

Clinical trials of antithrombotics for thrombosis prevention in orthopedic surgery

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1 antivitamins K

Trial	Treatments	Patients	Trials design and methods
vs no treatment			
Borsgtrom , 1965 n=29/29 follow-up: 65279;34 weeks	65279;Dicoumarol versus 65279;No treatment	HFS	Open
Phenindione vs no treatment			
Eskeland , 1966 n=100/100 follow-up: 3 months	Phenindione versus No treatment	HFS	Open
Hamilton , 1970 n=38/38 follow-up: 310 months	Phenindione versus No treatment	HFS	Open
Warfarin vs no treatment			
Pinto , 1970 n=25/25 follow-up: >3 weeks	Warfarin versus No treatment	Hip surgery	Open
Hume , 1973 n=17/19 follow-up: Discharge	Warfarin versus No treatment	THR	Open
Morris , 1976 n=80/80 follow-up: 3 months	Warfarin versus No treatment	HFS	Open
Powers , 1989 n=65/63 follow-up: 3 months	Warfarin versus No treatment	HFS	Open
Warfarin vs placebo			
Myrhe , 1969 n=50/55 follow-up: 3 weeks	Wwarfarin versus Placebo	HFS	double blind
Warfarin vs Ardeparin			
RD Heparin , 1994 n=403/770 follow-up: 3 months	Warfarin versus Ardeparin 50 anti-Xa IU /kg or 90 anti-Xa IU /kg x1	THR or TKR	Open
Heit , 1997 n=279/554 follow-up: Days 514	Warfarin versus Ardeparin 25, 35, 50 anti-Xa U /kg x2	TKR	double blind
Warfarin vs Aspirin			

continued...

Trial	Treatments	Patients	Trials design and methods
Lotke , 1997 n=146/166 follow-up: 6 months	Warfarin versus Aspirin 325 mg x2	THR or TKR (stratified)	Open
Powers , 1989 n=65/66 follow-up: 3 months	Warfarin versus Aspirin 650 mg x2	HFS	Open
Warfarin vs Dalteparin			
Francis , 1997 n=292/288 follow-up: Day 7 2	Warfarin versus Dalteparin 5000 anti-Xa IU x1	THR	Open
Hull , 2000 n=489/983 follow-up: Day 6 2	Warfarin versus Dalteparin 5000 anti-Xa IU x1	THR	double blind
Warfarin vs Danaparoid			
Gerhart , 1991 n=131/132 follow-up: 9 days	Warfarin versus Danaparoid 750 U x2	HFS	Open
van Comp , 1998 n=247/241 follow-up: 3 months	Warfarin versus Danaparoid 750 U x2	THR	Open
Warfarin vs Dextran			
Harris , 1972 n=114/113 follow-up: NA	Warfarin versus Dextran 40	THR	Open
Barber , 1977 n=58/51 follow-up: 1114 days	Warfarin versus Dextran 70	THR	Open
Francis , 1983 n=57/43 follow-up: 57 days	Warfarin versus Dextran 40	THR or TKR (stratified)65279;	Open
Myrhe , 1969 n=50/55 follow-up: 3 weeks	Warfarin versus Dextran 70	HFS	double blind
Warfarin vs Enoxaparin			
Leclerc , 1996 n=334/336 follow-up: 6 months	Warfarin versus Enoxaparin 30 mg x2	TKR	double blind
Colwell , 1999 n=1495/1516 follow-up: 3 months	Warfarin versus Enoxaparin 30 mg x2	THR	Open
Fitzgerald , 2001 n=176/173 follow-up: 3 weeks	Warfarin versus Enoxaparin 30 mg x2	TKR	Open
Warfarin vs Intermittent pneumatic compression			

continued...

