Appendix A.

Table 1: Various causes of villous atrophy (VA; Farrell and Kelly, Am J Gastro 2001;96:3237)

Celiac disease
Dermatitis herpetiformis
Cow's milk protein intolerance (children)
Post-gastroenteritis
Giardiasis
Peptic duodenitis
Crohn's disease
Small intestinal bacterial overgrowth
Eosinophilic gastroenteritis
Radiation or chemotherapy
Tropical sprue
Severe malnutrition
Diffuse small intestinal lymphoma
Graft versus host disease
Hypogammaglobulinemia
Alpha chain disease

Table 2: Marsh (Gastroenterology 1992;102:330) and Rostami (Am J Gastroenterol 1999;94:888) modified histological criteria for CD

Criteria		Rostami modification (1999)	Original Marsh (1992)
Marsh 0		Same as original	**Pre-infiltrative:** • Normal mucosal and villous architecture
Marsh I		Same as original	**Infiltrative:** • Normal mucosal and villous architecture • Increased numbers of IELs
Marsh II		Same as original	**Hyperplastic:** • Similar to above but with enlarged crypts, with increased crypt cell division
Marsh III	**a**	**Partial VA:** • Shortened blunt villi • Mild lymphocyte infiltration • Enlarged hyperplastic crypts	**Destructive lesion:** • Flat mucosa – complete loss of villi • Lymphocyte infiltration • Enlarged hyperplastic crypts
	b	**Sub-total VA:** • Clearly atrophic villi – but still recognizable • Enlarged crypts whose immature epithelial cells are generated at an increased rate • Influx of inflammatory cells	
	c	**Total VA:** • Nearly total VA • Severe Marsh atrophic, hyperplastic and infiltrative lesions	
Marsh IV		Same as original	**Hypoplastic:** • Total VA • Normal crypt height but hypoplasia • Normal IEL count • Many feel this doesn't exist and represents severe malnutrition
VA=villous atrophy IEL=intraepithelial lymphocytes			

Table 3: Revised ESPGAN criteria

Criteria	ESPGAN*- 1979	ESPGAN†- Revised 1990
Initial histology	- Absent or nearly absent villi - Recognized existence of less severe lesion - No consensus on verification of less severe lesions but recommended if possible continuing gluten diet and assess histology, or re-challenge after GFD, given the large differential of milder histologic lesions	- Biopsy must remain the initial step in the diagnosis (mandatory) - Recommend capsule over endoscopic biopsy - Large well oriented biopsy - Histology: hyperplastic VA with hyperplasia of the crypts and an abnormal surface epithelium. The IEL count is raised - Morphometery and histochemistry are important aids to diagnosis. - Monoclonal antibodies to IEL may be a future aid
Antibody studies	- n/a	- Recognize that IgA AGA, and EMA have a high degree of sensitivity and specificity for the diagnosis of CD - When such antibodies are present at the time of diagnosis in a child with a typical small intestinal mucosa, and when they disappear in parallel to a clinical response to a GFD, weight is added to the diagnosis of CD that may now be said to have been finally established - When biopsy is unavailable in communities were other causes of enteropathy are rare, the presence of abnormal concentrations of two antibodies strongly suggests that CD is a diagnostic possibility - Antibodies can be a marker of response to a GFD and a guide to dietary compliance
Improvement on GFD	- Recognized as central to the definition - Recognized that improvement need not be complete	- Second mandatory requirement remains a reasonably rapid (weeks rather than many months) clinical remission on a strict GFD - Control biopsy is always a suitable way of verifying the effect of GFD, and is required in asymptomatic pts
Gluten Challenge	- Importance of gluten challenge and re-biopsy emphasized to document “permanence” of gluten intolerance - However, the panel recognized that challenge was not being performed in routine practice (only 652 were performed among several thousand children with gluten intolerance)	- No longer a requirement - Should be used in equivocal cases such as when no initial biopsy was done, biopsy was inadequate or atypical, in communities with high rates of other enteropathies, or in situations when pts plan to abandon the GFD in an uncontrolled way - Challenge should be performed after obtaining a control biopsy on a GFD - Re-biopsy is performed 3-6 months later with the recognition that relapse can take 5-7 years or more to occur.
2-year rule	- To address the issue of transient gluten intolerance, the panel emphasized the usefulness of the 2-year rule after stopping a GFD - 619 of 652 gluten challenges redeveloped histology compatible with CD by 2 years	- The 2-year rule is practical in most cases, but several reports of relapse occurring 5-7 years after gluten rechallenge

*McNeish et al., Arch Dis Child 1979;54:783
†Walker-Smith et al., Arch Dis Child 1990:65:99
CD=celiac disease; n/a=not applicable; GFD=gluten-free diet

Appendix B. Search Strategies

Search Strategy 1

Celiac 1 – Diagnostic Tests

Test 1. EMA

MEDLINE on DIALOG

1. s anti(w)endomysial(w)antibod? OR antiendomysial(w)antibod?
2. s anti(w)endomysium(w)antibod? OR antiendomysium(w)antibod?
3. s endomysial(w)antibod? OR endomysium(w)antibod? OR endomysial(w)autoantibod? OR endomysium(w)autoantibod?
4. s endomysial(n3)iga OR antiendomysial(n3)iga OR iga(n)ema
5. s endomysium(n3)iga OR antiendomysium(n3)iga OR igg(n)ema
6. s immunoglobulin?(n3)endomysial OR immunoglobulin?(n3)antiendomysial
7. s immunoglobulin?(n3)endomysium OR immunoglobulin?(n3)antiendomysium
8. s ema(n3)antibod? OR ema(n3)autoantibod? OR anti(w)ema OR ema(n3)positiv?
9. s aea AND (endomysial OR endomysium OR antiendomys?) OR aea(n3)positiv? OR aea(n2)igg OR aea(n2)iga
10. c 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9
11. s (celiac OR celiacs OR coeliac OR coeliacs OR gluten OR glutens OR glutenin OR glutenins OR gliadin OR gliadins OR celiac disease/de) AND (ema OR aea)
12. s (celiac OR celiacs OR coeliac OR coeliacs OR gluten OR glutens OR glutenin OR glutenins OR gliadin OR gliadins OR celiac disease/de) AND autoantibod?(n2) positiv?
13. c 10 OR 11 OR 12
14. s epithelial(w)membrane(w)antigen
15. c 13 NOT 14
16. s s15/human
17. s s16/eng

EMBASE on DIALOG

1. s anti(w)endomysial(w)antibod? OR antiendomysial(w)antibod?
2. s anti(w)endomysium(w)antibod? OR antiendomysium(w)antibod?
3. s endomysial(w)antibod? OR endomysium(w)antibod? OR endomysial(w)autoantibod? OR endomysium(w)autoantibod? OR endomysium antibody/de
4. s endomysial(n3)iga OR antiendomysial(n3)iga OR iga(n)ema
5. s endomysium(n3)iga OR antiendomysium(n3)iga OR igg(n)ema 6. s immunoglobulin?(n3)endomysial OR immunoglobulin?(n3)antiendomysial
7. s immunoglobulin?(n3)endomysium OR immunoglobulin?(n3)antiendomysium
8. s ema(n3)antibod? OR ema(n3)autoantibod? OR anti(w)ema OR ema(n3)positiv?
9. s aea AND (endomysial OR endomysium OR antiendomys?) OR aea(n3)positiv? OR aea(n2)igg OR aea(n2)iga
10. c 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9
11. s (celiac OR celiacs OR coeliac OR coeliacs OR gluten OR glutens OR glutenin OR glutenins OR gliadin OR gliadins OR celiac disease/de) AND (ema OR aea)
12. s (celiac OR celiacs OR coeliac OR coeliacs OR gluten OR glutens OR glutenin OR glutenins OR gliadin OR gliadins OR celiac disease/de) AND autoantibod?(n2)positiv?
13. c 10 OR 11 OR 12

14. s epithelial(w)membrane(w)antigen
15. c 13 not 14
16. s s15/human
17. s s16/eng

Test 2. tTG

MEDLINE on DIALOG

1. s tissue(w)transglutaminase?? OR tissue(w)trans(w)glutaminase??
2. s antitissue(w)transglutaminase?? OR anti(w)transglutaminase??
3. s human(w)transglutaminase?? OR antitransglutaminase??(n3)antibod?
4. s (immunoglobulin? OR immunoglobulin a/de OR immunoglobulin g/de) AND (transglutaminase OR transglutaminases)
5. s ttg(n3)antibod? OR ttg(n3)autoantibod? OR ttg(w)(kit OR kits) OR ttga OR httg OR anti(w2)ttg OR human(w)ttg OR elisa(n)ttg OR attga
6. s (transglutaminase?? AND antibod?) OR (transglutaminase?? AND autoantibod?)
7. s transglutaminase??(n3)iga OR transglutaminase??(n3)igg OR tg2(n5)transglutaminase?? OR human(w) recombinant(w)tg2
8. s anti(w)gamma(w)glutamyltransferase AND (antibod? OR autoantibod?)
9. c 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8
10. s (celiac OR celiacs OR coeliac OR coeliacs OR gluten OR glutens OR glutenin OR glutenins OR gliadin OR gliadins OR celiac disease/de) AND (transglutaminase OR transglutaminases OR ttg OR tg2)
11. c 9 OR 10
12. s s11/human
13. s s12/eng

EMBASE on DIALOG

1. s tissue(w)transglutaminase?? OR tissue(w)trans(w)glutaminase??
2. s antitissue(w)transglutaminase?? OR anti(w)transglutaminase??
3. s human(w)transglutaminase?? OR antitransglutaminase??(n3)antibod?
4. s immunoglobulin OR immunoglobulin a/de OR immunoglobulin a1/de OR immunoglobulin a2/de
5. s immunoglobulin g/de OR immunoglobulin g1/de OR immunoglobulin g2/de OR immunoglobulin g2a/de OR immunoglobulin g2b/de OR immunoglobulin g3/de OR immunoglobulin g4/de
6. s transglutaminase OR transglutaminases
7. c 4 OR 5
8. c 7 AND 6
9. s ttg(n3)antibod? OR ttg(n3)autoantibod? OR ttg(w)(kit OR kits OR assay) OR ttga OR httg OR anti(w2)ttg OR human(w)ttg OR elisa(n)ttg OR attga
10. s (transglutaminase?? AND antibod?) OR (transglutaminase?? AND autoantibod?)
11. s transglutaminase??(n3)iga OR transglutaminase??(n3)igg OR tg2(n5)transglutaminase?? OR human(w) recombinant(w)tg2
12. s anti(w)gamma(w)glutamyltransferase AND (antibod? OR autoantibod?)
13. c 1 OR 2 OR 3 OR 8 OR 9 OR 10 OR 11 OR 12
14. s (celiac OR celiacs OR coeliac OR coeliacs OR gluten OR glutens OR glutenin OR glutenins OR gliadin OR gliadins OR celiac disease/de) AND (transglutaminase OR transglutaminases OR ttg OR tg2)
15. c 13 OR 14
16. s s15/human
17. s s16/eng

Test 3. AGA

MEDLINE on DIALOG

1. s gliadin(w)antibod? OR antigliadin(w)antibod? OR iga(n3)antigliadin OR igg(n3)antigliadin
2. s antigliadin AND (serology OR serological)
3. s iga(n2)aga OR igg(n2)aga OR aga(n3)positive? OR anti(w)aga
4. s (celiac OR celiacs OR coeliac OR coeliacs OR gluten OR glutens OR glutenin OR glutenins OR gliadin OR gliadins OR celiac disease/de) AND (aga OR antigliadin?)
5. c 1 OR 2 OR 3
6. c 5 OR 4
7. s s6/human
8. s s7/eng

EMBASE on DIALOG

1. s gliadin(w)antibod? OR antigliadin(w)antibod? OR iga(n3)antigliadin OR igg(n3)antigliadin
2. s antigliadin AND (serology OR serological)
3. s iga(n2)aga OR igg(n2)aga OR aga(n3)positive? OR anti(w)aga
4. s (celiac OR celiacs OR coeliac OR coeliacs OR gluten OR glutens OR glutenin OR glutenins OR gliadin OR gliadins OR celiac disease/de) AND (aga OR antigliadin? OR anti(w)gliadin?)
5. c 1 OR 2 OR 3
6. c 5 OR 4
7. s s6/human
8. s s7/eng

Test 4. HLA DQ2/DQ8

MEDLINE on DIALOG

1. s (leukocyte OR leukocytes OR leucocyte OR leucocytes) AND (antigen OR antigens)
2. s hla OR hla-dq antigens/de OR hla antigens/de OR hladq OR histocompatibility antigens/de OR histocompatibility testing/de OR histocompatibility
3. c 1 OR 2
4. s dq2? OR dq8? OR hladq2? OR hladq8? OR d2? OR d8?
5. c 3 AND 4
6. s celiac OR celiacs OR coeliac OR coeliacs OR gluten OR glutens OR glutenin OR glutenins OR gliadin OR gliadins OR celiac disease/de
7. s hla(w)antigen?? OR hla antigens/de OR hla-dq antigens/de
8. c 6 AND 7
9. c 5 OR 8
10. s s8/human
11. s s9/eng

EMBASE on DIALOG

1. s (leukocyte OR leukocytes OR leucocyte OR leucocytes) AND antigen
2. s (leukocyte OR leukocytes OR leucocyte OR leucocytes) AND antigens
3. s hla OR hla dq antigen/de OR hla antigen/de OR hladq OR histocompatibility antigen/de OR histocompatibility test/de OR histocompatibility/ti,ab,de
4. c 1 OR 2 OR 3
5. s dq2? OR dq8? OR hladq2? OR hladq8? OR d2? OR d8?
6. c 4 AND 5
7. s celiac OR celiacs OR coeliac OR coeliacs OR gluten OR glutens OR glutenin OR glutenins OR gliadin OR gliadins
8. s hla(w)antigens?? OR hla antigen/de OR hla dq antigen/de
9. c 7 AND 8
10. c 6 OR 9
11. s s10/human
12. s s11/eng

Test 5. Small bowel biopsy

MEDLINE on DIALOG

1. s celiac???(w)disease OR coeliac???(w)disease OR celiac(w)sprue OR coeliac(w)sprue OR celiac(w)syndrome OR coeliac(w)syndrome
2. s celiacs OR coeliacs OR celiac disease/de
3. s silent(w)celiac OR silent(w)coeliac OR asymptomatic(w)celiac OR asymptomatic(w)coeliac OR undetected(n3)(celiac OR coeliac)
4. s subclinical(w)celiac OR subclinical(w)coeliac OR sub(w)clinical(w)celiac OR sub(w)clinical(w)coeliac OR undiagnosed(n3)celiac OR undiagnosed(n3)coeliac
5. s nontropical(w)sprue OR non(w)tropical(w)sprue OR endemic(w)sprue
6. s gluten(n3)enteropath? OR gluten(n3)sensitiv? OR gluten(n3)hypersensitive? OR gluten(n3)intoleran? OR glutenin??(n3)hypersensitiv? OR glutenin??(n3) sensitiv? OR glutenin??(n3)intoleran?
7. s gliadin(n3)hypersentitiv? OR gliadin(n3)intoleran?
8. s wheat(n3)hypersensitiv? OR wheat(n3)intoleran? OR wheat hypersensitivity/de
9. s (wheat OR triticum OR gluten) AND food hypersensitivity/de
10. c 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. s celiac disease(l)pathology OR celiac disease(l)diagnosis OR wheat hypersensivitity(l)diagnosis OR wheat hypersensitivity(l)pathology
12. s (wheat OR triticum OR gluten) AND food hypersensitivity(l)diagnosis
13. s (wheat OR triticum OR gluten) AND food hypersensitivity(l)pathology
14. c 11 or 12 or 13
15. s intestine, small(l)pathology OR duodenum(l)pathology OR jejunum(l)pathology OR ileum(l)pathology OR small(n2)bowel/ti,ab OR small(n2)intestine?/ti,ab
16. s biopsy! OR biopsy/ti,ab OR biopsies/ti,ab
17. c 14 AND 15 AND 16
18. s small(w)(bowel OR intestine OR intestines) OR intestinal(w)mucosa
19. c 10 AND 16 AND 18
20. s (villi OR villus OR villous OR microvilli)(n3)atroph?
21. c (10 AND 20) OR (14 AND 20)
22. c 17 OR 19 OR 21
23. s s22/human
24. s s23/eng

EMBASE on DIALOG

1. s celiac???(w)disease OR coeliac???(w)disease OR celiac(w)sprue OR coeliac(w)sprue OR celiac(w)syndrome OR coeliac(w)syndrome
2. s celiacs OR coeliacs OR celiac disease/de
3. s silent(w)celiac OR silent(w)coeliac OR asymptomatic(w)celiac OR asymptomatic(w)coeliac OR undetected(n3)(celiac OR coeliac)
4. s subclinical(w)celiac OR subclinical(w)coeliac OR sub(w)clinical(w)celiac OR sub(w)clinical(w)coeliac OR undiagnosed(n3)celiac OR undiagnosed(n3)coeliac
5. s nontropical(w)sprue OR non(w)tropical(w)sprue OR endemic(w)sprue
6. s gluten(n3)enteropath? OR gluten(n3)sensitiv? OR gluten(n3)hypersensitive? OR gluten(n3)intoleran? OR glutenin??(n3)hypersensitiv? OR glutenin??(n3) sensitiv? OR glutenin??(n3)intoleran?
7. s gliadin(n3)hypersentitiv? OR gliadin(n3)intoleran?
8. s wheat(n3)hypersensitiv? OR wheat(n3)intoleran? OR wheat allergy/de
9. s (wheat OR triticum OR gluten OR glutens) AND food allergy/de
10. c 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. s small intestine/de OR duodenum/ti,ab,de OR jejunum/ti,ab,de OR ileum/ti,ab,de OR small(n2)bowel/ti,ab OR small(n2)intestine?/ti,ab OR duodenal/ti,ab OR jejunal/ti,ab OR ileal/ti,ab
12. s dc=a3.60.70? [small intestine]

13. s small(w)(bowel OR intestine OR intestines) OR intestinal(w)mucosa
14. s intestine mucosa/de or duodenum mucosa/de OR jejunum mucosa/de OR ileum mucosa/de
15. c 11 OR 12 OR 13 OR 14
16. s biopsy/ti,ab,de OR biopsies/ti,ab
17. c 15 AND 16
18. s intestine biopsy/de OR duodenum biopsy/de OR jejunum biopsy/de OR ileum biopsy/de
19. c 17 OR 18
20. c 10 AND 19
21. s (villi OR villus OR villous OR microvilli)(n3)atroph?
22. c 10 AND 21
23. c 20 OR 22
24. s s23/human
25. s s24/eng

Celiac 2 – Epidemiology

MEDLINE on DIALOG

1. s celiac???(w)disease OR coeliac???(w)disease OR celiac(w)sprue OR coeliac(w)sprue OR celiac(w)syndrome OR coeliac(w)syndrome
2. s celiacs OR coeliacs OR celiac disease/de
3. s silent(w)celiac OR silent(w)coeliac OR asymptomatic(w)celiac OR asymptomatic(w)coeliac OR undetected(n3)(celiac OR coeliac)
4. s subclinical(w)celiac OR subclinical(w)coeliac OR sub(w)clinical(w)celiac OR sub(w)clinical(w)coeliac OR undiagnosed(n3)celiac OR undiagnosed(n3)coeliac
5. s nontropical(w)sprue OR non(w)tropical(w)sprue OR endemic(w)sprue
6. s gluten(n3)enteropath? OR gluten(n3)sensitiv? OR gluten(n3)hypersensitive? OR gluten(n3)intoleran? OR glutenin??(n3)hypersensitiv? OR glutenin??(n3) sensitiv? OR glutenin??(n3)intoleran?
7. s gliadin(n3)hypersentitiv? OR gliadin(n3)intoleran?
8. s wheat(n3)hypersensitive? OR wheat(n3)intoleran? OR wheat hypersensitivity/de
9. s (wheat OR triticum OR gluten) AND food hypersensitivity/de
10. c 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. s celiac disease(l)epidemiology OR celiac disease(l)ethnology OR wheat hypersensitivity(l)epidemiology OR wheat hypersensitivity(l)ethnology
12. s (wheat OR triticum OR gluten) AND food hypersensitivity(l)epidemiology
13. s (wheat OR triticum OR gluten) AND food hypersensitivity(l)ethnology
14. s epidemiolog?/ti,de OR occurrence/ti,de OR prevalence/ti,de OR incidence/ti,de OR pedigree/de OR seroprevalence OR seroepidemiol? OR epidemiologic studies! OR epidemiologic measurements/de [check!!]
15. s population characteristics! OR population! OR demography! OR demographic?/ti,ab OR population?/ti,de
16. s minority groups/de OR ethnic groups! OR racial stocks!
17. s anemia(w2)iron(w)deficiency/de OR anemia(w)hypochromic/de OR iron(w)deficiency(w)anemia OR osteoporosis/ti,ab,de OR diabetes mellitus, insulin-dependent! OR juvenile(w)diabetes
18. s diabetes AND type(w)(1 OR I OR one)
19. s celiac disease(l)genetics OR gluten(l)genetics OR wheat hypersensitivity(l)genetics
20. s (wheat OR triticum OR gluten) AND food hypersensitivity(l)genetics
21. s family! OR genetic predisposition to disease! OR genetic(w)predisposition OR family(n3)(member OR members) OR familial
22. s family/ti,ab OR families/ti,ab OR familial/ti,ab OR brother/ti,ab OR brothers/ti,ab OR sister/ti,ab OR sisters/ti,ab OR aunt/ti,ab OR aunts/ti,ab OR uncle/ti,ab OR uncles/ti,ab OR cousin/ti,ab OR cousins/ti,ab
23. s parent/ti,ab OR parents/ti,ab OR mother/ti,ab OR mothers/ti,ab OR father/ti,ab OR fathers/ti,ab OR wife/ti,ab OR wives/ti,ab OR husband/ti,ab OR husbands/ti,ab
24. s son/ti,ab OR sons/ti,ab OR daughter/ti,ab OR daughters/ti,ab OR children/ti,ab OR relatives/ti,ab OR sibling/ti,ab OR siblings/ti,ab OR offspring/ti,ab
25. c 21 OR 22 OR 23 OR 24
26. c 19 OR 20
27. c 25 AND 26
28. c 14 OR 15 OR 16 OR 17 OR 18
29. c 10 AND 28
30. c 27 OR 29 OR 11 OR 12 OR 13
31. s s30/human
32. s s31/eng
33. s animal/de
34. c 32 NOT 33

EMBASE on DIALOG

1. s celiac???(w)disease OR coeliac???(w)disease OR celiac(w)sprue OR coeliac(w)sprue OR celiac(w)syndrome OR coeliac(w)syndrome
2. s celiacs OR coeliacs OR celiac disease/de
3. s silent(w)celiac OR silent(w)coeliac OR asymptomatic(w)celiac OR asymptomatic(w)coeliac OR undetected(n3)(celiac OR coeliac)
4. s subclinical(w)celiac OR subclinical(w)coeliac OR sub(w)clinical(w)celiac OR sub(w)clinical(w)coeliac OR undiagnosed(n3)celiac OR undiagnosed(n3)coeliac
5. s nontropical(w)sprue OR non(w)tropical(w)sprue OR endemic(w)sprue OR refractory(w)sprue
6. s gluten(n3)enteropath? OR gluten(n3)sensitiv? OR gluten(n3)hypersensitive? OR gluten(n3)intoleran? OR glutenin??(n3)hypersensitiv? OR glutenin??(n3) sensitiv? OR glutenin??(n3)intoleran?
7. s gliadin(n3)hypersentitiv? OR gliadin(n3)intoleran?
8. s wheat(n3)hypersensitive? OR wheat(n3)intoleran? OR wheat allergy/de OR cereal(w)allergy 9. s (wheat OR triticum OR gluten?? OR glutinin??) AND (food allergy/de OR allergy/de OR hypersensitivity/de OR food allergen/de)
10. c 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9
11. s epidemiology/de,id OR dc=c1.270? OR epidemiolog?/ti,ab OR seroepidemiol? OR epidemiological data/de 12. s occurrence/ti,de OR prevalence/ti,de OR incidence/ti,de OR pedigree/ti,de OR pedigree analysis/de OR dc=g1.385.170? OR seroprevalence
13. s dc= g1.250.710.715? OR dc= i1.700? OR demography/ti,ab,de OR demographic?/ti,ab OR population?/ti,de OR population research/de OR population risk/de
14. s minority(w)group?? OR ethnic(w)group?? OR minorities/ti,ab OR dc=g1.750? OR dc=i1.275? OR dc=m2? OR ethnology/ti,ab,de OR ethnic difference/de OR ethnicity/ti,ab
15. s iron(w)deficiency(w)anemia OR iron deficiency anemia/de OR anemia(n3)hypochromic/ti,ab
16. s osteoporosis/ti,ab,de OR dc= c2.275.540.110.650?
17. s insulin dependent diabetes mellitus/de OR juvenile(w)diabetes OR insulin(w)dependent(w)diabetes
18. s diabetes AND type(w)(1 OR i OR one)
19. s familial disease/de OR family study/de OR familial incidence/de
20. c 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19
21. s celiac disease/de OR gluten??/ti,ab OR wheat allergy/de OR cereal(w)allergy
22. s (wheat OR triticum OR gluten?? OR glutinin??) AND (food allergy/de OR allergy/de OR hypersensitivity/de OR food allergen/de)
23. c 21 OR 22
24. s genetics/de OR q1.340?
25. c 23 AND 24
26. s genetic(w)predisposition OR family(n3)(member OR members)
27. s family/ti,ab OR families/ti,ab OR familial/ti,ab OR brother/ti,ab OR brothers/ti,ab OR sister/ti,ab OR sisters/ti,ab OR aunt/ti,ab OR aunts/ti,ab OR uncle/ti,ab OR uncles/ti,ab OR cousin/ti,ab OR cousins/ti,ab
28. s parent/ti,ab OR parents/ti,ab OR mother/ti,ab OR mothers/ti,ab OR father/ti,ab OR fathers/ti,ab OR wife/ti,ab OR wives/ti,ab OR husband/ti,ab OR husbands/ti,ab
29. s son/ti,ab OR sons/ti,ab OR daughter/ti,ab OR daughters/ti,ab OR children/ti,ab OR relatives/ti,ab OR sibling/ti,ab OR siblings/ti,ab OR offspring/ti,ab
30. c 26 OR 27 OR 28 OR 29
31. c 25 AND 30
32. c 10 AND 20
33. c 31 OR 32
34. s celiac disease(l)epidemiology
35. s (celiac disease/de OR wheat allergy/de OR cereal(w)allergy) AND epidemiology/de
36. s (wheat OR triticum OR gluten?? OR glutinin??) AND (food allergy/de OR allergy/de OR hypersensitivity/de OR food allergen/de) AND epidemiology/de
37. c 34 OR 35 OR 36
38. c 33 OR 37
39. s s38/human
40. s s39/eng

