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[Intervention Review]

Home versus in-patient treatment for deep vein thrombosis

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ABSTRACT

Background

Deep vein thrombosis (DVT) occurs when a blood clot blocks blood flow through a vein, which can occur after surgery, after trauma, or when a person has been immobile for a long time. Clots can dislodge and block blood flow to the lungs (pulmonary embolism (PE)), causing death. DVT and PE are known by the term venous thromboembolism (VTE). Heparin (in the form of unfractionated heparin (UFH)) is a blood-thinning drug used during the first three to five days of DVT treatment. Low molecular weight heparins (LMWHs) allow people with DVT to receive their initial treatment at home instead of in hospital. This is an update of a review first published in 2001 and updated in 2007.

Objectives

To compare the incidence and complications of venous thromboembolism (VTE) in patients treated at home versus patients treated with standard in-patient hospital regimens. Secondary objectives included assessment of patient satisfaction and cost-effectiveness of treatment.

Search methods

For this update, the Cochrane Vascular Information Specialist searched the Cochrane Vascular Specialised Register (last searched 16 March 2017), the Cochrane Central Register of Controlled Trials (CENTRAL; 2017, Issue 2), and trials registries. We also checked the reference lists of relevant publications.

Selection criteria

Randomised controlled trials (RCTs) examining home versus hospital treatment for DVT, in which DVT was clinically confirmed and was treated with LMWHs or UFH.

Data collection and analysis

One review author selected material for inclusion, and another reviewed the selection of trials. Two review authors independently extracted data and assessed included studies for risk of bias. Primary outcomes included combined VTE events (PE and recurrent DVT), gangrene, heparin complications, and death. Secondary outcomes were patient satisfaction and cost implications. We performed meta-analysis using fixed-effect models with risk ratios (RRs) and 95% confidence intervals (CIs) for dichotomous data.

Main results

We included in this review seven RCTs involving 1839 randomised participants with comparable treatment arms. All seven had fundamental problems including high exclusion rates, partial hospital treatment of many in the home treatment arms, and comparison of UFH in hospital versus LMWH at home. These trials showed that patients treated at home with LMWH were less likely to have recurrence of VTE events than those given hospital treatment with UFH or LMWH (fixed-effect risk ratio (RR) 0.58, 95% confidence interval (CI) 0.39 to 0.86; 6 studies; 1708

participants; $P = 0.007$; low-quality evidence). No clear difference was seen between groups for major bleeding (RR 0.67, 95% CI 0.33 to 1.36; 6 studies; 1708 participants; $P = 0.27$; low-quality evidence), minor bleeding (RR 1.29, 95% CI 0.94 to 1.78; 6 studies; 1708 participants; $P = 0.11$; low-quality evidence), or mortality (RR 0.69, 95% CI 0.44 to 1.09; 6 studies; 1708 participants; $P = 0.11$; low-quality evidence). The included studies reported no cases of venous gangrene. We could not combine patient satisfaction and quality of life outcomes in meta-analysis owing to heterogeneity of reporting, but two of three studies found evidence that home treatment led to greater improvement in quality of life compared with in-patient treatment at some point during follow-up, and the third study reported that a large number of participants chose to switch from in-patient care to home-based care for social and personal reasons, suggesting it is the patient's preferred option (very low-quality evidence). None of the studies included in this review carried out a full cost-effectiveness analysis. However, a small randomised economic evaluation of the two alternative treatment settings involving 131 participants found that direct costs were higher for those in the in-patient group. These findings were supported by three other studies that reported on their costs (very low-quality evidence).

Quality of evidence for data from meta-analyses was low to very low. This was due to risk of bias, as many of the included studies used unclear randomisation techniques, and blinding was a concern for many. Also, indirectness was a concern, as most studies included a large number of participants randomised to the home (LMWH) treatment group who were treated in hospital for some or all of the treatment period. A further issue for some outcomes was heterogeneity that was evident in measurement and reporting of outcomes.

Authors' conclusions

Low-quality evidence suggests that patients treated at home with LMWH are less likely to have recurrence of VTE than those treated in hospital. However, data show no clear differences in major or minor bleeding, nor in mortality (low-quality evidence), indicating that home treatment is no worse than in-patient treatment for these outcomes. Because most healthcare systems are moving towards more LMWH usage in the home setting it is unlikely that additional large trials will be undertaken to compare these treatments. Therefore, home treatment is likely to become the norm, and further research will be directed towards resolving practical issues by devising local guidelines that include clinical prediction rules, developing biomarkers and imaging that can be used to tailor therapy to disease severity, and providing training for community healthcare workers who administer treatment and monitor treatment progress.

PLAIN LANGUAGE SUMMARY

Home versus in-patient treatment for deep vein blood clots

Background

Deep vein thrombosis (DVT) occurs when a blood clot blocks the flow of blood through a vein, generally in the legs. This can happen after surgery, after trauma, when a person is immobile for a long time, or for no obvious reason. Clots can dislodge and block blood flow to the lungs (pulmonary embolism (PE)), which can be fatal. DVT and PE are known as venous thromboembolism (VTE). Heparin is a blood-thinning drug that is used to treat DVT during the first three to five days. Unfractionated heparin (UFH) is administered intravenously in hospital with laboratory monitoring. Low molecular weight heparins (LMWHs) are given by subcutaneous injection once a day and can be given at home. Oral anticoagulants are then continued for three to six months. After recovery from the acute episode, people may develop post-thrombotic syndrome with leg swelling, varicose veins, and ulceration.

Study characteristics and key results

Seven randomised controlled trials involving 1839 patients with clinically confirmed DVT compared home (LMWH) versus hospital (unfractionated heparin, or LMWH in one trial) treatment. Trials had limitations, including high exclusion rates and designs that did not take into account short hospital stays for any of the people treated at home to allow fair comparison of heparin in hospital with LMWH at home.

Trials showed that patients treated at home with LMWH had less recurrence of VTE than hospital-treated patients. The review showed no clear differences between treatment groups for major bleeding, minor bleeding, or death. No study reported venous gangrene. We could not pool information on patient satisfaction and quality of life, as studies had different ways of reporting these, but two of the three studies reporting on quality of life provided evidence that home treatment led to greater improvement in quality of life compared with in-patient treatment, at some point during follow-up. The third study reported that a large number of participants chose to switch from in-patient care to home-based care for social and personal reasons, indicating that home treatment was better accepted than in-patient treatment. Studies that looked at cost found that cost of home management was lower per incident of treatment.

Quality of the evidence

Overall, the quality of evidence of the available data was low to very low owing to risk of bias, indirectness, and differences in measuring and reporting of outcomes. Risk of bias is a concern, as many of the included studies did not fully explain how they randomised and allocated participants to treatments, and blinding techniques described were not clear. Full blinding would be difficult if not impossible for these types of treatments (home vs hospital), but some techniques could be put in place such as using the same treatment medications or blinding those who measure outcomes. Another concern of reviewers was that in some studies, participants randomised to home treatment actually ended up being treated in hospital but remained in their assigned treatment for the analysis (this is known as indirectness). This makes it hard to determine whether trial results actually can be used to answer the question of whether home versus

hospital treatment for DVT is superior. A further concern regarding a few of outcomes is variation in the way outcomes were measured and reported.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Treatment of DVT at home compared with treatment in hospital

How does treatment of DVT at home compare with treatment in hospital?

Patient or population: people with diagnosed DVT

Setting: hospital and home

Intervention: treatment of DVT at home with LMWH^a

Comparison: treatment of DVT in hospital with UFH or LMWH^b

Outcomes	No. of participants (studies) Follow-up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)		Comments
				Risk with treatment of DVT in hospital	Risk difference with treatment of DVT at home	
Recurrence of VTE Follow-up: range 3 months to 12 months	1708 (6 RCTs)	⊕⊕⊕⊕ LOW ^{c,d}	RR 0.58 (0.39 to 0.86)	Study population 74 per 1000	 31 fewer per 1000 (45 fewer to 10 fewer)	
Venous gangrene	See comment.					This outcome was not reported by any of the included studies.
Major bleeding Follow-up: range 14 days to 12 months	1708 (6 RCTs)	⊕⊕⊕⊕ LOW ^{c,d}	RR 0.67 (0.33 to 1.36)	Study population 21 per 1000	 7 fewer per 1000 (14 fewer to 8 more)	
Minor bleeding Follow-up: range 14 days to 12 months	1708 (6 RCTs)	⊕⊕⊕⊕ LOW ^{c,d}	RR 1.29 (0.94 to 1.78)	Study population 72 per 1000	 21 more per 1000 (4 fewer to 56 more)	
Death fFollow-up: range 3 months to 12 months	1708 (6 RCTs)	⊕⊕⊕⊕ LOW ^{c,d}	RR 0.69 (0.44 to 1.09)	Study population 49 per 1000	 15 fewer per 1000	

				(28 fewer to 4 more)	
Patient satisfaction/Quality of life Follow-up: range 7 days to 6 months	1031 (3 RCTs)	⊕⊕⊕⊕ VERY LOW ^{c,d,e}	-	See comment.	Two studies reported greater improvement in QoL among participants treated at home than among those receiving in-patient treatment; the third study reported that a large number of participants chose to switch from in-patient care to home-based care, suggesting this may be patients' preferred option.
Cost-effectiveness^f Follow-up: range 10 days to 6 months	834 (4 RCTs)	⊕⊕⊕⊕ VERY LOW ^{c,d,e}	-	See comment.	One study carried out a randomised economic evaluation and reported that total direct costs were higher for participants in the in-patient strategy group (i.e. Swedish Crown (SEK) 16,400 per participant (EUR 1899) compared with SEK 12,100 per participant (EUR 1405)) than for those in the out-patient (home) strategy group (P < 0.0010). This was supported by 3 other studies that reported on costs.

*We calculated the assumed risk of the hospital treatment group from the average risk in the hospital treatment group (i.e. the number of participants with events divided by the total number of participants in the hospital treatment group included in the meta-analysis). **The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; DVT: deep vein thrombosis; LMWH: low molecular weight heparin; RR: risk ratio; UFH: unfractionated heparin; VTE: venous thromboembolism.

