Type 1 diabetes

Bibliographic reference	**Adlercreutz., EH. (2014).**
Study type	Cohort study
Study quality	The Joanna Briggs Institute Prevalence Critical Appraisal Tool (http://ijhpm.com/article_2870_607.html) 1. Was the sample representative of the target population? YES 2. Were study participants recruited in an appropriate way? NO – Unclear is consecutive sample recruited 3. Was the sample size adequate? YES 4. Were the study subjects and the setting described in detail? YES 5. Was the data analysis conducted with sufficient coverage of the identified sample? YES 6. Were objective, standard criteria used for the measurement of the condition? YES 7. Was the condition measured reliably? YES 8. Was there appropriate statistical analysis? YES

	9. Are all important confounding factors/subgroups/differences identified and accounted for? YES 10. Were subpopulations identified using objective criteria? NA Overall risk of bias = MODERATE
Patient characteristics	N = 662 Swedish children with T1D; 1080 Danish children with T1D; 309 healthy children from Sweden; 283 healthy Danish children. All children were diagnosed with T1D between 1995 and 2006. Samples were collected at the time of diagnosis. Healthy controls were recruited from local schools in both Denmark and Sweden. Swedish T1D: • N=662 • 305 = female • Median age = 10.2 (1 - 17.9) Danish T1D • N=1080 • Female = 518 • Median age = 10.3 (0.6 - 17.8)
Comorbid condition	Type 1 diabetes (T1D)
Investigations	Serological testing • Conjugated IgA/IgG DGP tTG • IgG tTG Celiac disease autoimmunity was defined as being positive for both IgA/G DGP tTG and IgG tTG HLA genotyping • HLA DQ genotyping
Results	Swedish T1D • Prevalence of CD = 17.2% (114/662) Danish T1D • Prevalence of CD = 11.7% (126/1080)
Funding	None listed
Other comments	NO Biopsy confirmed diagnosis of CD

Bibliographic reference	**Barbato et al. (1998)**
Study type	Cross-sectional survey
Study quality	The Joanna Briggs Institute Prevalence Critical Appraisal Tool (http://ijhpm.com/article_2870_607.html) 1. Was the sample representative of the target population? YES 2. Were study participants recruited in an appropriate way? YES (consecutive sample recruited) 3. Was the sample size adequate? YES 4. Were the study subjects and the setting described in detail? YES 5. Was the data analysis conducted with sufficient coverage of the identified sample? YES 6. Were objective, standard criteria used for the measurement of the condition? YES 7. Was the condition measured reliably? YES 8. Was there appropriate statistical analysis? YES 9. Are all important confounding factors/subgroups/differences identified and accounted for? YES 10. Were subpopulations identified using objective criteria? NA Overall risk of bias = LOW
Country	Italy
Number of patients	N=175 patients with insulin dependent diabetes
Study population	Inclusion: Patients with insulin dependent diabetes mellitus (no further inclusion criteria provided) 51.4% male Age from 1 to 30 years (102 were paediatric [between 6 and 14 years] and 73 were adults)
Control	none
Length of follow-up	n/a
Details of coeliac testing	IgA and IgG AGA (using fluorescent immunoenzymatic test, Eurospital) Anti-endomysium antibodies (AEA) (using indirect immuno-fluorescence with those who fluoresced only in reticular tissues as positive, Medic) anti-reticulin antibodies (ARA) (using indirect immuno-fluorescence with those who fluoresced only in reticular tissues as positive, Eurospital) If tests positive for AEA (with or without positivity for ARA and AGA), intestinal biopsy was performed
Results	Overall seroprevalence: 25.6% (45/175) Anti-endomysium antibodies (AEA) – 21 had pathological values

	23 had biopsy (21 with pathological values for AEA and 2 with pathological values for only ARA) – all 21 with pathological values for AEA had villous atrophy Prevalence of CD in children with diabetes: 8.8% (9/102; 95% CI 3.3 to 14.3) Prevalence of CD in adults with diabetes: 16.4% (12/73; 95% CI 7.9 to 24.9) Presenting symptoms at diagnosis included diarrhoea and weight loss in 2 (16 and 17 years old) and others had one or more of growth failure in height and/or weight, recurrent abdominal pain, abdominal distension, lack of appetite, mood changes, headache, sideropenic anaemia. (all symptoms disappeared after GFD was introduced)
Source of funding	Not reported
Conflicts of interest	Not reported
Comments	

