Reviewer’s report

Title: Cost-utility of enoxaparin compared with unfractionated heparin in unstable coronary artery disease

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Reviewer: Franco Sassi

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Accept after revision, which I do not need to see

1. The presentation of the study appears unbalanced, with very limited information in the text, particularly on methods and sources of data, and a large appendix. It is important that the authors include brief but informative details in the main text about the literature search methods, the characteristics of the trials that provide evidence of effectiveness, the population and methods used in the study from which quality of life information is drawn, the sources and calculation methods for cost data.

2. The authors correctly emphasise the risks involved in generalising results of economic studies undertaken in different countries or settings. However, they do not seem to be equally cautious in applying the results of the existing clinical trials in their cost-effectiveness calculations. The authors do mention that sub-group analysis at the country level would not be feasible, but fail to provide a qualitative discussion of the possible implications of differences between countries and settings, particularly with regard to the generalisability of effectiveness data.

3. Some concerns arise with regard to the assessment of the costs of the alternative strategies. Costing methods are illustrated in the appendix (although not mentioned in the text). These indicate that multiple sources have been used, ranging from commercial organisations to individual hospital Trusts, from Royal Colleges to published studies. The authors may have been looking for accurate sources for each cost item, but the resulting overall picture might be misleading. It would have made more sense to gather all the cost information from a single source, addressing the potential variability through a comparison of different settings and/or a sensitivity analysis. It is difficult to estimate what the impact of the costing methods used may be. On one hand, the analysis shows that under a wide range of assumptions, enoxaparin has a favourable economic impact. On the other hand, the analysis shows small differences between the alternative therapies, which could be overturned by estimation errors that may appear small if observed in isolation.

4. The authors do not explicitly mention a key assumption underlying their cost analysis, i.e. the assumption leading to the inclusion in the analysis of nursing time and of shares of capital equipment related to the administration of unfractionated heparin, computed at their full cost. This involves a
judgement on the opportunity cost of such components. The inclusion of nursing time and equipment costs reduces the overall cost difference between the two strategies. The consequences of this should be explained to the reader.

5. The three scenarios described on page 9 are redundant and confusing. If the perspective chosen for the analysis is that of the NHS, transfer payments (VAT, NI, superannuation) should be included and should form part of the base case analysis. Incidentally, I could not find an illustration of scenario 2 in the results table. The meaning of scenario no. 3 is most unclear. It should be clearly explained to the reader why treatment costs for cardiac events should be first excluded and then included in two separate scenarios, if there is a strong reason for doing so.

6. Two of the tables (1 and 5) are at the same time too large and not wholly informative. The authors should make an effort to select the most relevant information in the two tables but they should also make sure that the following information is included. In table 1, information on the outcomes assumed in previous economic evaluations should be added. Table 5 should include an indication of what the extremes of the sensitivity analysis refer to, without requiring the reader to look up table 4 or other information in the paper at the same time.

7. It may be important to discuss briefly the organisational implications of switching to enoxaparin for the patients examined, while unfractionated heparin may still be used for other patients. Another point for discussion is the possible existence of alternatives to the two drugs considered, which may change the terms of the cost-effectiveness comparison.

Minor comments:

1. Page 5, line 3: "unstable stable angina"
2. Page 5, lines 3 and 6: "non-Q-wave" is hyphenated in different ways
3. Page 5, last line of 2nd paragraph: what form of heterogeneity do the authors refer to? How is this related to the fact that studies use different pharmacological varieties?
4. Page 6, 5th line from bottom of page: "if" should be "is"
5. Page 7, 1st line of 4th paragraph: rephrase from "although ..."; this should read "The following limitations were detected in one study:..."
6. Page 9, 1st and 2nd lines: this sentence is unclear and should be reworded
7. Page 21, table 4: it should be made clear that values in the table represent differences between the two strategies

Competing interests:

None declared.