration of followup: Post-operative Followup: 100% in all arms Final: PE (post-operative) Intermediate: DVT, proximal DVT, distal DVT (post–operative) Adverse events: Bleeding complications (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Partially 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Ginsberg, 2009 RE-MOBILIZE	Publication type: Full text Geographic location: Canada, Mexico, USA, UK Funding: Industry Number of centers: 97 Randomization and allocation concealment: Randomly assigned to 1 of 3 treatment groups after surgery using an Interactive Voice Response System in blocks of 6 based on an independently generated scheme Outcome assessment: Diagnostic tests for VTE events were initially evaluated locally, subsequently reviewed by an independent central adjudication committee blinded to treatment allocation. An independent expert adjudication committee classified all bleeding events Total number randomized (number randomized in arms of interest): 2615 (2615)	Inclusion criteria: ≥18y and >40 kg, scheduled for primary elective unilateral TKA Exclusion criteria: Known inherited or acquired clinically significant bleeding disorder; major surgery, trauma, uncontrolled HTN or MI < 3m; hx of acute intracranial disease or hemorrhagic stroke; GI or urogenital bleeding or ulcer disease < 6m;severe liver disease; ALT or AST > 2X ULN range < last m; severe renal insufficiency; concomitant long acting NSAID therapy or anticoagulant during study drug treatment; active malignant disease; platelet count< 100 × 10^9/L; pregnant; nursing, or premenopausal women of child-bearing potential who were not practicing effective birth control; failure to provide informed consent Intervention 1: Dabigatran 75mg PO starting 6-12h post-operative followed by 150mg PO QD for a total duration of 12-15d post-operative Intervention 2: Dabigatran 110mg PO starting 6-12h post-operative followed by 220mg PO QD for a total duration of 12-15d post-operative Intervention 3: Enoxaparin 30mg SQ BID starting 12-24h post-operative for a total duration of 12-15d post-operative	Duration of followup: 90d Followup: 100% in all arms Final: Mortality due to bleeding, mortality (post-operative) Intermediate: Symptomatic DVT, proximal DVT, distal DVT (post-operative) Adverse events: Major bleeding, minor bleeding (post-operative during study period, post study period-90d); major bleeding leading to re-operation, surgical site bleeding (post-operative during study period)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Edwards, 2008	Publication type: Full text Geographic location: USA Funding: Industry Number of centers: NR Randomization and allocation concealment: NR Outcome assessment: Diagnosis of PE was adjudicated by a separate committee Total number randomized: 277 (277)	Inclusion criteria: Patients undergoing THA or TKA Exclusion criteria: Protocol violations such as missed ultrasound; surgery other than THA or TKA; previous history of thrombosis; prophylaxis other than LMWH Intervention: Enoxaparin 30 mg Q12h SQ from the morning after surgery until 7-8th post-operative day + IPC (ActiveCare DVT) on the calves of the patients in the operation room and worn until discharge Comparator: Enoxaparin 30 mg Q12h SQ from the morning after surgery until 7-8th post-operative day	Duration of followup: 90d Followup: 100% in all arms Final: PE, fatal PE, nonfatal PE (90d); mortality, mortality due to bleeding (post-operative) Intermediate: DVT, proximal DVT, distal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Partially 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Fuji, 2008 THA	Publication type: Full text Geographic location: Japan Funding: Industry Number of centers: 51 Randomization and allocation concealment: 1:1 ratio Outcome assessment: Objective tests for DVT and PE were centrally adjudicated by an independent expert panel blinded to treatment group; intra-abdominal or intracranial bleeding confirmed by US, CT, or MRI Total number randomized: 421 (421)	Inclusion criteria: Primary elective THA; ≥20y Exclusion criteria: Revision THA; CI to heparin therapy; positive clinical evidence of chronic postphlebitic syndrome or acute DVT within 12m of study drug treatment; allergy to iodine or contrast medium; CrCl <30 mL/min or plasma Cr level >1.5mg/dl; severe hepatic disease; uncontrolled HTN; illicit drug use of alcohol abuse; treatment with other investigation agents within 3m of surgery; failure to achieve post-operative hemostasis; females if pregnant or breastfeeding Intervention 1: Enoxaparin 40mg SQ daily starting 24-36h postoperatively for 14d Intervention 2: Enoxaparin 20mg SQ BID starting 24-36h postoperatively for 14d Comparator: Placebo (saline) injections	Duration of followup: Post-operative Followup: Enoxaparin 40mg 74.8%; enoxaparin 20mg 85.7%; placebo 81.9% Final: PE (during treatment period) Intermediate: DVT, proximal DVT (during treatment period) Adverse events: Major bleeding, minor bleeding (during treatment period)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Partially 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Fuji, 2008 TKA	Publication type: Full text Geographic location: Japan Funding: Industry Number of centers: 51 Randomization and allocation concealment: 1:1 ratio Outcome assessment: Objective tests for DVT and PE were centrally adjudicated by an independent expert panel blinded to treatment group; intra-abdominal or intracranial bleeding confirmed by US, CT, or MRI Total number randomized: 382 (382)	Inclusion criteria: Primary TKA; ≥20y Exclusion criteria: Revision TKA; CI to heparin therapy; positive clinical evidence of chronic postphlebitic syndrome or acute DVT within 12m of study drug treatment; allergy to iodine or contrast medium; CrCL <30 mL/min or plasma Cr >1.5 mg/dL; severe hepatic disease; uncontrolled HTN; illicit drug use of alcohol abuse; treatment with other investigation agents within 3m of surgery; failure to achieve post-operative hemostasis; females if pregnant or breastfeeding Intervention 1: Enoxaparin 40mg SQ daily starting 24-36h postoperatively for 14d Intervention 2: Enoxaparin 20mg SQ BID starting 24-36h postoperatively for 14d Comparator: Placebo (saline) injections	Duration of followup: During treatment period Followup: Enoxaparin 40mg 78.7%; enoxaparin 20mg 84.8%; placebo 82.3% Final: PE (during treatment period) Intermediate: DVT, proximal DVT (during treatment period) Adverse events: Major bleeding, minor bleeding (during treatment period)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Partially 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Thorey, 2008	Publication type: Full text Geographic location: Germany Funding: Unknown Number of centers: 1 Randomization and allocation concealment: NR Outcome assessment: NR Total number randomized (number randomized in arms of interest): 20 (20)	Inclusion criteria Patients undergoing simultaneous bilateral cemented TKA Exclusion criteria History of DVT; musculoskeletal infection in the lower extremities; bleeding diathesis; neurological problems; PVD Intervention 1: Tourniquet release and hemostasis before wound closure Intervention 2: Tourniquet release after wound closure and pressure dressing	Duration of followup: 180d Followup: 100% Final: NR Intermediate: DVT, asymptomatic DVT, symptomatic DVT, proximal DVT, distal DVT (180d) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Can't tell 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Poor

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Eriksson, 2007a RE-MODEL	Publication type: Full text Geographic location: Australia, Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Hungary, Italy, Poland, Netherlands, South Africa, Spain, Sweden Funding: Industry Number of centers: 105 Randomization and allocation concealment: Randomly assigned using a computer-generated central scheme stratified by study center in blocks of 6 Outcome assessment: All VTE and bleeding events reviewed by an independent central adjudication committee blinded to treatment allocation Total number randomized (number randomized in arms of interest): 2101 (2101)	Inclusion criteria ≥18y and >40 kg, scheduled for primary elective unilateral TKA Exclusion criteria Any bleeding diathesis; hx of acute intracranial disease or hemorrhagic stroke; major surgery, trauma, uncontrolled HTN or MI within the past 3m; GI or urogenital bleeding or ulcer disease within the past 6m; severe liver disease; AST or ALT levels >2 X ULN range within the past m; severe renal insufficiency; concomitant long-acting NSAID therapy; active malignant disease; and being female and of childbearing potential Intervention 1: Dabigatran 75mg PO starting 1-4h post-operative followed by 150mg PO QD for 6-10d post-operative Intervention 2: Dabigatran 110mg PO starting 1-4h post-operative followed by 220mg PO QD for 6-10d post-operative Intervention 3: Enoxaparin 40mg SQ QD starting evening before surgery (post-operative in some countries) for 6-10d post-operative	Duration of followup: 90d Followup: Dabigatran 150mg 88.90% Dabigatran 220mg 89.4% Enoxaparin 88.76% Final: Major VTE, fatal PE, nonfatal PE, PE, mortality due to bleeding, mortality (post-operative) Intermediate: Asymptomatic DVT, symptomatic DVT (post-operative) Adverse events: Major bleeding, minor bleeding, major bleeding leading to re-operation, bleeding leading to transfusion (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? No 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Eriksson, 2007b RE-NOVATE	Publication type: Full text Geographic location: Australia, Belgium, Czech Republic, Denmark, Finland, France, Germany, Hungary, Italy, Netherlands, Norway, Poland, South Africa, Spain, Sweden Funding: Industry Number of centers: 115 Randomization and allocation concealment: Randomly assigned stratified by study center with a central computer generated scheme in blocks of 6, with the lowest number allocated sequentially Outcome assessment: Diagnostic tests for VTE events were initially assessed locally, then by an independent central adjudication committee blinded to treatment allocation. Bleeding outcomes classified by an independent, expert adjudication committee Total number randomized (number randomized in arms of interest): 3494 (3494)	Inclusion criteria ≥18 y, ≥40 kg scheduled for primary elective unilateral THR Exclusion criteria Any bleeding diathesis; hx of acute intracranial disease or hemorrhagic stroke; major surgery, trauma, uncontrolled HTN, or MI in the past 3m; GI or urogenital bleeding, or ulcer disease in the past 6m; severe liver disease; ALT or AST concentrations >2X ULN range in the past m; severe renal insufficiency; use of long-acting NSAID; childbearing potential; allergy to radiopaque contrast media or heparin; and active malignant disease; > 3 attempts or traumatic placement of spinal or epidural anesthesia Intervention 1: Dabigatran 75mg PO starting 1-4h post-operative followed by 150mg PO QD for 28-35d post-operative until venography Intervention 2: Dabigatran 110mg PO starting 1-4h post-operative followed by 220mg PO QD for 28-35d post-operative until venography Intervention 3: Enoxaparin 40mg SQ QD starting evening before surgery (post-operative in some countries) for 28-35d post-operative until venography	Duration of followup: 94d Followup: 100% in all arms Final: Major VTE, fatal PE, nonfatal PE, PE, mortality due to bleeding, mortality (post-operative) Intermediate: Asymptomatic DVT, symptomatic DVT (post-operative) Adverse events: Major bleeding, minor bleeding, major bleeding leading to re-operation, bleeding leading to transfusion (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Lassen, 2007	Publication type: Full text Geographic location: Argentina, Australia, Canada, Mexico, Denmark, Israel, Poland, USA Funding: NR Number of centers: 97 Randomization and allocation concealment: Computer-generated allocation Outcome assessment: Efficacy, bleeding events and cause of death were adjudicated by an independent central committee unaware of treatment assignments Total number randomized (number randomized in arms of interest): 1238 (458)	Inclusion criteria: 18-90y; scheduled for TKR Exclusion criteria: Female w/child-bearing potential; bleeding/coagulation disorders; history of HIT; intracranial/ intraocular hemorrhage w/in past 5y; GI bleeding, brain, spinal, ophthalmologic or major surgery/trauma w/in 90d of surgery; ulcer disease w/in 30d before surgery; known VTE disease w/in past 12m; uncontrolled HTN, wound or other bleeding; malignant disease; active hepatobiliary disease; known or suspected GI disease that may affect absorption of study medication; ALT, AST or bilirubin >1.5 ULN; INR >1.4 or APTT >1.4 control; hypersensitivity to UFH, LMWH, VKA, porcine products or iodinated venography contrast medium; treatment with medications affecting coagulation/platelet function w/in 7d prior to surgery; traumatic or difficult lumbar puncture; use of epidural or intrathecal catheter post-operative Intervention 1: Enoxaparin 30mg SQ Q12h 12-24h after skin wound closure then Q12h for 12 $\pm$ 2d Intervention 2: Warfarin 5mg PO daily in evening starting evening of surgery for 12 $\pm$ 2d	Duration of followup: Post-operative Followup: 100% in all arms Final: Fatal PE, non-fatal PE, mortality, mortality due to bleeding (post-operative) Intermediate: Asymptomatic DVT, symptomatic DVT, proximal DVT (post-operative) Adverse events: Major bleeding, minor bleeding (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Partially 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Bonneux, 2006	Publication type: Full text Geographic location: Belgium Funding: NR Number of centers: 1 Randomization and allocation concealment: Randomized using a computer program Outcome assessment: NR Total number randomized (number randomized in arms of interest): 120 (120)	Inclusion criteria: Disabling knee conditions requiring TKA or revision of at least one of the metal components of previous TKA Exclusion criteria: Known hypersensitivity to enoxaparin sodium, fondaparinux or to any of the excipients, heparin, pork products; infectious arthritis; acute bacterial endocarditis; severe renal impairment; active ulcerative GI disease; active clinically significant bleeding; congenital or acquired bleeding disorder; recent intracranial hemorrhage; shortly after brain, spinal or ophthalmic surgery; low body weight (<50kg); suspicion of infection of previous TKA Intervention 1: Fondaparinux 2.5mg QD starting 6-12h post-operative for a duration of 6wks Intervention 2: Enoxaparin 40mg QD starting evening before surgery for a duration of 6wks postoperatively	Duration of followup: 42d Followup: 90.83% overall Final: NR Intermediate: Symptomatic DVT (post-operative) Adverse events: Re-operation (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? No 9. Was the differential loss to followup between the compared groups low (< 10%)? Can't tell 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Senaran, 2006	Publication type: Full text Geographic location: Turkey Funding: Industry Number of centers: 1 Randomization and allocation concealment: Randomized to either treatment groups Outcome assessment: NR Total number randomized (number randomized in arms of interest): 100 (100)	Inclusion criteria: ≥18y scheduled for THA Exclusion criteria: Hx of blood dyscrasia, HIT; allergy to enoxaparin or heparin that would preclude anticoagulant therapy Intervention 1: Enoxaparin 40mg SQ QD starting 12h before surgery for a duration of 7-10d post-operative or until discharge Intervention 2: Heparin 5000 IU SQ q8h starting 12h before surgery for a duration of 7-10d post-operative or until discharge	Duration of followup: 42d Followup: 100% in both arms Final: Symptomatic objectively confirmed VTE (post-operative until discharge, discharge-42d); fatal PE, nonfatal PE, PE, mortality due to bleeding, mortality (42d) Intermediate: DVT (post-operative until discharge, discharge-42d) Adverse events: Major bleeding, minor bleeding, surgical site bleeding, HIT, re-admission (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Westrich, 2006	Publication type: Full text Geographic location: USA Funding: Unknown Number of center: 1 Randomization and allocation concealment: Patients were divided into two groups using random numbers Outcome assessment: NR Total number randomized (number randomized in arms of interest): 118 (118)	Inclusion criteria: Patients undergoing primary TKA Exclusion criteria: History of previous thromboembolism; patients undergoing revision arthroplasty; patients taking Coumadin preoperatively for other medical reasons Intervention 1: Procedure modified to minimize the total amount of time the knee was hyperflexed and dislocated, the knee was extended during preparation of the femoral and tibial sides not to allow the knee to be in the flexed state for more than 4 min Intervention 2: Procedure according to normal protocol, which kept the knee in extreme flexion and maintained dislocation for the duration of the exposure, as in a standard knee replacement (i.e., extended only after the trial components were inserted and the patella to be cut)	Duration of followup: Post-operative Followup: 100% in both arms Final: NR Intermediate: DVT, proximal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Poor

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Eriksson, 2005 BISTRO II	Publication type: Full text Geographic location: Austria, Belgium, Czech Republic, Denmark, Finland, France, Hungary, Italy, Netherlands, Norway, South Africa, Sweden Funding: Industry Number of centers: 60 Randomization and allocation concealment: Assigned randomly to 5 treatment groups, stratified by the study center and surgical procedure (hip or knee replacement), using a computer-generated scheme Outcome assessment: All tests for VTE during the treatment period were first evaluated locally and subsequently by an independent central adjudication committee blinded to the treatment allocation. A centralized independent committee classified all bleeding events Total number randomized (number randomized in arms of interest): 1973 (1973)	Inclusion criteria: ≥18y, ≥40 kg scheduled for primary elective THR or TKR Exclusion criteria: Any bleeding diathesis; coagulation disorders; hx of or acute intracranial disease; major surgery or trauma within the last 3m; CVD including uncontrolled HTN or hx of MI within the last 6m; hx of stroke; DVT, GI or pulmonary bleeding within the last year; known liver; renal disease; use of long-term anticoagulants, antiplatelet drugs (except low-dose aspirin up to 160 mg daily), or fibrinolytics within 7d prior to surgery; allergy to radiopaque contrast media; TCP; active malignant disease; current cytostatic treatment or recent treatment with an investigational drug; women of childbearing potential; those with leg amputations and known alcohol or drug abuse Intervention1: Dabigatran 50mg PO BID Intervention 2: Dabigatran 150mg PO BID Intervention 3: Dabigatran 300mg PO QD Intervention 4: Dabigatran 225mg PO BID All dabigatran doses started within 1-4h post-operative and continued until venography (6-10d) Intervention 5: Enoxaprin 40mg SQ QD starting 12h before surgery and continued until venography (6-10d)	Duration of followup: 28-42d Followup: 100% in all arms Final: VTE (post-operative) Intermediate: Proximal DVT, distal DVT (post-operative) Adverse events: Major bleeding (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Farag, 2005	Publication type: Full text Geographic location: USA Funding: Unknown Number of centers: 1 Randomization and allocation concealment: Patients were randomized using cards generated from a computer-generated random number list into two groups Outcome assessment: NR Total number randomized (number randomized in arms of interest): 38 (38)	Inclusion criteria: Patients scheduled for TKR Exclusion criteria: In the epidural group, patients were excluded from the study if the epidural catheter could not be placed or maintained for the full study interval Intervention 1: Spinal anesthesia: 0.5% bupivacaine and analgesia with intravenous morphine via patient-controlled analgesia demand mode only Intervention 2: Epidural anesthesia: 1.0% ropivacaine with 1:200000 epinephrine and analgesia with 0.2% ropivacaine at 8 mL/h, maintained for 7d	Duration of followup: 10d Followup: 100% in both arms Final: NR Intermediate: DVT, asymptomatic DVT, symptomatic DVT, proximal DVT, distal DVT (10d) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Lachiewicz, 2004	Publication type: Full text Geographic location: USA Funding: Industry Number of centers: 1 Randomization and allocation concealment: Randomized using sealed envelopes Outcome assessment: Ultrasonography of the calf and thigh, as far cranially as the inguinal ligament, was performed by experienced vascular technicians who were blinded to treatment allocation Total number randomized (number randomized in arms of interest): 423 (423)	Inclusion criteria: Patients who had undergone primary or revision TKA Exclusion criteria: Hemophilia; allergy to aspirin; removal of an infected knee arthroplasty Intervention 1: IPC (Venaflow) applied to contralateral limb in operating room before the procedure and operated limb at the end of the procedure and worn continuously for at least 12 – 16h/d except for bathing and physiotherapy Intervention 2: IPC (Kendal) applied to contralateral limb in operating room before the procedure and operated limb at the end of the procedure and worn continuously for at least 12 – 16h/d except for bathing and physiotherapy	Duration of followup: 180d Followup: 100% in both arms Final: Fatal PE, nonfatal PE, PE, mortality, mortality due to bleeding (postoperative) Intermediate: DVT, proximal DVT, distal DVT (postoperative); symptomatic DVT (discharge-180d) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5 adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Silbersack, 2004	Publication type: Full text Geographic location: Germany Funding: Industry Number of centers: 1 Randomization and allocation concealment: Randomly assigned to either group Outcome assessment: Duplex ulrasonography performed by a independent angiologist unaware of the method of prophylaxis Total number randomized (number randomized in arms of interest): 131 (131)	Inclusion criteria: Patients >18y awaiting primary unilateral THR or TKR Exclusion criteria: History of cardiac insufficiency (NYHA III/IV); stage III chronic renal insufficiency; severe peripheral arterial disease; acute thrombophlebitis; neurological disorders or arthrodeses of lower limb; recent anticoagulation; hemorrhagic diathesis; allergy to heparins; active malignant disease Intervention 1: Enoxaparin 40mg SQ daily, starting evening prior to surgery and continued until 30d post –operative + IPC (Venaflow) bilaterally after operation in the recovery room and worn continuously until post-operative day 10 whenever the patient is in bed Intervention 2: Enoxaparin 40mg SQ daily, starting evening prior to surgery and continued until 30d post-operative + GCS (Comprinet Pro) bilaterally after operation for a maximum of 90d if without thromboembolic complications	Duration of followup: 84d Followup: 100% in both arms Final: PE, fatal PE, nonfatal PE (42-84th post-operative days) Intermediate: DVT, proximal DVT; distal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Eriksson, 2003	Publication type: Full text Geographic location: Europe and South America Funding: Industry Number of centers: Multicenter Randomization and allocation concealment: computer-generated randomization list balanced in blocks of equal numbers and stratified by center Outcome assessment: All efficacy outcomes and the safety outcomes bleeding and death were adjudicated by a central independent committee, the members of which were unaware of the patients' treatment assignment Total number randomized (number randomized in arms of interest): 656 (656)	Inclusion criteria: ≥18y old; undergoing standard surgery for fracture of the upper third of the femur, including femoral head and neck; surgery planned within 48h after admission Exclusion criteria: Trauma affecting more than 1 organ system or if more than 24h had elapsed between the causative trauma and hospital admission; active bleeding; documented congenital or acquired bleeding disorder; current ulceration or angiodysplastic GI disease; hemorrhagic stroke or brain, spinal, or ophthalmological surgery < 3m; difficulty in performing epidural or spinal anesthesia; planned indwelling intrathecal or epidural catheter >6h after surgery; contraindication to anticoagulant therapy; pregnancy; hypersensitivity to contrast media; SCr> 2.0 mg/dL in a well-hydrated patient; long-term anticoagulant treatment for a chronic comorbid condition; receiving any type of anticoagulant or fibrinolytic therapy or dextran from admission to first study drug administration or surgery Intervention 1: Fondaparinux 2.5mg SQ started <2h after randomization, then continued QD for 25-31d Intervention 2: Fondaparinux 2.5mg SQ QD started <2h after randomization, continued for 6-8d after surgery, then placebo 19-23d	Duration of followup: 32d Followup: 100% in both arms Final: VTE, fatal PE, nonfatal PE, PE, mortality (32d) Intermediate: DVT, symptomatic DVT, proximal DVT, distal DVT (32d) Adverse events: Major bleeding, minor bleeding, major bleeding leading to re-operation, surgical site bleeding, bleeding leading to infection, bleeding leading to transfusion (32d)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Kim, 2003	Publication type: Full text Geographic location: Korea Funding: Unknown Number of centers: 1 Randomization and allocation concealment: Randomization between cemented and cementless replacements in both groups was determined from a sequential pool maintained by statisticians, based on a table of randomized numbers Outcome assessment: NR Total number randomized (number randomized in arms of interest): 200 (200)	Inclusion criteria: Patients who had primary THR Exclusion criteria: NR Intervention 1: Cemented replacement Intervention 2: Uncemented replacement	Duration of followup: 180d Followup: 100% in both arms Final: NR Intermediate: DVT, proximal DVT; distal DVT (180d) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Can't tell 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Lassen, 2002	Publication type: Full text Geographic location: 16 European countries Funding: Industry Number of centers: 73 Randomization and allocation concealment: Blocks of four by a computer generated randomization list Outcome assessment: Efficacy outcomes, including review of all venograms, bleeding, and death were judged by a central independent committee, unaware of the patients' treatment assignment Total number randomized (number randomized in arms of interest): 2309 (2309)	Inclusion criteria: ≥18y scheduled for primary elective THR, or revision of at least one component of a previously implanted total hip prosthesis Exclusion criteria: Bilateral hip surgery planned during the same procedure or within 2wks after inclusion. active bleeding; acute bacterial endocarditis; documented congenital or acquired bleeding disorder; current ulceration or angiodysplastic gastrointestinal disease; haemorrhagic stroke or brain, spinal, or ophthalmological surgery within previous 3m; planned indwelling intrathecal or epidural catheter > 6h after end of surgery; hypersensitivity to heparin, LMWHs, porcine products, or iodinated contrast media; CI to anticoagulant treatment; concomitant intake of any drug that could not be combined with contrast media; addictive disorders; SCr >180 mmol/L in a well-hydrated patient; and platelet <$100X10^9$/L; patients who needed anticoagulant treatment or who had received any type of anticoagulant or fibrinolytic therapy or dextran within 2d preceding the first administration of the study drug Intervention 1: Fondaparinux 2.5mg SQ, starting 6± 2h postoperatively, then 12h after first dose, continued q24h for 5-9d post-operative Intervention 2: Enoxaparin 40mg SQ, starting 12 ± 2h preoperatively, then 12-24h after first dose, continued q24h for 5-9d post-operative	Duration of followup: 49d Followup: Fondaparinux: 78.6% Enoxaparin: 79.6% Final: Symptomatic objectively confirmed VTE, mortality, nonfatal PE, fatal PE (49d); mortality due to bleeding (11d) Intermediate: DVT, symptomatic DVT, proximal DVT, distal DVT (11d) Adverse events: Major bleeding, major bleeding leading re-operation, surgical site bleeding (11d)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? No 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? No 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Pitto, 2002	Publication type: Full text Geographic location: Germany Funding: Industry Number of centers: 1 Randomization and allocation concealment: Computer generated random number sheets Outcome assessment: Duplex images were analyzed by an observer who was blinded with regard to the method of fixation of femoral component. Venography results were analyzed by a single experienced radiologist blinded to findings of duplex USS Total number randomized (number randomized in arms of interest): 130 (130)	Inclusion criteria: Patients scheduled to have primary THA Exclusion criteria: history or symptoms of deep-vein thrombosis or pulmonary embolism, esophageal disease, or metabolic bone disease or current, ongoing anticoagulation therapy Intervention: Bone vacuum cementing technique Comparator: Standard cementing technique	Duration of followup: 45d Followup: 100% in both arms Final: Fatal PE, nonfatal PE, PE (45d) Intermediate: DVT, proximal DVT, distal DVT (45d) Adverse events: Major bleeding, minor bleeding (45d)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Prandoni, 2002	Publication type: Full text Geographic location: Italy Funding: Unknown Number of centers: 1 Randomization and allocation concealment: Computer generated list was used for randomization Outcome assessment: Information on all suspected (both asymptomatic and symptomatic) outcome events was reviewed and classified by an independent adjudication committee whose members were unaware of the treatment assignment. Total number randomized (number randomized in arms of interest): 360 (360)	Inclusion criteria: Consecutive patients who underwent elective THA and received warfarin prophylaxis during hospitalization; no previous hip surgery on the same side; no history of thromboembolic disorders Exclusion criteria: VTE complications or major bleeding during hospitalization; asymptomatic proximal DVT, as shown by a bilateral CUS examination performed before hospital discharge; need for long-term anticoagulation; unavailability for long-term followup; refusal to give written informed consent. Intervention 1: Warfarin 5mg PO daily starting on second pre-operative day for 28d Intervention 2: Warfarin 5mg PO daily starting on second pre-operative day and continued until hospital discharge	Duration of followup: 90d Followup: 100% in both arms Final: VTE, major VTE, mortality, mortality due to bleeding (90d); fatal PE, nonfatal PE, PE (28d) Intermediate: DVT, asymptomatic DVT, symptomatic DVT, proximal DVT (60d) Adverse events: Major bleeding (60d)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Can't tell 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Turpie, 2002 PENTATH -LON 2000	Publication type: Full text Geographic location: Canada, USA, Australia Funding: Industry Number of centers: 139 Randomization and allocation concealment: Randomly assigned to 2 treatment groups by a central computer-derived randomization scheme in blocks of four by an independent organization Outcome assessment: Efficacy outcomes, including review of all venograms, bleeding, and death were assessed by a central independent committee, who were unaware of the patients' treatment assignment Total number randomized (number randomized in arms of interest): 2275 (2275)	Inclusion criteria ≥18y undergoing a first elective THR or a revision of at least one component of a previously implanted total hip prosthesis Exclusion criteria: Planned bilateral hip surgery; women of childbearing age if pregnant or not using effective contraception; active bleeding; acute bacterial endocarditis; documented congenital or acquired bleeding disorder; current ulceration or angiodysplastic GI disease; hemorrhagic stroke or brain, spinal, or ophthalmological surgery <the previous 3m; planned indwelling, intrathecal, or epidural catheter during the study treatment period; unusual difficulty in achieving epidural or spinal anesthesia; hypersensitivity to heparin, LMWH, porcine products, or iodinated contrast medium; CI to anticoagulant treatment; concomitant intake of any drug that could not be combined with contrast medium; addictive disorders; concentration of SCr > 180 µmol/L in a well hydrated patient; platelet count < $100X10^9$/L; needed anticoagulant treatment or had received any type of anticoagulant, antiplatelet, or fibrinolytic treatment, or dextran within wk preceding the first administration of the study drug Intervention 1: Fondaparinux 2.5mg SQ QD starting 4-8h post-operative for 5-9d postoperative Intervention 2: Enoxaparin 30mg SQ BID starting between 12 and 24h post-operative for 5-9d post-operative	Duration of followup: 49d Followup: 100% in both arms Final: Symptomatic objectively confirmed VTE, fatal PE, nonfatal PE, fatal PE, mortality (49d); mortality due to bleeding (11d) Intermediate: DVT, symptomatic DVT, proximal DVT, distal DVT (11d) Adverse events: Major bleeding, major bleeding leading to re-operation (11d)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Warwick, 2002	Publication type: Full text Geographic location: UK Funding: NR Number of centers: 1 Randomization and allocation concealment: Random allocation using sealed envelope generated by a computer Outcome assessment: Venograms interpreted by two consultant radiologists with a particular interest in thromboembolism not aware of the outcome of randomization Total number randomized (number randomized in arms of interest): 229 (229)	Inclusion criteria: Patients scheduled for unilateral primary TKR Exclusion criteria: Refusal of consent; long-term warfarin therapy for pre-existing cardiac or cerebral disease; bleeding tendency; painful joints or wounds in the feet which would preclude the use of the foot pump; participating in an ongoing study of the early discharge of patients after joint arthroplasty Intervention 1: Enoxaparin 40mg SQ q24h starting 12h before surgery and continuing till discharge Intervention 2: VFP (AV Impulse system) applied in the recovery room and used whenever the patient was not bearing weight until discharge	Duration of followup: 90d Followup: Enoxaparin 79.46% VFP 84.62% Final: Fatal PE, mortality due to bleeding, mortality (post-operative) Intermediate: DVT, proximal DVT, distal DVT (post-operative) Adverse events: Re-admission (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? No 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Barden, 2001	Publication type: Full text Geographic location: Denmark Funding: Unknown Number of centers: 1 Randomization and allocation concealment: NR Outcome assessment: NR Total number randomized (number randomized in arms of interest): 160 (160)	Inclusion criteria: Patients undergoing primary THA Exclusion criteria: Marked main trunk and side branch varicosities; fractures; advance arterial diseases; CHF; severe liver disease; paresis or muscle atrophy; patients taking hormonal preparations, ASA, Vit K-antagonists, cytostatic agents. Intervention: Modified position to monitor femoral blood flow Comparator: Conventional figure of four positioning	Duration of followup: 3 to 3.6 months Followup: 100% in both arms Final: Fatal PE, nonfatal PE, PE (90d) Intermediate: Symptomatic DVT (90d) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Bauer, 2001	Publication type: Full text Geographic location: North America Funding: Industry Number of centers: 64 Randomization and allocation concealment: Randomly assigned in a 1:1 ratio in blocks of 4, stratified according to center, through a central computer derived randomization scheme Outcome assessment: Efficacy and safety outcomes adjudicated by a central independent committee unaware of the treatment assignments Total number randomized (number randomized in arms of interest): 1049 (1049)	Inclusion criteria: ≥ 18y undergoing elective major knee surgery: resection of the distal end of femur or proximal end of tibia or revision of at least one component of a previously implanted total knee prosthesis Exclusion criteria: Surgery in the contralateral knee was performed at the same time or within 2 wks after enrollment; pregnancy or not using active contraception; active bleeding disorder; current ulcerative or angiodysplastic GI disease; hemorrhagic stroke or brain , spinal, ophthalmologic surgery within the previous 3m; insertion of an indwelling intrathecal or epidural catheter during the treatment period; unusual difficulty in administering epidural or spinal anesthesia; hypersensitivity to heparin, LMWH, porcine products or iodinated contrast medium; CI to anticoagulant therapy; current addictive disorder, SCr concentration above 2mg/dL in a well hydrated patient; platelet count below 100,000/cubic mm; requiring anticoagulant Intervention 1: Fondaparinux 2.5mg SQ QD starting 6±2h postoperatively till 5th to 9th post-operative d. Intervention 2: Enoxaparin 30mg SQ BID starting 12-24h postoperatively till 5th to 9th post-operative d	Duration of followup: 49d Followup: 100% in all arms Final: Symptomatic objectively confirmed VTE, fatal PE, nonfatal PE, mortality (49d); PE, mortality due to bleeding (11d) Intermediate: DVT, symptomatic DVT, proximal DVT, distal DVT (11d) Adverse events: Major bleeding, major bleeding leading to reoperation (11d)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Comp, 2001	Publication type: Full text Geographic location: USA Funding: Industry Number of centers: Multicenter Randomization and allocation concealment: Computer-generated randomization scheme stratified by surgical procedure Outcome assessment: A central independent expert panel composed of at least three vascular radiologists blinded to the treatment assignment and outcome interpreted all venograms, ventilation-perfusion lung scans, and pulmonary angiograms made during the double-blind phase. The final diagnosis was assigned by a consensus method. The expert panel did not assess ultrasonograms Total number randomized (number randomized in arms of interest): 873 (873)	Inclusion criteria: Elective primary THR or TKR; written informed consent; received adequate medication during the open label phase of the study; did not require reoperation or have venous thrombosis or major hemorrhage during hospitalization; did not receive excluded concomitant medications Exclusion criteria: Multiple joint replacement or inability to achieve hemostasis <12 -24h after surgery; surgery on the ipsilateral hip/knee < 6m or on the ipsilateral knee/hip, the contralateral knee/hip, or the contralateral hip/knee < 3m; clinical evidence of chronic or acute DVT; hx of VTE<12m before surgery; generalized hemorrhagic diathesis or hypercoagulable syndrome; documented allergy to UFH; hx of heparin-associated thrombocytopenia; skin rash or necrosis; allergy to fish or swine products, iodine, or radiopaque contrast medium; current drug or alcohol abuse; surgery on the eye, spinal cord, or CNS; documented stroke or MI <1m prior to study; active ulcerative disease or GI tract angiodysplasia; active GIB < 6m; uncontrolled HTN; use of aspirin containing products or NSAIDs daily < 4d preceding hospitalization; receipt of another investigational drug < 4w; clinically relevant diseases or treatments that could interfere with study medications or their evaluation Intervention 1: Enoxaparin 30mg SQ BID starting12-24h post-operative for 7-10d, then 40mg SQ QD for 3w. Intervention 2: Enoxaparin 30mg SQ BID starting12-24h post-operative for 7-10d, then placebo injections SQ for 3w	Duration of followup: 90d Followup: 100% in both arms Final: VTE, fatal PE, nonfatal PE, PE, mortality due to bleeding, mortality (30d) Intermediate: DVT, proximal DVT, distal DVT (30d) Adverse events: Major bleeding (30d), readmission (90d)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Eriksson, 2001	Publication type: Full text Geographic location: 21 countries Funding: Industry Number of centers: 99 Randomization and allocation concealment: Randomly assigned to treatment groups in blocks of 4 with stratification according to center with the use of a computer generated randomization Outcome assessment: Efficacy and safety outcomes were adjudicated by a central independent committee whose members were unaware of the treatment assignments and included review of all venograms and reports of bleeding and death Total number randomized (number randomized in arms of interest): 1711 (1711)	Inclusion criteria: ≥18y scheduled to undergo standard surgery for fracture of the upper third of the femur, including the femoral head and neck, within 48h after admission Exclusion criteria: Multiple trauma affecting > 1 organ system; interval> 24h between the injury and hospital admission; pregnancy; active bleeding; documented congenital or acquired bleeding disorder; current ulcerative or angiodysplastic GI disease; hx of hemorrhagic stroke or brain, spinal, or ophthalmologic surgery within the previous 3m; planned use of an indwelling intrathecal or epidural catheter for more than 6h after surgery; hypersensitivity to heparin, LMWH, porcine products, or iodinated contrast medium; CI to anticoagulant therapy; current addictive disorder; SCr concentration above 2 mg/dL in a well-hydrated patient; and platelet count < 100,000/cubic mm; required anticoagulant therapy or received dextran or any type of anticoagulant or fibrinolytic therapy from admission to the time of 1st administration of the study drug or surgery Intervention 1: Fondaparinux 2.5mg SQ QD starting 6 6±2h post-operative if surgery was on time (if delayed dose given 12±2h preoperative) for 5-9d post-operative Intervention 2: Enoxaparin 40mg SQ QD starting 12±2h preoperative for 5-9d post-operative	Duration of followup: 49d Followup: Fondaparinux 75% Enoxaparin 74% Final: Symptomatic objectively confirmed VTE, fatal PE, nonfatal PE, mortality (49d); mortality due to bleeding (11d) Intermediate: DVT, symptomatic DVT, proximal DVT, distal DVT (11d) Adverse events: Major bleeding, minor bleeding, major bleeding leading to reoperation (11d)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? No 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? No 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Fitzgerald, 2001	Publication type: Full text Geographic location: NR Funding: Industry Number of centers: MC Randomization and allocation concealment: Randomization numbers generated by the study sponsor were affixed to the exterior of each sealed medication kit; randomization was performed by the investigator allocating the kits in ascending order Outcome assessment: In addition to the assessment by the investigator, a blinded, independent review of all venograms and ultrasonograms was carried out by a panel of vascular imaging specialists Total number randomized (number randomized in arms of interest): 349 (349)	Inclusion criteria: ≥38y; primary unilateral TKA; premenopausal women if surgically sterile or not pregnant Exclusion criteria: Wound hemorrhage continuing > 8h after wound closure; generalized hemorrhagic disorders or hypercoagulable syndrome, including chronic or acute DVT or hx of VTE; allergy to UFH, warfarin, fish or swine products, iodine, or contrast medium; hx of HIT or heparin or warfarin-associated skin rash or necrosis; asthma not under medical control; surgery on the ipsilateral knee < 6m or on the ipsilateral hip, contralateral hip, or contralateral knee < 3m; clinically important disease or requirement for treatment during the study period that could interfere with study drugs; hepatic disease; renal disease; current abuse of drugs or alcohol; surgery involving the eye, spinal cord, or central nervous system <3m; active ulcerative disease or angiodysplasia of the GI tract or active GI hemorrhage < 6m; HTN not under control; stroke or MI < 3m; treatment with aspirin, aspirin-containing products, or NSAID 4d before hospitalization or regular treatment with these products during hospitalization Intervention 1: Warfarin 7.5 mg PO starting within 8h after wound closure and dose adjusted to maintain between 2 and 3 for 4-14d postoperatively Intervention 2: Enoxaparin 30mg SQ q12h starting within 8h after wound closure for 4-14d postoperatively	Duration of followup: 21d Followup: 100% in both arms Final: PE, mortality due to bleeding, mortality (post-operative) Intermediate: DVT, proximal DVT, distal DVT (post-operative) Adverse events: Major bleeding, major bleeding leading to re-operation, minor bleeding, surgical site bleeding, re-operation (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Partially 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Hull, 2000	Publication type: Full text Geographic location: USA, Canada Funding: Industry, Academia Number of centers: 29 Randomization and allocation concealment: Randomized using a computer-derived treatment schedule to assign treatment regimens with the randomization list divided into consecutive blocks to obtain balance of treatments Outcome assessment: Venograms, lung scan, angiograms interpreted by the local radiologist and an independent, blinded central reader and disagreements resolved by a second blinded independent central interpretation. Two central committee members not involved in the patient's care independently adjudicated the bleeding data using the international classification Total number randomized (number randomized in arms of interest): 1472 (1472)	Inclusion criteria ≥18 y scheduled for elective unilateral THA (primary or revision) Exclusion criteria: Documented bleeding <3m before surgery; hypersensitivity to heparin, LMWH, warfarin, or contrast media; defective hemostasis; ongoing anticoagulants; pregnancy or breastfeeding; clinically significant hepatic dysfunction; renal insufficiency; severe HTN; septic endocarditis; < 40 kg; eye, ear, or central nervous system surgery <1m before surgery; diseases with unfavorable prognosis (eg, malignant neoplasms); inability to follow instructions or perform procedures; simultaneous participation in another pharmacological study or use of any investigational drug <30d before surgery; previous randomization into this study; or use of pneumatic compression stockings Intervention 1: Dalteparin 2500 IU SQ for the 1st dose followed by 5000 IU QD starting within 2h before surgery Intervention 2: Dalteparin 2500 IU SQ for the 1st dose followed by 5000 IU QD starting within 2h before surgery Intervention 3: Warfarin 10mg PO QD except for ≥70y or <57kg who received 5 mg for the first dose with subsequent doses adjusted to maintain an INR from 2.0 to 3.0 starting postoperatively on the evening of the surgery	Duration of followup: Post-operative Followup: 100% in both arms Final: Fatal PE, nonfatal PE, PE, mortality due to bleeding, mortality (post-operative) Intermediate: DVT, symptomatic DVT, proximal DVT (post-operative) Adverse events: Major bleeding, minor bleeding, surgical site bleeding (0-1d, 2-8d)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Kennedy, 2000	Publication type: Full text Geographic location: NR Funding: NR Number of centers: NR Randomization and allocation concealment: Randomly allocated by alternate selection to either group Outcome assessment: Doppler assessment was carried out by staff vascular medicine specialists who were blinded to the prophylactic regimen Total number randomized (number randomized in arms of interest): 160 (160)	Inclusion criteria Garden III or IV intracapsular hip fracture; ≤ 60y; direct admission to a hospital Exclusion criteria: Previous hx of DVT, PE, CVI or malignant tumor, peptic ulcer disease, gastritis, aspirin sensitivity or who were already on anticoagulation therapy Intervention 1: Aspirin 325mg PO BID starting on the day of surgery as soon as the patient was able to tolerate pills orally Intervention 2: VFP (AV impulse system) fitted in the recovery room on both feet with the inflatable pad placed under the plantar arch and secured in position for a minimum of 18h/d until the patient was fully ambulatory	Duration of followup: Post-operative Followup: Aspirin 91.25% VFP 87.5% Final: PE (post-operative) Intermediate: DVT, asymptomatic DVT, symptomatic DVT, proximal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? No 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Colwell, 1999	Publication type: Full text Geographic location: USA Funding: Industry Number of centers: 156 Randomization and allocation concealment: Randomly assigned to treatment groups Outcome assessment: NR Total number randomized (number randomized in arms of interest): 3011 (3011)	Inclusion criteria: ≥ 18y scheduled for elective unilateral primary hip arthroplasty Exclusion criteria: Hx of blood dyscrasia, HIT; allergy to warfarin or heparin Intervention 1: Enoxaparin 30mg SQ starting within 24h postoperatively and continuing q12h until discharge (mean of 7.3d) Intervention 2: Warfarin 7.5mg PO within 24h post-operative (could be initiated 48h pre-operatively) and continuing with dose adjusted to maintain an INR between 2.0-3.0 until discharge (mean of 7.3d)	Duration of followup: 90d Followup: 100% in both arms Final: Symptomatic objectively confirmed VTE, PE, fatal PE, mortality (90d) Intermediate: Symptomatic DVT (90d) Adverse events: Major bleeding, minor bleeding, surgical site bleeding, HIT (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Levy, 1999	Publication type: Full text Geographic location: Israel Funding: None Number of centers: 3 Randomization and allocation concealment: computer generated randomization list Outcome assessment: NR Total number randomized (number randomized in arms of interest): 58 (58)	Inclusion criteria: Oosteoarthritis of the knee; scheduled to have a unilateral TKA with cement Exclusion criteria: NR Intervention 1: Octacol F15 fibrin tissue adhesive (ten to twenty milliliters of combined product or one or two kits) was then applied by topical spraying with use of a double-syringe spray-device Comparator: No application of octacol F15 fibrin tissue adhesive	Duration of followup: Post-operative Followup: 100% in both arms Final: Fatal PE (post-operative) Intermediate: DVT, symptomatic DVT, asymptomatic DVT, proximal DVT, distal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Planes, 1999	Publication type: Full text Geographic location: France Funding: Industry Number of centers: 43 Randomization and allocation concealment: Stratification by study center performed by a computer generated randomization schedule balanced in blocks of four Outcome assessment: Bleeding and venograms were interpreted locally, then by centralized assessment by an independent expert blind to treatment allocation Total number randomized (number randomized in arms of interest): 499 (499)	Inclusion criteria: Patients age ≥ 40y; weight 50kg-90kg scheduled to undergo primary THR Exclusion criteria: Allergy to heparin, iodine or radioopaque contrast medium; acquired or hereditary hemostatic disorders; disorders contraindication anticoagulant prophylaxis; severe hepatic or renal failure; severe or malignant HTN; history of DVT or PE within previous 6m; MI or stroke within previous 6m; revision or conversion hip surgery or primary hip arthroplasty of the opposite hip performed <3m previously; advanced cancer; pregnancy Intervention 1: Enoxaparin 40mg SQ 12h before surgery, 12h post-surgery and then QD for 15d Intervention 2: Tinzaparin 4500 antifactor IU Xa SQ 12h before surgery, 12h post-surgery and then QD for 15d	Duration of followup: Post-operative Followup: 100% in both arms Final: Fatal PE, nonfatal PE, mortality, mortality due to bleeding (postoperative) Intermediate: DVT, symptomatic DVT, proximal DVT, distal DVT (post-operative) Adverse events: Major Bleeding, minor bleeding, surgical site bleeding, HIT (postoperative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
TIFDED Study Group, 1999	Publication type: Full text Geographic location: France, Belgium, Norway, Netherlands Funding: Government/foundation Number of centers: 4 Randomization and allocation concealment: Randomly assigned to one of three treatment groups stratified by center Outcome assessment: All venograms were coded and independently reviewed by a panel of experts unaware of treatment allocation. All information on patients with hemorrhage was adjudicated by an independent committee Total number randomized (number randomized in arms of interest): 197 (132)	Inclusion criteria: HFS within 24h of fracture and operated on within 48h after hospital entry Exclusion criteria: <45kg or > 100kg; history of bleeding diathesis; APTT >10% above reference range; uncontrolled HTN; hepatic failure; previous ischaemic or hemorrhagic CVA; fertile women; recent GI bleeding or peptic ulcer; recent use of oral anticoagulants or fibrinolytic drugs; contrast medium, iodine or glycosaminoglycuronan allergy Intervention 1: Enoxaparin† A: 20mg SQ 2h before surgery and then 40mg QD about 12h after surgery for 9-11d B: 20mg + 20mg SQ about 2h before surgery and then 40mg QD about 12h after surgery for 9-11d C: 20mg SQ BID the last preoperative dose about 2h before surgery and then 40mg QD about 12h after surgery for 9-11d Intervention 2: Dalteparin D: 2500U SQ starting about 2h before surgery then 2500U SQ about 12h after last preoperative dose, then 5000U SQ QD for 9-11d E: 2500U SQ BID the last preoperative dose not within 2h before surgery, 2500U SQ about 12h after last preoperative dose, then 5000U SQ QD for 9-11d	Duration of followup: Post-operative Followup: 100% in both arms Final: PE, fatal PE, nonfatal PE (post-operative) Intermediate: DVT, asymptomatic DVT, symptomatic DVT, proximal DVT (post-operative) Adverse events: Major bleeding, surgical site bleeding, (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Wakankar, 1999	Publication type: Full text Geographic location: UK Funding: None Number of centers: 1 Randomization and allocation concealment: Patients randomized into two groups using random numbers Outcome assessment: NR Total number randomized (number randomized in arms of interest): 77 (77)	Inclusion criteria Patients undergoing TKA Exclusion criteria: Diabetes; rheumatoid arthritis; previous thromboembolism; active malignancy; those having one-stage bilateral procedures Intervention 1: TKA under a tourniquet after the leg had been exsanguinated, tourniquet pressure was twice the systolic blood pressure. Comparator: No use of tourniquet	Duration of followup: 120d Followup: 100% in both arms Final: Mortality (120d) Intermediate: DVT, asymptomatic DVT, proximal DVT, distal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? No 6. Were methods for allocation concealment adequate? No 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Kim, 1998	Publication type: Full text Geographic location: Korea Funding: NR Number of centers: 1 Randomization and allocation concealment: NR Outcome assessment: NR Total number randomized: 150 (100)	Inclusion criteria Primary, uncemented THR; ≥18y; obtained informed consent Exclusion criteria History of aspirin intolerance; ingested aspirin containing compound or other antiplatelet within 14d prior to surgery Intervention: EC-aspirin 400mg po TID starting 48h pre-operatively and finishing 14d postoperatively Comparator: Control	Duration of followup: Post-operative Followup: 100% both arms Final: NR Intermediate: DVT (post-operative) Adverse events: Major bleeding (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Can't tell 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Lassen, 1998	Publication type: Full text Geographic location: Denmark Funding: Unknown Number of centers: 8 Randomization and allocation concealment: NR Outcome assessment: All venograms were evaluated by a panel of three radiologists who were unaware of the result of randomization Total number randomized (number randomized in arms of interest): 281 (281)	Inclusion criteria: All patients admitted for THA Exclusion criteria: Age < 18y; previous surgery in the study; simultaneous participation in other pharmacological studies; informed consent not obtained; high probability for drop-out; renal insufficiency; hepatic insufficiency and prothrombin < 0.7; platelet count < 100X 10^9/L; treatment with oral anticoagulants or heparin within 7d before inclusion; hypersensitivity to heparin, LMWH or contrast media; documented bleeding within 3m prior to surgery; intracranial bleeding within 3m prior to surgery; eye, ear, or central nervous system surgery within 1m prior to surgery; hypertension with diastolic pressure >120mmHg; septic endocarditis; body weight <40 kg; known pregnancy or lactation Intervention 1: Dalteparin 5000 antifactor Xa U SQ QD starting 12h before surgery, continuing for 7d post-operative. Same regimen was followed after randomization until 35d post-operative Intervention 2: Dalteparin 5000 antifactor Xa U SQ QD starting 12h before surgery, continuing for 7d post-operative, then placebo injections (isotonic sodium chloride) QD until 35d post-operative	Duration of followup: 35d Followup: 76% overall Final: NR Intermediate: DVT, asymptomatic DVT, proximal DVT (35d) Adverse events: Major bleeding, minor bleeding (35d)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5 Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? No 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Rader, 1998	Publication type: Full text Geographic location: Germany Funding: NR Number of centers: 1 Randomization and allocation concealment: NR Outcome assessment: NR Total number randomized (number randomized in arms of interest): 246 (246)	Inclusion criteria: High risk patient undergoing primary THA or TKA; hx of DVT >3y Exclusion criteria: Proximal fracture of the femur;<18y:long lasting immobilization; decompensated cardiac insufficiency; prolonged arterial sclerosis and occlusion; liver insuffiency; hemorrhagic diathesis; anticoagulation with pheprocoumon; apoplectic insult; pregnancy; tumor history; arthritis and arthrodesis of the lower extremity; manifest PE, DVT, thrombophlebitis; chronic paralysis; chronic muscular atrophies Intervention 1: Heparin 3 X 5000 IU for 3d, 3 X 7500 IU on 4th day to maintain a PTT of 40sec Intervention 2: Enoxaparin 40mg SQ QD for till hospital discharge (mean of 16.4d)	Duration of followup: Post-operative Followup: 100% in both arms Final: NR Intermediate: DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Can't tell 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)?Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Ryan, 1998	Publication type: Full text Geographic location: USA Funding: Industry Number of centers: 1 Randomization and allocation concealment: Randomized to two treatment groups Outcome assessment: All venography studies were interpreted by one of two senior radiologists blinded to patients treatment allocation Total number randomized (number randomized in arms of interest): 100 (100)	Inclusion criteria: Patients in whom primary THA has been performed Exclusion criteria: History of venous thrombi or PE; history of peripheral vascular disease; contraindication to aspirin or magnetic resonance imaging; indwelling vascular stent and/or IVC filter <6w before magnetic resonance venography Intervention 1: IPC (Venaflow) applied immediately post surgery and worn for first 24h, until patient stood for 1st time without help of physical therapy, then continuously for 4 – 5d Intervention 2: GCS (T.E.D.) applied immediately post surgery and worn for first 24h, until patient stood for 1st time without help of physical therapy, then continuously for 4 – 5d	Duration of followup: Post-operative Followup: 100% in both arms Final: PE, fatal PE, nonfatal PE (post-operative) Intermediate: Symptomatic DVT, proximal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Warwick, 1998	Publication type: Full text Geographic location: UK Funding: Industry, Government/Foundation Number of centers: 1 Randomization and allocation concealment: Randomization performed with use of sealed envelopes containing a slip indicating the allocation, which had been derived from a computer-generated sequence Outcome assessment: The venogram was interpreted by consensus between two consultant radiologists who had a special interest in thromboembolism and were not aware of the randomization category of the patient Total number randomized (number randomized in arms of interest): 290 (290)	Inclusion criteria: Patients scheduled for primary THR Exclusion criteria: Refusal of consent; long term anticoagulation therapy for preexisting cardiac or cerebrovascular disease; an active malignant tumor; GI ulceration; previous bleeding diatheses; wounds on or painful joints in the feet and enrollment in another trial necessitating planned early discharge from the hospital or modification of wound drainage Intervention 1: Enoxaparin 40mg SQ q24h starting 12h before surgery and continuing till 8th post-operative d Intervention 2: VFP (AV Impulse system) fitted on both legs in the recovery room and used whenever the patient was not bearing weight until 8th post-operative d	Duration of followup: 90d Followup: 100% in both arms Final: Fatal PE, nonfatal PE, PE, mortality due to bleeding, mortality (post-operative) Intermediate: DVT, symptomatic DVT, proximal DVT, distal DVT (post-operative) Adverse events: Discomfort, re-admission (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Partially 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Andersen, 1997	Publication type: Full text Geographic location: Denmark Funding: Government/foundation Number of centers: 1 Randomization and allocation concealment: NR Outcome assessment: phlebograms were evaluated by three independent radiologists who were unaware of the treatment Total number randomized (number randomized in arms of interest): 41 (41)	Inclusion criteria: Male or female, age ≥18y; monolateral THR (primary or revision); written informed consent from the patient; ability to continue medications after discharge Exclusion criteria: Previous participation in the study; participation in other studies that may influence the efficacy and safety of the study; expected low compliance; renal insufficiency measured within the last 3w before inclusion; liver insufficiency measured within the last week before inclusion; impaired hemostasis; treatment with oral anticoagulant heparin or LMWH within days before the inclusion; hypersensitivity to heparin, LMWH, or contrast media; GIB or cerebral bleeding within 3m prior to the inclusion; eye, ear or CNS surgery within 1m prior to the inclusion; HTN with diastolic pressure >120mm Hg; endocarditis; body weight < 40 kg; known pregnancy or lactation Intervention 1: Dalteparin 5,000IU SQ QD started the evening before operation, on the operation day, and 2 days after operation and thereafter for 35d Intervention 2: Dalteparin 5,000IU SQ QD started the evening before operation, on the operation day, and 2 days after operation and thereafter for 5-7d, then placebo injections for 28d	Duration of followup: 35d Followup: 100% in both arms Final: PE (35d) Intermediate: DVT, symptomatic DVT, asymptomatic DVT (35d) Adverse events: Reoperation (35d)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Dahl, 1997	Publication type: Full text Geographic location: Norway Funding: Unknown Number of centers: 2 Randomization and allocation concealment: NR Outcome assessment: venograms were evaluated blindly 6 months later by one specialist. VQ scans and X-rays were evaluated blindly after the study period by a specialist Total number randomized (number randomized in arms of interest): 265 (265)	Inclusion criteria: Consenting male and female patients age >18y admitted for elective primary or secondary arthroplasty of the hip Exclusion criteria: Known renal of liver insufficiency; cerebral bleeding <3m before surgery or known hemorrhagic diathesis; eye or ear surgery within 1m before surgery; severe hypertension; septic endocarditis; threatened arterial circulation in the leg; a body weight less than 40kg; anticoagulant therapy <1w before surgery; a known hypersensitivity to heparin, LMWH, dextran or contrast media; pregnancy or breastfeeding; inability to comply with the study protocol; previous surgery in the present study Intervention 1: Dalteparin 5000 IU SQ starting evening before surgery and continued daily for 7 days + dextran infusion 500-1000ml on 0d, 1500ml on 1d + below-knee GCS (Kendall) on both legs worn before operation, for first post-operative week. Patients with no DVT or PE during the first post-operative week continued dalteparin 5000 IU SQ daily until 35d Intervention 2: Dalteparin 5000 IU SQ starting evening before surgery and continued daily for 7 days + dextran infusion 500-1000ml on 0d, 1500ml on 1d + below-knee GCS (Kendall) on both legs worn before operation, for first post-operative week. Patients with no DVT or PE during the first post-operative week received placebo injections SQ daily until 35d	Duration of followup: 35d Followup: 100% in both arms Final: Fatal PE, nonfatal PE, PE (7-35d) mortality due to bleeding, mortality (35d) Intermediate: DVT (7d, 7-35d, 35d); Symptomatic DVT (7d, 35d); Proximal DVT (35d) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Eriksson, 1997a	Publication type: Full text Geographic location: Sweden, Denmark Funding: NR Number of centers: 11 Randomization and allocation concealment: Computer generated randomization scheme providing balanced blocks of patient numbers for each of the 2 treatment groups within each center, using a block size of 6 Outcome assessment: All venograms were centrally assessed by 2 independent expert radiologists who were unaware of the results recorded at the local centers Total number randomized (number randomized in arms of interest): 445 (445)	Inclusion criteria: ≥18y old, ≥50 kg scheduled to have an elective primary THR Exclusion criteria: Previous inclusion in the trial; childbearing potential; hemostatic or bleeding disorder; hip fracture or operation < 3m; major operation < last m; cerebral ischemic attack <last 6m; uncontrolled HTN; renal impairment; known allergy to hirudin, heparin, or contrast media Intervention 1: Desirudin 15mg SQ BID starting 30mins before surgery after induction of anesthesia for 8-11d postoperatively Intervention 2: UFH 5000 IU SQ TID starting 2h before surgery for 8-11d postoperatively	Duration of followup: 42d Followup: 100% in both arms Final: Fatal PE, nonfatal PE, PE, mortality due to bleeding; mortality (42d) Intermediate: DVT (post-operative, post-operative-42d); proximal DVT (post-operative) Adverse events: Major bleeding leading to re-operation (42d)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Partially 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Eriksson, 1997b	Publication type: Full text Geographic location: Austria, Belgium, Denmark, France, Germany, Italy, Netherlands, Spain, Sweden, Switzerland Funding: Industry Number of centers: 31 Randomization and allocation concealment: Randomized in a double-blind manner to 2 treatment groups Outcome assessment: All venograms were assessed in a central radiology department by consensus of two radiologists who were unaware of the results recorded at the local centers. An independent safety committee monitored reported adverse events, bleeding complications, laboratory abnormalities, and episodes of DVT as assessed locally Total number randomized (number randomized in arms of interest): 2079 (2079)	Inclusion criteria: ≥18 y, ≥50 kg scheduled to undergo elective primary THR Exclusion criteria: Childbearing potential; previous inclusion in the trial; bilateral hip operation; hip surgery or fracture of the leg < previous 3m; other major surgery < past m; hemostatic or bleeding disorders; hx of hemorrhagic stroke, intracranial or intraocular bleeding, or cerebral ischemic attacks < past 6m; GI or pulmonary bleeding < 3m; uncontrolled HTN; renal impairment, nephrectomy, or kidney transplantation; and known allergy to hirudin, heparin, or contrast medium Intervention 1: Desirudin 15mg BID starting within 30mins before surgery but after induction of regional block anesthesia for 8-12d postoperatively Intervention 2: Enoxaparin 40mg SQ QD staring on the evening before surgery for 8-12d postoperatively	Duration of followup: 42d Followup: Desirudin 77% Enoxaparin 76% Final: Major VTE (post-operative study period); PE (post-operative study period, after study period-42d); fatal PE (after study period-42d); mortality (42d) Intermediate: DVT (post-operative study period, study period-42d); proximal DVT (post-operative study period) Adverse events: Major bleeding (post-operative study period)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Partially 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? No 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? No 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Francis, 1997	Publication type: Full text Geographic location: USA Funding: NR Number of centers: 2 Randomization and allocation concealment: Randomly assigned to either of the two treatment groups Outcome assessment: All venograms were evaluated by a radiologist who had no knowledge of the treatment group assignment. All lung scans and pulmonary angiograms were reviewed by an independent third-party evaluator who did not have knowledge of the treatment-group assignment Total number randomized (number randomized in arms of interest): 580 (580)	Inclusion criteria 18y ≤ scheduled to have a unilateral primary or revision THA Exclusion criteria: SCr level of ≥1.7 mg/dl; defective hemostasis; documented GI or other bleeding <3m before the operation; cerebral hemorrhage <3m before the operation; operative procedure involving the eye, ear, or central nervous system<1m before the operation; a known hypersensitivity to heparin; severe HTN; and a weight < 41 kg; women who were pregnant or breastfeeding, those who had reproductive potential unless they had had a negative pregnancy test Intervention 1: Dalteparin SQ 2500 IU for the first 2 doses, 5000 IU QD on following post-operative days starting within 2h before surgery, continued until venography Intervention 2: Warfarin PO QD 5mg for ≤ 57kg, 7.5mg for >57kg for the first 2 doses with subsequent doses adjusted to maintain INR of 2.5 starting evening before surgery, continued until venography	Duration of followup: Post-operative Followup: 100% in both arms Final: NR Intermediate: DVT, proximal DVT, distal DVT (post-operative) Adverse events: Major bleeding, minor bleeding, major bleeding leading to re-operation, surgical site bleeding, bleeding leading to transfusion, re-operation (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Nilsson, 1997	Publication type: Full text Geographic location: Sweden Funding: Unknown Number of centers: 1 Randomization and allocation concealment: NR Outcome assessment: Each phlebogram was examined by a committee of three radiologists unaware of patients' group assignment. All interpretations and classifications were made before the randomization code was broken Total number randomized (number randomized in arms of interest): 262 (262)	Inclusion criteria: Patients undergoing primary elective hip arthroplasty Exclusion criteria: Renal insufficiency; hypersensitivity to contrast medium, heparin, or LMWH; a past or present risk of hemorrhage; endocarditis, severe liver disease, or untreated hypertension; VTE within the preceding three months; if they had received treatment with heparin, LMWH, oral anticoagulants, or NSAIDs within 5d before surgery; ipsilateral hip surgery within the preceding 6m; pregnant or lactating; lack of informed consent Intervention 1: Enoxaparin 40mg SQ QD starting 12h before surgery, then continued for 30 ±4d Intervention 2: Enoxaparin 40mg SQ QD starting 12h before surgery for 9 ±2d, then placebo for 21d	Duration of followup: 90d Followup: 100% in both arms Final: VTE, fatal PE, nonfatal PE, PE (30d); mortality due to bleeding, mortality (90d) Intermediate: DVT, asymptomatic DVT, symptomatic DVT, proximal DVT, distal DVT (30d) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Planes, 1997	Publication type: Full text Geographic location: France Funding: Industry Number of centers: 1 Randomization and allocation concealment: Randomization was balanced in blocks of four by a computer-generated randomization schedule. Outcome assessment: During the study period, patients were assessed by their attending physician, private nurses, or the medical staff of the convalescent homes who were all aware of the study protocol. The double blind for patient nurses, attending nursing and investigators was maintained until database was closed Total number randomized (number randomized in arms of interest): 179 (179)	Inclusion criteria: Consecutive hospital inpatients; > 45y; 45–95 kg; undergone primary THR or conversion or revision THR surgery; receiving LMWH prophylaxis for postoperative VTE; able to walk with crutches without assistance; did not have a diagnosis of DVT, as assessed by bilateral ascending contrast venography of the legs no more than 5d before discharge; availability for a followup assessment 21 days after discharge Exclusion criteria: History of documented DVT or PE in the previous 6m; active cancer; underlying bleeding disorders or hemostatic abnormalities; active gastroduodenal ulcer; a history of hypersensitivity to heparin or to radiopaque media; renal or hepatic insufficiency; uncontrolled hypertension; and recent stroke < 6m Intervention 1: Enoxaparin 40mg SQ QD starting immediately before surgery until just before hospital discharge, then continued for 21d postdischarge. Intervention 2: Enoxaparin 40mg SQ QD starting immediately before surgery until just before hospital discharge, then placebo injections for 21d postdischarge	Duration of followup: 90d Followup: Extended prophylaxis: 94.44% Control: 98.88% Final: fatal PE, nonfatal PE, PE (35d); mortality due to bleeding, mortality (35d, 90d) Intermediate: DVT, proximal DVT, distal DVT (35d) Adverse events: Major bleeding, minor bleeding, bleeding leading to transfusion (35d)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Samama, 1997	Publication type: Full text Geographic location: France Funding: NR Number of centers: 11 Randomization and allocation concealment: Computer-generated randomization schedule, which was equilibrated by study center and balanced in blocks of 4 patients Outcome assessment: Independent central reading committee for venographies, angiographies or lung scans, and if necessary 3rd party from data and safety monitoring review board; all venograms were evaluated by 2 independent radiologists unaware of the treatment Total number randomized: 170 (170)	Inclusion criteria: > 18 y; 45–95 kg; primary THR under regional anesthesia (subarachnoid block and catheter removed at the end of the surgical procedure); wearing GCS (started day before surgery) Exclusion criteria: Re-operation for THR; surgery under general anesthesia; nail extension before surgery; history of DVT, PE, or both; hepatic or renal insufficiency; lung or heart failure; anesthesia status >3, hemorrhagic disorders CI use of antithrombotic drugs (active ulcerative disease, uncontrolled arterial HTN, stroke within previous 6m or other known hemorrhagic disorders), occurrence of a bloody tap during spinal puncture; platelet <100 X 10^9 /L; history of HIT; allergic reaction to heparin, LMWH, or contrast dye; female of childbearing potential; heparin >24h before surgery; oral anticoagulant within 3d; antiplatelet drug for >8d; NSAID within 2d Intervention: Enoxaparin 40mg SQ daily for 10 ± 2d Comparator: Placebo (SQ saline injections)	Duration of followup: 10±2d Followup: Enoxaparin 91.8%, placebo 88.2% Final: PE, Fatal PE, non-fatal PE, mortality, mortality due to bleeding (10±2d) Intermediate: DVT, asymptomatic DVT, symptomatic DVT, proximal DVT, distal DVT (10±2d) Adverse events: Major bleeding, minor bleeding (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure / intervention status? Partially 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (<10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Eriksson, 1996	Publication type: Full text Geographic location: Europe Funding: NR Number of centers: 17 Randomization and allocation concealment: Randomized in equal numbers within each center Outcome assessment: All venograms were centrally assessed by two independent expert radiologists who were unaware of the recorded results at the local center Total number randomized (number randomized in arms of interest): 1119 (554)	Inclusion criteria: Patients scheduled to undergo elective primary THR Exclusion criteria: < 21 y; ≤50 kg; recent trauma, bleeding or surgery; bleeding diatheses; renal impairment; childbearing potential; previous inclusion in the trial; known allergy to hirudin, heparins or radiopaque contrast media Intervention 1: Desirudin 15mg BID starting before surgery after induction of regional block anesthesia for 8-11d postoperatively Intervention 2: UFH 5000 IU SQ TID starting 2h before surgery for 8-11d postoperatively	Duration of followup: 42d Followup: 100% in both arms Final: Fatal PE, nonfatal PE, PE, mortality due to bleeding (post-operative); mortality (42d) Intermediate: DVT, proximal DVT (post-operative) Adverse events: Major bleeding leading to re-operation, surgical site bleeding (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Partially 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Kalodiki, 1996	Publication type: Full text Geographic location: NR Funding: Industry Number of centers: 1 Randomization and allocation concealment: Patients given consecutive numbers with correspondingly-numbered boxes which contained prefilled syringes of placebo or enoxaparin and instructions whether GCS should be added; randomization performed by opening consecutively-numbered sealed envelopes Outcome assessment: Venograms and perfusion lung scans were reported on by a consultant radiologist who was not aware of the form of prophylaxis, venography results, or V/Q scan results Total number randomized: 78 (78)	Inclusion criteria: >40y, unilateral THR for the first time (with or without cement) under GA Exclusion criteria: Established documented coagulation tests+APTT including platelet counts <100 X 10^9/L; acute bleeding and/or recently documented hemorrhage and any other bleeding risk; anticoagulant therapy 14d before surgery or during study; aspirin 5d or NSAIDs 2d before surgery; severe arterial HTN, history of stroke or neurosurgery in previous 6m; endocarditis; ARF, CRF, severe hepatic or pancreatic disease; hypersensitivity to heparin or metabisulphite; allergy to porcine derived products, iodine or radio-opaque contrast media; history of HIT; previous surgery of the ipsilateral hip; surgery carried out under regional anesthesia; clinical signs of DVT and/or history of recent DVT and/or PE; presence of malignant growths; mental disorders and/or failure to give informed consent Intervention 1: Thigh-length GCS (TEDR) applied preoperatively bilaterally until discharge + enoxaparin 40mg SQ 12h preoperatively then QD until discharge Intervention 2: Enoxaparin 40mg SQ 12h preoperatively then QD until discharge Comparator: Placebo (SQ injections)	Duration of followup: Post-operative Followup: Total 100% Final: NR Intermediate: DVT, proximal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? 3. Were subjects and providers blind to the intervention status of participants? Partially 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? No 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Laupacis, 1996	Publication type: Full text Geographic location: Canada Funding: Government/foundation Number of centers: 1 Randomization and allocation concealment: Stratification by age and surgeon Outcome assessment: Venograms were read by one of two radiologists Total number randomized (number randomized in arms of interest): 250 (250)	Inclusion criteria: Patients undergoing unilateral, elective hip arthroplasty for osteoarthritis Exclusion criteria: NR Intervention 1: Cemented Mallory head prostehsis Comparator: Uncemented Mallory head prosthesis	Duration of followup: Post-operative Followup: 100% in both arms Final: PE (post-operative) Intermediate: DVT, proximal DVT, distal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Leclerc, 1996	Publication type: Full text Geographic location: Canada Funding: Industry Number of centers: 8 Randomization and allocation concealment: Randomized in a 1:1 blocks of four by a computer generated randomization list stratified by study center, hx of VTE, and use of a cemented or uncemented prosthesis. Outcome assessment: All diagnostic tests and bleeding episodes were adjudicated by a central committee that was unaware of treatment allocation or clinical findings Total number randomized (number randomized in arms of interest): 670 (670)	Inclusion criteria: Adult patients having knee arthroplasty Exclusion criteria: Allergy to contrast material; need for oral anticoagulant or antiplatelet agents; bleeding diathesis; GI hemorrhage < 3m of surgery; renal or hepatic insufficiency; uncontrolled HTN; illicit drug use or alcohol abuse; participation in the present study < last 3m; hemorrhagic stroke < 3m of surgery; receipt of other investigational drugs in the past m; warfarin allergy Intervention 1: Enoxaparin 30mg SQ, starting morning of first day after surgery, continued q12h for 14d or until hospital discharge whichever occurred first Intervention 2: Adjusted dose warfarin to maintain an INR between 2.0 and 3.0 starting evening of day of surgery, continued QD for 14d or until hospital discharge whichever occurred first	Duration of followup: 180d Followup: 100% in both arms Final: Symptomatic objectively confirmed VTE, mortality (180d); nonfatal PE, fatal PE, PE (post-operative) Intermediate: DVT, proximal DVT (post-operative) Adverse events: Major bleeding, minor bleeding (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Lotke, 1996	Publication type: Full text Geographic location: USA Funding: Government/foundation Number of centers: NR Randomization and allocation concealment: NR Outcome assessment: The VQ scans and venograms were interpreted without knowledge of prophylactic Regimen Total number randomized (number randomized in arms of interest): 388 (388)	Inclusion criteria: Consecutive patients having primary or revision THA or TKA Exclusion criteria: < 45y; refused consent; administrative omission in enrollment; allergy to contrast dye; either a postoperative VQ scan or postoperative venogram was not obtained Intervention 1: Aspirin 325 mg PO BID starting on the day of admission and continued for 6wks post-operative Intervention 2: Warfarin 10mg PO on the night of surgery, none the next day, and QD for 6wks to maintain PT between 1.2 and 1.5 X control value	Duration of followup: Post-operative Followup: 80.4% overall Final: NR Intermediate: DVT, proximal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Schwartsmann, 1996	Publication type: Full text Geographic location: Brazil Funding: NR Number of centers: NR Randomization and allocation concealment: Randomized to either treatment groups Outcome assessment: NR Total number randomized (number randomized in arms of interest): 99 (99)	Inclusion criteria: Elective primary THA; > 50 kg; > 40y Exclusion criteria: Coagulation disorders; hx of purpura or TCP; recent acute bleeding or bleeding risks; use of clotting or antiplatelet agents < 2 wks before surgery; moderate HTN; inflammatory disease; stroke; systemic infection or endocarditis; organ, kidney, liver or pancreatic insufficiency; hypersensitivity to heparin or LMWH; allergy to fish and swine products; allergy to iodine or radiological contrast media; previous episode of DVT or PE; previous THA; pregnancy or lactation; cancer; use or corticoids or estrogen; mental disorders Intervention 1: Enoxaparin 40mg SQ QD starting immediately post-operative for a duration of 10d post-operative Intervention 2: UFH 5000 IU SQ q8h starting immediately post-operative for a duration of 10d post-operative	Duration of followup: Post-operative Followup: 100% in both arms Final: Fatal PE, nonfatal PE, PE, mortality due to bleeding, mortality (post-operative) Intermediate: DVT, asymptomatic DVT< symptomatic DVT, proximal DVT, distal DVT(post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Stannard, 1996	Publication type: Full text Geographic location: USA Funding: NR Number of centers: 1 Randomization and allocation concealment: NR Outcome assessment: Surgeons and radiologists were blinded regarding the patient treatment groups Total number randomized (number randomized in arms of interest): 75 (75)	Inclusion criteria: Patients undergoing elective uncemented THA for underlying hip arthrosis Exclusion criteria: Patients with prior history of DVT or PE; femoral neck fracture; age<18y; preexisting extremity vascular disease Intervention 1: UFH 5000U SQ dialy X3d then EC-aspirin 325mg po BID Intervention 2: VFP (PlexiPulse) applied immediately after surgery bilaterally for 16h/d for first 3d and then 12h/d for the remainder of the study Intervention 3: UFH 5000U SQ daily X3d then EC-aspirin 325mg po BID plus VFP (PlexiPulse) applied immediately after surgery bilaterally for 16h/d for first 3d and then 12h/d for the remainder of the study	Duration of followup: Post-operative Followup: 100% in all arms Final: Mortality, mortality due to bleeding (post-operative) Intermediate: DVT, symptomatic DVT, asymptomatic DVT, proximal DVT, distal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Stone, 1996	Publication type: Full text Geographic location: UK Funding: NR Number of centers: NR Randomization and allocation concealment: Randomized to 2 treatment groups Outcome assessment: NR Total number randomized (number randomized in arms of interest): 50 (50)	Inclusion criteria Primary THR Exclusion criteria Antiplatelet therapy; known cancer; thromboembolism/PE; GI or ulcer in past year; social circumstances; complex medical problems; human error Intervention 1: IPC (Flowtron DVT garment) applied to the opposite limb during surgery and to the operated limb after the procedure, continuing until discharge or until 10d postoperatively Intervention 2: Enoxaparin 40mg SQ QD starting on the evening before surgery, continuing until discharge or 10d postoperatively	Duration of followup: Post-operative Followup: 100% in both arms Final: NR Intermediate: DVT, asymptomatic DVT, symptomatic DVT, proximal DVT, distal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Westrich, 1996	Publication type: Full text Geographic location: USA Funding: Unfunded Number of centers: 1 Randomization and allocation concealment: Randomized using a computer generated randomization table Outcome assessment: Radiologist who read the venogram and ultrasound was blinded to the study group Total number randomized: 122 (122)	Inclusion criteria: Primary unilateral or a one-stage bilateral TKA Exclusion criteria: History of DVT, PE, peptic ulcer disease or allergy to aspirin; current anticoagulation therapy Intervention: Aspirin 325mg PO BID starting post operatively on the night of the surgery for the study duration + VFP (PlexiPulse) applied in the recovery room and used while the patient was recumbent and removed only for walking and daily hygiene until venogram screening Comparator: Aspirin 325mg PO BID starting post operatively on the night of the surgery for the study duration	Duration of followup: Post-operative Followup: 100% in both arms Final: NR Intermediate: DVT, proximal DVT (post-operative) Adverse events: Major bleeding, minor bleeding (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Partially 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Williams-Russo, 1996	Publication type: Full text Geographic location: USA Funding: Government/Foundation Number of centers: 1 Randomization and allocation concealment: Randomized by a blocked schedule based on random numbers table Outcome assessment: Radiologist reading venograms and lung scan were blind to anesthesia status Total number randomized (number randomized in arms of interest): 262 (262)	Inclusion criteria: Patients undergoing elective primary unilateral TKR with participating orthopedic surgeons Exclusion criteria: Age≤ 40y; history of surgery performed with either a regional or general anesthetic in the 3m preceding TKR; presence of a contraindication to either epidural anesthesia or general anesthesia Intervention 1: General anesthesia: Induction: thiopental sodium, fentanyl, and vencuronium; maintenance: fentanyl, inhaled nitrous oxide (70%), and isoflurane; neuromuscular blockade was reversed with neostigmine and atropine or glycopyrrolate Intervention 2: Epidural anesthesia: Either lidocaine 2% or bupivacaine 0.75%, adjunctive medications for sedation included midazolam and fentanyl	Duration of followup: 180d Followup: 94.7% overall Final: Mortality (180d) Intermediate: DVT, proximal DVT, distal DVT (180d) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Abdel-Salam, 1995	Publication type: Full text Geographic location: England Funding: Unknown Number of centers: 1 Randomization and allocation concealment: Patients were allocated to one of two groups using a card system Outcome assessment: NR Total number randomized (number randomized in arms of interest): 80 (80)	Inclusion criteria: TKR patients; non-diabetic patients who had no previous knee surgery and who had a normal neurovascular supply to the leg (proved by Doppler studies) Exclusion criteria: NR Intervention1: A pneumatic tourniquet placed around the thigh and inflated. The limb was first exsanguinated by elevation for two minutes and the tourniquet was inflated to twice the systolic blood pressure Comparator: A pneumatic tourniquet placed around the thigh but not inflated.	Duration of followup: 730d Followup: 100% in all arms Final: NR Intermediate: DVT, proximal DVT, distal DVT (730d) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? No 6. Were methods for allocation concealment adequate? No 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Avikainen, 1995	Publication type: Full text Geographic location: Finland Funding: NR Number of centers: 1 Randomization and allocation concealment: Randomized to receive either of the two treatment arms in an unblinded fashion Outcome assessment: NR Total number randomized (number randomized in arms of interest): 167(167)	Inclusion criteria: Elective hip replacement; informed consent Exclusion criteria: Regular anticoagulant and/or antiplatelet (<14d before surgery); bleeding disorder; platelet (<100*109/l); acute or recent bleeding (<6wks); severe arterial HTN; hx of stroke during past 6m or paralysis of the lower limbs; endocarditis lenta; clinical signs of actual or hx of recent DVT (<3m); SCr>150µmol/l; severe hepatic and pancreatic disease; hypersensitivity to heparin; pregnancy and lactation; mental disorder and failure to give informed consent Intervention1: Enoxaparin 40mg/ 0.4ml SQ starting 12h before surgery and continued BID for 10d postoperatively Intervention2: UFH 500 IU SQ starting 2h before surgery and BID for 10d postoperatively	Duration of followup: Post-operative Followup: 100% in both arms Final: PE (post-operative) Intermediate: DVT, symptomatic DVT, proximal DVT, distal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? No 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Colwell, 1995	Publication type: Full text Geographic location: USA Funding: NR Number of centers: 25 Randomization and allocation concealment: Randomized to treatment groups Outcome assessment: Venograms and ultrasonograms read in a blinded manner by an institutionally qualified radiologist, physician or imaging specialist other than the principal investigator at each study site. Ultrasonogram videocassette recordings or hard copy format showing DVT were sent 2 experts for independent review. VQ scans and pulmonary angiogram assessments interpreted by qualified radiologist or physician other than principal investigator blinded to treatment regimens Total number randomized (number randomized in arms of interest): 453 (453)	Inclusion criteria: Male, premenopausal female(if documented to be not pregnant) or postmenopausal female patients 40y of age or older for elective TKA Exclusion criteria: Failure to achieve post-operative hemostasis; documented hx of positive clinical evidence of DVT; hx of generalized hemorrhagic disorders or any clinically significant diseases that might interfere with study medications; documented allergy to UFH, fish, swine products or radioopaque dye; uncontrolled asthma; hx of heparin associated TCP or skin rash; current evidence of drug or alcohol abuse; active ulcerative disease or GI hemorrhage within past 6m; uncontrolled HTN; surgery on the eye, spinal cord, or central nervous system within 3m; scheduled simultaneous multiple joint replacements; documented CVA within last 3m; treatment with aspirin or NSAID on a regular basis for 4d preceding hospitalization; pregnancy Intervention 1: Enoxaparin 30mg SQ q12h starting within 8h post-operative for 7d Intervention 2: Heparin 5000 U SQ q8h starting within 8h post-operative for 7.1d	Duration of followup: 21d after last medication dose Followup: 100% in both arms Final: PE, fatal PE, nonfatal PE (post-operative) Intermediate: DVT, proximal DVT, distal DVT (post-operative) Adverse events: Major bleeding, minor bleeding, surgical site bleeding (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Warwick, 1995	Publication type: Full text Geographic location: UK Funding: Government/foundation; academia Number of centers: 1 Randomization and allocation concealment: NR Outcome assessment: Venograms were interpreted by consensus of 2 consultant radiologists unaware of randomization Total number randomized: 156 (156)	Inclusion criteria Primary THR Exclusion criteria Recent aspirin consumption; medical requirement for continued NSAID intake; history of previous VTE Intervention: Enoxaparin 40mg SQ 12h pre- operatively, 12h and 36h for 3d. Comparator: Control	Duration of followup: Post-operative Followup: 100% in both arms Final: PE (post-operative) Intermediate: DVT, proximal DVT, distal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Colwell, 1994	Publication type: Full text Geographic location: USA Funding: Industry Number of centers: 34 Randomization and allocation concealment Randomly assigned to one of the 3 different treatment groups in a 1:1:1 ratio using a computer generated randomization schedule Outcome assessment: NR Total number randomized (number randomized in arms of interest): 610 (610)	Inclusion criteria: ≥40y scheduled for primary or revision hip replacement surgery Exclusion criteria: Operation on ipsilateral leg within previous 3m; hx of documented DVT or PE; heparin associated TCP; bleeding disorders; operation on the eye, spinal cord, nervous system within previous 3m; active ulcerative disease of the alimentary tract; uncontrolled HTN; use of NSAID during 4d before operation Intervention 1: Enoxaparin 30mg SQ q12h starting within 24h postoperatively and continued for 7d Intervention 2: Enoxaparin 40mg SQ QD starting within 24h postoperatively and continued for 7d Intervention 3: UFH 5000 U SQ q8h staring within 24h postoperatively and continued for 7d	Duration of followup: 42d Followup: 100% in both arms Final: PE, nonfatal PE (post-operative, discharge -42d) fatal PE, mortality (post-operative) Intermediate: DVT, proximal DVT, distal DVT (post-operative) Adverse events: Major bleeding, minor bleeding, surgical site bleeding, HIT(post-operative); readmission (discharge-42d)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Fauno, 1994	Publication type: Full text Geographic location: Finland, Denmark Funding: Industry Number of centers: 3 Randomization and allocation concealment: Randomized using sealed envelope Outcome assessment: All venograms examined independently by 3 radiologists who were unaware of the assigned drug Total number randomized (number randomized in arms of interest): 185 (185)	Inclusion criteria >40y, scheduled to have primary unilateral TKR and diagnosed as having osteoarthritis or rheumatoid arthritis Exclusion criteria Use of anticoagulant, platelet aggregation inhibitors, salicylates or NSAID within 7d before the operation; hx of bleeding disorder; abnormal preoperative coagulation values, including platelet count < 80 X 10^9/l or a PT outside range of 80-10 % of normal, indications of internal bleeding ; untreated HTN; hypersensitivity to heparin or contrast media; previous DVT or PE Intervention 1: Enoxaparin 40mg SQ QD staring on the evening before surgery for 7-10d postoperatively Intervention 2: UFH 5000 IU SQ TID starting evening before surgery for 7-10d postoperatively	Duration of followup: 60d Followup: 100% in both arms Final: Fatal PE, nonfatal PE, PE (post-operative) Intermediate: DVT, proximal DVT (post-operative); symptomatic DVT (post-operative-60d) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Partially 4. Were outcome assessors blind to exposure/intervention status? Partially 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Lieberman, 1994	Publication type: Full text Geographic location: USA Funding: Unfunded Number of centers: 1 Randomization and allocation concealment: Randomized to one of the 2 groups with the use of a random numbers table Outcome assessment: All venograms were analyzed in a blinded fashion by 1 radiologist Total number randomized (number randomized in arms of interest): 231 (231)	Inclusion criteria: Patients >39y; primary unilateral or bilateral hip arthroplasty under hypotensive epidural anesthesia Exclusion criteria: Previous VTE; allergy to aspirin or iodinated contrast medium; peptic ulcer disease; venous stasis ulcers of the lower extremity; hypercoagulable state or bleeding dyscrasia; CI to hypotensive epidural anesthesia Intervention: EC-aspirin 325 mg PO BID starting on the day of the operation for 3w+ IPC (Kendall SCD, thigh high) applied in the recovery room on the day of operation and worn continuously except when bathing or walking until venogram on postoperative day 6-8 Comparator: EC-aspirin 325 mg PO BID starting on the day of the operation for 3w	Duration of followup: 90d Followup: 100% in both arms Final: PE, fatal PE, nonfatal PE (90d); mortality, mortality due to bleeding (post-operative) Intermediate: Proximal DVT, distal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Menzin, 1994	Publication type: Full text Geographic location: USA Funding: Industry Number of centers: 32 Randomization and allocation concealment: NR Outcome assessment: NR Total number randomized (number randomized in arms of interest): 607 (607)	Inclusion criteria: Age≥ 37 undergoing elective hip replacement Exclusion criteria: Ipsilateral hip surgery in prior 3 months; history of VTE; bleeding dos or HIT; known allergy to UFH Intervention 1: Enoxaparin 30mg SQ q12h, starting within 24h after surgery for at least 7d Intervention 2: Enoxaparin 40mg SQ QD, starting within 24h of surgery, then continued for at least 7d Intervention 3: UFH 5000U SQ q8h, starting within 24h of surgery, then continued for at least 7d	Duration of followup: Post-operative Followup: 99.34% overall Final: NR Intermediate: DVT (post-operative) Adverse events: Major bleeding (postoperative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Santori, 1994	Publication type: Full text Geographic location: Italy Funding: NR Number of centers: NR Randomization and allocation concealment: Randomized by a casual numbers table, using sequentially numbered, sealed envelopes Outcome assessment: NR Total number randomized (number randomized in arms of interest): 132 (132)	Inclusion criteria: Patients undergoing primary THR under general anesthesia by a direct lateral approach Exclusion criteria: Previous hx of thromboembolism, varicose veins, venous insufficiency in the legs, or the presence of a malignant neoplasm Intervention 1: Heparin 5000 IU SQ TID starting the day before surgery for a duration of 10d Intervention 2: VFP (AV impulse system) fitted to both feet immediately after surgery and worn during all times in bed and interrupted only for physiotherapy and walking for 7-10d	Duration of followup: 42d Followup: 100% in both arms Final: Mortality due to bleeding, mortality (42d) Intermediate: DVT (42d) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Hull, 1993	Publication type: Full text Geographic location: USA, Canada Funding: Industry, Government/foundation Number of centers: 4 Randomization and allocation concealment: Randomized using a computer-derived treatment schedule balanced in blocks of 4, stratified into groups according to the study center Outcome assessment: Data on the outcome measures of effectiveness (venous thrombosis) and safety (bleeding complications) and on patients' deaths were interpreted by a central adjudicating committee. Two committee members not involved in the patient's care adjudicated, and disagreements were resolved by a third member Total number randomized (number randomized in arms of interest): 1436 (1436)	Inclusion criteria ≥18y scheduled to undergo THA or TKA Exclusion criteria: Currently active bleeding or disorders contraindicating anticoagulant therapy; hx of DVT or PE; allergy to heparin, bisulphites, or fish; allergy to radiopaque contrast medium; documented deficiency of antithrombin III, protein C, or protein S; hx of heparin-associated TCP; pregnancy; severe malignant HTN; severe hepatic failure (hepatic encephalopathy); severe renal failure necessitating dialysis; or geographic inaccessibility preventing them from making followup visits Intervention 1: Tinzaparin 75 IU/kg SQ QD starting 18-24h after surgery and continued until 14th postoperatively, venography or until discharge Intervention 2: Warfarin 10mg PO for the 1st dose with subsequent doses QD adjusted to maintain an INR between 2.0 and 3.0 starting on the evening before surgery and continued until 14th post-operative day, venography or discharge	Duration of followup: 90d Followup: 100% in both arms Final: Symptomatic objectively confirmed VTE, fatal PE, nonfatal PE (discharge - 90d), mortality due to bleeding, mortality (post-operative) Intermediate: DVT, proximal DVT (post-operative) Adverse events: Major bleeding, minor bleeding, surgical site bleeding (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Fordyce, 1992	Publication type: Full text Geographic location: UK Funding: None from any commercial party Number of centers: 1 Randomization and allocation concealment: Randomly assigned to 1 of the 2 groups by use of cards in sealed envelope Outcome assessment: Venograms independently assessed, blind, by 2 radiologists and vascular surgeon Total number randomized: 84 (84)	Inclusion criteria: Patients with osteoarthritis undergoing primary THR Exclusion criteria: NR Intervention: VFP (A-V Impulse System) applied postoperatively to the foot of operated limb Comparator: Control	Duration of followup: Post-operative Followup: VFP 92.86%; control 95.24% Final: NR Intermediate: DVT, proximal DVT, distal DVT (post-operative) Adverse events: Hemorrhagic complication (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Partially 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? No 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Francis, 1992	Publication type: Full text Geographic location: USA Funding: Government/foundation Number of centers: 2 Randomization and allocation concealment: Randomized using a computer generated randomization scheme Outcome assessment: Venograms were interpreted by a single radiologist unaware of the treatment group Total number randomized (number randomized in arms of interest): 232 (232)	Inclusion criteria Patients scheduled for primary THR Exclusion criteria: <18y; revision of a previous hip replacement; allergy to contrast media; receiving aspirin or long term anticoagulant therapy; underlying bleeding from GI or urinary tract Intervention 1: Warfarin PO 2 step regimen with dose adjustments to achieve an INR of 1.5 on the day of surgery and 2.5 postoperatively staring 10-14d pre-operatively, continued until venography Intervention 2: IPC (Kendall Inc.) applied in the operating room immediately before surgery worn at all times while in bed but removed as needed for nursing care or ambulation, continued until venography	Duration of followup: Post-operative Followup: 86.64% overall Final: Mortality due to bleeding, mortality (post-operative) Intermediate: DVT, proximal DVT (post-operative) Adverse events: Minor bleeding, major bleeding leading to re-operation, bleeding leading to transfusion (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? No 9. Was the differential loss to followup between the compared groups low (< 10%)? Can't tell 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Jorgensen, 1992	Publication type: Full text Geographic location: Denmark Funding: NR Number of centers: 1 Randomization and allocation concealment: NR Outcome assessment: NR Total number randomized: 82 (82)	Inclusion criteria: Patients admitted for hip fracture surgery; ≥ 40y Exclusion criteria: Bleeding disorders; hepatic or renal insufficiency; previous septic endocarditis; cerebral hemorrhage during the preceding 6m; hypersensitivity to heparin or iodine; anticoagulant therapy within 1w of surgery; patients from nursing homes Intervention: Dalteparin 2500 IU SQ 2h pre-operatively and 12h postoperatively, then 5000 IU daily for 6 days Comparator: Placebo (SQ saline injections)	Duration of followup: Post-operative Followup: Dalteparin 73.2%; placebo 92.7% Final: Mortality, mortality due to bleeding (post-operative) Intermediate: DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? No 9. Was the differential loss to followup between the compared groups low (< 10%)? No 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Wilson, 1992	Publication type: Full text Geographic location: UK Funding: NR Number of centers: 1 Randomization and allocation concealment: NR Outcome assessment: All venograms were independently assessed blind Total number randomized: 59 (59)	Inclusion criteria: Patients undergoing elective TKR with BiometAGC 2500 or Insall-Burnstein prostheses and a standard technique Exclusion criteria: NR Intervention: VFP (A-V Impulse System) fitted to the operated limb postoperatively and used continuously (except during mobilization) until ascending ipsilateral venography performed on 9th or 10th post-operative day Comparator: Control	Duration of followup: Post-operative Followup: 100% in both arms Final: PE, fatal PE, non-fatal PE (post-operative) Intermediate: DVT, proximal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Partially 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Bailey, 1991	Publication type: Full text Geographic location: USA Funding: Industry Number of centers: 1 Randomization and allocation concealment: Randomized to 1 of 2 treatment regimens using a standard computerized randomization program Outcome assessment: All venograms were carried out and interpreted by physicians blinded to the patients' treatment group Total number randomized (number randomized in arms of interest): 95 (95)	Inclusion criteria: Age≥40y scheduled for elective primary or revision THA Exclusion criteria: Active peptic ulcer disease; allergy to iodine contrast dye; underlying bleeding disorders; hx of CVAs, previous venous disease or hx or venous surgery Intervention 1: Low dose warfarin orally starting with 10mg the evening before surgery (adjusted to 7.5mg for women >70 and minor abnormal LFTs) and 5mg on the day of the surgery if PT and TT<15s. Subsequent doses adjusted to maintain PT of 14-18s Intervention 2: IPC (Kendall, Inc.) applied immediately after surgery in the recovery room and continuously except during bathing and physical therapy until hospital discharge	Duration of followup: Post-operative Followup: 100% in both arms Final: Mortality, mortality due to bleeding (post-operative) Intermediate: DVT, proximal DVT (post-operative) Adverse events: Readmission	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Eriksson, 1991	Publication type: Full text Geographic location: Sweden Funding: Government/Foundation Number of centers: NR Randomization and allocation concealment: Allocated to one of the two treatment groups in a randomized manner Outcome assessment: All phlebograms were made and analyzed by two experienced radiologists who were unaware of the assigned treatment. The pulmonary scintiscans were evaluated by an experienced clinical physiologist who was unaware of the phlebographic findings and the particular prophylactic treatment Total number randomized (number randomized in arms of interest): 136 (136)	Inclusion criteria: Patients admitted for THR ≥ 40y Exclusion criteria: Allergy to iodine or contrast medium; already receiving anticoagulant treatment; renal insufficiency; elevated levels of liver enzymes; hx of bleeding disorders, liver or renal disease; cerebral hemorrhage <6m before the time of the study; hypersensitivity to heparin or iodine; previous inclusion in the study Intervention 1: Dalteparin 5000 IU SQ QD starting evening before surgery for 10d postoperatively Intervention 2: UFH 5000 IU SQ TID starting 2h before surgery for 10d postoperatively	Duration of followup: Post-operative Followup: DVT: Dalteparin 94% UFH 86% PE: Dalteparin 97% UFH 90% Final: Fatal PE, nonfatal PE, PE, mortality due to bleeding; mortality (post-operative) Intermediate: DVT, asymptomatic DVT, symptomatic DVT (post-operative) Adverse events: Major bleeding, major bleeding leading to re-operation (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? No 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Jorgensen, 1991	Publication type: Full text Geographic location: Denmark Funding: Industry, government/foundation Number of centers: 1 Randomization and allocation concealment: NR Outcome assessment: Venograms were scrutinized by the same two experienced radiologist unaware of the anesthetic agent used Total number randomized (number randomized in arms of interest): 48 (48)	Inclusion criteria: Patients undergoing elective knee arthroplasty (primary or revision) Exclusion criteria: Patients receiving antithrombic medications; premenopausal women; history of venous thromboembolic disease; allergy to radioopaque contrast media Intervention 1: General anesthesia: Induction: thiopentone 3-5mg/kg, following intubation, lungs were ventilated with 66% NO in oxygen and diazepam 0.2mg/kg administered IV Intervention 2: Extradural anesthesia: 2% mepivacaine 3mL with adrenaline followed by 2% mepivacaine 8-15 mL through a lumbar extradural catheter. After surgery, 0.25% bupivacaine 5mL/hr was infused through the extradural catheter by infusion pump	Duration of followup: post-operative Followup: 81.25% in both arms Final: Nonfatal PE (post-operative) Intermediate: DVT, asymptomatic DVT, symptomatic DVT, proximal DVT, distal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Lassen, 1991	Publication type: Full text Geographic location: Denmark Funding: NR Number of centers: 2 Randomization and allocation concealment: Random numbers Outcome assessment: All venograms evaluated by a radiologist who was unaware of the randomization results Total number randomized: 210 (210)	Inclusion criteria: > 40y; scheduled for elective hip replacement Exclusion criteria: Treated with plasma expanders or investigational drugs within 4w prior to the operation; impaired renal or hepatic function; uncontrolled HTN (diastolic pressure >120mmHg); hemorrhagic diasthesis; pregnancy; confinement to bed; revision arthroplasty; hypersensitivity to radio-opaque dye, heparin, bisulfite, or benzyl alcohol; ongoing anticoagulant therapy; lack of informed consent Intervention: Tinzaparin 50 units anti-Xa/kg SQ daily starting 2h pre-operatively for 7d Comparator: Placebo (SQ saline injections)	Duration of followup: post-operative Followup: Tinzaparin 88.6%; placebo 92.4% Final: PE, Fatal PE, non-fatal (postoperatively); mortality (in-hospital) Intermediate: DVT, asymptomatic DVT, symptomatic DVT, proximal DVT, distal DVT (postoperatively) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Partially 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? No 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Levine, 1991	Publication type: Full text Geographic location: Canada Funding: Government/Foundation Number of centers: NR Randomization and allocation concealment: Randomized stratification by hospital, hx of documented VTE (present, absent) and by type of prosthesis (cement or uncemented) Outcome assessment: All venograms and bleeding episodes were interpreted by a central committee that was blinded to patients assigned treatment Total number randomized (number randomized in arms of interest): 665 (665)	Inclusion criteria: Consecutive patients undergoing elective hip replacement Exclusion criteria: < 40y; hx of underlying bleeding disorder; allergy to iodine or radiopaque dye; severe hepatic or renal disease; hx of MI or stroke < previous 6m; underlying psychiatric or addictive disorder; required to receive aspirin, long-term oral anticoagulant therapy, NSAIDs, indomethacin or other antlplatelet therapy during hospitalization Intervention 1: Enoxaparin 30mg SQ BID, starting 12-24h postoperatively and continued for 14d, or until discharge if it occurred sooner Intervention 2: UFH 7500 U SQ BID, starting 12-24h postoperatively and continued for 14d, or until discharge if it occurred sooner	Duration of followup: Postoperative Followup: 100% in both arms Final: Fatal PE, nonfatal PE, PE, mortality, mortality due to bleeding (post-operative) Intermediate: DVT, proximal DVT (post-operative) Adverse events: Major bleeding, minor bleeding, HIT (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Mitchell, 1991	Publication type: Full text Geographic location: USA Funding: Unknown Number of centers: 1 Randomization and allocation concealment: Patients were randomized prospectively based on their hospital number to receive either an epidural or general anesthetic Outcome assessment: bilateral contrast venography and ventilation-perfusion scanning were performed on the sixth, seventh, and eighth postoperative days and interpreted in a blinded fashion Total number randomized (number randomized in arms of interest): 72 (72)	Inclusion criteria: Age > 40y; normal hematological, renal, and nutritional parameters; history of osteoarthritis or rheumatoid arthritis with no previous surgery on the affected knee Exclusion criteria: Malignancy, history of DVT or PE Intervention 1: General anesthesia: Induction: sodium thiopental; maintenance: halogenated agent and nitrous oxide in oxygen Intervention 2: Epidural anesthesia: local anesthetic was then injected to obtain an anesthetic level adequate for the surgical procedure. Sedation was provided by incremental doses of intravenous narcotic and/or benzodiazepine	Duration of followup: Postoperative Followup: 100% in both arms Final: NR Intermediate: Proximal DVT(post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? No 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Planes, 1991	Publication type: Full text Geographic location: France Funding: Unknown Number of centers: 1 Randomization and allocation concealment: NR Outcome assessment: All venograms were examined by two experienced consultant radiologists without knowledge of group assignment. Total number randomized (number randomized in arms of interest): 194 (194)	Inclusion criteria: Age ≥ 45y; weighing ≥ 45 kg; undergoing elective hip replacement Exclusion criteria: Latent bleeding disorder; known allergy to iodine or radiopaque dye; renal insufficiency; previous replacement of the same hip; anticoagulant or antiplatelet therapy during the 8d prior to surgery; unable or unwilling to undergo general or spinal anesthesia Intervention 1: General anesthesia induced by fentanyl and thiopentone + enoxaparin 40 mg SQ 12 h prior to surgery, 12h after surgery then daily Intervention 2: Spinal anesthesia administered at the L3-L4 level + enoxaparin 20mg SQ 1h after onset of anesthesia then 40mg 12h after surgery and daily. Droperidol and/or midazolam were administered IV when sedation was necessary Intervention 3: Spinal anesthesia + enoxaparin 40mg SQ 12h after surgery then daily	Duration of followup: Post-operative Followup: 100% in all arms Final: Fatal PE, nonfatal PE, PE, mortality due to bleeding, mortality (post-operative) Intermediate: Proximal DVT, distal DVT (post-operative) Adverse events: Major bleeding, minor bleeding (post-operative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Torholm, 1991	Publication type: Full text Geographic location: Denmark Funding: NR Number of centers: 1 Randomization and allocation concealment: NR Outcome assessment: NR Total number randomized: 120 (120)	Inclusion criteria: THR patients ≥ 40y Exclusion criteria: Bleeding disorders; hepatic or renal insufficiency; previous septic endocarditis; cerebral hemorrhage during the past 6m; hypersensitivity to heparin or iodine; anticoagulant therapy within 1w of surgery Intervention: Dalteparin 2500 IU SQ 2h before surgery and 12h after surgery, then 5000 IU SQ daily for 6d Comparator: Placebo (SQ saline injections)	Duration of followup: Post-operative Followup: Dalteparin 96.7%; placebo 90% Final: Mortality, mortality due to bleeding (post-operative) Intermediate: DVT, proximal DVT, distal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? No 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Woolson, 1991	Publication type: Full text Geographic location: USA Funding: Unfunded Number of centers: 1 Randomization and allocation concealment: Random assignment to groups was carried out with the use of sealed envelopes Outcome assessment: NR Total number randomized: 196 (196)	Inclusion criteria: Primary or revisions THR patients >39y Exclusion criteria: Allergy to aspirin or warfarin; recently had a peptic ulcer or other bleeding diathesis; taken any drug that affect platelet function within two weeks before operation; expected to remain in bed for more than 4d postoperatively Intervention 1: IPC (Sequential Compression Device) thigh-high, worn bilaterally during surgery and until screening for DVT + aspirin 650mg po BID beginning the evening before surgery Intervention 2: IPC (Sequential Compression Device) thigh-high, worn bilaterally during surgery and until screening for DVT + warfarin 7.5mg or 10mg po the evening before surgery then adjusted according to prothrombin time to 1.2 to 1.3 X the control Comparator: IPC (Sequential Compression Device) thigh-high, worn bilaterally during surgery and until screening for DVT	Duration of followup: Post-operative Followup: 100% in all arms Final: PE (post-operative) Intermediate: Proximal DVT (post-operative) Adverse: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Cant' tell 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Haas, 1990	Publication type: Full text Geographic location: USA Funding: NR Number of centers: 1 Randomization and allocation concealment: Randomized to 2 treatment groups Outcome assessment: All venograms were interpreted by 1 radiologist unaware of the prophylactic regimen Total number randomized (number randomized in arms of interest): 119 (119)	Inclusion criteria: >39y scheduled for primary unilateral or one stage bilateral TKA Exclusion criteria: Hx of PE; receiving anticoagulant; hx of allergy to aspirin or massive bleeding in the stomach or duodenum Intervention 1: IPC (Kendall, Inc.) placed on the uninvolved limb just before surgery and on the operated limb after the surgery, worn continuously and removed only for washing or when patient was walking until morning after post-operative lung scan Intervention 2: Aspirin 650mg PO BID starting day before surgery and continued until patient was discharged from the hospital	Duration of followup: Post-operative Followup: 100% in both arms Final: NR Intermediate: DVT, proximal DVT, distal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Sorensen, 1990	Publication type: Full text Geographic location: Denmark Funding: NR Number of centers: 1 Randomization and allocation concealment: NR Outcome assessment: NR Total number randomized (number randomized in arms of interest): 70 (70)	Inclusion criteria: Patients aged ≥40y undergoing THR Exclusion criteria: NR Intervention: Tinzaparin 50 anti-Xa U/kg SQ daily starting 2h before surgery and continued for 7 consecutive days Comparator: Placebo (SQ saline injections)	Duration of followup: Post-operative Followup: 100% in both arms Final: Mortality, mortality due to bleeding (post-operative) Intermediate: DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Can' tell 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Can't tell 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? No 8. Was intention to treat analysis used? No 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Dechav-anne, 1989	Publication type: Full text Geographic location: France Funding: NR Number of centers: 2 Randomization and allocation concealment: Randomly allocated to 1 of 3 treatment groups using a sealed envelope Outcome assessment: NR Total number randomized (number randomized in arms of interest): 124 (124)	Inclusion criteria: >40y undergoing elective hip replacement under general anesthesia Exclusion criteria: Hemorrhagic diathesis; severe hepatic or renal insufficiency; active peptic ulcer disease; taking aspirin or drugs known to affect platelet function during 2 days prior to surgery Intervention 1: Dalteparin 2500 anti-Xa U SQ q12h starting 2h before surgery for 10-13d post-operative Intervention 2: Dalteparin 2500 anti-Xa U for the first 48h followed by 5000 anti-Xa U QD SQ starting 2h before surgery for 10-13d post-operative Intervention 3: Heparin 5000 IU SQ twice daily with dose adjusted after 2nd d according to APTT starting 2h before surgery for 10-13d post-operative	Duration of followup: Post-operative Followup: 100% in both arms Final: NR Intermediate: DVT, proximal DVT, distal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Can't tell 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Monreal, 1989	Publication type: Full text Geographic location: Spain Funding: NR Number of centers: NR Randomization and allocation concealment: Allocated by numbers from a randomization list; sealed envelope guaranteed that in case of emergency, type of prophylaxis could be checked without breaking code for other patients Outcome assessment: NR Total number randomized (number randomized in arms of interest): 90 (90)	Inclusion criteria: >40y admitted for HFS on the day of fracture Exclusion criteria: Underlying bleeding disorder Intervention1: Dalteparin 2,500U SQ 2h before surgery followed by 5000 U SQ QD for 9d post-operative Intervention2: Heparin 5000 U SQ starting 2h before surgery and q8h for 9d post-operative	Duration of followup: Post-operative Followup: PE: 100% in both arms DVT: Dalteparin 69.57% Heparin 68.18% Final: Fatal PE, nonfatal PE, PE, mortality due to bleeding, mortality (post-operative) Intermediate: DVT, proximal DVT, distal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? No 9. Was the differential loss to followup between the compared groups low (< 10%)?Yes 10. Was the overall loss to followup low (< 20%)? No 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Powers, 1989	Publication type: Full text Geographic location: Canada Funding: Industry; government Number of centers: 3 Randomization and allocation concealment: Patients were allocated using sealed envelopes to treatment groups, according to a prescribed randomized arrangement, balanced in blocks of 3 and 6 Outcome assessment: All diagnostic results and suspected hemorrhagic complications were adjudicated by an independent panel unaware of treatment allocation. Total number randomized: 194 (194)	Inclusion criteria: 18-90y; entering hospital for HFS Exclusion criteria: Allergy to aspirin, warfarin or radiopaque dye; inability to undergo I-25 fibrinogen leg scanning or impedence plethysmography; medical need to continue aspirin or other antiplatelet therapy; could not be randomized within 24h of hospital admission with fractured hip; refused to give informed consent Intervention 1: Warfarin 10mg PO given after surgery up to 21d postoperatively or discharge whichever occurred first; Intervention 2: EC-aspirin 650mg PO BID starting postoperatively up to 21d or discharge whichever occurred first Comparator: Placebo	Duration of followup: 90d Followup: 100% in all arms Final: PE, fatal PE, non-fatal PE, mortality due to bleeding (21d); mortality (90d) Intermediate: NR Adverse events: Major bleeding (postoperatively)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Partially 4. Were outcome assessors blind to exposure/intervention status? Partially 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Planes, 1988	Publication type: Full text Geographic location: France Funding: Unknown Number of centers: 7 Randomization and allocation concealment: NR Outcome assessment: All venograms interpreted by central committee of 3 radiologists independently without knowledge of treatment assignment Total number randomized (number randomized in arms of interest): 237 (237)	Inclusion criteria: Age >45y and undergoing elective hip replacement Exclusion criteria: Underlying bleeding disorder; hx of allergy to iodine or radiopaque dye; renal insufficiency with Cr >30mg/l; hx of DVT associated with previous hip surgery; hx of replacement of the same hip, or taken anticoagulant or antiplatelet therapy during the 8d prior to surgery. Intervention 1: Enoxaparin 40mg SQ, QD, started 12h before surgery, and continued until 14d or hospital discharge Intervention 2: UFH 5000IU SQ, q8h daily, started 12h before surgery, and continued until 14d or hospital discharge	Duration of followup: Post-operative Followup: 100% in both arms Final: Fatal, non- fatal PE, mortality due to bleeding, mortality (post-operative) Intermediate: DVT, proximal DVT, distal DVT (post-operative) Adverse events: Major bleeding, minor bleeding (postoperative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Barre, 1987	Publication type: Full text Geographic location: France Funding: NR Number of centers: NR Randomization and allocation concealment: Randomly allocated to treatment groups Outcome assessment: NR Total number randomized (number randomized in arms of interest): 80 (80)	Inclusion criteria: Age≥40y who had to undergo THR under epidural anesthesia Exclusion criteria: Hemorrhagic past history; severe hepatic or renal insufficiency; femoral neck fracture; progressive cancer Intervention 1: Dalteparin 2,500 anti-Xa U SQ 2h before surgery, continued q12h postoperatively for 10d Intervention 2: Heparin 3750 IU SQ 2h before surgery, continued q8h postoperatively for 10d with dose adjustment using thrombin time and/or cephalin plus activator time	Duration of followup: 60d Followup: 100% in both arms Final: Mortality, mortality due to bleeding, PE, nonfatal PE, fatal PE (60d) Intermediate: DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Paiement, 1987	Publication type: Full text Geographic location: USA Funding: Industry, government/foundation Number of centers: 1 Randomization and allocation concealment: NR Outcome assessment: The radiologists who interpreted the phlebography were unaware of the prophylactic regimen used. Total number randomized (number randomized in arms of interest): 163 (163)	Inclusion criteria: Age >39y and undergoing total hip replacement Exclusion criteria: Patients found before or at operation to require more than 3 weeks of postoperative bed rest because of the complexities of the operation were excluded. Intervention 1: Low dose warfarin started the night before surgery, then 5 mg on the night of surgery adjusted to maintain PTT for control at 11-12 s, and continued until at least 2d after radiographic phlebography, if the result was negative Intervention 2: IPC (Gaymar) started postoperatively in the recovery room and worn bilaterally continuously, except during brief periods of skin care and when the patient was ambulating	Duration of followup: Post-operative Followup: 100% in both arms Final: Fatal PE, nonfatal PE, PE (post-operative) Intermediate: DVT, proximal DVT, distal DVT (post-operative) Adverse events: Major bleeding, minor bleeding (postoperative)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Alfaro, 1986	Publication type: Full text Geographic location: Spain Funding: Government Number of centers: 1 Randomization and allocation concealment: NR Outcome assessment: NR Total number randomized (number randomized in arms of interest): 120 (90)	Inclusion criteria: > 40y; admitted for THR and gave informed consent Exclusion criteria: Pregnancy; history of peptic ulcers; hematemesis or sensitivity to salicylates; ingested aspirin or other antiplatelet agent in week prior to admission Intervention 1: Aspirin 500mg PO BID beginning preoperatively for 7d Intervention 2: Aspirin 125mg PO BID beginning preoperatively for 7d Comparator: Control	Duration of followup: Post-operative (minimum 7d) Followup: 100% in both arms Final: PE (post-operative) Intermediate: DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Can't tell 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Can't tell 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Poor

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Turpie, 1986	Publication type: Full text Geographic location: Canada Funding: Government/foundation Number of centers: Multicenter Randomization and allocation concealment: NR Outcome assessment: Venograms and bleeding episodes were interpreted by a central committee unaware of the assigned treatment Total number randomized (number randomized in arms of interest): 100 (100)	Inclusion criteria: ≥40y undergoing elective hip replacement. Exclusion criteria: Underlying bleeding disorder; history of allergy to iodine or radiopaque dye; DVT related to hip surgery; surgery on ipsilateral hip; taking aspirin during hospitalization; previous VTE; previous hip surgery Intervention: Enoxaparin 30mg SQ BID starting 12-24h after surgery for 14d or until discharge Comparator: Placebo (SQ saline injection)	Duration of followup: Post-operative Followup: 100% in both arms Final: PE, fatal PE, nonfatal PE, mortality due to bleeding, mortality (post-operative) Intermediate: DVT, proximal DVT (post-operative) Adverse events: Major bleeding, minor bleeding (post-operative	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Partially 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
McKenzie, 1985	Publication type: Full text Geographic location: UK Funding: Unknown Number of centers: 1 Randomization and allocation concealment: Patients allocated randomly to received subarachnoid blockade or general anesthesia Outcome assessment: NR Total number randomized (number randomized in arms of interest): 40 (40)	Inclusion criteria: Patients admitted for HFS Exclusion criteria: NR Intervention 1: General anesthesia: Induced with althesin 1-3ml IV, following the administration of suxamethonium 50mg, the trachea was intubated with a cuffed endotracheal tube and anesthesia was maintained with 66% nitrous oxide and 0.75-1.25% halothane in oxygen Intervention 2: Subarachnoid blockade: Hyperbaric cinchocaine 1.2-1.5ml injected slowly to the subarachnoid space at the L3-4 or L4-5 space via a 22-gauge spinal needle. The block was performed with the partient in the horizontal lateral position with fractured hip dependent. Small doses of diazepam were administered IV if sedation was necessary.	Duration of followup: 365d postoperatively Followup: 100% in both arms Final: Mortality (365d) Intermediate: DVT, symptomatic DVT, asymptomatic DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Welin-Berger, 1982	Publication type: Full text Geographic location: Sweden Funding: Government / foundation Number of centers: 1 Randomization and allocation concealment: NR Outcome assessment: NR Total number randomized: 60 (40)	Inclusion criteria: THR; no history of previous DVT and with normal venous outflow capacity of both legs determined pre-operatively Exclusion criteria: NR Intervention: Heparin 5000IE SQ preoperatively and repeated every 12h during 1st post-operative week Comparator: Control	Duration of followup: Post-operative Followup: 100% in both arms Final: PE (post-operative) Intermediate: DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Can't tell 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Poor

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Modig, 1981	Publication type: Full text Geographic location: Sweden Funding: Government/Foundation; industry Number of centers: 1 Randomization and allocation concealment: The patients were randomly allotted, according to their date of birth Outcome assessment: All phlebograms were scrutinized by an experienced radiologist unaware of the type of anesthetic regiment used in any particular patient. Total number randomized (number randomized in arms of interest): 30 (30)	Inclusion criteria: Severe osteoarthrosis of the hip joint and undergoing THR; no history of heart or lung disease, diabetes, previous thromboembolism, varicose veins, or leg ulcers Exclusion criteria: NR Intervention 1: General anesthesia: Artificial ventilation with nitrous oxide/oxygen via an endotracheal tube and intravenously administered fentanyl and pancuronium bromide, narcotic analgesics were given intramuscularly on demand for pain relief Intervention 2: Epidural anesthesia: Bupivacaine with epinephrine prolonged into the postoperative period for pain relief	Duration of followup: 14d Followup: 100% in both arms Final: PE (14d) Intermediate: DVT, proximal DVT, distal DVT (14d) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? No 6. Were methods for allocation concealment adequate? Can't tell 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
McKenna, 1980	Publication type: Full text Geographic location: USA Funding: NR Number of centers: 1 Randomization and allocation concealment: Computer-generated random number table Outcome assessment: NR Total number randomized (number randomized in arms of interest): 46 (21)	Inclusion criteria: Patients aged >40y admitted for TKR Exclusion criteria: History of DVT or PE in the 6m prior to study Intervention: Aspirin 325mg PO TID immediately after admission and continued until discharge Comparator: Placebo (tablet)	Duration of followup: Post-operative Followup: Aspirin 81.82%; Placebo 100% Final: Mortality, mortality due to bleeding (post-operative) Intermediate: DVT, proximal DVT, distal DVT (post-operative) Adverse events: NR	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Can't tell 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Can't tell 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? No 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

*Duration of followup is reported as the original study's longest reported followup for outcomes of interest and followup percent is reported for the study's pre-specified primary outcome

† A=Patient operated within 12h of randomization, B= Patient operated 12-24h after randomization. C= Patient operated >24h after randomization. D= Patient operated within 8h of randomization. E= Patient operated >8h after randomization.