GRADE Working Group grades of evidence.

High quality: We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

^aHome treatment refers to treatment for DVT with an LMWH that occurs outside of a hospital or in-patient setting and can include the medication being administered by the participant or by a caregiver.

^bHospital treatment refers to treatment for DVT with an LMWH or a UFH in a hospital or in-patient setting that is administered by care staff.

^cDowngraded one level owing to risk of bias from unclear randomisation techniques and blinding measures in most included studies.

^dDowngraded one level owing to indirectness because most of the included studies had few participants actually treated at home with an LMWH, and many were treated in hospital.

^eDowngraded one level owing to heterogeneity because the included studies used different methods and time points for gathering information on this outcome.

^fWe are reporting on the cost-effectiveness analysis reported in the included studies. We have not carried out an economic analysis ourselves.

BACKGROUND

Description of the condition

Deep vein thrombosis (DVT) is a frequent disorder in western medical practice, affecting one to two per thousand of the adult population annually. DVT occurs in conjunction with malignancy, after surgery, and after trauma and immobilisation, and can occur spontaneously. It manifests in the acute stage with leg symptoms and, in a small minority, with potentially fatal pulmonary embolism (PE). Venous thromboembolism (VTE) is a term that refers to both DVT and PE. After recovery from the acute episode, people may develop post-thrombotic syndrome with leg swelling, varicosis, and ulceration. Gold standard techniques for diagnosing DVT include ascending venography and duplex ultrasound scanning. Deep vein thrombosis is most commonly managed by anticoagulants to prevent spread of the clot proximally and to allow it to become adherent or undergo fibrinolysis, thus reducing the risk of PE. Currently used anticoagulant treatments include unfractionated and low molecular weight heparin (UFH and LMWH, respectively), as well as vitamin K antagonists (VKAs), primarily warfarin, and direct oral anticoagulants (DOACs) (NICE 2012; Robertson 2015; van Es 2014).

Description of the intervention

In the hospitalised patient, UFH is usually administered intravenously, with laboratory monitoring for about five days, overlapping with oral anticoagulants, which are continued for three to six months. LMWH is administered daily by subcutaneous injection; it can be delivered at home without the need for continuous laboratory monitoring and may be followed by an oral anticoagulant regimen.

Why it is important to do this review

Development of LMWHs has resulted in many trials investigating their efficaciousness and safety, as compared with UFH. These studies show that LMWH is at least as effective as UFH; some meta-analyses and reviews show that LMWH is more effective and safer than UFH (Erkens 2010; Leizorovicz 1994; Lensing 1995). Because LMWH is given subcutaneously once per day and requires no laboratory monitoring, it is possible to treat people with LMWH at home. Although LMWH has been available since 1976, home treatment has not been investigated further since the time it was first reported in 1988 (Bakker 1988). Rigorous evaluation of home versus in-patient care is required to inform policy on alternative strategies for treating patients with DVT. Home treatment of DVT offers potential cost savings and improved social acceptability for the patients. This review aims to update the review that was first published in 2001 and updated in 2007 (Othieno 2007).

OBJECTIVES

To compare the incidence and complications of venous thromboembolism (VTE) in patients treated at home versus patients treated with standard in-patient hospital regimens. Secondary objectives included assessment of patient satisfaction and cost-effectiveness of treatment.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) in which participants were randomised to home or in-patient treatment. Exclusion criteria before randomisation had to be stated and the trial author's policy regarding protocol violations and withdrawals known (i.e. intention-to-treat basis).

Types of participants

We included people with proven VTE who had no contraindication to heparin therapy, and whose home circumstances were adequate. Participants had to present with objective evidence of DVT such as duplex scanning and/or venography.

Types of interventions

We included studies that compared home versus hospital management with LMWH (which can be used in either setting) or UFH (which is used in hospital only). Trials involving a placebo group are not ethically acceptable.

Types of outcome measures

Primary outcomes

- Recurrence of VTE: PE or recurrence of DVT (depending on length of follow-up)
- Venous gangrene
- Heparin complications: major and minor bleeding (the former defined as bleeding within the abdomen, cranium, or eye, or requiring transfusion, or causing a fall in haemoglobin ≥ 2 g/dL)
- Death

Ideally, evidence of PE is derived from lung scans, spiral computed tomography (CT), or pulmonary angiography, but as these methods were not likely to be widely available, we considered X-rays, electrocardiograms (ECGs), and strong clinical signs acceptable. In the event of death, postmortem evidence was desirable.

Secondary outcomes

- Patient satisfaction and quality of life
- Cost-effectiveness of treatment (as reported by individual studies)

We will also report on other outcomes of interest (i.e. post-thrombotic syndrome or length of stay in hospital), when reported by individual studies.

Search methods for identification of studies

Electronic searches

For this update, the Cochrane Vascular Information Specialist (CIS) searched the following databases for relevant trials.

- Cochrane Vascular Specialised Register (16 March 2017).
- Cochrane Central Register of Controlled Trials (CENTRAL; 2017, Issue 2) via the Cochrane Register of Studies Online.

See [Appendix 1](#) for details of the search strategy used for CENTRAL.

The Cochrane Vascular Specialised Register is maintained by the CIS and is constructed from weekly electronic searches of MEDLINE Ovid, Embase Ovid, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), and the Allied and Complementary Medicine Database (AMED), as well as through handsearching of relevant journals. The full list of databases, journals, and conference proceedings searched, as well as the search strategies used, are described in the [Specialised Register](#) section of the Cochrane Vascular module in the Cochrane Library (www.cochranelibrary.com).

In addition, the CIS searched the following trial databases for details of ongoing and unpublished studies (16 March 2017). See [Appendix 2](#).

- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) Search Portal (apps.who.int/trialsearch).
- ClinicalTrials.gov (clinicaltrials.gov).
- International Standard Randomised Controlled Trial Number (ISRCTN) Registry (www.isrctn.com).

Searching other resources

We identified additional articles by reviewing the references of relevant papers identified by the initial search.

Data collection and analysis

Selection of studies

For this update, three review authors (RO, EO, RF) independently selected trials. Final selection of articles was agreed upon through discussion and consensus.

Data extraction and management

Two review authors (RO, EO) independently extracted data from existing and newly included trials using the criteria designated by Cochrane Vascular. For some references, we sought clarification from trial authors. Two review authors (RO, EO) performed data entry.

Assessment of risk of bias in included studies

Two review authors (RO, EO) independently assessed the risk of bias of all included studies using Cochrane's 'Risk of bias' tool, as described in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)). We rated studies as having 'low risk of bias' (plausible bias that is unlikely to seriously alter the results); 'high risk of bias' (plausible bias that seriously weakens confidence in the results); or 'unclear risk of bias' (plausible bias that raises some doubt about results). We assessed included RCTs against the six domains listed below.

- Sequence generation: Was the allocation sequence adequately described?
- Allocation concealment: Was allocation adequately concealed?
- Blinding of participants, personnel, and outcome assessors: Was knowledge of the allocation intervention adequately prevented during the study?
- Incomplete outcome data: Were incomplete outcome data adequately addressed?

- Selective outcome reporting: Are reports of the study free of the suggestion of selective outcome reporting?
- Other sources of bias: Did the study appear to be free of other problems that could put it at high risk of bias?

Measures of treatment effect

Two review authors (RO, EO) performed the data analysis according to the statistical guidelines provided for review authors by Cochrane Vascular. When data were sufficient, we calculated risk ratios (RRs) with 95% confidence intervals (CIs) using Review Manager software ([RevMan 2014](#)).

Unit of analysis issues

None of the included studies applied non-standard designs, such as cross-over trials or cluster-randomised trials. Therefore we made no adjustments for measurement effects. The individual participant was the unit of analysis.

Dealing with missing data

We aimed to conduct a complete-case analysis in this Cochrane Review, such that we included in the analysis all participants with a recorded outcome. We analysed data on an intention-to-treat basis as far as possible. When data were missing, we made attempts to obtain them from the original investigators. When they were unobtainable, we analysed only available data, based on the numerator and the denominator reported in study results or calculable from reported percentages.

Assessment of heterogeneity

We examined heterogeneity between trials by visually examining forest plots to judge whether any differences between studies in direction or size of the treatment effect were apparent. We also considered I^2 and Tau^2 statistics and the P value of the Chi^2 test for heterogeneity. If we identified heterogeneity among trials (i.e. if the value of I^2 was greater than 30%, and the value of Tau^2 was greater than zero or the P value of the Chi^2 test for heterogeneity was lower than 0.1), we planned to explore heterogeneity by performing prespecified sensitivity analysis as described below.

Assessment of reporting biases

In view of the difficulty involved in detecting and correcting for publication bias and other reporting biases, we aimed to minimise their potential impact by ensuring a comprehensive search for eligible studies and by staying alert for duplication of data. We planned to use a funnel plot to assess the possibility of small-study effects (a tendency for estimates of the intervention effect to be more beneficial in smaller studies) for the primary review outcomes when we included 10 or more studies in meta-analyses ([Higgins 2011](#)). We intended to cautiously consider visible asymmetry in the funnel plot as a possible indication of publication bias.

Data synthesis

We carried out statistical analysis using Review Manager software ([RevMan 2014](#)). We used a fixed-effect meta-analysis for combining data when it was reasonable to assume that studies were estimating the same underlying treatment effect (i.e. when trials were examining the same intervention, and when we judged that trial populations and methods were sufficiently similar).

We planned to use random-effects meta-analysis if clinical heterogeneity was sufficient to expect that underlying treatment effects differed between trials, or if we detected substantial statistical heterogeneity.

Subgroup analysis and investigation of heterogeneity

If identified, we planned to explore any possible evidence of heterogeneity within meta-analyses by performing subgroup analysis. We planned to perform no other subgroup analyses.

Sensitivity analysis

We performed sensitivity analyses by excluding studies that we judged to be at high risk of bias to determine effects on overall findings. We also performed sensitivity analysis if a single study carried most of the weight when we included three or more studies in an analysis. We performed additional sensitivity analysis to determine the robustness of findings that included data from [Koopman 1996](#), [Levine 1996](#), and [Ramacciotti 2004](#), when we found that participants randomised to LMWH were treated only at home, as determined by a clinician, but were not specifically assigned to home treatment.