Celiac 3 – Lymphomas

MEDLINE on DIALOG

1. s celiac???(w)disease OR coeliac???(w)disease OR celiac(w)sprue OR coeliac(w)sprue OR celiac(w)syndrome OR coeliac(w)syndrome
2. s celiacs OR coeliacs OR celiac disease/de
3. s silent(w)celiac OR silent(w)coeliac OR asymptomatic(w)celiac OR asymptomatic(w)coeliac OR undetected(n3)(celiac OR coeliac)
4. s subclinical(w)celiac OR subclinical(w)coeliac OR sub(w)clinical(w)celiac OR sub(w)clinical(w)coeliac OR undiagnosed(n3)celiac OR undiagnosed(n3)coeliac
5. s nontropical(w)sprue OR non(w)tropical(w)sprue OR endemic(w)sprue
6. s gluten(n3)enteropath? OR gluten(n3)sensitiv? OR gluten(n3)hypersensitive? OR gluten(n3)intoleran? OR glutenin??(n3)hypersensitiv? OR glutenin??(n3) sensitiv? OR glutenin??(n3)intoleran?
7. s gliadin(n3)hypersentitiv? OR gliadin(n3)intoleran?
8. s wheat(n3)hypersensitive? OR wheat(n3)intoleran? OR wheat hypersensitivity/de
9. s (wheat OR triticum OR gluten) AND food hypersensitivity/de
10. c 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. s (villi OR villus OR villous OR microvilli)(n3)atroph?
12. c 10 OR 11
13. s lymphoma/ti,ab,de OR lymphomas/ti,ab,de OR lymphoma! OR hodgkin?/ti,ab,de
14. s intestine/ti,ab,de OR intestinal/ti,ab,de OR duodenum/ti,ab,de OR duodenal/ti,ab.de OR jejunum/ti,ab,de OR jejunal/ti,ab,de OR ileum/ti,ab,de OR ileal/ti,ab,de
15. s small(n2)bowel/ti,ab OR small(n2)intestine?/ti,ab OR large(n2)intestine?/ti,ab OR large(n2)bowel/ti,ab OR intestines!
16. s gastric/ti,ab,de OR gastro?/ti,ab,de OR gi/ti,ab OR stomach/ti,ab,de OR pylorus/ti,ab,de OR pyloric/ti,ab,de OR esophagogastr?
17. c 14 or 15 or 16
18. c 12 AND 13 AND 17
19. s s18/human
20. s s19/eng

EMBASE on DIALOG

1. s celiac???(w)disease OR coeliac???(w)disease OR celiac(w)sprue OR coeliac(w)sprue OR celiac(w)syndrome OR coeliac(w)syndrome
2. s celiacs OR coeliacs OR celiac disease/de
3. s silent(w)celiac OR silent(w)coeliac OR asymptomatic(w)celiac OR asymptomatic(w)coeliac OR undetected(n3)(celiac OR coeliac)
4. s subclinical(w)celiac OR subclinical(w)coeliac OR sub(w)clinical(w)celiac OR sub(w)clinical(w)coeliac OR undiagnosed(n3)celiac OR undiagnosed(n3)celiac
5. s nontropical(w)sprue OR non(w)tropical(w)sprue OR endemic(w)sprue
6. s gluten(n3)enteropath? OR gluten(n3)sensitiv? OR gluten(n3)hypersensitive? OR gluten(n3)intoleran? OR glutenin??(n3)hypersensitiv? OR glutenin??(n3) sensitiv? OR glutenin??(n3)intoleran?
7. s gliadin(n3)hypersentitiv? OR gliadin(n3)intoleran? Or gluten free diet/de OR gluten(w)free
8. s wheat(n3)hypersensitive? OR wheat(n3)intoleran? OR wheat allergy/de OR cereal(w)allergy
9. s (wheat OR triticum OR gluten?? OR glutinin??) AND (food allergy/de OR allergy/de OR hypersensitivity/de)
10. c 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. s (villi OR villus OR villous OR microvilli)(n3)atroph?
12. s refractory/ti,ab OR non(w)respond?/ti,ab OR nonrespond?/ti,ab OR non(w)responsiv?/ti,ab OR nonresponsiv?/ti,ab
13. s sprue OR celiac OR coeliac OR celiac disease/de
14. c 12 AND 13
15. c 10 OR 11 OR 14

16. s lymphoma/ti,ab,de OR lymphomas/ti,ab,de OR hodgkin?/ti,ab,de
17. s dc = c2.385.520.500.510? OR dc = c2.385.520.510.500? OR dc = c6.610.50.50? OR dc = c6.610.75.520.510? [var. lymphoma]
18. c 16 OR 17
19. s small intestine/de OR small(n2)bowel/ti,ab OR small(n2)intestine?/ti,ab OR duodenum/ti,ab,de OR duodenal/ti,ab OR jejunum/ti,ab,de OR jejunal/ti,ab OR ileum/ti,ab,de OR ileal/ti,ab
20. s large(n2)intestine?/ti,ab OR large(n2)bowel/ti,ab OR cecum/ti,ab,de OR colon/ti,ab,de OR colonic/ti,ab,de OR rectum/ti,ab,de OR rectal/ti,ab,de OR anus/ti,ab,de
21. s intestine/ti,ab,de OR intestinal/ti,ab,de OR dc = a3? [digestive system]
22. s intestine mucosa/de OR duodenum mucosa/de OR jejunum mucosa/de OR ileum mucosa/de OR intestinal(w)mucosa OR colon mucosa/de OR rectum mucosa/de OR small intestine mucosa/de
23. s gastric/ti,ab,de OR gastro?/ti,ab,de OR gi/ti,ab OR stomach/ti,ab,de OR cardia/ti,ab,de OR pylorus/ti,ab,de OR pyloric/ti,ab,de OR esophagogastr?
24. s digestive system cancer/de OR dc = c2.220.230.210? OR dc = c2.220.230.210? [digestive system cancer]
25. c 19 OR 20 OR 21 OR 22 OR 23 OR 24
26. c 15 AND 18 AND 25
27. s stomach lymphoma/de OR intestine lymphoma/de
28. c 15 AND 27
29. c 26 OR 28
30. s s29/human
31. s s30/eng

Celiac 4 – Screening

MEDLINE on DIALOG

1. s celiac???(w)disease OR coeliac???(w)disease OR celiac(w)sprue OR coeliac(w)sprue OR celiac(w)syndrome OR coeliac(w)syndrome
2. s celiacs OR coeliacs OR celiac disease/de
3. s silent(w)celiac OR silent(w)coeliac OR asymptomatic(w)celiac OR asymptomatic(w)coeliac OR undetected(n3)(celiac OR coeliac)
4. s subclinical(w)celiac OR subclinical(w)coeliac OR sub(w)clinical(w)celiac OR sub(w)clinical(w)coeliac OR undiagnosed(n3)celiac OR undiagnosed(n3)coeliac
5. s nontropical(w)sprue OR non(w)tropical(w)sprue OR endemic(w)sprue
6. s gluten(n3)enteropath? OR gluten(n3)sensitiv? OR gluten(n3)hypersensitive? OR gluten(n3)intoleran? OR glutenin??(n3)hypersensitiv? OR glutenin??(n3) sensitiv? OR glutenin??(n3)intoleran?
7. s gliadin(n3)hypersentitiv? OR gliadin(n3)intoleran?
8. s wheat(n3)hypersensitive? OR wheat(n3)intoleran? OR wheat hypersensitivity/de
9. s (wheat OR triticum OR gluten) AND food hypersensitivity/de
10. c 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. s screen/ti,ab OR screens/ti,ab OR screening/ti,ab OR screened/ti,ab OR mass screening!
12. c 10 AND 11
13. s celiac disease(l)diagnosis OR celiac disease(l)pathology
14. s “sensitivity and specificity”/de
15. s physician’s practice patterns/de
16. s reference standards/de OR quality control/de OR evaluation studies/de OR predictive value of tests/de OR incidental findings/de
17. s reproducibility of results/de OR physical examination(l)standards OR diagnosis, differential/de OR diagnostic errors! OR follow-up studies/de
18. s public health/de OR public health practice/de OR population surveillance/de OR clinical protocols/de OR critical pathways/de
19. s quality assurance, health care! OR guideline adherence/de OR social control, formal/de OR “outcome assessment (health care)”/de
20. c 14 or 15 or 16 or 17 or 18 or 19
21. c 13 AND 20
22. c 12 OR 21
23. s s22/human
24. s s23/eng

EMBASE on DIALOG

1. s celiac???(w)disease OR coeliac???(w)disease OR celiac(w)sprue OR coeliac(w)sprue OR celiac(w)syndrome OR coeliac(w)syndrome
2. s celiacs OR coeliacs OR celiac disease/de
3. s silent(w)celiac OR silent(w)coeliac OR asymptomatic(w)celiac OR asymptomatic(w)coeliac OR undetected(n3)(celiac OR coeliac)
4. s subclinical(w)celiac OR subclinical(w)coeliac OR sub(w)clinical(w)celiac OR sub(w)clinical(w)coeliac OR undiagnosed(n3)celiac OR undiagnosed(n3)coeliac
5. s nontropical(w)sprue OR non(w)tropical(w)sprue OR endemic(w)sprue
6. s gluten(n3)enteropath? OR gluten(n3)sensitiv? OR gluten(n3)hypersensitiv? OR gluten(n3)intoleran? OR glutenin??(n3)hypersensitiv? OR glutenin??(n3) sensitiv? OR glutenin??(n3)intoleran?
7. s gliadin(n3)hypersentitiv? OR gliadin(n3)intoleran?
8. s wheat(n3)hypersensitiv? OR wheat(n3)intoleran?
9. s (wheat OR triticum OR gluten) AND (food allergy/de OR hypersensitivity/de)
10. c 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. s mass screening/de OR mass(w)screen? OR genetic screening/de OR genetic(w)screen? OR newborn screening/de OR newborn??(n3)screen?

12. 10 AND 11
13. s screen/ti,ab OR screens/ti,ab OR screening/ti,ab OR screened/ti,ab
14. s dc=J2.10? [controlled study]
15. s dc=J2.40.10? [clinical study]
16. s dc=J2.50? [methodology]
17. s evaluation(w)study OR evaluation(w)studies OR physical examination/de OR follow-up studies/de
18. s dc=E1.215? [diagnosis]
19. s dc=N7.700? [practice guideline]
20. s dc=Q1.550.75? [social medicine]
21. c 14 or 15 or 16 or 17 or 18 or 19 or 20
22. c 10 AND 13 AND 21
23. c 12 OR 22
24. s s23/human
25. s s24/eng

CAB and AGRICOLA on DIALOG

1. s celiac???(w)disease OR coeliac???(w)disease OR celiac(w)sprue OR coeliac(w)sprue OR celiac(w)syndrome OR coeliac(w)syndrome
2. s celiacs OR coeliacs OR celiac syndrome/de
3. s silent(w)celiac OR silent(w)coeliac OR asymptomatic(w)celiac OR asymptomatic(w)coeliac OR undetected(n3)(celiac OR coeliac)
4. s subclinical(w)celiac OR subclinical(w)coeliac OR sub(w)clinical(w)celiac OR sub(w)clinical(w)coeliac OR undiagnosed(n3)celiac OR undiagnosed(n3)coeliac
5. s nontropical(w)sprue OR non(w)tropical(w)sprue OR endemic(w)sprue
6. s gluten(n3)enteropath? OR gluten(n3)sensitiv? OR gluten(n3)hypersensitiv? OR gluten(n3)intoleran? OR glutenin??(n3)hypersensitiv? OR glutenin??(n3) sensitiv? OR glutenin??(n3)intoleran?
7. s gliadin(n3)hypersentitiv? OR gliadin(n3)intoleran?
8. s wheat(n3)hypersensitiv? OR wheat(n3)intoleran?
9. s (wheat OR triticum OR gluten) AND (food allergies/de OR hypersensitivity/de)
10. c 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. s mass(w)screen? OR genetic(w)screen? OR newborn??(n3)screen?
12. c 10 AND 11
13. s screen/ti,ab OR screens/ti,ab OR screening/ti,ab OR screened/ti,ab
14. s evaluation(w)study OR evaluation(w)studies
15. c 10 AND 13 AND 14
16. c 12 OR 15
17. s s16/human
18. s s17/eng

PsycInfo on DIALOG

1. s celiac???(w)disease OR coeliac???(w)disease OR celiac(w)sprue OR coeliac(w)sprue OR celiac(w)syndrome OR coeliac(w)syndrome
2. s celiacs OR coeliacs
3. s silent(w)celiac OR silent(w)coeliac OR asymptomatic(w)celiac OR asymptomatic(w)coeliac OR undetected(n3)(celiac OR coeliac)
4. s subclinical(w)celiac OR subclinical(w)coeliac OR sub(w)clinical(w)celiac OR sub(w)clinical(w)coeliac OR undiagnosed(n3)celiac OR undiagnosed(n3)coeliac
5. s nontropical(w)sprue OR non(w)tropical(w)sprue OR endemic(w)sprue
6. s gluten(n3)enteropath? OR gluten(n3)sensitiv? OR gluten(n3)hypersensitiv? OR gluten(n3)intoleran? OR glutenin??(n3)hypersensitiv? OR glutenin??(n3) sensitiv? OR glutenin??(n3)intoleran?
7. s gliadin(n3)hypersentitiv? OR gliadin(n3)intoleran?
8. s wheat(n3)hypersensitiv? OR wheat(n3)intoleran?
9. s (wheat OR triticum OR gluten) AND food allergies/de
10. c 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9

11. s mass(w)screen? OR genetic(w)screen? OR newborn??(n3)screen? OR screening/de OR screening tests/de OR health screening/de
12. c 10 AND 11
13. s screen/ti,ab OR screens/ti,ab OR screening/ti,ab OR screened/ti,ab
14. s evaluation(w)study OR evaluation(w)studies OR physical examination/de OR followup studies/de OR evaluation/de
15. c 10 AND 13 AND 14
16. c 12 OR 15
17. s s16/human
18. s s17/eng

Sociological Abstracts at CAB

Limits set to English

1. celiac (KW) OR celiacs (KW) OR coeliac (KW) OR coeliacs (KW)
2. wheat (KW) OR gluten* (KW) OR gliadin* OR food (DE) OR foods (KW)
3. allergy (KW) OR allergies (KW) OR hypersensitivit* (KW) OR sensitive* (KW) OR intolerance* (KW)
4. mass public (DE) OR screen (KW OR screens (KW) OR screening (KW) OR screened (KW)
5. 1 AND 4
6. 2 and 3 AND 4
7. 5 OR 6

Celiac 5 – Dietary Compliance

MEDLINE on DIALOG:

Part 1

1. s celiac disease(l)psychology OR diet therapy(l)education OR diet therapy(l)methods OR diet therapy(l)standards OR diet therapy(l)trends OR diet therapy(l)utilization OR diet therapy(l)psychology
2. s diet(l)methods OR diet(l)trends OR diet(l)psychology OR diet(l)standards OR diet(l)utilization
3. s psychological tests/de OR health behavior/de OR patient acceptance of health care! OR health education/de OR patient education/de OR nutrition(l)education OR teaching!
4. s quality of life/de OR menu planning/de OR food habits/de OR feeding behavior/de OR quality of health care/de OR compliance/ti,ab OR adherence/ti,ab OR motivation/ti,ab,de
5. s achievement/de OR motivation/de OR directive counseling/de OR counseling/de OR psychology, applied/de OR psychology, educational/de OR learning/de OR child guidance/de
6. s adaptation, psychological/de OR attitude/de OR attitude of health personnel/de OR professional-patient relations! OR attitude to health!
7. s health promotion/de OR decision making! OR risk reduction behavior/de OR early(w)intervention/de OR intervention/ti,ab OR interventions/ti,ab OR data collection/de
8. s diet, protein-restricted(l)methods OR diet, protein-restricted(l)trends OR diet, protein-restricted(l)psychology OR diet, protein-restricted(l)standards OR diet, protein-restricted(l)utilization
9. s health surveys/de OR nutrition assessment! OR Behavioral Risk Factor Surveillance System/de OR interviews! OR questionnaire?/ti,ab,de
10. s guideline adherence/de OR evaluation studies/de OR “outcome assessment (health care)” OR “process assessment (health care)” OR food labeling/de
11. c 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10
12. s celiac disease(l)diet therapy
13. c 11 AND 12
14. s triticum(l)adverse effects OR wheat hypersensitivity/de OR gluten(n2)withdraw? OR gluten(l)adverse effects OR gliadin(l)adverse effects OR gluten(w)free
15. s diet OR dietary OR diets OR nutrition OR nutritional
16. c 14 AND 15
17. c 13 OR 16
18. s s17/human
19. s s18/eng

Part 2

1. s food labeling/de
2. s celiac OR coeliac OR triticum OR wheat hypersensitivity/de OR gluten OR gliadin OR celiac disease/de
3. c 1 and 2
4. s s3/human
5. s s4/eng

EMBASE on DIALOG

1. s celiac???(w)disease OR coeliac???(w)disease OR celiac(w)sprue OR coeliac(w)sprue OR celiac(w)syndrome OR coeliac(w)syndrome OR celiac(w)syndrome
2. s celiacs OR coeliacs OR celiac disease/de
3. s silent(w)celiac OR silent(w)coeliac OR asymptomatic(w)celiac OR asymptomatic(w)coeliac OR undetected(n3)(celiac OR coeliac)
4. s subclinical(w)celiac OR subclinical(w)coeliac OR sub(w)clinical(w)celiac OR sub(w)clinical(w)coeliac OR undiagnosed(n3)celiac OR undiagnosed(n3)coeliac
5. s nontropical(w)sprue OR non(w)tropical(w)sprue OR endemic(w)sprue

6. s gluten(n3)enteropath? OR gluten(n3)sensitiv? OR gluten(n3)hypersensitive? OR gluten(n3)intoleran? OR glutenin??(n3)hypersensitiv? OR glutenin??(n3) sensitiv? OR glutenin??(n3)intoleran?
7. s gliadin(n3)hypersentitiv? OR gliadin(n3)intoleran?
8. s wheat(n3)hypersensitive? OR wheat(n3)intoleran? OR wheat allergy/de
9. s (wheat OR triticum OR gluten) AND (hypersensitivity/de OR food allergy/de)
10. c 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. s diet restriction/de OR gluten(w)free(w)diet?? OR diet therapy/de OR diet?(w)intervention OR therapeutic(w)diet?? OR diet OR dietary OR diets OR nutrition OR nutritional OR dietary(w) restriction?? OR dietary(n3)guideline??
12. s intervention??/ti,ab,de OR feeding behavior/de OR gluten(w)free(w)food?/ti,ab OR nutritional intolerance/de
13. c 11 OR 12
14. c 10 AND 13
15. s health behavior/de OR illness behavior/de OR adaptive behavior/de OR behavior modification/de OR patient attitude/de OR patient compliance/de OR patient education/de OR patient guidance/de OR patient counseling/de
16. s quality of life/de OR coping(w)behavior/ti,ab OR adjustment??/ti,ab,de OR decision making/de OR early(w)intervention/ti,ab,de OR compliance/ti,ab OR adherence/ti,ab OR motivation/ti,ab,de OR coping behavior/de OR coping/ti,ab,de
17. s psychosocial(n3)aspect?? OR habit??/ti,ab,de OR attitude??/ ti,ab,de OR psychologic test /de OR counsel?/ti,ab,de OR psychological factor/de OR psycholog?/ti,ab,de
18. c 15 OR 16 OR 17
19. c 14 AND 18
20. s s19/human, eng

CAB and AGRICOLA on DIALOG

1. s celiac???(w)disease OR coeliac???(w)disease OR celiac(w)sprue OR coeliac(w)sprue OR celiac(w)syndrome OR coeliac(w)syndrome OR celiac(w)syndrome
2. s celiacs OR coeliacs OR celiac syndrome/de
3. s silent(w)celiac OR silent(w)coeliac OR asymptomatic(w)celiac OR asymptomatic(w)coeliac OR undetected(n3)(celiac OR coeliac)
4. s subclinical(w)celiac OR subclinical(w)coeliac OR sub(w)clinical(w)celiac OR sub(w)clinical(w)coeliac OR undiagnosed(n3)celiac OR undiagnosed(n3)coeliac
5. s nontropical(w)sprue OR non(w)tropical(w)sprue OR endemic(w)sprue
6. s gluten(n3)enteropath? OR gluten(n3)sensitiv? OR gluten(n3)hypersensitive? OR gluten(n3)intoleran? OR glutenin??(n3)hypersensitiv? OR glutenin??(n3) sensitiv? OR glutenin??(n3)intoleran?
7. s gliadin(n3)hypersentitiv? OR gliadin(n3)intoleran?
8. s wheat(n3)hypersensitive? OR wheat(n3)intoleran?
9. s (wheat OR triticum OR gluten) AND (hypersensitivity/de OR food allergies/de)
10. c 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. s gluten(w)free(w)diet?? OR diet treatment/de OR diet?(w)intervention OR therapeutic diets/de OR diet OR dietary OR diets OR nutrition OR nutritional
12. s dietary(w)restriction?? OR dietary(n3)guideline?? OR intervention??/ti,ab,de OR feeding behavior/de OR gluten(w)free(w)food?/ti,ab OR
13. c 11 OR 12
14. c 10 AND 13
15. s behavior modification/de OR patient compliance/de OR patient education/de
16. s quality of life/de OR coping(w)behavior/ti,ab OR adjustment??/ti,ab,de OR decision making/de OR early(w)intervention/ti,ab,de OR compliance/ti,ab OR adherence/ti,ab OR motivation/ti,ab,de OR coping/ti,ab
17. s psychosocial(n3)aspect?? OR habit??/ti,ab,de OR attitude??/ ti,ab,de OR counsel?/ti,ab,de OR psychological factors/de OR psycholog?/ti,ab,de
18. c 15 OR 16 OR 17
19. c 14 AND 18
20. s s19/human

21. s s20/eng

PsycInfo on DIALOG

1. s celiac???(w)disease OR coeliac???(w)disease OR celiac(w)sprue OR coeliac(w)sprue OR celiac(w)syndrome OR coeliac(w)syndrome OR celiac(w)syndrome
2. s celiacs OR coeliacs
3. s silent(w)celiac OR silent(w)coeliac OR asymptomatic(w)celiac OR asymptomatic(w)coeliac OR undetected(n3)(celiac OR coeliac)
4. s subclinical(w)celiac OR subclinical(w)coeliac OR sub(w)clinical(w)celiac OR sub(w)clinical(w)coeliac OR undiagnosed(n3)celiac OR undiagnosed(n3)coeliac
5. s nontropical(w)sprue OR non(w)tropical(w)sprue OR endemic(w)sprue
6. s gluten(n3)enteropath? OR gluten(n3)sensitiv? OR gluten(n3)hypersensitive? OR gluten(n3)intoleran? OR glutenin??(n3)hypersensitiv? OR glutenin??(n3) sensitiv? OR glutenin??(n3)intoleran?
7. s gliadin(n3)hypersentitiv? OR gliadin(n3)intoleran?
8. s wheat(n3)hypersensitive? OR wheat(n3)intoleran? OR wheat(n3)(allergy OR allergies)
9. s (wheat OR triticum OR gluten) AND food allergies/de
10. c 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. s gluten(w)free(w)diet?? OR diet?(w)intervention OR therapeutic(w)diet?? OR diet OR dietary OR diets OR nutrition OR nutritional OR dietary(w)restriction?? OR dietary(n3)guideline??
12. s intervention??/ti,ab OR gluten(w)free(w)food?/ti,ab
13. c 11 OR 12
14. c 10 AND 13
15. s health behavior/de OR illness behavior/de OR adaptive behavior/de OR behavior modification/de
16. s quality of life/de OR coping(w)behavior/ti,ab OR adjustment??/ti,ab,de OR decision making/de OR early(w)intervention/ti,ab,de OR compliance/ti,ab OR adherence/ti,ab OR motivation/ti,ab,de OR coping behavior/de OR coping/ti,ab
17. s psychosocial(n3)aspect?? OR habit??/ti,ab,de OR attitude??/ti,ab,de OR counsel?/ti,ab,de OR psycholog?/ti,ab,de
18. c 15 OR 16 OR 17
19. c 14 AND 18
20. s s19/human
21. s s20/eng

Sociological Abstracts at CAB

Limits set to English

1. celiac (KW) OR celiacs (KW) OR coeliac (KW) OR coeliacs (KW)
2. wheat (KW) OR food (DE) OR foods (kw) OR gluten* (KW) OR gliadin*
3. allergy (KW) OR allergies (KW) OR hypersensitive* (KW) OR intoleran* (KW) OR sensitive* (KW)
4. feeding practices (DE) OR feeding (DE)
5. diet (DE) OR nutrition (DE)
6. diet (KW) OR diets(KW) OR nutrition (KW)OR nutritional (KW)
7. 2 AND 3
8. 4 OR 5 OR 6
9. 1 AND 8
10. 7 AND 8
11. 9 OR 10

Appendix C. Data Assessment and Data Abstraction Forms

Data Assessment Forms

Level 1 Screening

Objective 1:

1. Does this refer to determining the sensitivity or specificity of one of the following tests for celiac disease? (biopsy, anti-htTG, anti-endomysial, anti-gliadin antibody, anti-gliadin antibody, HLA DQ2/DQ8).
    a. This citation refers to another objective and should be moved or copied
    b. **No** (move on to next citation)
    c. **Yes**
    d. Can't tell

Objective 2:

1. Does this refer to the prevalence or incidence of **celiac disease**?
    a. This citation refers to another objective and should be moved or copied
    b. **No** (move on to next citation)
    c. **Yes**
    d. Can't tell

Objective 3:

1. Does this refer to an association between **celiac and GI lymphoma**?
    a. This citation refers to another objective and should be moved or copied
    b. **No** (move on to next citation)
    c. **Yes**
    d. Can't tell

Objective 4:

1. Does this refer to expected consequences of testing for celiac disease
    a. This citation refers to another objective and should be moved or copied
    b. **No** (move on to next citation)
    c. **Yes**
    d. Can't tell

Objective 5:

1. Does this refer to identifying or assessing interventions for promoting or monitoring adherence to a gluten free diet?
    a. This citation refers to another objective and should be moved or copied
    b. **No** (move on to next citation)
    c. **Yes**
    d. Can't tell

Level 2 Screening

Objective 1:

1. Does this refer **specifically** to determining the sensitivity or specificity of one of the identified tests for celiac disease? **Note: for biopsy and HLA**, we may not see sensitivity or specificity – keep if you can get data on use as diagnostic test or accuracy as a test or if it distinguishes celiac from other diseases etc.
    a. **Yes.** If this citation also refers to another objective(s), please state objective number(s):
    b. **No.** If this citation refers to another objective(s), please state objective number(s): (move on to next citation)

2. Is this a review article?
    a. Yes (keep for references)
    b. No

3. What is the test(s) being studied? (Note: we are not interested in any other type of test!)
    a. Biopsy
    b. Anti-htTG
    c. Anti-endomysial antibody (EMA)
    d. Anti-gliadin antibody (AGA)
    e. HLA DQ2/DQ8 (note: we are not interested in pathophysiology does the article give data using HLA to distinguish celiac from non celiac)
    f. If none of above then – reject citation

4. What is the "gold standard" the test(s) is compared to?
    a. Biopsy
    b. Anti-htTG
    c. Anti-endomysial antibody (EMA)
    d. Anti-gliadin antibody (AGA)
    e. HLA DQ2/DQ8
    f. Other (list in box)

5. What is the patient population?
    a. Adults

b. Paediatric
c. General unselected
d. Specific ethnic groups (fill in box)
e. Patients with suspected celiac (symptomatic)
f. Patients at risk of celiac disease (asymptomatic - relatives of celiac, diabetes, Fe Diff, infertility, osteoporosis, short stature)
g. Other (fill in box)

Objective 2:

1. Does this refer **specifically** to the prevalence or incidence of **celiac disease**? Please remember we are only really interested in the incidence / prevalence of celiac in population X or disease X **NOT** vice verse.
   a. **Yes**.
   b. **No. Exclude**
   c. **No.** But this referrers to an association between celiac and another disease to state in background /discussion

2. Is this a review article?
   a. Yes (keep for references)
   b. No

3. Does the prevalence or incidence refer to:
   a. Classical celiac
   b. Atypical celiac (i.e., Fe diff, infertility, short stature, osteoporosis)
   c. Asymptomatic celiac
   d. Other or (fill in box)

4. What is the patient population that was tested?
   a. Unselected – general population (e.g., blood donors, routine physical etc)
   b. Patients with suspected celiac
   c. Relatives of celiac patients
   d. Iron deficiency
   e. Osteoporosis
   f. Short stature
   g. Infertility
   h. Other (fill in box)

5. What was the screening test(s) used?
   a. Biopsy
   b. Anti-htTG
   c. Anti-endomysial antibody (EMA)
   d. Anti-gliadin antibody (AGA)
   e. HLA DQ2/DQ8
   f. Other (fill in box)

6. What is the country/region of origin of the study (fill in box)?

Objective 3:

1. Does this refer **specifically** to an association between **celiac and GI lymphoma**?
    a. **Yes**.
    b. **No. Exclude**

2. Is this a review article?
    a. Yes (keep for references)
    b. No

3. Does this give **data** on the risk of developing GI lymphoma in celiac?
    a. Yes
    b. No

4. What is the country/region of origin of the study? (fill in box)

5. What celiac population was evaluated?
    a. Classical celiac
    b. Atypical celiac (i.e., fe dif, infertility, short stature, osteoporosis)
    c. Asymptomatic celiac
    d. Other (fill in box)

Objective 4:

1. Does this refer **specifically** to expected **consequences of testing for celiac disease?**
    a. **Yes**.
    b. **No. Exclude**

2. Is this a review article?
    a. Yes (keep for references)
    b. No

3. What consequences were assessed:
    a. False-positive results
    b. Follow-up testing
    c. Invasive procedures (biopsy)
    d. Costs
    e. Cases diagnosed
    f. Patients complying with treatment
    g. Response to treatment
    h. Clinical outcome (reduced risk of complication etc)
    i. Other (fill in box)

4. What is the country/region of origin of the study? (fill in box)

5. What is the patient population that was tested?
    a. Unselected – general population (e.g., blood donors, routine physical, etc.)
    b. Patients with symptoms suggestive of celiac.
    c. Asymptomatic at risk populations (relatives of celiac patients, iron deficiency, osteoporosis, infertility short, stature)
    d. Other (fill in box).

