Evidence table – Canavan et al. (2011)

Study type	Non-randomised comparative case series
Country	UK
Number of patients	N=7527 adults with undetected CD
quality	1. Did the study have a clearly focused aim? Yes 2. Was the cohort recruited in an acceptable way? Yes 3. Was the exposure accurately measured to minimise bias? Yes 4. Was the outcome accurately measured to minimise bias? Yes 5. Have the authors identified all important confounding factors? Have they taken account of confounding factors in the design/analysis? Yes 6. Was the follow-up of subjects complete enough? Was the follow-up of subjects long enough? Yes - roughly 16 years 7. What are the results? Undetected CD in adults over the age of 45 does not confer increased mortality risk 8. How precise are the results? Precise but cross line no effect 9. Do you believe the results? Yes 10. Can the results be applied to the local population? Yes 11. Do the results fit with other available evidence? Yes 12. What are the implications of this study for practice? Nil
Study population	Inclusion: patients from the Cambridge General Practice Health Study on bone density in the general population (people registered at 12 general practices in Cambridge between 1990 and 1995) who were between 45 and 76 years old and, in 2001, invited to participate (completing a questionnaire and physical assessment including blood samples) Exclusion: patients on a GFD
Control	None
Length of follow-	117 914 patient years (median 16.8)

up	(patients were followed up until the end of 2009)
Details of coeliac testing	IgA EMA (indirect immunofluorescence on commercial monkey oesophagus sections; The Binding Site, Birmingham, UK with 1 in 10 dilution) Validation with human tTGA was used for all positive samples Undetected coeliac disease was defined as patients who did not report a diagnosis of coeliac disease and were not on a GFD but had EMA positivity
Results	Of 7550 tested in 2001, 23 were excluded: 3 had probably treated CD (on a GFD and coded as having malabsorption), 1 had probable coeliac disease but untreated (EMA positive, was not on a GFD but was coded as having malabsorption) and 19 with possible coeliac disease (those on a GFD but did not report having a malabsorption and who were EMA negative).

It total, 1.2% (87/7527) of patients were EMA positive

Multivariate logistic regression:

	EMA negative (n=7440)	EMA positive (n=87)	Odds ratio for positive EMA (95% CI)	
			Univariate	Multivariate
Proportion women	59% (4387)	65.5% (57)	1	1
Proportion men	41% (3053)	35.5% (30)	0.76 (0.49-1.18)	0.83 (0.52-1.34)
Age group: < 55 55-64 ≥65	37.6% (2794) 30.6% (2280) 31.8% (2366)	42.5% (37) 34.5% (30) 23% (20)	1 0.99 (0.61-1.61) 0.64 (0.37-1.10)	1 1.01 (0.62-1.65) 0.67 (0.38-1.16)

Mortality rate:

	Mortality rate per 1000 person years (95% CI)
Women	10.3 (9.6-11.1)
Men	16.2 (15.1-17.4)

Mortality rate by EMA status (using Cox multivariate regression):

	Persons at risk	Deaths	Mortality rate per 1000 person years (95%CI)	Hazard ratio for mortality (95% CI)		
				Unadjusted	Age and gender adjusted	Multivariate adjusted*
EMA negative	7440	1479	12.7 (12.1-13.4)	1	1	1
EMA positive	87	13	9.4 (5.4-16.1)	0.73 (0.42-12.6)	0.91 (0.53-1.58)	0.98 (0.57-1.69)

* Adjusted for age, gender, socioeconomic group and smoking status

Mortality rate attributed to cancer or cardiovascular disease by EMA status (using Cox multivariate regression):

	Mortality rate per 1000 person years (95%CI)		Hazard ratio for mortality (95% CI)					
			Unadjusted		Age and gender adjusted		Multivariate adjusted*	
	EMA negative	EMA positive	EMA negative	EMA positive	EMA negative	EMA positive	EMA negative	EMA positive
Cancer	4.2 (3.8-4.6)	4.3 (1.9-9.6)	1	1.03 (0.46-2.30)	1	1.18 (0.53-2.65)	1	1.27 (0.57-2.85)
Cardiovascular disease	5.1 (4.7-5.5)	5.0 (2.4-10.6)	1	0.99 (0.47-2.08)	1	1.31 (0.62-2.76)	1	1.39 (0.66-2.92)

* Adjusted for age, gender, socioeconomic group and smoking status

Source of funding	NIHR Clnical Fellowship held by one of the authors and the NIHR Clniical Scientist position held by another author (funding for the original study was from Coeliac UK project grant in 2001)
Conflicts of interest	Study reports no personal interests
Comments	

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