Table 6: Evidence table – Zugna et al. (2013)

<table>
<tr><td>Study type</td><td>Case control</td></tr>
<tr><td>Country</td><td>Sweden</td></tr>
<tr><td>Number of patients</td><td>N=12,919 children born to mothers with undiagnosed CD
N=53,186 children used as controls
N=3202 children born to mothers with diagnosed CD</td></tr>
<tr><td>Quality</td><td>1. Did the study have a clearly focused aim? No - many different sub questions and populations embedded in study
2. Was the cohort recruited in an acceptable way? Yes
3. Was the exposure accurately measured to minimise bias? Difficult to determine how mortality was defined - mortality at birth? Or throughout childhood? Or both?
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
7. What are the results? No increased mortality in children born to mothers with undiagnosed CD
8. How precise are the results? Imprecise
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? Not clear
12. What are the implications of this study for practice? Not clear</td></tr>
<tr><td>Study population</td><td>Children born to women with undiagnosed CD who gave birth to a live singleton infant between 1961 and 2009 taken from computerised biopsy report data from all Swedish pathology departments

Of all mothers with CD (diagnosed or undiagnosed):
<table>
<tr><th></th><th>With CD
(16, 121 births)</th><th>Without CD
(61, 782 births)</th></tr>
<tr><td>Sex of child</td><td>50.7% (8179) male</td><td>51.3% (31, 712) male</td></tr>
<tr><td>Mothers with type I diabetes</td><td>1.4% (227)</td><td>0.3% (175)</td></tr>
<tr><td>Mothers with thyroid disease</td><td>7.7% (1239)</td><td>2.9% (1807)</td></tr>
<tr><td>Mothers with rheumatoid arthritis</td><td>1.3% (206)</td><td>0.8% (466)</td></tr>
<tr><td>Non-smoking mothers</td><td>39.6% (6378)</td><td>37.4% (23, 085)</td></tr>
</table>
</td></tr>
</table>

Control

5 per patient matched for age, sex, calendar year of birth and county of residence taken asa sample of all Swedish residents (data from Statistics Sweden) with no prior duodenal or jejunal biopsy (exclusion: those with a duodenal or jejunal biopsy during following, those who died before the hypothetical biopsy date [based on those of the matched index], and those whose matched index case with CD was excluded)

Length of follow-up

n/a

Details of coeliac testing

Not described

Results

Risk of death in children born to mothers with undiagnosed CD or no CD:

	Crude HR (95% CI)	Adjusted HR (95% CI) [a]
No CD	1.0	1.0
Undiagnosed CD	1.10 (0.95, 1.26) [b]	1.08 (0.94, 1.25) [b]

(unclear if authors have used correct calculation of OR for matched study designs)

[a] adjusted for maternal age, maternal country of birth, maternal educational level, maternal total number of children, infant's year of birth (calendar year of birth, appearance of maternal diabetes, thyroid disease and rheumatoid arthritis were all considered as time-dependent variables in the models)

[b] no difference between male and female children

Risk of nonaccidental death in children:

	HR (95% CI)*
Undiagnosed CD	1.07 (0.92, 1.26)
Diagnosed CD	1.30 (0.65, 2.58)

* unclear if this HR is adjusted

Risk of death in children (5 year follow-up only):

	HR (95% CI)*
Undiagnosed CD	1.23 (0.99, 1.54)
Diagnosed CD	1.22 (0.60, 2.48)

* unclear if this HR is adjusted

Risk of death in children (children born from 1982 onwards):

	Adjusted HR (95% CI)*
Undiagnosed CD	1.27 (0.80, 2.00)

	<table><tr><td>Diagnosed CD</td><td>1.12 (0.54, 2.32)</td></tr></table> * adjusted for prenatal smoking exposure and civil status Post hoc analysis of risk of death in children (restricted to the first year of follow-up only): <table><tr><td></td><td>HR (95% CI)*</td></tr><tr><td>Undiagnosed CD</td><td>0.74 (0.30, 1.85)</td></tr><tr><td>Diagnosed CD</td><td>1.32 (1.03, 1.67)</td></tr></table> * unclear if this HR is adjusted
Source of funding	One author was partially supported by grants from The Campagnia san Paolo/Firms and the Italian Association for Cancer Research, 2 authors were supported by the Swedesh Society of Medicine, and one was supoorted by the Swedish Society of Medicine, the Swedish Research Council-Medicine, the Swedish Celiac Society,and the Fulbright Commission (authors state that none of the funders had any role in the design or conduct of the study, in the collection, management, analysis and interpretation of data, or in the preparation, review or approval of the manuscript)
Conflicts of interest	None declared
Comments	

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