Trial	Treatments	Patients	Trials design and methods
Francis , 1992 n=103/98 follow-up: 68 days	Warfarin versus IPC	THR	Open
Paiement , 1987 n=80/83 follow-up: 12 days	Warfarin versus IPC	THR	Open
Bailey , 1991 n=45/50 follow-up: 57 days	Warfarin versus IPC	THR	Open
Kaempffe , 1991 n=52/48 follow-up: At least 2 months	Warfarin versus IPC	THR or TKR (stratified)	Open
Warfarin vs Logiparin			
Hull , 1993 n=721/715 follow-up: 65279;Day 14 or discharge	Warfarin versus Logiparin 75 anti-Xa IU /kg x1	65279;THR or TKR (stratified)	double blind
Acenocoumarol vs Nadroparin			
Hamulyak , 1994 n=342/330 follow-up: Day 10 2	Acenocoumarol versus Nadroparin 60 anti-Xa IU /kg x1	THR or TKR (stratified)	single blind
Acenocoumarol vs Reviparin			
Samama , 2001 n=645/644 follow-up: 6 weeks	Acenocoumarol versus Reviparin 4200 anti-Xa IU x1	THR	Open
Warfarin vs Sudoxicam			
Hume , 1973 n=52/51 follow-up: Discharge	Warfarin versus Sudoxicam	THR	single blind
Acenocoumarol vs unfractionated heparin			
van Geloven , 1977 n=11/11 follow-up: NA	Acenocoumarol versus UFH 4000 x2	THR	double blind
Warfarin vs unfractionated heparin			
Hume , 1973 n=17/18 follow-up: Discharge	Warfarin versus UFH 5000 x3	THR	Open
Barber , 1977 n=58/19 follow-up: 1114 days	Warfarin versus UFH 5000 x2	THR	Open

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2 direct factor Xa inhibitors

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Trial	Treatments	Patients	Trials design and methods
edoxaban vs placebo			
DU176b-04 <i>ongoing</i> [NCT01203072] n=NA follow-up:	edoxaban 5, 15, 30, 60 mg once daily for 2 weeks versus placebo	elective total knee arthroplasty	parallel groups double-blind Japan
apixaban vs enoxaparin			
ADVANCE 3 , 2010 [NCT00423319] n=2708/2699 follow-up: 35 days (+60)	apixaban 2.5mg twice daily for 35 days versus enoxaparin 40mg once daily for 35 days	patients undergoing elective total hip replacement surgery	Parallel groups double blind 21 countries
edoxaban vs enoxaparin			
DU176b-B-J302 <i>ongoing</i> [NCT01181102] n=NA follow-up:	edoxaban 30mg once daily versus enoxaparin sodium (enoxaparin sodium 20mg(=2000IU)/0.2ml twice daily, subcutaneous injection)	elective total knee arthroplasty	parallel groups double-blind Japan
DU176b-B-J303 <i>ongoing</i> [NCT01181141] n=NA follow-up:	edoxaban 30mg once daily versus Enoxaparin sodium 20mg(=2000IU)/0.2ml twice daily, subcutaneous injection	elective hip fracture surgery	open Japan

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Trial	Treatments	Patients	Trials design and methods
DU176b-B-J304 <i>ongoing</i> [NCT01181167] n=NA follow-up:	edoxaban 30mg once daily versus (enoxaparin sodium 20mg(=2000IU)/0.2ml twice daily, subcutaneous injection	elective total hip arthroplasty	parallel groups double-blind Japan
rivaroxaban vs enoxaparin			
RECORD 1 , 2008 [NCT00329628] n=2266/2275 follow-up: 36 days (range 30-42)	rivaroxaban 10mg once daily for 35 days versus enoxaparin 40mg subcutaneous once daily for 31-39 days	patients undergoing total hip arthroplasty	Parallel groups double blind 27 countries worldwide
apixaban vs enoxaparin (europe regimen)			
ADVANCE 2 , 2010 [NCT00452530] n=1528/1529 follow-up: 12 days	apixaban 2.5mg twice daily during 12 days versus enoxaparin 40mg once daily 12 days	patients undergoing elective unilateral or bilateral total knee replacement	Parallel groups double blind 27 countries
rivaroxaban vs enoxaparin (europe regimen)			
RECORD 3 , 2008 [NCT00361894] n=1254/1277 follow-up: 13-17 days	rivaroxaban 10 mg once daily for 10- 14 days versus enoxaparin 40 mg subcutaneous once daily for 10-14 days	patients undergoing total knee arthroplasty	Parallel groups double blind 19 countries worldwide
edoxaban vs enoxaparin (short duration)			
STARS J-V [NCT01181167] n=255/248 follow-up:	edoxaban 30 mg once daily for 11 to 14 days versus subcutaneous enoxaparin 2,000 IU, equivalent to 20 mg, twice daily (BID) for 11 to 14 days	total hip arthroplasty	Parallel groups double-blind japan
rivaroxaban vs enoxaparin (short duration)			
ODIXa-HIP 10mg , 2006 n=142/157 follow-up: 5-9 days	rivaroxaban 10mg daily for 59 days versus once-daily subcutaneous enoxaparin dose of 40 mg for 59 days	patients undergoing elective total hip replacement	Parallel groups double blind Europe, Israel
rivaroxaban (long duration) vs enoxaparin (short duration)			
RECORD 2 , 2008 [NCT00332020] n=1252/1257 follow-up: 30-42 days	extended thromboprophylaxis with rivaroxaban 10mg once daily for 31-39 days versus enoxaparin 40mg subcutaneous once daily for 10-14 days	patients undergoing elective total hip replacement	Parallel groups double blind 21 countries worldwide
apixaban vs enoxaparin (US regimen)			
APROPOS 2.5mg , 2007 [NCT00097357] n=153/152 follow-up: 12 days	apixaban 2.5mg BID for 12 days versus enoxaparin 30mg twice daily for 12 days	patients undergoing elective total knee replacement surgery	Parallel groups double blind
rivaroxaban vs enoxaparin (US regimen)			

