Reviewer's report

**Title:** The Association between Statin Therapy during Intensive Care Unit Stay and the Incidence of Venous Thromboembolism: A Propensity Adjusted Analysis

**Version:** 2  **Date:** 23 April 2013

**Reviewer:** Peter Kruger

**Reviewer's report:**

The authors report the results of a secondary analysis of data from a prior study conducted in 2006 to 2008. The original study is “in press” and not presented for comment but from the title looked at intermittent vs. graduated compression stockings in DVT prevention.

In this current analysis the authors presents the results of a propensity score adjusted analysis that suggests statin use had no impact of either DVT rates or 30day / hospital mortality.

The paper is well written and reads well.

I have several concerns about the data and the analysis presented.

**Major issues (compulsory).**

1. The prior study, while cited needs to presented in more detail. Please provide some detail on the intervention / treatment allocation / outcomes in the main study and the intervention could readily influence the outcomes assessed in this study. Ideally the full manuscript would be available to reviewers of these subsequent studies and available as a full citation for any sub studies (including this current one)

2. Limited data is provided or presented on the study cohort. In particular how the propensity score was arrived at and what actually was performed when providing the adjustments reported in table 1. This must be expanded in considerable detail.

3. The groups are very very different at baseline with numerous major significant differences. It is almost implausible they would in fact have similar outcomes for either DVT or mortality. I think the raw data for outcomes and the adjusted analysis would both need to be presented and significant discussions of the major limitation on interpretation of the results that such different groups may place on a post hoc non-randomised study.

4. I have significant concern over the data presented in figure 1. This would suggest a that no patients died in the first approx 4 days and the cohort had almost a 75 % one month mortality – this should be clarified and the additional clinical detail described above may help place this in context for the reader.
5. More detailed information is required regarding statin use. It is mentioned which statin but it is not clear on prior use / duration prior use / continued in ICU / commenced in ICU etc.

6. The significant difference in sequential stocking, unfractionated heparin and enoxaparin use between the groups represents a major confounder. Perhaps one could argue you may expect from some of the demographics the statin group to have a higher incidence of DVT (older / sicker / more bed bound / etc) so that fact they are similar incidence represents an effect?

7. Like many of the other studies in this field the end point chosen has a major limitation and inherent bias that must be acknowledged both in the way the results are presented and in the limitations section of the discussion. By design the investigators and the readers can not know a true denominator of incidence – we are only aware of DVT in the patients it was clinically suspected rather than all patients. The study should therefore report number for both those assessed / those +ve and those not assessed rather than just DVT in 6 patients and 51 patients.

Minor (essential)

1. Does Central venous line present – mean any location or just Femoral – it might be worth separating these in a study about DVT or acknowledge this as a limitation

2. Similarly for Dialysis catheter present – femoral vs other site would be relevant

3. Does “dialysis catheter present” equate to renal replacement therapy performed – this should be made clear in the additional demographic data.

4. As the primary outcome was DVT – the figure representing this should be prior to the mortality figure in the manuscript (ie Fig 1 rather than fig 2)

5. Define in methods “bedridden” – it is described in table as “3 days” - perhaps needs a bit more explanation? had these patients been in hospital longer prior to ICU than non statin users

6. Line 7 of the study design section – delete the repeated words about study approval.

7. Reference 16 mentioned in discussion – seems an odd comparison to make statin vs thyroid replacement – if mentioning this it may require some clarification for the reader about why the comparator was chosen (in an effort to find a cohort on an agent not thought to influence DVT incidence).

Minor (Discretionary)

1. In the 3rd sentence of the background – it might be more accurate to state the incidence in critically ill patients is “up to” 10 %
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

'I declare that I have no competing interests’