

Thank you for your review of our original manuscript titled '**FOCUS: Future of fecal calprotectin utility study in inflammatory bowel disease**'. Please find below responses to reviewer comments:

Response to Reviewer *03478404 comments*

1. Among exclusion criteria, according to the literature, patients with polyps/polyposis, allergic digestive disorders, concomitant celiac disease or mucoviscidosis should have been also excluded, as they may have high levels of FC. This is not mentioned in the manuscript.

The authors acknowledge the potential impact of the aforementioned co-morbidities on the specificity of an elevated calprotectin result, and the limitation of not excluding patients with such co-morbidities. A statement reflecting this limitation has been added to the discussion (Given this was a real-life study, there was also unavoidable potential for inclusion of patients with co-existing undiagnosed conditions that could influence the FC level such as colonic polyps or additional immunologically driven digestive disorders)

For many patients, endoscopic procedures had not occurred prior to the performance of FC, and accordingly luminal pathologies such as those mentioned above were not known prior to patient inclusion in the study. When endoscopic findings for an elevated FC beyond IBD were identified subsequently to inclusion, reference was made to this in study results. (See Figure 6)

2. The sentence "It was at the discretion of the individual treating physician as to how the FC result was to be interpreted." is not clear. The negative and positive values should have been mentioned for the CF test and interpreted accordingly, not arbitrarily. If it is really true that any physician interpreted the FC results in his/her own way, then the results of this survey are not reliable at all. However, later in the manuscript the authors mentioned that "Given the heterogeneity in the indication for FC in the study cohort as well as the uncertainty in the current literature relating to what is considered a 'positive' and 'negative' FC, the primary outcome of change in management was analysed according to a positive result being >250 microg/g as well as >100 microg/g. Within the follow up subset, a FC result of >100microg/g was considered positive." Which one then? Please clarify. It is explained somehow in the "Results" and "Discussions", but not in "Material and methods".

At commencement of the study, FC result of >250 was regarded as a cut-off for a positive result. This has now been included in the Material and Methods. (Physician were informed that a

FC level of > 250 was considered indicative of inflammatory activity, however it was at the discretion of the individual treating physician as to how incorporate the FC result into the patient's management) *At the time of follow-up analysis, the consideration of a more sensitive cut-off for FC was also considered of interest, and accordingly cut off of 100 was also analysed.*

3. Please use IBD U (IBD unclassified) instead of "indeterminant colitis", as this is the term used nowadays, according to the new classification. It is unacceptable to use the old term in the Abstract.

Thank you for highlighting this change in terminology. The manuscript (abstract and results) has been adjusted accordingly.

4. Seventy five % of complete responses = acceptable for a survey, if there is a balanced geographical distribution of the GIs. Two thirds are from academic centers, which is good.

Majority of the patients were from the greater Vancouver area. The remaining thirty patients were from a regional area. Twenty- three (76%) of patients returned surveys from this area, consistent with the overall compete response.

5. I would include the "FOCUS - fecal calprotectin requisition survey" in the main manuscript, not as a supplementary material (appendix 1), as it is necessary to know what the questions were. This is very important. Readers should know what was asked, since the answers are provided (in the Results) and Discussed. Especially about ordering FC

This recommendation is noted. Upon the advice of the editor, the surveys have been incorporated as supplementary material for ease of publication with respect to article length

Response to Reviewer 00503587 Comments

Specific Comments

1. The term indeterminate colitis is used incorrectly. This should be IBDU
Thank you for highlighting this change in terminology. The manuscript (abstract and results) has been adjusted accordingly.

2. In the INTRODUCTION one particular product is specified but others are not. No product names required here (to avoid bias)
Product name has been removed from the introduction.

3. Parts of the METHODS and RESULTS are long and hard to read. Shortening may be advantageous

These sections have been shortened.

4. The first part of the RESULTS does not have a subheading currently

*A subheading has been allocated to the first section of Results: **Baseline patient demographics***

5. On page 9 it is stated that 177 patients were from academic centres. However two pages later this figure is given as 210

177 of patients returning kits were from academic centres. (There were additional patients from academic centres who did not return the kits). When the follow-up analysis occurred, reference to 210 patients with available follow-up data included both those returning and not returning the kit. The latter was also considered in order to determine the outcomes of patients who did not return the kit. There were five patients whose medical records were unavailable to reviewed. (Accordingly 172 patients with follow up as opposed to 177)

6. On page 13, a sentence refers firstly to seven patients and then to eight: one of these numbers is incorrect

This has been amended to the correct number of 8.

7. The DISCUSSION could be shortened and made more focused to enhance readability

The Discussion has been shortened.

8. The Figure legends (page 19) do not include figure titles Subsequently the Figures are provided with contradictory titles.

The Figure titles and legends have been amended.

9. Table legend/title could be improved also

As above