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Trial	Treatments	Patients	Trials design and methods
ODIXa-KNEE , 2005 n=102/105 follow-up: 5-9 days	BAY 59-7939 5mg b.i.d. for 59 days versus enoxaparin 30 mg b.i.d. for 59 days	patients undergoing elective total knee replacement	Parallel groups double blind North America
RECORD 4 , 2009 [NCT00362232] n=1584/1564 follow-up: 40 days	rivaroxaban 10mg once daily for 10 to 14 days versus enoxaparin 30 mg twice daily by subcutaneous injection for 10-14 days	patients who had undergone total-knee-replacement surgery	Parallel groups double blind 12 countries

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STARS J-V, 0:

ODIXa-HIP 10mg, 2006:

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3 extended prophylaxis

Trial	Treatments	Patients	Trials design and methods
out of hospital Ardeparin vs standard prophylaxis			
Heit , 2000 n=589/572	65279;in hospital thromboprophylaxis followed by out of hospital Ardeparin 100 IU/kg once a day for a total duration of 42 days versus Ardeparin 50 IU/kg twice a day for 4-10 days	THR or TKR	
out of hospital Dalteparin vs standard prophylaxis			
Dahl , 1997 n=134/131	65279;in hospital thromboprophylaxis followed by out of hospital Dalteparin 5000 IU once a day for a total duration of 35 days versus Dalteparin 5000 IU once a day for 7 days (dextran day 0 and day 1)	THR	
Lassen , 1998 n=140/141	65279;in hospital thromboprophylaxis followed by out of hospital Dalteparin 5000 IU once a day for a total duration of 35 days versus Dalteparin 5000 IU once a day for 7 days	THR	
Hull , 2000 n=389/180	65279;in hospital thromboprophylaxis followed by out of hospital Dalteparin 5000 IU once a day for a total duration of 35 days versus Dalteparin 5000 IU once a day or warfarin for 6 days	THR	
out of hospital Enoxaparin vs standard prophylaxis			
Bergqvist , 1996 n=117/116	65279;in hospital thromboprophylaxis followed by out of hospital Enoxaparin 40 mg once a day for a total duration of 30 days versus 65279;Enoxaparin 40 mg once a day for 10-11 days	65279;THR	
Planes , 1996 n=90/89	65279;in hospital thromboprophylaxis followed by out of hospital Enoxaparin 40 mg once a day for a total duration of 35 days versus Enoxaparin 40 mg once a day for 13-15 days	THR	

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Trial	Treatments	Patients	Trials design and methods
Comp , 2001 n=441/432	65279;in hospital thromboprophylaxis followed by out of hospital Enoxaparin 40 mg once a day for a total duration of 27-29 days versus Enoxaparin 30 mg twice a day for 7-10 days	THR or TKR	
out of hospital Nadroparin vs standard prophylaxis			
NPHDO , 1998 n=173/173	65279;in hospital thromboprophylaxis followed by out of hospital Nadroparin weight-adjusted for a total duration of 37-38 days versus Nadroparin weight-adjusted for 16-17 days	THR	
out of hospital UFH vs standard prophylaxis			
Manganelli , 1998 n=79/80	65279;in hospital thromboprophylaxis followed by out of hospital UFH 5000 IU three times a day for a total duration of 30 days versus UFH 5000 IU three times a day for 15 days	THR	

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4 Graduated compression stockings

Trial	Treatments	Patients	Trials design and methods
compression stocking group vs control (on top fondaparinux)			
Cohen (L8405) , 2007 n=426/430 follow-up: 42 days	fondaparinux 2.5mg plus graduated compression stockings versus fondaparinux 2.5mg daily	patients undergoing elective or emergency hip surgery	Parallel groups open Brazil, UK, Hong Kong, Spain

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5 Low molecular weight heparin

Trial	Treatments	Patients	Trials design and methods
semuloparin vs enoxaparin			
SAVE-HIP1 , 2012 [NCT00697099] n=1161/1165 follow-up:	Semuloparin 20 mg once-daily versus Enoxaparin 40 mg once-daily	-	
SAVE-KNEE , 2012 [NCT00718224] n=-576/574 follow-up:	Semuloparin 20 mg once-daily versus Enoxaparin 30 mg twice-daily	-	
SAVE-HIP 2 , 2012 [NCT00721760] n=500/503 follow-up:	Semuloparin 20 mg once-daily versus Enoxaparin 40 mg once-daily	hip fracture surgery	Parallel groups

continued...