Objective 5:

1. Does this **specifically** refer to identifying or assessing an intervention(s) for promoting or monitoring adherence to a gluten free diet?
    a. **Yes**.
    b. **No. Exclude**

2. Is this a review article?
    a. Yes (keep for references)
    b. No

3. Does this refer to:
    a. Promoting adherence
    b. Monitoring adherence
    c. Both

4. What intervention was assessed? (If **monitoring adherence**)
    a. Biopsy
    b. Antibody testing

5. What intervention was used? (If **promoting adherence**) – fill in box

Level 3 Screening

Celiac 1: Sensitivity and specificity of screening tests:

Inclusion criteria: (a **No** answer to any of the below excludes the article)

1. For serology - the study publication date is 1990 or more recent (biopsy studies can be earlier)
    a. Yes (include)
    b. No (exclude)

2. For AGA - the studies uses a standardized commercial ELISA kit (or this study is testing such a kit or technique)
    a. Yes (include)
    b. No (exclude)

3. For EMA – the substrate is monkey esophagus or human umbilical cord
    a. Yes (include)
    b. No (exclude)

4. For tTG – study uses ELISA with the substrate for tTG being guinea pig or human recombinant tTG.
    a. Yes (include)
    b. No (exclude)

5. For any serology and HLA studies – the control group(s) are appropriate and controls evaluated with the reference test (i.e., biopsy)?
    a. Yes (include)
    b. No (exclude)

6. The paper allows for the extraction of the sensitivity or specificity of the test in question (AGA, EMA, tTG, HLA DQ2/8, biopsy)?
    a. Yes (include)
    b. No (exclude)

7. Was the diagnosis of celiac disease appropriate in the celiac disease group
    a. Yes (include)
    b. No (exclude)

Celiac 2: Prevalence and incidence of celiac disease:

Inclusion Criteria: (a **No** answer to any of the below excludes the article)

1. The country of origin must be **Western Europe, North America, Australia, New Zealand**.
    a. Yes (include)
    b. No (exclude)

2. The publication date was >= 1990 if serology was used to screen (but can be earlier for biopsy)
    a. Yes (include)
    b. No (exclude)

3. The screening test was biopsy, standardized ELISA AGA, EMA (monkey esophagus or human umbilical cord), tTG (guinea pig, or human recombinant)
    a. Yes (include)
    b. No (exclude)

4. The screened population must belong to one of these groups:
        a. Unselected – General population (e.g. Blood donors, routine physical etc)
        b. Patients with suspected celiac
        c. Relatives of celiac patients
        d. Iron deficiency
        e. Osteoporosis
        f. Diabetes

        a. Yes (include)
        b. No (exclude)

Celiac 3: Prevalence/incidence of lymphoma in celiac disease

1. Does this study specifically give the **incidence**, **prevalence** or a **measure of risk** of GI lymphoma (Includes malignant histiocytosis) in a population of celiac patients? (Note: we are not interested in other cancers, and we are not interested in how many lymphoma patients have celiac disease)

   OR

   Does this study discuss ulcerative jejuno-ileitis or refractory sprue as a precursor or marker for GI lymphoma in patients with celiac disease?

   a. Yes (include lymphoma)
   b. Yes (include jejuno-ileitis/refractory sprue)
   c. No (exclude)

Celiac 4: Consequences of testing for celiac disease

1. Does this paper report a consequence of testing for celiac listed below: (note: false positive, and negative results, follow-up testing and need for invasive testing is obtained from Celiac 1 objective)
   a. **Costs**
   b. Patients complying with treatment
   c. **Response to treatment** – i.e., **clinical outcome** (reduced risk of complication – osteoporosis, lymphoma, anemia, symptoms)

      i. Yes (include)
      ii. No (exclude)

2. Did the population include one of the following (note: nothing more than listed):
   a. Patients with symptoms suggestive of celiac disease
   b. Asymptomatic, at-risk populations (affected family members, patients with type 1 diabetes, osteoporosis, Fe Diff)
   c. General population

      i. Yes (include)
      ii. No (exclude)

Note: a **No** to either question excludes the study

Celiac 5: Monitoring or promoting adherence to a GFD

If a monitoring question:

Does this paper report monitoring adherence based on **serology** (standardized ELISA **AGA publication date >= 1990**, **EMA** (monkey esophagus or human umbilical cord), **tTG** (guinea pig, or human recombinant) or **biopsy**?

Note: If this is a study of sensitivity or specificity – it must include actual extractable follow-up data (like drop in titre or improvement in biopsy)

OR

If a promoting adherence question:

Does this paper report on an intervention that was used to promote adherence to Gluten free diet?

a. Yes (include promoting)
b. Yes (include Monitoring)
c. No (exclude)

Data Abstraction Forms

Celiac 1: Serology

1. Paper #:
2. Title:
3. Author/year:
4. Reference:
5. Reviewer:

6. Publication type:
    a. Journal
    b. Conference abstract
    c. Other:

7. Is this a duplicate publication (state refid of duplicate):

8. Study type:
    a. Relevant clinical population: (cases and controls defined from the population based on the results of the test under study)
    b. Case Control: (groups are predefined and may come from different populations):
    c. Other: (list)

9. Country:

10. Racial Groups and % if different from country: *list in box*

11. Group demographics

	Celiac		Control			
	Group 1	Group 2	group1	group 2	group 3	group 4
Group name						
Age groups						
Mean age						
Age range						
% female						
Gluten intake						

12. Type of population (applies to 8 a): (*from level 2 database)*
    a. Unselected – general population (e.g., blood donors, routine physical, etc.)
    b. Patients with suspected celiac
    c. Relatives of celiac patients
    d. Diabetes
    e. Iron deficiency
    f. Osteoporosis
    g. Other (fill in box): *not part of extraction – background / discussion only*

13. Case and control group types (applies to 8 b):
    a. Celiac group 1
        i. Untreated
            1. Classic
            2. Silent celiac
            3. Atypical celiac
            4. Other
        ii. Treated On GFD
        iii. Refractory (implies on GFD) / ulcerative jejuno-ileitis
        iv. Other/can't tell: text box

    b. Celiac group 2 – if applicable
        i. Untreated
            1. Classic
            2. Silent celiac
            3. Atypical celiac
            4. Other
        ii. Treated on GFD
        iii. Refractory (implies on GFD) / ulcerative jejuno-ileitis
        iv. Other/can't tell: text box

Note: Control groups must have had a negative biopsy otherwise should have been excluded at level 3

    c. Control group 1:
        i. Unselected – general population (e.g., blood donors, routine physical, etc.)
        ii. Patients with suspected celiac
        iii. Relatives of celiac patients
        iv. Diabetes
        v. Iron deficiency
        vi. Osteoporosis
        vii. Other disease controls
        viii. Other (fill in box):

    d. Control group 2 (if applicable):
        i. Unselected – general population (e.g., blood donors, routine physical, etc.)
        ii. Patients with suspected celiac
        iii. Relatives of celiac patients
        iv. Diabetes
        v. Iron deficiency
        vi. Osteoporosis
        vii. Other disease controls
        viii. Other (fill in box):

e. Control group 3 (if applicable):
    i. Unselected – general population (e.g., blood donors, routine physical, etc)
    ii. Patients with suspected celiac
    iii. Relatives of celiac patients
    iv. Diabetes
    v. Iron deficiency
    vi. Osteoporosis
    vii. Other disease controls
    viii. Other (fill in box):

f. Control group 4 (if applicable):

    i. Unselected – general population (e.g., blood donors, routine physical, etc.)
    ii. Patients with suspected celiac
    iii. Relatives of celiac patients
    iv. Diabetes
    v. Iron deficiency
    vi. Osteoporosis
    vii. Other disease controls
    viii. Other (fill in box):

14. Reference test(s) for cases (i.e., how was celiac diagnosed):
    a. Biopsy (required):
        i. endoscopic
        ii. capsule
            1. list type: text box
        iii. how many samples taken (text box)
    b. Serology (check as many as applicable)
        i. AGA (date >1990)
        ii. EMA
        iii. tTG
    c. Comments:

15. What test was conducted first
    a. Biopsy
    b. Serology
    c. Simultaneous
    d. Mixed
    e. Unsure/other: comment in box

16. Reference test for control (s) 1-----2-----3-----4
    a. Include biopsy (required)
    b. Otherwise excluded

17. Detail biopsy criteria used to define celiac (ESPGAN, Marsh, Rostami) and state what grades were used (i.e., Marsh I and above? etc.)

18. Was IgA deficiency assessed (if applicable):
    a. Yes
    b. No
    c. N/A
    d. Comments: text box)

19. Overall number:

20. Number of:
    a. Cases 1
    b. Cases 2 (if applicable):
    c. Control group 1:
    d. Control group 2 (if applicable):
    e. Control group 3 (if applicable):
    f. Control group 4 (if applicable):

21. Intervention: (***may be up to 8+ tests studied – distinguish IgG from IgA***)

				Results (4x4 table)				
Test name	Methodology	Cut-off (criteria)	Group	a	b	c	d	

22. Stated results if raw data not given:

Test name	Sensitivity	Specificity	PPV	NPV	Prevalence

23. Comments regarding study: test box

Notes for reference:

Test name can be:

1) Anti-htTG
2) Anti-endomysial antibody (EMA)
3) Anti-gliadin antibody (AGA)

TEST: _____		BIOPSY (gold standard) positive	BIOPSY (gold standard) negative
	positive	a	b
	negative	c	d

Calculate automatically

- Prevalence: (a+c)/(a+b+c+d)
- Sensitivity: (a/(a+c));
- Specificity: d/(b+d);
- PPV: a/(a+b)
- NPV: d/(c+d)

Celiac 1: HLA

1. Paper #:
2. Title:
3. Author/year:
4. Reference:
5. Reviewer:

6. Publication type:
   a. Journal
   b. Conference abstract
   c. Other:

7. Is this a duplicate publication (state refid of duplicate):

8. Country:

9. Racial groups and % if different from country: *list in box*

10. Age groups (ped, adult, both):

11. Mean age:

12. Range of age:

13. Percent female:

14. Study type:
    d. Relevant clinical population: (cases and controls defined from the population based on the results of the test under study)
    e. Case control: (groups are predefined and may come from different populations:
    f. Cross-sectional screening study
    g. Other: (list)

15. Type of population (applies to 14 a, c):
    a. Unselected – general population (e.g., blood donors, routine physical etc)
    b. Patients with suspected celiac
    c. Relatives of celiac patients
    d. Diabetes
    e. Iron deficiency
    f. Osteoporosis
    g. Other (fill in box): *not part of extraction – background / discussion only*

16. Case and control group types (applies to 14b):
    h. Celiac group 1
        i. Untreated
            1. Classic
            2. Silent celiac
            3. Atypical celiac
            4. Other
        ii. Treated on GFD
        iii. Refractory (implies on GFD) / ulcerative jejuno-ileitis
        iv. Other/can't tell: text box Celiac group 2

    i. Celiac group 2 – if applicable
        i. Untreated
            1. Classic
            2. Silent celiac
            3. Atypical celiac
            4. Other
        ii. Treated on GFD
        iii. Refractory (implies on GFD) / ulcerative jejuno-ileitis
        iv. Other/can't tell: text box

Note: Control groups must have had a negative biopsy otherwise should have been excluded at level 3

j. Control group 1:
    i. Unselected – general population (e.g., blood donors, routine physical, etc.)
    ii. Patients with suspected celiac
    iii. Relatives of celiac patients
    iv. Diabetes
    v. Iron deficiency
    vi. Osteoporosis
    vii. Other disease controls
    viii. Other (fill in box):

k. Control group 2 (if applicable):
    i. Unselected – general population (e.g., blood donors, routine physical, etc.)
    ii. Patients with suspected celiac
    iii. Relatives of celiac patients
    iv. Diabetes
    v. Iron deficiency
    vi. Osteoporosis
    vii. Other disease controls
    viii. Other (fill in box):

l. Control group 3 (if applicable):
    i. Unselected – general population (e.g., blood donors, routine physical, etc.)
    ii. Patients with suspected celiac
    iii. Relatives of celiac patients
    iv. Diabetes
    v. Iron deficiency
    vi. Osteoporosis
    vii. Other disease controls
    viii. Other (fill in box):

m. Control group 4 (if applicable):

    i. Unselected – general population (e.g., blood donors, routine physical, etc.)
    ii. Patients with suspected celiac
    iii. Relatives of celiac patients
    iv. Diabetes
    v. Iron deficiency
    vi. Osteoporosis
    vii. Other disease controls
    viii. Other (fill in box):

17. Reference test for cases
    n. Biopsy:
        i. endoscopic
        ii. capsule
            1. list type: text box

    o. Serology (check as many as applicable)
        i. AGA (date >1990)
        ii. EMA
        iii. tTG

18. Reference test for control 1-----2------3-----4
    p. Biopsy
    q. Serology (list)
    r. Can't tell

19. Overall number:

20. Number of:
    s. Cases 1
    t. Cases 2 (if applicable):
    u. Control group 1:
    v. Control group 2 (if applicable):
    w. Control group 3 (if applicable):
    x. Control group 4 (if applicable):

21. HLA tested

				Results (4x4 table)				
Test name	Methodology	Cut-off (criteria)	Group	a	b	c	d	

22. Stated results if raw data not given:

Test name	Sensitivity	Specificity	PPV	NPV	Prevalence

23. Narrative result if data not extractable: text box

24. Comments regarding study: text box

Celiac 2: Prevalence and Incidence of Celiac Disease

1. Paper #:
2. Title:
3. Author/year:
4. Reference:
5. Reviewer:

Patient population:

6. Publication type:
    a. Journal
    b. Conference abstract
    c. Etc (your list)

7. Is this a duplicated: list refid

8. Study type:
    a. Cross-sectional prevalence
    b. Cohort
    c. Case control
    d. Incidence study
    e. Other: (list)

9. Country:

10. Racial groups and % if different from country: *list in box*

11. Type of patients screened:
    a. Unselected – general population (e.g., blood donors, routine physical etc)
    b. Patients with suspected celiac
    c. Relatives of celiac patients
    d. Diabetes
    e. Iron deficiency
    f. Osteoporosis
    g. Other (fill in box): *not part of extraction – background / discussion only*

12. Age groups (ped, adult or both): *from level 2 database*

13. Mean age:

14. Range of age:

15. Percent female:

Intervention:

				Results	
Test name	Methodology	# screened	Cases detected	Incidence (time period)	Prevalence

Note: distinguish IgG from IgA. Also the screen may be single test, or combination of tests. So list each strategy used as a "test name"

16. State control reference and methodology of incidence study: (fill in box)

17. Confirmatory test
    a. None
    b. Biopsy
    c. Other serology
    d. Other: fill in box

18. Was IgA deficiency assessed (if applicable):
    a. Yes
    b. No
    c. N/A
    d. Comments: (text box)

19. Comments about study: text box

Celiac 3: Lymphoma

1. Paper #:
2. Title:
3. Author/year:
4. Reference:
5. Reviewer:

6. Publication type:
    a. Journal
    b. Conference abstract
    c. Etc (your list)

7. Study type:
    a. Cross-sectional prevalence
    b. Case series
    c. Cohort
        i. Prospective
        ii. Retrospective
    d. Case control
    e. Other: (list)

8. Country: *from level 2 database*

9. Racial groups and % if different from country: *list in box*

10. Study population type(s) – this is the population of "lymphoma" in case control **OR** the overall population in a screening/prevalence study and cohort studies: Check multiple if study included different populations

    a. Classic celiac:
        1) Treated celiac
        2) Untreated celiac
        3) Non-compliant
        4) Unclear about treatment
    b. Asymptomatic (silent celiac)
    c. Atypical celiac (found on basis of
    d. Latent celiac (normal histology)
    e. Refractory celiac
    f. Ulcerative jejuno-ileitis
    g. Other celiac complications
    h. Patients on Immunosuppression:
    i. Other:

11. How were celiac patients identified (text box)

12. How were cases of lymphoma identified? (i.e., registry, administrative database, etc.) text box

13. Group demographics

	Overall population study type a, b, c	Case group	Control group
Age groups			
Mean age			
Age range			
% female			
Disease duration			

14. For **case control** study:
    a. Control population type (those without lymphoma)
        i. Unselected general population
        ii. Other disease controls: state disease(s)
        iii. A celiac population
            1. Classic celiac:
                a. Treated celiac
                b. Untreated celiac
                c. Non-compliant
                d. Unclear about treatment
            2. Asymptomatic (silent celiac)
            3. Atypical celiac (found on basis of
            4. Latent celiac (normal histology)
            5. Refractory celiac
            6. Ulcerative jejuno-ileitis
            7. Other celiac complications
        iv. Patients on immunosuppression:
    b. # of cases:
    c. # of controls:
    d. Risk factor used to calculate odds ratio
        i. Celiac itself
            1. classic
            2. refractory
            3. ulcerative jejuno-ileitis
        ii. Compliance with diet
        iii. Disease duration
        iv. Other: state in text box
    e. Raw data (if possible)

Table for case control study

Risk factor	Lymphoma present	Lymphoma absent
Present		
Absent		

15. For **cohort study**
    f. Length of F/U of cohort:
    g. Timeline:
        iii. Prospective cohort
        iv. Retrospective cohort:

    h. Risk factor used to calculate Relative Risk if one population used
        v. Celiac itself
            1. classic
            2. atypical
            3. silent
            4. refractory
            5. ulcerative jejuno-ileitis
        vi. Compliance with diet
        vii. Disease duration
        viii. Other: state in text box

    i. If a celiac cohort was compared to another population to obtain another risk estimate (i.e., standardized mortality or morbidity ratios). Describe control population.

        ix. Unselected general population
        x. Other disease controls: state disease(s)
        xi. A celiac population
            1. Classic celiac:
                a. Treated celiac
                b. Untreated celiac
                c. Non-compliant
                d. Unclear about treatment
            2. Asymptomatic (silent celiac)
            3. Atypical celiac (found on basis of
            4. Latent celiac (normal histology)
            5. Refractory celiac
            6. Ulcerative jejuno-ileitis
            7. Other celiac complications
        xii. Patients on immunosuppression
        xiii. Other: (fill in text box)

    j. Overall number in cohort:
        xiv. Number of cases identified:
    k. Number in control population (if applicable)
        xv. Number of lymphomas identified
        xvi. Raw data if available:

16. Table for classic cohort study

Risk factor	Lymphoma present	Lymphoma absent
Present		
Absent		

17. For cross sectional studies: study population in Q #10
    l. Overall number screened:
    m. Number of cases identified:

18. Results (text boxes)
    n. Lymphoma type
    o. Prevalence of lymphoma in celiac:
    p. Incidence of lymphoma in celiac:
    q. Odds ratio (95% confidence interval)
    r. Relative risk (95% confidence interval):
    s. Standardized mortality ratio
    t. Standardized morbidity ratio
    u. Other risk estimate:

19. Study comments:

Celiac 4: Consequences of Testing

1. Paper #:
2. Title:
3. Author/year:
4. Reference:
5. Reviewer:

Patient population:

6. Publication type:
    a. Journal
    b. Conference abstract
    c. Etc (your list)

7. Study type:
    a. Diagnostic test
    b. Cross-sectional prevalence
    c. Cohort
    d. Case control
    e. Other: (list)

8. Country: *from level 2 database*

9. Racial groups and % if different from country: *list in box*

10. Type of patients tested (*from level 2 database)*
    a. Unselected – general population (e.g., blood donors, routine physical, etc.)
    b. Patients with suspected celiac
    c. Relatives of celiac patients
    d. Diabetes
    e. Iron deficiency
    f. Osteoporosis
    g. Other (fill in box):

11. Type of celiac patients identified:
    a. Classic celiac
    b. Asymptomatic
    c. Atypical celiac
        i. Fe deficiency
        ii. Osteoporosis
        iii. Other
    d. Complicated celiac
        i. Refractory
        ii. Jejuno-ileitis
        iii. Lymphoma)

e. Other

12. Intervention:
    a. Test(s) used to identify celiac patients:
        i. Biopsy
        ii. AGA ELISA (publication date >1990)
        iii. AMA
        iv. tTG:

13. Was IgA deficiency assessed (if applicable):
    a. Yes
    b. No
    c. N/A
    d. Comments: text box)

14. Length of F/U:

15. How were patients followed (if applicable): test box

16. Outcomes:

Outcome	**Result**	**Notes**
Costs		
Cases diagnosed		
Patients complying with treatment		
Response to treatment		
Clinical outcome (reduced risk of complication, etc)		
Other (fill in box)		

17. Comments regarding study: Fill in text box

Celiac 5: Promoting and Monitoring Adherence to Gluten-Free Diet

1. Paper #:
2. Title:
3. Author/year:
4. Reference:
5. Reviewer:

Patient population:

6. Publication type:
    a. Journal
    b. Conference abstract
    c. Etc (your list)

7. Study type:
    a. Diagnostic test
    b. Cross-sectional prevalence
    c. Cohort
    d. Case control
    e. Other: (list)

8. Country: *from level 2 database*

9. Racial groups and % if different from country: *list in box*

10. Age groups (ped, adult, both): *from level 2 database*

11. Mean age:

12. Range of age:

13. Percent female:

14. Disease duration: state in box

15. Type of celiac studied
    a. Classic celiac
    b. Asymptomatic celiac
    c. Atypical celiac (Fe deficiency, osteoporosis, etc.)
    d. Refractory celiac
    e. Ulcerative jejuno-ileitis
    f. IgA deficient celiac
    g. Other:

16. Does this refer to:

a. Promoting adherence
b. Monitoring adherence
c. Both

17. What intervention was assessed? (if **monitoring adherence**)

	Result (normalization of biopsy or drop in antibody titres - list result details)
Biopsy	
Antibody testing (state test used)	
Other: _____	

18. Did this study determine the sensitivity/specificity of the intervention during follow-up or with different histologic grades:
    a. No
    b. Yes: detail in text box

19. Was IgA deficiency assessed (if applicable):
    a. Yes
    b. No
    c. N/A
    d. Comments: text box

20. What intervention was used? (if **promoting adherence**) – fill in box

Intervention	Result

Comments about the study: fill in text box

Appendix D. Quality Assessment Forms

QUADAS Checklist

Item		Yes	No	Unclear
1.	Was the spectrum of patients representative of the patients who will receive the test in practice?			
2.	Were selection criteria clearly described?			
3.	Is the reference standard likely to correctly classify the target condition?			
4.	Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?			
5.	Did the whole sample or a random selection of the sample, receive verification using a reference standard of diagnosis?			
6.	Did patients receive the same reference standard regardless of the index test result?			
7.	Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)?			
8a.	Was the execution of the index test described in sufficient detail to permit replication of the test?			
8b.	Was the execution of the reference standard described in sufficient detail to permit its replication?			
9a.	Were the index test results interpreted without knowledge of the results of the reference standard?			
9b.	Were the reference standard results interpreted without knowledge of the results of the index test?			
10.	Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?			
11.	Were uninterpretable/ intermediate test results reported?			
12.	Were withdrawals from the study explained?			

Cross-Sectional/Prevalence Study Quality

Item	Yes	No	Unclear
1) Define the source of information (survey, record review)			
2) List inclusion and exclusion criteria for exposed and unexposed subjects (cases and controls) or refer to previous publications			
3) Indicate time period used for identifying patients			
4) Indicate whether or not subjects were consecutive if not population-based			
5) Indicate if evaluators of subjective components of study were masked to other aspects of the status of the participants			
6) Describe any assessments undertaken for quality assurance purposes (e.g., test/retest of primary outcome measurements)			
7) Explain any patient exclusions from analysis			
8) Describe how confounding was assessed and/or controlled.			
9) If applicable, explain how missing data were handled in the analysis			
10) Summarize patient response rates and completeness of data collection			
11) Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained			

Newcastle–Ottawa Quality Assessment Scale: Cohort Studies

Note: a study can be awarded a maximum of one star for each numbered item within the selection. A maximum of two stars can be given for comparability and selection.

1) Representativeness of the exposed cohort
   a) truly representative of the average _____ (describe) in the community ☸
   b) somewhat representative of the average _____ in the community ☸
   c) selected group of users e.g. nurses, volunteers
   d) no description of the derivation of the cohort
2) Selection of the non exposed cohort
   a) drawn from the same community as the exposed cohort ☸
   b) drawn from a different source
   c) no description of the derivation of the non exposed cohort
3) Ascertainment of exposure
   a) secure record (e.g. surgical records) ☸
   b) structured interview ☸
   c) written self report
   d) no description
4) Demonstration that outcome of interest was not present at start of study
   a) yes ☸
   b) no

Comparability
1) Comparability of cohorts on the basis of the design or analysis
   a) study controls for _____ (select the most important factor) ☸
   b) study controls for any additional factor ☸ (This criteria could be modified to indicate specific control for a second important factor.)