Abbreviations: ALT=Alanine aminotransferase; APTT= activated partial thromboplastin time; ARF=acute renal failure; AST=aspartate aminotransferase; BID= twice daily; BMI=body mass index ; CHF=congestive heart failure; CI=contraindication; CNS=central nervous system; Cr=creatinine; CRF=chronic renal failure; CT=computed tomography scan; CUS=continuous ultrasonography; CVA= cerebraovascular accident;

CVI= chronic venous insufficiency; d=day(s); dL=deciliter; DUS= Doppler ultrasound; DVT=deep vein thrombosis; EC=enteric coated; GA=general anesthesia; GCS=graduated compression stocking; GI=gastrointestinal; h=hour(s); HFS=hip fracture surgery; HIT=heparin-induced thrombocytopenia; HTN=hypertension; hx=history; INR=international normalized ratio; IPC=intermittent pneumatic compression; IU=international units; IV=intravenous; IVC=inferior vena cava; kg=kilograms; L=liter; LMWH=low molecular weight heparin; m=months; MC=multicenter; MI=myocardial infarction; min=minute(s); mg=milligrams; mmHg=millimeters of mercury; mL=mililiters; MRI=magnetic resonance imaging; NR=not reported; NSAID=nonsteroidal anti-inflammatory drug; NYHA=New York heart association PE=pulmonary embolism; PO=by mouth; PT=prothrombin time; PTS=post thrombotic syndrome; PVD=peripheral vascular disease; QD=daily; SCr= serum creatinine; SQ=subcutaneously; TCP=thrombocytopenia; THA=total hip arthroplasty; TKA=total knee arthroplasty; THR=total hip replacement; TKR=total knee replacement; TT=thromboplastin time; UFH=unfractionated heparin; UK=United Kingdom; ULN=upper limit of normal; US=ultrasound; USA=United States of American; VFP=venous foot pump; VTE=venous thromboembolism; VQ=ventilation perfusion; w=week(s); y=year(s)

Table 4. Quality and characteristics of randomized controlled trials evaluating nonmajororthopedic surgery

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Lapidus, 2007	Publication type: Full text Geographic location: Sweden Funding: Industry/Government Number of centers: 1 Randomization and allocation concealment: Patients were consecutively included and randomized(by computer) into the study immediately after surgery at theoutpatient surgery unit. Outcome assessment: The radiologist on duty made a preliminary evaluation of the phlebography for clinical purposes. A standardized, secondary evaluation was then carried out by an experienced independent radiologist blinded to the randomization and previous phlebographic findings. Total number randomized (number randomized in arms of interest): 105 (105)	Inclusion criteria: Patients age18 to 75 years with acute (0-72h) Achilles tendon rupture accepted for surgery admitted Exclusion criteria: Inability or refusal to give informed consent for participation in the study, ongoing treatment with anticoagulant therapy, known allergy for contrast media, intended followup at another hospital, an inability to comply with the study instructions (because of drug or alcohol abuse, cognitive dysfunction, etc), known kidney disorder, a recent thromboembolic event (during the preceding 3 months), recent surgery (during the preceding month), the presence of known malignancy, a current bleeding disorder, pregnancy, treatment with high doses of acetylsalicylic acid (325 mg) other platelet inhibitors, and other injuries Intervention 1: Dalteparin 5000 units SC QD started a few hours after surgery and continued until hospital discharge for a total duration of 6 weeks Intervention 2: Placebo (sodium chloride) injections SC QD started a few hours after surgery and continued until hospital discharge for a total duration of 6 weeks	Duration of followup: 42d Followup: 100% in all arms Final: PE, Fatal PE, Non-fatal PE (42d) Intermediate: DVT, proximal DVT (42d) Adverse events: Major bleeding (42d)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? Yes 4. Were outcome assessors blind to exposure/intervention status? Yes 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? Yes Overall quality rating: Good

Study, year	Trial characteristics	Population and interventions	Followup* and Outcomes of interest (Timing)	Quality assessment
Michot, 2002	Publication type: Full text Geographic location: Switzerland Funding: Unknown Number of centers: 1 Randomization and allocation concealment: Sealed envelopes Outcome assessment: NR Total number randomized (number randomized in arms of interest): 130 (130)	Inclusion criteria Patients aged18 to 80 years referred for diagnostic or therapeutic arthroscopic knee surgery Exclusion criteria Inability or unwillingness to given written informed consent; history of DVT or PE; known deficiency of antithrombin III, protein C, protein S, or presence of a resistance to activated protein C; malignancy; pregnancy; ongoing treatment with steroids, anticoagulant or antiplatelet agents, long-term use of NSAIDs; hypersensitivity to heparin; history of GI bleeding in the past 2 weeks; history of cerebrovascular accident in the past 6 months; or severe renal or hepatic failure Intervention 1: Dalteparin 2500 units for patients 70kg or less and Dalteparin 5000 units for patients over 70kg given SC QD starting 60-120 mins before operation for 30d Intervention 2: No prophylaxis (Control group)	Duration of followup: 30d Followup: 100% Final: PE (30d) Intermediate: DVT, proximal DVT, distal DVT (30d) Adverse events: Major bleeding, minor bleeding (30d)	1. Were the groups similar at baseline in terms of baseline characteristics and prognostic factors? Yes 2. Were outcomes assessed using a valid methodology and criteria? Yes 3. Were subjects and providers blind to the intervention status of participants? No 4. Were outcome assessors blind to exposure/intervention status? Can't tell 5. Were the methods used for randomization adequate? Yes 6. Were methods for allocation concealment adequate? Yes 7. Were incomplete outcome data adequately addressed? Yes 8. Was intention to treat analysis used? Yes 9. Was the differential loss to followup between the compared groups low (< 10%)? Yes 10. Was the overall loss to followup low (< 20%)? Yes 11. Conflict of interest reported and insignificant? No Overall quality rating: Fair

*Duration of followup is reported as the original study's longest reported followup for outcomes of interest and followup percent is reported for the study's pre-specified primary outcome

Abbreviations: d=day(s); DVT=deep vein thrombosis; GI=gastrointestinal; mins=minutes; PE=pulmonary embolism; QD=once daily; SC=subcutaneously; w=week(s); y=year(s)

Table 5. Quality and characteristics of observational studies

Study, year	Study characteristics	Population, intervention, followup	Followup*, outcomes of interest (timing)	Quality assessment
Bozic, 2010	Publication type: Full text Geographical location: US Study design: Retrospective cohort Funding: Government/Foundation Number of centers: 307 Outcome assessment: ICD-9 codes as reported in hospital database Number of participants enrolled: 93,840 (56,642)	Inclusion criteria: ≥18 y; primary TKA as their principal procedure during hospitalization Exclusion criteria: No charges for any VTE prophylaxis treatment; had charges for VTE treatment in formulations representing therapeutic rather than prophylactic anticoagulation Intervention: Warfarin Comparator: Aspirin	Duration of followup (d): 30 Covariates/potential confounders adjusted for: Patient characteristics and comorbidities along with propensity score Final: Mortality (30d) Intermediate: NR Adverse: Surgical site bleeding (30d)	1. Unbiased selection of the cohort? Yes 2. Selection minimizes baseline differences in prognostic factors? No 3. Sample size calculated? No 4. Adequate description of the cohort? Yes 5. Validated method to ascertain exposure? Yes 6. Validated method for ascertaining clinical outcomes? Partially 7. Outcome assessment blinded to exposure? Can't tell 8. Adequate followup period? Yes 9. Completeness of followup? Yes 10. Analysis controls for confounding? Yes Overall quality rating: Good

Study, year	Study characteristics	Population, intervention, followup	Followup*, outcomes of interest (timing)	Quality assessment
Cusick, 2009	Publication type: Full text Geographical location: Ireland Study design: Prospective Funding: NR Number of centers: 1 Outcome assessment: Data recorded prospectively in a database within the orthopedics department by a designated team of outcomes assessment nurses Number of participants enrolled: THR: 2,203 (2,203) TKR: 2,050 (2,050)	Inclusion criteria: Consecutive patients undergoing primary THR or TKR Exclusion criteria: NR Intervention 1: Aspirin 150mg po QD starting postoperative day 1 for 6w Intervention 2: Warfarin Comparator: No prophylaxis	Duration of followup (d): 90 Covariates/potential confounders adjusted for: Unadjusted Final: Fatal PE, non-fatal PE, mortality (90d) Intermediate: NR Adverse: NR	1. Unbiased selection of the cohort? Yes 2. Selection minimizes baseline differences in prognostic factors? Yes 3. Sample size calculated? No 4. Adequate description of the cohort? No 5. Validated method to ascertain exposure? Yes 6. Validated method for ascertaining clinical outcomes? Yes 7. Outcome assessment blinded to exposure? Can't tell 8. Adequate followup period? Yes 9. Completeness of followup? Yes 10. Analysis controls for confounding? No Overall quality rating: Fair

Study, year	Study characteristics	Population, intervention, followup	Followup*, outcomes of interest (timing)	Quality assessment
Froimson, 2009	Publication type: Full text Geographical location: US Study design: Retrospective Funding: Unfunded Number of centers: 1 Outcome assessment: Objectively confirmed pathologies were recorded Number of participants enrolled: 1,810 (1,810)	Inclusion criteria: Consecutive patients 18 to 90y in age; undergoing elective primary or revision hip or knee replacement surgery Exclusion criteria: Patients treated for tumor, fracture, or resection arthroplasty Intervention: IPC (ActiveCare CECT system) applied immediately pre-operatively on contralateral leg the bilateral postoperatively for duration of hospital stay or diagnosis of VTE Comparator: IPC (Flowtron excel pump) applied immediately pre-operatively on contralateral leg the bilateral postoperatively for duration of hospital stay or diagnosis of VTE	Duration of followup (d): 30d Covariates/potential confounders adjusted for: Unadjusted Final: Fatal PE, non-fatal PE, mortality, mortality due to bleeding (30d) Intermediate: DVT (30d) Adverse: NR	1. Unbiased selection of the cohort? Yes 2. Selection minimizes baseline differences in prognostic factors? No 3. Sample size calculated? No 4. Adequate description of the cohort? Partially 5. Validated method to ascertain exposure? Yes 6. Validated method for ascertaining clinical outcomes? Yes 7. Outcome assessment blinded to exposure? Can't tell 8. Adequate followup period? Yes 9. Completeness of followup? Yes 10. Analysis controls for confounding? No Overall quality rating: Fair

Study, year	Study characteristics	Population, intervention, followup	Followup*, outcomes of interest (timing)	Quality assessment
Gandhi, 2009	Publication type: Full text Geographical location: Canada Study design: Registry Funding: NR Number of centers: 1 Outcome assessment: Diagnosis of DVT assessed by a physician, who ordered a Doppler ultrasound based on clinical symptoms of excessive pain and swelling Number of participants enrolled: 1460 (1460)	Inclusion criteria: ≥18 y; primary or secondary osteoarthritis scheduled for primary TKR Exclusion criteria: NR Comparisons: Patients with metabolic syndrome were compared to patients without metabolic syndrome to determine the effect of metabolic syndrome on the incidence of symptomatic DVT	Duration of followup (d): 90d Covariates/potential confounders adjusted for: Adjusted for age, sex, BMI, Charleston Index and education Final: NR Intermediate: Symptomatic DVT (90d) Adverse: NR	1. Unbiased selection of the cohort? Yes 2. Selection minimizes baseline differences in prognostic factors? Yes 3. Sample size calculated? No 4. Adequate description of the cohort? Yes 5. Validated method to ascertain exposure? Yes 6. Validated method for ascertaining clinical outcomes? Yes 7. Outcome assessment blinded to exposure? Can't tell 8. Adequate followup period? Yes 9. Completeness of followup? Yes 10. Analysis controls for confounding? Yes Overall quality rating: Good

Study, year	Study characteristics	Population, intervention, followup	Followup*, outcomes of interest (timing)	Quality assessment
McNamara, 2009	Publication type: Full text Geographical location: UK Study design: Prospective observational Funding: NR Number of centers: 1 Outcome assessment: All symptomatic DVT confirmed by ultrasound, venography, or at autopsy and all symptomatic PE confirmed by nuclear medicine isotope scan, CT angiography or autopsy Number of participants enrolled: 5300 (5300)	Inclusion criteria: >16 y admitted for HFS Exclusion criteria: Hip fracture treated non-surgically Comparisons: Patients who developed thromboembolic complications were compared to patients who did not develop thromboembolic complications to assess risk factors for symptomatic VTE	Duration of followup (d): 365d Covariates/potential confounders adjusted for: Age, sex Final: Symptomatic VTE (365d) Intermediate: NR Adverse: NR	1. Unbiased selection of the cohort? Yes 2. Selection minimizes baseline differences in prognostic factors? Yes 3. Sample size calculated? No 4. Adequate description of the cohort? Yes 5. Validated method to ascertain exposure? Yes 6. Validated method for ascertaining clinical outcomes? Yes 7. Outcome assessment blinded to exposure? Can't tell 8. Adequate followup period? Yes 9. Completeness of followup? Yes 10. Analysis controls for confounding? Yes Overall quality rating: Good

Study, year	Study characteristics	Population, intervention, followup	Followup*, outcomes of interest (timing)	Quality assessment
Dorr, 2007	Publication type: Full text Geographical location: USA Study design: Retrospective cohort Funding: Industry Number of centers: 1 Outcome assessment: All patients had Doppler ultrasound within 24h before discharge and symptomatic patients suggestive of PE had VQ scan for PE Number of participants enrolled: 970 (970)	Inclusion criteria: Patients who underwent total knee or hip arthroplasties between January 2002 and July 2003 Exclusion criteria: NR Comparisons: No/Low risk group was compared to high risk group for the prevalence of thromboembolic complications	Duration of followup (d): 180d Covariates/potential confounders adjusted for: Unadjusted Final: Non-fatal PE, mortality (180d) Intermediate: DVT, proximal DVT, distal DVT (180d) Adverse: NR	1. Unbiased selection of the cohort? Yes 2. Selection minimizes baseline differences in prognostic factors? No 3. Sample size calculated? No 4. Adequate description of the cohort? Yes 5. Validated method to ascertain exposure? Yes 6. Validated method for ascertaining clinical outcomes? Yes 7. Outcome assessment blinded to exposure? Can't tell 8. Adequate followup period? Partialy 9. Completeness of followup? Yes 10. Analysis controls for confounding? No Overall quality rating: Fair

Study, year	Study characteristics	Population, intervention, followup	Followup*, outcomes of interest (timing)	Quality assessment
Shorr, 2007	Publication type: Full text Geographical location: US Study design: Retrospective cohort Funding: Unknown Number of centers: 509 Outcome assessment: ICD-9 codes as reported in hospital database Number of participants enrolled: 144,806 (144,860) 257,380† (257,380)†	Inclusion criteria: ≥18 y; primary or secondary diagnosis for hip replacement, knee replacement, or hip fracture surgery during the index hospitalization; received dalteparin, enoxaparin, fondaparinux, or UFH within 1d prior or 2d after hip or knee replacement or hip fracture surgery Exclusion criteria: Received more than 1 anticoagulant of interest on their 1st d of injectable anticoagulant therapy; received UFH only at subtherapeutic prophylactic doses (heparin flush or <5,000 U); admitted diagnosis of VTE [ACS]†; outpatient emergency room or hospital outpatient clinic visit including a VTE diagnosis [ACS diagnosis]† during the 3m prior to initial hospital stay; [no recorded surgery day]† Intervention 1: Fondaparinux Intervention 2: Enoxaparin or dalteparin Intervention 4: UFH Intervention 5:† No prophylaxis	Duration of followup (d): 60d postdischarge Covariates/potential confounders adjusted for: Age†, gender†, orthopedic surgery type†, comorbidities (Charlson-Deyo score)†, LOS†, cancer diagnosis†, number of hospitalizations prior to orthopedic surgery hospitalization†, hospital geographic location (Northeast, West, Midwest, and South)†, hospital type (teaching, non-teaching)†, urban vs. rural hospital location†, and hospital size (number of beds)† Final: Mortality (inhospital) Intermediate: NR Adverse: Major bleeding (60d postdischarge)	1. Unbiased selection of the cohort? Yes 2. Selection minimizes baseline differences in prognostic factors? Yes 3. Sample size calculated? No 4. Adequate description of the cohort? Yes 5. Validated method to ascertain exposure? Partially 6. Validated method for ascertaining clinical outcomes? Partially 7. Outcome assessment blinded to exposure? Can't tell 8. Adequate followup period? Yes 9. Completeness of followup? Yes 10. Analysis controls for confounding? Partially Overall quality rating: Fair

Study, year	Study characteristics	Population, intervention, followup	Followup*, outcomes of interest (timing)	Quality assessment
Leirozovicz, 2004 SMART study	Publication type: Full text Geographical location: Bangladesh, China, India, Indonesia, South korea, Malaysia, Pakistan, Phillipines, Singapore, Taiwan, Thailand Study design: Prospective cohort Funding: Industry Number of centers: 39 Outcome assessment: DVT was confirmed by ultrasonography and venography, PE was confirmed by VQ scan (PIOPED), angiography, CT scan or autopsy. All outcomes were adjudicated by an independent Committee Number of participants enrolled: 2420 (2420)	Inclusion criteria: Asian patients atleast 40y, hospitalized for THR, TKR or HFS Exclusion criteria: Patients scheduled to receive thromboprophylactic drugs during their hospital stay; patients who received antiplatelet agents or vitamin K antagonists within the week preceding inclusion Comparisons: Patients who developed VTE or sudden death were compared to patients who did not to determine the potential predictive factors	Duration of followup (d): 30d Covariates/potential confounders adjusted for: Unadjusted Final: Symptomatic VTE, mortality (30d) Intermediate: NR Adverse: NR	1. Unbiased selection of the cohort? Yes 2. Selection minimizes baseline differences in prognostic factors? Yes 3. Sample size calculated? Yes 4. Adequate description of the cohort? Yes 5. Validated method to ascertain exposure? Yes 6. Validated method for ascertaining clinical outcomes? Yes 7. Outcome assessment blinded to exposure? Yes 8. Adequate followup period? No 9. Completeness of followup? Yes 10. Analysis controls for confounding? No Overall quality rating: Good

Study, year	Study characteristics	Population, intervention, followup	Followup*, outcomes of interest (timing)	Quality assessment
Sachs, 2003	Publication type: Full text Geographical location: US Study design: Controlled observational Funding: Unfunded Number of centers: MC Outcome assessment: Charts screened by nurse-research assistant using standardized tool in duplicate Number of participants enrolled: 1,742 (1,742)	Inclusion criteria: Patients undergoing unilateral primary TKA Exclusion criteria: Bilateral or revision TKA; already on warfarin for chronic AF; selected for warfarin prophylaxis due to previous chronic AF or thromboembolic events Intervention: Warfarin adjusted bi-weekly to maintain INR of 1.6-2.2 for 6w Comparator: No prophylaxis	Duration of followup (d): 90d Covariates/potential confounders adjusted for: Unadjusted Final: Mortality (90d) Intermediate: Symptomatic DVT (90d) Adverse: Bleeding leading to transfusion, readmission, reoperation (90d)	1. Unbiased selection of the cohort? Yes 2. Selection minimizes baseline differences in prognostic factors? Partially 3. Sample size calculated? No 4. Adequate description of the cohort? Partially 5. Validated method to ascertain exposure? Yes 6. Validated method for ascertaining clinical outcomes? Yes 7. Outcome assessment blinded to exposure? Can't tell 8. Adequate followup period? Yes 9. Completeness of followup? Yes 10. Analysis controls for confounding? No Overall quality rating: Fair

Study, year	Study characteristics	Population, intervention, followup	Followup*, outcomes of interest (timing)	Quality assessment
Ryan, 1998	Publication type: Full text Geographical location: US, Canada Study design: Retrospective cohort Funding: Academia, foundation Number of centers: 4 Outcome assessment: Venograms performed postoperatively were interpreted by blinded radiologists and clinically evident bleeding were identified. Number of participants enrolled: 825 (825)	Inclusion criteria: Patients with THR or TKR recruited for one of six prospective studies comparing different antithrombotic prophylaxis regimens Exclusion criteria: <18y; allergic to contrast media; receiving aspirin or long term anticoagulation therapy; underlying bleeding disorder or recent bleeding from GI or urinary tract; pregnancy; SCr>1.7mg/dL; recent eye, ear or CNS surgery; known hypersensitivity to heparin; severe HTN; weight<90lbs Comparisons: Patients with Factor V Leiden mutation was compared to patients without Factor V Leiden mutation to determine its association with DVT and bleeding complications	Duration of followup (d): Postoperative Covariates/potential confounders adjusted for: Age; sex; history of DVT or PE; type of venograms Final: NR Intermediate: DVT (postoperative) Adverse: Major bleeding, minor bleeding (postoperative)	1. Unbiased selection of the cohort? Yes 2. Selection minimizes baseline differences in prognostic factors? Yes 3. Sample size calculated? Yes 4. Adequate description of the cohort? Yes 5. Validated method to ascertain exposure? Yes 6. Validated method for ascertaining clinical outcomes? Yes 7. Outcome assessment blinded to exposure? Partially 8. Adequate followup period? No 9. Completeness of followup? Yes 10. Analysis controls for confounding? Yes Overall quality rating: Good

Study, year	Study characteristics	Population, intervention, followup	Followup*, outcomes of interest (timing)	Quality assessment
Lieberman, 1997	Publication type: Full text Geographical location: US Study design: Before and after study (before and after discharge) Funding: Unfunded Number of centers: 1 Outcome assessment: Outcomes were recorded prospectively into a database Number of participants enrolled: 1042 (1042)	Inclusion criteria: THR; received low-dose warfarin prophylaxis Exclusion criteria: Use of anti-inflammatory agent or aspirin; placement of Greenfield filter; use of warfarin for extended period postoperatively Intervention: Patient cohort prior to discharge Comparator: Patient cohort after discharge for 3 months	Duration of followup (d): 90d Covariates/potential confounders adjusted for: Unadjusted Final: PE (90d) Intermediate: DVT (90d) Adverse: Major bleeding (90d)	1. Unbiased selection of the cohort? Yes 2. Selection minimizes baseline differences in prognostic factors? Partially 3. Sample size calculated? No 4. Adequate description of the cohort? Partially 5. Validated method to ascertain exposure? Yes 6. Validated method for ascertaining clinical outcomes? Can't tell 7. Outcome assessment blinded to exposure? Can't tell 8. Adequate followup period? Yes 9. Completeness of followup? Yes 10. Analysis controls for confounding? No Overall quality rating: Fair

Study, year	Study characteristics	Population, intervention, followup	Followup*, outcomes of interest (timing)	Quality assessment
Haas, 1992	Publication type: Full text Geographical location: US Study design: Cohort Funding: Unfunded Number of centers: 1 Outcome assessment: NR Number of participants enrolled: 1257 (1257)	Inclusion criteria: Primary TKA; unilateral or bilateral who completed standard surveillance protocol Exclusion criteria: NR Intervention: Patients with DVT were compared to those without DVt to assess the risk of pulmonary embolism	Duration of followup (d): Postopertaive Covariates/potential confounders adjusted for: Unadjusted Final: PE (postoperative) Intermediate: DVT, distal DVT, proximal DVT (postoperative) Adverse: NR	1. Unbiased selection of the cohort? Yes 2. Selection minimizes baseline differences in prognostic factors? Partially 3. Sample size calculated? No 4. Adequate description of the cohort? Partially 5. Validated method to ascertain exposure? Yes 6. Validated method for ascertaining clinical outcomes? Can't tell 7. Outcome assessment blinded to exposure? Can't tell 8. Adequate followup period? Yes 9. Completeness of followup? Yes 10. Analysis controls for confounding? No Overall quality rating: Fair

Study, year	Study characteristics	Population, intervention, followup	Followup*, outcomes of interest (timing)	Quality assessment
Lemos, 1991	Publication type: Full text Geographical location: US Study design: Nested Case-control Funding: NR Number of centers: 1 Outcome assessment: Chest roengenogram and VQ scans were performed and confirmed by angiogram Number of participants enrolled: 2348 (240)	Inclusion criteria: Patients undergoing TKA or THA Exclusion criteria: NR Comparisons: Patients with PE after THA or TKA were compared with a matched control of patients without PE for determining risk factors for PE	Duration of followup (d): Postoperative Covariates/potential confounders adjusted for: Gender; procedure Final: PE (postoperative) Intermediate: NR Adverse: NR	1. Unbiased selection of the cohort? Yes 2. Selection minimizes baseline differences in prognostic factors? Partially 3. Sample size calculated? No 4. Adequate description of the cohort? Partially 5. Validated method to ascertain exposure? Yes 6. Validated method for ascertaining clinical outcomes? Yes 7. Outcome assessment blinded to exposure? Can't tell 8. Adequate followup period? No 9. Completeness of followup? Yes 10. Analysis controls for confounding? Partially Overall quality rating: Fair

*Duration of followup is reported as the original study's longest reported followup for outcomes of interest and followup percent is reported for the study's pre-specified primary outcome
† From Happe 2007

Abbreviations: ACS=acute coronary syndrome; AF=atrial fibrillation; ASA=aspirin; CECT=continuous enhanced circulation therapy; d=day(s); DVT=deep vein thrombosis; GI:=gastrointestinal; ICD-9=International Classification of Disease, Ninth Revision; ICD-9-CM=International Classification of Disease, Ninth Revision, Clinical Modification; Inc=incorporated; IPC-intermittent pneumatic compression; kg=kilograms; LMWH=low molecular weight heparin; LOS=length of stay; MC=multicenter; mg=milligrams; NOS=not otherwise specified; NR=not reported; PE=pulmonary embolism; PO=by mouth; QD=daily; SQ=subcutaneous; THR=total hip replacement; TKA=total knee arthroplasty; TKR=total knee replacement; UFH=unfractionated heparin; U=units; US=United States; VTE=venous thromboembolism; w=weeks; y=years

Appendix E. Baseline and procedural characteristics of included trials and studies

Table 6. Baseline characteristics of patient enrolled in randomized controlled trials evaluating major orthopedic surgery

Study, Year	Group	N	Age mean (SD)	Female %	Wt kg mean (SD)	Smoker %	Obese %	Hx VTE %	Vari-cosity %	Estro-gen %	DM %	CA %	CVD %	Prior ortho-pedic sx %
Fuji, 2010	Dabigatran 150mg	126	70.9 (7.7)	83.3	59.8 (11.1)	---	---	0	---	---	---	0	---	---
	Dabigatran 220mg	129	72.7 (6.8)	84.5	60.3 (10.7)	---	---	0	---	---	---	0	---	---
	Placebo	124	71.3 (8.5)	84.7	60.8 (11.2)	---	---	0	---	---	---	0	---	---
Chin, 2009	Enoxaparin	110	67 (52-78)*	91.82	---	6.36	---	0	0	---	---	0	---	---
	Control	110	65 (47-77)*	91.81	---	3.64	---	0	0	---	---	0	---	---
Ginsberg, 2009	Dabigatran 150mg QD	871	65.9 (9.5)	58.2	87.6 (20.0)	---	---	---	---	---	---	---	---	---
	Dabigatran 220mg QD	857	66.2 (9.5)	56.7	88.4 (19.1)	---	---	---	---	---	---	---	---	---
	Enoxaparin	868	66.3 (9.6)	58.1	88.0 (19.2)	---	---	---	---	---	---	---	---	---
Edwards, 2008 THA	Enoxaparin + IPC	65	64.2 (31.6-87.7)*	55.4	79.5 (48.6-143.2)*	---	---	0	---	---	---	16.9	---	---
	Enoxaparin	59	67.7 (33.7-86.6)*	59.3	78.8 (40.9-154.6)*	---	---	0	---	---	---	18.6	---	---
Edwards, 2008 TKA	Enoxaparin + IPC	76	68.1 (46.4-87.4)*	63.1	88 (48.2-135.5)*	---	---	0	---	---	---	17.1	---	---
	Enoxaparin	77	68.7 (48.7-88.1)*	55.8	87.7 (53.6-145.5)*	---	---	0	---	---	---	15.6	---	---
Fuji, 2008 THA	Enoxparin 40mg QD	80	60.6 (9.9)	92.5	54.2 (9.8)	12.5	32.5†	---	---	---	---	---	---	---
	Enoxaparin 20mg BID	90	63.0 (9.3)	83.3	54.3 (9.4)	17.8	34.4†	---	---	---	---	---	---	---
	Placebo	86	62.0 (10.3)	87.2	56.0 (10)	16.3	39.5†	---	---	---	---	---	---	---
Fuji, 2008 TKA	Enoxparin 40mg QD	74	70.0 (9.4)	85.1	57.6 (10.5)	9.5	59.4†	---	---	---	---	---	---	---
	Enoxaparin 20mg BID	84	68.3 (8.7)	94.0	54.0 (8.3)	7.1	41.7†	---	---	---	---	---	---	---
	Placebo	79	68.7 (9.5)	81.0	57.2 (9.5)	13.9	50.6†	---	---	---	---	---	---	---

Study, Year	Group	N	Age mean (SD)	Female %	Wt kg mean (SD)	Smoker %	Obese %	Hx VTE %	Vari-cosity %	Estro-gen %	DM %	CA %	CVD %	Prior ortho-pedic sx %
Thorey, 2008	Early release tourniquet	20	67 (11)	65	83	---	---	0	---	---	---	---	---	---
	Late release tourniquet	20	67 (11)	65	83	---	---	0	---	---	---	---	---	---
Eriksson, 2007a	Dabigatran 150mg QD	703	68 (9)	64	83 (15)	---	---	---	---	---	---	0	0	---
	Dabigatran 220mg QD	679	67 (9)	65	82 (15)	---	---	---	---	---	---	0	0	---
	Enoxaparin	694	68 (9)	69	82 (15)	---	---	---	---	---	---	0	0	---
Eriksson, 2007b	Dabigatran 150mg QD	1163	63 (11)	57	79 (15)	---	---	2	---	---	---	---	---	---
	Dabigatran 220mg QD	1146	65 (10)	56	79 (15)	---	---	3	---	---	---	---	---	---
	Enoxaparin	1154	64 (11)	56	78 (15)	---	---	3	---	---	---	---	---	---
Lassen, 2007	Enoxaparin	152	66.5 (36-88)*	61.8	83.1 (17.6)	---	---	0	---	---	---	0	---	---
	Warfarin	153	66.8 (43-85)*	60.8	83.7 (16)	---	---	0	---	---	---	0	---	---
Bonneux, 2006	Fondaparinux	55	66.9 (8.5)	78.18	---	---	---	---	---	---	---	---	---	---
	Enoxaparin	54	65.7 (10.4)	79.63	---	---	---	---	---	---	---	---	---	---
Senaran, 2006	Enoxaparin	50	55.2 (8.4)	76	---	---	---	---	---	---	---	---	---	---
	Heparin	50	52.4 (11.2)	66	---	---	---	---	---	---	---	---	---	---
Westrich, 2006	Minimum hyperflexed knee	55	68.1 (8.7)‡	70.3‡	---	---	---	0	---	---	---	---	---	---
	Standard hyperflexed knee	63			---	---	---	0	---	---	---	---	---	---
Eriksson, 2005	Dabigatran 50mg BID	389	66.1 (31-88)*	57.3	79 (46-125)*	---	---	---	---	---	---	0	0	---
	Dabigatran 150mg BID	390	65.9 (34-89)*	64.6	79 (44-130)*	---	---	---	---	---	---	0	0	---
	Dabigatran 300mg QD	385	66.5 (21-88)*	63.9	79 (43-128)*	---	---	---	---	---	---	0	0	---

Study, Year	Group	N	Age mean (SD)	Female %	Wt kg mean (SD)	Smoker %	Obese %	Hx VTE %	Vari-cosity %	Estro-gen %	DM %	CA %	CVD %	Prior ortho-pedic sx %
	Dabigatran 225mg BID	393	65.9 (33-93)*	58.3	79 (44-130)*	---	---	---	---	---	---	0	0	---
	Enoxaparin	392	65.0 (20-86)*	61.5	79 (47-125)*	---	---	---	---	---	---	0	0	---
Farag, 2005	Epidural Anesthesia	16	63 (8)	81	94 (28)	---	---	---	---	---	---	---	---	---
	Spinal Anesthesia	22	64 (13)	59	100 (26)	---	---	---	---	---	---	---	---	---
Lachiewicz, 2004	IPC (Venaflow)	206	67.3 (23-89)*	62.14	87.7 (50 -146.8)*	---	---	---	---	---	---	---	---	---
	IPC (Kendal)	217	66.4 (30-94)*	66.82	86.6 (45.4-147.7)*	---	---	---	---	---	---	---	---	---
Silbersack, 2004	Enoxaparin + IPC	68	63 (29-90)*	58.82	78 (50-108)*	14.7	---	7.35	66.18	5.88	17.65	5.88	17.65	---
	Enoxaparin + GCS	63	65 (36-87)*	69.84	77 (42-110)*	9.52	---	4.76	61.90	3.17	19.05	3.17	20.63	---
Eriksson, 2003	Extended fondaparinux	327	79 (23-94)[§]	71.9	65 (39-115)[§]	---	7.8	4	---	---	---	---	---	4.9
	Fondaparinux	329	79 (28-96)[§]	70.2	66 (41-127)[§]	---	8.0	3.6	---	---	---	---	---	3.6
Kim, 2003	Cemented	51	54.9 (42-73)*[‡]	46	---	---	---	---	---	---	---	---	---	---
	Non-cemented	51		46	---	---	---	---	---	---	---	---	---	---
Lassen, 2002	Fondaparinux	1140	66 (29-92)*	57	75 (40- 135)*	---	20	4	---	---	---	---	---	10
	Enoxaparin	1133	67 (24-97)*	68	75 (40-145)*	---	24	5	---	---	---	---	---	9
Pitto, 2002	Bone vacuum cement technique	65	73.5 (9.4)	52.3	---	---	---	0	---	---	---	---	---	---
	Standard cement technique	65	71.6 (8.9)	58.5	---	---	---	0	---	---	---	---	---	---
Prandoni, 2002	Extended warfarin	184	68 (48-82)*	54.89	---	---	9.2	---	7.6	1.5	---	2.5	---	---
	Warfarin	176	69 (44-87)*	55.13	---	---	9.7	---	8.5	2.3	---	1.7	---	---
Turpie, 2002	Fondaparinux	1128	67 (18-92)[§]	51	81 (36-169)[§]	---	33	5	---	---	---	---	---	12
	Enoxaparin	1129	67 (19-91)[§]	54	80 (35-226)[§]	---	34	6	---	---	---	---	---	11

Study, Year	Group	N	Age mean (SD)	Female %	Wt kg mean (SD)	Smoker %	Obese %	Hx VTE %	Vari-cosity %	Estro-gen %	DM %	CA %	CVD %	Prior ortho-pedic sx %
Warwick, 2002	Enoxaparin	112	71 (10)	66.96	69 (11)	4.46	---	3.57	6.25	---	---	---	---	---
	VFP	117	73 (9)	63.25	71 (11)	4.27	---	5.98	10.26	---	---	---	---	---
Barden, 2001	Modified position	84	71.2 (54-87)*	71.4	73.4 (43-115)*	---	---	---	---	0	---	0	---	---
	Conventional figure four positioning	76	72.3 (61-84)*	71.0	75.2 (58-118)*	---	---	---	---	0	---	0	---	---
Bauer, 2001	Fondaparinux	517	67.5 (10.7)	60.54	89.0 (20.0)	---	53.3[ll]	4.4	---	---	---	---	---	16.8
	Enoxaparin	517	67.5 (10.2)	56.87	88.4 (19.6)	---	53.3[ll]	5.4	---	---	---	---	---	14.9
Comp, 2001 THR	Extended enoxaparin	224	64.4 (28-90)*	50.45	81.4 (40.4-149.7)*	---	51.3	---	---	---	---	---	---	---
	Enoxaparin	211	63.4 (26-88)*	49.76	82.7 (40.8-139.3)*	---	55.9	---	---	---	---	---	---	---
Comp, 2001 TKR	Extended enoxaparin	217	66.2 (39-87)*	58.99	88.7 (52.2-147.4)*	---	75.1	---	---	---	---	---	---	---
	Enoxaparin	221	66.3 (34-88)*	55.66	89.2 (45.5-147.4)*	---	73.8	---	---	---	---	---	---	---
Eriksson, 2001	Fondaparinux	831	76.8 (12.3)	77.50	64.3 (13.1)	---	5.4	3.5	---	---	---	9.5	---	4.0
	Enoxaparin	842	77.3 (12.6)	73.40	64.2 (13.8)	---	7.6	3.8	---	---	---	8.8	---	3.1
Fitzgerald, 2001	Warfarin	176	68.2 (9.7)	55.1	84.2	---	---	0	---	---	---	---	---	---
	Enoxaparin	173	67.9 (8.5)	57.2	85.9	---	---	0	---	---	---	---	---	---
Hull, 2000	Dalteparin (preoperative)	496	64 (12)	50	81 (18)	---	---	4.64	16.13	---	---	11.90	---	---
	Dalteparin (postoperative)	487	63 (13)	55.03	80 (19)	---	---	3.49	16.43	---	---	9.45	---	---
	Warfarin	489	63 (13)	50.51	80 (17)	---	---	4.29	13.29	---	---	7.57	---	---
Kennedy, 2000	Aspirin	73	75	50.68	---	---	---	0	0	---	---	0	---	---
	VFP	70	78	54.29	---	---	---	0	0	---	---	0	---	---
Colwell, 1999	Enoxaparin	1516	63.9 (13.17)	55.3	---	---	32.3	---	---	---	---	---	---	---
	Warfarin	1495	64.1 (13.21)	55.9	---	---	27.5	---	---	---	---	---	---	---

Study, Year	Group	N	Age mean (SD)	Female %	Wt kg mean (SD)	Smoker %	Obese %	Hx VTE %	Vari-cosity %	Estro-gen %	DM %	CA %	CVD %	Prior ortho-pedic sx %
Levy, 1999	Fibrin adhesive	29	68.9 (6.3)	79.3	76.7	---	---	---	---	---	---	---	---	---
	No fibrin adhesive	29	70.2 (8.2)	79.3	76.9	---	---	---	---	---	---	---	---	---
Planes, 1999	Enoxaparin	248	64 (11)	55.24	71 (13)	---	---	9	---	---	---	---	---	---
	Tinzaparin	251	65 (11)	56.97	71 (11)	---	---	11	---	---	---	---	---	---
TIFDED Study Group, 1999	Enoxaparin	66	77 (11)	72.73	---	---	---	3.1	---	---	---	3.1	---	---
	Dalteparin	66	76 (10)	78.79	---	---	---	6.1	---	---	---	6.1	---	---
Wakankar, 1999	Tourniquet	37	72.5 (57-85)*	70.2	---	---	---	0	---	---	0	---	---	---
	No tourniquet	40	71.8 (43-91)*	65	---	---	---	0	---	---	0	---	---	---
Kim, 1998	Aspirin	50	---	24.0	---	---	---	---	---	---	---	---	---	---
	Control	50	---	18.0	---	---	---	---	---	---	---	---	---	---
Lassen, 1998	Extended dalteparin	140	68 (30-94)*	52.86	75 (43-125)*	---	---	7.1	15	---	---	2.1	10	---
	Dalteparin	141	70 (28-91)*	56.03	72 (43-105)*	---	---	3.5	18.4	---	---	2.1	10.6	---
Rader, 1998	Heparin	116	68.3 (11)	78.45	74 (19)	12.07	---	11.21	---	2.59	5.18	0	---	---
	Enoxaparin	130	69.6 (13)	62.31	78 (12)	10.00	---	4.64	---	0.77	6.15	0	---	---
Ryan, 1998	IPC	50	70.1	62	71.5	---	---	---	---	---	---	---	---	---
	GCS	50	67.5	62	73.4	---	---	---	---	---	---	---	---	---
Warwick, 1998	Enoxaparin	143	68 (11)	39.16	71 (10)	---	---	2	---	---	---	---	---	---
	VFP	147	68 (11)	36.05	71 (12)	---	---	1	---	---	---	---	---	---
Andersen, 1997	Extended dalteparin	20	67 (52-84)*	40	76 (50-104)*	---	---	---	---	---	---	---	---	---
	Dalteparin	21	67 (34-84)*	48	73 (52-94)*	---	---	---	---	---	---	---	---	---
Dahl, 1997	Extended dalteparin	117	70.9	68.4	73.2	---	---	8.5	---	---	---	9.4	---	---
	Dalteparin	110	71.4	73.6	71.6	---	---	4.5	---	---	---	9.1	---	---

Study, Year	Group	N	Age mean (SD)	Female %	Wt kg mean (SD)	Smoker %	Obese %	Hx VTE %	Vari-cosity %	Estro-gen %	DM %	CA %	CVD %	Prior ortho-pedic sx %
Eriksson, 1997a	Desirudin	225	68.6 (9.3)	58	74.8 (12.3)	19	37	4	20	---	---	3	0.89	16
	UFH	220	68.2 (9.8)	58	73.7 (13.2)	18	32	2	16	---	---	3	5	15
Eriksson, 1997b	Desirudin	1043	66 (27-90)[§]	56.6	73 (42-120)[§]	15.1	41.0	6.5	---	---	---	12.3	---	---
	Enoxaparin	1036	67 (18-87)[§]	60.0	74 (43-128)[§]	18.0	41.6	6.0	---	---	---	12.4	---	---
Francis, 1997	Dalteparin	271	63 (13)	53.14	80 (19)	---	---	9.59	---	---	---	---	---	---
	Warfarin	279	63 (14)	52.69	80 (18)	---	---	8.96	---	---	---	---	---	---
Nilsson, 1997	Extended enoxaparin	131	70 (44-87)*	57.25	---	---	---	6	21	---	---	---	---	---
	Enoxaparin	131	70 (44-87)*	56.49	---	---	---	9	24	---	---	---	---	---
Planes, 1997	Extended enoxaparin	90	70 (9.1)	47.78	---	---	---	2.22	14.44	---	---	---	---	13.33[¶]
	Enoxaparin	89	68 (8.2)	38.2	---	---	---	1.12	14.61	---	---	---	---	10.11
Samama, 1997	Enoxaparin	85	67.2 (31.6-9.21)[§]	31.8	74.4 (12.1)	---	---	0	---	---	---	---	---	---
	Placebo	85	67.2 (31.6-87.5)[§]	51.8	71.4 (11.1)	---	---	0	---	---	---	---	---	---
Eriksson, 1996	Desirudin	277	66.6 (9.7)	60.3	73.1 (12.6)	16.7	39.4	3.6	18.1	---	---	4.3	7.9	18.1
	UFH	277	66.7 (9.8)	64.3	72.9 (13.9)	18.8	35.4	4.7	18.4	---	---	2.5	4.7	14.1
Kalodiki, 1996	Enoxaparin + GCS	32	69 (54-85)*	40.63	---	---	34.38	0	46.88	---	---	3.12	---	---
	Enoxaparin	32	67(53-82)*	59.38	---	---	34.38	3.13	43.75	---	---	3.13	---	---
	Placebo	14	72 (60-83)*	57.14	---	---	21.43	7.14	28.57	---	---	7.14	---	---
Laupacis, 1996	Cemented	124	63.9 (7.6)	48.4	---	---	---	3.2	---	---	---	---	---	---
	Non-cemented	126	63.9 (7.4)	46	---	---	---	4.8	---	---	---	---	---	---
Leclerc, 1996	Warfarin	334	69.2 (9.2)	63.2	78.2 (15.9)	---	---	10.2	---	---	---	---	---	---
	Enoxaparin	336	68.0 (9.4)	63.1	79.2 (16.0)	---	---	9.5	---	---	---	---	---	---
Lotke, 1996	Aspirin	166	66.4	61.2[‡]	---	---	---	---	---	---	---	---	---	---
	Warfarin	136	67.1		---	---	---	---	---	---	---	---	---	---

Study, Year	Group	N	Age mean (SD)	Female %	Wt kg mean (SD)	Smoker %	Obese %	Hx VTE %	Vari-cosity %	Estro-gen %	DM %	CA %	CVD %	Prior ortho-pedic sx %
Schwarts-mann, 1996	Enoxaparin	52	62 (10)	58	69 (12)	3.8	15.4	0	3.8	0	---	0	---	---
	UFH	47	58 (11)	60	69 (12)	4.2	23.4	0	2.1	0	---	0	---	---
Stannard, 1996	UFH then ASA + VFP	25	65.0 (51-79)*	---	---	---	---	---	---	---	---	---	---	---
	UFH then aspirin	25	69.7 (28-86)*	---	---	---	---	---	---	---	---	---	---	---
	VFP	25	68.7 (48-86) *	---	---	---	---	---	---	---	---	---	---	---
Stone, 1996	Enoxaparin	25	64 (37-82)*	68	67 (41-92)*	---	---	0	---	---	---	0	---	---
	IPC	25	64 (42-83)*	60	69 (48-90)*	---	---	0	---	---	---	0	---	---
Westrich, 1996	Aspirin + VFP	61	---	67.12‡	---	---	---	0	---	---	---	---	---	---
	Aspirin	61	---		---	---	---	0	---	---	---	---	---	---
Williams-Russo, 1996	General Anesthesia	81	68 (9)	65	---	---	38	10	---	---	---	---	---	---
	Regional Anesthesia	97	68 (8)	74	---	---	33	3	---	---	---	---	---	---
Abdel-Salam, 1995	Tourniquet	40	72 (65-80)*	57.5	---	---	---	---	---	---	0	---	---	---
	No tourniquet	40	74 (64-82)*	62.5	---	---	---	---	---	---	0	---	---	---
Avikainen, 1995	Enoxaparin	83	65 (27-86)*	63.86	72 (39-110)*	---	---	2.41# 0**	9.64	---	---	---	---	30.12
	UFH	84	66 (34-86)*	70.24	71 (36-126)*	---	---	3.57# 2.38**	7.14	---	---	---	---	27.38
Colwell, 1995	Enoxaparin	228	67.5 (9.5)	53.1	86.9 (17.9)	---	---	0	---	---	---	---	---	---
	Heparin	225	68.6 (8.8)	59.6	84.8 (17.3)	---	---	0	---	---	---	---	---	---
Warwick, 1995	Enoxaparin	78	---	---	---	---	---	---	---	---	---	---	---	---
	Control	78	---	---	---	---	---	---	---	---	---	---	---	---
Colwell, 1994	Enoxaparin 30mg Q12h	195	65.6 (10.97)	49.74	78.4 (17.12)	---	---	0	---	---	---	---	---	---

Study, Year	Group	N	Age mean (SD)	Female %	Wt kg mean (SD)	Smoker %	Obese %	Hx VTE %	Vari-cosity %	Estro-gen %	DM %	CA %	CVD %	Prior ortho-pedic sx %
	Enoxaparin 40mg QD	203	65.0 (11.31)	51.23	78.8 (17.84)	---	---	0	---	---	---	---	---	---
	UFH	209	65.6 (10.65)	51.67	78.2 (15.96)	---	---	0	---	---	---	---	---	---
Fauno, 1994	Enoxaprain	92	71 (11)	61.96	78 (14)	---	---	0	23.91	---	---	---	---	---
	UFH	93	70 (10)	59.14	72 (14)	---	---	0	19.35	---	---	---	---	---
Lieberman, 1994	Aspirin + IPC	113	67 (40-87)*	59.29	75 (45-100)*	---	---	0	---	---	---	---	---	---
	Aspirin	118	66 (40-80)*	55.93	75 (48-106)*	---	---	0	---	---	---	---	---	---
Menzin, 1994	UFH	209	65.7 (10.7)	52	---	---	---	0	---	---	16	---	---	---
	Enoxaparin 40mg QD	202	65.0 (11.3)	51	---	---	---	0	---	---	20	---	---	---
	Enoxaparin 30mg Q12h	192	65.8 (11.0)	49	---	---	---	0	---	---	14	---	---	---
Santori, 1994	Heparin	65	69.8 (6.22)	76.92	---	---	---	0	0	---	---	0	---	---
	VFP	67	72.4 (6.65)	71.64	---	---	---	0	0	---	---	0	---	---
Hull, 1993	Tinzaparin	715	66 (12)	56.08	---	---	---	0	---	---	8.67	8.67	2.80	---
	Warfarin	721	66 (12)	61.44	---	---	---	0	---	---	7.63	8.60	4.88	---
Fordyce, 1992	VFP	39	68.1	61.54	69.75	---	---	0	41.03	---	---	---	---	---
	Control	40	71.2	62.5	69.9	---	---	0	55.00	---	---	---	---	---
Francis, 1992	Warfarin	103	64 (12)	49.51	---	---	---	5.83	---	---	---	---	---	---
	IPC	98	64 (12)	56.12	---	---	---	7.14	---	---	---	---	---	---
Jorgensen, 1992	Dalteparin	30	79 (57-95) §	70.0	---	---	---	10.0	---	---	---	0	---	---
	Placebo	38	80 (61-90) §	81.6	---	---	---	0	---	---	---	9	---	---
Wilson, 1992	VFP	28	71.1 (6.7)	82.14	---	---	---	---	---	---	---	---	---	---
	Control	31	70.1 (6.8)	67.74	---	---	---	---	---	---	---	---	---	---

Study, Year	Group	N	Age mean (SD)	Female %	Wt kg mean (SD)	Smoker %	Obese %	Hx VTE %	Vari-cosity %	Estro-gen %	DM %	CA %	CVD %	Prior ortho-pedic sx %
Bailey, 1991	Warfarin	45	64.4 (45-80)*	51	81.3 (35.7-120)*	---	---	---	---	---	---	---	---	---
	IPC	50	65.3 (41-88)*	52	72.2 (42-109)*	---	---	---	---	---	---	---	---	---
Eriksson, 1991	Dalteparin	67	68.4 (8.2)	59.70	---	20.89	---	10.45	28.36	2.99	10.45	---	4.48	52.24
	UFH	69	69.0 (8.0)	56.52	---	14.49	---	14.49	33.33	0	2.90	---	5.80	47.83
Jorgensen, 1991	General Anesthesia	22	64 (38-85)*	68.1	---	---	---	0	13.6	---	---	---	---	---
	Epidural Anesthesia	17	70.5 (52-87)*	76.5	---	---	---	0	11.8	---	---	---	---	---
Lassen, 1991	Tinzaparin	93	67 (40-85)[§]	51.6	73 (40-101)[§]	---	---	6.5	34.4	---	---	3.2	---	---
	Placebo	97	67 (40-86)[§]	51.5	74 (48-126)[§]	---	---	6.2	28.9	---	---	4.1	---	---
Levine, 1991	Enoxaparin	333	66.2 (10.39)	56.5	---	---	---	9.61	---	---	---	---	---	39.34
	UFH	332	66.8 (9.09)	51.8	---	---	---	10.84	---	---	---	---	---	42.47
Mitchell, 1991	General Anesthesia	38	64 (38-84)*[‡]	37.5[‡]	---	---	---	---	---	---	---	---	---	---
	Epidural Anesthesia	34			---	---	---	---	---	---	---	---	---	---
Planes, 1991	General Anesthesia + Enoxaparin	62	66.1 (1)	54.8	68.9 (1.5)	---	32.3	9.7	43.6	---	---	4.8	---	---
	Epidural Anestheisa + Enoxaparin	61	66.8 (1.1)	47.5	70.8 (1.3)	---	41.0	4.9	39.3	---	---	1.6	---	---
	Epidural Anesthesia alone	65	66.7 (1.2)	55.6	68.7 (1.6)	---	33.9	7.7	44.6	---	---	0	---	---
Torholm, 1991	Dalteparin	58	67 (43-85)[§]	60.3	---	---	---	8.6	---	---	---	0	---	---
	Placebo	54	64 (43-81)[§]	50.0	---	---	---	9.3	---	---	---	1.9	---	---
Woolson, 1991	Aspirin + IPC	70	62.3	50[††]	74	---	---	6[††]	7[††]	---	---	---	---	---
	Warfarin + IPC	69	67.6	55[††]	75	---	---	14[#††]	13[††]	---	---	---	---	---
	IPC	73	66.3	63	71	---	---	7[#††]	8[††]	---	---	---	---	---

Study, Year	Group	N	Age mean (SD)	Female %	Wt kg mean (SD)	Smoker %	Obese %	Hx VTE %	Vari-cosity %	Estro-gen %	DM %	CA %	CVD %	Prior ortho-pedic sx %
Haas, 1990 Unilateral	Aspirin	36	70.2	69.44	---	5.56	58.33	8.33	25.00	---	8.33	---	19.44	---
	IPC	36	67.7	72.22	---	13.89	50.00	5.56	19.44	---	8.33	---	13.89	---
Haas, 1990 Bilateral	Aspirin	22	71.1	68.18	---	0	59.09	0	18.18	---	0	---	18.18	---
	IPC	25	69.9	52.00	---	28.00	52.00	4.00	16.00	---	12.00	---	16.00	---
Sorensen, 1990	Tinzaparin	31	---	64.42‡	---	---	---	---	---	---	---	---	---	---
	Placebo	33	---		---	---	---	---	---	---	---	---	---	---
Dechav-anne,1989	Dalteparin 2500U Q12h	41	65.1 (10.8)	60.98	66.5 (11.3)	---	---	7.32	36.59	---	---	0	---	48.78
	Dalteparin 5000U QD	41	62.8 (10.6)	53.66	70.8 (13.6)	---	---	4.88	36.59	---	---	2.44	---	36.59
	Heparin	40	62.8 (10.6)	50	70.0 (12.9)	---	---	12.5	42.5	---	---	7.5	---	45
Monreal, 1989	Dalteparin	46	75.73 (9.86)	80.43	---	---	---	---	---	---	---	4.35	---	---
	Heparin	44	78.31(12.1)	84.09	---	---	---	---	---	---	---	2.27	---	---
Powers, 1989	Warfarin	65	74.5 (43-90)*	64.62	---	---	---	6.15	---	---	---	---	---	---
	Aspirin	66	73.0 (48-87)*	71.21	---	---	---	4.55	---	---	---	---	---	---
	Placebo	63	76.6 (30-91)*	80.95	---	---	---	6.35	---	---	---	---	---	---
Planes, 1988	Enoxaparin	124	65.4 (9.1)	50.81	69.1 (13.4)	---	34.68	---	25	0.81	---	---	---	35.48
	Heparin	113	66.3 (12.5)	59.3	65.3 (12.5)	---	23.89	---	29.20	0.88	---	---	---	29.20
Barre, 1987	Dalteparin	40	63.1	62.5	69.2	---	---	7.5	45	---	---	0	---	---
	Heparin	40	63.3	45	73.3	---	---	7.5	55	---	---	5.0	---	
Paiement, 1987	Warfarin	72	---	---	---	---	---	---	---	---	---	---	---	---
	IPC	66	---	---	---	---	---	---	---	---	---	---	---	---
Alfaro, 1986	Aspirin 250 mg/d	30	66.06 (8.93)	43.3	---	---	---	6.7	33.3	---	---	0	13.3	16.7
	Aspirin 1 g/d	30	62.04 (10.99)	50.0	---	---	---	3.3	36.7	---	---	0	6.7	10.0

Study, Year	Group	N	Age mean (SD)	Female %	Wt kg mean (SD)	Smoker %	Obese %	Hx VTE %	Vari-cosity %	Estro-gen %	DM %	CA %	CVD %	Prior ortho-pedic sx %
	Control	30	61.99 (7.17)	36.7	---	---	---	0	33.3	---	---	0	16.7	13.3
Turpie, 1986	Enoxaparin	50	66.82 (9.55)	44.0	---	---	---	10.0	---	---	---	0	---	22.0
	Placebo	50	67.3 (8.85)	60.0	---	---	---	10.0	---	---	---	0	---	18.0
McKenzie, 1985	General Anesthesia	20	72.3 (3.8)	70	---	---	---	---	---	---	---	---	---	---
	Spinal Anesthesia	20	73.9 (4.1)	80	---	---	---	---	---	---	---	---	---	---
Welin-Berger, 1982	Heparin	20	66.8 (8.3)	71.7‡	---	---	---	---	---	---	---	---	---	---
	Control	20	65.7 (10.6)		---	---	---	---	---	---	---	---	---	---
Modig, 1981	General Anesthesia	15	65.4 (6.3)	53.3	---	---	---	0	0	---	0	---	0	---
	Epidural Anesthesia	15	66.5 (5.5)	46.7	---	---	---	0	0	---	0	---	0	---
McKenna, 1980	Aspirin	9	72	100	---	---	0	0	---	0	---	0	---	---
	Placebo	12	66	81.82	---	---	0	0	---	0	---	0	---	---

*Mean (range)
†BMI>25
‡Value for the total study population
§Median (range)
‖BMI≥30
¶Conversion or revision of total hip replacement
patients with history of DVT
**patients with history of PE
††Percent of hips

Abbreviations: ASA=aspirin; BID=twice daily; CA=cancer; CVD=cardiovascular disease; DM=diabetes mellitus; d=day; GCS=graduated compression stocking; HFS=hip fracture surgery; g=gram; hx=history; IPC=intermittent pneumatic compression; kg=kilograms; mg=milligram; N=total number of patients; QD=daily; SD=standard deviation; sx=surgery; THR=total hip replacement; TKR=total knee replacement; UFH=unfractionated heparin; VFP=venous foot pump; VTE=venous thromboembolism; Wt=weight

Table 7. Procedural characteristics of randomized controlled trials KQ 5

Study, Year	Group	N	Primary surgery %	Cemented fixation %	Surgical approach %	Mean duration of surgery min (SD)	Mean duration of anesthesia min (SD)	Anesthesia %	Mean LOS, d
Fuji, 2010	Dabigatran 150mg	126	100	---	---	109.2 (44.2)	---	GA: 77.0 Non-GA: 23.0	---
	Dabigatran 220mg	129	100	---	---	108.9 (44.2)	---	GA: 74.4 Non-GA: 25.6	---
	Placebo	124	100	---	---	108.8 (46.9)	---	GA: 74.2 Non-GA: 25.8	---
Chin, 2009	Enoxaparin	110	---	---	---	93.0 (55-155)*	---	GA: 58.18 RA: 41.82	8.1 (4-19)*
	Control	110	---	---	---	94.2 (45-195)*	---	GA: 57.27 RA: 42.73	7.9 (4-24)*
Ginsberg, 2009	Dabigatran 150mg QD	871	100	---	---	91 (30)	---	GA: 54.0 RA: 45.8	---
	Dabigatran 220mg QD	857	100	---	---	91 (28)	---	GA: 52.9 RA: 46.3	---
	Enoxaparin	868	100	---	---	90 (28)	---	GA: 51.7 RA: 47.5	---
Edwards, 2008 THA	Enoxaparin + IPC	65	---	---	---	---	---	---	3.0
	Enoxaparin	59	---	---	---	---	---	---	3.13
Edwards, 2008 TKA	Enoxaparin + IPC	76	---	---	---	---	---	---	3.1
	Enoxaparin	77	---	---	---	---	---	---	3.3
Fuji, 2008 THA	Enoxaparin 40mg QD	80	100	43.8	---	123.6 (39)	---	GA: 16.3 RA: 0	---
	Enoxaparin 20mg BID	90	100	46.7	---	123 (39.6)	---	GA: 21.1 RA: 0	---
	Placebo	86	100	40.7	---	129 (46.8)	---	GA: 16.3 RA: 0	---
Fuji, 2008 TKA	Enoxaparin 40mg QD	74	100	77.0	---	132 (46.8)	---	GA: 18.9 RA: 0	---
	Enoxaparin 20mg BID	84	100	84.5	---	127.2 (37.2)	---	GA: 21.4 RA: 0	---
	Placebo	79	100	78.5	---	126.6 (39)	---	GA: 12.7 RA: 0	---
Thorey, 2008	Early release tourniquet	20	---	100	---	58 (18)	---	GA: 100	---
	Late release tourniquet	20	---	100	---	51 (17)	---	GA: 100	---
Eriksson, 2007a	Dabigatran 150mg QD	703	100	---	---	91 (30)	---	GA: 24 RA: 47 GA+RA: 29	---

Study, Year	Group	N	Primary surgery %	Cemented fixation %	Surgical approach %	Mean duration of surgery min (SD)	Mean duration of anesthesia min (SD)	Anesthesia %	Mean LOS, d
	Dabigatran 220mg QD	679	100	---	---	91 (28)	---	GA: 22 RA: 49 GA+RA: 29	---
	Enoxaparin	694	100	---	---	90 (28)	---	GA: 22 RA: 48 GA+RA: 30	---
Eriksson, 2007b	Dabigatran 150mg QD	1163	100	---	---	85 (29)	---	GA: 24 RA: 66 GA+RA: 10	9 (7-12)†
	Dabigatran 220mg QD	1146	100	---	---	85 (29)	---	GA: 26 RA: 66 GA+RA: 8	9 (7-12)†
	Enoxaparin	1154	100	---	---	87 (29)	---	GA: 24 RA: 68 GA+RA: 8	9 (7-12)†
Lassen, 2007	Enoxaparin	152	---	---		96 (42-199.8)*	---	GA: 30.2 RA: 54.4	6 (2-24)*
	Warfarin	153	---	---		96.6 (40.2- 250.2)*	---	GA: 35.8 RA: 50.3	6 (3-38)*
Bonneux, 2006	Fondaparinux	55	96.36	---	---	---	---	GA+RA:100	---
	Enoxaparin	54	92.59	---	---	---	---	GA+RA:100	---
Senaran, 2006	Enoxaparin	50	---	---	---	---	---	GA: 100	---
	Heparin	50	---	---	---	---	---	GA: 100	---
Westrich, 2006	Minimum hyperflexed knee	55	100	100	---	---	---	RA: 100	---
	Standard hyperflexed knee	63	100	100	---	---	---	RA: 100	---
Eriksson, 2005	Dabigatran 50mg BID	389	100	---	---	84 (30-234)*	---	GA: 26.3 RA:73.7	---
	Dabigatran 150mg BID	390	100	---	---	90 (30-324)*	---	GA: 27.3 RA: 72.7	---
	Dabigatran 300mg QD	385	100	---	---	84 (30-234)*	---	GA: 25.8 RA: 74.2	---
	Dabigatran 225mg BID	393	100	---	---	84 (30-216)*	---	GA: 27.5 RA: 72.5	---
	Enoxaparin	392	100	---	---	90 (24-276)*	---	GA: 27.9 RA: 72.1	---
Farag, 2005	Epidural Anesthesia	16	---	---	---	---	---	RA: 100	---

Study, Year	Group	N	Primary surgery %	Cemented fixation %	Surgical approach %	Mean duration of surgery min (SD)	Mean duration of anesthesia min (SD)	Anesthesia %	Mean LOS, d
	Spinal Anesthesia	22	---	---	---	---	---	RA: 100	---
Lachiewicz, 2004	IPC (Venaflow)	206	86.89	---	---	---	---	GA: 14.56 RA: 84.95 GA+RA: 0.49	---
	IPC (Kendal)	217	82.95	---	---	---	---	GA: 11.98 RA: 87.56 GA+RA: 0.46	---
Silbersack, 2004	Enoxaparin + IPC	68	100	42.65	---	89 (55-177)*	133 (80-195)*	GA: 27.94 RA: 72.06	---
	Enoxaparin + GCS	63	100	46.03	---	93 (46-159)*	137 (70-210)*	GA: 26.98 RA: 73.02	---
Eriksson, 2003	Extended fondaparinux	327	---	23.9	---	99 (27-335)*	---	GA: 31.2 RA: 67.6 GA+RA: 1.2	---
	Fondaparinux	329	---	25.2	---	95 (27-255)*	---	GA: 31.0 RA: 67.5 GA+RA: 1.5	---
Kim, 2003	Cemented	51	---	50	---	---	---	---	---
	Non-cemented	51	---		---	---	---	---	---
Lassen, 2002	Fondaparinux	1140	89	60	---	138 (48)	---	GA: 35 RA: 61 GA+RA: 5	---
	Enoxaparin	1133	87	60	---	144 (52.2)	---	GA: 38 RA: 57 GA+RA: 4	---
Pitto, 2002	Bone vacuum cement technique	65	100	100	DL: 100	75 (8)	---	GA: 100	11.5 (2)
	Standard cement technique	65	100	100	DL: 100	71 (11)	---	GA: 100	12 (2.5)
Prandoni, 2002	Extended warfarin	184	---	---	---	---	---	GA: 97.0	9 (5-18)*
	Warfarin	176	---	---	---	---	---	GA: 97.2	9 (4-20)*
Turpie, 2002	Fondaparinux	1128	84	51	---	148.8 (57)	---	GA: 70 RA: 26 GA+RA: 4	---

Study, Year	Group	N	Primary surgery %	Cemented fixation %	Surgical approach %	Mean duration of surgery min (SD)	Mean duration of anesthesia min (SD)	Anesthesia %	Mean LOS, d
	Enoxaparin	1129	87	53	---	147 (57)	---	GA: 72 RA: 23 GA+RA: 5	---
Warwick, 2002	Enoxaparin	112	100	---	---	---	---	RA: 83	---
	VFP	117	100	---	---	---	---	RA: 86	---
Barden, 2001	Modified position	84	100	100	AL: 100	---	---	---	---
	Conventional figure four positioning	76	100	100	AL: 100	---	---	---	---
Bauer, 2001	Fondaparinux	517	92.5	93.2	---	127 (39)	---	GA: 74.7 RA: 24.4 GA+RA: 1.0	---
	Enoxaparin	517	92.6	93.6	---	128 (42)	---	GA:71.4 RA: 27.5 GA+ RA: 1.2	---
Comp, 2001 THR	Extended enoxaparin	224	78.6	---	---	---	---	GA: 75.0 RA: 25.0	---
	Enoxaparin	211	78.2	---	---	---	---	GA: 69.7 RA: 30.3	---
Comp, 2001 TKR	Extended enoxaparin	217	72.4	---	---	---	---	GA: 67.7 RA: 32.3	---
	Enoxaparin	221	76.0	---	---	---	---	GA: 67.9 RA: 32.1	---
Eriksson, 2001	Fondaparinux	831	---	21.2	---	101 (39)	---	GA:31.5 RA: 66.7 GA+RA: 1.8	---
	Enoxaparin	842	---	21.8	---	104 (44)	---	GA:32.8 RA: 65.2 GA+RA: 2.0	---
Fitzgerald, 2001	Warfarin	176	100	92.0	---	121.2 (55.8)	---	GA: 61.9 RA: 38.1	---
	Enoxaparin	173	100	91.3	---	119.4 (44.4)	---	GA: 64.7 RA: 35.3	---

Study, Year	Group	N	Primary surgery %	Cemented fixation %	Surgical approach %	Mean duration of surgery min (SD)	Mean duration of anesthesia min (SD)	Anesthesia %	Mean LOS, d
Hull, 2000	Dalteparin (preoperative)	496	81.85	22.58	---	---	---	---	---
	Dalteparin (postoperative)	487	81.52	25.05	---	---	---	---	---
	Warfarin	489	85.89	22.49	---	---	---	---	---
Kennedy, 2000	Aspirin	73	---	100	---	64	---	GA: 45.21 RA: 54.79	---
	VFP	70	---	100	---	59	---	GA: 60 RA: 41.43	---
Colwell, 1999	Enoxaparin	1516	100	---	---	---	---	---	---
	Warfarin	1495	100	---	---	---	---	---	---
Levy, 1999	Fibrin adhesive	29	---	100	---	---	---	---	---
	No fibrin adhesive	29	---	100	---	---	---	---	---
Planes, 1999	Enoxaparin	248	100	---	---	89 (44)	161 (56)	---	---
	Tinzaparin	251	100	---	---	87 (39)	159 (61)	---	---
TIFDED Study Group, 1999	Enoxaparin	66	---	---	---	69 (33)	---	---	---
	Dalteparin	66	---	---	---	70 (26)	---	---	---
Wakankar, 1999	Tourniquet	37	---	100	---	---	---	GA: 100	---
	No tourniquet	40	---	100	---	---	---	GA: 100	---
Kim, 1998	Aspirin	50	100	0	Modified Gibson: 100	---	---	GA: 100	---
	Control	50	100	0	Modified Gibson: 100	---	---	GA: 100	---
Lassen, 1998	Extended dalteparin	140	88.2‡	61.43	PL: 100	110 (55-280)*	---	GA: 37.14 RA: 62.86	---
	Dalteparin	141		67.38	PL: 100	105 (50-275)*	---	GA: 38.30 RA: 61.70	---
Rader, 1998	Heparin	116	100	---	THA L: 100 TKA AM: 100	THA: 72(14) TKA: 86(18)	---	GA:45.69 RA:54.31	16.4 (13-21)*‡
	Enoxaparin	130	100	---	THA L:100 TKA AM: 100	THA:74(17) TKA: 88(15)	---	GA:40.77 RA:59.23	
Ryan, 1998	IPC	50	100	---	---	---	---	RA: 100	---

Study, Year	Group	N	Primary surgery %	Cemented fixation %	Surgical approach %	Mean duration of surgery min (SD)	Mean duration of anesthesia min (SD)	Anesthesia %	Mean LOS, d
	GCS	50	100	---	---	---	---	RA: 100	---
Warwick, 1998	Enoxaparin	143	100	64.34	P: 61	---	---	RA: 87	---
	VFP	147	100	66.67	P: 56	---	---	RA: 84	
Andersen, 1997	Extended dalteparin	20	---	35	---	99 (60-140)*	149 (120-180)*	---	---
	Dalteparin	21	---	43	---	105 (60-180)*	165 (120-270)*	---	---
Dahl, 1997	Extended dalteparin	117	92.5‡	79.1	---	107	---	GA: 0.88‡ RA: 99.12‡	---
	Dalteparin	110		84.1	---	107	---		---
Eriksson, 1997a	Desirudin	225	100	81	---	101 (30)	---	GA:5 RA: 88 GA+RA: 6	---
	UFH	220	100	75	---	104 (30)	---	GA:6 RA: 86 GA+RA: 9	---
Eriksson, 1997b	Desirudin	1043	100	44.6	---	82.0 (22-297)†	---	RA: 55.7	---
	Enoxaparin	1036	100	44.3	---	80.0 (25-345)†	---	RA: 55.8	---
Francis, 1997	Dalteparin	271	76.38	29.52	---	161 (72)	221 (75)	GA:67.53 RA:32.47	---
	Warfarin	279	69.53	29.75	---	163 (62)	225 (67)	GA:63.44 RA:36.56	---
Nilsson, 1997	Extended enoxaparin	131	100	---	L:100	102 (66-312)*	---	GA: 3.8 RA: 86.3 GA+RA: 9.9	---
	Enoxaparin	131	100	---	L: 100	114 (60-300)*	---	GA: 6.1 RA: 84.0 GA+RA: 9.9	---
Planes, 1997	Extended enoxaparin	90	---	---	AL: 6.36‡ PL: 93.64‡	---	127.67 (19.95)	GA: 58.38‡ RA: 41.62‡	---
	Enoxaparin	89	---	---		---	125.83 (19.77)		---
Samama, 1997	Enoxaparin	85	100	74.1	A: 24.7 P: 71.8	70.1 (27.3)	---	RA: 100	---

Study, Year	Group	N	Primary surgery %	Cemented fixation %	Surgical approach %	Mean duration of surgery min (SD)	Mean duration of anesthesia min (SD)	Anesthesia %	Mean LOS, d
	Placebo	85	100	67.1	A: 21.2 P: 71.6	69.2 (27.9)	---	RA: 100	---
Eriksson, 1996	Desirudin	277	100	67.7	---	---	---	RA: 51.5	---
	UFH	277	100	67.5	---	---	---	RA: 51.6	---
Kalodiki, 1996	Enoxaparin + GCS	32	100	0	---	98 (50-185)*	---	GA: 100	---
	Enoxaparin	32	100	0	---	98 (45-215)*	---	GA: 100	---
	Placebo	14	100	0	---	96 (60-135)*	---	GA: 100	---
Laupacis, 1996	Cemented	124	100	100	DL: 100	---	---	GA: 85.5 RA: 14.5	---
	Non-cemented	126	100	100	DL: 100	---	---	GA: 90.5 RA: 9.5	---
Leclerc, 1996	Warfarin	334	93.4	89.2	---	124.3 (38.5)	---	GA:85.9 RA:14.1	---
	Enoxaparin	336	92.3	89.0	---	126.2 (44.7)	---	GA:87.2 RA:12.8	---
Lotke,1996	Aspirin	166	---	---	---	---	---	---	---
	Warfarin	136	---	---	---	---	---	---	---
Schwartsmann, 1996	Enoxaparin	52	100	62	AL: 100	90.8	---	RA: 100	---
	UFH	47	100	47	AL: 100	93.6	---	GA: 2 RA: 97.87 GA+RA: 0	---
Stannard, 1996	UFH then aspirin + VFP	25	88.0	0	P: 100	106 (85-128)*	---	GA: 16.0 RA: 84.0	---
	UFH then aspirin	25	100	0	P: 100	111 (87-140)*	---	GA: 12.0 RA: 88.0	---
	VFP	25	92.0	0	P: 100	113 (91-135)*	---	GA: 20.0 RA: 80.0	---
Stone, 1996	Enoxaparin	25	100	100	P: 100	---	---	---	---
	IPC	25	100	100	P: 100	---	---	---	---
Westrich, 1996	Aspirin + VFP	61	100	100	---	---	---	RA: 100	---
	Aspirin	61	100	100	---	---	---	RA: 100	---

Study, Year	Group	N	Primary surgery %	Cemented fixation %	Surgical approach %	Mean duration of surgery min (SD)	Mean duration of anesthesia min (SD)	Anesthesia %	Mean LOS, d
Abdel-Salam, 1995	Tourniquet	40	100	100	---	60-105[§]	---	GA: 100	12 (9-20)*
	No tourniquet	40	100	100	---	60-95[§]	---	GA: 100	12 (8-19)*
Avikainen, 1995	Enoxaparin	83	---	42.17	---	---	---	GA:29.69 RA:78.31	---
	UFH	84	---	30.95	---	---	---	GA:1.19 RA: 72.62	---
Colwell, 1995	Enoxaparin	228	---	---	---	---	---	---	---
	Heparin	225	---	---	---	---	---	---	---
Warwick, 1995	Enoxaparin	78	100	---	---	---	---	---	---
	Control	78	100	---	---	---	---	---	---
Williams-Russo, 1996	General Anesthesia	81	100	100	---	88 (32)	---	GA: 100	12.7 (4.3)
	Regional Anesthesia	97	100	100	---	85 (33)	---	RA: 100	12.1 (4.5)
Colwell, 1994	Enoxaparin 30mg Q12h	195	86	23	---	---	---	GA:66 RA:33	---
	Enoxaparin 40mg QD	203	83	27	---	---	---	GA:63 RA:35	---
	UFH	209	87	29	---	---	---	GA:65 RA:34	---
Fauno, 1994	Enoxaparin	92	100	65.22	---	104 (20)	---	GA: 10.87	---
	UFH	93	100	62.37	---	102 (24)	---	GA: 19.35	---
Leiberman, 1994	Aspirin + IPC	113	100	17.74[‖]	PL: 100	86	---	Hypotensive regional: 100	---
	Aspirin	118	100	13.49[‖]	PL: 100	87	---	Hypotensive regional: 100	---
Menzin, 1994	UFH	209	---	---	---	162 (78)	---	---	11.3
	Enoxaparin 40mg QD	202	---	---	---	156 (84)	---	---	9.9
	Enoxaparin 30mg Q12h	192	---	---	---	150 (66)	---	---	9.5
Santori,1994	Heparin	65	100	---	DL: 100	65 (9.89)	---	GA: 100	---
	VFP	67	100	---	DL: 100	70 (11.98)	---	GA: 100	---
Hull, 1993	Tinzaparin	715	84.62	54.13	---	---	128 (52)	GA:53.85 RA: 20.97 GA+RA: 25.17	---

Study, Year	Group	N	Primary surgery %	Cemented fixation %	Surgical approach %	Mean duration of surgery min (SD)	Mean duration of anesthesia min (SD)	Anesthesia %	Mean LOS, d
	Warfarin	721	84.47	57.98	---	---	127 (48)	GA:53.81 RA: 20.94 GA+RA: 25.24	---
Fordyce, 1992	VFP	39	100	100	DL: 12.82 P: 87.18	---	104.5	GA: 7.69	---
	Control	40	100	100	DL: 17.50 P: 82.50	---	112.6	GA: 15.00	---
Francis, 1992	Warfarin	103	100	24.53	AL: 100	---	198 (36)	GA: 69.90 RA: 30.10	9[‡]
	EPC	98	100	25.51	AL: 100	---	205 (40)	GA: 61.22 RA: 38.78	
Jorgensen, 1992	Dalteparin	30	---	---	---	57 (25 -115)[†]		GA: 66.67 RA: 30	14 (2-117)[†]
	Placebo	38	---	---	---	60 (35-105)[†]		GA: 53 RA: 45	16 (3-50)[†]
Wilson, 1992	VFP	28	---	---	---	139.2 (34.9)	---	---	---
	Control	31	---	---	---	132.1 (32.4)	---	---	---
Bailey, 1991	Warfarin	45	57.8	80.9	L:100	---	---	GA: 82.2 RA:6.7	---
	IPC	50	54	75.5	L:100	---	---	GA: 80 RA:14	---
Eriksson,1991	Dalteparin	67	---	79.10	AL: 100	123 (22)	---	GA: 14.93 RA:85.07	---
	UFH	69	---	79.71	AL: 100	124 (29)	---	GA: 7.25 RA:92.75	---
Jorgensen, 1991	General Anesthesia	22	---	---	---	---	---	GA: 100	---
	Epidural Anesthesia	17	---	---	---	---	---	RA: 100	---
Lassen, 1991	Tinzaparin	93	100	65.6	PL: 100	117 (55-200)[†]	---	GA: 72.0 RA: 28.0	---
	Placebo	97	100	71.1	PL: 100	123 (50-250)[†]	---	GA: 69.1 RA: 30.9	---
Levine, 1991	Enoxaparin	333	---	38.74	---	166 (56.6)	---	---	---
	UFH	332	---	39.16	---	172 (67.7)	---	---	---
Mitchell, 1991	General Anesthesia	38	100	76.4	---	121	---	GA: 100	11

Study, Year	Group	N	Primary surgery %	Cemented fixation %	Surgical approach %	Mean duration of surgery min (SD)	Mean duration of anesthesia min (SD)	Anesthesia %	Mean LOS, d
	Epidural Anesthesia	34	100		---	122	---	RA: 100	10.4
Planes, 1991	General Anesthesia + Enoxaparin	62	100	---	PL: 100	73.7 (2.4)	---	GA: 100	---
	Epidural Anestheisa + Enoxaparin	61	100	---	PL: 100	73.3 (2.3)	---	RA: 100	---
	Epidural Anesthesia alone	65	100	---	PL: 100	74.9 (1.7)	---	RA: 100	---
Torholm, 1991	Dalteparin	58	76	---	---	---	---	GA: 88 RA: 12	---
	Placebo	54	80	---	---	---	---	GA: 81 RA: 19	---
Woolson, 1991	Aspirin + IPC	70	75[‖]	65[‖]	TT: 25[‖] PL: 75[‖]	124	---	---	9
	Warfarin + IPC	69	68[‖]	68[‖]	TT: 32[‖] PL: 68[‖]	125	---	---	9
	IPC	73	72[‖]	63[‖¶]	TT: 28[‖] PL: 72[‖]	121	---	---	10
Haas, 1990 Unilateral	Aspirin	36	100	---	---	---	---	RA: 97[‡]	---
	IPC	36	100	---	---	---	---		---
Haas, 1990 Bilateral	Aspirin	22	100	---	---	---	---	RA: 97[‡]	---
	IPC	25	100	---	---	---	---		---
Sorenson, 1990	Tinzaparin	31	---	---	---	---	---	---	---
	Placebo	33	---	---	---	---	---	---	---
Dechavanne, 1989	Dalteparin 2500U Q12h	41	---	61.9	PL: 88	121.1 (59.1)	---	GA: 100	16.6 (4.8)
	Dalteparin 5000U QD	41	---	46.3	PL: 92	112.4 (34.3)	---	GA: 100	17.1 (4.7)
	Heparin	40	---	56.1	PL: 83	115.1 (51.7)	---	GA: 100	17.2 (5.4)
Monreal, 1989	Dalteparin	46	---	---	---	94 (54)	---	---	---
	Heparin	44	---	---	---	91 (51)	---	---	---
Powers, 1989	Warfarin	65	---	---	---	---	---	---	---
	Aspirin	66	---	---	---	---	---	---	---
	Placebo	63	---	---	---	---	---	---	---
Planes, 1988	Enoxaparin	124	---	62.1	---	63 (30)	138.9 (78.3)	GA: 100	---

Study, Year	Group	N	Primary surgery %	Cemented fixation %	Surgical approach %	Mean duration of surgery min (SD)	Mean duration of anesthesia min (SD)	Anesthesia %	Mean LOS, d
	Heparin	113	---	69.91	---	66 (23)	141.9 (73.2)	GA: 100	---
Barre, 1987	Dalteparin	40	---	100	---	73.8 (50-115)*	---	RA:100	15.6
	Heparin	40	---	100	---	86.1 (50-160)*	---	RA:100	15.2
Paiement, 1987	Warfarin	72	---	---	---	---	---	---	---
	IPC	66	---	---	---	---	---	---	---
Alfaro, 1986	Aspirin 250mg/d	30	---	---	---	---	---	---	---
	Aspirin 1g/d	30	---	---	---	---	---	---	---
	Control	30	---	---	---	---	---	---	---
Turpie, 1986	Enoxaparin	50	---	---	---	128.84 (26.23)	---	---	---
	Placebo	50	---	---	---	122.78 (23.20)	---	---	---
McKenzie, 1985	General Anesthesia	20	---	---	---	79.4 (4.1)	---	GA: 100	---
	Spinal Anesthesia	20	---	---	---	93.5 (5.6)	---	RA: 100	---
Welin-Berger, 1982	Heparin	20	---	---	---	118	---	---	---
	Control	20	---	---	---	103	---	---	---
Modig, 1981	General Anesthesia	15	---	100	---	161.3 (34.5)	---	GA: 100	---
	Epidural Anesthesia	15	---	100	---	147 (27.9)	---	RA: 100	---
McKenna, 1980	Aspirin	9	---	---	---	---	---	---	16‡
	Placebo	12	---	---	---	---	---	---	

*Mean (range)
†Median (range)
‡Value for the total study population
§Range
||Percent of hips
¶ Cemented or hybrid prosthesis

Abbreviations: A=anterior; AL=anteriolateral; AM=anteriomedial; ASA=aspirin; BID=twice daily; d=days; DL=direct lateral; GA=general anesthesia; GCS=graduated compression stockings; HFS=hip fracture surgery; IPC=intermittent pneumatic compression device; L=lateral; LOS=length of stay; min=minutes; mg=milligram; ML=midline longitudinal; N=number enrolled; P=posterior; PL=posteriolateral; QD=daily; RA=regional anesthesia; SD=standard deviation; THA=total hip arthroplasty; THR=total hip replacement; TKA= total knee arthroplasty; TKR=total knee replacement; TT=transtrochanteric; UFH=unfractionated heparin; VFP=venous foot pump

Table 8. Baseline characteristics of randomized controlled trials in nonmajor orthopedic surgery

Study, Year	Group	N	Age mean (SD)	Female %	Wt kg mean (SD)	Smoker %	Obese %	Hx VTE %	Varicosity %	Estrogen %	DM %	CA %	CVD %	Previous orthopedic surgery %
Lapidus, 2007	Dalteparin	52	37 (8)	21	80 (12)	17.3	---	0	5.8	0	0	---	---	---
	Placebo	52	42 (9)	21	81 (11)	15.1	---	0	11.3	1.9	3.8	---	---	---
Michot, 2002	Dalteparin	66	42 (14.7)	39.4	---	---	---	---	12.1	6.1	---	0	0	---
	Control	64	46.5 (13.2)	28.1	---	---	---	---	14.1	0	---	0	0	---

Abbreviations: CA=cancer; CVD=cardiovascular disease; DM=diabetes mellitus; Hx=history; kg=kilograms; N=number of participants; SD=standard deviation; Wt=weight

Table 9. Procedural characteristics of randomized controlled trials in nonmajor orthopedic surgery

Study, Year	Group	N	Primary surgery %	Cemented fixation %	Surgical approach %	Mean duration of surgery min (SD)	Mean duration of anesthesia min (SD)	Anesthesia %	Mean LOS, d
Lapidus, 2007	Dalteparin	52	---	---	---	44 (18)	---	GA: 0 RA: 100	---
	Placebo	53	---	---	---	45 (18)	---	GA: 0 RA: 100	---
Michot, 2002	Dalteparin	66	---	---	---	91 (30)	---	GA: 33.3 RA: 66.7 GA+RA: 3.0	---
	Control	64	---	---	---	90 (28)	---	GA: 29.7 RA: 70.3 GA+RA: 3.1	---

Abbreviations: d= days; GA= general anesthesia; LOS= length of stay; N= total number of patients; RA= regional anesthesia; SD= standard deviation

Table 10. Baseline characteristics of observational studies evaluating venous thromboembolism prophylaxis in major orthopedic surgery.

Study, Year	Group	N	Age mean (SD)	Female %	Wt kg mean (SD)	Smoker %	Obese %	Hx VTE %	Varic-osity %	Estr-ogen %	DM %	CA %	CVD %	Previous ortho-pedic surgery %
Bozic, 2010	Warfarin	51923	67.3 (10.4)	65.17	---	5	12	---	---	---	17	0.6	---	---
	Aspirin	4719	66.4 (10.7)	64.42	---	6	18	---	---	---	16	0.4	---	---
Cusick, 2009 THR	Aspirin	2094	68 (19-93)* †	---	---	---	---	---	---	---	---	---	---	---
	Warfarin	6		---	---	---	---	---	---	---	---	---	---	---
	Control	86		---	---	---	---	---	---	---	---	---	---	---
Cusick, 2009 TKR	Aspirin	1966	71 (31-93)* †	---	---	---	---	---	---	---	---	---	---	---
	Warfarin	5		---	---	---	---	---	---	---	---	---	---	---
	Control	50		---	---	---	---	---	---	---	---	---	---	---
Froimson, 2009	IPC (ActiveCare)	223	66 (11.5)	---	---	---	---	---	---	---	---	---	---	---
	IPC (Flowtron)	1354	64.3 (13.7)	---	---	---	---	---	---	---	---	---	---	---
Gandhi, 2009	Metabolic syndrome	135	66.1 (9.2)	67.00	---	---	---	---	---	---	---	---	---	---
	Without metabolic syndrome	1325	66.6 (9.9)	63.5	---	---	---	---	---	---	---	---	---	---
McNamara, 2009	Thrombosis	117	79(12)	82.91	---	14.02	---	---	---	---	---	---	---	---
	No thrombosis	5183	80 (11)	78.37	---	12.53	---	---	---	---	---	---	---	---
Dorr, 2007	Low risk	856	64.9 (11.9)†	56.9†	83.9 (21.1)†	---	---	---	---	---	---	---	---	---
	High risk	114		---		---	---	---	---	---	---	---	---	---
Shorr, 2007	Fondaparinux	12532	69	63.4	---	---	---	---	---	---	---	---	---	---

Study, Year	Group	N	Age mean (SD)	Female %	Wt kg mean (SD)	Smoker %	Obese %	Hx VTE %	Varic-osity %	Estr-ogen %	DM %	CA %	CVD %	Previous ortho-pedic surgery %
	Enoxaparin	97827	70	65.2	---	---	---	---	---	---	---	---	---	---
	Dalteparin	16109	68	63.5	---	---	---	---	---	---	---	---	---	---
	UFH	18338	69	63.6	---	---	---	---	---	---	---	---	---	---
	Control	112574	68	63.0	---	---	---	---	---	---	---	---	---	---
Leirozovicz,2005	sVTE or death	28	72 (68-80)*	67.9	---	---	18.2	3.6	14.3	0.0/ 0.0‡	---	7.1	---	---
	No sVTE or death	2392	68 (60-75)*	67.3	---	---	12.1	0.2	4.2	0.2/ 0.5‡	---	3.2	---	---
Sachs, 2003	Warfarin	957	70	56†	---	---	---	---	---	---	---	---	---	---
	Control	785	70		---	---	---	---	---	---	---	---	---	---
Ryan, 1998	Factor V Leiden mutation	32	66.0 (12.1)	47	---	---	---	4	---	---	---	---	---	---
	Without Factor V Leiden mutation	793	66.9 (11.1)	57	---	---	---	8.6	---	---	---	---	---	---
Lieberman, 1997	Before hospital discharge	1042†	59 (19-90)*†	---	---	---	----	20†§	---	---	---	---	---	---
	After hospital discharge			---	---	---	---		---	---	---	---	---	---
Haas, 1992	No thrombi	498	---	---	---	---	---	---	---	---	---	---	---	---
	Calf thrombi	655	---	---	---	---	---	---	---	---	---	---	---	---
	Proximal thrombi	104	---	---	---	---	---	---	---	---	---	---	---	---
Lemos, 1991	PE	81	---	---	---	---	---	---	---	---	---	---	---	---
	Without PE	159	---	---	---	---	---	---	---	---	---	---	---	---

*Mean(range)
†Value for the total study population
‡Estrogen/HRT use
§History of symptomatic pulmonary embolism or deep vein thrombosis

Abbreviations: BMI=body mass index; CA=cancer; CVD=cardiovascular disease; DM=diabetes mellitus; hx=history; IPC=intermittent pneumatic compression; kg=kilograms; LMWH=low molecular weight heparin; PE=pulmonary embolism; SD=standard deviation; sVTE=symptomatic venous thromboembolism; THR=total hip replacement; TKR=total knee replacement; UFH=unfractionated heparin; VTE=venous thromboembolism; Wt=weight

Table 11. Procedural characteristics of observational studies evaluating venous thromboembolism prophylaxis in major orthopedic surgery.

Study, Year	Group	N	Primary surgery %	Cemented fixation %	Surgical approach %	Mean duration of surgery min (SD)	Mean duration of anesthesia min (SD)	Anesthesia %	Mean LOS, d
Bozic, 2010	Warfarin	51923	100	---	---	---	---	---	3 (3-4)*
	Aspirin	4719	100	---	---	---	---	--	3 (3-4)*
Cusick, 2009 THR	Aspirin	2094	100	---	P: 100	---	---	---	---
	Warfarin	6	100	---	P: 100	---	---	---	---
	Control	86	100	---	P: 100	---	---	---	---
Cusick, 2009 TKR	Aspirin	1966	100	---	MP: 100	---	---	---	---
	Warfarin	5	100	---	MP: 100	---	---	---	---
	Control	50	100	---	MP: 100	---	---	---	---
Froimson, 2009	IPC (ActiveCare)	223	77.13	---	---	---	---	---	4.2 (3.2)
	IPC (Flowtron)	1354	79.84	---	---	---	---	---	5 (3.7)
Gandhi, 2009	Metabolic syndrome	135	100	---	---	---	---	RA: 100	---
	Without metabolic syndrome	1325	100	---	---	---	---	RA: 100	---
McNamara, 2009	Thrombosis	117	---	---	---	---	60	---	---
	No thrombosis	5183	---	---	---	---	60	---	---
Dorr, 2007	Low risk	856	100	---	P: 100	---	---	---	---
	High risk	114	100	---	MP: 100	---	---	---	---

Study, Year	Group	N	Primary surgery %	Cemented fixation %	Surgical approach %	Mean duration of surgery min (SD)	Mean duration of anesthesia min (SD)	Anesthesia %	Mean LOS, d
Shorr, 2007	Fondaparinux	12532	---	---	---	---	---	---	4.4 (2.6)
	Enoxaparin	97827	---	---	---	---	---	---	5.1 (4.1)
	Dalteparin	16109	---	---	---	---	---	---	4.6 (3.3)
	UFH	18338	---	---	---	---	---	---	5.6 (6.2)
	Control	112574	---	---	---	---	---	---	4.1 (2.5)
Leirozovicz, 2005	sVTE or death	28	100	---	MP: 100	---	---	---	---
	No sVTE or death	2392	100	---	MP: 100	---	---	---	---
Sachs, 2003	Warfarin	957	100	---	---	---	---	---	---
	Control	785	100	---	---	---	---	---	---
Ryan, 1998	Factor V Leiden mutation	32	---	---	---	---	---	---	4.4 (2.6)
	Without Factor V Leiden mutation	793	---	---	---	---	---	---	5.1 (4.1)
Lieberman, 1997	Before hospital discharge	1042†	607†	---	---	---	---	---	11 (4-53)†‡
	After hospital discharge								
Haas, 1992	No thrombi	498	100	100	---	---	---	---	---
	Calf thrombi	655	100	100	---	---	---	---	---
	Proximal thrombi	104	100	100	---	---	---	---	---
Lemos, 1991	PE	81	---	---	---	---	---	---	4.6 (3.3)
	Without PE	159	---	---	---	---	---	---	5.6 (6.2)

*Median(range)
†Value for the total population
‡Mean(range)

Abbreviations: d=day(s); GA=general anesthesia; IPC=intermittent pneumatic compression; LMWH=low molecular weight heparin; LOS=length of stay; min=minute; MP=medial parapatellar; N=total population; P=posterior; PE=pulmonary embolism; RA=regional anesthesia; SD=standard deviation; sVTE=symptomatic venous thromboembolism; THR=total hip replacement; TKR=total knee replacement; UFH=unfractionated heparin

Appendix F. Additional evidence tables

Table 12. Final health outcomes in randomized controlled trials evaluating patients who had major orthopedic surgery

Study, Year	Group	Symptomatic objectively confirmed VTE n/N	Major VTE n/N	Fatal PE n/N	Nonfatal PE n/N	PE n/N	PTS n/N	Mortality n/N	Mortality due to bleeding n/N
Fuji, 2010	Dabigatran 150mg	---	2/113	0/126	0/126	0/126	---	0/126	0/126
	Dabigatran 220mg	---	0/102	0/129	0/129	0/129	---	0/129	0/129
	Placebo	---	6/104	0/124	0/124	0/124	---	0/124	0/124
Chin, 2009	Enoxaparin	---	---	---	---	0/110	---	---	---
	Control	---	---	---	---	1/110	---	---	---
Ginsberg, 2009	Dabigatran 150mg QD	---	---	---	---	---	---	1/871	0/871
	Dabigatran 220mg QD	---	---	---	---	---	---	1/857	0/857
	Enoxaparin	---	---	---	---	---	---	0/868	0/868
Edwards, 2008 THA	Enoxaparin + IPC	---	---	0/65	0/65	0/65	---	0/65	0/65
	Enoxaparin	---	---	0/59	0/59	0/59	---	0/59	0/59
Edwards, 2008 TKA	Enoxaparin + IPC	---	---	0/76	1/76	1/76	---	0/76	0/76
	Enoxaparin	---	---	0/77	1/77	1/77	---	0/77	0/77
Fuji, 2008 THA	Enoxaparin 40mg QD	---	---	---	---	1/80	---	---	---
	Enoxaparin 20 mg BID	---	---	---	---	0/90	---	---	---
	Placebo	---	---	---	---	0/86	---		
Fuji, 2008 TKA	Enoxaparin 40mg QD	---	---	---	---	1/74	---	---	---
	Enoxaparin 20 mg BID	---	---	---	---	0/84	---	---	---
	Placebo	---	---	---	---	1/79	---	---	---
Thorey, 2008	Early release tourniquet	---	---	---	---	---	---	---	---
	Late release tourniquet	---	---	---	---	---	---	---	---
Eriksson, 2007a	Dabigatran 150mg QD	---	20/527	0/696	1/696	1/696	---	1/696	0/703
	Dabigatran 220mg QD	---	13/506	0/675	0/675	0/675	---	1/675	0/679
	Enoxaparin	---	18/511	1/685	0/685	1/685	---	1/685	0/694
Eriksson, 2007b	Dabigatran 150mg QD	---	38/888	1/1156	0/1156	1/1156	---	3/1156	1/1163
	Dabigatran 220mg QD	---	28/909	0/1137	5/1137	5/1137	---	3/1137	1/1146

Study, Year	Group	Symptomatic objectively confirmed VTE n/N		Major VTE n/N	Fatal PE n/N	Nonfatal PE n/N	PE n/N	PTS n/N	Mortality n/N	Mortality due to bleeding n/N
	Enoxaparin	---		36/917	0/1142	3/1142	3/1142	---	0/1142	0/1154
Lassen, 2007	Enoxaparin	---		---	0/109	2/109	2/109	---	0/109	0/109
	Warfarin	---		---	0/109	0/109	0/109	---	0/109	0/109
Bonneux, 2006	Fondaparinux	---		---	---	---	---	---	---	---
	Enoxaparin	---		---	---	---	---	---	---	---
Senaran, 2006	Enoxaparin	0/50	2/50*	---	0/50	0/50	0/50	---	0/50	0/50
	Heparin	2/50	0/50*	---	0/50	0/50	0/50	---	0/50	0/50
Westrich, 2006	Minimum hyperflexed knee	---		---	---	---	---	---	---	---
	Standard hyperflexed knee	---		---	---	---	---	---	---	---
Eriksson, 2005	Dabigatran 50mg BID	2/302	2/302†	---	---	0/300 1/302†	---	---	1/389	0/389
	Dabigatran 150mg BID	2/282	1/282†	---	---	2/282 0/282†	---	---	0/390	0/282
	Dabigatran 300mg QD	0/283	2/283†	---	---	0/283 0/283†	---	---	0/385	0/283
	Dabigatran 225mg BID	0/297	0/297†	---	---	0/297 0/297†	---	---	1/393	0/297
	Enoxaparin	1/300	0/300†	---	---	0/300 0/300†	---	---	0/392	0/300
Farag, 2005	Epidural Anesthesia	---		---	---	---	---	---	---	---
	Spinal Anesthesia	---		---	---	---	---	---	---	---
Lachiewicz, 2004	IPC (Venaflow)	---		---	0/206	0/206	0/206	---	0/206	0/206
	IPC (Kendal)	---		---	0/217	1/217	1/217	---	1/217	0/217
Silbersack, 2004	Enoxaparin + IPC	---		---	0/68‡	0/68‡	0/68‡	---	---	---
	Enoxaparin + GCS	---		---	0/63‡	0/63‡	0/63‡	---	---	---
Eriksson, 2003	Extended fondaparinux	1/326		---	0/326	0/326	0/326	---	---	6/327
	Fondaparinux	9/330		---	1/330	2/330	3/330	---	---	8/329
Kim, 2003	Cemented	---		---	---	---	0/200§	---	---	2/200§
	Non-cemented	---		---	---	---		---	---	
Lassen, 2002	Fondaparinux	12/1129		---	1/1129	3/1129	---	---	2/1140	0/1140

Study, Year	Group	Symptomatic objectively confirmed VTE n/N	Major VTE n/N	Fatal PE n/N	Nonfatal PE n/N	PE n/N	PTS n/N	Mortality n/N	Mortality due to bleeding n/N
	Enoxaparin	9/1123	---	0/1123	3/1123	---	---	4/1133	0/1133
Pitto, 2002	Bone vaccum cement technique	---	---	0/65	0/65	0/65	---	---	---
	Standard cement technique	---	---	0/65	0/65	0/65	---	---	---
Prandoni, 2002	Extended warfarin	3/184	3/184	0/184	0/184	0/184	---	0/184	0/184
	Warfarin	9/176	9/176	0/176	1/176	1/176	---	0/176	0/176
Turpie, 2002	Fondaparinux	29/1126	---	1/1126	11/1126	---	---	6/1128	0/1126
	Enoxaparin	13/1128	---	2/1128	2/1128	---	---	3/1129	0/1128
Warwick, 2002	Enoxaparin	---	---	0/112	---	---	---	1/112	0/112
	VFP	---	---	2/117	---	---	---	3/117	0/117
Barden, 2001	Modified position	---	---	0/83	0/83	0/83	---	---	---
	Conventional figure four positioning	---	---	0/76	0/76	0/76	---	---	---
Bauer, 2001	Fondaparinux	5/517	---	1/517	2/517	1/517	---	2/517	0/517
	Enoxaparin	10/517	---	1/517	4/517	4/517	---	3/517	0/517
Comp, 2001 THR	Extended enoxaparin	18/224	---	0/224	0/224	0/224	---	0/224	0/224
	Enoxaparin	49/211	---	0/211	1/211	1/211	---	0/211	0/211
Comp, 2001 TKR	Extended enoxaparin	38/217	---	0/217	0/217	0/217	---	0/217	0/217
	Enoxaparin	46/221	---	0/221	2/221	2/221	---	0/221	0/221
Eriksson, 2001	Fondaparinux	17/831	---	8/831	3/831	---	---	38/831	0/831
	Enoxaparin	13/840	---	7/840	4/840	---	---	42/842	1/842
Fitzgerald, 2001	Warfarin	---	---	---	---	1/176	---	3/176	1/176
	Enoxaparin	---	---	---	---	0/173	---	1/173	0/173
Hull, 2000	Dalteparin (pre-operative)	---	---	0/496	0/496	0/496	---	2/496	0/496
	Dalteparin (post-operative)	---	---	0/487	0/487	0/487	---	0/487	0/487
	Warfarin	---	---	0/489	0/489	0/489	---	2/489	0/489
Kennedy, 2000	Aspirin	---	---	---	---	1/73	---	---	---
	VFP	---	---	---	---	0/70	---	---	---
Colwell, 1999	Enoxaparin	55/1516	---	1/1516	---	15/1516	---	9/1516	---

Study, Year	Group	Symptomatic objectively confirmed VTE n/N	Major VTE n/N	Fatal PE n/N	Nonfatal PE n/N	PE n/N	PTS n/N	Mortality n/N	Mortality due to bleeding n/N
	Warfarin	56/1495	---	0/1495	---	12/1495	---	10/1495	---
Levy, 1999	Fibrin adhesive	---	---	0/29	---	---	---	---	---
	No fibrin adhesive	---	---	1/29	---	---	---	---	---
Planes, 1999	Enoxaparin	---	---	1/248	1/248	---	---	1/248	0/248
	Tinzaparin	---	---	0/251	1/251	---	---	0/251	0/251
TIFDED Study Group, 1999	Enoxaparin	---	---	0/66	0/66	0/66	---	---	---
	Dalteparin	---	---	0/66	0/66	0/66	---	---	---
Wakankar, 1999	Tourniquet	---	---	---	---	---	---	1/37	---
	No tourniquet	---	---	---	---	---	---	2/40	---
Kim, 1998	Aspirin	---	---	---	---	---	---	---	---
	Control	---	---	---	---	---	---	---	---
Lassen, 1998	Extended dalteparin	---	---	---	---	---	---	---	---
	Dalteparin	---	---	---	---	---	---	---	---
Rader, 1998	Heparin	---	---	---	---	---	---	---	---
	Enoxaparin	---	---	---	---	---	---	---	---
Ryan, 1998	IPC	---	---	0/50	0/50	0/50	---	---	---
	GCS	---	---	0/50	0/50	0/50	---	---	---
Warwick, 1998	Enoxaparin	---	---	0/138	0/138	0/138	---	0/143	0/143
	VFP	---	---	0/136	1/136	1/136	---	0/147	0/147
Andersen, 1997	Extended dalteparin	---	---	---	---	0/20	---	---	---
	Dalteparin	---	---	---	---	1/21	---	---	---
Dahl, 1997	Extended dalteparin	---	---	0/111	0/111	4/111	---	1/134	0/134
	Dalteparin	---	---	1/106	2/106	7/106	---	1/131	0/131
Eriksson, 1997a	Desirudin	---	---	0/180	0/180	0/180	---	0/180	0/180
	UFH	---	---	0/180	4/180	4/180	---	2/180	0/180
Eriksson, 1997b	Desirudin	---	39/802	1/802[ll]	---	2/802 1/802[ll]	---	4/802	---
	Enoxaparin	---	60/785	0/785[ll]	---	2/785 5/785[ll]	---	1/785	---
Francis, 1997	Dalteparin	---	---	---	---	---	---	---	---

Study, Year	Group	Symptomatic objectively confirmed VTE n/N	Major VTE n/N	Fatal PE n/N	Nonfatal PE n/N	PE n/N	PTS n/N	Mortality n/N	Mortality due to bleeding n/N
	Warfarin	---	---	---	---	---	---	---	---
Nilsson, 1997	Extended enoxaparin	2/131	---	0/131	0/131	0/131	---	0/131	0/131
	Enoxaparin	10/131	---	0/131	2/131	2/131	---	0/131	0/131
Planes, 1997	Extended enoxaparin	---	---	0/85	0/85	0/85	---	0/85	0/85
	Enoxaparin	---	---	0/88	0/88	0/88	---	0/88	0/88
Samama, 1997	Enoxaparin	---	---	0/85	0/85	0/85	---	0/85	0/85
	Placebo	---	---	0/84	0/84	0/84	---	0/84	0/84
Eriksson, 1996	Desirudin	---	---	0/202	1/202	1/202	---	0/202	0/202
	UFH	---	---	0/229	0/229	0/229	---	1/229	0/229
Kalodiki, 1996	Enoxaparin + GCS	---	---	---	---	---	---	---	---
	Enoxaparin	---	---	---	---	---	---	---	---
	Placebo	---	---	---	---	---	---	---	---
Laupacis, 1996	Cemented	---	---	---	---	3/124	---	---	---
	Non-cemented	---	---	---	---	1/125	---	---	---
Leclerc, 1996	Enoxaparin	3/336	---	0/336	1/336	1/336	---	1/336	0/336
	Warfarin	1/334	---	0/334	3/334	3/334	---	1/334	0/334
Lotke, 1996	Aspirin	---	---	---	---	---	---	---	---
	Warfarin	---	---	---	---	---	---	---	---
Schwartsmann, 1996	Enoxaparin	---	---	0/52	0/52	0/52	---	0/52	0/52
	UFH	---	---	0/47	0/47	0/47	---	0/47	0/47
Stannard, 1996	UFH then aspirin + VFP	---	---	---	---	---	---	0/25	0/25
	UFH then aspirin	---	---	---	---	---	---	0/25	0/25
	VFP	---	---	---	---	---	---	0/25	0/25
Stone, 1996	Enoxaparin	---	---	---	---	---	---	---	---
	IPC	---	---	---	---	---	---	---	---
Westrich, 1996	Aspirin + VFP	---	---	---	---	---	---	---	---
	Aspirin	---	---	---	---	---	---	---	---
Williams-Russo, 1996	General Anesthesia	---	---	---	---	3/178[§]	---	1/81	---
	Regional Anesthesia	---	---	---	---		---	1/97	---

Study, Year	Group	Symptomatic objectively confirmed VTE n/N	Major VTE n/N	Fatal PE n/N	Nonfatal PE n/N	PE n/N	PTS n/N	Mortality n/N	Mortality due to bleeding n/N
Abdel-Salam, 1995	Tourniquet	---	---	---	---	---	---	---	---
	No tourniquet	---	---	---	---	---	---	---	---
Avikainen, 1995	Enoxaparin	---	---	---	---	0/83	---	---	---
	UFH	---	---	---	---	1/84	---	---	---
Colwell, 1995	Enoxaparin	---	---	0/228	0/228	0/228	---	---	---
	Heparin	---	---	1/225	1/225	2/225	---	---	---
Warwick, 1995	Enoxaparin	---	---	---	---	1/78	---	---	---
	Control	---	---	---	---	2/78	---	---	---
Colwell, 1994	Enoxaparin 30mg Q12h	---	---	0/195	0/195 0/195*	0/195 0/195*	---	1/195	---
	Enoxaparin 40mg QD	---	---	0/203	0/203 0/203*	0/203 0/203*	---	0/203	---
	UFH	---	---	0/209	1/209 3/209*	1/209 3/209*	---	2/209	---
Fauno, 1994	Enoxaprain	---	---	0/92	0/92	0/92	---	---	---
	UFH	---	---	0/93	0/93	0/93	---	---	---
Leiberman, 1994	Aspirin + IPC	---	---	0/113	0/113	1/113	---	1/113	0/113
	Aspirin	---	---	0/118	0/118	1/118	---	0/118	0/118
Menzin, 1994	UFH	---	---	---	---	---	---	---	---
	Enoxaparin 40mg QD	---	---	---	---	---	---	---	---
	Enoxaparin 30mg Q12h	---	---	---	---	---	---	---	---
Santori, 1994	Heparin	---	---	---	---	---	---	1/65	0/65
	VFP	---	---	---	---	---	---	0/67	0/67
Hull, 1993 THR	Tinzaparin	6/398[¶]	---	0/398[¶]	1/398[¶]	1/398[¶]	---	5/715[#]	0/398
	Warfarin	2/397[¶]	---	0/397[¶]	0/397[¶]	0/397[¶]	---	5/721[#]	0/397
Hull, 1993 TKR	Tinzaparin	1/317[¶]	---	0/317[¶]	0/317[¶]	0/317[¶]			0/317
	Warfarin	1/324	---	0/324[¶]	1/324[¶]	1/324[¶]			0/324
Fordyce, 1992	VFP	---	---	---	---	---	---	---	---
	Control	---	---	---	---	---	---	---	---
Francis, 1992	Warfarin	---	---	---	---	---	---	1/103	0/103
	IPC	---	---	---	---	---	---	1/98	0/98

Study, Year	Group	Symptomatic objectively confirmed VTE n/N	Major VTE n/N	Fatal PE n/N	Nonfatal PE n/N	PE n/N	PTS n/N	Mortality n/N	Mortality due to bleeding n/N
Jorgensen, 1992	Dalteparin	---	---	---	---	---	---	3/30	0/30
	Placebo	---	---	---	---	---	---	4/38	0/38
Wilson, 1992	VFP	---	---	0/28	0/28	0/28	---	---	---
	Control	---	---	0/32	0/32	0/32	---	---	---
Bailey, 1991	Warfarin	---	---	---	---	---	---	0/45	0/45
	IPC	---	---	---	---	---	---	0/50	0/50
Eriksson, 1991	Dalteparin	---	---	0/65	8/65	8/65	---	0/67	0/67
	UFH	---	---	0/62	19/62	19/62	---	1/69	0/69
Jorgensen, 1991	General Anesthesia	---	---	---	1/22	---	---	---	---
	Epidural Anesthesia	---	---	---	0/17	---	---	---	---
Lassen, 1991	Tinzaparin	---	---	0/93	1/93	1/93	---	1/93	---
	Placebo	---	---	0/97	1/97	1/97	---	1/97	---
Levine, 1991	Enoxaparin	---	---	0/333	0/333	0/333	---	0/333	0/333
	UFH	---	---	0/332	2/332	2/332	---	0/332	0/332
Mitchell, 1991	General Anesthesia	---	---	---	---	---	---	---	---
	Epidural Anesthesia	---	---	---	---	---	---	---	---
Planes, 1991	General Anesthesia + Enoxaparin	---	---	0/62	0/62	0/62	---	0/62	0/62
	Epidural Anestheisa + Enoxaparin	---	---	0/61	0/61	0/61	---	1/61	0/61
	Epidural Anesthesia alone	---	---	0/65	0/65	0/65	---	0/65	0/65
Torholm, 1991	Dalteparin	---	---	---	---	---	---	1/58	0/58
	Placebo	---	---	---	---	---	---	0/54	0/54
Woolson, 1991	Aspirin + IPC	---	---	---	---	1/70	---	---	---
	Warfarin + IPC	---	---	---	---	0/69	---	---	---
	IPC	---	---	---	---	0/73	---	---	---
Haas, 1990 Unilateral TKA	Aspirin	---	---	---	---	---	---	---	---
	IPC	---	---	---	---	---	---	---	---
Haas, 1990 Bilateral TKA	Aspirin	---	---	---	---	---	---	---	---

Study, Year	Group	Symptomatic objectively confirmed VTE n/N	Major VTE n/N	Fatal PE n/N	Nonfatal PE n/N	PE n/N	PTS n/N	Mortality n/N	Mortality due to bleeding n/N
	IPC	---	---	---	---	---	---	---	---
Sorensen, 1990	Tinzaparin	---	---	---	---	---	---	1/31	0/31
	Placebo	---	---	---	---	---	---	1/33	0/33
Dechavanne, 1989	Dalteparin 2500U Q12h	---	---	---	---	---	---	---	---
	Dalteparin 5000U QD	---	---	---	---	---	---	---	---
	Heparin	---	---	---	---	---	---	---	---
Monreal, 1989	Dalteparin	---	---	0/46	6/46	6/46	---	2/46	0/46
	Heparin	---	---	0/44	0/44	0/44	---	3/44	1/44
Powers, 1989	Warfarin	---	---	0/65	0/65	0/65	---	5/65	0/65
	Aspirin	---	---	1/66	0/66	1/66	---	5/66	0/66
	Placebo	---	---	0/63	2/63	2/63	---	3/63	0/63
Planes, 1988	Enoxaparin	---	---	0/120	0/120	---	---	0/120	0/120
	Heparin	---	---	0/108	1/108	---	---	0/108	0/108
Barre, 1987	Dalteparin	---	---	0/40	0/40	0/40	---	0/40	0/40
	Heparin	---	---	0/40	0/40	0/40	---	0/40	0/40
Paiement, 1987	Warfarin	---	---	0/72	0/72	0/72	---	---	---
	IPC	---	---	0/66	0/66	0/66	---	---	---
Alfaro, 1986	Aspirin 250mg/d	---	---	---	---	0/30	---	---	---
	Aspirin 1g/d	---	---	---	---	0/30	---	---	---
	Control	---	---	---	---	1/30	---	---	---
Turpie, 1986	Enoxaparin	---	---	0/50	0/50	0/50	---	0/50	0/50
	Placebo	---	---	0/50	1/50	1/50	---	1/50	1/50
McKenzie, 1985	General Anesthesia	---	---	---	---	---	---	5/20	---
	Spinal Anesthesia	---	---	---	---	---	---	3/20	---
Welin-Berger, 1982	Heparin	---	---	---	---	0/20	---	---	---
	Control	---	---	---	---	1/20	---	---	---
Modig, 1981	General Anesthesia	---	---	---	---	7/15	---	---	---
	Epidural Anesthesia	---	---	---	---	2/15	---	---	---

Study, Year	Group	Symptomatic objectively confirmed VTE n/N	Major VTE n/N	Fatal PE n/N	Nonfatal PE n/N	PE n/N	PTS n/N	Mortality n/N	Mortality due to bleeding n/N
McKenna, 1980	Aspirin	---	---	---	---	---	---	0/9	0/9
	Placebo	---	---	---	---	---	---	0/12	0/12

*Discharge-42days; †After study period-30 or 42days; ‡42-82days;§number of events out of the total population; ||After study period-42days; ¶Discharge-90days; #number of events out of combined THR and TKR population

Abbreviations: BID=twice daily; d=days; g=grams; GCS=graduated compression stockings; h=hours; IPC=intermittent pneumatic compression device; mg=milligram; n/N= total number of events/total population; PE=pulmonary embolism; PTS=post thrombotic syndrome; QD=daily; SD=standard deviation; THA=total hip arthroplasty; THR=total hip replacement; TKA=total knee arthroplasty; TKR=total knee replacement; U=units; UFH=unfractionated heparin; VFP=venous foot pump; VTE=venous thromboembolism

Table 13. Final health outcomes in randomized controlled trials in KQ 10

Study, Year	Group	Symptomatic objectively confirmed VTE n/N	Major VTE n/N	Fatal PE n/N	Non- fatal PE n/N	PE n/N	PTS n/N	Mortality n/N	Mortality due to bleeding n/N
Lapidus, 2007	Dalteparin	---	---	0/52	0/52	0/52	---	---	---
	Placebo	---	---	0/53	0/53	0/53	---	---	---
Michot, 2002	Dalteparin	---	---	---	---	1/66	---	---	---
	Control	---	---	---	---	0/64	---	---	---

Abbreviations: n/N= total number of events/total population; PE=pulmonary embolism; PTS=post thrombotic syndrome; VTE=venous thromboembolism

Table 14. Final health outcomes in observational studies evaluating venous thromboembolism prophylaxis in major orthopedic surgery

Study, Year	Group	Symptomatic objectively confirmed VTE n/N	Major VTE n/N	Fatal PE n/N	Nonfatal PE n/N	PE n/N	PTS n/N	Mortality n/N	Mortality due to bleeding n/N
Bozic, 2010	Warfarin	---	---	---	---	---	---	54/51923	---
	Aspirin	---	---	---	---	---	---	9/4719	---
Cusick, 2009 THR	Aspirin	---	---	1/2094	27/4060*	---	---	5/2094	---
	Warfarin	---	---	0/6	0/11*	---	---	0/6	---

Study, Year	Group	Symptomatic objectively confirmed VTE n/N	Major VTE n/N	Fatal PE n/N	Nonfatal PE n/N	PE n/N	PTS n/N	Mortality n/N	Mortality due to bleeding n/N
	Control	---	---	0/86	0/136*	---	---	0/86	---
Cusick, 2009 TKR	Aspirin	---	---	2/1966		---	---	8/1966	---
	Warfarin	---	---	0/5		---	---	0/5	---
	Control	---	---	0/50		---	---	0/50	---
Froimson, 2009	IPC (ActiveCare)	---	---	0/223	0/223	---	---	0/223	0/223
	IPC (Flowtron)	---	---	0/1354	9/1354	---	---	0/1354	0/1354
Shorr, 2007	Fondaparinux	---	---	---	---	---	---	75/12532	---
	Enoxaparin or dalteparin	---	---	---	---	---	---	1253/113936	---
	UFH	---	---	---	---	---	---	403/18338	---
	Control	---	---	---	---	---	---	---	---
Sachs, 2003	Warfarin	---	---	---	---	---	---	1/957	---
	Control	---	---	---	---	---	---	2/785	---

* The nonfatal PE data reflect the entire study population. THR and TKR was not broken down.

Abbreviations: IPC=intermittent pneumatic compression; PE=pulmonary embolism; PTS=post-thrombotic syndrome; THR=total hip replacement; TKR=total knee replacement; UFH=unfractionated heparin; VTE=venous thromboembolism

Table 15. Intermediate health outcomes from randomized controlled trials evaluating patients who had major orthopedic surgery

Study, Year	Group	DVT n/N	Asymptomatic DVT n/N	Symptomatic DVT n/N	Proximal DVT n/N	Distal DVT n/N
Fuji, 2010	Dabigatran 150mg	34/104	32/104	2/126	2/113	---
	Dabigatran 220mg	23/96	22/96	1/129	0/102	---
	Placebo	57/101	55/101	2/124	6/104	---
Chin, 2009	Enoxaparin	6/110	---	---	1/110	5/110
	Control	24/110	---	---	3/110	21/110
Ginsberg, 2009	Dabigatran 150mg QD	---	---	6/649	20/649	198/649
	Dabigatran 220mg QD	---	---	7/604	14/604	167/604
	Enoxaparin	---	---	5/643	10/643	148/643
Edwards, 2008 THA	Enoxaparin + IPC	1/65	---	---	0/65	1/65
	Enoxaparin	2/59	---	---	0/59	2/59

Study, Year	Group	DVT n/N	Asymptomatic DVT n/N	Symptomatic DVT n/N		Proximal DVT n/N	Distal DVT n/N
Edwards, 2008 TKA	Enoxaparin + IPC	5/76	---	---		0/76	5/76
	Enoxaparin	8/77	---	---		0/77	8/77
Fuji, 2008 THA	Enoxaparin 40mg QD	27/80	---	---		6/80	---
	Enoxaparin 20 mg BID	18/90	---	---		3/90	---
	Placebo	36/86	---	---		9/86	---
Fuji, 2008 TKA	Enoxaparin 40mg QD	25/74	---	---		3/74	---
	Enoxaparin 20 mg BID	25/84	---	---		0/84	---
	Placebo	48/79	---	---		6/79	---
Thorey, 2008	Early release tourniquet	0/20	0/20	0/20		0/20	0/20
	Late release tourniquet	0/20	0/20	0/20		0/20	0/20
Eriksson, 2007a	Dabigatran 150mg QD	---	208/524	3/696		---	---
	Dabigatran 220mg QD	---	181/503	1/675		---	---
	Enoxaparin	---	184/511	8/685		---	---
Eriksson, 2007b	Dabigatran 150mg QD	---	63/871	9/1156		---	---
	Dabigatran 220mg QD	---	40/874	6/1137		---	---
	Enoxaparin	---	56/894	1/1142		---	---
Lassen, 2007	Enoxaparin	---	14/109	1/109		1/109	---
	Warfarin	---	28/109	1/109		2/109	---
Bonneux, 2006	Fondaparinux	---	---	2/55		---	---
	Enoxaparin	---	---	1/54		---	---
Senaran, 2006	Enoxaparin	0/50	---	2/50*		---	---
	Heparin	2/50	---	0/50*		---	---
Westrich, 2006	Minimum hyperflexed knee	30/79[†]	---	---		13/79[†]	---
	Standard hyperflexed knee	39/93[†]	---	---		11/92[†]	---
Eriksson, 2005 THR	Dabigatran 50mg BID	49/208	---	2/302[‡]	1/302[‡§]	12/208	42/208
	Dabigatran 150mg BID	26/201	---	0/282[‡]	1/282[‡§]	8/201	22/201
	Dabigatran 300mg QD	25/191	---	0/283[‡]	2/283[‡§]	3/191	22/191
	Dabigatran 225mg BID	17/204	---	0/297[‡]	0/297[‡§]	4/204	14/204
	Enoxaparin	31/208	---	1/300[‡]	0/300[‡§]	11/208	26/208
Eriksson, 2005 TKR	Dabigatran 50mg BID	37/94	---	2/302[‡]	1/302[‡§]	3/94	37/94
	Dabigatran 150mg BID	21/81	---	0/282[‡]	1/282[‡§]	1/81	21/81

Study, Year	Group	DVT n/N	Asymptomatic DVT n/N	Symptomatic DVT n/N		Proximal DVT n/N	Distal DVT n/N
	Dabigatran 300mg QD	22/92	---	0/283[‡]	2/283[‡§]	3/92	21/92
	Dabigatran 225mg BID	22/93	---	0/297[‡]	0/297[‡§]	1/93	22/93
	Enoxaparin	41/92	---	1/300[‡]	0/300[‡§]	6/92	41/92
Farag, 2005	Epidural Anesthesia	0/10	0/10	0/10		0/10	0/10
	Spinal Anesthesia	0/14	0/14	0/14		0/14	0/14
Lachiewicz, 2004	IPC (Venaflow)	16/232	---	0/206[‖]		1/232	15/232
	IPC (Kendal)	36/240	---	0/217[‖]		6/240	30/240
Silbersack, 2004	Enoxaparin + IPC	0/68	---	---		0/68	0/68
	Enoxaparin + GCS	18/63	---	---		2/63	16/63
Eriksson, 2003	Extended fondaparinux	3/208	---	1/326		2/221	1/207
	Fondaparinux	74/218	---	6/330		35/222	42/211
Kim, 2003	Cemented	31/150	---	---		19/150	22/150
	Non-cemented	41/150	---	---		23/150	30/150
Lassen, 2002	Fondaparinux	36/908	---	3/1129		6/922	30/909
	Enoxaparin	83/918	---	1/1123		23/927	67/917
Pitto, 2002	Bone vaccum cement technique	2/65	---	---		0/65	2/65
	Standard cement technique	12/65	---	---		7/65	5/65
Prandoni, 2002	Extended warfarin	3/184	1/184	2/184		1/184	---
	Warfarin	8/176	5/176	3/176		3/176	---
Turpie, 2002	Fondaparinux	44/784	---	5/1126		14/816	34/796
	Enoxaparin	65/796	---	0/1128		10/830	54/800
Warwick, 2002	Enoxaparin	48/89	---	---		0/89	48/89
	VFP	57/99	---	---		4/99	53/99
Barden, 2001	Modified position	---	---	0/83		---	---
	Conventional figure four positioning	---	---	3/76		---	---
Bauer, 2001	Fondaparinux	45/361	---	3/517		9/368	35/372
	Enoxaparin	98/361	---	4/517		20/372	78/366
Comp, 2001 THR	Extended enoxaparin	18/224	---	---		6/224	12/224
	Enoxaparin	49/211	---	---		27/211	22/211
Comp, 2001 TKR	Extended enoxaparin	38/217	---	---		9/217	29/217

Study, Year	Group	DVT n/N	Asymptomatic DVT n/N	Symptomatic DVT n/N	Proximal DVT n/N	Distal DVT n/N
	Enoxaparin	46/221	---	---	17/221	27/221
Eriksson, 2001	Fondaparinux	49/624	---	1/831	6/650	42/627
	Enoxaparin	117/623	---	1/840	28/646	94/626
Fitzgerald, 2001	Warfarin	79/176	---	---	20/176	75/176
	Enoxaparin	44/173	---	---	3/173	44/173
Hull, 2000	Dalteparin (pre-operative)	36/337	---	5/337	3/354	---
	Dalteparin (post-operative)	44/336	---	10/336	3/358	---
	Warfarin	81/338	---	15/338	11/363	---
Kennedy, 2000	Aspirin	7/73	3/73	4/73	---	---
	VFP	4/70	2/70	2/70	4/70	---
Colwell, 1999	Enoxaparin	---	---	49/1516	---	---
	Warfarin	---	---	47/1495	---	---
Levy, 1999	Fibrin adhesive	0/29	0/29	0/29	0/29	0/29
	No fibrin adhesive	0/29	0/29	0/29	0/29	0/29
Planes, 1999	Enoxaparin	44/219	---	3/219	23/219	21/219
	Tinzaparin	48/221	---	2/221	21/221	27/221
TIFDED Study Group, 1999	Enoxaparin	8/52	8/52	0/52	2/52	---
	Dalteparin	5/57	5/57	0/57	3/57	---
Wakankar, 1999	Tourniquet	1/37	1/37	---	1/37	0/37
	No tourniquet	0/40	0/40	---	0/40	0/40
Kim, 1998	Aspirin	6/50	---	---	---	---
	Control	10/50	---	---	---	---
Lassen, 1998	Extended dalteparin	5/113	3/113	---	1/111	---
	Dalteparin	12/102	9/102	---	5/101	---
Rader, 1998 THA	Heparin	1/56	---	---	---	---
	Enoxaparin	2/70	---	---	---	---
Rader, 1998 TKA	Heparin	1/60	---	---	---	---
	Enoxaparin	6/60	---	---	---	---
Ryan, 1998	IPC	---	---	0/50	4/50	---
	GCS	---	---	0/50	11/50	---

Study, Year	Group	DVT n/N	Asymptomatic DVT n/N	Symptomatic DVT n/N	Proximal DVT n/N	Distal DVT n/N
Warwick, 1998	Enoxaparin	18/138	---	1/138	12/138	6/138
	VFP	24/136	---	0/136	17/136	7/136
Andersen, 1997	Extended dalteparin	2/20	1/20	1/20	---	---
	Dalteparin	3/21	2/21	1/21	---	---
Dahl, 1997	Extended dalteparin	11/93[¶]	---	8/114	10/114	---
	Dalteparin	2/89[¶]	---	4/104	14/104	---
Eriksson, 1997a	Desirudin	13/180	---	2/180[#]	5/174	---
	UFH	42/180	---	3/180[#]	28/177	---
Eriksson, 1997b	Desirudin	142/773	---	6/773[#]	36/802	---
	Enoxaparin	196/768	---	3/768[#]	59/785	---
Francis, 1997	Dalteparin	28/192	---	---	10/192	21/192
	Warfarin	49/190	---	---	16/190	43/190
Nilsson, 1997	Extended enoxaparin	21/131	19/131	2/131	8/131	13/131
	Enoxaparin	43/131	35/131	8/131	28/131	15/131
Planes, 1997	Extended enoxaparin	6/85	---	---	5/85	1/85
	Enoxaparin	17/88	---	---	7/88	10/88
Samama, 1997	Enoxaparin	11/78	10/78	1/78	2/78	8/78
	Placebo	28/75	27/75	1/75	12/75	13/75
Eriksson, 1996	Desirudin	37/202	---	---	6/195	---
	UFH	77/229	---	---	43/219	---
Kalodiki, 1996	Enoxaparin + GCS	8/32	---	---	4/32	---
	Enoxaparin	12/32	---	---	9/32	---
	Placebo	13/14	---	---	8/14	---
Laupacis, 1996	Cemented	36/72	---	---	2/67	36/72
	Non-cemented	33/70	---	---	3/63	32/69
Leclerc, 1996	Enoxaparin	76/336	---	---	24/336	---
	Warfarin	109/334	---	---	22/334	---
Lotke, 1996	Aspirin	94/166	---	---	16/166	---
	Warfarin	78/146	---	---	18/146	---
Schwartsmann, 1996	Enoxaparin	5/52	2/52	3/52	4/52	1/52
	UFH	5/47	2/47	3/47	5/47	0/47
Stannard, 1996	UFH then aspirin + VFP	0/25	0/25	0/25	0/25	0/25

Study, Year	Group	DVT n/N	Asymptomatic DVT n/N	Symptomatic DVT n/N	Proximal DVT n/N	Distal DVT n/N
	UFH then aspirin	5/25	2/25	3/25	5/25	0/25
	VFP	0/25	0/25	0/25	0/25	0/25
Stone, 1996	Enoxaparin	1/25	1/25	0/25	1/25	0/25
	IPC	1/25	1/25	0/25	1/25	0/25
Westrich, 1996	Aspirin + VFP	11/41 22/81†	---	---	0/41 0/81†	---
	Aspirin	26/39 49/83†	---	---	5/39 12/83†	---
Williams-Russo, 1996	General Anesthesia	39/81	---	---	0/81	39/81
	Regional Anesthesia	39/97	---	---	0/97	39/97
Abdel-Salam, 1995	Tourniquet	4/40	---	---	4/40	0/40
	No tourniquet	0/40	---	---	0/40	0/40
Avikainen, 1995	Enoxaparin	1/83	---	1/83	1/83	0/83
	UFH	4/84	---	4/84	4/84	0/84
Colwell, 1995	Enoxaparin	56/228	---	---	5/228	51/228
	Heparin	77/225	---	---	22/225	54/225
Warwick, 1995	Enoxaparin	22/78	---	---	12/78	10/78
	Control	33/78	---	---	14/78	19/78
Colwell, 1994	Enoxaparin 30mg Q12h	9/194	---	---	4/194	4/194
	Enoxaparin 40mg QD	30/203	---	---	8/203	20/203
	UFH	24/207	---	---	10/207	11/207
Fauno, 1994	Enoxaparin	21/92	---	0/92**	3/92	18/92
	UFH	25/93	---	1/93**	5/93	20/93
Leiberman, 1994	Aspirin + IPC	---	---	---	0/124††	1/126††
	Aspirin	---	---	---	7/124††	8/126††
Menzin, 1994	UFH	24/209	---	---	---	---
	Enoxaparin 40mg QD	30/202	---	---	---	---
	Enoxaparin 30mg Q12h	9/192	---	---	---	---
Santori, 1994	Heparin	23/65	---	---	---	---
	VFP	9/67	---	---	---	---
Hull, 1993 THR	Tinzaparin	69/332	---	---	16/332	---
	Warfarin	79/340	---	---	13/340	---
Hull, 1993 TKR	Tinzaparin	116/258	---	---	20/258	---
	Warfarin	152/277	---	---	34/277	---

Study, Year	Group	DVT n/N	Asymptomatic DVT n/N	Symptomatic DVT n/N	Proximal DVT n/N	Distal DVT n/N
Fordyce, 1992	VFP	4/39	---	---	2/39	2/39
	Control	16/40	---	---	5/40	3/40
Francis, 1992	Warfarin	32/103	---	---	3/103	---
	IPC	26/98	---	---	12/98	---
Jorgensen, 1992	Dalteparin	5/30	---	---	---	---
	Placebo	18/38	---	---	---	---
Wilson, 1992	VFP	14/28[†]	---	---	0/28[†]	5/28[†]
	Control	22/32[†]	---	---	6/32[†]	13/32[†]
Bailey, 1991	Warfarin	12/45	---	---	0/45	---
	IPC	3/50	---	---	2/50	---
Eriksson, 1991	Dalteparin	19/63	17/63	2/63	---	---
	UFH	25/59	23/59	2/59	---	---
Lassen, 1991	Tinzaparin	29/93	29/93	0/93	24/93	5/93
	Placebo	44/97	44/97	0/97	35/97	9/97
Jorgensen, 1991	General Anesthesia	13/22	11/22	2/22	3/22	10/22
	Epidural Anesthesia	3/17	3/17	0/17	1/17	2/17
Levine, 1991	Enoxaparin	50/258	---	---	14/258	---
	UFH	61/263	---	---	17/263	---
Mitchell, 1991	General Anesthesia				24/38	
	Epidural Anesthesia				16/34	
Planes, 1991	General Anesthesia + Enoxaparin	---	---	---	4/62	0/62
	Epidural Anestheisa + Enoxaparin	---	---	---	4/60	3/60
	Epidural Anesthesia alone	---	---	---	4/65	7/65
Torholm, 1991	Dalteparin	8/58	---	---	0/58	8/58
	Placebo	16/54	---	---	4/54	12/54
Woolson, 1991	Aspirin + IPC	---	---	---	7/72[††]	---
	Warfarin + IPC	---	---	---	6/69[††]	---
	IPC	---	---	---	9/76[††]	---
Haas, 1990 Unilateral TKA	Aspirin	17/36	---	---	0/36	17/36

Study, Year	Group	DVT n/N	Asymptomatic DVT n/N	Symptomatic DVT n/N	Proximal DVT n/N	Distal DVT n/N
	IPC	8/36	---	---	0/36	8/36
Haas, 1990 Bilateral TKA	Aspirin	15/22	---	---	1/22	14/22
	IPC	12/25	---	---	2/25	10/25
Sorensen, 1990	Tinzaparin	17/31	---	---	---	---
	Placebo	16/33	---	---	---	---
Dechavanne, 1989	Dalteparin 2500U Q12h	2/41	---	---	1/41	1/41
	Dalteparin 5000U QD	3/41	---	---	1/41	2/41
	Heparin	4/40	---	---	3/40	1/40
Monreal, 1989	Dalteparin	14/32	---	---	12/32	2/32
	Heparin	6/30	---	---	5/30	1/30
Powers, 1989	Warfarin	---	---	---	---	---
	Aspirin	---	---	---	---	---
	Placebo	---	---	---	---	---
Planes, 1988	Enoxaparin	15/120	---	---	9/120	6/120
	Heparin	27/108	---	---	20/108	7/108
Barre, 1987	Dalteparin	7/40	---	---	---	---
	Heparin	4/40	---	---	---	---
Paiement, 1987	Warfarin	12/72	---	---	5/72	8/72
	IPC	11/66	---	---	10/66	2/66
Alfaro, 1986	Aspirin 250mg/d	1/30	---	---	---	---
	Aspirin 1g/d	1/30	---	---	---	---
	Control	9/30	---	---	---	---
Turpie, 1986	Enoxaparin	4/37	---	---	2/37	---
	Placebo	20/39	---	---	9/39	---
McKenzie, 1985	General Anesthesia	15/20	15/20	0/20	---	---
	Spinal Anesthesia	8/20	5/20	3/20	---	---
Welin-Berger, 1982	Heparin	8/20	---	---	---	---
	Control	5/20	---	---	---	---
Modig, 1981	General Anesthesia	11/15	---	---	11/15	11/15
	Epidural Anesthesia	5/15	---	---	3/15	4/15
McKenna, 1980	Aspirin	7/9	---	---	3/9	4/9

Study, Year	Group	DVT n/N	Asymptomatic DVT n/N	Symptomatic DVT n/N	Proximal DVT n/N	Distal DVT n/N
	Placebo	9/12	---	---	5/12	4/12

*Discharge-42days
†Number of events out of total knees
‡Number of events out of the combined THR and TKR population
§After study period-30 or 42days
||Discharge to 180days
¶7-35days; After study period-42days
**Discharge-60days
††Number of events out of total hips

Abbreviations: BID=twice daily; d=day; DVT=deep vein thrombosis; g=gram; GCS=graduated compression stockings; h=hours; IPC=intermittent pneumatic compression device; mg=milligram; n/N= total number of events/total population; QD=daily; THA=total hip arthroplasty; THR=total hip replacement; TKA=total knee arthroplasty; TKR=total knee replacement; U=units; UFH=unfractionated heparin; VFP=venous foot pump

Table 16. Intermediate health outcomes in randomized controlled trials evaluating patients who had nonmajor orthopedic surgery

Study, Year	Group	DVT n/N	Asymptomatic DVT n/N	Symptomatic DVT n/N	Proximal DVT n/N	Distal DVT n/N
Lapidus, 2007	Dalteparin	18/49	---	---	1/49	---
	Placebo	19/47	---	---	3/47	---
Michot, 2002	Dalteparin	1/66	---	---	0/66	1/66
	Control	10/64	---	---	0/64	10/64

Abbreviations: N=number of participants; n=number of participants with the event

Table 17. Intermediate health outcomes in observational studies evaluating venous thromboembolism prophylaxis in major orthopedic surgery

Study, Year	Group	DVT n/N	Asymptomatic DVT n/N	Symptomatic DVT n/N	Proximal DVT n/N	Distal DVT n/N
Bozic, 2010	Warfarin	---	---	---	---	---
	Aspirin	---	---	---	---	---
Cusick, 2009 THR	Aspirin	---	---	---	---	---
	Warfarin	---	---	---	---	---
	Control	---	---	---	---	---
Cusick, 2009 TKR	Aspirin	---	---	---	---	---
	Warfarin	---	---	---	---	---

Study, Year	Group	DVT n/N	Asymptomatic DVT n/N	Symptomatic DVT n/N	Proximal DVT n/N	Distal DVT n/N
	Control	---	---	---	---	---
Froimson, 2009	IPC (ActiveCare)	3/223	---	---	---	---
	IPC (Flowtron)	49/1354	---	---	---	---
Shorr, 2007	Fondaparinux	---	---	---	---	---
	Enoxaparin or dalteparin	---	---	---	---	---
	UFH	---	---	---	---	---
	Control	---	---	---	---	---
Sachs, 2003	Warfarin	---	---	2/957	---	---
	Control	---	---	0/785	---	---

Abbreviations: DVT=deep vein thrombosis; IPC=intermittent pneumatic compression; THR=total hip replacement; TKR=total knee replacement; UFH=unfractionated heparin

Table 18. Major and minor bleeding from randomized controlled trials evaluating patients who had major orthopedic surgery

Study, Year	Group	Major Bleeding n/N	Major Bleeding Definition	Minor Bleeding n/N	Minor Bleeding Definition
Fuji, 2010	Dabigatran 150mg	0/126	Fatal bleeding; clinically overt bleeding associated with a fall ≥Hb 20g/L, transfusion of ≥2U PRBC or whole blood, retroperitoneal or intracranial bleeding, bleeding warranting treatment cessation	12/126	Per European guidelines
	Dabigatran 220mg	3/129		9/129	---
	Placebo	1/124		6/124	---
Chin, 2009	Enoxaparin	---	---	---	---
	Control	---	---	---	---
Ginsberg, 2009	Dabigatran 150mg	5/871 2/871*	Fatal bleeding; clinically overt bleeding in excess of expected and associated with a fall of 2g/L of Hb and/or leading to transfusion of ≥2U packed cells or whole blood; symptomatic retroperitoneal, intracranial, intraocular, or intraspinal bleeding; bleeding requiring treatment cessation and/or operation	22/871 5/871*	Spontaneous skin hematoma >25 cm2; wound hematoma >100 cm2; spontaneous nose bleeding or gingival bleeding lasting >5 min; spontaneous rectal bleeding creating more than a spot on toilet paper; macroscopic hematuria either spontaneous or, if associated with an intervention (e.g. Foley catheter) lasting >24h; other bleeding event considered clinically relevant by the investigator not qualifying as a major bleed
	Dabigatran 220mg	5/857 1/857*		23/857 6/857*	

Study, Year	Group	Major Bleeding n/N	Major Bleeding Definition	Minor Bleeding n/N	Minor Bleeding Definition
	Enoxaparin	12/868 0/868*		21/868 3/868*	
Edwards, 2008 THA	Enoxaparin + IPC	---	---	---	---
	Enoxaparin	---	---	---	---
Edwards, 2008 TKA	Enoxaparin + IPC	---	---	---	---
	Enoxaparin	---	---	---	---
Fuji, 2008 THA	Enoxaparin 40mg QD	2/102	Retroperitoneal, intracranial, or intraocular; associated with death, transfusion of ≥2U of PRBC or whole blood (not autologous), reduction in Hb ≥2 g/dl; serious or life-threatening clinical event that required medical intervention	7/102	Epistaxis lasting >5 min or requiring intervention; ecchymosis or hematoma with a maximum size of >5 cm; hematuria not associated with urinary catheter trauma; GI hemorrhage not related to intubation or NG tube; wound hematoma or hemorrhagic wound complications not associated with major hemorrhage; subconjunctival hemorrhage requiring cessation of medication
	Enoxaparin 20mg BID	3/104		4/104	
	Placebo	0/101		2/101	
Fuji, 2008 TKA	Enoxaparin 40mg QD	1/91	Retroperitoneal, intracranial, or intraocular; associated with death, transfusion of ≥2U of PRBC or whole blood (not autologous), reduction in Hb ≥2 g/dl; serious or life-threatening clinical event that required medical intervention	6/91	Epistaxis lasting >5 min or requiring intervention; ecchymosis or hematoma with a maximum size of >5 cm; hematuria not associated with urinary catheter trauma; GI hemorrhage not related to intubation or NG tube; wound hematoma or hemorrhagic wound complications not associated with major hemorrhage; subconjunctival hemorrhage requiring cessation of medication
	Enoxaparin 20mg BID	3/95		10/95	
	Placebo	4/89		4/89	
Thorey, 2008	Early release tourniquet	---	---	---	---
	Late release tourniquet	---	---	---	---
Eriksson, 2007a	Dabigatran 150mg QD	9/703	Defined according to accepted guidelines	59/703	Defined according to accepted guidelines
	Dabigatran 220mg QD	10/679		60/679	
	Enoxaparin	9/694		69/694	
Eriksson, 2007b	Dabigatran 150mg QD	15/1163	Defined according to accepted guidelines	72/1163	Defined according to accepted guidelines

Study, Year	Group	Major Bleeding n/N	Major Bleeding Definition	Minor Bleeding n/N	Minor Bleeding Definition
	Dabigatran 220mg QD	23/1146		70/1146	
	Enoxaparin	18/1154		74/1154	
Lassen, 2007	Enoxaparin	0/149	Accompanied by a reduction in Hb of >2 g/dl (relative to the postsurgical value) and/or a requirement for transfusion of > 2U of blood product; need to discontinue study medication; intracranial, intraspinal, retroperitoneal, or in the operated joint necessitating re-operation or intervention, intrapericardial, intraocular or fatal	6/149	Defined as other bleeding not meeting the definition of “major”
	Warfarin	0/151		8/151	
Bonneux, 2006	Fondaparinux	---	---	---	---
	Enoxaparin	---	---	---	---
Senaran, 2006	Enoxaparin	2/50	Overt bleeding associated with ≥1 of the following events: death or a life-threatening clinical event; bleeding confirmed to be retroperitoneal, intracranial, intraocular; postoperative transfusion of >2U of PRBC or whole blood; decrease in the Hb > 20g/L compared with the relevant postoperative level	1/50	Overt bleeding episode that did not meet the criterion for classification as a major bleeding episode, or absence of any simultaneous bleeding other than the surgical wound
	Heparin	0/50		4/50	
Westrich, 2006	Minimum hyperflexed knee	---	---	---	---
	Standard hyperflexed knee	---	---	---	---
Eriksson, 2005 THR	Dabigatran 50mg BID	0/265	Clinically overt bleeding associated with > 20 g/L fall in Hb; clinically overt leading to transfusion of >2U packed cells or whole blood; fatal, retroperitoneal, intracranial, intraocular or intraspinal bleeding; bleeding warranting treatment cessation or leading to reoperation	11/265	Minor bleeding events were defined as those not fulfilling the criteria of major or clinically significant bleeding
	Dabigatran 150mg BID	10/266		23/266	
	Dabigatran 300mg QD	12/258		22/258	
	Dabigatran 225mg BID	12/270		28/270	
	Enoxaparin	6/270		14/270	

Study, Year	Group	Major Bleeding n/N	Major Bleeding Definition	Minor Bleeding n/N	Minor Bleeding Definition
Eriksson, 2005 TKR	Dabigatran 50mg BID	1/124	Clinically overt bleeding associated with >20 g/L fall in Hb; clinically overt leading to transfusion of >2U packed cells or whole blood; fatal, retroperitoneal, intracranial, intraocular or intraspinal bleeding; bleeding warranting treatment cessation or leading to reoperation	7/124	Minor bleeding events were defined as those not fulfilling the criteria of major or clinically significant bleeding
	Dabigatran 150mg BID	6/124		8/124	
	Dabigatran 300mg QD	6/127		15/127	
	Dabigatran 225mg BID	3/123		10/123	
	Enoxaparin	2/122		11/122	
Farag, 2005	Epidural Anesthesia	---	---	---	---
	Spinal Anesthesia	---	---	---	---
Lachiewicz, 2004	IPC (Venaflow)	---	---	---	---
	IPC (Kendal)	---	---	---	---
Silbersack, 2004	Enoxaparin + IPC	---	---	---	---
	Enoxaparin + GCS	---	---	---	---
Eriksson, 2003	Extended fondaparinux	8/327	Fatal, retroperitoneal, intracranial, or intraspinal bleeding; bleeding that involved any other critical organ; bleeding leading to reoperation; overt bleeding with a bleeding index ≥ 2	5/327	---
	Fondaparinux	2/329		2/329	---
Kim, 2003	Cemented	---	---	---	---
	Non-cemented	---	---	---	---
Lassen, 2002	Fondaparinux	47/1140	Fatal, retroperitoneal, intracranial, or intraspinal bleeding; bleeding that involved any other critical organ; bleeding leading to reoperation; overt bleeding with a bleeding index ≥ 2	---	---
	Enoxaparin	32/1133		---	---
Pitto, 2002	Bone vaccum cement technique	0/65	Major bleeding from a wound (wound hematoma requiring operative decompression), or major bleeding not related to a wound (gastrointestinal or intracerebral hemorrhage).	5/65	Minor bleeding from a wound (bleeding at the injection site, epistaxis, or wound hematoma not requiring operative decompression)

Study, Year	Group	Major Bleeding n/N	Major Bleeding Definition	Minor Bleeding n/N	Minor Bleeding Definition
	Standard cement technique	0/65		4/65	
Prandoni, 2002	Extended warfarin	1/184	Clinically overt bleeding associated with either a decrease in Hb ≥2 g/dL or a need for a transfusion of ≥2U RBC; intracranial or retroperitoneal; resulted in the permanent discontinuation of anticoagulation	---	---
	Warfarin	0/176		---	---
Turpie, 2002	Fondaparinux	20/1128	Fatal, retroperitoneal, intracranial, or intraspinal bleeding; bleeding that involved any other critical organ; bleeding leading to reoperation; overt bleeding with a bleeding index ≥ 2	---	---
	Enoxaparin	11/1129		---	---
Warwick, 2002	Enoxaparin	---	---	---	---
	VFP	---	---	---	---
Barden, 2001	Modified position	---	---	---	---
	Conventional figure four positioning	---	---	---	---
Bauer, 2001	Fondaparinux	11/517	Fatal, retroperitoneal, intracranial, or intraspinal bleeding; bleeding that involved any other critical organ; bleeding leading to reoperation; overt bleeding with a bleeding index ≥ 2	---	---
	Enoxaparin	1/517		---	---
Comp, 2001 THR	Extended enoxaparin	0/224	Clinically overt bleeding resulting in death, transfusion of ≥2U blood products, decrease in the Hb level of ≥2.0 g/dL (≥20g/L) compared with the most recent preceding postoperative value; serious or life-threatening clinical event; one requiring surgical intervention; retroperitoneal, intracranial, or intraocular in location	---	Overt bleeding that did not meet the criteria for major hemorrhage and associated with ≥1 of the following: epistaxis lasting more than 5min or requiring intervention, ecchymosis or hematoma >5cm at its greatest dimension, hematuria not associated with urinary catheter related trauma, GI hemorrhage not related to intubation or placement of a NG tube, wound hematoma or complications, subconjunctival hemorrhage necessitating cessation of medication
	Enoxaparin	0/211		---	

Study, Year	Group	Major Bleeding n/N	Major Bleeding Definition	Minor Bleeding n/N	Minor Bleeding Definition
Comp, 2001 TKR	Extended enoxaparin	0/217	Clinically overt bleeding resulting in death, transfusion of ≥2U blood products, decrease in the Hb level of ≥2.0 g/dL (≥20g/L) compared with the most recent preceding postoperative value; serious or life-threatening clinical event; one requiring surgical intervention; retroperitoneal, intracranial, or intraocular in location	---	Overt bleeding that did not meet the criteria for major hemorrhage and associated with ≥1 of the following: epistaxis lasting more than 5min or requiring intervention, ecchymosis or hematoma >5cm at its greatest dimension, hematuria not associated with urinary catheter related trauma, GI hemorrhage not related to intubation or placement of a NG tube, wound hematoma or complications, subconjunctival hemorrhage necessitating cessation of medication
	Enoxaparin	1/221		---	
Eriksson, 2001	Fondaparinux	18/831	Fatal, retroperitoneal, intracranial, or intraspinal bleeding; bleeding that involved any other critical organ; bleeding leading to reoperation; overt bleeding with a bleeding index ≥ 2	34/831	Overt bleeding that did not meet the criteria for major bleeding
	Enoxaparin	19/842		18/842	
Fitzgerald, 2001	Warfarin	4/176	Fulfilled ≥1 of the following: resulted in transfusion of ≥2U PRBC; resulted in a decrease in the Hb ≥20 g/L compared with the postoperative Hb concentration before the administration of any study medication; retroperitoneal, intracranial, or intraocular; resulted in a serious life-threatening clinical event or death	37/176	---
	Enoxaparin	9/173		49/173	
Hull, 2000	Dalteparin (pre-operative)	33/496[†] 11/496[‡]	Clinically overt and associated with a decrease in Hb≥20 g/L or required transfusion of ≥ 2U of blood; intracranial, intraocular, intraspinal or retroperitoneal; occurred into a prosthetic joint	3/496[†] 6/496[‡]	Clinically overt without meeting the major bleeding criteria and as trivial if it was clearly of no consequence
	Dalteparin (post-operative)	28/487[†] 4/487[‡]		3/487[†] 8/487[‡]	
	Warfarin	20/489[†] 2/489[‡]		2/489[†] 8/489[‡]	
Kennedy, 2000	Aspirin	---	---	---	---

Study, Year	Group	Major Bleeding n/N	Major Bleeding Definition	Minor Bleeding n/N	Minor Bleeding Definition
	VFP	---	---	---	---
Colwell, 1999	Enoxaparin	18/1516	Overt bleeding associated with ≥1 of the following: death or life threatening clinical event; bleeding confirmed to be retroperitoneal, intracranial, or intraocular; post-operative blood transfusion ≥2U PRBC or whole blood; decrease in Hb>20g/L	143/1516	Overt bleeding that did not meet the criteria for major bleeding
	Warfarin	8/1495		106/1495	
Levy, 1999	Fibrin adhesive	---	---	---	---
	No fibrin adhesive	---	---	---	---
Planes, 1999	Enoxaparin	4/248	Overt and associated with either a fall in Hb≥2g/dl, need for transfusion of ≥2U blood, or if retroperitoneal, intracranial, or intraocular	21/248	Overt bleeding not meeting the criteria for major bleeding
	Tinzaparin	2/251		13/251	
TIFDED Study Group, 1999	Enoxaparin	2/66	Bleeding leading to death or re-operation; intracranial bleeding; bleeding into organs; associated with a decrease in Hb>32g/L within 72h	---	Other bleedings (e.g. small wound hematoma or oozing)
	Dalteparin	1/66		---	
Wakankar, 1999	Tourniquet	---	---	---	---
	No tourniquet	---	---	---	---
Kim, 1998	Aspirin	0/50	---	---	---
	Control	0/50	---	---	---
Lassen, 1998	Extended dalteparin	0/140	---	18/140	---
	Dalteparin	1/141	---	11/141	---
Rader, 1998	Heparin	---	---	---	---
	Enoxaparin	---	---	---	---
Ryan, 1998	IPC (Kendal)	---	---	---	---
	GCS	---	---	---	---
Warwick, 1998	Enoxaparin	---	---	---	---
	VFP	---	---	---	---
Andersen, 1997	Extended dalteparin	---	---	---	---

Study, Year	Group	Major Bleeding n/N	Major Bleeding Definition	Minor Bleeding n/N	Minor Bleeding Definition
	Dalteparin	---	---	---	---
Dahl, 1997	Extended dalteparin	---	---	---	---
	Dalteparin	---	---	---	---
Eriksson, 1997a	Desirudin	---	---	---	---
	UFH	---	---	---	---
Eriksson, 1997b	Desirudin	20/1028	Serious bleeding defined as any of the following: perioperative transfusion of ≥5U of whole blood, red-cell concentrate, or both; transfusion of ≥7U whole blood, red-cell concentrate, or both, at any time; transfusion of a total of >3500 mL of blood	---	---
	Enoxaparin	20/1023		---	---
Francis, 1997	Dalteparin	6/271	Bleeding which was fatal or if they required a transfusion, reoperation, or prolonged hospital stay	16/271	Minor bleeding in the GI or urinary tract and hematoma at the site of an injection
	Warfarin	4/279		10/279	
Nilsson, 1997	Extended enoxaparin	---	---	---	---
	Enoxaparin	---	---	---	---
Planes, 1997	Extended enoxaparin	0/90	Overt bleeding associated with a decrease in Hb ≥2 g/dL compared with the last postoperative value; need for transfusion of ≥2U PRBC; retroperitoneal or intracranial	17/90	Overt bleeding that did not meet the criteria for major hemorrhage
	Enoxaparin	0/89		4/89	
Samama, 1997	Enoxaparin	1/78	Overt, associated with decrease in Hb ≥ 2/dl or required ≥2 transfusions; Intracranial, retroperitoneal, or led to surgical intervention or death	32/78	Overt but did not meet criteria for “major”
	Placebo	1/75		21/75	
Eriksson, 1996	Desirudin	---	---	---	---
	UFH	---	---	---	---
Kalodiki, 1996	Enoxaparin + GCS	---	---	---	---
	Enoxaparin	---	---	---	---
	Placebo	---	---	---	---

Study, Year	Group	Major Bleeding n/N	Major Bleeding Definition	Minor Bleeding n/N	Minor Bleeding Definition
Laupacis, 1996	Cemented	---	---	---	---
	Non-cemented	---	---	---	---
Leclerc, 1996	Enoxaparin	7/336	Overt bleeding that decreased the Hb ≥20 g/L, necessitated transfusion of ≥2U packed red cells, hemarthrosis requiring evacuation, discontinuation of prophylaxis, or interruption of physiotherapy for at least 24 hours	94/336	Overt bleeding not meeting the criteria for major hemorrhage
	Warfarin	6/334		83/334	
Lotke, 1996	Aspirin	---	---	---	---
	Warfarin	---	---	---	---
Schwartsmann, 1996	Enoxaparin	---	---	---	---
	UFH	---	---	---	---
Stannard, 1996	UFH then aspirin + VFP	---	---	---	---
	UFH then aspirin	---	---	---	---
	VFP	---	---	---	---
Stone, 1996	Enoxaparin	---	---	---	---
	IPC	---	---	---	---
Westrich, 1996	Aspirin + VFP	0/61	---	0/61	---
	Aspirin	0/61	---	0/61	---
Williams-Russo, 1996	General Anesthesia	---	---	---	---
	Regional Anesthesia	---	---	---	---
Abdel-Salam, 1995	Tourniquet	---	---	---	---
	No tourniquet	---	---	---	---
Avikainen, 1995	Enoxaparin	---	---	---	---
	UFH	---	---	---	---
Colwell, 1995	Enoxaparin	3/228	---	43/228	---
	Heparin	3/225	---	49/225	---
Warwick, 1995	Enoxaparin	---	---	---	---
	Control	---	---	---	---

Study, Year	Group	Major Bleeding n/N	Major Bleeding Definition	Minor Bleeding n/N	Minor Bleeding Definition
Colwell, 1994	Enoxaparin 30mg Q12h	8/195	Overt bleeding associated with ≥1of the following: death or a life threatening clinical event; acute MI or stroke; bleeding at the operative site; retroperitoneal, intracranial or GI; postoperative transfusion >2U PRBC; decrease in Hb >20g/L compared with the relevant post-operative value	16/195	Overt bleeding episode that did not meet the criteria for classification of a major episode
	Enoxaparin 40mg QD	3/203		18/203	
	UFH	13/209		12/209	
Fauno, 1994	Enoxaparin	---	---	---	---
	UFH	---	---	---	---
Leiberman, 1994	Aspirin + IPC	---	---	---	---
	Aspirin	---	---	---	---
Menzin, 1994	UFH	13/209	Overt and associated with death or life threatening clinical event, a decrease in Hb from baseline of >20g/L or a post-operative transfusion>2U of non-autologous blood	---	---
	Enoxaparin 40mg QD	3/202		---	---
	Enoxaparin 30mg Q12h	8/192		---	---
Santori, 1994	Heparin	---	---	---	---
	VFP	---	---	---	---
Hull, 1993 THR	Tinzaparin	11/398	---	5/398	---
	Warfarin	6/397	---	9/397	---
Hull, 1993 TKR	Tinzaparin	9/317	---	5/317	---
	Warfarin	3/324	---	5/324	---
Fordyce, 1992	VFP	---	---	---	---
	Control	---	---	---	---
Francis, 1992	Warfarin	---	---	3/103	Hematemesis , hemoptysis, hematuria
	IPC	---	---	4/98	
Jorgensen, 1992	Dalteparin	---	---	---	---
	Placebo	---	---	---	---
Wilson, 1992	VFP	---	---	---	---

Study, Year	Group	Major Bleeding n/N	Major Bleeding Definition	Minor Bleeding n/N	Minor Bleeding Definition
	Control	---	---	---	---
Bailey, 1991	Warfarin	---	---	---	---
	IPC	---	---	---	---
Eriksson, 1991	Dalteparin	0/67	---	---	---
	UFH	0/69	---		
Jorgensen, 1991	General Anesthesia	---	---	---	---
	Epidural Anesthesia	---	---	---	---
Lassen, 1991	Tinzaparin	---	---	---	---
	Placebo	---	---	---	---
Levine, 1991	Enoxaparin	11/333	Overt and associated with either a fall in Hb level ≥2g/L, a need for transfusion of ≥2U of blood, or retroperitoneal or intracranial	6/333	Overt bleeding not meeting criteria for major bleeding
	UFH	19/332		12/332	
Mitchell, 1991	General Anesthesia	---	---	---	---
	Epidural Anesthesia	---	---	---	---
Planes, 1991	General Anesthesia + Enoxaparin	2/62	NR	0/62	NR
	Epidural Anestheisa + Enoxaparin	1/61		0/61	
	Epidural Anesthesia alone	1/65		0/65	
Torholm, 1991	Dalteparin	---	---	---	---
	Placebo	---	---	---	---
Woolson, 1991	Aspirin + IPC	---	---	---	---
	Warfarin + IPC	---	---	---	---
	IPC	---	---	---	---
Haas, 1990 Unilateral TKA	Aspirin	---	---	---	---
	IPC	---	---	---	---
Haas, 1990 Bilateral TKA	Aspirin	---	---	---	---
	IPC	---	---	---	---
Sorensen, 1990	Tinzaparin	---	---	---	---

Study, Year	Group	Major Bleeding n/N	Major Bleeding Definition	Minor Bleeding n/N	Minor Bleeding Definition
	Placebo	---	---	---	---
Dechavanne, 1989	Dalteparin 2500U Q12h	---	---	---	---
	Dalteparin 5000U QD	---	---	---	---
	Heparin	---	---	---	---
Monreal, 1989	Dalteparin	---	---	---	---
	Heparin	---	---	---	---
Powers, 1989	Warfarin	5/65	Overt and associated with a decrease in Hb ≥20g/l; led to transfusion of ≥2U of blood; retroperitoneal or intracranial bleeding	---	---
	Aspirin	1/66		---	---
	Placebo	5/63		---	---
Planes, 1988	Enoxaparin	2/124	Overt and associated with either a fall in Hb level ≥2g/dl, need for transfusion of ≥2U of blood, or if it was retroperitoneal or intracranial	1/124	Overt but did not meet the other criteria for major bleeding
	Heparin	0/112		2/112	
Barre, 1987	Dalteparin	---	---	---	---
	Heparin	---	---	---	---
Paiement, 1987	Warfarin	0/72	Overt and associated with a decrease in the Hb ≥2 g/dL; led to transfusion of ≥2U of blood; retroperitoneal, intracranial or occurred in a major prosthetic joint	3/72	Minor post-operative wound bleed
	IPC	0/66		3/66	
Alfaro, 1986	Aspirin 250mg/d	---	---	---	---
	Aspirin 1g/d	---	---	---	---
	Control	---	---	---	---
Turpie, 1986	Enoxaparin	1/50	Overt, associated with decrease in Hb ≥2/dL; required transfusion of ≥2U of blood; intracranial or retroperitoneal	1/50	Overt bleeding that did not meet criteria for “major”
	Placebo	2/50		0/50	
McKenzie, 1985	General Anesthesia	---	---	---	---
	Spinal Anesthesia	---	---	---	---

Study, Year	Group	Major Bleeding n/N	Major Bleeding Definition	Minor Bleeding n/N	Minor Bleeding Definition
Welin-Berger, 1982	Heparin	---	---	---	---
	Control	---	---	---	---
Modig, 1981	General Anesthesia	---	---	---	---
	Epidural Anesthesia	---	---	---	---
McKenna, 1980	Aspirin	---	---	---	---
	Placebo	---	---	---	---

*After study period-90days
†Days 0-1
‡Days 2-8

Abbreviations: BID=twice daily; cm=centimeters; d=day; dL=deciliter; DVT=deep vein thrombosis; g=gram; GCS=graduated compression stockings; GI=gastrointestinal; h=hours; Hb=hemoglobin; HFS=hip fracture surgery; IPC=intermittent pneumatic compression; mg=milligram; min=minutes; mL=mililiter; N=number of participants; n=number of participants with the event; NG=nasogastric; PRBC=packed red blood cells; QD= once daily; RBC=red blood cell; THA=total hip arthroplasty; THR=total hip replacement; TKA=total knee arthroplasty; TKR=total knee replacement; U=units; UFH=unfractionated heparin; VFP= venous foot pump

Table 19. Bleeding outcomes in randomized controlled trials evaluating …….