Trial	Treatments	Patients	Trials design and methods
enoxaparin vs no treatment			
Warwick , 1995 n=78/78 follow-up: 8-10 days	enoxaparin 4000x1 + elastic stockings versus no treatment + elastic stockings	Elective hip	open
nadroparin vs no treatment			
Yoo , 1997 n=50/50 follow-up: 10 days	nadroparin 41/kgx1 days 1-3, 62/kg x1 days 4-11+elastic stockings versus no treatment	Elective hip	open
ardeparin vs placebo			
Levine , 1996 n=122/124 follow-up: 14 days	ardeparin 50/kgx2 +elastic stockings versus Placebo+elastic stockings	Knee	double blind
dalteparin vs placebo			
Jorgensen , 1989 n=30/38 follow-up: 9 days	dalteparin 5000 x1 versus Placebo	Hip fracture	double blind
Torholm , 1991 n=58/54 follow-up: 9 days	dalteparin 5000x1 versus Placebo	Elective hip	double blind
enoxaparin vs placebo			
Kalodiki , 1996 n=13/14 follow-up: discharge (8-12 days)	enoxaparin 4000x1 versus Placebo	Elective hip	double blind
Leclerc , 1991 n=65/64 follow-up: 14 days	Enoxaparin 3000 x2 versus Placebo	Knee	double blind
Samama , 1997 n=85/85 follow-up: 8-12 days	enoxaparin 4000x1+elastic stockings versus Placebo+elastic stockings	Elective hip	double blind
Turpie , 1986 n=50/50 follow-up: 14 days or discharge	Enoxaparin 3000 x2 versus Placebo	Elective hip	double blind
nadroparin vs placebo			
Sourmelis , 1995 n=72/78 follow-up: 10-12 days	nadroparin 3075x1 preop, 6150x1 post op versus Placebo	Hip fracture	double blind
tinzaparin vs placebo			
Lassen , 1991 n=105/105 follow-up: 8-10 days	tinzaparin 50/kg x1 +elastic stockings versus Placebo+elastic stockings	Elective hip	double blind
dalteparin vs Dextran			

continued...

Trial	Treatments	Patients	Trials design and methods
Matzsch , 1991 n=120/123	dalteparin versus Dextran	Elective hip	
Eriksson , 1988 n=50/50	dalteparin versus Dextran	Elective hip	
Matzsch , 1988 n=48/52	dalteparin versus Dextran	Elective hip	
enoxaparin vs Dextran			
DES Group , 1991 n=120/126	Enoxaparin versus Dextran	Elective hip	
certoparin + DHE vs Unfractionated heparin			
Haas , 1987 n=80/80	Sandoz +0.5mg DHE versus Unfractionated heparin	Elective hip	
Lassen , 1989 n=68/71 follow-up: 6 days	certoparin 3000+0.5mg DHE x1 versus placebo	Hip fracture	double blind
Lassen , 1988 n=118/122 follow-up: 6 days	certoparin 3000+0.5mg DHE, x1 versus Placebo	Elective hip	double blind
dalteparin vs Unfractionated heparin			
Binsack , 1986 n=48/47	dalteparin versus Unfractionated heparin	Elective hip	
Barre , 1987 n=40/40	dalteparin versus Unfractionated heparin	Elective hip	
Dechavanne , 1989 n=82/40	dalteparin versus Unfractionated heparin	Elective hip	
Eriksson , 1989 n=67/69	dalteparin versus Unfractionated heparin	Elective hip	
Haas , 1985 n=65/65	dalteparin versus Unfractionated heparin	Elective hip	
Monreal , 1989 n=46/44	dalteparin versus Unfractionated heparin	Hip	
enoxaparin vs Unfractionated heparin			

continued...