Outcome
1) Assessment of outcome
   a) independent blind assessment ☸
   b) record linkage ☸
   c) self report
   d) no description
2) Was follow-up long enough for outcomes to occur
   a) yes (select an adequate follow up period for outcome of interest) ☸
   b) no
3) Adequacy of follow up of cohorts
   a) complete follow up - all subjects accounted for ☸
   b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost) ☸
   c) follow up rate < ____% (select an adequate %) and no description of those lost
   d) no statement

Newcastle–Ottawa Quality Assessment Scale: Case Control Studies

Note: a study can be awarded a maximum of one star for each numbered item within the selection and exposure categories. A maximum of two stars can be given for comparability.

Selection

1) Is the case definition adequate?
   a) yes, with independent validation ☸
   b) yes, e.g. record linkage or based on self reports
   c) no description
2) Representativeness of the cases
   a) consecutive or obviously representative series of cases ☸
   b) potential for selection biases or not stated
3) Selection of Controls
   a) community controls ☸
   b) hospital controls
   c) no description
4) Definition of Controls
   a) no history of disease (endpoint) ☸
   b) no description of source

Comparability

1) Comparability of cases and controls on the basis of the design or analysis
   a) study controls for _____ (Select the most important factor.) ☸
   b) study controls for any additional factor ☸ (This criteria could be modified to indicate specific control for a second important factor.)

Exposure

1) Ascertainment of exposure
   a) secure record (e.g. surgical records) ☸
   b) structured interview where blind to case/control status ☸
   c) interview not blinded to case/control status
   d) written self report or medical record only
   e) no description
2) Same method of ascertainment for cases and controls
   a) yes ☸
   b) no
3) Non-Response rate
   a) same rate for both groups ☸
   b) non respondents described
   c) rate different and no designation

Appendix E. Summary ROC Curves

Summary ROC curves as calculated by the methods of Moses and Shapiro (meta-analysis text). For all figures below, the middle curve is the summary ROC, the other curves are upper and lower 96% CI, and the vertical line is the point were sensitivity = specificity; dots are individual studies

Figure 1. Summary ROC HLA average-risk with 95% CIs

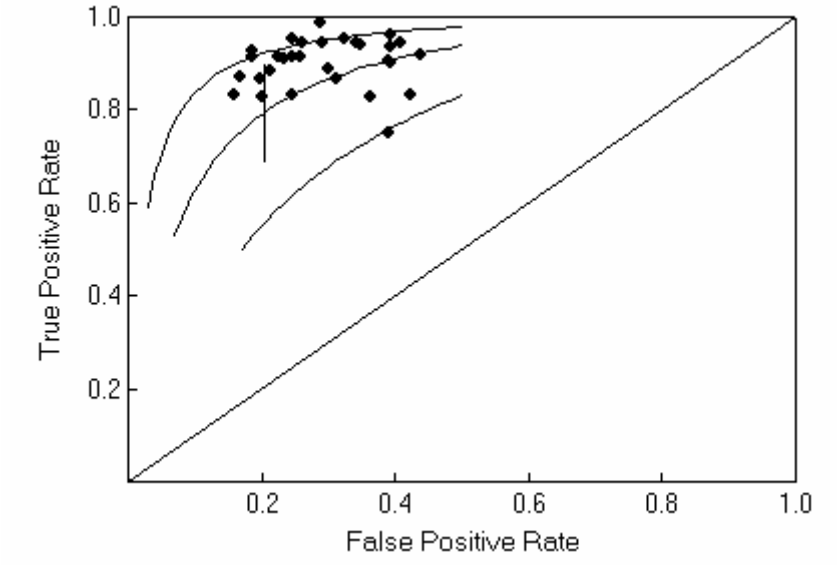


Figure 2. Summary ROC IgA-AGA–adults

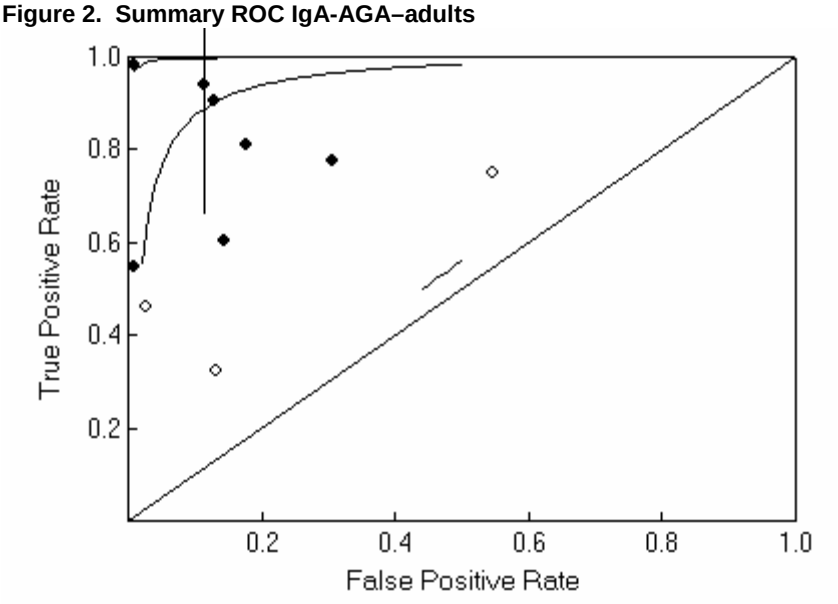


Figure 3. Summary ROC IgG-AGA–adults

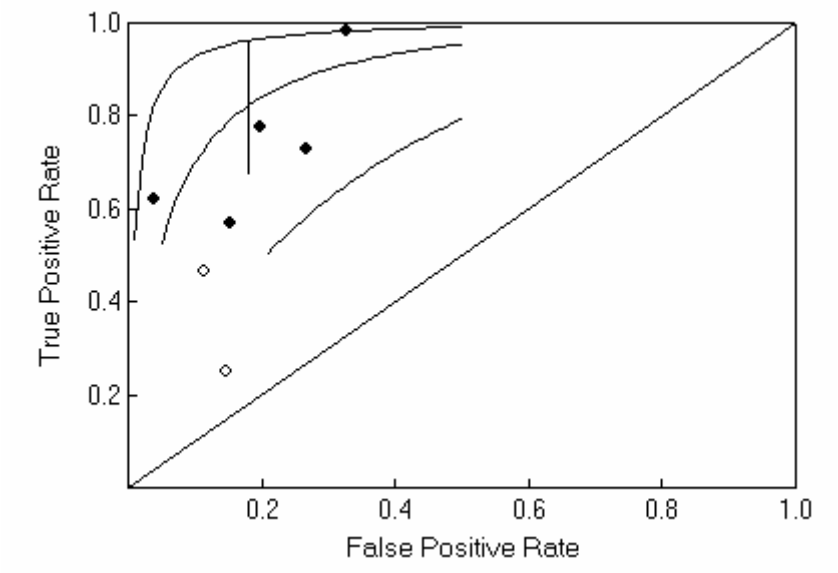


Figure 4. Summary ROC IgA-EMA-EM–adults

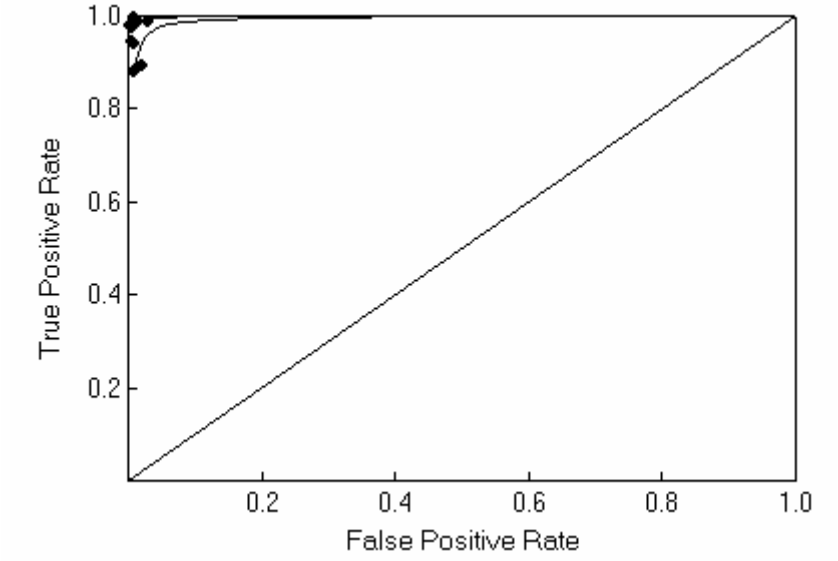


Figure 5. Summary ROC IgA-EMA-HU–adults

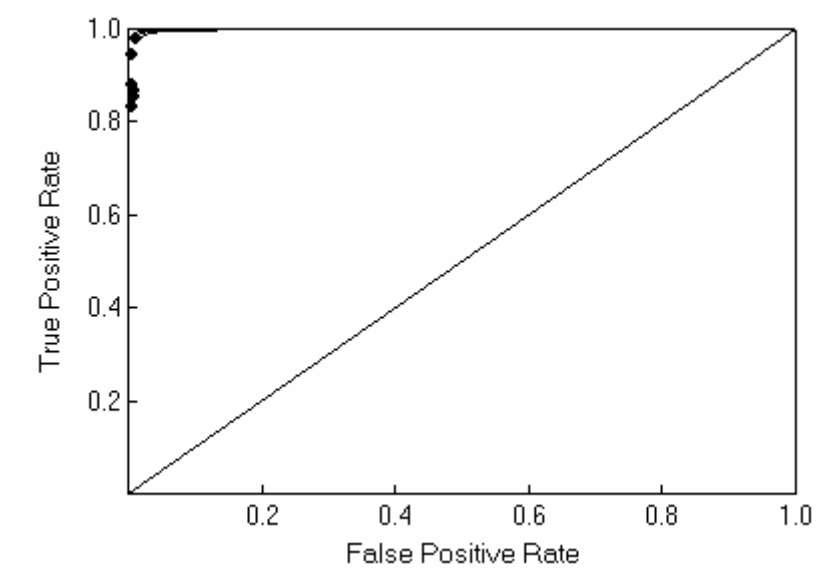


Figure 6. Summary ROC IgA-tTG-GP–adults

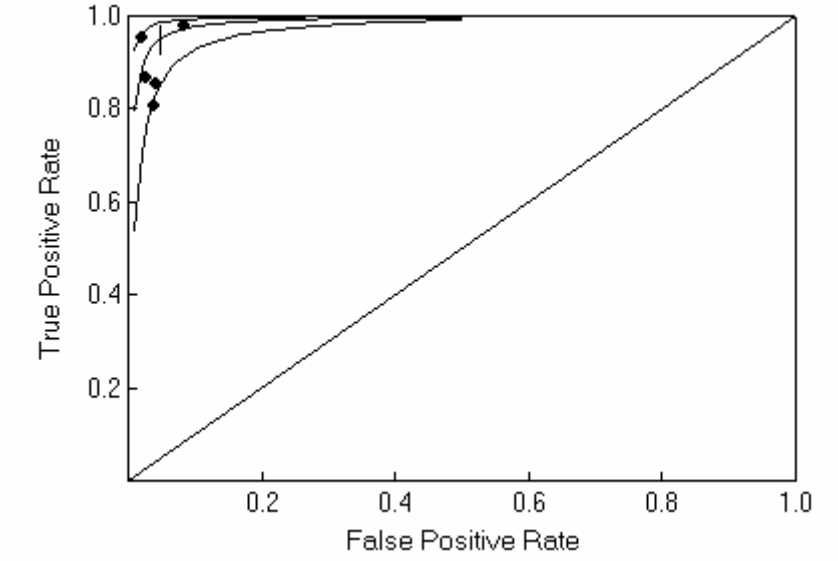


Figure 7. Summary ROC IgA-tTG-HR–adults

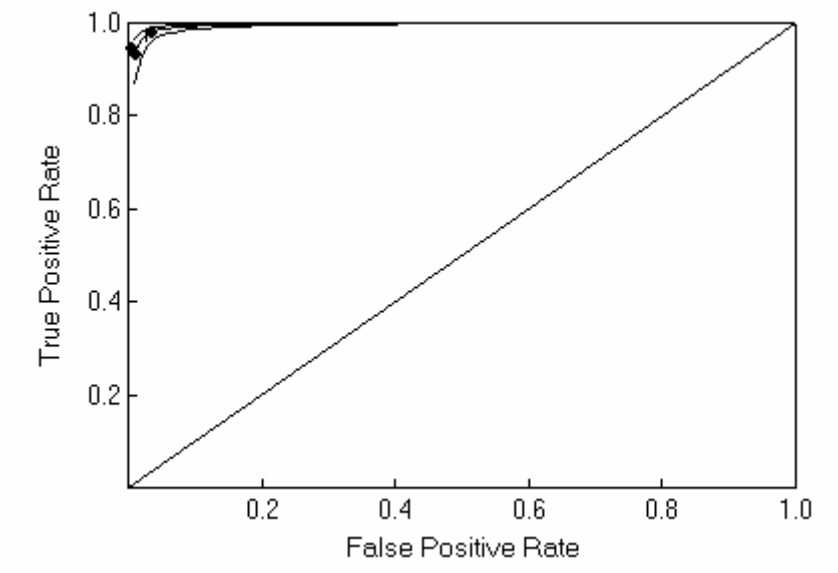


Figure 8. Summary ROC IgA-AGA–child

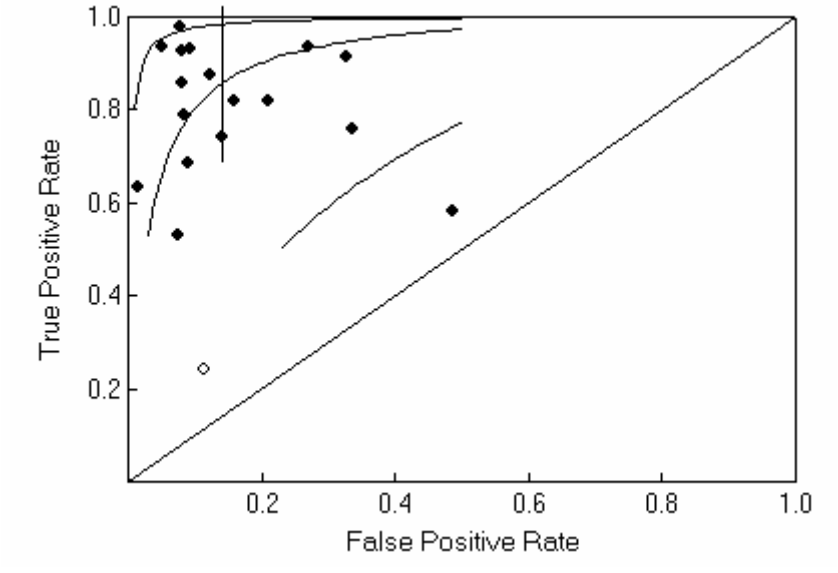


Figure 9. Summary ROC IgG-AGA–child

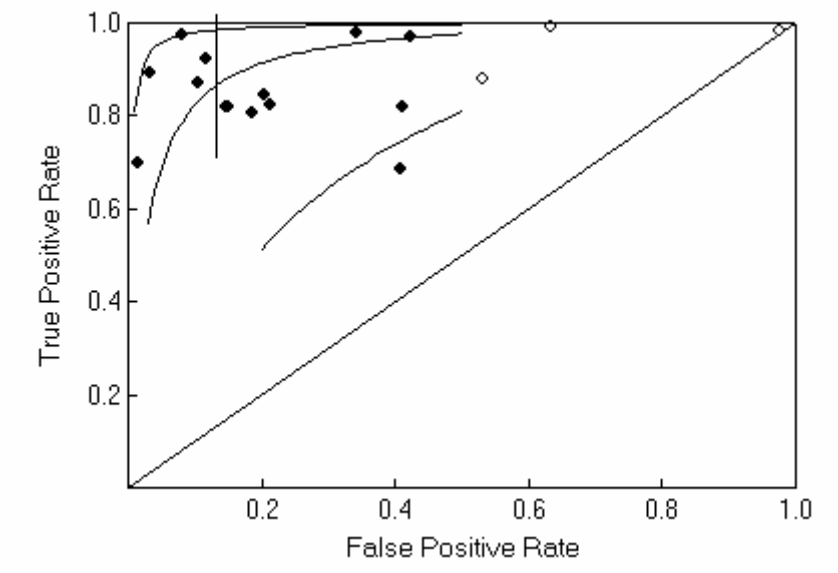


Figure 10. Summary ROC IgA-EMA-ME–child

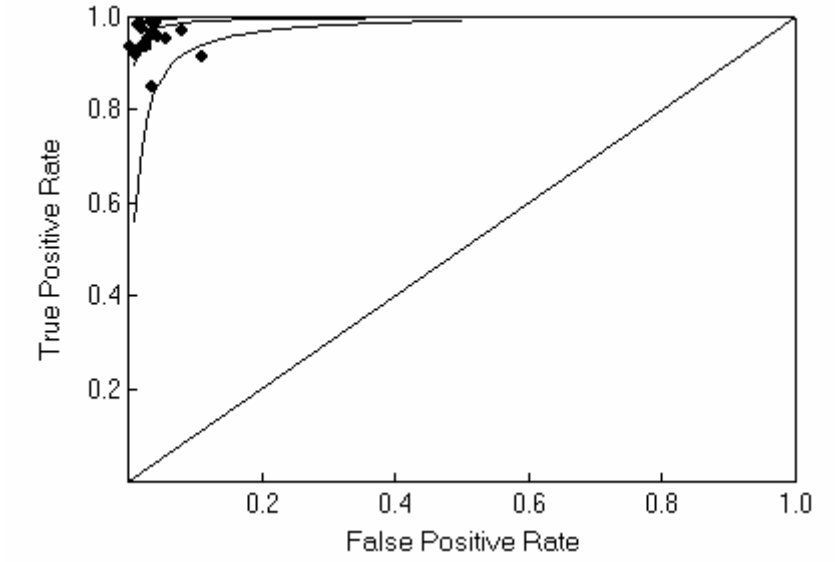


Figure 11. Summary ROC IgA-EMA-HU–child

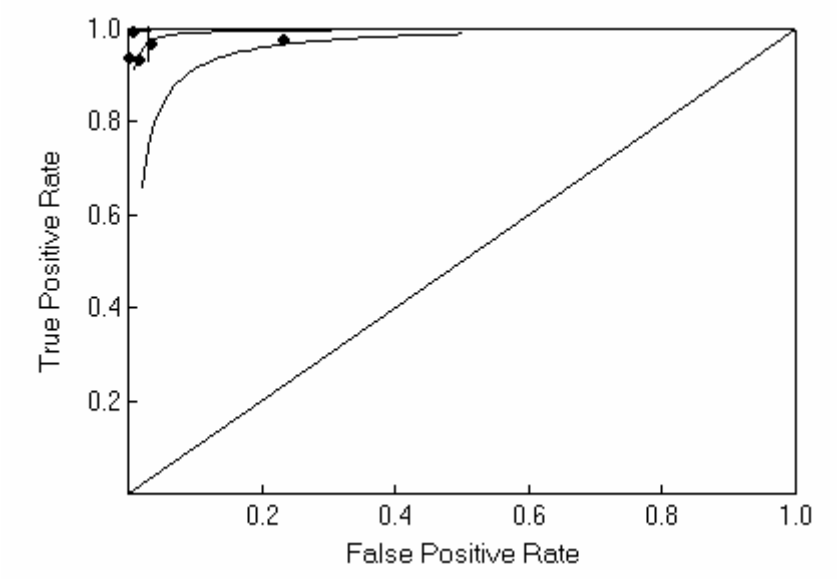


Figure 12. Summary ROC IgA-tTG-GP–child

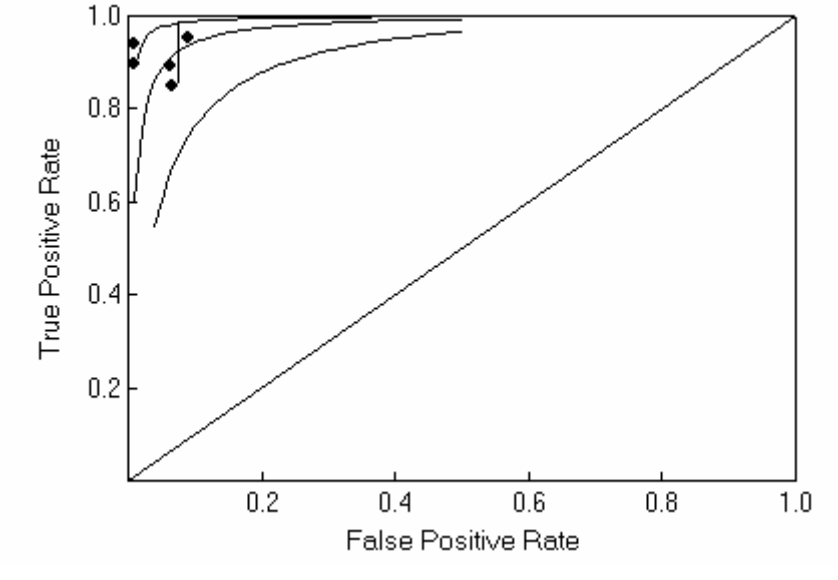


Figure 13. Summary ROC IgA-tTG-HR–child

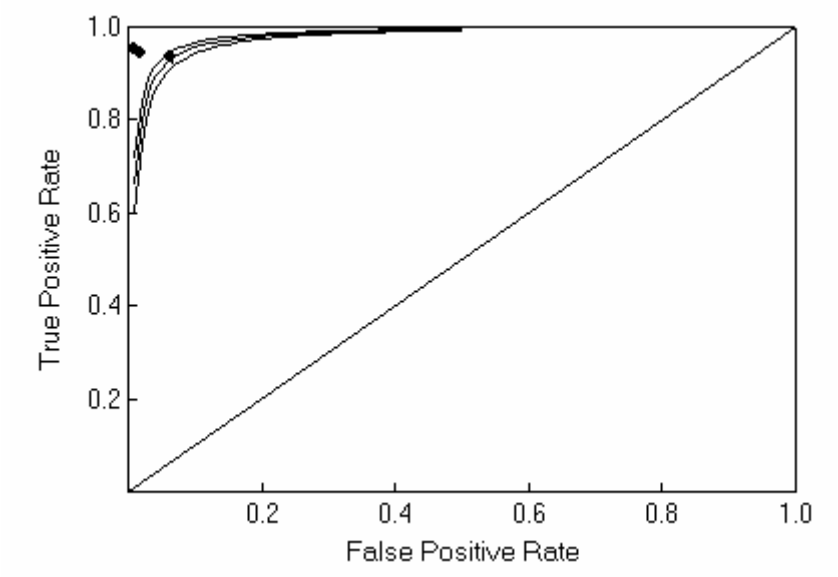


Figure 14. Summary ROC IgA-AGA–mixed-age populations

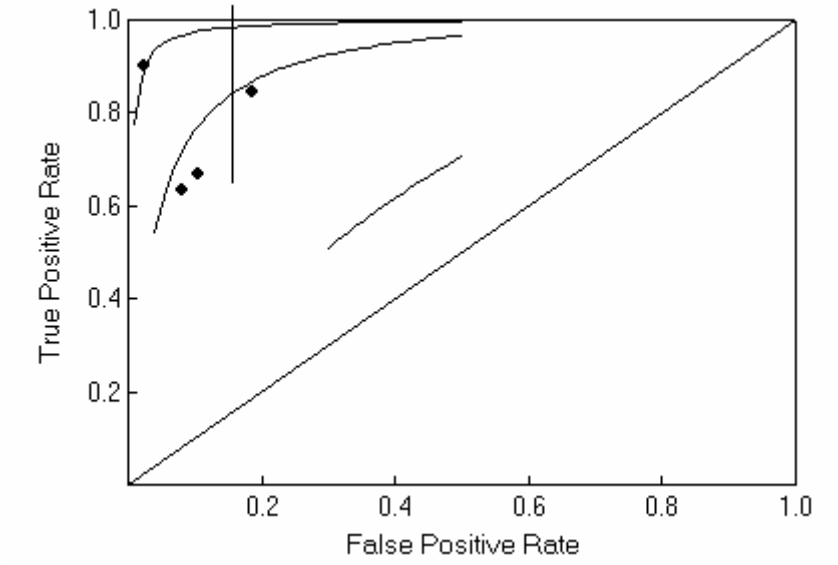


Figure 15. Summary ROC IgG-AGA–mixed-age populations

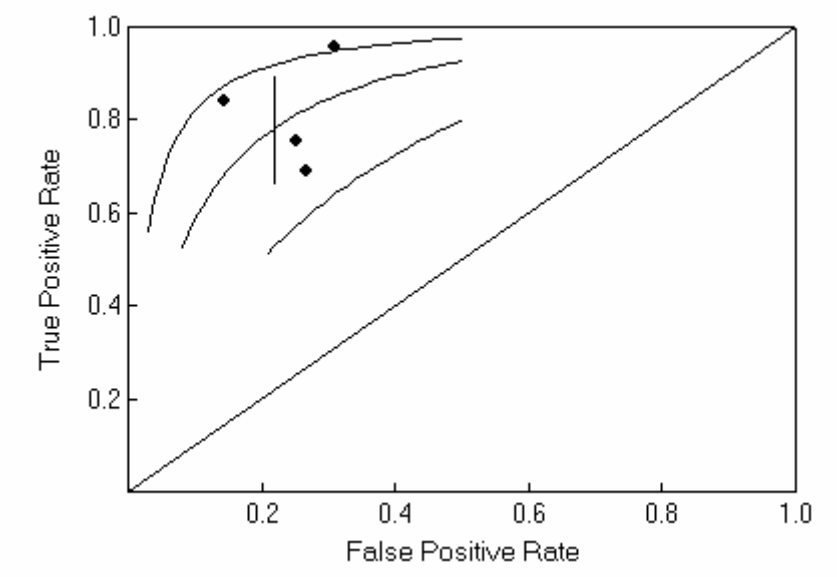


Figure 16. Summary ROC IgA-EMA-ME–mixed-age populations

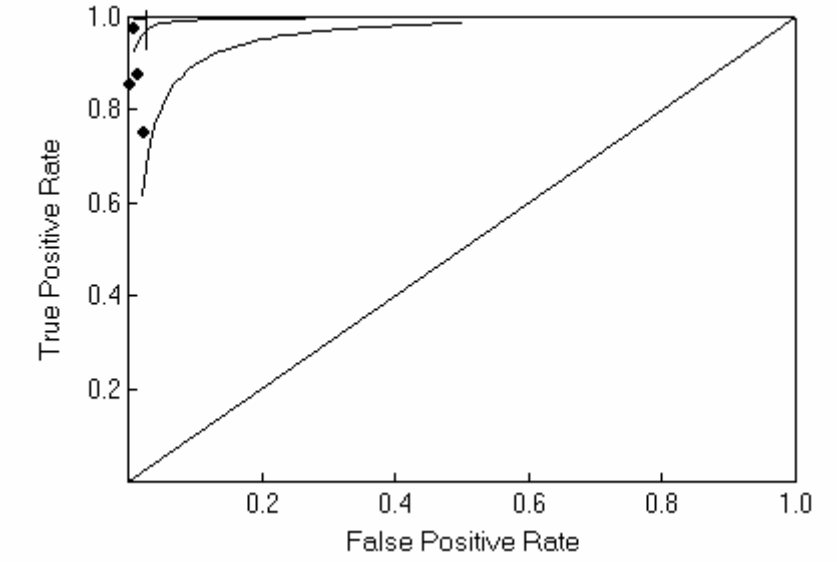
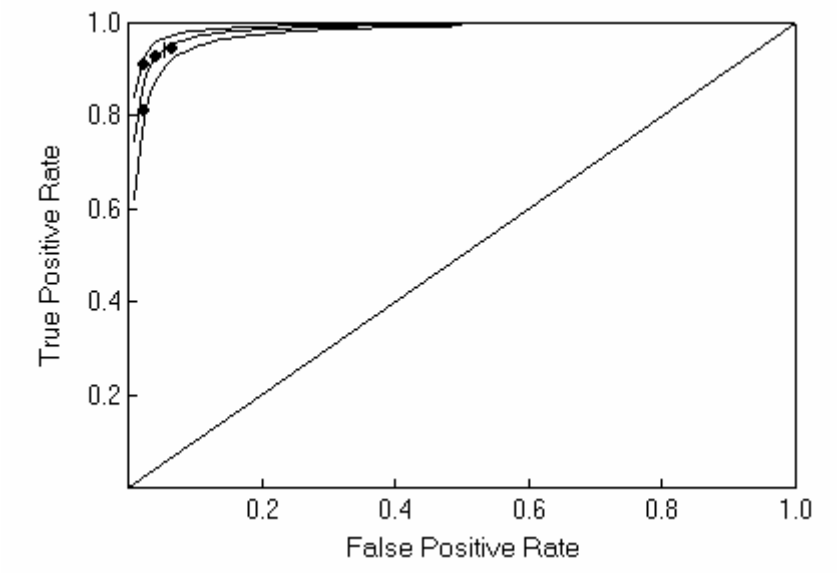


