

Reviewer #1:

Specific Comments to Authors: You did a great research.

Response: Thank you very much.

Reviewer #2:

Specific Comments to Authors: Manuscript titled "Systematic review of the prevalence and development of osteoporosis or low bone mineral density and its risk factors in patients with inflammatory bowel disease" deal an important issue of osteoporosis. The aim of this review was to assess prevalence and development of osteoporosis and low bone mineral density (BMD), and its risk factors, in IBD patients. This Systematic review of population-based studies is interesting and well written, innovative and well described.

Moreover, minor revisions are needed to update the introduction (too poor) based on the current literature. Please add a sentence or improve the current ruling regarding the osteoporosis, eg. Adding the importance of physical activity in osteoporosis. Please quote adequate missing references as follow: The importance of physical activity in osteoporosis. From the molecular pathways to the clinical evidence. *Histol Histopathol.* 2016 Nov;31(11):1183-94. RANKL is downregulated in bone cells by physical activity (treadmill and vibration stimulation training) in rat with glucocorticoid-induced osteoporosis. *Histol Histopathol.* 2013 Sep;28(9):1185-96. The effects of physical activity on apoptosis and lubricin expression in articular cartilage in rats with glucocorticoid-induced osteoporosis. *J Bone Miner Metab.* 2013 May;31(3):274-84.

Response: Thank you for this input. This has been added in the introduction, page 5

In the conclusion section please add the clinical relevance of your work.

Response: The clinical relevance of our work has been added in the conclusion on pp. 26-27

Reviewer #3:

Specific Comments to Authors: Overall this is a nice review of Osteoporosis and IBD, though no meta-analysis was performed. 1) Original findings indicate that CD, more than UC, seems to be associated with Osteoporosis (though data specifically in UC is lacking from the studies). 2&3) This study also suggests associations between BMI/gender and osteoporosis, though there was a lack of ability to perform a true meta-analysis. As such, it is more of a narrative review. Additionally, while similar results have been reported previously (PMID: 31720198), this study highlights the lack of uniformity both in measurements as well as design across studies, and emphasizes the need for further investigation (particularly with stratification between UC and CD). Comments

-Would change the sentence "Among healthy controls, prevalence of osteoporosis was 3% and 10%." Would note from 2 different studies and among age and sex matched controls. On first read was confusing.

Response: We agree with the reviewer and have corrected the sentence, and like sentences, on pp. 3, 18, 23 and 29 in the manuscript.

-Would note which gender in Haugeberg study was associated with Osteoporosis in Table 3.

Response: We agree with the reviewer and have corrected the sentence on p. 19 in the manuscript.

-When describing associations should note the direction for each: "Overall, a CD diagnosis, body mass index (BMI), body weight and gender were associated with osteoporosis or low BMD." Should note which gender, direction of BMI etc.

Response: We agree with the reviewer and have corrected the sentence, and sentences like this, on pp. 3, 4, 18, 23, 24, 26 and 29 in the manuscript. We have concluded that the statement that gender is associated with low BMD might be misleading and have made changes throughout the manuscript.

-For Table 4 would note the time period that BMD was assessed over for each study. I would include a range in the text to give the reader an idea of the duration

Response: This has been added in the text on p. 20 as well as in the description for table 4 on page 21 and in the description for supplementary table 3.

-Since a meta-analysis was not able to be completed, it's more a narrative review in essence.

Response: We performed a systematic search of the literature for this study and therefore we think that the study should be categorized as a systematic review. This is reflected in the title of the manuscript.

-Would explicitly mention that data just for UC patients is lacking much earlier in the paper - not explicitly mentioned until the limitations.

Response: We agree with the reviewer and have stated this on p. 11.

-Sig. limitation as noted is the difference in measurements among the studies as well as other heterogeneous features that preclude a true meta-analysis.

Response: We agree with the reviewer, that the available population-based literature did not allow for a meta-analysis. We have mentioned this in the discussion, page 26.

Science Editor:

(3) Format: There are 4 tables and 1 figure. A total of 31 references are cited, including 8 references published in the last 3 years. There are no self-citations. We suggest the authors to cite their own research works in the review paper.

Response: Thank you. We have added references on work from our group.

5 Issues raised:

(1) I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

Response: Figure 1 has now been prepared and submitted in a separate in PowerPoint format. It has also been included in the manuscript as an editable figure.

(2) I found the authors did not add the PMID and DOI in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout; and

Response: PMID and DOI numbers are now added in the reference list. However, it has not been possible for us to find a DOI number for the article written by Schoon et al (PMID 11232491).

(3) I found the authors did not write the "article highlight" section. Please write the "article highlights" section at the end of the main text

Response: Highlight section has now been added on p. 28.