Trial	Treatments	Patients	Trials design and methods
Levine , 1991 n=333/332	Enoxaparin versus Unfractionated heparin	Elective hip	
Planes , 1988 n=124/113	Enoxaparin versus Unfractionated heparin	Elective hip	
fluxum vs Unfractionated heparin			
Chiapuzzo , 1988 n=70/70	Fluxum versus Unfractionated heparin	Elective hip	
Pini , 1989 n=25/24	Fluxum versus Unfractionated heparin	Hip	
nadroparin vs Unfractionated heparin			
Leyvraz , 1991 n=203/206 follow-up:	Fraxiparin versus Unfractionated heparin	Elective hip	

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6 oral direct thrombin inhibitor

Trial	Treatments	Patients	Trials design and methods
ximelagatran vs Dalteparin			
METHRO I , 2002 n=103 follow-up: 69 days	Melagatran 14 mg s.c. immediately before surgery, melagatran at 20.00 hours, then ximelagatran 624 mg orally b.d. for 69 days versus Dalteparin 5000 IU o.d., started evening before surgery for 69 days	adults undergoing hip or knee replacement	parallel group open Swedish
METHRO II , 2002 n=1495/381 follow-up: 710 days	Melagatran 13 mg s.c. immediately before surgery, melagatran same day, then ximelagatran 824 mg orally b.d. for 710 days versus Dalteparin 5000 IU o.d., started evening before surgery for 710 days	undergoing hip or knee replacement	Parallel groups double-blind
dabigatran 150mg vs enoxaparin			
RE-NOVATE (150mg) , 2007 [NCT00168818] n=1174/1162 follow-up: 28-35 days, median 33d	dabigatran etexilate 150 mg q.d. 28-35 days versus Enoxaparin 40 mg q.d. for 28-25 days	Total hip replacement	double blind Europe, Australia, South Africa
dabigatran 220mg vs enoxaparin			
RE-NOVATE 2 unpublished [NCT00657150] n=1010/1003 follow-up: 28-35 days (mean 32d)	dabigatran 220mg once daily for 28-35 Days versus enoxaparin 40mg subcutaneous once daily for 28-35 Days	patients undergoing total hip-replacement surgery	Parallel groups double-blind

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Trial	Treatments	Patients	Trials design and methods
RE-NOVATE (220mg) , 2007 [NCT00168818] n=1157/1162 follow-up: 28-35 days, median 33d	dabigatran etexilate 220 mg q.d. for 28-35 days versus Enoxaparin 40 mg q.d. for 23-35 days	Total hip replacement	Parallel groups double blind Europe, Australia, South Africa
ximelagatran vs Enoxaparin			
Platinum (Colwell) , 2003 n=906/910 follow-up: 712 days	Ximelagatran 24 mg orally b.d., starting at least 12 h after surgery for 712 days versus Enoxaparin 30 mg s.c. b.d.,starting at least 12 h after surgery for 712 days	adults undergoing hip replacement	parallel group double-blind USA, Canada, Israel, Mexico,Argentina, South Africa
METHRO III , 2002 n=2788 follow-up: 811 days	Melagatran 3 mg s.c. 412h after surgery, then ximelagatran24 mg orally b.d. for 710 days versus Enoxaparin 40 mg s.c. o.d. 12 h before surgery for 710 days	hip or knee replacement	double-blind Europe, South Africa
Phase II (Heit) , 2001 n=600 follow-up: 612 days	Ximelagatran 8, 12, 18 or 24 mg orally b.d., at least 12 h after surgery for 612 days versus Enoxaparin 30 mg s.c. b.d.,starting at least 12 h after surgery for 612 days	adults (age>18 years and weight at least 40 kg) undergoing knee replacements	parallel group double-blind North American
EXPRESS , 2003 n=2835 follow-up: 811 days	Melagatran 2 mg s.c. up to 30 min before surgery, then melagatran 3 mg at least 8 hafter surgery, then ximelagatran 24 mg orally b.d. for 811 days versus Enoxaparin 40 mg s.c. o.d.,starting 12 h before surgery for 811 days	hip or knee replacement	parallel group double-blind Europe
dabigatran 150mg vs enoxaparin (europe regimen)			
RE-MODEL (150mg) , 2007 n=708/699 follow-up: 6-10 days, mean 8 days	dabigatran etexilate 150 mg q.d. for 6-10 days versus Enoxaparin 40 mg q.d. for 6-10 days	Total knee replacement	Parallel groups double blind Europe, Australia, South Africa
dabigatran 220mg vs enoxaparin (europe regimen)			
RE-MODEL (220mg) , 2007 n=694/699 follow-up: 6-10 days, mean 8 days	dabigatran etexilate 220 mg q.d. 6-10 days versus Enoxaparin 40 mg q.d. for 6-10 days	patients undergoing total knee replacement	double blind Europe, Australia, South Africa
dabigatran 150mg vs enoxaparin (US regimen)			
RE-MOBILIZE (150mg) , 2008 n=877/876 follow-up: 12-15 days, median 14d	dabigatran etexilate 150 mg q.d. for 12-15 days versus enoxaparin 30 mg SC BID after surgery for 12-15 days	Total knee replacement	double blind US, Canada, Mexico, UK
dabigatran 220mg vs enoxaparin (US regimen)			