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

Bibliographic reference	**Cev et al. (2010)**
Study type	Cross-sectional data from case series
Study quality	The Joanna Briggs Institute Prevalence Critical Appraisal Tool (http://ijhpm.com/article_2870_607.html) 1. Was the sample representative of the target population? YES 2. Were study participants recruited in an appropriate way? NO – Unclear is consecutive sample recruited 3. Was the sample size adequate? YES 4. Were the study subjects and the setting described in detail? YES 5. Was the data analysis conducted with sufficient coverage of the identified sample? YES 6. Were objective, standard criteria used for the measurement of the condition? YES 7. Was the condition measured reliably? YES 8. Was there appropriate statistical analysis? YES 9. Are all important confounding factors/subgroups/differences identified and accounted for? YES 10. Were subpopulations identified using objective criteria? NA Overall risk of bias = MODERATE
Country	Romania
Number of patients	N=307 patients with T1D

Study population	Inclusion: patients with T1D prospectively enrolled from January 2004 to December 2008 who had presented at a centre for evaluation and rehabilitation for children and adolescents 158 females, 149 males Median age 27 years (range 14-38)
Control	None
Length of follow-up	n/a
Details of coeliac testing	tTGA (IgA and IgG) (ELISA with human recombinant tTG as antigen with Test ESKULISA, CeliCheck, Germany; values greater than 24 U/ml were considered positive) If positive, IgA EMA (indirect immunofluorescence using unfixed cryosections of monkey oesophagus) If positive on tTGA, duodenal biopsy assessed with Marsh system
Results	5.5% (17) with positive tTGA 16 has biopsy 3.9% (12) with biopsy-confirmed CD - four Marsh 0 (not considered CD) - 2 Marsh 1 - 1 Marsh 2 - 9 Marsh 3
Source of funding	Not reported
Conflicts of interest	Not reported
Comments	Study also reports results after treatment on GFD but this was not extracted here

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

Bibliographic reference	**Djurić et al. (2010)**
Study type	Cross-sectional survey
Study quality	The Joanna Briggs Institute Prevalence Critical Appraisal Tool (http://ijhpm.com/article_2870_607.html) 1. Was the sample representative of the target population? YES 2. Were study participants recruited in an appropriate way? NO – Unclear is consecutive sample recruited 3. Was the sample size adequate? YES 4. Were the study subjects and the setting described in detail? YES 5. Was the data analysis conducted with sufficient coverage of the identified sample? YES 6. Were objective, standard criteria used for the measurement of the condition? YES 7. Was the condition measured reliably? YES

	8. Was there appropriate statistical analysis? YES 9. Are all important confounding factors/subgroups/differences identified and accounted for? YES 10. Were subpopulations identified using objective criteria? NA Overall risk of bias = MODERATE
Country	Serbia
Number of patients	N=121 children and adolescents with T1D N=125 healthy children and adolescents as control
Study population	Inclusion: children and adolescent with T1D who were admitted to a university hospital or observed on an outpatient basis from October 2004 to December 2007 70 girls, 51 boys Mean age 10.4 years
Control	Healthy children and adolescents identified as healthy from their medical records and routine physical examinations from south east Serbia
Length of follow-up	n/a
Details of coeliac testing	Serum IgA Anti-tTG IgA (ELISA, Euroimmun; 20 RU/ml was cut-off) / anti-tTG IgG (ELISA) if IgA deficient Biopsy if serologically positive (ESPGHAN criteria)
Results	9 (7.4%) were serologically positive on tTG IgA Of 4 with selective IgA deficiency, all had negative IgG tTG Biopsy-proven CD: 5.79%(7) vs 0.8% (1) ($p < 0.05$) (T1D group: 2 had Marsh IIIa, 3 had Marsh IIIb, 2 had Marsh IIIc; the positive control participant had Marsh IIIa)
Source of funding	Not reported
Conflicts of interest	Not reported
Comments	