Study, Year	Group	Major Bleeding n/N	Major Bleeding Definition	Minor Bleeding n/N	Minor Bleeding Definition
Lapidus, 2007	Dalteparin	0/52	Bleeding requiring blood transfusion or bleeding in a critical site (such as intraocular, intracranial, intraspinal, or retroperitoneal bleeding)	---	---
	Placebo	0/53		---	---
Michot, 2002	Dalteparin	0/66	Overt bleeding associated with transfusion of packed red blood cells or surgical interventions or when it led to permanent disability.	8/66	Overt bleeding that did not meet the other criteria for major hemorrhage (soft-tissue hematoma at the operation site or at the LMWH injection site, hemarthrosis, GI bleeding).
	Control	0/64		4/64	

Abbreviations: N=number of participants; n=number of participants with the event

Table 20. Major and minor bleeding outcomes in observational studies evaluating venous thromboembolism prophylaxis in major orthopedic surgery

Study, Year	Group	Major bleeding n/N	Major bleeding definition	Minor bleeding n/N	Minor bleeding definition
Bozic, 2010	Warfarin	---	---	---	---
	Aspirin	---	---	---	---
Cusick, 2009 THR	Aspirin	---	---	---	---
	Warfarin	---	---	---	---
	Control	---	---	---	---
Cusick, 2009 TKR	Aspirin	---	---	---	---
	Warfarin	---	---	---	---
	Control	---	---	---	---
Froimson, 2009	IPC (ActiveCare)	---	---	---	---
	IPC (Flowtron)	---	---	---	---
Shorr, 2007	Fondaparinux	188/12532	ICD-9 codes for hemoperitoneum bleed (568.81), intracranial hemorrhage/hemorrhagic stroke (430-432), hemorrhage complicating a procedure (98.11), or other bleeding accompanied by greater than 2 units of blood transfused as recorded in the billing file	---	---
	Enoxaparin or dalteparin	1709/113936		---	---
	UFH	---		---	---
	Control	---		---	---
Sachs, 2003	Warfarin	---	---	---	---
	Control	---	---	---	---

Abbreviations: ICD-9=International Classification of Disease, Ninth Revision; IPC=intermittent pneumatic compression; THR=total hip replacement; TKR=total knee replacement; UFH=unfractionated heparin

Table 21. Adverse outcomes from randomized controlled trials evaluating patients who had major orthopedic surgery

Study, Year	Group	Major bleeding leading to reoperation n/N	Surgical site bleeding n/N	Bleeding leading to infection n/N	Bleeding leading to transfusion n/N	HIT n/N	Discomfort n/N	Readmission n/N	Reoperation n/N
Fuji, 2010	Dabigatran 150mg	0/126	---	---	0/126	---	---	---	---
	Dabigatran 220mg	1/129	---	---	1/129	---	---	---	---
	Placebo	0/124	---	---	0/124	---	---	---	---
Chin, 2009	Enoxaparin	---	---	---	---	---	---	---	---
	Control	---	---	---	---	---	---	---	---
Ginsberg, 2009	Dabigatran 150mg QD	0/871	3/871	---	---	---	---	---	---
	Dabigatran 220mg QD	0/857	2/857	---	---	---	---	---	---
	Enoxaparin	1/868	11/868	---	---	---	---	---	---
Edwards, 2008 THA	Enoxaparin + IPC	---	---	---	---	---	---	---	---
	Enoxaparin	---	---	---	---	---	---	---	---
Edwards, 2008 TKA	Enoxaparin + IPC	---	---	---	---	---	---	---	---
	Enoxaparin	---	---	---	---	---	---	---	---
Fuji, 2008 THA	Enoxaparin 40mg QD	---	---	---	---	---	---	---	---
	Enoxaparin 20mg BID	---	---	---	---	---	---	---	---
	Placebo	---	---	---	---	---	---	---	---
Fuji, 2008 TKA	Enoxaparin 40mg QD	---	---	---	---	---	---	---	---
	Enoxaparin 20mg BID	---	---	---	---	---	---	---	---
	Placebo	---	---	---	---	---	---	---	---
Thorey, 2008	Early release tourniquet	---	---	---	---	---	---	---	---
	Late release tourniquet	---	---	---	---	---	---	---	---
Eriksson, 2007a	Dabigatran 150mg QD	1/703	---	---	6/703	---	---	---	---
	Dabigatran 220mg QD	3/679	---	---	8/679	---	---	---	---
	Enoxaparin	1/694	---	---	5/694	---	---	---	---
Eriksson, 2007b	Dabigatran 150mg QD	3/1163	---	---	8/1163	---	---	---	---
	Dabigatran 220mg QD	2/1146	---	---	21/1146	---	---	---	---
	Enoxaparin	3/1154	---	---	16/1154	---	---	---	---

Study, Year	Group	Major bleeding leading to reoperation n/N	Surgical site bleeding n/N	Bleeding leading to infection n/N	Bleeding leading to transfusion n/N	HIT n/N	Discomfort n/N	Readmission n/N	Reoperation n/N
Lassen, 2007	Enoxaparin	---	---	---	---	---	---	---	---
	Warfarin	---	---	---	---	---	---	---	---
Bonneux, 2006	Fondaparinux	---	---	---	---	---	---	---	4/55
	Enoxaparin	---	---	---	---	---	---	---	1/54
Senaran, 2006	Enoxaparin	---	3/50	---	---	0/50	---	2/50	---
	Heparin	---	4/50	---	---	0/50	---	0/50	---
Westrich, 2006	Minimum hyperflexed knee	---	---	---	---	---	---	---	---
	Standard hyperflexed knee	---	---	---	---	---	---	---	---
Eriksson, 2005	Dabigatran 50mg BID	---	---	---	---	---	---	---	---
	Dabigatran 150mg BID	---	---	---	---	---	---	---	---
	Dabigatran 300mg QD	---	---	---	---	---	---	---	---
	Dabigatran 225mg BID	---	---	---	---	---	---	---	---
	Enoxaparin	---	---	---	---	---	---	---	---
Farag, 2005	Epidural Anesthesia	---	---	---	---	---	---	---	---
	Spinal Anesthesia	---	---	---	---	---	---	---	---
Lachiewicz, 2004	IPC (Venaflow)	---	---	---	---	---	---	---	---
	IPC (Kendal)	---	---	---	---	---	---	---	---
Silbersack, 2004	Enoxaparin + IPC	---	---	---	---	---	---	---	---
	Enoxaparin + GCS	---	---	---	---	---	---	---	---
Eriksson, 2003	Extended fondaparinux	2/327	6/327	0/327	29/327	---	---	---	---
	Fondaparinux	2/329	0/329	0/329	20/329	---	---	---	---
Kim, 2003	Cemented	---	---	---	---	---	---	---	---
	Non-cemented	---	---	---	---	---	---	---	---
Lassen, 2002	Fondaparinux	5/1140	40/1140	---	---	---	---	---	---
	Enoxaparin	3/1133	29/1133	---	---	---	---	---	---
Pitto, 2002	Bone vacuum cement technique	---	---	---	---	---	---	---	---

Study, Year	Group	Major bleeding leading to reoperation n/N	Surgical site bleeding n/N	Bleeding leading to infection n/N	Bleeding leading to transfusion n/N	HIT n/N	Discomfort n/N	Readmission n/N	Reoperation n/N
	Standard cement technique	---	---	---	---	---	---	---	---
Prandoni, 2002	Extended warfarin	---	---	---	---	---	---	---	---
	Warfarin	---	---	---	---	---	---	---	---
Turpie, 2002	Fondaparinux	2/1128	---	---	---	---	---	---	---
	Enoxaparin	2/1129	---	---	---	---	---	---	---
Warwick, 2002	Enoxaparin	---	---	---	---	---	---	3/112	
	VFP	---	---	---	---	---	---	4/117	
Barden, 2001	Modified position	---	---	---	---	---	---	---	---
	Conventional figure four positioning	---	---	---	---	---	---	---	---
Bauer, 2001	Fondaparinux	2/517	---	---	---	---			
	Enoxaparin	1/517	---	---	---	---			
Comp, 2001 THR	Extended enoxaparin	---	---	---	---	---	---	3/224	---
	Enoxaparin	---	---	---	---	---	---	22/211	---
Comp, 2001 TKR	Extended enoxaparin	---	---	---	---	---	---	7/217	---
	Enoxaparin	---	---	---	---	---	---	12/221	---
Eriksson, 2001	Fondaparinux	3/831	---	---	---	---	---	---	---
	Enoxaparin	2/842	---	---	---	---	---	---	---
Fitzgerald, 2001	Warfarin	0/176	6/176	---	---	---	---	---	0/176
	Enoxaparin	0/173	12/173	---	---	---	---	---	0/173
Hull, 2000	Dalteparin (pre-operative)	---	32/496[*] 9/496[†] 0/496[‡] 0/496[§]	---	---	---	---	---	---
	Dalteparin (post-operative)	---	27/487[*] 3/487[†] 1/487[‡] 2/487[§]	---	---	---	---	---	---

Study, Year	Group	Major bleeding leading to reoperation n/N	Surgical site bleeding n/N	Bleeding leading to infection n/N	Bleeding leading to transfusion n/N	HIT n/N	Discomfort n/N	Readmission n/N	Reoperation n/N
	Warfarin	---	17/489[*] 2/489[†] 0/489[‡] 0/489[§]	---	---	----	---	---	---
Kennedy, 2000	Aspirin	---	---	---	---	---	---	---	---
	VFP	---	---	---	---	---	---	---	---
Colwell, 1999	Enoxaparin	---	62/1516[‖] 14/1516[¶]	---	---	0/1516	---	---	---
	Warfarin	---	45/1495[‖] 5/1495[¶]	---	---	0/1495	---	---	---
Levy, 1999	Fibrin adhesive	---	---	---	---	---	---	---	---
	No fibrin adhesive	---	---	---	---	---	---	---	---
Planes, 1999	Enoxaparin	---	4/248	---	---	1/248	---	---	---
	Tinzaparin	---	2/251	---	---	0/251	---	---	---
TIFDED Study Group, 1999	Enoxaparin	---	0/66	---	---	---	---	---	---
	Dalteparin	---	1/66	---	---	---	---	---	---
Wakankar, 1999	Tourniquet	---	---	---	---	---	---	---	---
	No tourniquet	---	---	---	---	---	---	---	---
Kim, 1998	Aspirin	---	---	---	---	---	---	---	---
	Control	---	---	---	---	---	---	---	---
Lassen, 1998	Extended dalteparin	---	---	---	---	---	---	---	---
	Dalteparin	---	---	---	---	---	---	---	---
Rader, 1998	Heparin	---	---	---	---	---	---	---	---
	Enoxaparin	---	---	---	---	---	---	---	---
Ryan, 1998	IPC (Kendal)	---	---	---	---	---	---	---	---
	GCS	---	---	---	---	---	---	---	---
Warwick, 1998	Enoxaparin	---	---	---	---	---	17/122	1/143	---
	VFP	---	---	---	---	---	35/124	1/147	---
Andersen, 1997	Extended dalteparin	---	---	---	---	---	---	---	0/20
	Dalteparin	---	---	---	---	---	---	---	2/21

Study, Year	Group	Major bleeding leading to reoperation n/N	Surgical site bleeding n/N	Bleeding leading to infection n/N	Bleeding leading to transfusion n/N	HIT n/N	Discomfort n/N	Readmission n/N	Reoperation n/N
Dahl, 1997	Extended dalteparin	---	---	---	---	---	---	---	---
	Dalteparin	---	---	---	---	---	---	---	---
Eriksson, 1997a	Desirudin	0/225				---			
	UFH	0/220				---			
Eriksson, 1997b	Desirudin	---	---	---	---	---	---	---	---
	Enoxaparin	---	---	---	---	---	---	---	---
Francis, 1997	Dalteparin	1/271	12/271	---	5/271	---	---	---	41/192
	Warfarin	0/279	3/279	---	3/279	---	---	---	48/190
Nilsson, 1997	Extended enoxaparin	---	---	---	---	---	---	---	---
	Enoxaparin	---	---	---	---	---	---	---	---
Planes, 1997	Extended enoxaparin	---	---	---	0/90	---	---	---	---
	Enoxaparin	---	---	---	0/89	---	---	---	---
Samama, 1997	Enoxaparin	0/78	---	---	---	---	---	---	---
	Placebo	0/75	---	---	---	---	---	---	---
Eriksson, 1996	Desirudin	4/277	8/277	---	---	---	---	---	---
	UFH	2/277	7/277	---	---	---	---	---	---
Kalodiki, 1996	Enoxaparin + GCS	---	---	---	---	---	---	---	---
	Enoxaparin	---	---	---	---	---	---	---	---
	Placebo	---	---	---	---	---	---	---	---
Laupacis, 1996	Cemented	---	---	---	---	---	---	---	---
	Non-cemented	---	---	---	---	---	---	---	---
Leclerc, 1996	Enoxaparin	---	---	---	---	---	---	---	---
	Warfarin	---	---	---	---	---	---	---	---
Lotke,1996	Aspirin	---	---	---	---	---	---	---	---
	Warfarin	---	---	---	---	---	---	---	---
Schwartsmann, 1996	Enoxaparin	---	---	---	---	---	---	---	---
	UFH	---	---	---	---	---	---	---	---
Stannard, 1996	UFH then aspirin + VFP	---	---	---	---	---	---	---	---
	UFH then aspirin	---	---	---	---	---	---	---	---

Study, Year	Group	Major bleeding leading to reoperation n/N	Surgical site bleeding n/N	Bleeding leading to infection n/N	Bleeding leading to transfusion n/N	HIT n/N	Discomfort n/N	Readmission n/N	Reoperation n/N
	VFP	---	---	---	---	---	---	---	---
Stone, 1996	Enoxaparin	---	---	---	---	---	---	---	---
	IPC	---	---	---	---	---	---	---	---
Westrich, 1996	Aspirin+ VFP	---	---	---	---	---	---	---	---
	Aspirin	---	---	---	---	---	---	---	---
Williams-Russo, 1996	General Anesthesia	---	---	---	---	---	---	---	---
	Regional Anesthesia	---	---	---	---	---	---	---	---
Abdel-Salam, 1995	Tourniquet	---	---	---	---	---	---	---	---
	No tourniquet	---	---	---	---	---	---	---	---
Avikainen, 1995	Enoxaparin	---	---	---	---	---	---	---	---
	UFH	---	---	---	---	---	---	---	---
Colwell, 1995	Enoxaparin	---	9/228	---	---	---	---	---	---
	Heparin	---	5/225	---	---	---	---	---	---
Warwick, 1995	Enoxaparin	---	---	---	---	---	---	---	---
	Control	---	---	---	---	---	---	---	---
Colwell, 1994	Enoxaparin 30mg Q12h	---	6/195	---	---	0/195	---	3/195	---
	Enoxaparin 40mg QD	---	1/203	---	---	0/203	---	1/203	---
	UFH	---	7/209	---	---	1/209	---	4/209	---
Fauno, 1994	Enoxaparin	---	---	---	---	---	---	---	---
	UFH	---	---	---	---	---	---	---	---
Lieberman, 1994	Aspirin + IPC	---	---	---	---	---	---	---	---
	Aspirin	---	---	---	---	---	---	---	---
Menzin, 1994	UFH	---	---	---	---	---	---	---	---
	Enoxaparin 40mg QD	---	---	---	---	---	---	---	---
	Enoxaparin 30mg Q12h	---	---	---	---	---	---	---	---
Santori, 1994	Heparin	---	---	---	---	---	---	---	---
	VFP	---	---	---	---	---	---	---	---
Hull,1993	Tinzaparin	---	18/715[||] 0/715[¶]	---	---	---	---	---	---

Study, Year	Group	Major bleeding leading to reoperation n/N	Surgical site bleeding n/N	Bleeding leading to infection n/N	Bleeding leading to transfusion n/N	HIT n/N	Discomfort n/N	Readmission n/N	Reoperation n/N
	Warfarin	---	7/721[‖] 1/721[¶]	---	---	---	---	---	---
Fordyce, 1992	VFP	---	---	---	---	---	---	---	---
	Control	---	---	---	---	---	---	---	---
Francis, 1992	Warfarin	0/103	---	---	0/103	---	---	---	---
	IPC	0/98	---	---	0/98	---	---	---	---
Jorgensen, 1992	Dalteparin	---	---	---	---	---	---	---	---
	Placebo	---	---	---	---	---	---	---	---
Wilson, 1992	VFP	---	---	---	---	---	---	---	---
	Control	---	---	---	---	---	---	---	---
Bailey, 1991	Warfarin	---	---	---	---	---	---	0/45	---
	IPC	---	---	---	---	---	---	1/50	---
Eriksson,1991	Dalteparin	0/67	---	---	---	---	---	---	---
	UFH	0/69	---	---	---	---	---	---	---
Jorgensen, 1991	General Anesthesia	---	---	---	---	---	---	---	---
	Epidural Anesthesia	---	---	---	---	---	---	---	---
Lassen, 1991	Tinzaparin	---	---	---	---	---	---	---	---
	Placebo	---	---	---	---	---	---	---	---
Levine, 1991	Enoxaparin	---	---	---	---	0/333	---	---	---
	UFH	---	---	---	---	9/332	---	---	---
Mitchell, 1991	General Anesthesia	---	---	---	---	---	---	---	---
	Epidural Anesthesia	---	---	---	---	---	---	---	---
Planes, 1991	General Anesthesia + Enoxaparin	---	---	---	---	---	---	---	---
	Epidural Anestheisa + Enoxaparin	---	---	---	---	---	---	---	---
	Epidural Anesthesia alone	---	---	---	---	---	---	---	---
Torholm, 1991	Dalteparin	---	---	---	---	---	---	---	---
	Placebo	---	---	---	---	---	---	---	---

Study, Year	Group	Major bleeding leading to reoperation n/N	Surgical site bleeding n/N	Bleeding leading to infection n/N	Bleeding leading to transfusion n/N	HIT n/N	Discomfort n/N	Readmission n/N	Reoperation n/N
Woolson, 1991	Aspirin + IPC	---	---	---	---	---	---	---	---
	Warfarin + IPC	---	---	---	---	---	---	---	---
	IPC	---	---	---	---	---	---	---	---
Haas, 1990 Unilateral TKA	Aspirin	---	---	---	---	---	---	---	---
	IPC	---	---	---	---	---	---	---	---
Haas, 1990 Bilateral TKA	Aspirin	---	---	---	---	---	---	---	---
	IPC	---	---	---	---	---	---	---	---
Sorensen, 1990	Tinzaparin	---	---	---	---	---	---	---	---
	Placebo	---	---	---	---	---	---	---	---
Dechavanne, 1989	Dalteparin 2500U Q12h	---	---	---	---	---	---	---	---
	Dalteparin 5000U QD	---	---	---	---	---	---	---	---
	Heparin	---	---	---	---	---	---	---	---
Monreal, 1989	Dalteparin	---	---	---	---	---	---	---	---
	Heparin	---	---	---	---	---	---	---	---
Powers, 1989	Warfarin	---	---	---	---	---	---	---	---
	Aspirin	---	---	---	---	---	---	---	---
	Placebo	---	---	---	---	---	---	---	---
Planes, 1988	Enoxaparin	---	---	---	---	---	---	---	---
	Heparin	---	---	---	---	---	---	---	---
Barre, 1987	Dalteparin	---	---	---	---	---	---	---	---
	Heparin	---	---	---	---	---	---	---	---
Paiement, 1987	Warfarin	---	---	---	---	---	---	---	---
	IPC	---	---	---	---	---	---	---	---
Alfaro, 1986	Aspirin 250mg/d	---	---	---	---	---	---	---	---
	Aspirin 1g/d	---	---	---	---	---	---	---	---
	Control	---	---	---	---	---	---	---	---
Turpie, 1986	Enoxaparin	---	---	---	---	---	---	---	---
	Placebo	---	---	---	---	---	---	---	---

Study, Year	Group	Major bleeding leading to reoperation n/N	Surgical site bleeding n/N	Bleeding leading to infection n/N	Bleeding leading to transfusion n/N	HIT n/N	Discomfort n/N	Readmission n/N	Reoperation n/N
McKenzie, 1985	General Anesthesia	---	---	---	---	---	---	---	---
	Spinal Anesthesia	---	---	---	---	---	---	---	---
Welin-Berger, 1982	Heparin	---	---	---	---	---	---	---	---
	Control	---	---	---	---	---	---	---	---
Modig, 1981	General Anesthesia	---	---	---	---	---	---	---	---
	Epidural Anesthesia	---	---	---	---	---	---	---	---
McKenna, 1980	Aspirin	---	---	---	---	---	---	---	---
	Placebo	---	---	---	---	---	---	---	---

* major surgical bleeding on days 0-1
†major surgical bleeding on days 2-8
‡minor surgical bleeding on days 0-1
§minor surgical bleeding on days 2-8
||minor surgical site bleeding
¶major surgical site bleeding

Abbreviations: BID=twice daily; d=day; g=gram; GCS= graduated compression stockings; h=hours; HFS=hip fracture surgery; HIT=heparin-induced thrombocytopenia; IPC=intermittent pneumatic compression device; mg=milligram; n/N= total number of events/total population; QD=daily; THA=total hip arthroplasty; THR=total hip replacement; TKA=total knee arthroplasty; TKR=total knee replacement; U=units; UFH=unfractionated heparin; VFP=venous foot pump

Table 22. Adverse outcomes in randomized controlled trials evaluating nonmajor orthopedic suregery

Study, Year	Group	Major bleeding leading to re-operation n/N	Surgical site bleeding n/N	Bleeding leading to infection n/N	Bleeding leading to transfusion n/N	HIT n/N	Discomfort n/N	Re-admission n/N	Re-operation n/N
Lapidus, 2007	Dalteparin	---	---	---	---	---	---	---	---
	Placebo	---	---	---	---	---	---	---	---
Michot, 2002	Dalteparin	---	---	---	---	---	---	---	---
	Control	---	---	---	---	---	---	---	---

Abbreviations: HIT= heparin induced thrombocytopenia; N=number of participants; n=number of participants with the event

Table 23. Additional adverse events in observational studies evaluating venous thromboembolism prophylaxis in major orthopedic surgery

Study, Year	Group	Major bleeding leading to reoperation n/N	Surgical site bleeding n/N	Bleeding leading to infection n/N	Bleeding leading to transfusion n/N	HIT n/N	Discomfort n/N	Readmission n/N	Reoperation n/N
Bozic, 2010	Warfarin	---	548/51923	---	---	---	---	---	---
	Aspirin	---	30/4719	---	---	---	---	---	---
Cusick, 2009 THR	Aspirin	---	---	---	---	---	---	---	---
	Warfarin	---	---	---	---	---	---	---	---
	Control	---	---	---	---	---	---	---	---
Cusick, 2009 TKR	Aspirin	---	---	---	---	---	---	---	---
	Warfarin	---	---	---	---	---	---	---	---
	Control	---	---	---	---	---	---	---	---
Froimson, 2009	IPC (ActiveCare)	---	---	---	---	---	---	---	---
	IPC (Flowtron)	---	---	---	---	---	---	---	---
Shorr, 2007	Fondaparinux	---	---	---	---	---	---	---	---
	Enoxaparin or dalteparin	---	---	---	---	---	---	---	---
	UFH	---	---	---	---	---	---	---	---
	Control	---	---	---	---	---	---	---	---
Sachs, 2003	Warfarin	---	---	---	1/957	---	---	17/957	11/957
	Control	---	---	---	0/785	---	---	7/785	2/785

Abbreviations: HIT=heparin-induced thrombocytopenia; IPC=intermittent pneumatic compression; THR=total hip replacement; TKR=total knee replacement; UFH=unfractionated heparin

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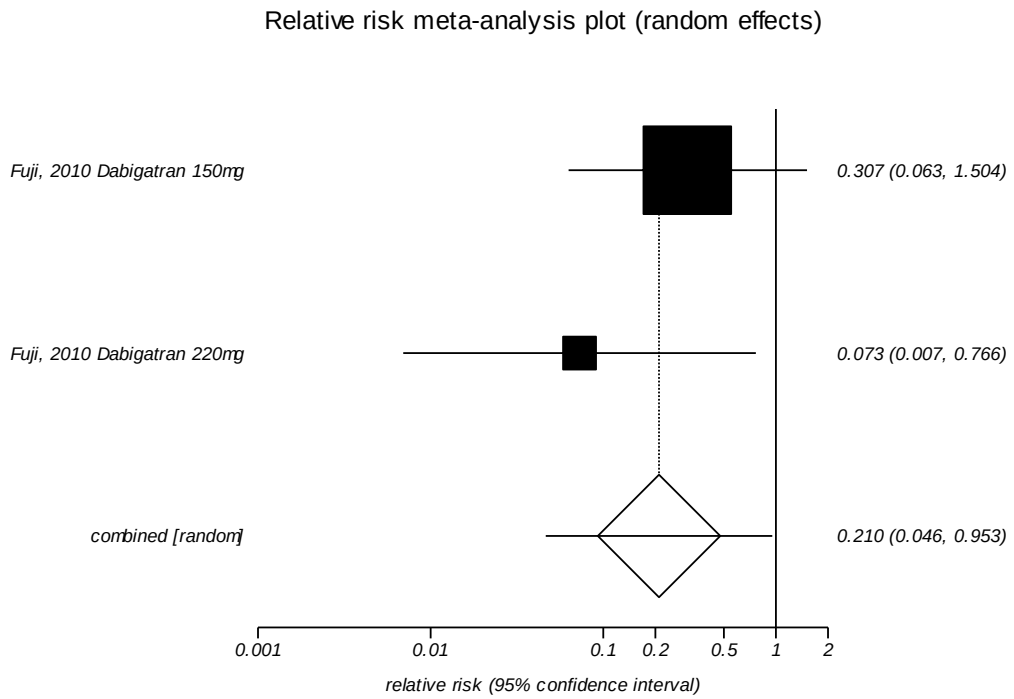
Froimson MI, Murray TG, Fazekas AF. Venous thromboembolic disease reduction with a portable pneumatic compression device. J Arthroplasty 2009;24:310-6. PMID: 18534456

Appendix G. Forest plots

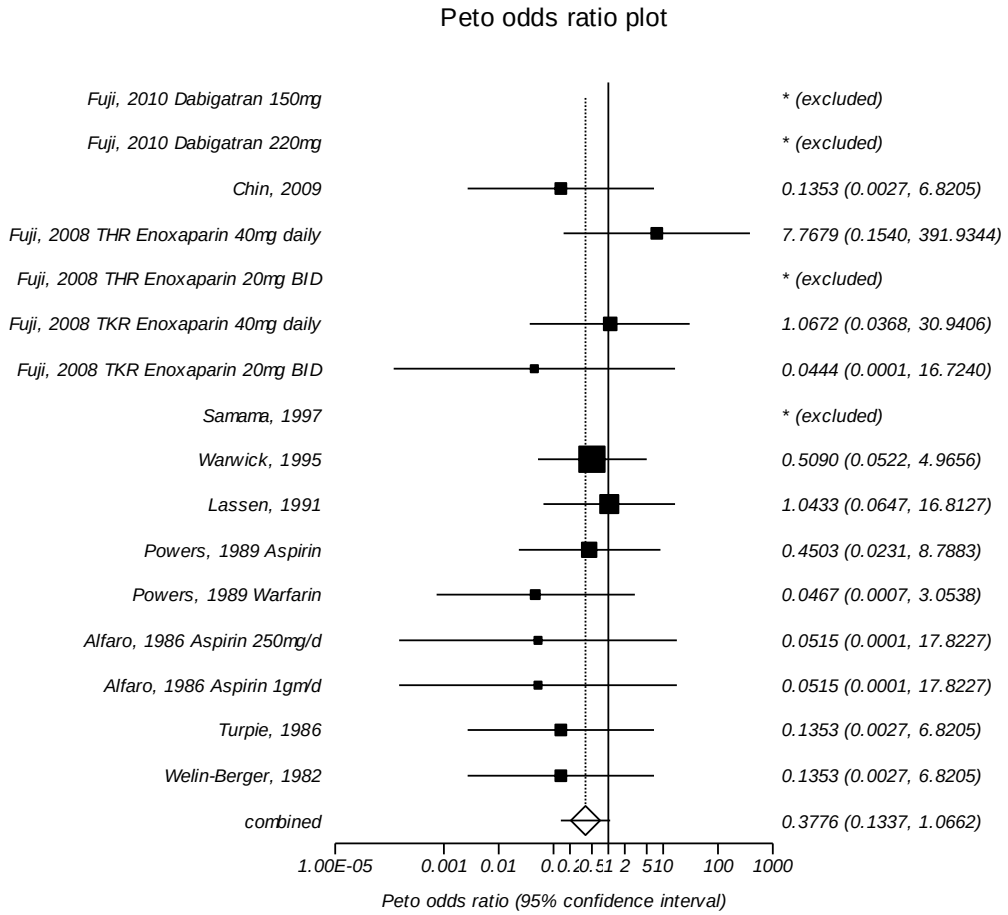
Figure 1. Impact of pharmacologic prophylaxis versus no prophylaxis on major venous thromboembolism in patients who had major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

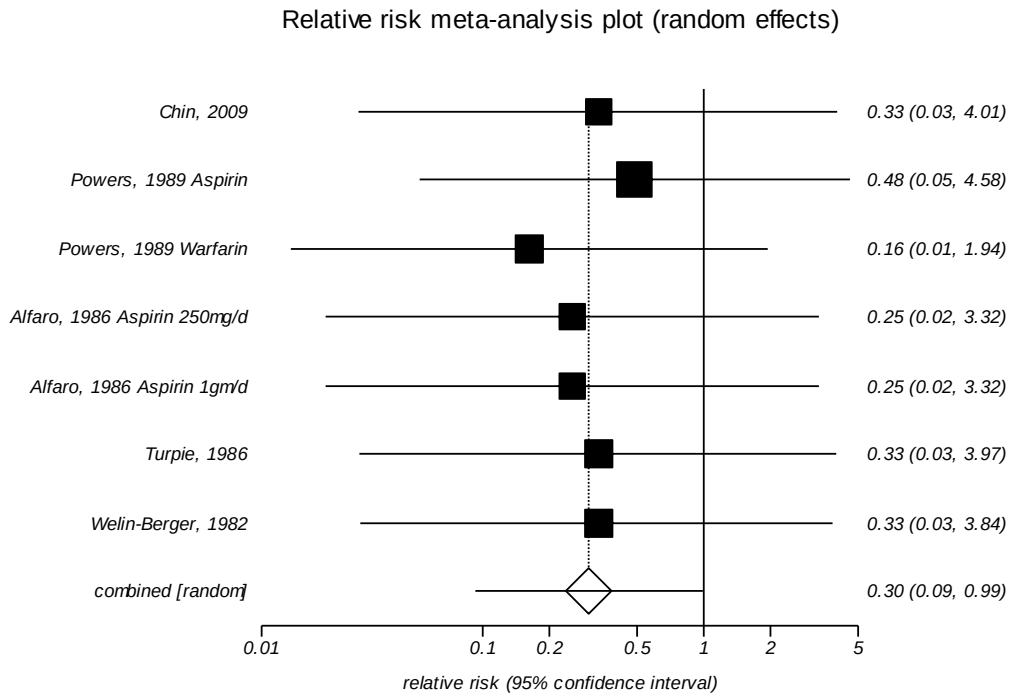
Figure 2. Impact of pharmacologic prophylaxis versus no prophylaxis on pulmonary embolism in patients who had major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.063

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

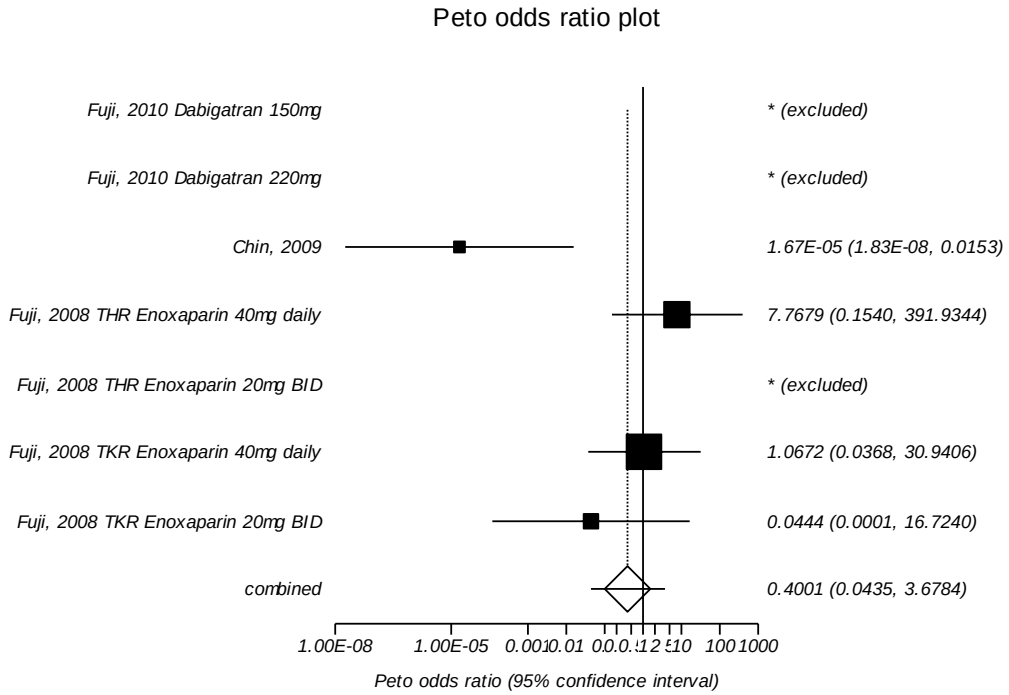
Figure 3. Impact of pharmacologic prophylaxis versus no prophylaxis on pulmonary embolism in patients who had major orthopedic surgery limited to truly no prophylaxis trials



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

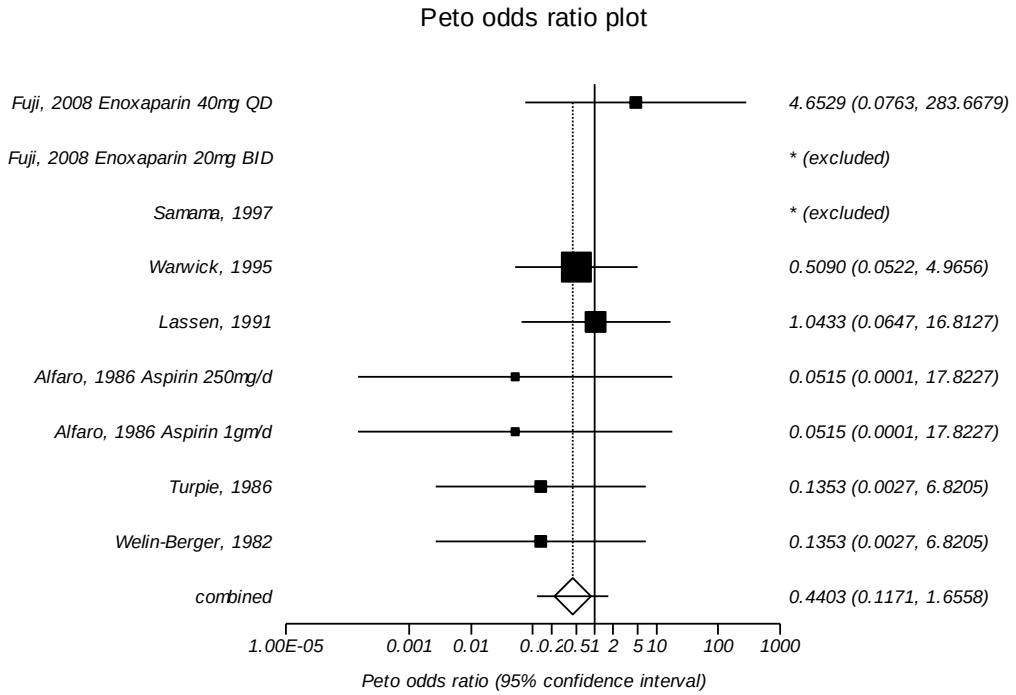
Figure 4. Impact of pharmacologic prophylaxis versus no prophylaxis on pulmonary embolism in patients who had major orthopedic surgery limited to trials published from 2001-present



I^2: 73.8 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

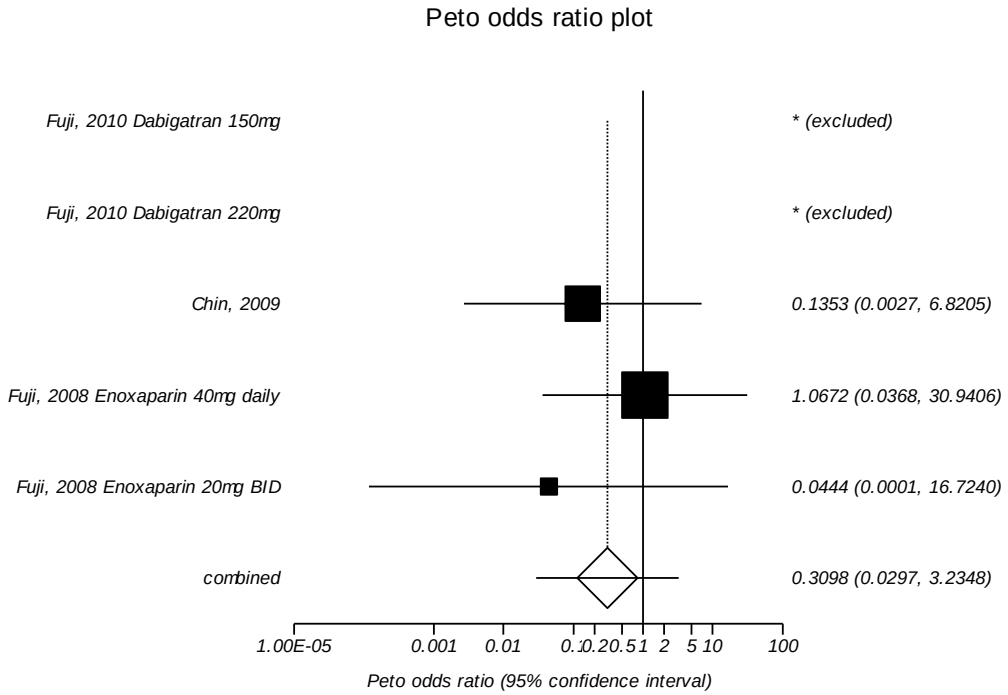
Figure 5. Impact of pharmacologic prophylaxis versus no prophylaxis on pulmonary embolism in patients who had major orthopedic surgery limited total hip replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

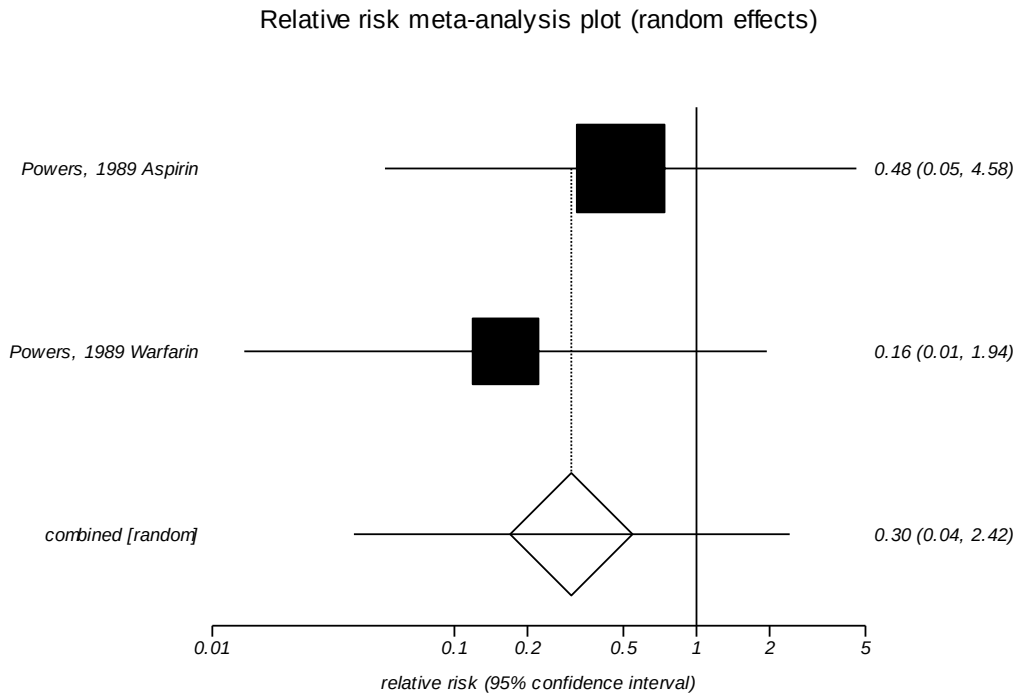
Figure 6. Impact of pharmacologic prophylaxis versus no prophylaxis on pulmonary embolism in patients who had major orthopedic surgery limited total knee replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

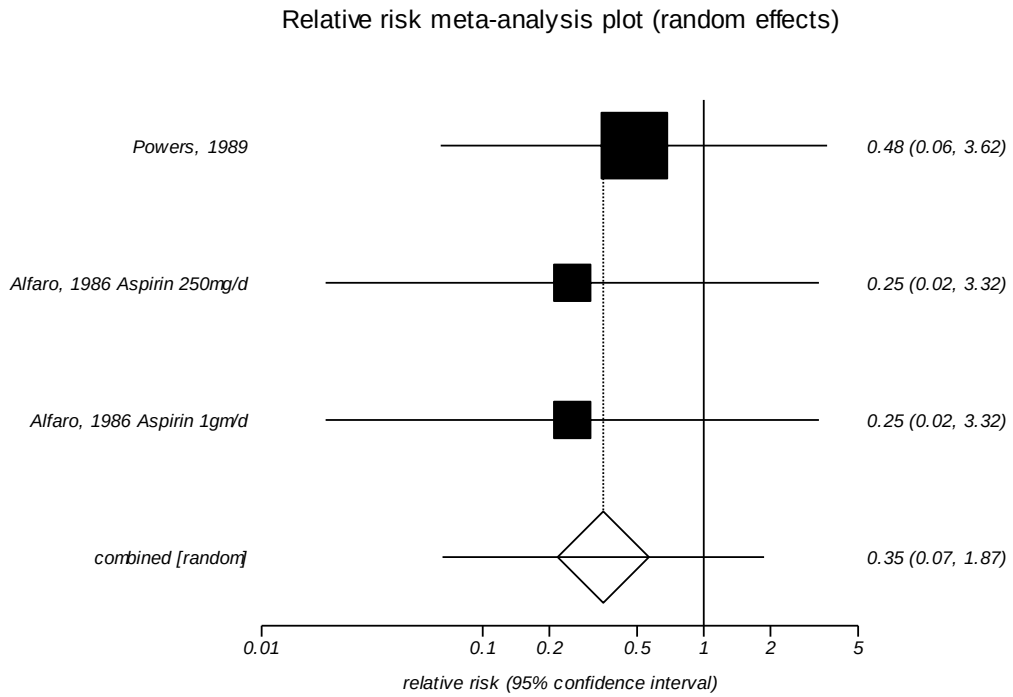
Figure 7. Impact of pharmacologic prophylaxis versus no prophylaxis on pulmonary embolism in patients who had major orthopedic surgery limited hip fracture surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

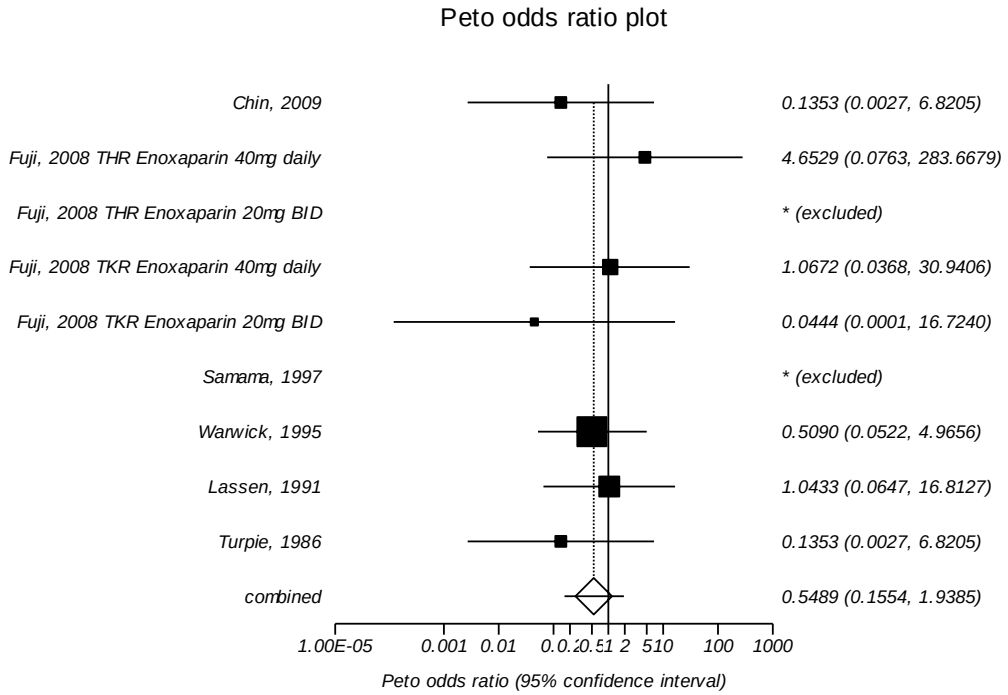
Figure 8. Impact of oral antiplatelet agents versus no prophylaxis on pulmonary embolism in patients who had major orthopedic surgery



I^2: 0 percent
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

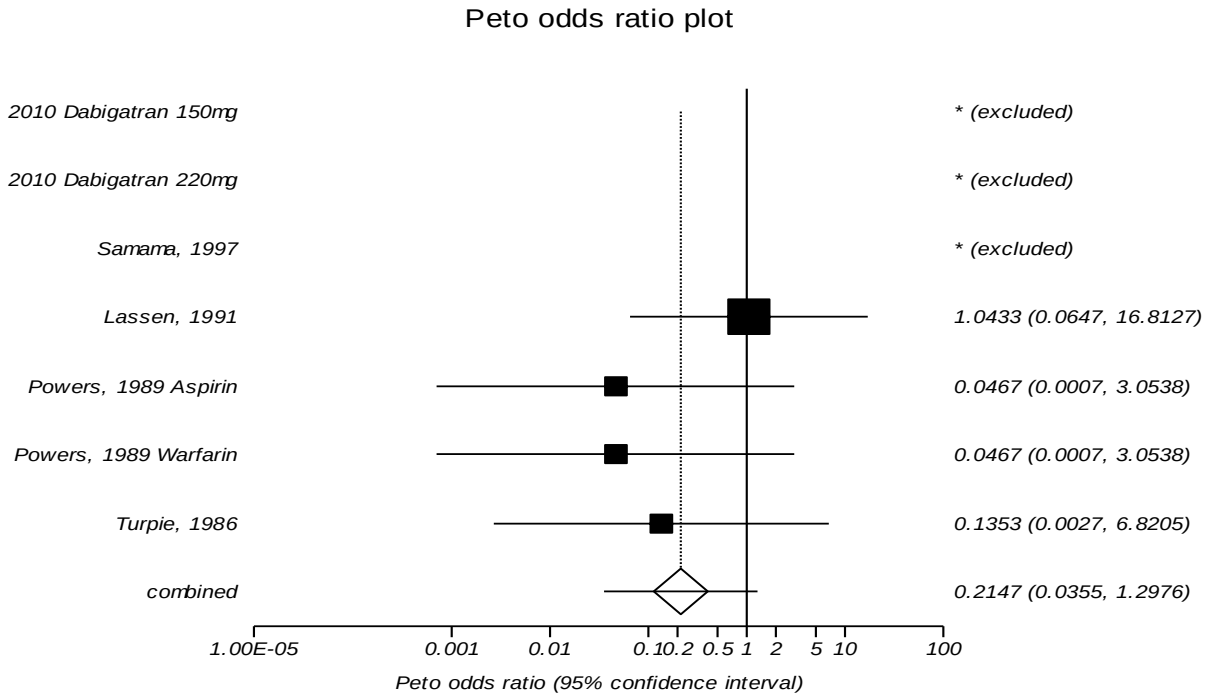
Figure 9. Impact of injectable low molecular weight heparins versus no prophylaxis on pulmonary embolism in patients who had major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.446

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

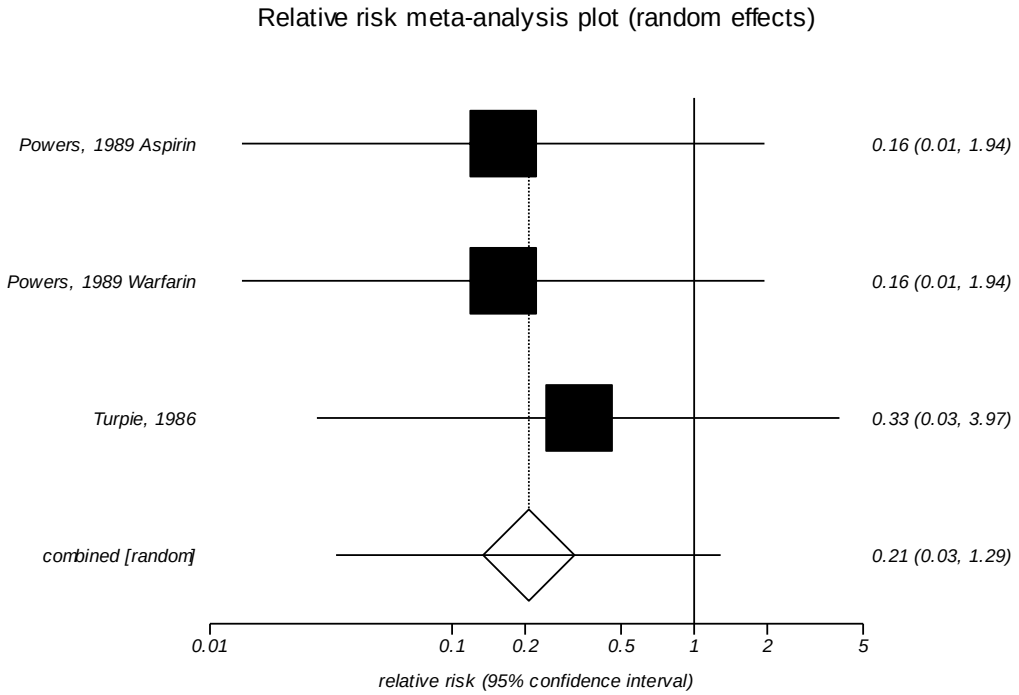
Figure 10. Impact of pharmacologic prophylaxis versus no prophylaxis on nonfatal pulmonary embolism in patients who had major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.009

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

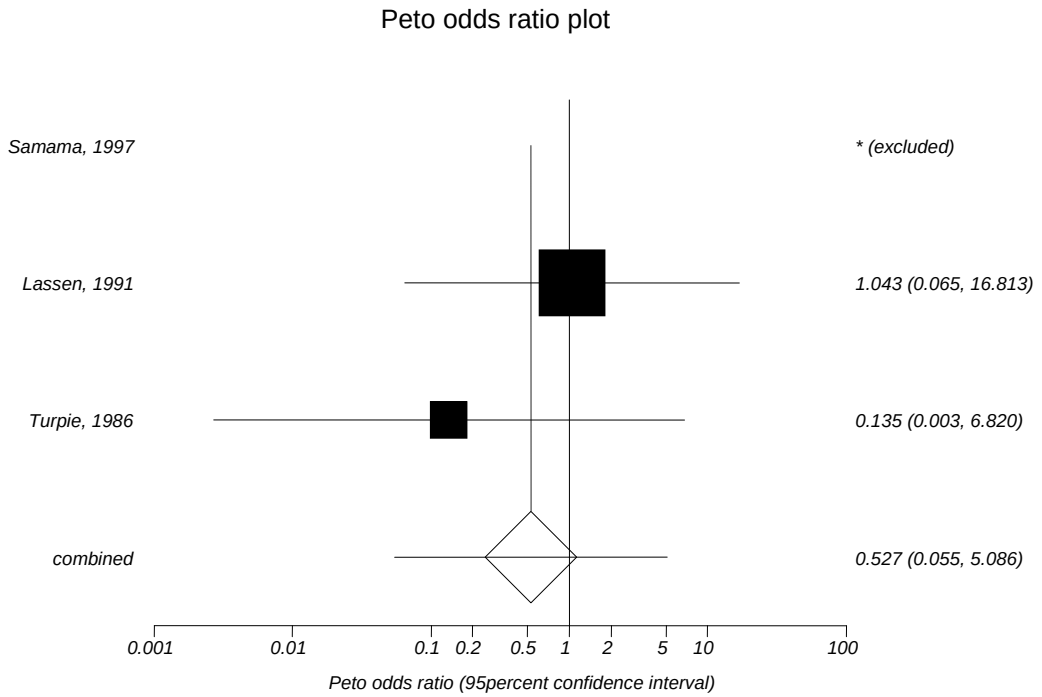
Figure 11. Impact of pharmacologic prophylaxis versus no prophylaxis on nonfatal pulmonary embolism in patients who had major orthopedic surgery limited to truly no prophylaxis trials



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

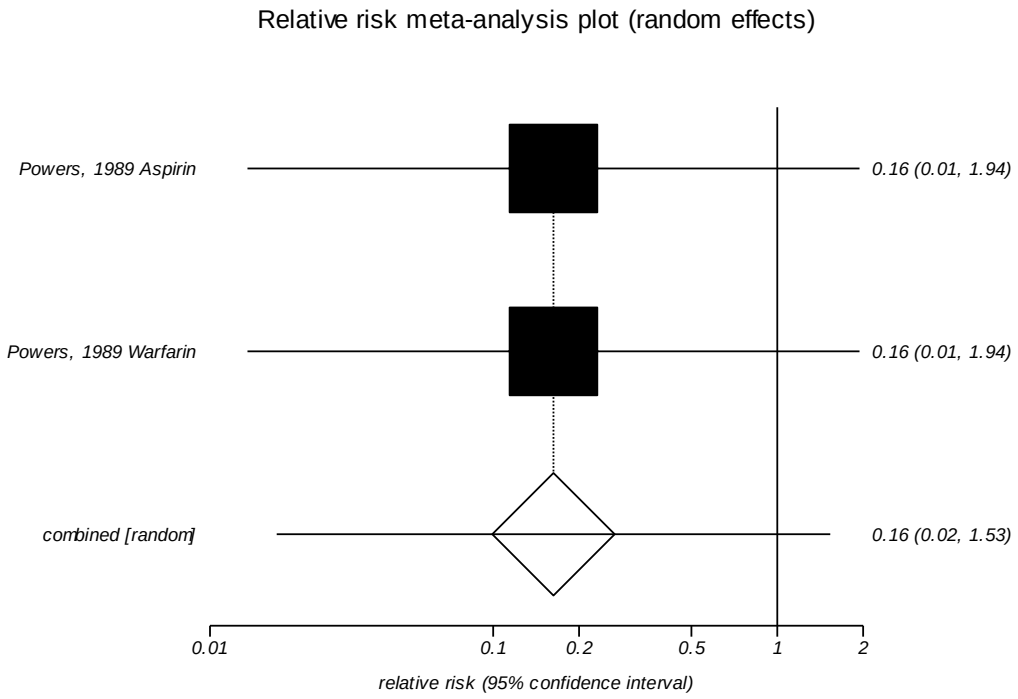
Figure 12. Impact of pharmacologic prophylaxis versus no prophylaxis on nonfatal pulmonary embolism in patients who had major orthopedic surgery limited to total hip replacement (same as injectable low molecular weight heparins versus no prophylaxis in patients who had major orthopedic surgery)



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

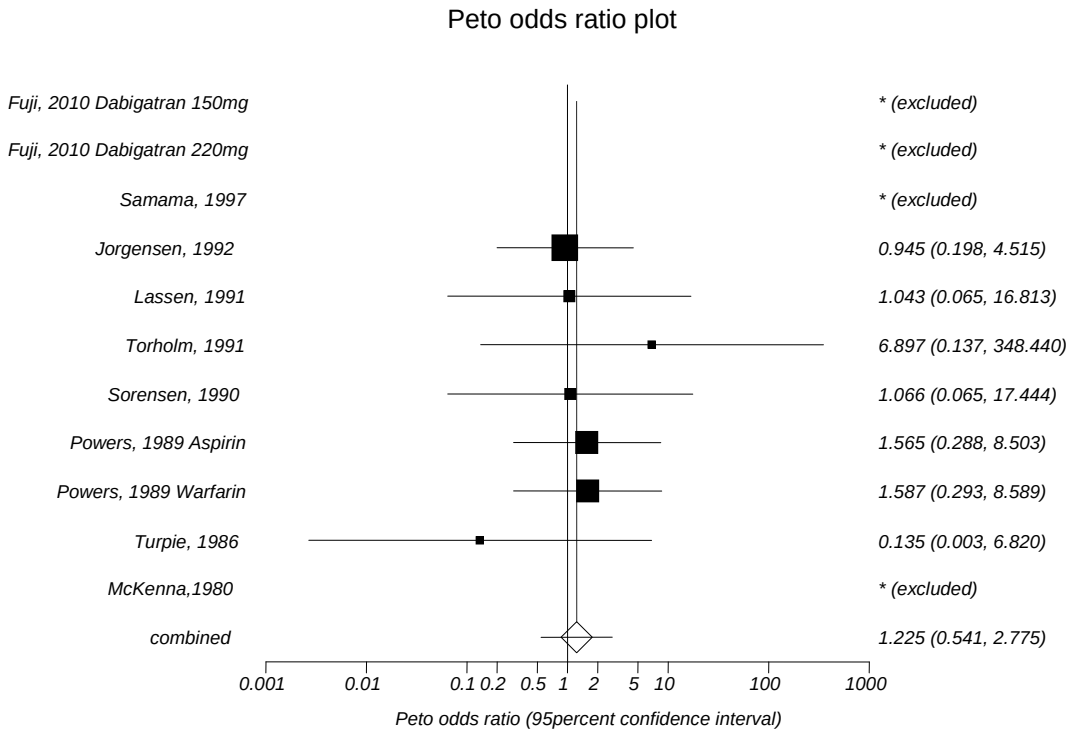
Figure 13. Impact of pharmacologic prophylaxis versus no prophylaxis on nonfatal pulmonary embolism in patients who had major orthopedic surgery limited to hip fracture surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

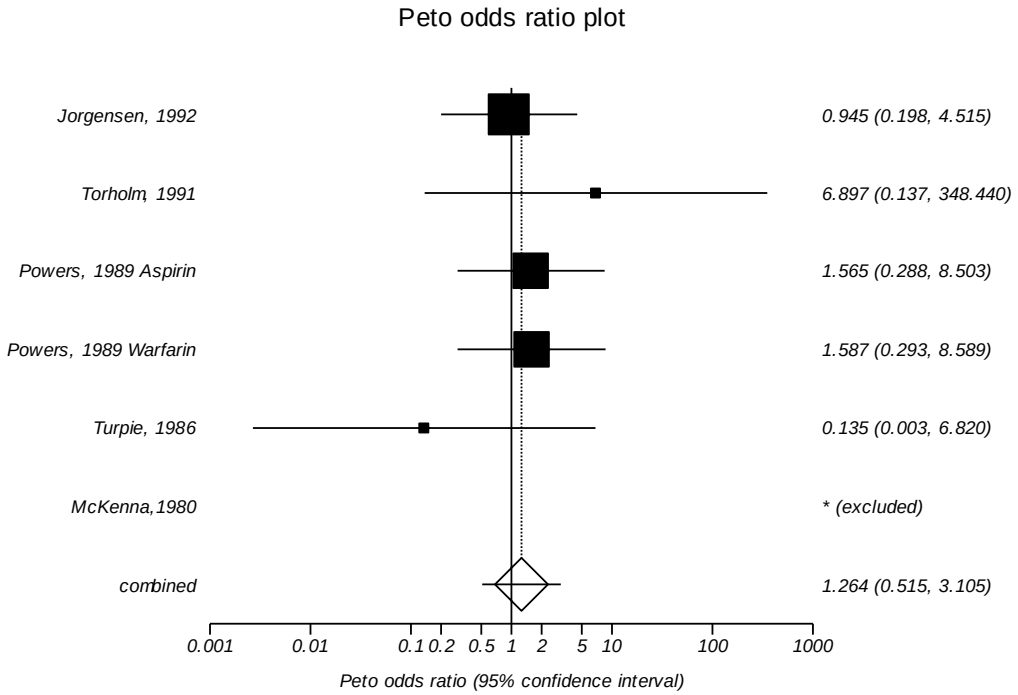
Figure 14. Impact of pharmacologic prophylaxis versus no prophylaxis on mortality in patients who had major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.757

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

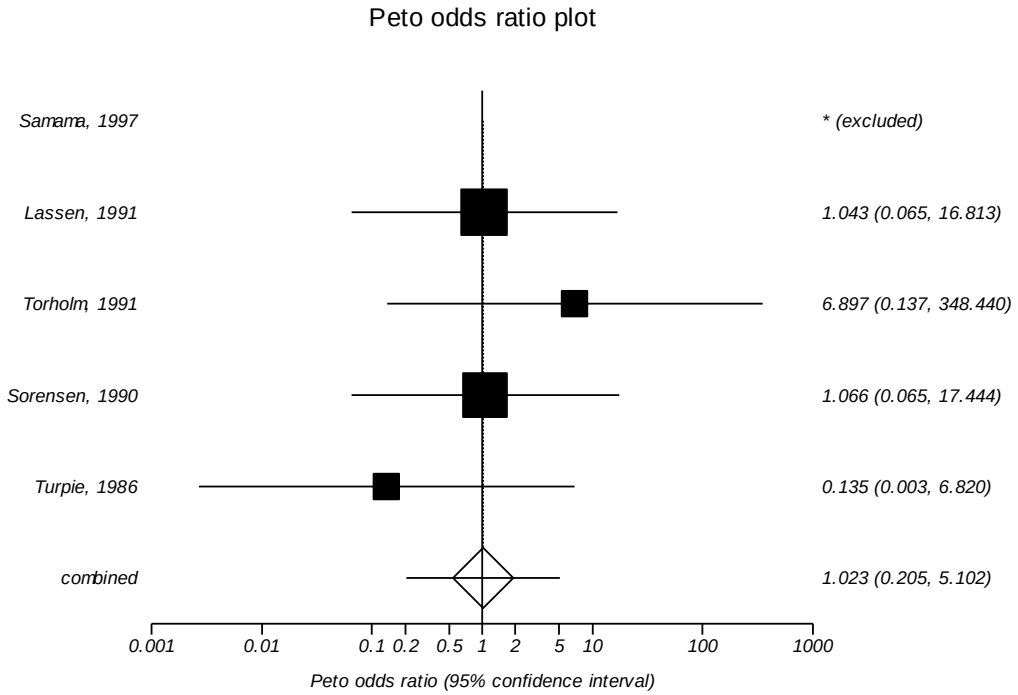
Figure 15. Impact of pharmacologic prophylaxis versus no prophylaxis on mortality in patients who had major orthopedic surgery limited to truly no prophylaxis trials



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

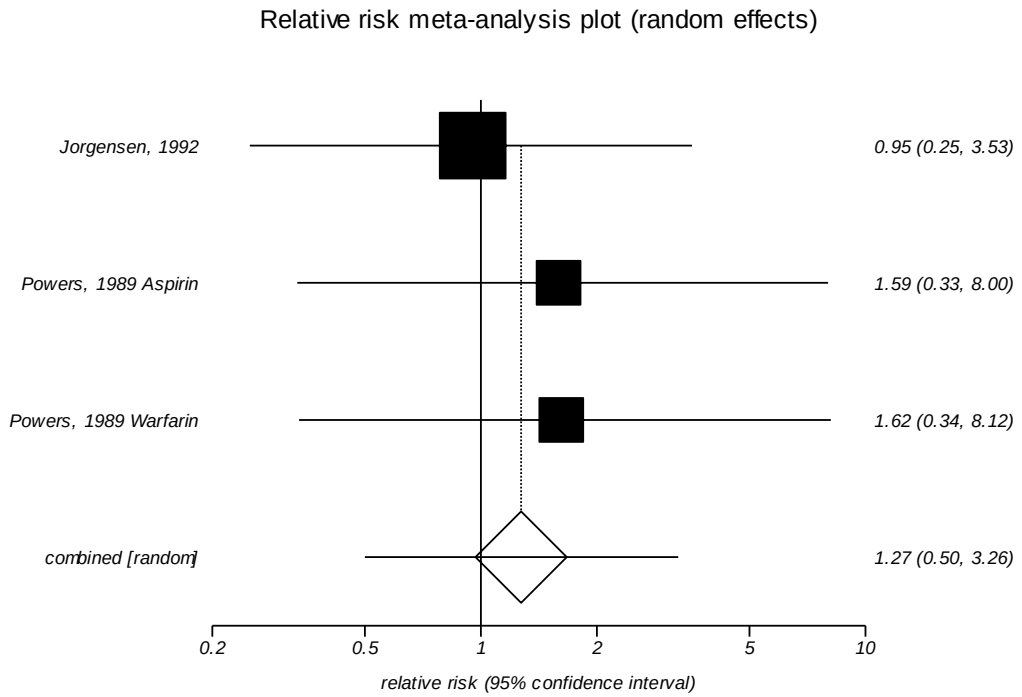
Figure 16. Impact of pharmacologic prophylaxis versus no prophylaxis on mortality in patients who had major orthopedic surgery limited to total hip replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

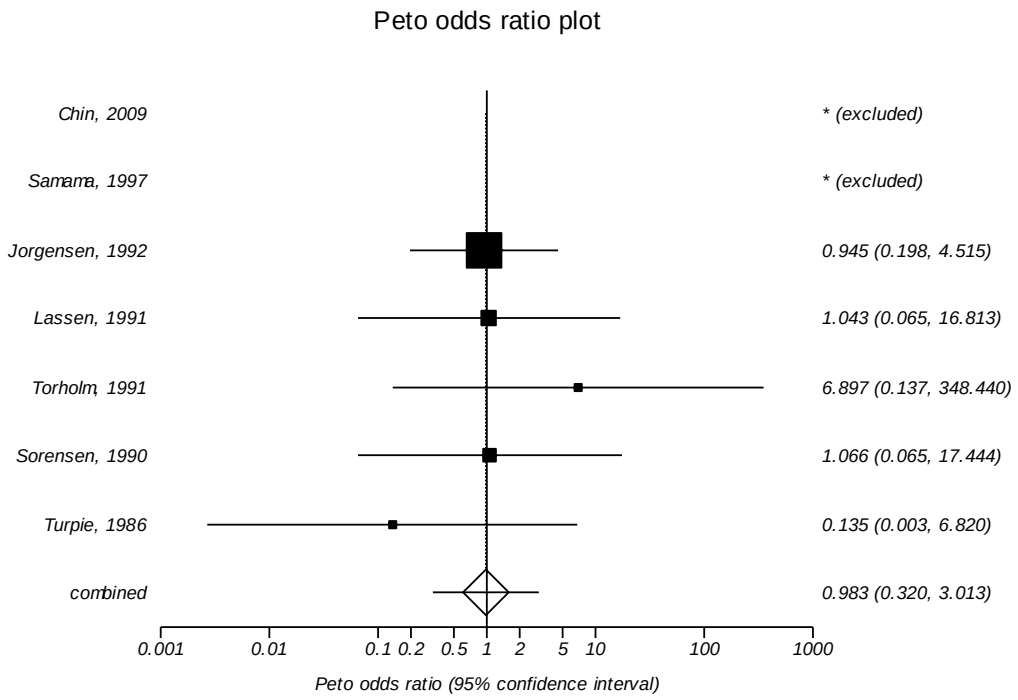
Figure 17. Impact of pharmacologic prophylaxis versus no prophylaxis on mortality in patients who had major orthopedic surgery limited to hip fracture surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

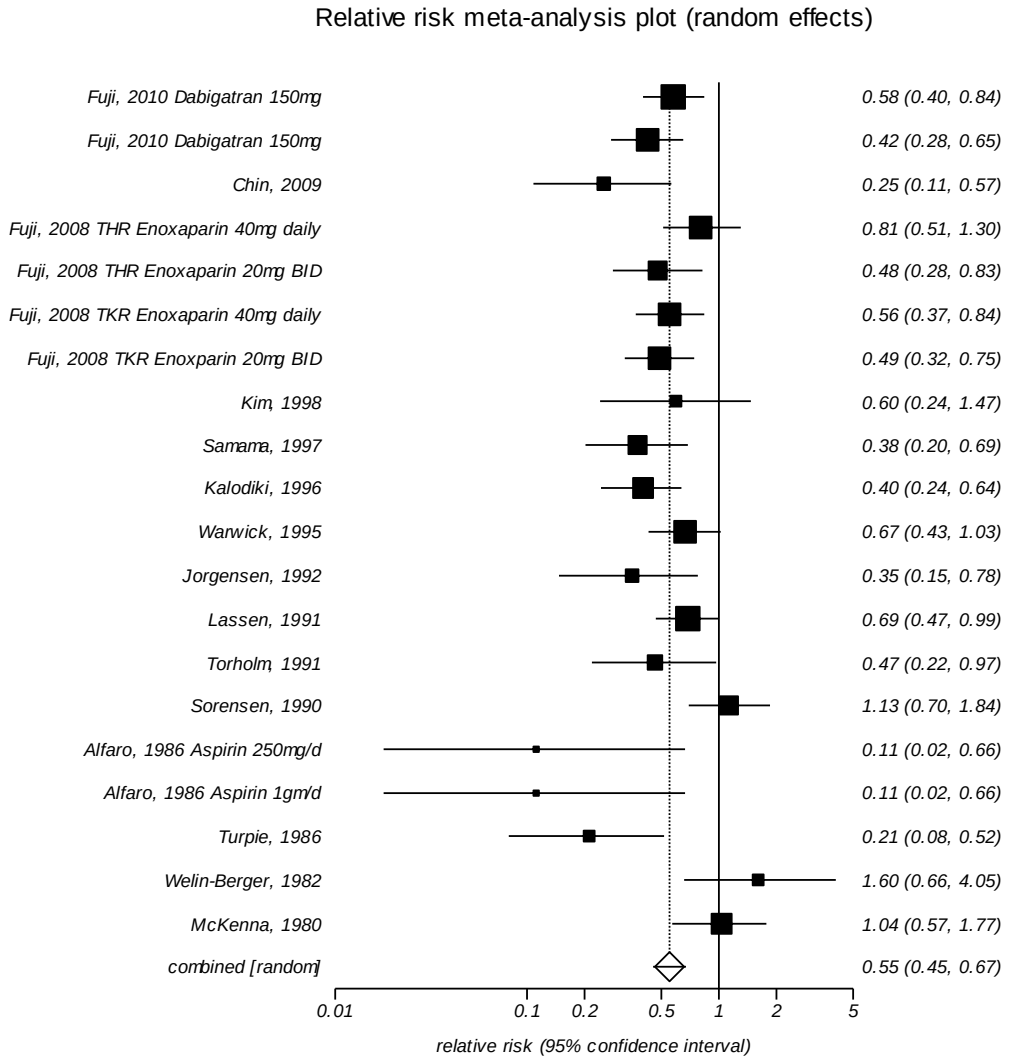
Figure 18. Impact of injectable low molecular weight heparins versus no prophylaxis on mortality in patients who had major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.962

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

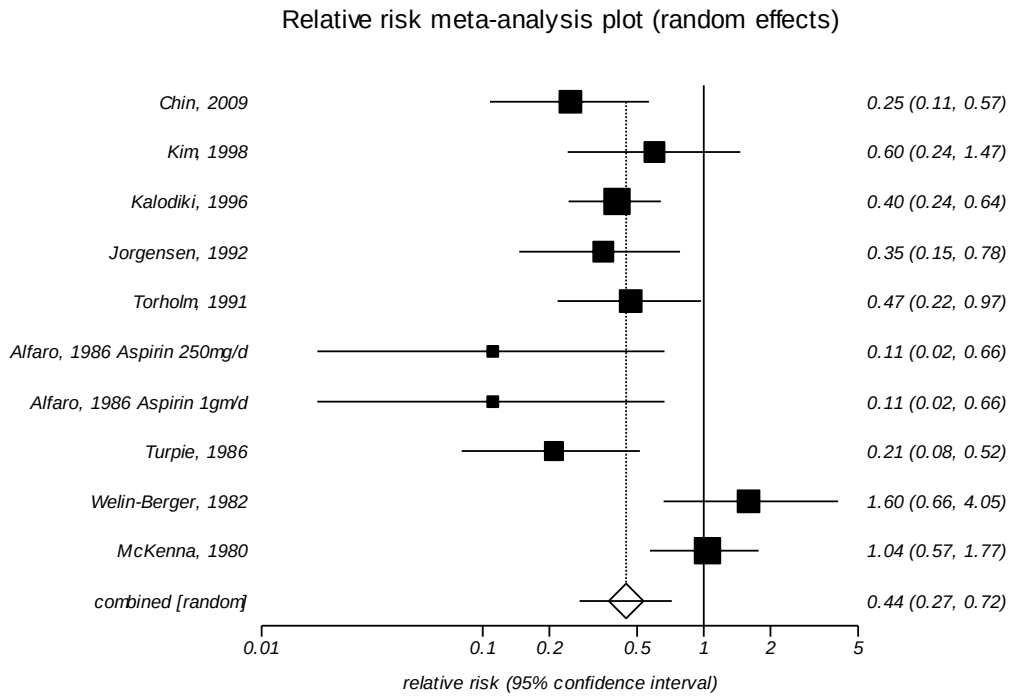
Figure 19. Impact of pharmacologic prophylaxis versus no prophylaxis on deep vein thrombosis in patients who had major orthopedic surgery



I^2: 56.6 percent
Egger's p-value: 0.080

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

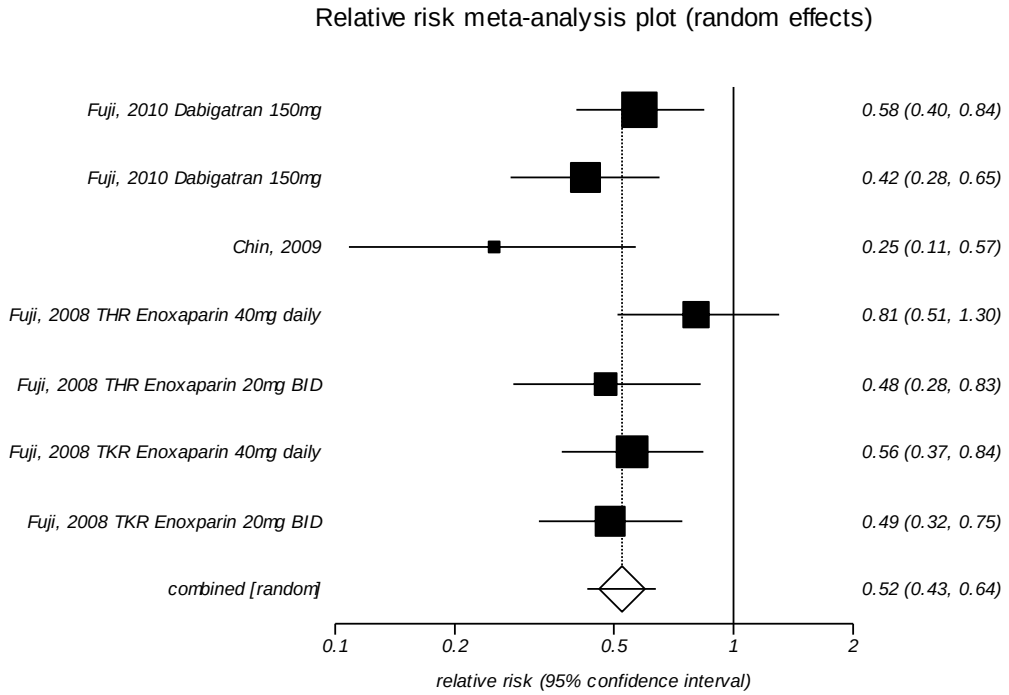
Figure 20. Impact of pharmacologic prophylaxis versus no prophylaxis on deep vein thrombosis in patients who had major orthopedic surgery limited to truly no prophylaxis trials



I^2: 69 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

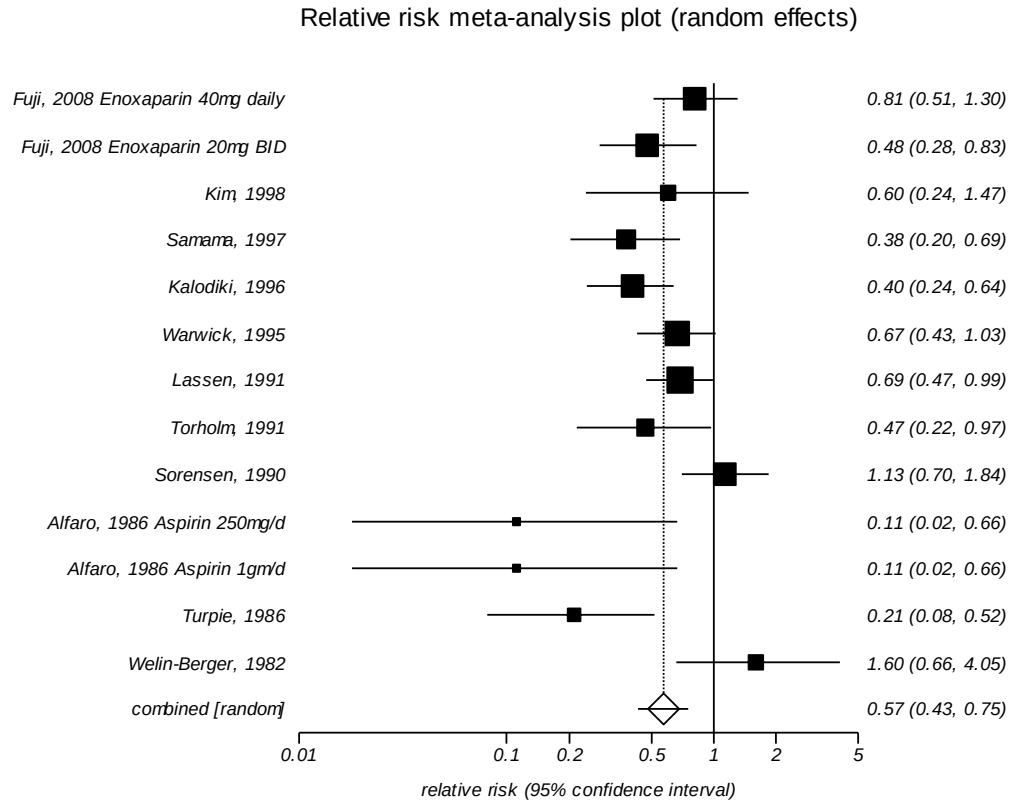
Figure 21. Impact of pharmacologic prophylaxis versus no prophylaxis on deep vein thrombosis in patients who had major orthopedic surgery limited to trials published from 2001-present



I^2: 22.8 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

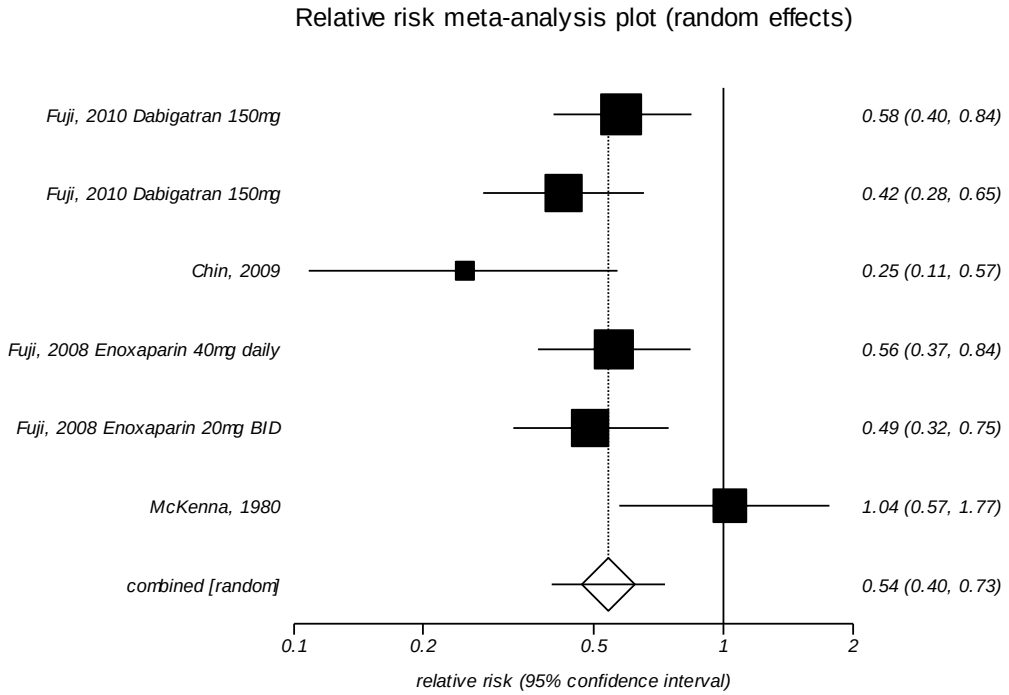
Figure 22. Impact of pharmacologic prophylaxis versus no prophylaxis on deep vein thrombosis in patients who had major orthopedic surgery limited to total hip replacement surgery



I^2: 58.8 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

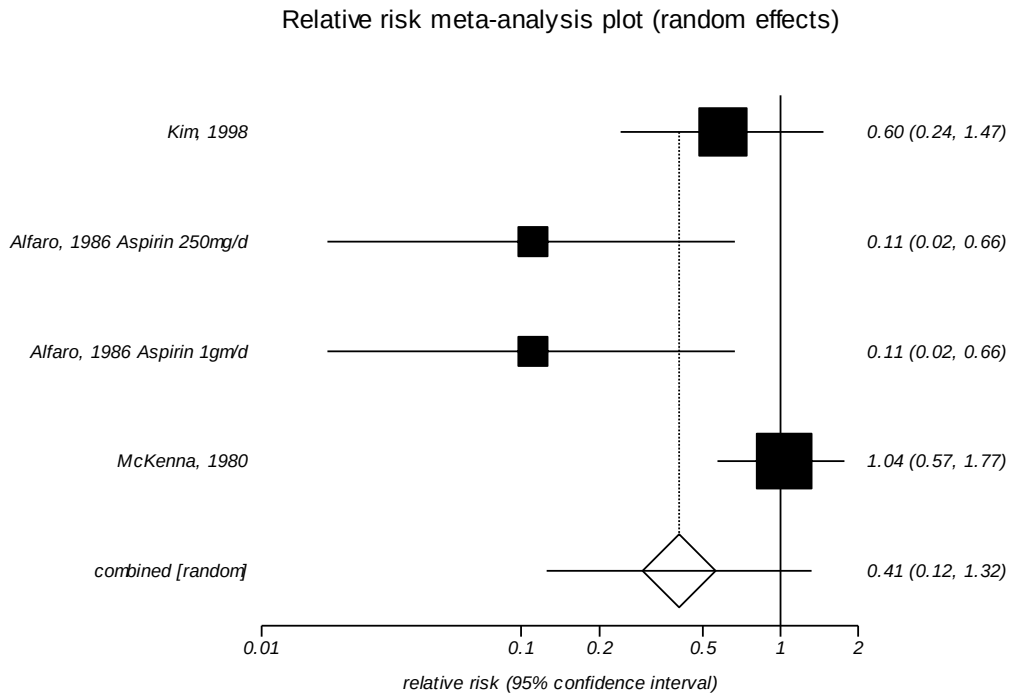
Figure 23. Impact of pharmacologic prophylaxis versus no prophylaxis on deep vein thrombosis in patients who had major orthopedic surgery limited to total knee replacement surgery



I^2: 61.4 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

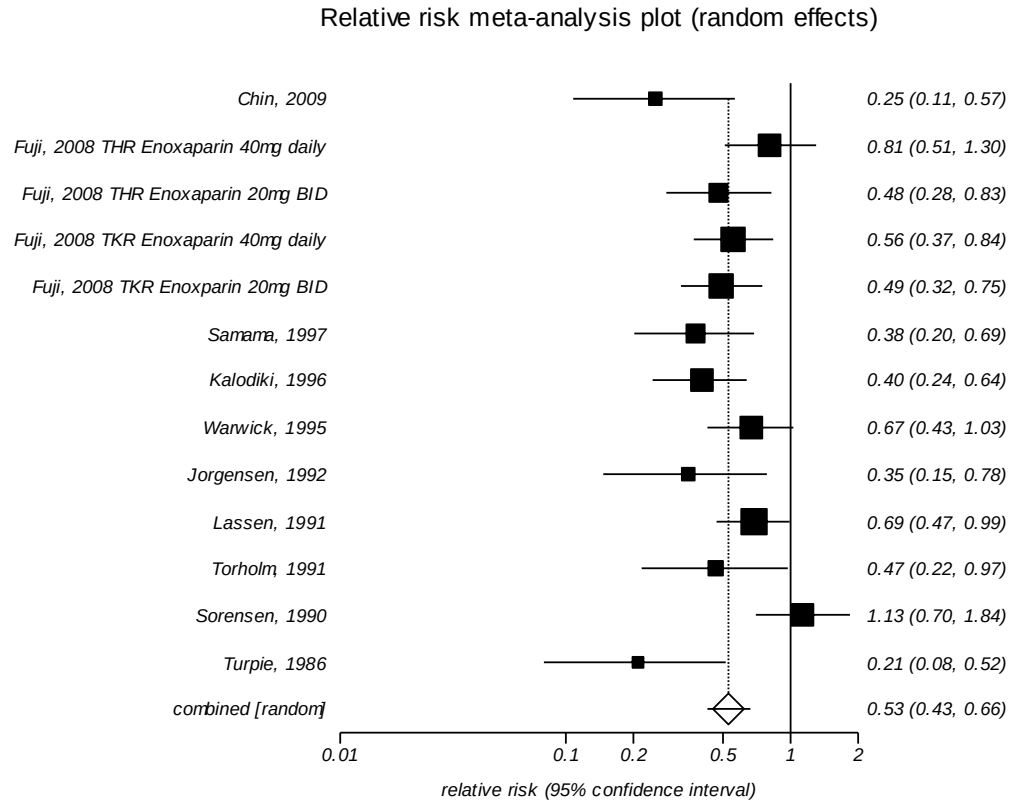
Figure 24. Impact of oral antiplatelet agents versus no prophylaxis on deep vein thrombosis in patients who had major orthopedic surgery



I^2: 76 percent
Egger's p-value: 0.002

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

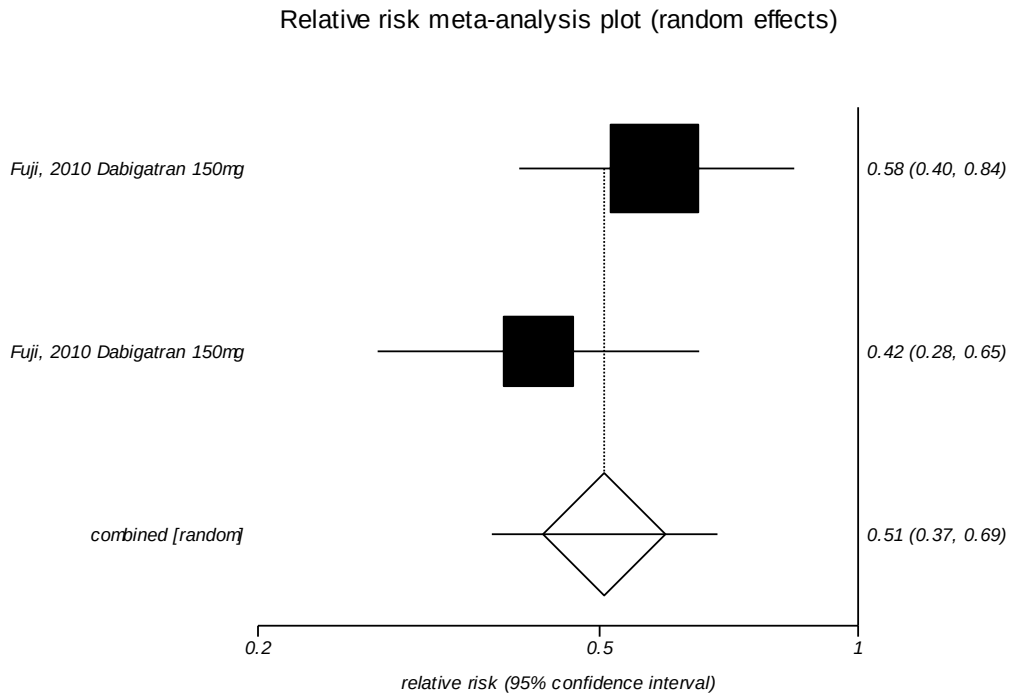
Figure 25. Impact of injectable low molecular weight heparins versus no prophylaxis on deep vein thrombosis in patients who had major orthopedic surgery



I^2: 53.3 percent
Egger's p-value: 0.023

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

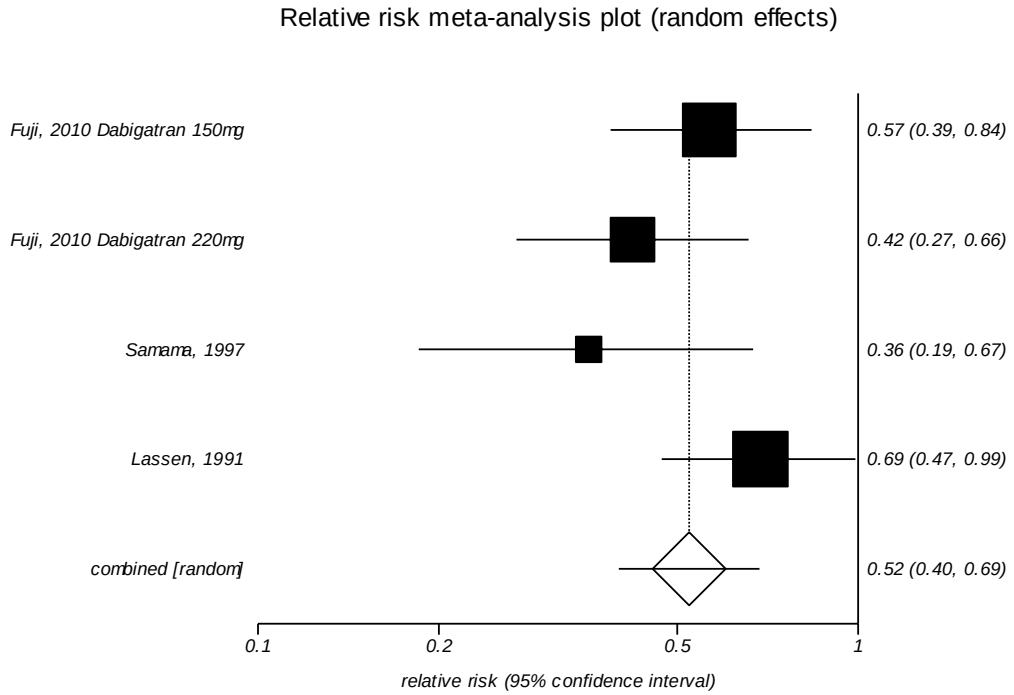
Figure 26. Impact of injectable or oral direct thrombin inhibitors versus no prophylaxis on deep vein thrombosis in patients who had major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

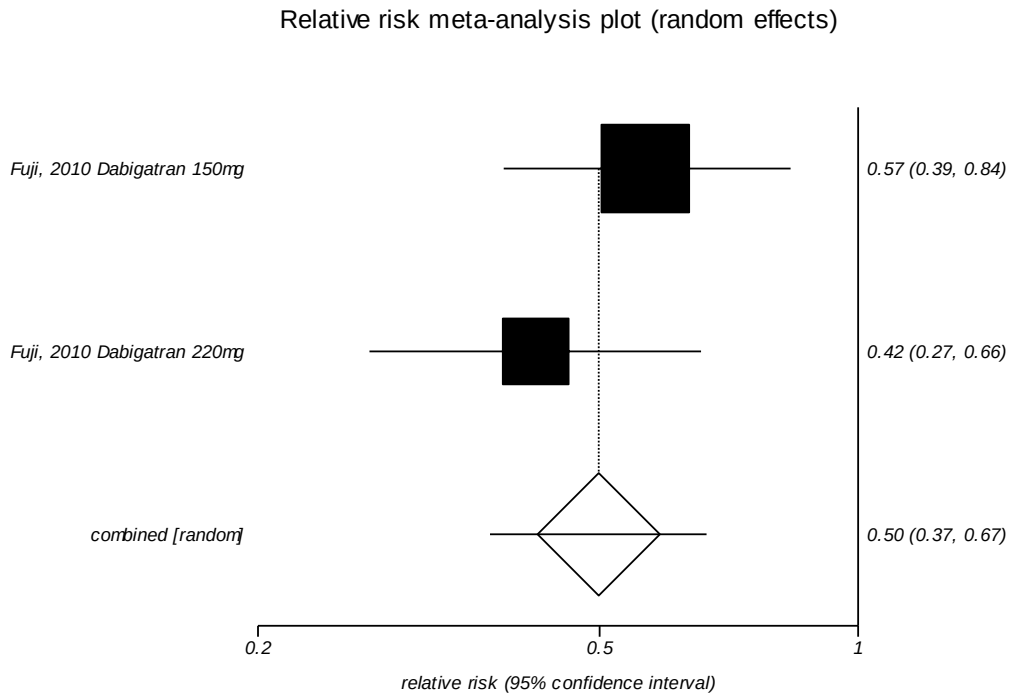
Figure 27. Impact of pharmacologic prophylaxis versus no prophylaxis on asymptomatic deep vein thrombosis in patients who had major orthopedic surgery



I^2: 32.7 percent
Egger's p-value: 0.168

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

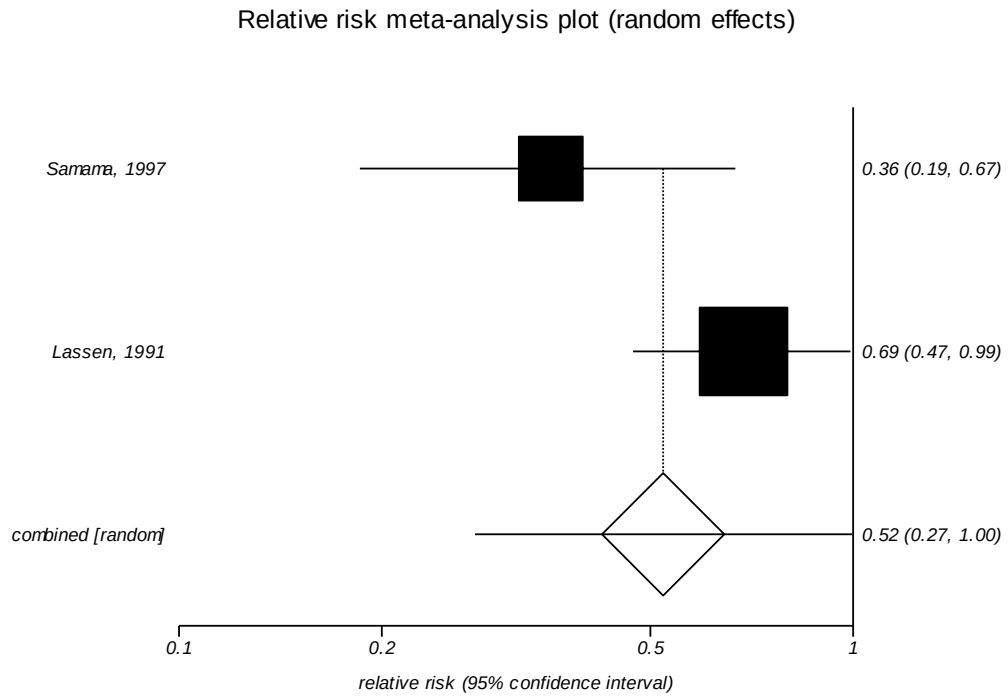
Figure 28. Impact of pharmacologic prophylaxis versus no prophylaxis on asymptomatic deep vein thrombosis in patients who had major orthopedic surgery limited to trials published from 2001-present (same analysis as limited to total knee replacement; same analysis as injectable or oral direct thrombin inhibitors versus no prophylaxis in major orthopedic surgery)



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

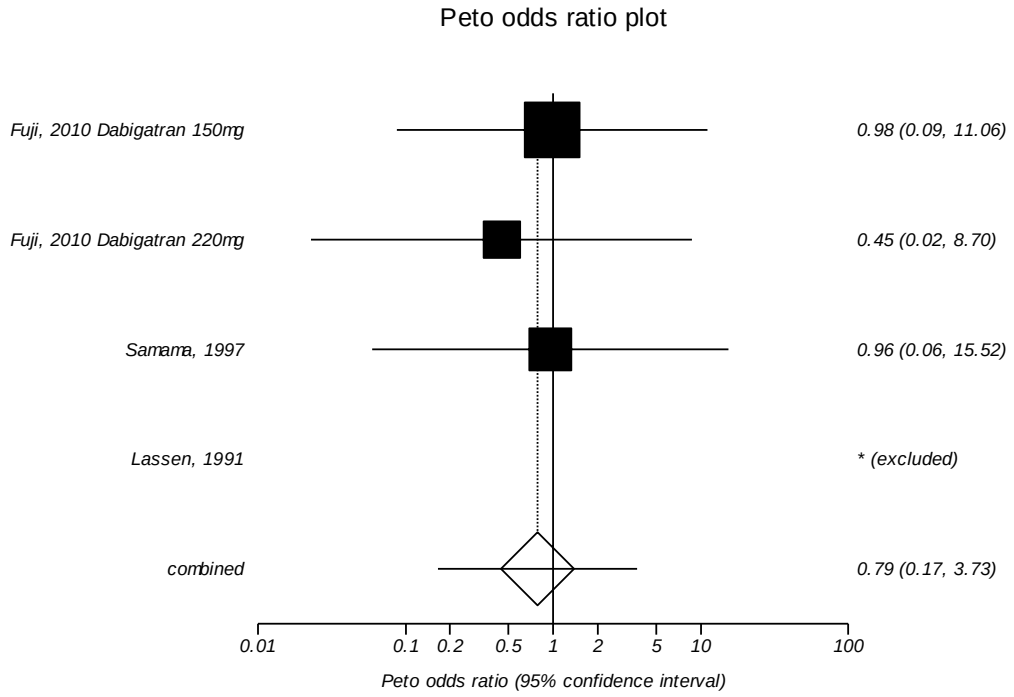
Figure 29. Impact of pharmacologic prophylaxis versus no prophylaxis on asymptomatic deep vein thrombosis in patients who had major orthopedic surgery limited to total hip replacement (same analysis as low molecular weight heparin versus no prophylaxis in major orthopedic surgery)



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

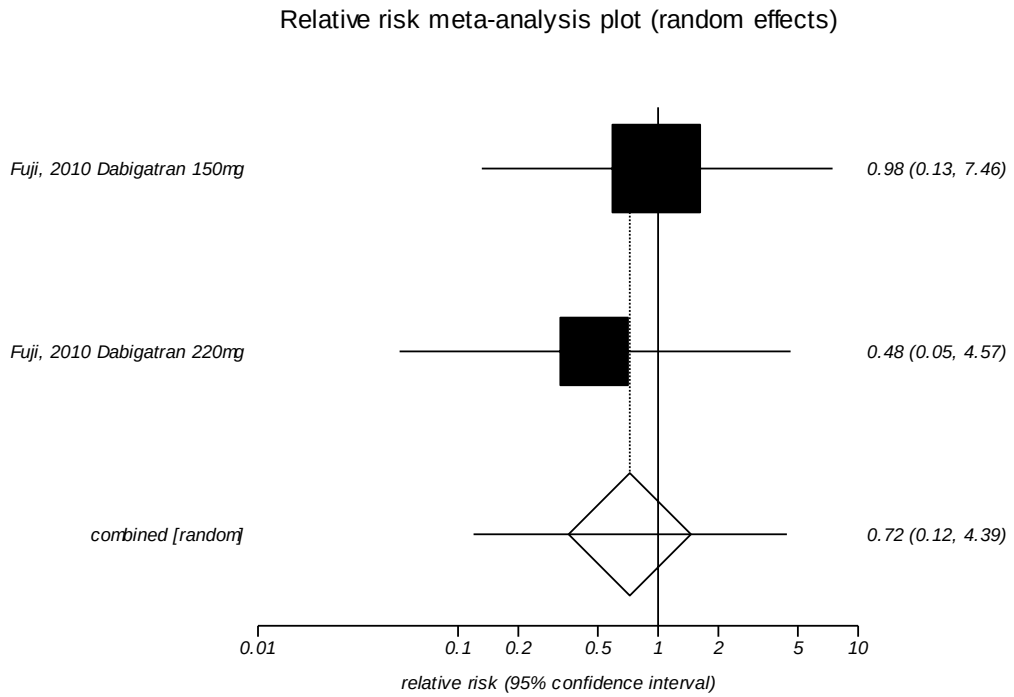
Figure 30. Impact of pharmacologic prophylaxis versus no prophylaxis on symptomatic deep vein thrombosis in patients who had major orthopedic surgery



I^2: 0 percent
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

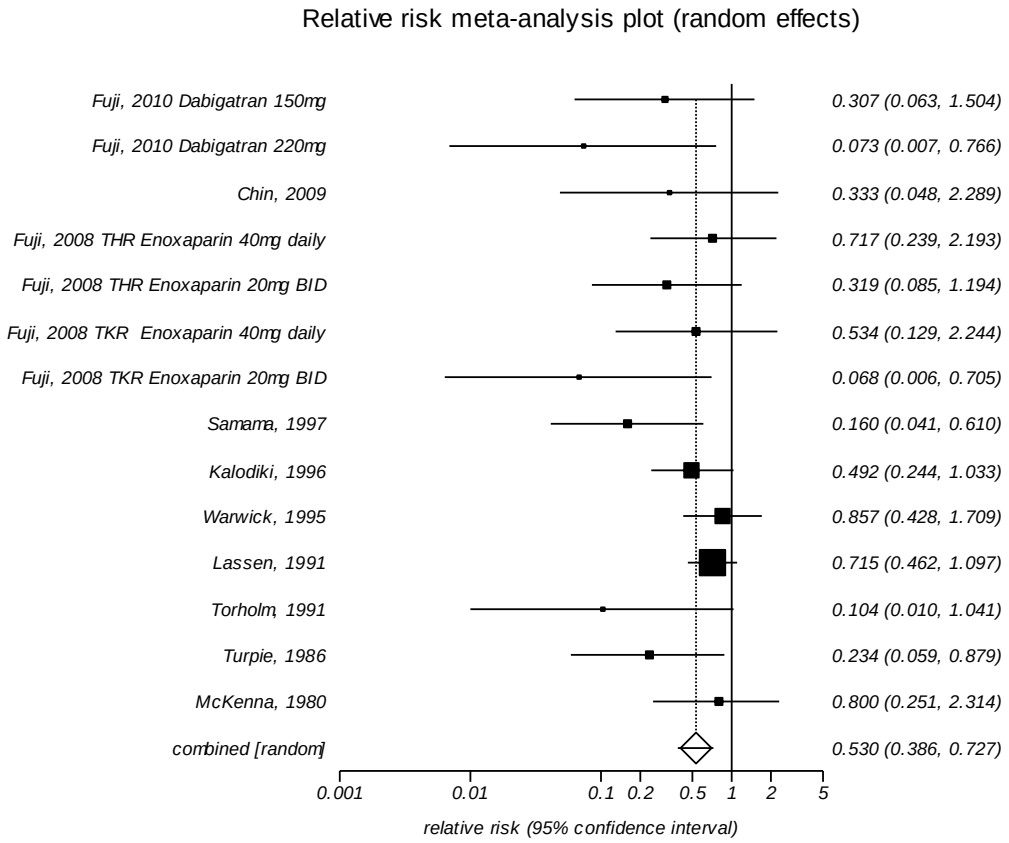
Figure 31. Impact of pharmacologic prophylaxis versus no prophylaxis on symptomatic deep vein thrombosis in patients who had major orthopedic surgery limited to trials published in 2001-present (same analysis as limited to total knee replacement; same analysis as injectable or oral direct thrombin inhibitors versus no prophylaxis in major orthopedic surgery)



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

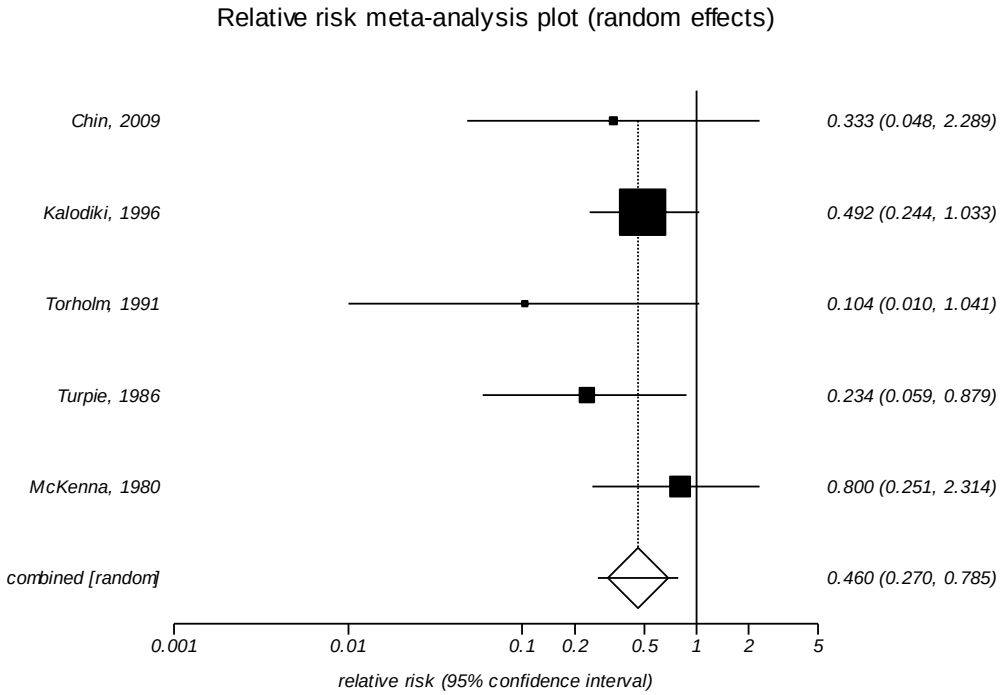
Figure 32. Impact of pharmacologic prophylaxis versus no prophylaxis on proximal deep vein thrombosis in patients who had major orthopedic surgery



I^2: 10.7 percent
Egger's p-value: 0.001

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

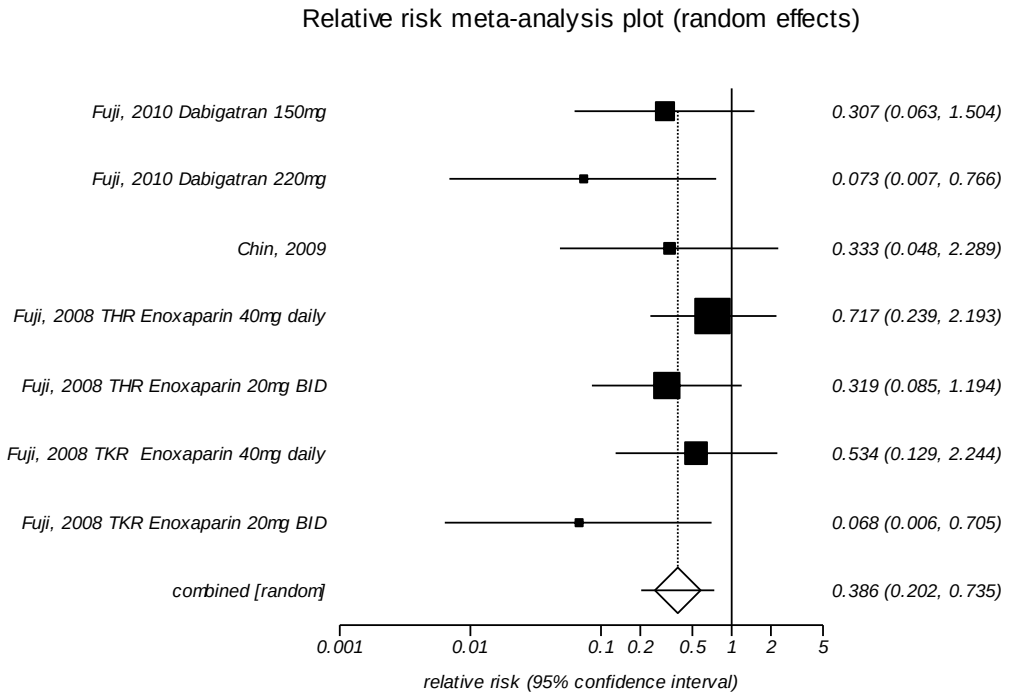
Figure 33. Impact of pharmacologic prophylaxis versus no prophylaxis on proximal deep vein thrombosis in patients who had major orthopedic surgery limited to truly no prophylaxis trials



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

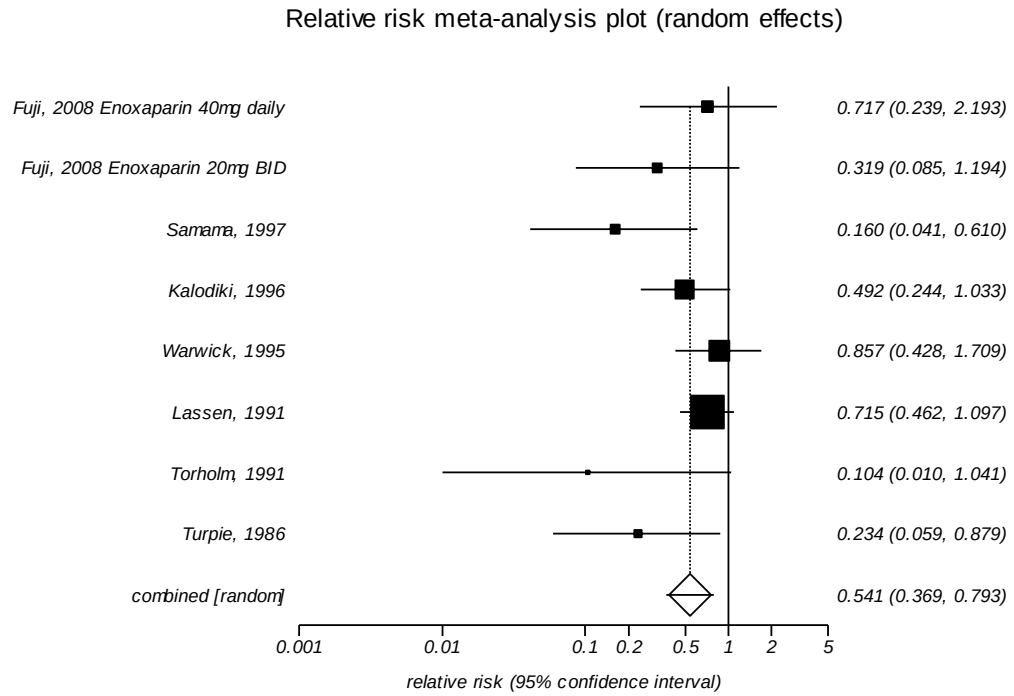
Figure 34. Impact of pharmacologic prophylaxis versus no prophylaxis on proximal deep vein thrombosis in patients who had major orthopedic surgery limited to trials published from 2001-present



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

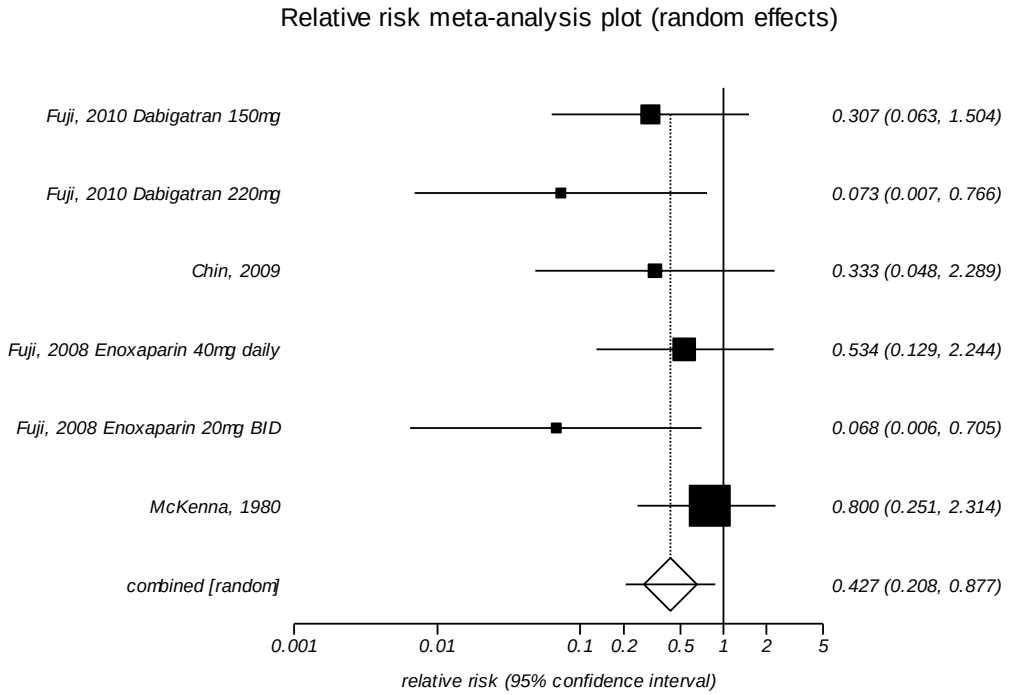
Figure 35. Impact of pharmacologic prophylaxis versus no prophylaxis on proximal deep vein thrombosis in patients who had major orthopedic surgery limited to total hip replacement



I^2: 23.9 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

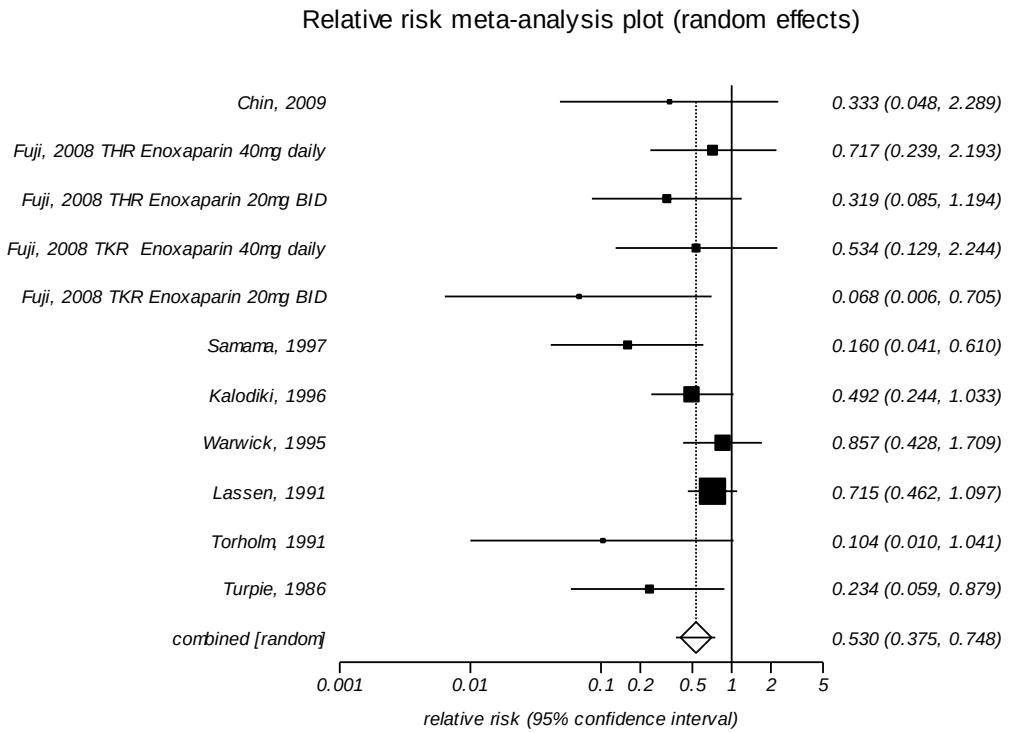
Figure 36. Impact of pharmacologic prophylaxis versus no prophylaxis on proximal deep vein thrombosis in patients who had major orthopedic surgery limited to total knee replacement



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

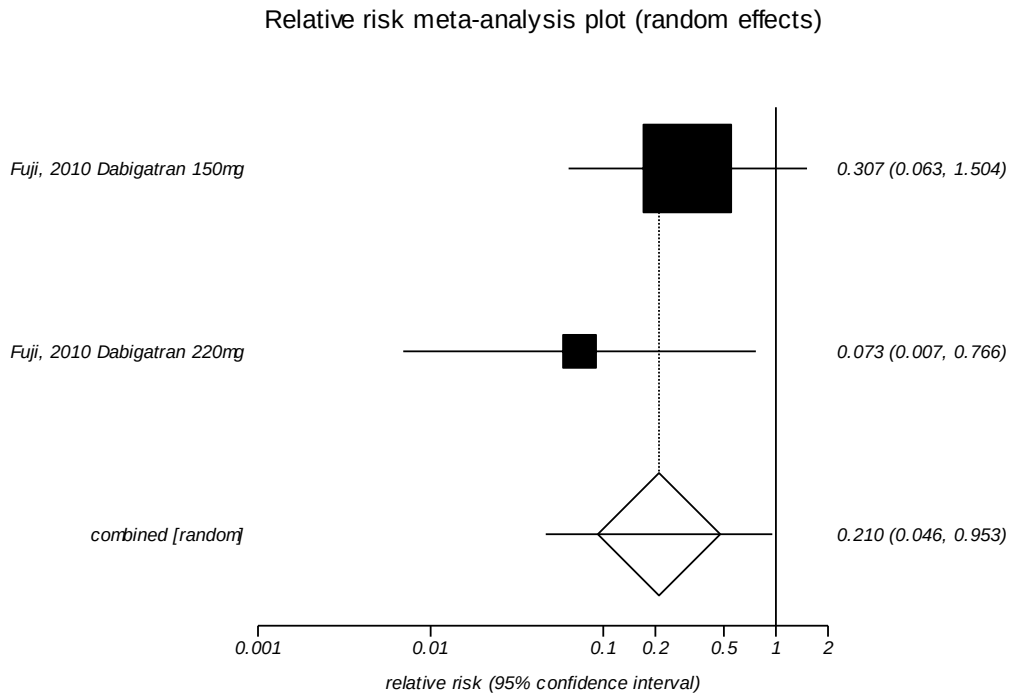
Figure 37. Impact of injectable low molecular weight heparins versus no prophylaxis on proximal deep vein thrombosis in patients who had major orthopedic surgery



I^2: 14.3 percent
Egger's p-value: 0.003

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

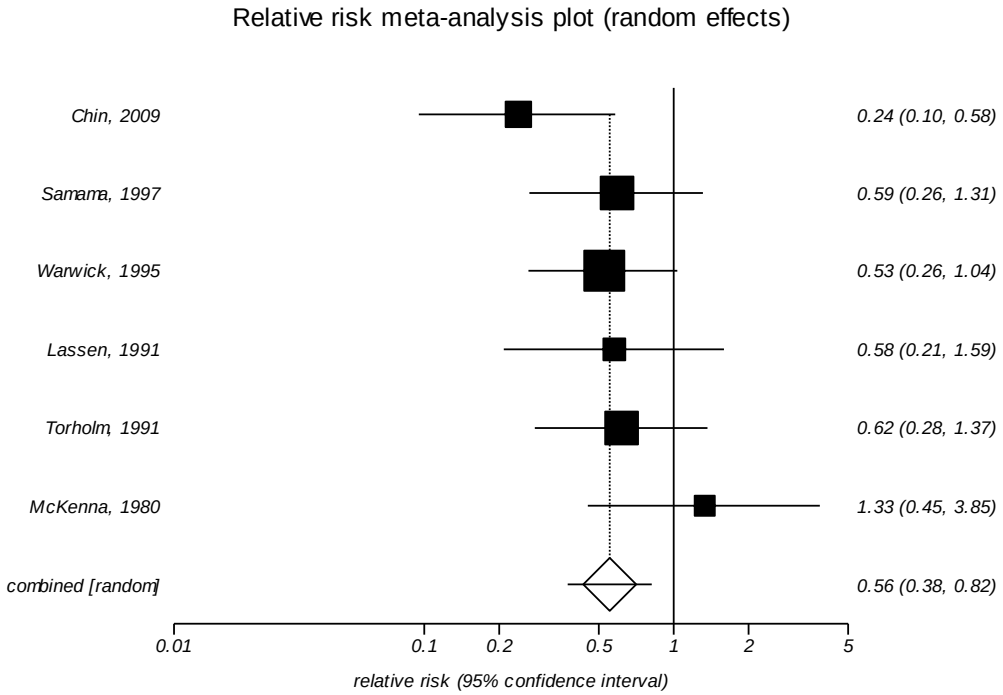
Figure 38. Impact of injectable or oral direct thrombin inhibitors versus no prophylaxis on proximal deep vein thrombosis in patients who had major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

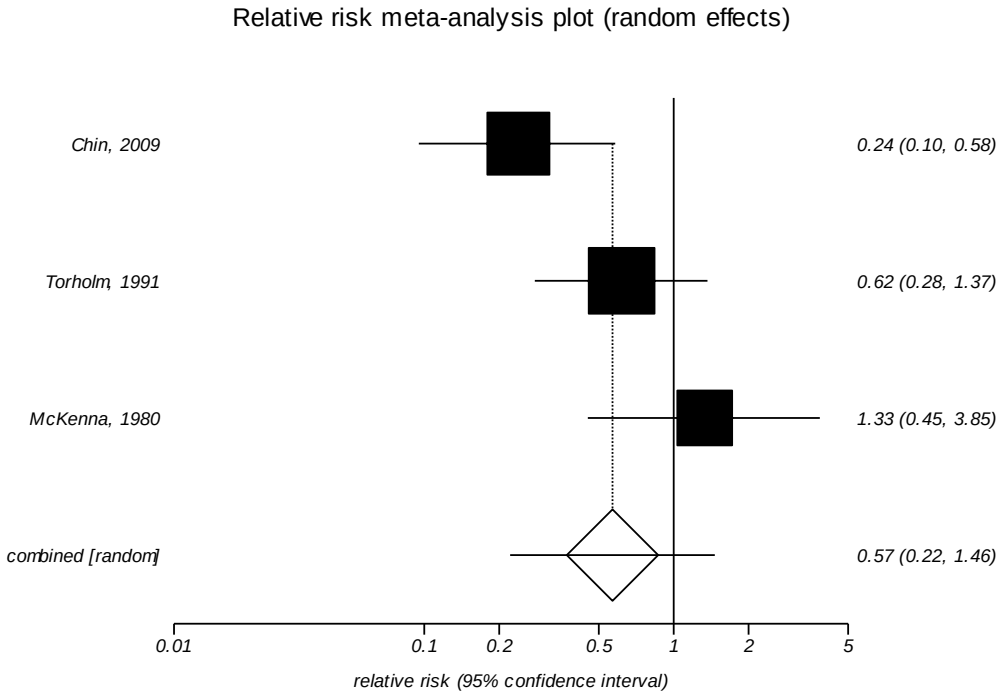
Figure 39. Impact of pharmacologic prophylaxis versus no prophylaxis on distal deep vein thrombosis in patients who had major orthopedic surgery



I^2: 15.4 percent
Egger's p-value: 0.666

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

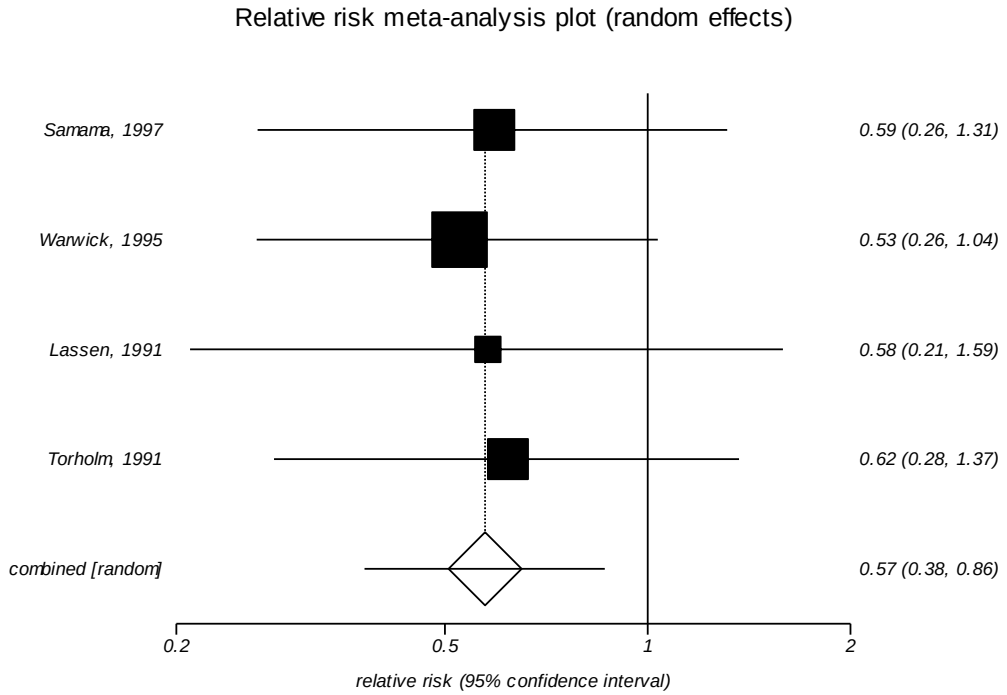
Figure 40. Impact of pharmacologic prophylaxis versus no prophylaxis on distal deep vein thrombosis in patients who had major orthopedic surgery limited to truly no prophylaxis trials



