

Dear Editor

Please find attached our revised manuscript.

We sent our paper to a second native speaker who corrected it extensively.

Please find also in details a point by point answer to your requests.

- The main problem of the paper is the part dedicated to meta-analysis. This meta-analysis has been poorly performed (see PRISMA recommendations) and the results do not add important issues to the current literature (see ref. 33). For these reasons the part concerning the meta-analysis should be removed (title, Metanalysis paragraph, figure 2).  
We removed the section related to the meta-analysis (title, paragraph). We explained more extensively ref 33, citing also in Figure 2, which has been changed.
- Paragraph 'Minor studies assessing use of ESCHERICHIA COLI NISSLE 1917 in UC'. P value of 54% vs 89% is wrongly reported ( $p < 0.005$ ). The true value of P is  $< 0.05$ .  
We correct the data by entering the correct value ' $p < 0.05$ '
- In the text there are numerous grammatical errors and misspellings (Trulov Witts criteria, Calprotectine, omogeneous, respectively, topycal, homogeneity, Interengly, of 12 month, wit just, and so on). Moreover, even in figure 1 there is another misspelling (IMMUE-). The manuscript may well benefit from language editing.  
We modified the text according following your suggestions.
- In abstract, I would like to see a conclusion of the review. In conclusion, a perspective would be appreciated.  
In both paragraphs we have included future perspectives. In particular, respectively:  
    'Further studies may be helpful for this subject to further the full use of potential of ECN'  
    'Further studies may be helpful to further dissect mechanisms of actions and perhaps optimize dose and newer indication of ECN.'
- A short legend to fig1 would be useful.  
We have introduced a short legend; we have not further deepened as not to repeat what is shown and written in the text.
- In Matthes trial, the volume of enema does not indicate the amount of bacteria  $10^8$ /ml, it must be indicated in text and table 1.  
We modified the text following your suggestions.
- Please state the date (1999) where Rembacken et al [28] is cited in the text so as to be homogenous with other 2 trials.

We modified the text following your suggestions.

- Typographical errors such as omogeneous instead of homogenous in chapter “Minor studies assessing use of.....” have to be corrected.

We modified the text following your suggestions.

We hope our manuscript is now ready for publication.

Kind regards

Franco Scaldaferri on behalf of all authors.