Critical Review Form
Critical Review Form **Therapy** Lagerstedt CI, Olsson CG, Fagher BO, Oqvist BW, Albrechtsson U. Need for long-term anticoagulant treatment in symptomatic calf-vein thrombosis. Lancet. 1985 Sep 7;2(8454):515-8.

Objectives: to assess "the need for oral anticoagulation in calf-vein DVT."

Methods: This prospective, randomized controlled trial was conducted from 1981 to 1984 at University Hospital in Lund, Sweden. Patients admitted to the medical department with symptoms due to a DVT confined to the calf veins were eligible for inclusion. Exclusion criteria included extension of thrombus to the popliteal vein, PE, malignancy, conditions predisposing to recurrent thrombosis (not defined), or history of recurrent thrombosis requiring long-term anticoagulation.

All patients received a 5-day course of IV heparin (500-600 IU/kg/day in six divided doses). Patients were randomized via the use of sealed envelopes to receive either warfarin or no further anticoagulation. Warfarin was started as soon as a diagnosis was confirmed, with a goal INR of 2.5-4.2.

All patients underwent physical exam and ^{99m}Tc-plasmin testing at days 5, 14, 30, and 90, as well as a V/Q scan on day 90 in some patients. At the end of the study, patients were contacted by telephone or had records obtained from their family physician.

A total of 52 patients were enrolled (24 in the warfarin group and 28 in the control group. One patient in the warfarin group was excluded as she was taken off warfarin by her physician and did not attend follow-up, leaving 23 patients in the warfarin group. The mean age in the two groups was 65.0 and 60.9 years, respectively.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis (answer the questions posed below)?**	
1.	Were patients randomized?	Yes, although the method of sequence generation was in no way described.
2.	Was randomization concealed (blinded)? In other words, was it possible to subvert the randomization process to ensure that a patient would be "randomized" to a particular group?	Uncertain. The investigators used sealed envelopes in the allocation process, but do not specify if these were opaque. It is possible that the randomization scheme could have been subverted (allocation concealment).
3.	Were patients analyzed in the groups to	Yes. One patient in the warfarin group who

	which they were randomized?	was taken off anticoagulation was excluded, though this appears to be due to loss to follow-up. One patient in the control group was deemed on review of the initial studies to have had clot extension into the popliteal vein at the time of enrollment. He was still included in the study in order to adhere to the intention to treat principle. No further treatment crossover was mentioned.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	Uncertain. The authors provide very little information regarding prognostic factors and medical comorbidities. Patients in the control group were twice as likely to have a history of prior thrombosis (n = 6 vs. n = 3), but otherwise we are given no information regarding past history.
B.	**Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)?**	
1.	Were patients aware of group allocation?	Yes. This was an unblinded study, although it seems unlikely that performance bias on the part of patients would influence outcomes.
2.	Were clinicians aware of group allocation?	Yes. This was an unblinded study, although it seems unlikely that performance bias on the part of clinicians would influence outcomes.
3.	Were outcome assessors aware of group allocation?	This was an unblinded study, and it is possible the knowledge of treatment group could have affected the interpretation of follow-up phlebography (observer bias).
4.	Was follow-up complete?	Mostly yes. One patient in the warfarin group was lost to follow-up. However, the authors do not indicate what percent of patients were followed up by phone call and/or what percent were followed by medical record review.
II.	**What are the results (answer the questions posed below)?**	
1.	How large was the treatment effect?	• No patients in the warfarin group had a recurrent clot at 90 days, compared to 8 (29%) in the control group: RR of 0, and a NNT of 3.5, 95% CI 2.2-8.5, p < 0.01. Five of these recurrences involved proximal extension. • One patients in the warfarin group had

		a recurrent clot at 1 year compared to 9 in the control group: RR 0.13, 95% CI 0.02-0.99. • No patients in the warfarin group had a PE compared to 1 patient in the control group.
2.	How precise was the estimate of the treatment effect?	See above.
III.	**How can I apply the results to patient care (answer the questions posed below)?**	
1.	Were the study patients similar to my patient?	Not entirely. This study looked at patients "admitted to the medical department because of symptoms due to DVT confined to the calf veins." (p. 515) The diagnosis was made by physical exam and a technetium-plasma test, then confirmed by phlebography. Such tests are no longer routinely performed. Instead, venous duplex ultrasonography is the standard of care for diagnosing DVT.
2.	Were all clinically important outcomes considered?	No. The primary outcome was recurrent clot. This does not seem to be a very patient-centered outcome. More important outcomes, such as propagation of clot or development of PE, would better serve to guide care.
3.	Are the likely treatment benefits worth the potential harm and costs?	Uncertain. This was a very small study conducted in the 1980s with outcomes of uncertain clinical interest. The results suggest that use of anticoagulation reduces the risk of "recurrent clot," but do not demonstrate a reduction in clot propagation or risk of PE.

Limitations:

1. The authors failed to adhere to CONSORT guidelines for the reporting of trials.

    a. There is no description of how patients were randomized, how the randomization sequence was generated, or what (if any) measures were used to ensure allocation concealment.

      b. **There is no flow chart depicting eligible vs. enrolled patients, and no assessment of whether patients were eligible but not enrolled were similar to those who were enrolled.**

      c. **There is very little information regarding demographics or medical comorbidities.**

2. **The patients, clinicians, and investigators were not blinded to group allocation, raising the possibility of <u>performance bias</u>.**

3. **The primary outcome analyzed was recurrence of clot by 90 days. This does not seem to be a very <u>patient-centered outcome</u>. More important outcomes, such as propagation of clot or development of PE, would better serve to guide care.**

4. **The study was conducted over 30 years ago, using vastly different techniques to diagnose and characterize venous thrombosis. It is unclear if these results could be applied to current practice (<u>external validity</u>).**

<u>Bottom Line:</u>

This small, randomized controlled study from the 1980s demonstrated a reduction in the risk of recurrent clot at 90 days with the use of anticoagulation, with a NNT of 3.5. The study did not demonstrate any change in more <u>patient-centered outcomes</u> and used techniques to diagnose and characterize DVTs that are now outdated. More modern studies will need to evaluate outcomes that are more relevant to patient care.