

## 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

<b>Risk factors for reduced BMD</b>	<b>Andreassen et al (1998) [14]</b>	<b>Andreassen et al (1999) [15]</b>	<b>Haugeberg et al (2001) [17]</b>	<b>Jahnsen et al (1997) [12]</b>	<b>Schoon et al (2000) [13]</b>	<b>Bernstein et al (2003, May) [21]</b>	<b>Bernstein et al (2003, November) [22]</b>	<b>Leslie et al (2008) [19]</b>	<b>Leslie et al (2009) [20]</b>	<b>Comments</b>
<b>Patient cohort</b>	Only CD	Only CD	Only CD	Only CD	Only CD	CD & UC	CD & UC	CD & UC	CD & UC	
<b>GENERAL RISK FACTORS</b>										
<b>Gender</b>			+f	+ m	-				+f	
<b>Age</b>		+	+			-		(+)	-	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.
<b>Weight</b>		-f,+m	+			+			+
<b>Total fat</b>									+/-
<b>Total lean tissue</b>									+
<b>Total fat fraction</b>									+
<b>BMI</b>		-f,+m	+/-	+					+
<b>Height</b>			+/-			-			+
<b>Previous corticosteroid use</b>									-
<b>Ever use of prednisolone</b>			+						
<b>Ever use of steroids</b>		-m,+f							
<b>Use of</b>				+^					

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



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

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



<b>Serum phosphate</b>	-								+		
<b>Total alkaline phosphatase</b>									+		
<b>Bone specific alkaline phosphatase</b>									+		
<b>Bone alkaline phosphate</b>	+										
<b>N-telopeptide</b>									+		
<b>Vitamin D deficiency</b>	+										
<b>Serum 1,25(OH<sub>2</sub>)D</b>	-										

+ = 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

\*\* = in males and premenopausal females

\* = only in postmenopausal females

.. = 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

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

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	-				

<b>Initial BMD measurements</b>	+				
<b>Osteoporosis at baseline measurements</b>	-				
<b>DISEASE SPECIFIC RISK FACTORS</b>					
<b>Diagnosis</b>			-	+ <sup>^</sup> , <sup>-</sup>	- <sup>-</sup> ,+ <sup>^</sup> , <sup>-</sup>
<b>Small bowel resection</b>	-				
<b>Large bowel disease only</b>	+				
<b>Disease location</b>	-				
<b>Disease activity</b>					-
<b>Inactive disease</b>					-
<b>Active disease</b>					+
<b>MEDICATION &amp; SUPPLEMENTS</b>					
<b>Osteoporosis medication use</b>		+			
<b>Corticosteroid treatment during follow-up</b>	-				
<b>Corticosteroid dosis</b>	-				
<b>Previous corticosteroid use</b>			-		

Cumulative prednisolone dose					+/-
Cumulative prednisolone dose < 450 mg					-
Cumulative prednisolone dose > 450 mg					+
<b>SERUM MARKERS</b>					
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	+	-			

<b>Haemoglobin</b>					-
<b>Final serum C-telopeptide</b>					+
<b>Bone specific alkaline phosphatase</b>		+			
<b>Total alkaline phosphatase</b>		+			
<b>N-telopeptide</b>		+			

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*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<sup>[16]</sup>; Leslie et al: 2.3 ± 0.3 years<sup>[19]</sup>; Leslie et al: 2.3 ± 0.3 years<sup>[20]</sup>; Targownik et al 4.3 ± 0.3 years<sup>[3]</sup>; Tsai et al: 6.49 ± 3.09 years<sup>[18]</sup>.*