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

Bibliographic reference	**Galván et al. (2008)**
Study type	Cross-sectional survey
Study quality	The Joanna Briggs Institute Prevalence Critical Appraisal Tool (http://ijhpm.com/article_2870_607.html)

	1. Was the sample representative of the target population? YES 2. Were study participants recruited in an appropriate way? NO – Unclear is consecutive sample recruited 3. Was the sample size adequate? YES 4. Were the study subjects and the setting described in detail? YES 5. Was the data analysis conducted with sufficient coverage of the identified sample? YES 6. Were objective, standard criteria used for the measurement of the condition? YES 7. Was the condition measured reliably? YES 8. Was there appropriate statistical analysis? YES 9. Are all important confounding factors/subgroups/differences identified and accounted for? YES 10. Were subpopulations identified using objective criteria? NA Overall risk of bias = MODERATE
Country	Cuba
Number of patients	N=208 patients with T1D
Study population	Inclusion: patients with T1D who were diagnosed as positive for antibodies against islet cells and/or glutamic acid decarboxylase isoform 65 (antibodies against GAD65) requiring insulin treatment at diagnosis Mean 19 years old (range 2-58) 116 male, 92 female
Control	none
Length of follow-up	n/a
Details of coeliac testing	tTGA IgA (immunochromatographic test, HeberFast Line® anti-transglutaminase and also ELISA) Biopsy if positive tTGA
Results	14 patients were positive on both arrays (2 had symptoms) 6 agreed to biopsy (including the 2 with symptoms) and had features consistent with CD with 2.88% (6/208) biopsy-confirmed prevalence: - 5 had partial villous atrophy with elevated IEL counts - 1 had subtotal villous atrophy - (mean age at diagnosis: 11.00 ±4.56 years
Source of funding	Not reported
Conflicts of interest	Not reported

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

Bibliographic reference	**Kakleas et al. (2010)**
Study type	Comparative cross-sectional survey
Study quality	The Joanna Briggs Institute Prevalence Critical Appraisal Tool (http://ijhpm.com/article_2870_607.html) 1. Was the sample representative of the target population? YES 2. Were study participants recruited in an appropriate way? NO – Unclear is consecutive sample recruited 3. Was the sample size adequate? YES 4. Were the study subjects and the setting described in detail? YES 5. Was the data analysis conducted with sufficient coverage of the identified sample? YES 6. Were objective, standard criteria used for the measurement of the condition? YES 7. Was the condition measured reliably? YES 8. Was there appropriate statistical analysis? YES 9. Are all important confounding factors/subgroups/differences identified and accounted for? YES 10. Were subpopulations identified using objective criteria? NA Overall risk of bias = MODERATE
Country	Greece
Number of patients	N=105 children and adolescents with type 1 diabetes mellitus
Study population	Inclusion: children and adolescents with T1DM regularly followed at the Diabetic Clinic of the Second University Department of Paediatrics between 2005 and 2007 Mean ± SD: Age: 12.44 ± 4.76 years Duration of diabetes: 4.41 ±3.70 Age at diabetes diagnosis: 8.01 ± 3.17 years 50.4% male HbA1c levels: 8.13 ± 1.70%
Control	Study compared those with and without tTG IgA seropositivity for CD
Length of follow-up	n/a
Details of coeliac	Anti-tTG IgA class antibodies were detected by ELISA (using DYNEX DSX ELISA analyser; human native tissues transglutaminase