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Trial	Treatments	Patients	Trials design and methods
RE-MOBILIZE (220mg) , 2008 n=862/876 follow-up: 12-15 days, median 14d	dabigatran etexilate 220 mg for 12-15 days versus Enoxaparin 30mg SC BID after surgery for 12-15 days	Total knee replacement	Parallel groups double blind US, Canada, Mexico, UK

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7 platelet aggregation inhibitors

19

Trial	Treatments	Patients	Trials design and methods
Aspirin vs no treatment			
Pasteyer , 1977 n=20/20 follow-up: 2 weeks	Aspirin 1000mg daily + Hep versus control (Hep alone)	Elective orthopaedic surgery	Parallel groups
Rocha , 1986 n=60/30 follow-up: 1 weeks	Aspirin 250mg or 1000mg daily versus control (combination of heparin plus dihydroergotamine)	total hip replacement	Parallel groups open
aspirin + dipyridamol vs no treatment			
Morris-B , 1977 n=32/32 follow-up:	Aspirin 900 mg daily + dipyridamole versus control	elderly patients with hip fractures	Parallel groups open
Lyon-I , 1975 n=20/20 follow-up: 2 weeks	Aspirin 1500 mg daily + Dipyridamole versus control	Elective orthopaedic surgery	
dipyridamol vs no treatment			
Morris-A , 1977 n=24/24 follow-up:	dipyridamole versus control	elderly patients with hip fractures	Parallel groups open
Flurbiprofen vs no treatment			
Mocris-C , 1977 n=20/20 follow-up:	Flurbiprofen versus control	elderly patients with hip fractures	Parallel groups open

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Trial	Treatments	Patients	Trials design and methods
Hydroxychloroquine vs no treatment			
Massachusetts-I , 1981 n=50/25 follow-up:	Aspirin 1200mg daily, Aspirin 1200mg daily + hydroxychloroquine 300 mg b.i.d. versus control	patients with upper femoral fractures	Parallel groups open
aspirin vs placebo			
Zekert-I , 1974 n=138/140 follow-up:	Aspirin 1500mg daily versus placebo	patients undergoing surgery of hip-joint proximal fractures	Parallel groups double-blind
Powers , 1976 n=66/63	A1300 versus placebo	traumatic orthopaedic surgery	
Erfurt-B , 1979 n=44/44 follow-up:	A1500 versus placebo	traumatic orthopaedic surgery	double-blind
PEP hip-fracture , 2000 n=6679/6677 follow-up: 35 days	aspirin 160mg/d started preoperatively and continued for 35 days versus placebo	patients undergoing surgery for hip fracture	Parallel groups Double blind Australia, New Zealand, South Africa,
Stockholm-I , 1975 n=26/25 follow-up: 2 weeks	Aspirin 2000mg daily versus placebo	elective surgery of the hip	double blind
Harris-I , 1977 n=58/59 follow-up: 1 weeks	Aspirin 1200mg daily versus placebo	patients over 40 years of age, who had undergone total hip replacement	Parallel groups double-blind
McKenna-I , 1980 n=24/12 follow-up: 2 weeks	Aspirin 975mg or 3900mg daily versus placebo	total knee replacement	Parallel groups double-blind
Sautter , 1983 n=68/77 follow-up: 3 weeks	Aspirin 900mg daily + sulfapyrazone versus placebo	patient with total hip replacement	Parallel groups
McBride , 1983 n=21/22 follow-up: 1 weeks	A1800+Dipyridamole versus placebo	Elective orthopaedic surgery	
aspirin + dipyridamol vs placebo			
Encke-II , 1976 n=34/25 follow-up:	Aspirin 1500mg daily, Aspirin 990mg daily + dipyridamol versus placebo	patients with abdominal operations	Parallel groups double-blind
Hamburg , 1976 n=21/11 follow-up: 3 weeks	A+Dipyridamole,A1000 versus placebo	Elective orthopaedic surgery	
Hydroxychloroquine vs placebo			

continued...