'Summary of findings'

We presented the main findings of the review concerning quality of evidence, magnitude of effect of interventions examined, and the sum of available data for all outcomes of this review ([Types of outcome measures](#)) in a 'Summary of findings' table, according to GRADE principles, as described by [Higgins 2011](#) and [Atkins 2004](#). We evaluated evidence on the basis of risk of bias of the included studies, inconsistency, indirectness, and imprecision of data, as well as publication bias. We used GRADEprofiler (GRADEpro) software to assist in preparation of the 'Summary of findings' table ([GRADEProGDT 2015](#)), and we used the [Ryan 2016](#) publication to prepare GRADE ratings.

RESULTS

Description of studies

Results of the search

See [Figure 1](#).

Figure 1. Study flow diagram.

Included studies

In total, seven studies with a total of 1839 participants were eligible for inclusion in this review (Bäckman 2004; Boccalon 2000; Chong 2005; Daskalopoulos 2005; Koopman 1996; Levine 1996; Ramacciotti 2004). We identified one new study for inclusion in this review update (Bäckman 2004). This study had previously been excluded on the grounds that it did not assess any of the primary outcomes, but after further assessment, we decided we should include it, as the study did report on economic data.

Three large trials randomised 298 (150 home and 148 hospital), 400 (202 home and 198 hospital), and 500 participants (247 home and 253 hospital), respectively (Chong 2005; Koopman 1996; Levine 1996). Three trials were smaller (Boccalon 2000; Daskalopoulos 2005; Ramacciotti 2004). Boccalon 2000 reported results on 201 randomised participants (99 home and 102 hospital); Ramacciotti 2004 reported results on 104 home and 97 hospital randomised participants; and in Daskalopoulos 2005, investigators randomised 108 participants (55 to home and 53 to hospital). Bäckman 2004 evaluated and compared direct and indirect medical costs during a three-month period for 131 randomised participants (65 out-patient/home and 66 in-patient).

Bäckman 2004 did not report on any of the predefined outcomes of this review other than costs; therefore we did not include this study in any meta-analyses for these outcomes.

The three major trials (Chong 2005; Koopman 1996; Levine 1996) were similar in construction and results but differed in their exclusion rates (see [Characteristics of included studies](#); further discussed in [Overall completeness and applicability of evidence](#)). Of the seven trials, only Boccalon 2000 and Bäckman 2004 used LMWH in both treatment arms; the other five used LMWH in home treatment arms and UFH in hospital treatment arms.

See [Characteristics of included studies](#) tables for further details of the included studies.

Excluded studies

For this update, we excluded an additional five studies (Aujesky 2011; Hull 2009; Modesto-Alapont 2006; Otero 2010; Wilson 2003), for a total of 26 excluded studies (Aujesky 2011; Belcaro 1999; Blattler 1998; Buller 2004; Conner 1999; Fitzmaurice 2000; Frank 1998; Goldhaber 1998; Grau 1998; Grau 2001; Green 1998; Hull

2000; Hull 2002; Hull 2009; Lindmarker 1996; Miles 1998; Modesto-Alapont 2006; O'Shaughnessy 1998; Otero 2010; Pineo 2003; Rymes 2002; Ting 1998; Wells 1998; White 1989; Wilson 2003; Wimperis 1998).

Eight were uncontrolled studies (Conner 1999; Grau 1998; Green 1998; Lindmarker 1996; Miles 1998; O'Shaughnessy 1998; Ting 1998; Wimperis 1998), and two were retrospective studies (Grau 2001; Rymes 2002). We excluded the remaining 16 trials for a variety of reasons. We excluded two reported controlled trials because participants were not actually randomised but instead were treated according to their expressed therapeutic preferences (Blattler 1998; Frank 1998). We excluded Wells 1998 because this study compared patient-administered versus nurse-administered injections rather than the location of treatment; Goldhaber 1998 because participants randomised to treatment with LMWH in a home setting were first required to be treated in hospital for several days; Otero 2010 and Aujesky 2011 because these studies focussed on PE - not DVT; Belcaro 1999 because this was primarily a trial of formulations of heparin rather than a trial of home versus hospital treatment; Hull 2000 and Modesto-Alapont 2006 because investigators were concerned with prophylactic regimens including LMWH for patients undergoing hip arthroplasty and for those with VTE in obstructive pulmonary disease, respectively; Pineo 2003 and Hull 2002 because they investigated two protocols on long-term effects of LMWH treatment - not location; and two other trials because they did not include in-patient arms - Wilson 2003 compared anticoagulant clinics versus family clinics, and Hull 2009 compared long-term subcutaneous tinzaparin versus initial tinzaparin followed by long-term warfarin in the community as opposed to home patients versus in-patients. White 1989 and Fitzmaurice 2000 were concerned with monitoring oral anticoagulation at home or in general practitioner (GP) surgery. Buller 2004 compared once-daily LMWH versus twice-daily doses in the out-patient setting, and LMWH versus UFH in the out-patient setting - not hospital versus home.

See also [Characteristics of excluded studies](#).

Risk of bias in included studies

Figure 2 gives an overall view of our assessment of included studies' risk of bias, and Figure 3 shows the 'Risk of bias' summary presented as percentages across all included studies. See also [Characteristics of included studies](#).

Figure 2. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Bäckman 2004	?	+	+	-	+	+	?
Boccalon 2000	?	+	+	-	-	+	+
Chong 2005	?	?	-	+	+	+	?
Daskalopoulos 2005	+	?	-	+	+	+	+
Koopman 1996	?	+	-	+	+	+	?
Levine 1996	?	+	-	+	+	+	?
Ramacciotti 2004	?	-	-	-	-	+	?

Figure 3. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Allocation

We considered the following methods of allocation concealment adequate.

- Central allocation, including telephone randomisation.
- Use of sequentially numbered, opaque, sealed envelopes.

We deemed risk of bias as low if study authors described one of these methods. We deemed risk of bias as unclear if researchers described the trial as randomised but did not describe the method used for allocation concealment.

All included trials were reported as randomised controlled trials (RCTs). Random sequence generation was unclear in six studies (Bäckman 2004; Boccalon 2000; Chong 2005; Koopman 1996; Levine 1996; Ramacciotti 2004) but was adequate in a single trial (Daskalopoulos 2005) as these investigators reported using a computerised process.

Four trials adequately concealed allocation (Bäckman 2004; Boccalon 2000; Koopman 1996; Levine 1996). Daskalopoulos 2005 did not report the method used, and Chong 2005 did not report allocation concealment, so we rated both as having unclear risk of bias. In the Ramacciotti 2004 study, researchers performed randomisation by using blocks in an 'open manner'; we rated this study as having high risk of bias.

Blinding

Blinding refers to whether participants and study personnel knew which participants were treated in hospital, and which received treatment at home. By the nature of this study, blinding was never going to be easy to achieve. Five studies were open, non-blinded studies (Chong 2005; Daskalopoulos 2005; Koopman 1996; Levine 1996; Ramacciotti 2004); we judged them to be at high risk of bias. Participants in Bäckman 2004 were allowed to change their assigned treatment or to leave the study after randomisation, but we determined the risk of performance bias as low for the outcomes of this study. Although Boccalon 2000 reported no blinding of participants or personnel, both groups

received the same treatment. All participants received an oral anticoagulant for the first three days. The review authors deemed that outcomes were unlikely to have been affected by lack of blinding of participants or personnel, and so we judged this trial to be at low risk of bias.

Four studies had independent outcome assessors, and we deemed them to have low risk of detection bias (Chong 2005; Daskalopoulos 2005; Koopman 1996; Levine 1996). Three studies did not report blinding of outcome assessors; therefore we deemed these studies to be at high risk of detection bias (Bäckman 2004; Boccalon 2000; Ramacciotti 2004).

Incomplete outcome data

Five of the seven included studies either reported on all participants or adequately described their loss to follow-up; we rated them as low risk (Bäckman 2004; Chong 2005; Daskalopoulos 2005; Koopman 1996; Levine 1996). Ramacciotti 2004 and Boccalon 2000 had a high rate of attrition, and we rated them as high risk.

Selective reporting

We assessed a study for risk of selective outcome reporting according to the following.

- The published report included all expected outcomes.
- Outcomes were reported systematically for all comparison groups, based on prospectively collected data.

We deemed risk of bias to be low if both of these criteria were met, unclear if these criteria were not met, and high if evidence indicated that data had been collected on outcomes of interest but were not reported in the study publication.

We did not find any indication suggesting that outcomes were selectively reported in the included studies, so we rated all studies as low risk.

Other potential sources of bias

We had no concerns regarding other potential sources of bias for two studies (Boccalon 2000; Daskalopoulos 2005). For Bäckman 2004, Chong 2005, Koopman 1996, Levine 1996, and Ramacciotti 2004, information was insufficient for review authors to judge whether there was potential for other bias; we rated these as having unclear risk, as each study included a large number of participants in the LMWH/home treatment group who were treated in hospital. Koopman 1996, Levine 1996, and Ramacciotti 2004 differed methodologically, as participants randomised to LMWH were treated only at home, as determined by a clinician, but were not specifically assigned to home treatment. We evaluated these studies by performing sensitivity analysis to assess their impact on evidence obtained through meta-analysis. We have discussed these issues further in the section [Overall completeness and applicability of evidence](#).

Effects of interventions

See: [Summary of findings for the main comparison Treatment of DVT at home compared with treatment in hospital](#)

We have presented a summary of the findings of this review in [Summary of findings for the main comparison](#), and a summary of outcomes of included trials in [Table 1](#).

Recurrent VTE (PE or recurrence of DVT)

Six studies reported on this outcome (Boccalon 2000; Chong 2005; Daskalopoulos 2005; Koopman 1996; Levine 1996; Ramacciotti 2004). Outcome follow-up time ranged from three months to one year. Pooled results showed differences in recurrence of VTE between home and hospital treatment, with home treatment carrying less risk of recurrent VTE (RR 0.58, 95% CI 0.39 to 0.86; 1708 participants; 6 studies; $I^2 = 0\%$; $P = 0.007$; [Analysis 1.1](#)). We rated the evidence as low quality owing to risk of bias and indirectness concerns.