I^2: 66.8 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

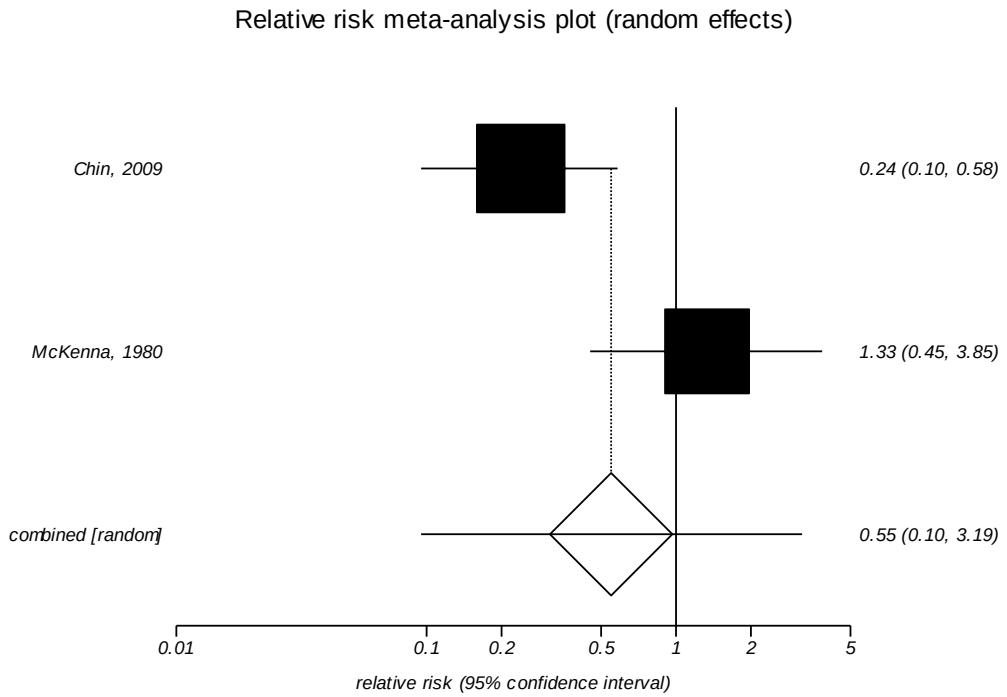
Figure 41. Impact of pharmacologic prophylaxis versus no prophylaxis on distal deep vein thrombosis in patients who had major orthopedic surgery limited to total hip replacement



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

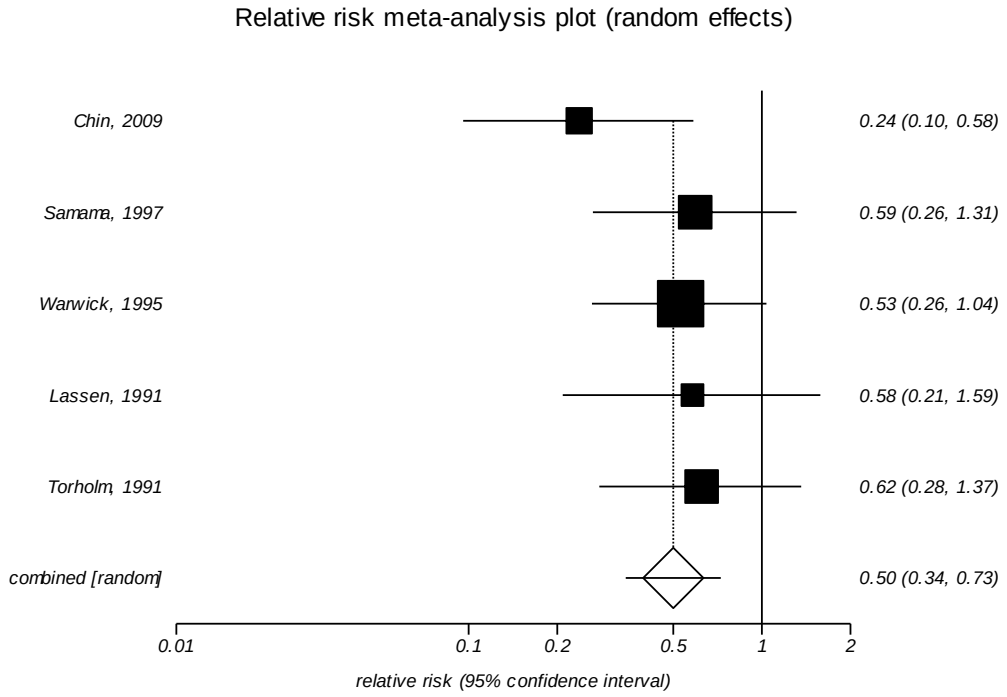
Figure 42. Impact of pharmacologic prophylaxis versus no prophylaxis on distal deep vein thrombosis in patients who had major orthopedic surgery limited to total knee replacement



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

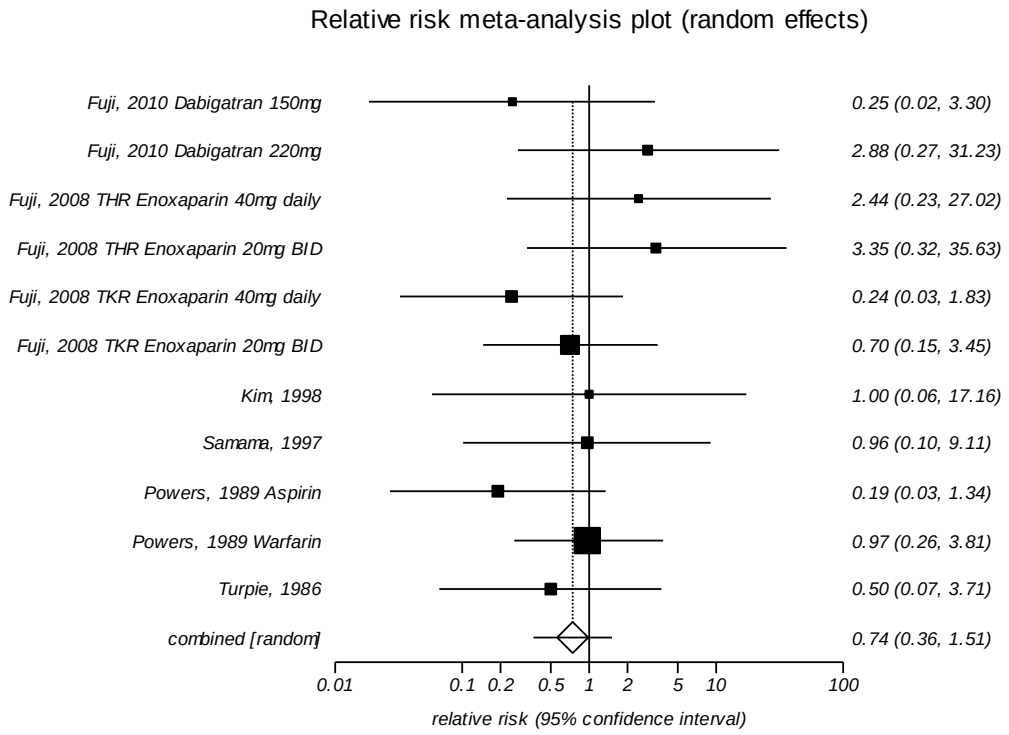
Figure 43. Impact of injectable low molecular weight heparins versus no prophylaxis on distal deep vein thrombosis in patients who had major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.615

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

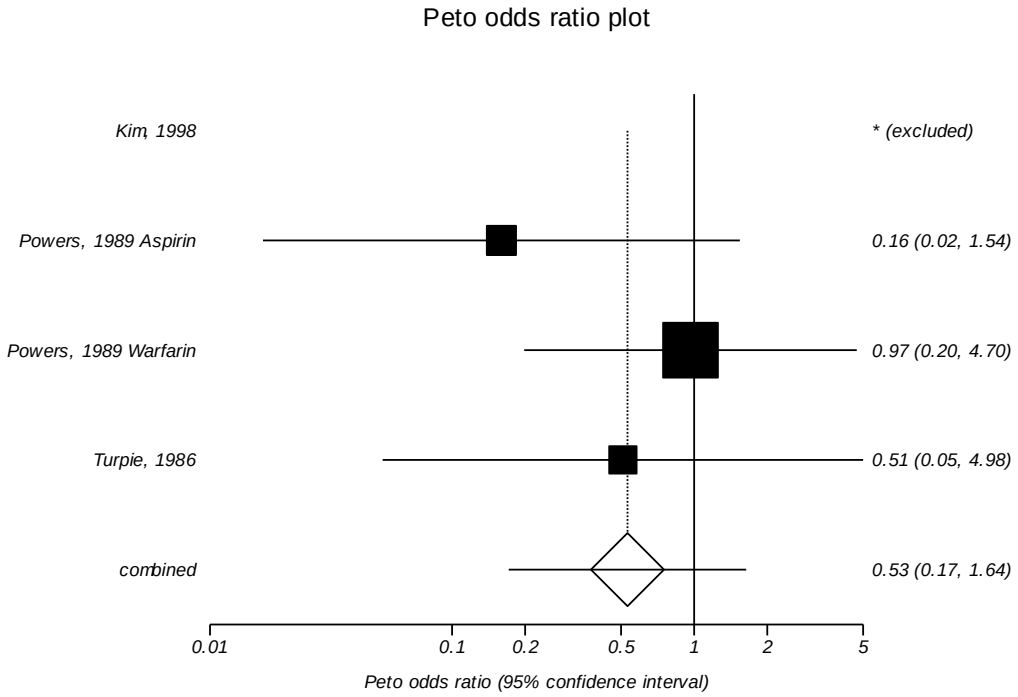
Figure 44. Impact of pharmacologic prophylaxis versus no prophylaxis on major bleeding in patients who had major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.707

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

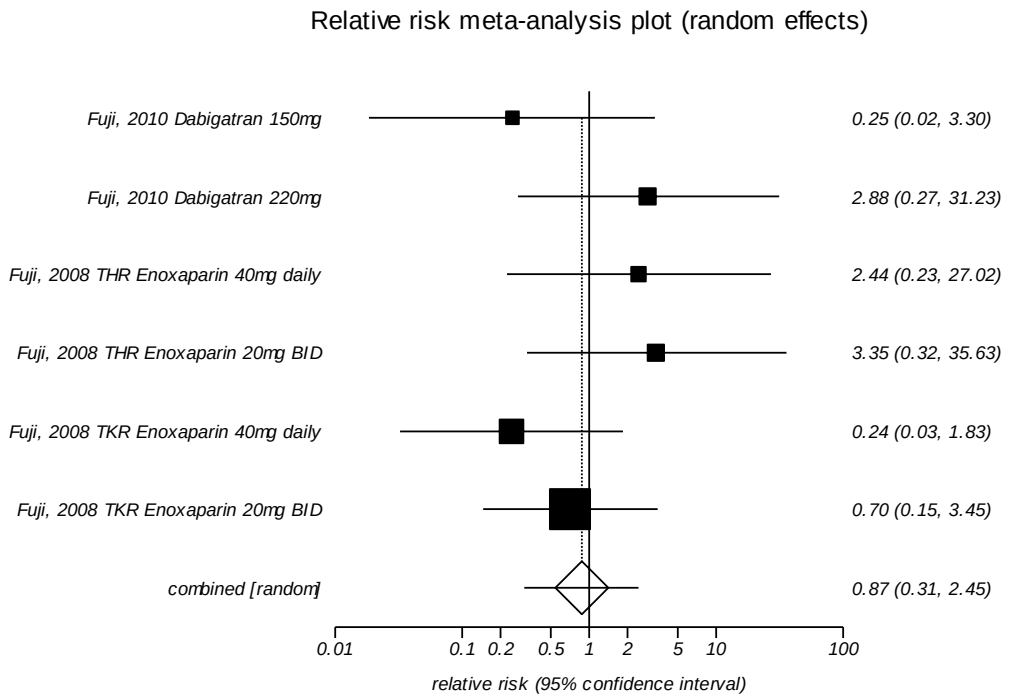
Figure 45. Impact of pharmacologic prophylaxis versus no prophylaxis on major bleeding in patients who had major orthopedic surgery limited to truly no prophylaxis trials



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

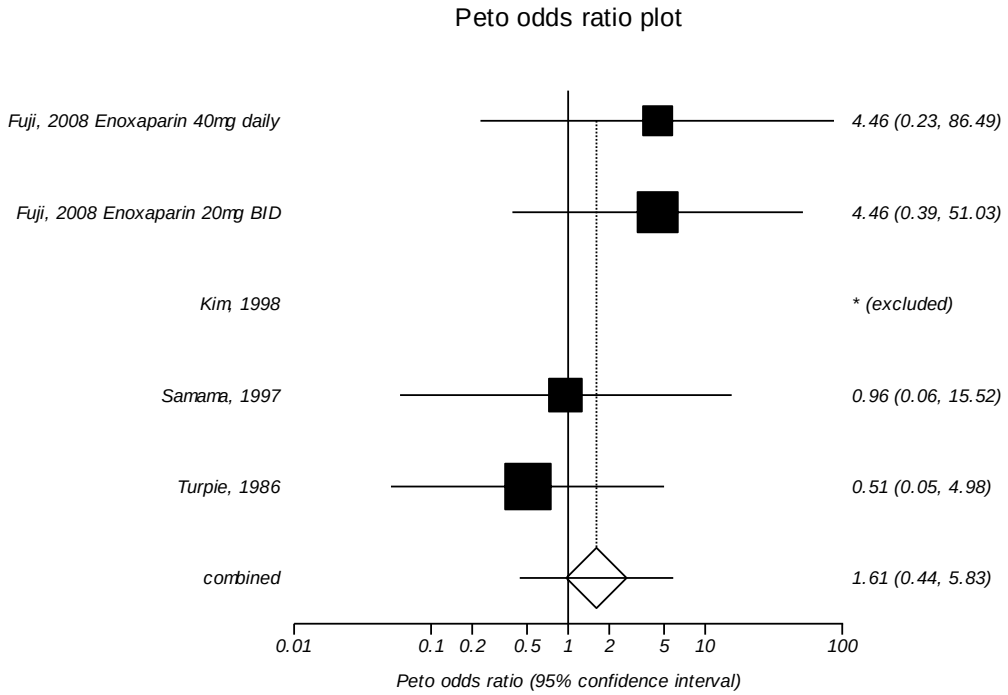
Figure 46. Impact of pharmacologic prophylaxis versus no prophylaxis on major bleeding in patients who had major orthopedic surgery limited to trials published from 2001-present



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

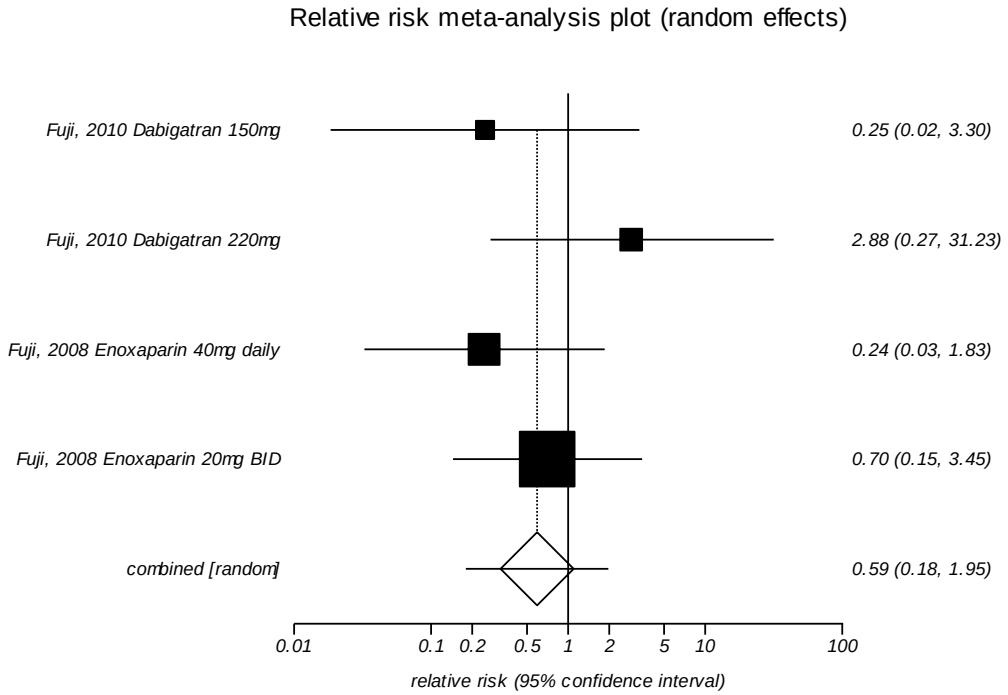
Figure 47. Impact of pharmacologic prophylaxis versus no prophylaxis on major bleeding in patients who had major orthopedic surgery limited to total hip replacement



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

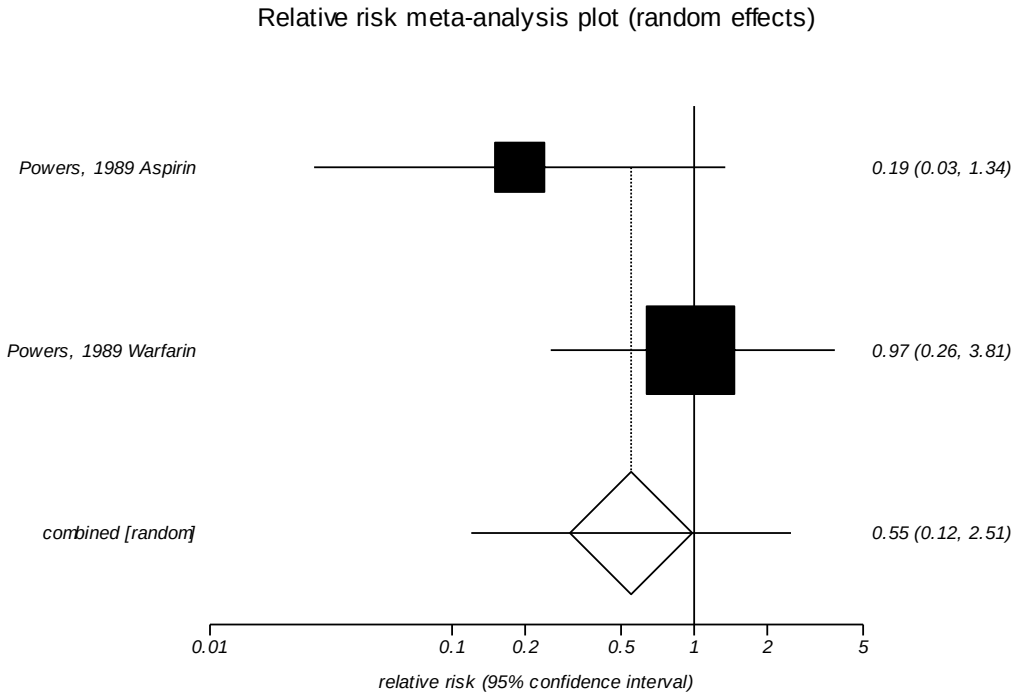
Figure 48. Impact of pharmacologic prophylaxis versus no prophylaxis on major bleeding in patients who major orthopedic surgery limited to total knee replacement



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

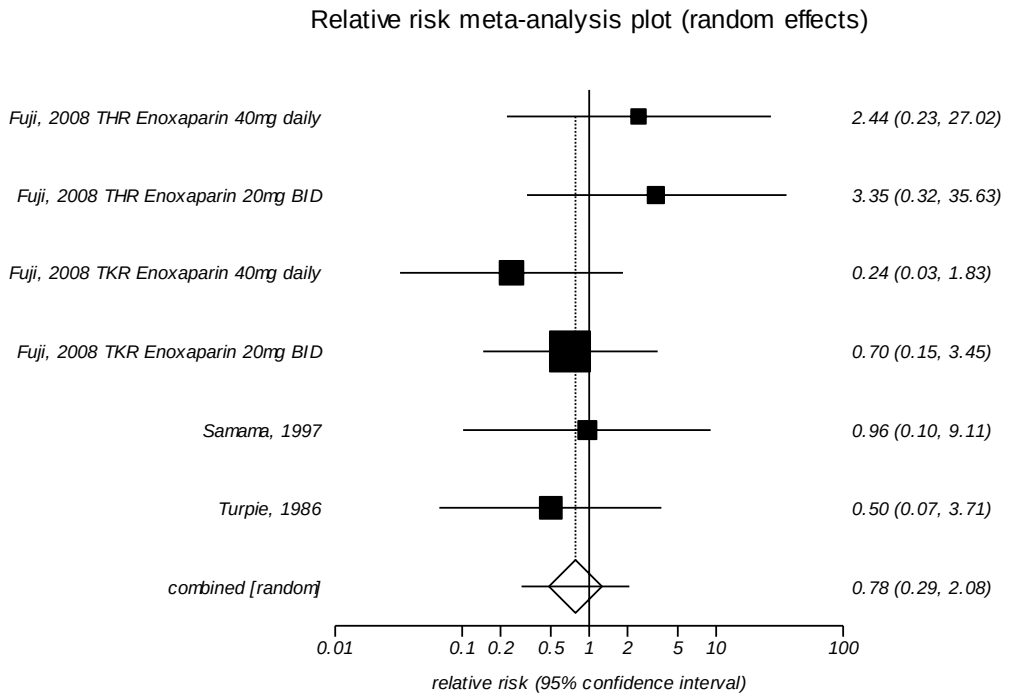
Figure 49. Impact of pharmacologic prophylaxis versus no prophylaxis on major bleeding in patients who had major orthopedic surgery limited to hip fracture surgery



I^2: too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

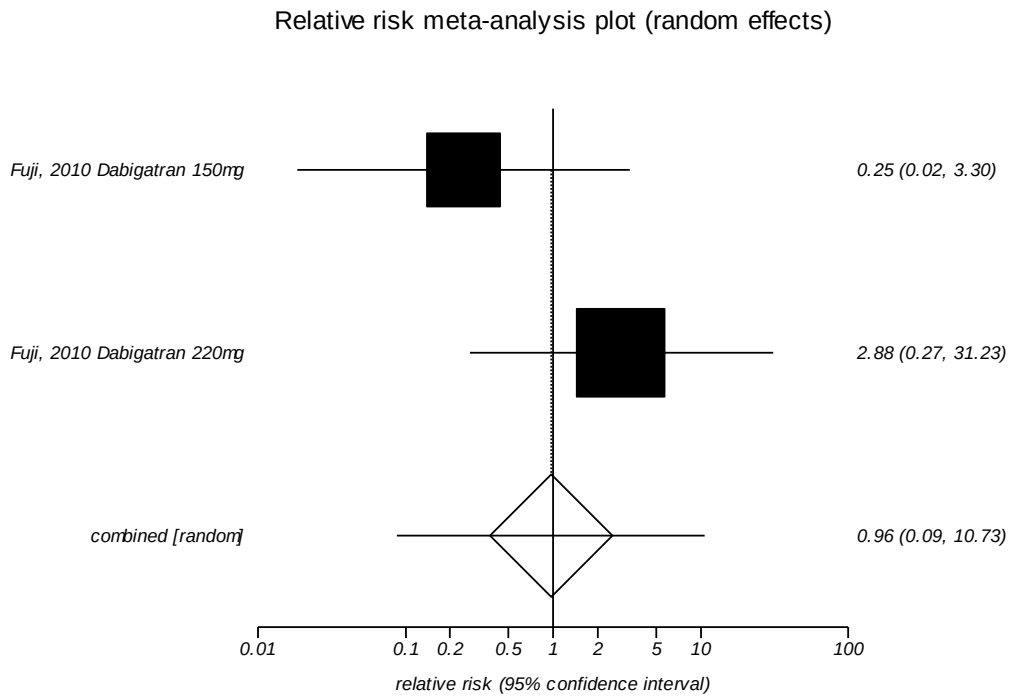
Figure 50. Impact of injectable low molecular weight heparins versus no prophylaxis on major bleeding in patients who had major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.275

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

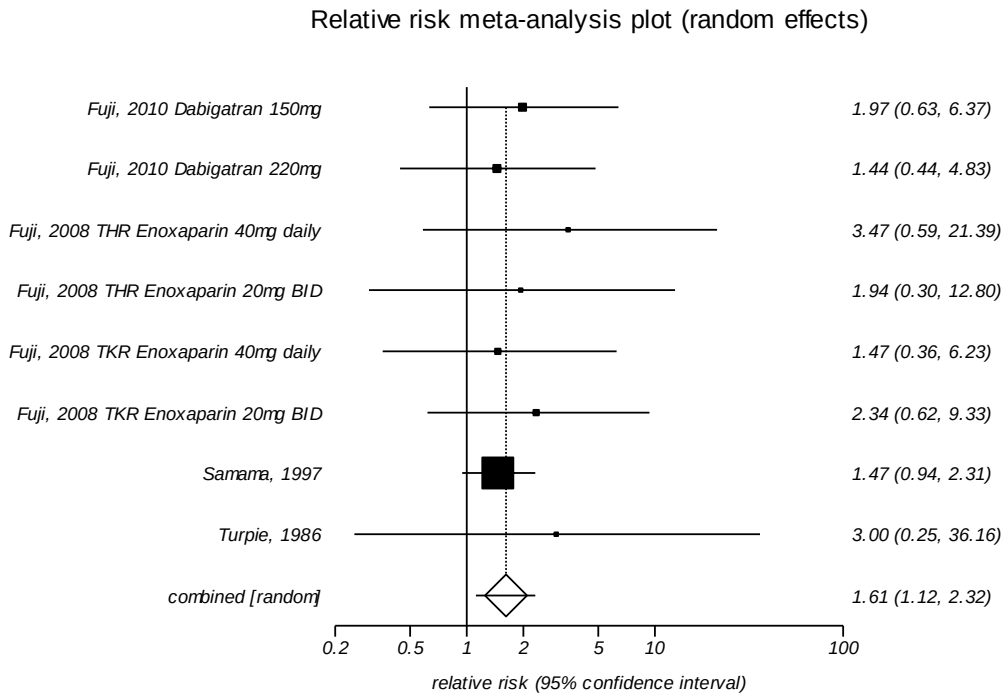
Figure 51. Impact of injectable or oral direct thrombin inhibitors versus no prophylaxis on major bleeding in patients who had major orthopedic surgery



I^2: too few strata
Egger's p-value: too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

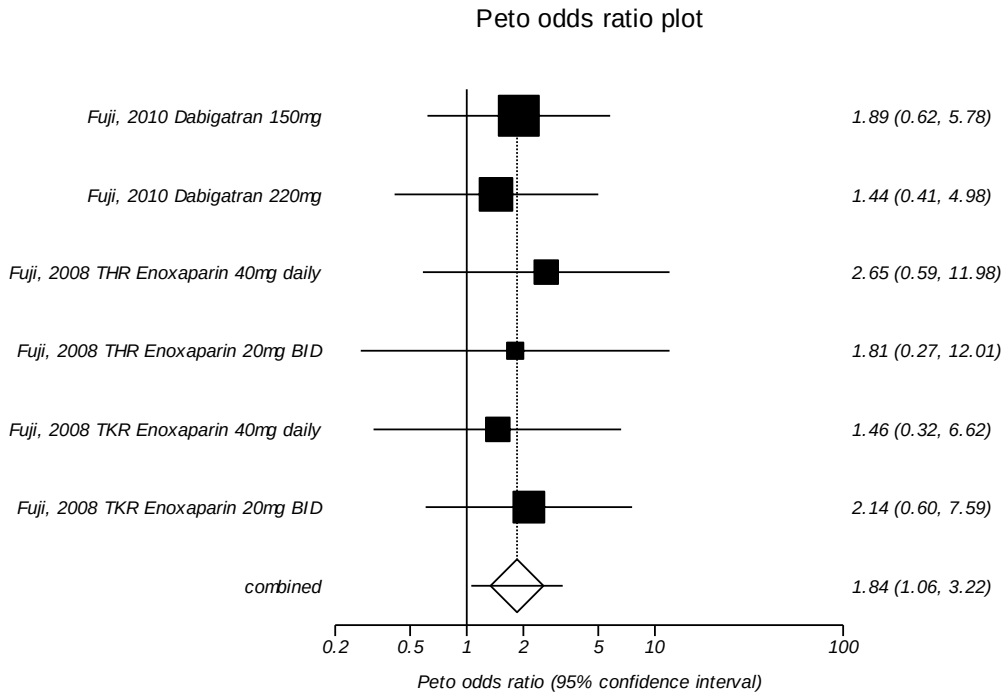
Figure 52. Impact of pharmacologic prophylaxis versus no prophylaxis on minor bleeding in patients who had major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.030

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

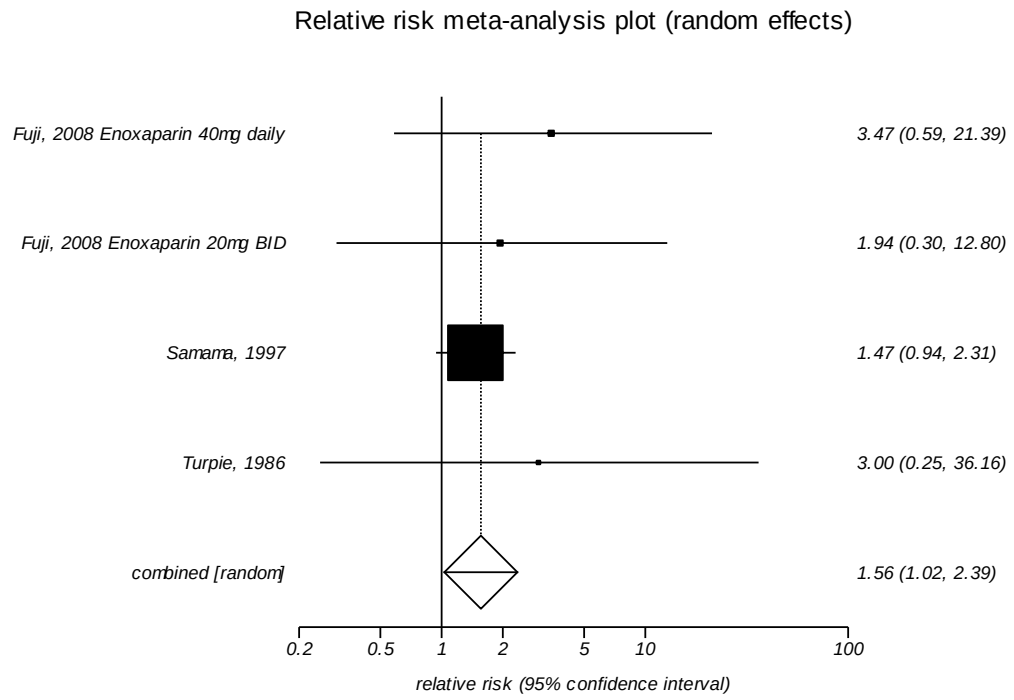
Figure 53. Impact of pharmacologic prophylaxis versus no prophylaxis on minor bleeding in patients who had major orthopedic surgery limited to trials published from 2001-present



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

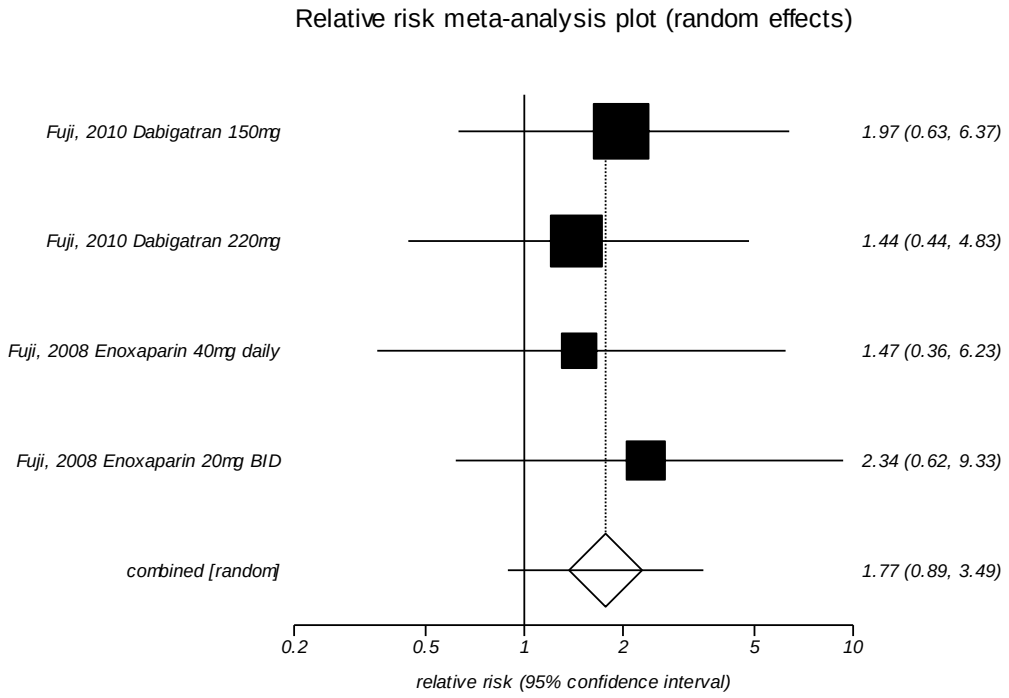
Figure 54. Impact of pharmacologic prophylaxis versus no prophylaxis on minor bleeding in patients who had major orthopedic surgery limited to total hip replacement



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

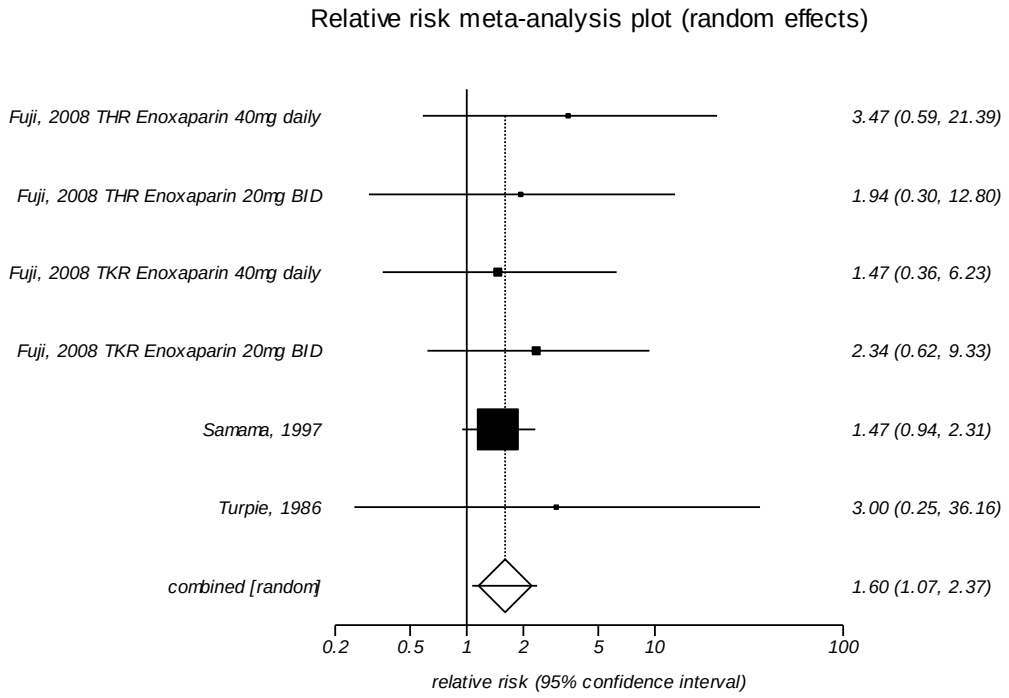
Figure 55. Impact of pharmacologic prophylaxis versus no prophylaxis on minor bleeding in patients who had major orthopedic surgery limited to total knee replacement



I^2: 0 percent
Egger's p-value: 0.974

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

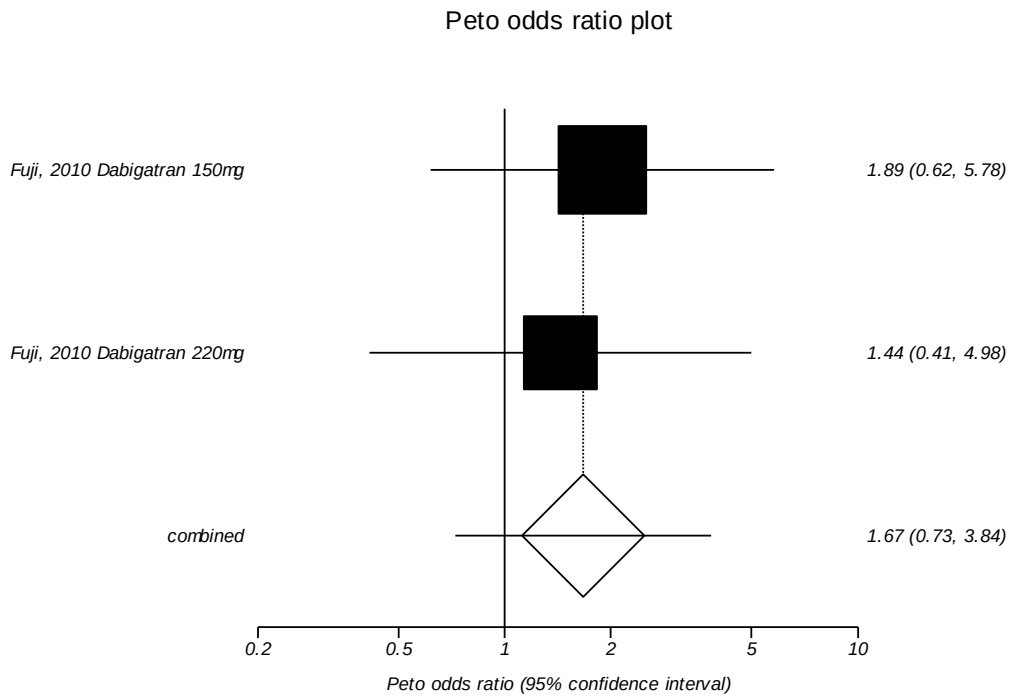
Figure 56. Impact of injectable low molecular weight heparins versus no prophylaxis on minor bleeding in patients who had major orthopedic surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

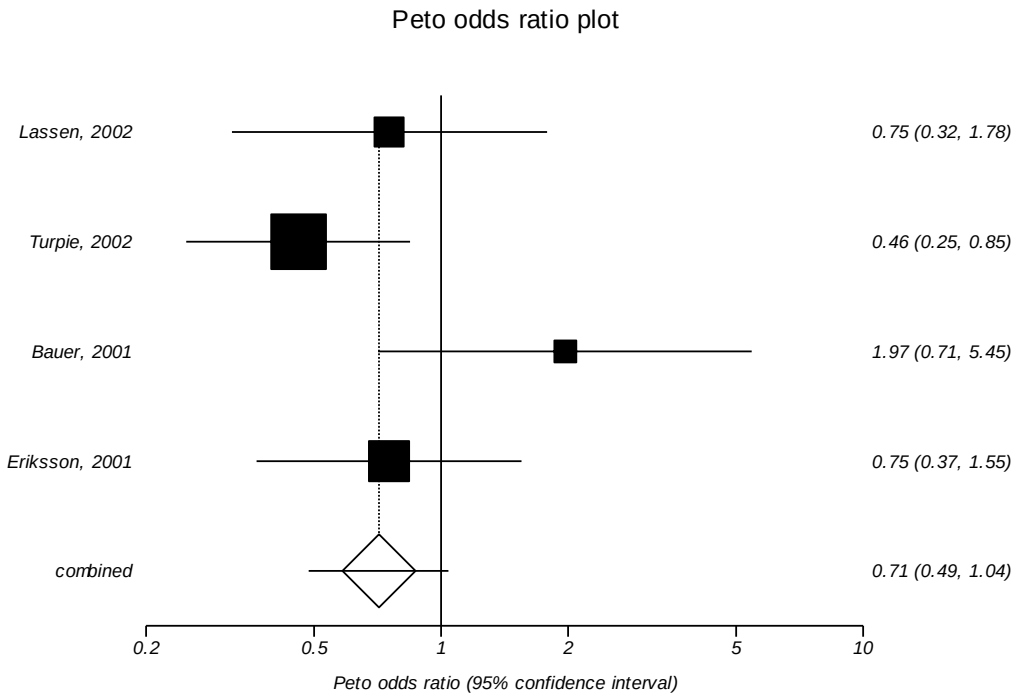
Figure 57. Impact of injectable or oral direct thrombin inhibitors versus no prophylaxis on minor bleeding in patients who had major orthopedic surgery



I^2: too few strata
Egger's p-value: too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

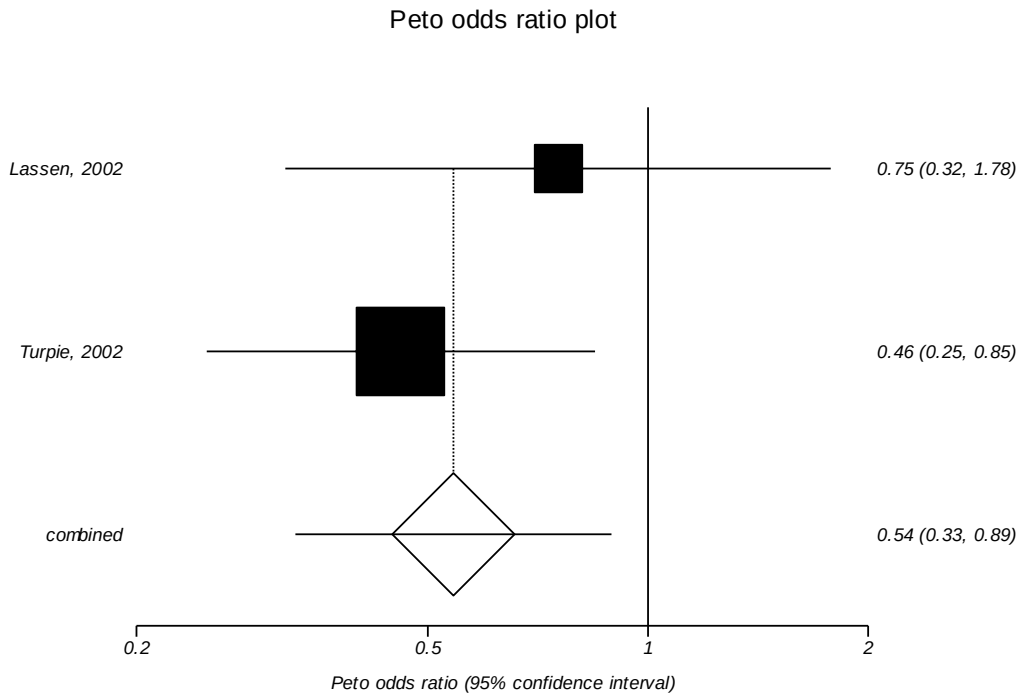
Figure 58. Impact of injectable low molecular weight heparin versus injectable or oral factor Xa inhibitors on symptomatic objectively confirmed venous thromboembolism in patients undergoing major orthopedic surgery (same as analysis limited to trials published from 2001 to the present)



I^2: 48.6 percent
Egger's p-value: 0.061

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

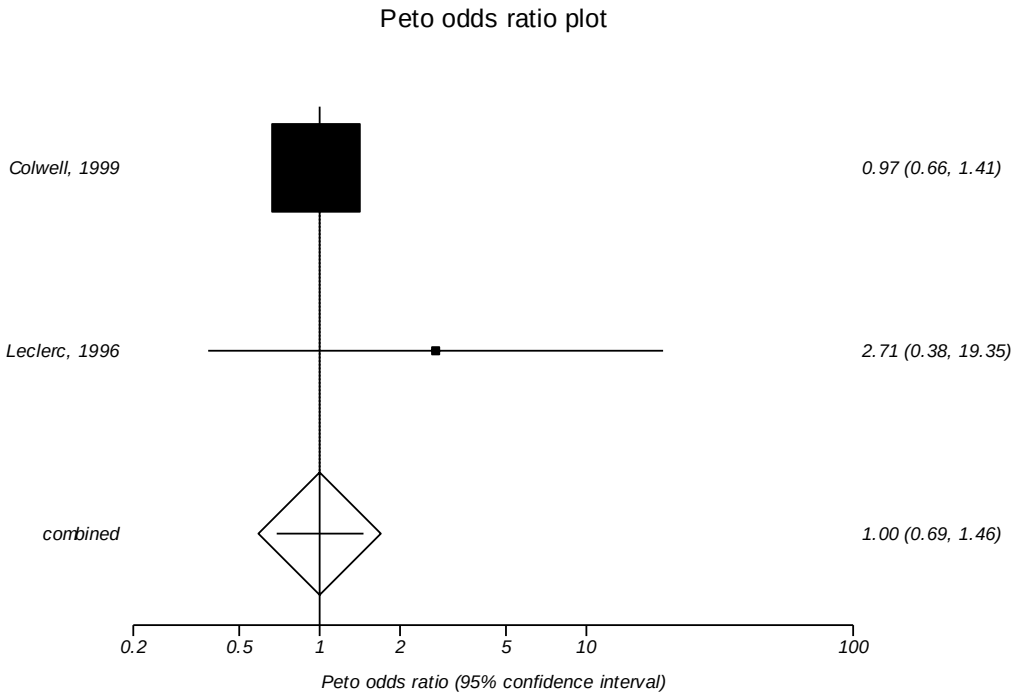
Figure 59. Impact of injectable low molecular weight heparin versus injectable or oral factor Xa inhibitors on symptomatic objectively confirmed venous thromboembolism in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

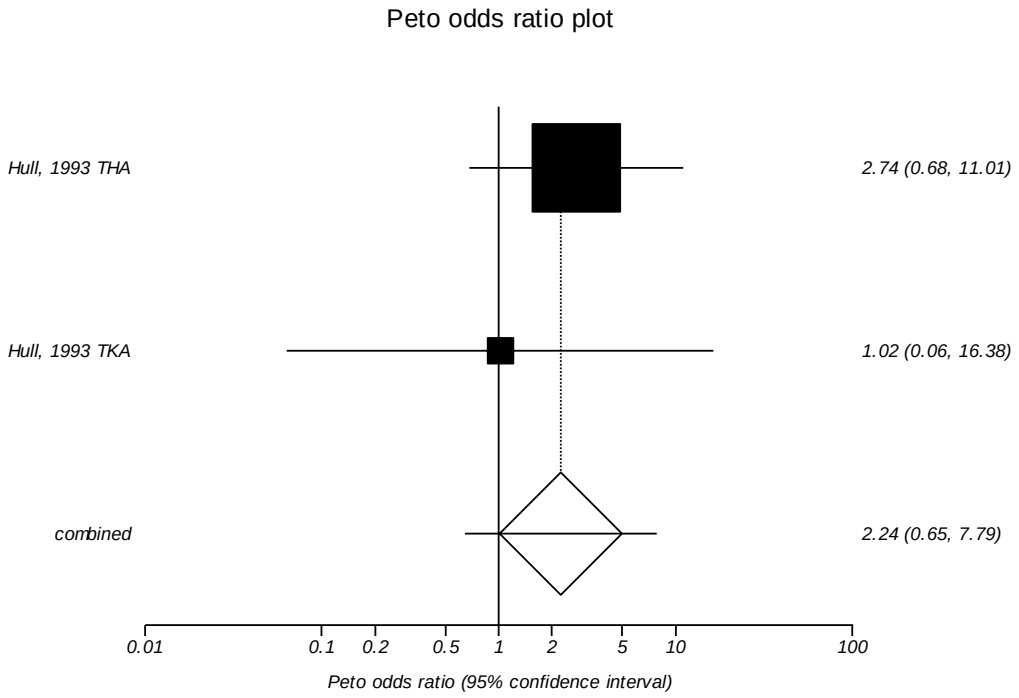
Figure 60. Impact of injectable low molecular weight heparin prophylaxis versus oral vitamin K antagonist prophylaxis on symptomatic objectively confirmed venous thromboembolism in patients undergoing major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

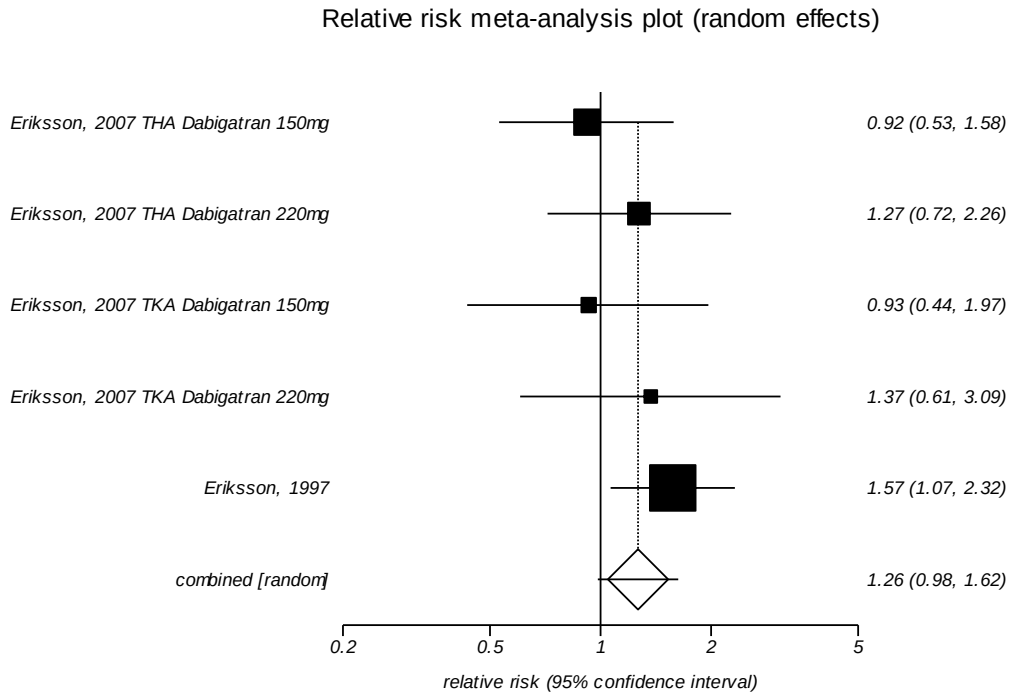
Figure 61. Impact of injectable low molecular weight heparin versus oral vitamin K antagonists on symptomatic objectively confirmed venous thromboembolism during the postdischarge period in patients who had major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

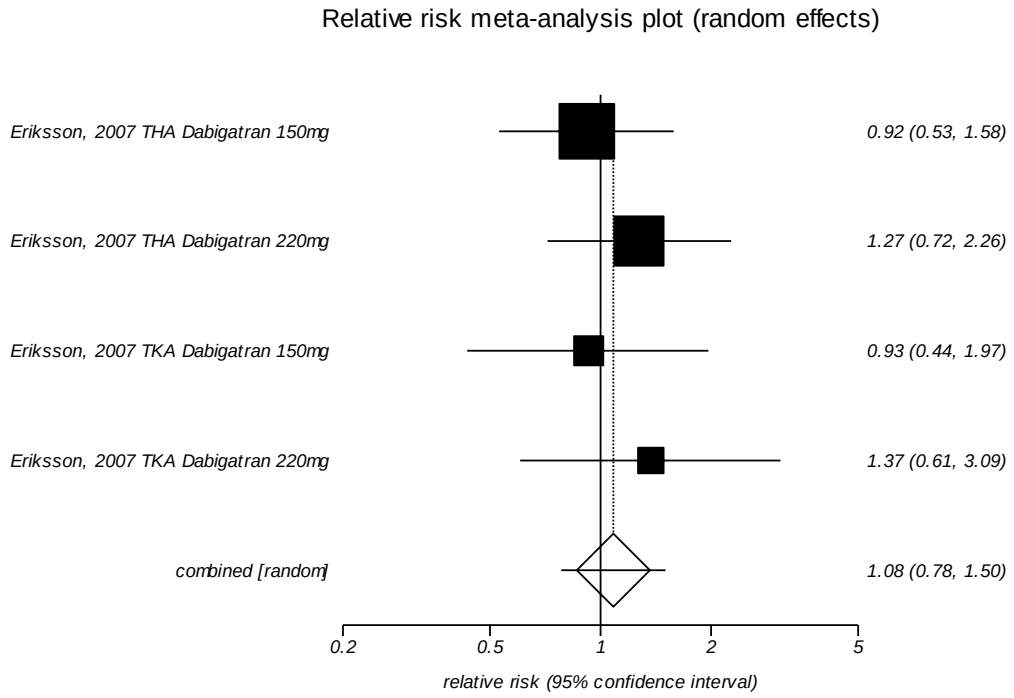
Figure 62. Impact of injectable low molecular weight heparin versus oral or injectable direct thrombin inhibitors on major venous thromboembolism in patients undergoing major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.326

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

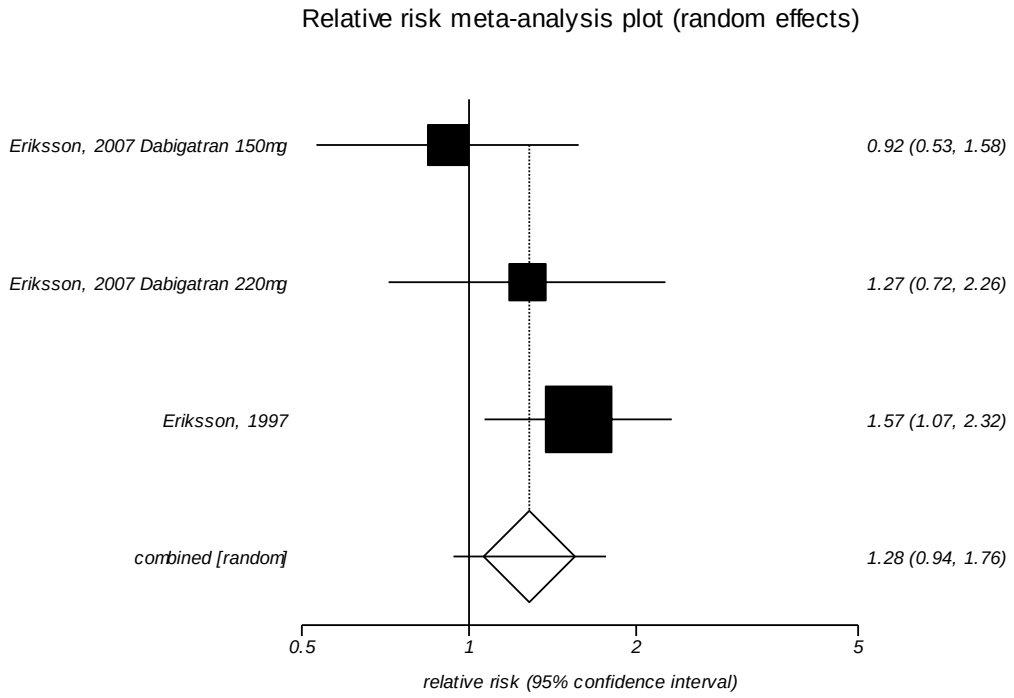
Figure 63. Impact of injectable low molecular weight heparin versus oral or injectable direct thrombin inhibitors on major venous thromboembolism in patients undergoing major orthopedic surgery limited to trials published from 2001 to the present



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

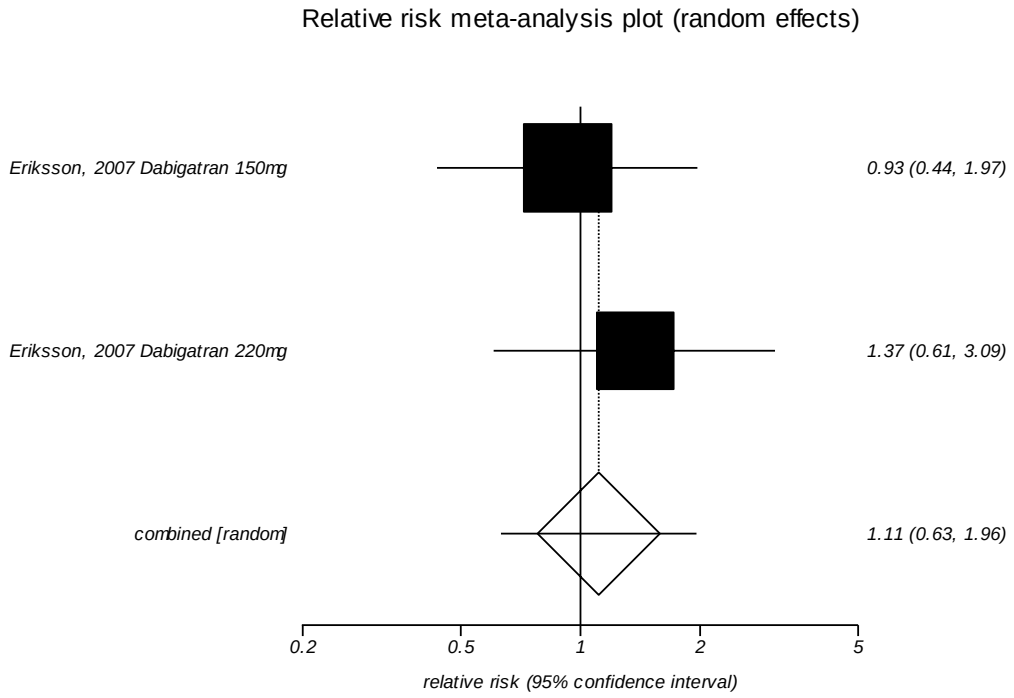
Figure 64. Impact of injectable low molecular weight heparin versus oral or injectable direct thrombin inhibitors on major venous thromboembolism in patients undergoing major orthopedic surgery limited to total hip replacement



I^2: 18.6 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

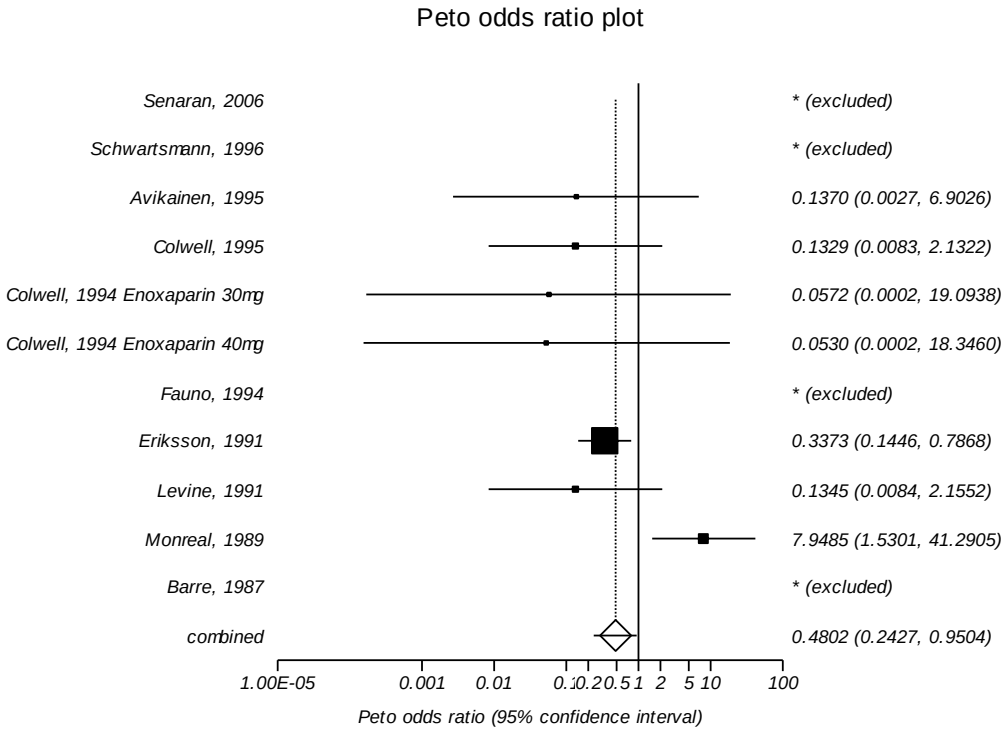
Figure 65. Impact of injectable low molecular weight heparin versus oral or injectable direct thrombin inhibitors on major venous thromboembolism in patients undergoing major orthopedic surgery limited to total knee replacement



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

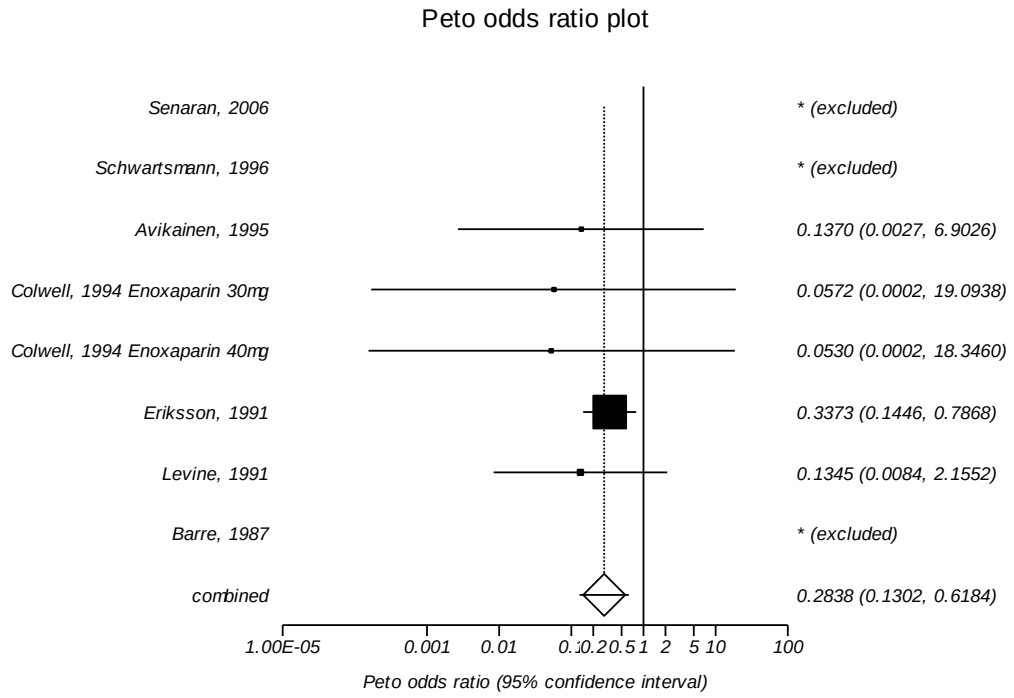
Figure 66. Impact of injectable low molecular weight heparin versus injectable unfractionated heparin on pulmonary embolism in patients undergoing major orthopedic surgery



I^2: 59.7
Egger's p-value: 0.629

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

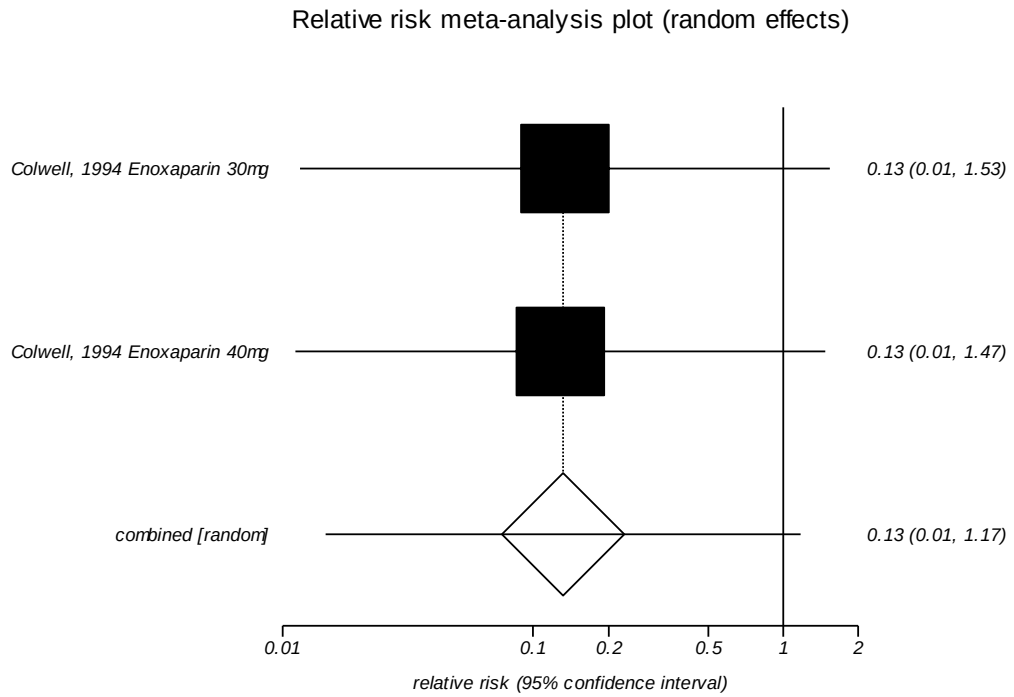
Figure 67. Impact of injectable low molecular weight heparin versus injectable unfractionated heparin on pulmonary embolism in patients undergoing major orthopedic surgery limited to total hip replacement



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

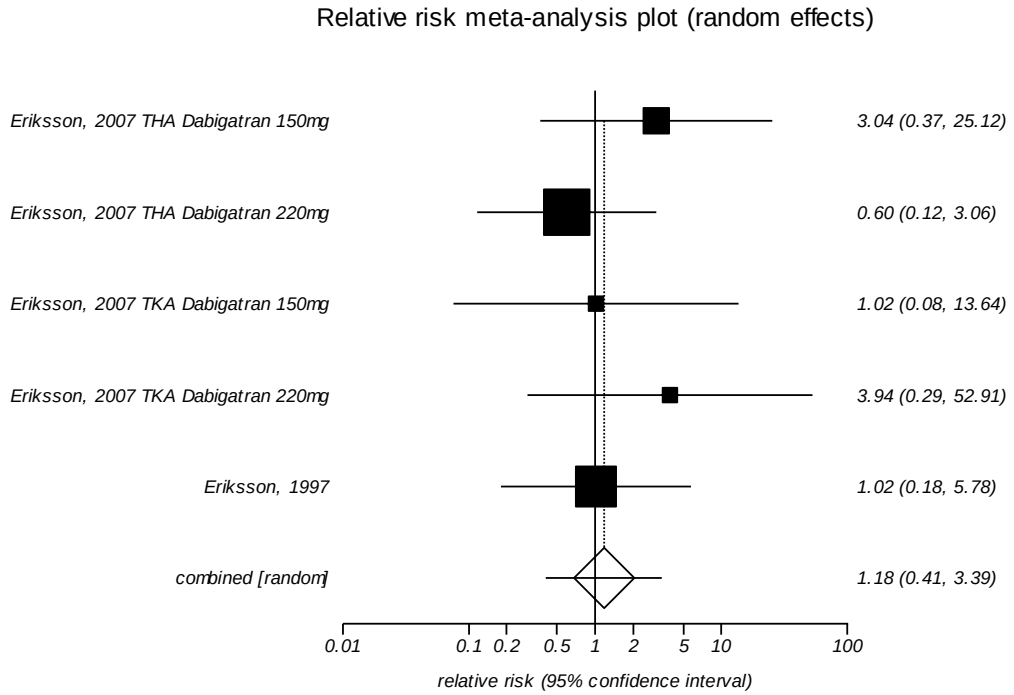
Figure 68. Impact of injectable low molecular weight heparin versus injectable unfractionated heparin on pulmonary embolism during the postdischarge period in patients who had total hip replacement surgery (same as analysis of nonfatal pulmonary embolism during the post discharge period)



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

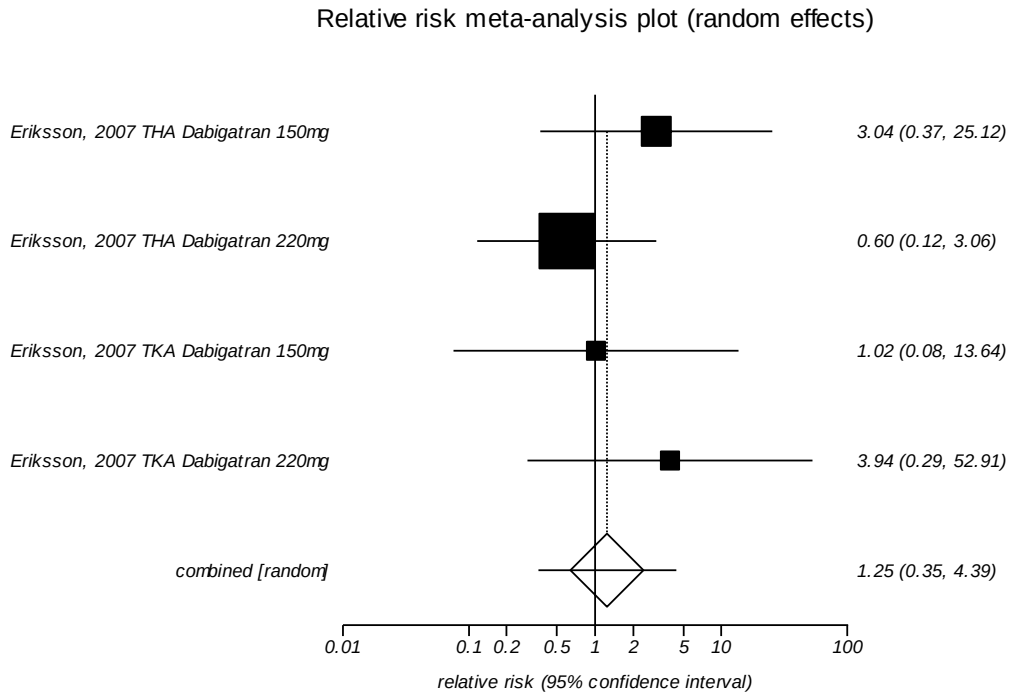
Figure 69. Impact of injectable low molecular weight heparin versus oral or injectable direct thrombin inhibitors on pulmonary embolism in patients undergoing major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.208

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

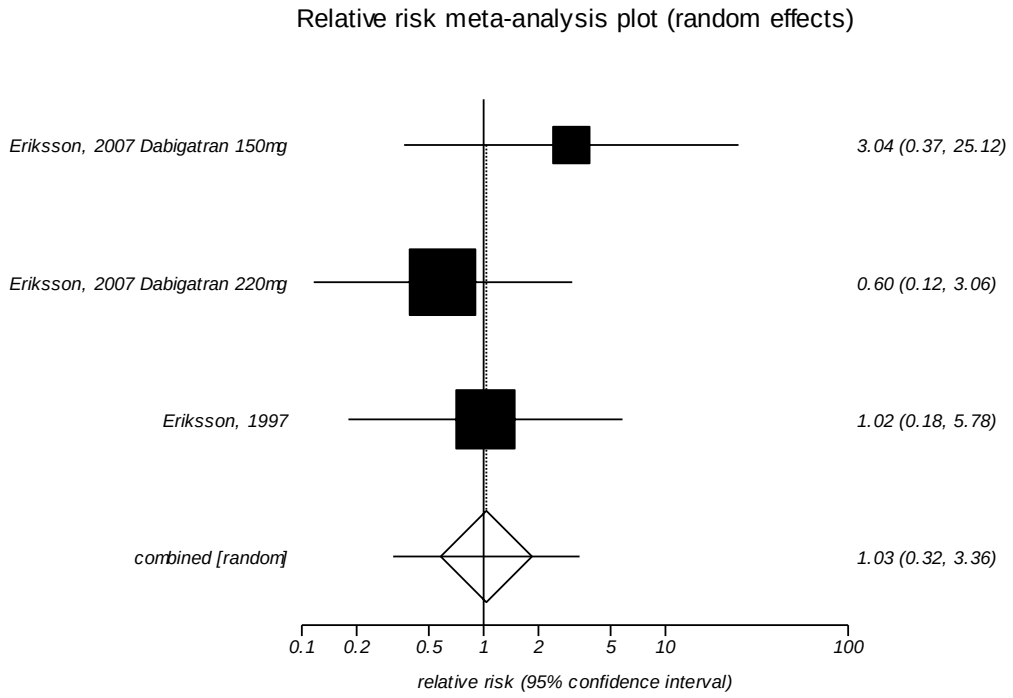
Figure 70. Impact of injectable low molecular weight heparin versus oral or injectable direct thrombin inhibitors on pulmonary embolism in patients undergoing major orthopedic surgery limited to trials published from 2001 to the present



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

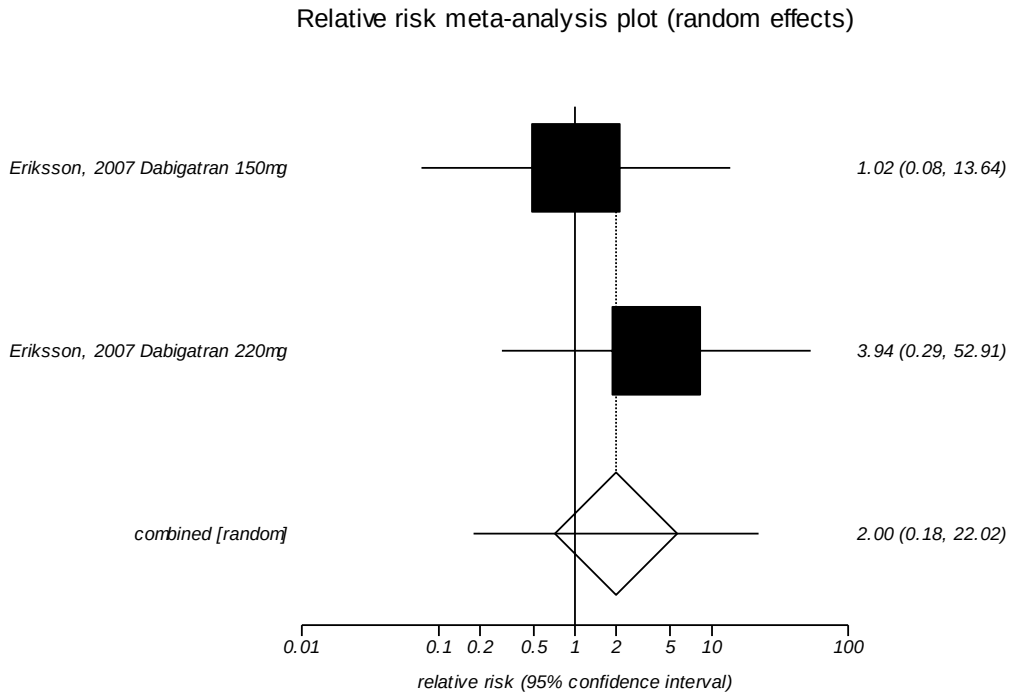
Figure 71. Impact of injectable low molecular weight heparin versus oral or injectable direct thrombin inhibitors on pulmonary embolism in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

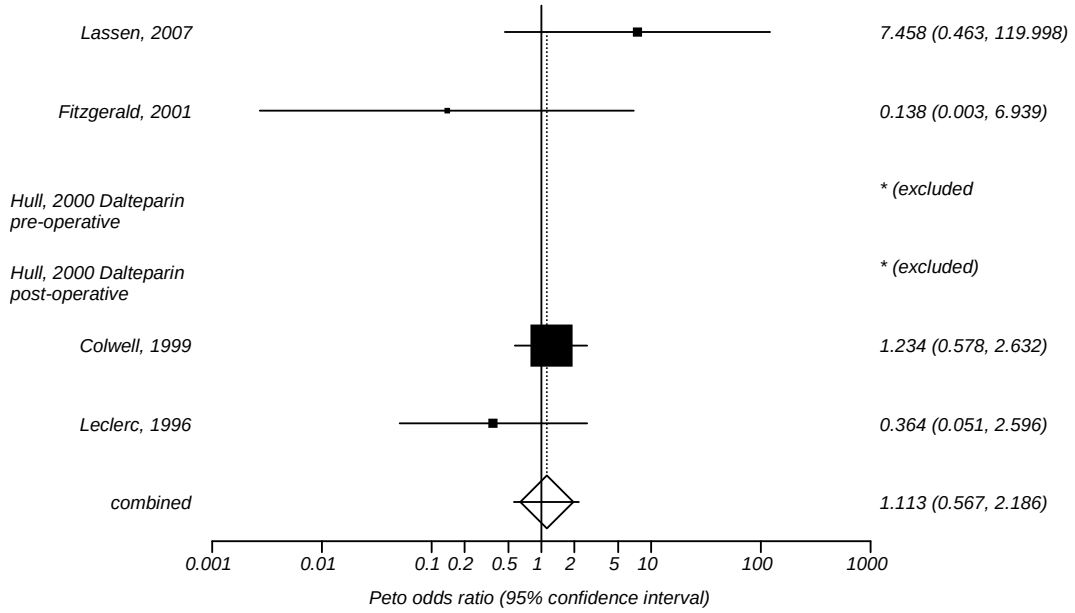
Figure 72. Impact of injectable low molecular weight heparin versus oral or injectable direct thrombin inhibitors on pulmonary embolism in patients undergoing major orthopedic surgery limited to total knee replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

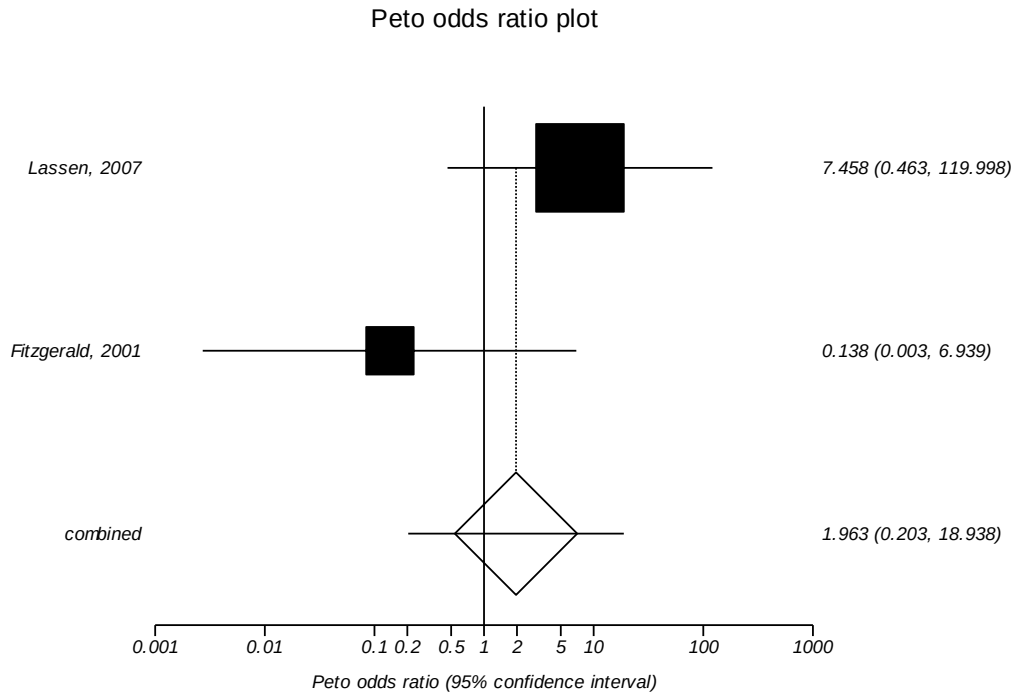
Figure 73. Impact of injectable low molecular weight heparin versus oral vitamin k antagonists on pulmonary embolism in patients undergoing major orthopedic surgery



I^2: 28.7 percent
Egger's p-value: 0.762

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

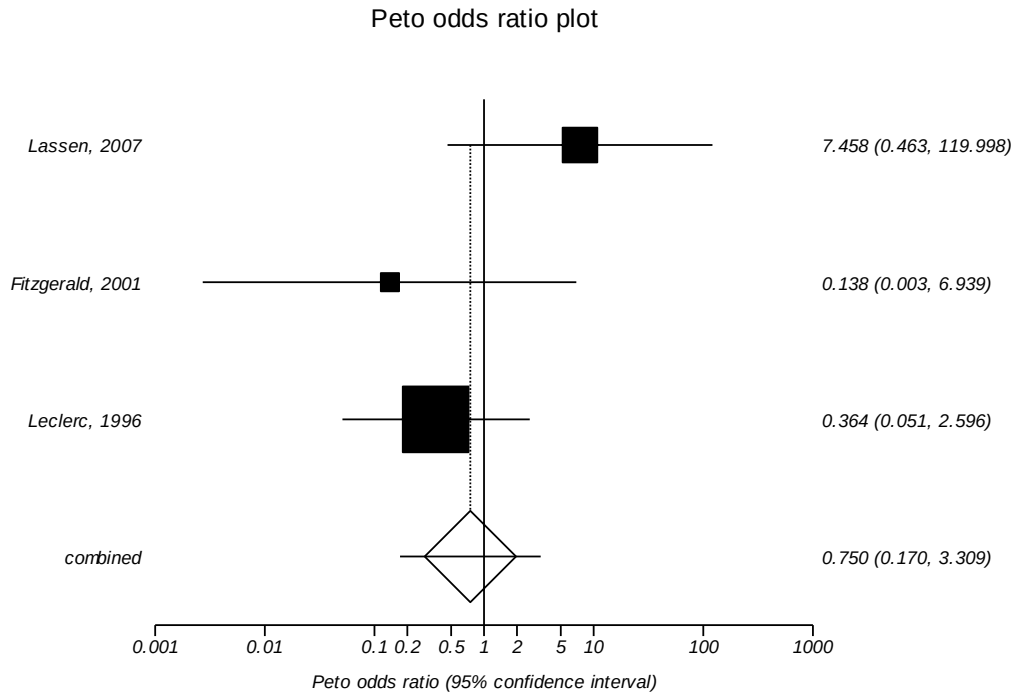
Figure 74. Impact of injectable low molecular weight heparin versus oral vitamin K antagonists on pulmonary embolism in patients undergoing major orthopedic surgery limited to trials published from 2001 to the present



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

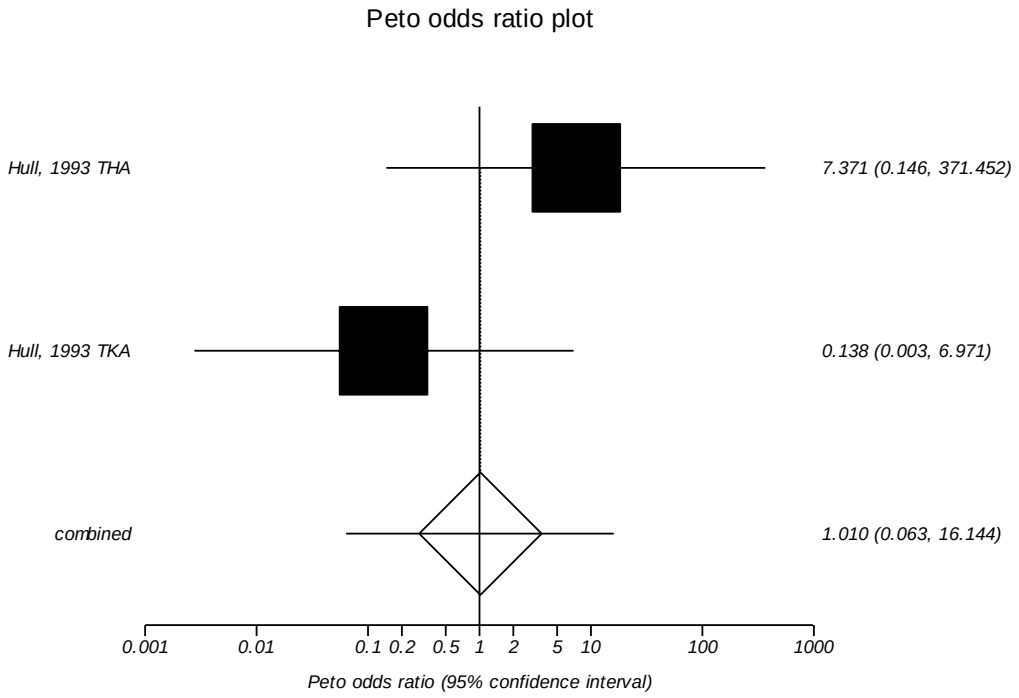
Figure 75. Impact of injectable low molecular weight heparin versus oral vitamin K antagonists on pulmonary embolism in patients undergoing major orthopedic surgery limited total knee replacement surgery



I^2: 48.2 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

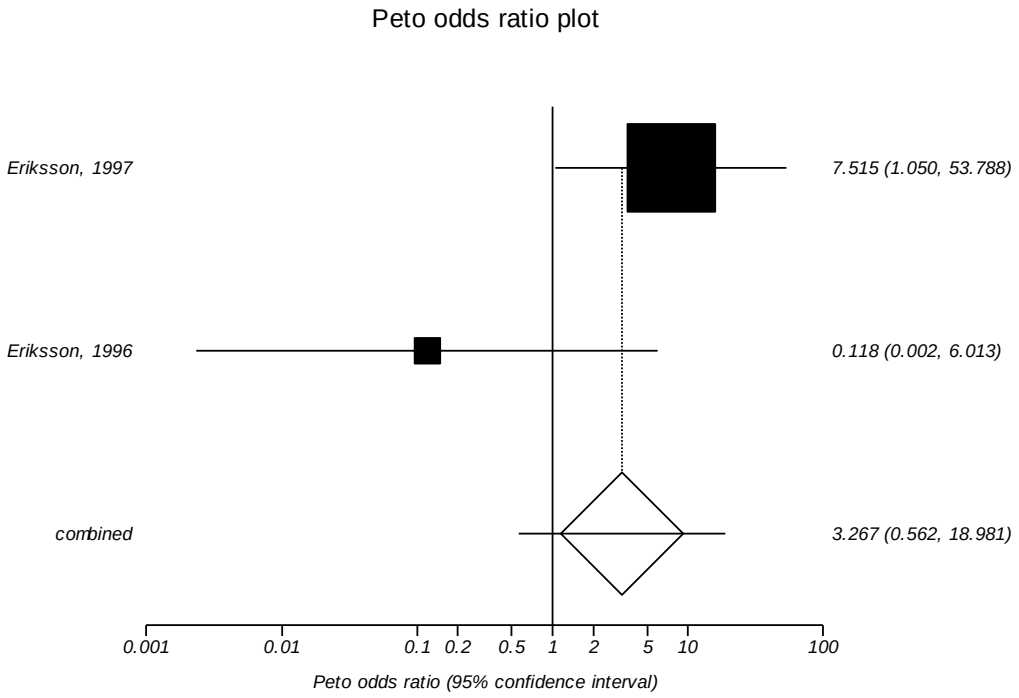
Figure 76. Impact of injectable low molecular weight heparin versus oral vitamin K antagonists on pulmonary embolism during the postdischarge period in patients who had major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

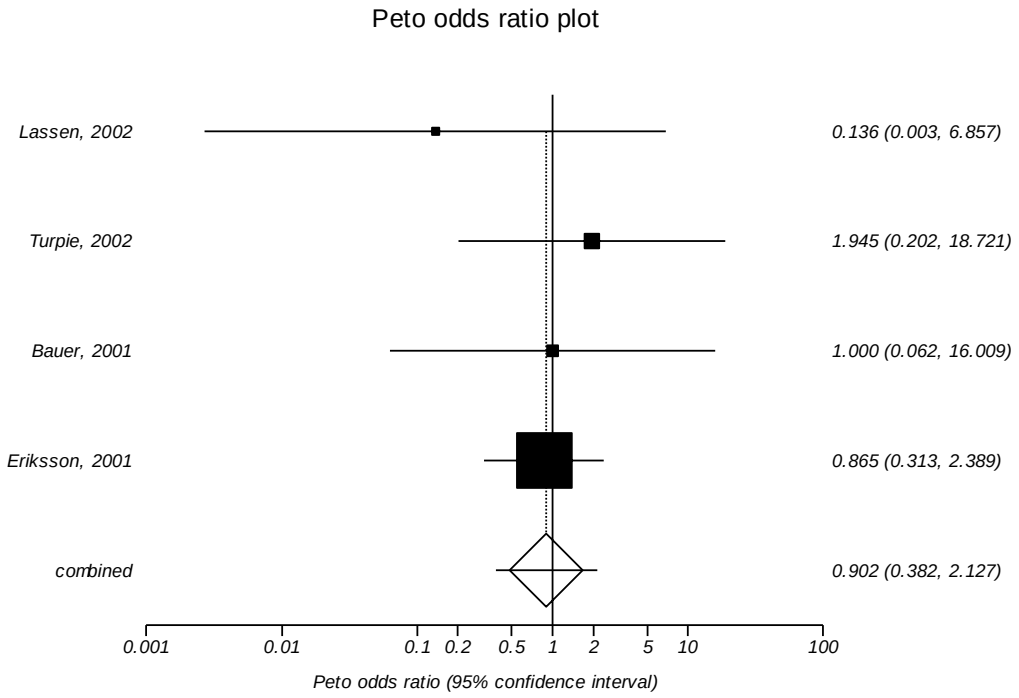
Figure 77. Impact of injectable unfractionated heparin versus oral or injectable direct thrombin inhibitors on pulmonary embolism in patients undergoing major orthopedic surgery (same as limited to total hip replacement surgery)



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

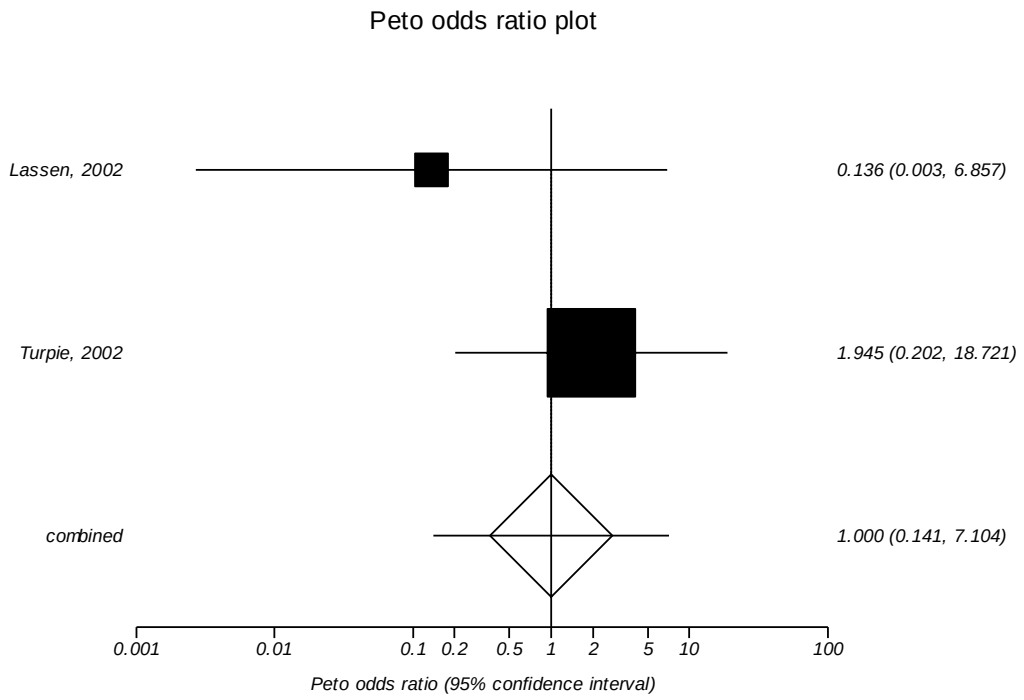
Figure 78. Impact of injectable low molecular weight heparin versus injectable or oral factor Xa inhibitors on fatal pulmonary embolism in patients undergoing major orthopedic surgery (Same as analysis limited to trials published from 2001-present)



I^2: 0 percent
Egger's p-value: 0.744

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

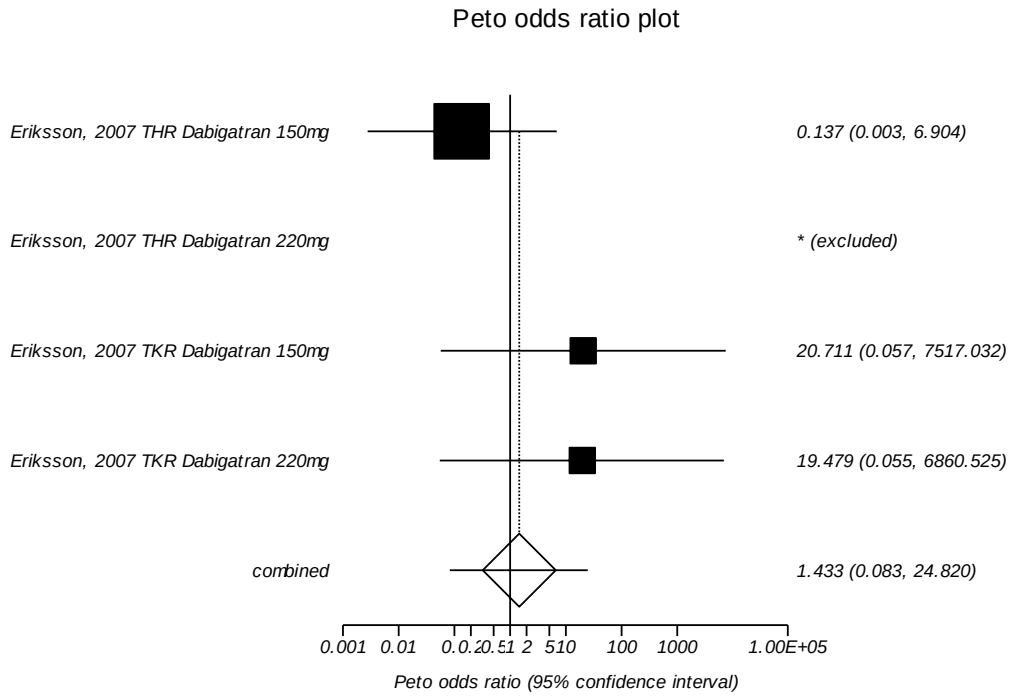
Figure 79. Impact of injectable low molecular weight heparin versus injectable or oral factor Xa inhibitors on fatal pulmonary embolism in patients undergoing major orthopedic surgery limited to total hip replacement



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

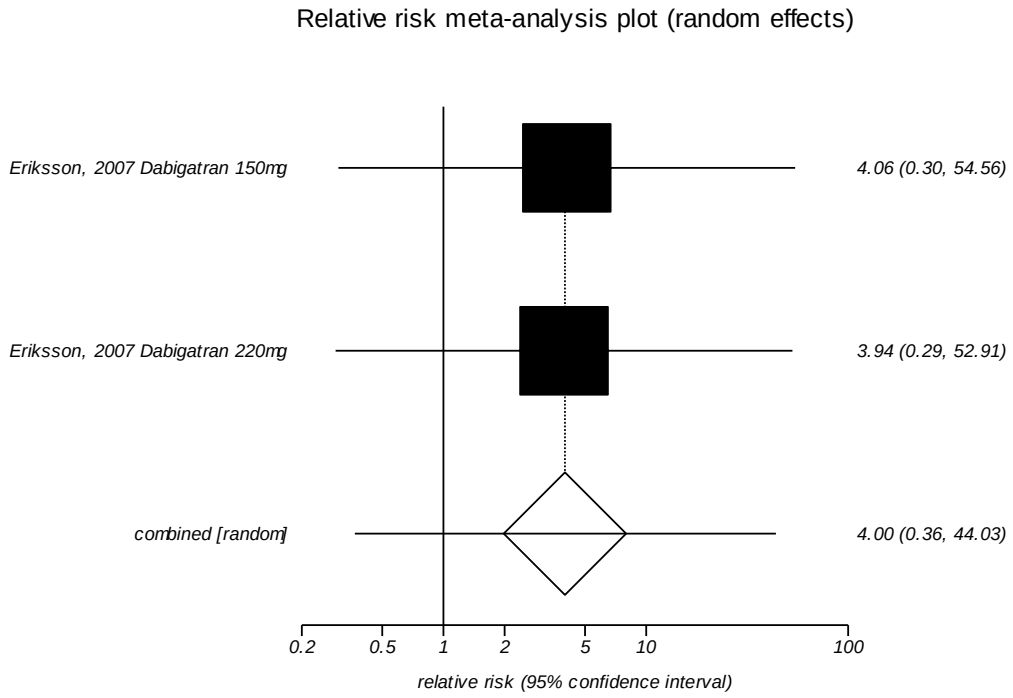
Figure 80. Impact of injectable low molecular weight heparin versus injectable or oral direct thrombin inhibitors on fatal pulmonary embolism in patients undergoing major orthopedic surgery (Same as analysis limited to trials published from 2001-present)



I^2: 31.7 percent
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

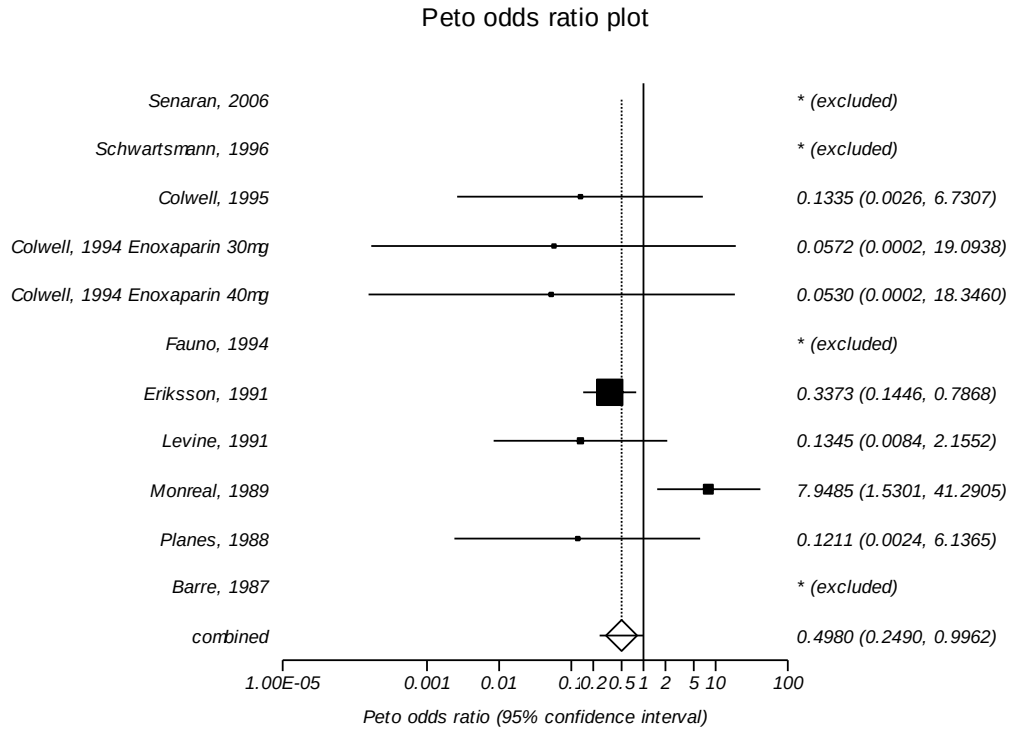
Figure 81. Impact of injectable low molecular weight heparin versus injectable or oral direct thrombin inhibitors on fatal pulmonary embolism in patients undergoing major orthopedic surgery limited to total knee replacement



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

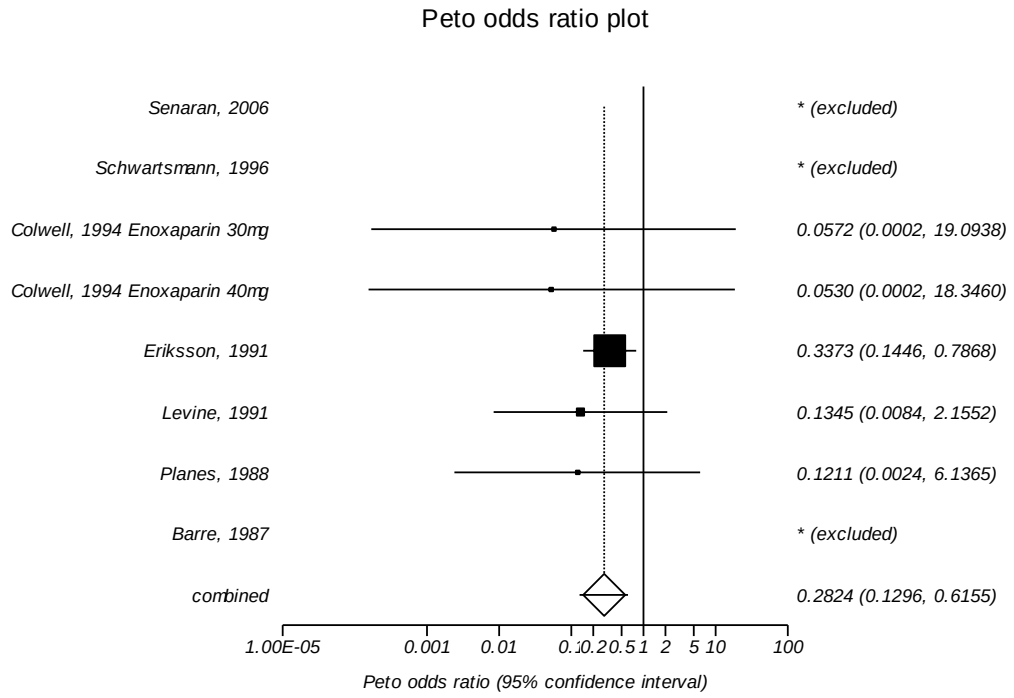
Figure 82. Impact of injectable low molecular weight heparin versus injectable unfractionated heparin on nonfatal pulmonary embolism in patients undergoing major orthopedic surgery



I^2: 58.8 percent
Egger's p-value: 0.634

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

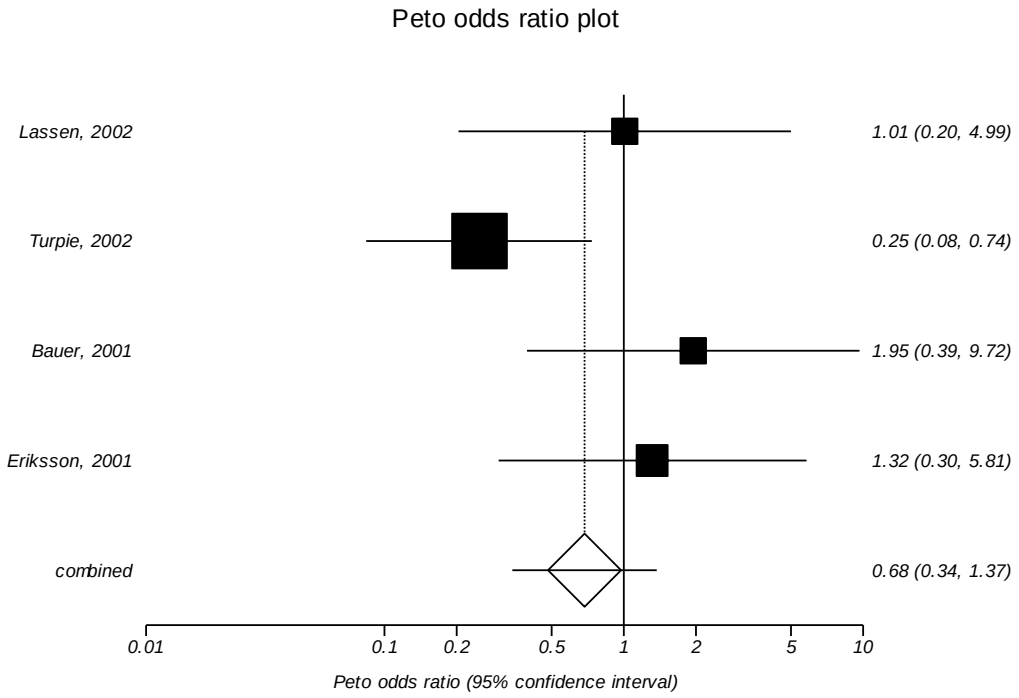
Figure 83. Impact of injectable low molecular weight heparin versus injectable unfractionated heparin on nonfatal pulmonary embolism in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

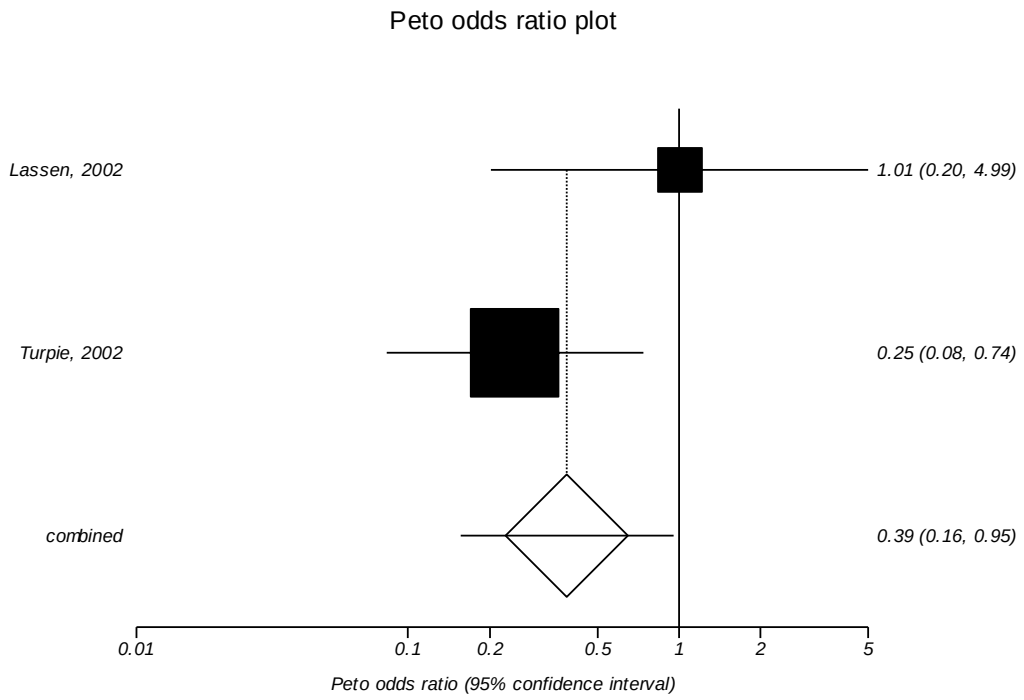
Figure 84. Impact of injectable low molecular weight heparin versus injectable or oral factor Xa inhibitors on nonfatal pulmonary embolism in patients undergoing major orthopedic surgery (same as analysis limited to trials published from 2001-present)



I^2: 49.5 percent
Egger's p-value: 0.040

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

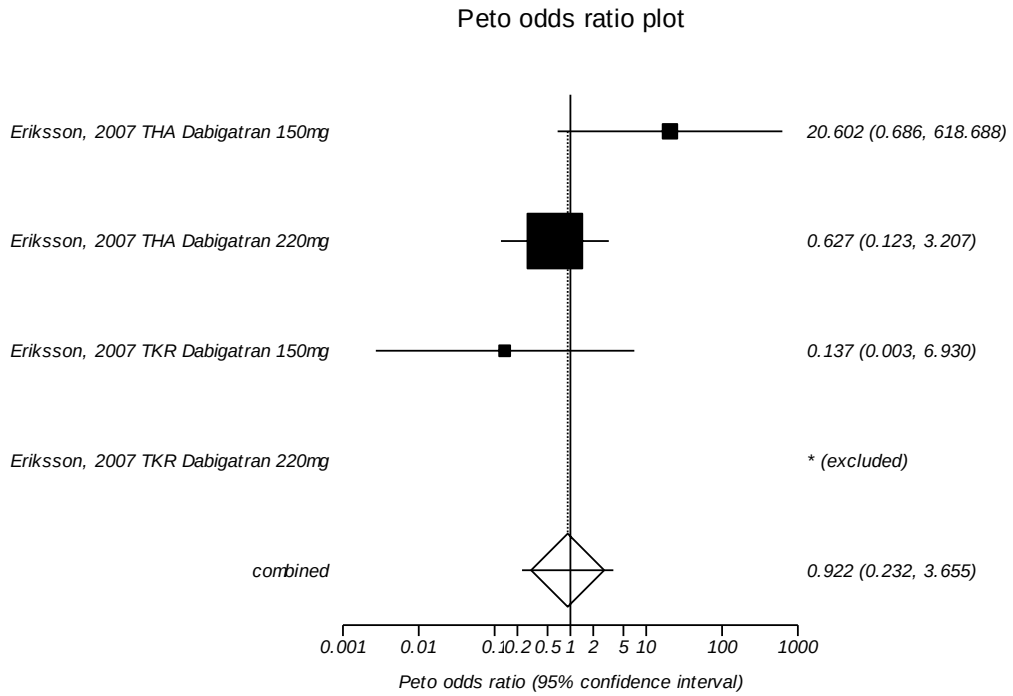
Figure 85. Impact of injectable low molecular weight heparin versus injectable or oral factor Xa inhibitors on nonfatal pulmonary embolism in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

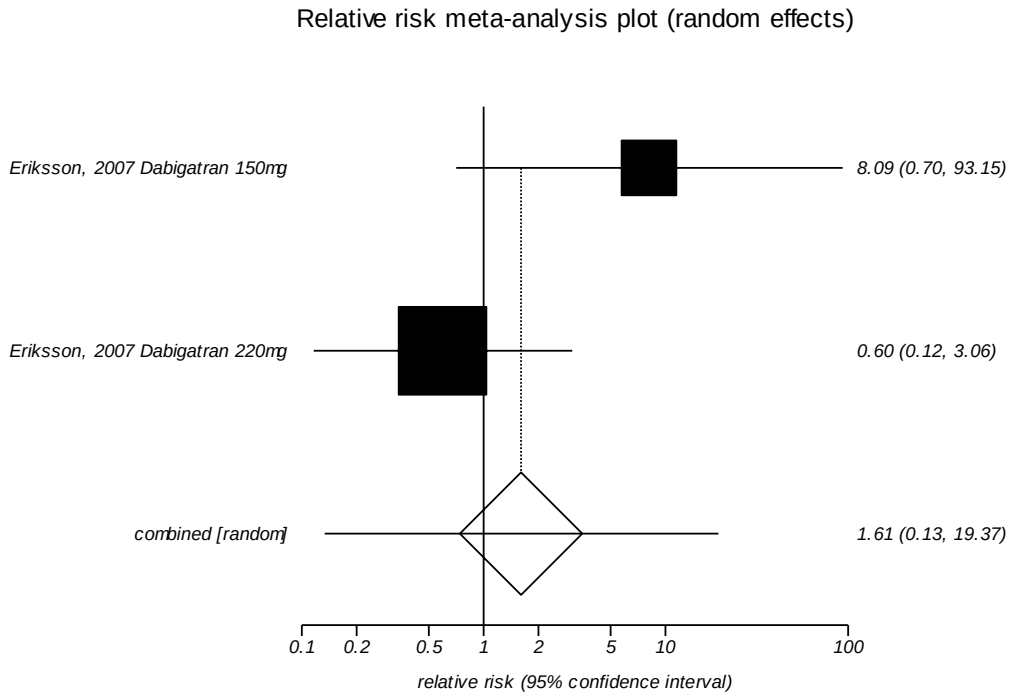
Figure 86. Impact of injectable low molecular weight heparin versus injectable or oral direct thrombin inhibitors on nonfatal pulmonary embolism in patients undergoing major orthopedic surgery (same as analysis limited to trials published from 2001 to the present)



I^2: 53.7 percent
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

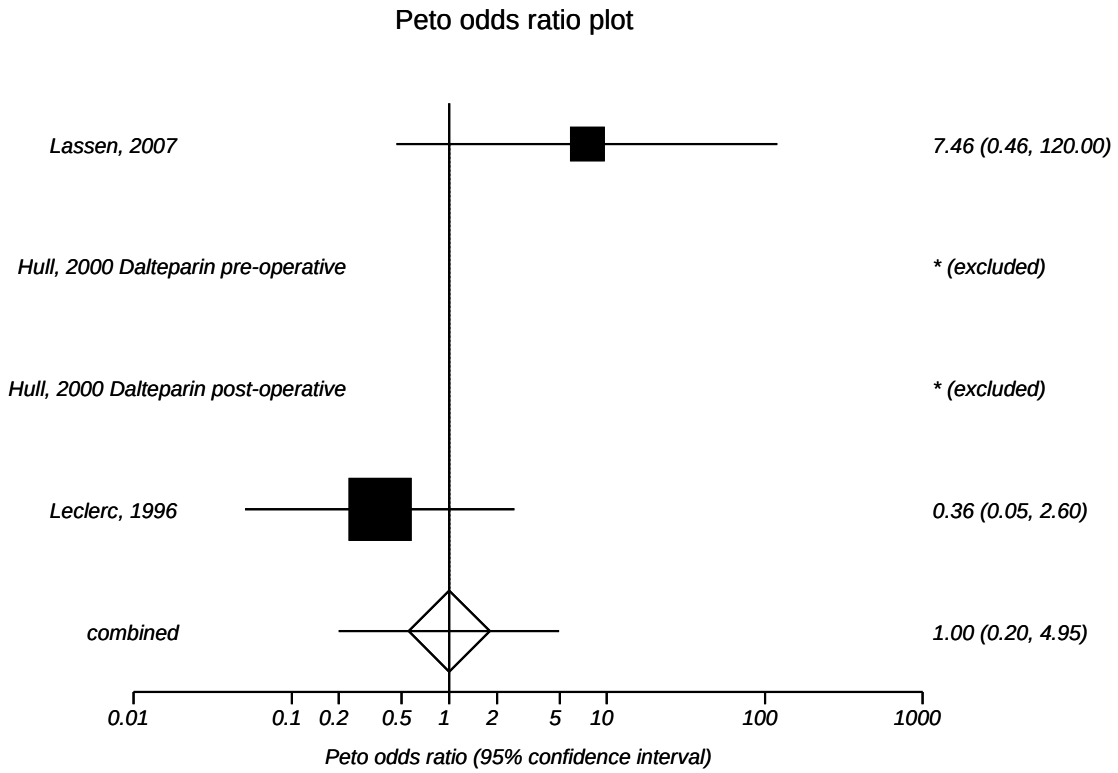
Figure 87. Impact of injectable low molecular weight heparin versus injectable or oral direct thrombin inhibitors on nonfatal pulmonary embolism in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

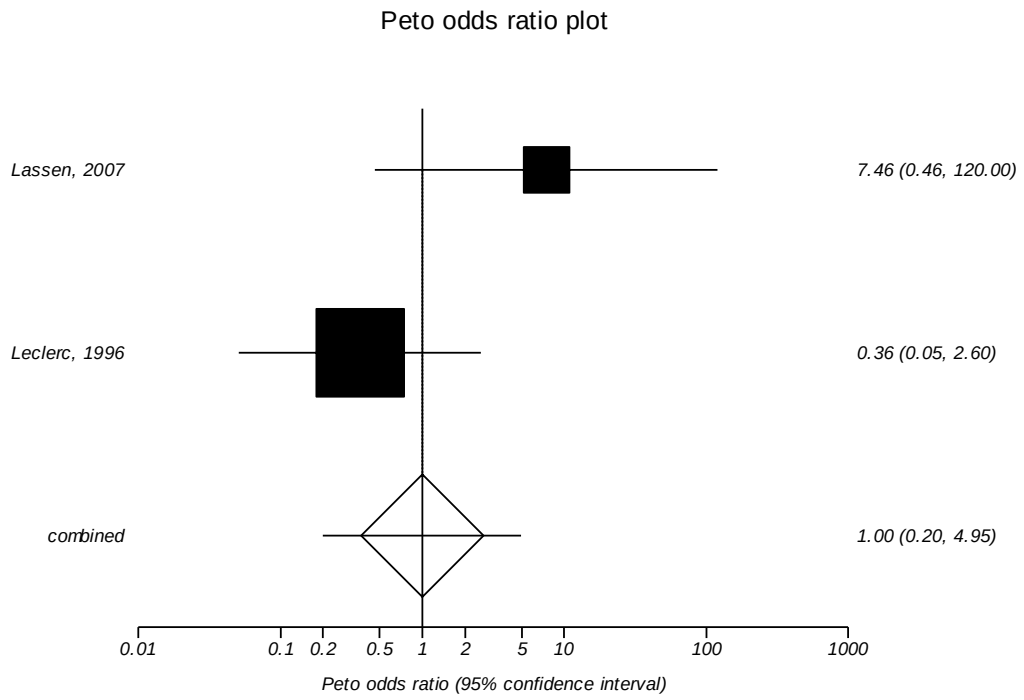
Figure 88. Impact of injectable low molecular weight heparin versus oral vitamin k antagonists on nonfatal pulmonary embolism in patients undergoing major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

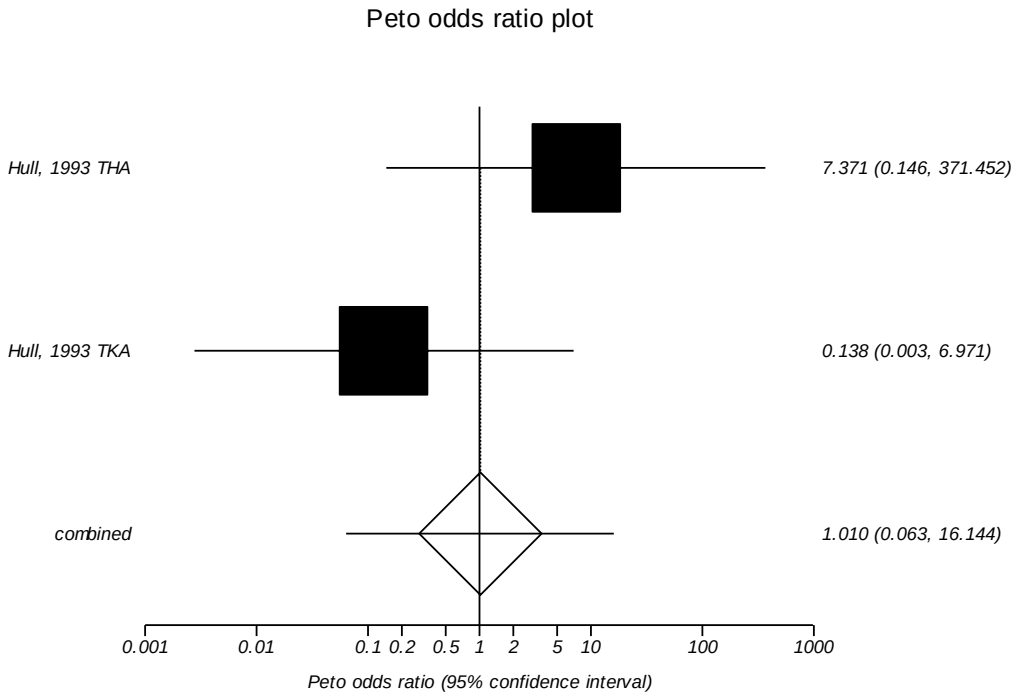
Figure 89. Impact of injectable low molecular weight heparin versus oral vitamin k antagonists on nonfatal pulmonary embolism in patients undergoing major orthopedic surgery limited to total knee replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

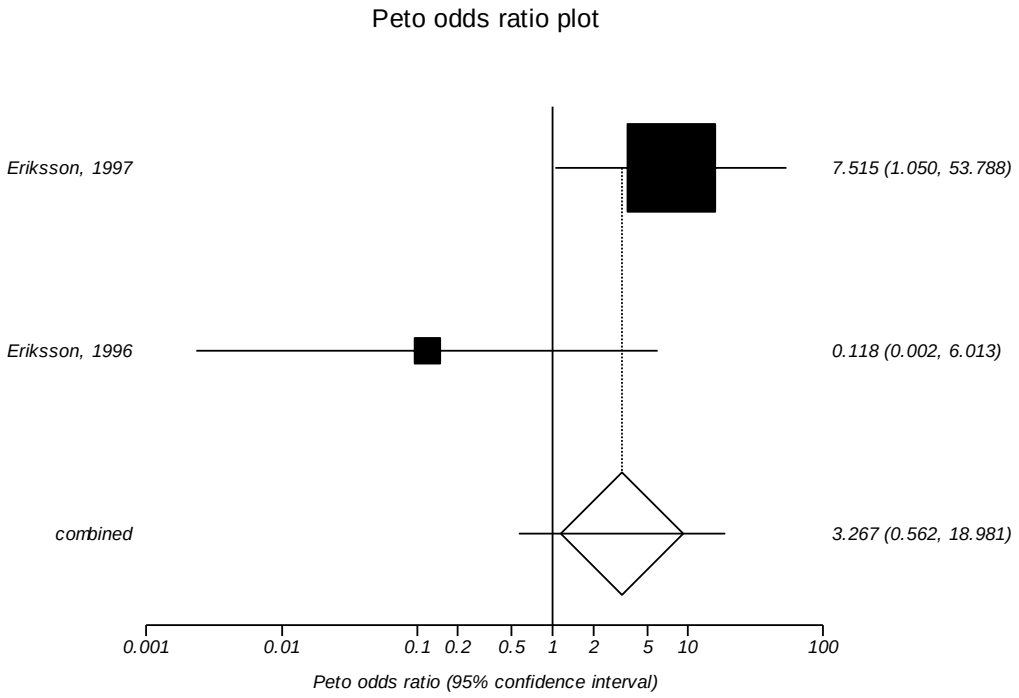
Figure 90. Impact of injectable low molecular weight heparin versus oral vitamin K antagonists on nonfatal pulmonary embolism during the postdischarge period in patients who had major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

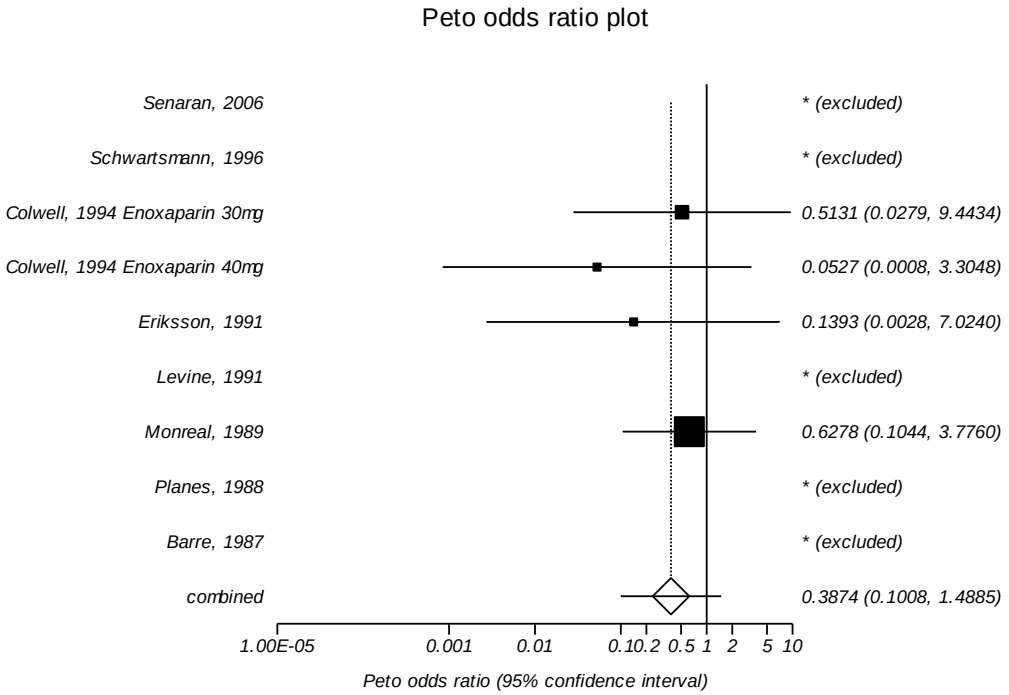
Figure 91. Impact of injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors on nonfatal pulmonary embolism in patients undergoing major orthopedic surgery (same as analysis limited to total hip replacement)



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

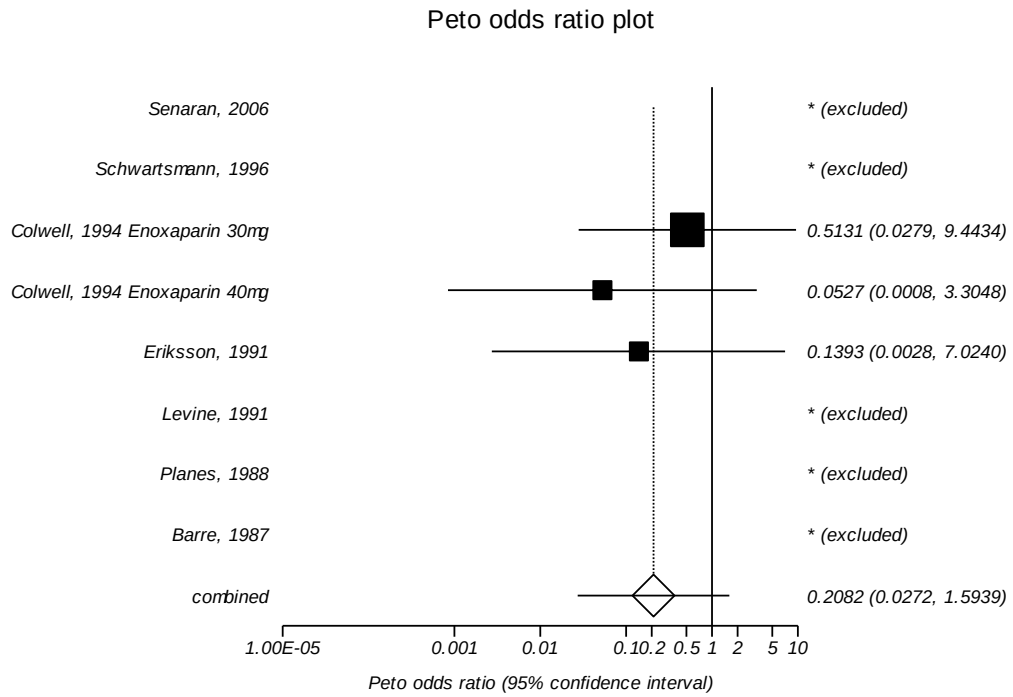
Figure 92. Impact of injectable low molecular weight heparin prophylaxis versus injectable unfractionated heparin prophylaxis on mortality in patients who had major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.102

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

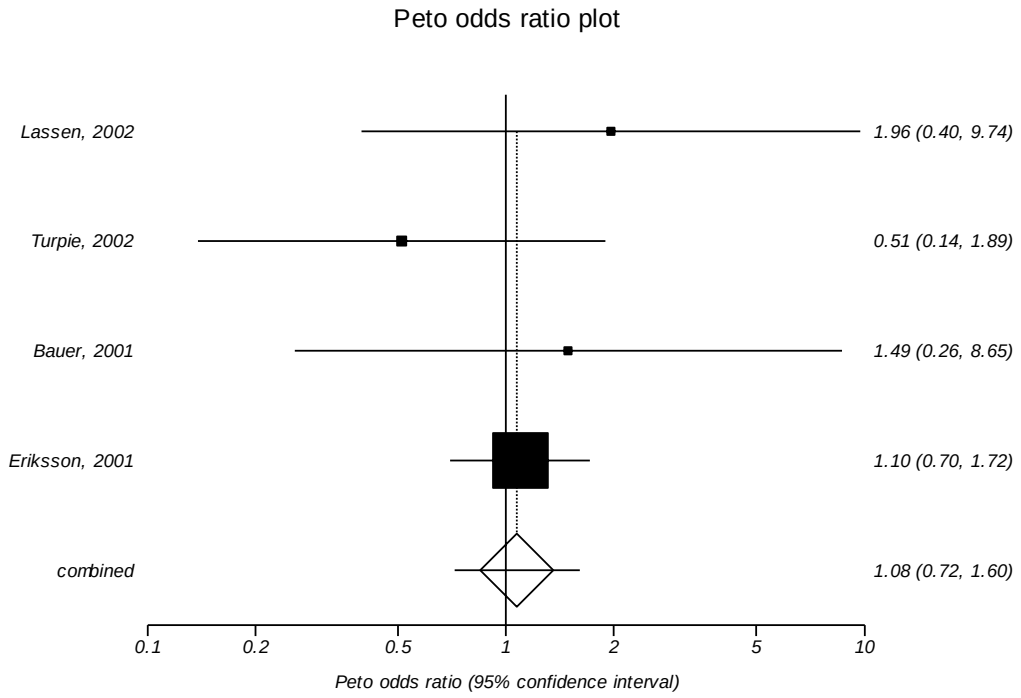
Figure 93. Impact of injectable low molecular weight heparin prophylaxis versus injectable unfractionated heparin prophylaxis on mortality in patients who had major orthopedic surgery limited to total hip replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

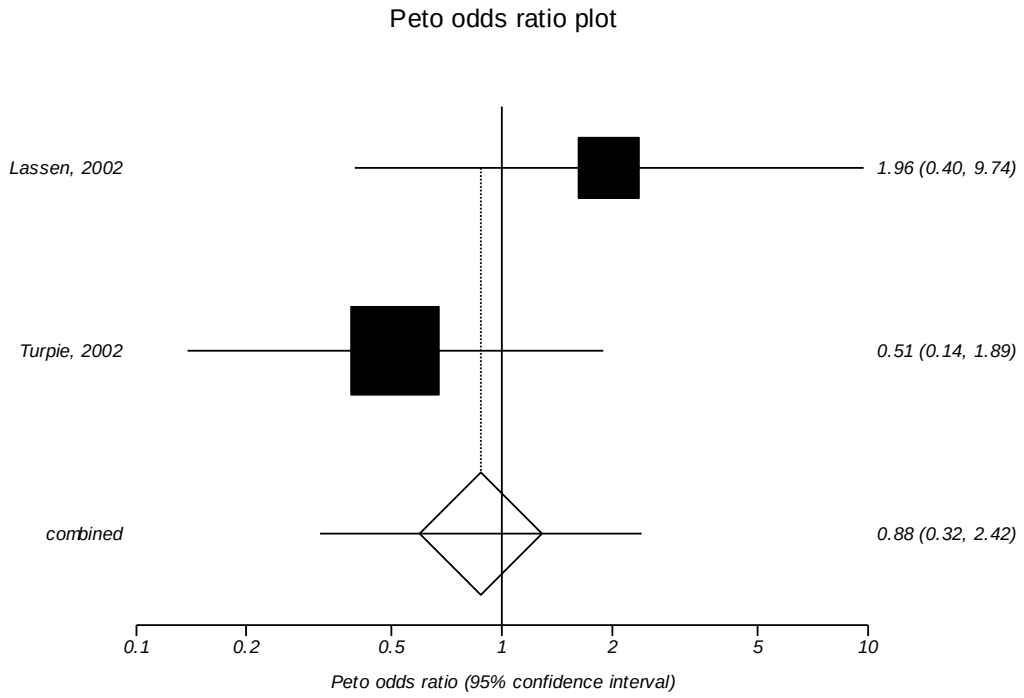
Figure 94. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral factor Xa inhibitor prophylaxis on mortality in patients who had major orthopedic surgery (same as analysis limited to 2001 to present)



I^2: 0 percent
Egger's p-value: P = 0.952

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

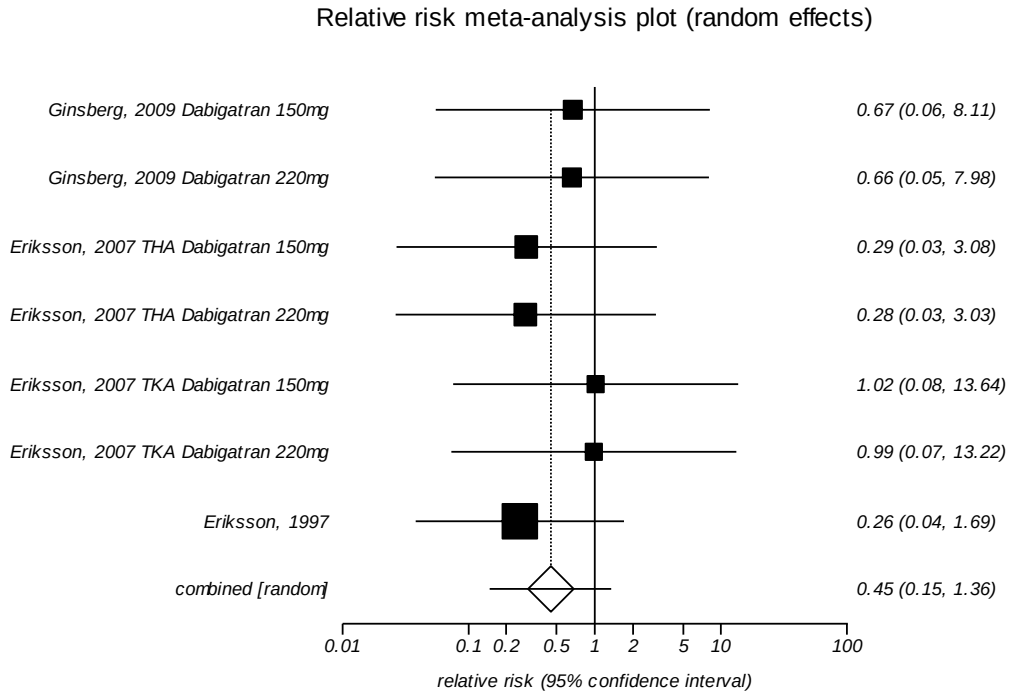
Figure 95. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral factor Xa inhibitor prophylaxis on mortality in patients who had major orthopedic surgery limited to total hip replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

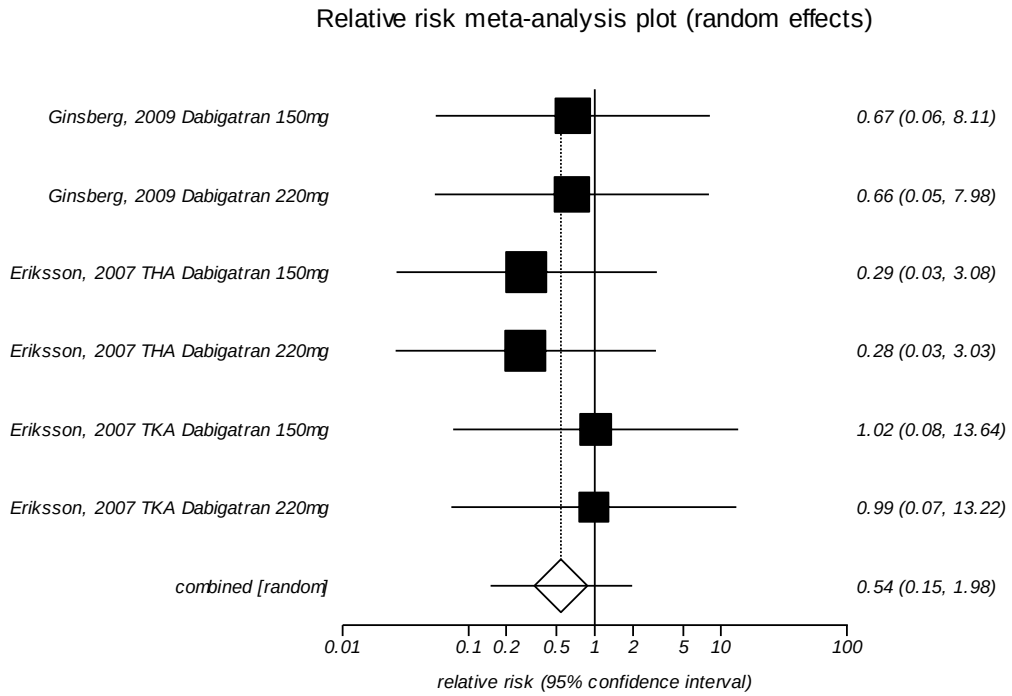
Figure 96. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral direct thrombin inhibitor prophylaxis on mortality in patients who had major orthopedic surgery