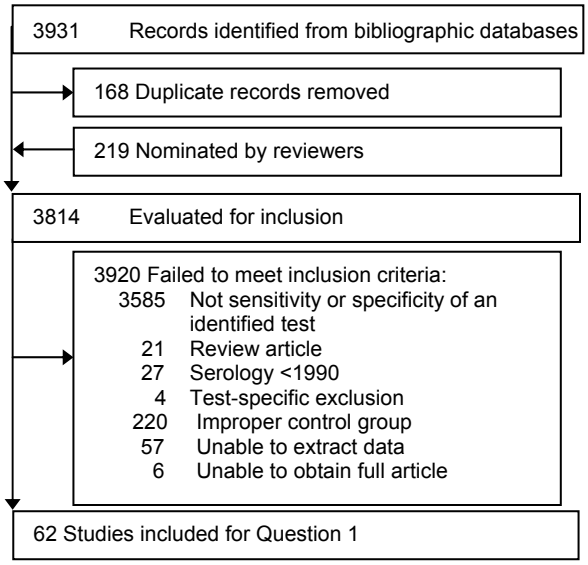
Figure 17. Summary ROC IgA-tTG-GP–mixed-age populations



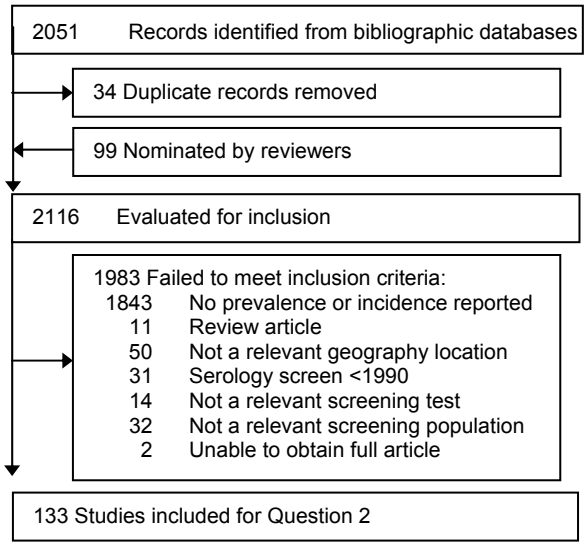
Appendix F. Modified QUOROM Flow Chart

Modified QUOROM Flow Charts

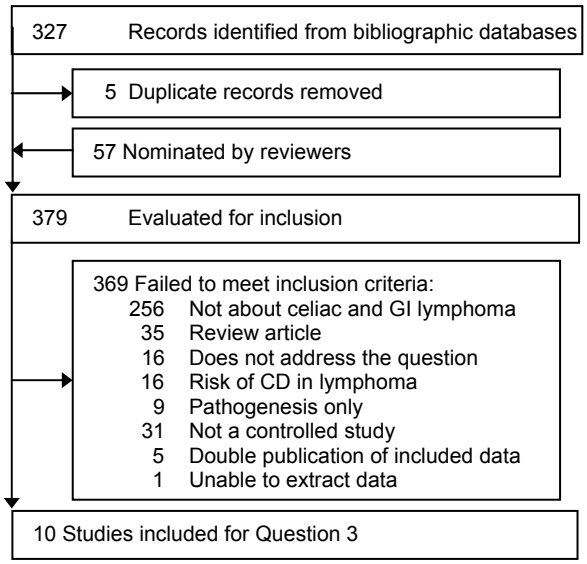
Objective 1 – Sensitivity and Specificity of Tests for CD



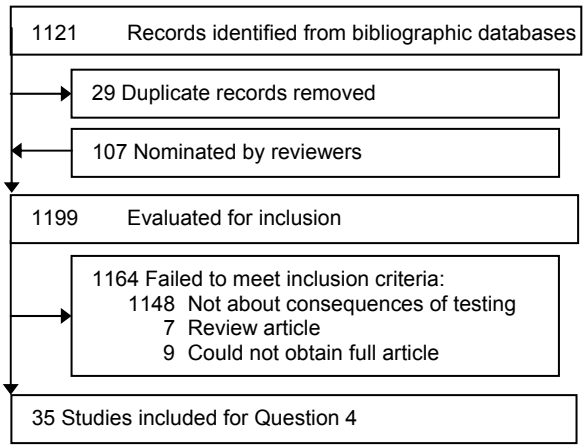
Objective 2 – Prevalence and Incidence of CD



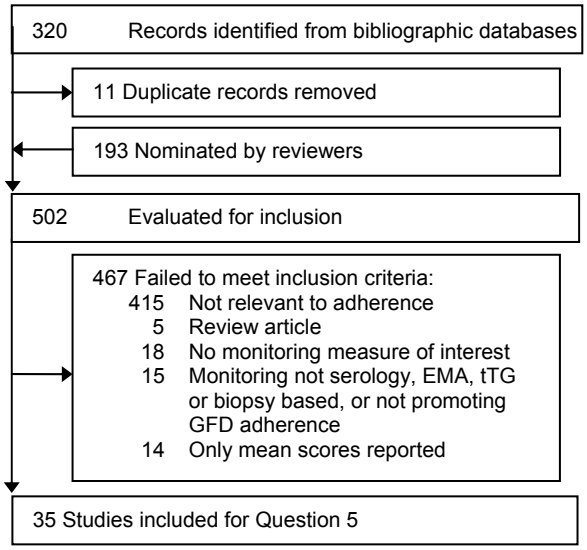
Objective 3 – Celiac Associated Lymphoma



Objective 4 – Expected Consequences of Testing for CD



Objective 5 – Promoting or Monitoring Adherence to a GFD



Appendix G. Raw Pooled Data

All raw pooled data by antibody test and study types showing number of studies and total patient numbers.

AGA - ELISA														
Population	Pooled Number		IgA					Pooled Number		IgG				
	Studies	Patients	Sens	Spec	PPV	NPV	Prev	Studies	Patients	Sens	Spec	PPV	NPV	Prev
Case Control														
Adults	2	336	57.9	92.6	93.2	55.7	0.40	1	157	78.0	80.7	87.6	67.6	56.7
Children	5	412	76.6	79.9	81.1	75.2	0.5	5	412	84.4	60.3	70.5	77.5	0.5
Both	1	343	84.6	81.6	75.2	88.9	0.4	1	343	69.1	73.4	63.1	78.4	0.4
Relevant CP														
Adults	8	946	71.0	81.1	61.7	86.8	0.35	6	652	65.6	85.7	70.7	82.7	31.9
Children	14	1382	80.1	89.9	78.7	90.7	0.3	12	1189	89.3	83.6	68.1	95.2	0.3
Both	3	737	68.2	92.7	91.5	71.5	0.5	3	737	83.8	79.5	82.6	80.9	0.5

EMA – Monkey Esophagus IF														
Study Population	Pooled Number		IgA					Pooled Number		IgG				
	Studies	Patients	Sens	Spec	PPV	NPV	Prev	Studies	Patients	Sens	Spec	PPV	NPV	Prev
Case Control														
Adults	6	706	97.3	100.0	100.0	97.1	50.7	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Children	12	1038	96.5	98.7	98.6	96.6	0.5	1*	153	100	100	100	100	0.1
Both	1	131	75.3	98.3	98.2	76.0	0.6	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Relevant CP														
Adults	5	692	95.0	99.4	98.1	98.5	22.4	1	89	39.3	98.4	91.7	77.9	0.14
Children	6	868	93.2	95.4	88.3	97.4	0.3	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Both	3	737	87.9	99.7	99.7	87.6	0.5	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Note: *this study was conducted in CD patients known to be IgA-EMA negative, and 50% had IgA deficiency														

EMA – Human Umbilical Cord - IF														
Population	Pooled Number		IgA					Pooled Number		IgG				
	Studies	Patients	Sens	Spec	PPV	NPV	Prev	Studies	Patients	Sens	Spec	PPV	NPV	Prev
Case Control														
Adults	5	578	90.3	100.0	100.0	93.7	37.2	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Children	4	375	96.6	100.0	100.0	97.1	0.5	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Both	2	428	92.5	99.6	99.5	93.8	0.5	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Relevant CP														
Adults	1	92	87.5	100.0	100.0	98.8	7.6	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Children	2	172	70.5	86.7	64.6	89.5	0.3	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Both	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a

tTG - Guinea Pig Liver - ELISA														
Population	Pooled Number		IgA					Pooled Number		IgG				
	Studies	Patients	Sens	Spec	PPV	NPV	Prev	Studies	Patients	Sens	Spec	PPV	NPV	Prev
Case Control														
Adults	3	368	83.4	97.1	97.0	84.2	45.1	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Children	3	270	92.3	99.2	99.2	92.0	0.5	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Both	3	559	91.2	94.7	94.3	91.8	0.5	1	85	61.5	100.0	100.0	44.4	0.8
Relevant CP														
Adults	2	327	100.0	94.2	66.7	100.0	15.6	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Children	2	176	95.1	93.0	87.9	97.3	0.3	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Both	1	111	91.7	98.4	97.8	93.9	0.4	1	111	22.9	98.4	91.7	62.6	0.4

tTG – Human Recombinant - ELISA														
Population	Pooled Number		IgA					Pooled Number		IgG				
	Studies	Patients	Sens	Spec	PPV	NPV	Prev	Studies	Patients	Sens	Spec	PPV	NPV	Prev
Case Control														
Adults	1	63	95.2	100.0	100.0	97.7	31.7	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Children	2	115	95.3	98.0	98.4	94.3	0.6	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Both	1	85	90.8	100.0	100.0	76.9	0.8	1	85	67.7	100.0	100.0	48.8	0.8
Relevant CP														
Adults	2	299	100.0	97.8	84.2	100.0	12.7	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Children	1	101	96.2	100.0	100.0	96.1	0.5	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Both	1	426	90.0	94.9	96.2	87.0	0.6	n/a	n/a	n/a	n/a	n/a	n/a	n/a

Appendix H. Biopsy Results

Relationship of Serology to Histology

CD clearly exists in patients with histological grades milder than Marsh IIIa, and given that the sensitivity of biopsy is improved by using a lower grade as a cut-off, an important question arises—what test is most sensitive for detecting CD with mild histologic changes, biopsy or serology?

Fasano,[1] in a large American prevalence study of CD in at risk and not at risk populations, found that only 34% of biopsied EMA-positive subjects had subtotal or total VA (modified Marsh IIIb or IIIc). In this study, no EMA-positive patient had a Marsh 1 lesion, 26% of EMA-positive patients had a Marsh II lesion, and 40% had a Marsh IIIa lesion. All newly-diagnosed, EMA-positive CD patients with (n=98) or without (n=114) biopsy had HLA DQ2, DQ8 or both, as apposed to 59% of EMA-negative subjects (n=92). The results of this study once again suggest that applying a criterion of subtotal or total VA would miss 66% of CD patients. The absence of Marsh I lesions in EMA-screened subjects is not surprising (discussed below), given the lower sensitivity of this test in lower-grade histologic lesions of CD, suggesting that the CD may have been unrecognized in some EMA-negative subjects. Unfortunately, HLA was not evaluated in all subjects and assessment of the correlation with serology in the population at large or systematically with biopsy grade was not reported.

Rostami et al.[2] evaluated the diagnostic value of IgA EMA and AGA in 101 untreated CD patients. The diagnosis of CD was made on the basis of "appropriate histopathological features" (Marsh IIIa or greater) and clinical improvement on a gluten-free diet (GFD). Sixteen first-degree relatives with minor histologic abnormalities (Marsh I-II) were used as controls. Sixteen patients were excluded for not meeting diagnostic criteria, IgA deficiency, or undergoing serology while on GFD.

Rostami et al.[2]	Marsh I-II (controls)	Marsh IIIa	Marsh IIIb	Marsh IIIc
Biopsy	16	29 (%)	23 (%)	17 (%)
AGA	3 (21%)	9 (31%)	16 (70%)	14 (82%)
EMA	0	9 (31%)	16 (70%)	17 (100%)

The combination of the two tests showed an overall sensitivity of 76%. Unfortunately, the authors, as is commonly done, considered Marsh I-II as controls; it is unclear if any of these, particularly those who were AGA positive, actually have CD. As will be described below, there is a subset of patients with Marsh I-II who are serology negative who have CD. In any case, this study demonstrates an important finding, i.e., that the sensitivity of the studied serological markers varies with the severity of the histologic grade. Alarmingly, the sensitivity even for CD patients with Marsh IIIa lesions is close to 30%. This is partially at odds with the results of the Fasano study[1] where only 34% of the identified patients were found to have Marsh IIIb or greater

grade lesions, with the rest having grade II to IIIa lesions. In both studies, no EMA-positive Marsh I lesions were found. The Fasano study, being a population-based screening study, obviously did not biopsy all screened patients. This begs the question of how many grade IIIb or less patients with CD were missed based on the findings of Rostami and Tursi (detailed below).

Tursi et al.[3] assessed the relationship of the histologic grade of 119 consecutive adult patients with CD defined by characteristic duodenal biopsy and "permanent gluten-sensitive enteropathy." The following table summarizes the main findings.

Tursi et al.[3]	Marsh I	Marsh II	Marsh IIIa	Marsh IIIb	Marsh IIIc
Biopsy	13 (11%)	24 (20%)	27 (23%)	31 (26%)	24 (20%)
tTG positive	1 (8%)	8 (33%)	15 (56%)	26 (84%)	23 (96%)
Mean tTG level UA/mL	7.3	18.5	n/a	36	74.95

In this study, 69% of CD patients had VA (Marsh IIIa or greater). The frequency of tTG-positivity (sensitivity) and mean tTG levels were greatest with the highest Marsh grade and dropped steadily with milder histologic grades, reaching a low of only 8%-positivity in CD patients with Marsh I lesions. Since these patients all have "permanent gluten-sensitive enteropathy," it is clear that tTG would have missed 76% of this cohort of CD patients with Marsh I or II lesions who were picked up by biopsy.

Tursi et al.,[4] also assessed 123 adult patients (possibly the same patients cohort from the above study) with either subclinical (equivalent to atypical in this review) or silent CD. All patients were biopsied and CD was diagnosed on the basis of "permanent-gluten sensitive enteropathy", and histology was classified with the modified Marsh criteria. The subclinical group included patients with associated CD conditions such as iron deficiency but without GI symptoms, while silent CD patients were asymptomatic patients screened in at risk groups such as first-degree relatives or type 1 diabetes. EMA was positive in 77/96 (80.8%) of subclinical CD cases and 17/27 (63.0%) of silent CD cases. EMA was negative in patients with Marsh I lesions. Once again, assuming that all these patients with "permanent gluten-sensitive enteropathy" are truly CD patients, then EMA would miss 19% of subclinical CD patients, and 37% of silent CD that were picked-up by biopsy.

In what appears to be a partial duplicate publication, Tursi et al.[5] demonstrated similar results with AGA, and EMA in 115 patients with subclinical or silent CD.

Patients with subclinical CD

Tursi et al[5]	Marsh I	Marsh II	Marsh IIIa	Marsh IIIb	Marsh IIIc
Biopsy	2	10	18	25	30
AGA pos.	0	3 (30%)	14 (77%)	21 (84%)	27 (90%)
EMA pos	0	4 (40%)	16 (88.9%)	23 (92%)	29 (96.7%)

Patients with silent CD

Tursi et al[5]	Marsh I	Marsh II	Marsh IIIa	Marsh IIIb	Marsh IIIc
Biopsy	2	2	5	6	9
AGA pos.	0	0	3 (60%)	4 (66.7%)	7 (77.8%)
EMA pos	0	0	4 (80.0%)	5 (83.3%)	8 (88.9%)

As before, in this group of CD patients, serology would miss patients that would be picked up by biopsy.

Demir et al.[6] (Celiac 4) studied the presentation and clinical features of 104 newly diagnosed Turkish children. EMA and biopsy correlation was available for 72 children. Similar to what was described above, EMA was positive in 92% of children with Marsh III compared with 66.6% of children with Marsh I-II.

Kotze et al.[7,8] assessed 47 symptomatic subjects with CD with intestinal biopsy, tTG and EMA antibodies. Forty were suspected of having CD (9 were children) and the investigations were performed together, while seven were biopsy-diagnosed CD who were already on a GFD. Both EMA and tTG antibodies were negative in these seven patients. The findings of the 40 suspected CD patients are presented in the following table.

Kotze et al[7,8]							
Normal biopsy	7	8	2		1 (child)		
Partial VA			1		1		
Total VA			1	3	7	8 (child)	8
Mean tTG titer	8.14	11.87	41.5	181.7	356.3	307.4	432.8
Mean EMA titer	neg	1/2.5	1/5	1/10	1/20	1/40	1/80
Notes: Titers of EMA and tTg antibodies of 1/2.5 and 20 U, respectively VA= VA							

The authors used an older histology grading system, and did not systematically report on the overall number of "normal biopsies" with raised IELs. They also did not report on the number of subjects with the Marsh II hyperplastic lesion, nor did they distinguish between Marsh IIIa and IIIb (lumped as "partial VA"). Nonetheless, the authors report that in the eight subjects with positive-EMA antibodies (>1/2.5) yet negative for tTG antibodies (<20), the mucosa showed normal villous structure but raised levels of IELs. These eight subjects responded to a GFD and were considered to have CD. The correlation between the two serological tests was high (Pearson's Chi square [the large R is 'accountable' variance]; r=0.797). However, the same finding as in the previous studies is repeated again. CD occurred in eight patients with negative tTG antibodies, and the titres of both EMA and tTG antibodies correlated with histologic grade, once again suggesting that serology alone would miss CD patients who would be picked-up by biopsy. This is a very recent study and it would shed a great deal of light on the false-positive and negative-rate of biopsy if the authors would publish a follow-up study on: (1) the status of the three subjects who were positive for EMA and tTG antibodies yet had "normal" biopsies (IEL status not reported); (2) the seven subjects who were negative for all tests; and (3) the histologic and clinical response to GFD in those who were diagnosed with CD.

Hoffenberg et al.[9] studied a group of children at risk of CD who were part of a large prospective study of the genetic and environmental factors associated with autoimmune diseases. For the CD portion, newborns were screened for the presence of HLA DR3/3, DR3/4, or DR3/x as markers for DQ2. In another group, at risk children with type I diabetes, first-degree relatives of type 1 diabetics, and first-degree relatives of CD patients, were studied. Thirty anti-tTG positive subjects among these screened patients were enrolled in the study (14 diabetics, 11 first-degree relatives, and five HLA DR3). All 30 children underwent Marsh biopsy grading. No relationship was found between Marsh grade and the genetic risk factor leading to screening. A significant correlation was found between Marsh grade and anti-tTG (r=0.57, p<0.01). The calculated mean anti-tTG titers are presented in parentheses in the table below.

Biopsy results of 30 tTG-positive children

Hoffenberg et al[9]	Marsh 0	Marsh I	Marsh II	Marsh III
Biopsy	5 (16.7%)	4 (13.3%)	2 (6.7%)	19 (63%)
Mean tTG level UA/mL	< 0.6	< 0.6	< 0.6	> 0.6 (0.70)

Unlike the other studies presented in this series, this study selected patients at risk of CD who were anti-tTG positive. Unfortunately, this makes direct comparisons difficult, but in essence this study supports the notion of a greater sensitivity of tTG in high-grade histologic lesions through the finding that high-grade lesions are associated with higher anti-tTG titres.

In a small case control study assessing the diagnostic value of EMA, Sategna-Guidetti,[10] also found that in patients with documented CD, EMA positivity correlated with the severity of the histologic grade. In this study, EMA was falsely negative in 50% of CD patients without VA.

Other Histological Features

Several other histological features have been studied in an attempt to improve the accuracy of biopsy in the diagnosis of CD. Some of these features include: assessment of small bowel mucosal mast cells,[11-14] mucosal fat,[15] and endocrine cell hyperplasia.[16] Discussion of these features is beyond the scope of this review.

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Appendix I. Evidence Tables

List of abbreviations used in the evidence tables

Ab=antibody	n=number of patients
AGA=anti-gliadin antibodies	n/a=not applicable
ARA=antireticulin antibodies	NHL=non-Hodgkin's lymphoma
Bx=biopsy	n/r=not reported
CD=celiac disease	OR=odds ratio
CI=confidence interval	pt=patient
CO=control	RR=relative risk
Dx=diagnosis	SD=standard deviation
EGD=esophagogastroduodenoscopy	TGA=anti-thyroglobulin
EIA=enzyme immunoassay	tTG=anti-tissue transglutaminase
EMA=anti-endomysium antibodies	UTCD=untreated celiac disease
F=female	VA=villous atrophy
GC=gluten challenge	y=year
GCD=gluten-containing diet	
GERD=gastroesophageal reflux disease	
GFD=gluten-free diet	
GI=gastrointestinal	
GP=guinea pig	
Hb-hemoglobin	
HLA=human leukocyte antigens	
HU=human umbilical cord	
HUVEC= human umbilical vein endothelial cells	
JAB=human jejunal antibodies	
IBS=irritable bowel syndrome	
IDA=iron deficiency anemia	
IDDM=insulin-dependent diabetes mellitus	
IF=immunofluorescence	
M=male	
ME=monkey esophagus	
mos=months	

Celiac 1: Sensitivity and Specificity of Tests for CD

Serology

Evidence Table 1: Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Altuntas, 1998 Turkey	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** • endoscopic biopsy **First test:** • serology test **Controls biopsied:** • yes **Biopsy criteria:** • subtotal or total VA, crypt hyperplasia, increased IEL **Checked IgA def.** • n/r **Studied tests** • IgA-AGA • IgG-AGA **Methodology:** • ELISA **Cut-off:** • levels between 25 and 50 RU/mL were accepted as weakly positive and levels >50 RU/mL as strongly positive	**Celiac Group 1** • 26 short-statured children with probable CD on biopsy • mean age: n/r • % F: n/r	**Group 1:** • 21 short-statured children without CD on biopsy; • median age: n/r • % F: n/r	**celiac 1 vs control 1** IgA AGA	6	20	2	19	23	90	75	48
				celiac 1 vs control 1 IgG AGA	26	0	21	0	100	0	55	0

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Artan, 1998, Turkey	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** • biopsy **First test:** • simultaneous **Controls biopsied:** • yes **Biopsy criteria:** • ESPGAN **Checked IgA def.** • n/r **Studied tests** IgA-AGA; IgG-AGA; IgA and IgG; IgA or IgG **Methodology:** • ELISA **Cut-off:** • >25 arbitrary units (did not adjust for age)	**Celiac Group 1** • 24 children with CD by ESPGAN, out of 63 suspected CD pts • age: n/r • % F: n/r	**Group 1:** • 39 of 63 with normal intestinal villous structure. • Age: n/r • % F: n/r	celiac 1 vs control 1-IgA-AGA celiac 1 vs control 1-IgG-AGA IgA AND IgG IgA OR IgG	14 20 12 20	10 4 12 4	19 16; 13; 25;	20; 23 26 14	58 83 50 83	51 59 67 36	42.4 55.6 48 44	66.7 85.2 68.4 77.8

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Ascher, 1996 Sweden	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** • n/r **First test:** • biopsy and serum tests obtained simultaneously **Controls biopsied:** • yes **Biopsy criteria:** • ESPGAN **Checked IgA def.** • Yes **Studied tests** • EIA IgA; EIA IgG; DIG-ELISA IgA; DIG-ELISA IgG; ARA; Human JAB; Rat JAB; EMA **Methodology:** for EIA IgA and IgG: ELISA; for ARA: IF; for EMA, JAB: immunohistochemical method **Cut-off:** EIA IgA and IgG: 35 AU (arbitrary units) for children <5 y; and 20 AU for children >5 y; DIG-ELISA: IgA values >13 mm and IgG values >16 mm were considered positive in children <5 y; IgA values <11 mm and IgG values >14 mm - in children >5 y	**Celiac Group 1** • 55 pts with biopsy proven CD • mean age: n/r; <5 y n=22; >5 y n=33 • % female: n/r **Celiac Group 2** • 36 out of initial 55 pts who were treated with GFD of 1 y; • mean age: n/r; <5 y n=21; >5 y n=15 • % female: n/r **Celiac Group 3** • 21 pts on a gluten-challenge diet of 3-6 mos • mean age: n/r; <5 y n=18; >5 y n=3; • % female: n/r NB: group 2: biopsy proven CD on a GFD of > 1 y; group 3: biopsy proven CD on a gluten challenge of 3-6 mos duration	**Group 1:** • 65 disease controls with biopsy proven normal intestinal mucosa; • mean age: n/r; <5 y n=18; >5 y n=47 • % female: n/r	group 1 vs control, EIA IgA	50	5	1	64	90.9	98.5		
				group 1 vs control, EIA IgG	53	2	20	45	96.4	69.2		
				group 1 vs control, DIG-ELISA IgA	50	5	2	63	90.9	96.9		
				group 1 vs control, DIS-ELISA IgA	48	7	9	56	87.3	86.2		
				group 1 vs control ARA	48	6	18	47	88.9	72.3		
				group 1 vs control, Human JAB	55	0	18	47	100	72.3		
				group 1 vs control, RAT JAB	55	0	11	54	100	83.1		
				group 1 vs control, EMA	54	1	0	65	98.2	100		
				group 3 vs control, EIA IgA	20	1	1	64	95.5	98.5		
				group 3 vs control, EIA IgG	19	2	20	45	90.5	69.2		
				group 3 vs control, DIG-ELISA IgA	17	4	2	63	80.9	96.9		
				group 3 vs control, DIS-ELISA IgA	15	5	9	56	75	86.1		
				group 3 vs control, ARA	18	3	18	47	85.7	72.3		
				group 3 vs control, Human JAB	21	0	18	47	100	72.3		
				group 3 vs control, RAT JAB	18	3	11	54	85.7	83		
				group 3 vs control, EMA	19	2	0	65	90.5	100		

