Reviewer’s report

Title: The GRADE approach for assessing new technologies: the case of apheresis in Ulcerative Colitis.

Version: 1 Date: 24 August 2009

Reviewer: Hindrik Vonderling

Detailed comments:

P1 Department of gastroenterology instead of digestive department?

P2 Be more explicit: e.g. methods section line 3: At the end the overall quality of the evidence for each question was considered for the formulation of recommendations.

P2 and 3 It is unclear to what method of formulating HTA recommendations the GRADE method is compared in this study. What is common practice in your centre and/or in your country?

P3 The final sentence touches upon the distinction between assessment and appraisal. This could be elaborated upon a bit in the discussion section of the article.

P4 For non-clinicians: what is steroid tapering?

P5 The objective of the study was explorative, a kind of feasibility- or pilot study (the authors use the latter term in the discussion). At first sight, however, one would expect a comparative study, e.g. with SIGN. I guess the reader would like to know why the methodological advances of a controlled study have not been realised here! This could be briefly touched upon on page 5 and perhaps in a more elaborative way in the discussion. Does the SWOT analysis really compensate for this?

P6 The essential difference between treatment indications seems to be corticosteroid dependent versus non-corticosteroid dependent and corticosteroid resistant versus non-corticosteroid resistant ulcerative colitis. This requires some more information and explanation as part of the background section (page 4) where (it seems) these conditions are not explicitly described. Why are these the most important treatment-indication combinations (in accordance with the PICO model)?

(For research question 2 the difference between mild, moderate and severe UC is most important, which has been adequately described).

P6 Mild adverse events instead of effects?
Isn’t the IBDQ relevant as an outcome measure in the context of the first question as well?

How was consensus reached on the importance of the defined outcomes?? This is important for the replicability of the study. The same goes for the definition of the cut-off points. And how sensitive are the results to the choice of cut-off points?? How, if at all, did patient’s values play a role in the procedure?

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Assessment of the outcomes. The criteria may need a bit more explanation (the reader now has to continue two more pages to learn more).

How did you agree on recommendations? Could you give a few examples of your considerations in specific cases (e.g. in text boxes)? What was the impact of the process review by the Grade working group member and the clinical expert? Could the expert veto a judgment? Why only one clinical expert?

On page 6 you write that you will use the Endoscopic Mayo Subindex to assess endoscopic remission. How does this compare to the information on page 10 on the Rachmilevich Endoscopic Index? Why is a before-after mean EI defined and used as an indirect measure for endoscopic remission?

Balance between risks and benefits. It seems that a decision on the choice of treatment for each (sub)indication goes together with/is based on many different considerations. The last sentence of the first paragraph only seems to cover some of these, for particular patients. In general, there seems some room for apheresis systems, even beyond those patients presenting toxicity to corticosteroids, wouldn’t you agree?

And why do you specifically mention children here? For non-clinicians this may need some explanation.

Based on the evidence you are presenting I would agree with the conclusion that apheresis systems should not be first choice in all patients covered by research question 1.

Remarks: If available, some quantitative information on the cost/cost differences of treatment alternatives would fit perfectly here. Now the information on lower costs of corticosteroids ‘falls from heaven’ while it seems to have profound (?) influence on the judgment you provide.

Considering the evidence provided, isn’t your statement at the bottom of page 11 a bit too strict/too restrictive towards apheresis systems?

Page 12 Recommendation 1: Shouldn’t you write: for most corticosteroid dependent etc. ?

Can only one subgroup of patients be identified for which the second recommendation applies?

Perhaps add ‘weak treatment recommendation, very low quality of evidence’ to the second recommendation as well.
P12 Why was the study with the prednisolone resistant or dependent patients excluded?

P13 Balance between risks and benefits. There seems to be more benefits than harms of apheresis systems treatment?

P14 Please explain how the SWOT analysis process considers patients values and why the outcomes reported in the literature need to be avoided. For example, is endoscopic remission of limited importance compared to clinical remission or is the relation between the two not straightforward?

P15 halfway the page: strength of recommendations?

P18 Conclusions. How about this formulation? Our study suggests that the GRADE approach could be a proper approach to make the process of the formulation of recommendations a more transparent part of the overall process of producing HTA reports.

This formulation would show that your approach is all-inclusive, in contrast with the assessment-appraisal approach.

Please elaborate a bit on the relationship of your work with the value of information approach to new research.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that (as a reviewer) I have no competing interests.