testing	from red blood cells was used; 20-30 units was considered to be weakly positive [Inova Diagnostics, USA]) If high values of tTG IgA was discovered on 2 consecutive measurements (60 units or more), jejunal biopsy was performed Conclusive diagnosis on typical mucosal findings including lymphocytic infiltration, hypertrophy of the crypts and villous atrophy(Marsh II) Serum total IgA levels were determined to detect IgA deficiency
Results	Serological results: **Anti-tTG IgA positivity: 8.6% (9/105)** (only 5 had mild intestinal symptoms, iron deficiency anaemia and growth retardation) No differences between males/females, BMIHbA1c levels, but patients with positive anti-tTG IgA were significant younger (p=0.038), had shorter T1DM duration (p=0.056) and shorter height (p=0.055) Univariate regression analyses showed that the likelihood of anti-tTG IgA positivity was: - approximately 18% greater [95% CI 0.68-0.99) in younger patients with T1DM - 30% greater in those with short T1DM duration [95% CI: 0.48, 1.04]) Multivariate logistic regression indicated that the patients' present age was the only determinant associated with anti-tTG IgA positivity: younger children with T1DM had 22% more odds of presenting with anti-tTG IgA positivity (OR:1.22, 95% CI 1.01-1.45) Biopsy results: **5 patients (4.8%) had biopsy-proven CD** (the same 5 were those who had symptoms and anti-tTG IgA positivity with high titres 60 or more units)
Source of funding	Not reported
Conflicts of interest	Study reports that there are none
Comments	

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

Bibliographic reference	**Leeds et al. (2010)**
Study type	Cross-sectional data (for prevalence) and case-control
Study quality	The Joanna Briggs Institute Prevalence Critical Appraisal Tool (http://ijhpm.com/article_2870_607.html) 1. Was the sample representative of the target population? YES 2. Were study participants recruited in an appropriate way? NO – Unclear is consecutive sample recruited 3. Was the sample size adequate? YES 4. Were the study subjects and the setting described in detail? YES

<table>
<tr><td></td><td>5. Was the data analysis conducted with sufficient coverage of the identified sample? YES
6. Were objective, standard criteria used for the measurement of the condition? YES
7. Was the condition measured reliably? YES
8. Was there appropriate statistical analysis? YES
9. Are all important confounding factors/subgroups/differences identified and accounted for? YES
10. Were subpopulations identified using objective criteria? NA
Overall risk of bias = MODERATE</td></tr>
<tr><td>Country</td><td>UK</td></tr>
<tr><td>Number of patients</td><td>For cross-sectional data: N=1000 with T1D; N=1200 healthy controls
For case-control: N=12 with newly diagnosed CD and T1D, N=24 matched controls with T1D but not CD</td></tr>
<tr><td>Study population</td><td>Inclusion: patients with T1D aged >16 years
Exclusion: patients < 16 years, inability to consent , diabetes other than type 1

43 patients refused to participate, resulting in 1000 included overall
Mean age 43.2 years
439 females
21 patients already had established CD and T1D and were included in the analyses</td></tr>
<tr><td>Control</td><td>For cross-sectional data: screening of 1200 healthy volunteers from 5 separate general practices in Sheffield
For case-control: 2 control subjects with T1D, matched for every case by age, sex, weight, and diabetes duration</td></tr>
<tr><td>Length of follow-up</td><td>Not reported here</td></tr>
<tr><td>Details of coeliac testing</td><td>IgA EMA, IgA anti-tTG and total IgA
All with either positive antibody or low IgA level were offered a duodenal biopsy; histological features consistent with CD were classified according to Marsh staging with grade 3 changes(villous atrophy) considered diagnostic for CD</td></tr>
<tr><td>Results</td><td>Prevalence of CD:
<table>
<tr><td></td><td>Newly diagnosed</td><td>Including the 21 who already had established CD</td><td>Control group</td><td>Comparison of all CD patients with control group</td></tr>
<tr><td>Prevalence of CD</td><td>12% (12/1000)*</td><td>3.3% (33/1000; 95%CI 2.3-4.6)</td><td>1% (12/1200; 95%CI 0.5-1.7)</td><td>OR 3.3 (95%CI 1.7-6.6, p< 0.0001)</td></tr>
</table>
*6 had GI symptoms, 1 was anaemic, 2 were negative for EMA) – 12% undetected CD

4 patients with positive antibodies refused to be tested. Authors calculated that if all had biopsy-proven CD, the prevalence would be 3.7% (37/1000; 95%CI 2.6-5.1)