Venous gangrene

Included studies reported no cases of venous gangrene.

Heparin complications including major and minor bleeding

Six studies reported on this outcome (Boccalon 2000; Chong 2005; Daskalopoulos 2005; Koopman 1996; Levine 1996; Ramacciotti 2004). Outcome follow-up ranged from 14 days to one year.

Pooling of results on major bleeding revealed no clear differences between home and hospital treatment groups (RR 0.67, 95% CI 0.33 to 1.36; 1708 participants; 6 studies; $I^2 = 0\%$; $P = 0.27$; [Analysis 1.2](#)). We rated the evidence as low quality owing to risk of bias and indirectness concerns.

For the outcome of minor bleeding, data show no clear differences between hospital and home treatment arms (RR 1.29, 95% CI 0.94 to 1.78; 1708 participants; 6 studies; $I^2 = 0\%$; $P = 0.11$; [Analysis 1.3](#)). We rated the evidence as low quality owing to risk of bias and indirectness concerns.

Death

Six studies included reports on death, with follow-up ranging from three months to one year (Boccalon 2000; Chong 2005; Daskalopoulos 2005; Koopman 1996; Levine 1996; Ramacciotti

2004). Meta-analysis of trial results showed no clear differences in numbers of deaths between home- and hospital-treated groups (RR 0.69, 95% CI 0.44 to 1.09; 1708 participants; 6 studies; $I^2 = 0\%$; $P = 0.11$; [Analysis 1.4](#)). We rated the evidence as low quality owing to risk of bias and indirectness concerns.

Patient satisfaction and quality of life

Three studies included data on quality of life (QoL) (Bäckman 2004; Koopman 1996; Levine 1996). Bäckman 2004 assessed QoL using the EuroQoL tool based on five dimensions (EQ-5D) and found no differences between treatment groups in mean QoL scores, nor in the proportion of participants showing improvement in self-rated health state. QoL was assessed immediately after treatment and after three months. A substantial number of participants randomised to in-patient care in this study chose out-patient treatment, predominantly as a personal/social preference. The Koopman 1996 trial measured QoL by using the Medical Outcome Study Short Form 20 as a generic measure of physical and mental health, as well as an adapted version of the Rotterdam Symptom Checklist, which is specific to thrombosis; measurements were taken at baseline, at end of treatment course, and at 12 weeks and 24 weeks after treatment. At 24 weeks after treatment, over 80% of both trial groups had completed the QoL questionnaires. Overall, participants in both groups showed improvement in QoL; two out of six criteria (physical activity and social functioning) showed an advantage for those in the LMWH group at completion of initial treatment, but this difference was not seen at 12 weeks or at 24 weeks after treatment. Levine 1996 reported on QoL seven days after treatment using the Medical Outcomes Study Short Form 36, which reports on eight physical and mental health domains. Only the social functioning domain showed greater improvement among participants treated at home compared with those given heparin treatment; data show no differences between the two treatment groups in terms of the other domains (O'Brien 1999). We could not carry out meta-analysis for this outcome owing to heterogeneity in reporting of QoL and the paucity of data reported by trial authors.

We rated the quality of evidence for this outcome as very low owing to risk of bias, indirectness, and heterogeneity of measurement and reporting.

Cost-effectiveness of treatment

Bäckman 2004, Boccalon 2000, Daskalopoulos 2005, and Koopman 1996 all reported on cost-effectiveness of compared treatments, but because of the way investigators presented data, we could perform no meta-analysis for this outcome.

In Bäckman 2004, which reported on costs within three months of treatment, 224 participants were eligible, 131 entered the trial, and 124 completed the economic portion of the study. Total direct costs were higher for participants in the in-patient strategy group (i.e. Swedish Crown (SEK) 16,400 per participant (Euro (EUR) 1899) compared with SEK 12,100 per participant (EUR 1405)) than for those in the out-patient (home) strategy group ($P < 0.0010$).

Koopman 1996 followed participants for six months and used trial results to compare cost of treatment calculations between the two arms of the trial (van den Belt 1998). Data show a 64% savings among those treated with LMWH as opposed to UFH, largely owing to lower hospital costs. Trialists stated that this was a conservative estimate of the potential reduction in costs. Similarly, an evaluation

of participants entered into the [Levine 1996](#) trial showed cost savings of 57% ([O'Brien 1999](#)); researchers followed participants for three months. This latter figure is confirmed by [Boccalon 2000](#), which showed that the mean cost of in-patient treatment over 10 days was over 55% higher than the mean cost of out-patient treatment over the same time period. Similarly, in [Daskalopoulos 2005](#), which reported on 12 months of follow-up, estimated costs slightly favoured the LMWH group because of the significant cut in hospitalisation.

We rated the quality of evidence for this outcome as very low owing to risk of bias, indirectness, and heterogeneity of measurement and reporting.

Other outcomes of interest

None of the included trials considered the incidence of post-thrombotic syndrome.

Mean hospital stay for participants without events such as bleeding or (suspected) recurrences in [Koopman 1996](#) was 8.1 days for the hospital-treated 'control' group, and 2.7 days for the home-treated 'treatment' group. In the other large trial ([Levine 1996](#)), mean hospital stay was 6.5 days for the hospital-treated control group and 2.1 days for the home-treated group. Mean hospital stay in [Boccalon 2000](#) was 9.6 days for the hospital-treated group and one day for the home-treated group. [Ramacciotti 2004](#) reported a mean hospital stay of three days for home-treated participants and seven days for hospital-treated participants. Three studies did not report duration of hospital stay ([Bäckman 2004](#); [Chong 2005](#); [Daskalopoulos 2005](#)).

Thirty-six per cent of participants in [Koopman 1996](#) were treated entirely at home, 39% had a short hospital stay, and 25% were entirely hospital treated. Fifty per cent of participants in [Levine 1996](#) were treated entirely at home. In [Daskalopoulos 2005](#), no participant allocated to receive treatment with LMWH underwent any hospitalisation.

Seventy-seven per cent of participants in the home arm (LMWH group) of the [Chong 2005](#) trial were admitted to hospital. Twelve per cent were released on the day of admission, 34% were kept for one day, and 31% were kept for two or more nights. [Ramacciotti 2004](#) reported hospitalisation for all hospital-treated participants and for 64% of home-treated participants.

Heterogeneity, subgroup analysis, and sensitivity analysis

We found heterogeneity in pooled effect estimates to be very low and had no reason to further investigate. When we performed sensitivity analysis, we found no difference in the effect when we removed studies at high risk of bias ([Ramacciotti 2004](#)). No analyses showed a majority weight by a single study, so we performed no sensitivity analyses on these criteria. We performed sensitivity analysis by evaluating the impact of the [Koopman 1996](#), [Levine 1996](#), and [Ramacciotti 2004](#) trials given that participants randomised to LMWH were treated only at home, as determined by a clinician, but were not specifically assigned to home treatment. This sensitivity analysis did not change the findings.

DISCUSSION

Summary of main results

This review presents low-quality evidence suggesting that patients treated at home with low molecular weight heparin (LMWH) are less likely to have recurrence of venous thromboembolism (VTE) than those treated in an in-patient (hospital) setting. Data show no clear differences in major or minor bleeding events nor in mortality (all low-quality evidence), indicating that home treatment is no worse for these outcomes when compared with in-patient treatment.

Overall completeness and applicability of evidence

Although the results of this review are promising, review authors have several concerns about the applicability of the evidence. Our primary concern is that a large number of participants in the home treatment group were not treated solely at home. Also, there was heterogeneity in the findings of the larger trials, making it difficult to interpret and apply the results. Finally, a large number of eligible participants were excluded from trials before randomisation, raising concerns about applicability.

Many of the participants randomised to home treatment with LMWH were not actually treated fully at home but were hospitalised for some or all of the treatment period (see [Table 2](#) for details). Only 40% (in [Bäckman 2004](#)), 23% (in [Chong 2005](#)), 36% (in [Koopman 1996](#)), 48.5% (in [Levine 1996](#)), and 36% (in [Ramacciotti 2004](#)) of those randomised to home treatment were treated wholly at home, making trial results difficult to interpret. In three trials, participants randomised to LMWH treatment, as opposed to unfractionated heparin (UFH), could be treated at home or in an in-patient setting at the discretion of clinicians or investigators ([Koopman 1996](#); [Levine 1996](#); [Ramacciotti 2004](#)). This creates the concern that data collected and reported in meta-analyses may not directly speak to the question at hand. To address these issues, we conducted extensive sensitivity analyses and found no differences in our findings when we excluded the findings of these studies. This issue is a problem not just with these few trials; rather, it is an overall, possibly insurmountable problem, as deep vein thrombosis (DVT) and its complications by their nature may require in-patient treatment, even if a person is deemed acceptable for home treatment. However, these trials have shown that patients treated at home with LMWH are less likely to have recurrence of VTE than their counterparts treated in hospital with UFH or LMWH. Also, researchers found that participants preferred to have treatment at home. Concerns presented here most likely contribute to dilution of review conclusions.

The three major randomised controlled trials (RCTs) compared UFH in hospital versus LMWH at home ([Chong 2005](#); [Koopman 1996](#); [Levine 1996](#)). A more methodologically sound trial would have compared LMWH in both groups, and this would have been justified by the many trials and three meta-analyses showing that LMWH is at least as effective as UFH ([Erkens 2010](#); [Leizorovicz 1994](#); [Lensing 1995](#)).

Another factor limiting review conclusions was the very high prerandomisation exclusion rate reported by several trials ([Boccalon 2000](#); [Koopman 1996](#); [Levine 1996](#)). [Koopman 1996](#) reported exclusion of 31% of eligible participants, and [Levine 1996](#) reported exclusion of 67%. Similarly, [Boccalon 2000](#) (78%) and [Bäckman 2004](#) (42%) reported high exclusion rates. Exclusion

criteria were very diffuse and could have been less strict. [Daskalopoulos 2005](#) presented a contrasting low exclusion rate (7%). [Ramacciotti 2004](#) and [Chong 2005](#) did not report on prerandomisation exclusions, except for three participants in the [Chong 2005](#) trial, who were enrolled but were not randomised because they did not receive study treatment or did not provide treatment-related data.

