

Table 4: Evidence table –Sánchez et al. (2011)

Study type	Cross-sectional data from cohort study																
Country	Argentina																
Number of patients	N=265 adults (223 female and 42 male) with a diagnosis of coeliac disease N=530 controls																
Quality	<ol style="list-style-type: none"> 1. Did the study have a clearly focused aim? Yes - 2 clear aims 2. Was the cohort recruited in an acceptable way? No - not clear recruitment strategy 3. Was the exposure accurately measured to minimise bias? No - questionnaire data highly biased 4. Was the outcome accurately measured to minimise bias? Yes CD clearly defined 5. Have the authors identified all important confounding factors? Have they taken account of confounding factors in the design/analysis? No - many important confounding factors, namely memory bias and personal recollection bias, no supporting info source 6. Was the follow-up of subjects complete enough? Was the follow-up of subjects long enough? Na 7. What are the results? CD group showed higher incidence rate of fracture 8. How precise are the results? Precise - tight CI 9. Do you believe the results? No - questionnaire data nit appropriate way of addressing research aim 10. Can the results be applied to the local population? Not clear 11. Do the results fit with other available evidence? Yes 12. What are the implications of this study for practice? Not clear 																
Study population	<p>Patients who attended gastroenterology units in four medical centres from March 2007 to November 2009</p> <p>Inclusion: diagnosis confirmed at least 5 years prior to entry into the study</p> <p>Exclusion: patients diagnosed with other disorders that could independently reduce bone health (ie. uncontrolled thyroid dysfunction, rheumatoid arthritis, inflammatory bowel disease, diabetes), who took medications that could affect bone metabolism (ie. steroids, calcium, vitamin D, alendronate, anticonvulsants, thyroid hormones, estrogen or androgen replacement) and who had complicated CD.</p> <table border="1"> <thead> <tr> <th></th> <th>Coeliac disease (N=265)</th> <th>Control (N=530)</th> <th>p value</th> </tr> </thead> <tbody> <tr> <td>Proportion female</td> <td>84% (223)</td> <td>84% (530)</td> <td rowspan="3">Not reported</td> </tr> <tr> <td>Median age (range)</td> <td>42 (18-85)</td> <td>43 (16-87)</td> </tr> <tr> <td>Median age at diagnosis (range)</td> <td>30 (1-80)</td> <td>-</td> </tr> </tbody> </table>				Coeliac disease (N=265)	Control (N=530)	p value	Proportion female	84% (223)	84% (530)	Not reported	Median age (range)	42 (18-85)	43 (16-87)	Median age at diagnosis (range)	30 (1-80)	-
	Coeliac disease (N=265)	Control (N=530)	p value														
Proportion female	84% (223)	84% (530)	Not reported														
Median age (range)	42 (18-85)	43 (16-87)															
Median age at diagnosis (range)	30 (1-80)	-															

	Mean BMI (kg/m ²) ±SE	22.5 ± 0.2	24.3 ±0.2	0.001
	Median age at menarche (range)	13 (9-17)	12 (9-20)	Not reported
	Median age at menopause (range)	48 (30-54)	49 (36-59)	
Control	2 age and sex matched controls (for each patient with CD) with functional gastrointestinal disorders (based on Rome III criteria)			
Length of follow-up	Person-years before diagnosis: 7028 (cases) vs 14532 (controls) (of cases 6480 were attributed to females and 647 males)			
Details of coeliac testing	Based on combination of positive clinical findings (symptoms or risk factors such as family history), characteristic enteropathy at the time of diagnosis, positive CD0specific serology and positive clinical and/or histological response to GFD; positive serological tests (antigliadin antibodies, anti-tissue transglutaminase antibodies and/or antimysium antibodies) were considered sufficient for a diagnosis of CD			
Results	Fracture rate before diagnosis:			
		Coeliac disease (N=265)	Control (N=530)	
	Proportion of patients with at least one fracture	15.1% (40)	8.5% (45)	
	Median age at first fracture (range)	10 (2-61)	15 (1-74)	
	(Asked by questionnaire of patients and confirmed in patient records)			
	Characteristics of patients with coeliac disease:			
		Female (N=223)	Male (N=42)	p value
	Median age (range)	42 (18-62)	35 (18-66)	0.04
	Median age at diagnosis (range)	31 (1-80)	19 (1-52)	0.003
	Mean BMI (kg/m ²) ±SE	22.5 ± 0.5	23.7 ±0.6	0.01
Proportion with at least one fracture before diagnosis	13% (29)	26% (11)	0.05	
Median age at first fracture before diagnosis (range)	14 (2-61)	10 (6-32)	0.04	
Risk of fracture				
	Coeliac disease (N=265)	Control (N=530)	HR (95% CI) p value	Adjusted HR (95% CI)
All - incidence ratio	8.67	5.64	1.53 (1.05-2.14), p=0.01	1.78 (1.23-2.56)*, p=0.02
Females – incidence ratio	6.58	5.09	1.28 (0.87-1.88), p=NS	1.52 (0.99-2.32)*, p=0.052

Appendix D: Evidence tables

	Males – incidence ratio	29.35	10.20	2.67 (1.37 -5.22), p=0.004	2.63 (1.24-5.59)*, p=0.01
	* adjusted by age at enrolment, age at diagnosis, BMI, smoking habits and menopause				
Source of funding	Partially from Asociacion para el estudio de las Enfermedades del Intestino				
Conflicts of interest	Not reported				
Comments	Authors included any events occurring during the first year after diagnosis of coeliac disease in the ‘before diagnosis’ category because coeliac disease is a long-term disease and GFD may only provide a slow recovery				

Definitions of abbreviations are given at the end of this document.