I^2: 0 percent
Egger's p-value: P = 0.023

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

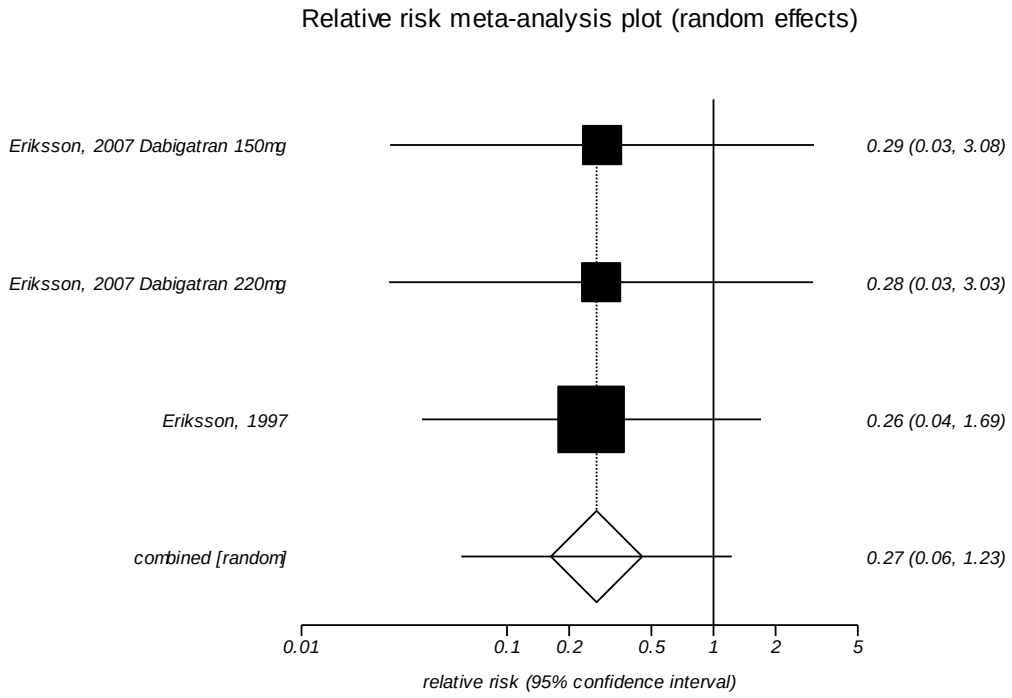
Figure 97. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral direct thrombin inhibitor prophylaxis on mortality in patients who had major orthopedic surgery limited to trials published from 2001 to present



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

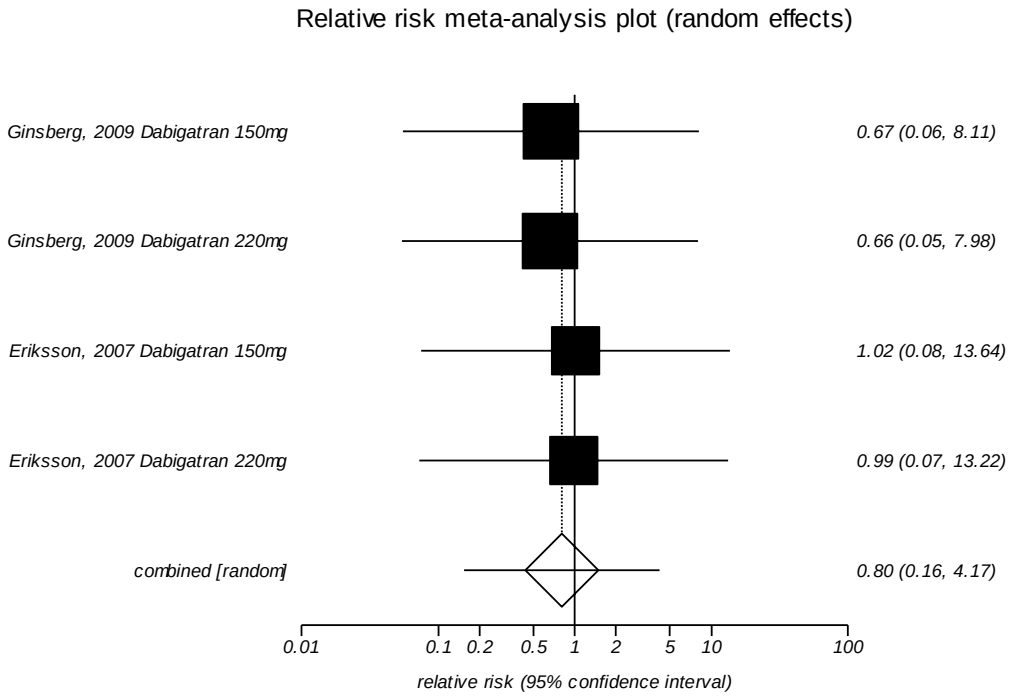
Figure 98. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral direct thrombin inhibitor prophylaxis on mortality in patients who had major orthopedic surgery limited to total hip replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

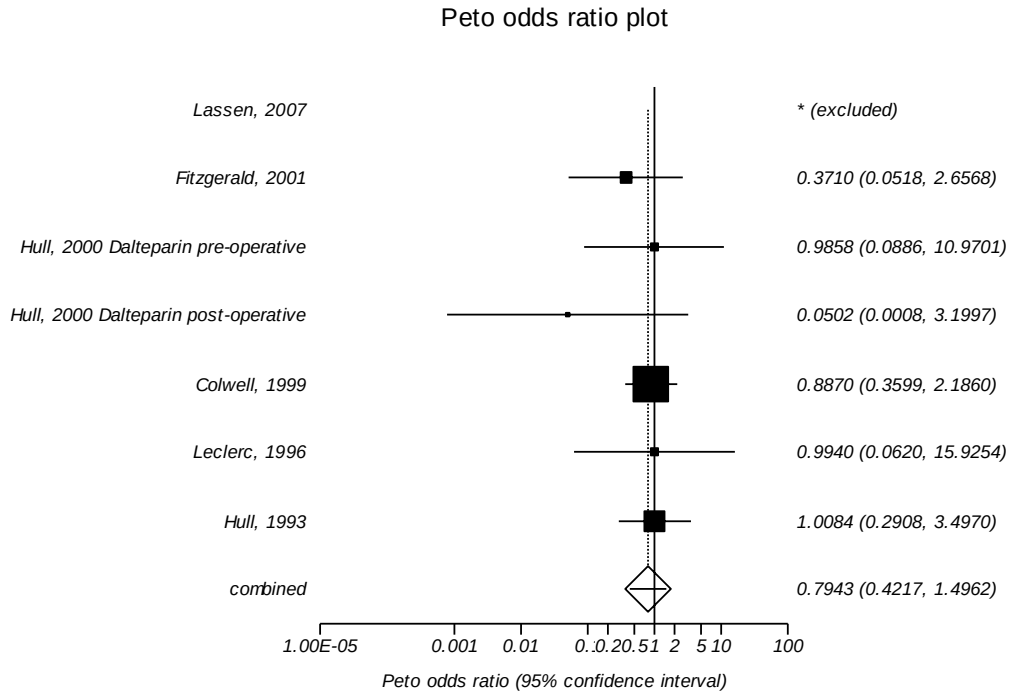
Figure 99. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral direct thrombin inhibitor prophylaxis on mortality in patients who had major orthopedic surgery limited to total knee replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

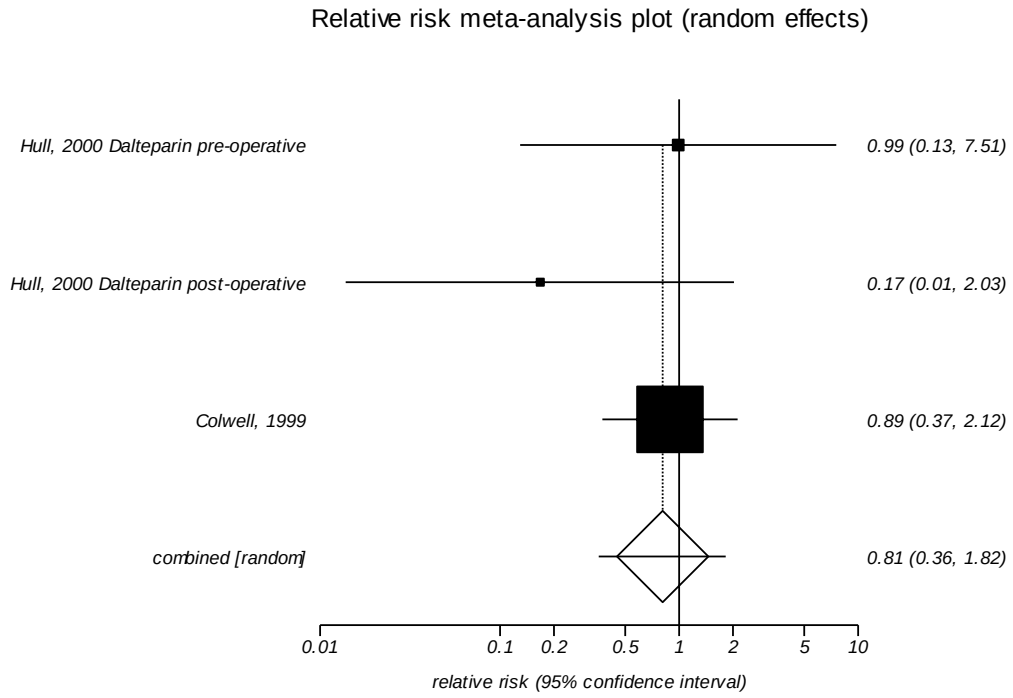
Figure 100. Impact of injectable low molecular weight heparin prophylaxis versus oral vitamin K antagonist prophylaxis on mortality in patients who had major orthopedic surgery



I^2: 0 percent
Egger's p-value: P = 0.188

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

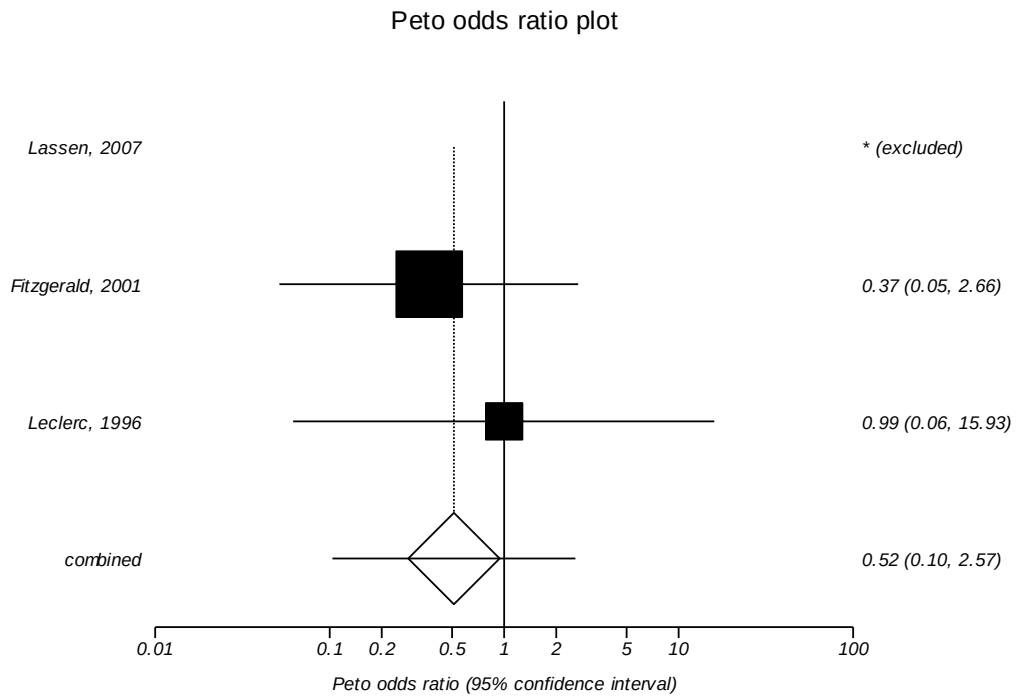
Figure 101. Impact of injectable low molecular weight heparin prophylaxis versus oral vitamin K antagonist prophylaxis on mortality in patients who had major orthopedic surgery limited to total hip replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

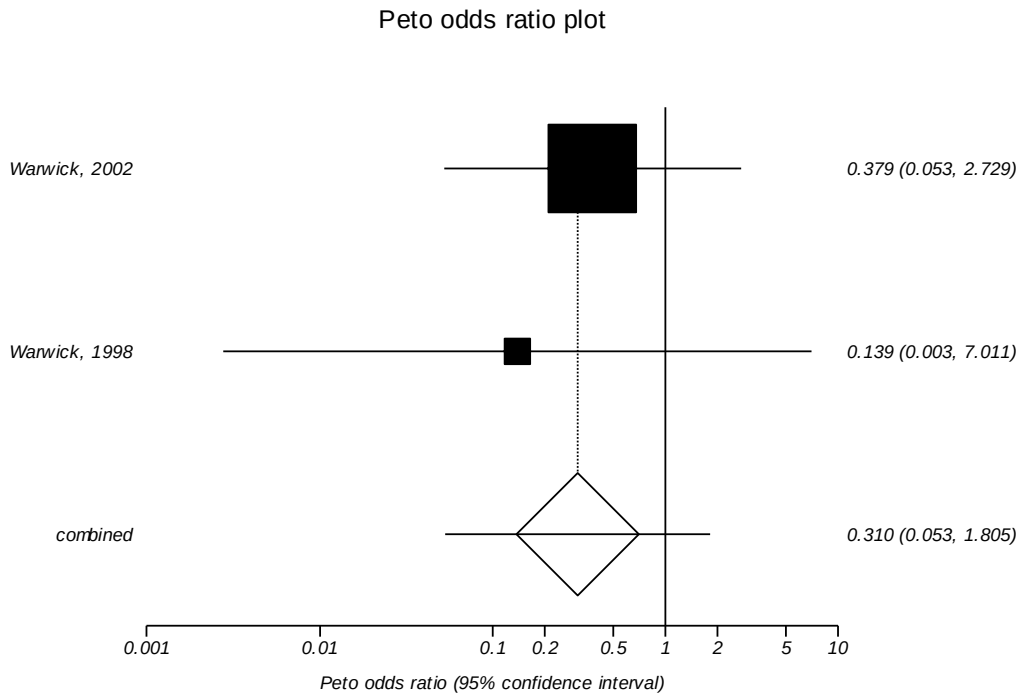
Figure 102. Impact of injectable low molecular weight heparin prophylaxis versus oral vitamin K antagonist prophylaxis on mortality in patients who had major orthopedic surgery limited to total knee replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

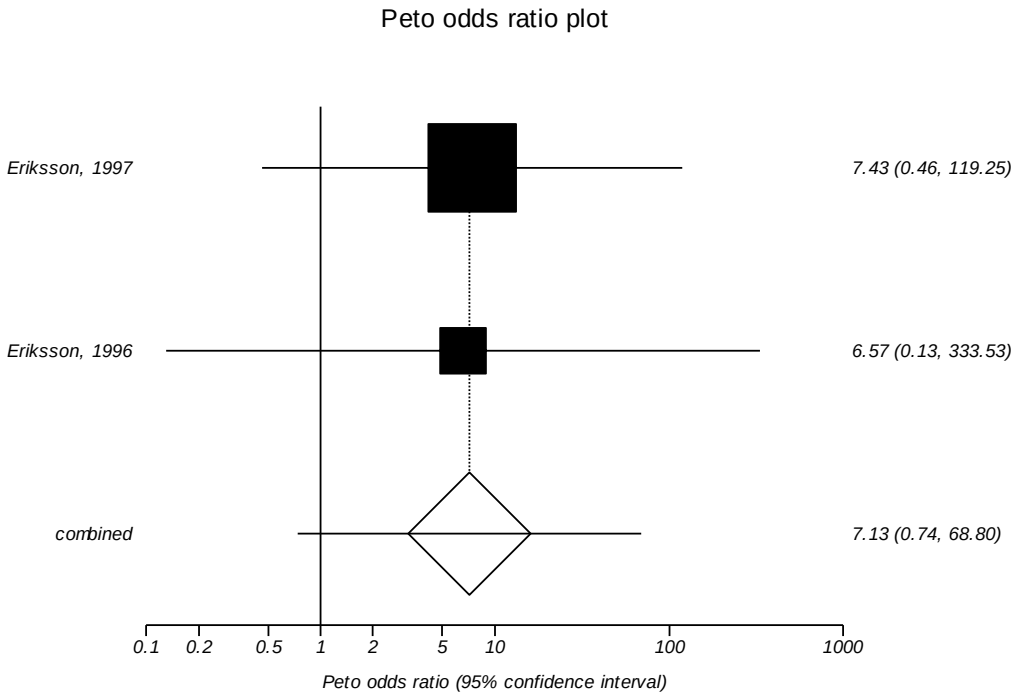
Figure 103. Impact of injectable low molecular weight heparin prophylaxis versus mechanical prophylaxis on mortality in patients who had major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

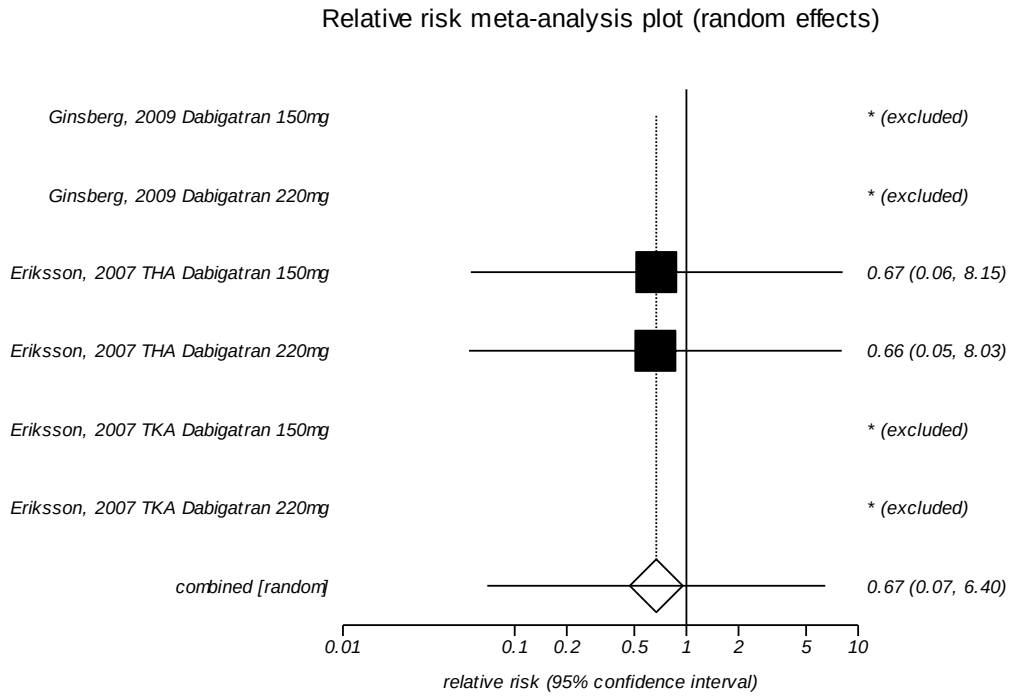
Figure 104. Impact of injectable unfractionated heparin prophylaxis versus injectable or oral direct thrombin inhibitor prophylaxis on mortality in patients who had major orthopedic surgery (same as analysis limited to total hip replacement surgery)



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

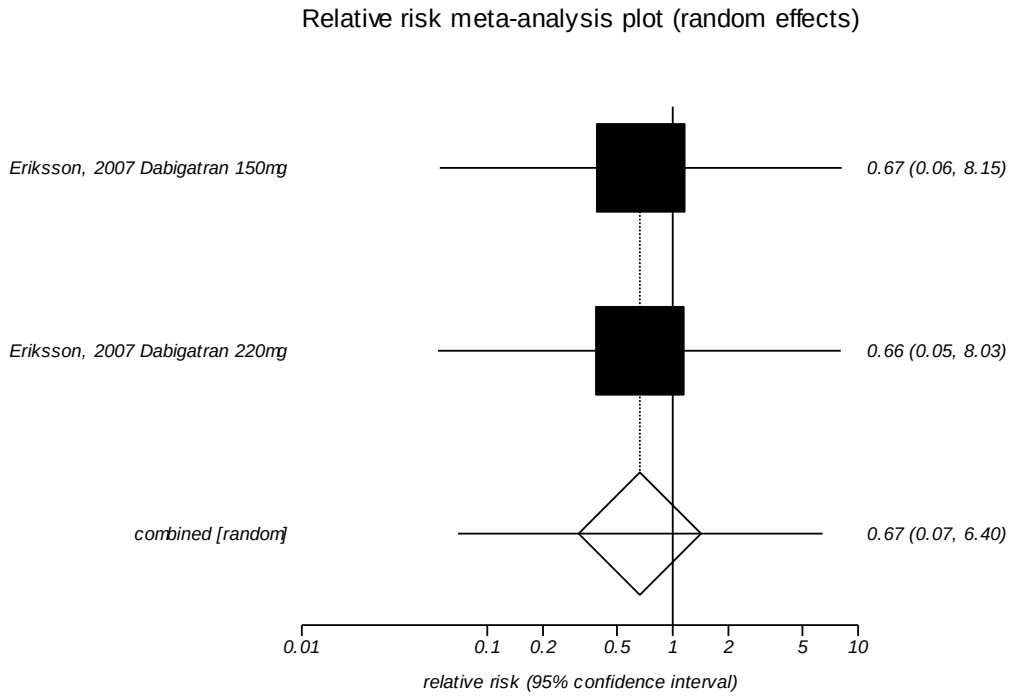
Figure 105. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral direct thrombin inhibitor prophylaxis on mortality due to bleeding in patients who had major orthopedic surgery (same as analysis limited to 2001 to present)



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

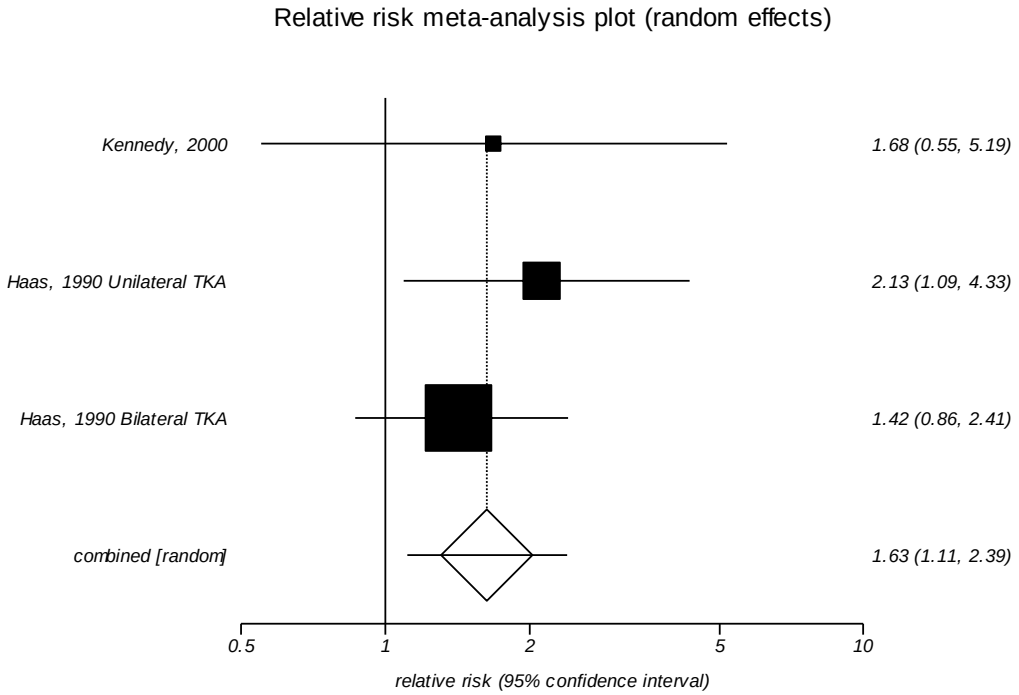
Figure 106. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral direct thrombin inhibitor prophylaxis on mortality due to bleeding in patients who had major orthopedic surgery limited to total hip replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

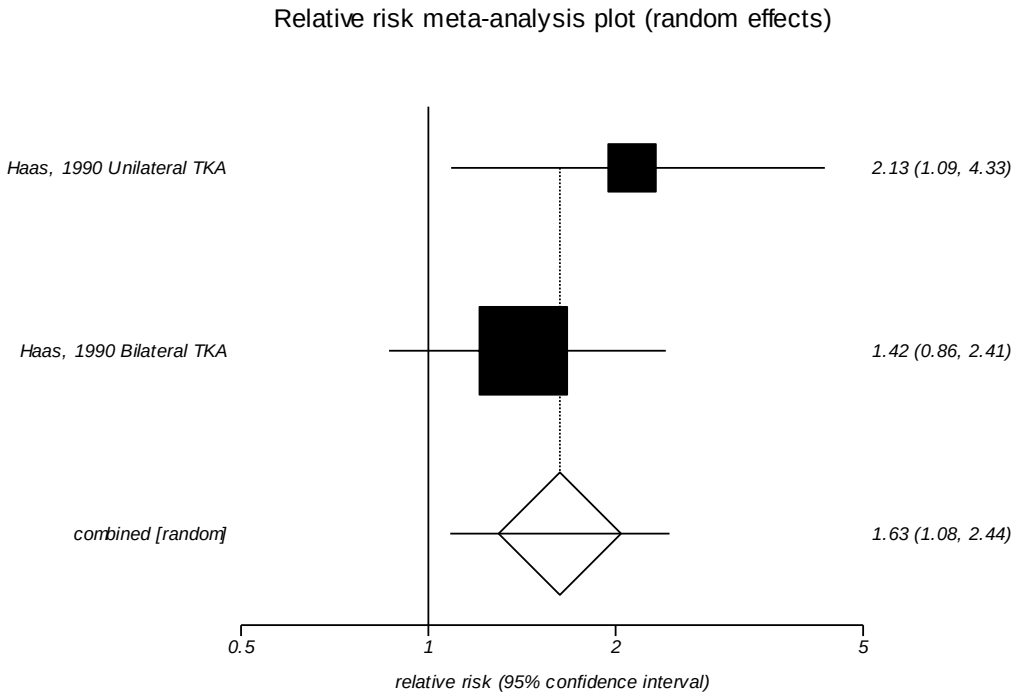
Figure 107. Impact of oral antiplatelet prophylaxis versus mechanical prophylaxis on deep vein thrombosis in patients undergoing major orthopedic surgery



I^2: 0 percent
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

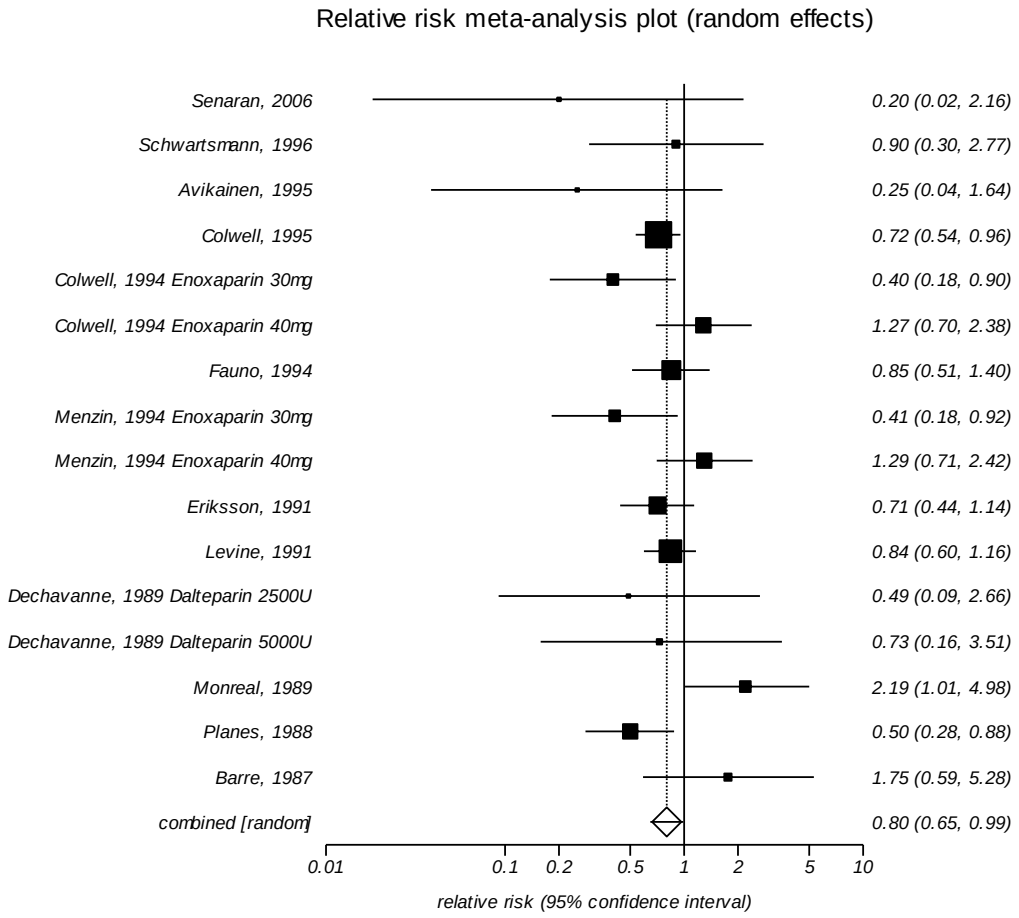
Figure 108. Impact of oral antiplatelet prophylaxis versus mechanical prophylaxis on deep vein thrombosis in patients undergoing major orthopedic surgery limited to total knee replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

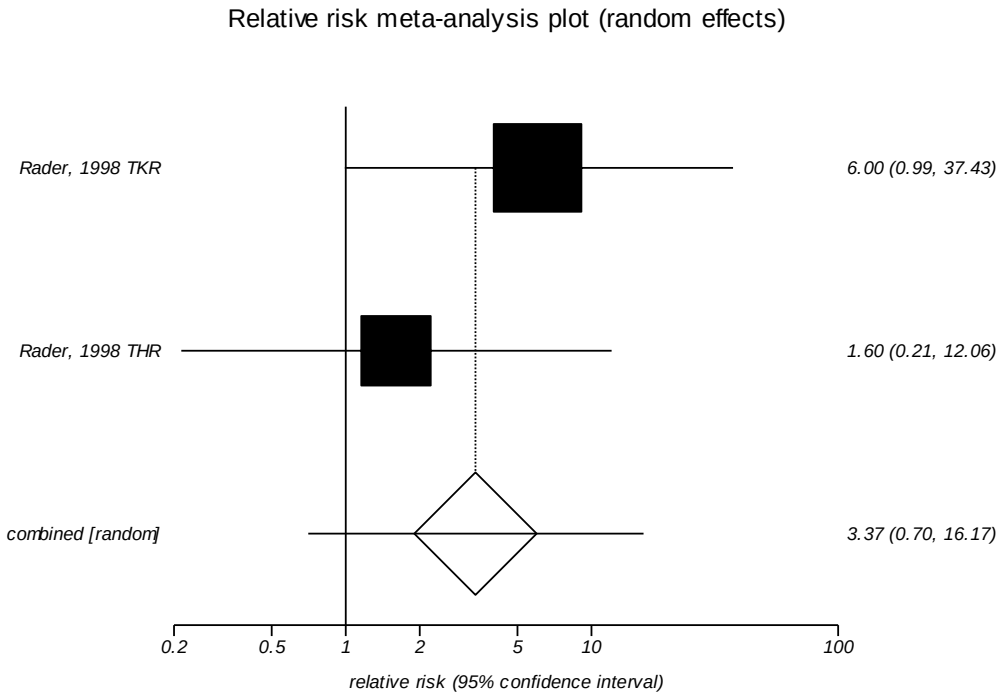
Figure 109. Impact of injectable low molecular weight heparin prophylaxis versus injectable unfractionated heparin prophylaxis on deep vein thrombosis in patients undergoing major orthopedic surgery



I^2: 34.4 percent
Egger's p-value: 0.808

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

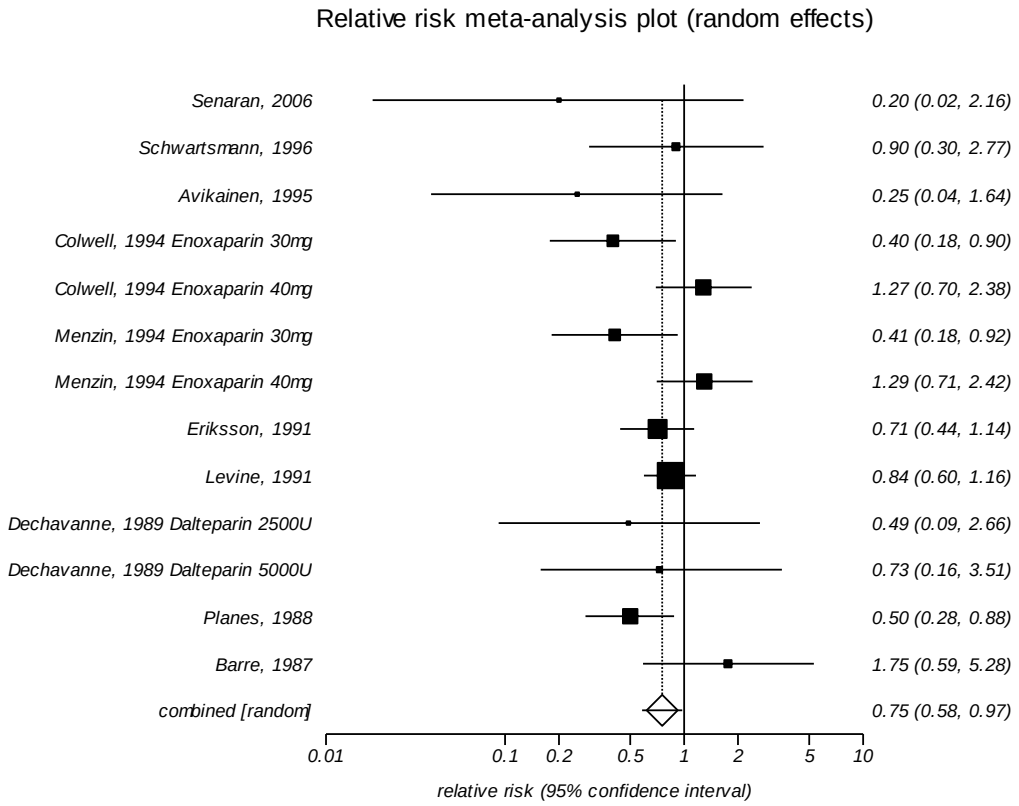
Figure 110. Impact of injectable low molecular weight heparin versus injectable unfractionated heparin on deep vein thrombosis in patients who all received unfractionated heparin before randomization and underwent major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

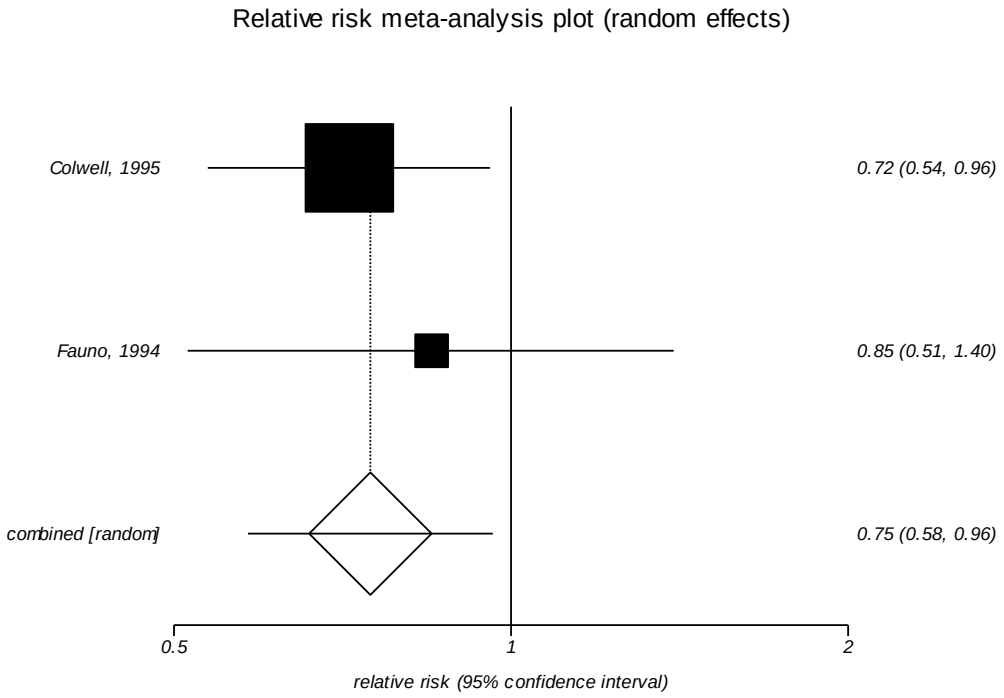
Figure 111. Impact of injectable low molecular weight heparin prophylaxis versus injectable unfractionated heparin prophylaxis on deep vein thrombosis in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: 26.4 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

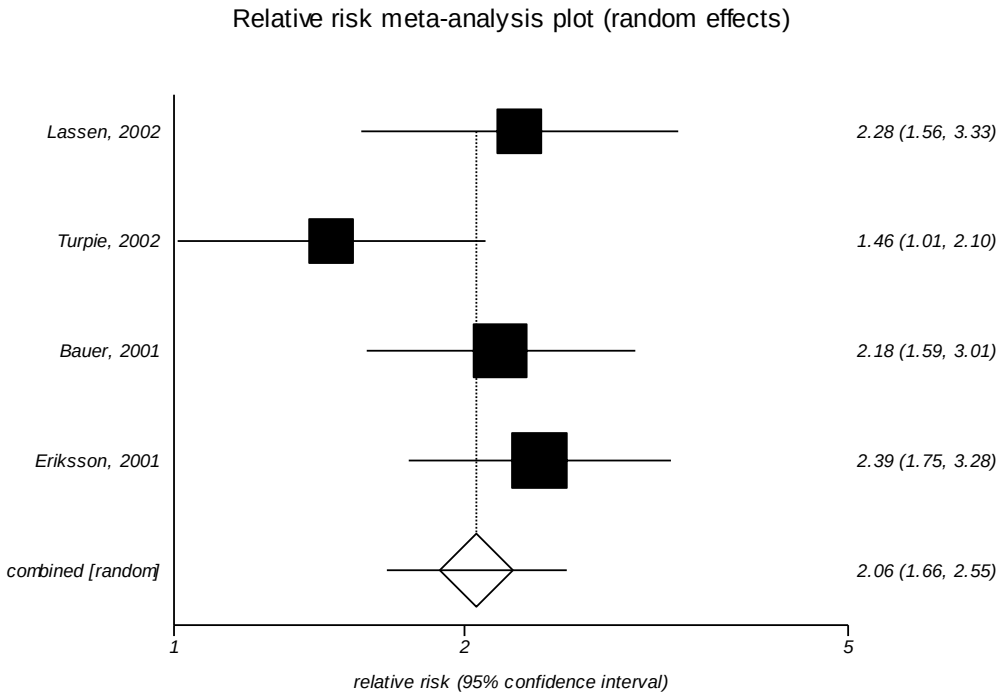
Figure 112. Impact of injectable low molecular weight heparin prophylaxis versus injectable unfractionated heparin prophylaxis on deep vein thrombosis in patients undergoing major orthopedic surgery limited to total knee replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

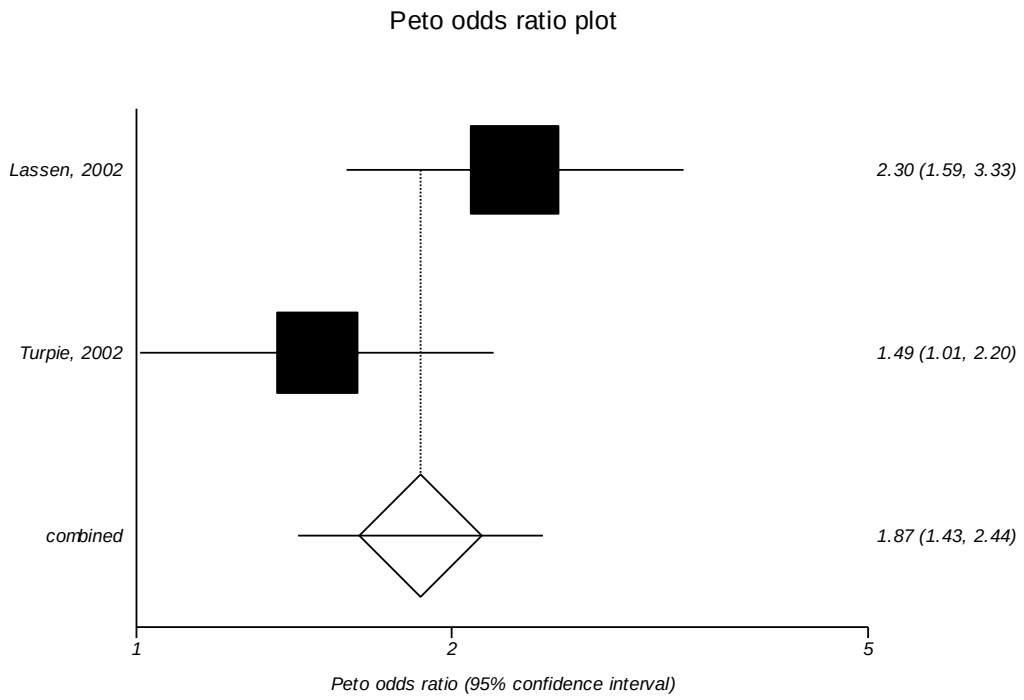
Figure 113. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral factor Xa inhibitor prophylaxis on deep vein thrombosis in patients undergoing major orthopedic surgery (same as limited from 2001 to present)



I^2: 35.5 percent
Egger's p-value: 0.473

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

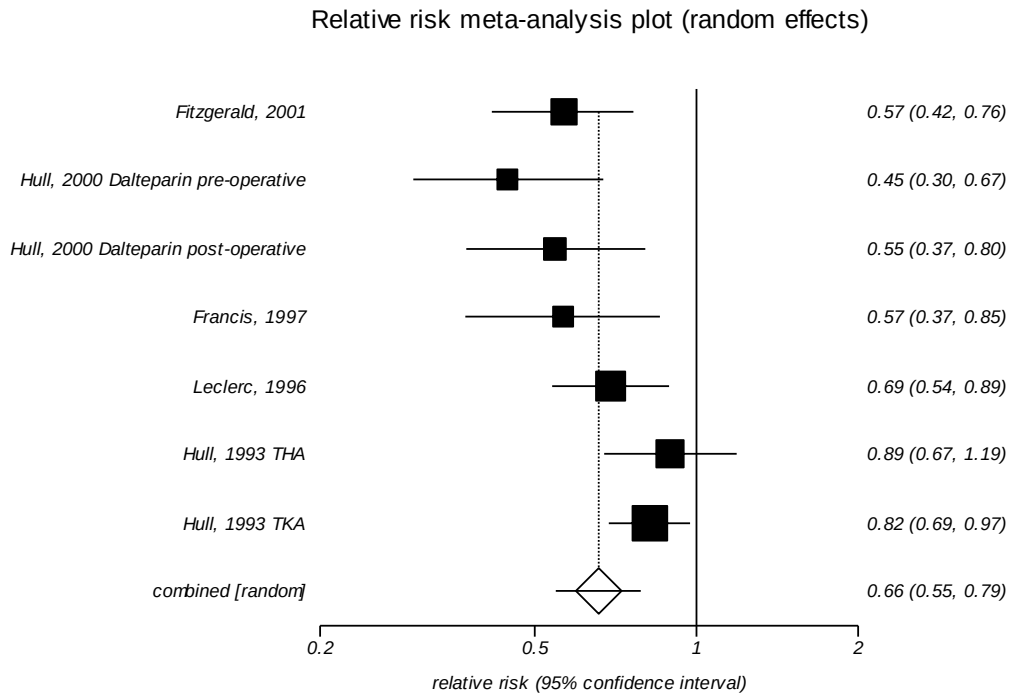
Figure 114. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral factor Xa inhibitor prophylaxis on deep vein thrombosis in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

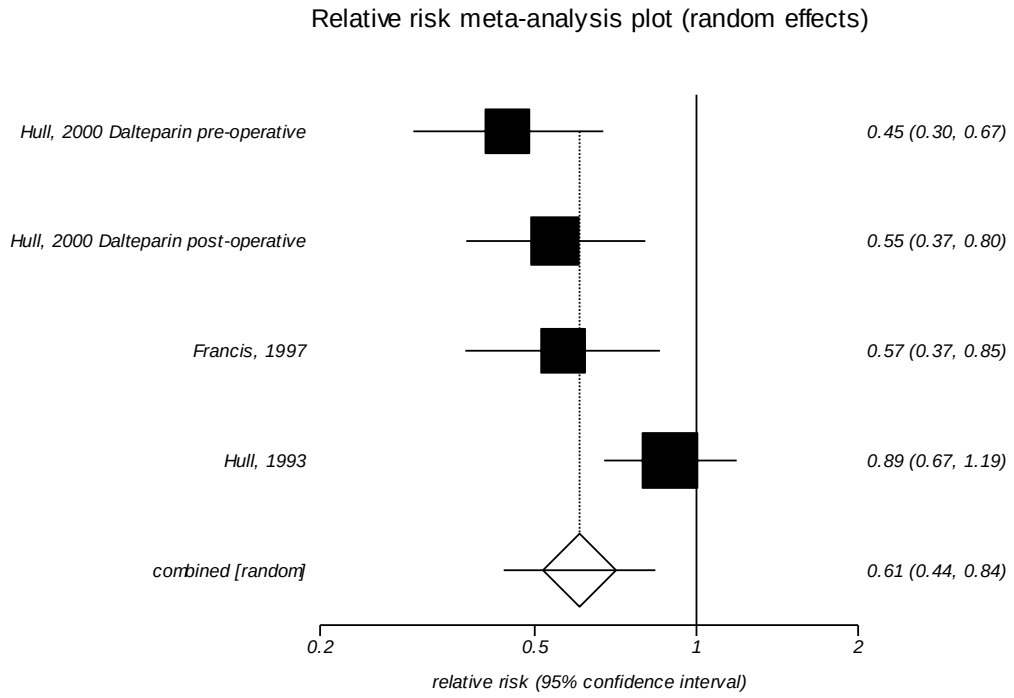
Figure 115. Impact of injectable low molecular weight heparin prophylaxis versus oral vitamin K antagonist prophylaxis on deep vein thrombosis in patients undergoing major orthopedic surgery



I^2: 60.9 percent
Egger's p-value: 0.033

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

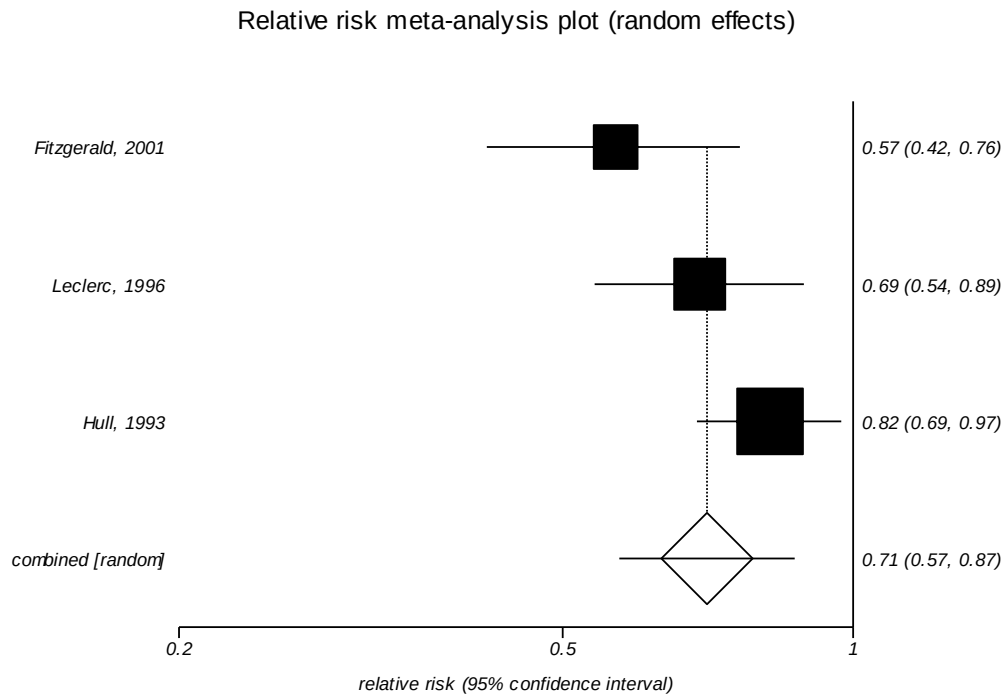
Figure 116. Impact of injectable low molecular weight heparin prophylaxis versus oral vitamin K antagonist prophylaxis on deep vein thrombosis in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: 67.6 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

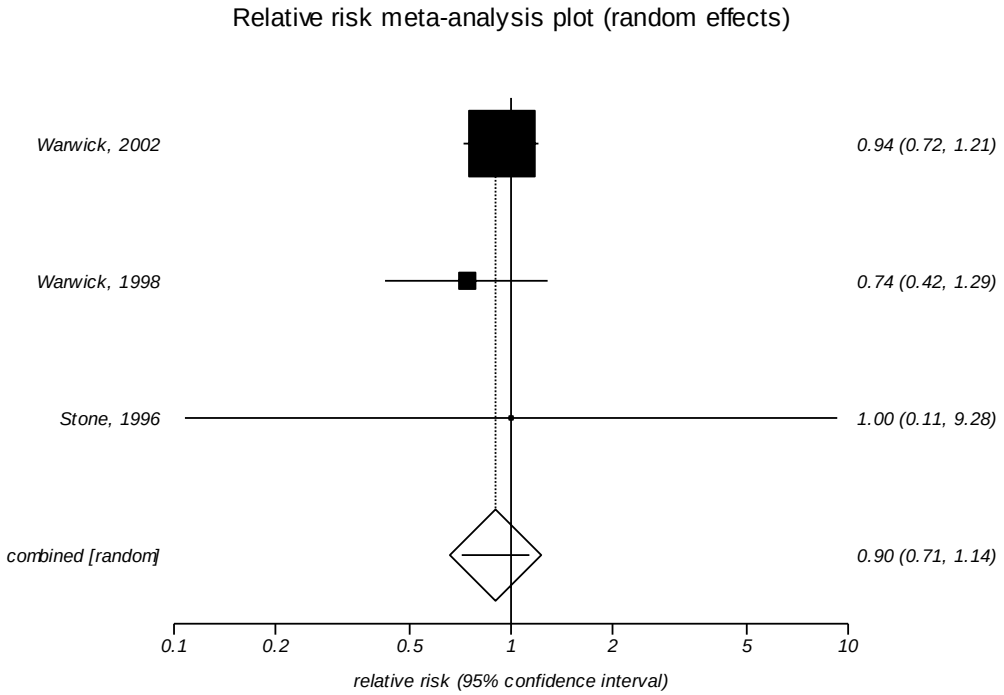
Figure 117. Impact of injectable low molecular weight heparin prophylaxis versus oral vitamin K antagonist prophylaxis on deep vein thrombosis in patients undergoing major orthopedic surgery limited to total knee replacement surgery



I^2: 57.2 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

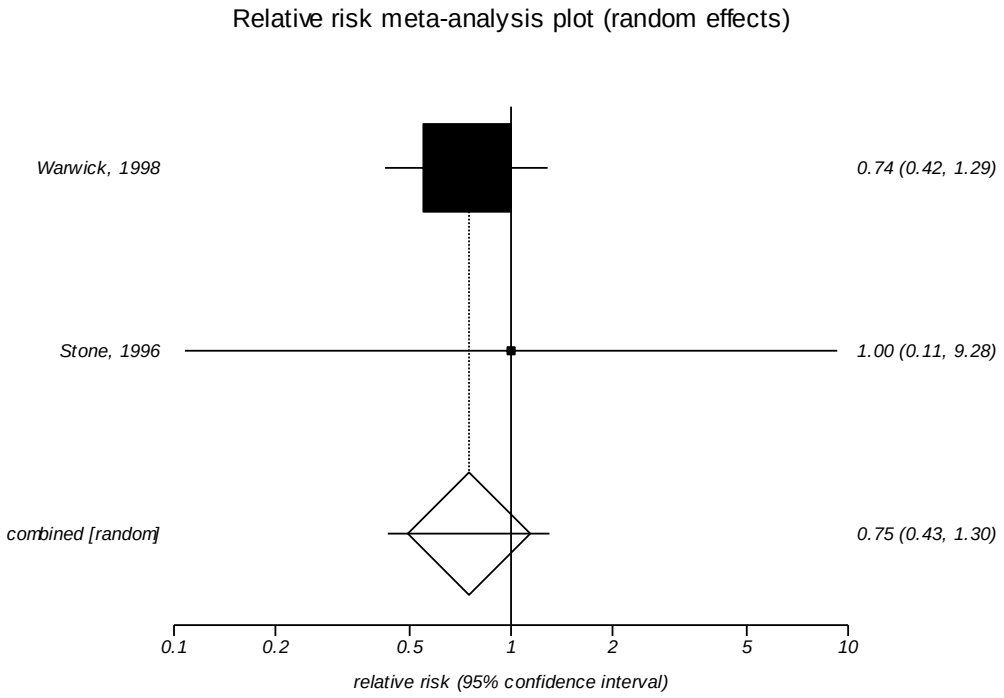
Figure 118. Impact of injectable low molecular weight heparin prophylaxis versus mechanical prophylaxis on deep vein thrombosis in patients undergoing major orthopedic surgery



I^2: 0 percent
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

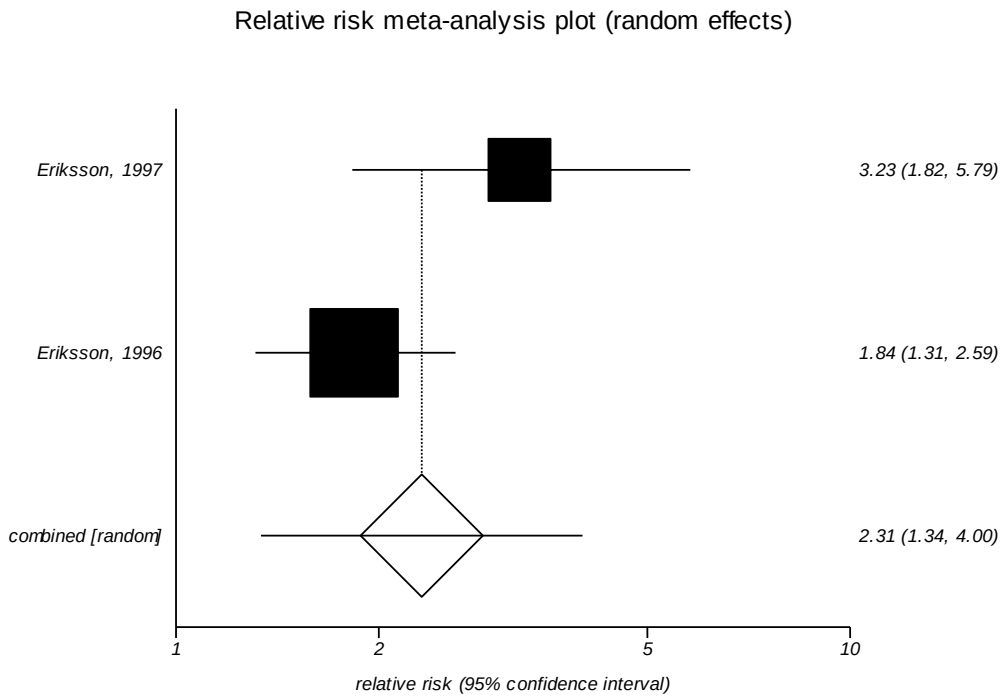
Figure 119. Impact of injectable low molecular weight heparin prophylaxis versus mechanical prophylaxis on deep vein thrombosis in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

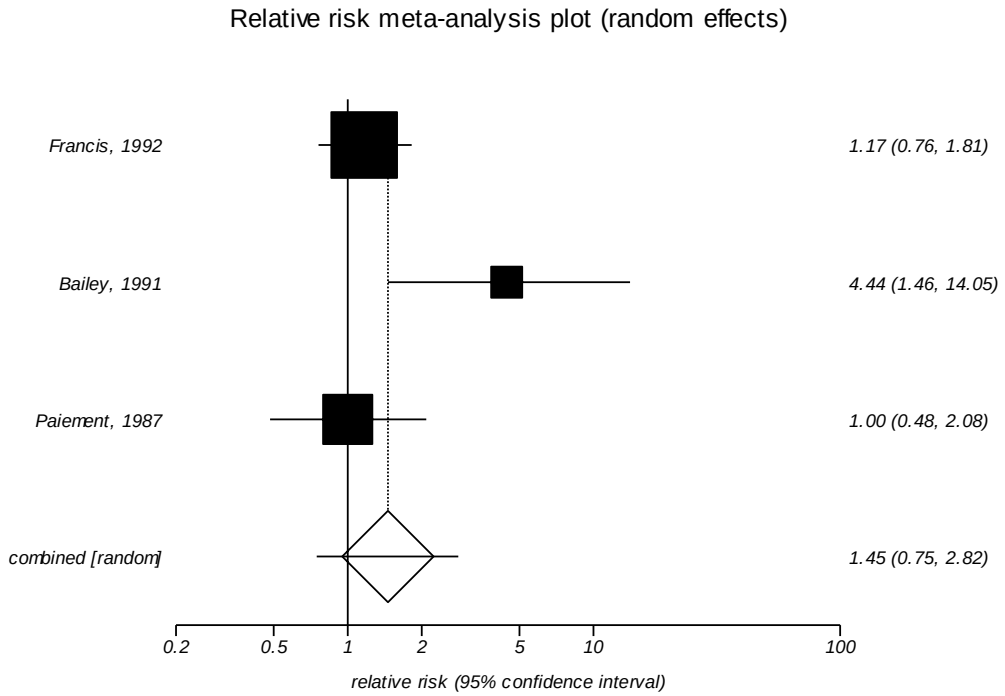
Figure 120. Impact of injectable unfractionated heparin prophylaxis versus injectable or oral direct thrombin inhibitor prophylaxis on deep vein thrombosis in patients undergoing major orthopedic surgery (same as total hip replacement therapy)



I^2: 0 percent
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

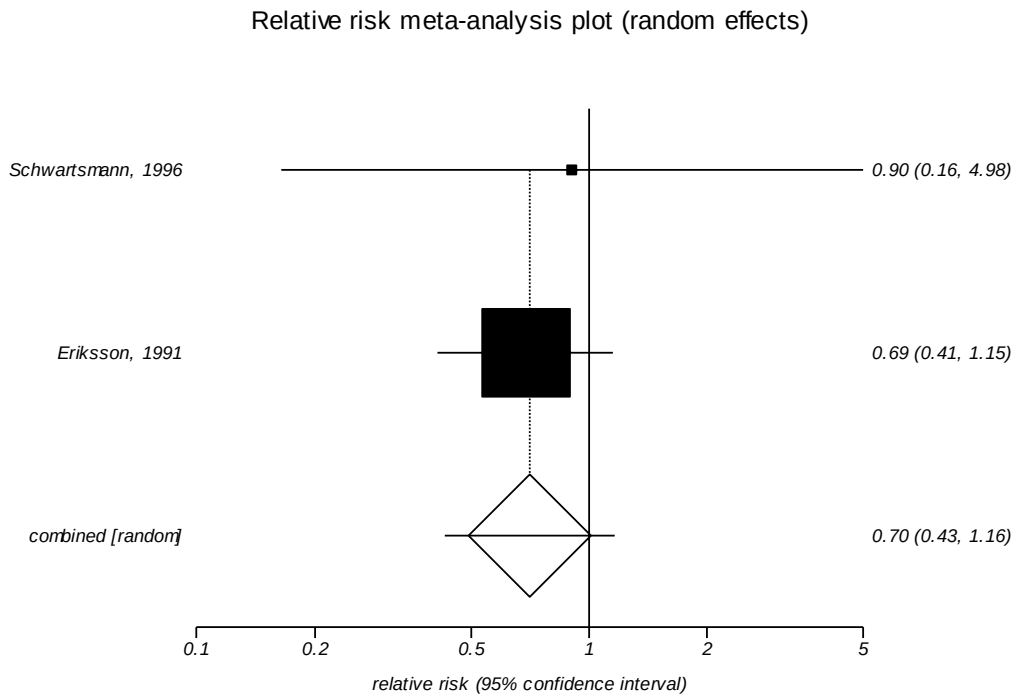
Figure 121. Impact of oral vitamin K antagonist prophylaxis versus mechanical prophylaxis on deep vein thrombosis in patients undergoing major orthopedic surgery (same as limited to total hip replacement surgery)



I^2: 58.5 percent
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

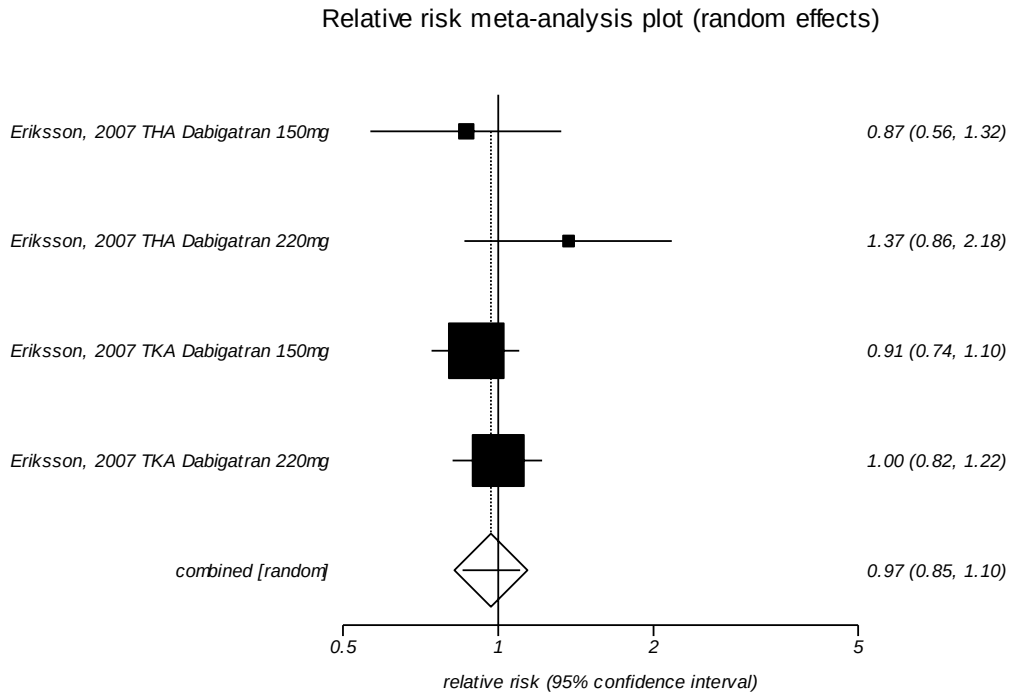
Figure 122. Impact of injectable low molecular weight heparin versus injectable unfractionated heparin on asymptomatic deep vein thrombosis in patients undergoing major orthopedic surgery (same as analysis limited to total hip replacement surgery)



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

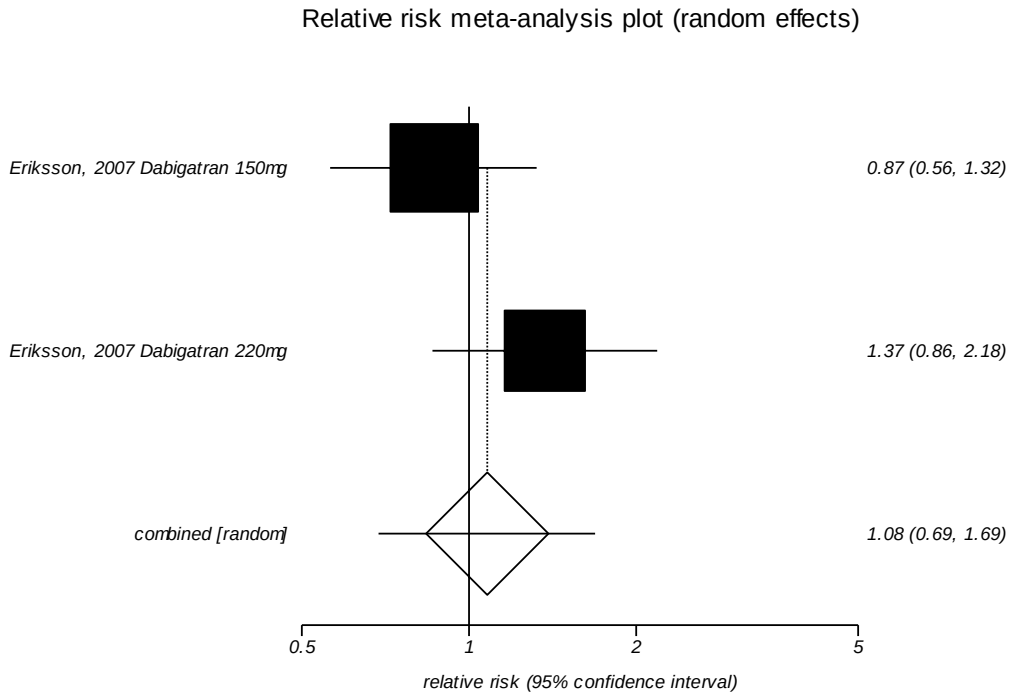
Figure 123. Impact of injectable low molecular weight heparin versus injectable or oral direct thrombin inhibitors on asymptomatic deep vein thrombosis in patients undergoing major orthopedic surgery (same as analysis limited to trials published from 2001-present)



I^2: 0 percent
Egger's p-value: 0.536

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

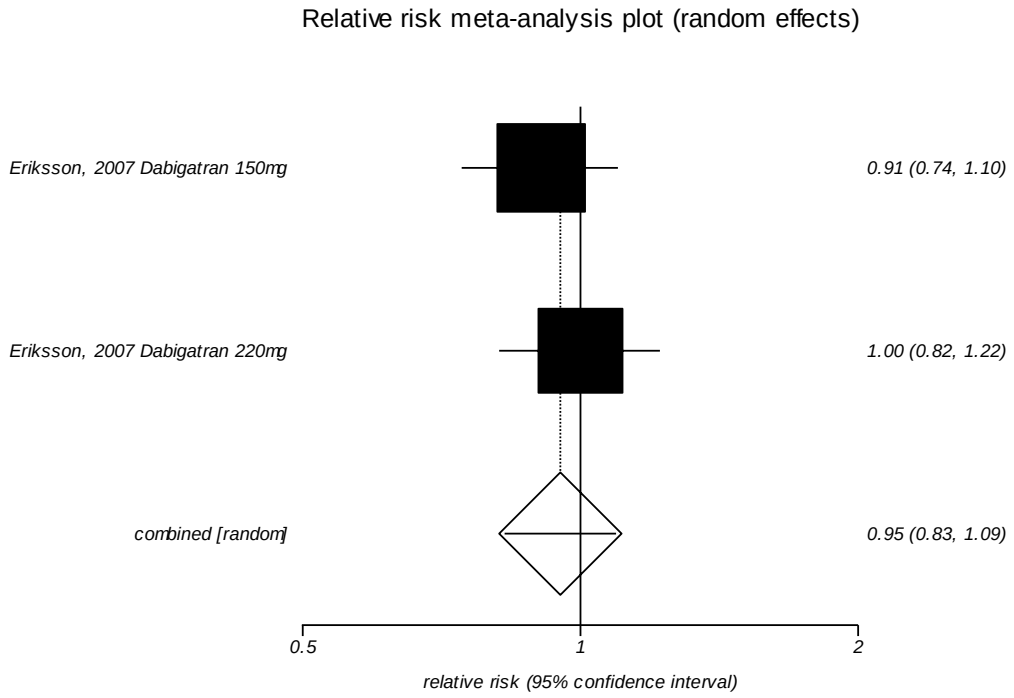
Figure 124. Impact of injectable low molecular weight heparin versus injectable or oral direct thrombin inhibitors on asymptomatic deep vein thrombosis in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

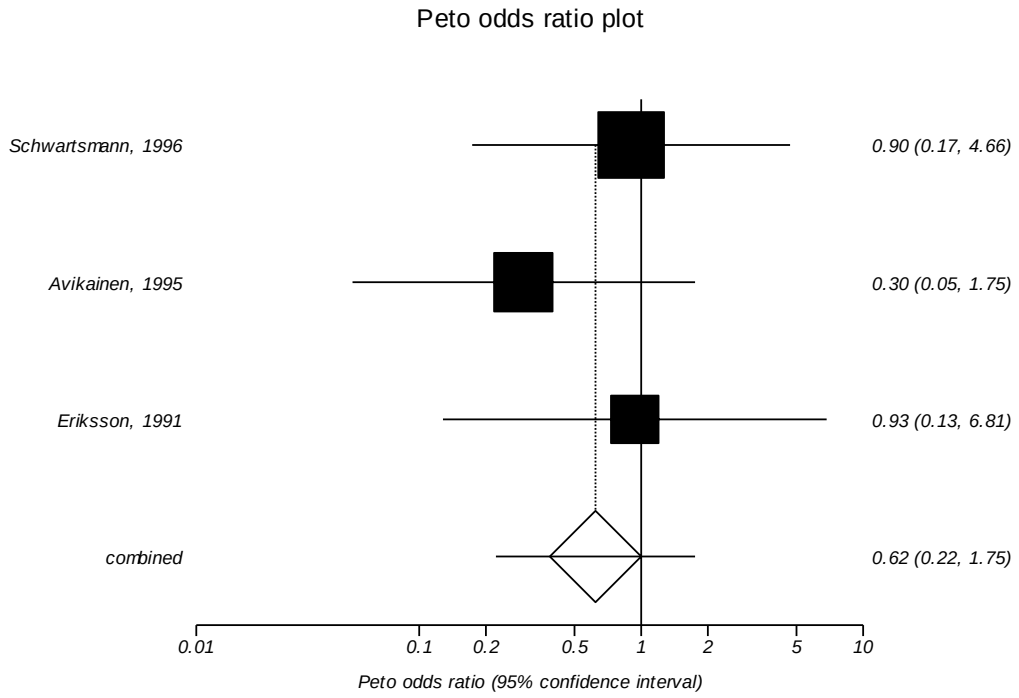
Figure 125. Impact of injectable low molecular weight heparin versus injectable or oral direct thrombin inhibitors on asymptomatic deep vein thrombosis in patients undergoing major orthopedic surgery limited to total knee replacement



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

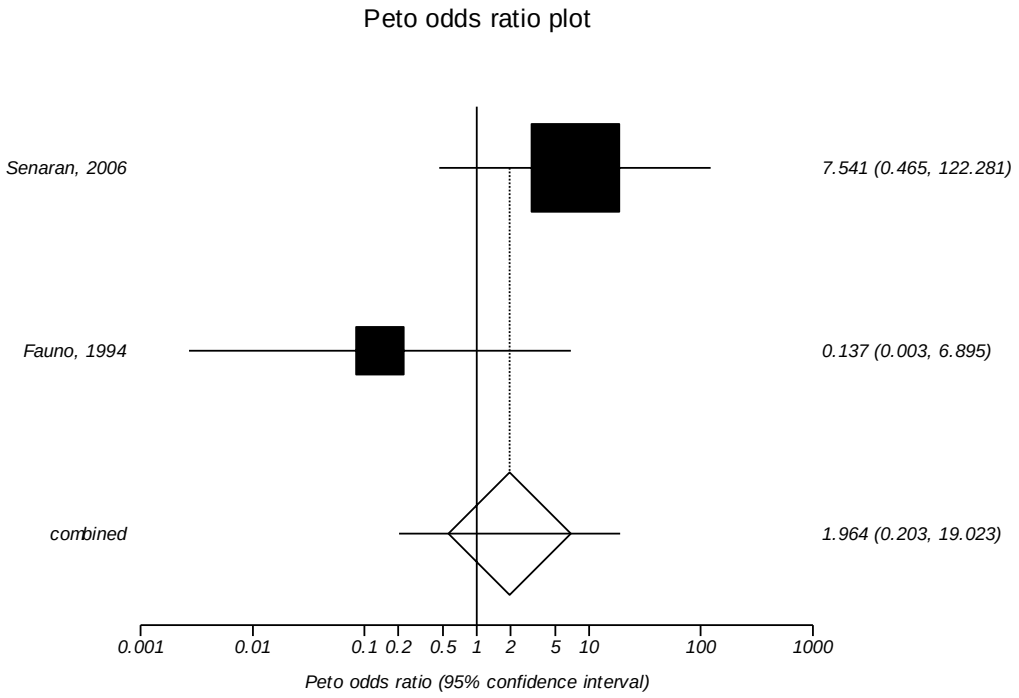
Figure 126. Impact of injectable low molecular weight heparin versus injectable unfractionated heparin on symptomatic deep vein thrombosis in patients undergoing major orthopedic surgery (same as analysis limited to total hip replacement)



I^2: 0 percent
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

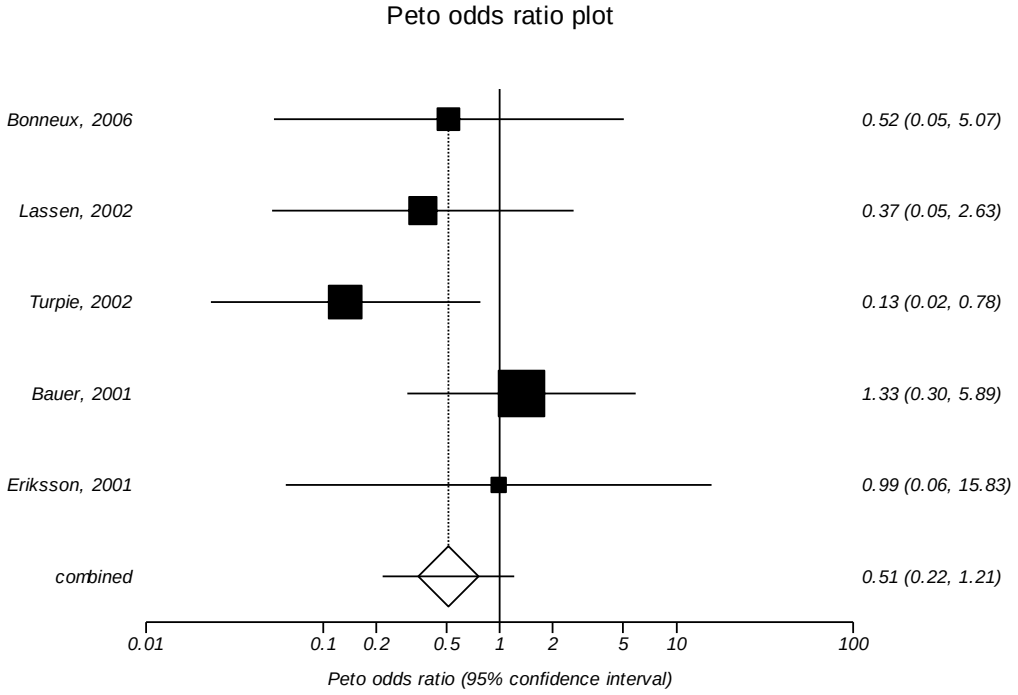
Figure 127. Impact of injectable low molecular weight heparin versus injectable unfractionated heparin on symptomatic deep vein thrombosis during the postdischarge period in patients who had major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

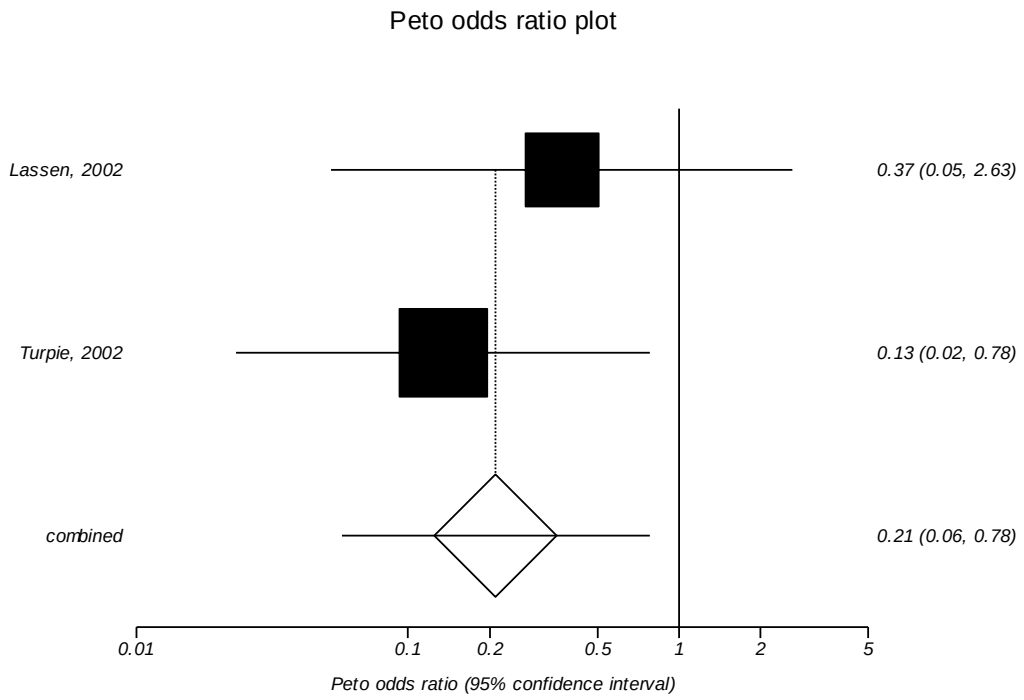
Figure 128. Impact of injectable low molecular weight heparin versus injectable or oral factor Xa inhibitors on symptomatic deep vein thrombosis in patients undergoing major orthopedic surgery (same as analysis limited to trials published from 2001-present)



I^2: 3.5 percent
Egger's p-value: 0.878

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

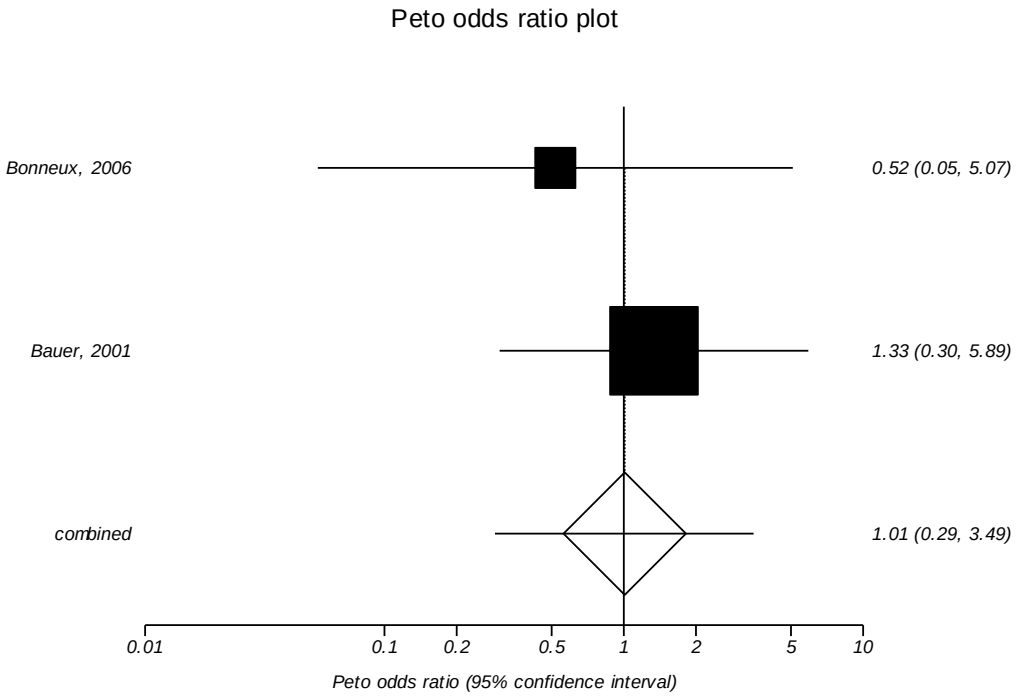
Figure 129. Impact of injectable low molecular weight heparin versus injectable or oral factor Xa inhibitors on symptomatic deep vein thrombosis in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

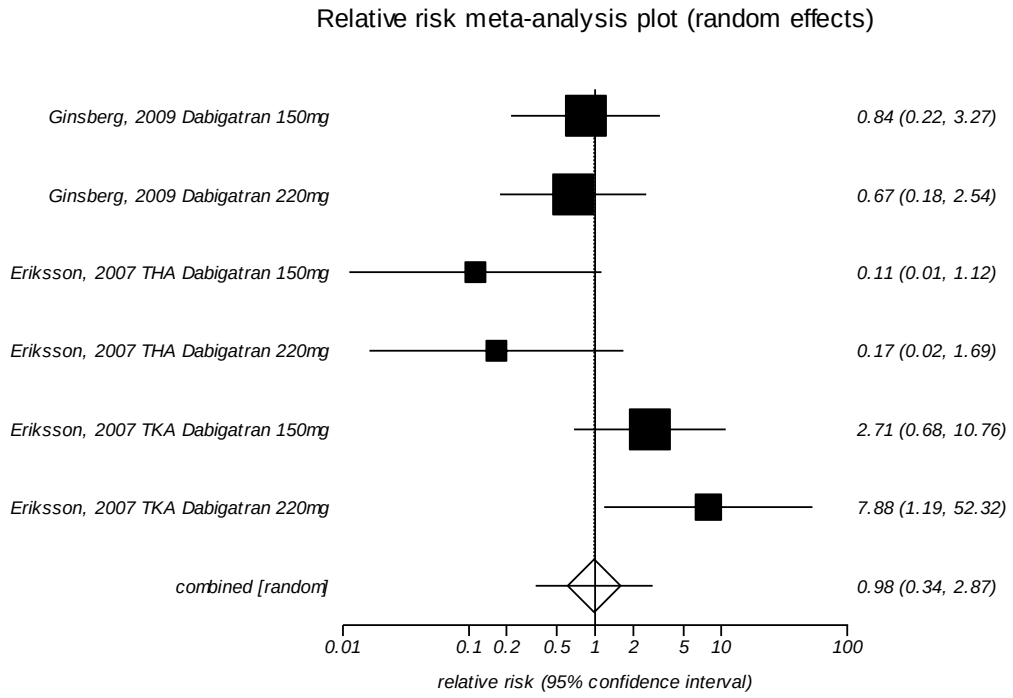
Figure 130. Impact of injectable low molecular weight heparin versus injectable or oral factor Xa inhibitors on symptomatic deep vein thrombosis in patients undergoing major orthopedic surgery limited to total knee replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

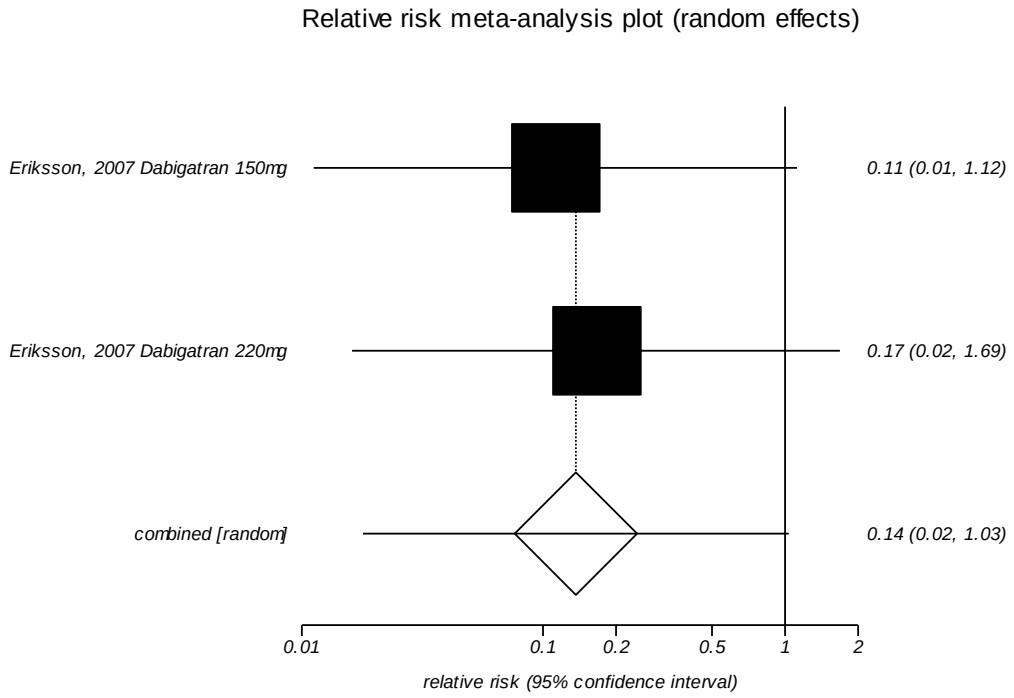
Figure 131. Impact of injectable low molecular weight heparin versus injectable or oral direct thrombin inhibitors on symptomatic deep vein thrombosis in patients undergoing major orthopedic surgery (same as analysis limited to trials published from 2001-present)



I^2: 47.5 percent
Egger's p-value: 0.476

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

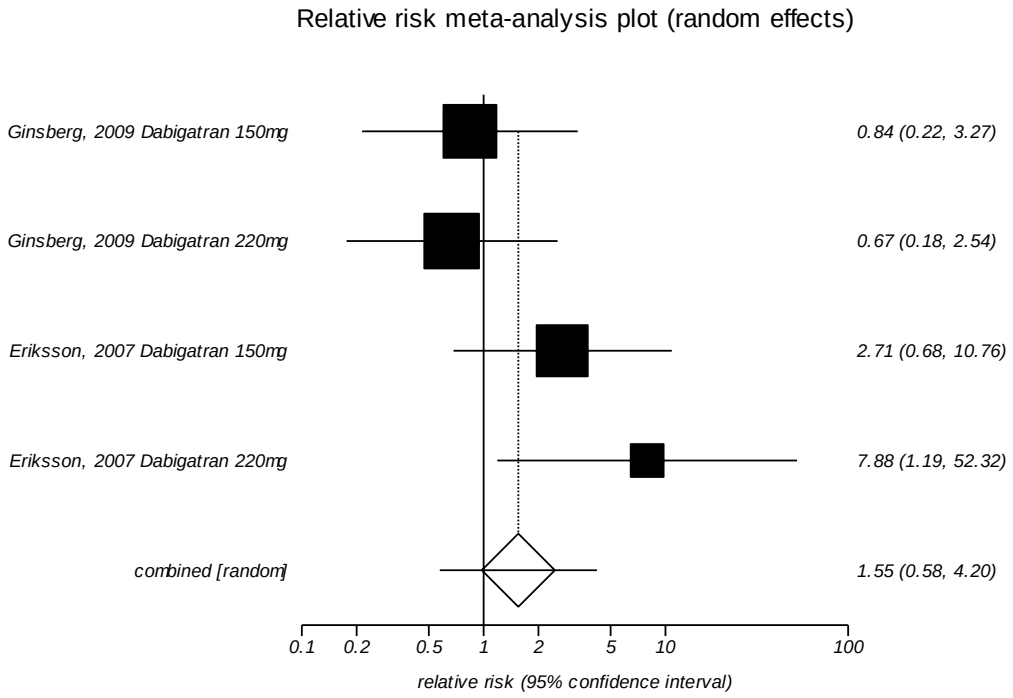
Figure 132. Impact of injectable low molecular weight heparin versus injectable or oral direct thrombin inhibitors on symptomatic deep vein thrombosis in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

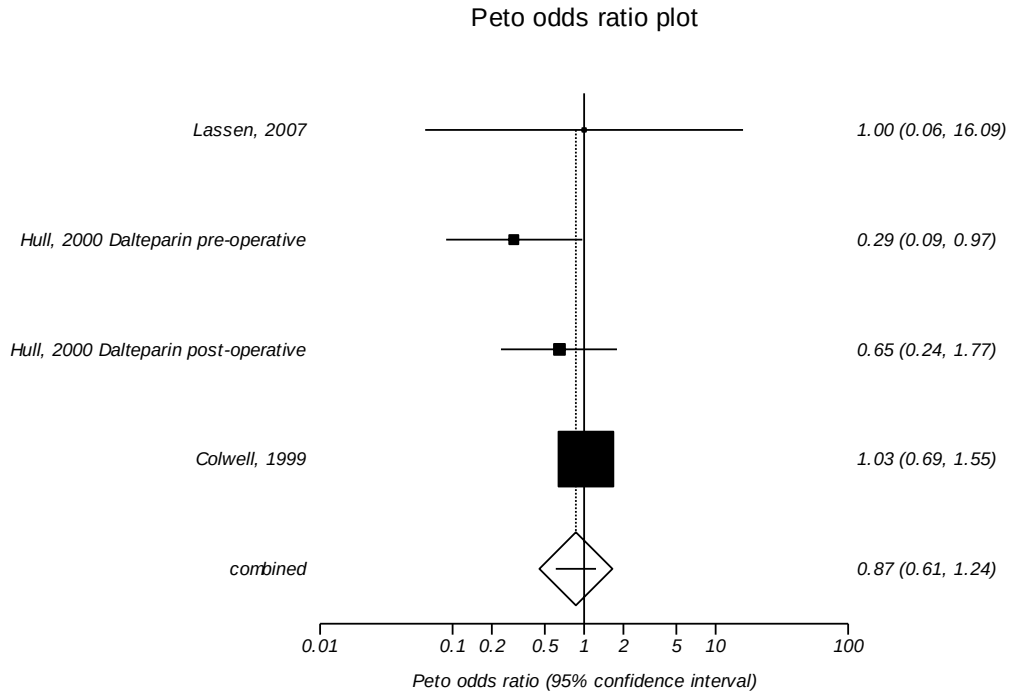
Figure 133. Impact of injectable low molecular weight heparin versus injectable or oral direct thrombin inhibitors on symptomatic deep vein thrombosis in patients undergoing major orthopedic surgery limited to total knee replacement surgery



I^2: 35 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

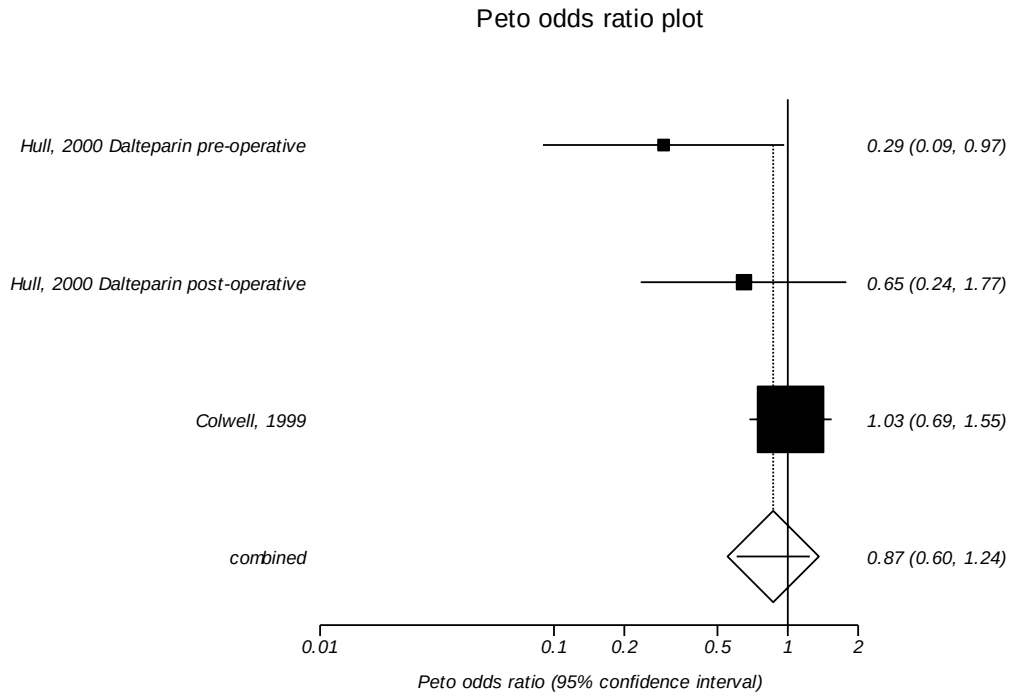
Figure 134. Impact of injectable low molecular weight heparin versus oral vitamin K antagonists on symptomatic deep vein thrombosis in patients undergoing major orthopedic surgery



I^2: 28.4 percent
Egger's p-value: 0.376

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

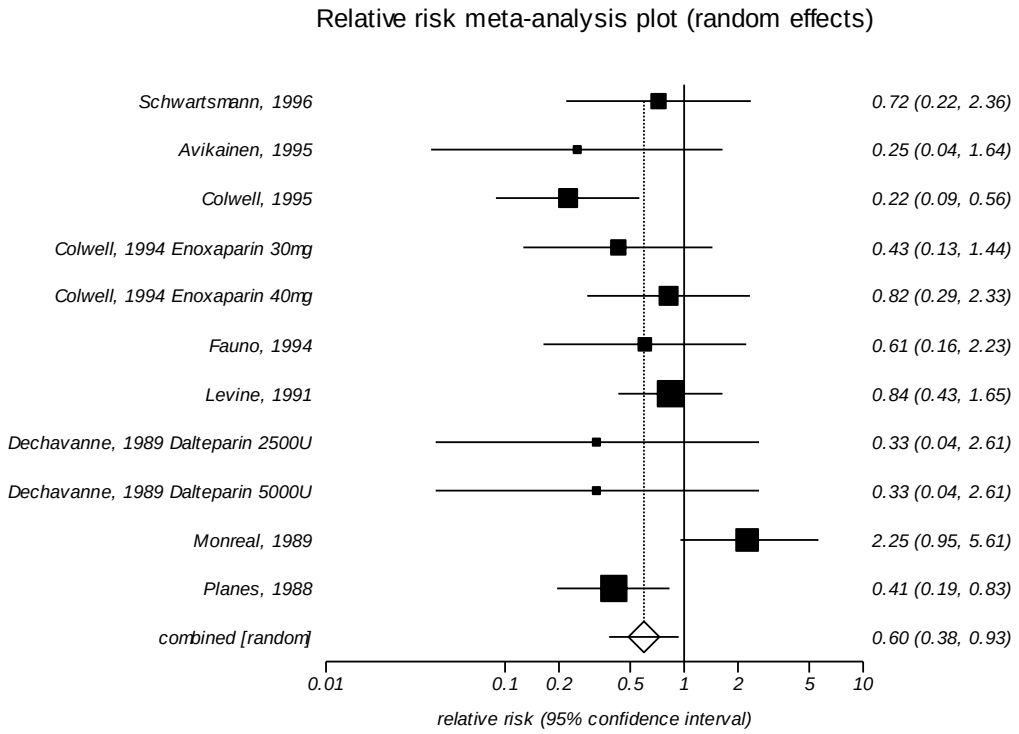
Figure 135. Impact of injectable low molecular weight heparin versus oral vitamin K antagonists on symptomatic deep vein thrombosis in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: 52.2 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

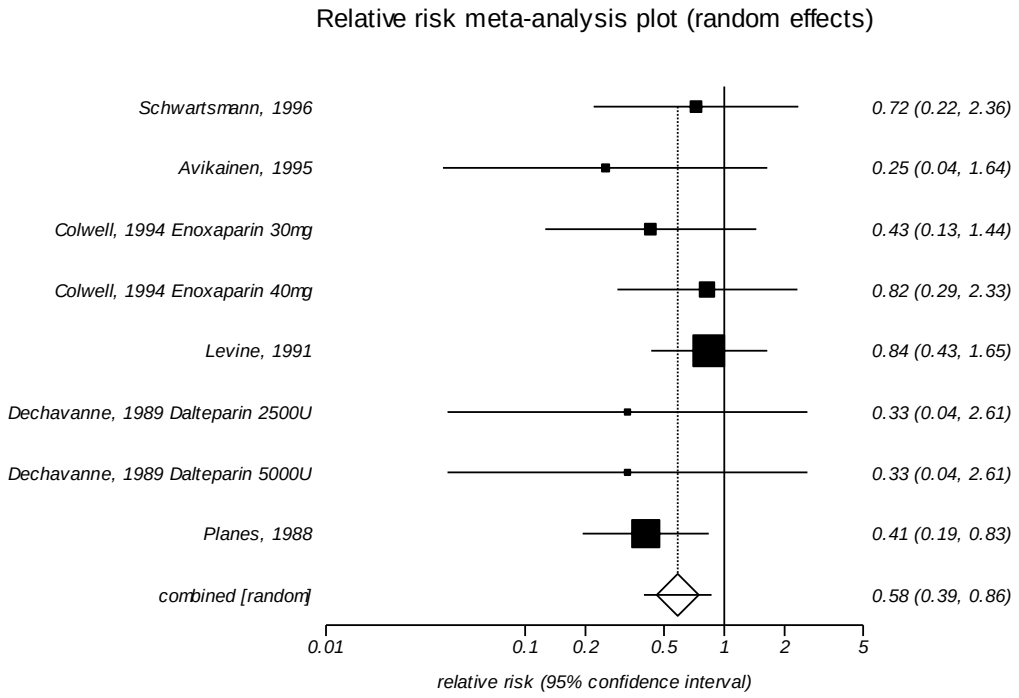
Figure 136. Impact of injectable low molecular weight heparin prophylaxis versus injectable unfractionated heparin prophylaxis on proximal deep vein thrombosis in patients undergoing major orthopedic surgery



I^2: 37 percent
Egger's p-value: 0.450

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

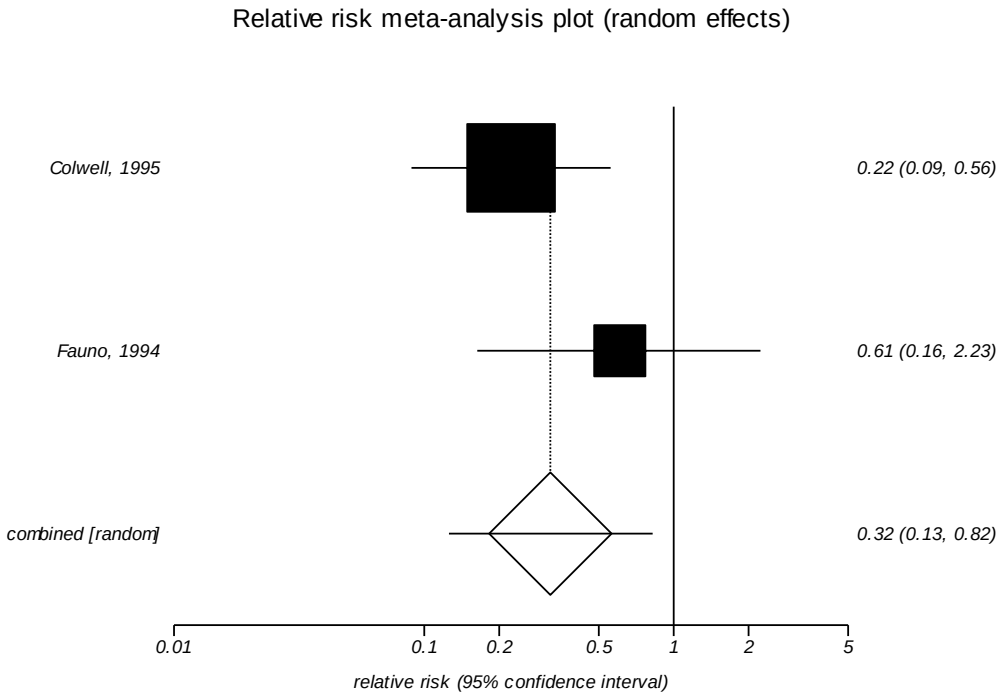
Figure 137. Impact of injectable low molecular weight heparin prophylaxis versus injectable unfractionated heparin prophylaxis on proximal deep vein thrombosis in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

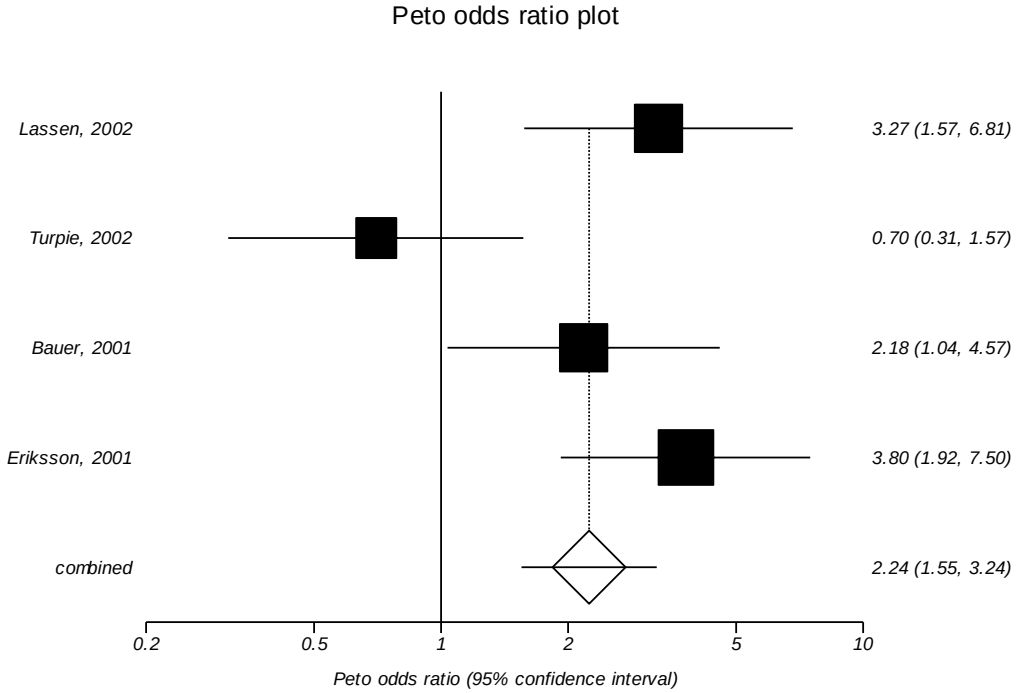
Figure 138. Impact of injectable low molecular weight heparin prophylaxis versus injectable unfractionated heparin prophylaxis on proximal deep vein thrombosis in patients undergoing major orthopedic surgery limited to total knee replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

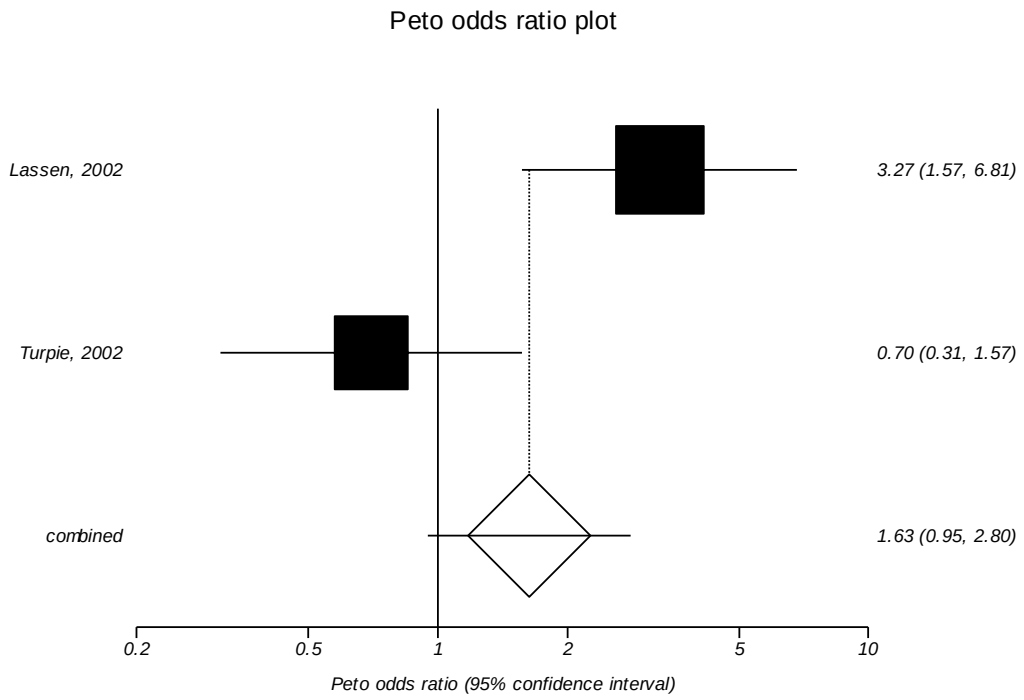
Figure 139. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral factor Xa inhibitor prophylaxis on proximal deep vein thrombosis in patients undergoing major orthopedic surgery (same as 2001 to present)



I^2: 73.5 percent
Egger's p-value: 0.070

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

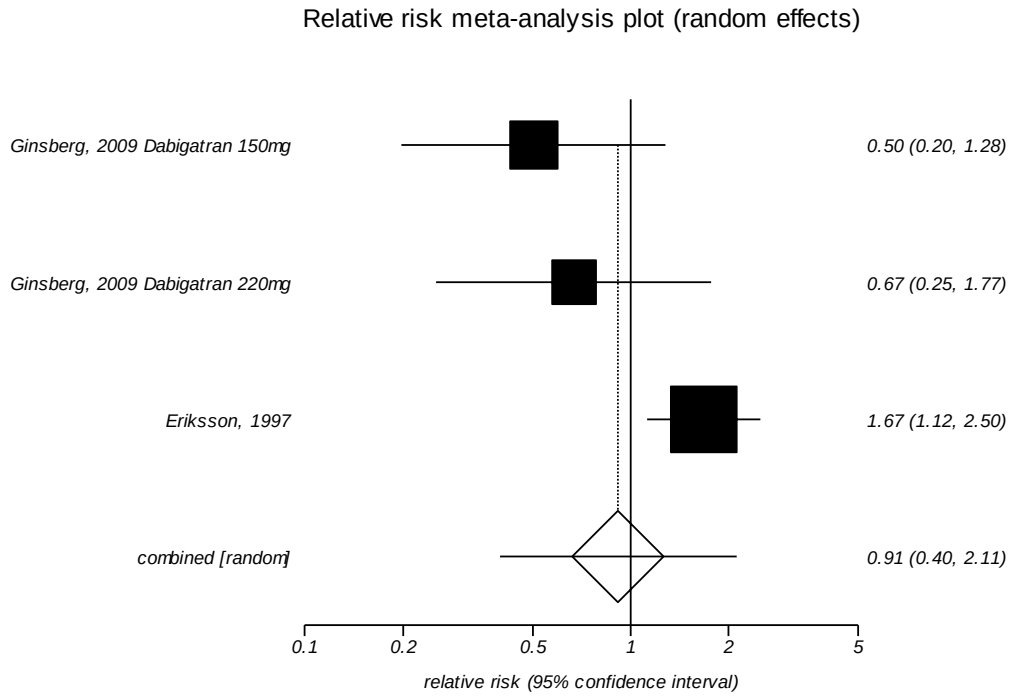
Figure 140. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral factor Xa inhibitor prophylaxis on proximal deep vein thrombosis in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

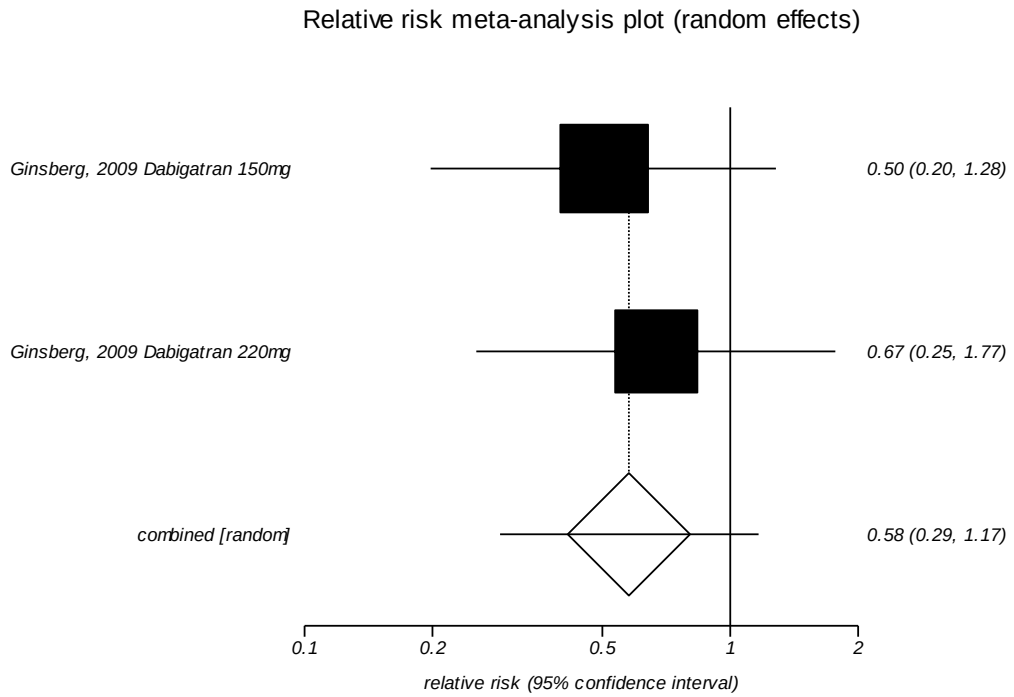
Figure 141. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral direct thrombin inhibitor prophylaxis on proximal deep vein thrombosis in patients undergoing major orthopedic surgery



I^2: 70.8 percent
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Figure 142. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral direct thrombin inhibitor prophylaxis on proximal deep vein thrombosis in patients undergoing major orthopedic surgery limited to trials published from 2001 to present (same as original analysis limited to total knee replacement surgery)



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

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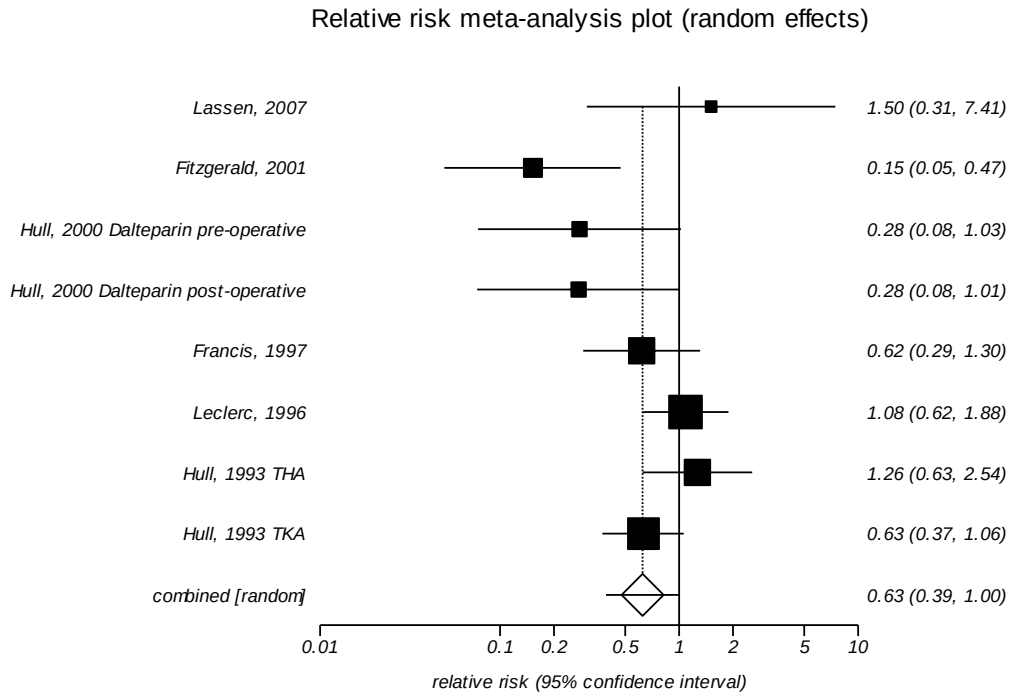
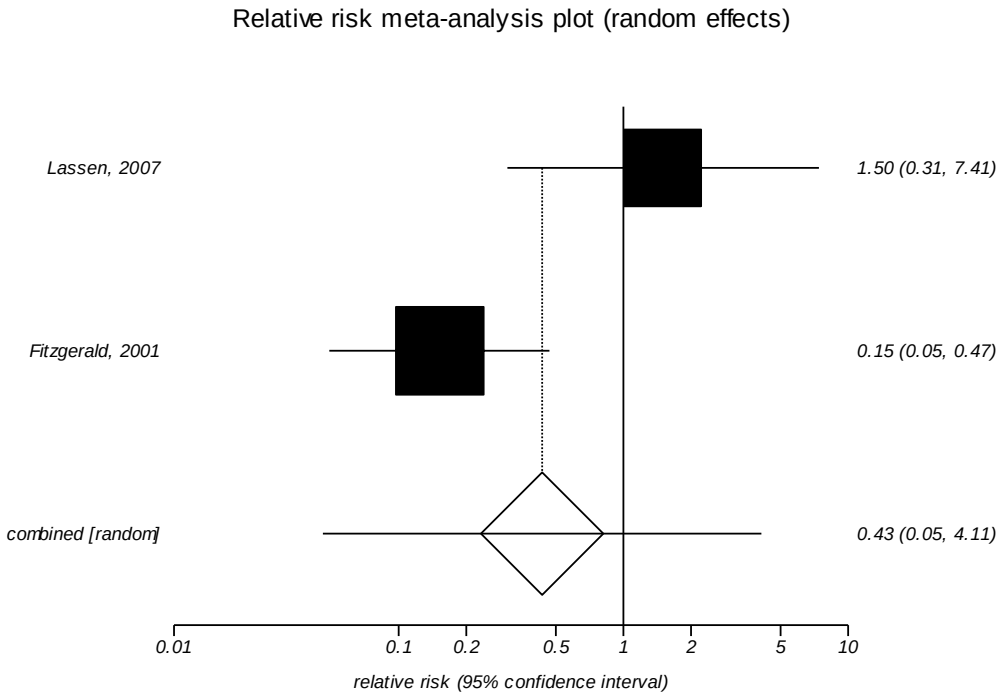
Figure 143. Impact of injectable low molecular weight heparin prophylaxis versus oral vitamin K antagonist prophylaxis on proximal deep vein thrombosis in patients undergoing major orthopedic surgery



I^2: 55.3 percent
Egger's p-value: 0.224

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

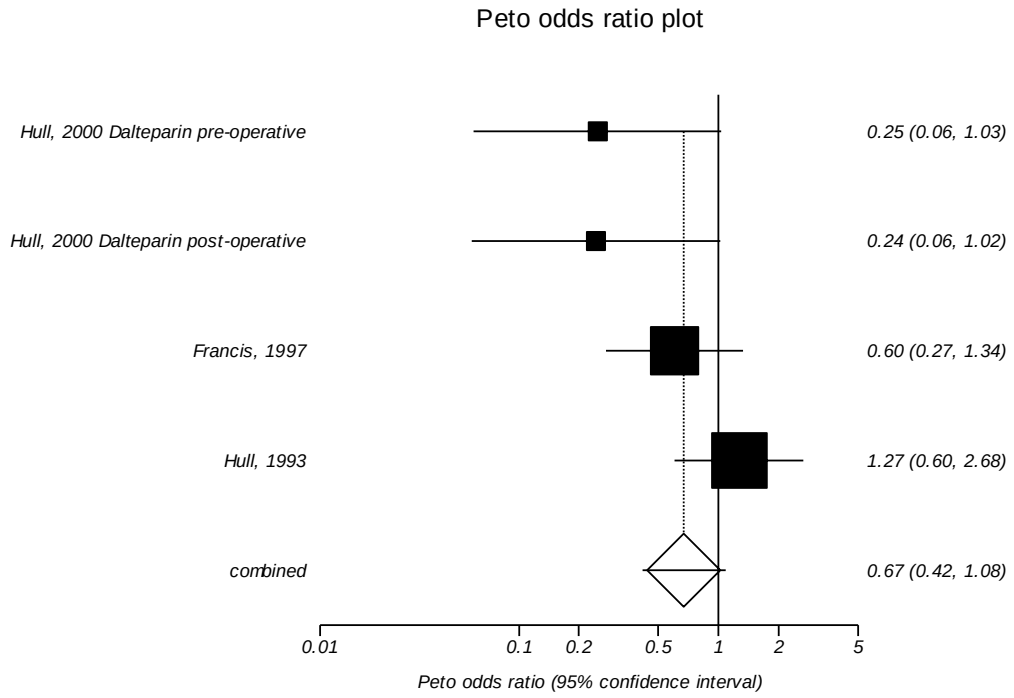
Figure 144. Impact of injectable low molecular weight heparin prophylaxis versus oral vitamin K antagonist prophylaxis on proximal deep vein thrombosis in patients undergoing major orthopedic surgery limited to trials published from 2001 to present



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

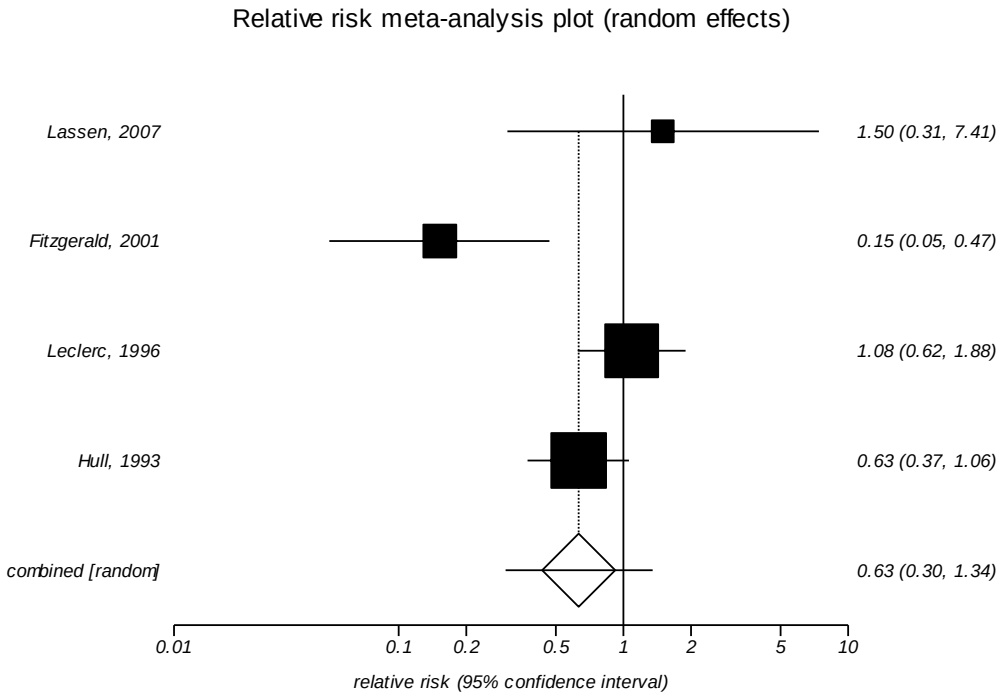
Figure 145. Impact of injectable low molecular weight heparin prophylaxis versus oral vitamin K antagonist prophylaxis on proximal deep vein thrombosis in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: 55.3 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

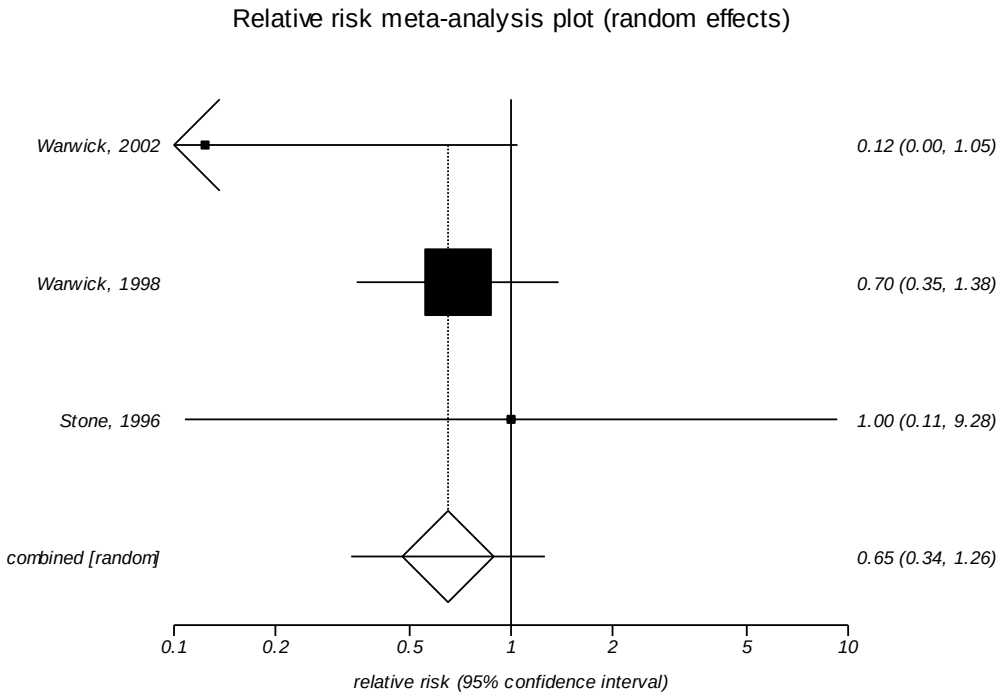
Figure 146. Impact of injectable low molecular weight heparin prophylaxis versus oral vitamin K antagonist prophylaxis on proximal deep vein thrombosis in patients undergoing major orthopedic surgery limited to total knee replacement surgery



I^2: 68.9 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

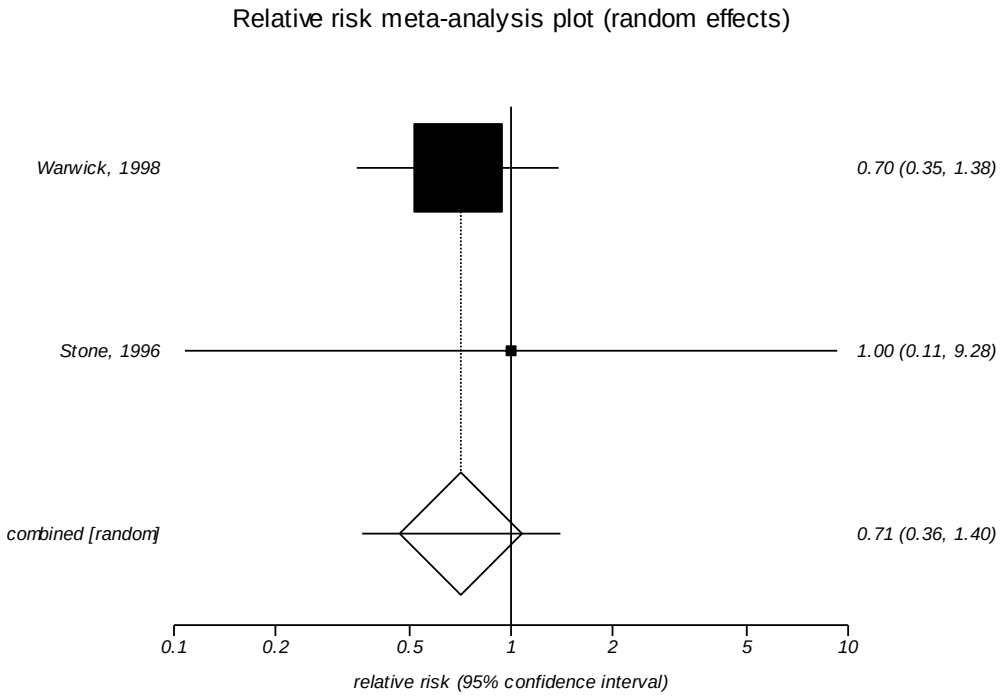
Figure 147. Impact of injectable low molecular weight heparin prophylaxis versus mechanical prophylaxis on proximal deep vein thrombosis in patients undergoing major orthopedic surgery



I^2: 0 percent
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

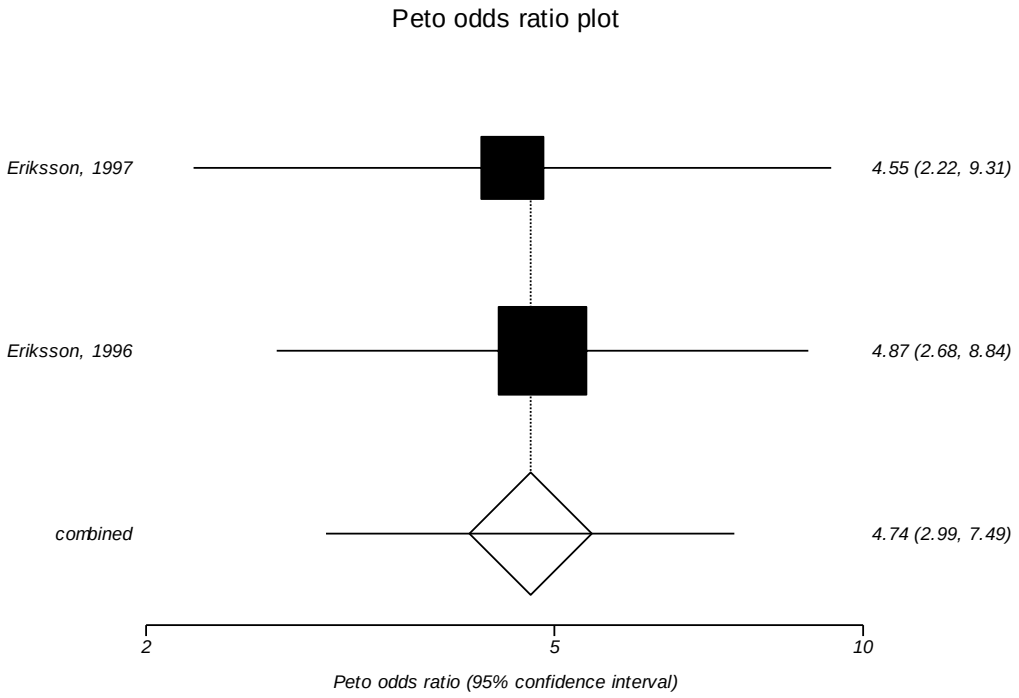
Figure 148. Impact of injectable low molecular weight heparin prophylaxis versus mechanical prophylaxis on proximal deep vein thrombosis in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

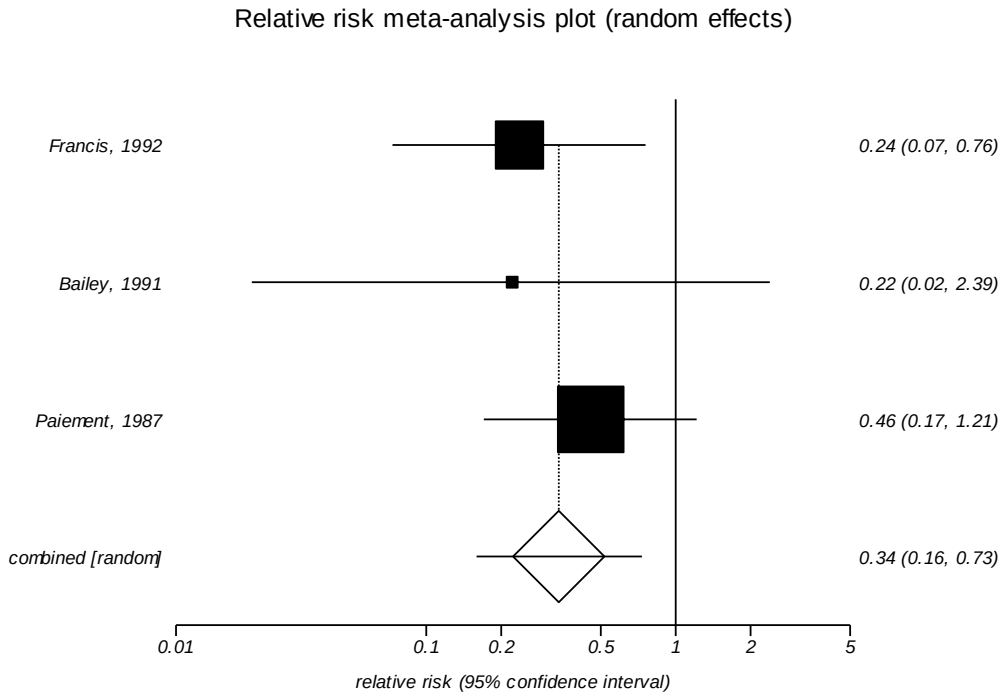
Figure 149. Impact of injectable unfractionated heparin prophylaxis versus injectable or oral direct thrombin inhibitor prophylaxis on proximal deep vein thrombosis in patients undergoing major orthopedic surgery (same as limited to total hip replacement surgery)



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

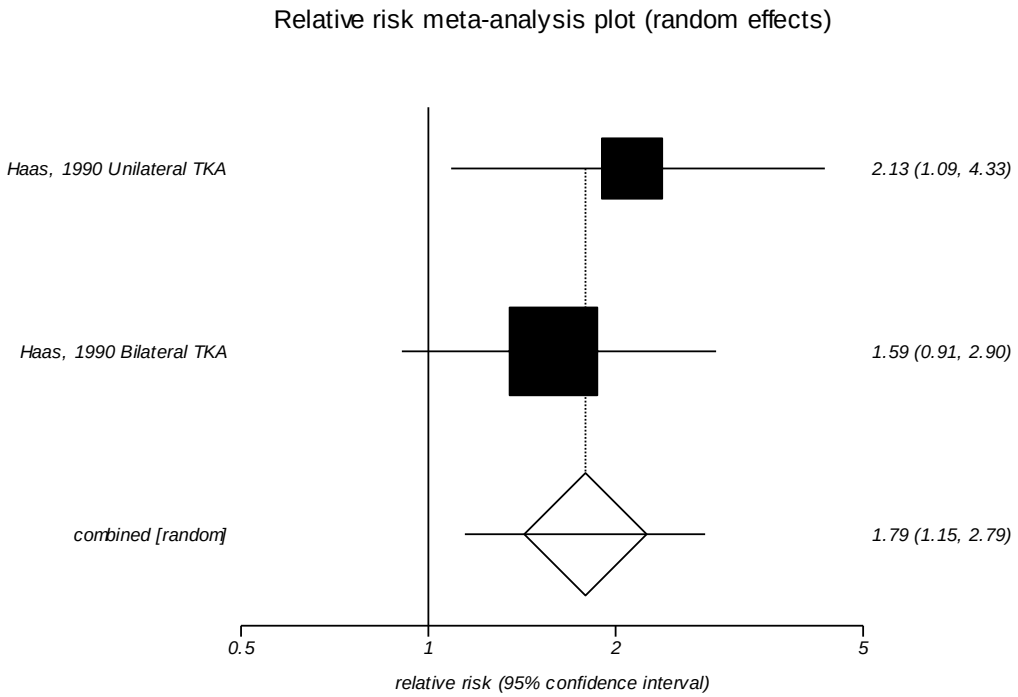
Figure 150. Impact of oral vitamin K antagonist prophylaxis versus mechanical prophylaxis on proximal deep vein thrombosis in patients undergoing major orthopedic surgery (same as limited to total hip replacement surgery)



I^2: 0 percent
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

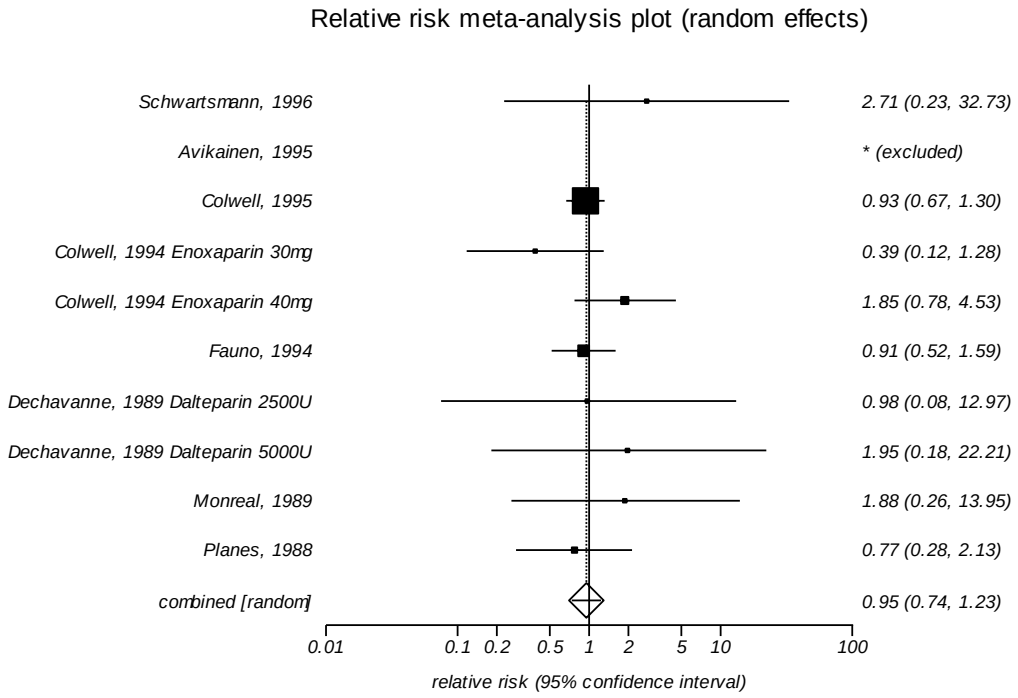
Figure 151. Impact of oral antiplatelet prophylaxis versus mechanical prophylaxis on distal deep vein thrombosis in patients undergoing major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

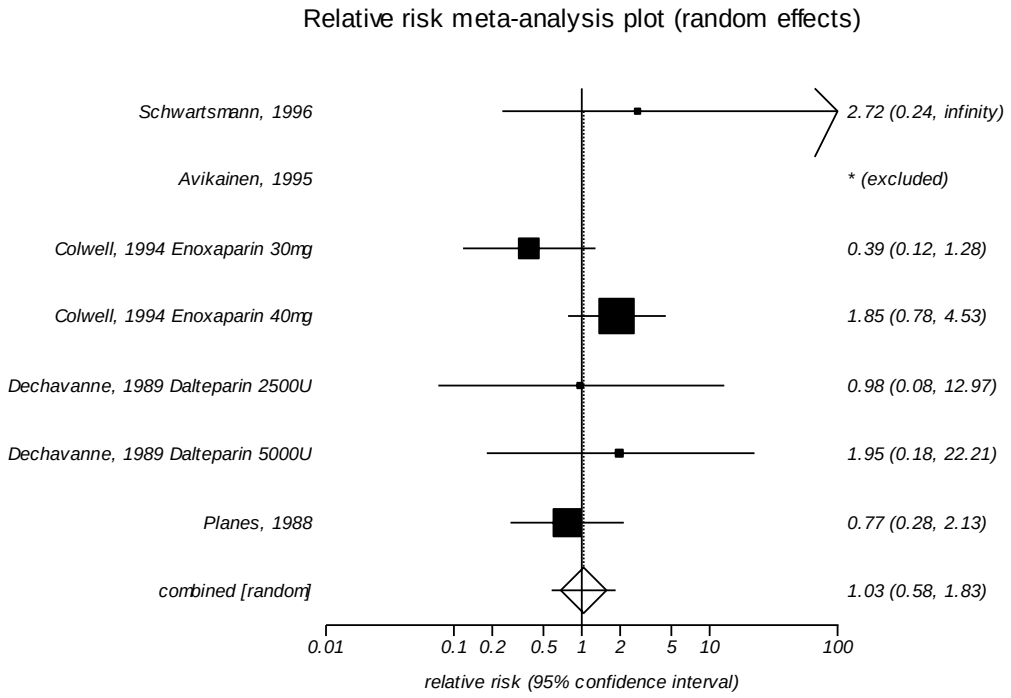
Figure 152. Impact of injectable low molecular weight heparin prophylaxis versus injectable unfractionated heparin prophylaxis on distal deep vein thrombosis in patients undergoing major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.544

