Reviewer’s report

Title: ALICAT: A feasibility study to inform the design of a randomised controlled trial to identify the most clinically and cost effective Anticoagulation Length with low molecular weight heparin In the treatment of Cancer Associated Thrombosis: a study protocol.

Version: 1 Date: 6 February 2014

Reviewer: Sarah Damery

Reviewer’s report:

This protocol outlines an interesting study which has the potential to provide clear evidence determining the length of anticoagulation treatment that provides the best outcomes for patients and the NHS in patients with cancer associated thrombosis. The authors outline a mixed methods feasibility trial which encompasses an RCT, embedded qualitative study and nationwide survey.

Although complex, the study is well designed and very clearly described. Indeed, in the main, this protocol was a pleasure to read, and it was well referenced. I have suggested a few alterations which may improve the paper below.

Major compulsory revisions

1. It would be helpful if the authors could provide a precise definition of what they mean by ‘active cancer’. Is this only cancer in which tumour growth is occurring? Or metastatic cancer? Or does it also include cancer where a tumour may be shrinking due to chemotherapy or radiotherapy but is not yet considered ‘in remission’? Greater clarity here would be useful. If the authors simply mean (as they write elsewhere in the protocol) locally advanced or metastatic cancer, it may be better to use the latter terms rather than ‘active cancer’

2. The protocol does not describe whether there would be any stopping rules for the trial component of the research – please clarify whether and if there would be any circumstances (e.g. high rate of severe bleeding events etc.) that would lead to the trial being stopped, particularly in the intervention group receiving the extended period of anticoagulation treatment.

3. Methods, randomised controlled trial section, participant recruitment para 1: Some more detail on how patients will be identified from the primary care perspective would be useful. The authors state that primary and secondary care clinical databases will be used. For the secondary care patients, this seems straightforward as they will already be undergoing treatment, but it is not clear how the primary care section of patients will be identified.

4. Methods, paragraph preceding ‘trial treatment arm’ section: the first sentence seems tautological here “Information on all eligible patients will be recorded including whether or not patients were eligible for the trial”. If patients are
'eligible', surely they will be eligible for the trial? Perhaps the authors intend to make a distinction between those who are POTENTIALLY eligible and those who (after screening for eligibility according to inclusion/exclusion criteria) are ACTUALLY eligible to participate. If so, this sentence could be made clearer.

5. The methods section notes that patients will complete 3 baseline QoL questionnaires. From its position in the text, it seems that these questionnaires will be completed after randomisation, yet there is no reference to them in Figure 1, despite the same questionnaires being mentioned in Figure 1 as part of the data collection in follow-up. For consistency, it would be useful to add the baseline data collection into Figure 1 so that the figure matches the text.

6. Table 4 seems unnecessary as its contents are entirely and clearly described in the text relating to the patient/carer semi-structured interviews. As there are currently 5 tables and 1 figure, I would suggest that table 4 is removed.

7. How feasible is it that clinician focus groups will be possible at national meetings and educational events? It is not clear whether the clinician focus group participants will be recruited regionally (i.e. in the centres in which the trial will run) or whether this is will be national recruitment. Do the authors have any experience of using the method of running focus groups at national events that suggests that it will be successful (or can they cite any literature from other studies that has used this method?)

8. Please clarify how clinicians will be identified for invitation to participate in the focus group study – will this be from a pre-existing mailing list, or via personal contacts of members of the research team?

9. Methods, paragraph preceding ‘statistical analysis’ section. Please clarify the sorts of things that will be included in the assessment of ‘use of NHS resources’

10. The nationwide survey is under-described in the protocol. What are the ‘relevant stakeholders’ in primary and secondary care? Does this include commissioners for example? What sorts of questions will be asked in the survey? Why have the authors chosen to perform telephone piloting when the survey will be administered in a web-based format? Will questions be closed or open, or a mixture of the two? Is there any idea of the number of responses that will be required to give a robust sample size? The protocol would benefit from greater detail in this section.

Minor issues not for publication

1. Background, para 1, 2nd sentence: There is/are missing word(s) here “Within the UK, the cost to of managing VTE...”

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable
**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.