Dalteparin reduced venous thromboembolic events without increased bleeding in acutely ill medical patients

We discussed this article (1) at our "evidence for clinical decisions" meeting and have some comments.

With regard to the applicability of the title and conclusion: We think the title is too strong a statement and may lead to recommendation and application of this treatment for all unselected acutely ill medical patients. We feel there should be more reservation in recommendations for the use of prophylactic dalteparin in the title and commentary for the following reasons: 1) The primary outcome was a composite endpoint, and the validity of such an approach has been questioned (2). 2) Participants were included if they had ≥ 1 risk factor for VTE. The control event rate may be lower in unselected acutely ill medical patients and hence may lead to an increase in the number needed to treat. 3) Patients at "high risk for bleeding" were excluded. In unselected acutely ill medical patients, the risk for bleeding may be higher and therefore result in a reduced number needed to harm. 4) The study had pharmaceutical company sponsorship (3).

Routine prophylactic anticoagulation for medical patients is an issue of great importance to physicians. We are concerned that this *ACP Journal Club* item may be interpreted to recommend that dalteparin-based prophylactic anticoagulation should be given to all acutely ill medical patients without proper risk stratification and with the risk for bleeding as a complication underestimated.

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References

1. Dalteparin reduced venous thromboembolic events without increased bleeding in acutely ill medical patients [Abstract]. ACP J Club. 2005 Mar-Apr;142:40. Abstract of: Leizorovicz A, Cohen AT, Turpie AG, et al. Randomized, placebo-controlled trial of dalteparin for the prevention of venous thromboembolism in acutely ill medical patients. Circulation. 2004;110:874-9.
2. **Montori VM, Permanyer-Miralda G, Ferreira-Gonzalez I, et al.** Validity of composite end points in clinical trials. BMJ. 2005;330:594-6.
3. **Lexchin J, Bero LA, Djulbegovic B, Clark O.** Pharmaceutical industry sponsorship and research outcome and quality: systematic review. BMJ. 2003; 326:1167-70.

IN RESPONSE:

We thank Drs. von Garnier and Ryan for their insightful and stimulating comments. The title that *ACP Journal Club* provides for an abstract is intended to represent, at face value, the principal findings of the study as reported, as denoted by the use of the past tense in our title ("Dalteparin reduced…").

Beyond our initial screening (www.acpjc.org/shared/purpose_and_procedure.htm), the interpretation of the study findings (and our title), including further assessment of validity and generalizability, is left to the commentator and readers. The concern that our title and abstract for this study might convey the message that all medical patients should receive anticoagulant prophylaxis for deep venous thrombosis (DVT) is acknowledged. However, the commentator suggests the need for DVT prophylaxis only for those patients "at risk," and not all medical patients, including those at increased risk for bleeding. It may be argued that the trial justifiably excluded such patients, in whom anticoagulant DVT prophylaxis would not be appropriate.

We also acknowledge the limitations of composite outcomes, although it may be argued that, for this study, combining proximal asymptomatic DVT (which most physicians would consider clinically important) with symptomatic DVT is reasonable.

Finally, we agree about the need for vigilance of industry-sponsored trials and make a point of stating the source of funding for all studies that are abstracted in *ACP Journal Club*. Furthermore, we encourage commentators to place a drug evaluated in a trial in the context of alternative treatment options. For this trial, we believe the commentator has provided a balanced and generic assessment of anticoagulant options available for DVT prophylaxis in medical patients.

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Correction: Dalteparin reduced venous thromboembolic events without increased bleeding in acutely ill medical patients

In the Table of the abstract "Dalteparin reduced venous thromboembolic events without increased bleeding in acutely ill medical patients" (1), the relative risk increase for major bleeding of 2% should be 206%.

Reference

1. Dalteparin reduced venous thromboembolic events without increased bleeding in acutely ill medical patients [Abstract]. ACP J Club. 2005 Mar-Apr;142:40. Abstract of: Leizorovicz A, Cohen AT, Turpie AG, et al. Randomized, placebo-controlled trial of dalteparin for the prevention of venous thromboembolism in acutely ill medical patients. Circulation. 2004;110:874-9.