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

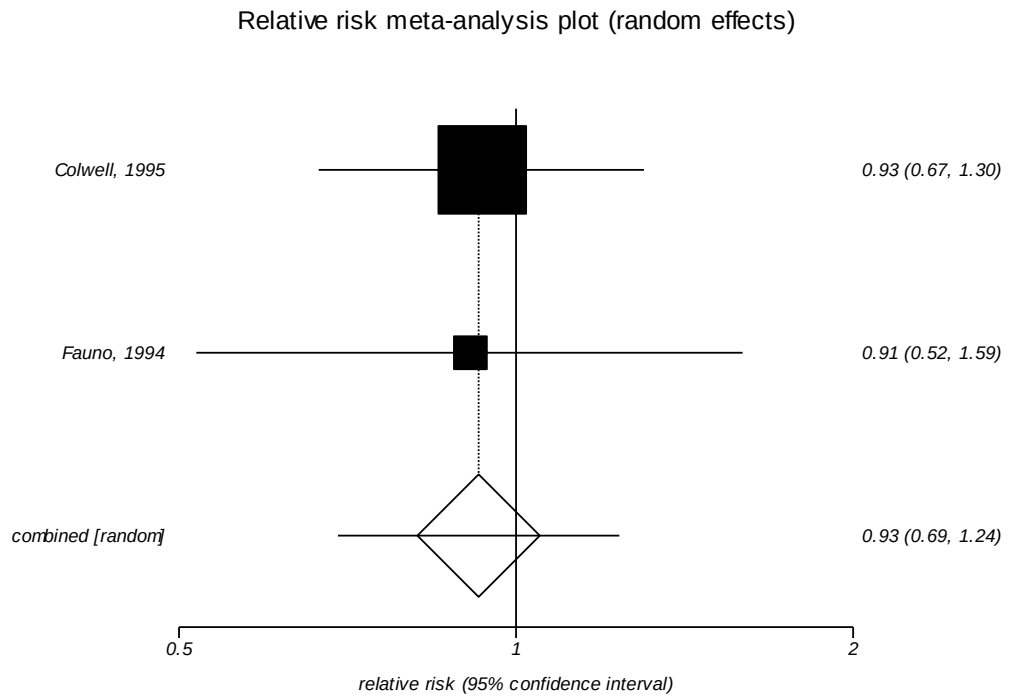
Figure 153. Impact of injectable low molecular weight heparin prophylaxis versus injectable unfractionated heparin prophylaxis on distal deep vein thrombosis in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

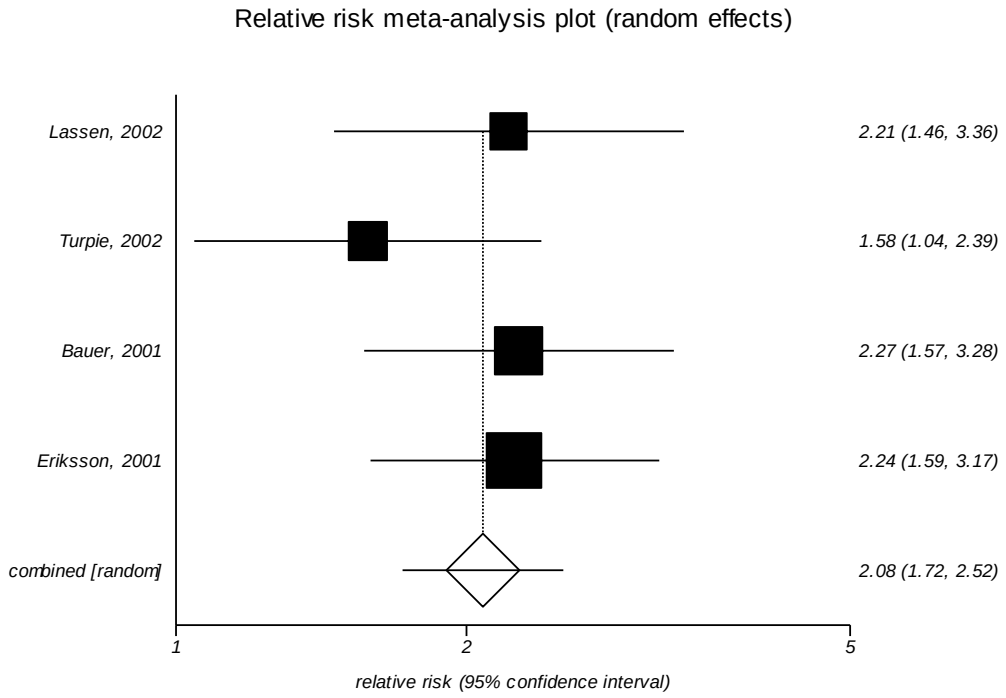
Figure 154. Impact of injectable low molecular weight heparin prophylaxis versus injectable unfractionated heparin prophylaxis on distal deep vein thrombosis in patients undergoing major orthopedic surgery limited to total knee replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

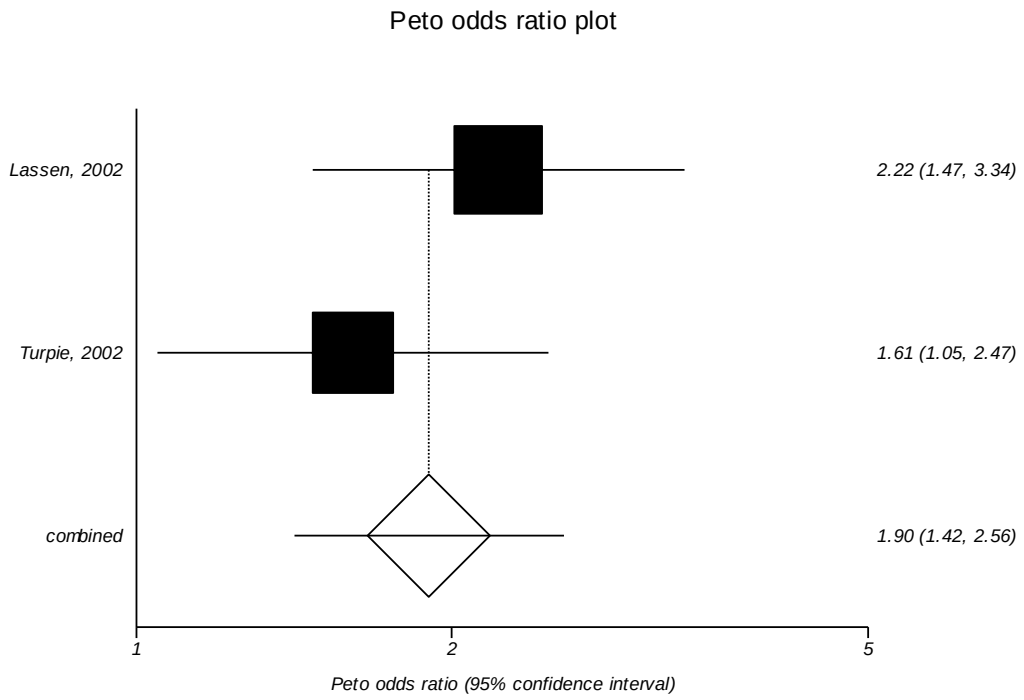
Figure 155. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral factor Xa inhibitor prophylaxis on distal deep vein thrombosis in patients undergoing major orthopedic surgery (same as limited to 2001 to present)



I^2: 0 percent
Egger's p-value: 0.418

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

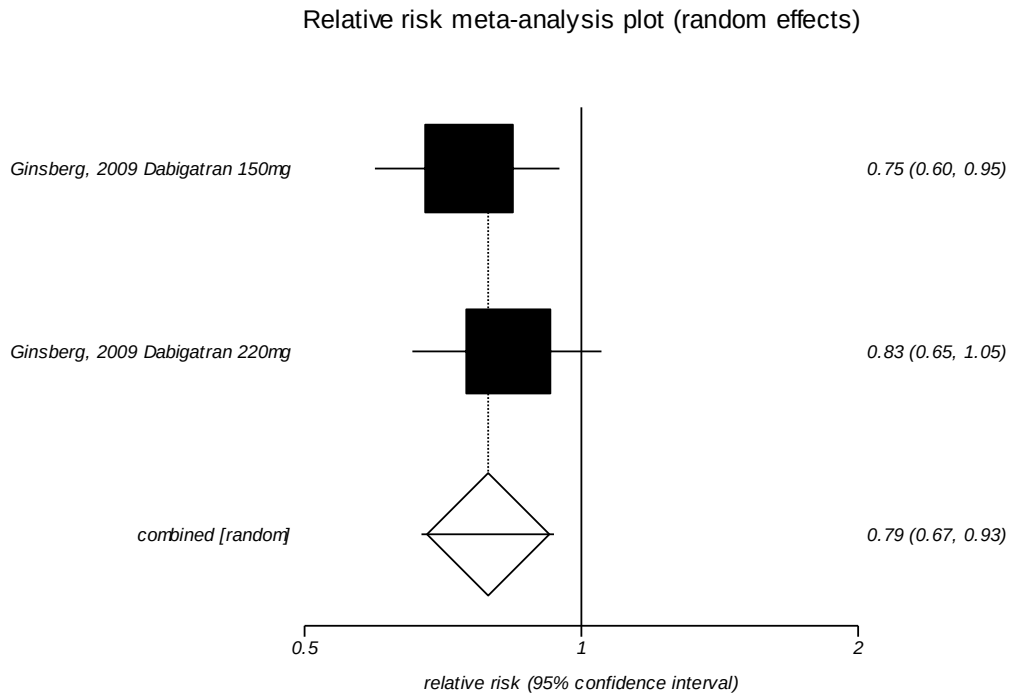
Figure 156. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral factor Xa inhibitor prophylaxis on distal deep vein thrombosis in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

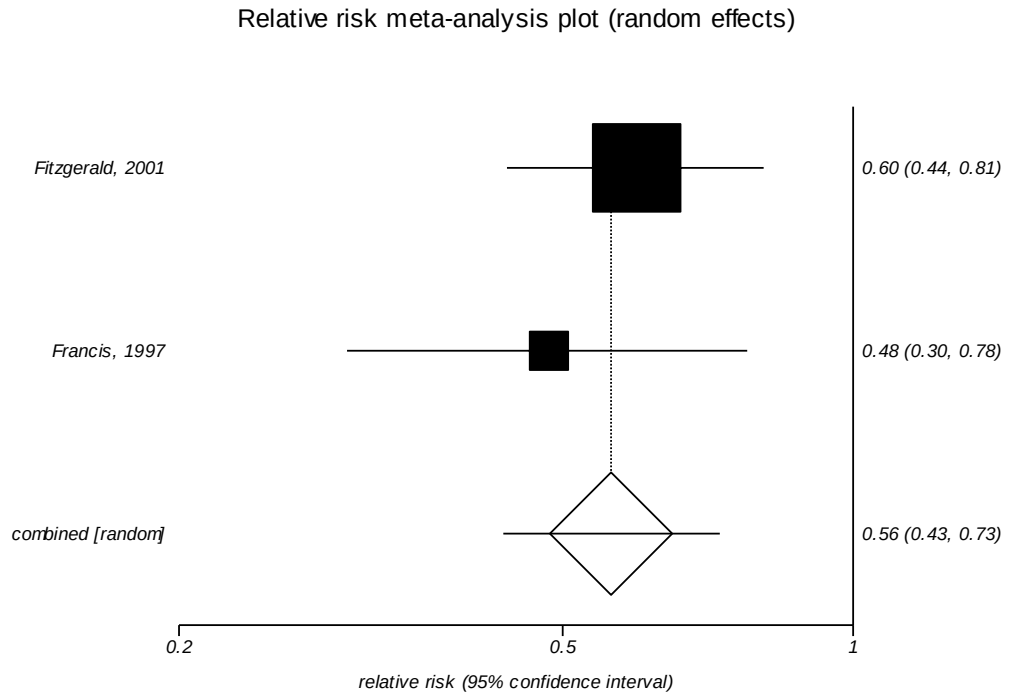
Figure 157. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral direct thrombin inhibitor prophylaxis on distal deep vein thrombosis in patients undergoing major orthopedic surgery (same as limited to 2001 to present, same as limited to total hip replacement surgery)



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

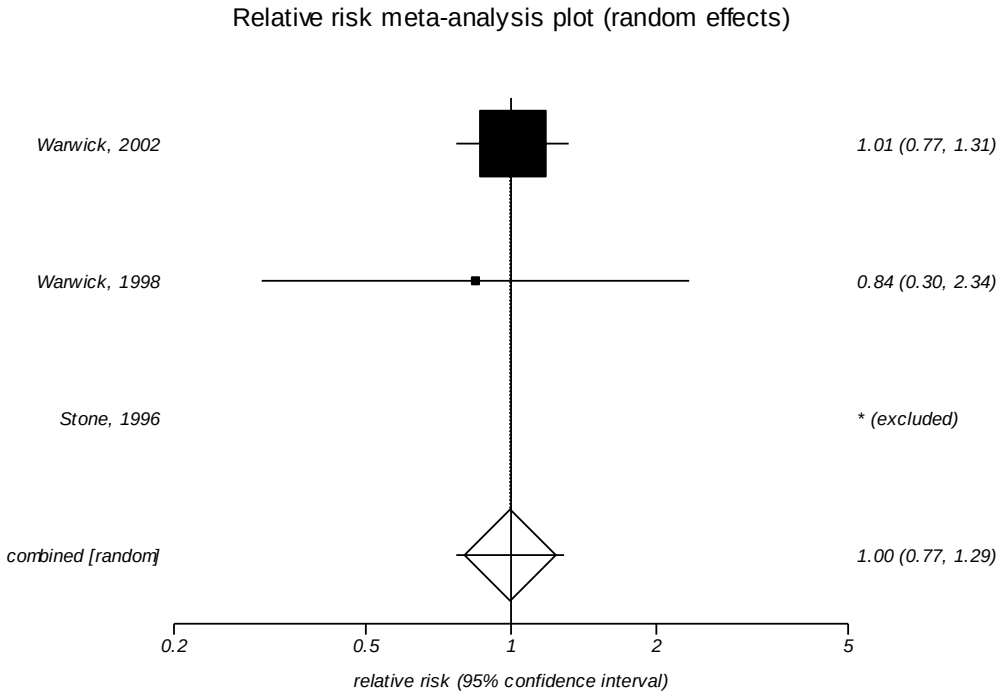
Figure 158. Impact of injectable low molecular weight heparin prophylaxis versus oral vitamin K antagonist prophylaxis on distal deep vein thrombosis in patients undergoing major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

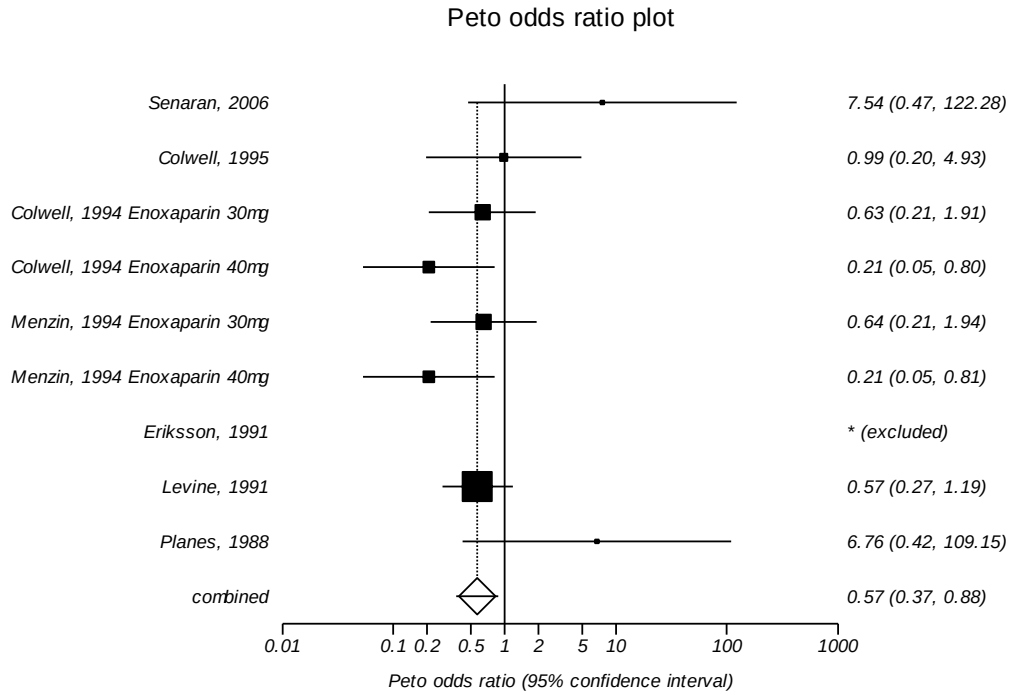
Figure 159. Impact of injectable low molecular weight heparin prophylaxis versus mechanical prophylaxis on distal deep vein thrombosis in patients undergoing major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

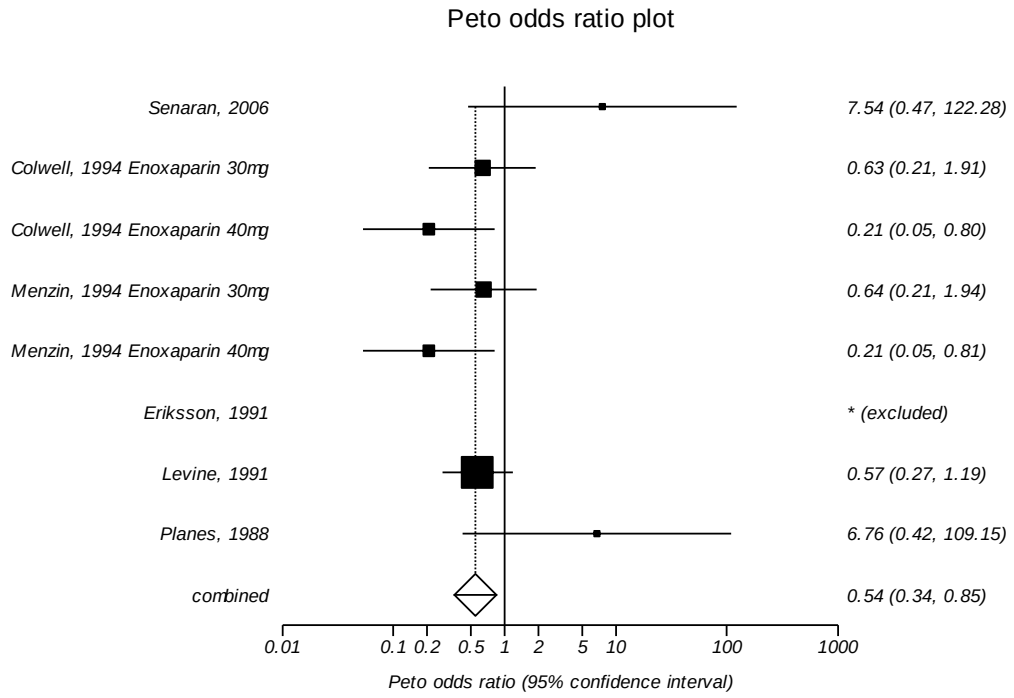
Figure 160. Impact of injectable low molecular weight heparin versus injectable unfractionated heparin on major bleeding in patients undergoing major orthopedic surgery



I^2: 37.1 percent
Egger's p-value: 0.201

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

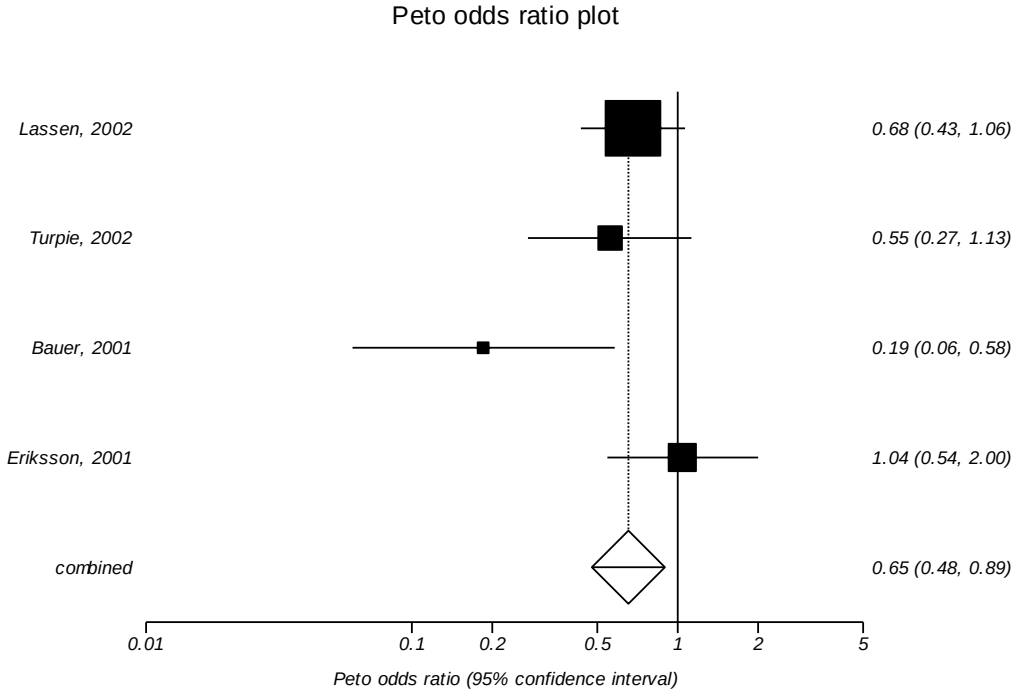
Figure 161. Impact of injectable low molecular weight heparin versus injectable unfractionated heparin on major bleeding in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: 43.5 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

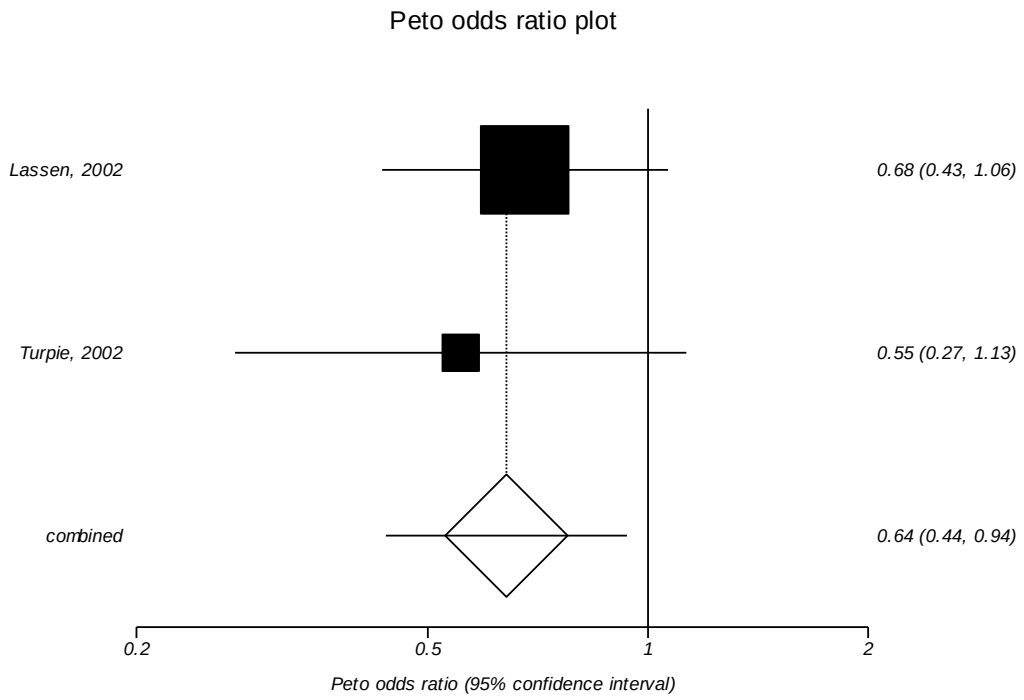
Figure 162. Impact of injectable low molecular weight heparin versus injectable or oral factor Xa inhibitors on major bleeding in patients undergoing major orthopedic surgery (same as analysis limited to trials published from 2001 to the present)



I^2: 56.6 percent
Egger's p-value: 0.347

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

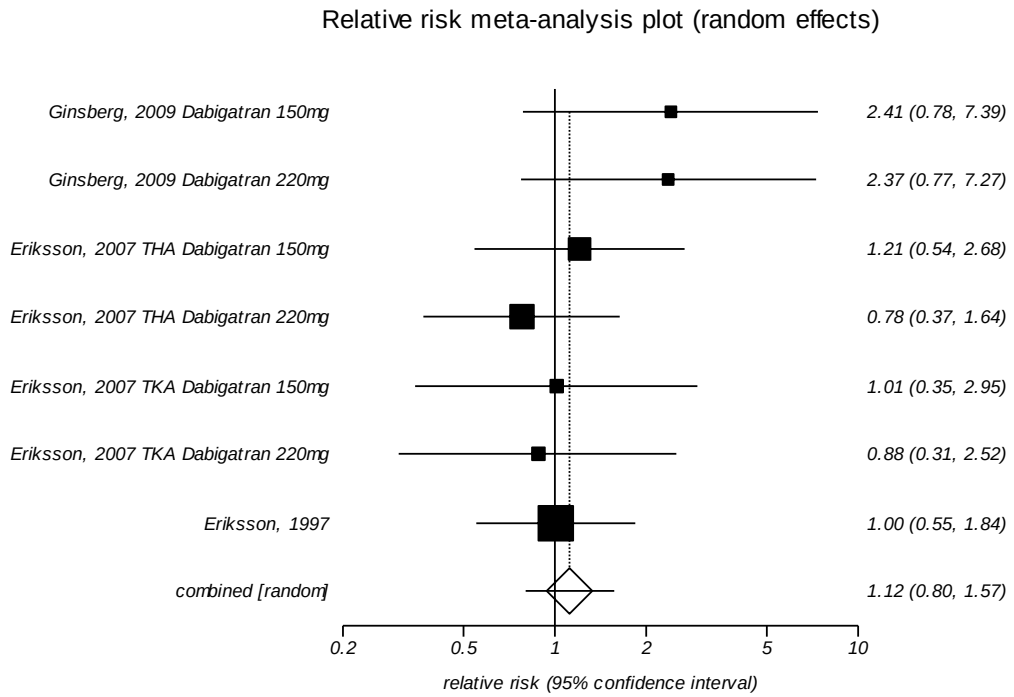
Figure 163. Impact of injectable low molecular weight heparin versus injectable or oral factor Xa inhibitors on major bleeding in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

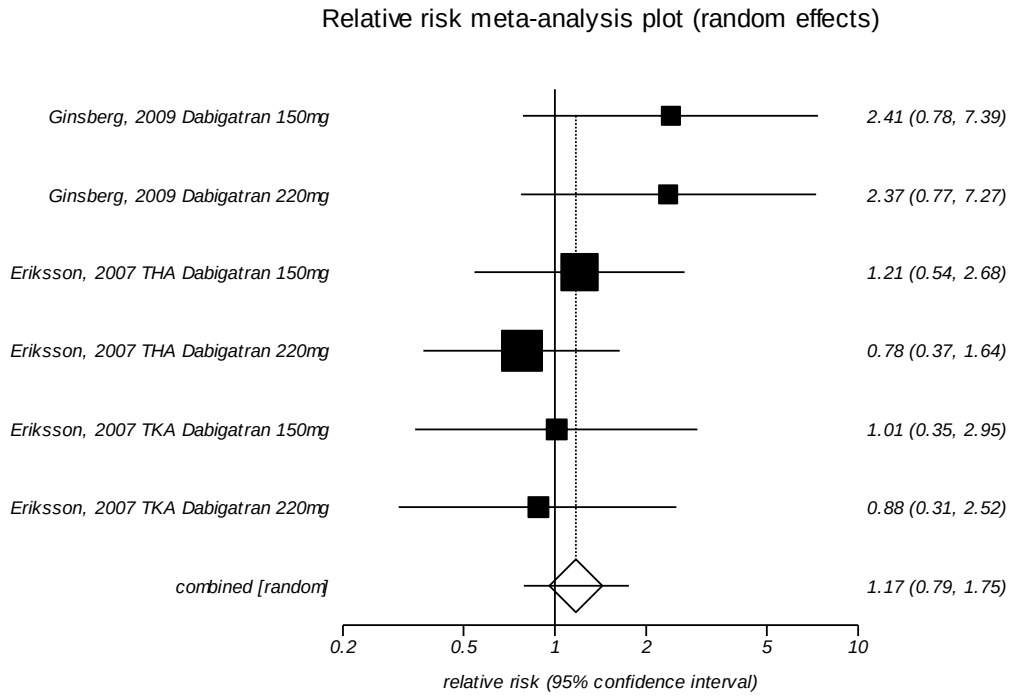
Figure 164. Impact of injectable low molecular weight heparin versus injectable or oral direct thrombin inhibitors on major bleeding in patients undergoing major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.175

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

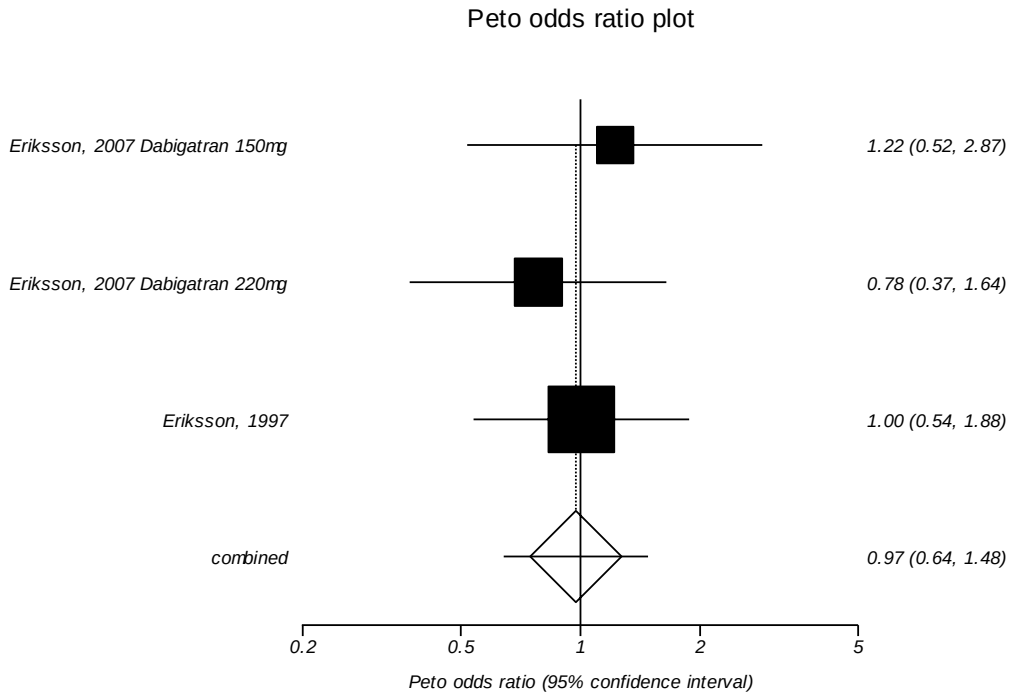
Figure 165. Impact of injectable low molecular weight heparin versus injectable or oral direct thrombin inhibitors on major bleeding in patients undergoing major orthopedic surgery limited to trials published from 2001 to the present



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

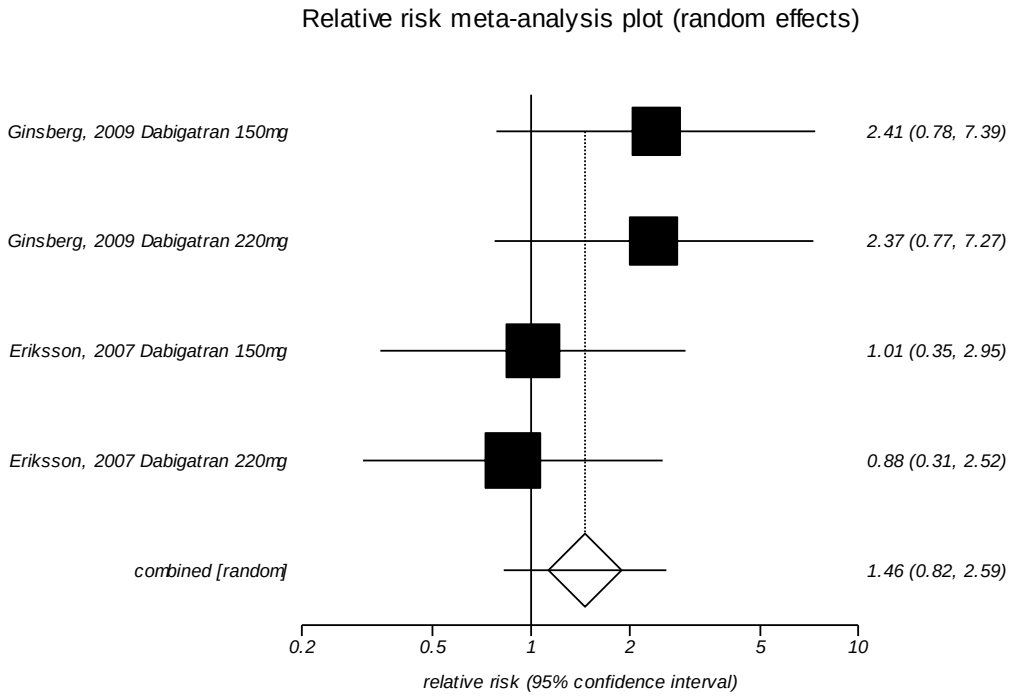
Figure 166. Impact of injectable low molecular weight heparin versus injectable or oral direct thrombin inhibitors on major bleeding in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

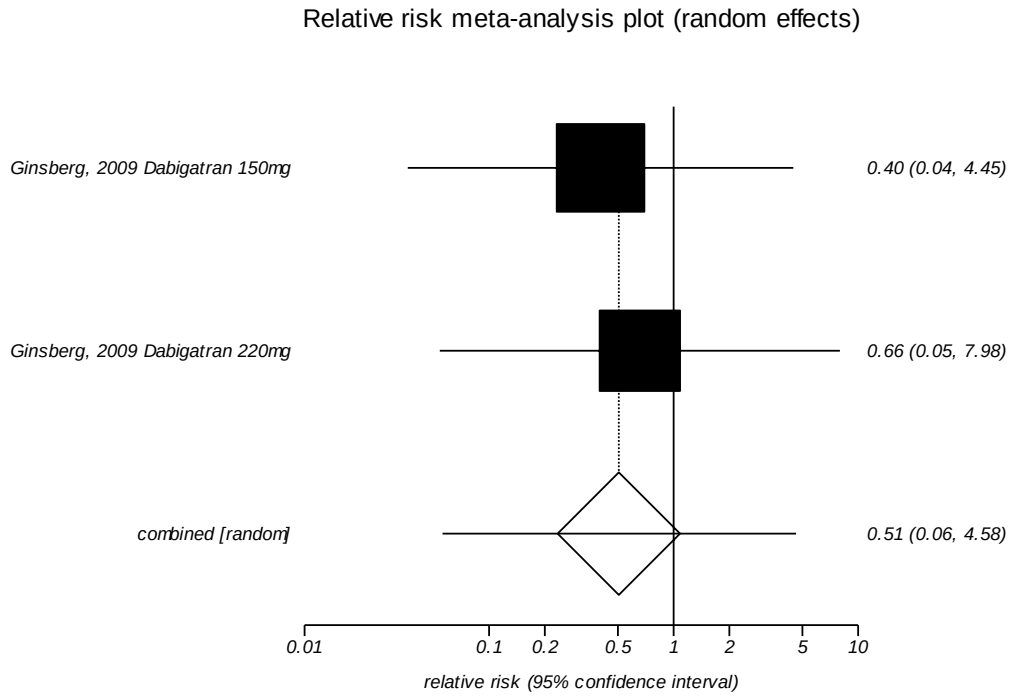
Figure 167. Impact of injectable low molecular weight heparin versus injectable or oral direct thrombin inhibitors on major bleeding in patients undergoing major orthopedic surgery limited to total knee replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

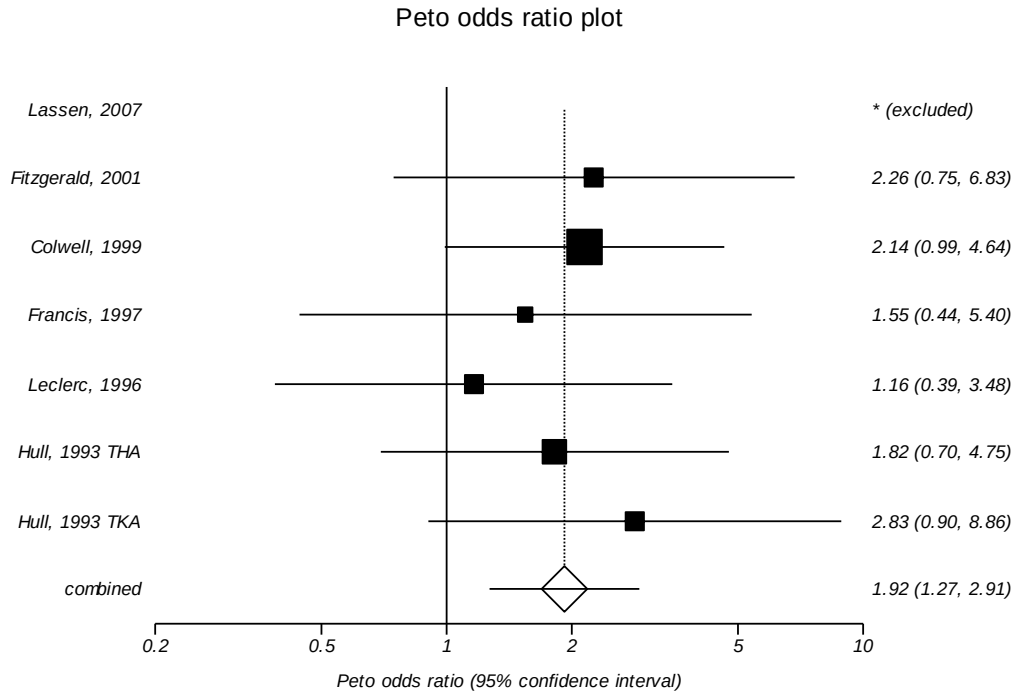
Figure 168. Impact of injectable low molecular weight heparin versus injectable or oral direct thrombin inhibitors on major bleeding during the postdischarge period in patients who had total knee replacement surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

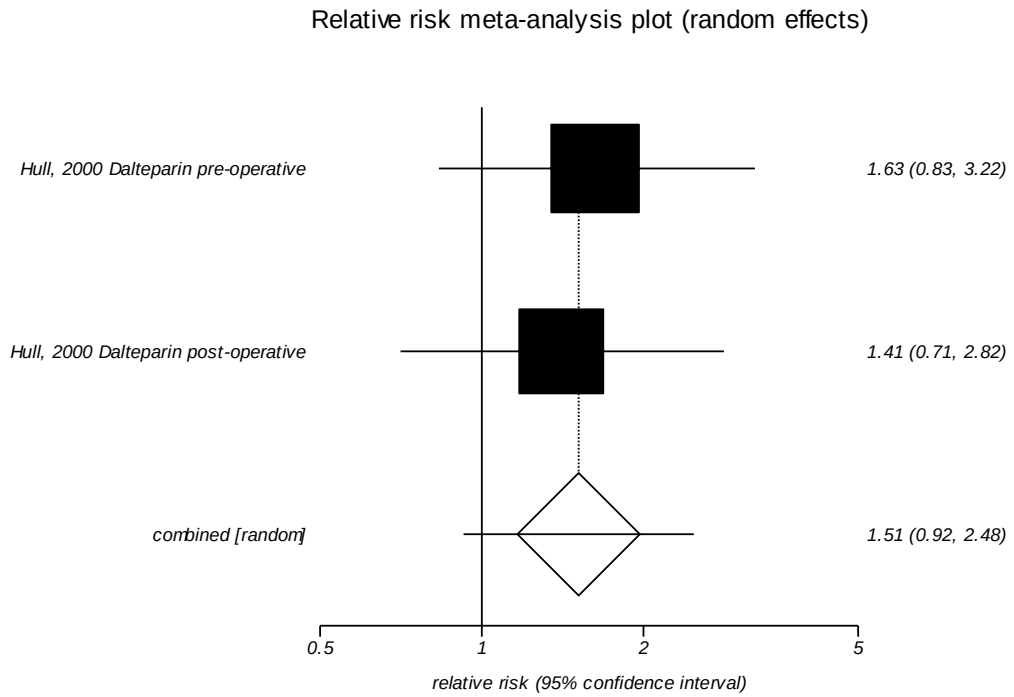
Figure 169. Impact of injectable low molecular weight heparin versus oral vitamin K antagonists on major bleeding in patients undergoing major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.661

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

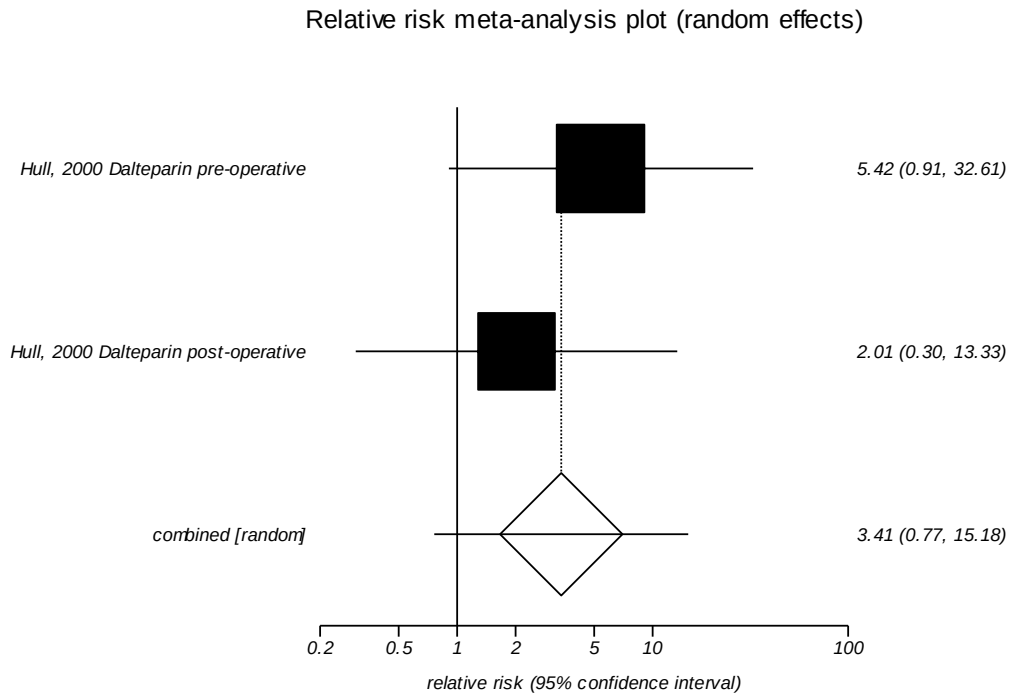
Figure 170. Impact of injectable low molecular weight heparin versus oral vitamin K antagonists on major bleeding during days 0 to 1 in patients who had total hip replacement surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

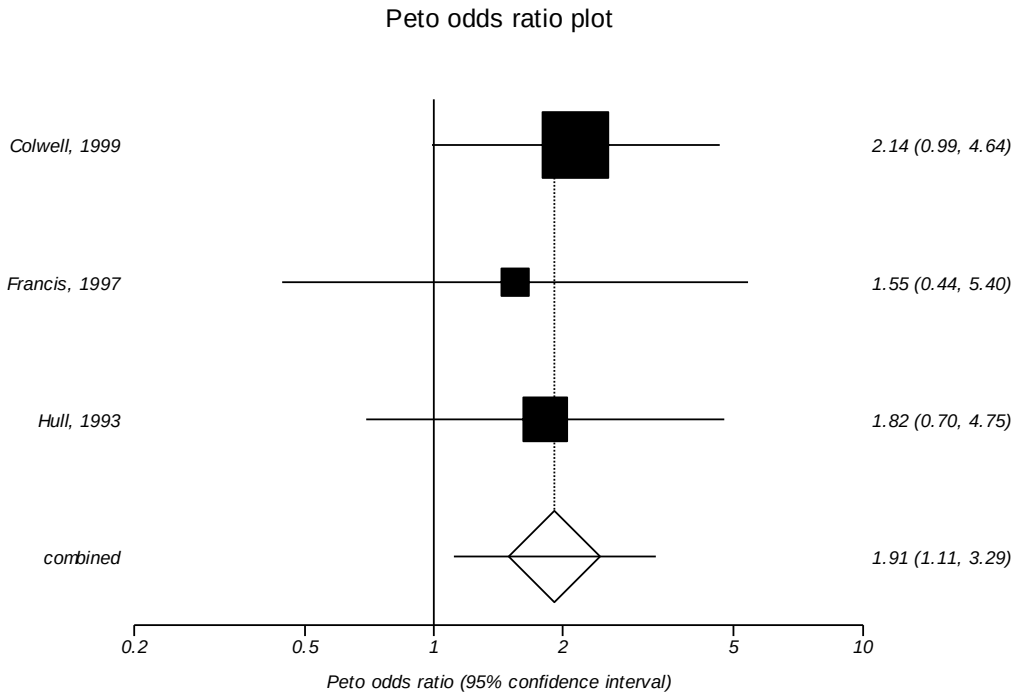
Figure 171. Impact of injectable low molecular weight heparin versus oral vitamin K antagonists on major bleeding during days 2 to 8 in patients who had total hip replacement surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

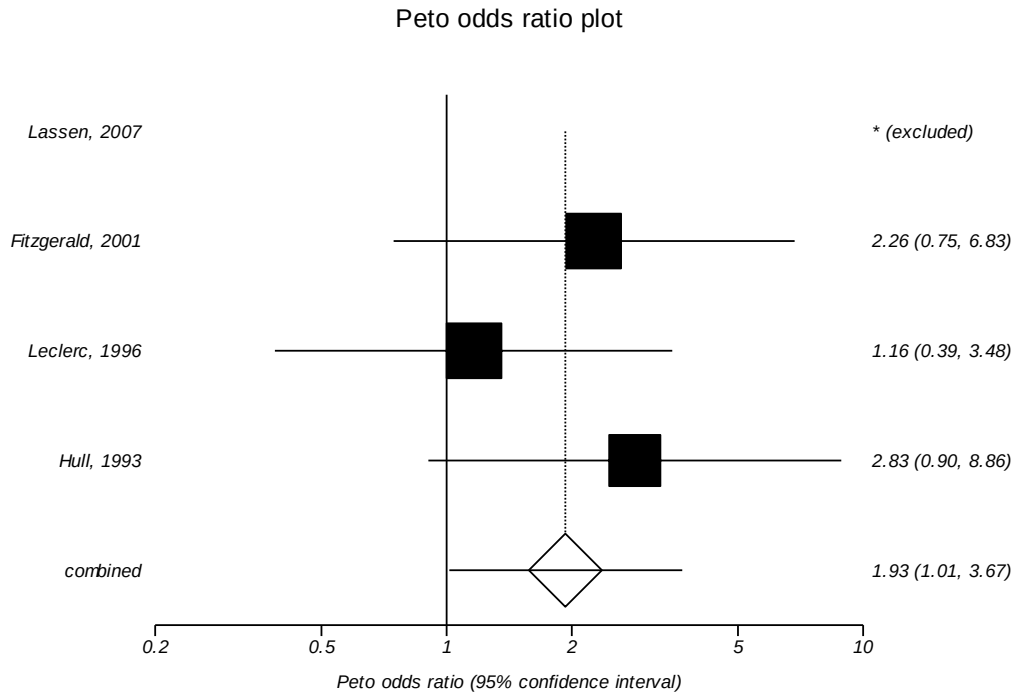
Figure 172. Impact of injectable low molecular weight heparin versus oral vitamin k antagonists on major bleeding in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

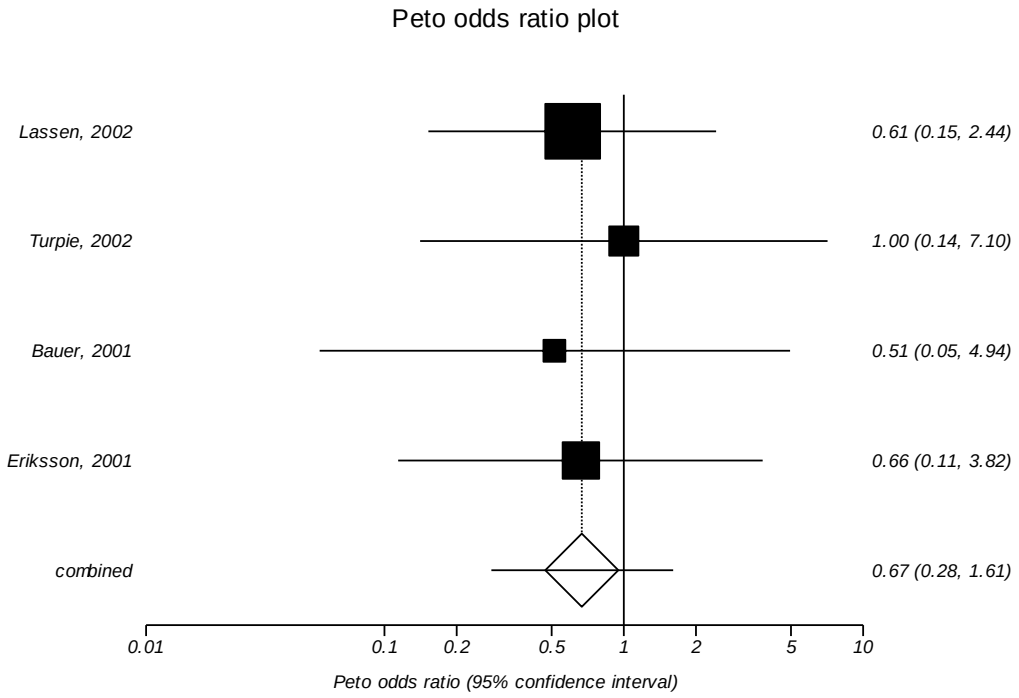
Figure 173. Impact of injectable low molecular weight heparin versus oral vitamin K antagonists on major bleeding in patients undergoing major orthopedic surgery limited to total knee replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

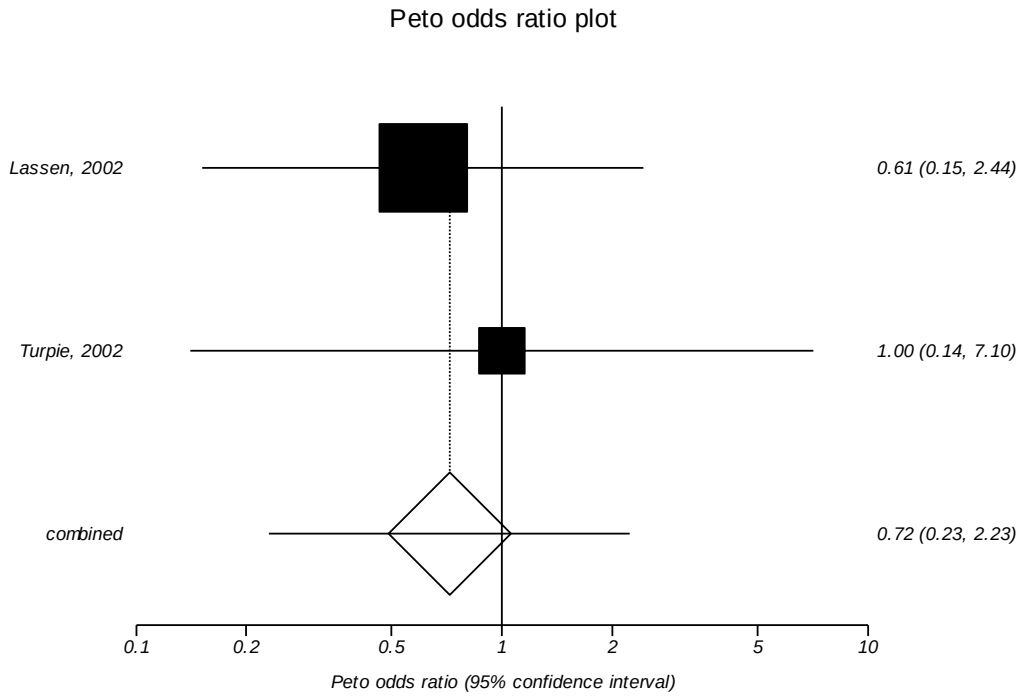
Figure 174. Impact of injectable low molecular weight heparin versus injectable or oral factor Xa antagonists on major bleeding leading to reoperation (same as analysis limited to trials published from 2001-present)



I^2: 0 percent
Egger's p-value: 0.855

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

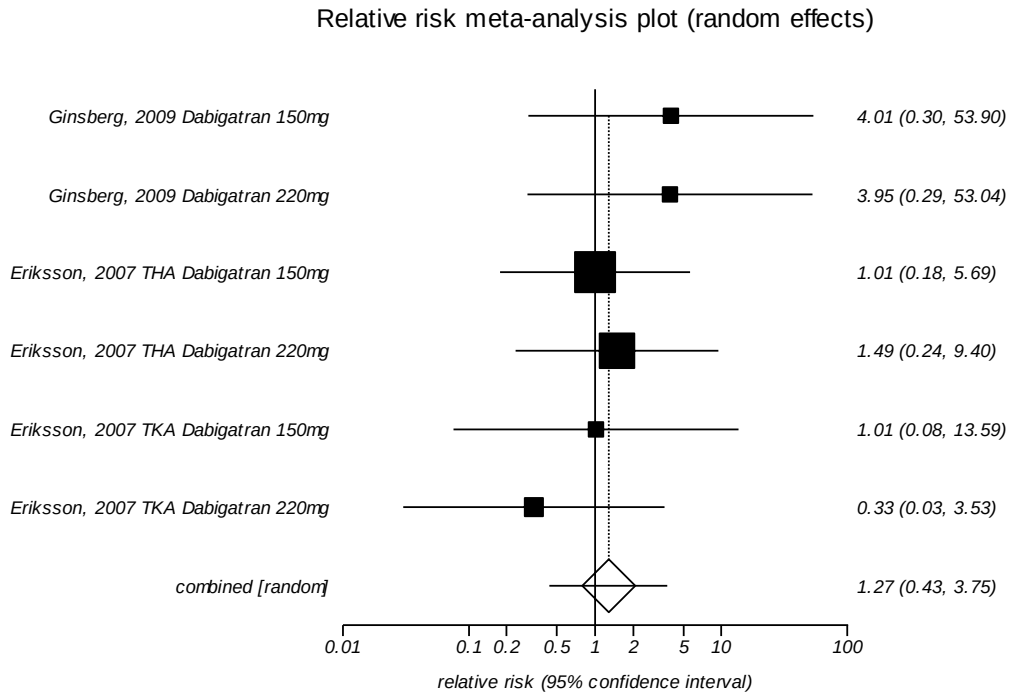
Figure 175. Impact of injectable low molecular weight heparin versus injectable or oral factor Xa antagonists on major bleeding leading to reoperation in patients undergoing major orthopedic surgery limited to total hip replacement



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

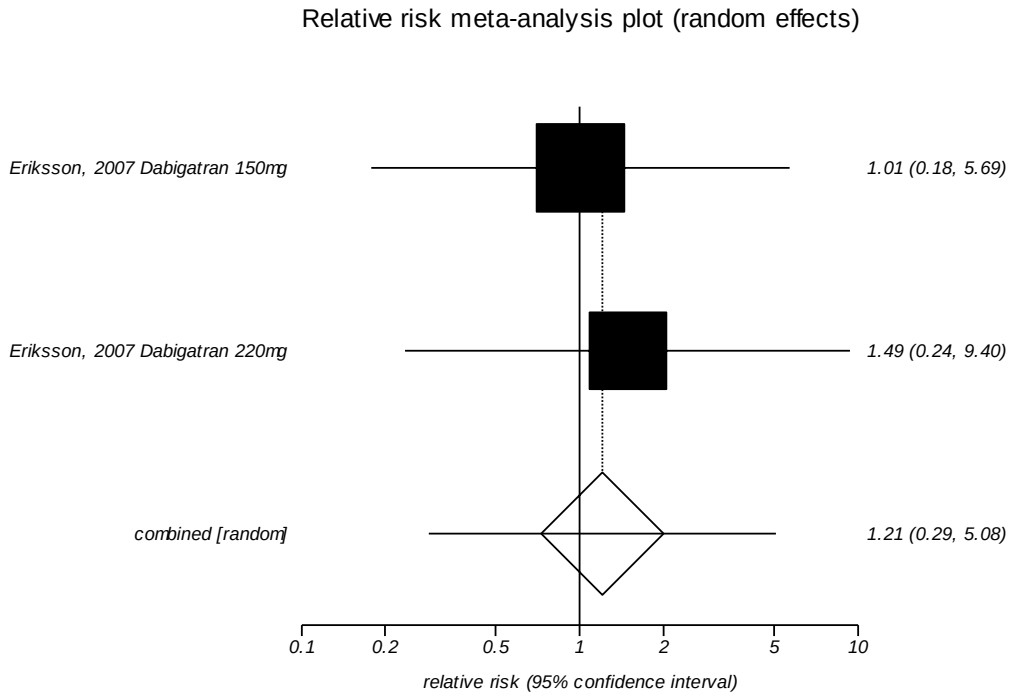
Figure 176. Impact of injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors on major bleeding leading to reoperation in patients who had major orthopedic surgery (same as analysis limited to trials published from 2001-present)



I^2: 0 percent
Egger's p-value: 0.614

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

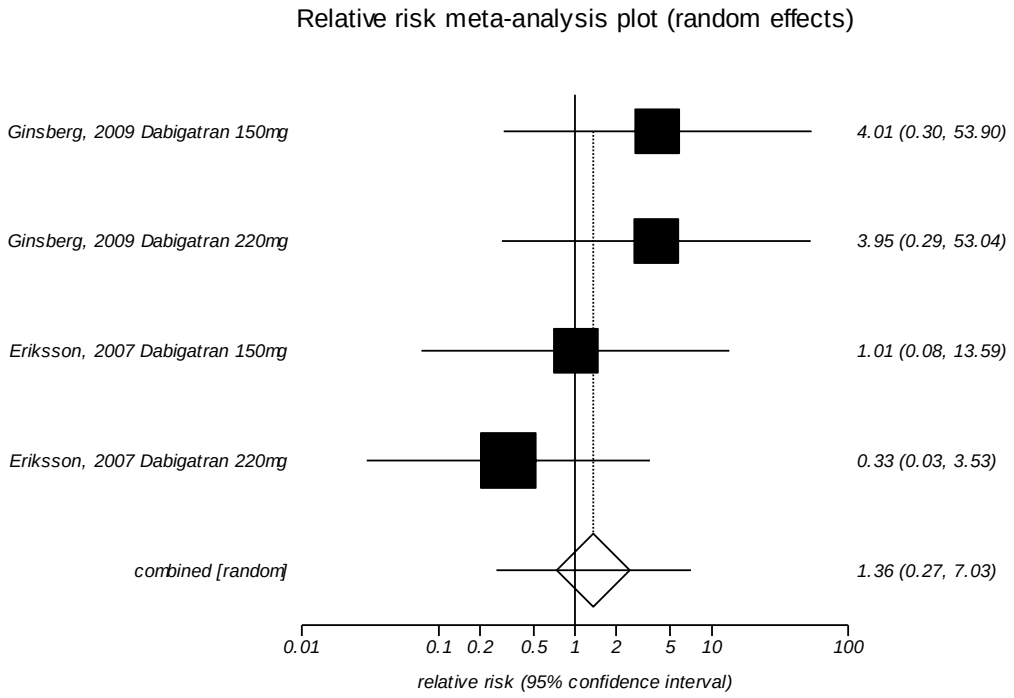
Figure 177. Impact of injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors on major bleeding leading to reoperation in patients who had major orthopedic surgery limited to total hip replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

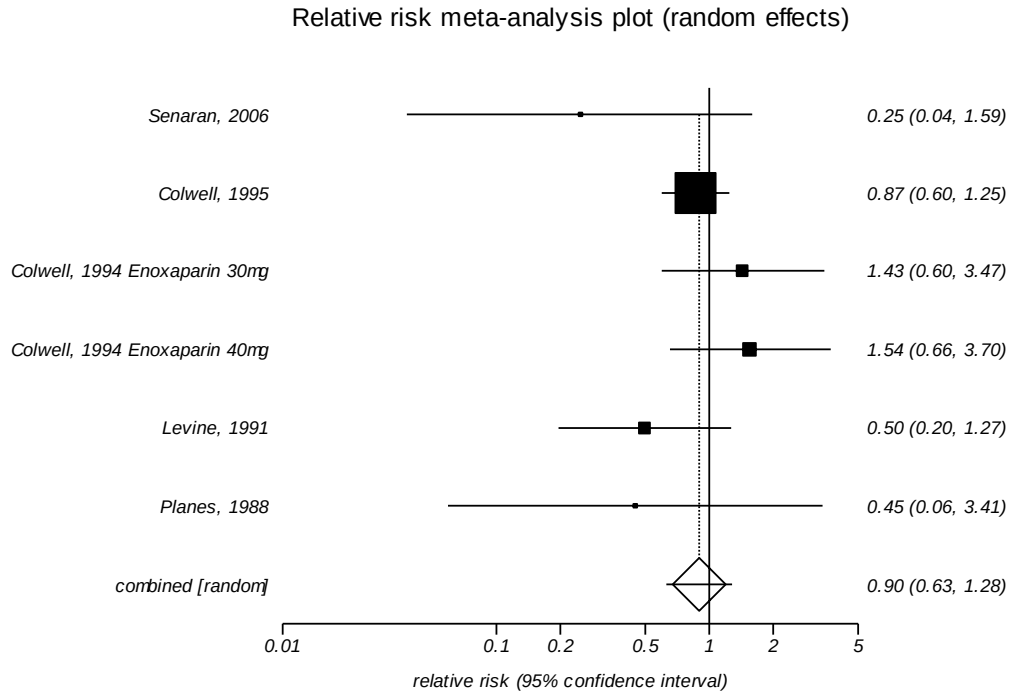
Figure 178. Impact of injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors on major bleeding leading to reoperation in patients who had major orthopedic surgery limited to total knee replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

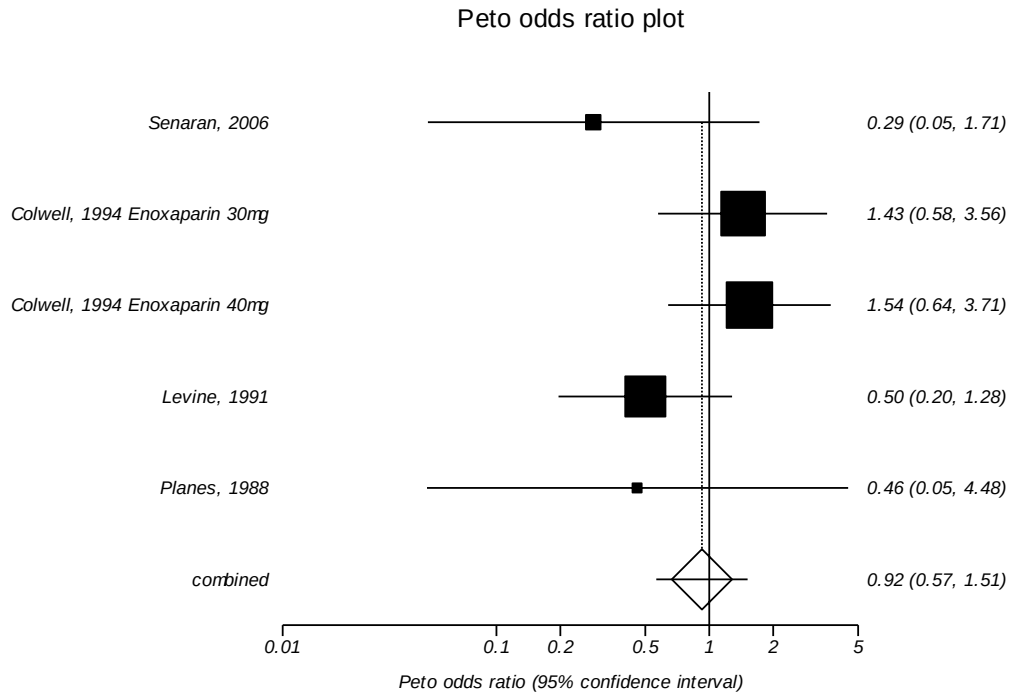
Figure 179. Impact of injectable low molecular weight heparin versus injectable unfractionated heparin on minor bleeding in patients undergoing major orthopedic surgery



I^2: 9.9 percent
Egger's p-value: 0.608

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

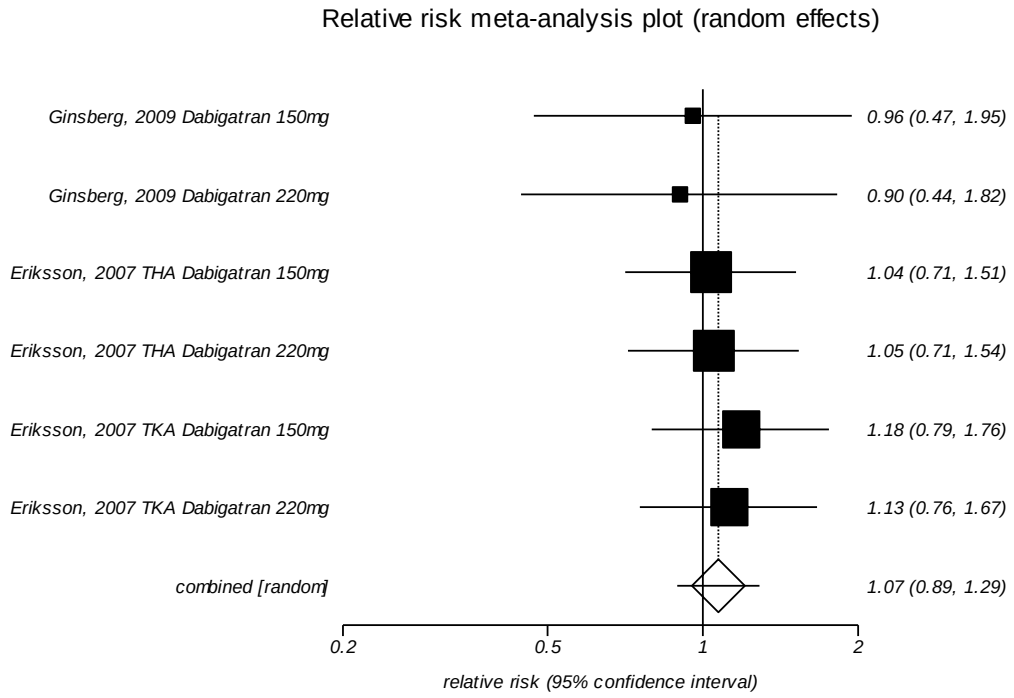
Figure 180. Impact of injectable low molecular weight heparin versus injectable unfrationated heparin on minor bleeding in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: 0 percent
Egger's p-value: 0.132

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

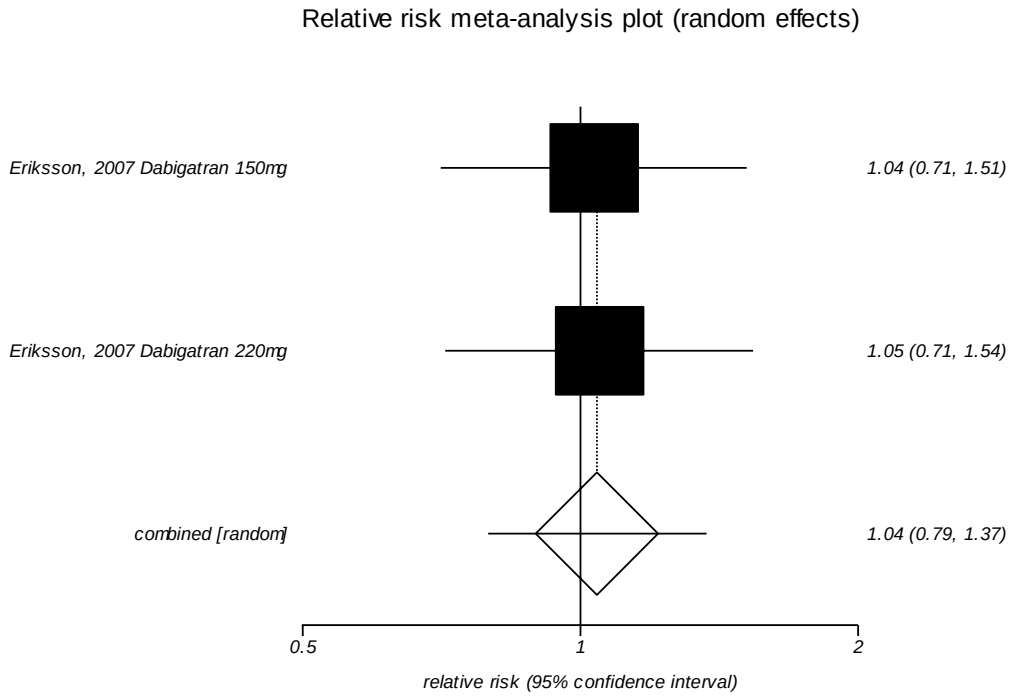
Figure 181. Impact of injectable low molecular weight heparin versus injectable or oral direct thrombin inhibitors on minor bleeding in patients undergoing major orthopedic surgery (same as analysis limited to trials published from 2001-present)



I^2: 0 percent
Egger's p-value: 0.132

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

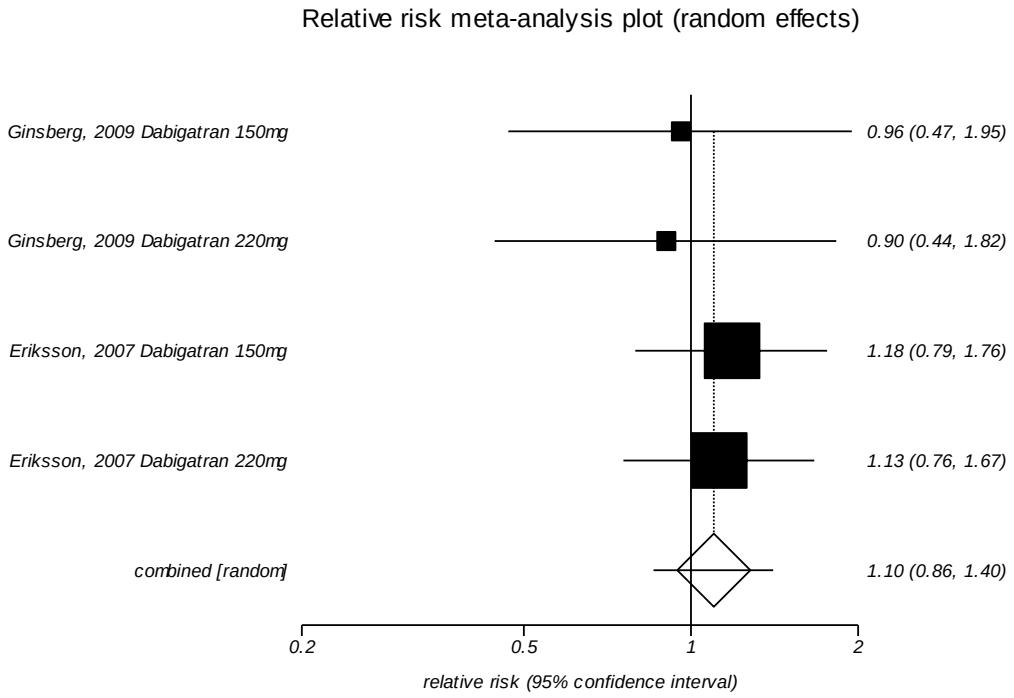
Figure 182. Impact of injectable low molecular weight heparin versus injectable or oral direct thrombin inhibitors on minor bleeding in patients undergoing major orthopedic surgery limited to total hip replacement



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

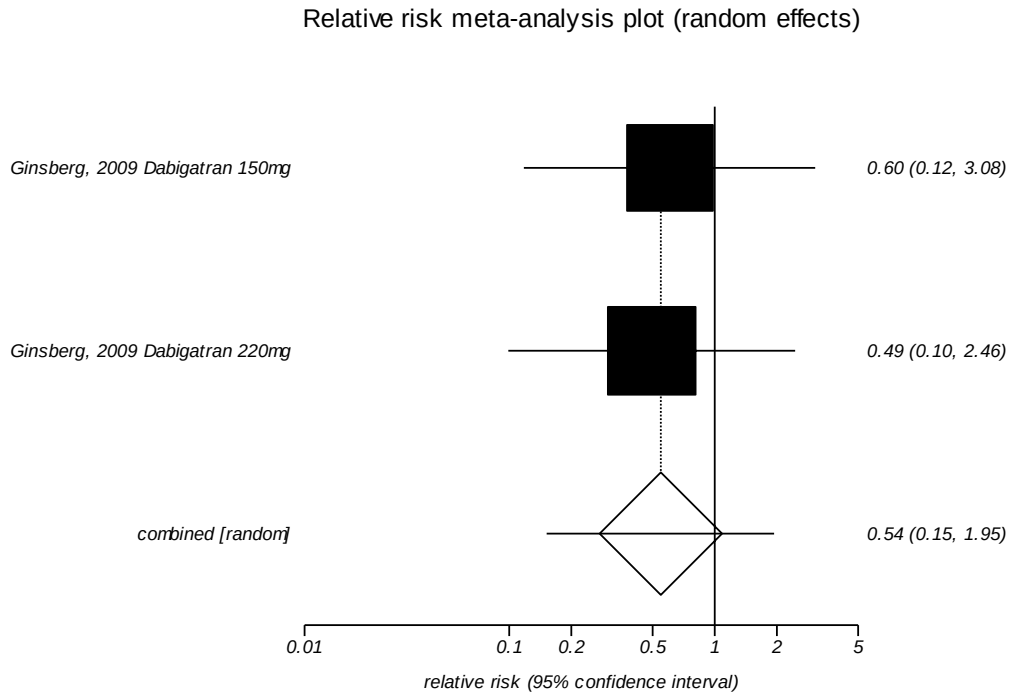
Figure 183. Impact of injectable low molecular weight heparin versus injectable or oral direct thrombin inhibitors on minor bleeding in patients undergoing major orthopedic surgery limited to total knee replacement



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

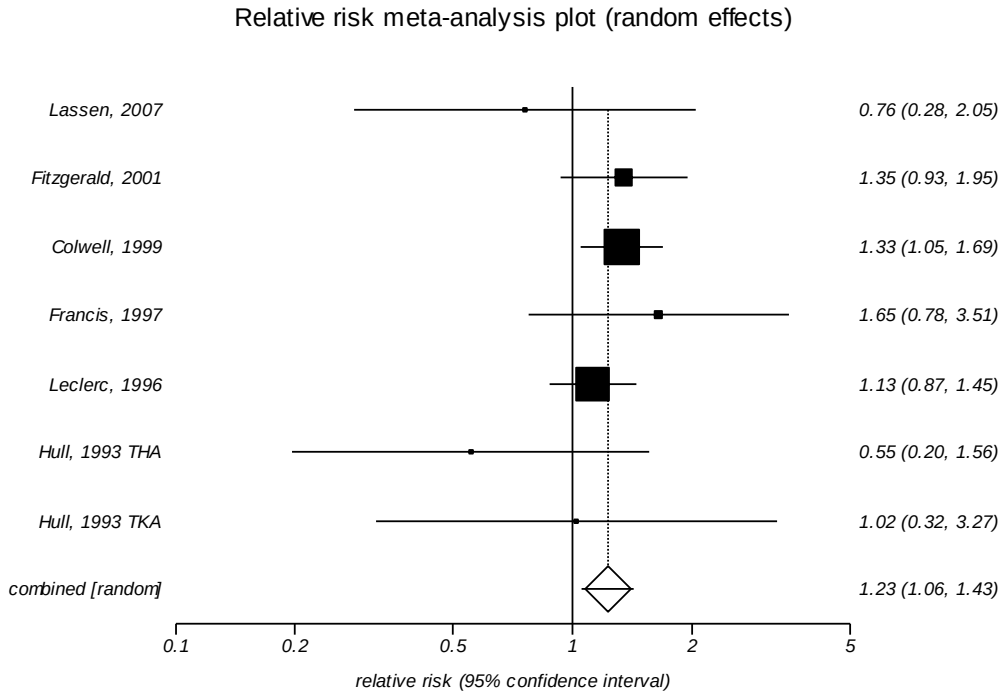
Figure 184. Impact of injectable low molecular weight heparin versus injectable or oral direct thrombin inhibitors on minor bleeding during the postdischarge period in patients who had total knee replacement surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

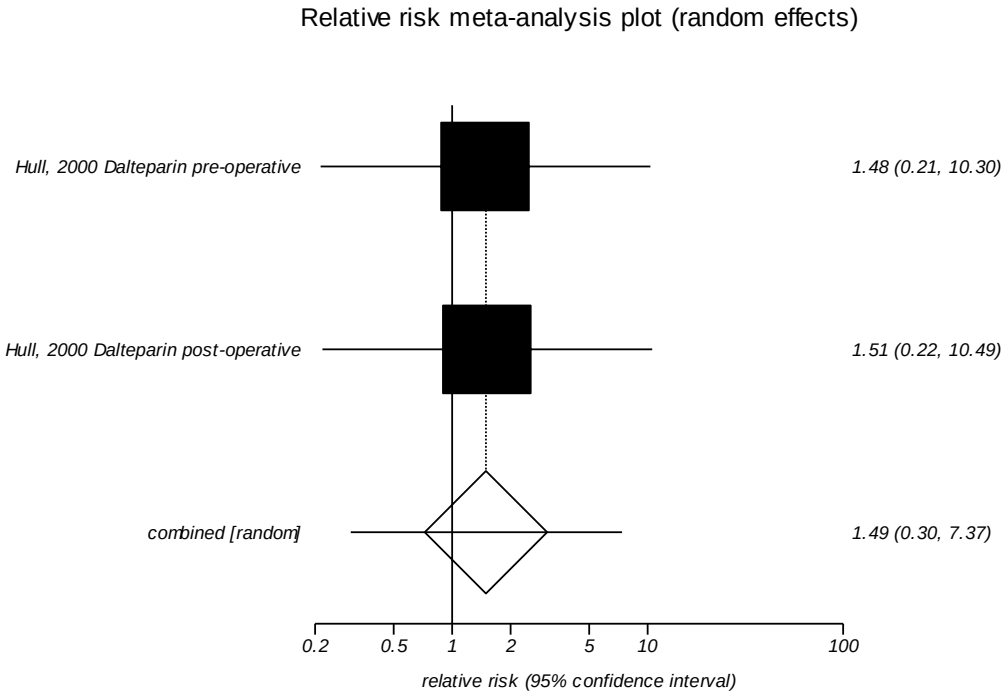
Figure 185. Impact of injectable low molecular weight heparin versus oral vitamin K antagonists on minor bleeding in patients undergoing major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.311

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

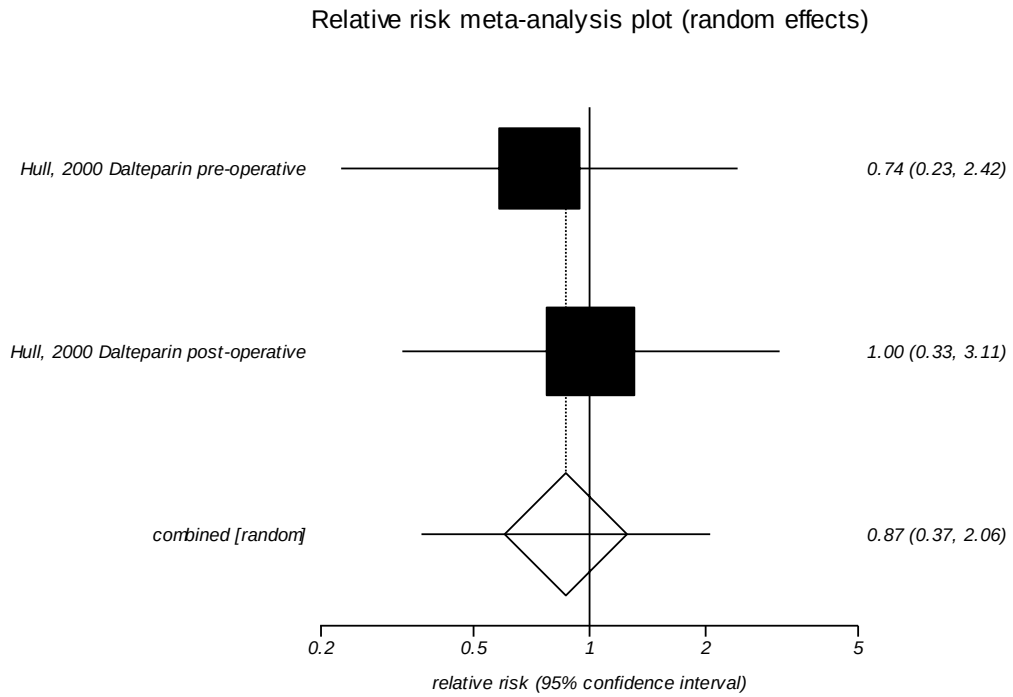
Figure 186. Impact of injectable low molecular weight heparin versus oral vitamin K antagonists on minor bleeding during days 0 to 1 in patients who had total hip replacement surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

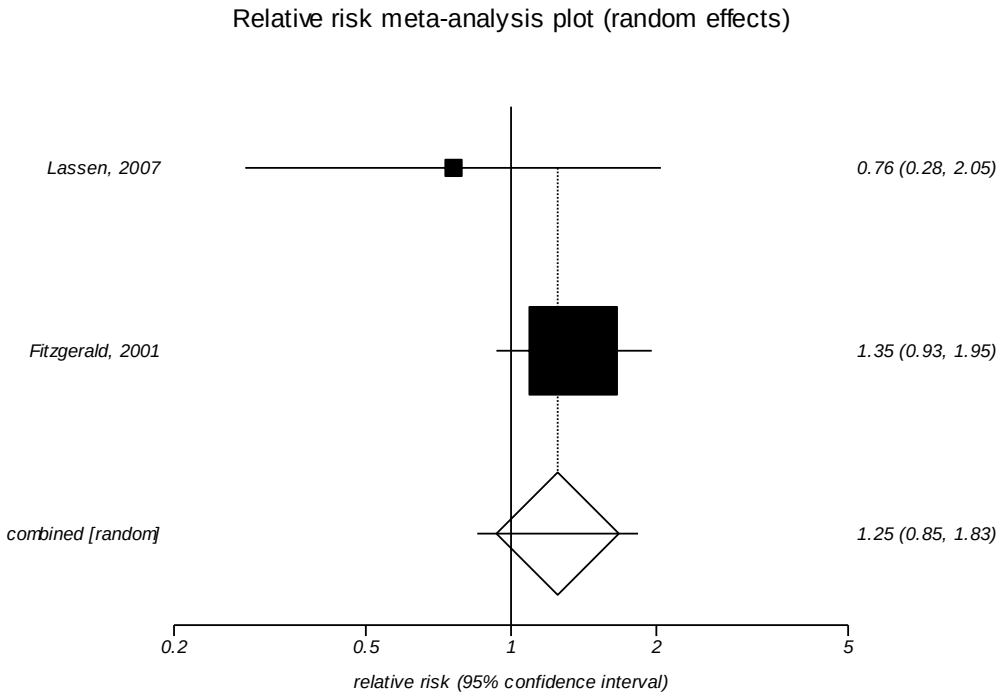
Figure 187. Impact of injectable low molecular weight heparin versus oral vitamin K antagonists on minor bleeding during days 2 to 8 in patients who had total hip replacement surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

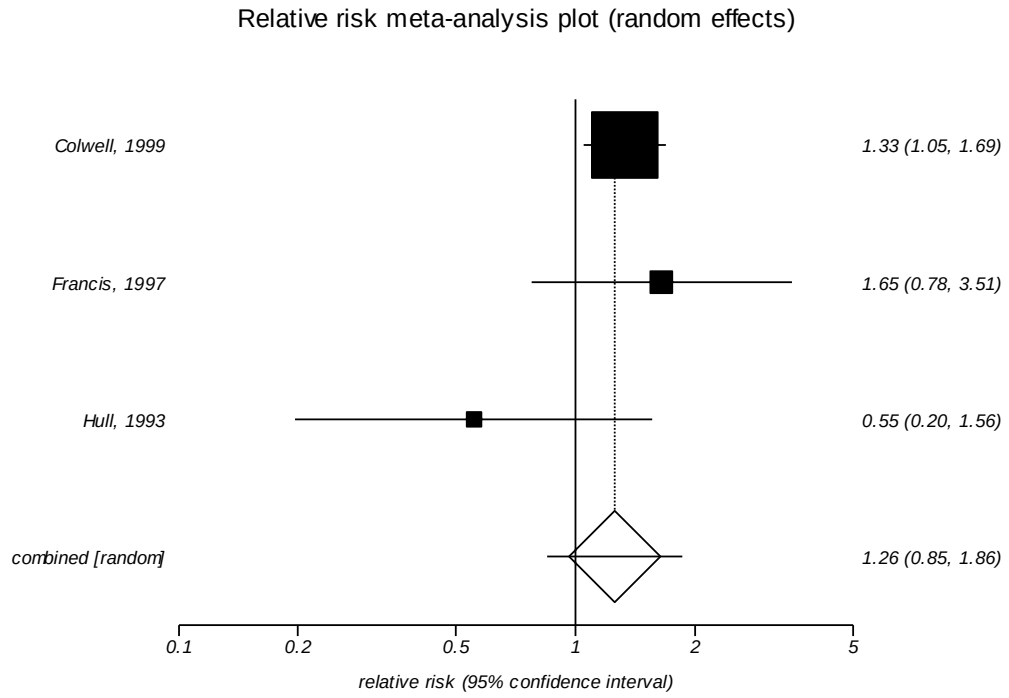
Figure 188. Impact of injectable low molecular weight heparin versus oral vitamin K antagonists on minor bleeding in patients undergoing major orthopedic surgery limited to trials published from 2001-present



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

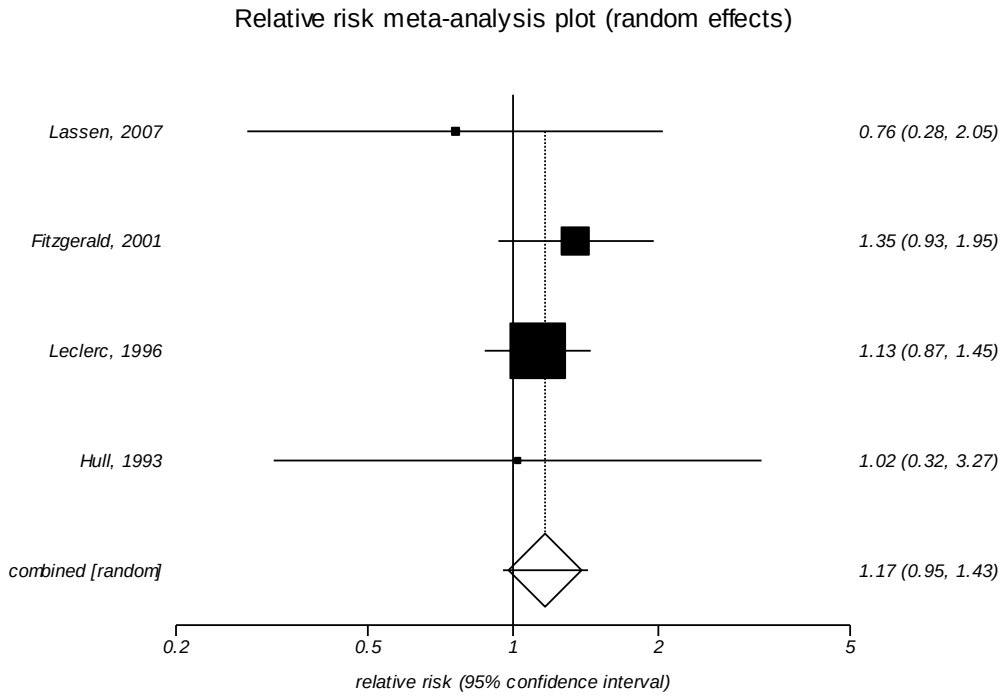
Figure 189. Impact of injectable low molecular weight heparin versus oral vitamin K antagonists on minor bleeding in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: 27.8 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

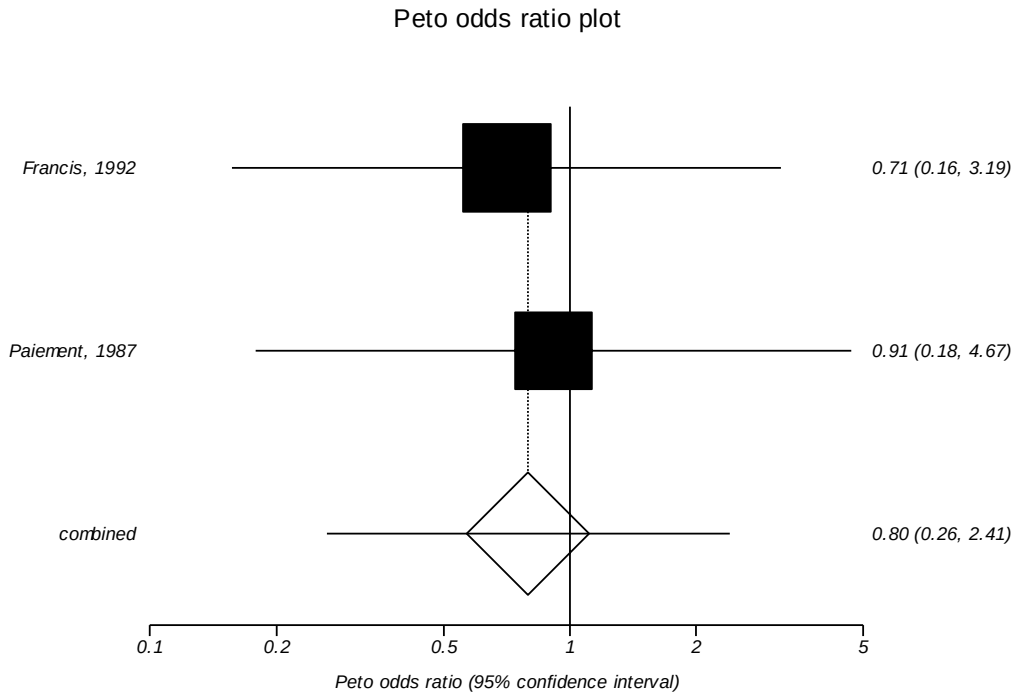
Figure 190. Impact of injectable low molecular weight heparin versus oral vitamin K antagonists on minor bleeding in patients undergoing major orthopedic surgery limited to total knee replacement



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

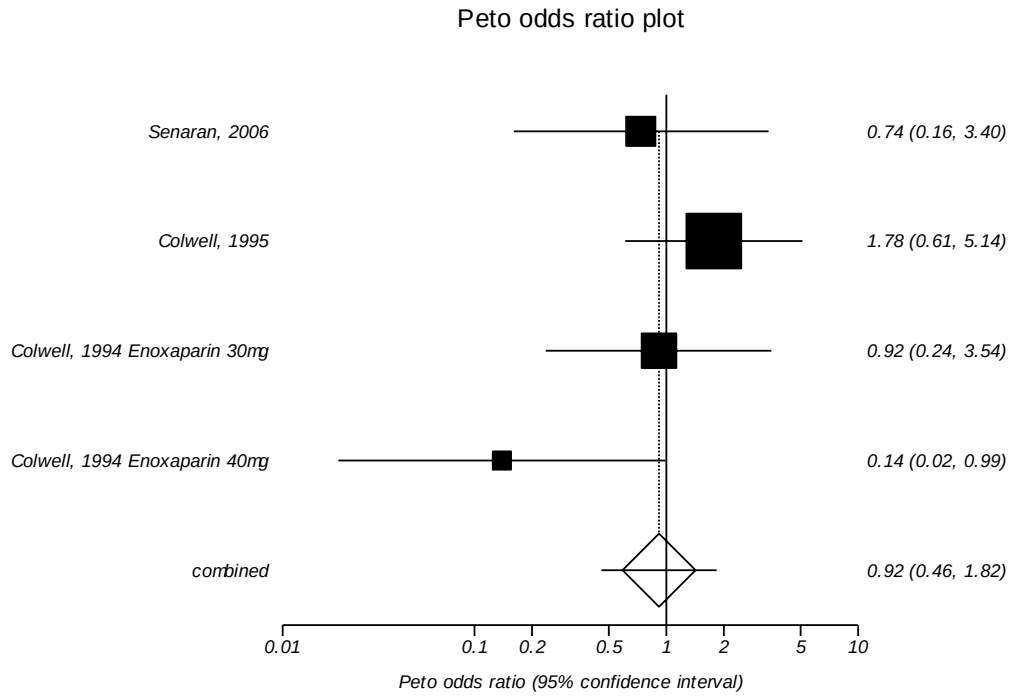
Figure 191. Impact of oral vitamin K antagonists versus mechanical prophylaxis on minor bleeding in patients undergoing major orthopedic surgery (same as analysis limited to total hip replacement)



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

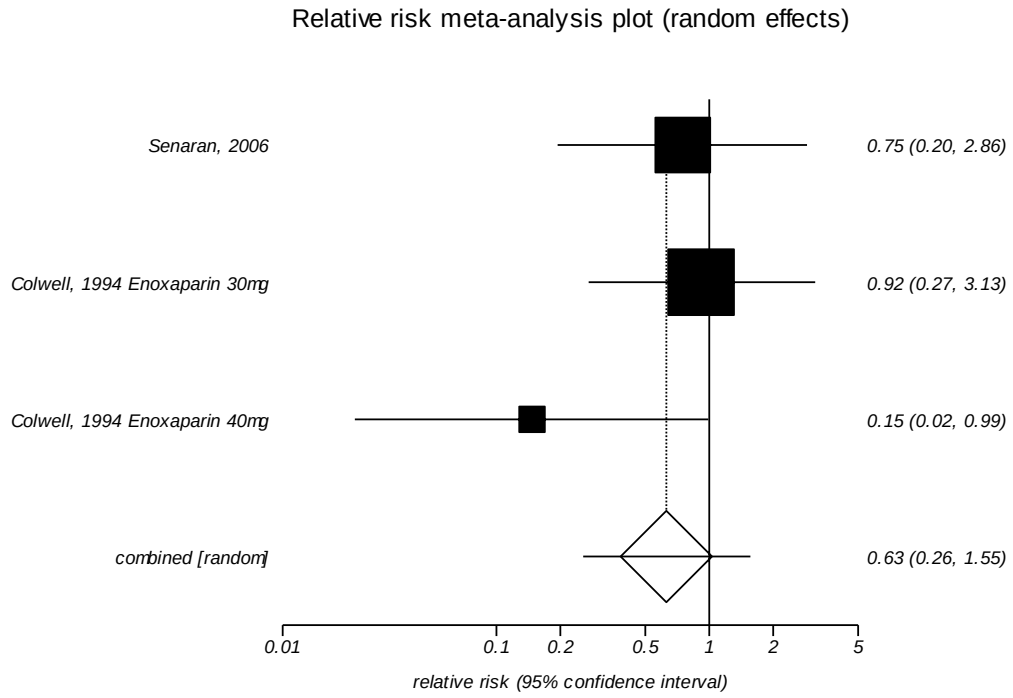
Figure 192. Impact of injectable low molecular weight heparin prophylaxis versus injectable unfractionated heparin prophylaxis on surgical site bleeding in patients undergoing major orthopedic surgery



I^2: 41.4 percent
Egger's p-value: 0.021

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

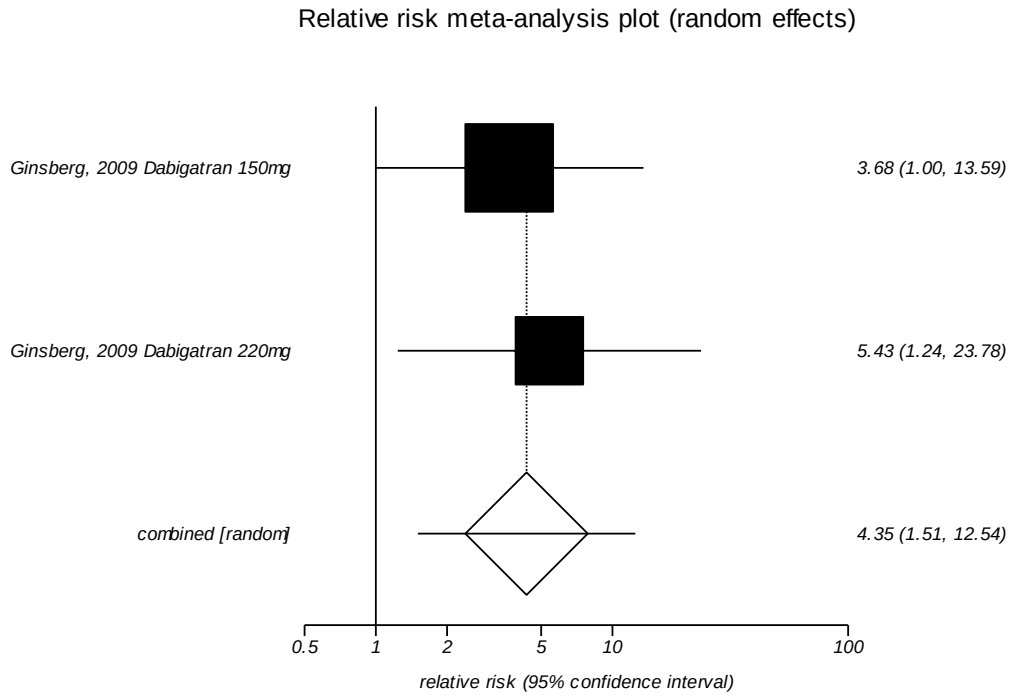
Figure 193. Impact of injectable low molecular weight heparin prophylaxis versus injectable unfractionated heparin prophylaxis on surgical site bleeding in patients undergoing major orthopedic surgery limited to total hip replacement surgery



I^2: 3.1 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

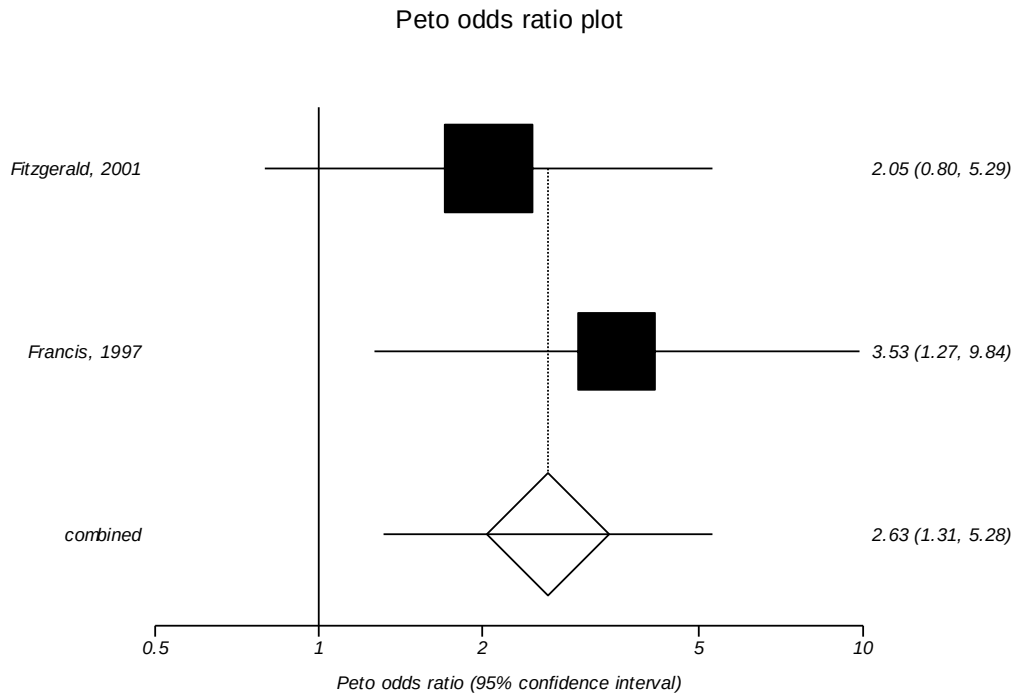
Figure 194. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral direct thrombin inhibitor prophylaxis on surgical site bleeding in patients undergoing major orthopedic surgery (same as 2001-present, same as limited to total knee replacement



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

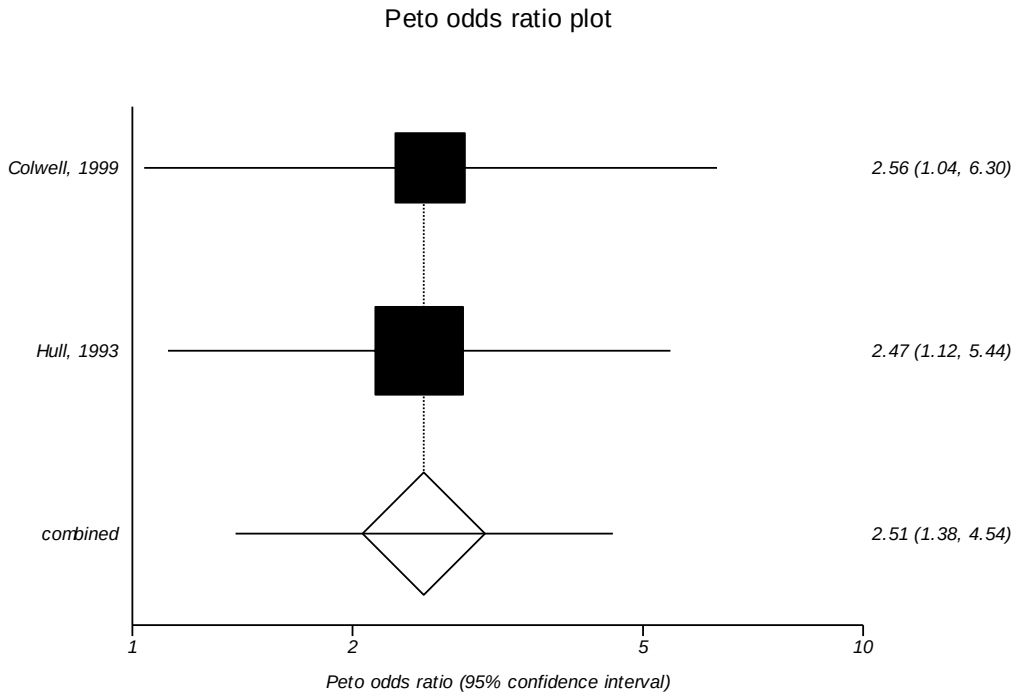
Figure 195. Impact of injectable low molecular weight heparin prophylaxis versus oral vitamin K antagonist prophylaxis on surgical site bleeding in patients undergoing major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

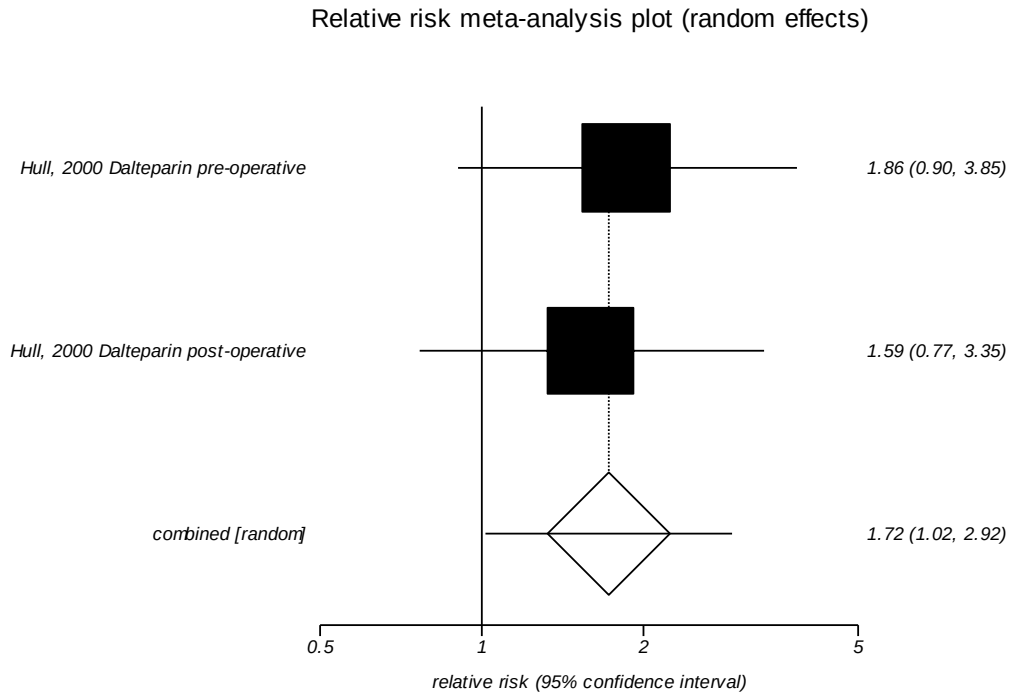
Figure 196. Impact of injectable low molecular weight heparin prophylaxis versus oral vitamin K antagonist prophylaxis on major surgical site bleeding in patients undergoing major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

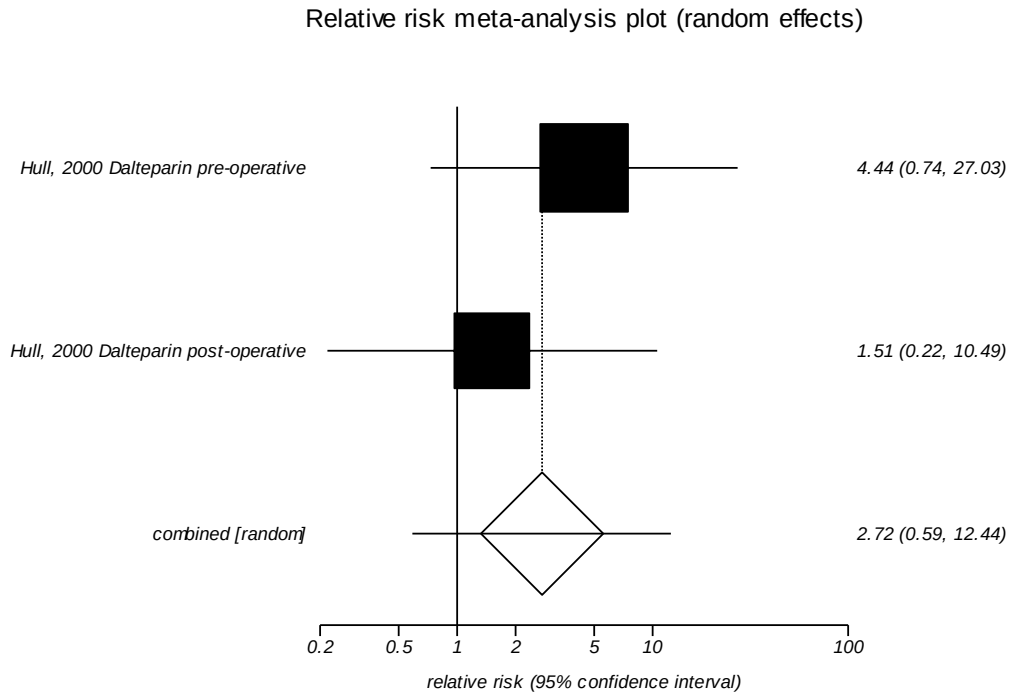
Figure 197. Impact of injectable low molecular weight heparin versus oral vitamin K antagonists on major surgical site bleeding during days 0 to 1 in patients who had total hip replacement surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

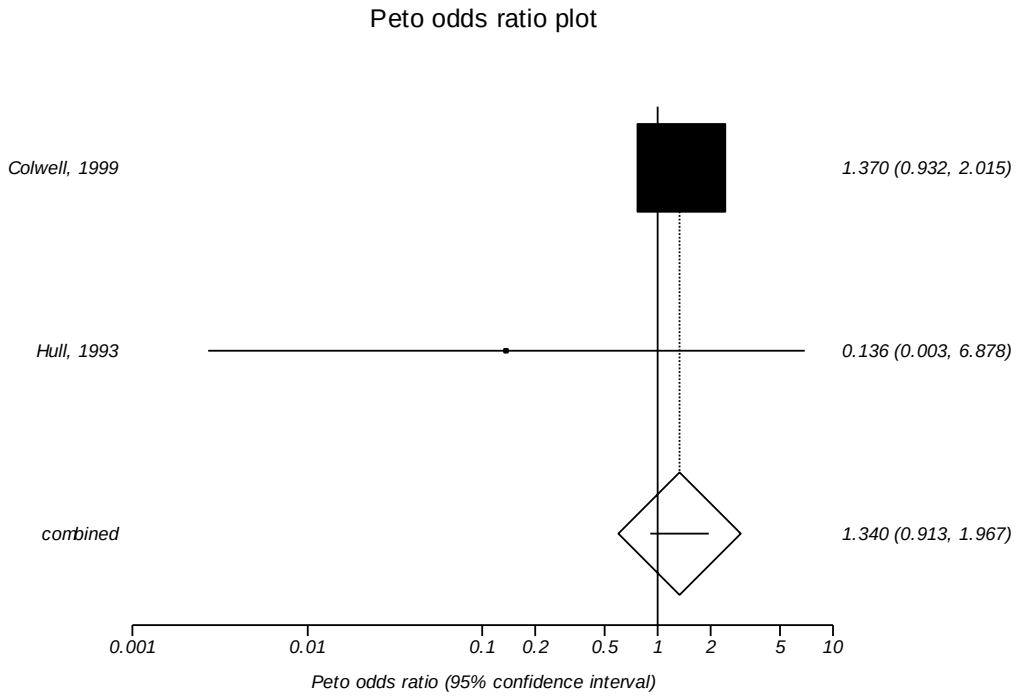
Figure 198. Impact of injectable low molecular weight heparin versus oral vitamin K antagonists on major surgical site bleeding during days 2 to 8 in patients who had total hip replacement surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

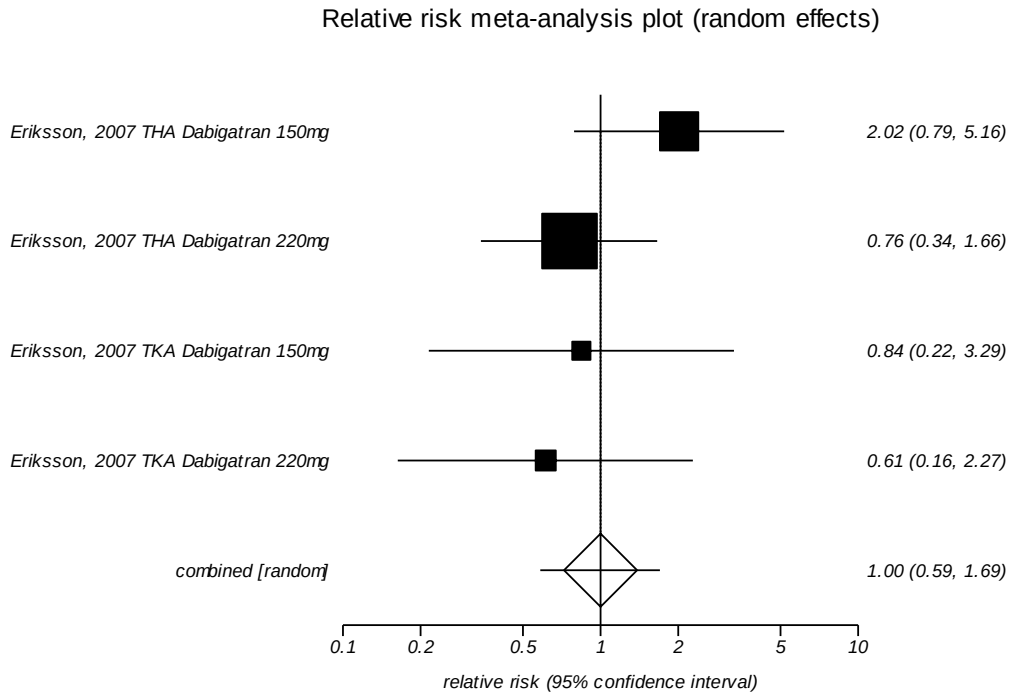
Figure 199. Impact of injectable low molecular weight heparin prophylaxis versus oral vitamin K antagonist prophylaxis on minor surgical site bleeding in patients undergoing major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

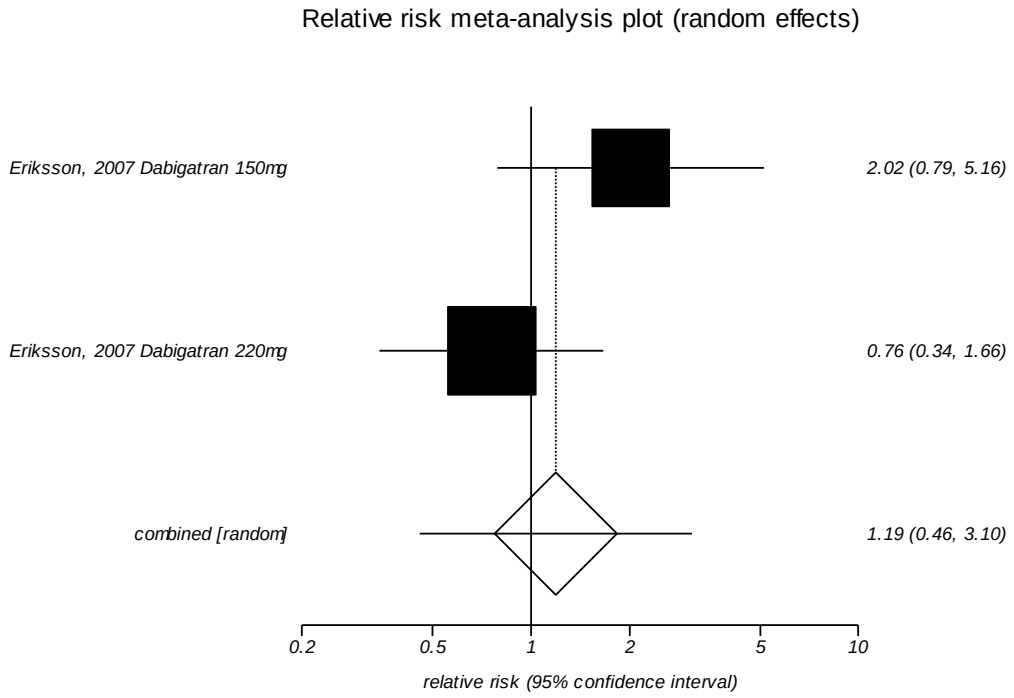
Figure 200. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral direct thrombin inhibitor prophylaxis on bleeding leading to transfusion in patients who had major orthopedic surgery (same as analysis of 2001-present)



I^2: 0 percent
Egger's p-value: P = 0.823

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

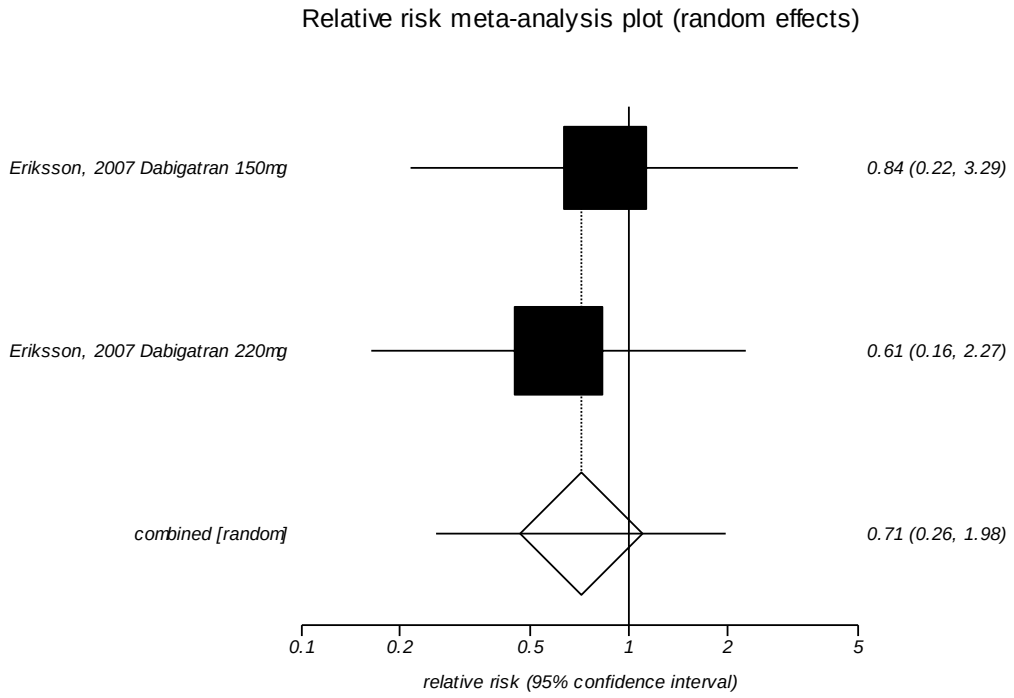
Figure 201. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral direct thrombin inhibitor prophylaxis on bleeding leading to transfusion in patients who had major orthopedic surgery limited to total hip replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

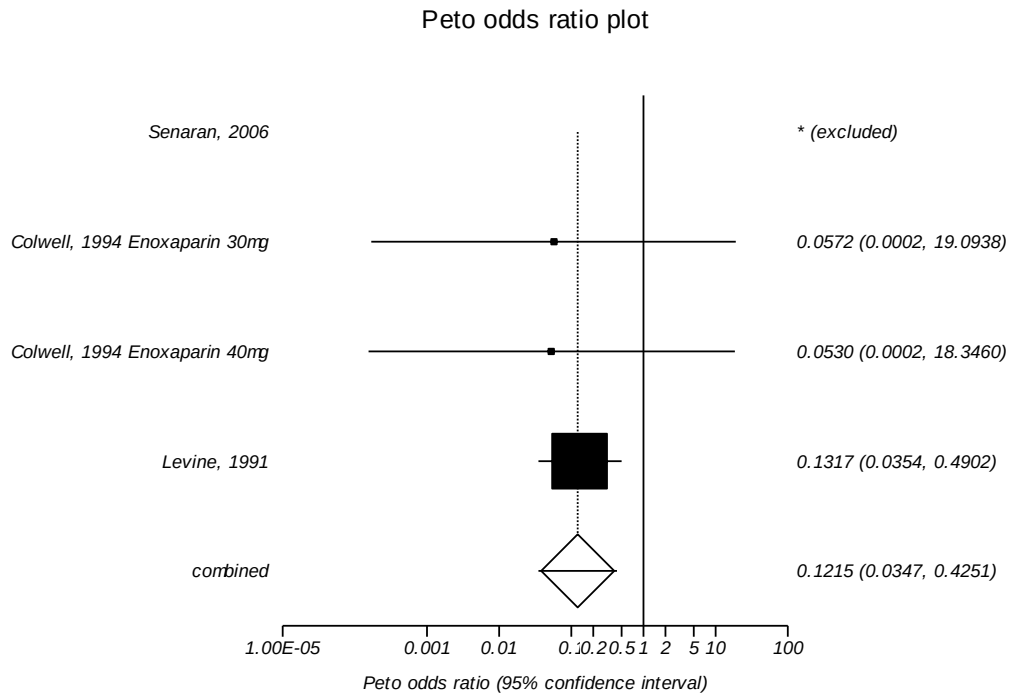
Figure 202. Impact of injectable low molecular weight heparin prophylaxis versus injectable or oral direct thrombin inhibitor prophylaxis on bleeding leading to transfusion in patients who had major orthopedic surgery limited to total knee replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

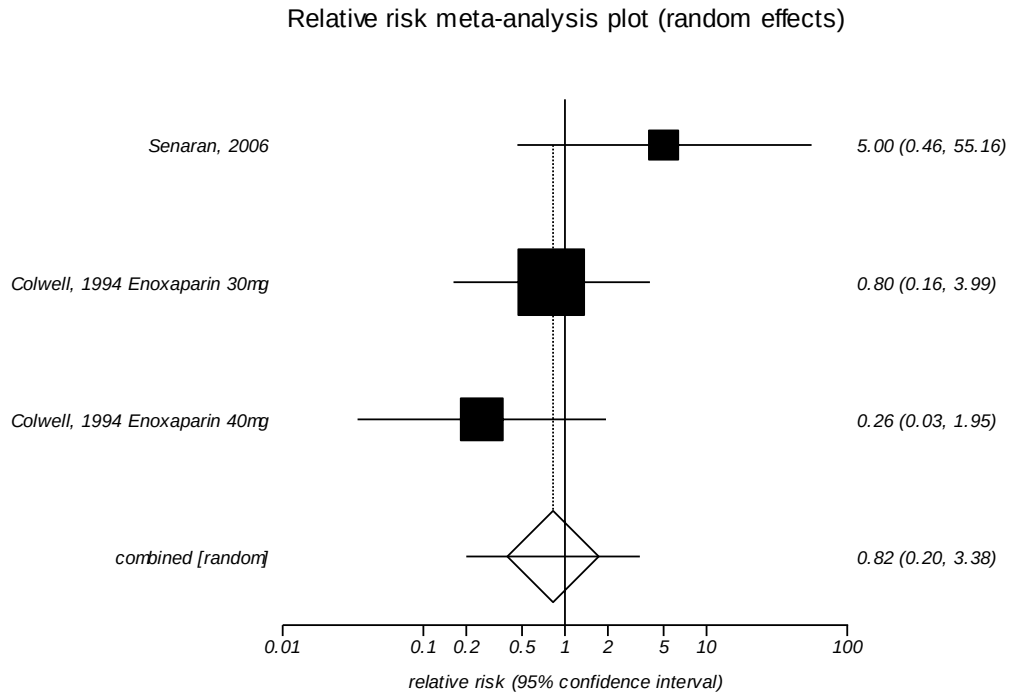
Figure 203. Impact of injectable low molecular weight heparin prophylaxis versus injectable unfractionated heparin prophylaxis on heparin-induced thrombocytopenia in patients who had major orthopedic surgery (same as analysis limited to total hip replacement surgery)



I^2: 0 percent
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

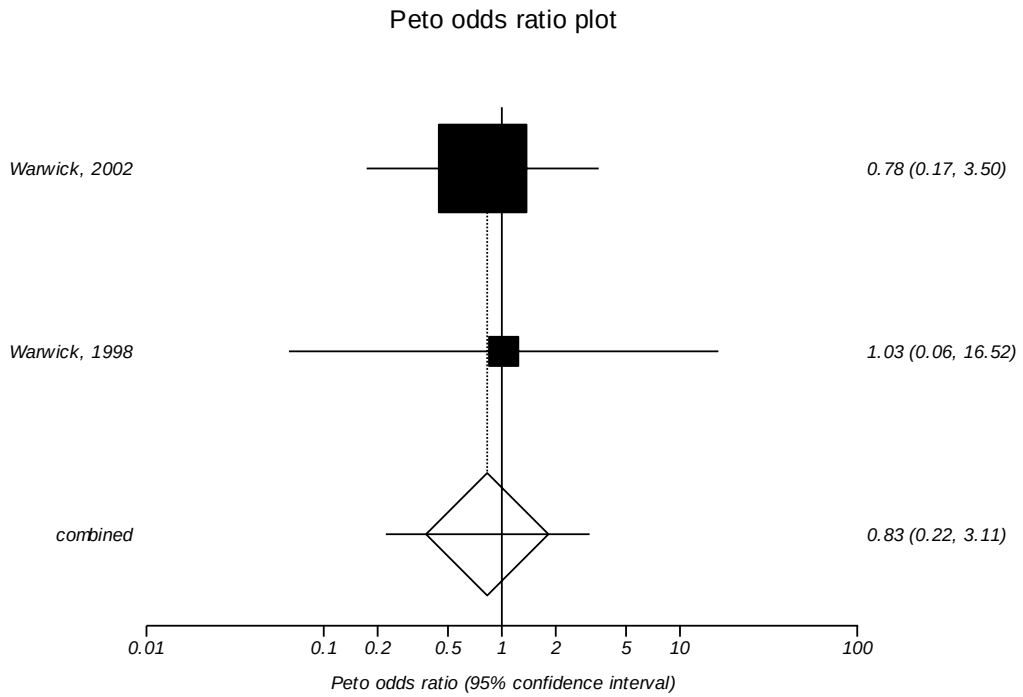
Figure 204. Impact of injectable low molecular weight heparin prophylaxis versus injectable unfractionated heparin prophylaxis on readmission in patients who had major orthopedic surgery (same as analysis limited to total hip replacement surgery)



I^2: 14.1 percent
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

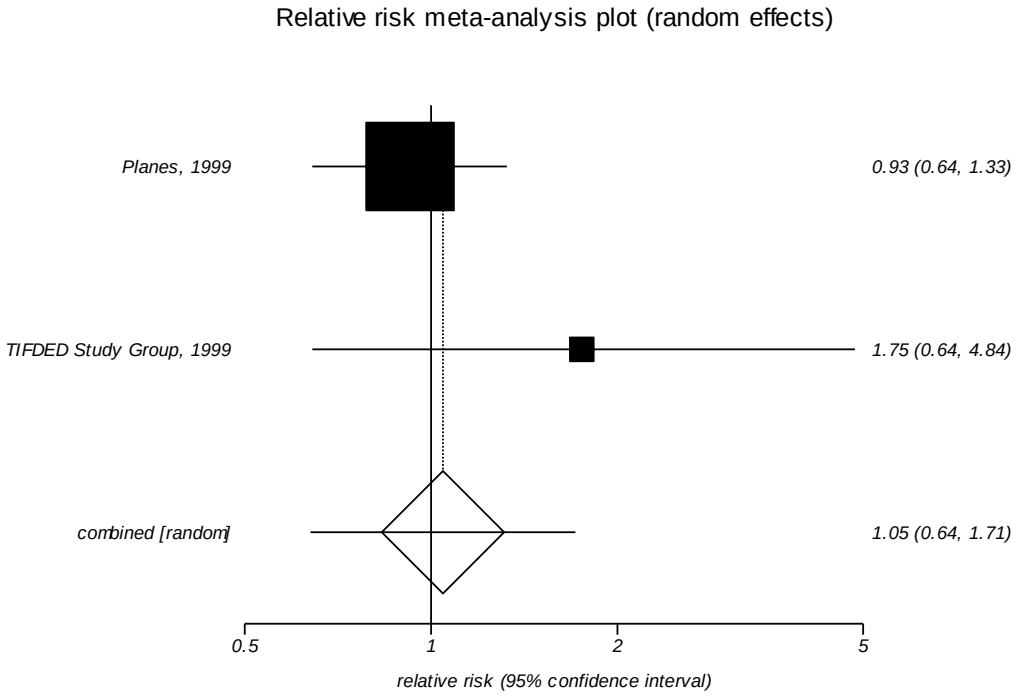
Figure 205. Impact of injectable low molecular weight heparin prophylaxis versus mechanical prophylaxis on readmission in patients who had major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

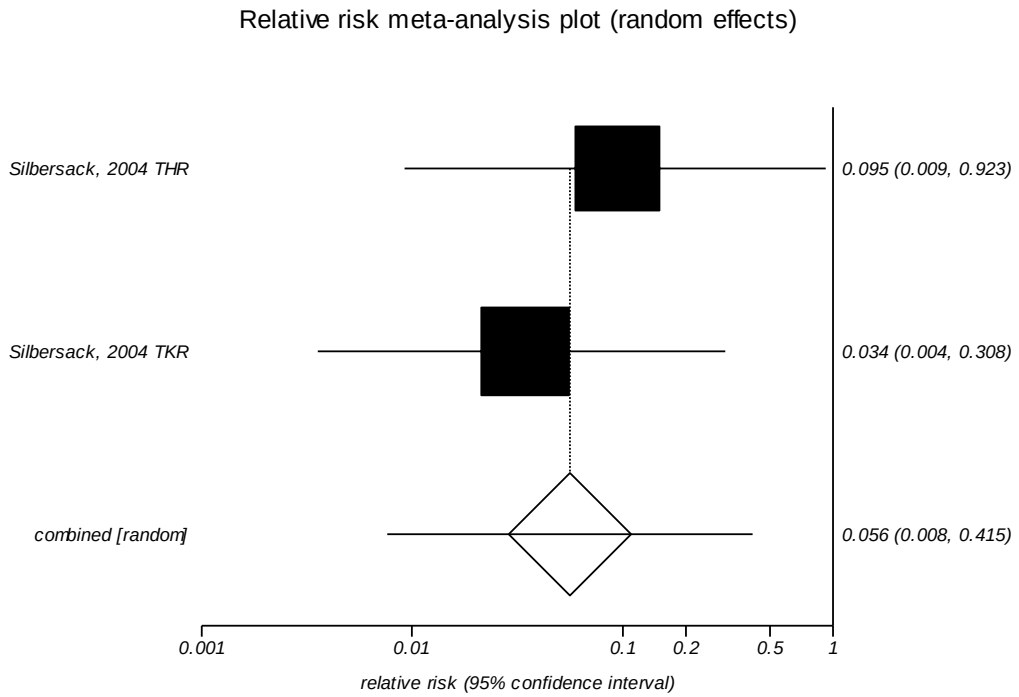
Figure 206. Impact of enoxaparin versus other low molecular weight heparin agents on deep vein thrombosis in patients who had major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

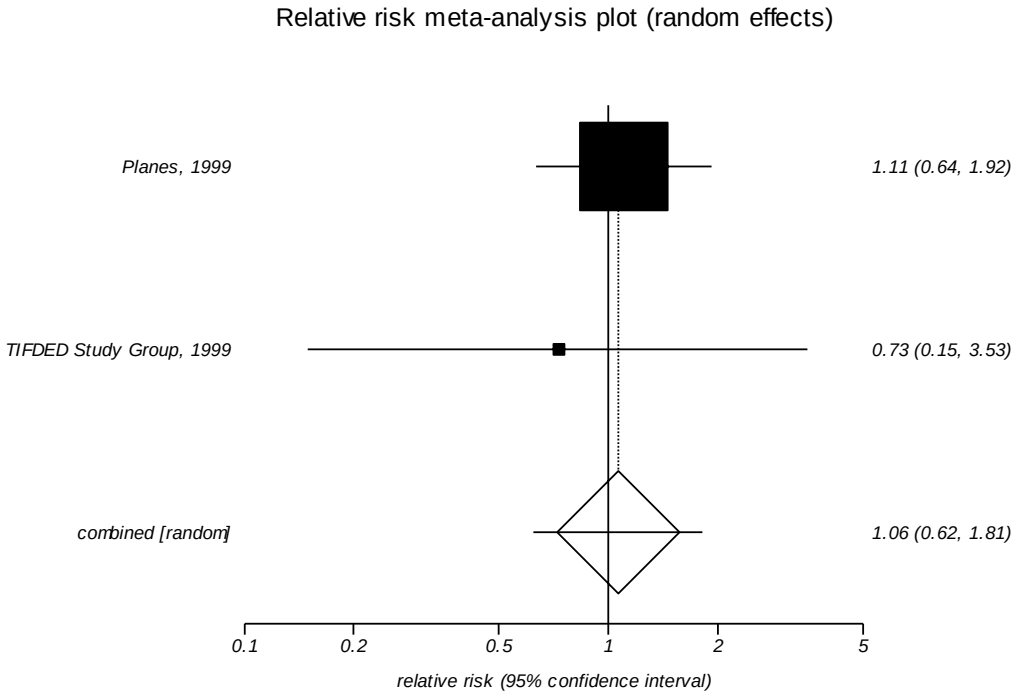
Figure 207. Impact of intermittent pneumatic compression versus graduated compression on deep vein thrombosis in patients who had major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

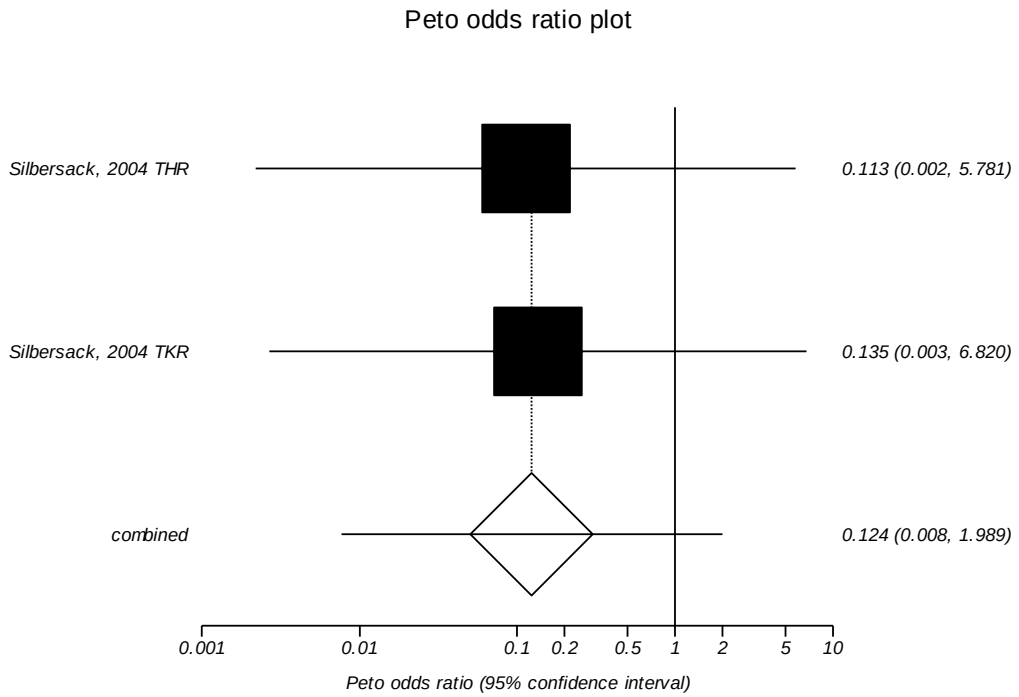
Figure 208. Impact of enoxaparin versus other low molecular weight heparin agents on proximal deep vein thrombosis in patients who had major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