21 patients tested positive for EMA but did not have biopsy considered CD so were considered to have potential CD – 18 of these had completely normal biopsies but 3 had increased IELs; these patients were not included in the overall rate of CD and were excluded from</td></tr>
</table>

	investigations in this study A comparison between those with T1D and newly diagnosed CD and matched controls showed that patients were well matched but that those with CD and T1D had significantly higher HbA1C (median 8.2% vs 7.5%, p=0.05), significantly lower cholesterol (median 4.1 vs 4.9 mmol/L, p=0.014), and significantly lower HDL (median 1.1 vs 1.56 mmol/L, p=0.017). These patients also had a significantly higher proportion with nephrology stage > 3 (41.6% vs 4.2%) and advanced retinopathy (58.3% vs 25%). However, there was no difference in quality of life, cholesterol-toHDL ratio, triglycerides, eGFR, or proportion with peripheral neuropathy. Of those with newly identified CD, 3/12 had abnormal bone density (on DEXA scan) and 16.7% (2/12) were considered as having osteoporosis and 8.3% (1/12) considered as having osteopenia.
Source of funding	Bardhan Research and Education Trust of Rotherham and Solvay
Conflicts of interest	Paper reports no potential conflicts relevant to the article
Comments	This is data from a larger study considering the prevalence of microvascualr complications in adults with T1D and newly diagnosed CD; data was available after 1 year but as this included patients on a GFD, this data was not extracted here.

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

Bibliographic reference	**Pham-Short et al. (2010)**
Study type	Case series
Study quality	The Joanna Briggs Institute Prevalence Critical Appraisal Tool (http://ijhpm.com/article_2870_607.html) 1. Was the sample representative of the target population? YES 2. Were study participants recruited in an appropriate way? NO – Unclear is consecutive sample recruited 3. Was the sample size adequate? YES 4. Were the study subjects and the setting described in detail? YES 5. Was the data analysis conducted with sufficient coverage of the identified sample? YES 6. Were objective, standard criteria used for the measurement of the condition? YES 7. Was the condition measured reliably? YES 8. Was there appropriate statistical analysis? YES 9. Are all important confounding factors/subgroups/differences identified and accounted for? YES 10. Were subpopulations identified using objective criteria? NA Overall risk of bias = MODERATE
Country	Australia
Number of	N=4379 young people with T1D

<table>
<tr><td>patients</td><td></td></tr>
<tr><td>Study population</td><td>Inclusion: people aged 18 years or younger with T1D attending a tertiary diabetes centre in New South Wales between January1990 and December 2009

49% (2147) male
Mean age at diabetes diagnosis was 6.6 ± 4.0 compared with 8.4 ± 4.1 in those without CD (P< 0.001)</td></tr>
<tr><td>Control</td><td>None</td></tr>
<tr><td>Length of follow-up</td><td>Study conducted over a 20-year period</td></tr>
<tr><td>Details of coeliac testing</td><td>Screening for coeliac disease at diagnosis and 1-2yearly using anti-EMA IgA and/or anti tTG IgA antibodies
(EMA used until June 2004 with indirect immunofluorescence and anti-tTG IgA after June 2004 with enzyme-linked immunosorbent assay)
CD diagnosed with small bowel biopsy based on Marsh scores III or greater</td></tr>
<tr><td>Results</td><td>4.2% (185/4379) were diagnosed with coeliac disease (45% within 2 years, 78% within 5 years, and 94% within 10 years of diabetes diagnosis)
Of these 33% (61) were EMA or anti tTG IgA positive at diagnosis of diabetes

Incidence of coeliac disease:
<table>
<tr><td>Time period</td><td>Incidence of CD (95% CI)</td></tr>
<tr><td>Over entire 20 year period</td><td>7.7 per 1000 person years (6.6-8.9)</td></tr>
<tr><td>1990-1999</td><td>7.5 per 1000 person years (5.8-9.5)</td></tr>
<tr><td>2000-2009</td><td>7.7 per 1000 person years (6.4-9.3)</td></tr>
</table>
(difference between the 2 decades was not significant)

In 2009, the prevalence of CD was 7.1% (95% CI 5.6-8.8) (75 were biopsy-proven over 1051 clinic population)