Although we have included 'economic analysis' as an outcome, a comprehensive economic analysis is beyond the scope/expertise of this review, so we have reported only limited data available from the included studies.

Other issues that may affect applicability of our review include the limited number of participants from developing countries, and the fact that no high-quality RCTs have been published since 2005.

Trends in the treatment of individuals with VTE have been changing recently, with practitioners moving away from UFH and using more LMWHs along with the newer class of direct oral anticoagulants (DOACs). Treatment with LMWHs and DOACs has been shown to be efficacious, with no increase in clinically relevant complications ([Robertson 2015](#); [Robertson 2017](#)). Although UFH treatment is not going to disappear completely, practitioners have been moving away from its usage and embracing LMWH and DOACs owing to monitoring requirements and subsequent costs of treatment with UFH. However, clinicians using DOACs to treat patients with VTE have to reckon with their complexity, involving appropriate dose selection for the relevant indication, avoidance of drug-drug and drug-disease interactions, and consideration of dose adjustments in specific clinical situations, such as organ dysfunction ([Finks 2016](#)). This review did not evaluate any studies that included the use of DOACs, such as rivaroxaban or dabigatran, as no such studies met our inclusion criteria. We therefore have presented limited evidence in this review for detailed discussion of their use.

Quality of the evidence

Strengths of the evidence include the consistency and homogeneity of results from individual studies, as well as sufficient numbers of participants and events included for each outcome. However, we downgraded evidence generated in this review to low quality owing to concerns about risk of bias of individually included studies, as well as indirectness of the data due to issues surrounding hospitalisation of participants randomised to home treatment, as discussed in the previous section. A major concern associated with risk of bias was selection bias: All seven included studies were at unclear or high risk for concerns with random sequence generation or allocation concealment. Although minimising performance bias would be very difficult owing to the open nature of the treatment, making blinding of participants and personnel nearly impossible, these issues could be addressed in other ways, such as keeping treatment drugs consistent between interventions or demonstrating more stringent control of detection bias. Risk of bias concerns led us to downgrade the quality of evidence by one level. These concerns reduce the robustness of findings. See [Summary of findings for the main comparison](#) for further information.

We conducted sensitivity analysis by evaluating the strength of evidence in light of risk of bias issues, as well as concerns with indirectness, and we found that findings did not change when we removed studies with high risk of bias, or studies that may not have directly contributed to the objectives of the review.

We did not investigate publication bias for the review because we included fewer than 10 studies in the individual meta-analyses, precluding robust results in the funnel plots used to investigate publication bias.

Potential biases in the review process

During the review process, we adhered to all possible measures to reduce potential biases, including conducting a comprehensive search, performing double data extraction, and grading the evidence. We made attempts to identify relevant studies and discussed disagreements thoroughly.

Agreements and disagreements with other studies or reviews

The results of uncontrolled trials encompass a considerable body of evidence ([Table 3](#)), particularly in relation to practical questions (see [Implications for research](#)). An observational study that included 334 participants concluded that community-based treatment of individuals with thromboembolism was safe and effective ([Hyers 2007](#)). Home treatment has also been investigated in specific pathological communities, including individuals with cancer, and was found to be a suitable alternative to in-patient care ([Ageno 2005](#)).

In the UK, some local health authorities (Trusts) have published the results of uncontrolled studies. Swindon Trust reported that 373 patients were referred to the programme, of whom 32% had proven DVT and 37.5% were treated wholly or partially at home ([Green 1998](#)). Chertsey Trust reported on 1093 referrals, of which 160 were proven to have a diagnosis of DVT. All but one (i.e. 159 patients) were home-treated ([O'Shaughnessy 1998](#)). Researchers have reported no complications apart from two minor bleeds and estimated savings to Chertsey Trust as £320,000 over 22 months. In a combined presentation to the American Thoracic Society, three trusts reported that they managed the care of 966 patients with DVT, of whom only 10% were admitted to hospital ([Miles 1998](#)). In Norwich, 447 patients were referred over a six-month period, scans were positive in 30%, and 20% of these were considered unsuitable for home treatment ([Wimperis 1998](#)). Thus, 105 were treated and five had to be readmitted - two with suspected pulmonary embolism (PE) (negative scans), one with PE, one with stroke, and one with an unrelated illness ([Wimperis 1998](#)).

A study from Melbourne presented 100 participants with proven DVT ([Ting 1998](#)). Fifty-three participants had proximal thrombosis and were admitted for one day for investigation, including lung scan: 16 scans were positive, although participants were asymptomatic and the result did not affect their management at home. The 47 participants with distal thrombosis were treated entirely at home. The clot was initially extended in 13.2% of distal and 2.7% of proximal thromboses, but at follow-up scans at six months, 60.7% of distal and 18.5% of proximal thromboses had completely resolved. The only complications were six minor bleeds. The numbers of participants referred but cleared of DVT, and the numbers rejected by the protocol, were not mentioned. In a Swedish study, 434 participants with DVT were treated in hospital for three days before discharge home on treatment ([Lindmarker 1996](#)). Three participants had proven PE: One major bleed and 16 minor ones occurred. Data show no deaths in the acute stage and no extension of thromboses. In [Grau 1998](#), 39 out of 71 participants with DVT were treated at home. Investigators reported no instance

of PE and only one minor bleed. These trials all reported worthwhile cost savings. Only one uncontrolled study reported on patient satisfaction (Conner 1999). Seventy-nine per cent of participants were happy to be treated at home, 12% would have preferred hospital treatment, and 9% had no preference.

Although not based on evidence from RCTs, cost savings in favour of home treatment have been shown when calculated. Hospital Episode Statistics for the UK for 1993 show 17,000 admissions for PE and 25,000 for DVT, with an average in-patient stay of 7.2 days (Griffin 1996). At an estimated cost of £200 per in-patient day (1998 figures), hospitalisation costs alone amounted to £60,480,000. If this could be reduced to, say, two days in 75% of cases, at a cost of £12,600,000, a savings of £47,880,000 on bed costs per annum would be realisable. Although it was not in the remit of this review, it is worth noting that surveillance of participants up to four years after randomisation to home or hospital regimens revealed no differences between groups (Grau 2001).

Regarding the results of quality of life outcomes reported in Bäckman 2004, Blattler 1998 (excluded from our review as it was not an RCT) observed a similar preference in two-thirds of participants, who challenged hospital confinement and stated that they would not choose hospitalisation another time. The Blattler trial also reported that its home treatment group was free of symptoms a day earlier and returned to work a week earlier than the hospital treatment group (Blattler 1998).

AUTHORS' CONCLUSIONS

Implications for practice

This review presents low-quality evidence suggesting that patients treated at home with low molecular weight heparin (LMWH) are less likely to have recurrence of venous thromboembolism (VTE) than those treated in hospital. Researchers have found no clear differences in major or minor bleeding complications, nor in mortality (low-quality evidence), indicating that treatment at home with LMWH is not more harmful than treatment in an in-patient setting with LMWH or unfractionated heparin (UFH). Despite the limitations of reviewed trials, low-quality evidence suggests that home treatment of patients with DVT is more effective than standard hospital treatment.

Implications for research

It is unlikely that definitive evidence on the safety of home treatment will be forthcoming for reasons addressed in the discussion. This is underscored by the fact that during our

search, we identified no other high-quality randomised controlled trials published after 2005. Also, treatment of individuals with thromboembolism with LMWH is being incorporated into local health authority guidelines that include at-home administration practices (East Lancashire Health Economy 2015; Wong 2014). A larger database of accumulated uncontrolled studies that can be compared only with historical controls is needed. Anecdotal notes may describe treatment failure but as these occurrences will be rare, it is possible that they will not be published.

It has been suggested by Baron 1999 that patients should be allocated on a triage basis: (1) standard in-patient regimen for those with intercurrent illness or massive VTE; (2) partial home treatment for those receiving the diagnosis in hospital but fit enough for discharge; and (3) complete home treatment. The ideal trial would compare LMWH only in each arm, would exclude 25% or fewer participants from entry into the trial, and would present trial results in three groups. These issues should be given further examination.

Some practical issues remain to be resolved.

- Should the patient be admitted at all if suitable for home treatment?
- Should LMWH be given on suspicion or only on confirmation of the diagnosis?
- How would the treatment comparison be changed by use of newer direct oral anticoagulants versus more traditional LMWH?
- Should exclusion criteria be relaxed to favour greater entry to home treatment? For example, should a healthy pregnancy preclude home treatment?
- Should a screening test such as D-dimer levels be used?
- Should the system be controlled by the traditional physician's team, or should specialist anticoagulant nurses be trained? If so, will a lead clinician continue to accept overall responsibility?
- How should local guidelines be developed that include clinical prediction rules, biomarkers, and imaging that can be used to tailor therapy to disease severity?
- How should community healthcare workers be trained to administer treatment and monitor treatment progress?