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Ascher, 1990 Sweden	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** • Watson capsule **First test:** • biopsy and serum tests obtained simultaneously **Controls biopsied:** • yes **Biopsy criteria:** ESPGAN **Checked IgA def.** Yes **Studied tests** • Pharmacia Gluten IgA-AGA measured by enzyme immunoassay (PG IgA-EIA) **Methodology:** • ELISA **Cut-off:** • 35 AU (arbitrary units)	**Celiac Group 1** • 36 pts with CD out of 130 consecutive group of children who had a small intestinal biopsy due to symptoms suggestive of CD; out of 36 pts with CD, 28 have been verified according to ESPGAN criteria; • mean age: n/r • % female: n/r **Celiac Group 2** • children with CD according to ESPGAN's criteria, differing with regard to gluten content of diet: first biopsy on a gluten-containing diet (n=29); at the second biopsy after 1 y on GFD (n=45); at the third biopsy after gluten-challenge (n=45); • mean age: n/r • % F: n/r **Celiac Group 3** • children with an initial abnormal mucosa that normalized on a GFD but did not relapse after gluten challenge during 3-31 mos • mean age: n/r • % F: n/r	**Group 1:** • 92 children taken from consecutive group of 130 children who did not have CD; 12 had other food intolerance, 1 had cystic fibrosis and 79 had no intestinal disorder	group 1 vs control PG IgA-EIA	35	1	7	85	97	92	83.3	98.8

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Bahia, 2001 Brazil	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/a **Population Type:** • suspected CD **Reference test:** • Carey capsule **First test:** • n/r **Controls biopsied:** • yes **Biopsy criteria:** • severe VA **Checked IgA def.** • n/r **Studied tests** • IgA and IgG-AGA **Methodology:** • ELISA **Cut-off:** • mean+2 SD for a group of 20 normal children: 0.022 for IgA (mean=0.0065, SD=0.0076); and 0.103 for IgG (mean=0.0393, SD=0.032)	**Celiac Group 1** • 22 pts with CD • age (mos): mean/SD: 30.6+/-28.8; • % F: 54.5 • median w/range: 19.3 (6.0-135.6) • % female: 54.5 **Celiac Group 2** • 61 pts with other enteropathies (OE); • age (mos): mean/SD: 43.3+-38.1; • median w/range: 27.9 (4.8-156.5); • % F: 59	**Group 1:** • 46 controls with biopsy-proven non-CD enteropathies (CO) • age (mos): mean/SD: 96.9+/-48.5; median w/range: 92.6 (12.2-170.8); • % F: 54.5	IgA group 1 vs CO IgA group 1 vs OE+CO IgG group 1 vs CO IgG group 1 vs OE+CO	21 21 20 20	1 1 2 2	2 9 1 12	46 98 45 95	95.5 95.5 90.9 90.9	95.6 91.6 97.8 88.7	when prevalence is 1:500 PPV for IgA is 4.8%; in prevalence of 1:1000 PPV=2.0; in prevalence of 1:2000, PPV=1.1	in any prevalence of CD NPV for IgA is 99.9%

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Bardela, 2001 Italy	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/a **Population Type:** • suspected CD **Reference test:** • endoscopic biopsy **First test:** • n/r **Controls biopsied:** • yes **Biopsy criteria:** • Marsh, no grade reported **Checked IgA def.** • Yes and excluded **Studied tests** • IgA-AGA; IgA-EMA; IgA-tTGA **Methodology:** • ELISA for AGA; ELISA for tTGA GP liver; IF for EMA ME **Cut-off:** • AGA: 12 AU/mL; tTGA: >10 AU/mL; EMA: antibody titre > 1:10	**Celiac Group 1** • 40 untreated biopsy-proven CD pts • age (y): mean 38, range 16-77 • % F: 72.5 **Celiac Group 2** • 195 treated CD pts; biopsy proven on GFD • age (y): mean 38, range 16-79 • % F: 70.2	**Group 1:** • 110 biopsy proven non-CD disease controls (CO): inflammatory bowel disease (n=22); IBS (n=29); peptic ulcer (n=7); diverticular disease (n=6); pancreatitis (n=5); non- ulcer dyspepsia(n=14); anemia not due to malabsorption (n=7); reflux esophagitis (n=3); atrophic gastritis (n=2); acute appendicitis (n=1) • age (y): mean 41, range 14-80 • % F: 75.7;	AGA group 1 vs CO EMA group 1 vs CO tTGA group 1 vs CO	38 40 40	2 0 0	12 3 2	98 107 108	95 100 100	89 97.2 98.2	when expected prevalence is 0.5%, PPV for AGA is 4.2%; for EMA - 15.7% and for tTGA - 21.8%; when expected prevalence of CD is 50%, PPV for AGA is 89.7%, for EMA - 97.4% and for tTGA - 98.2%	when expected prevalence is 0.5%, NPV for AGA is 99.9%; for EMA - 100% and for tTGA - 100%; when expected prevalence of CD is 50%, NPV for AGA is 94.7%, for EMA - 100% and for tTGA - 100%

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Berger, 1996 Switzerland	**Publication type:** • journal **Study design:** • case-control **Ethnicity:** • n/a **Population Type:** • suspected CD **Reference test:** • endoscopic biopsy **First test:** • n/r **Controls biopsied:** • yes **Biopsy criteria:** •ESPGAN revised with complete VA **Checked IgA def.** • n/r **Studied tests** •5 different AGA assays: Eurospital; Labodia; Pharmacia; FIST-IF; Granditsch; IgA EMA **Methodology:** • for AGA - ELISA; for EMA - IF **Cut-off:** For IgG Eurospital: index30-50; in Pharmacia units: 30-50 AU; Labodia: 30 U/mL; in Pharmacia units-18; Pharmacia: 20-100 AU; FIST: titer 1:20; in Pharmacia units-13 AU; Granditsch: 0.350 OD; in Pharmacia units: 70 AU; for IgA Eurospital: index 8-20; in Pharmacia units: 53-132 AU; Labodia: 15 U/mL; in Pharmacia units-28; Pharmacia: 20-35 AU; FIST: titer 1:20; in Pharmacia units-34 AU; Granditsch: 0.250 OD; in Pharmacia units: 38 AU	**Celiac Group 1** • 67 biopsy proven CD pts • age: n/r • % F: n/r	**Group 1 (CO):** •54 biopsy proven non-CD pts: transient GI problems (n=39), ulcerative colitis (n=2), Crohn's disease (n=8), duodenal ulcer (n=3), short stature (n=2) •age: n/r •% F: n/r	**CD vs CO**								
				Eurospital IgG	55	12	27	27	82	50	67	69
				FIST IgG	56	11	53	1	84	2	51	8
				Granditsch IgG	55	12	46	8	82	15	54	36
				Labodia IgG	61	6	42	12	91	22	59	57
				Pharmacia IgG	46	21	22	32	69	59	68	53
				Eurospital IgA	41	26	3	51	61	94	93	57
				FIST IgA	44	23	49	5	66	9	47	17
				Granditsch IgA	53	14	23	31	79	57	70	59
				Labodia IgA	58	9	35	19	87	35	62	58
				Pharmacia IgA;	51	16	18	36	76	67	74	59

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Biagi, 2001 Italy	**Publication type:** • journal **Study design:** • case-control **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** • Carey capsule **First test:** • n/r **Controls biopsied:** • yes **Biopsy criteria:** • partial VA or greater **Checked IgA def.** • Only in EMA (neg) pts in CD group **Studied tests** • IgA-tTG • IgA-EMA **Methodology:** • TTG-GP; EMA -ME **Cut-off:** • on the basis of ROC analysis performed on the preliminary results (group of 30 controls) results >0.65 OD (optical density) were considered positive; <0.35 OD - negative and 0.35-0.65 OD - borderline	**Celiac Group 1** • 56 pts with biopsy-proven CD • age (y): mean/SD: 39.2+-19.2; range 4-79 • % F: 76	**Group 1:** • 52 disease controls (biopsy-proven non-SD enteropathies) with irritable bowel disease (n=29); Crohn's disease (n=9); gastric lymphoma (n=7); Whipple disease (n=3); giardiasis (n=2); systemic mastocytosis (n=1); IgE-mediated food sensitivity • mean age (y): 40.4+-19.9; range 14-79; • % F:	IgA TTG group 1 vs CO when considering borderline results as positive	55	1	8	44	98.2	84.6	87.3	97.7
				IgA-tTG group 1 vs CO when considering borderline results as negative	49	7	1	51	87.5	98.1	98	87.9
				IgA EMA group 1 vs CO	53	3	0	52	94.6	100	100	94.5

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Bode, 1993 Denmark	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** • n/r **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** •typical biopsy and response to a GFD (likely ESPGAN) **Checked IgA def.** • yes **Studied tests** • serum IgG-AGA • serum IgA-AGA **Methodology:** •DIG-ELISA - diffusion in gel ELISA **Cut-off:** • 1) old limits: positive test for IgA AGA was defined as >10.5 mm and/or IgG level >14 mm; 2) new limits for children: for IgA >10 mm and for IgG >13 mm	**Celiac Group 1** • 14 of 233 consecutive children with untreated CD • median age for the 233: 2.75; range 0.33-15.5) • 117 males; 74 females **Celiac Group 2a** •T-CD - group 2a) 47 children with CD on GFD •age (y): median 11.83, range 1-17.92 •% F: 61.7 **Celiac Group 2b** • 14 children with known CD on gluten challenge	**Group 1:** • 177 children with non-CD diseases: postenteritis diarrhea (n=43), short stature (n=25), diarrhea (n=25), failure to thrive (n=22), food allergy (n=11), dissaccharide intolerance (n=8), dietary problems (n=8), giardiasis (n=4), ulcerative colitis (n=3), recurrent abdominal pain (3), constipation (n=2), recurrent infections (n=2), acute gastroenteritis (n=1), Crohn's disease (n=1), other GI diseases (n=4), other non-GI diseases (n=15) **Group 2:** • 8 children not CD/GFD and gluten challenge • age (y): median 2.5, range 1.17-7.5 • % F: 37.5	group 1 vs control 1, serum AGA-IgA; in brackets data according to new cut off					64 (79)	99 (98)	90 (79)	97 (98)
				group 1 vs control 1, serum AGA-IgG; in brackets data according to new cut off limits					71 (93)	99 (98)	100 (76)	98 (99)
				group 1 vs control 1, serum AGA-IgA/IgG; in brackets data according to new cut-off limits					86 (100)	99 (97)	92 (70)	99 (100)

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Bode, 1994 Denmark	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** • n/r **First test:** • n/r **Controls biopsied:** • yes **Biopsy criteria:** • Crypt hyperplasia, VA and increase inflammatory cells **Checked IgA def.** • n/r **Studied tests** • serum IgG-AGA • serum IgA-AGA **Methodology:** • DIG-ELISA - diffusion in gel ELISA **Cut-off:** • positive test for IgA AGA was >10.5 mm; for IgG - >14 mm; borderline levels for IgA was between 9.5 mm and 10.5 mm; and for IgG - between 13 mm and 14 mm	**Celiac Group 1** • 100 consecutive adult pts admitted for a small intestinal biopsy on suspicion of CD • age (y): median 51, range 17-81 • % F: 64; 13 CD pts **Celiac Group 2** • 118 adult pts with increased or borderline (gliadin antibodies) AGA • age (y): median 48, range 19-95 • % F: 72; • 55 children pts with increased or borderline (gliadin antibodies) AGA • age (y): median 4, range 7 mos-17 • % F: 56	**Group 1:** • 87 out of 100 suspected of CD who did not have CD by biopsy	group 1 IgA-AGA					46	98	75	92
				group 1 IgG-AGA					62	97	73	94
				group 1 IgA/IgG-AGA					77	95	71	97

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Bonamico, 2001 Italy	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** • biopsy **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** •ESPGAN (severe VA and crypt hyperplasia) **Checked IgA def.** • Yes **Studied tests** • tTG-HR (RIA) • tTG-GP (ELISA) • IF-EMA **Methodology:** • tTG-HR • tTG-GP • EMA-ME IF **Cut-off:** • RIA anti-tTG Ab ≥0.05 index as selected on ROC plot analysis; ELISA anti-tTG Ab ≥7 AU; IF-EMA - n/r (appearance of fluorescence)	**Celiac Group 1** • 62 pts; untreated with biopsy-proven celiac CD • median age 7, age range 1-23 • % F: n/r **Celiac Group 2** • 78 pts; GFD treated, at least 6 mos • median age, age range • % F: n/r **Celiac Group 3** • 14 pts; on gluten-challenge at least 3 mos • median age, age range • % F: n/r	**Group 1:** • 56 disease controls; chronic diarrhea, short stature, recurrent abdominal pain; age and sex-matched controls • median age, age range • % F: n/r	RIA group 1 vs control	62	0	0	56	100	100	100	100
				RIA group 2 vs control	34	44	0	56	43.5	100	100	56
				RIA group 3 vs control	14	0	0	14	100	100	100	100
				ELISA group 1 vs control	56	6	0	56	90.3	100	100	90.3
				ELISA group 2 vs control	7	71	0	56	9.8	100	100	44
				ELISA group 3 vs control	11	3	0	56	78.5	100	100	94.9
				IF-EMA group 1 vs control	59	3	1	55	95.1	98.2	98.3	94.8
				IF-EMA group 2 vs control	9	69	1	55	11.5	98.2	90	44.3
				IF-EMA group 3 vs control	13	1	1	55	92.8	98.2	92.8	98.2

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Bottaro, 1997 Italy	**Publication type:** • journal **Study design:** • case-control **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** • n/r **First test:** • n/r **Controls biopsied:** • yes **Biopsy criteria:** •ESPGAN **Checked IgA def.** • Yes **Studied tests** serum AGA-IgG serum AGA-IgA serum EMA-IgA serum ARA-IgA **Methodology:** •for AGA ELISA; for AGA-IgA IF; for EMA-IgA IF using ME or HU **Cut-off:** • AGA: for IgA 10% and for IgG 25%, resulting the mean+-SD of values obtained from children proven normal	**Celiac Group 1** • 50 children with biopsy proven CD • age: median 2.5 y, range 7 mos - 15 y • % F: 68	**Group 1:** • 25 control group of children (CO) • age: median 3.0 y, range 9 mos - 14 y • % F: 52	group 1 vs control 1, serum AGA IgA	46	4	8	17	92	68	85.2	80.9;
				group 1 vs control 1, serum AGA IgG	50	0	16	9	100	36	75.7	100
				group 1 vs control 1, serum EMA-IgA, HUC	47	3	0	25	94	100	100	89.2
				group 1 vs control 1, serum EMA-IgA, ME	48	2	1	24	96	96	97.9	92.3
				group 1 vs control 1, serum ARA IgA								

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Carroccio 2002 Italy	**Publication type:** • journal **Study design:** • case-control **Ethnicity:** • n/a **Population Type:** • suspected CD **Reference test:** children: Crosby capsule; adults: endoscopic biopsy **First test:** • n/r **Controls biopsied:** • yes **Biopsy criteria:** Marsh; CD was diagnosed as enlarged crypts and/or VA - with normalization on GFD **Checked IgA def.** • Yes **Studied tests** Serum AGA-IgG; Serum AGA-IgA; Serum EMA; Culture EMA; Culture EMA+gliadin **Methodology:** ELISA for AGA; indirect IF on ME for serum EMA; biopsy specimen incubation in a culture medium with gliadin peptide and further IF on ME **Cut-off:** AGA-results expressed as a % of reference serum: 20% was upper normal limit for IgG and 10% for IgA antibodies; EMA-semi-quantified as follows: 0=not detectable; 1=positive at dilutions between 1/5 and 1/20; 2=positive between 1/40 and 1/80; 3=positive at 1/100; 4=positive at 1/200; 5=positive at >1/200; EMA in culture-same as serum EMA and for IgG 25%, resulting the mean+-SD of values obtained from children proven normal	**Celiac Group 1** • 91 pts with biopsy proven CD • age (y): median 2; range 7 mos - 84 y • % F: 56 **Celiac Group 2** • 21 treated CD pts on a GFD with normal intestinal architecture • age (y): median 5, range 3-51 • % F: 62	**Group 1:** • 100 subjects with a normal intestinal morphology or diseases other than CD (biopsy proven) • age (y): median 21 y, range 9 mos-76 y • % F: 56 **Group 2:** • 22 disease controls (biopsy-proven non-CD) with GERD-like symptoms • age (y): median 33, range 4-60 • % F: 54.5	group 1 vs control 1, serum AGA IgG	69	22	25	75	76	75	73.4	77.3
				group 1 vs control 1, serum AGA IgA	61	30	10	90	67	90	86	75
				group 1 vs control 1, serum EMA	80	11	1	99	88	99	98.7	90
				group 1 vs control 1, culture EMA	82	9	0	100	90	100	100	91.7
				group 1 vs control 1, culture EMA+gliadin	87	4	0	100	96	100	100	96
				group 2 vs control 2, culture EMA+gliadin	10	11	0	22	47.6	100	100	66.7

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Carroccio 1993 Italy	**Publication type:** • journal **Study design:** • case-control **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** • Biopsy Watson capsule **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** •Biopsies confirmed at diagnosis, on GFD, and rechallenge (severity grade-not reported) **Checked IgA def.** • n/r **Studied tests** IgA-AGA IgG-AGA IgA-EMA **Methodology:** •ELISA; IF likely ME **Cut-off:** • AGA mean +2 SD	**Celiac Group 1** • infants with CD on gluten diet; biopsy proven • median age 2.6; range 0.8-10 • 21 males; 22 females	**Group 1:** • 60 infants disease controls; biopsy proven non-CD • median age 1.2; range 0.9-9 • 32 males; 28 females	celiac 1 vs control	31 40 45	14 5 0	5 32 2	55 28 58	68 88.9 100	91.7 46.7 96.7	86.1 55.6 95.7	79.7 84.8 100

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Carroccio 2002 Italy	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** gastroduodenoscopy and biopsy **First test:** • simultaneously **Controls biopsied:** • yes **Biopsy criteria:** •Ferguson and Murray; partial or total VA **Checked IgA def.** yes (none of CD pts showed IgA deficiency **Studied tests** EMA-IgA; anti-GP-tTG IgA (GP used); anti-h-tTG IgA (HR) **Methodology:** for EMA - IF ME; for tTG–ELISA **Cut-off:** anti-h-tTG IgA-results were expressed as a % of the positive control serum. Normal values were taken as <7%, which represented a value >2 SD above the mean of 850 healthy individuals; anti-gp-tTG IgA-values >95th percentile of a control group were considered positive;	**Celiac Group 1** • 24 consecutive pts with untreated biopsy proven CD • age (y): median 30, range 18-80 • % F: 58	**Group 1:** • 183 consecutive pts with biopsy proven non-CD disorders: IBS (n=70), esophagatis (n=45), peptic ulcers (n=41), Crohn's disease (n=15), Food intolerance (10), chronic liver disease (n=6), gastric cancer (n=2), right colon cancer (n=2), collagenous colitis (n=1), intestinal bacterial overgrowth syndrome (n=1), psoriasis (n=1) • age (y): median 46, range 17-84 • % F: 51	CD vs CO: EMA	24	0	0	183	100	100	100	100
				CD vs CO: anti-GP-tTG IgA	24	0	15	168	100	92	60	100
				CD vs CO: anti-h-tTG IgA	24	0	6	177	100	97	80	100

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Cataldo, 2000 Italy	**Publication type:** • journal **Study design:** • case-control **Ethnicity:** • n/a **Population Type:** • IgA deficient adults and children **Reference test:** • n/r **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** Original & revised criteria? **Checked IgA def.** • Yes **Studied tests** IgG-EMA IgA-EMA IgG-tTG IgA-tTG IgG-AGA IgA-AGA **Methodology:** •IgG-EMA, ME; IgG-tTG, human serum albumin **Cut-off:** • n/a	**Celiac Group 1** • 20 untreated CD (biopsy proven) with IgAD • age/gender: n/a **Celiac Group 2** • 11 untreated CD without IgAD • age/gender: n/a	**Group 1:** • 10 healthy IgAD controls on GD (healthy controls (not biopsied - not used) • age: n/a • gender: adults and children **Group 2** •25 healthy controls on a GD, first degree relatives of CD pts, adult or paediatric pts with GI diseases i.e. mild protein intolerance, pstenteritis syndrome, Crohn's disease, ulcerative colitis, or giardiasis •age/gender: n/a	Celiac 1 vs control 1	20 0 20 0 20 0	0 20 0 20 0 20	0 0 2 0 0 0	10 10 8 10 10 10	100 0 100 0 100 0	100 100 80 100 100 100	100 0 90.1 0 100 0	100 33.3 100 33.3 100 33.3

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Chan, 2001 Canada	**Publication type:** • journal **Study design:** • case-control **Ethnicity:** • n/a **Population Type:** • suspected CD **Reference test:** • Carey capsule or 4 to 6 duodenal biopsies at endoscopy **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** Villous atrophy, crypt hyperplasia, increase lymphocytes **Checked IgA def.** • Yes **Studied tests** IgA-EMA; IgA-tTG **Methodology:** •EMA-ME; IgA tTG ELISA GP liver **Cut-off:** • EMA:≥1:10; tTG: >20	**Celiac Group 1** • 9 untreated CD (biopsy + from a group of 77 children • age: 2 mos -16 y **Celiac Group 2** • 12 suspected CD with DM from a group of 16 DMs • age: 3-18Y **Celiac Group 3** • 2 IgAD pts, one biopsy positive, (excluded in the analysis)	**Group 1:** • 62 disease controls with negative biopsy with abdominal pain, diarrhea, failure to thrive/short stature, family history of CD, Crohn's disease, vomiting, abdominal distension, ulcerative colitis, autoimmune thyroiditis/short stature, trisomy, (from a total of 77) • age 2 mos to 16 y **Group 2** •2 DM from a group of 16 DMs	celiac 1 vs control 1	8 8	1 1	2 4	64 62	89 89	97 94	80 67	98 98

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Chartrand 1997 Canada	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/a **Population Type:** • suspected CD **Reference test:** • Biopsy - endoscopic **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** ESPGAN - with flat mucosal biopsy **Checked IgA def.** • yes - 2 of false negatives were IgA def **Studied tests** IgA–AGA IgG-AGA IgG or IgA **Methodology:** •ELISA **Cut-off:** • 0.25 for IgA, 0.3 for IgG (optical density)	**Celiac Group 1** • 30 of 176 children suspected of CD • mean age: 5.2; range 0.5-18; • % F: n/r	**Group 1:** •146 with suspected CD - biopsy excluded •mean age: n/r •% F: n/r	Celiac 1 vs Control	24 25 28	6 5 2	12 31 42	134 115 104	80 83 93	92 79 71	67 45 43	96 96 98

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Chirdo 1999 Argentina	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/a **Population Type:** • suspected CD **Reference test:** • n/r **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** Total or subtotal VA **Checked IgA def.** • n/a **Studied tests** IgG commercial gliadin; IgG ethanolic extract; IgG ω-gliadins ; IgA commercial gliadin; IgA ethanolic extract; IgA IgG ω-Gliadins **Methodology:** •ELISA **Cut-off:** • n/r	**Celiac Group 1** • 28 pts, biopsy proven untreated • mean age: 7 y; range 13 mos-14 y • % F: 15 (54%)	**Group 1:** •31 disease controls; chronic diarrhea, short stature, abdominal distension •mean age: 5.4 y, 2-12 y •13 F, 18 M	Celiac 1 vs Control	24 23 25 21 18 24	4 5 3 7 10 4	6 8 5 4 3 1	25 23 26 27 28 30	85.7 82.1 89.3 75 64.3 85.7	80.6 74.2 83.9 87.1 90.3 96.8	80 74 83 84 86 96	86 82 90 80 74 88

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Chirdo 2000 Argentina	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** Intestinal biopsy **First test:** • biopsy **Controls biopsied:** • only group 3 **Biopsy criteria:** ESPGAN **Checked IgA def.** • Yes **Studied tests** IgA w-AGA; IgG w-AGA; not a commercial kit (not used) IgA-EMA (used) **Methodology:** • IgA-EMA-ME IF **Cut-off:** • cut-off value for each antigen by using the same set of samples. Five control samples used as reference to normalize the day-to-day variation	**Celiac Group 1** • 105 untreated CD pts (biopsy proven) • mean age: 6.5 y; range 16 mos-15 y • % F: n/r	**Group 1:** • 45 healthy controls • mean age 8.5 y; range 3-14 y **Group 2:** • 36 healthy blood donors • mean age 36, range 22-45 y **Group 3:** • 46 biopsy negative disease control; presenting with short stature, chronic diarrhoea, parasitic infection • mean age 5.2 y; range 1.5-14 y this group used for analysis **Group 4:** • 27 disease controls with Crohn's disease, ulcerative colitis, or Helicobacter pylori infection	Celiac 1 vs control 3	94 100 97	11 5 8	5 9 0	41 37 46	89.5 95.2 92.4	89.1 80.4 100	94.9 91.7 100	78.8 88.1 85.2

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Dahele 2001 Scotland	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/a **Population Type:** • suspected CD **Reference test:** duodenal biopsy **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** Included partial VA or greater **Checked IgA def.** • Yes **Studied tests** IgA AGA; IgG AGA; IgA EMA; IgA tTG **Methodology:** • IgA AGA, ELISA; IgG-AGA, ELISA; IgA-EMA, HU; IgA-tTG ELISA GP liver **Cut-off:** • for IgA & IgG AGA: ≥30 unit/mL & ≥45 units/mL, respectively	**Celiac Group 1** • 53 untreated CD pts (biopsy proven) • median age 51 y; range 22-77 y • 39 F; 14 M	**Group 1:** • 65 control pts • median age: 45 y; range 17-90 y • 46 F; 19 M	Celiac 1 vs Control 1	34 44 40 35;	19 8 13 18	10 14 0 3	55 51 65 62	64 83 75 66	85 78 100 92	77 76 100 92	74 86 83 78

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Dahele 2001 Scotland NB: update of Dahele et al., Dig Dis Sci; 2001;46: 214	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/a **Population Type:** • suspected CD **Reference test:** duodenal biopsy **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** Included 6 with IEL, rest partial VA or greater **Checked IgA def.** • yes - 2 IgA deficient excluded (114/116 CD used) **Studied tests** IgA AGA; IgA AEM; IgA tTG **Methodology:** • IgA-AGA, ELISA; IgG-AGA, ELISA; IgA-EMA, HU; IgA tTG ELISA GP liver **Cut-off:** • for IgA & IgG AGA: ≥30 unit/mL & ≥45 units/mL, respectively	**Celiac Group 1** • 116 untreated CD pts (biopsy proven) • median age: 47 y; range 15-78 y • 74 F; 42 M	**Group 1:** • 65 control pts (suspected CD pts with normal biopsy) • median age 45 y; range 16-90 y • 45 F; 20 M	Celiac 1 vs Control 1	69 99 92	45 15 22	9 0 2	56 65 63	61 87 81	86 100 97	88.5 100 97.9	42.7 81.3 74.1