Comparison of age at diagnosis of diabetes:
<table>
<tr><td rowspan="2"></td><td colspan="3">Age at diabetes diagnosis</td><td rowspan="2">p value*</td></tr>
<tr><td>< 5 years (n=80)</td><td>5-10 years (n=61)</td><td>≥10 years (n=44)</td></tr>
<tr><td>Mean age at CD diagnosis (SD)</td><td>7.1 (3.4)</td><td>10.5 (2.6)</td><td>13.3 (1.6)</td><td>Not reported</td></tr>
<tr><td>Male gender</td><td>50%</td><td>46%</td><td>51%</td><td>NS</td></tr>
<tr><td>Median time in years to diagnosis of CD after diabetes diagnosis (range)</td><td>3.0 (0.1-14.3)</td><td>2.1 (0.1-10)</td><td>0.7 (0.2-3.8)</td><td>< 0.001</td></tr>
<tr><td>Diagnosed with CD within</td><td>33%</td><td>48%</td><td>75%</td><td><0.01</td></tr>
</table>
</td></tr>
</table>

	2 years of diabetes				
	Incidence of CD per 100 person years (95%CI)	10.4 (8.2-13.0)	6.5 (4.7-8.8)	6.4 (4.9-8.2)	<0.01
	* <5 years compared to ≥10 years				
Source of funding	Not reported				
Conflicts of interest	Authors state that there is nothing to declare				
Comments					

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

Bibliographic reference	**Picarelli et al. (2005)**
Study type	Case control
Study quality	The Joanna Briggs Institute Prevalence Critical Appraisal Tool (http://ijhpm.com/article_2870_607.html) 1. Was the sample representative of the target population? YES 2. Were study participants recruited in an appropriate way? Yes (consecutive sample recruited) 3. Was the sample size adequate? YES 4. Were the study subjects and the setting described in detail? YES 5. Was the data analysis conducted with sufficient coverage of the identified sample? YES 6. Were objective, standard criteria used for the measurement of the condition? YES 7. Was the condition measured reliably? YES 8. Was there appropriate statistical analysis? YES 9. Are all important confounding factors/subgroups/differences identified and accounted for? YES 10. Were subpopulations identified using objective criteria? NA Overall risk of bias = LOW
Country	Italy
Number of patients	N=94 adults with insulin-dependent diabetes mellitus 1 N=83 control
Study population	Inclusion: consecutive adult patients with IDDM1 regularly attending a centre for the study of diabetes, N=43 male, N=51 female, mean age 46.9yrs (range 18 to 70yrs), none had any symptoms attributable to enteropathy, any evidence of malabsorbtion or been previously diagnosed with coeliac disease, all on gluten containing diet
Control	blood donors without IDDM1, CD, other auto-immune conditions, or first-degree relative with any autoimmune condition

Details of coeliac testing	
Results	All had IDDM1 for >15yrs and satisfactory metabolic control N=13 (6.4%) with coeliac disease EMA =ve vs. EMA –ve
Source of funding	Ministry of University and Research (MIUR), the non-governmental association for research on coeliac disease and diabetes mellitus
Conflicts of interest	
Comments	

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

Bibliographic reference	**Salardi et al. (2008)**
Study type	Case series (retrospective and prospective)
Study quality	The Joanna Briggs Institute Prevalence Critical Appraisal Tool (http://ijhpm.com/article_2870_607.html) 1. Was the sample representative of the target population? YES 2. Were study participants recruited in an appropriate way? YERS (consecutive sample recruited) 3. Was the sample size adequate? YES 4. Were the study subjects and the setting described in detail? YES 5. Was the data analysis conducted with sufficient coverage of the identified sample? YES 6. Were objective, standard criteria used for the measurement of the condition? YES 7. Was the condition measured reliably? YES 8. Was there appropriate statistical analysis? YES 9. Are all important confounding factors/subgroups/differences identified and accounted for? YES 10. Were subpopulations identified using objective criteria? NA Overall risk of bias = LOW
Country	Italy
Number of patients	N=331 children with type I diabetes
Study population	Consecutive children newly diagnosed with type I diabetes mellitus in a paediatric clinic between 1987 and 2004 (sera was stored between 1987 and 1993 and this was retrospectively tested for CD-related antibodies) Mean age: 8.1 ± 4.3 years (range 0.08-14.9)

