# Microscopic colitis is a risk factor for low bone density: a systematic 

## review and meta-analysis

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## Introduction

Microscopic colitis (MC) is a chronic inflammatory disease of the large bowel characterized by watery diarrhoea, which substantially decreases the patient's quality of life. Moreover, low bone density (LBD) has been associated with the disease. Furthermore, many risk factor contribute to the random coincidence of the two conditions. We aimed to investigate whether MC is a risk factor in LBD development and measure the proportions of bone mineral modulations in the MC population.

## Methods

Our protocol was prospectively registered with PROSPERO (CRD42021283392). We performed a comprehensive literature search in five databases (Pubmed, Embase, Cochrane, Scopus, Web of Science) from inception to the 16th of October, 2021. All studies that reported the number of adult patients with MC diagnosed by histopathologic criteria with BMD evaluation were eligible. We used the random-effect model to calculate pooled odds ratios (ORs) and pooled event rates with $95 \%$ confidence intervals (CI). We assessed the risk of bias using the QUIPS tool for our prognostic question, and we applied the JBI Critical Appraisal Checklist for Prevalence Studies in the proportional measurements. To ascertain the quality of evidence for our outcomes, we followed the recommendations of the GRADE working group.



We analyzed 111 patients with MC; 67 had LBD compared to 265 controls with 110 LBD cases. The odds of having LBD was threefold higher ( $O R=2.96, \mathrm{CI}$ : 1.15-7.59) in the presence of MC. Our proportional analysis showed that from 276, 182 and 182 patients with MC a total of 189, 92 and 20 patients had LBD, osteopenia and osteoporosis, respectively. The proportion of LBD was 0.68 (CI: 0.56-0.78), osteopenia was 0.51 (CI: 0.43-0.58), and osteoporosis was 0.11 (CI: 0.07-0.16) among the MC population. We determined the low number of participants studies being at high risk of bias, and downgraded the certainty of evidence to very low level due to the small sample size and the use of a surrogate outcome, measuring the bone mineral density.

## Conclusion

## Results

The systematic search yielded a total of 3046 articles. Four articles were found eligible for our quantitative synthesis.

| Author | LBD | MC |  |  |  |  | Proportion | 95\% CI |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Lörinczy et al. 2011 | 8 | 14 |  |  | 1 |  | 0.57 | [0.33; 0.79] |
| Wildt et al. 2018 | 29 | 50 |  |  | - |  | 0.58 | [0.44; 0.71] |
| Graziano et al. 2021 | 75 | 118 |  |  | $\square$ |  | 0.64 | [0.55; 0.72] |
| Greenberg et al. 2019 | 77 | 94 |  |  |  | - | 0.82 | [0.73; 0.88] |
| Overall effect$I^{2}=75 \%[31 \% ; 91 \%]$ | 189 | 276 |  |  | $\cdots$ |  | 0.68 | [0.56; 0.78] |
|  |  |  | 0.2 | 0.4 | 0.6 | 0.8 | 1 |  |
| Author | OPE | MC |  |  |  |  | Proportion | 95\% CI |
| Wildt et al. 2018 | 22 | 50 |  | - |  |  | 0.44 | [0.31; 0.58] |
| Lörinczy et al. 2011 | 7 | 14 |  |  |  |  | 0.50 | [0.27; 0.73] |
| Graziano et al. 2021 | 63 | 118 |  |  | - |  | 0.53 | [0.44; 0.62] |
| Overall effect$I^{2}=0 \%[0 \% ; 90 \%]$ | 92 | 182 |  | $<$ |  |  | 0.51 | [0.43; 0.58] |
|  |  |  | 00.2 |  |  | 0.8 |  |  |
| Author | OPO | MC |  |  |  |  | Proportion | 95\% CI |
| Lörinczy et al. 2011 | 1 | 14 | + |  |  |  | 0.07 | [0.00; 0.34] |
| Graziano et al. 2021 | 12 | 118 | + |  |  |  | 0.10 | [0.06; 0.17] |
| Wildt et al. 2018 | 7 | 50 | + |  |  |  | 0.14 | [0.07; 0.26] |
| Overall effect $I^{2}=0 \%[0 \% ; 90 \%]$ | 20 | 182 | $\bigcirc$ |  |  |  | 0.11 | [0.07; 0.16] |
|  |  |  | $0 \quad 0.2$ | 0.4 | 0.6 | 0.8 |  |  |
| Fiqure 3. Forest plot presenting the proportions of low bone density, osteopenia, and osteoporosis in patients with microscopic colitis. $\angle B D=10$.bone density. MC $=$ microscopic |  |  |  |  |  |  |  |  |

The odds of having LBD is tripled in the presence of MC. We highly suggest screening patients with MC for BMD at the moment of diagnosis.