Trial	Treatments	Patients	Trials design and methods
Danish-A , 1976 n=48/50 follow-up:	Hydroxychloroquine sulphate versus placebo	patients with fractures of the hip, pelvis, or thoracolumbar spine	Parallel groups double-blind
Danish-B , 1976 n=27/28 follow-up:	Hydroxychloroquine sulphate versus placebo	patients with fractures of the hip, pelvis, or thoracolumbar spine	Parallel groups
Massachusetts-II , 1976 n=51/51 follow-up: 3 weeks	Hydroxychloroquine 600mg daily versus placebo	fractures or orthopaedic operations involving the skeleton between the knee and the pelvis	
Cooke , 1977 n=25/25 follow-up: 2 weeks	Hydroxychloroquine versus placebo	elective surgery on the hip	Parallel groups double-blind
Hume-A , 1977 n=20/20 follow-up: 2 weeks	Hydroxychloroquine versus placebo	total hip replacement	
Stockholm-II , 1981 n=18/17 follow-up: 2 weeks	Hydroxychloroquine versus placebo	total hip replacement	
RA233 vs placebo			
65279;Wood , 1973 n=21/9 follow-up:	RA233; Aspirin 600mg daily +RA233 versus placebo	traumatic orthopaedic surgery	
Ticlopidine vs placebo			
McKenna-II , 1983 n=29/29 follow-up: 2 weeks	Ticlopidine versus placebo	Elective orthopaedic surgery	
Lyon-II , 3000 n=20/20 follow-up: 3 weeks	Ticlopidine versus placebo	Elective orthopaedic surgery	
Gardecki , 3000 n=48/46 follow-up: 2 weeks	Ticlopidine versus placebo	Elective orthopaedic surgery	

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8 recombinant hirudin

Trial	Treatments	Patients	Trials design and methods
desirudin vs enoxaparin			
Ericksson , 1997 n=NA follow-up:	desirudin 15mg SC twice daily for 8-12 days versus enoxaparin 40mg once daily for 8-12 days	Patients who undergo total hip replacement	Parallel groups double blind Europe
desirudin vs UFH			
REVASC , 1997 n=225/220 follow-up:	desirudin 15mg twice daily versus unfractionated heparin 5000 IU three times a day	patients having a primary elective total hip replacement	Parallel groups

continued...

Trial	Treatments	Patients	Trials design and methods
Eriksson , 1996 n=1119 follow-up:	recombinant hirudin, desirudin (CGP 39393) 10, 15, or 20 mg twice daily started just before surgery and continued for 8-11 days versus unfractionated heparin 5000 IU three times daily started just before surgery and continued for 8-11 days	patients undergoing elective hip surgery	Parallel groups double blind Europe

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9 synthetic oligosaccharide

Trial	Treatments	Patients	Trials design and methods
fondaparinux vs control			
NCT00320398 <i>ongoing</i> [NCT00320398] n=NA follow-up:	-	patients undergoing either an elective primary total hip replacement (THR) surgery or a revision of a THR	double-blind Japan
fondaparinux vs placebo			
DRI4757 n=345/87 follow-up: 14 days	fondaparinux subcutaneously at 0.75, 1.5, 2.5, and 3.0 mg for at least 10 calendar days, (with a maximum of 14 days) versus placebo	Japanese patients undergoing elective total knee replacement surgery	Parallel groups double blind Japan
fondaparinux vs enoxaparin			
L8541 n=119/118 follow-up: 9 days (49d)	fondaparinux 2.5mg subcutaneous once-daily for 7+/-2 days versus enoxaparin 40mg s.c. once-daily	chinese patients undergoing major orthopaedic surgery of the lower limbs	Parallel groups single-blind China

continued...