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Di Leo 1999 Italy	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** biopsy **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** ESPGAN **Checked IgA def.** • yes **Studied tests** EIA-IgA; EIA-IgG; DIG-ELISA IgA; DIG-ELISA IgG; ARA; human JAB-IgA; Rat JAB; EMA-IgA **Methodology:** •for EIA-IgA and IgG-ELISA; for ARA-IF; for EMA, JAB-immunohistochemical method •**Cut-off:** EIA IgA and IgG: 35 AU (arbitrary units) for children <5 y; and 20 AU for children >5 y; DIG-ELISA: IgA values >13 mm and IgG values >16 mm were considered positive in children <5 y; IgA values <11 mm and IgG values >14 mm - in children >5 y	**Celiac Group 1** • 45 untreated pts (biopsy proven untreated) • mean age: 6.11 y; range 9 mos-17 y • 32 F, 13 M **Celiac Group 2** • 18 GDF pts (celiac on GFD) • mean age: 13.2 y; range 3 y 8 mos-16 y 6 mos • 13 F, 5 M	**Group 1:** • 67 healthy controls • mean age: 8 y. 9 mos; range 1 y. 4 mos-16 y. 9 mos • 43 F, 24 M	group 1 vs control, EIA IgA	50	5	1	64	90.9	98.5		
				group 1 vs control, EIA IgG	53	2	20	45	96.4	69.2		
				group 1 vs control, DIG-ELISA IgA	50	5	2	63	90.9	96.9		
				group 1 vs control, DIS-ELISA IgA	48	7	9	56	87.3	86.2		
				group 1 vs control, ARA	48	6	18	47	88.9	72.3		
				group 1 vs control, Human JAB	55	0	18	47	100	72.3		
				group 1 vs control, RAT JAB	55	0	11	54	100	83.1		
				group 1 vs control, EMA	54	1	0	65	98.2	100		
				group 3 vs control, EIA IgA	20	1	1	64	95.5	98.5		
				group 3 vs control, EIA IgG	19	2	20	45	90.5	69.2		
				group 3 vs control, DIG-ELISA IgA	17	4	2	63	80.9	96.9		
				group 3 vs control, DIS-ELISA IgA	15	5	9	56	75	86.1		
				group 3 vs control, ARA	18	3	18	47	85.7	72.3		
				group 3 vs control, Human JAB	21	0	18	47	100	72.3		
				group 3 vs control, RAT JAB	18	3	11	54	85.7	83		
				group 3 vs control, EMA	19	2	0	65	90.5	100		

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Dickey 2001 Northern Ireland	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** • n/a **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** VA **Checked IgA def.** • no **Studied tests** EMA (excluded); tTGA; EMA and/or tTGA **Methodology:** •EMA=ME; tTGa, ELISA GP liver **Cut-off:** >30 as positive	**Celiac Group 1** • 73 untreated biopsy-proven CD pts • age 13-72 y • 45 F, 28 M	**Group 1:** 58 disease controls; diarrhea, anaemia, family history of celiac and others	Celiac 1 vs Control 1	55 68	18 5	1 2	57 56	75.3 93.2	98.3 96.6	98.2 97.1	76.0 91.8

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Faith-Magnusson 1994 Sweden	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/a **Population Type:** • suspected CD **Reference test:** • Watson capsule or Stortz **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** ESPGAN+ Alexander grading IV, grade III to IV callenge **Checked IgA def.** • no **Studied tests** DIG - ELISA combined IgA & IgG; ELISA combined IgA & IgG **Methodology:** •ELISA; DIG-ELISA **Cut-off:** DIG ELISA (mm) combined IgA+IgG ≥ 6 and /or; ≥10; ≥12; ≥14; ≥16; ELISA (mm) for combined IgA+IgG ≥0.25; and; ≥0.8; ≥0.9; ≥1.0; ≥1.1	**Celiac Group 1** • 116 pts; biopsied twice; median time on GFD pre 2nd biopsy 13 mos (10-24 mos) • age @ 1st biopsy median 13 mos, range 0.7-16.7 y, age @ 2nd biopsy 29 mos range 1.6-17.8 y • 73 F; 43 M	**Group 1:** • 199 disease controls; poor weight gain; diarrhea; stature • median age 22 mos range 0.7-16.8 y • 105 F; 94 M	Celiac 1 vs Control 1	n/r	n/r	n/r	n/r	98.1 95.2 91.4 88.6 93.3 88.7 88.7 88.7	27.8 39.5 70.5 92.3 64.6 75.8 82.3 93.5		

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Gilbert 2000 Canada	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/a **Population Type:** • n/r **Reference test:** • biopsy **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** mild, moderate, severe VA **Checked IgA def.** • n/r **Studied tests** IgA-EMA; IgA-tTG **Methodology:** •EMA-HU •tTG- HR **Cut-off:** EMA:≥1:5; tTG: >400u	**Celiac Group 1** • 21 CD adults • age: n/r • % F: n/r	**Group 1:** • biopsied disease controls with CD excluded • age: n/r • % F: n/r	Celiac 1 vs Control	21 20	0 1	0 0	42 42	100 95.2	100 100		

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Gonczi 1991 Australia	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/r **Population Type:** • suspected celiac; single institution 1977-1983; mean age 3.97 (range 1 mos-16 y) **Reference test:** • biopsy technique not reported (likely capsule) **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** ESPGAN no details on biopsy findings **Checked IgA def.** • yes - 1 CD child **Studied tests** IgA AGA; IgG-AGA **Methodology:** •ELISA mean + 2 SD; IgA 25 AU; IgG 46 **Cut-off:** 20.2%	**Celiac Group 1** • 20 children untreated biopsy-proven CD • age: n/r • % F: n/r **Celiac Group 2** • 25 untreated adults biopsy-proven CD • age: n/r • % F: n/r	**Group 1:** • 79 children biopsy-negative controls w sx • age: n/r • % F: n/r **Group 2:** • 34 adult disease controls • age: n/r • % F: n/r	celiac 1 vs control 1-IgA-AGA	19	1	6	73	95	92.4	76	98.6
				celiac 1 vs control 1-IgG – AGA	20	0	6	73	100	92.4	76.9	100
				celiac 1 vs control 1-IgA+IgG	20	0	1	78	100	98.7	95.2	98.7
				celiac 2 vs control 2-IgA-AGA	23	2	4	30	92	88.2	85.2	93.8
				celiac 2 vs control 2-IgG – AGA	25	0	11	23	100	69.7	69.4	100
				celiac 2 vs control 2-IgA+IgG	25	0	1	33	100;	97.1	96.2	100

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Hallstrom 1989 Findland	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/r **Population Type:** • n/a **Reference test:** • biopsy **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** Flat mucosa **Checked IgA def.** • yes **Studied tests** IgA - EMA **Methodology:** •EMA-ME **Cut-off:** n/r	**Celiac Group 1** • 32 untreated adult CD pts • mean age 36 y; range 18-63 y) • % F: n/r **Celiac Group 2** • 18 children with untreated CD • mean age 1; range 2-16 • % F: n/r	**Group 1:** • 24 non-CD children by biopsy, with various abdominal symptoms • mean age 7.5 y; range 1-15 • % F: n/r	celiac 1 vs control 1	29	3	0	24	90.6	100	100	88.9
				celiac 2 vs control 1	18	0	0	24	100	100	100	100

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Hansson 2000 Sweden	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/r **Population Type:** • n/a **Reference test:** • n/r **First test:** • serology test **Controls biopsied:** • no **Biopsy criteria:** ESPGAN **Checked IgA def.** • no **Studied tests** IgA EMA; IgA serum; IgG AGA; IgA tTG; human erythrocyte tTG; tTG GP liver **Methodology:** •IgA-EMA-ME; tTG, ELISA (human) **Cut-off:** n/r	**Celiac Group 1** • 22 untreated pts (biopsy proven CD) • median age 3 y; range 1-16 y • 14 F, 8 M	**Group 1:** • 23 disease controls (note: no biopsy for the 5/23 control group); GI symptoms; inflammatory bowel disease; cow's milk protein intolerance; food intolerance; miscellaneous GI disorders 17 confirmed biopsy negatives • median age: 6 y, range 1-16 y • 9 F, 13 M	Celiac 1 vs Control 1	21 21 18 21 22 20	1 1 4 1 0 2	0 6 4 1 0 1	23 17 19 22 23 22	95.5 95.5 81.8 95.5 100 90.9	100 73.9 82.6 95.7 100 95.7	100 77.8 81.8 95.5 100 95.2	95.8 94.4 82.6 95.7 100 91.7

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Iltanen 1999 Finland	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/r **Population Type:** • 78 children with suspected CD **Reference test:** • biopsy **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** ESPGAN - CD confirmed at follow-up **Checked IgA def.** • n/r **Studied tests** IgA - EMA **Methodology:** •HU - IF **Cut-off:** >=1:5	**Celiac Group 1** • 23 CD children out of 78 evaluated for suspected CD • median age: overall group 6.5; range 0.5-15.8 • % F: n/r	**Group 1:** • 57 biopsy negative children who were suspected of CD • age: n/r • % F: n/r	celiac 1 vs control 1	20	0	13	44	100	77.1	60.1	100

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Kaukinen, 2000 Finland	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/r **Population Type:** • pts suspected of CD with self reported symptoms upon gluten ingestion **Reference test:** • biopsy **First test:** • simultaneous **Controls biopsied:** • yes **Biopsy criteria:** Villous height to crypt ration <2.0; IEL and HLA also tested **Checked IgA def.** • n/r **Studied tests** IgA EMA; IgA htTg; IgA AGA; IgG AGA **Methodology:** •IF-EMA-HU; Human recombinant TTG ELISA (from Enova Diagnostics web site); AGA ELISA **Cut-off:** ≥1:5; ≥20 U; IgA-AGA ≥0.2 EU/mL; IgG-AGA ≥10 EU/mL	**Celiac Group 1** • 93 pts with self-reported suffering from GI symptoms upon gluten ingestion • mean age: 39 y; range 17-73 y; 9 CD pts • % F: 70; 23 M	**Group 1:** • 84 of 93 with negative biopsy • age: n/r • % F: n/r	celiac 1 vs control 1	7 8	1 0	0 0	84 84	88.9 100 83 17	100 100 45 86	100 100	98.9 100

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Kolho, 1997 Finland	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/r **Population Type:** • suspected CD; or reason to exclude CD **Reference test:** • Biopsy either ingestible capsule technique or endoscopically **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** revised ESPGAN **Checked IgA def.** • yes – in pts with neg serology **Studied tests** EMA (HU); EMA (ME) **Methodology:** •EMA-ME •EMA-HU **Cut-off:** cut off level was 20% for class IgA and IgG antibodies	**Celiac Group 1** • 53 pts newly diagnosed CD (biopsy proven) • mean age: 6.46 y (range 0.77-19.7 y) • gender: n/r **Celiac Group 2** • 22 pts with CD in remission (CD on GFD) • age (range 0.77-19.7 y) • gender: n/r **Celiac Group 3** • 13 CD pts gluten challenge • age range: 0.77-19.7 y • gender: n/r	**Group 1:** • 48 pts children/adolescents GI complaints; disturbed growth or elevated AGA titres (normal biopsy) • median age 5.39 y (age range 0.63-13.3 y) • % F: n/r **Group 2:** • 20 pts with cow's milk sensitivity enteropathy n/r **Group 3:** • 23 pts with inflammatory bowel disease n/r **Group 4:** • 23 pts with diabetes mellitus n/r	CD untreated and on gluten challenge (group 1) vs control groups 1-4 (combined in the study) CD gluten challenged vs control EMA	50 50 13 13	3 3 0 0	0 0 0 0	114 114 13 13	95 95 100 100	100 100 100 100	100 100 100 100	97 97 100 100

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Kumar, 1989 USA, Israel	**Publication type:** • journal **Study design:** • relevant clinical population and control cases **Ethnicity:** • n/r **Population Type:** • suspected CD; asymptomatic family members **Reference test:** • Crosby-Kugler capsule **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** ESPGAN + Townley **Checked IgA def.** • no **Studied tests** IgA-EMA **Methodology:** •IgA EMA, IF studies; ME **Cut-off:** n/r	**Celiac Group 1** • 38 children (biopsy proven); untreated CD • age: n/r • gender n/r **Celiac Group 2** • 37 pts; GFD treated. • age: n/r • gender: n/r **Celiac Group 3** • 30 suspected CD; on gluten diet **Celiac Group 4** • 30 suspected cd on GFD	**Group 1:** • 106 asymptomatic family members • age & gender: n/r **Group 2:** • 52 children with chronic diarrhea; 30 ulcerative colitis; 65 Crohn's disease; 21 liver disease; 34 recurrent abdominal pain • age & gender: n/r **Group 3:** • 87 healthy subjects • age & gender: n/r	CD untreated and suspected untreated and 8 biopsy + family members vs Control 1 (106-8), 2, 3	73	3	11	376	96	89	87	96.7

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Ladinser, 1994 Italy	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/r **Population Type:** • n/r **Reference test:** • endoscopic biopsy; IgA EMA **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** revised ESPGAN **Checked IgA def.** • IgA deficiency excluded by serum testing **Studied tests** IgA EMA **Methodology:** • IgA-EMA, IF studies HU smooth muscle; IgA-EMA, IF studies ME **Cut-off:** n/r	**Celiac Group 1** • 20 biopsy-proven CD pts • mean age: 35 y (range 5-68) • % F: 67%; 20 on gluten-containing diet **Celiac Group 2** • 10 pts GFD (subset of original 30). • age: n/r • gender: n/r	**Group 1:** • 35 pts (CD on GFD) with positive AGA serum samples no histological abnormalities • Mean age: 40 y (range 3-65) • % F: 57% **Group 2:** • 40 non-celiac pts without GI disorder with AGA below average range (IgA<5 and IgG <15) • mean age: 37 y (range 5-65) • % F: 50%	20 active untreated cases vs control group; IgA-EMA (HU) 20 active untreated cases vs control group IgA-EMA (ME)	20 18	0 2	0 0	75 75	100 90	100 100	100 100	100 98

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Lerner, 1994 USA, Israel NB: duplicate of Pacht et al., Isr J Med Sci 1995;31:218 (used data from Lerner et al, 1994 since more complete and larger control group)	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/r **Population Type:** • n/r **Reference test:** • Crosby capsule **First test:** • simultaneous Biopsy & serology **Controls biopsied:** • yes **Biopsy criteria:** criteria of Townley modified by Ingkaran **Checked IgA def.** • no **Studied tests** IgA -AGA; IgG-AGA; IgA-ARA (rat kidney); IgA-ARA (mouse kidney); IgA-EMA ME **Methodology:** AGA=ELISA; ARA=IF rat & mouse kidney; EMA=IF ME **Cut-off:** ELISA 2 SD above the mean of normal value considered positive	**Celiac Group 1** • 34 biopsy proven CD • mean age: 9.6 (range 1.7-17 y) • male:female: 0.6:1.0	**Group 1:** • 9 pts abnormal biopsy pathological control grade II-IV atrophy; (3) Giardia lamblia (3) protracted diarrhea (1) Crohn's (1) HSP (1) intestinal lymphangectasis (1) hypogammaglobulinaemia • mean age 9.3 y (range 2-16 y) • male:female 1.2:1 **Group 2:** • 32 pts with normal intestinal morphology (GCD) • mean age: 8.4 y (range 1-16 y) • male:female 0.9:1	CD1 vs CO IgA-AGA					52	94	87	74
				CD1 vs CO IgG-AGA					88	92	88	92
				CD1 vs CO IgA-ARA-r					65	100	100	77
				CD1vs CO IgA-ARA-m					53	100	100	71
				CD1 vs CO IgA-EMA;					97	98	97	98

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Lindberg, 1985 Sweden NB: duplicate Jardas et al., Pol J Immunol 1994;19:49	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/r **Population Type:** • suspected malabsorption **Reference test:** • biopsy duodenojejunal flexure Watson pediatric capsule EMA **First test:** • biopsy & serology simultaneous (sera collected ± 2 weeks of biopsy) **Controls biopsied:** • yes **Biopsy criteria:** ESPGAN and Alexander grades; reported sensitivity and specificity for pts with severely damaged mucosa **Checked IgA def.** • yes **Studied tests** IgA-AGA; IgG-AGA; combined IgA/IgG **Methodology:** •DIG-ELISA **Cut-off:** 11 mm IgA; 14mm IgG combined	**Celiac Group 1** • 25 pts untreated CD; 29 pts probable CD • mean age: 12 months (range 7-132 mos) • gender: n/r • 58 pts in total used (with severely damaged mucosa) **Celiac Group 2** • 32 pts CD treated GFD (2nd biopsy) • mean age: 30 mos (range 18-168 mos) • gender: n/r **Celiac Group 3** • 37pts confirmed CD challenged period with gluten • mean age: 36 mos (range 16-192 mos) • gender: n/r	**Group 1:** • 121 pts with other GI disorders i.e., unspecified diarrhea, cow's milk protein intolerance, multiple food allergies, post infectious diarrhea, diarrhea caused by Yersinia enterocolitica • mean age 14 mos (7-130 mos) • gender: n/r **Group 2:** • 23 pts short stature no GI symptoms • mean age: 48 mos (range 12-180 mos) • gender: n/r NB: the study combined control 1 and control 2 (132 pts)	Author reports groups as: CD severely damaged intestinal mucosa vs control IgA AGA CD severely damaged intestinal mucosa vs control IgG AGA CD severely damaged intestinal mucosa vs control IgA/IgG AGA					88 93 97	88 89 83		

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Lindquist, 1994 Sweden	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/r **Population Type:** • suspected CD **Reference test:** • paediatric Watson capsule **First test:** • Simultaneous biopsy & serology **Controls biopsied:** • yes **Biopsy criteria:** ESPGAN; subtotal or partial VA **Checked IgA def.** • yes **Studied tests** IgA-EMA IgA-AGA **Methodology:** IgA-EMA, indirect IF & ME; IgA-AGA, DIG-ELISA **Cut-off:** IgA-AGA >11mm regarded as positive	**Celiac Group 1** • 42 confirmed CD pts (meets ESPGAN criteria) • mean age: 2.7 y (range 5 mos-14.4 y) • % F: 48 **Celiac Group 2** • 10 suspected CD pts with characteristic biopsy but repeat biopsy on GFD was pending • mean age: 2.7 y (range 5 mos-14.4 y) • % F: 48	**Group 1:** • 25 pts with other pathology (CD excluded) • mean age: 2.7 y (range 5 mos-14.4 y) • % F: 48	Celiac 1 & 2 vs control 1 EMA	51	1	3	38	98.1	92.7	94.4	97.5
				Celiac 1 & 2 vs control 1 IgA	45	7	3	39	86.5	92.7	93.7	85

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Maki, 1991 Finland	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/r **Population Type:** • suspected celiac **Reference test:** • paediatric Watson capsule **First test:** • Simultaneous Biopsy & serology **Controls biopsied:** • yes **Biopsy criteria:** ESPGAN; subtotal or partial VA **Checked IgA def.** • yes **Studied tests** IgA-EMA IgA-AGA **Methodology:** IgA-EMA, indirect IF & ME; IgA-AGA, DIG-ELISA **Cut-off:** IgA-AGA > 11mm regarded as positive	**Celiac Group 1** • 42 confirmed CD pts (meets ESPGAN criteria) • mean age: 2.7 y (range 5 mos-14.4 y) • % F: 48 **Celiac Group 2** • 10 suspected CD with characteristic biopsy but repeat biopsy on GFD was pending • mean age: 2.7 y (range 5 mos-14.4 y) • % F: 48	**Group 1:** • 25 pts with other pathology (CD excluded) • mean age: 2.7 y (range 5 mos-14.4 y) • % F: 48	Celiac 1 & 2 vs control 1 EMA	51	1	3	38	98.1	92.7	94.4	97.5
				Celiac 1 & 2 vs control 1 IgA	45	7	3	39	86.5	92.7	93.7	85

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
McMillan, 1991 Ireland	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/r **Population Type:** • suspected celiac **Reference test:** • Crosby capsule "muzzle loaded" **First test:** • simultaneous Biopsy & serology **Controls biopsied:** • yes **Biopsy criteria:** revised ESPGAN **Checked IgA def.** • yes **Studied tests** IgG-AGA; IgA-AGA; IgG-AGA; IgA-AGA; IgG-EMA; IgA-EMA; IgA jejunum; IgG jejunum **Methodology:** • AGA by indirect IF; AGA by ELISA; EMA by IF, ME; jejunum, IF with sections of black hooded rat jejunum as antigen **Cut-off:** titre of one in 20 or greater were considered positive	**Celiac Group 1** • 23 biopsy proven CD + 5 probable CD = 28 pts • Adults age (y): 16-89 • % F: n/r	**Group 1:** • 7 pts 2 did not respond to GFD 4 had ulcerative colitis (1 of those pts had partial VA); 1 had IBS • mean age: n/r • % F: n/r **Group 2:** • 61 normal results of jejunal biopsies	Celiac group 1 vs control group 2	21 21 16 28 11 25 15 21	7 7 12 0 17 3 13 7	4 0 9 0 1 0 0 0	57 61 52 61 60 61 61 61	75 75 57 100 39 89.2 54 75	93.4 100 85 100 98.3 100 92 100	84 100 64 100 92 100 75 100	89 90 81 100 78 95.3 81 90

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Meini, 1996 Italy	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/r **Population Type:** • 65/85 IgA-def pts seen in single immunology clinic 1989-93 (76.5%) **Reference test:** • Watson capsule **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** partial VA or total VA **Checked IgA def.** • yes **Studied tests** IgA-AGA; IgG-AGA **Methodology:** ELISA **Cut-off:** 25 AU/dL	**Celiac Group 1** • 5 pts; untreated; IgA-deficient • mean age: 8.8 y; range 7-11 y • % F: 80	**Group 1:** • 60 biopsy-negative IgA-deficient	celiac 1 vs control 1	0 5	5 0	0 11	55 44	0 100	100 80	- 31.2	91.7 100

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Picarelli, 2000 Italy	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/r **Population Type:** • suspected CD **Reference test:** • EMA; biopsy (EGD) 2 biopsies **First test:** • EMA serology **Controls biopsied:** • yes **Biopsy criteria:** ESPGAN **Checked IgA def.** • yes 9 of 18 IgA deficient **Studied tests** IgG-EMA; IgA-AGA; IgG-AGA **Methodology:** EMA, indirect IF ME; AGA, in house ELISA **Cut-off:** 0.9 for AGA-IgA and 1.1 for AGA-IgG	**Celiac Group 1** • 30 EMA neg suspected CD; 18 confirmed cases CD • mean age: 10.6 y (age range 2-16 y) • % F: 60	**Group 1:** • 60 disease control (other GI diseases) • mean age: 11.3 y (age range 4-16) • % F: 55 **Group 2:** • 63 healthy children • mean age 10.5 y (age range 3-16 y) • % F: 52 - this group not biopsied so not used **Group 3:** • 12 suspected CD pts biopsy negative	celiac 1 vs control 1 and EMA	18	0	0	135	100	100	100	100
				celiac 1 vs control 3 for IgA-AGA	4	14	4	8	22.2	66.7	50	36.3
				IgG-AGA	6	12	5	7	33.3	58.3	54.5	36.8;

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Poddar, 2002 India	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/r **Population Type:** • suspected CD **Reference test:** • biopsy - endoscopic **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** ESPGAN (VA and unequivocal response to GFD) **Checked IgA def.** • n/r **Studied tests** IgA–AGA **Methodology:** ELISA **Cut-off:** 5U/mL	**Celiac Group 1** • 50 CD children of 100 biopsied for suspected CD • mean age: 6.3; range 2.5-12 y • % F: n/r	**Group 1:** • 44 biopsy-negative controls who were suspected of CD	celiac 1 vs control 1	47	3	4	43	94	91.5	92	93.5

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Rich, 1990 USA	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** pediatric suction biopsy technique under fluoroscopic control **First test:** • n/r **Controls biopsied:** • yes **Biopsy criteria:** n/r - state "severe" lesion **Checked IgA def.** • n/r **Studied tests** xylose; IgA-AGA; IgG-AGA **Methodology:** D-xylose absorption test; for AGA - ELISA **Cut-off:** xylose ≤25 mg/dL was considered abnormal; AGA - Ab levels >2 SD above the mean of the reference group of normal subjects were considered to be abnormal	**Celiac Group 1** • 15 biopsy-proven CD pts out of 60 consecutive group of children suspicious of having CD • age: n/r • % F: n/r	**Group 1:** • 45 non-CD biopsies out of 60 consecutive group of children suspicious of having CD • age: n/r • % F: n/r	celiac vs CO: Xylose celiac vs CO: IgG AGA celiac vs CO: IgA AGA	14 15 8	1 0 7	24 19 3	21 26 42	93 100 53	47 58 93	36.8 44 72.7	84 100 85.7

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Russo, 1999 Canada	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** endoscopic biopsy **First test:** • n/r **Controls biopsied:** • yes **Biopsy criteria:** ESPGAN **Checked IgA def.** yes (1 pts with CD were found to be IgA deficient) **Studied tests** AGA-IgA; AGA-IgG; EMA ME; EMA HU **Methodology:** for AGA-IgA and IgG ELISA; for EMA - IF on either ME, or HU **Cut-off:** for AGA-gA cut-off was 0.25 EU and for AGA-IgG 0.3 EU; for EMA positive results were considered when a characteristic honeycomb pattern was observed around the smooth muscle	**Celiac Group 1** • 24 pediatric pts with CD (biopsy proven) diagnosed by evaluating consecutive group of 95 children with suspected CD • age: mean 3.5 y, range 7 mos-11 y • % F: 50	**Group 1:** • 71 children with biopsy proved non-CD enteropathies or normal mucosa • age: n/r • % F: n/r	celiac vs control IgG-AGA celiac vs control IgA-AGA; celiac vs control EMA ME celiac vs control EMA HU parallel series					83.3 83.3 75 45.8 100 100	84.5 85.9 88.7 95.8 73 93	64.5 66.7 69.2 78.6 57 86	93.8 93.8 91.3 84 82 100

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Salmaso, 2001 Italy	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/a **Population Type:** consecutive CD Dx 1996-99 **Reference test:** • no info on biopsy **First test:** • biopsy? **Controls biopsied:** • yes **Biopsy criteria:** grades 1-1V Marsh with response to GFD **Checked IgA def.** yes; IgA deficients were excluded **Studied tests** IgA-EMA; IgA-tTG **Methodology:** UC EMA; GP-tTG antigen **Cut-off:** tTG=20 AU	**Celiac Group 1** • 23 adult untreated CD pts • median age: 50; range 27-96 • % F: 56.5 **Celiac Group 2** • 59 children with untreated CD • median age: 8.2 y; range 2-14 • % F: 37.3	**Group 1:** 58 adult age-matched biopsy-negative controls **Group 2:** 48 children age-matched biopsy-neg controls	celiac 1 vs control 1 celiac 2 vs control 2	20 20 59 56	3 3 0 3	0 2 0 0	58 56 48 48	87 87 100 95	100 97 100 100	100 90.9 100 100	95.1 94.9 100 94.1