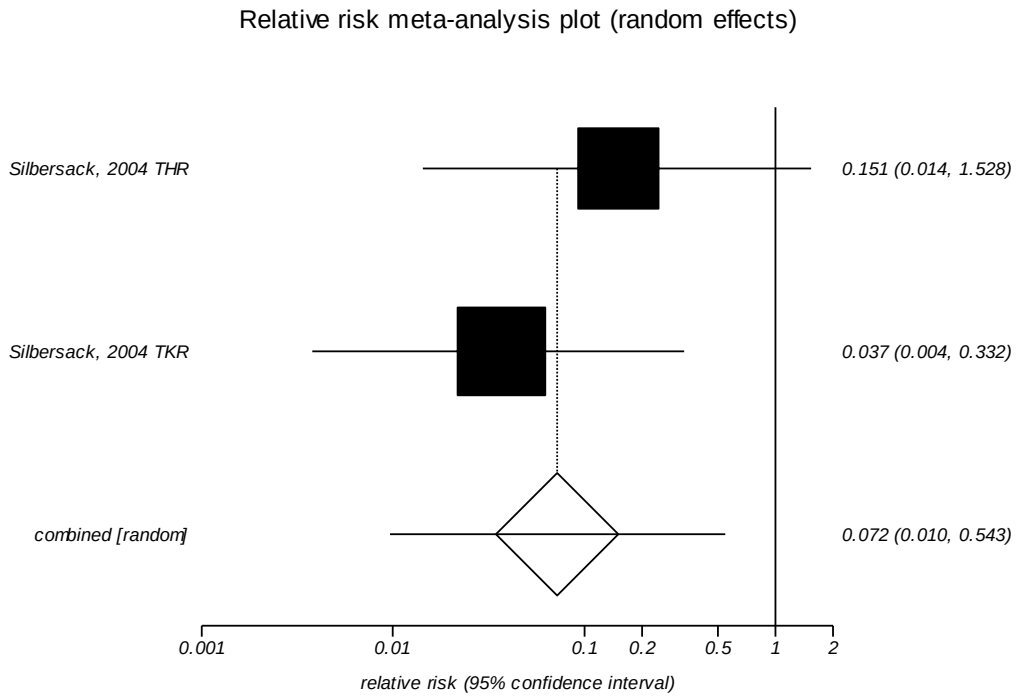
Figure 209. Impact of intermittent pneumatic compression versus graduated compression on proximal deep vein thrombosis in patients who had major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

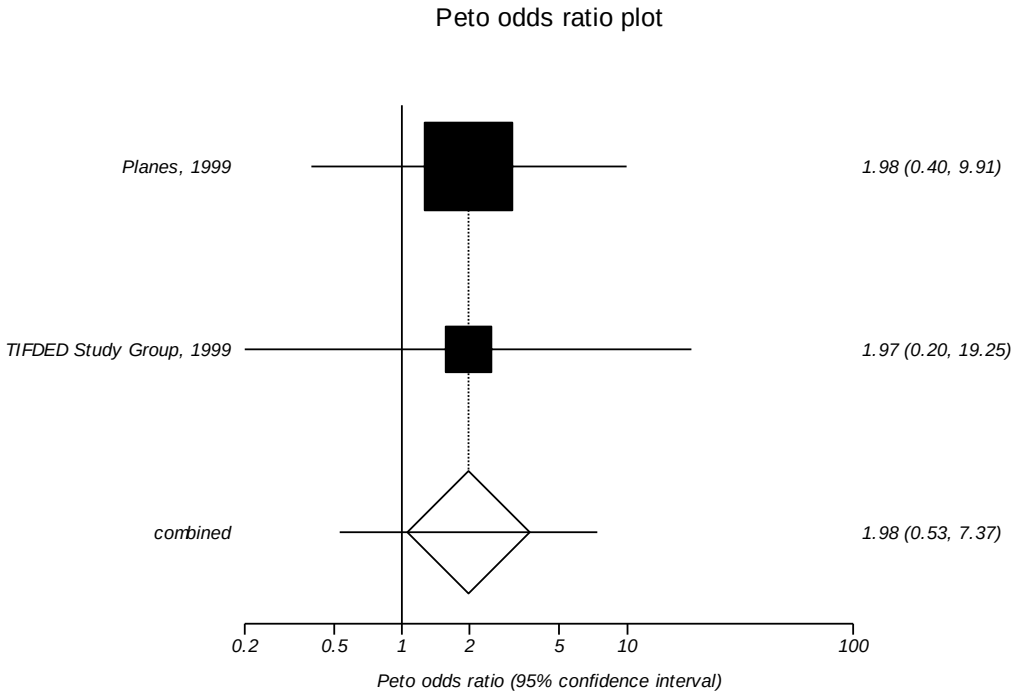
Figure 210. Impact of intermittent pneumatic compression versus graduated compression on distal deep vein thrombosis in patients who had major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

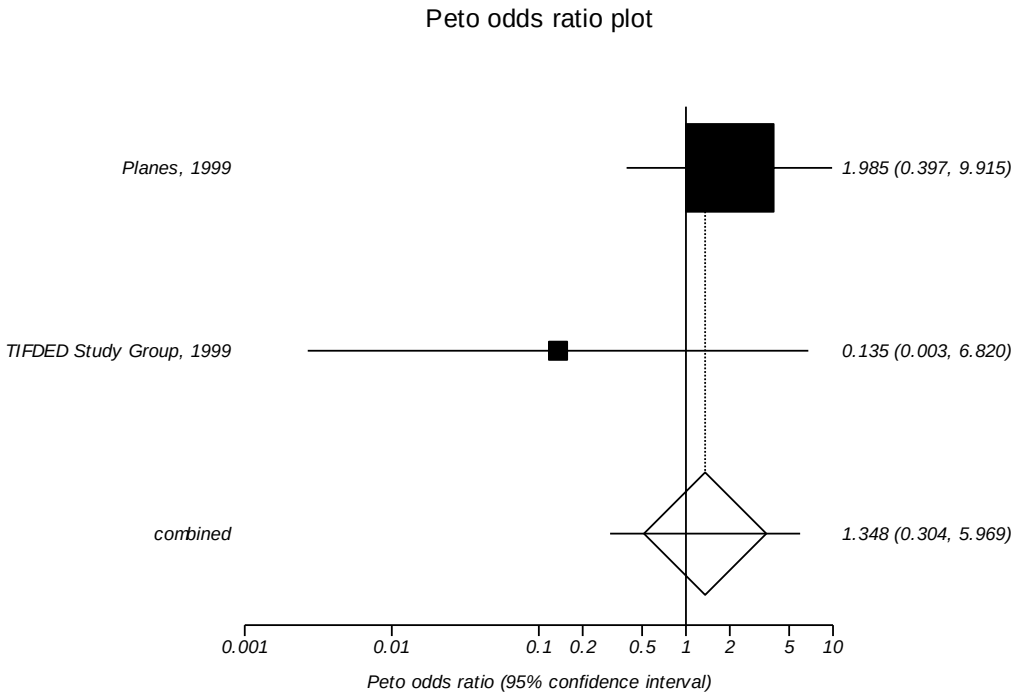
Figure 211. Impact of enoxaparin versus other low molecular weight heparin agents on major bleeding in patients who had major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

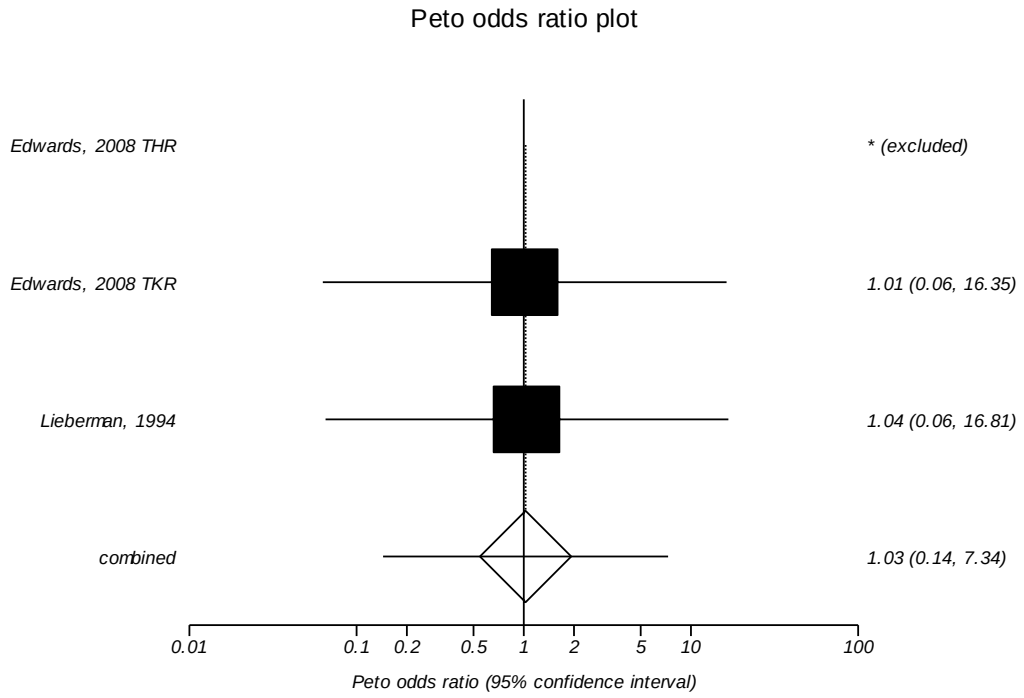
Figure 212. Impact of enoxaparin versus other low molecular weight heparin agents on surgical site bleeding in patients who had major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

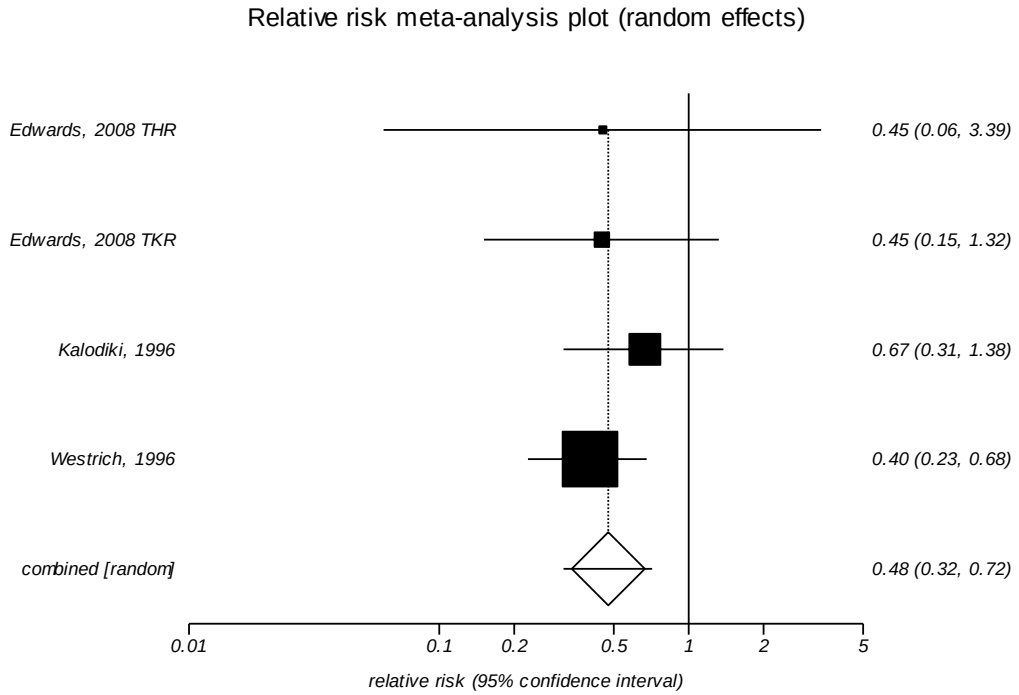
Figure 213. Impact of pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis alone on pulmonary embolism in patients who had major orthopedic surgery (same as the analysis of nonfatal pulmonary embolism)



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

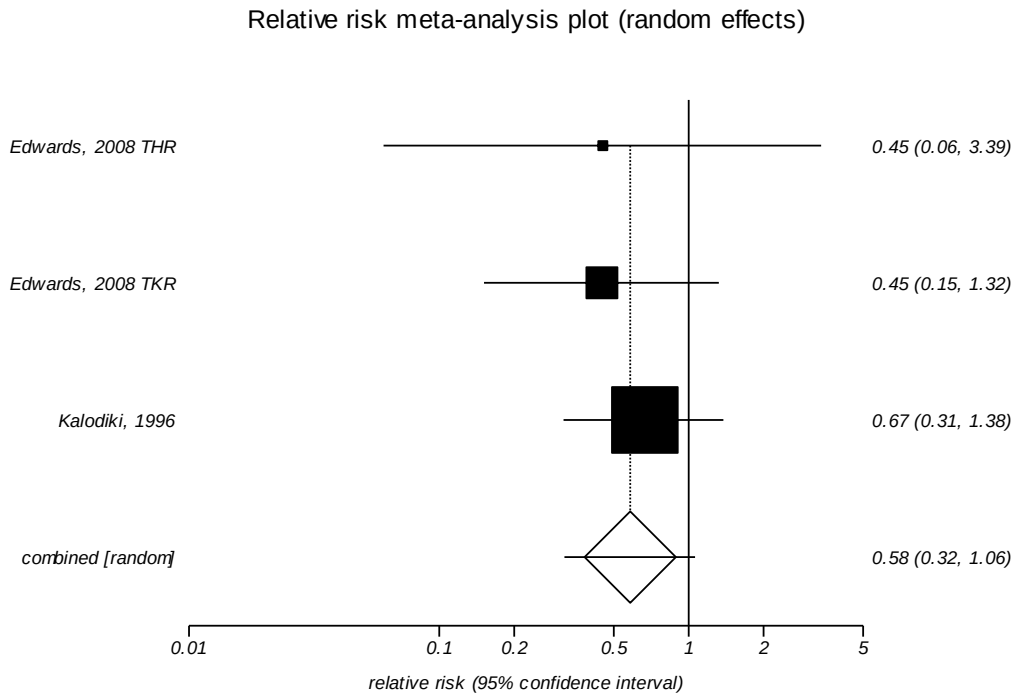
Figure 214. Impact of pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis alone on deep vein thrombosis in patients who had major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.831

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

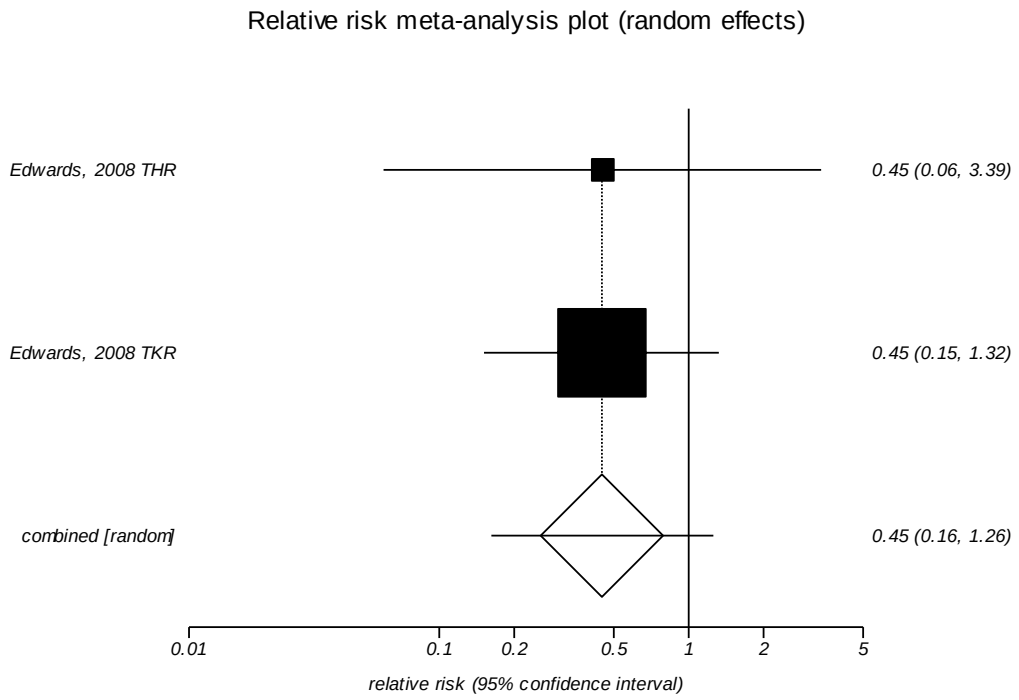
Figure 215. Impact of anticoagulant plus mechanical prophylaxis versus anticoagulant prophylaxis alone on deep vein thrombosis in patients who had major orthopedic surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

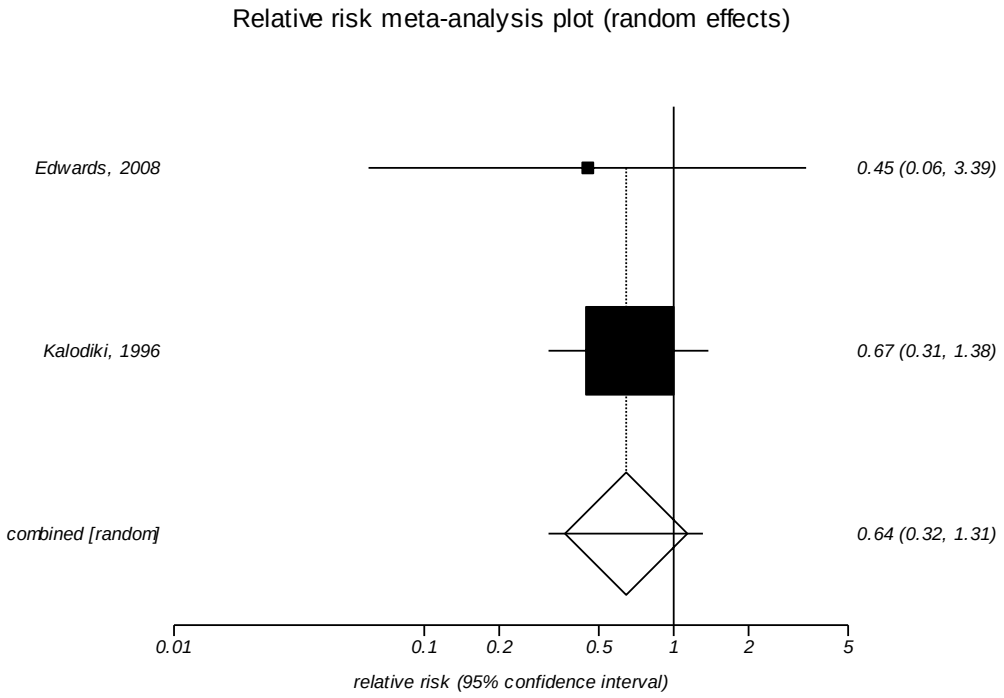
Figure 216. Impact of pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis alone on deep vein thrombosis in patients who had major orthopedic surgery limited to trials published from 2001-present



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

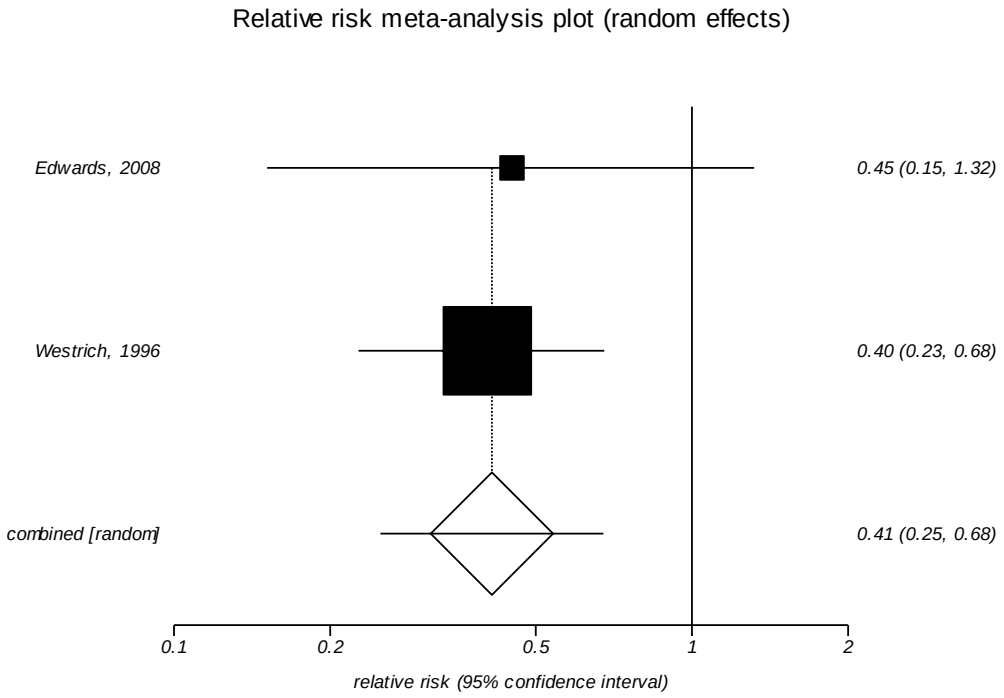
Figure 217. Impact of pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis alone on deep vein thrombosis in patients who had major orthopedic surgery limited to total hip replacement



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

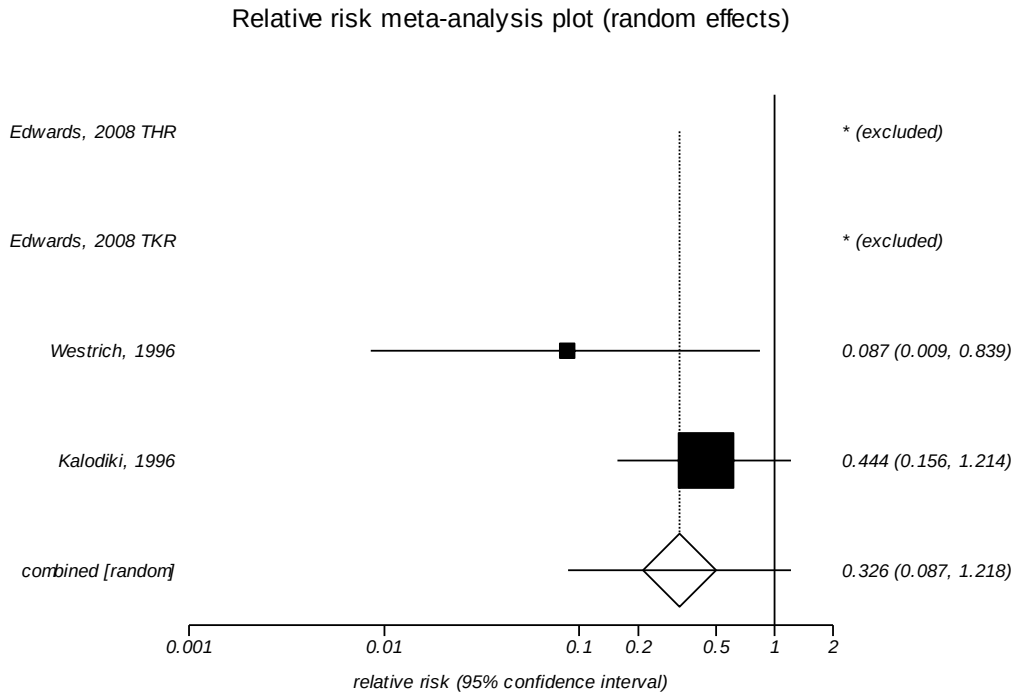
Figure 218. Impact of pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis alone on deep vein thrombosis in patients who had major orthopedic surgery limited to total knee replacement



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

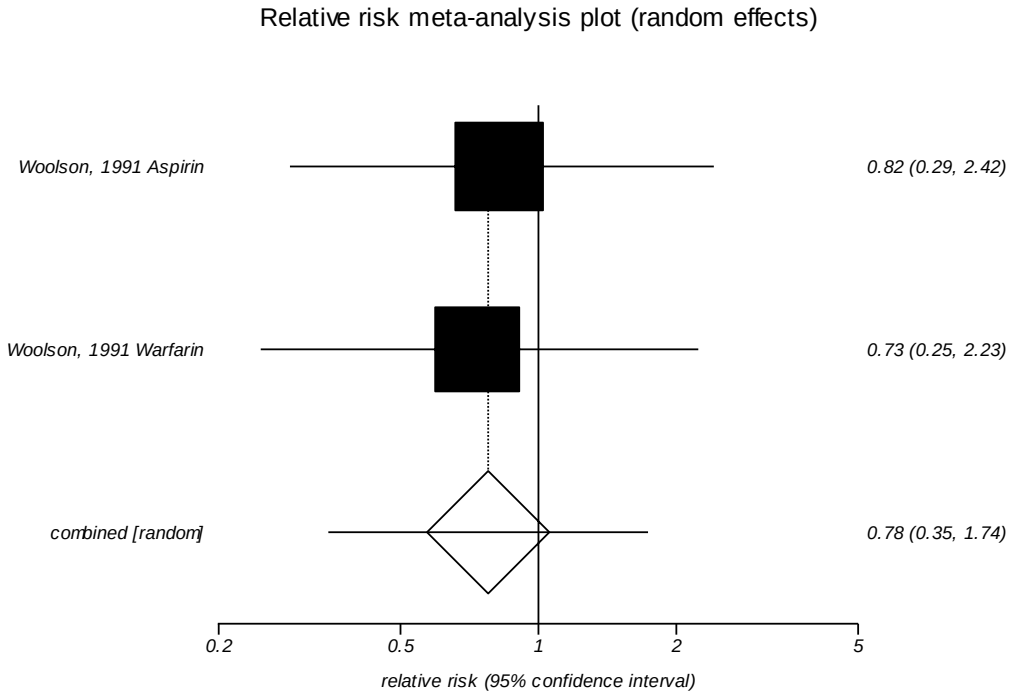
Figure 219. Impact of pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis alone on proximal deep vein thrombosis in patients who had major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

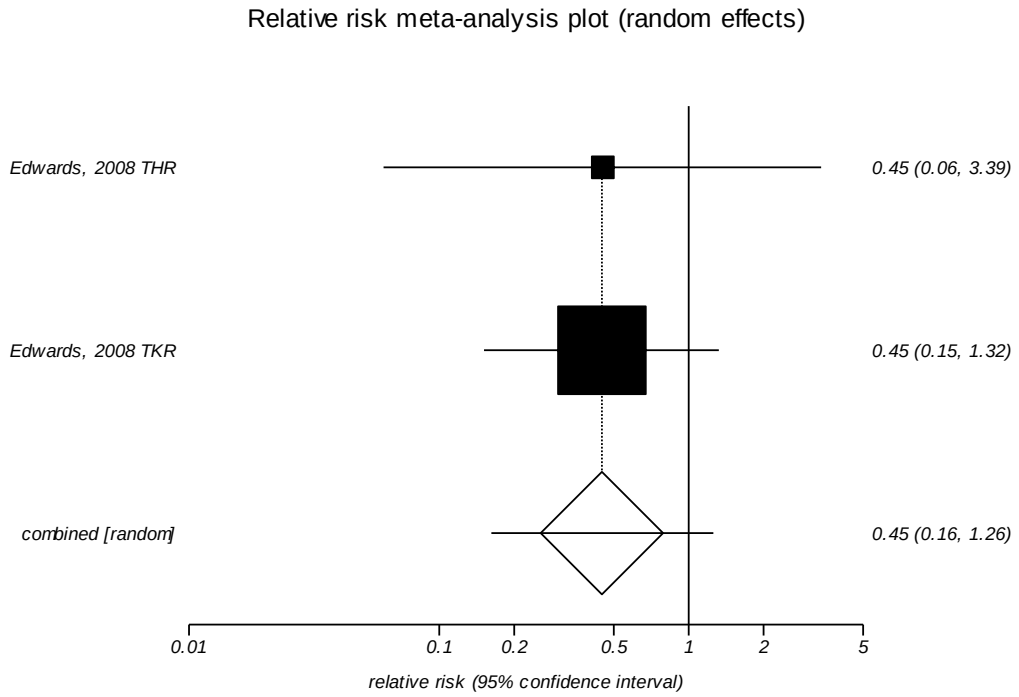
Figure 220. Impact of pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis alone on proximal deep vein thrombosis in patients who had major orthopedic surgery



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

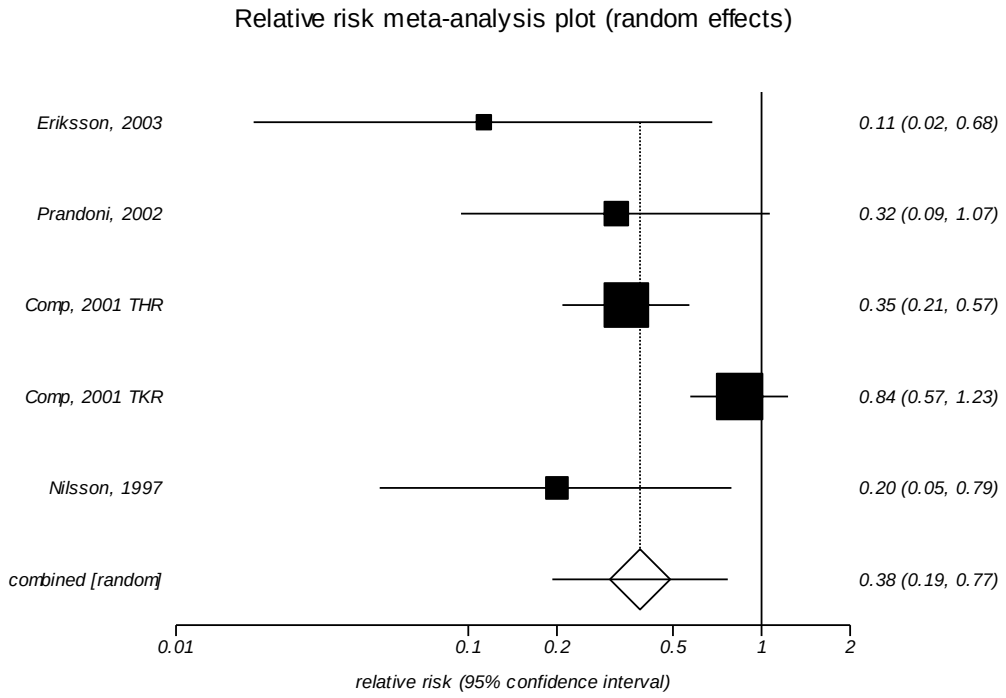
Figure 221. Impact of pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis alone on distal deep vein thrombosis in patients who had major orthopedic surgery (same as the analysis of trial published from 2001-present; same as the comparison of anticoagulant plus mechanical prophylaxis versus anticoagulant alone in patients who had major orthopedic surgery)



I^2: Too few strata
Egger's p-value: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

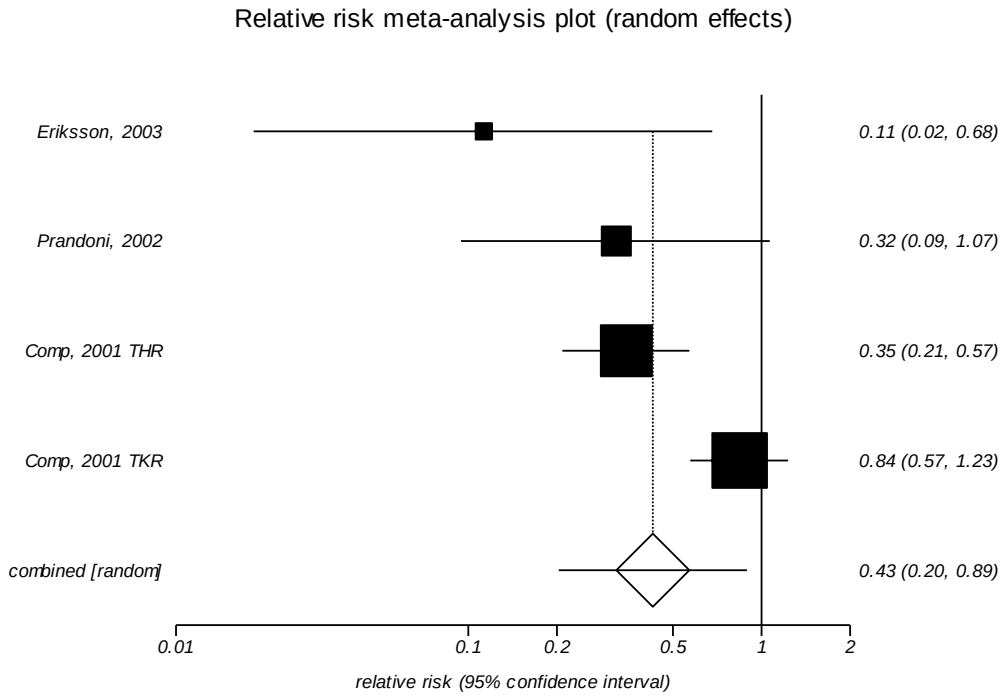
Figure 222. Impact of prolonged prophylaxis versus standard duration of prophylaxis on symptomatic objectively confirmed venous thromboembolism in patients who had major orthopedic surgery



I^2: 69.1 percent
Egger's p-value: 0.150

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

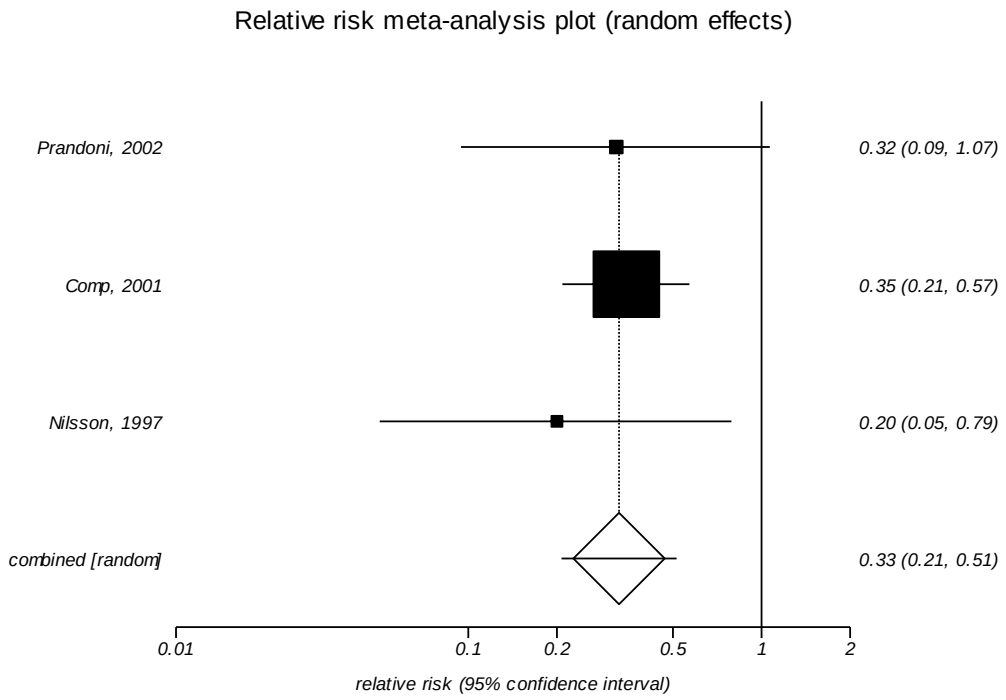
Figure 223. Impact of prolonged prophylaxis versus standard duration of prophylaxis on symptomatic objectively confirmed venous thromboembolism in patients who had major orthopedic surgery limited to trial published from 2001-present



I^2: 72.9 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

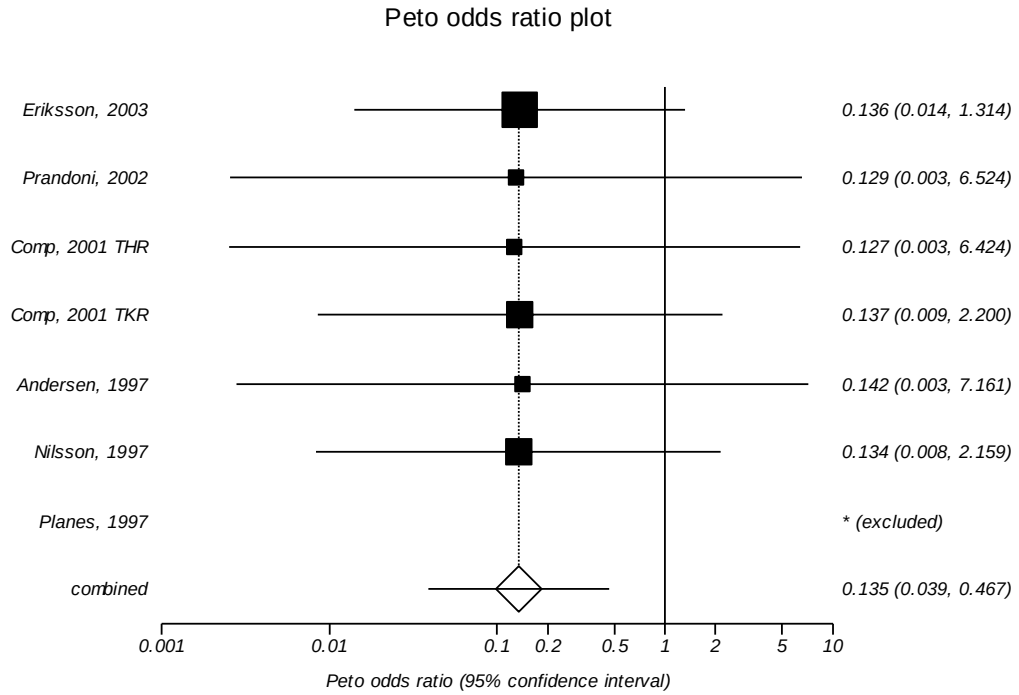
Figure 224. Impact of prolonged prophylaxis versus standard duration of prophylaxis on symptomatic objectively confirmed venous thromboembolism in patients who had major orthopedic surgery limited to total hip replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

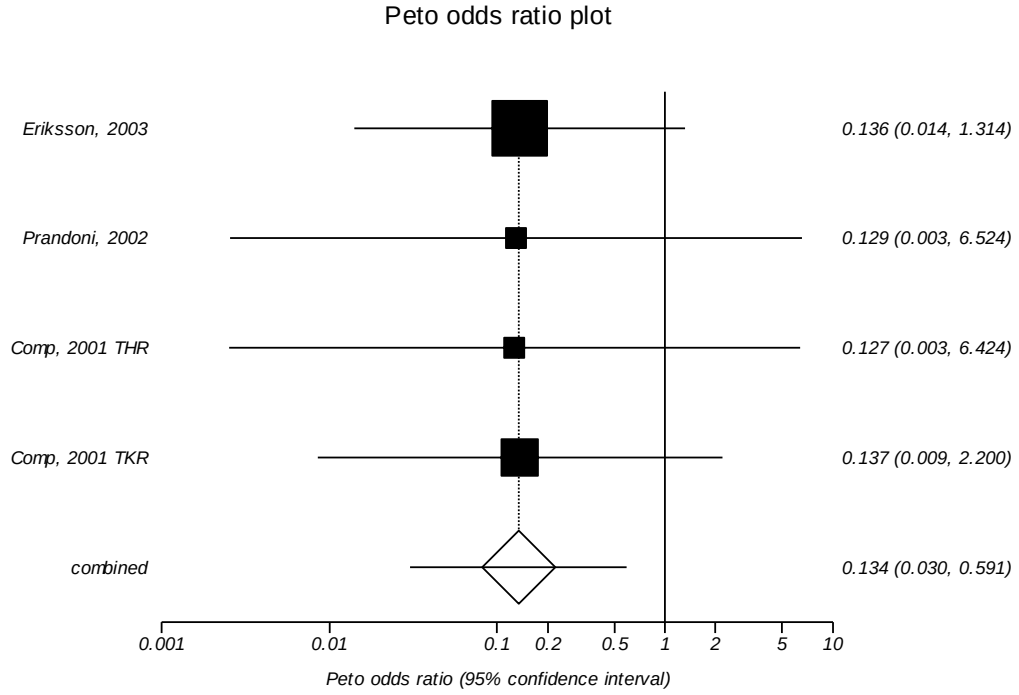
Figure 225. Impact of prolonged prophylaxis versus standard duration of prophylaxis on pulmonary embolism in patients who had major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.471

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

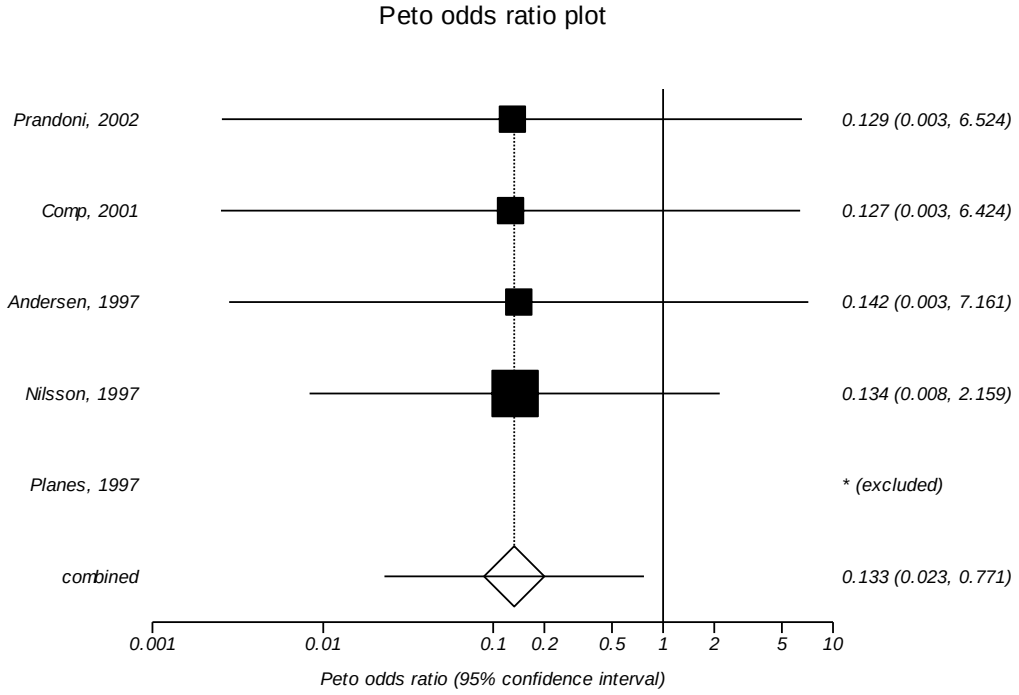
Figure 226. Impact of prolonged prophylaxis versus standard duration of prophylaxis on pulmonary embolism in patients who had major orthopedic surgery limited to trials published from 2001-present



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

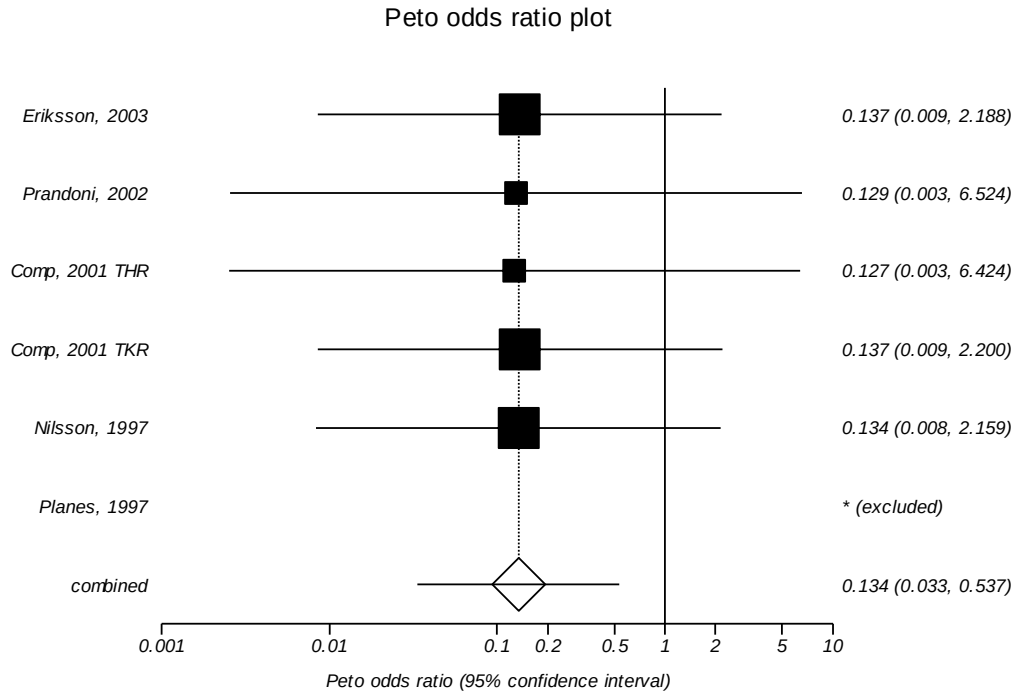
Figure 227. Impact of prolonged prophylaxis versus standard duration of prophylaxis on pulmonary embolism in patients who had major orthopedic surgery limited to total hip replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

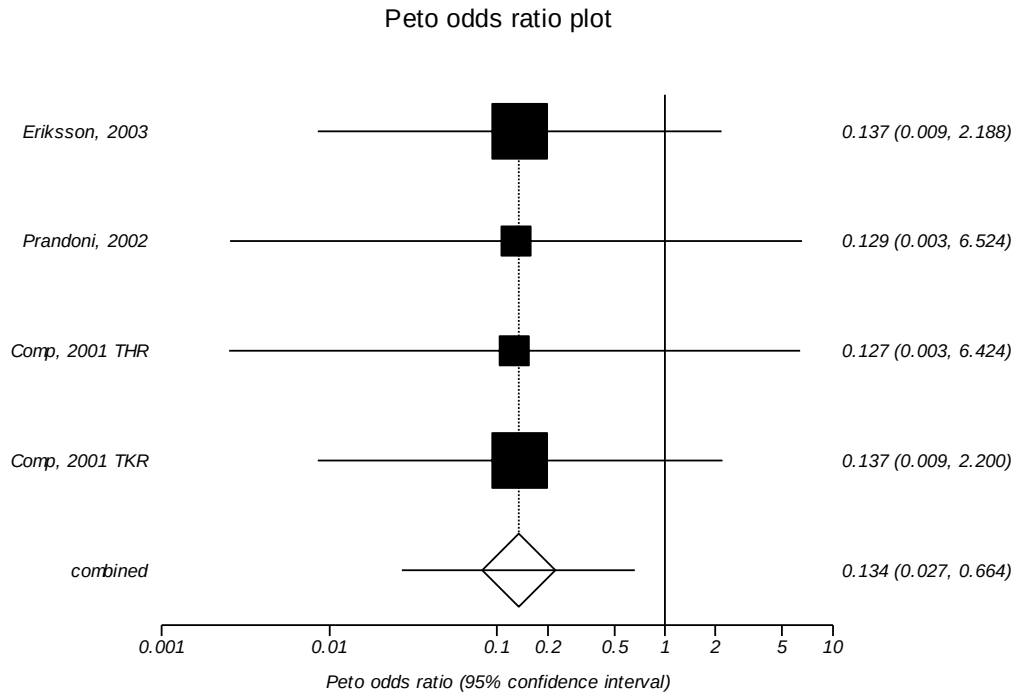
Figure 228. Impact of prolonged prophylaxis versus standard duration of prophylaxis on nonfatal pulmonary embolism in patients who had major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.016

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

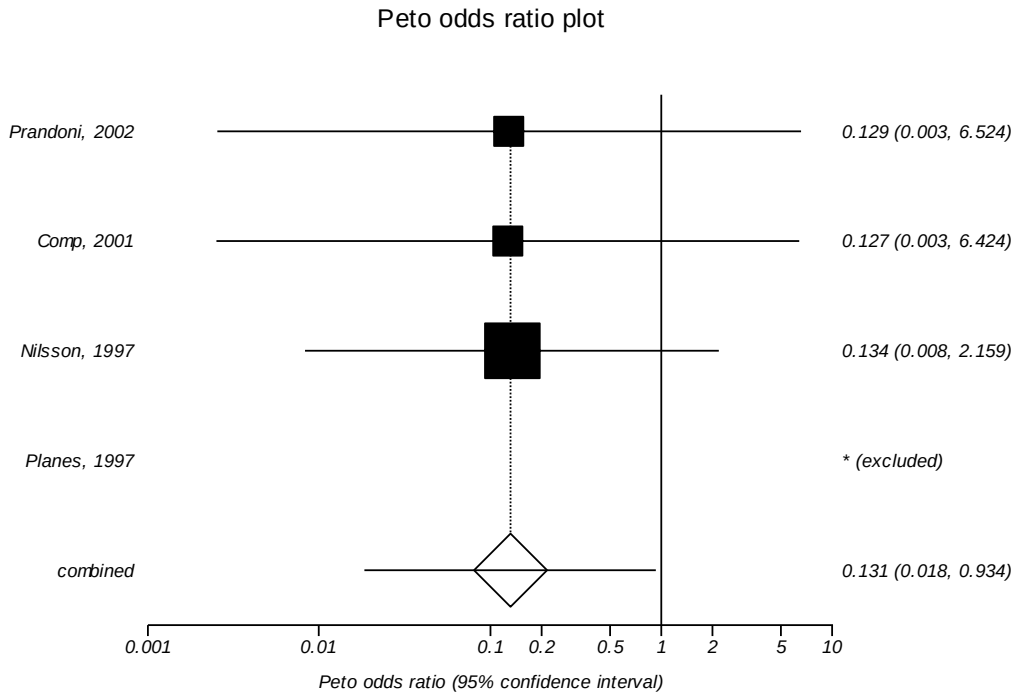
Figure 229. Impact of prolonged prophylaxis versus standard duration of prophylaxis on nonfatal pulmonary embolism in patients who had major orthopedic surgery limited to trials published from 2001-present



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

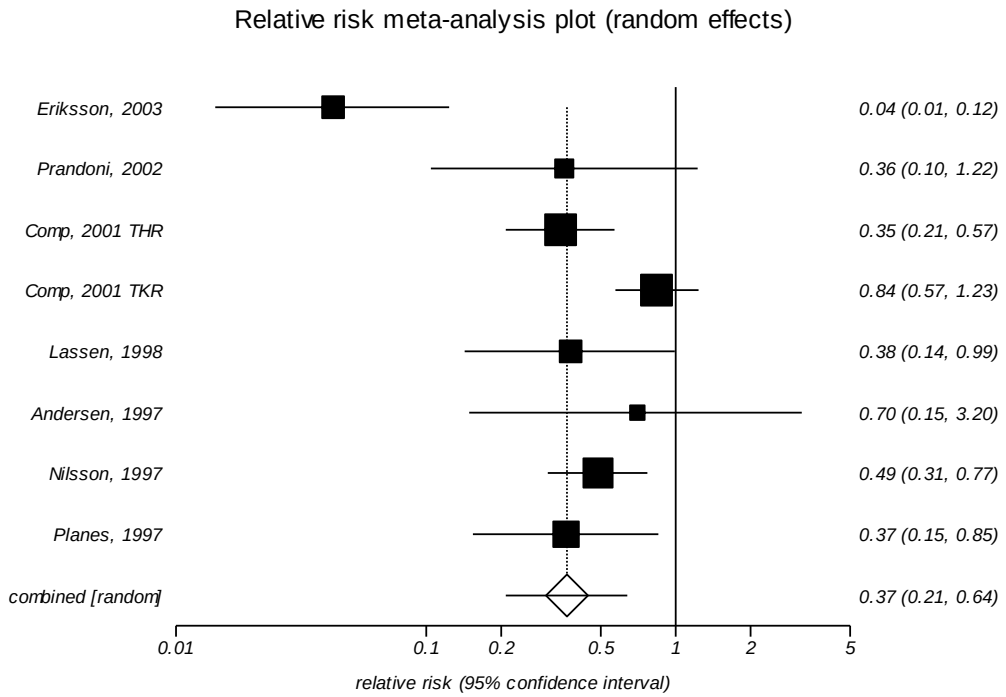
Figure 230. Impact of prolonged prophylaxis versus standard duration of prophylaxis on nonfatal pulmonary embolism in patients who had major orthopedic surgery limited to total hip replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

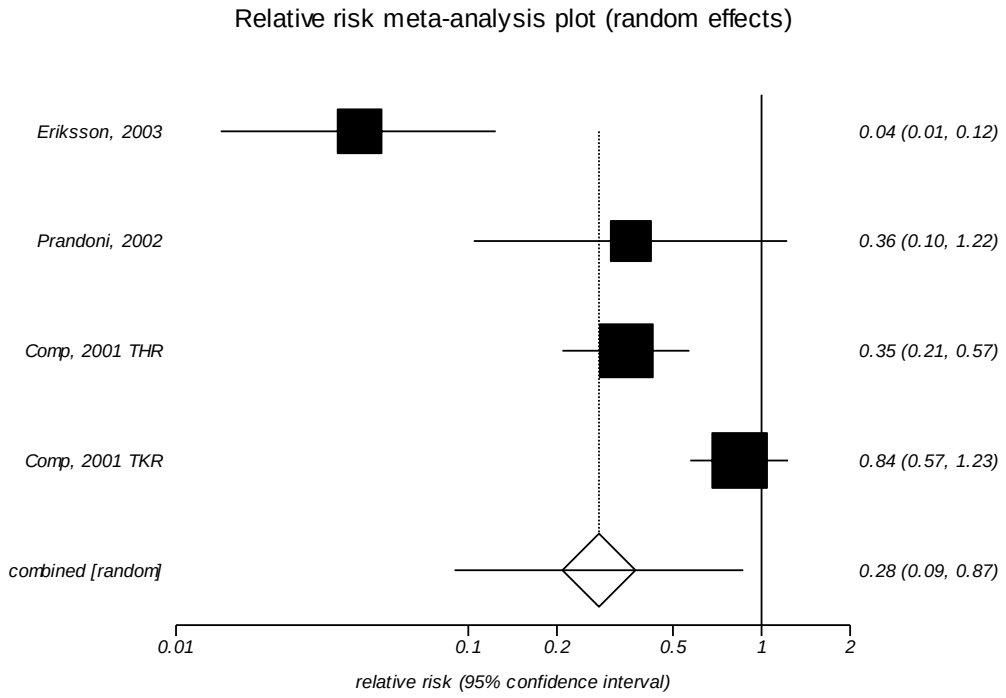
Figure 231. Impact of prolonged prophylaxis versus standard duration of prophylaxis on deep vein thrombosis in patients who had major orthopedic surgery



I^2: 78.3 percent
Egger's p-value: 0.164

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

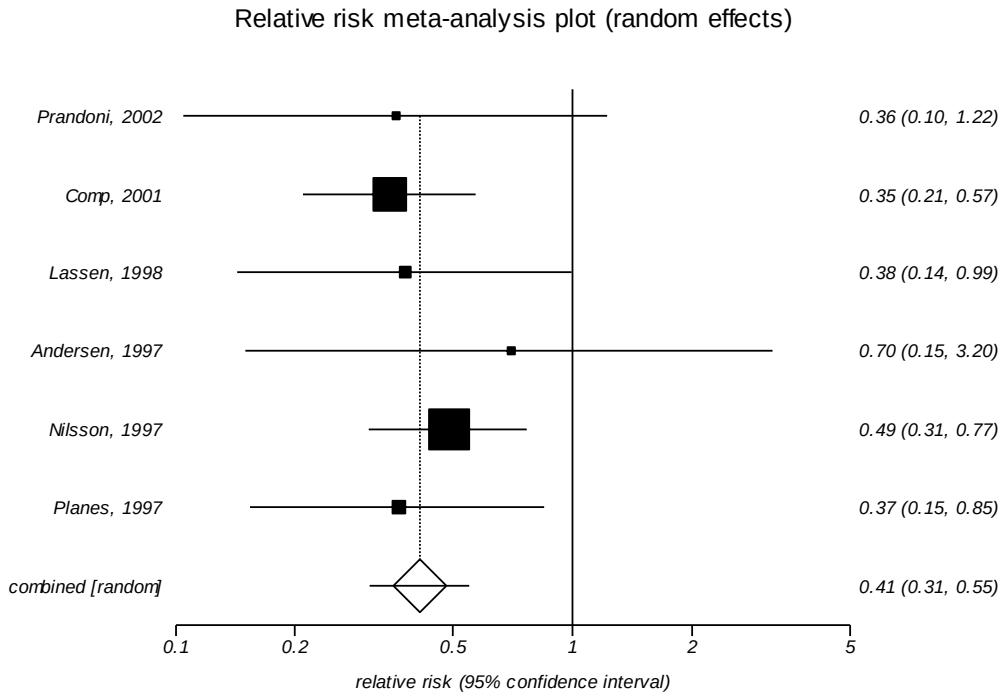
Figure 232. Impact of prolonged prophylaxis versus standard duration of prophylaxis on deep vein thrombosis in patients who had major orthopedic surgery limited to trials published from 2001-present



I^2: 90.9 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

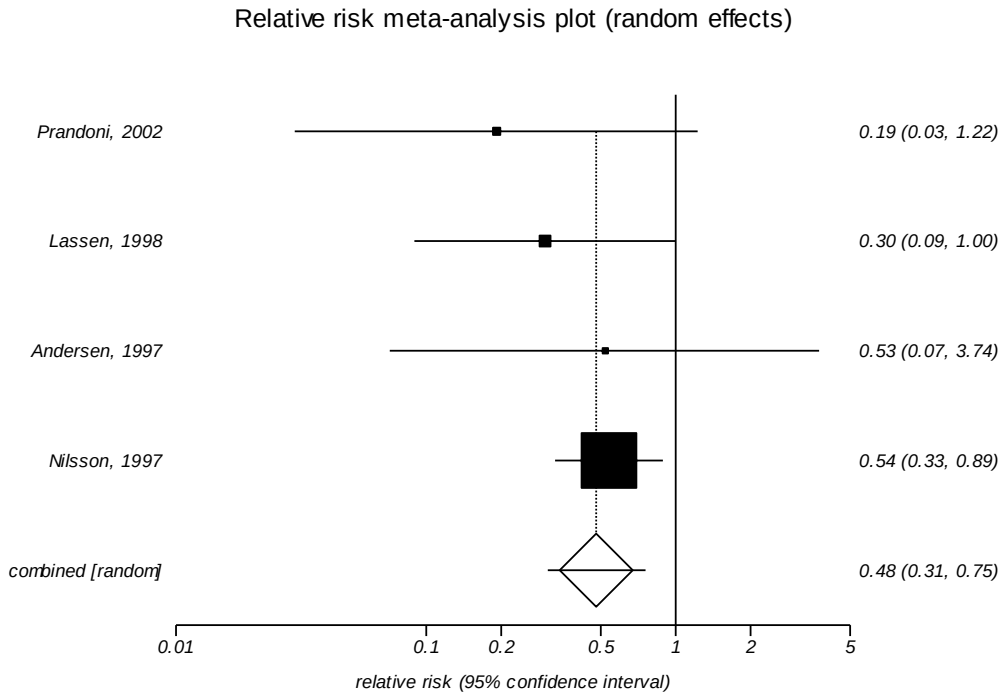
Figure 233. Impact of prolonged prophylaxis versus standard duration of prophylaxis on deep vein thrombosis in patients who had major orthopedic surgery limited to total hip replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

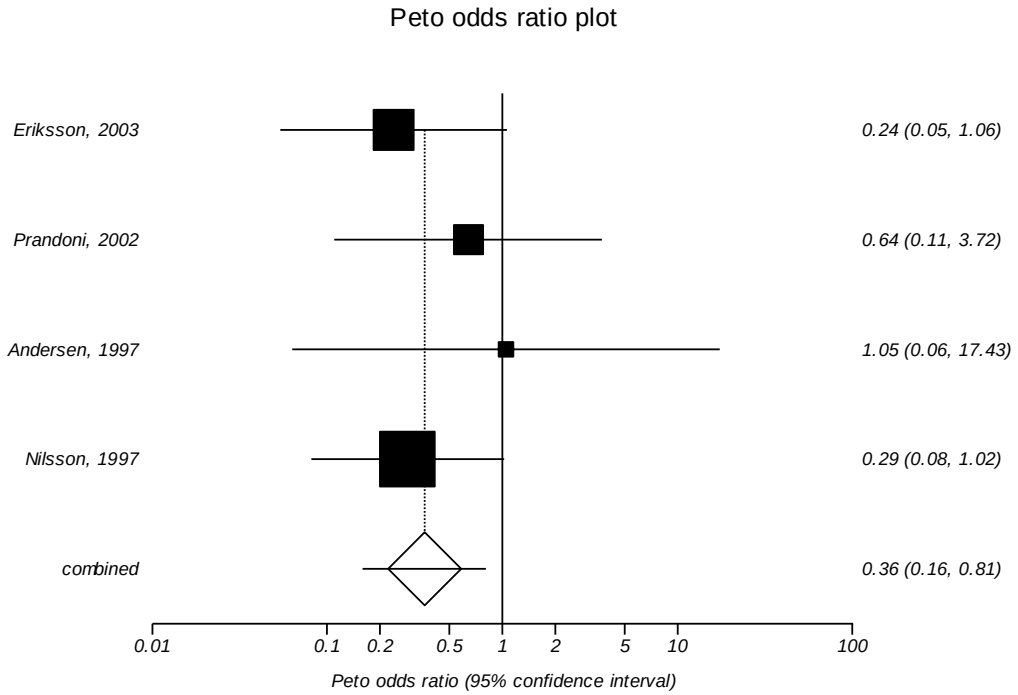
Figure 234. Impact of prolonged prophylaxis versus standard duration of prophylaxis on asymptomatic deep vein thrombosis in patients who had major orthopedic surgery (same as limited to total hip replacement surgery)



I^2: 0 percent
Egger's p-value: 0.252

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

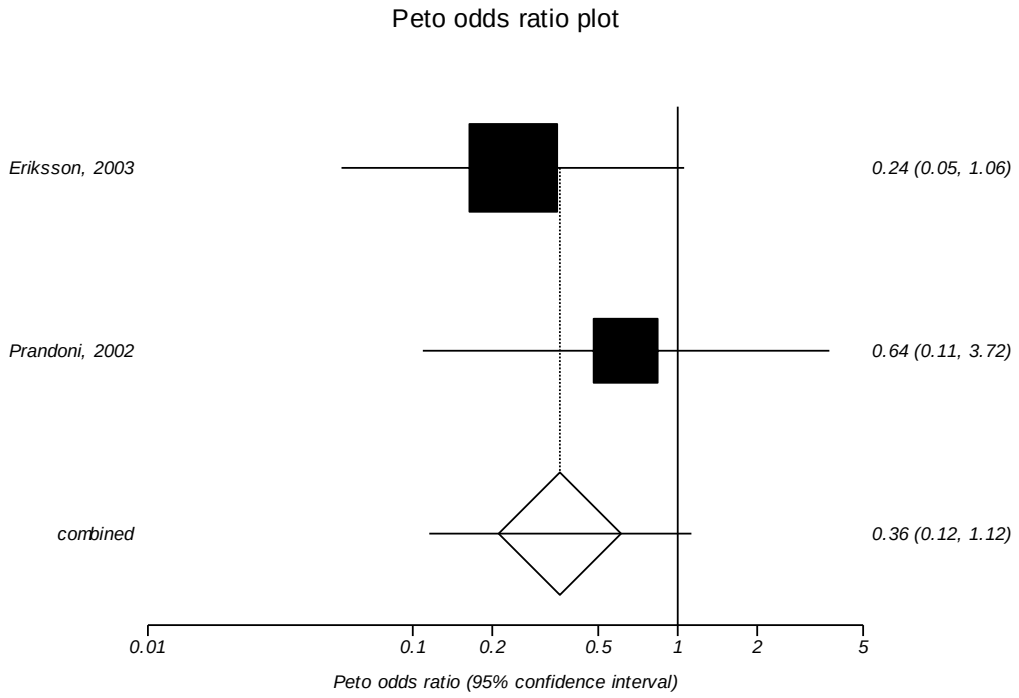
Figure 235. Impact of prolonged prophylaxis versus standard duration of prophylaxis on symptomatic deep vein thrombosis in patients who had major orthopedic surgery



I^2: 0 percent
Egger's p-value: 0.155

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

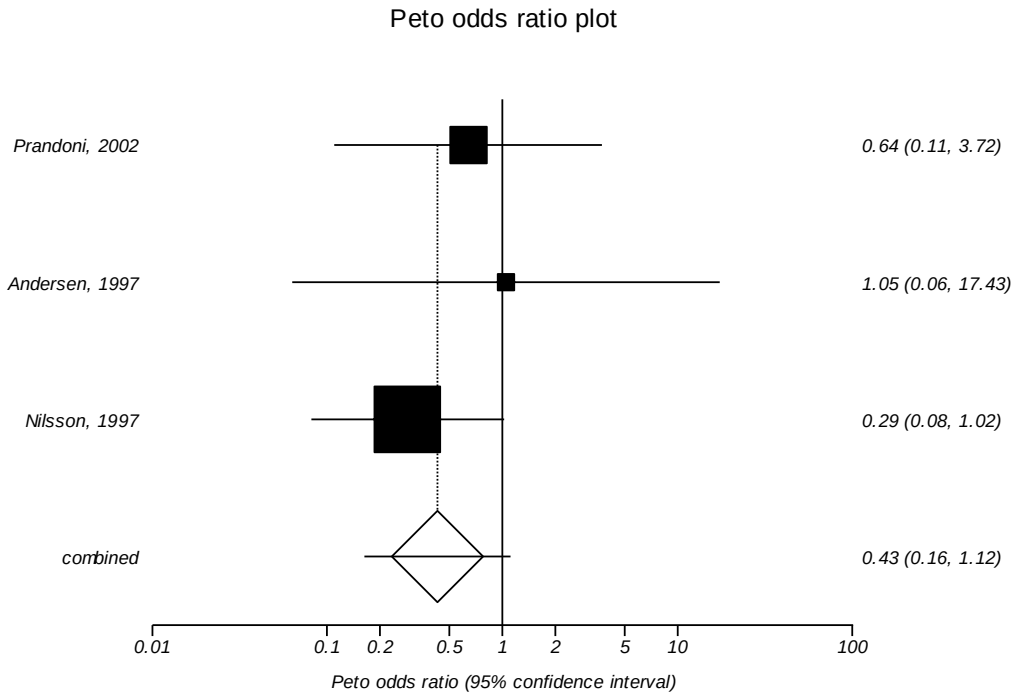
Figure 236. Impact of prolonged prophylaxis versus standard duration of prophylaxis on symptomatic deep vein thrombosis in patients who had major orthopedic surgery limited to trials published from 2001-present



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

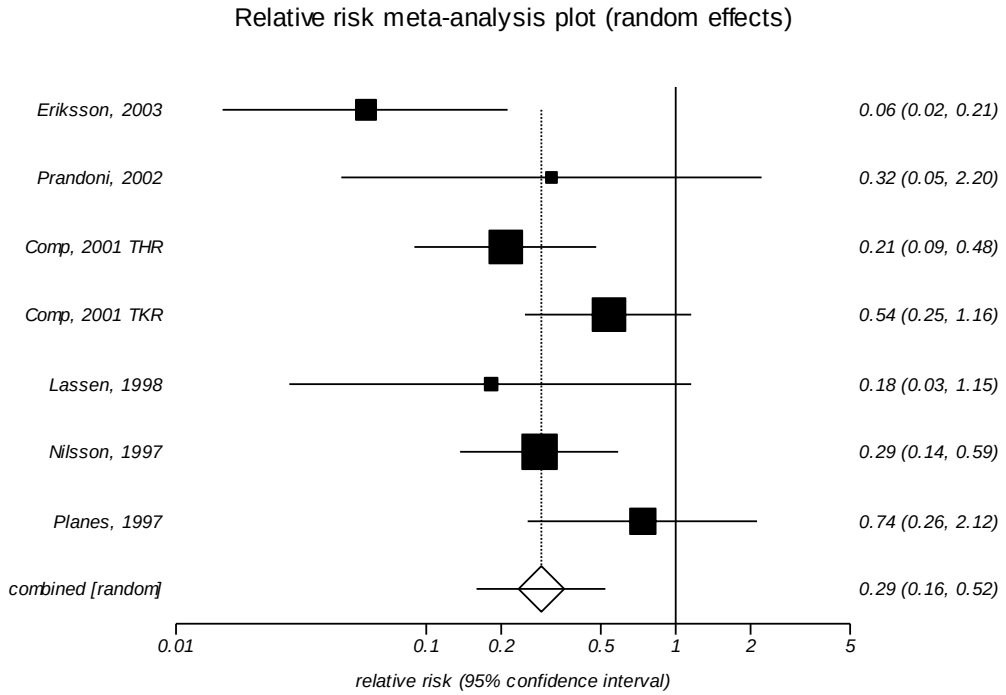
Figure 237. Impact of prolonged prophylaxis versus standard duration of prophylaxis on symptomatic deep vein thrombosis in patients who had major orthopedic surgery limited to total hip replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

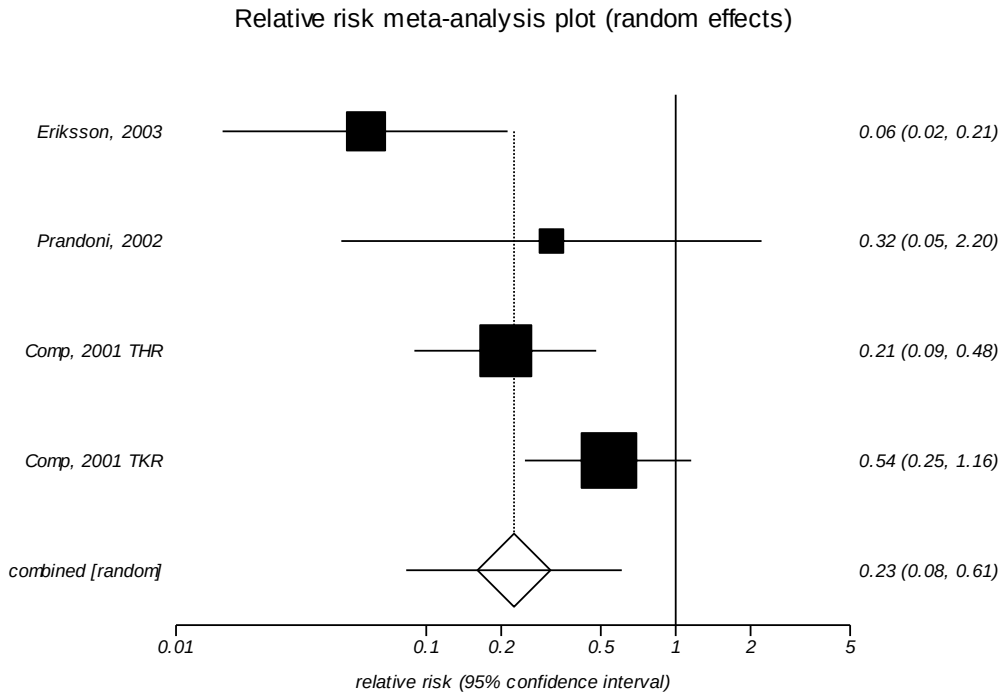
Figure 238. Impact of prolonged prophylaxis versus standard duration of prophylaxis on proximal deep vein thrombosis in patients who had major orthopedic surgery



I^2: 48.1 percent
Egger's p-value: 0.507

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

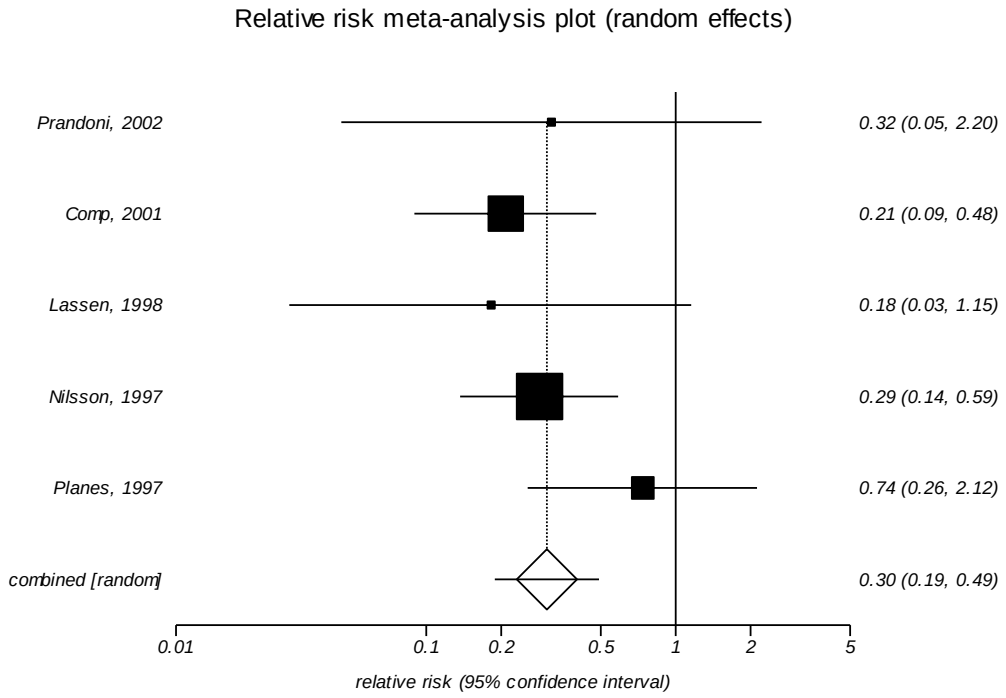
Figure 239. Impact of prolonged prophylaxis versus standard duration of prophylaxis on proximal deep vein thrombosis in patients who had major orthopedic surgery limited to trials published from 2001-present



I^2: 65.5 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

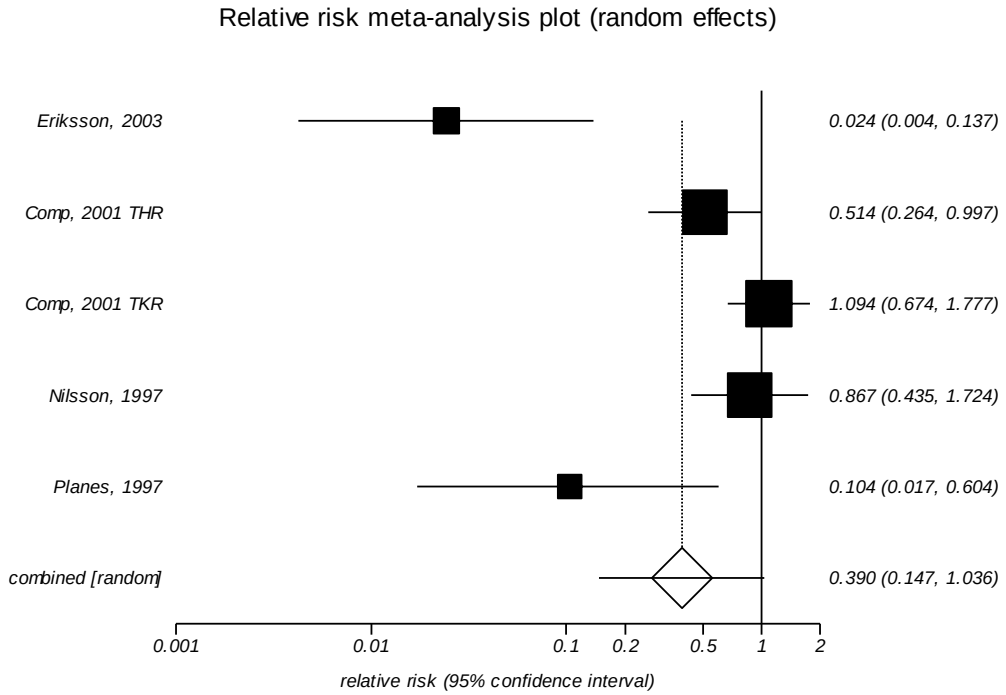
Figure 240. Impact of prolonged prophylaxis versus standard duration of prophylaxis on proximal deep vein thrombosis in patients who had major orthopedic surgery limited total hip replacement surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

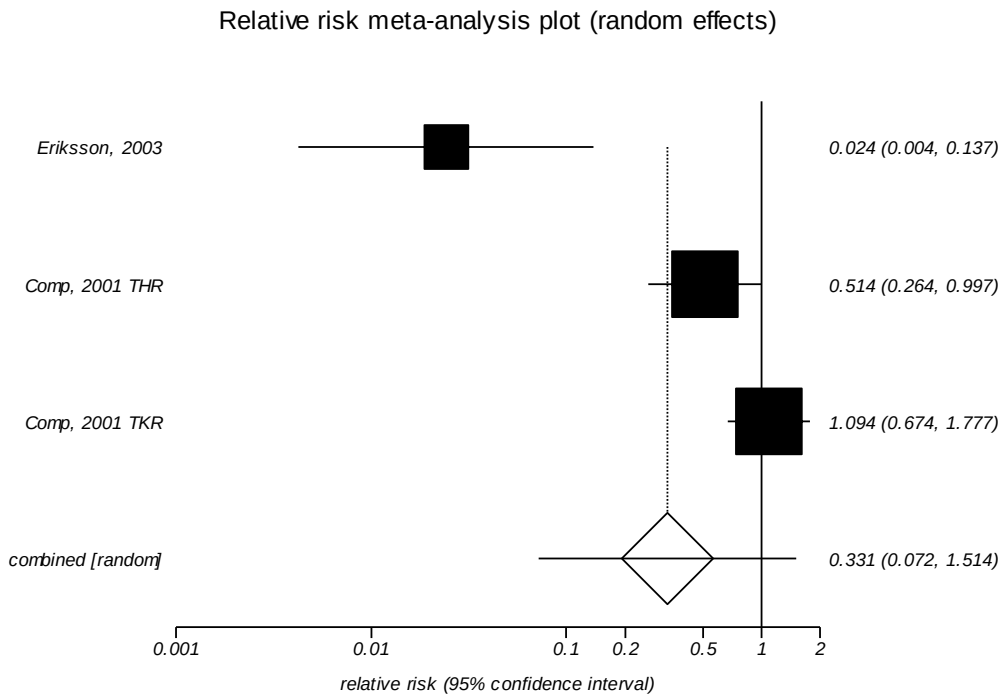
Figure 241. Impact of prolonged prophylaxis versus standard duration of prophylaxis on distal deep vein thrombosis in patients who had major orthopedic surgery



I^2: 83.6 percent
Egger's p-value: 0.023

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

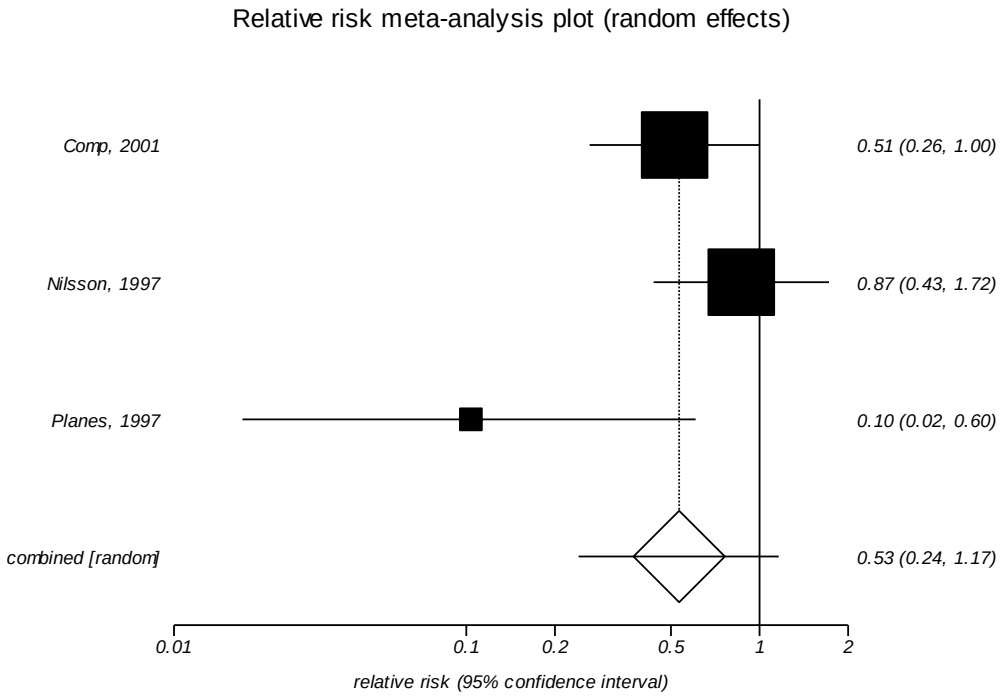
Figure 242. Impact of prolonged prophylaxis versus standard duration of prophylaxis on distal deep vein thrombosis in patients who had major orthopedic surgery limited to trials published from 2001-present



I^2: 90.3 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

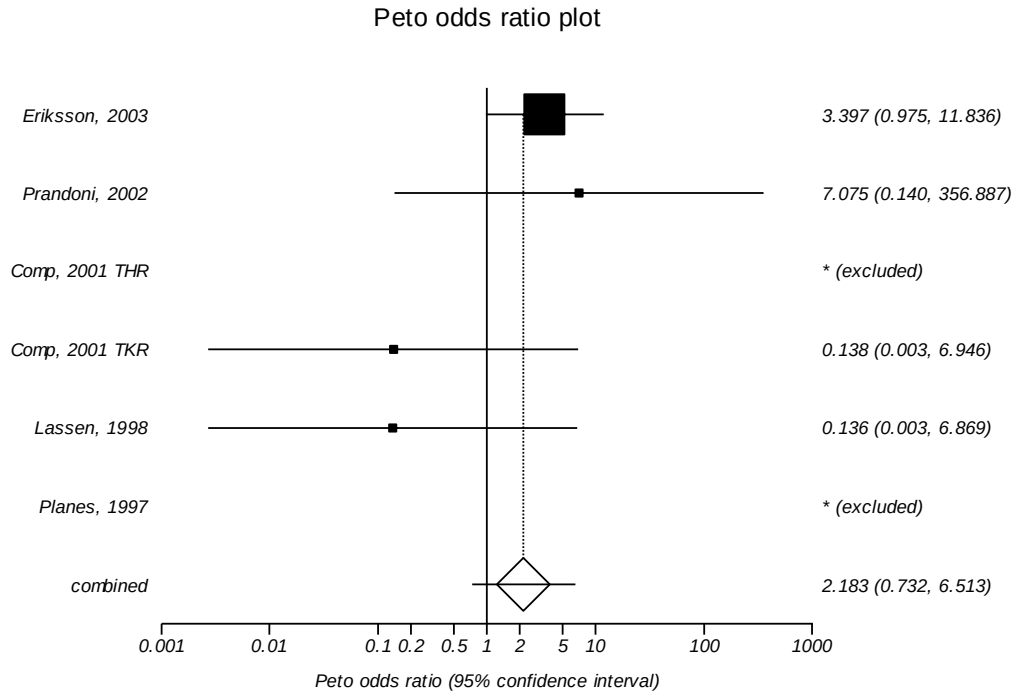
Figure 243. Impact of prolonged prophylaxis versus standard duration of prophylaxis on distal deep vein thrombosis in patients who had major orthopedic surgery limited to total hip replacement surgery



I^2: 53.4 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

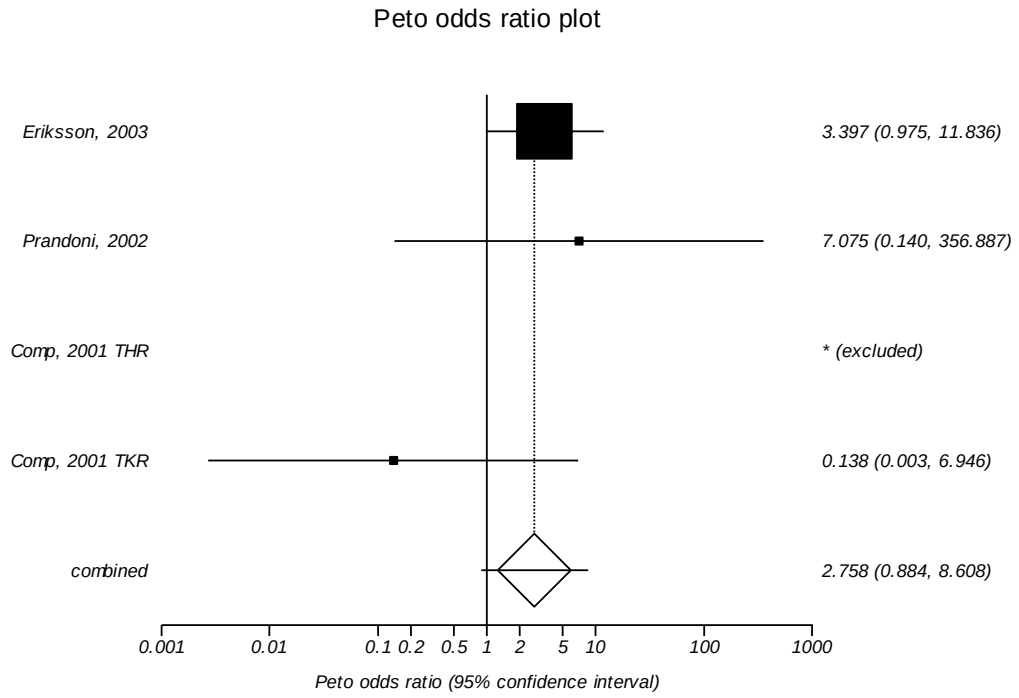
Figure 244. Impact of prolonged prophylaxis versus standard duration of prophylaxis on major bleeding in patients who had major orthopedic surgery



I^2: 35.6 percent
Egger's p-value: 0.334

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

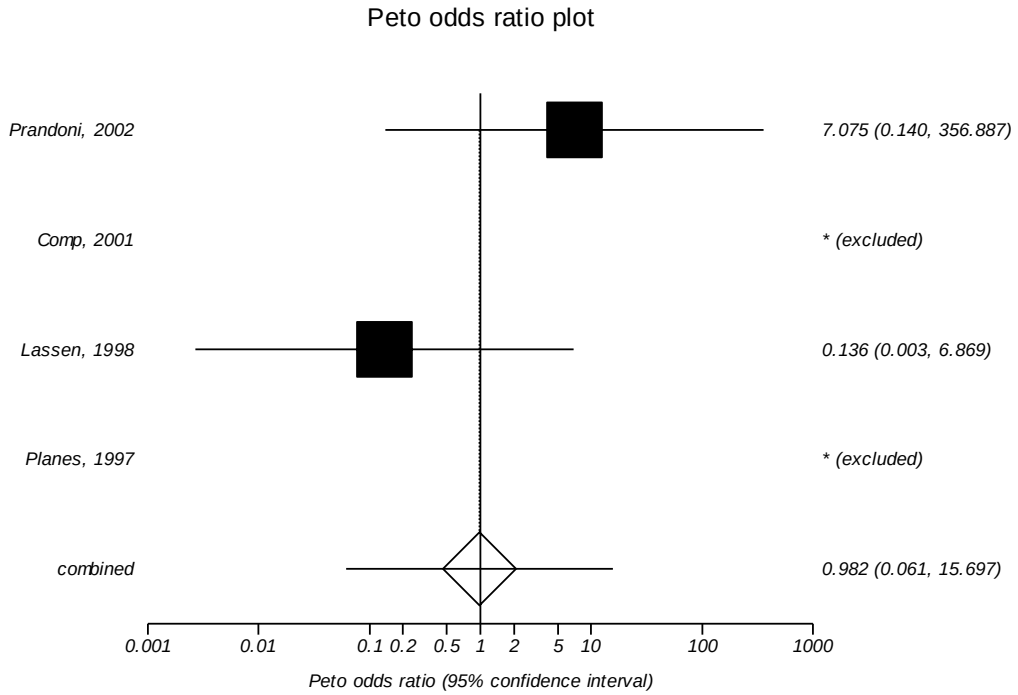
Figure 245. Impact of prolonged prophylaxis versus standard duration of prophylaxis on major bleeding in patients who had major orthopedic surgery limited to trials published from 2001-present



I^2: 22.3 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

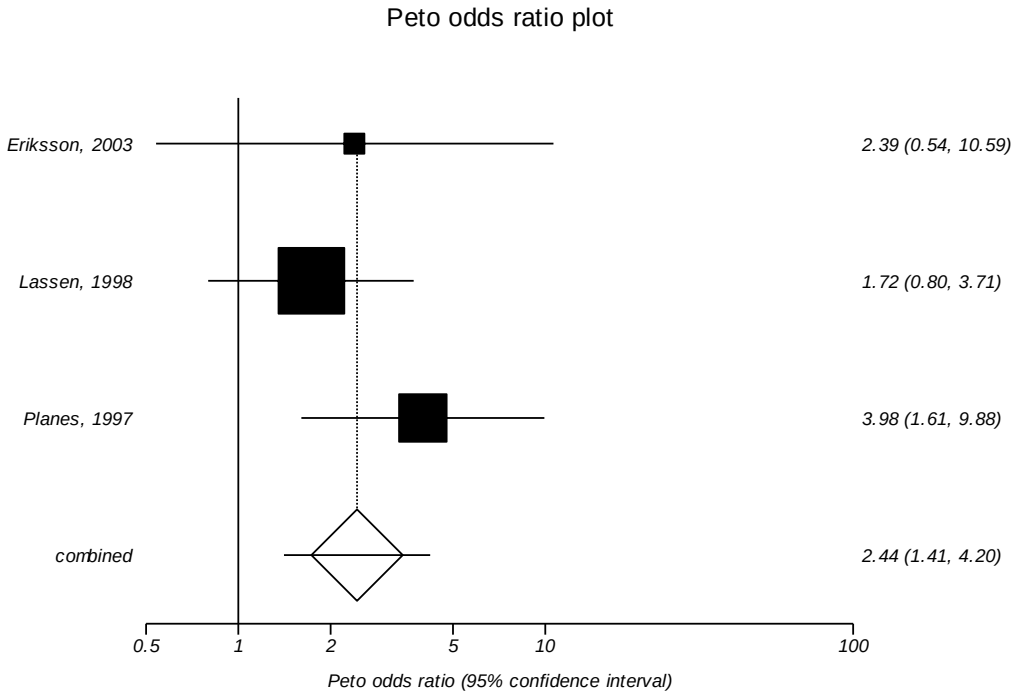
Figure 246. Impact of prolonged prophylaxis versus standard duration of prophylaxis on major bleeding in patients who had major orthopedic surgery limited to total hip replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each tudy in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

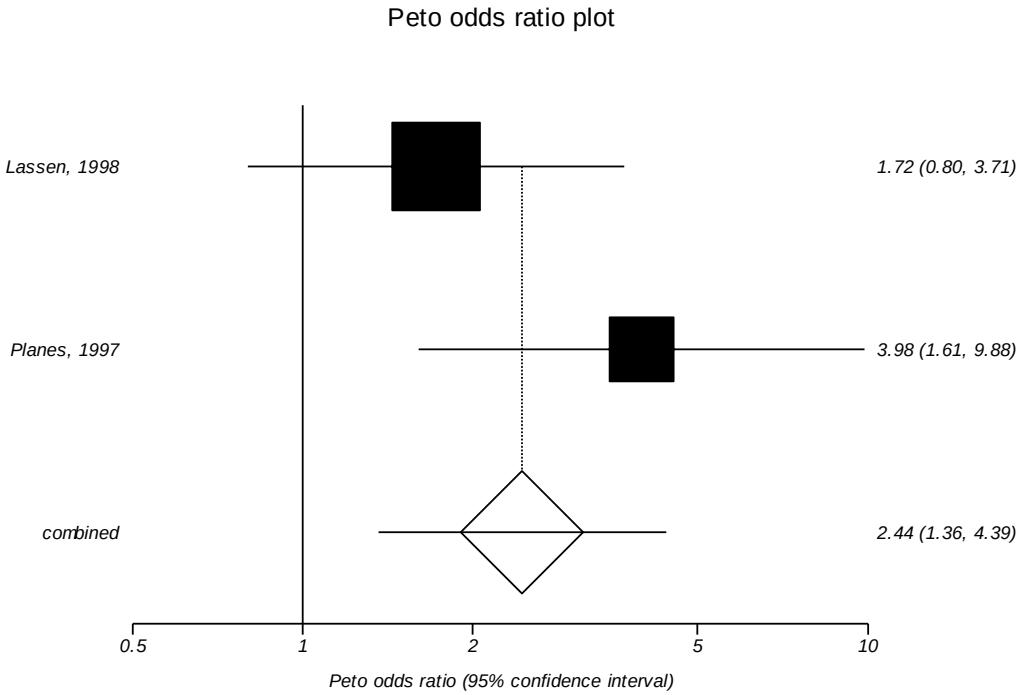
Figure 247. Impact of prolonged prophylaxis versus standard duration of prophylaxis on minor bleeding in patients who had major orthopedic surgery



I^2: 0 percent

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

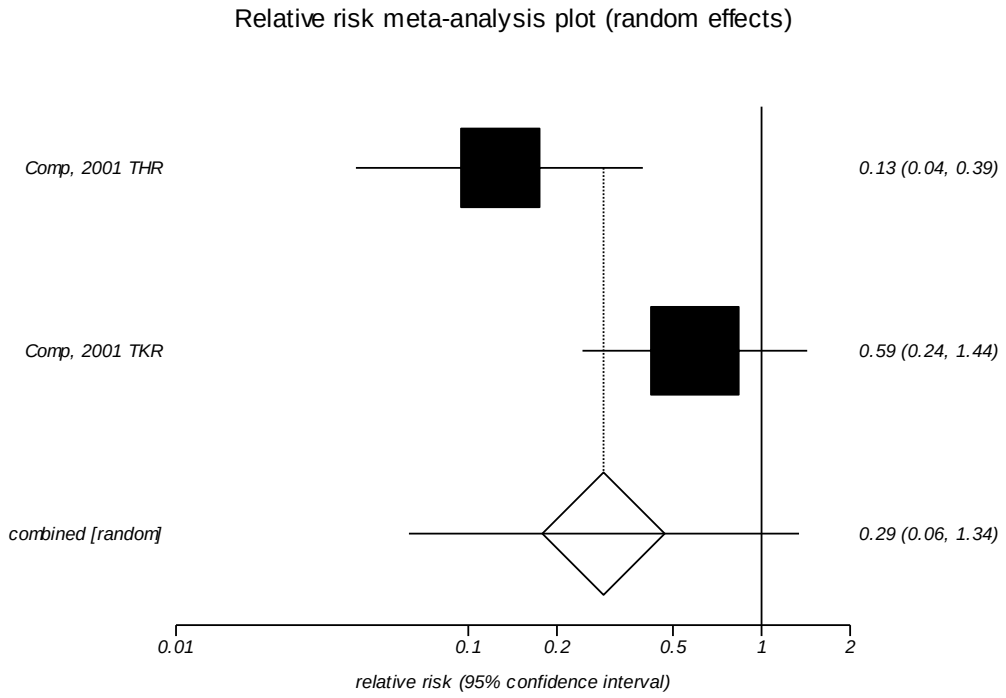
Figure 248. Impact of prolonged prophylaxis versus standard duration of prophylaxis on minor bleeding in patients who had major orthopedic surgery limited to total hip replacement surgery



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Figure 249. Impact of prolonged prophylaxis versus standard duration of prophylaxis on readmission in patients who had major orthopedic surgery (same as limited to trials published from 2001-present)



I^2: Too few strata

Legend: The squares represent individual point estimates. The size of the square represents the weight given to each study in the meta-analysis. Horizontal lines through each square represent 95 percent confidence intervals. The diamond represents the combined results. The solid vertical line extending from 1 is the null value.

Appendix H. Strength of evidence rating

Table 24. Strength of evidence for the incidence of final, intermediate and adverse outcomes in total hip replacement surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major venous thromboembolism	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	5	RCT	Very serious limitation	Very serious inconsistency	No indirectness	Serious imprecision	Low
Fatal pulmonary embolism	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Nonfatal pulmonary embolism	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Deep vein thrombosis	8	RCT	Very serious limitation	Very serious inconsistency	No indirectness	No imprecision	Low
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	4	RCT	Serious limitation	Very serious inconsistency	No indirectness	Serious imprecision	Low
Distal deep vein thrombosis	2	RCT	Very serious limitation	Serious inconsistency	No indirectness	Very serious imprecision	Low
Major bleeding	5	RCT	Serious limitation	No inconsistency	No indirectness	No imprecision	Moderate
Major bleeding leading to reoperation	2	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Minor bleeding	5	RCT	Serious limitation	Very serious inconsistency	No indirectness	Serious imprecision	Low
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 25. Strength of evidence for the incidence of final, intermediate and adverse outcomes in total knee replacement surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	3 (2,1)	RCT, OBS	Very serious limitation	No inconsistency	No indirectness	No imprecision	Low
Fatal pulmonary embolism	2 (1,1)	RCT, OBS	Very serious limitation	NA	No indirectness	NA	Insufficient
Nonfatal pulmonary embolism	2 (1,1)	RCT, OBS	Very serious limitation	NA	No indirectness	NA	Insufficient
Deep vein thrombosis	4 (2,1)	RCT, OBS	Very serious limitation	Serious inconsistency	No indirectness	Very serious imprecision	Low
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	2	RCT	Very serious limitation	Serious inconsistency	No indirectness	Very serious imprecision	Low
Distal deep vein thrombosis	2	RCT	Very serious limitation	No inconsistency	No indirectness	No imprecision	Low
Major bleeding	2	RCT	Serious limitation	No inconsistency	No indirectness	Serious imprecision	Low
Major bleeding leading to reoperation	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Minor bleeding	2	RCT	Serious limitation	No inconsistency	No indirectness	No imprecision	Moderate
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 26. Strength of evidence for the incidence of final, intermediate and adverse outcomes in hip fracture surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Fatal pulmonary embolism	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Nonfatal pulmonary embolism	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Deep vein thrombosis	1	RCT	Very serious limitation	NA	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	1	RCT	Very serious limitation	NA	No indirectness	NA	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 27. Strength of evidence for the impact of spinal versus epidural anesthesia on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 28. Strength of evidence for the impact of general versus regional anesthesia on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	2	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	6(4,2)	RCT, OBS	Serious limitation	Serious inconsistency	No indirectness	NA	Low
Asymptomatic deep vein thrombosis	2	RCT	Serious limitation	Serious inconsistency	No indirectness	NA	Insufficient
Symptomatic deep vein thrombosis	2	RCT	Serious limitation	NA	No indirectness	NA	Low
Proximal deep vein thrombosis	5	RCT	Serious limitation	Serious inconsistency	No Indirectness	NA	Low
Distal deep vein thrombosis	4	RCT	Serious limitation	Serious inconsistency	No indirectness	NA	Insufficient
Major bleeding	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 29. Strength of evidence for the impact of cemented versus noncemented arthroplasty on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	5 (2,3)	RCT, OBS	Serious limitation	Serious inconsistency	No indirectness	NA	Low
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	2	RCT	Serious limitation	No inconsistency	No Indirectness	NA	Low
Distal deep vein thrombosis	2	RCT	Serious limitation	Serious inconsistency	No indirectness	NA	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 30. Strength of evidence for the impact of bone vacuum cement versus standard cement on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	RCT	No limitations	NA	No indirectness	NA	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	RCT	No limitations	NA	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	1	RCT	No limitations	NA	No indirectness	NA	Insufficient
Distal deep vein thrombosis	1	RCT	No limitations	NA	No indirectness	NA	Insufficient
Major bleeding	1	RCT	No limitations	NA	No indirectness	NA	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	1	RCT	No limitations	NA	No indirectness	NA	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 31. Strength of evidence for the impact of tourniquet versus no tourniquet on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	RCT	Serious limitation	No inconsistency	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Symptomatic deep vein thrombosis	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Proximal deep vein thrombosis	2	RCT	Serious limitation	No inconsistency	No indirectness	NA	Insufficient
Distal deep vein thrombosis	2	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 32. Strength of evidence for the impact of tourniquet release prior to wound closure versus tourniquet release after wound closure on the risk of venous thromboembolic or bleeding outcomes.

Outcome	Number of studies	Design	Risk of Bias	Quality Assessment Consistency	Directness	Precision	Summary of Findings Quality
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	RCT	Very serious limitation	NA	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 33. Strength of evidence for the impact of modified position to maintain femoral blood flow versus standard figure four position on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Fatal pulmonary embolism	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Nonfatal pulmonary embolism	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	1	RCT	Serious limitations	NA	No indirectness	NA	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 34. Strength of evidence for the impact of minimum hyperflexed knee versus standard hyperflexed knee on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	RCT	Very serious limitation	NA	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	1	RCT	Very serious limitation	NA	No indirectness	NA	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 35. Strength of evidence for the impact of tissue fibrin adhesive versus no adhesive on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Symptomatic deep vein thrombosis	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Proximal deep vein thrombosis	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Distal deep vein thrombosis	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 36. Strength of evidence for the impact of primary versus revision surgery on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	OBS	Serious limitation	NA	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational ; VTE=venous thromboembolism

Table 37. Strength of evidence for the impact of perioperative blood loss on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	OBS	Serious limitation	NA	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational ; VTE=venous thromboembolism

Table 38. Strength of evidence for the impact of operative time on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	OBS	Serious limitation	NA	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 39. Strength of evidence for the impact of blood transfusions on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	OBS	Serious limitation	NA	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational ; VTE=venous thromboembolism

Table 40. Strength of evidence for the impact of congestive heart failure on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	2	OBS	No limitations	No inconsistency	No indirectness	NA	Moderate
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	1	OBS	Serious limitation	NA	No indirectness	NA	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational ; VTE=venous thromboembolism

Table 41. Strength of evidence for the impact of inactive malignancy on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	1	OBS	Serious limitation	NA	No indirectness	NA	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	1	OBS	Serious limitation	NA	No indirectness	NA	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational ; VTE=venous thromboembolism

Table 42. Strength of evidence for the impact of hormone replacement therapy on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	1	OBS	Serious limitation	NA	No indirectness	NA	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	1	OBS	Serious limitation	NA	No indirectness	NA	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 43. Strength of evidence for the impact of age on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	2	OBS	Serious limitation	No inconsistency	No indirectness	NA	Low
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	OBS	Serious limitation	NA	No indirectness	NA	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	3	OBS	Serious limitation	Serious inconsistency	No indirectness	NA	Low
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Proximal deep vein thrombosis	2	OBS	Very serious limitation	No inconsistency	No indirectness	NA	Low
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 44. Strength of evidence for the impact of living at home on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 45. Strength of evidence for the impact of intertrochanteric fractures on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 46. Strength of evidence for the impact of subtrochanteric fractures on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 47. Strength of evidence for the impact of increased hemoglobin on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 48. Strength of evidence for the impact of gender on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	2	OBS	No limitations	Serious inconsistency	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 49. Strength of evidence for the impact of history of venous thromboembolism on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 50. Strength of evidence for the impact of varicose veins on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 51. Strength of evidence for the impact of genitourinary infection on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	OBS	Serious limitations	NA	No indirectness	NA	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 52. Strength of evidence for the impact of cardiovascular disease on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	OBS	Serious limitations	NA	No indirectness	NA	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 53. Strength of evidence for the impact of thyroid hormone replacement on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	OBS	Serious limitation	NA	No indirectness	NA	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 54. Strength of evidence for the impact of phlebitis on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	OBS	Serious limitation	NA	No indirectness	NA	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 55. Strength of evidence for the impact of peripheral vascular disease on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	OBS	Serious limitation	NA	No indirectness	NA	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 56. Strength of evidence for the impact of weight on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	3	OBS	Very serious limitations	Serious inconsistency	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 57. Strength of evidence for the impact of smoking on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	OBS	Serious limitations	NA	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	1	OBS	Serious limitations	NA	No indirectness	NA	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 58. Strength of evidence for the impact of height on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	OBS	Serious limitations	NA	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 59. Strength of evidence for the impact of factor V Leiden mutation on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 60. Strength of evidence for the impact of blood disorders on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	1	OBS	Serious limitations	NA	No indirectness	NA	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 61. Strength of evidence for the impact of metabolic syndrome on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 62. Strength of evidence for the impact of education on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 63. Strength of evidence for the impact of diabetes mellitus on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 64. Strength of evidence for the impact of hypertension on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 65. Strength of evidence for the impact of hyperlipidemia on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 66. Strength of evidence for the impact of comorbidities on the risk of venous thromboembolic or bleeding outcomes.

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	1	OBS	No limitations	NA	No indirectness	NA	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 67. Strength of evidence for the causal link between deep vein thrombosis and pulmonary embolism in major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	11 (9,2)	RCT, OBS	Serious risk of bias	Serious inconsistency	Indirectness	NA	Insufficient

Abbreviations: RCT: randomized controlled trial; VTE=venous thromboembolism

Table 68. Strength of evidence for final, intermediate and adverse outcomes comparing pharmacologic prophylaxis to no prophylaxis in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	1	RCT	No limitations	Serious limitation	No indirectness	Serious imprecision	Low
Pulmonary Embolism	11	RCT	No limitations	No serious inconsistency	No indirectness	Very serious imprecision	Low
Fatal pulmonary embolism	6 (5,1)	RCT, OBS	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Nonfatal pulmonary embolism	6 (5,1)	RCT, OBS	No limitations	No serious inconsistency	No indirectness	Serious imprecision	Low
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	11 (9, 2)	RCT , OBS	No limitations	No serious inconsistency	No indirectness	Serious imprecision	Low
Mortality due to bleeding	8	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	16	RCT	Serious limitations	Serious inconsistency	No indirectness	No imprecision	Moderate
Asymptomatic deep vein thrombosis	3	RCT	No limitations	No inconsistency	No indirectness	No imprecision	Moderate
Symptomatic deep vein thrombosis	4 (3,1)	RCT , OBS	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Proximal deep vein thrombosis	11	RCT	No limitations	No inconsistency	No indirectness	No imprecision	Moderate
Distal deep vein thrombosis	6	RCT	No limitations	No inconsistency	No indirectness	No imprecision	Moderate
Major bleeding	7	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Major bleeding leading to reoperation	2	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Minor bleeding	5	RCT	No limitations	No inconsistency	No indirectness	No imprecision	High
Surgical site bleeding	0	---	---	---	---	---	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	1	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	1	OBS	Serious risk of bias	NA	No indirectness	NA	Insufficient
Reoperation	1	OBS	Serious risk of bias	NA	No indirectness	NA	Insufficient

Abbreviations: NA=not applicable; RCT= randomized controlled trial; OBS=observational; VTE=venous thromboembolism

Table 69. Strength of evidence for final, intermediate and adverse outcomes comparing mechanical prophylaxis to no prophylaxis in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Fatal pulmonary embolism	1	RCT	Serious limitation	NA	No indirectness	Serious imprecision	Insufficient
Nonfatal pulmonary embolism	1	RCT	Serious limitation	NA	No indirectness	Serious imprecision	Insufficient
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	0	---	---	---	---	---	Insufficient
Mortality due to bleeding	0	---	---	---	---	---	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	RCT	No limitation	NA	No indirectness	No imprecision	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	1	RCT	No limitation	NA	No indirectness	Serious imprecision	Insufficient
Distal deep vein thrombosis	1	RCT	No limitation	NA	No indirectness	Serious imprecision	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 70. Strength of evidence for final, intermediate and adverse outcomes comparing oral antiplatelet agents prophylaxis to oral vitamin K antagonists prophylaxis in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Fatal pulmonary embolism	2 (1,1)	RCT, OBS	No limitations	NA	No indirectness	Very serious imprecision	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Nonfatal pulmonary embolism	2 (1,1)	RCT, OBS	No limitations	NA	No indirectness	NA	Insufficient
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	3 (1, 2)	RCT, OBS	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Mortality due to bleeding	1	RCT	No limitations	NA	No indirectness	NA	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	RCT	Serious limitation	NA	No indirectness	Serious imprecision	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	1	RCT	Serious limitation	NA	No indirectness	Serious imprecision	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	1	RCT	No limitations	NA	No indirectness	Serious imprecision	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	1	OBS	No limitations	NA	No indirectness	Serious imprecision	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT: randomized controlled trial; OBS=observational; VTE=venous thromboembolism

Table 71. Strength of evidence for final, intermediate and adverse outcomes comparing oral antiplatelet agents prophylaxis to mechanical prophylaxis in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	RCT	Serious limitation	NA	No indirectness	Very serious imprecision	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	0	---	---	---	---	---	Insufficient
Mortality due to bleeding	0	---	---	---	---	---	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	2	RCT	Serious limitation	No inconsistency	No indirectness	No imprecision	Moderate
Asymptomatic deep vein thrombosis	1	RCT	Serious limitation	NA	No indirectness	Very serious imprecision	Insufficient
Symptomatic deep vein thrombosis	1	RCT	Serious limitation	NA	No indirectness	Very serious imprecision	Insufficient
Proximal deep vein thrombosis	1	RCT	Serious limitation	NA	No indirectness	Very serious imprecision	Insufficient
Distal deep vein thrombosis	1	RCT	Serious limitation	No inconsistency	No indirectness	No imprecision	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Readmission	0	---	---	---	---	---	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 72. Strength of evidence for final, intermediate and adverse outcomes comparing injectable low molecular weight heparin prophylaxis to injectable unfractionated heparin prophylaxis in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	1	RCT	Serious limitation	NA	No indirectness	Very serious imprecision	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	10	RCT	No limitations	Serious inconsistency	No indirectness	No imprecision	Moderate
Fatal pulmonary embolism	10	RCT	Serious limitation	NA	No indirectness	Very serious imprecision	Insufficient
Nonfatal pulmonary embolism	10	RCT	No limitations	Serious inconsistency	No indirectness	Serious imprecision	Low
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	8	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Mortality due to bleeding	7	RCT	Serious limitation	NA	No indirectness	Very serious imprecision	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	14	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Asymptomatic deep vein thrombosis	2	RCT	Serious limitation	No inconsistency	No indirectness	No imprecision	Low
Symptomatic deep vein thrombosis	3	RCT	Serious limitation	No inconsistency	No indirectness	Serious imprecision	Low
Proximal deep vein thrombosis	9	RCT	No limitations	No inconsistency	No indirectness	No imprecision	High
Distal deep vein thrombosis	8	RCT	No limitations	No inconsistency	No indirectness	No imprecision	High

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Major bleeding	7	RCT	No limitations	No inconsistency	No indirectness	No imprecision	High
Major bleeding leading to reoperation	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Minor bleeding	5	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Surgical site bleeding	3	RCT	Serious limitation	No inconsistency	No indirectness	Serious imprecision	Low
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	3	RCT	Serious limitation	No inconsistency	No indirectness	No imprecision	Moderate
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	2	RCT	Serious limitation	No inconsistency	No indirectness	Serious imprecision	Low
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT= randomized controlled trial; VTE=venous thromboembolism

Table 73. Strength of evidence for final, intermediate and adverse outcomes comparing injectable low molecular weight heparin prophylaxis to injectable or oral factor Xa inhibitor prophylaxis in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	4	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Low
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	RCT	No limitations	NA	No indirectness	Serious imprecision	Insufficient
Fatal pulmonary embolism	4	RCT	No limitations	No inconsistency	No indirectness	Very serious imprecision	Low
Nonfatal pulmonary embolism	4	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Mortality	4	RCT	No limitations	No inconsistency	No indirectness	No imprecision	Moderate
Mortality due to bleeding	4	RCT	Serious limitation	NA	No indirectness	Very serious imprecision	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	4	RCT	No limitations	No inconsistency	No indirectness	No imprecision	High
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	5	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Proximal deep vein thrombosis	4	RCT	No limitations	Serious inconsistency	No indirectness	No imprecision	Moderate
Distal deep vein thrombosis	4	RCT	No limitations	No inconsistency	No indirectness	No imprecision	High
Major bleeding	5	RCT	No limitations	Serious inconsistency	No indirectness	No imprecision	Moderate
Major bleeding leading to reoperation	4	RCT	No limitation	No inconsistency	No indirectness	Serious imprecision	Moderate
Minor bleeding	1	RCT	No limitations	NA	No indirectness	Serious imprecision	Insufficient
Surgical site bleeding	1	RCT	No limitations	NA	No indirectness	Serious imprecision	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient
Reoperation	1	RCT	Serious limitation	NA	No indirectness	Serious imprecision	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 74. Strength of evidence for final, intermediate and adverse outcomes comparing injectable low molecular weight heparin prophylaxis to injectable or oral direct thrombin inhibitors prophylaxis in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	3	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Pulmonary Embolism	3	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Fatal pulmonary embolism	3	RCT	No limitations	No inconsistency	No indirectness	Very serious imprecision	Low
Nonfatal pulmonary embolism	2	RCT	No limitations	Serious inconsistency	No indirectness	Serious imprecision	Low
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	5	RCT	No limitation	No inconsistency	No indirectness	Serious imprecision	Moderate
Mortality due to bleeding	3	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	RCT	No limitations	NA	No indirectness	No imprecision	Insufficient
Asymptomatic deep vein thrombosis	2	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Symptomatic deep vein thrombosis	4	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Proximal deep vein thrombosis	3	RCT	No limitations	Serious inconsistency	No indirectness	Serious imprecision	Low
Distal deep vein thrombosis	1	RCT	No limitations	No inconsistency	No indirectness	No imprecision	Insufficient
Major bleeding	4	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Major bleeding leading to reoperation	3	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Minor bleeding	3	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Surgical site bleeding	1	RCT	No limitations	No inconsistency	No indirectness	Very serious imprecision	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	2	RCT	No limitations	No inconsistency	No indirectness	No imprecision	High
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT: randomized controlled trial; VTE=venous thromboembolism

Table 75. Strength of evidence for final, intermediate and adverse outcomes comparing injectable low molecular weight heparin prophylaxis to oral vitamin K antagonists prophylaxis in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	2	RCT	No limitations	Serious inconsistency	No indirectness	Serious imprecision	Low
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	5	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Fatal pulmonary embolism	4	RCT	Serious limitation	NA	No indirectness	Very serious imprecision	Insufficient
Nonfatal pulmonary embolism	3	RCT	No limitations	Serious inconsistency	No indirectness	Serious imprecision	Low
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	6	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Mortality due to bleeding	4	RCT	Serious limitation	NA	No indirectness	Very serious imprecision	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Deep vein thrombosis	5	RCT	Serious limitation	Serious inconsistency	No indirectness	No imprecision	Low
Asymptomatic deep vein thrombosis	1	RCT	No limitations	NA	No indirectness	No imprecision	Insufficient
Symptomatic deep vein thrombosis	3	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Proximal deep vein thrombosis	6	RCT	No limitations	Serious inconsistency	No indirectness	Serious imprecision	Low
Distal deep vein thrombosis	2	RCT	Serious limitation	No inconsistency	No indirectness	No imprecision	Moderate
Major bleeding	7	RCT	No limitations	No inconsistency	No indirectness	No imprecision	High
Major bleeding leading to reoperation	2	RCT	Serious limitation	NA	No indirectness	Very serious imprecision	Insufficient
Minor bleeding	8	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Surgical site bleeding	2	RCT	Serious limitation	No inconsistency	No indirectness	Serious imprecision	Low
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	1	RCT	Serious limitation	NA	No indirectness	Serious imprecision	Insufficient
Heparin-induced thrombocytopenia	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient
Reoperation	2	RCT	Serious limitation	NA	No indirectness	Serious imprecision	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 76. Strength of evidence for final, intermediate and adverse outcomes comparing injectable low molecular weight heparin prophylaxis to mechanical prophylaxis in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Fatal pulmonary embolism	2	RCT	No limitations	NA	No indirectness	Serious imprecision	Insufficient
Nonfatal pulmonary embolism	1	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	2	RCT	No limitations	No inconsistency	No indirectness	Very serious imprecision	Low
Mortality due to bleeding	2	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	3	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Asymptomatic deep vein thrombosis	1	RCT	Serious limitation	NA	No indirectness	Very serious imprecision	Insufficient
Symptomatic deep vein thrombosis	2	RCT	No limitation	NA	No indirectness	Very serious imprecision	Insufficient
Proximal deep vein thrombosis	3	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Distal deep vein thrombosis	3	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	1	RCT	No limitations	NA	No indirectness	No imprecision	Insufficient
Readmission	2	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Low
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 77. Strength of evidence for final, intermediate and adverse outcomes comparing injectable unfractionated heparin prophylaxis to injectable or oral direct thrombin inhibitors prophylaxis in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	2	RCT	No limitations	Serious inconsistency	No indirectness	Very serious imprecision	Low
Fatal pulmonary embolism	2	RCT	No limitations	NA	No indirectness	NA	Insufficient
Nonfatal pulmonary embolism	2	RCT	No limitations	Serious inconsistency	No indirectness	Very serious imprecision	Low
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	2	RCT	No limitations	No inconsistency	No indirectness	Very serious imprecision	Low
Mortality due to bleeding	2	RCT	No limitations	NA	No indirectness	NA	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	2	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	2	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	2	RCT	Serious limitation	NA	No indirectness	Serious imprecision	Low
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	1	RCT	Serious limitation	NA	No indirectness	Serious imprecision	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 78. Strength of evidence for final, intermediate and adverse outcomes comparing injectable unfractionated heparin prophylaxis to injectable or oral factor Xa inhibitors prophylaxis in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	1	OBS	Serious limitation	NA	No indirectness	NA	Insufficient
Mortality due to bleeding	0	---	---	---	---	---	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	1	OBS	Serious limitation	NA	No indirectness	Serious imprecision	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 79. Strength of evidence for final, intermediate and adverse outcomes comparing injectable unfractionated heparin prophylaxis to mechanical prophylaxis in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	1	RCT	Serious limitation	NA	No indirectness	Very serious imprecision	Insufficient
Mortality due to bleeding	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	RCT	Serious limitation	NA	No indirectness	No imprecision	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Readmission	0	---	---	---	---	---	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 80. Strength of evidence for final, intermediate and adverse outcomes comparing oral vitamin K antagonists prophylaxis to mechanical prophylaxis in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Fatal pulmonary embolism	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Nonfatal pulmonary embolism	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	2	RCT	Serious limitation	NA	No indirectness	Very serious imprecision	Insufficient
Mortality due to bleeding	2	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	3	RCT	Serious limitation	Serious inconsistency	No indirectness	Serious imprecision	Low
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	3	RCT	Serious limitation	No inconsistency	No indirectness	No imprecision	Moderate
Distal deep vein thrombosis	1	RCT	Serious limitation	NA	No indirectness	Very serious imprecision	Insufficient
Major bleeding	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Major bleeding leading to reoperation	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Minor bleeding	2	RCT	Serious limitation	No inconsistency	No indirectness	Serious imprecision	Low
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	1	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT: randomized controlled trial; VTE=venous thromboembolism

Table 81. Strength of evidence for final, intermediate and adverse outcomes comparing enoxaparin prophylaxis to other low molecular weight heparin agents in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Fatal pulmonary embolism	2	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Nonfatal pulmonary embolism	2	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	1	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Mortality due to bleeding	1	RCT	No limitations	NA	No indirectness	NA	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	2	RCT	No limitations	Serious inconsistency	No indirectness	Serious imprecision	Low
Asymptomatic deep vein thrombosis	1	RCT	Serious limitation	NA	No indirectness	Serious imprecision	Insufficient
Symptomatic deep vein thrombosis	2	RCT	No limitations	NA	No indirectness	Serious imprecision	Insufficient
Proximal deep vein thrombosis	2	RCT	No limitations	Serious inconsistency	No indirectness	Serious imprecision	Low
Distal deep vein thrombosis	1	RCT	No limitations	NA	No indirectness	No imprecision	Insufficient
Major bleeding	2	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Moderate
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	1	RCT	No limitations	NA	No indirectness	Serious imprecision	Insufficient
Surgical site bleeding	2	RCT	No limitations	No inconsistency	No indirectness	Very serious imprecision	Low
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Heparin-induced thrombocytopenia	1	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 82 . Strength of evidence for final, intermediate and adverse outcomes comparing the intermittent pneumatic compression device by Kendall to the Venaflow intermittent pneumatic compression device in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Fatal pulmonary embolism	1	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Nonfatal pulmonary embolism	1	RCT	No limitations	No inconsistency	No indirectness	Very serious imprecision	Insufficient
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	1	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Mortality due to bleeding	1	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	1	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Distal deep vein thrombosis	1	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 83. Strength of evidence for final, intermediate and adverse outcomes comparing the ActiveCare intermittent pneumatic compression device to the Flowtron intermittent pneumatic compression device in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	1	OBS	Serious limitations	NA	No indirectness	NA	Insufficient
Nonfatal pulmonary embolism	1	OBS	Serious limitations	NA	No indirectness	NA	Insufficient
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	1	OBS	Serious limitations	NA	No indirectness	NA	Insufficient
Mortality due to bleeding	1	OBS	Serious limitations	NA	No indirectness	NA	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	OBS	Serious limitations	NA	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; OBS=observational; VTE=venous thromboembolism

Table 84. Strength of evidence for final, intermediate and adverse outcomes comparing intermittent pneumatic compression versus graduated compression stockings in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	2	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Fatal pulmonary embolism	2	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Nonfatal pulmonary embolism	2	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Mortality	0	---	---	---	---	---	Insufficient
Mortality due to bleeding	0	---	---	---	---	---	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	RCT	Serious limitation	NA	No indirectness	No imprecision	Low
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	1	RCT	Serious limitation	NA	No indirectness	NA	Insufficient
Proximal deep vein thrombosis	2	RCT	Serious limitation	No inconsistency	No indirectness	Serious imprecision	Low
Distal deep vein thrombosis	1	RCT	No limitations	No inconsistency	No indirectness	No imprecision	Low
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 85. Strength of evidence for final, intermediate and adverse outcomes comparing pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis alone in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	2	RCT	No limitations	No serious inconsistency	No indirectness	Very serious imprecision	Low
Fatal pulmonary embolism	2	RCT	No limitations	NA	No indirectness	NA	Insufficient
Nonfatal pulmonary embolism	2	RCT	No limitations	No serious inconsistency	No indirectness	Very serious imprecision	Low
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	3	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Mortality due to bleeding	3	RCT	No limitations	NA	No indirectness	NA	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	4	RCT	No limitations	No serious inconsistency	No indirectness	No imprecision	Moderate
Asymptomatic deep vein thrombosis	1	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Symptomatic deep vein thrombosis	1	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Proximal deep vein thrombosis	5	RCT	No limitations	No serious inconsistency	No indirectness	Very serious imprecision	Low
Distal deep vein thrombosis	3	RCT	No limitations	No serious inconsistency	No indirectness	Serious imprecision	Moderate
Major bleeding	1	RCT	No limitations	NA	No indirectness	NA	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	1	RCT	No limitations	NA	No indirectness	NA	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 86. Strength of evidence for final, intermediate and adverse outcomes comparing pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis alone in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	RCT	Serious limitations	NA	No indirectness	Very serious imprecision	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	1	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Mortality due to bleeding	1	RCT	No limitations	NA	No indirectness	NA	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	RCT	No limitations	NA	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	1	RCT	No limitations	NA	No indirectness	NA	Insufficient
Symptomatic deep vein thrombosis	1	RCT	No limitations	NA	No indirectness	NA	Insufficient
Proximal deep vein thrombosis	2	RCT	Serious limitation	No serious inconsistency	No indirectness	Serious imprecision	Low
Distal deep vein thrombosis	1	RCT	No limitations	NA	No indirectness	NA	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 87. Strength of evidence for final, intermediate and adverse outcomes comparing extended duration prophylaxis versus standard duration prophylaxis in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	4	RCT	No limitations	Serious inconsistency	No indirectness	No imprecision	Moderate
Major VTE	1	RCT	Serious limitation	NA	No indirectness	Serious imprecision	Insufficient
Pulmonary Embolism	7	RCT	No limitations	No inconsistency	No indirectness	No imprecision	High
Fatal pulmonary embolism	6	RCT	No limitations	NA	No indirectness	Serious imprecision	Insufficient
Nonfatal pulmonary embolism	6	RCT	Serious limitation	No inconsistency	No indirectness	No imprecision	Moderate
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	6	RCT	No limitations	NA	No indirectness	Serious imprecision	Insufficient
Mortality due to bleeding	5	RCT	No limitations	NA	No indirectness	NA	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	8	RCT	No limitations	Serious inconsistency	No indirectness	No imprecision	Moderate
Asymptomatic deep vein thrombosis	4	RCT	No limitations	No inconsistency	No indirectness	No imprecision	High
Symptomatic deep vein thrombosis	5	RCT	No limitations	No inconsistency	No indirectness	No imprecision	High
Proximal deep vein thrombosis	7	RCT	No limitations	No inconsistency	No indirectness	No imprecision	High
Distal deep vein thrombosis	4	RCT	Serious limitation	Serious inconsistency	No indirectness	Serious imprecision	Low
Major bleeding	5	RCT	No limitations	No inconsistency	No indirectness	Very serious imprecision	Low
Major bleeding leading to reoperation	1	RCT	No limitations	NA	No indirectness	Very serious imprecision	Insufficient
Minor bleeding	3	RCT	No limitations	No inconsistency	No indirectness	No imprecision	High
Surgical site bleeding	1	RCT	No limitations	NA	No indirectness	No imprecision	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	2	RCT	No limitations	NA	No indirectness	Serious imprecision	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	1	RCT	No limitations	No inconsistency	No indirectness	Serious imprecision	Low
Reoperation	1	RCT	Serious limitation	NA	No indirectness	Serious imprecision	Insufficient

Abbreviations: NA=not applicable; RCT=randomized controlled trial; VTE=venous thromboembolism

Table 88. Strength of evidence for final, intermediate and adverse outcomes comparing inferior vena cava filters to mechanical prophylaxis in patients who had major orthopedic surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major VTE	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Nonfatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	0	---	---	---	---	---	Insufficient
Mortality due to bleeding	0	---	---	---	---	---	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: VTE=venous thromboembolism

Table 89. Strength of evidence for final, intermediate and adverse outcomes comparing prophylaxis versus no prophylaxis in patients who had knee arthroscopy

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major venous thromboembolism	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	RCT	Serious risk of bias	NA	No indirectness	NA	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Non-fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	0	---	---	---	---	---	Insufficient
Mortality due to bleeding	0	---	---	---	---	---	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	RCT	Serious risk of bias	NA	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	1	RCT	Serious risk of bias	NA	No indirectness	NA	Insufficient
Distal deep vein thrombosis	1	RCT	Serious risk of bias	NA	No indirectness	NA	Insufficient
Major bleeding	1	RCT	Serious risk of bias	NA	No indirectness	NA	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	1	RCT	Serious risk of bias	NA	No indirectness	NA	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: RCT: randomized controlled trial; VTE=venous thromboembolism

Table 90. Strength of evidence for final, intermediate and adverse outcomes comparing prophylaxis versus no prophylaxis in patients who had surgical repair of a lower extremity injury distal to the hip

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major venous thromboembolism	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	1	RCT	No risk of bias	NA	No indirectness	NA	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Non-fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	0	---	---	---	---	---	Insufficient
Mortality due to bleeding	0	---	---	---	---	---	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	1	RCT	No risk of bias	NA	No indirectness	NA	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	1	RCT	No risk of bias	NA	No indirectness	NA	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	1	RCT	No risk of bias	NA	No indirectness	NA	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: RCT: randomized controlled trial; VTE=venous thromboembolism

Table 91. Strength of evidence for final, intermediate and adverse outcomes comparing prophylaxis versus no prophylaxis in patients who had elective spine surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major venous thromboembolism	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Non-fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	0	---	---	---	---	---	Insufficient
Mortality due to bleeding	0	---	---	---	---	---	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: RCT: randomized controlled trial; VTE=venous thromboembolism

Table 92. Strength of evidence for final, intermediate and adverse outcomes comparing injectable pharmacologic prophylaxis versus mechanical prophylaxis in patients who had knee arthoscopy

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major venous thromboembolism	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Non-fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	0	---	---	---	---	---	Insufficient
Mortality due to bleeding	0	---	---	---	---	---	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: RCT: randomized controlled trial; VTE=venous thromboembolism

Table 93. Strength of evidence for final, intermediate and adverse outcomes comparing injectable pharmacologic prophylaxis versus mechanical prophylaxis in patients who had surgical repair of a lower extremity injury distal to the hip

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major venous thromboembolism	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Non-fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	0	---	---	---	---	---	Insufficient
Mortality due to bleeding	0	---	---	---	---	---	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: RCT: randomized controlled trial; VTE=venous thromboembolism

Table 94. Strength of evidence for final, intermediate and adverse outcomes comparing injectable pharmacologic prophylaxis versus mechanical prophylaxis in patients who had elective spine surgery

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Symptomatic objectively confirmed VTE	0	---	---	---	---	---	Insufficient
Major venous thromboembolism	0	---	---	---	---	---	Insufficient
Pulmonary Embolism	0	---	---	---	---	---	Insufficient
Fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Non-fatal pulmonary embolism	0	---	---	---	---	---	Insufficient
Post thrombotic syndrome	0	---	---	---	---	---	Insufficient
Mortality	0	---	---	---	---	---	Insufficient
Mortality due to bleeding	0	---	---	---	---	---	Insufficient
Health related quality of life	0	---	---	---	---	---	Insufficient
Deep vein thrombosis	0	---	---	---	---	---	Insufficient
Asymptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Symptomatic deep vein thrombosis	0	---	---	---	---	---	Insufficient
Proximal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Distal deep vein thrombosis	0	---	---	---	---	---	Insufficient
Major bleeding	0	---	---	---	---	---	Insufficient
Major bleeding leading to reoperation	0	---	---	---	---	---	Insufficient
Minor bleeding	0	---	---	---	---	---	Insufficient
Surgical site bleeding	0	---	---	---	---	---	Insufficient
Bleeding leading to infection	0	---	---	---	---	---	Insufficient
Bleeding leading to transfusion	0	---	---	---	---	---	Insufficient
Heparin-induced thrombocytopenia	0	---	---	---	---	---	Insufficient

				Quality	Assessment		Summary of Findings
Outcome	**Number of studies**	**Design**	**Risk of Bias**	**Consistency**	**Directness**	**Precision**	**Quality**
Discomfort	0	---	---	---	---	---	Insufficient
Readmission	0	---	---	---	---	---	Insufficient
Reoperation	0	---	---	---	---	---	Insufficient

Abbreviations: RCT: randomized controlled trial; VTE=venous thromboembolism

Appendix I. Applicability rating for individual trials and studies and the body of evidence

Table 95. Evaluation of applicability for individual randomized controlled trials

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Fuji, 2010	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Assessed final health outcomes 2. Assessed adverse outcomes 3. Used intention-to-treat analysis 4. Adequate sample size	Population, Outcomes, Setting	• High female to male ration (F:84%, M:16%) • Only patients undergoing TKA • Conducted in Japan • Duration of followup for final and intermediate health outcomes (postoperative) • Only primary surgery
Chin, 2009	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Assessed final health outcomes 2. Assessed adverse outcomes 3. Used intention-to-treat analysis 4. Adequate sample size	Population, Outcomes, Setting	• High female to male ratio (F:92%, M:8%) • Only patients undergoing TKR • Conducted in Singapore • Duration of followup for final and intermediate health outcomes (postoperative) • Primary or revision surgery not reported
Ginsberg, 2009	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing TKA • Only primary surgery • Duration of followup for final and intermediate health outcomes (postoperative) • Conducted in 4 countries including USA
Edwards, 2008	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Assessed final health outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Outcomes	• Primary or revision surgery not reported • DVT outcomes and mortality assessed postoperatively • Did not report adverse outcomes

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Fuji, 2008 THA	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Assessed final health outcomes 2. Assessed adverse outcomes 3. Used intention-to-treat analysis 4. Adequate sample size	Population, Outcomes, Setting	• High female to male ratio (F:87%, M:13 %) • Only patients undergoing THA • Conducted in Japan • Duration of followup for final and intermediate health outcomes (postoperative) • Only primary surgery
Fuji, 2008 TKA	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Assessed final health outcomes 2. Assessed adverse outcomes 3. Used intention-to-treat analysis 4. Adequate sample size	Population, Outcomes, Setting	• High female to male ratio (F:87%, M:13 %) • Only patients undergoing TKA • Conducted in Japan • Duration of followup for final and intermediate health outcomes (postoperative) • Only primary surgery
Thorey, 2008	Study Designation: Efficacy Study Composite Score: 3 of 7	1. Enrolled primary care population 2. Used intention-to-treat analysis 3. Adequate study duration with clinically relevant treatment	Population, Outcomes, Setting	• Only patients undergoing TKA • Primary or revision surgery not reported • Did not assess final health outcomes • Did not assess adverse outcomes • Small sample size (N=20) • Conducted in Germany
Eriksson, 2007a	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing TKA • Only primary surgery • Did not use intention-to-treat analysis • Duration of followup for final and intermediate health outcomes (postoperative) • Conducted in 105 centers not including USA

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Eriksson, 2007b	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing THR • Only primary surgery • Duration of followup for final and intermediate health outcomes (postoperative) • Conducted in 115 centers not including USA
Lassen, 2007	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing TKR • Primary or revision surgery not repotted • Duration of followup for final and intermediate health outcomes (postoperative) • Conducted in 97 centers including USA
Bonneux, 2006	Study Designation: Efficacy Study Composite Score: 1 of 7	1. Assessed adverse outcomes	Population, Outcomes, Setting	• High female to male ratio (F:79%; M:21%) • Only patients undergoing TKA • Mainly primary surgery (revision surgery:5%) • Did not assess final health outcomes • Did not use intention-to-treat analysis • Small sample size (N=120) • Duration of followup for final and intermediate health outcomes (post-operartive) • Conducted in Belgium
Westrich, 2006	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled primary care population 2. Used intention-to-treat analysis 3. Adequate sample size 4. Adequate study duration with clinically relevant treatment	Population, Outcomes	• Only patients undergoing TKA • Only primary surgery • Did not assess final health outcomes • Did not assess adverse outcomes • Small sample size (N=118) • Duration of followup for intermediate health outcomes (post-operartive)

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Kalodiki, 1996	Study Designation: Efficacy Study Composite Score: 1 of 7	1. Enrolled primary care population	Outcomes, Setting	• Only patients undergoing THR • Geographical location not reported • Only primary surgery (100%) • Small sample size (N=78) • Did not use intention -to- treat analysis • Did not report final health outcomes • Did not report adverse outcomes • Duration of followup for intermediate health outcomes (post-operative)
Senaran, 2006	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Less stringent eligibility criteria 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis	Population, Outcomes, Setting	• Mean age 53.8 years • High female to male ratio (F:71%; M:29%) • Only patients undergoing THA • Primary or revision surgery not reported • Small sample size (N=100) • Duration of followup for final and intermediate health outcomes (42d or until discharge) • Conducted in Turkey
Eriksson,2005	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Intervention, Outcomes, Setting	• Only primary surgery • Duration of followup for final and intermediate health outcomes (post-operative or 30d-42d) • Did not use any of the doses included in Phase 3 trials • Conducted in 60 centers not including USA
Farag, 2005	**Study Designation:** Efficacy Study **Composite Score:** 4 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Used intention-to-treat analysis 4. Adequate study duration with clinically relevant treatment	Population, Outcomes, Setting	• Only patients undergoing TKA • Primary or revision surgery not reported • Did not assess final health outcomes • Did not assess adverse otucomes • Small sample size (N=38) • Duration of followup for intermediate health outcomes (10d)

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Lachiewicz, 2004	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Assessed final health outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes	• Only patients undergoing TKA • Duration of followup for final and intermediate health outcomes (post-operative) • Did not report adverse outcomes
Silbersack, 2004	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Used intention-to-treat analysis 4. Adequate sample size	Outcomes, Setting	• Only primary surgery • Duration of followup for final and intermediate health outcomes (post-operative) • Did not report adverse outcomes • Conducted in Germany
Eriksson, 2003	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Assessed final health outcomes 2. Assessed adverse outcomes 3. Used intention-to-treat analysis 4. Adequate sample size 5. Adequate study duration with clinically relevant treatment	Population, Outcomes, Setting	• High female to male ratio (F:71%; M:29%) • Only patients undergoing HFS • Primary or revision surgery not reported • Duration of followup for final health outcomes (32d) • Conducted in Europe and South America
Kim, 2003	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Less stringent eligibility criteria 2. Assessed final health outcomes 3. Used intention-to-treat analysis 4. Adequate sample size 5. Adequate study duration with clinically relevant treatment	Population, Outcomes, Setting	• Mean age 54.9 yrs • Only patients undergoing THR • Primary or revision surgery not reported • Did not assess adverse outcomes • Duration of followup for final and intermediate health outcomes (7d) • Conducted in Korea
Lassen, 2002	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing THR • Mainly primary surgery (revision:12%) • Did not use intention-to-treat analysis • Duration of followup for final and intermediate health outcomes (49d) • Conducted in 73 centers not including USA