Trial	Treatments	Patients	Trials design and methods
L8635 n=28/23 follow-up: 10 days	Fondaparinux 2.5mg once daily subcutaneously for 7 days versus enoxaparin 40mg once daily SC for 7 days	Taiwanese patients undergoing elective knee replacement	Parallel groups open, blind assessment Taiwan
PENTAMAKS (Bauer) , 2001 n=517/517 follow-up: 11 days	fondaparinux 2.5-mg once-daily subcutaneous, starting 6 hours after surgery versus enoxaparin 30mg twice daily (North america recommendation)	elective major knee surgery	Parallel groups double blind North america
PENTHIFRA (Eriksson) , 2001 n=831/840 follow-up: 11 days	fondaparinux 2.5-mg once-daily subcutaneous, starting 6 hours after surgery versus enoxaprin 40mg once daily	hip fracture surgery	Parallel groups double blind 21 countries
EPHESUS (Lassen) , 2002 n=1155/1154 follow-up: 11 days (6 weeks)	fondaparinux 2.5-mg once-daily subcutaneous, starting 6 hours after surgery versus enoxaprin 40mg once daily	elective hip replacement surgery	Parallel groups double blind 16 European countries
PENTATHLON (Turpie) , 2002 n=1138/1137 follow-up: 11 days	fondaparinux 2.5-mg once-daily subcutaneous, starting 6 hours after surgery versus enoxaparin 30mg twice daily (North america recommendation)	elective hip replacement surgery	Parallel groups double blind USA, Canada, Australia
Turpie , 2001 n=673/260 follow-up: >15 days	pentasaccharide Org31540/SR90107A subcutaneous once daily at doses 0.75 mg, 1.5 mg, 3.0 mg, 6.0 mg, and 8.0 mg versus enoxaparin 30mg once daily subcutaneous	patients undergoing total hip replacement	Parallel groups double blind US, Canada, Australia
SR123781A vs enoxaparin			
DRIVE , 2008 [NCT00338897] n=854/169 follow-up: 5-10 days	SR123781A for 5-10 days, doses ranging from 0.25 to 4.0 mg daily for 10 days versus enoxaparin 40 mg	patients undergoing total hip replacement surgery	Parallel groups double blind 12 countries
extended prophylaxis vs standard prophylaxis			
PENTHIFRAPLUS (Eriksson) , 2003 n=656 follow-up: 19-23 days	25-31 days of fondaparinux 2.5-mg once-daily versus 6-8 days of fondaparinux 2.5-mg once-daily	patients undergoing hip fracture surgery	Parallel groups double blind

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L8541, 0:

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10 unfractionated heparin

Trial	Treatments	Patients	Trials design and methods
UFH vs no treatment			
Bergqvist , 1979 n=84/77	UFH twice daily for 5 days versus no treatment	elective orthopedic surgery	
Bergqvist , 1979 n=32/23	UFH twice daily for 5 days versus no treatment	traumatic orthopedic surgery	
Dechavanne , 1974 n=29/29	UFH 3 times daily for 10 days versus no treatment	elective orthopedic surgery	
Dechavanne , 1975 n=20/21	UFH 3 times daily for 10 days versus no treatment	elective orthopedic surgery	
Galasko , 1976 n=50/50	UFH twice daily (duration unknown) versus no treatment	traumatic orthopedic surgery	

continued...

Trial	Treatments	Patients	Trials design and methods
Gallus , 1973 n=23/23	UFH 3 times daily for A versus no treatment	traumatic orthopedic surgery	
Mannucci , 1976 n=23/24	UFH 3 times daily for 7 days versus no treatment	elective orthopedic surgery	
Morris , 1974 n=36/36	UFH twice daily for 10 days versus no treatment	elective orthopedic surgery	
Morris , 1977 n=24/24	UFH 3 times daily for 10 days versus no treatment	traumatic orthopedic surgery	
VTCSG , 1975 n=34/30	UFH twice daily for 10 days versus no treatment	elective orthopedic surgery	
Welin-Berger , 1982 n=20/20	UFH twice daily for 7 days versus no treatment	elective orthopedic surgery	
UFH vs placebo			
Abraham-Inpijn , 1975 n=12/13	UFH twice daily for 8 days versus placebo	elective orthopedic surgery	
Hampson , 1974 n=48/52	UFH 3 times daily for 7- 10 days versus placebo	elective orthopedic surgery	
Lahnborg , 1980 n=70/69	UFH twice daily for 10 days versus placebo	traumatic orthopedic surgery	
Lowe , 1981 n=51/49	UFH twice daily for 16 days versus placebo	elective orthopedic surgery	
Moskovitz , 1978 n=29/23	UFH 3 times daily for 7 days versus placebo	traumatic orthopedic surgery	
Moskovitz , 1978 n=35/32	UFH 3 times daily for 7 days versus placebo	elective orthopedic surgery	
Svend-Hansen , 1981 n=65/65	UFH 3 times daily for 14 days versus placebo	traumatic orthopedic surgery	
Williams , 1978 n=106/106	UFH twice daily for 14 days versus placebo	elective orthopedic surgery	

continued...

Trial	Treatments	Patients	Trials design and methods
Xabregas , 1977 n=27/26	UFH twice daily for 14 days versus placebo	traumatic orthopedic surgery	

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