

Supplementary material

Supplementary table 1: Search strategy

PubMed search

1. Inflammatory bowel disease
2. Crohn disease
3. Ulcerative colitis
4. 1 OR 2 OR 3
5. Osteoporosis
6. Osteopenia
7. Bone mass density
8. BMD
9. 5 OR 6 OR 7 OR 8
10. Cohort
11. Prospective
12. Case-control
13. Follow-Up
14. Longitudinal
15. Retrospective
16. Cross-Sectional
17. 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16
18. 4 AND 9 AND 17

Embase search

1. 'inflammatory bowel disease'
2. 'crohn disease'
3. 'ulcerative colitis'
4. #1 OR #2 OR #3
5. 'osteoporosis'
6. 'osteopenia'
7. Bone AND mass AND density

8. bmd
9. #5 OR #6 OR #7 OR #8
10. cohort
11. prospective
12. 'case-control'
13. 'follow-up'
14. longitudinal
15. retrospective
16. 'cross-sectional'
17. #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16
18. #4 AND #9 AND #17
19. #18 AND 'article'/it
20. #18 AND 'article'/it AND [embase]/lim NOT ([embase]/lim AND [medline]/lim)

Supplementary table 2: Detailed overview of all investigated risk factors for low bone mineral density

Risk factors for reduced BMD	Andreassen et al (1998) [14]	Andreassen et al (1999) [15]	Haugeberg et al (2001) [17]	Jahnsen et al (1997) [12]	Schoon et al (2000) [13]	Bernstein et al (2003, May) [21]	Bernstein et al (2003, November) [22]	Leslie et al (2008) [19]	Leslie et al (2009) [20]	Comments
Patient cohort	Only CD	Only CD	Only CD	Only CD	Only CD	CD & UC	CD & UC	CD & UC	CD & UC	
GENERAL RISK FACTORS										
Gender			+ ^f	+ ^m	-				+ ^f	
Age		+	+			-		(+)	-	Leslie et al (2009) found no correlation in a multiple linear regression analysis made on a cohort in which only 10% was above age

										65. Haugeberg et al found patients with low BMD to be younger than patients with normal BMD.
Weight		- ^f , + ^m	+			+			+	
Total fat									+/-	
Total lean tissue									+	
Total fat fraction									+	
BMI		- ^f , + ^m	+/-	+					+	
Height			+/-			-			+	
Previous corticosteroid use									-	
Ever use of prednisolone			+							
Ever use of steroids		- ^m , + ^f								
Use of				+^						

corticosteroids										
Cumulative prednisolone dose		***,-	+							
Highest daily prednisolone dose			+/-							
Maintenance prednisolone dose			+/-							
Mean age at first prednisone dose						-				
Prednisone > 1 month at any time						-				
Prednisolone treatment last year			-							
Current prednisolone treatment			-							
Duration of prednisolone treatment			+							
Postmenopausal		+	-	-	+/-					

[illegible]

DISEASE SPECIFIC RISK FACTORS										
Site of disease	-		-			-				
Disease duration		-+*	-	-		-				
UC diagnosis						-			-	
CD diagnosis						-			+	
CD diagnosis when not treated with steroids				-						
CD diagnosis when treated with steroids				+						
CD lifetime steroid dose				+						
Diagnosis (post- or pre puberty)						-				
Colon surgery			+/-							
GI surgery		-	+/-			-				
Small bowel			-	-						

resection										
Total colectomy			-							
Length of resected ileum		-								
Mean age at diagnosis			+/-		+	-				
Perianal fistulas						-				
Serum osteocalcin			+/-							
MEDICATION & SUPPLEMENTS										
Daily vitamin D intake							-			
Daily calcium intake							-			
Vitamin D supplement			-			-				
Calcium supplement			-			-				
Sex hormone						-				

[illegible]

.. = only in Ulcerative colitis

^ = only in Crohn's Disease

f = only in females

m = only in males

Supplementary to table 3. A plus sign means that a significant association was found and a minus sign means that no association was found. If there were discrepancies in the results depending on what statistical analysis that was made in one study, both signs are present

Supplementary table 3: Detailed overview of all investigated risk factors for change in BMD over time

Risk factors for change in BMD	Jahnsen et al (2004) ^[16]	Leslie et al (2008) ^[19]	Leslie et al (2009) ^[20]	Tsai et al (2015) ^[18]	Targownik et al (2012) ^[3]
Patient cohort	Only CD	CD & UC	CD & UC	CD+UC	CD & UC
GENERAL RISK FACTORS					
Gender		-	-	+ ^{f,m}	-
Height					-
Smoking	-				
Menstrual status	-				
Age		-	+	+	
Age < 50 or > 65 years				-	

Age 50-64 years				+	
Age >< 50 years		+	+		+/-
Increase in weight			+		
Greater weight at baseline measurement			+		
Weight change			+		+
Total fat change			+		
Total lean change			+		
Lean mass			+		
Total fat fraction change			-		
Fat mass			+		
BMI increase					-
BMI decrease					+/-
BMI			+		
BMI change					+
% change in BMI	+				
Comorbidities				+/-	
No comorbidities				+	
Previous fractures	-				

Initial BMD measurements	+				
Osteoporosis at baseline measurements	-				
DISEASE SPECIFIC RISK FACTORS					
Diagnosis			-	+ [^] , - ^{••}	- ^{••} , + [^] , -
Small bowel resection	-				
Large bowel disease only	+				
Disease location	-				
Disease activity					-
Inactive disease					-
Active disease					+
MEDICATION & SUPPLEMENTS					
Osteoporosis medication use		+			
Corticosteroid treatment during follow-up	-				
Corticosteroid dosis	-				
Previous corticosteroid use			-		

Cumulative prednisolone dose					+/-
Cumulative prednisolone dose < 450 mg					-
Cumulative prednisolone dose > 450 mg					+
SERUM MARKERS					
Poor vitamin D status with secondary hyperparathyroidism	-				
Serum albumin					-
Serum creatinine		+			-
Serum calcium					-
Serum 25-OH D	+	+			-
Serum parathyroid hormone					-
Serum estradiol					-
Serum testosterone					-
Serum C-reactive protein					-
Serum phosphate					+
Alkaline phosphate					+
Serum PTH	+	-			

Haemoglobin					-
Final serum C-telopeptide					+
Bone specific alkaline phosphatase		+			
Total alkaline phosphatase		+			
N-telopeptide		+			

+ = positive association

- = no association

+/- = significant association and no association were found depending on the type of statistical analysis

CD = Crohn's Disease

UC = Ulcerative Colitis

.. = only in Ulcerative colitis

^ = only in Crohn's Disease

^f = only in females

^m = only in males

Supplementary to table 4. A plus sign means that a significant association was found and a minus sign means that no association was found.

If there were discrepancies in the results depending on what statistical analysis that was made in one study, both signs are present. Follow-up time for the respective studies was as follows: Jahnsen et al: 2 years^[16]; Leslie et al: 2.3 ± 0.3 years^[19]; Leslie et al: 2.3 ± 0.3 years^[20]; Targownik et al 4.3 ± 0.3 years^[3]; Tsai et al: 6.49 ± 3.09 years^[18].