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Boccalon 2000

Methods	<p>Study design: randomised controlled trial</p> <p>Exclusions post randomisation: One patient withdrew consent following randomisation, 7 withdrew owing to severe complications (3 DVT extensions, 4 major haemorrhages).</p> <p>Losses to follow-up: 38 participants did not complete the 6-month follow-up (those treated in hospital were twice as likely to withdraw).</p> <p>Intention-to-treat analysis: not indicated</p>
Participants	<p>Country: France</p> <p>Setting: home or hospital</p> <p>N: 204 randomised, 201 included (102 hospital, 99 home), representing 11.8% of those eligible</p>

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Boccalon 2000 (Continued)

Age: mean 63.8 ± 14.1 years, range 18 to 85 years

Sex: 113 male; 88 female

Inclusion criteria: confirmed diagnosis (by ultrasonography or venography) of proximal DVT not more than 30 days before enrolment

Exclusion criteria: thrombus in the inferior vena cava, a floating thrombus, history of DVT within the previous 6 months, DVT with symptomatic PE, a clinical condition requiring hospitalisation, contraindication to anticoagulant treatment, pregnancy, heparin treatment within the 48 hours preceding inclusion, home or hospital treatment impossible for any reason, participant lived too far away from the trial centre, written consent not given

Participants were also examined, although not necessarily excluded, for risk factors for DVT, including previous thromboembolism, varicose veins, immobilisation, surgery, trauma, cancer, use of oral contraceptives, known or inherited clotting disorders, other comorbidities such as cardiovascular disease with right ventricular failure

Interventions	<p>Treatment: sc injection of LMWH (dalteparin sodium, enoxaparin sodium, or nadroparin calcium, as chosen by the attending physician) at the recommended dose, followed by anticoagulant for 6 months at home</p> <p>Control: sc injection of LMWH (dalteparin sodium, enoxaparin sodium, or nadroparin calcium, as chosen by the attending physician) at the recommended dose, followed by anticoagulant for 6 months initially in hospital for 10 ± 2 days, then at home</p> <p>Anticoagulants: oral VKA or fluindione, 20 mg/d for the first 3 days, followed by regimen to maintain INR between 2.0 and 3.0 for up to 6 months</p> <p>Participants were also given compression stockings and were encouraged to return to physical activity according to a schedule approved by general practitioner and nurse.</p>
Outcomes	<p>Primary: recurrent VTE, PE, major bleeding</p> <p>Secondary: death, minor bleeding, economic analysis</p> <p>Duration of follow-up: 6 months</p>
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Low risk	Sealed envelopes were used.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Although no blinding of participant or personnel was reported, both groups received the same treatment. All participants received an oral anticoagulant for the first 3 days. Outcome is unlikely to have been affected by lack of blinding of participants or personnel.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Blinding of outcome assessors was not reported. Outcomes could have been influenced by lack of blinding.
Incomplete outcome data (attrition bias) All outcomes	High risk	38 participants did not complete the 6-month follow-up (those treated in hospital were twice as likely to withdraw).

Boccalon 2000 (Continued)

Selective reporting (reporting bias)	Low risk	All prespecified outcomes were reported.
Other bias	Low risk	No other potential bias was identified.

Bäckman 2004

Methods	<p>Study design: randomised multi-centre trial</p> <p>Exclusions post randomisation: 7 patients excluded (5 randomised to in-patient treatment refused to co-operate; 2 randomised to outpatient/home treatment had a drug reaction and haematuria, respectively)</p> <p>Losses to follow-up: none</p> <p>Intention-to-treat analysis: yes</p>
Participants	<p>Country: Sweden</p> <p>Setting: in-patient or out-patient/home</p> <p>N: 224 met inclusion criteria, 131 randomised (66 in-patient, 65 out-patient/home), representing 58% of those eligible</p> <p>Age: mean 66 (33 to 87) years, in-patient group; 67 (25 to 91) years, out-patient/home group</p> <p>Sex, male/female ratio: 34/34 in-patient group; 34/31 out-patient group</p> <p>Inclusion criteria: acute symptomatic DVT confirmed by phlebography or ultrasound in patients aged 18 years and older presenting at the emergency department</p> <p>Exclusion criteria: not clearly stated</p>
Interventions	<p>All participants were provided with intervention stockings. Both groups were treated with LMWH administered sc once daily, adjusted for body weight, for at least 5 days until prothrombin time was < 25% (INR > 2.0) for at least 1 day.</p> <p>Out-patient/home: Treatment included a daily visit to the out-patient department at a primary care centre or a visit by the district nurse at the participant's home, depending on local circumstances or patient preference.</p> <p>In-patient: Participants were admitted to the ward.</p>
Outcomes	<p>Direct medical and direct non-medical costs</p> <p>Duration of follow-up: 3 months</p>
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	The method used to generate the random sequence was not described by trial authors.
Allocation concealment (selection bias)	Low risk	Randomisation was performed centrally by means of codes in envelopes in batches of 20. in accordance with Zelen 1979.

Bäckman 2004 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Although participants were allowed to change their assigned treatment or to leave the study after randomisation, the review authors determined that the risk of performance bias was low.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not described; outcomes could have been influenced by lack of blinding.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No data were missing.
Selective reporting (reporting bias)	Low risk	Prespecified outcomes were included.
Other bias	Unclear risk	Information was insufficient to reveal whether other potential bias exists; only 40% of participants randomised to treatment with LMWH were actually treated at home.

Chong 2005

Methods	<p>Study design: randomised parallel-group open study</p> <p>Exclusions post randomisation: 63 (20%) were not included in the primary outcome analysis</p> <p>Losses to follow-up: 45 had no analysis at 24 weeks</p> <p>Intention-to-treat analysis: yes</p>
Participants	<p>Countries: Australia, New Zealand, Poland, South Africa</p> <p>Setting: out-patient or hospital</p> <p>N: 301 enrolled; 298 randomised (148 hospital, 150 home)</p> <p>Age: 18+ years</p> <p>Sex: 156 male, 142 female</p> <p>Inclusion criteria: diagnosis of symptomatic lower extremity DVT (proximal or distal) confirmed by contrast venography and/or ultrasonography, suitable for treatment in an out-patient setting, prepared to self-administer daily sc injections, life expectancy > 6 months</p> <p>Exclusion criteria: received therapeutic doses of heparin for more than 24 hours before randomisation; clinically overt signs or symptoms of PE or evidence of PE on lung scanning or pulmonary angiography; impending venous gangrene; previous HIT or another hypersensitivity reaction to heparin; platelet count < 50 × 10⁹/L; treatment with fibrinolytics or oral anticoagulants within the previous 5 days, or with other investigational therapeutic agents within the previous 4 weeks; pregnancy or lactation; any clinically significant medical condition other than DVT that would prevent discharge from hospital</p>
Interventions	<p>Treatment: once-daily sc injection of LMWH enoxaparin 1.5 mg/kg for a minimum of 5 days plus 10 mg of warfarin for 3 months with dose adjusted to achieve and maintain INR above 2 and within range accepted by the investigator</p> <p>Control: 5000 IU bolus of UFH for a minimum of 5 days, plus 10 mg warfarin started on day 1 of treatment, for 3 months</p>
Outcomes	Primary: efficacy endpoint: incidence of symptomatic recurrent DVT

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Chong 2005 (Continued)

Safety endpoint: incidence of adverse effect, major or minor bleeding during the first 14 days

Secondary: incidence of PE, recurrent VTE

Duration of follow-up: 24 weeks

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Did not report use of adequate random sequence generation
Allocation concealment (selection bias)	Unclear risk	Did not report use of adequate concealment technique
Blinding of participants and personnel (performance bias) All outcomes	High risk	Treatment was not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessors were independent of the study and investigators and were unaware of the treatments that participants were receiving.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All outcome data were reported.
Selective reporting (reporting bias)	Low risk	All prespecified primary and secondary safety endpoints were reported.
Other bias	Unclear risk	Information was insufficient to reveal whether other potential bias exists; only 23% of participants randomised to treatment with LMWH were actually treated exclusively at home.

Daskalopoulos 2005

Methods	<p>Study design: prospective randomised trial</p> <p>Exclusions post randomisation: 6 patients withdrew consent following randomisation</p> <p>Losses to follow-up: none</p> <p>Intention-to-treat analysis: yes</p>
Participants	<p>Country: Greece</p> <p>Setting: out-patient or hospital</p> <p>N: 108 randomised (55 LMWH, 53 UFH)</p> <p>Age: 18 years and over, range 23 to 95, mean 58.6 years</p> <p>Sex: 61 female, 41 male</p>

Daskalopoulos 2005 (Continued)

Inclusion criteria: acute proximal DVT confirmed by colour duplex ultrasound scan not more than 1 week from onset

Exclusion criteria: segmental DVT restricted to infrapopliteal deep veins or calf muscles, as determined by duplex ultrasonography; symptomatic or clinically suspected PE; history of recently diagnosed (within 12 months) DVT or PE; already receiving anticoagulant therapy; bleeding tendency objectively confirmed; hypersensitivity to heparin preparations or coumarin derivatives; uncontrolled hypertension; history of recently diagnosed (less than 1 month) cerebrovascular accident, intracranial artery aneurysm, infectious endocarditis, thrombocytopenia, active peptic ulcer, hepatic or renal failure, history of asthma, recent spinal or epidural anaesthesia, or intraspinal paracentesis (less than 5 days); recent surgery (less than 5 days); recently performed thrombolysis or receiving antiplatelet therapy; body weight less than 35 kg; pregnancy; illicit drug addiction; altered mental status or impaired cognitive function with inability to comply with study protocol

Interventions	<p>Treatment: single sc injection of LMWH (tinzaparin sodium) at a weight-adjusted dose (175 anti Xa IU/Kg) daily for 6 months</p> <p>Control: iv bolus of 5000 IU UFH followed by iv infusion of UFH for 5 to 7 days. APTT was measured after 4 hours of initiation of heparin administration and was repeated 6 hours thereafter to reach the therapeutic range (ratio: 1.5 to 2.5).</p> <p>Oral anticoagulant was commenced on the third day following UFH therapy.</p>
Outcomes	<p>Primary: recanalisation of thrombosed veins, major events</p> <p>Secondary: recurrent DVT, PE, major bleeding, minor bleeding, thrombocytopenia, death</p> <p>Duration of follow-up: 12 months</p>
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was done by means of a computer schedule.
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Study was open-label.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Because a double-blind study was not feasible, all objective diagnostic tests were interpreted by specialists including Coagulation Unit staff and Radiology staff who were not involved in the study.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All outcome data were reported.
Selective reporting (reporting bias)	Low risk	All predefined data endpoints were reported.
Other bias	Low risk	No other potential bias was identified.