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Pitto, 2002	**Study Designation:** Effectiveness Study **Composite Score:** 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate study duration with clinically relevant treatment	Population, Outcomes, Setting	• Only patients undergoing TKA • Only primary surgery • Did not assess adverse outcomes • Small sample size (N=130) • Duration of followup for final health outcomes (45d) • Conducted in Germany
Prandoni, 2002	Study Designation: Effectiveness Study Composite Score: 7 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Assessed final health outcomes 4. Assessed adverse outcomes 5. Used intention-to-treat analysis 6. Adequate sample size 7. Adequate study duration with clinically relevant treatment	Population, Setting	• Only patients undergoing THA • Primary or revision surgery not reported • Duration of followup for final health outcomes (28d, 90d) • Conducted in Italy
Turpie, 2002	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes Setting	• Only patients undergoing THR • Duration of followup for final and intermediate health outcomes (11d, 42d) • Conducted in 3 countries including USA
Warwick, 2002	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing TKR • Only primary surgery • Did not use intention-to-treat analysis • Duration of followup for final and intermediate health outcomes (postoperative) • Conducted in UK

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Barden, 2001	**Study Designation:** Efficacy Study **Composite Score:** 3 of 7	1. Assessed final health outcomes 2. Used intention-to-treat analysis 3. Adequate sample size	Population, Outcomes, Setting	• High female to male ratio (F:71%; M:29%) • Only patients undergoing THR • Only primary surgery • Did not assess adverse outcomes • Conducted in Denmark
Bauer, 2001	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes	• Only patients undergoing TKR • Mainly primary surgery (revision surgery:7.5%) • Duration of followup for final and intermediate health outcomes (49d and 11d)
Comp, 2001	Study Designation: Effectiveness Study Composite Score: 6 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size 6. Adequate study duration with clinically relevant treatment	Outcomes	• Duration of followup for final health outcomes (30d)
Eriksson, 2001	Study Designation: Efficacy Study Composite Score: 3 of 7	1. Assessed final health outcomes 2. Assessed adverse outcomes 3. Adequate sample size	Population, Outcomes, Setting	• High female to male ratio (F:75%; M:25%) • Only patients undergoing HFS • Primary or revision surgery not reported • Did not use intention-to-treat analysis • Duration of followup for final and intermediate health outcomes (49d and 11d) • Conducted in 21 countries; unknown if USA also included

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Fitzgerald, 2001	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing TKA • Only primary surgery • Duration of followup for final and intermediate health outcomes (post-operative) • Conducted as multicenter (location unknown)
Hull, 2000	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing THR • Duration of followup for final and intermediate health outcomes (post-operative) • Conducted in USA and Canada
Kennedy, 2000	Study Designation: Efficacy Study Composite Score: 3 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing HFS • Primary or revision surgery not reported • Did not assess adverse outcomes • Did not use intention-to-treat analysis • Duration of followup for final and intermediate health outcomes (post-operative) • Study location not reported
Colwell, 1999	Study Designation: Effectiveness Study Composite Score: 7 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Assessed final health outcomes 4. Assessed adverse outcomes 5. Used intention-to-treat analysis 6. Adequate sample size 7. Adequate study duration with clinically relevant treatment	Population	• Only patients undergoing THR • Only primary surgery

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Levy, 1999	**Study Designation:** Effectiveness Study **Composite Score:** 5 of 7	1. Less stringent eligibility criteria 2. Assessed final health outcomes 3. Used intention-to-treat analysis 4. Adequate sample size 5. Adequate study duration with clinically relevant treatment	Population, Outcomes, Setting	• High female to male ratio (F:79%; M:21%) • Only patients undergoing TKA • Primary or revision surgery not reported • Did not assess adverse outcomes • Small sample size (N=58) • Duration of followup for final and intermediate health outcomes (post-operartive) • Conducted in Israel
Planes, 1999	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Assessed final health outcomes 2. Assessed adverse outcomes 3. Adequate sample size 4. Used intention-to-treat analysis	Population, Outcomes, Setting	• Only patients undergoing THR • Only primary surgery • Duration of followup for final, intermediate and adverse health outcomes (postoperative) • Conducted in France
TIFDED Study group, 1999	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Assessed final health outcomes 2. Assessed adverse outcomes 3. Adequate sample size 4. Used intention-to-treat analysis	Population, Setting	• High female to male ratio (F:79%, M:21%) • Only patients undergoing HFS • Primary versus revision surgery not reported • Duration of followup for final and intermediate health outcomes (postoperative) • Conducted in France, Belgium, Norway, Netherlands
Wakankar, 1999	**Study Designation:** Efficacy Study **Composite Score:** 4 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Used intention-to-treat analysis 4. Adequate study duration with clinically relevant treatment	Population, Outcomes, Setting	• Only patients undergoing TKA • Primary or revision surgery not reported • Did not assess adverse outcomes • Small sample size (N=77) • Duration of followup for intermediate health outcomes (post-operative) • Conducted in UK

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Kim, 1998	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Less stringent eligibility criteria 2. Adequate study duration with clinically relevant treatments 3. Assessed adverse outcomes 4. Used intention-to-treat analysis	Population, Outcomes, Setting	• Small sample size (N=100) • Mean age not reported • High male to female ratio (F:21%, M:79 %) • Only patients undergoing THR • Conducted in Korea • Only primary surgery • Duration of followup for intermediate health outcomes (post-operative) • Final health outcomes not assessed
Lassen, 1998	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled primary care population 2. Assessed adverse outcomes 3. Adequate sample size 4. Adequate study duration with clinically relevant treatment	Population, Outcomes, Setting	• Only patients undergoing THA • Mainly primary surgery (revision surgery 12%) • Did not assess final health outcomes • Did not use intention-to-treat analysis • Conducted in Denmark
Rader, 1998	Study Designation: Efficacy Study Composite Score: 3 of 7	1. Enrolled primary care population 2. Used intention-to-treat analysis 3. Adequate sample size	Population, Outcomes, Setting	• Only primary surgery • Did not assess final health outcomes • Did not assess adverse outcomes • Conducted in Germany
Ryan, 1998	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled a primary care population 2. Less stringent eligibility criteria 3. Assessed final health outcomes 4. Used intention-to-treat analysis	Population, Outcomes	• Only patients undergoing THA • Only primary surgery • Duration of followup for final and intermediate health outcomes (postoperative) • Did not evaluate adverse outcomes • Small sample size (N=100)

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Warwick,1998	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing THR • Only primary surgery • Duration of followup for final and intermediate health outcomes (post-operative) • Conducted in UK
Andersen, 1997	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Used intention-to-treat analysis 4. Adequate study duration with clinically relevant treatment	Population, Outcomes, Setting	• Only patients undergoing THA • Primary or revision not reported • Did not assess adverse outcomes • Small sample size (N=41) • Duration of followup for final health outcomes (35d) • Conducted in Denmark
Dahl, 1997	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing THA • Mainly primary surgery (revision surgery 8%) • Duration of followup for final and intermediate health outcomes (35d, 7d, 7-35d) • Conducted in Norway
Eriksson, 1997a	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing THR • Only primary surgery • Duration of followup for final and intermediate health outcomes (42d or post-operative) • Conducted in Sweden & Denmark
Eriksson, 1997b	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing THR • Only primary surgery • Did not use intention-to-treat analysis • Duration of followup for final and intermediate health outcomes (42d or post-operative) • Conducted in 31 centers not including USA

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Francis,1997	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled primary care population 2. Assessed adverse outcomes 3. Used intention-to-treat analysis 4. Adequate sample size	Population, Outcomes	• Only patients undergoing THR • Only primary surgery • Did not assess final health outcomes • Duration of followup for intermediate health outcomes (post-operative)
Nilsson, 1997	Study Designation: Effectiveness Study Composite Score: 6 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Assessed final health outcomes 4. Assessed adverse outcomes 5. Adequate sample size 6. Used intention-to-treat analysis	Population, Outcomes, Setting	• Only patients undergoing THA • Only primary surgery • Duration of followup for final health outcomes (30d, 90d) • Conducted in Sweden
Planes, 1997	Study Designation: Effectiveness Study Composite Score: 6 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size 6. Adequate study duration with clinically relevant treatment	Population, Setting	• Only patients undergoing THA • Primary or revision not reported • Duration of followup for final health outcomes (35d, 90d) • Conducted in France
Samama, 1997	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size.	Population, Outcomes, Setting	• Only patients undergoing THR • Conducted in France • Only primary surgery • Duration of followup for final and intermediate health outcomes (post-operative)
Eriksson, 1996	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing THR • Only primary surgery • Duration of followup for final and intermediate health outcomes (post-operative) • Conducted in Europe

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Kalodiki, 1996	Study Designation: Efficacy Study Composite Score: 1 of 7	1. Enrolled primary care population	Outcomes, Outcomes, Setting	• Small sample size (N=78) • Only patients undergoing THR • Geographic location not reported • Only primary surgery • Did not assess final health outcomes • Duration of followup for intermediate health outcomes (post-operative) • Did not assess adverse outcomes • Did not use intention to treat analysis
Laupacis, 1996	Study Designation: Effectiveness Study Composite Score: 6 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Assessed final health outcomes 4. Used intention-to-treat analysis 5. Adequate sample size 6. Adequate study duration with clinically relevant treatment	Population, Outcomes, Setting	• Only patients undergoing THR • Only primary surgery • Did not assess final health outcomes • Did not assess adverse outcomes • Duration of followup for final and intermediate health outcomes (post-operartive) • Conducted in Canada
Leclerc, 1996	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing TKR • Mainly primary surgery (revision:7%) • Duration of followup for final and intermediate health outcomes (post-operative) • Conducted in Canada
Lotke, 1996	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Used intention-to-treat analysis 4. Adequate sample size	Population, Outcomes	• Primary or revision surgery not reported • Did not assess final health outcomes • Did not assess adverse outcomes • Duration of followup for intermediate health outcomes (post-operative)

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Schwartsmann, 1996	Study Designation: Efficacy Study Composite Score: 3 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Used intention-to-treat analysis	Population, Outcomes, Setting	• Only patients undergoing THR • Only primary surgery • Did not assess adverse outcomes • Small sample size (N=99) • Duration of followup for final and intermediate health outcomes (post-operative) • Conducted in Brazil
Stannard, 1996	Study Designation: Efficacy Study Composite Score: 3 of 7	1. Less stringent enrollment criteria 2. Assessed final health outcomes 3. Used intent to treat analysis	Population, Outcomes,	• Only patients undergoing THR • Gender not reported • Low percent of revision surgery (0-12%) • Duration of followup (postoperative) • Did not assess adverse outcomes • Small sample size (N=75)
Stone, 1996	Study Designation: Efficacy Study Composite Score: 2 of 7	1. Enrolled primary care population 2. Used intention-to-treat analysis	Population, Outcomes, Setting	• Only patients undergoing THR • Only primary surgery • Did not assess final health outcomes • Did not assess adverse outcomes • Small sample size (N=50) • Duration of followup for intermediate health outcomes (post-operative) • Conducted in UK
Westrich, 1996	Study Designation: Efficacy Study Composite Score: 3 of 7	1. Less stringent eligibility criteria 2. Assessed adverse outcomes 3. Used intention-to-treat analysis	Population, Outcomes	• Mean age not reported • Only patients undergoing TKR • Only primary surgery (100%) • Small sample size (N=122) • Did not report final health outcomes • Duration of followup for intermediate health outcomes (post-operative)

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Williams-Russo, 1996	Study Designation: Effectivenss Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Assessed final health outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes	• Only patients undergoing TKA • Only primary surgery • Did not assess adverse outcomes • Primary anesthetic for GA is not available in the US
Abdel-Salam, 1995	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Used intention-to-treat analysis 4. Adequate study duration with clinically relevant treatment	Population, Outcomes, Setting	• Only patients undergoing TKA • Only primary surgery • Did not assess final health outcomes • Did not assess adverse outcomes • Small sample size (N=80) • Conducted in England
Avikainen, 1995	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Used intention-to-treat analysis 4. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing THR • Primary or revision surgery not reported • Did not assess adverse outcomes • Duration of followup for final and intermediate health outcomes (post-operative) • Conducted in Finland
Colwell, 1995	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes	• Only patients undergoing TKR • Primary or revision surgery not reported • Duration of followup for final and intermediate health outcomes (post-operative)

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Warwick, 1995	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Less stringent eligibility criteria 2. Assessed final health outcomes 3. Used intention-to-treat analysis 4. Adequate sample size.	Population, Outcomes, Setting	• Gender not reported • Only patients undergoing THR • Conducted in United Kingdom • Duration of followup for final and intermediate health outcomes (postoperative) • Mean age not reported • Only primary surgery • Did not assess adverse outcomes
Colwell, 1994	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes	• Only patients undergoing THR • Mainly primary surgery (revision: 14%) • Duration of followup for final and intermediate health outcomes (post-operative or 42d)
Fauno, 1994	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Used intention-to-treat analysis 4. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing TKR • Only primary surgery • Did not assess adverse outcome • Duration of followup for final and intermediate health outcomes (post-operative) • Conducted in Finland and Denmark
Lieberman, 1994	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Adequate sample size 4. Used intention to treat analysis	Population, Outcomes	• Only primary surgery • Only patient undergoing THR • Duration of followup for mortality and intermediate outcomes (postoperative) • Did not assess adverse outcomes

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Menzin, 1994	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes	• Only patients undergoing THR • Primary or revision surgery not reported • Did not assess final health outcomes • Duration of followup for final and intermediate health outcomes (post-operative)
Santori, 1994	Study Designation: Efficacy Study Composite Score: 3 of 7	1. Less stringent eligibility criteria 2. Assessed final health outcomes 3. Used intention-to-treat analysis	Population, Outcomes, Setting	• High female to male ratio (F:74%; M:26%) • Only patients undergoing THR • Only primary surgery • Did not assess adverse outcomes • Small sample size (N=132) • Duration of followup for final and intermediate health outcomes (42d) • Conducted in Italy
Hull, 1993	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing THR and TKR • Duration of followup for final and intermediate health outcomes (post-operative or 90d) • Conducted in USA and Canada
Fordyce, 1992	Study Designation: Efficacy Study Composite Score: 3 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Adequate study duration with clinically relevant treatments 4. Assessed adverse outcomes	Population, Outcomes, Setting	• High female to male ratio (F:66%; M:34%) • Only patients undergoing THR • Small sample size (N=84) • Conducted in United Kingdom • Did not assess final health outcomes • Duration of followup for intermediate health outcomes (post-operative) • Only primary surgery • Did not use intention to treat analysis

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Francis, 1992	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Assessed final health outcomes 4. Assessed adverse outcomes 5. Adequate sample size	Population, Outcomes	• Only patients undergoing THR • Only primary surgery • Did not use intention-to-treat analysis • Duration of followup for final and intermediate health outcomes (post-operative)
Jorgensen, 1992	Study Designation: Efficacy Study Composite Score: 1 of 7	1. Assessed final health outcomes	Population, Outcomes, Setting	• High female to male ratio (F:76%, M:24%) • Only patients undergoing HFS • Small sample size (N=82) • Conducted in Denmark • Duration of followup for final and intermediate health outcomes (postoperative) • Did not assess adverse events • Primary or revision surgery not reported • Did not use intention to treat analysis
Wilson, 1992	Study Designation: Efficacy Study Composite Score: 2 of 7	1. Assessed final health outcomes 2. Used intention-to-treat analysis	Population, Outcomes, Setting	• High female to male ratio (F:75%, M:25%) • Only patients undergoing TKR • Small sample size (N=59) • Conducted in the United Kingdom • Duration of followup for final and intermediate health outcomes (postoperative) • Did not assess adverse events • Primary or revision surgery not reported
Bailey, 1991	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Assessed final health outcomes 4. Assessed adverse outcomes 5. Used intention-to-treat analysis	Population, Outcomes	• Only patients undergoing THR • Small sample size (N=95) • Duration of followup for final and intermediate health outcomes (post-operative)

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Eriksson, 1991	Study Designation: Efficacy Study Composite Score: 3 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes	Population, Outcomes, Setting	• Only patients undergoing THR • Primary or revision surgery not reported • Did not use intention-to-treat analysis • Small sample size (N=136) • Duration of followup for final and intermediate health outcomes (post-operative) • Conducted in Sweden
Jorgensen, 1991	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Assessed final health outcomes 4. Used intention-to-treat analysis	Population, Outcomes, Setting	• Only patients undergoing TKA • Primary or revision surgery not reported • Did not assess adverse outcomes • Small sample size (N=48) • Duration of followup for final and intermediate health outcomes (post-operartive) • Conducted in Denmark
Lassen, 1991	Study Designation: Efficacy Study Composite Score: 3 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Adequate sample size.	Population, Outcomes, Setting	• Only patients undergoing THR • Conducted in Denmark • Duration of followup for final and intermediate health outcomes (postoperative) • Only primary surgery • Did not use intention to treat analysis • Did not assess adverse outcomes
Levine, 1991	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing THR • Primary or revision surgery not reported • Duration of followup for final and intermediate health outcomes (post-operative) • Conducted in Canada

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Mitchell, 1991	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Used intention-to-treat analysis 4. Adequate sample size	Population, Outcomes	• Only patients undergoing TKA • Only primary surgery • Did not assess final health outcomes • Did not assess adverse outcomes • Small sample size (N=72) • Duration of followup for final and intermediate health outcomes (post-operartive) • Drug regimen used for epidermal anesthesia was NR, agents used for GA are not available/limited availability in the US
Planes, 1991	Study Designation: Efficacy Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing THR • Only primary surgery • Duration of followup for final and intermediate health outcomes (post-operartive) • Primary anesthetics used are not available in the US • Conducted in France
Torholm, 1991	Study Designation: Efficacy Study Composite Score: 2 of 7	1. Enrolled primary care population 2. Assessed final health outcomes	Population, Outcomes, Setting	• Only patients undergoing THR • Small sample size (N=120) • Conducted in Denmark • Duration of followup for final and intermediate health outcomes (postoperative) • Did not assess adverse events • Did not use intention to treat analysis
Woolson, 1991	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Assessed final health outcomes 4. Adequate sample size 5. Intention to treat analysis	Population, Outcomes	• Only patients undergoing THR • Duration of followup for intermediate and final health outcomes (postoperative) • Did not assess adverse outcomes

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Haas, 1990	Study Designation: Efficacy Study Composite Score: 3 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Used intention-to-treat analysis	Population, Outcomes	• Only patients undergoing TKR • Only primary surgery • Did not assess final health outcomes • Did not assess adverse outcomes • Small sample size (N=119) • Duration of followup for intermediate health outcomes (post-operative)
Sorensen, 1990	Study Designation: Efficacy Study Composite Score: 2 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Assessed final health outcomes	Population, Outcomes, Setting	• Only patients undergoing THR • Small sample size (N=70) • Conducted in Denmark • Mean age not reported • Duration of followup for final and intermediate health outcomes (postoperative) • Did not assess adverse outcomes events • Primary or revision surgery not reported • Did not use intention to treat analysis
Dechavanne, 1989	Study Designation: Efficacy Study Composite Score: 3of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Used intention-to-treat analysis	Population, Outcomes, Setting	• Only patients undergoing THR • Primary or revision surgery not reported • Did not assess final health outcomes • Did not assess adverse outcomes • Small sample size (N=124) • Duration of followup for intermediate health outcomes (post-operative) • Conducted in France

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Monreal, 1989	Study Designation: Efficacy Study Composite Score: 3 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Assessed final health outcomes	Population, Outcomes, Setting	• High female to male ratio (F:82%; M:18%) • Only patients undergoing HFS • Primary or revision surgery not reported • Did not assess adverse outcomes • Did not use intention-to-treat analysis • Small sample size (N=90) • Duration of followup for final and intermediate health outcomes (post-operative) • Conducted in Spain
Powers, 1989	Study Designation: Effectiveness Study Composite Score: 6 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size 6. Adequate study duration with clinically relevant treatment	Population, Outcomes, Setting	• High female to male ratio (F:72%, M:28%) • Only patients undergoing HFS • Conducted in Canada • Primary or revision surgery not reported • Duration of followup for final health outcomes (21-90d)
Planes, 1988	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing THR • Primary or revision surgery not reported • Duration of followup for final and intermediate health outcomes (post-operative) • Conducted in France
Barre, 1987	Study Designation: Efficacy Study Composite Score: 3 of 7	1. Enrolled primary care 2. Assessed final health outcomes 3. Used intention-to-treat analysis	Population, Outcomes, Setting	• Only patients undergoing THR • Primary or revision surgery not reported • Did not assess adverse outcomes • Small sample size (N=80) • Duration of followup for final and intermediate health outcomes (60d) • Conducted in France

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Paiement, 1987	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Less stringent eligibility criteria 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis 5. Adequate sample size	Population, Outcomes	• Age and gender not reported • Only patients undergoing THR • Primary or revision surgery not reported • Duration of followup for final and intermediate health outcomes (post-operative)
McKenzie, 1985	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Less stringent eligibility criteria 2. Assessed final health outcomes 3. Used intention-to-treat analysis 4. Adequate sample size	Population, Outcomes, Setting	• High female to male ratio (F:75%; M:25%) • Only patients undergoing HFS • Primary or revision surgery not reported • Did not assess adverse outcomes • Small sample size (N=48) • Duration of followup for final and intermediate health outcomes (post-operartive) • Primary anesthetics used are not available in the US • Conducted in UK
Alfaro, 1986	Study Designation: Efficacy Study Composite Score: 3 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Used intention-to-treat analysis	Population, Outcomes, Setting	• Only patients undergoing THR • Small sample size (N=90) • Conducted in Spain • Duration of followup for final and intermediate health outcomes (post-operative) • Did not assess adverse events • Primary or revision surgery not reported
Turpie, 1986	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Assessed adverse outcomes 4. Used intention-to-treat analysis	Population, Outcomes, Setting	• Only patients undergoing THR • Small sample size (N=100) • Conducted in Canada • Duration of followup for final and intermediate health outcomes (postoperatively) • Primary or revision surgery not reported

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Welin-Berger, 1982	Study Designation: Efficacy Study Composite Score: 2 of 7	1. Assessed final health outcomes 2. Used intention-to-treat analysis	Population, Outcomes, Setting	• High female to male ratio (F:72%, M:28%) • Only patients undergoing THR • Small sample size (N=40) • Conducted in Sweden • Duration of followup for final and intermediate health outcomes (postoperative) • Did not assess adverse events • Primary or revision surgery not reported
Modig, 1981	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled primary care population 2. Assessed final health outcomes 3. Used intention-to-treat analysis 4. Adequate sample size	Population, Outcomes, Setting	• Only patients undergoing THR • Primary or revision surgery not reported • Did not assess adverse outcomes • Small sample size (N=30) • Duration of followup for final and intermediate health outcomes (14d) • Primary anesthetic used for GA is not available in the US • Conducted in Sweden
McKenna, 1980	Study Designation: Efficacy Study Composite Score: 1 of 7	1. Assessed final health outcomes	Population, Outcomes, Setting	• High female to male ratio (F:90%, M:10%) • Only patients undergoing TKR • Small sample size (N=21) • Duration of followup for final and intermediate health outcomes (postoperative) • Did not assess adverse events • Primary or revision surgery not reported • Did not use intention to treat analysis

Abbreviations: d=days; F=female; HFS=hip fracture surgery; M=male; N=total population; THA=total hip arthroplasty; TKA=total knee arthrosplasty; TKR=total knee replacement; THR=total hip replacement;

Table 96. Evaluation of applicability for individual randomized controlled trials in nonmajor orthopedic surgery

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Lapidus, 2007	Study Designation: Effectiveness Study Composite Score: 5 of 7	4. Enrolled primary care population 5. Assessed final health outcomes 6. Assessed adverse outcomes 7. Used intention-to-treat analysis 8. Adequate study duration with clinically relevant treatment	Population, Outcomes, Setting	• Duration of followup for final health outcomes (45d) • Conducted in Sweden
Michot, 2002	Study Designation: Efficacy Study Composite Score: 5 of 7	5. Enrolled primary care population 6. Assessed final health outcomes 7. Assessed adverse outcomes 8. Used intention-to-treat analysis 9. Adequate study duration with clinically relevant treatment	Population, Outcomes, Setting	• Duration of followup for final health outcomes (30d) • Conducted in Switzerland

Abbreviations: d=days; F=female; M=male; N=total population

Table 97. Evaluation of applicability for individual observational studies evaluating ……

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Bozic, 2010	Study Designation: Effectiveness Study Composite Score: 5 of 7	5. Enrolled primary care population 6. Less stringent eligibility criteria 7. Assessed final health outcomes 8. Assessed adverse	Population, Outcomes	• Only patients undergoing TKR • Only primary surgery (100%) • Did not use intention-to-treat analysis • Duration of followup for final health outcome (30d)

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
		outcomes 9. Adequate sample size		
Cusick, 2009	Study Designation: Effectiveness Study Composite Score: 5 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Assessed final health outcomes 4. Adequate sample size 5. Adequate study duration with clinically relevant treatment	Population, Outcomes, Setting	• Only primary surgery (100%) • Gender not reported • Did not assess adverse outcomes • Did not use intention-to-treat analysis • Duration of followup for mortality (90d) • Conducted in Ireland
Froimson, 2009	Study Designation: Efficacy Study Composite Score: 4 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Assessed final health outcomes 4. Adequate sample size	Population, Outcomes	• Only primary surgery (100%) • Gender not reported • Did not assess adverse outcomes • Did not use intention-to-treat analysis • Duration of followup for final health outcomes (30d)
Gandhi, 2009	Study Designation: Efficacy Study Composite Score: 4 of 7	9. Enrolled primary care population 10. Less stringent eligibility criteria 11. Adequate study duration 12. Adequate sample size	Population, Outcomes, Setting	• Only primary surgery • Did not assess final health outcomes • Did not assess adverse outcomes • Conducted in Canada • Did not use intention- to-treat analysis
McNamara, 2009	Study Designation: Efficacy Study Composite Score: 4 of 7	10. Less stringent eligibility criteria 11. Adequate study duration 12. Assessed final health outcomes 13. Adequate sample size	Population, Outcomes, Setting	• High female to male ratio (F=78.5%: M=21.5%) • Did no report primary or secondary surgery • Did not assess adverse outcomes • Conducted in UK • Did not use intention-to- treat analysis

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Dorr, 2007	Study Designation: Effectiveness Study Composite Score: 5 of 7	5. Enrolled primary care population 6. Less stringent eligibility criteria 7. Adequate study duration 8. Assessed final health outcomes 9. Adequate sample size	Population, Outcomes	• Only primary surgery • Did not assess adverse outcomes • Did not use intention-to-treat analysis
Shorr, 2007	Study Designation: Efficacy Study Composite Score: 4 of 7	5. Enrolled primary care population 6. Assessed final health outcomes 7. Assessed adverse outcomes 8. Adequate sample size	Population, Outcomes	• Primary or secondary surgery not reported • Duration of followup for final health outcomes (in-hospital) • Did not use intention-to-treat analysis
Leirozovicz, 2004	Study Designation: Efficacy Study Composite Score: 3 of 7	6. Less stringent eligibility criteria 7. Assessed final health outcomes 8. Adequate sample size	Population, Outcomes, Setting	• Only primary surgery • Did not assess adverse outcomes • Duration of followup for final health outcomes (30d) • Conducted in Asia • Did not use intention-to-treat analysis
Sachs, 2003	Study Designation: Effectiveness Study Composite Score: 6 of 7	1. Enrolled primary care population 2. Less stringent eligibility criteria 3. Assessed final health outcomes 4. Assessed adverse outcomes 5. Adequate sample size 6. Adequate study duration with clinically relevant treatments	Population, Outcomes	• Only patients undergoing TKA • Only primary surgery (100%) • Duration of followup for mortality (90d) • Did not use intention-to-treat analysis

Author, Year	Effectiveness Study Designation and Composite Score	Effectiveness Study Criteria Met	Applicability Limitation Category	Specific Factors Limiting Applicability
Ryan, 1998	Study Designation: Efficacy Study Composite Score: 3 of 7	6. Enrolled primary care population 7. Assessed adverse outcomes 8. Adequate sample size	Population, Outcomes, Setting	• Did not report primary or secondary surgery • Did not assess final health outcomes • Duration of followup for intermediate and adverse health outcomes (postoperative) • Conducted in USA and Canada • Did not use intention-to-treat analysis
Lemos, 1991	Study Designation: Efficacy Study Composite Score: 2 of 7	4. Less stringent eligibility criteria 5. Assessed final health outcomes	Population, Outcomes, Setting	• Did not report male or female percentage • Did not report primary or secondary surgery • Did not assess adverse outcomes • Duration of followup for final health outcomes (postoperative) • Small sample size (240) • Did not use intention-to-treat analysis

Abbreviations: TKR=total knee replacement; THR=total hip replacement; TKA=total knee replacement

Table 98. Strength of applicability for the body of evidence evaluating the link between deep vein thrombosis and pulmonary embolism in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Relationship between deep vein thrombosis and pulmonary embolism in major orthopedic surgery	Moderate	There is insufficient evidence to determine the relationship between intermediate and final health outcomes in patients who had major orthopedic surgery. Overall applicability is limited because the majority of data is within knee replacement surgery (57.8%) and little is within hip fracture surgery (4.4%). However, the majority of data is derived from trials conducted in the United States and published in the 1990's.

Table 99. Strength of applicability for the body of evidence evaluating symptomatic venous thromboembolism in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Incidence of symptomatic venous thrombomebolism in total hip replacement	NA	No data
Incidence of symptomatic venous thrombomebolism in total knee replacement	NA	No data
Incidence of symptomatic venous thrombomebolism in hip fracture surgery	NA	No data
Impact of congestive heart failure	Moderate	Congestive heart failure significantly increases the odds of symptomatic objectively confirmed venous thromboembolism. Data is highly applicable to primary major orthopedic surgery although only one of the two studies was conducted in the United States which did not include hip fracture surgery.
Impact of inactive cancer	Moderate	Inactive cancer significantly increases the odds of symptomatic objectively confirmed venous thromboembolism. Data is highly applicable to hip or knee replacement surgery although not applicable to hip fracture surgery.
Impact of hormone replacement therapy	Moderate	Hormone replacement therapy significantly increases the odds of symptomatic objectively confirmed venous thrombembolism. Data is highly applicable to hip or knee replacement surgery although not applicable to hip fracture surgery.
Impact of age	Moderate	Age did not influence the odds of symptomatic objectively confirmed venous thrombembolism. Data is applicable to all three major orthopedic surgeries although the trial evaluating hip fracture surgery was conducted in the United Kingdom.
Impact of living at home	Low	Living at home significantly increases the odds of symptomatic objectively confirmed venous thrombembolism. Data is more applicable to females than males and is highly applicable to hip fracture surgery although the trial was conducted in the United Kingdom. Data is not applicable to knee or hip replacement surgery.
Impact of intertrochanteric fracture	Low	Intertrochanteric fractures significantly increases the odds of symptomatic objectively confirmed venous thrombembolism. Data is more applicable to females than males and is highly applicable to hip fracture surgery although the trial was conducted in the United Kingdom. Data is not applicable to knee or hip replacement surgery.

Comparison	Strength of applicability	Conclusion with description of applicability
Impact of subtrochanteric fracture	Low	Subtrochanteric fractures significantly increases the odds of symptomatic objectively confirmed venous thrombembolism. Data is more applicable to females than males and is highly applicable to hip fracture surgery although the trial was conducted in the United Kingdom. Data is not applicable to knee or hip replacement surgery.
Impact of elevated hemoglobin	Low	Elevated hemoglobin significantly increases the odds of symptomatic objectively confirmed venous thrombembolism. Data is more applicable to females than males and is highly applicable to hip fracture surgery although the trial was conducted in the United Kingdom. Data is not applicable to knee or hip replacement surgery.
Impact of gender	Low	Male gender did not influence the odds of symptomatic objectively confirmed venous thrombembolism. Data is more applicable to females than males and is highly applicable to hip fracture surgery although the trial was conducted in the United Kingdom. Data is not applicable to knee or hip replacement surgery.
Impact of history of venous thrombomebolism	Low	History of venous thrombomebolism significantly increases the odds of symptomatic objectively confirmed venous thrombembolism. Data is applicable to all major orthopedic surgeries although the trial was conducted in Asia an therefore overall applicability is limited.
Impact of varicose veins	Low	Varicose veins significantly increases the odds of symptomatic objectively confirmed venous thrombembolism. Data is applicable to all major orthopedic surgeries although the trial was conducted in Asia and therefore overall applicability is limited.
Pharmacologic prophylaxis versus no prophylaxis	NA	No data
Mechanical prophylaxis versus no prophylaxis	NA	No data
Oral antiplatelet agents versus oral vitamin K antagonists	NA	No data
Oral antiplatelet agents versus mechanical prophylaxis	NA	No data
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	Low	Compared with injectable unfractionated, patients who had major orthopedic surgery and received injectable low molecular weight heparin did not have a difference in the odds of symptomatic venous thromboembolism. Data is highly applicable to injectable low molecular weight heparin agents versus injectable unfractionated heparin in patients undergoing total hip replacement during the first 42 days after surgery. Applicability is limited because the type of surgery; primary or revision was not reported and because the one available trial was conducted in Turkey.
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	Moderate	Compared with injectable or oral factor Xa inhibitors, patients who had major orthopedic surgery and received low molecular weight heparin agents did not have a difference in the odds of symptomatic venous thromboembolism. Data is highly applicable to primary or revision total hip replacement surgery. Data has a low level of applicability to primary or revision surgery for total knee replacement or hip fracture surgery.
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	Moderate	Compared with received oral vitamin K antagonists, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of symptomatic venous thrombomebolism. Data is highly applicable to total knee or hip replacement surgery and is not applicable to primary or revision hip fracture surgery.
Injectable low molecular weight heparin agents versus mechanical prophylaxis	NA	No data
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data
Oral vitamin K antagonists versus mechanical prophylaxis	NA	No data
Enoxaparin versus other low molecular weight heparin agents	NA	No data
Intermittent pneumatic compression versus intermittent pneumatic compression devices	NA	No data
Intermittent pneumatic compression by Kendall versus the Venaflow intermittent pneumatic compression device	NA	No data
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	NA	No data
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	Low	Compared to 7 to 10 days of prophylaxis, patients who had major orthopedic surgery and received 28 days or more of prophylaxis had a decreased risk of symptomatic venous thromboembolism. Applicability is limited because the majority of trials were conducted outside of the United States. Data is highly applicable to primary hip replacement surgery with the use of injectable low molecular weight heparin agents. Data has a low level of applicability to the use of injectable factor Xa inhibitors, oral vitamin K antagonists, revision surgery, and total knee replacement surgery. Data is moderately applicable to hip fracture surgery.
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=Not applicable

Table 100. Strength of applicability for the body of evidence evaluating major venous thromboembolism in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Incidence of major venous thrombomebolism in total hip replacement	NA	No data
Incidence of major venous thrombomebolism in total knee replacement	NA	No data
Incidence of major venous thrombomebolism in hip fracture surgery	NA	No data
Pharmacologic prophylaxis versus no prophylaxis	Low	Compared with no prophylaxis, patients who had major orthopedic surgery and received pharmacologic prophylaxis had a decreased risk of major venous thromboembolism. Data is highly applicable to dabigatran, primary total knee replacement surgery but is not applicable to total hip replacement or hip fracture surgery. Applicability is limited due to the short duration of followup and because the only trial available was conducted in Japan.
Mechanical prophylaxis versus no prophylaxis	NA	No data
Oral antiplatelet agents versus oral vitamin K antagonists	NA	No data
Oral antiplatelet agents versus mechanical prophylaxis	NA	No data
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	NA	No data
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	NA	No data
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	Low	Compared with injectable or oral direct thrombin inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the risk of major venous thromboembolism. Data is moderately applicable to primary total hip replacement surgery. Data has low applicability to primary total knee replacement surgery. Data is not applicable to primary or revision surgery for hip fracture. Applicability is limited because all trials were conducted outside of the United States.
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	NA	No data
Injectable low molecular weight heparin agents versus mechanical prophylaxis	NA	No data
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Oral vitamin K antagonists versus mechanical prophylaxis	NA	No data
Enoxaparin versus other low molecular weight heparin agents	NA	No data
Intermittent pneumatic compression by Kendall versus the Venaflow intermittent pneumatic compression device	NA	No data
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus graduated compression	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	NA	No data
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	Low	Compared to 7 to 10 days of prophylaxis, patients who had major orthopedic surgery and received 28 days of prophylaxis did not have a difference in the odds of major venous thromboembolism. Applicability is limited because the trial was conducted in Italy. Data is highly applicable to the use of oral vitamin K antagonists and to primary total hip replacement. Data is not applicable to primary or revision total knee replacement or hip fracture surgery or other pharmacologic methods of prophylaxis.
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=Not applicable

Table 101. Strength of applicability for the body of evidence evaluating pulmonary embolism in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Incidence of pulmonary embolism in total hip replacement	Low	The pooled incidence of pulmonary embolism in patients who had total hip replacement surgery was 6 percent. Overall applicability is limited because all trials were conducted outside of the United States and four of the five trials were published in the 1980's.
Incidence of pulmonary embolism in total knee replacement	Low	The pooled incidence of pulmonary embolism in patients who had total knee replacement surgery was 1 percent. Overall applicability is limited because both trials were conducted outside of the United States.
Incidence of pulmonary embolism in hip fracture surgery	Low	Based on one trial, the incidence of pulmonary embolism was 3 percent in patients who had hip fracture surgery. Overall applicability is limited because this trial was conducted in Canada and published in 1989.
General versus regional anesthesia	Low	There is insufficient data to determine the impact of general versus regional anesthesia on the risk of pulmonary embolism. Data is not applicable to knee replacement or hip fracture surgery. Data is highly applicable to hip replacement surgery although both trials were conducted outside of the United States with anesthetics currently unavailable in the United States.

Comparison	Strength of applicability	Conclusion with description of applicability
Cemented versus noncemented arthroplasty	Low	There was insufficient data to determine the impact of cemented versus noncemented arthroplasty on the risk of pulmonary embolism. Data is highly applicable to primary hip replacement surgery although overall applicability is limited as this trial was conducted in Canada and had a short duration of followup. Data is not applicable to knee replacement or hip fracture surgery.
Maintained femoral blood flow versus standard procedure	NA	No data
Impact of age	Moderate	Age increases the odds of pulmonary embolism. Data is applicable to hip or knee replacement surgery although is not applicable to hip fracture surgery. Overall applicability is limited due to shorter duration n=of followup.
Impact of genitourinary infection	Moderate	Genitourinary infection increases the odds of pulmonary embolism. Data is applicable to hip or knee replacement surgery although is not applicable to hip fracture surgery. Overall applicability is limited due to shorter duration of followup.
Impact of cardiovascular disease	Moderate	Cardiovascular disease decreases the odds of pulmonary embolism. Data is applicable to hip or knee replacement surgery although is not applicable to hip fracture surgery. Overall applicability is limited due to shorter duration of followup.
Impact of phlebitis	Moderate	Phlebitis has no impact on the odds of pulmonary embolism. Data is applicable to hip or knee replacement surgery although is not applicable to hip fracture surgery. Overall applicability is limited due to shorter duration of followup.
Impact of thyroid hormone replacement therapy	Moderate	Thyroid hormone replacement therapy has no impact on the odds of pulmonary embolism. Data is applicable to hip or knee replacement surgery although is not applicable to hip fracture surgery. Overall applicability is limited due to shorter duration of followup.
Impact of a history of pulmonary embolism	Moderate	History of pulmonary embolism has no impact on the odds of pulmonary embolism. Data is applicable to hip or knee replacement surgery although is not applicable to hip fracture surgery. Overall applicability is limited due to shorter duration of followup.
Impact of varicosity	Moderate	Varicosity has no impact on the odds of pulmonary embolism. Data is applicable to hip or knee replacement surgery although is not applicable to hip fracture surgery. Overall applicability is limited due to shorter duration of followup.
Impact of phlebitis in the other extremity	Moderate	Phlebitis in the other extremity has no impact on the odds of pulmonary embolism. Data is applicable to hip or knee replacement surgery although is not applicable to hip fracture surgery. Overall applicability is limited due to shorter duration of followup.
Impact of peripheral vascular disease	Moderate	Peripheral vascular disease has no impact on the odds of pulmonary embolism. Data is applicable to hip or knee replacement surgery although is not applicable to hip fracture surgery. Overall applicability is limited due to shorter duration of followup.
Pharmacologic prophylaxis versus no prophylaxis	Low	Compared to no prophylaxis, patients who had major orthopedic surgery and received pharmacologic prophylaxis did not have a difference in the odds of pulmonary embolism. Data is highly applicable to total hip replacement. Applicability to total knee replacement and primary versus revisions surgery is limited. Data is not applicable to hip fracture surgery. Applicability is limited due to the short duration of follow up and because the majority of trials were conducted outside of the United States.
Mechanical prophylaxis versus no prophylaxis	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Oral antiplatelet agents versus oral vitamin K antagonists	Low	Compared with oral vitamin K antagonists, patients who had major orthopedic surgery and received oral antiplatelet agents did not have a difference in the odds of pulmonary embolism. Data is highly applicable to hip fracture surgery. Applicability Is limited because the type of surgery; primary or revision was not reported. Data is not applicable to primary or revision total hip or knee replacement surgery.
Oral antiplatelet agents versus mechanical prophylaxis	Low	Compared with mechanical prophylaxis, patients who had major orthopedic surgery and received oral antiplatelet agents did not have a difference in the odds of pulmonary embolism. Data is highly applicable to primary hip fracture surgery. Data is not applicable to primary or revision total hip or knee replacement surgery.
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	Low	Compared with injectable unfractionated heparin, patients who had major orthopedic surgery and received injectable low molecular weight heparin had a decreased in the odd of pulmonary embolism. Data is moderately applicable to total hip replacement surgery. Data has limited applicability to total knee and hip fracture surgery. Applicability Is limited because the type of surgery; primary or revision was not reported, there was a short duration of follow up and the majority of trials were conducted outside of the United States.
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	Low	Compared with injectable or oral factor Xa inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of pulmonary embolism. Data is highly applicable to revision surgery for total knee replacement. Data is not applicable to primary or revision total hip or hip fracture surgery.
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	Low	Compared with injectable or oral direct thrombin inhibitors, patients who had major orthopedic surgery and injectable low molecular weight heparin agents did not have a difference in the risk of pulmonary embolism. Data is moderately applicable to primary total hip replacement surgery. Data has low applicability to primary total knee replacement surgery. Applicability is limited because all of the trials were conducted outside of the United States. Data is not applicable to primary or revision surgery for hip fracture.
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	Moderate	Compared with oral vitamin K antagonists, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of pulmonary embolism. Applicability is limited due to the short duration of follow up. Data has high applicability to total hip replacement surgery and moderate applicability to total knee replacement surgery. Data is not applicable to hip fracture surgery.
Injectable low molecular weight heparin agents versus mechanical prophylaxis	Low	Compared with mechanical prophylaxis, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of pulmonary embolism. Data is highly applicable primary total hip replacement surgery. Data is not applicable to primary or revision total knee or hip fracture surgery and has limited applicability because the one available trial was conducted in the United Kingdom.
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	Low	Compared with injectable or oral direct thrombin inhibitors, patients who had major orthopedic surgery and received injectable unfractionated heparin did not have a difference in the odds of pulmonary embolism. Data is highly applicable to primary total hip replacement surgery. Data is not applicable to primary or revision total knee or hip fracture surgery and has limited applicability because the trials were conducted outside of the United States.
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data
Oral vitamin K antagonists versus mechanical prophylaxis	NA	No data
Enoxaparin versus other low molecular weight heparin agents	NA	No data
Intermittent pneumatic compression by Kendall versus Venaflow intermittent pneumatic compression devices	Low	Compared to intermittent pneumatic compression device by Kendall, patients who had major orthopedic surgery and received prophylaxis with the Venaflow intermittent pneumatic compression device did not have a difference in the odds of pulmonary embolism. Data is highly applicable to primary or revision total knee replacement surgery. Data is not applicable to primary or revision total hip replacement or hip fracture surgery.
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus graduated compression	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	Moderate	Compared with pharmacologic prophylaxis alone, patient who had major orthopedic surgery and received pharmacologic plus mechanical prophylaxis had no difference in the odds of pulmonary embolism. Data is highly applicable to total hip replacement surgery, moderately applicable to total knee replacement surgery and not applicable to hip fracture surgery or revision surgery.
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	Low	Compared with mechanical prophylaxis alone, patient who had major orthopedic surgery and received pharmacologic plus mechanical prophylaxis had no difference in the risk of pulmonary embolism. Applicability is limited due to the short duration of followup. Data is highly applicable to primary or revision total hip replacement surgery and not applicable to total knee replacement or hip fracture surgery.
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	Low	Compared to 7 to 10 days of prophylaxis, patients who had major orthopedic surgery and received 28 days or more of prophylaxis had a decrease in the odds of pulmonary embolism. Applicability is limited due to the short duration of follow up and because the trials were conducted outside of the United States. Data is moderately applicable to the used of injectable low molecular weight heparin agents and has a low level of applicability to the use of injectable factor Xa inhibitors and oral vitamin K antagonists. Data is highly applicable to primary or revision total hip replacement surgery. Data has a low level of applicability to hip fracture surgery and is not applicable to knee replacement surgery.
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=not applicable

Table 102. Strength of applicability for the body of evidence evaluating fatal pulmonary embolism in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Incidence of fatal pulmonary embolism in total hip replacement	Low	Based on one trial, the incidence of fatal pulmonary embolism was zero percent in patients who had total hip replacement surgery. Overall applicability is limited because this trial was conducted in Canada and published in 1986.
Incidence of fatal pulmonary embolism in total knee replacement	Low	Based on one trial the incidence of fatal pulmonary embolism was 0 percent. Overall applicability is limited because this trial was conducted in the United Kingdom.
Incidence of fatal pulmonary embolism in hip fracture surgery	Low	Based on one trial, the incidence of fatal pulmonary embolism was 0 percent in patients who had hip fracture surgery. Overall applicability is limited because this trial was conducted in Canada and published in 1989.
Tissue fibrin adhesive versus none	Low	Compared to surgery without tissue fibrin adhesive, patients who received tissue fibrin adhesive did not have a difference in the risk of fatal pulmonary embolism. Data is highly applicable to knee replacement surgery although is limited because the trial was conducted in Israel and had shorter duration of followup. Data is not applicable to other major orthopedic surgeries.
Pharmacologic prophylaxis versus no prophylaxis	Low	Compared to no prophylaxis, patients who had major orthopedic surgery and received pharmacologic prophylaxis did not have a difference in the odds of fatal pulmonary embolism. Data is applicable to total hip replacement but has limited applicability to total knee replacement and hip fracture surgery. Data has limited applicability to primary and revision surgery. Applicability is limited due to the short duration of follow up.
Mechanical prophylaxis versus no prophylaxis	NA	No data
Oral antiplatelet agents versus oral vitamin K antagonists	Low	Compared with oral vitamin K antagonists, patients who had major orthopedic surgery and received oral antiplatelet agents did not have a difference in the odds of fatal pulmonary embolism. Data is highly applicable to hip fracture surgery. Applicability Is limited because the type of surgery; primary or revision was not reported. Data is not applicable to primary or revision total hip or knee replacement surgery.
Oral antiplatelet agents versus mechanical prophylaxis	NA	No data
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	Low	Compared to injectable unfractionated heparin, patients who had major orthopedic surgery and received injectable low molecular weight heparin did not have a difference in the odds of fatal pulmonary embolism. Data is highly applicable to total knee replacement surgery. Applicability Is limited because the type of surgery; primary or revision was not reported and due to the short duration of follow up. Data is not applicable to total hip replacement or hip fracture surgery,
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	Low	Compared to injectable or oral factor Xa, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of fatal pulmonary embolism. Data is moderately applicable to primary or revision for total hip replacement surgery. Applicability is limited for primary or revision surgery in the total knee and hip fracture surgery population and because the majority of trials were conducted outside of the United States

Comparison	Strength of applicability	Conclusion with description of applicability
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	Low	Compared to injectable or oral direct thrombin, patients who had major orthopedic surgery and received inhibitors injectable low molecular weight heparin agents did not have a difference in the odds of fatal pulmonary embolism. Data is moderately applicable to primary or revision total knee and total hip replacement surgery. Data is not applicable to primary or revision hip fracture surgery and overall has limited applicability because the trials were conducted outside of the United States.
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	Low	Compared to oral vitamin K antagonists, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of fatal pulmonary embolism. Data is highly applicable to primary total hip replacement and is not applicable to other major orthopedic surgeries. Applicability is limited due to the short duration of follow up.
Injectable low molecular weight heparin agents versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of fatal pulmonary embolism. Data is highly applicable to primary total knee replacement surgery. Data is not applicable to primary or revision total hip replacement or hip fracture surgery and has limited applicability because the trials were conducted outside of the United States.
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data
Oral vitamin K antagonists versus mechanical prophylaxis	NA	No data
Enoxaparin versus other low molecular weight heparin agents	Low	Compared to other low molecular weight heparin agents, patients who had major orthopedic surgery and received enoxaparin did not have a difference in the odds of fatal pulmonary embolism. Applicability is limited due to the short duration of follow up and because the trials were conducted outside of the United States. Data is highly applicable to the use of tinzaparin in primary total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip fracture surgery.
Intermittent pneumatic compression by Kendall versus the Venaflow intermittent pneumatic compression device	NA	No data
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus graduated compression	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	NA	No data
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	Low	Compared to 7 to 10 days of prophylaxis, patients who had major orthopedic surgery and received 28 days or more of prophylaxis did not have a difference in the odds of fatal pulmonary embolism. Applicability is limited due to the short duration of follow up and because the trials were conducted outside of the United States. Data is highly applicable to the use of injectable factor Xa inhibitors during hip fracture surgery. Data is not applicable to primary or revision total hip or total knee replacement surgery.
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=not applicable

Table 103. Strength of applicability for the body of evidence evaluating nonfatal pulmonary embolism in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Incidence of nonfatal pulmonary embolism in total hip replacement	Low	Based on one trial, the incidence of nonfatal pulmonary embolism was 2 percent in patients who had total hip replacement surgery. Overall applicability is limited because this trial was conducted in Canada and published in 1986.
Incidence of nonfatal pulmonary embolism in total knee replacement surgery	Low	Based on one trial the incidence of nonfatal pulmonary embolism was 0 percent. Overall applicability is limited because this trial was conducted in the United Kingdom.
Incidence of fatal pulmonary embolism in hip fracture surgery	Low	Based on one trial, the incidence of nonfatal pulmonary embolism was 3 percent in patients who had hip fracture surgery. Overall applicability is limited because this trial was conducted in Canada and published in 1989.
Pharmacologic prophylaxis versus no prophylaxis	Low	Compared to no prophylaxis, patients who had major orthopedic surgery and received pharmacologic prophylaxis did not have a difference in the risk of nonfatal pulmonary embolism. Data is applicable to total hip replacement but has limited applicability to total knee replacement and hip fracture surgery. Data has limited applicability to primary and revision surgery. Applicability is limited due to the short duration of follow up and because the majority of trials were conducted outside of the United States.
Mechanical prophylaxis versus no prophylaxis	NA	No data
Oral antiplatelet agents versus oral vitamin K antagonists	Low	Compared to oral vitamin K antagonists, patients who had major orthopedic surgery and received oral antiplatelet agents did not have a difference in the percent of nonfatal pulmonary embolism. Data is moderately applicable to primary total hip and total knee replacement surgery. Data is not applicable to primary or revision hip fracture surgery.
Oral antiplatelet agents versus mechanical prophylaxis	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	Low	Compared with injectable unfractionated heparin, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of nonfatal pulmonary embolism. Applicability is limited due to the short duration of follow up. Data is moderately applicable to total hip replacement surgery. Applicability is limited because the type of surgery; primary or revision is not reported and because the majority of the trials were conducted outside of the United States. Applicability to total knee replacement and hip fracture surgery is limited.
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	Low	Compared to injectable or oral factor Xa inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of nonfatal pulmonary embolism. Data is moderately applicable to primary or revision for total hip replacement surgery. Applicability is limited for primary or revision surgery in the total knee and hip fracture surgery population.
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	Low	Compared to injectable or oral direct thrombin inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of nonfatal pulmonary embolism. Data is moderately applicable to primary or revision total knee and total hip replacement surgery. Data is not applicable to primary or revision hip fracture surgery and has limited applicability because the trials were conducted outside of the United States.
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	Low	Compared to oral vitamin K antagonists, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of nonfatal pulmonary embolism. Data is highly applicable to primary or revision total knee replacement surgery and is not applicable to other major orthopedic surgeries. Applicability was limited due to the short duration of follow up.
Injectable low molecular weight heparin agents versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who had major orthopedic surgery and received, injectable low molecular weight heparin agents did not have a difference in the odds of nonfatal pulmonary embolism. The data is highly applicable to primary total hip replacement surgery. The data is not applicable to primary or revision total knee or hip fracture surgery and has limited applicability because the trial was conducted in United Kingdom.
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	Low	Compared to injectable or oral direct thrombin inhibitors, patients who had major orthopedic surgery and received injectable unfractionated heparin did not have a difference in the odds of nonfatal pulmonary embolism. Applicability is limited by the short duration of follow up and because the trials were conducted outside of the United States. Data is highly applicable to primary total hip replacement surgery. Data is not applicable to primary or revision total knee or hip fracture surgery.
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data
Oral vitamin K antagonists versus mechanical prophylaxis	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Enoxaparin versus other low molecular weight heparin agents	Low	Compared to other low molecular weight heparin agents, patients who had major orthopedic surgery and received enoxaparin did not have a difference in the odds of nonfatal pulmonary embolism. Applicability is limited due to the short duration of follow up and because the trials wer conducted outside of the United States. Data is highly applicable to the use of tinzaparin in primary total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip fracture surgery.
Intermittent pneumatic compression by Kendall versus the Venaflow intermittent pneumatic compression device	Low	Compared to the intermittent pneumatic compression device by Kendall, patients who had major orthopedic surgery and received the Venaflow intermittent pneumatic compression device did not have a difference in the odds of nonfatal pulmonary embolism. Applicability is limited due to the short duration of follow up. Data is moderately applicable to primary or revision total hip replacement surgery. Data is moderately applicable to primary or revision total knee replacement surgery. Data is not applicable to primary or revision hip fracture surgery.
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	Moderate	Compared to the Flowtron device, patients who had major orthopedic surgery and received ActiveCare device did not have a difference in the odds of nonfatal pulmonary embolism. Data is highly applicable to total hip or knee replacement surgery but is not applicable to hip fracture surgery.
Intermittent pneumatic compression versus graduated compression	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	Moderate	Compared with pharmacologic prophylaxis alone, patient who had major orthopedic surgery and received pharmacologic plus mechanical prophylaxis had no difference in the odds of nonfatal pulmonary embolism. Data is highly applicable to total hip replacement surgery, moderately applicable to total knee replacement surgery and not applicable to hip fracture surgery or revision surgery.
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	Low	Compared to 7 to 10 days of prophylaxis, patients who had major orthopedic surgery and received 28 days or more of prophylaxis had decreased odds of nonfatal pulmonary embolism. Applicability is limited because the included trials were conducted outside of the United States. Data is moderately applicable to the use of injectable low molecular weight heparin agents during primary total hip replacement surgery. Data has a low level of applicability to oral vitamin K antagonists and injectable factor Xa inhibitors or to hip fracture surgery. Data is not applicable to knee replacement surgery.
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=not applicable

Table 104. Strength of applicability for the body of evidence evaluating post thrombotic syndrome in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Pharmacologic prophylaxis versus no prophylaxis	NA	No data
Mechanical prophylaxis versus no prophylaxis	NA	No data
Oral antiplatelet agents versus oral vitamin K antagonists	NA	No data
Oral antiplatelet agents versus mechanical prophylaxis	NA	No data
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	NA	No data
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	NA	No data
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	NA	No data
Injectable low molecular weight heparin agents versus mechanical prophylaxis	NA	No data
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data
Oral vitamin K antagonists versus mechanical prophylaxis	NA	No data
Enoxaparin versus other low molecular weight heparin agents	NA	No data
Intermittent pneumatic compression by Kendall versus the Venaflow intermittent pneumatic compression device	NA	No data
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus graduated compression	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	NA	No data
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	NA	No data
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=Not applicable

Table 105. Strength of applicability for the body of evidence evaluating mortality in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Pharmacologic prophylaxis versus no prophylaxis	Low	Compared to no prophylaxis, patients who had major orthopedic surgery and received pharmacologic prophylaxis did not have a difference in the odds of mortality. Data is highly applicable to hip replacement surgery, but has limited applicability to total knee replacement and hip fracture surgery. Data has limited applicability to primary and no applicability to revision surgery. Applicability is limited due to the short duration of follow up and because the majority of trials were conducted outside of the United States.
Mechanical prophylaxis versus no prophylaxis	NA	No data
Oral antiplatelet agents versus oral vitamin K antagonists	Low	Compared to oral vitamin K antagonists, patients who had major orthopedic surgery and received oral antiplatelet agents did not have a difference in the risk of mortality. Applicability is limited because the type of surgery; primary or revision was not reported. Data is highly applicable to the hip fracture surgery. Data is not applicable to primary or revision total hip or knee replacement surgery.
Oral antiplatelet agents versus mechanical prophylaxis	NA	No data
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	Low	Compared to injectable unfractionated heparin, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of mortality. Applicability is limited by the short duration of follow up and because the majority of trials were conducted outside of the United States. Applicability is limited because the type of surgery; primary or revision is not reported. Data is moderately applicable to total hip replacement and hip fracture surgery. Data is not applicable to total knee replacement surgery.
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	Low	Compared to injectable or oral factor Xa inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of mortality. Applicability is limited by the duration of follow up. Data has moderate applicability to primary or revision total hip replacement surgery. Data has a low level of applicability to primary hip fracture surgery and revision total knee replacement surgery.
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	Low	Compared to injectable or oral direct thrombin inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the risk of mortality. Applicability is limited by the duration of follow up and because the majority of trials were conducted outside of the United States. Data is moderately applicable to primary total knee or total hip replacement surgery. Data is not applicable to primary or revision hip fracture surgery.
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	Moderate	Compared to oral vitamin K antagonists, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of mortality. Applicability is limited due to the short duration of follow up. Data is highly applicable to primary or revision total knee and hip replacement surgery but not applicable to primary or revision hip fracture surgery.

Comparison	Strength of applicability	Conclusion with description of applicability
Injectable low molecular weight heparin agents versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of mortality. Applicability is limited due to the short duration of follow up and because the trials were conducted outside of the United States. Data is moderately applicable to primary total knee and hip replacement surgery. Data is not applicable to primary or revision hip fracture surgery.
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	Low	Compared to injectable or oral direct thrombin patients who had major orthopedic surgery and inhibitors injectable unfractionated heparin did not have a difference in the odds of mortality. Applicability is limited due to the short duration of follow up. Applicability is limited because the type of surgery; primary or revision is not reported and because the trials were conducted outside of the United States. Data is moderately applicable to total knee and hip replacement and hip fracture surgery.
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	Low	Compared to injectable unfractionated heparin patients who had major orthopedic surgery and received injectable or oral factor Xa inhibitors had a decreased rate of mortality. Applicability is limited due to the short duration of follow up. Data is highly applicable to primary total hip replacement surgery. Data is not applicable to primary or revision total knee or hip fracture surgery.
Injectable unfractionated heparin versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who had major orthopedic surgery and received injectable unfractionated heparin did not have a difference in the odds of mortality. Applicability is limited due to the short duration of follow up and because the trial was conducted in Italy. Data is highly applicable to primary total hip replacement surgery. Data is not applicable to revision or primary total knee replacement or hip fracture surgery.
Oral vitamin K antagonists versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who had major orthopedic surgery and received oral vitamin K antagonists did not have a difference in the odds of mortality. Applicability is limited due to the short duration of follow up. Data is highly applicable to primary total hip replacement surgery. Data is not applicable to revision or primary total knee replacement or hip fracture surgery.
Enoxaparin versus other low molecular weight heparin agents	Low	Compared to other low molecular weight heparin agents, patients who had major orthopedic surgery and received enoxaparin did not have a difference in the odds of mortality. Applicability is limited due to the short duration of follow up and because the trials were conducted outside of the United States. Data is highly applicable to the use of tinzaparin in primary total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip facture surgery.
Intermittent pneumatic compression by Kendall versus the Venaflow intermittent pneumatic compression device	Low	Compared to the intermittent pneumatic compression device by Kendall, patients who had major orthopedic surgery and received intermittent pneumatic compression device by Venaflow did not have a difference in the odds of mortality. Applicability is limited due to the short duration of follow up. Data is highly applicable to primary or revision total knee replacement surgery. Data is not applicable to primary or revision total hip replacement or hip fracture surgery.
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Intermittent pneumatic compression versus graduated compression	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	Low	Compared with pharmacologic prophylaxis alone, patient who had major orthopedic surgery and received pharmacologic plus mechanical prophylaxis do not have a difference in the odds of mortality. Data is highly applicable to patients who had primary total hip replacement surgery and received aspirin plus IPC versus aspirin alone. Data is not applicable to other major orthopedic or revision surgeries.
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	Low	Compared to 7 to 10 days of prophylaxis, patients who had major orthopedic surgery and received 28 days or more of prophylaxis did not have a difference in the odds of mortality. Applicability is limited due to the short duration of follow up and because the trials were conducted outside of the United States. Data is moderately applicable to the use of injectable low molecular weight heparin agents. Data has a low level of applicability to oral vitamin K antagonists and injectable factor Xa inhibitors. Data is highly applicable to primary total hip replacement surgery, moderately applicable to hip fracture surgery and has low applicability to hip fracture surgery.
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=Not applicable

Table 106. Strength of applicability for the body of evidence evaluating mortality due to bleeding in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Pharmacologic prophylaxis versus no prophylaxis	Low	Compared to no prophylaxis, patients who had major orthopedic surgery and received pharmacologic prophylaxis did not have a difference in the odds of mortality due to bleeding. Data is highly applicable to the use of enoxaparin in hip replacement surgery, but has limited applicability to total knee replacement and hip fracture surgery. Data has limited applicability to primary and no applicability to revision surgery. Applicability is limited due to the short duration of follow up and because the trial available was conducted in Denmark.
Mechanical prophylaxis versus no prophylaxis	NA	No data
Oral antiplatelet agents versus oral vitamin K antagonists	NA	No data.
Oral antiplatelet agents versus mechanical prophylaxis	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	Low	Compared to unfractionated heparin, patients who had major orthopedic surgery and injectable low molecular weight heparin agents did not have a difference in the odds of mortality due to bleeding. Applicability is limited due to the short duration of follow up and because the available trial was conducted in Spain. Data is highly applicable to primary hip fracture surgery. Data is not applicable to primary or revision total knee or hip replacement surgery.
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	Low	Compared to injectable or oral factor Xa inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents, did not had a difference in the odds of mortality due to bleeding. Applicability is limited due to the short duration of follow up. Data is highly applicable to primary hip fracture surgery. Data is not applicable to primary or revision total knee or hip replacement surgery.
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	Low	Compared to injectable or oral direct thrombin inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not had a difference in the risk of mortality due to bleeding. Applicability is limited due to the short duration of follow up and because the trial was conducted outside of the United States. Data is highly applicable to primary total knee replacement surgery. Data is not applicable to primary or revision hip fracture or total hip replacement surgery.
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	Low	Compared to oral vitamin K antagonists, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of mortality due to bleeding. Applicability is limited due to the short duration of follow up. Data is highly applicable to primary total knee replacement surgery. Data is not applicable to primary or revision hip fracture or total hip replacement surgery.
Injectable low molecular weight heparin agents versus mechanical prophylaxis	Low	Compared to oral vitamin K antagonists, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of mortality due to bleeding. Applicability is limited due to the short duration of follow up. Data is highly applicable to primary total hip replacement surgery. Data is not applicable to primary or revision hip fracture or total knee replacement surgery.
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data
Oral vitamin K antagonists versus mechanical prophylaxis	NA	No data
Enoxaparin versus other low molecular weight heparin agents	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Intermittent pneumatic compression by Kendall versus the Venaflow intermittent pneumatic compression device	NA	No data
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus graduated compression	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	NA	No data
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	NA	No data.
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=Not applicable

Table 107. Strength of applicability for the body of evidence evaluating health related quality of life in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Pharmacologic prophylaxis versus no prophylaxis	NA	No data
Mechanical prophylaxis versus no prophylaxis	NA	No data
Oral antiplatelet agents versus oral vitamin K antagonists	NA	No data
Oral antiplatelet agents versus mechanical prophylaxis	NA	No data
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	NA	No data
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	NA	No data
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	NA	No data
Injectable low molecular weight heparin agents versus mechanical prophylaxis	NA	No data
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data
Oral vitamin K antagonists versus mechanical prophylaxis	NA	No data
Enoxaparin versus other low molecular weight heparin agents	NA	No data
Intermittent pneumatic compression by Kendall versus the Venaflow intermittent pneumatic compression device	NA	No data
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus graduated compression	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	NA	No data
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=Not applicable

Table 108. Strength of applicability for the body of evidence evaluating deep vein thrombosis in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Incidence of deep vein thrombosis in patients who had total hip replacement surgery	Low	The pooled incidence of deep vein thrombosis in patients who had total hip replacement surgery was 39 percent. Overall applicability is limited because seven of the eight trials were conducted outside of the United States while the eight did not report location.
Incidence of deep vein thrombosis in patients who had total knee replacement surgery	Low	The pooled incidence of deep vein thrombosis in patients who had total knee replacement surgery was 46 percent. Overall applicability is limited because the majority of data is derived from the study conducted in Singapore while only a small percent (<10 percent) of data is derived from the study conducted in the United States. One trial was published in 2009 while the other in 1980.
Incidence of deep vein thrombosis in patients who had hip fracture surgery	Low	Based on one trial, the incidence of deep vein thrombosis was 47 percent in patients who had hip fracture surgery. Overall applicability is limited because the trial was conducted in Denmark and published in 1992.
Spinal versus epidural anesthesia	NA	No data
General versus regional anesthesia	Low	Patients who received general anesthesia may have a higher risk of deep vein thrombosis compared to those who received regional anesthesia in major orthopedic surgery. Overall applicability is limited as the majority of trials were conducted outside of the United States using anesthetics that are not available in the United States, additionally followup was generally shorter and primary versus revision surgery was usually not reported.
Cemented versus cementless arthroplasty	Low	Compared to patients who had cementless arthroplasty, those who had cemented arthroplasty had no difference in the risk of deep vein thrombosis. Data is highly applicable to hip replacement surgery although overall applicability is limited as the majority of studies were conducted outside of the United States and had a short duration of followup. Data is not applicable to knee replacement or hip fracture surgery.
Bone vacuum cement versus standard procedure	Low	Compared to standard procedure, patients who received bone vacuum cement had a lower risk of deep vein thrombosis. Data is highly applicable to primary total knee replacement surgery although overall applicability is limited as the trial was conducted in Germany and had a short duration of followup. Data is not applicable to hip replacement or hip fracture surgery.
Early versus late release of tourniquet	NA	No data
Limited time in flexion/dislocation versus standard procedure	Low	Compared to standard procedure, patients whose limb was in flexion and dislocation for a limited time did not have a difference in the risk of deep vein thrombosis. Data is highly applicable to primary hip replacement surgery although the duration of followup was short. Data is not applicable to other major orthopedic surgeries.

Comparison	Strength of applicability	Conclusion with description of applicability
Primary versus revision surgery	Low	Compared to revision surgery, primary surgery impacts the risk of deep vein thrombosis (although direction or magnitude is unknown). Data is highly applicable to hip replacement surgery and not applicable to other major orthopedic surgeries.
Impact of perioperative blood loss	Low	Perioperative blood loss does not impact the odds of deep vein thrombosis. Data is highly applicable to hip replacement surgery and not applicable to other major orthopedic surgeries.
Impact of blood transfusions	Low	Blood transfusion does not impact the odds of deep vein thrombosis. Data is highly applicable to hip replacement surgery and not applicable to other major orthopedic surgeries.
Impact of operative time	Low	Operative time does not impact the odds of deep vein thrombsis.
Impact of age	Low	Age increases the odds of deep vein thrombosis. Data is highly applicable to hip replacement surgery although most data is derived from trials conducted outside of the United States. Data is not applicable to knee replacement or hip fracture surgery.
Impact of obesity / weight	Low	There is insufficient data to determine the impact of obesity / weight on deep vein thrombosis. Data is highly applicable to hip replacement surgery although both studies were conducted outside of the United States. Data is not applicable to knee replacement or hip fracture surgery.
Impact of gender	Low	There is insufficient data to determine the impact of gender on deep vein thrombosis. Data is highly applicable to hip replacement surgery and is not applicable to knee replacement or hip fracture surgery.
Impact of smoking	Low	There is little to no effect of smoking on the odds of deep vein thrombosis (although magnitude and direction are unknown). Data is highly applicable to hip replacement surgery although the trial was conducted outside of the United States. Data is not applicable to knee replacement or hip fracture surgery.
Impact of height	Low	Height does not impact the odds of deep vein thrombosis. Data is highly applicable to hip replacement surgery and is not applicable to knee replacement or hip fracture surgery.
Impact of Factor V Leiden mutation	Moderate	Factor V Leiden mutation does not impact the odds of deep vein thrombosis. Data is applicable to hip or knee replacement surgery although not applicable to hip fracture surgery. Overall applicability is limited due to a shorter duration of followup.
Pharmacologic prophylaxis versus no prophylaxis	Low	Compared to no prophylaxis, patients who had major orthopedic surgery and received pharmacologic prophylaxis had a decrease in the risk of deep vein thrombosis. Data is highly applicable to primary hip replacement surgery, but has limited applicability to total knee replacement and hip fracture surgery. The data has no applicability to revision surgery. Applicability is limited due to the short duration of follow up and because the majority of trials were conducted outside of the United States.
Mechanical prophylaxis versus no prophylaxis	Low	Compared to no prophylaxis, patients who had major orthopedic surgery and received mechanical prophylaxis had a decrease in the risk of deep vein thrombosis. Data is highly applicable to patients receiving prophylaxis with venous foot pump undergoing primary total hip replacement but not applicable to total hip replacement or hip fracture surgery. Applicability is limited due to the short duration of follow up and because the one available trial was conducted in the United Kingdom.

Comparison	Strength of applicability	Conclusion with description of applicability
Oral antiplatelet agents versus oral vitamin K antagonists	Low	Compared to oral vitamin K antagonists patients who had major orthopedic surgery and received oral antiplatelet agents did not have a difference in the risk of deep vein thrombosis. Applicability is limited due to the short duration of follow up. Data is moderately applicable to primary or revision total hip and total knee replacement surgery. Data is not applicable to primary or revision hip fracture surgery.
Oral antiplatelet agents versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis patients who had major orthopedic surgery and received oral antiplatelet agents had an increased risk of deep vein thrombosis. Applicability is limited due to the short duration of follow up. Data is moderately applicable to primary total knee replacement and hip fracture surgery. Data is not applicable to primary or revision total hip replacement surgery.
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	Low	Compared to injectable unfractionated heparin, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents had a decreased risk of deep vein thrombosis. Applicability is limited due to the short duration of follow up and because the majority of trials were conducted outside of the United States. Applicability to primary or revision surgery is limited. Data is moderately applicable to total hip replacement surgery. Data has a low level of applicability to total knee and hip fracture surgery.
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	Low	Compared to injectable or oral factor Xa inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents had an increased risk of deep vein thrombosis. Data is highly applicable to primary hip fracture surgery. Data is not applicable to primary or revision total knee or hip replacement surgery.
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	Low	Compared to injectable or oral direct thrombin inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents had an increased risk of deep vein thrombosis. Data is highly applicable to primary total hip replacement. Data is not applicable to primary or revision total knee or hip fracture surgery and has limited applicability because the trial was conducted outside of the United States.
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	Moderate	Compared to oral vitamin K antagonists, patients who received injectable low molecular weight heparin agents had a decreased risk of deep vein thrombosis. Applicability is limited due to the short duration of follow up. Data has high applicability to primary or revision total hip or knee replacement surgery And is not applicable to primary or revision hip fracture surgery.
Injectable low molecular weight heparin agents versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who received injectable low molecular weight heparin agents did not have a difference in the risk of deep vein thrombosis. Applicability is limited due to the short duration of follow up and because all trials were conducted outside of the United States. Data is moderately applicable to primary total knee and total hip replacement surgery. Data is not applicable to primary or revision hip fracture surgery.
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	Low	Compared to injectable or oral direct thrombin inhibitors, patients who had major orthopedic surgery and received injectable unfractionated heparin had an increased risk of deep vein thrombosis. Data is highly applicable to primary total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip fracture surgery and has limited applicability because all trials were conducted outside of the United States.
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Injectable unfractionated heparin versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who had major orthopedic surgery and received injectable unfractionated heparin had an increased risk of deep vein thrombosis. Data is highly applicable to primary total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip fracture surgery and has limited applicability because the trial was conducted in Italy.
Oral vitamin K antagonists versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who had major orthopedic surgery and received oral vitamin K antagonists did not have a difference in the risk of deep vein thrombosis. Applicability is limited due to the short duration of follow up. Applicability is limited base on the type of surgery; primary or revision. Data is highly applicable to total hip replacement surgery. Data is not applicable to total knee replacement or hip fracture surgery.
Enoxaparin versus other low molecular weight heparin agents	Low	Compared to other low molecular weight heparin agents, patients who had major orthopedic surgery and received enoxaparin did not have a difference in the risk of deep vein thrombosis. Applicability is limited due to the short duration of follow up and because the trials wer conducted outside of the United States. Data has a low level of applicability to primary total hip replacement and hip fracture surgery. Data is not applicable to primary or revision total knee replacement surgery.
Intermittent pneumatic compression device by Kendall versus Venaflow intermittent pneumatic compression device	Low	Compared to the intermittent pneumatic compression device by Kendall, patients who had major orthopedic surgery and received intermittent pneumatic compression device by Venaflow had a decreased risk of deep vein thrombosis. Applicability is limited due to the short duration of follow up. Data is moderately applicable to primary or revision total hip replacement surgery. Data is moderately applicable to primary or revision total knee replacement surgery. Data is not applicable to primary or revision hip fracture surgery.
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	Moderate	Compared to the Flowtron device, patients who had major orthopedic surgery and received ActiveCare device did not have a difference in the percent of deep vein thrombosis. Data is highly applicable to total hip or knee replacement surgery but is not applicable to hip fracture surgery.
Intermittent pneumatic compression versus graduated compression	Low	Compared to graduated compression stockings, patient who had major orthopedic surgery and received intermittent pneumatic compression devices had a decreased risk of deep vein thrombosis. Data is highly applicable to the Venaflow intermittent pneumatic compression device and Comprinet Pro graduated compression stockings. Data is highly applicable to total hip or knee replacement surgery but is not applicable to hip fracture surgery. Overall applicability is limited because the trial was conducted outside of the United States.
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	Moderate	Compared with pharmacologic prophylaxis alone, patients who had major orthopedic surgery and received pharmacologic plus mechanical prophylaxis had a decreased risk of deep vein thrombosis. Data is highly applicable to primary total hip or total knee replacement surgery, has limited applicability to revision surgery and is not applicable to hip fracture surgery.
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	Moderate	Compared to 7 to 10 days of prophylaxis, patients who had major orthopedic surgery and received 28 days or more of prophylaxis had a decreased risk of deep vein thrombosis. Data is highly applicable to the use of injectable low molecular weight heparin agents although applicability is limited because the majority of trials were conducted outside of the United States. Data has a low level of applicability to oral vitamin K antagonists and injectable factor Xa inhibitors. Data is highly applicable to primary or revision total hip replacement surgery, moderately applicable ot hip fracture surgery and has low applicability to total knee replacement surgery.
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=Not applicable

Table 109. Strength of applicability for the body of evidence evaluating asymptomatic deep vein thrombosis in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Incidence of asymptomatic deep vein thrombosis in patients who had total hip replacement surgery	NA	No data
Incidence of asymptomatic deep vein thrombosis in patients who had total knee replacement surgery	NA	No data
Incidence of asymptomatic deep vein thrombosis in patients who had hip fracture surgery	NA	No data
General versus regional anesthesia	Low	There is insufficient data to determine the impact of general versus regional anesthesia on the risk of asymptomatic deep vein thrombosis in patients who had major orthopedic surgery. Data is not applicable to hip replacement surgery. Overall applicability is limited because both studies were conducted outside of the United States and one used anesthetics unavailable in the United States. Additionally primary versus revision surgery was not reported and duration of followup was short.
Tourniquet use versus none	Low	Compared to no use of a tourniquet, those who had surgery with a tourniquet did not have a difference in the risk of asymptomatic deep vein thrombosis. Data is highly applicable to knee replacement surgery although the trial was conducted in the United Kingdom and had a short duration of followup. Data is not applicable to other major orthopedic surgeries.
Pharmacologic prophylaxis versus no prophylaxis	Low	Compared to no prophylaxis, patients who had major orthopedic surgery and received pharmacologic prophylaxis had a decrease in the risk of asymptomatic deep vein thrombosis. Data is applicable to primary total hip replacement, has limited applicability to primary knee replacement and no applicability to hip fracture surgery. Applicability is limited due to the short duration of follow up and because all trials were conducted outside of the United States.
Mechanical prophylaxis versus no prophylaxis	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Oral antiplatelet agents versus oral vitamin K antagonists	NA	No data
Oral antiplatelet agents versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis patients who had major orthopedic surgery and received oral antiplatelet agents did not have a difference in the odds of asymptomatic deep vein thrombosis. Applicability is limited due to the short duration of follow up. Data is highly applicable to primary hip fracture surgery. Data is not applicable to primary or revision total hip or total knee replacement surgery.
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	Low	Compared to injectable unfractionated heparin, patients who had major orthopedic surgery and received injectable low molecular weight agents did not have a difference in the risk of asymptomatic deep vein thrombosis. Applicability is limited due to the short duration of follow up and because all trials were conducted outside of the United States. Data is highly applicable to total hip replacement surgery. Applicability is limited based on the type of surgery; primary or secondary. Data is not applicable to primary or revision total knee or hip replacement surgery.
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	NA	No data
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	Moderate	Compared to injectable or oral direct thrombin inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the risk of asymptomatic deep vein thrombosis. Data is moderately applicable to primary total knee and total hip replacement surgery. Data is not applicable to primary or revision hip fracture surgery and has limited applicability because the trials were conducted outside of the United States.
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	Low	Compared to oral vitamin K antagonists, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents had a decreased risk of asymptomatic deep vein thrombosis. Applicability is limited due to the short duration of follow up and because the type of surgery (primary versus revision) was not reported. Data is highly applicable to total knee replacement and not applicable to other major orthopedic surgeries.
Injectable low molecular weight heparin agents versus mechanical prophylaxis	Low	Compared to, mechanical prophylaxis patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of asymptomatic deep vein thrombosis. Applicability is limited due to the short duration of follow up and because this trial was conducted in the United Kingdom. Data is highly applicable to primary total hip replacement. Data is not applicable to primary or revision total knee or hip fracture surgery.
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Oral vitamin K antagonists versus mechanical prophylaxis	NA	No data
Enoxaparin versus other low molecular weight heparin agents	Low	Compared to other low molecular weight heparin agents, patients who had major orthopedic surgery and received enoxaparin did not have a difference in the risk of asymptomatic deep vein thrombosis. Applicability is limited due to the short duration of follow up and because the trials wer conducted outside of the United States. Data has a high applicability to the use of dalteparin in hip fracture surgery and is not applicable in other major orthopedic surgeries.
Intermittent pneumatic compression device by Kendall versus Venaflow intermittent pneumatic compression device	NA	No data
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus graduated compression	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	Low	Compared with pharmacologic prophylaxis alone, patients who had major orthopedic surgery and received pharmacologic plus mechanical prophylaxis did not have a difference in the risk of asymptomatic deep vein thrombosis. Data is highly applicable to patients who had primary total hip replacement and received a sequential pharmacologic therapy of unfractionated heparin for 3 days then aspirin plus the mechanical prophylaxis of venous foot pumps versus the pharmacologic prophylaxis alone. Data is not applicable to other major orthopedic surgeries.
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	Low	Compared to 7 to 10 days of prophylaxis, patients who had major orthopedic surgery and received 28 days or more of prophylaxis had a decreased risk of asymptomatic deep vein thrombosis. Data is highly applicable to the use of injectable low molecular weight heparin agents although overall applicability is limited because all trials were conducted outside of the United States. Data has a low level of applicability to oral vitamin K antagonists. Data is highly applicable to primary or revision total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip fracture surgery.
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=Not applicable

Table 110. Strength of applicability for the body of evidence evaluating symptomatic deep vein thrombosis in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Incidence of symptomatic deep vein thrombosis in patients who had total hip replacement surgery	NA	No data
Incidence of symptomatic deep vein thrombosis in patients who had total knee replacement surgery	NA	No data
Incidence of symptomatic deep vein thrombosis in patients who had hip fracture surgery	NA	No data
General versus regional anesthesia	Low	Compared to patients who received regional anesthesia, those who received general anesthesia did not have a difference in the risk of symptomatic deep vein thrombosis. Data is not applicable to hip replacement surgery. Overall applicability is limited because both studies were conducted outside of the United States and one used anesthetics unavailable in the United States. Additionally primary versus revision surgery was not reported and duration of followup was short.
Tourniquet use versus none	Low	Compared to those who had no tourniquet, patients who had surgery with a tourniquet did not have a difference in the risk of symptomatic deep vein thrombosis. Data is highly applicable to primary knee replacement surgery although the trial was conducted in England. Data is not applicable to other major orthopedic surgeries.
Maintained femoral blood flow versus standard procedure	Low	Compared to standard procedure, patients who had surgery to maintain femoral blood flow did not have a difference in the risk of symptomatic deep vein thrombosis. Overall applicability is limited as this intervention is only for experimentation purposes and the trial was conducted in hip replacement surgery therefore inapplicable to other major orthopedic surgeries.
Impact of metabolic syndrome	Low	Metabolic syndrome increases the odds of symptomatic deep vein thrombosis. Data is highly applicable to primary knee replacement surgery although not applicable to the other major orthopedic surgeries. Overall applicability is limited as this study was conducted in Canada.
Impact of age	Low	Age does not impact the odds of symptomatic deep vein thrombosis. Data is highly applicable to primary knee replacement surgery although not applicable to the other major orthopedic surgeries. Overall applicability is limited as this study was conducted in Canada.
Impact of education	Low	Education does not impact the odds of symptomatic deep vein thrombosis. Data is highly applicable to primary knee replacement surgery although not applicable to the other major orthopedic surgeries. Overall applicability is limited as this study was conducted in Canada.
Impact of diabetes	Low	Diabetes does not impact the odds of symptomatic deep vein thrombosis. Data is highly applicable to primary knee replacement surgery although not applicable to the other major orthopedic surgeries. Overall applicability is limited as this study was conducted in Canada.

Comparison	Strength of applicability	Conclusion with description of applicability
Impact of hypertension	Low	Hypertension does not impact the odds of symptomatic deep vein thrombosis. Data is highly applicable to primary knee replacement surgery although not applicable to the other major orthopedic surgeries. Overall applicability is limited as this study was conducted in Canada.
Impact of hypercholesterolemia	Low	Hypercholesterolemia does not impact the odds of symptomatic deep vein thrombosis. Data is highly applicable to primary knee replacement surgery although not applicable to the other major orthopedic surgeries. Overall applicability is limited as this study was conducted in Canada.
Impact of body mass index	Low	Body mass index does not impact the odds of symptomatic deep vein thrombosis. Data is highly applicable to primary knee replacement surgery although not applicable to the other major orthopedic surgeries. Overall applicability is limited as this study was conducted in Canada.
Impact of comorbidities	Low	Presence of comorbidities does not impact the odds of symptomatic deep vein thrombosis. Data is highly applicable to primary knee replacement surgery although not applicable to the other major orthopedic surgeries. Overall applicability is limited as this study was conducted in Canada.
Pharmacologic prophylaxis versus no prophylaxis	Low	Compared to no prophylaxis, patients who had major orthopedic surgery and received pharmacologic prophylaxis did not have a difference in the risk of symptomatic deep vein thrombosis. Data is applicable to primary total hip replacement, has limited applicability to primary knee replacement and no applicability to hip fracture surgery. Applicability is limited due to the short duration of follow up and because all trials were conducted outside of the United States.
Mechanical prophylaxis versus no prophylaxis	NA	No data
Oral antiplatelet agents versus oral vitamin K antagonists	NA	No data
Oral antiplatelet agents versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who had major orthopedic surgery and received oral antiplatelet agents did not have a difference in the odds of symptomatic deep vein thrombosis. Applicability is limited due to the short duration of follow up. Data is highly applicable to primary hip fracture surgery. Data is not applicable to primary or revision total hip or total knee replacement surgery.
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	Low	Compared to injectable unfractionated heparin, patients who had major orthopedic surgery and received injectable low molecular weight agents did not have a difference in the odds of symptomatic deep vein thrombosis. Applicability is limited due to the short duration of follow up and because the trials were conducted outside of the United States. Data is highly applicable to total hip replacement surgery. Data is moderately applicable to primary total knee replacement surgery. Applicability is limited based on the type of surgery; primary or secondary. Data is not applicable to primary or revision hip replacement surgery.

Comparison	Strength of applicability	Conclusion with description of applicability
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	Moderate	Compared to injectable or oral factor Xa inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of symptomatic deep vein thrombosis. Data is moderately applicable to primary or revision total hip replacement surgery. Data is moderately applicable to revision total knee replacement surgery. Data has a low level of applicability to primary hip fracture surgery and overall is limited because the majority of trials were conducted outside of the United States.
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	Low	Compared to injectable or oral direct thrombin inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the risk of symptomatic deep vein thrombosis. Overall applicability is limited because the majority of trials were conducted outside of the United States. Data is moderately applicable to primary total knee replacement surgery. Data has a low level of applicability to primary total hip replacement surgery. Data is not applicable to revision total knee, total hip or hip fracture surgery.
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	Low	Compared to oral vitamin K antagonists, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of symptomatic deep vein thrombosis. Applicability is limited due to the short duration of follow up. Data is highly applicable to primary or revision total hip replacement surgery and moderate applicable to total knee replacement surgery. Data is not applicable to primary or revision hip fracture surgery.
Injectable low molecular weight heparin agents versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of symptomatic deep vein thrombosis. Data is highly applicable to primary total hip replacement surgery. Data is not applicable to primary or revision total knee or hip fracture surgery and has limited applicability because the trials were conducted outside of the United States.
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	NA	No data.
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data
Oral vitamin K antagonists versus mechanical prophylaxis	NA	No data
Enoxaparin versus other low molecular weight heparin agents	Low	Compared to other low molecular weight heparin agents, patients who had major orthopedic surgery and received enoxaparin did not have a difference in the odds of symptomatic deep vein thrombosis. Applicability is limited due to the short duration of follow up and because the trials wer conducted outside of the United States. Data is highly applicable to the use of tinzaparin in primary total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip fracture surgery.

Comparison	Strength of applicability	Conclusion with description of applicability
Intermittent pneumatic compression device by Kendall versus Venaflow intermittent pneumatic compression device	NA	No data
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus graduated compression	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	Low	Compared with pharmacologic prophylaxis alone, patients who had major orthopedic surgery and received pharmacologic plus mechanical prophylaxis did not have a difference in the risk of symptomatic deep vein thrombosis. Data is highly applicable to patients who had primary total hip replacement and received a sequential pharmacologic therapy of unfractionated heparin for 3 days then aspirin plus the mechanical prophylaxis of venous foot pumps versus the pharmacologic prophylaxis alone. Data is not applicable to other major orthopedic surgeries.
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	Moderate	Compared to 7 to 10 days of prophylaxis, patients who had major orthopedic surgery and received 28 days or more of prophylaxis had a decreased risk of symptomatic deep vein thrombosis. Data is moderately applicable to the use of injectable low molecular weight heparin agents. Data has a low level of applicability to oral vitamin K antagonists and injectable factor Xa inhibitors. Data is highly applicable to primary or revision total hip replacement surgery, has moderate applicability to hip fracture surgery and is not applicable to primary or revision total knee replacement. Overall applicability is limited because all trials were conducted outside of the United States.
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=Not applicable

Table 111. Strength of applicability for the body of evidence evaluating proximal deep vein thrombosis in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Incidence of proximal deep vein thrombosis in patients who had total hip replacement surgery	Low	The pooled incidence of proximal deep vein thrombosis was 32 percent in patients who had total hip replacement surgery. Overall applicability is limited because all trials were conducted outside of the United States.
Incidence of proximal deep vein thrombosis in patients who had total knee replacement surgery	Low	The pooled incidence of proximal deep vein thrombosis in patients who had total knee replacement surgery was 17 percent. Overall applicability is limited because the majority of data is derived from the study conducted in Singapore while only a small percent (<10 percent) of data is derived from the study conducted in the United States. One trial was published in 2009 while the other in 1980.
Incidence of proximal deep vein thrombosis in patients who had hip fracture surgery	NA	No data
General versus regional anesthesia	Low	Compared to patients who received regional anesthesia, those who received general anesthesia have no difference in the risk of proximal deep vein thrombosis. Data is not applicable to hip fracture surgery. Although trials were conducted in the United States, the majority overall used anesthetics unavailable in the United States, and had a short duration of followup.
Cemented versus cementless arthroplasty	Low	Compared to patients who had cementless arthroplasty, those who had cemented arthroplasty had no difference in the risk of proximal deep vein thrombosis. Data is highly applicable to hip replacement surgery although overall applicability is limited as both trials were conducted outside of the United States and had a short duration of followup. Data is not applicable to knee replacement or hip fracture surgery.
Bone vacuum cement versus standard procedure	Low	Compared to standard procedure, patients who received bone vacuum cement had a lower risk of proximal deep vein thrombosis. Data is highly applicable to primary total knee replacement surgery although overall applicability is limited as the trial was conducted in Germany and had a short duration of followup. Data is not applicable to hip replacement or hip fracture surgery.
Tourniquet use versus none	Low	Compared to those who had no tourniquet, patients who had surgery with a tourniquet did not have a difference in the risk of proximal deep vein thrombosis. Data is highly applicable to primary knee replacement surgery although the trial was conducted in England. Data is not applicable to other major orthopedic surgeries.
Limited time in flexion/dislocation versus standard procedure	Low	Compared to standard procedure, patients whose limb was in flexion and dislocation for a limited time did not have a difference in the risk of proximal deep vein thrombosis. Data is highly applicable to primary hip replacement surgery although the duration of followup was short. Data is not applicable to other major orthopedic surgeries.
Impact of congestive heart failure	Moderate	Congestive heart failure significantly increases the odds of proximal deep vein thrombosis. Data is highly applicable to hip or knee replacement surgery although not applicable to hip fracture surgery.
Impact of age	Moderate	Insufficient data is available to determine the impact of age on the odds of proximal deep vein thrombosis. Data is highly applicable to hip or knee replacement surgery although not applicable to hip fracture surgery.
Impact of prior deep vein thrombosis	Moderate	Prior deep vein thrombosis has no impact on the odds of proximal deep vein thrombosis. Data is highly applicable to hip or knee replacement surgery although not applicable to hip fracture surgery.

Comparison	Strength of applicability	Conclusion with description of applicability
Impact of inactive malignancy	Moderate	Inactive malignancy has no impact on the odds of proximal deep vein thrombosis. Data is highly applicable to hip or knee replacement surgery although not applicable to hip fracture surgery.
Impact of current hormone replacement therapy	Moderate	Current hormone replacement therapy has no impact on the odds of proximal deep vein thrombosis. Data is highly applicable to hip or knee replacement surgery although not applicable to hip fracture surgery.
Impact of chronic tobacco use	Moderate	Chronic tobacco use has no impact on the odds of proximal deep vein thrombosis. Data is highly applicable to hip or knee replacement surgery although not applicable to hip fracture surgery.
Impact of blood disorders	Moderate	Presence of blood disorders has no impact on the odds of proximal deep vein thrombosis. Data is highly applicable to hip or knee replacement surgery although not applicable to hip fracture surgery.
Pharmacologic prophylaxis versus no prophylaxis	Low	Compared to no prophylaxis, patients who had major orthopedic surgery and received pharmacologic prophylaxis had a decrease in the risk of proximal deep vein thrombosis. Data is highly applicable to primary hip replacement surgery, moderately applicable to knee replacement surgery and not applicable to hip facture surgery. Data is not applicable to revision surgery. Applicability is limited due to the short duration of follow up and because all trials were conducted outside of the United States.
Mechanical prophylaxis versus no prophylaxis	Low	Compared to no prophylaxis, patients who had major orthopedic surgery and received mechanical prophylaxis did not have a difference in the risk of proximal deep vein thrombosis. Data is highly applicable to patients receiving prophylaxis with venous foot pump undergoing primary total hip replacement but not applicable to total hip replacement or hip fracture surgery. Applicability is limited due to the short duration of follow up and because the one available trial was conducted outside of the United States.
Oral antiplatelet agents versus oral vitamin K antagonists	Low	Compared to oral vitamin K antagonists, patients who had major orthopedic surgery and received oral antiplatelet agents did not have a difference in the risk of proximal deep vein thrombosis. Applicability is limited due to the short duration of follow up. Data is moderately applicable to primary or revision total knee or total hip replacement surgery. Data is not applicable to primary or revision hip fracture surgery.
Oral antiplatelet agents versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who had major orthopedic surgery and received oral antiplatelet agents did not have a difference in the odds of proximal deep vein thrombosis. Applicability is limited due to the short duration of follow up. Applicability is limited because data is only available for bilateral total knee replacement. Data has a low level of applicability to bilateral total knee replacement. Data is not applicable to primary or revision total hip replacement or hip fracture surgery.
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	Low	Compared to injectable unfractionated heparin, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents had a decreased risk of proximal deep vein thrombosis. Applicability is limited due to the short duration of follow up and because the majority of trials were conducted outside of the United States. Applicability is limited based on the type of surgery; primary or revision. Data is moderately applicable to total hip replacement surgery. Data has a low level of applicability to total knee and hip fracture surgery.

Comparison	Strength of applicability	Conclusion with description of applicability
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	Low	Compared to injectable or oral factor Xa inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents had an increase in the odds of proximal deep vein thrombosis. Applicability is limited by the duration of follow up. Data has moderate applicability to primary or revision total hip replacement surgery. Data has a low level of applicability to primary hip fracture surgery and revision total knee replacement surgery.
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	Moderate	Compared to injectable or oral direct thrombin, patients who had major orthopedic surgery and received inhibitors injectable low molecular weight heparin agents did not have a difference in the risk of proximal deep vein thrombosis. Applicability is limited by the duration of follow up. Data is moderately applicable to primary total knee or total hip replacement surgery. Data is not applicable to primary or revision hip fracture surgery.
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	Moderate	Compared to oral vitamin K antagonists, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the risk of proximal deep vein thrombosis. Applicability is limited by the short duration of follow up. Data is highly applicable to primary and revision total hip and total knee or hip replacement surgery and is not applicable to primary or revision hip fracture surgery.
Injectable low molecular weight heparin agents versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the risk of proximal deep vein thrombosis. Data is moderately applicable to primary total hip replacement surgery. Data has a low level of applicability to primary total knee replacement surgery. Data is not applicable to primary or revision hip fracture surgery and is limited overall because the trials were conducted outside of the United States.
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	Low	Compared to injectable or oral direct thrombin inhibitors, patients who had major orthopedic surgery and received injectable unfractionated heparin agents had an increase in the odds of proximal deep vein thrombosis. Data is moderately applicable to primary total hip and total knee replacement surgery. Data is not applicable to primary or revision hip fracture surgery and is limited overall because the trials were conducted outside of the United States.
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data
Oral vitamin K antagonists versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who had major orthopedic surgery and received oral vitamin K antagonists had a decrease in the risk of proximal deep vein thrombosis. Applicability is limited due to the short duration of follow up. Data is highly applicable to primary or revision total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip fracture surgery.
Enoxaparin versus other low molecular weight heparin agents	Low	Compared to other low molecular weight heparin agents, patients who had major orthopedic surgery and received enoxaparin did not have a difference in the risk of proximal deep vein thrombosis. Data has a low level of applicability to primary total hip replacement surgery and primary hip fracture surgery. Data is not applicable to primary or revision total knee replacement surgery. Applicability is limited because the trials were conducted outside of the United States

Comparison	Strength of applicability	Conclusion with description of applicability
Intermittent pneumatic compression device by Kendall versus Venaflow intermittent pneumatic compression device	Low	Compared to prophylaxis with the Venaflow intermittent pneumatic compression device, patients who had major orthopedic surgery and received the device by Kendall had no difference in the odds of proximal deep vein thrombosis. Data is moderately applicable to primary or revision total hip replacement surgery. Data is moderately applicable to primary or revision total knee replacement surgery. Data is not applicable to primary or revision hip fracture surgery.
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus graduated compression	Moderate	Compared to prophylaxis with intermittent pneumatic compression devices, patients who had major orthopedic surgery and received prophylaxis with graduated compression stockings did not have a difference in the odds of proximal deep vein thrombosis. Data is moderately applicable to primary and revision total knee and total hip replacement surgery. Data is not applicable to primary or revision hip fracture surgery.
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	Moderate	Compared with pharmacologic prophylaxis alone, patients who had major orthopedic surgery and received pharmacologic plus mechanical prophylaxis did not have a difference in the risk of proximal deep vein thrombosis. Applicability is limited due to the short duration of followup. Data is highly applicable to both primary total hip and knee replacement surgery although not applicable to hip fracture surgery or revision surgery.
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	Low	Compared with pharmacologic prophylaxis alone, the hips of patients which underwent replacement surgery and received pharmacologic plus mechanical prophylaxis did not have a difference in the risk of proximal deep vein thrombosis. Applicability is limited because only one trial was available. Applicability is high for primary or revision total hip replacement surgery although not applicable to other major orthopedic surgeries.
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	Moderate	Compared to 7 to 10 days of prophylaxis, patients who had major orthopedic surgery and received 28 days or more of prophylaxis had a decreased risk of proximal deep vein thrombosis. Data is highly applicable to primary hip replacement surgery with the use of injectable low molecular weight heparin agents. Data has a low level of applicability to oral vitamin K antagonists and injectable factor Xa inhibitors. Data has a moderate level of applicability to hip fracture surgery and a low level of applicability to total knee replacement surgery. Overall applicability is limited because the majority of trials were conducted outside of the United States.
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=not applicable

Table 112. Strength of applicability for the body of evidence evaluating distal deep vein thrombosis in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Incidence of distal deep vein thrombosis in patients who had total hip replacement surgery	Low	The pooled incidence of distal deep vein thrombosis in patients who had total hip replacement surgery was 30 percent. Overall applicability is limited because both trials were conducted outside of the United States and one was published in 2009 while the other in 1980.
Incidence of distal deep vein thrombosis in patients who had total knee replacement surgery	Low	The pooled incidence of distal deep vein thrombosis in patients who had total knee replacement surgery was 22 percent. Overall applicability is limited because the majority of data is derived from the study conducted in Singapore while only a small percent (<10 percent) of data is derived from the study conducted in the United States. One trial was published in 2009 while the other in 1980.
Incidence of distal deep vein thrombosis in patients who had hip fracture surgery	NA	No data
General versus regional anesthesia	Low	There was insufficient evidence to determine the impact of general versus regional anesthesia on the risk of distal deep vein thrombosis. Data is not applicable to hip fracture surgery. Overall applicability is limited because the majority of data is derived from trials conducted outside of the United States using agents that are currently not available in the United States.
Cemented versus cementless arthroplasty	Low	Compared to patients who had cementless arthroplasty, those who had cemented arthroplasty had no difference in the risk of distal deep vein thrombosis. Data is highly applicable to hip replacement surgery although overall applicability is limited as both trials were conducted outside of the United States and had a short duration of followup. Data is not applicable to knee replacement or hip fracture surgery.
Bone vacuum cement versus standard procedure	Low	Compared to standard procedure, patients who received bone vacuum cement did not have a difference in the risk of distal deep vein thrombosis. Data is highly applicable to primary total knee replacement surgery although overall applicability is limited as the trial was conducted in Germany and had a short duration of followup. Data is not applicable to hip replacement or hip fracture surgery.
Tourniquet use versus none	NA	No data
Pharmacologic prophylaxis versus no prophylaxis	Low	Compared to no prophylaxis, patients who had major orthopedic surgery and received pharmacologic prophylaxis had a decrease in the risk of distal deep vein thrombosis. Data is highly applicable to primary total hip replacement, moderately applicable to total knee replacement and not applicable to hip fracture surgery. Applicability is limited by the short duration of follow up and because all of the trials were conducted outside of the United States.
Mechanical prophylaxis versus no prophylaxis	Low	Compared to no prophylaxis, patients who had major orthopedic surgery and received mechanical prophylaxis had no difference in the risk of distal deep vein thrombosis. Data is highly applicable to patients receiving prophylaxis with venous foot pump undergoing primary total hip replacement but not applicable to total hip replacement or hip fracture surgery. Applicability is limited due to the short duration of follow up and because the one available trial was conducted outside of the United States.
Oral antiplatelet agents versus oral vitamin K antagonists	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Oral antiplatelet agents versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who had major orthopedic surgery and received oral antiplatelet agents had an increase in the risk of distal deep vein thrombosis. Applicability is limited due to the short duration of follow up. Applicability is limited because data is only available for bilateral total knee replacement. Data has a low level of applicability to bilateral total knee replacement. Data is not applicable to primary or revision total hip replacement or hip fracture surgery.
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	Low	Compared to injectable unfractionated heparin, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the risk of distal deep vein thrombosis. Applicability is limited due to the short duration of follow up and because the majority of trials were conducted outside of the United States. Applicability is limited based on the type of surgery; primary or revision. Data is moderately applicable to total hip replacement surgery. Data has a low level of applicability to total knee and hip fracture surgery.
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	Low	Compared to injectable or oral factor Xa inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents had an increased risk of distal deep vein thrombosis. Applicability is limited by the duration of follow up. Data has moderate applicability to primary or revision total hip replacement surgery. Data has a low level of applicability to primary hip fracture surgery and revision total knee replacement surgery.
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	Low	Compared to injectable or oral direct thrombin inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents had a decreased risk of distal deep vein thrombosis. Data is highly applicable to primary total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip fracture surgery.
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	Low	Compared to oral vitamin K antagonists, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents had a decreased risk of distal deep vein thrombosis. Applicability is limited due to the short duration of follow up. Data is highly applicable to primary total hip or knee replacement surgery although is not applicable to revision surgery or hip fracture surgery.
Injectable low molecular weight heparin agents versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the risk of distal deep vein thrombosis. Data is moderately applicable to primary total hip replacement surgery. Data has a low level of applicability to primary total knee replacement surgery. Data is not applicable to primary or revision hip fracture surgery and overall is limited because the trials were conducted outside of the United States.
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Oral vitamin K antagonists versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who had major orthopedic surgery and received oral vitamin K antagonists did not have a difference in the odds of distal deep vein thrombosis. Applicability is limited due to the short duration of follow up. Applicability is limited because the type of surgery; primary or revision was not reported. Data is moderately applicable to total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip fracture surgery.
Enoxaparin versus other low molecular weight heparin agents	Low	Compared to other low molecular weight heparin agents, patients who had major orthopedic surgery and received enoxaparin did not have a difference in the odds of distal deep vein thrombosis. Applicability is limited due to the short duration of follow up and because the trials were conducted outside of the United States. Data is highly applicable to the use of tinzaparin in primary total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip fracture surgery.
Intermittent pneumatic compression device by Kendal versus the Venaflow intermittent pneumatic compression device	Low	Compared to prophylaxis with the intermittent pneumatic compression device by Kendal, patients who had major orthopedic surgery and received the Venaflow device had a decreased risk of distal deep vein thrombosis. Data is moderately applicable to primary or revision total hip replacement surgery. Data is moderately applicable to primary or revision total knee replacement surgery. Data is not applicable to primary or revision hip fracture surgery.
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus graduated compression	Moderate	Compared to graduated compression stockings, patient who had major orthopedic surgery and received intermittent pneumatic compression devices had a decreased risk of distal deep vein thrombosis. Data is highly applicable to the Venaflow intermittent pneumatic compression device and Comprinet Pro graduated compression stockings. Data is highly applicable to total hip or knee replacement surgery but is not applicable to hip fracture surgery.
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	Low	Compared with pharmacologic prophylaxis alone, patients who had major orthopedic surgery and received pharmacologic plus mechanical prophylaxis did not have a difference in the risk of distal deep vein thrombosis. Applicability is limited because only one trial was available comparing enoxaparin plus IPC versus enoxaparin alone and the duration of followup was short. Data is highly applicable to total hip or knee replacement surgery and not applicable to hip fracture surgery.
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	Moderate	Compared to 7 to 10 days of prophylaxis, patients who had major orthopedic surgery and received 28 days or more of prophylaxis did not have a difference in the risk of distal deep vein thrombosis. Data is highly applicable to primary hip replacement surgery with the use of injectable low molecular weight heparin agents. Data has a low level of applicability to oral vitamin K antagonists and injectable factor Xa inhibitors. Data has a moderate level of applicability to hip fracture surgery and a low level of applicability to total knee replacement surgery. Overall applicability is limited because the majority of trials were conducted outside of the United States.

Comparison	Strength of applicability	Conclusion with description of applicability
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=not applicable

Table 113. Strength of applicability for the body of evidence evaluating major bleeding in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Incidence of major bleeding in patients who had total hip replacement surgery	Low	The pooled incidence of major bleeding in patients who had total hip replacement surgery was 1 percent. Overall applicability is limited because 4 of the 5 trials were conducted outside of the United States and the trial conducted in the United States contributed a small percent of the overall population (17 percent).
Incidence of major bleeding in patients who had total knee replacement surgery	Low	The pooled incidence of major bleeding in patients who had total knee replacement surgery was 3 percent. Overall applicability was limited because both trials were conducted in Japan.
Incidence of major bleeding in patients who had hip fracture surgery	Low	Based on one trial, the incidence of major bleeding in patients who had hip fracture surgery was 8 percent. Overall applicability is limited because this trial was conducted in Canada and published in 1989.
General versus regional anesthesia	Low	There was insufficient evidence to determine the impact of general versus regional anesthesia on the risk of major bleeding. Data is highly applicable to primary hip replacement surgery although overall applicability is limited because the trial was conducted in France using agents that are currently not available in the United States.
Pharmacologic prophylaxis versus no prophylaxis	Low	Compared to no prophylaxis, patients who had major orthopedic surgery and received pharmacologic prophylaxis had no difference in the risk of major bleeding. Data is highly applicable to primary hip replacement surgery, moderately applicable to primary knee replacement and hip fracture surgery. Applicability is limited because the majority of trials were conducted outside of the United States.
Mechanical prophylaxis versus no prophylaxis	NA	No data
Oral antiplatelet agents versus oral vitamin K antagonists	Low	Compared to oral vitamin K antagonists, patients who had major orthopedic surgery and received oral antiplatelet agents did not have a difference in the risk of major bleeding. Applicability is limited because the type of surgery; primary or revision was not reported. Data is moderately applicable to hip fracture surgery. Data is not applicable to primary or revision total knee or total hip replacement surgery.
Oral antiplatelet agents versus mechanical prophylaxis	NA	No data
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	Low	Compared to injectable unfractionated heparin, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents had a decrease in the odds of major bleeding. Applicability is limited because the type of surgery; primary or revision was not reported. Data is highly applicable to total hip replacement surgery. Data has a low level of applicability to total knee replacement surgery. Data is not applicable to primary or revision hip fracture surgery.

Comparison	Strength of applicability	Conclusion with description of applicability
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	Low	Compared to injectable or oral factor Xa inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents had a decrease in the odds of major bleeding. Data has moderate applicability to primary or revision total hip replacement surgery. Data has a low level of applicability to primary hip fracture surgery and revision total knee replacement surgery.
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	Low	Compared to injectable or oral direct thrombin inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the risk of major bleeding. Applicability is limited because the majority of trials were conducted outside of the United States. Data is moderately applicable to primary total knee and total hip replacement surgery. Data is not applicable to primary or revision hip fracture surgery.
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	Moderate	Compared to oral vitamin K antagonists patients who had major orthopedic surgery and received injectable low molecular weight heparin agents had an increase in the odds of major bleeding. Applicability is limited by the type of surgery; primary or revision. Data is highly applicable to total hip and total knee replacement surgery and not applicable to primary or revision hip fracture surgery.
Injectable low molecular weight heparin agents versus mechanical prophylaxis	NA	No data
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	Moderate	Compared to injectable or oral factor Xa inhibitors, patients who had major orthopedic surgery and received injectable unfractionated heparin agents had an increase in the odds of major bleeding. Applicability is limited because the type of surgery; primary or revision was not reported. Data is moderately applicable to total hip replacement, total knee replacement and hip fracture surgery.
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data
Oral vitamin K antagonists versus mechanical prophylaxis	NA	No data
Enoxaparin versus other low molecular weight heparin agents	Low	Compared to other low molecular weight heparin agents, patients who had major orthopedic surgery and received enoxaparin did not have a difference in the risk of major bleeding. Data has a low level of applicability to primary total hip replacement surgery and primary hip fracture surgery. Data is not applicable to primary or revision total knee replacement surgery. Applicability is limited because the trials were conducted outside of the United States
Intermittent pneumatic compression device by Kendal versus the Venaflow intermittent pneumatic compression device	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus graduated compression	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	NA	No data
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	Moderate	Compared to 7 to 10 days of prophylaxis, patients who had major orthopedic surgery and received 28 days or more of prophylaxis did not have a difference in the odds of major bleeding. Data is moderately applicable to the use of injectable low molecular weight heparin agents. Data has a low level of applicability to oral vitamin K antagonists and injectable factor Xa inhibitors. Data is highly applicable to primary total hip replacement surgery, moderately applicable to hip fracture surgery and has low applicability to hip fracture surgery. Overall applicability is limited because the majority of trials were conducted outside of the United States.
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=Not applicable

Table 114. Strength of applicability for the body of evidence evaluating major bleeding leading to reoperation in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Incidence of major bleeding leading to reoperation in patients who had total hip replacement surgery	Moderate	Based on two trials the incidence of major bleeding leading to reoperation was 0 percent in patients who had total hip replacement surgery. Overall applicability is limited moderate because the majority of data is derived from a study conducted in the United States although this trial was published in 1992 while the second trial was published in 1997.
Incidence of major bleeding leading to reoperation in patients who had total knee replacement surgery	Low	Based on one trial, the incidence of major bleeding leading to reoperation was 0 percent. Overall applicability is limited because the trial was conducted in Japan.
Incidence of major bleeding leading to reoperation in patients who had hip fracture surgery	NA	No data
General versus regional anesthesia	NA	No data
Bone vacuum cement versus standard procedure	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Pharmacologic prophylaxis versus no prophylaxis	Low	Compared to no prophylaxis, patients who had major orthopedic surgery and received pharmacologic prophylaxis had no difference in the risk of major bleeding leading to reoperation. Data is highly applicable to primary total knee and hip replacement and total knee replacement. Data is not applicable to hip fracture surgery. Applicability is limited because all trials were conducted outside of the United States.
Mechanical prophylaxis versus no prophylaxis	NA	No data
Oral antiplatelet agents versus oral vitamin K antagonists	NA	No data
Oral antiplatelet agents versus mechanical prophylaxis	NA	No data
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	NA	No data
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	Low	Compared to injectable or oral factor Xa inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of major bleeding leading to reoperation. Data has moderate applicability to primary or revision total hip replacement surgery. Data has a low level of applicability to primary hip fracture surgery and revision total knee replacement surgery.
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	Low	Compared to injectable or oral direct thrombin inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the risk of major bleeding leading to reoperation. Data is moderately applicable to primary total knee replacement surgery. Data has a low level of applicability to primary total hip replacement surgery. Data is not applicable to primary or revision hip fracture surgery and is limited because the trials were conducted outside of the United States.
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	Low	Compared to oral vitamin K antagonists patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of major bleeding leading to reoperation. Data is moderately applicable to primary total knee replacement surgery and is not applicable to other major orthopedic surgeries.
Injectable low molecular weight heparin agents versus mechanical prophylaxis	NA	No data
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	Low	Compared to injectable or oral direct thrombin inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of major bleeding leading to reoperation. Data is highly applicable to primary total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip fracture surgery and has limited applicability because the trials were conducted outside of the United States.

Comparison	Strength of applicability	Conclusion with description of applicability
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data
Oral vitamin K antagonists versus mechanical prophylaxis	NA	No data
Enoxaparin versus other low molecular weight heparin agents	NA	No data
Intermittent pneumatic compression device by Kendal versus the Venaflow intermittent pneumatic compression device	NA	No data
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus graduated compression	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	NA	No data
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	Low	Compared to 7 to 10 days of prophylaxis, patients who had major orthopedic surgery and received 28 days or more of prophylaxis did not have a difference in the odds of major bleeding leading to reoperation. Data is highly applicable to the use of injectable factor Xa inhibitors and hip fracture surgery. Data is not applicable to injectable low molecular weight heparin agents or oral vitamin K antagonists or to primary or revision total hip replacement or total knee replacement surgery. Overall applicability is limited because the trial was conducted outside of the United States.
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=Not applicable

Table 115. Strength of applicability for the body of evidence evaluating minor bleeding in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Incidence of minor bleeding in patients who had total hip replacement surgery	Moderate	The pooled incidence of minor bleeding in patients who had total hip replacement surgery was 6 percent. Overall applicability is moderate as half of the data is derived from trials conducted in the Unite States. Two trials were published in the 90's, two in the 80's and one in 2008.
Incidence of minor bleeding in patients who had total knee replacement surgery	Low	The pooled incidence of minor bleeding in patients who had total knee replacement surgery was 6 percent. Overall applicability was limited because both trials were conducted in Japan.
Incidence of minor bleeding in patients who had hip fracture surgery	NA	No data
General versus regional anesthesia	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Bone vacuum cement versus standard procedure	Low	Compared to standard procedure, patients who received bone vacuum cement did not have a difference in the risk of minor bleeding. Data is highly applicable to primary total knee replacement surgery although overall applicability is limited as the trial was conducted in Germany and had a short duration of followup. Data is not applicable to hip replacement or hip fracture surgery.
Pharmacologic prophylaxis versus no prophylaxis	Moderate	Compared to no prophylaxis, patients who had major orthopedic surgery and received pharmacologic prophylaxis had an increase in the risk of minor bleeding. Data is highly applicable to primary total knee and hip replacement and total knee replacement. Data is not applicable to hip fracture surgery. Applicability is limited because all of the trials were conducted outside of the United States.
Mechanical prophylaxis versus no prophylaxis	NA	No data
Oral antiplatelet agents versus oral vitamin K antagonists	NA	No data
Oral antiplatelet agents versus mechanical prophylaxis	NA	No data
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	Low	Compared to injectable unfractionated heparin, patients who had major orthopedic surgery and received injectable low molecular weight heparin did not have a difference in the risk of minor bleeding. Applicability is limited because the type of surgery; primary or revision was not reported and because the majority of trials were conducted outside of the United States. Data is moderately applicable to total hip replacement surgery. Data has a low level of applicability to total knee replacement surgery. Data is not applicable to primary or revision hip fracture surgery.
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	Low	Compared to injectable or oral factor Xa inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin had a decrease in the odds of minor bleeding. Data is highly applicable to primary hip fracture surgery. Data is not applicable to primary or revision total knee or total hip replacement surgery.
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	Low	Compared to injectable or oral direct thrombin inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in risk of minor bleeding. Applicability is limited because the majority of trials were conducted outside of the United States. Data is moderately applicable to primary total knee and total hip replacement surgery. Data is not applicable to primary or revision hip fracture surgery.
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	Moderate	Compared to oral vitamin K antagonists, patients who had major orthopedic surgery and received injectable low molecular weight heparin had an increased risk of minor bleeding. Data is highly applicable to primary or revision total hip or knee replacement surgery although is not applicable to primary or revision hip fracture surgery.
Injectable low molecular weight heparin agents versus mechanical prophylaxis	NA	No data
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data
Oral vitamin K antagonists versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who had major orthopedic surgery and received oral vitamin K antagonists did not have a difference in the odds of minor bleeding. Applicability is limited due to the type of surgery; primary or revision. Data is highly applicable to total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip fracture surgery.
Enoxaparin versus other low molecular weight heparin agents	Low	Compared to other low molecular weight heparin agents, patients who had major orthopedic surgery and received enoxaparin did not have a difference in the odds of minor bleeding. Data is highly applicable to primary total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip fracture surgery. Applicability is limited because the trials wer conducted outside of the United States
Intermittent pneumatic compression device by Kendal versus the Venaflow intermittent pneumatic compression device	NA	No data
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus graduated compression	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	NA	No data
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	Moderate	Compared to 7 to 10 days of prophylaxis, patients who had major orthopedic surgery and received 28 days or more of prophylaxis had an increase in the odds of minor bleeding. Data has a low level of applicability to the use of injectable factor Xa inhibitors. Data is highly applicable to injectable low molecular weight heparin agents. And primary or revision hip replacement surgery. Data is not applicable to the use of oral vitamin K antagonists or to knee replacement surgery. Data has a moderate level of applicability to hip fracture surgery. Overall applicability is limited because the majority of trials were conducted outside of the United States.
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=Not applicable

Table 116. Strength of applicability for the body of evidence evaluating surgical site bleeding in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Incidence of surgical site bleeding in patients who had total hip replacement surgery	NA	No data
Incidence of surgical site bleeding in patients who had total knee replacement surgery	NA	No data
Incidence of surgical site bleeding in patients who had hip fracture surgery	NA	No data
Pharmacologic prophylaxis versus no prophylaxis	NA	No data
Mechanical prophylaxis versus no prophylaxis	NA	No data
Oral antiplatelet agents versus oral vitamin K antagonists	Low	Compared to oral vitamin K antagonists, patients who had major orthopedic surgery and received oral antiplatelet agents did not have a difference in the odds of surgical site bleeding. Applicability is limited due to the type of surgery; primary or revision. Data is highly applicable to total knee replacement surgery. Data is not applicable to primary or revision total hip replacement or hip fracture surgery.
Oral antiplatelet agents versus mechanical prophylaxis	NA	No data
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	Low	Compared to injectable unfractionated heparin, patients who had major orthopedic surgery and received low molecular weight heparin agents did not have a difference in the odds of surgical site bleeding. Applicability is limited because the type of surgery; primary or revision was not reported. Data is moderately applicable to total hip replacement surgery. Data has a low level of applicability to total knee replacement surgery. Data is not applicable to primary or revision hip fracture surgery.
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	Low	Compared to injectable or oral factor Xa inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odd of surgical site bleeding. Applicability is limited because the trial was conducted outside of the United States. Data is highly applicable to primary total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip fracture surgery.
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	Low	Compared to injectable or oral direct thrombin, patients who had major orthopedic surgery and received inhibitors injectable low molecular weight heparin agents had an increased risk of surgical site bleeding. Data is highly applicable to primary total knee replacement surgery. Data is not applicable to primary or revision total hip replacement or hip fracture surgery.
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	Low	Compared to oral vitamin K antagonists, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents had an increase in the odds of surgical site bleeding. Data is highly applicable to primary total hip or knee replacement surgery and is not applicable to revision surgery or hip fracture surgery.

Comparison	Strength of applicability	Conclusion with description of applicability
Injectable low molecular weight heparin agents versus mechanical prophylaxis	NA	No data
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	Low	Compared to injectable or oral direct thrombin inhibitors, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of surgical site bleeding. Applicability is limited because the trial was conducted outside of the United States. Data is highly applicable to primary total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip fracture surgery.
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data
Oral vitamin K antagonists versus mechanical prophylaxis	NA	No data
Enoxaparin versus other low molecular weight heparin agents	Low	Compared to other low molecular weight heparin agents, patients who had major orthopedic surgery and received enoxaparin did not have a difference in the odds of surgical site bleeding. Applicability is limited due to the type of surgery; primary or revision and because the trials were conducted outside of the United States. Data is highly applicable to total knee replacement surgery. Data is not applicable to primary or revision total hip replacement or hip fracture surgery.
Intermittent pneumatic compression device by Kendal versus the Venaflow intermittent pneumatic compression device	NA	No data
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus graduated compression	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	NA	No data
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	Low	Compared to 7 to 10 days of prophylaxis, patients who had major orthopedic surgery and received 28 days or more of prophylaxis had an increase in the odds of surgical site bleeding. Data is highly applicable to the use of injectable factor Xa inhibitors and hip fracture surgery. Data is not applicable to injectable low molecular weight heparin agents or oral vitamin K antagonists or to primary or revision total hip replacement or total knee replacement surgery. Overall applicability is limited because the trial was conducted outside of the United States.
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=Not applicable

Table 117. Strength of applicability for the body of evidence evaluating bleeding leading to infection in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Incidence of surgical site bleeding in patients who had total hip replacement surgery	NA	No data
Incidence of surgical site bleeding in patients who had total knee replacement surgery	NA	No data
Incidence of surgical site bleeding in patients who had hip fracture surgery	NA	No data
Pharmacologic prophylaxis versus no prophylaxis	NA	No data
Mechanical prophylaxis versus no prophylaxis	NA	No data
Oral antiplatelet agents versus oral vitamin K antagonists	NA	No data
Oral antiplatelet agents versus mechanical prophylaxis	NA	No data
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	NA	No data
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	NA	No data
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	NA	No data
Injectable low molecular weight heparin agents versus mechanical prophylaxis	NA	No data
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data
Oral vitamin K antagonists versus mechanical prophylaxis	NA	No data
Intermittent pneumatic compression device by Kendal versus the Venaflow intermittent pneumatic compression device	NA	No data
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus intermittent pneumatic compression devices	NA	No data
Intermittent pneumatic compression versus graduated compression	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	NA	No data
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	NA	No data
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=Not applicable

Table 118. Strength of applicability for the body of evidence evaluating bleeding leading to transfusion in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Incidence of bleeding leading to transfusion in patients who had total hip replacement surgery	Moderate	Based on one trial, the incidence of bleeding leading to transfusion was 0 percent in patients who had total hip replacement surgery. Overall applicability was limited because the trial was conducted in 1992.
Incidence of bleeding leading to transfusion in patients who had total knee replacement surgery	Low	Based on one trial, the incidence of bleeding leading to transfusion was 0 percent in patients who had total knee replacement surgery. Overall applicability was limited because the trial was conducted in Japan.
Incidence of bleeding leading to transfusion in patients who had hip fracture surgery	NA	No data
Pharmacologic prophylaxis versus no prophylaxis	Low	Compared to no prophylaxis, patients who had major orthopedic surgery and received pharmacologic prophylaxis had no difference in the odds of bleeding leading to transfusion. Data is highly applicable to the use of dabigatran in primary total knee replacement surgery. Data is not applicable to total hip replacement or hip fracture surgery. Applicability is limited because the one trial available was conducted in Japan.
Mechanical prophylaxis versus no prophylaxis	NA	No data
Oral antiplatelet agents versus oral vitamin K antagonists	NA	No data
Oral antiplatelet agents versus mechanical prophylaxis	NA	No data
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	NA	No data
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	Low	Compared to injectable unfractionated heparin, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the risk of bleeding leading to transfusion. Data is moderately applicable to primary total knee replacement and total hip replacement surgery. Data is not applicable to primary or revision hip fracture surgery and is limited because the trials were conducted outside of the United States.
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	Low	Compared to oral vitamin K antagonists, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the odds of bleeding leading to transfusion. Data is moderately applicable to primary total hip replacement surgery and is not applicable to other major orthopedic surgeries.
Injectable low molecular weight heparin agents versus mechanical prophylaxis	NA	No data
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data
Oral vitamin K antagonists versus mechanical prophylaxis	NA	No data
Enoxaparin versus other low molecular weight heparin agents	NA	No data
Intermittent pneumatic compression device by Kendal versus the Venaflow intermittent pneumatic compression device	NA	No data
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus graduated compression	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	NA	No data
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	Low	Compared to 7 to 10 days of prophylaxis, patients who had major orthopedic surgery and received 28 days or more of prophylaxis did had a difference in the odds of bleeding leading to transfusion. Data is highly applicable to the use of injectable factor Xa inhibitors and hip fracture surgery. Data is not applicable to injectable low molecular weight heparin agents or oral vitamin K antagonists or to primary or revision total hip replacement or total knee replacement surgery. Overall applicability is limited because the trial was conducted outside of the United States.
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=Not applicable

Table 119. Strength of applicability for the body of evidence evaluating heparin induced thrombocytopenia in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Pharmacologic prophylaxis versus no prophylaxis	NA	No data
Mechanical prophylaxis versus no prophylaxis	NA	No data
Oral antiplatelet agents versus oral vitamin K antagonists	NA	No data
Oral antiplatelet agents versus mechanical prophylaxis	NA	No data
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	Low	Compared to injectable unfractionated heparin, patients who had major orthopedic surgery and received injectable low molecular weight heparin had a decrease in the odds of heparin induced thrombocytopenia. Applicability is limited because the type of surgery; primary or revision is not reported. Data is highly applicable to total hip replacement surgery. Data is moderately applicable to total knee replacement surgery. Data is not applicable to primary or revision hip fracture surgery.
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	NA	No data
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	NA	No data
Injectable low molecular weight heparin agents versus mechanical prophylaxis	NA	No data
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data
Oral vitamin K antagonists versus mechanical prophylaxis	NA	No data
Enoxaparin versus other low molecular weight heparin agents	Low	Compared to other low molecular weight heparin agents, patients who had major orthopedic surgery and received enoxaparin did not have a difference in the odds of heparin induced thrombocytopenia. Data is highly applicable to the use of tinzaparin in primary total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip fracture surgery. Applicability is limited because the trials were conducted outside of the United States
Intermittent pneumatic compression device by Kendal versus the Venaflow intermittent pneumatic compression device	NA	No data
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus graduated compression	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	NA	No data
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	NA	No data
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=Not applicable

Table 120. Strength of applicability for the body of evidence evaluating discomfort in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Pharmacologic prophylaxis versus no prophylaxis	NA	No data
Mechanical prophylaxis versus no prophylaxis	NA	No data
Oral antiplatelet agents versus oral vitamin K antagonists	NA	No data
Oral antiplatelet agents versus mechanical prophylaxis	NA	No data
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	NA	No data
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	NA	No data
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Injectable low molecular weight heparin agents versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who had major orthopedic surgery and received low molecular weight heparin agents had a decreased risk of discomfort. Applicability is limited because the trial was conducted outside of the United States. Data is highly applicable to primary total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip fracture surgery.
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data
Oral vitamin K antagonists versus mechanical prophylaxis	NA	No data
Enoxaparin versus other low molecular weight heparin agents	NA	No data
Intermittent pneumatic compression device by Kendal versus the Venaflow intermittent pneumatic compression device	NA	No data
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus graduated compression	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	NA	No data
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	NA	No data
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=Not applicable

Table 121. Strength of applicability for the body of evidence evaluating readmission in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Pharmacologic prophylaxis versus no prophylaxis	Low	Compared to no prophylaxis, patients who had major orthopedic surgery and received pharmacologic prophylaxis had no difference in the rate of readmission. Data is highly applicable to the use of warfarin in primary total knee replacement surgery. Data is not applicable to total hip replacement or hip fracture surgery.
Mechanical prophylaxis versus no prophylaxis	NA	No data
Oral antiplatelet agents versus oral vitamin K antagonists	NA	No data
Oral antiplatelet agents versus mechanical prophylaxis	NA	No data
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	Low	Compared to injectable unfractionated heparin patients who had major orthopedic surgery and received low molecular weight heparin agents did not have a difference in the risk of readmission. Data is highly applicable to primary or revision total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip fracture surgery.
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	NA	No data
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	NA	No data
Injectable low molecular weight heparin agents versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the risk of readmission. Applicability is limited because the trials were conducted outside of the United States. Data is moderately applicable to primary total knee and total hip replacement surgery. Data is not applicable to primary or revision hip fracture surgery.
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
Oral vitamin K antagonists versus mechanical prophylaxis	Low	Compared to mechanical prophylaxis, patients who had major orthopedic surgery and received oral vitamin K antagonists did not have a difference in the odds of readmission. Data is highly applicable to primary or revision total hip replacement surgery. Data is not applicable to primary or revision total knee replacement or hip fracture surgery.
Enoxaparin versus other low molecular weight heparin agents	NA	No data
Intermittent pneumatic compression device by Kendal versus the Venaflow intermittent pneumatic compression device	NA	No data
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus graduated compression	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	NA	No data
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	Low	Compared to 7 to 10 days of prophylaxis, patients who had major orthopedic surgery and received 28 days or more of prophylaxis did not have a difference in the risk of readmission. Data is highly applicable to the use of injectable low molecular weight heparin agents in primary total hip or knee replacement surgery. Data is not applicable to primary or revision hip fracture surgery. Data is not applicable to revision total knee or total hip replacement surgery.
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=Not applicable

Table 122. Strength of applicability for the body of evidence evaluating reoperation in patients who had major orthopedic surgery

Comparison	Strength of applicability	Conclusion with description of applicability
Pharmacologic prophylaxis versus no prophylaxis	Low	Compared to no prophylaxis, patients who had major orthopedic surgery and received pharmacologic prophylaxis had an increase in the rate of reoperation. Data is highly applicable to the use of warfarin in primary total knee replacement surgery. Data is not applicable to total hip replacement or hip fracture surgery.

Comparison	Strength of applicability	Conclusion with description of applicability
Mechanical prophylaxis versus no prophylaxis	NA	No data
Oral antiplatelet agents versus oral vitamin K antagonists	NA	No data
Oral antiplatelet agents versus mechanical prophylaxis	NA	No data
Injectable low molecular weight heparin agents versus injectable unfractionated heparin	NA	No data
Injectable low molecular weight heparin agents versus injectable or oral factor Xa inhibitors	Low	Compared to injectable or oral factor Xa, patients who had major orthopedic surgery and received inhibitors injectable low molecular weight heparin agents did not have a difference in the risk of reoperation. Applicability is limited because the trial was conducted outside of the United States. Data is highly applicable to revision total knee replacement surgery. Data is not applicable to primary or revision total hip replacement or hip fracture surgery.
Injectable low molecular weight heparin agents versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable low molecular weight heparin agents versus oral vitamin K antagonists	Low	Compared to, oral vitamin K antagonists patients who had major orthopedic surgery and received injectable low molecular weight heparin agents did not have a difference in the risk of reoperation. Data is moderately applicable to primary total knee replacement surgery and is not applicable to other major orthopedic surgeries.
Injectable low molecular weight heparin agents versus mechanical prophylaxis	NA	No data
Injectable unfractionated heparin versus injectable or oral direct thrombin inhibitors	NA	No data
Injectable unfractionated heparin versus injectable or oral factor Xa inhibitors	NA	No data
Injectable unfractionated heparin versus mechanical prophylaxis	NA	No data
Oral vitamin K antagonists versus mechanical prophylaxis	NA	No data
Enoxaparin versus other low molecular weight heparin agents	NA	No data
Intermittent pneumatic compression device by Kendal versus the Venaflow intermittent pneumatic compression device	NA	No data

Comparison	Strength of applicability	Conclusion with description of applicability
ActiveCare intermittent pneumatic compression device versus Flowtron intermittent pneumatic compression device	NA	No data
Intermittent pneumatic compression versus graduated compression	NA	No data
Pharmacologic plus mechanical prophylaxis versus pharmacologic prophylaxis	NA	No data
Pharmacologic plus mechanical prophylaxis versus mechanical prophylaxis	NA	No data
Effect of prolonging prophylaxis for 28 days compared to prophylaxis for 7 to 10 days	Low	Compared to 7 to 10 days of prophylaxis, patients who had major orthopedic surgery and received 28 days or more of prophylaxis did not have a difference in the risk of reoperation. Data is highly applicable to the use of injectable low molecular weight heparin agents in primary or revision total hip replacement surgery. Data is not applicable to primary or revision hip fracture surgery or total knee replacement surgery. Overall applicability is limited because the trial was conducted outside of the United States.
Inferior vena cava filter versus mechanical prophylaxis	NA	No data

Abbreviations: NA=Not applicable

Appendix J. Glossary

Confidence Intervals (CIs): A range that is likely to include the given value. Usually presented as a percent (%). For example, a value with 95% confidence interval implies that when a measurement is made 100 times, it will fall within the given range 95% of the time.
Deep Venous Thrombosis (DVT): A blood clot occurring in a leg vein and verified with Doppler ultrasound or venography. Proximal deep vein thrombosis was defined as blood clot occurring in either popliteal, femoral, or any deep veins of the pelvis. Distal vein thrombosis was defined as blood clot occurring distal to the popliteal vein in the calf veins of the leg. When both bilateral and unilateral clots data were available, unilateral clots data was used for the analysis.
DerSimonian and Laird Random-Effects Model: A statistical method based on the assumption that the effects observed in different studies (in a meta-analysis) are truly different.
Egger's Weighted Regression Statistics: A method of identifying and measuring publication bias.
Hip Fracture Surgery (HFS): The surgical procedure to treat hip fracture.
I^2: Measure of degree of variation due to statistical heterogeneity. Usually reported as a percent ranging from 0 to100.
Major Orthopedic Surgery: Total hip arthroplasty, total knee arthroplasty, hip fracture surgery
Meta-Analysis: The process of extracting and pooling data from several studies investigating a similar topic to synthesize a final outcome.
Other Orthopedic Surgery: knee arthroscopy, surgical repair of a lower extremity injury distal to the hip (open reduction internal fixation of the femur, tibia, ankle or foot, intermedullary fixation, ankle fusion, osteotomy of the tibia or femur, open ligament reconstruction of the knee or ankle, and tendon repair) or elective spine surgery (anterior or posterior spinal fusion +/- decompression, laminectomy, or diskectomy all of the lumbar region).
Peto's Odds Ratio (OR): An odds ratio is the ratio of an event occurring in an exposed group to an event occurring in the nonexposed group in a given population. A ratio of one indicates no difference in the odds between the two groups. Peto's odds ratios are used to compare two groups when the number of events is rare.
Publication Bias: The possibility that published studies may not represent all the studies that have been conducted, and therefore, create bias by being left out of a meta-analysis.
Pulmonary Embolism (PE): A blood clot in the vasculature of the lung. In order to have a pulmonary embolism in our review, it needed to be verified with spiral computed tomography angiography or ventilation/perfusion scan with either Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) criteria or high clinical suspicion based on symptoms for pulmonary embolism.
Relative Risks (RRs): The ratio of an event occurring in an exposed group to an event occurring in a non-exposed group in a given population. A ratio of one indicates no difference in the risk between the two groups.
Sensitivity Analyses: A 'what if' analysis that helps determine the robustness of a study. Helps determine the degree of importance of each variable for a given outcome.
Standard Deviations (SDs): A measure of the variability of a data set. For a simple data set with numbers, can be calculated using the following formula: $\sigma = ((\sum(x-x_m))^2/N)^{0.5}$ where σ is standard deviation, x_m is the average, $\sum(x-x_m)$ is the sum of x_m subtracted from each individual number x, N is the total number of values.

Statistical Heterogeneity: Variability in the observed effects among studies in a meta-analysis.
Total Hip Arthroplasty (THR): The surgical replacement of the hip.
Total Knee Arthroplasty (TKA): The surgical replacement of the knee.
Venous Thromboembolism (VTE): The occurrence of either a deep venous thrombosis or pulmonary embolism.