Control	None
Length of follow-up	Immunological evaluation at diagnosis of diabetes, every 6 to 12mths after (duration 1 to 18yrs, mean 9yrs)
Details of coeliac testing	IgA EMA (indirect immunuofluorescence using monkey oesophagus commercial kits, Eurospital, Trieste, Italy) and human umbilical cord cryostat sections (were tested to the dilution of 1:5 and were titrated to the end point if positive) Diagnosis was confirmed by intestinal biopsy with gastroduodenoscopy and multiple biopsies with specimens graded according to Marsh classification
Results	Apart from 2/331 patients who were diagnosed with CD before they were diagnosed with diabetes, 29 additional patients had positive EMA assay – 6 did not have biopsy as they had borderline EMA positivity (n=2) or because EMA became negative without a GFD (n=4). 23 patients had biopsy – 18 had typical CD lesions and 5 had normal mucosa; however, 2 of these 5 had a second biopsy at 1 and 4.5 years after the onset of symptoms showing typical CD lesions 6.0% (20/331) had biopsy-proven CD (an additional 2 patients had been diagnosed with CD before being diagnosed with diabetes and were on a GFD) (After 1994, the prevalence was 10.6% [16/151] and before 1994 it was 3.3% [6/180] [p=0.015])
Source of funding	Not reported
Conflicts of interest	Not reported
Comments	(author's comment: same screening methods (EMA), all tests carried out in the same reference lab, consistent assay performance, population referring to the clinic did not change over time, suggest that the risk of CD increased in diabetic children after 1994)

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

Bibliographic reference	**Smith et al. (2000)**
Study type	Cross-sectional data (for prevalence) from case series
Study quality	The Joanna Briggs Institute Prevalence Critical Appraisal Tool (http://ijhpm.com/article_2870_607.html) 1. Was the sample representative of the target population? YES 2. Were study participants recruited in an appropriate way? YES – (unselected population) 3. Was the sample size adequate? YES 4. Were the study subjects and the setting described in detail? YES 5. Was the data analysis conducted with sufficient coverage of the identified sample? YES 6. Were objective, standard criteria used for the measurement of the condition? YES 7. Was the condition measured reliably? YES

	8. Was there appropriate statistical analysis? YES 9. Are all important confounding factors/subgroups/differences identified and accounted for? YES 10. Were subpopulations identified using objective criteria? NA Overall risk of bias = LOW
Country	Australia
Number of patients	N=281 children and adolescents with T1D
Study population	Inclusion: children and adolescents with diabetes mellitus attending a paediatric diabetes clinic between January 1993 and December 1998 Mean and SD: Age 9.9 ± 3.8 years (range 1.3 to 18 years) 133 females/136 males One patient had prior diagnosis of CD before onset of diabetes
Control	None
Length of follow-up	Only cross-sectional data extracted
Details of coeliac testing	AGA-IgG and AGA-IgA If positive AGA-IgG and undetectable AGA-IgA, total serum was measured to exclude IgA deficiency Those with double positive AGAs had gastro-duodenoscopy and multiple biopsy to confirm CD according to ESPGAN criteria CD diagnosis was based on increased IELs, crypt hyperplasia and/or increase in inflammatory cells in the lamina propria in addition to either total or partial villous atrophy
Results	Double positive AGAs: 12.5% (35/280) None had IgA deficiency **Overall CD prevalence: 5.7% (16/281)** (with initial biopsies confirming CD diagnosis; this rate includes the one patient with previously diagnosed CD) Of those diagnosed on biopsy, 7 had gluten challenge and third a biopsy under ESPGHAN criteria to confirm the diagnosis, and 4 have completed 2 biopsies; one declined a gluten challenge after the initial biopsy due to extreme gluten sensitivity and four had yet to complete a confirmatory biopsy on a GFD and/or gluten challenge at the writing of the paper) 5 with double positive antibodies did not have biopsy: one because of loss to follow-up and 4 declined because they were asymptomatic
Source of funding	Not reported
Conflicts of interest	Not reported
Comments	The purpose of the study was to look at the prevalence of CD in diabetese mellitus and also consider the longitudinal changes in AGA status – only the cross-sectional data on prevalence was included here.