Koopman 1996

Methods	<p>Study design: randomised controlled trial</p> <p>Exclusions post randomisation: 2 (both withdrew consent, 1 from each group)</p> <p>Losses to follow-up: 2 participants in each group were lost to follow-up at 12 weeks</p> <p>Intention-to-treat analysis: yes</p>
Participants	<p>Countries: The Netherlands, France, Italy, New Zealand, Australia</p> <p>Setting: home or hospital</p> <p>N: 400 randomised (202 LMWH, 198 UFH)</p> <p>Age: 59 ± 17 years LMWH group, 62 ± 16 years UFH group</p> <p>Sex: 203 male; 197 female</p> <p>Inclusion criteria: acute symptomatic proximal DVT proven by venography or duplex scan</p> <p>Exclusion criteria: VTE within previous 2 years, suspected PE at presentation, geographic inaccessibility, PTS, less than 18 years old, pregnancy, life expectancy less than 6 months, previous treatment with heparin for longer than 24 hours</p>
Interventions	<p>Treatment: twice-daily injections of LMWH (nadroparin calcium (Fraxiparine) at a dose adjusted for participant's weight) at home when appropriate; participants were instructed by nurse on how to administer the injections themselves</p> <p>Control: UFH (APTT adjusted dose, continuous iv infusion of 1250 IU per hour after initial iv bolus of 5000 IU) in hospital</p> <p>Duration: minimum 5 days, maximum 24 weeks</p> <p>Oral anticoagulation: Warfarin commenced on day 1 and continued for 3 months, with dose adjusted to attain INR 2.0 to 3.0</p>
Outcomes	<p>Primary: symptomatic recurrent VTE</p> <p>Secondary: major haemorrhage, death, quality of life comparisons, comparison of costs (in-patient vs home)</p> <p>Duration of follow-up: 6 months</p>
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of random sequence generation was not reported.
Allocation concealment (selection bias)	Low risk	Allocation was performed by means of a central 24-hour telephone service.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unblinded trial

Koopman 1996 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Objective testing was done blindly; documentation of all potential outcome events was assessed by an independent adjudication committee whose members were unaware of treatment assignments,
Incomplete outcome data (attrition bias) All outcomes	Low risk	All losses to follow-up were reported.
Selective reporting (reporting bias)	Low risk	All prespecified outcome measures were reported.
Other bias	Unclear risk	Information was insufficient to determine whether other potential bias exists; only 36% of participants randomised to treatment with LMWH were actually treated at home.

Levine 1996

Methods	Study design: randomised controlled trial Exclusions post randomisation: not stated Losses to follow-up: none Intention-to-treat analysis: not indicated, but analysis included all randomised participants
Participants	Country: Canada Setting: home or hospital N: 500 randomised (247 LMWH, 253 UFH) Age: mean 57 ± 17 years LMWH group, 59 ± 15 years UFH group Sex: 301 male; 199 female Inclusion criteria: acute proximal DVT proven on venography or duplex scan Exclusion criteria: 2 or more previous episodes of DVT or PE; active bleeding; active peptic ulcer; coagulation disorder; symptomatic PE; possibility of non-compliance; contraindications to LMWH; pregnancy; pretreatment with heparin for longer than 48 hours; inability to make follow-up visits due to geographical inaccessibility; presence of known deficiency of antithrombin III, protein C, or protein S
Interventions	Treatment: sc LMWH (enoxaparin 1 mg per kg body weight twice a day) primarily at home Control: UFH (APTT adjusted dose, continuous iv infusion of 20,000 IU after initial iv bolus of 5000 IU) in hospital Duration: minimum 5 days Anticoagulants: Warfarin sodium was started on evening of day 2 and was continued for at least 3 months. First dose of 10 mg was thereafter adjusted to maintain INR between 2.0 and 3.0.
Outcomes	Primary: symptomatic recurrent DVT or PE within 90 days of randomisation, major bleeding, minor bleeding during study period and up to 48 hours after discontinuation of study medication Secondary: death, economic evaluation Duration of follow-up: 3 months

Levine 1996 (Continued)

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of random sequence generation was not reported.
Allocation concealment (selection bias)	Low risk	Treatment was assigned over the telephone from a central site.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unblinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Testing and assessment for recurrent VTE and bleeding were conducted by a committee unaware of treatment assignments.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow-up were reported.
Selective reporting (reporting bias)	Low risk	All prespecified outcomes were reported.
Other bias	Unclear risk	Information was insufficient to determine whether other potential bias exists; only 48.5% of participants randomised to treatment with LMWH were actually treated at home.

Ramacciotti 2004

Methods	<p>Study design: randomised, open-label, multi-centre clinical trial</p> <p>Exclusions post randomisation: not stated</p> <p>Losses to follow-up: 53.6% at 6-month follow-up</p> <p>Intention-to-treat analysis: not indicated but analysis included all randomised participants</p>
Participants	<p>Country: Brazil</p> <p>Setting: home or hospital</p> <p>N: 201 randomised (104 enoxaparin, 97 UFH)</p> <p>Age (years): mean 64 for home, 44 for hospitals</p> <p>Sex: 69 male, 132 female</p> <p>Inclusion criteria: age greater than or equal to 18 years, weight greater than or equal to 50 kg and < 110 kg, DVT symptoms for 10 days or longer, proximal lower limb DVT (confirmed by duplex ultrasound or venography), ready access to local health service, capable of using enoxaparin at home</p> <p>Exclusion criteria: history of HIT or allergy to heparin; haemorrhagic diathesis; surgery within 7 days; symptoms of PE, bilateral DVT; survival prognosis < 6 months; hepatic or renal failure; received therapeutic doses of UFH or LMWH for 24 hours or longer in the previous 48 hours; in hospital for another</p>

Ramacciotti 2004 (Continued)

reason, with stay anticipated to last > 3 days; initial platelet count < 100,000/mL; uncontrolled hypertension, with DBP greater than or equal to 180; initial APTT > 1.3 times the normal value; INR > 1.5 at enrolment; indication for thrombolysis or venous thrombectomy

Interventions	<p>Treatment: once-daily sc injection of LMWH enoxaparin at a dose of 1.5 mg/kg for 5 to 10 days, given at home or in hospital at the discretion of the healthcare provider</p> <p>Control: iv bolus injection of 5000 IU of UFH followed by iv 500 IU/kg/d adjusted to maintain an APTT of 1.5 to 2.5 times the normal value for 5 to 10 days in hospital</p> <p>Anticoagulant: All participants received warfarin (with a targeted INR 2 to 3) for at least 3 months, starting at day 1 or 2 of treatment.</p>
Outcomes	<p>Primary: recurrent DVT, PE</p> <p>Secondary: major and minor bleeding</p> <p>Duration of follow-up: 6 months</p>
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation was by block 1:1 at each centre to ensure balance in each treatment arm, but method of random sequence generation was not reported.
Allocation concealment (selection bias)	High risk	Each investigator received the randomisation scheme specifying the treatment allocation for each participant enrolled in the study. Thus the investigator could foresee assignments and introduce selection bias.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	Only 32.7% of enoxaparin and 46.4% UFH participants were followed up after 6 months.
Selective reporting (reporting bias)	Low risk	All prespecified safety endpoints were reported.
Other bias	Unclear risk	Information was insufficient to determine whether other potential bias exists; only 36% of participants randomised to treatment with enoxaparin were actually treated at home.

APTT: activated partial thromboplastin time.

DBP: diastolic blood pressure.

DVT: deep vein thrombosis.

HIT: heparin-induced thrombocytopenia.

INR: international normalised ratio.

IU: international units.

iv: intravenous.

LMWH: low molecular weight heparin.

PE: pulmonary embolism.
PTS: post-thrombotic syndrome.
PTT: partial thromboplastin time.
sc: subcutaneous.
UFH: unfractionated heparin.
VKA: vitamin K antagonist.
VTE: venous thromboembolism.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Aujesky 2011	Assessed effectiveness, safety, and efficacy of outpatient vs inpatient care for patients with acute PE - not DVT
Belcaro 1999	Participants were randomised to different forms of heparin rather than to home or hospital treatment.
Blattler 1998	Although this study is published as an RCT, the method described in the study report does not meet the criteria for an RCT.
Buller 2004	Compared once-daily LMWH vs twice-daily doses in the outpatient setting - not hospital vs home
Conner 1999	Uncontrolled trial
Fitzmaurice 2000	This study was concerned with monitoring of oral anticoagulation at home or in the GP surgery.
Frank 1998	Although this study is published as an RCT, the method described in the study report does not meet the criteria for an RCT.
Goldhaber 1998	Participants randomised to home care with LMWH were first required to be treated in hospital before being discharged.
Grau 1998	Not a randomised trial
Grau 2001	Retrospective study
Green 1998	Uncontrolled trial
Hull 2000	Trial concerned with prophylactic regimens using LMWH in patients undergoing hip arthroplasty
Hull 2002	Trial concerned with evaluating 2 long-term LMWH treatment protocols
Hull 2009	Not home vs in-patient care; both groups of participants treated outside hospital. Usual care was defined as tinzaparin for 5 days or longer, followed by warfarin for 12 weeks.
Lindmarker 1996	Uncontrolled trial
Miles 1998	Uncontrolled trial
Modesto-Alapont 2006	Investigated the use of LMWH administered at home for prevention of VTE in patients with severe chronic obstructive pulmonary disease
O'Shaughnessy 1998	Uncontrolled trial
Otero 2010	Focussed on PE - not DVT

Study	Reason for exclusion
Pineo 2003	Trial concerned with evaluating 2 long-term LMWH treatment protocols
Rymes 2002	Retrospective study
Ting 1998	Uncontrolled trial
Wells 1998	Controlled trial of nurse vs patient injection. Not related to admission or home treatment
White 1989	This trial was concerned with monitoring of oral anticoagulation at home or in the GP surgery.
Wilson 2003	Study design not home vs in-patient, anticoagulant clinics vs family physician clinic. Intervention was oral anticoagulant - not LMWH. Study population included anyone who required warfarin for at least 3 months - not specifically for DVT.
Wimperis 1998	Uncontrolled trial

DVT: deep vein thrombosis.

LMWH: low molecular weight heparin.

PE: pulmonary embolism.

RCT: randomised controlled trial.

VTE: venous thromboembolism.

DATA AND ANALYSES

Comparison 1. Treatment of DVT at home versus treatment in hospital

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Recurrence of VTE	6	1708	Risk Ratio (M-H, Fixed, 95% CI)	0.58 [0.39, 0.86]
2 Major bleeding	6	1708	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.33, 1.36]
3 Minor bleeding	6	1708	Risk Ratio (M-H, Fixed, 95% CI)	1.29 [0.94, 1.78]
4 Death	6	1708	Risk Ratio (M-H, Fixed, 95% CI)	0.69 [0.44, 1.09]

Analysis 1.1. Comparison 1 Treatment of DVT at home versus treatment in hospital, Outcome 1 Recurrence of VTE.