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

Bibliographic reference	**Uibo et al. (2010)**
Study type	Cross-sectional survey and prospective case series of some patients
Study quality	The Joanna Briggs Institute Prevalence Critical Appraisal Tool (http://ijhpm.com/article_2870_607.html) 1. Was the sample representative of the target population? YES 2. Were study participants recruited in an appropriate way? NO – Unclear is consecutive sample recruited 3. Was the sample size adequate? YES 4. Were the study subjects and the setting described in detail? YES 5. Was the data analysis conducted with sufficient coverage of the identified sample? YES 6. Were objective, standard criteria used for the measurement of the condition? YES 7. Was the condition measured reliably? YES 8. Was there appropriate statistical analysis? YES 9. Are all important confounding factors/subgroups/differences identified and accounted for? YES 10. Were subpopulations identified using objective criteria? NA Overall risk of bias = MODERATE
Country	Estonia
Number of patients	N=271 children with type 1 diabetes
Study population	Inclusion: T1D patients from 2 main children's hospitals in Estonia who were investigated between 1995 and 2006 (T1D definition made according to the WHO and International Society for Paediatric Adolescent Diabetes criteria) For cross-sectional data/initial screening study (n=271): 57% male Mean age: 10.6 years (range 1.7-18.0) Mean age at diagnosis of T1D: 8.3 years (range 1.6-17.7) N=122 at diagnosis of T1D N=149 after diagnosis of T1D (0.1 to 14.8 years after diagnosis) For prospective case series: N=73 of the 271 patients included in the initial screening study (56.2% male, age range: 1.7-16.2)
Control	none
Length of follow-	n/a for cross-sectional data Not reported for case series

up

Details of coeliac testing

IgA EMA and IgA tTGA (until 2000, only EMA; in 2003 all who had been tested so far were re-tested with tTGA)
(IgA levels were tested to rule out IgA deficiency with DPS Immulite assay)
Those with antibodies and/or with coeliac-disease related symptoms were invited for small intestinal biopsy
Diagnosis of CD according to criteria recommended by ESPGHAN

Results

Results of testing:

	Initial screening/cross-sectional survey (n=271)			Prospective follow-up (n=73)		
	Rate with/without symptoms (95% CI)[1]	tTGA/EMA results	Biopsy results[4]	Those who continued in prospective study	tTGA/EMA results	Biopsy results
With symptoms	2.2% (6/271; 95% CI 0.90-4.99)	5/6 negative	Marsh 0-5[2]	0	n/a	n/a
		1/6 positive	n/a (refused)	1	Negative	n/a
Without symptoms	265/271	254 negative	NA	73	71 negative 2 positive	n/a MIIIa&IIIb[3]
		11 positive	1 M0 1 MIIIa[3] 1MIIIb[3] 1 n/a (refused)	0	n/a	n/a

[1] not a statistically significant difference, [2] authors considered this to be normal mucosa, [3] considered to be coeliac disease, [4] rate of those with biopsy-proven CD was considered statically significant than the EMA/tTG negative group ($p<0.01$)

(none had IgA deficiency)

Rate of CD:

	Rate (95% CI)	Patient characteristics of those diagnosed	Presence of symptoms in those diagnosed
Primary screening (n=271)	3.3% (9/271; 95% CI 1.63-6.42)*	Mean age 9.9 years (3.1-16.2)	None
Prospective case series (n=73)	2.7% (2/73; 95% CI 0-0.072)	Both 10 years with duration of T1D 3.2 and 3.3 years	None
Overall in 1995-2006	4.1% (11/271)	7 girls, 4 boys	None

* CD was diagnosed simultaneously with T1D in 2 patients but mean 3.4 years (range 0.9-6.9) after the T1D diagnosis in the other 7.

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Conflicts of

Not reported

interest	
Comments	

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