Study or subgroup	Treatment (Home)	Control (Hospital)	Risk Ratio		Weight	Risk Ratio
	n/N	n/N	M-H, Fixed, 95% CI			
Boccalon 2000	1/99	2/102			3.11%	0.52[0.05,5.59]
Chong 2005	4/150	14/148			22.24%	0.28[0.09,0.84]
Daskalopoulos 2005	3/55	6/53			9.64%	0.48[0.13,1.83]
Koopman 1996	14/202	17/198			27.09%	0.81[0.41,1.59]
Levine 1996	13/247	17/253			26.5%	0.78[0.39,1.58]
Ramacciotti 2004	2/104	7/97			11.43%	0.27[0.06,1.25]

			Favours home 0.01 0.1 1 10 100 Favours hospital			

Favours home

Favours hospital

Analysis 1.2. Comparison 1 Treatment of DVT at home versus treatment in hospital, Outcome 2 Major bleeding.

Analysis 1.3. Comparison 1 Treatment of DVT at home versus treatment in hospital, Outcome 3 Minor bleeding.

Analysis 1.4. Comparison 1 Treatment of DVT at home versus treatment in hospital, Outcome 4 Death.

ADDITIONAL TABLES

Table 1. Summary of outcomes

Study	Setting	Number of participants entered	Heparin type	Mean hospital stay (days)	Recurrence of VTE (%)	Major bleeding (%)	Minor bleeding (%)	Death (%)	Mean total direct costs per participant
Bäckman 2004									
	Hospital	65	LMWH	3.6	-	-	-	-	SEK 16,400
	Home	66	LMWH	1.6	-	-	-	-	SEK 12,100
Boccalon 2000									
	Hospital	102	LMWH	9.5	2.0	2.0	10.8	2.0	Fr 20,932
	Home	99	LMWH	1.4	1.0	2.0	17.2	0	Fr 9230
Chong 2005									
	Hospital	148	UFH	-	9.5	2.0	11.5	1.4	-
	Home	150	LMWH	-	2.7	0	10.0	1.3	-
Daskalopoulos 2005									
	Hospital	53	UFH	-	11.3	7.5	5.7	3.8	-
	Home	55	LMWH	-	9.1	3.6	5.5	1.8	-
Koopman 1996									
	Hospital	198	UFH	8.1	8.6	2.0	7.6	8.1	-
	Home	202	LMWH	2.7	6.9	0.5	13.4	6.9	-
Levine 1996									
	Hospital	253	UFH	6.5	6.7	1.2	2.3	6.7	-
	Home	247	LMWH	2.1	5.3	2.0	2.4	4.5	-

Table 1. Summary of outcomes (Continued)

Ramacciotti 2004

Hospital	97	LMWH	3	2	2	12	-	-
Home	104	UFH	7	7	3	9	-	-

LMWH: low molecular weight heparin.

UFH: unfractionated heparin.

VTE: venous thromboembolism.

Table 2. Percentage of participants treated at home

Participants	Bäckman 2004	Boccalon 2000	Chong 2005	Daskalopoulos 2005	Koopman 1996	Levine 1996	Ramacciotti 2004
Randomised (N)	131	201	298	108	400	500	201
Excluded after randomisation (%)	5.3	18.9	20	5.5	0	0	0
Randomised to home/LMWH treatment and were actually treated at home (not hospitalised) (%)	40 ^a	74	23 ^b	100 ^c	36	48.5	36

^aBäckman 2004 reported that 40% of those randomised to home treatment remained at home, and 40% were hospitalised; it is unclear what happened with the remaining 20%; 36 randomised participants changed treatment, 26 of whom changed from hospital to home, and 10 from home to hospital.

^bChong 2005 reported that 23% of those randomised to home treatment were exclusively treated at home, 12% were hospitalised and discharged within a day, and 35% were hospitalised for one night, 23% for two nights, and 8% for three or more nights.

^cDaskalopoulos 2005 initially reported: "Patients allocated to receive treatment with LMWH underwent no hospitalizations at all", but later in the text trial authors state: "The number of major events requiring hospitalization was significantly lower in the LMWH group", making it unclear whether those randomised to LMWH were exclusively treated at home.

LMWH: low molecular weight heparin.

Table 3. Uncontrolled trials - participant demographics

Trial author	Referrals	Positive scans	% home treated
Grau 1998	-	71	55.0
Green 1998	373	119	37.5
Lindmarker 1996	-	434 ^a	100.0
Miles 1998	-	966	90.0
O'Shaughnessy 1998	1093	160	99.9
Ting 1998	-	53 ^b	100.0
Wimperis 1998	447	134	80.0
Total		1451	

^a3 days' hospital treatment before discharge.

^bExcluding distal thrombosis.

APPENDICES

Appendix 1. CENTRAL search strategy

#1	MESH DESCRIPTOR Thrombosis	1261
#2	MESH DESCRIPTOR Thromboembolism	919
#3	MESH DESCRIPTOR Venous Thromboembolism	257
#4	MESH DESCRIPTOR Venous Thrombosis EXPLODE ALL TREES	2036
#5	(thrombus* or thrombopro* or thrombotic* or thrombotic* or thromboemboli* or thrombos* or embol*):TI,AB,KY	18960
#6	MESH DESCRIPTOR Pulmonary Embolism EXPLODE ALL TREES	746
#7	(PE or DVT or VTE):TI,AB,KY	4979
#8	((vein* or ven*) near thromb*):TI,AB,KY	6702
#9	(blood near3 clot*):TI,AB,KY	2963
#10	(pulmonary near3 clot*):TI,AB,KY	5
#11	(lung near3 clot*):TI,AB,KY	4
#12	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11	24595
#13	MESH DESCRIPTOR Outpatients	983

(Continued)

#14	MESH DESCRIPTOR Inpatients	703
#15	MESH DESCRIPTOR Patient Care EXPLODE ALL TREES	48022
#16	MESH DESCRIPTOR Ambulatory Care	2843
#17	MESH DESCRIPTOR Home Nursing	253
#18	MESH DESCRIPTOR Hospitalization EXPLODE ALL TREES	10891
#19	MESH DESCRIPTOR Outpatient Clinics, Hospital	541
#20	in-patient:TI,AB,KY	4947
#21	inpatient:TI,AB,KY	5166
#22	hospitali*:TI,AB,KY	25539
#23	bed-ridden:TI,AB,KY	20
#24	bedridden:TI,AB,KY	107
#25	home:TI,AB,KY	19783
#26	out-patient:TI,AB,KY	1246
#27	outpatient:TI,AB,KY	15589
#28	ambulatory*:TI,AB,KY	14873
#29	domicil*:TI,AB,KY	383
#30	#13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29	108891
#31	#12 AND #30	3043

Appendix 2. Trials registries searches

Clinicaltrials.gov

44 studies found for: embolism AND home

WHO

809 records for 256 trials for: embolism AND home

ISRCTN

18 records for: embolism AND home

FEEDBACK

Anticoagulant feedback, 14 February 2011

Summary

Feedback received on this review, and other reviews and protocols on anticoagulants, is available on the Cochrane Editorial Unit website at <http://www.editorial-unit.cochrane.org/anticoagulants-feedback>.

Home versus in-patient treatment for deep vein thrombosis (Review)

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WHAT'S NEW

Date	Event	Description
29 May 2017	New search has been performed	Searches rerun. One new study included and five new studies excluded
29 May 2017	New citation required but conclusions have not changed	Searches rerun. One new study included and five new studies excluded. Review text updated to incorporate updated Cochrane requirements. New headings added, included studies assessed for risk of bias, GRADE ratings generated, and 'Summary of findings' table populated. Conclusions not changed

HISTORY

Protocol first published: Issue 2, 2000

Review first published: Issue 2, 2001

Date	Event	Description
14 February 2011	Amended	Link to anticoagulant feedback added
13 May 2008	Amended	Converted to new review format
9 November 2007	New search has been performed	No new trials found. One additional secondary reference added to Ramacciotti 2004 (included study). Conclusions not changed
22 May 2007	New citation required but conclusions have not changed	New team of review authors. Two new included trials and six new excluded trials. Overall conclusions strengthened with further evidence
27 May 2004	New search has been performed	No new trials found. Review updated as it stands

CONTRIBUTIONS OF AUTHORS

RO: independently selected articles; assessed studies for inclusion; assessed the methodological quality of selected trials; extracted data; and contributed to discussion of the final report of the review.

EO: independently selected articles, assessed studies for inclusion, and assessed the methodological quality of selected trials; extracted data; performed data entry and analysis and drafted the report; evaluated evidence for the review; and contributed to discussion of the final report of the review.

RF: performed data entry and analysis; drafted the report; evaluated evidence for the review; and contributed to discussion of the final report of the review.

DECLARATIONS OF INTEREST

RO: none known.

EO: none known.

RF: none known.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We assessed the methodological quality of included studies by using Cochrane's 'Risk of bias' tool presented in [Higgins 2011](#) instead of the method previously used for [Jadad 1996](#). We added a 'Summary of findings' table and assessed the quality of evidence according to the GRADE method ([Atkins 2004](#)).

We broadened the secondary outcome of patient satisfaction to include quality of life, as this outcome is more commonly used and is well accepted.

We renamed outcomes 'PE' and 'recurrent DVT' as 'recurrence of VTE'.

INDEX TERMS

Medical Subject Headings (MeSH)

*Home Care Services; *Hospitalization; Cost-Benefit Analysis; Fibrinolytic Agents [*therapeutic use]; Hemorrhage [chemically induced]; Heparin [adverse effects] [*therapeutic use]; Heparin, Low-Molecular-Weight [adverse effects] [therapeutic use]; Randomized Controlled Trials as Topic; Recurrence; Secondary Prevention; Thrombolytic Therapy [standards]; Venous Thrombosis [*drug therapy] [mortality]

MeSH check words

Humans