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Sategna-Guidetti, 1995 Italy	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** endoscopic biopsy **First test:** • n/r **Controls biopsied:** yes, except pts with ulcerative colitis **Biopsy criteria:** Roy-Choudhury criteria; partial or total VA **Checked IgA def.** yes **Studied tests** AGA-IgA; AGA-IgG; Ig AGA total Ig; EMA IgA (ME); JAB IgA **Methodology:** for AGA-IgA and IgG: ELISA; for Ig-AGA, EMA, JAB: IF **Cut-off:** for AGA-IgA and IgG: mean±2 SD of control absorbance index values; for Ig AGA: endpoint still generating a pertubular and a periglomerular reticular pattern; for EMA: results considered when a characteristic honeycomb pattern was observed around the smooth muscle; for JAB: IF at a dilution of 1:5 in phosphate-buffered saline	**Celiac Group 1** • 100 untreated biopsy-proven CD pts • age (y): mean/median n/r; range 14-79 • % F: 71	**Group 1:** • 52 healthy volunteers recruiting among medical and nursing staff • **Group 2:** • 57 pts with non-CD conditions: Crohn's disease (n=38), ulcerative colitis (n=5), lymphoma (n=7), Whipple's disease (n=1), irritable bowel disease (n=6) • age: n/r	celiac vs CO EMA	100	0	0	109	100	100	100	100
				celiac vs CO JAB	100	0	0	109	100	100	100	100
				celiac vs CO IgA-AGA	55	45	0	109	55	100	100	70.8
				celiac vs CO IgG-AGA	78	22	18	91	78	83.5	81.3	80.5
				celiac vs CO Ig-AGA	92	8	5	104	92	95	96	90

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Sblaterro, 2000 Italy	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** n/r **First test:** • biopsy **Controls biopsied:** ESPGHAN **Biopsy criteria:** ESPGHAN **Checked IgA def.** yes **Studied tests** EMA-IgA; GP-tTG IgG and IgA; HR tTG **Methodology:** for tTG: ELISA; for EMA: IF **Cut-off:** normal values for IgA HR-tTG were taken as <13% and for IgG HR-tTG <30%; normal values for IgA GP-tTG were taken as <7% and <16%	**Celiac Group 1** • 65 pts with biopsy proven CD • age (y): median 12, range 2-60 • % F: 52.3	**Group 1:** • 150 healthy donors and 20 pts with Crohn's disease (biopsy proven non-CD enteropathies or normal mucosa) • age: mean/media n/r; range 12-60 y • % F: 44	celiac vs CO EMA	60	5	0	170	93	100	100	97
				celiac vs CO IgG GP-tTG	40	25	3	167	61	98	93	87
				celiac vs CO IgA GP-tTG	53	12	3	167	84	98	94.6	88
				IgG/IgA GP-tTG	58	7	6	164	90	96	91	98
				celiac vs CO IgG HR-tTG	44	21	7	163	67.6	96	86.3	88.6
				celiac vs CO IgA HR-tTG	59	6	1	169	91.5	99	98.3	96.6
				IgG/IgA HR-tTG	64	1	8	162	98.5	95	88.9	99.4

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Sulkanen, Collin, et al. 1998 Finland N.B: used adult group of Sulkanen, Collin, et al., 1998; more complete data located in Sulkanen, Halttunen, et al. 1998	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** n/r **First test:** • n/r **Controls biopsied:** • yes **Biopsy criteria:** subtotal or severe partial VA, crypt hyperplasia, increased IEL **Checked IgA def.** yes (4 pts with CD and 1 CO had IgA deficiency) **Studied tests** HU IgA; HU IgG; ARA IgA and IgG; AGA IgA and IgG **Methodology:** for AGA ELISA; for ARA IF; for HU IF using HU **Cut-off:** HU-Ab positivity included a specific honey-comb IF around the smooth-muscle fibres; AGA IgA - cut off level-0.2 EU/mL; AGA IgG cut off level - 10.0 EU/mL; ARA test was considered positive when the characteristic R1-type ARA pattern was found	**Celiac Group 1** •92 consecutive adult pts with biopsy-proven CD •age (y): median 43; range 20-72 • % F: 71.7	**Group 1:** • 95 disease controls with biopsy proven non-CD enteropathies: 52 undergoing gastroscopic exam for dyspepsia; 14 with Crohn's disease, 29 with ulcerative colitis • age (y): median 44; range 16-76	celiac vs control IgA-HU	78	12	0	95	84.8	100	100	87
				celiac vs control IgG-HU	11	81	0	95	12	100	100	54
				celiac vs control IgA-ARA	72	20	0	95	78.2	100	100	82.6
				celiac vs control IgG-ARA	12	80	2	93	13	98	85.7	53.7
				celiac vs control IgA-AGA	74	18	13	82	80.4	86.3	85	82
				celiac vs control IgG-AGA	35	57	3	92	38	96.8	92	61.7

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Sulkanen, Halttunen, et al. 1998 Finland	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/a **Population type:** • n/a **Reference test:** Watson capsule **First test:** • n/r **Controls biopsied:** • yes **Biopsy criteria:** ESPGAN **Checked IgA def.** yes (n=14) **Studied tests** IgA tTG; IgA EMA; IgA-ARA; IgA-AGA; IgG-AGA **Methodology:** tTG-source n/r ELISA; IgA-EMA-HU; IgA and IgG-AGA-ELISA; IgA ARA-IF) **Cut-off:** for IgA tTG cut off level-10 AU	**Celiac Group 1** • 136 consecutive pts with untreated CD (biopsy proven) • age (y): median 10.7, range 0.8-69.3 • % F: n/r **Celiac Group 2** • 38 pts with CD on GFD of a median duration 48 mos • age: median, range n/r • % F: n/r **Celiac Group 3** • 18 pts on a gluten-challenge • age: median, range n/r • % F: n/r • 11 pts after reintroduction of a GFD (group 4) • age (y): median, range n/r • % F: n/r	**Group 1:** • 154 disease CO with suspicion of CD but biopsy proven non-CD • age (y): median 10, range 0.8-76.0 • % F: n/r	CD group1 vs CO IgA-tTG	129	7	13	194	95	93.7	90.8	96.5
				CD group1 vs CO IgA-EMA	126	10	1	206	92.6	99.5	99.2	94.9
				CD group1 vs CO IgA-ARA	125	11	8	199	92	96.1	94	94.7
				CD group1 vs CO IgA-AGA	115	21	38	169	84.5	81.6	75.2	89
				CD group1 vs CO all IgG-AGA	94	42	55	152	69	73.4	63	78.3

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Tesei, 2003 Argentina	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** endoscopic biopsy **First test:** Simultaneously **Controls biopsied:** yes **Biopsy criteria:** Marsh 2 to 4 - with confirmation **Checked IgA def.** yes (11 pts were diagnosed as IgA deficient having dermatitis herpetiformis) **Studied tests** HU-anti-tTG IgA-HR; EMA-IgA; AGA-IgA; AGA-IgG **Methodology:** for HU-anti-tTG, ELISA; for EMA, ME IF; for AGA, ELISA **Cut-off:** for HU-anti-tTG - 7 AU/mL; for AGA - 20 AU/mL; for EMA - florescence at dilution of 1:5	**Celiac Group 1** • 250 consecutive pts with biopsy proven CD • age (y): mean 39, range 13-79 • % F: 74	**Group 1:** • 176 biopsy proven non-CD disease controls: chronic diarrhea (n=78), chronic microcitic anemia (n=33), first-degree relatives of index cases (n=32), healthy individuals (n=11), malabsorption (n=4), miscellaneous (n=12), undernutrition (n=6) • age (y): mean 40, range 17-83 • % F: 75	CD vs CO: HU-anti-tTG IgA CD vs CO: EMA CD vs CO: AGA IgA CD vs CO: AGA IgG	225 214 159 210	25 36 91 40	9 0 14 25	167 176 162 151	91 86 64 84	96 100 92 86	97 100 92 89	87 83 64 79

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Troncone, 1999 Italy	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** n/r **First test:** • n/r **Controls biopsied:** • yes **Biopsy criteria:** ESPGAN **Checked IgA def.** yes (none of celiac or CO suffered from IgA deficiency) **Studied tests** anti-tTG IgA; anti-tTG IgG; IgA EMA **Methodology:** for tTG-GP, ELISA; for EMA, ME IF **Cut-off:** for anti-tTG - at the 97th percentile of the control group (9% of the reference serum for IgA and 60% - for IgG); for EMA - as the highest dilution giving a positive result (a thin fluorescent network around the smooth muscle fibres)	**Celiac Group 1** • 48 biopsy proven CD pts • age (y): mean 5.7, range 0.9-20 • % F: 58 **Celiac Group 2** • 33 pts who were on GFD of at least 2 y • age (y): mean 7.3, range 4.3-18 • % F: 60.6 **Celiac Group 3** • 10 pts from group 2 who were reintroduced to gluten-containing diet	**Group 1:** • 63 biopsy proven non-CD disease controls: chronic diarrhea (n=16), failure to thrive (n=14), Crohn's disease (n=10), cow's milk protein allergy (n=5), GERD (n=5), recurrent abdominal pain (n=4), sideropenic anemia (n=4), hepatatis C (n=3), Cystic fibrosis (n=2) • age (y): mean 4.2, range 1.1-17 • % F: 49	CD vs CO: anti-tTG IgA CD vs CO: anti-tTG IgG	44 11	4 37	1 1	62 62	91.7 23	98 98	98 92	94 63

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Valdimarsson, 1996 Sweden	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** Watson capsule in 91 pts; fiberoptic endoscopy - in 65 pts **First test:** • biopsy **Controls biopsied:** • yes **Biopsy criteria:** Alexander's classification; partial or subtotal VA **Checked IgA def.** yes (5 had IgA deficiency) **Studied tests** IgA AGA; IgA EMA **Methodology:** for AGA, ELISA; for EMA, IF ME **Cut-off:** for AGA-IgA, 30 units (>92nd percentile in healthy blood donors); for AGA-IgG, 20 units (>91.3th percentile in healthy blood donors); for IgA EMA, characteristic honeycomb pattern was observed around the smooth muscle	**Celiac Group 1** • 19 pts with CD (biopsy-proven) out of 156 pts referred for symptoms suspicious for CD • age: n/r • % F: n/r	**Group 1:** • 137 pts with biopsy proven non-CD; 5 had IgA deficiency and 7-dermatitis herpetiformis • age: n/r • NB: pts with IgA deficiency and dermatitis herpetiformis were excluded from the analysis of sensitivity, specificity, so that CO group was composed of 125 pts	celiac vs CO IgA EMA	14	5	0	125	74	100	100	96
				celiac vs CO IgA AGA	15	4	38	87	79	70	28	96

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Valentini, 1994 Italy	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** multipurpose biopsy tube, endoscopic **First test:** • simultaneously **Controls biopsied:** • yes **Biopsy criteria:** partial VA or greater **Checked IgA def.** n/r **Studied tests** IgA-AGA; IgG-AGA; IgA-EMA ME **Methodology:** for IgA/IgG AGA, ELISA; for IgA-EMA, IF **Cut-off:** lower limit of AGA positive was 1 EU, based on the mean+-2 SD of the results obtained in a large series of healthy adults; IgA-EMA identified by their reticulin-like staining of the smooth muscle; sera containing antibody at a titre of 1:5 or greater were considered to be positive	**Celiac Group 1** • 100 consecutive adult untreated pts with CD (biopsy proven) • age (y): mean 37.4+-15.4, range 17-79 • % F: 77 **Celiac Group 2** • 33 pts out of 100 group 1 who were on GFD of at least 6 mos (mean 9.9 mos, range 6-12 mos);	**Group 1:** • 30 disease controls (CO) with biopsy proven non-CD conditions: ulcerative colitis (n=8), gastric lymphoma (n=8), Crohn's disease (n=5), Whipple disease (n=3), IBS (n=3), giardiasis (n=2), Graves disease (n=1) • age (y): mean 40+-13, range 18-60 • % F: 47	celiac vs CO IgA EMA	99	1	0	30	99	100	100	96.7
				celiac vs CO IgA/IgG AGA	92	8	3	27	92	90	96.8	77.1

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Vitoria, 2001 Italy	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** n/r **First test:** • n/r **Controls biopsied:** • yes **Biopsy criteria:** subtotal VA **Checked IgA def.** n/r **Studied tests** IgA tTG-ab; IgA EMA **Methodology:** tTG-HR, ELISA; IgA-EMA, IF ME **Cut-off:** for tTG, values of 9 U/mL and more were considered positive; for EMA, reticular pattern of fluorescence in the muscular mucosa at a dilution of serum 1:5 were considered positive	**Celiac Group 1** • 42 biopsy proven CD pts • age: mean 4.2±4.2 y • % F: n/r	**Group 1:** • 28 biopsy proven non-CD disorders • age: mean 6.1+-5.2 y • % F: n/r	celiac vs CO: tTG celiac vs CO: EMA	40 42	2 0	0 0	28 28	95 100	100 100	100 100	93 100

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Vogelsang, 1995 Austria	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/r **Population Type:** • suspected CD **Reference test:** biopsy **First test:** • endoscopic biopsy distal duodenum or Baumgartner-Classen capsule from duodenojejunal flexure **Controls biopsied:** • yes **Biopsy criteria:** modified ESPGAN; flat mucosa; crypt hyperplasia raised IELs **Checked IgA def.** yes; no cases found **Studied tests** IgA-AGA; IgG-AGA; IgA-EMA **Methodology:** ELISA; >95th percentile; ME **Cut-off:** AGA 0.2 AU/mL	**Celiac Group 1** • 49 untreated biopsy-proven CD • age: median 35; range 17-75	**Group 1:** • 53 biopsy-neg controls; median age 31; range 15-79; Crohn's (17); IBS (16); lactase def (7); fibroma (1); duodenitis (1); gastroparesis (3); gastritis (2); chron pancr (1); UC (1); coll colitis (1)	celiac 1 vs control 1	40 36 49	9 13 0	9 14 0	44 39 53	81.6 73.5 100	83 73.6 100	81.6 72 100	83 75 100

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Volta, 1995 Italy	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** n/r **First test:** • n/r **Controls biopsied:** • only disease CO **Biopsy criteria:** Roy-Choudhury criteria **Checked IgA def.** n/r **Studied tests** IgA-EMA on ME; IgA-EMA on HU **Methodology:** IF **Cut-off:** staining of the endomysium around the smooth muscle was considered as a positive result	**Celiac Group 1** • 60 untreated pts with biopsy-proven CD • age (y): median 41, range 14-68 • % F: 70 **Celiac Group 2** • 36 pts with CD on GFD of 12 mos duration	**Group 1:** • 100 disease CO (biopsy proven non-CD in disease CO): ulcerative colitis (n=25), Crohn's disease (n=35), various other GI diseases (n=40) • age (y): median 44, range 25-70 • % F: 68 **Group 2:** • 100 healthy CO (not biopsied) • age: median, range n/r • % F: n/r	celiac vs CO IgA-EMA ME celiac vs CO IgA-EMA HU	57 57	3 3	0 0	100 100	95 95	100 100	100 100	97.1 97.1

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Whelan, 1996 Ireland	**Publication type:** • journal **Study design:** • case control **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** n/r **First test:** • n/r **Controls biopsied:** • only disease CO **Biopsy criteria:** subtotal VA **Checked IgA def.** n/r **Studied tests** HUVEC IgA - human umbilical vein endothelial cells; EMA IgA; (ME) ARA IgA (rat liver); only EMA used for analysis **Methodology:** HUVEC - IF; EMA - IF; ARA - IF **Cut-off:** n/a	**Celiac Group 1** • 25 untreated CD (biopsy-proven) – (UTCD) • age: median, range n/r • % F: n/r **Celiac Group 2** • 16 treated CD on GFD – TCD • age: median, range n/r • % F: n/r	**Group 1:** • 20 disease CO (biopsy proven non-CD in disease CO) - 10 pts with ulcerative colitis and 10 - with Crohn's disease • age: median, range n/r • % F: n/r **Group 2:** • 16 CO with normal intestinal mucosa • age: median, range n/r • % F: n/r	UTCD vs CO: HUVEC UTCD vs CO: EMA ME UTCD vs CO: ARA	25 25 21	0 0 4	0 0 0	36 36 36	100 100 84	100 100 100	100 100 100	100 100 90

Evidence Table 1 (cont'd): Included studies of the sensitivity and specificity of serology for CD

Author, Year, Location	Study Design	Study Population	Control Population	Results								
					4X4 table							
				Comparison	a	c	b	d	Sens	Spec	PPV	NPV
Wolters, 2002 Netherlands	**Publication type:** • journal **Study design:** • cohort **Ethnicity:** • n/a **Population Type:** • n/a **Reference test:** endoscopic biopsy **First test:** • n/r **Controls biopsied:** • yes **Biopsy criteria:** subtotal VA with crypt hyperplasia **Checked IgA def.** n/r **Studied tests** IgA-AGA; IgG-AGA; IgA-EMA; IgA-GP-tTG; IgA-HU-tTG **Methodology:** for AGA-ELISA; for EMA–IF ME; for tTG - ELISA **Cut-off:** for AGA: Ab titers were considered positive if IgA-AGA exceeded 4 U/mL and IgG-AGA exceeded 150 U/mL; for EMA - fluorescence in the muscularis mucosa at a serum dilution equal to or greater than 1:5	**Celiac Group 1** • 52 pediatric pts with biopsy proven CD • age: mean 4.0 y, range 1.1-14.4 y • % F: 73	**Group 1:** • 49 disease CO pts with biopsy proven non-CD • age: mean 5.1 y, range 0.8-19.2 y • % F: 41	CD vs CO: IgA AGA	43	9	10	39	83	86	81	81
				CD vs CO: IgG AGA	43	9	7	42	83	80	86	82
				CD vs CO: IgA EMA	48	4	5	44	92	90	90.5	92
				CD vs CO: anti-GP-tTG IgA	50	2	4	45	96	92	92.6	95.7
				CD vs CO: anti-h-tTG IgA	50	2	0	49	96	100	100	96

HLA DQ2/DQ8

Evidence Table 2: Case-control study evidence for the use of HLA as a marker of CD

Author, Year, Location	Study Design	Study Population	Control Population	Results		
					Control	
				Celiac Group	Group 1	Group 2
Iltanen, 1999, Finland	• case control • monoclonal antibodies used to stain jejunal IELs and mucosal HLA-DR; DQA1*0501 and DQB1*0201 alleles determined	• 21 children with biopsy-confirmed CD • CD criteria: ESPGAN • mean age: 6.1 y, range 0.5-16.3 y • % F: n/r • ethnicity: n/r	**Group 1:** • 67 ethnically-, age-matched pts with biopsy-negative CD • ethnicity: n/r	• DQ2: 19 (90.48) • DQ8: n/a • DQ2 or 8: n/a Prevalence of CD: 0.24	• DQ2: 29.85 Sens: 0.90 Spec: 0.70 PPV: 0.49 NPV: 0.96 • DQ8: n/a • DQ2 or 8: n/a	

Evidence Table 2 (cont'd): Case-control study evidence for the use of HLA as a marker of CD

Author, Year, Location	Study Design	Study Population	Control Population	Results		
				Celiac Group	Control	
					Group 1	Group 2
Sacchetti, 1998, Southern Italy	• case control • used PCR to examine prevalence of HLA heterodimer and HLA DRB104 alleles in healthy subjects, in CD-affected children, and in other age-matched subjects affected by confounding disease	• 122 children with biopsy-confirmed CD • CD criteria: ESPGAN • ethnicity: Italian	**Group 1:** • 32 age-matched pts with GI symptoms but negative biopsy for CD • Ethnicity: Italian **Group 2:** • 116 ethnically-matched healthy adult controls	• DQ2: 106 (86.89%) • DQ8: n/a • DQ2 or 8: n/a	• prevalence of CD: 0.79 • DQ2: 6 (18.75%) Sens: 0.87 Spec: 0.81 PPV: 0.95 NPV: 0.62 • DQ8: n/a • DQ2 or 8: n/a	• Prevalence of CD: 0.51 • DQ2: 31 (26.72%) Sens: 0.87 Spec: 0.73 PPV: 0.77 NPV: 0.84 • DQ8: n/a • DQ2 or 8: n/a

Celiac 2: Incidence and Prevalence of CD

Incidence of CD in the General Population

Evidence Table 3. Incidence of CD in the general population

Study, year; country	Group at risk	Case ascertainment	Incidence	Other observations
Bode, 1996 Denmark	**Region:** County of Copenhagen **Period:** 1976-1991 retrospective **Age groups:** all adults>15 **Size:** 480,581 in 1976; 503,283 in 1992	**Institution(s):** sole 3 teaching hospitals + clinic of region **Register(s):** Discharged Dx w ICD 269-0.01; all small bowel biopsy from path depts; case register of all celiacs **Verification of accuracy:** review of case records **Dx Criteria:** at least 1 biopsy; good response to GFD; gluten challenge with re-biopsy if Dx uncertain **% capture:**	**Outcome measures:** cumulative incidence avg incidence rates adjusted for age/sex **Results:** **# cases:** 101 (64F/37M) **Characteristics of cases:** **median age at Dx:** 40.1 y (range 16-81) **crude incidence:** 1.27/100,000 **cumulative incidence:** 19 y: 198/1000 births	**Women:** **Crude incidence:** 1.55/100,000 **Lifetime cumulative incidence:** 55.8/100,000 **Men:** **Crude incidence:** 0.96/100,000 **Lifetime cumulative incidence:** 35.3/100,000 **Prevalence (1992):** 45.9/100,000

Evidence Table 3 (cont'd). Incidence of CD in the general population

Study, year; country	Group at risk	Case ascertainment	Incidence	Other observations
Collin 1997 Finland	**Region:** Tampere City **Period:** 1975-94 **Age groups:** Adult **Size:** 121,000 in 1970; 147,000 in 1994 **Note:** Screening of high-risk groups in effect Systematic small bowel biopsy during gastroscopy	**Institution(s):** Sole 3 centers that perform gastroscopy; The University Hospital. The City Hospital and the local health centre **Register(s):** Membership list of local Coeliac Society **Verification of accuracy:** All case records and specimen of CD pts were verified **Dx Criteria:** Subtotal or severe partial VA and crypt hyperplasia; clinical or histological improvement on GFD **% capture:** NR	**Outcome measures:** Prevalence: All adult CD pts living in Tampere on Dec 31 1994 per 100 000 population. 5-y Incidence: All adult CD pts dx'ed between 1975 and 1994 per 100,000 pop. **Results:** **# cases:** 301 cases (222 F/79 M) **Characteristics of cases:** **Crude incidence (/100,000 pop/yr):** 1975-79: 1.6 1980-84: 6.8 1985-89: 13 1990-94: 17.2 **Cumulative incidence:** NR	**Median age at Dx:** 39 y (range 1-80) **Prevalence in 1994:** 204/100,000 (95% CI 181-231) **Mode of presentation:** Apparent symptoms: 24% Minor symptoms: 37% Screening: 27% Chance at endoscopy: 13% **Causes for increased incidence:** Use of serologic screening Performance of small bowel biopsy on all pts undergoing gastroscopy Ability of all GP to refer pts to gastroscopy

Evidence Table 3 (cont'd). Incidence of CD in the general population

Study, year; country	Group at risk	Case ascertainment	Incidence	Other observations
Corrao, 1996 Italy	**Region:** Provinces of Turin, Cuneo, Brescia, Umbria region, Sardinia region **Period:** 1990-91 prospective vs retrospective **Age groups:** All ages **Size:** Italian population census in 1991 6,339,194 in 1991 (11.0% Italy); 107,048 live births (9.4% Italy)	**Institution(s):** Dx lists of peds, med, GI depts in all hosp; Dx lists leading Italian hosp **Register(s):** National Health Service records; local Italian Coeliac Society **Verification of accuracy:** capture-recapture method **Dx Criteria:** biopsy without challenge in 47.2% ESPGAN in 52.8% **% capture:** 85.6% **Exclusion(s):** pts residing outside Dx area	**Outcome measures:** crude incidence: #new Dx/yr/100,000 pop cumulative incidence: #cases over period/100,000 births **Results:** **# cases:** 270 (181F/89M) **Characteristics of cases:** **mean age at Dx:** children 3.7; adults 34; overall 21 **Crude incidence:** 2.13/100,000/y **Cumulative incidence (/10,000 births):** 2 y: 5.75 5 y: 8.08 10 y: 10.30 15 y: 11.42	**RR according to gender** (95% CI**):** Male: 1.0 Female: 1.90 (1.48, 2.45) **RR according to age (95% CI):** 0-15: 1.0 16-39:0.33 (0.25-0.44) 40-59:0.21 (0.15-0.30) >60: 0.11 (0.06-0.18)

Evidence Table 3 (cont'd). Incidence of CD in the general population

Study, year; country	Group at risk	Case ascertainment	Incidence	Other observations
Hawkes, 2000 England	**Region:** South Glamorgan **Period:** 1980-95 retrospective **Age groups:** all ages **Size:** Registrar General mid-yr estimates for total pop, pop <16yr, total live births 415,900 in 1995	**Institution(s):** sole 3 teaching hospitals in Cardiff **Register(s):** Local Celiac Society, letters to GP from consultants **Verification of accuracy:** pathology & dietetic records from the 3 Cardiff teaching hospitals **Dx Criteria:** ESPGAN **% capture:** 100%	**Outcome measures:** Crude incidence: age-weighed avg/100,000 pop **Results:** **# cases:** 137 (98F/39M) **Characteristics of cases:** **mean age at Dx:** children 5.3 yrs (range 0.9-14.9); adults 49.1 yrs (range 19.9-88.2) **Crude incidence:** **children (/100,000/yr):** 1981-85: 2.08 1986-90: 2.53 1991-95: 2.15 **adults (/100,000/yr):** 1981-85: 1.32 1986-90: 2.15 1991-95: 3.08 **Cumulative incidence:** NR	

Evidence Table 3 (cont'd). Incidence of CD in the general population

Study, year; country	Group at risk	Screening	Incidence	Other observations	Incidence	Other observations
Hoffenberg 2003 US	**Region:** Denver Colorado **Period:** 1993-99 prospective **Age groups:** Birth to 7 y; 987 for at least 1 y; 386 for at least 5 y **Size:** Sample from 22 346 newborns screened for HLA, i.e. 987 infants from one institution (St Joseph's Hospital). **Ethnicity:** 56% non Hispanic white 30% Hispanic 7% African American 2% Asian American 5% biracial/other **Genotypes:** HLA-DR3/3; DR3/4, DQB1*0302; DR4, DQ8; DR5/7	**Intervention:** HLA type newborn; follow-up of selected genotypes **Follow-up:** CD serology at 9, 15 and 24 months of age, then yearly. If positive tTG on 2 separate occasions, or if positive tTG plus clinical suspicion, evaluation for small bowel biopsy. **CD serology:** EMA IgA 1993-98; tTG IgA 1998-99; Retesting of EMA positive samples with tTG once test available; Total IgA; tTG IgG used on IgA deficients. **Dx criteria:** Either positive tTG plus biopsy (Marsh 2 or greater), or two consecutive tTG positives 6 months apart	**Outcome measures:** Time to the event of evidence of CD; Cumulative probability of being event-free for the entire population; Cumulative incidence of evidence of CD, stratified by genotype (DR3/3; DR3/x, DRx/x); RR evidence of CD by genotype **Results:** **# cases:** 40 tTG pos at least once; 19 with evidence of CD; 10 biopsy-confirmed; 9 with pos tTG at least twice **Characteristics of cases:** 13F/6M Mean age 4.6 (range 2.6-6.5) 84% non-hispanic whites **Crude incidence:** NR **Cumulative incidence at age 5:** 9/1000 births (95% CI 4-20) **Cumulative incidence at age 5 according to genotype:** HLA-DR3/3: 32/1000 (95% CI 10-110) HLA-DR3/x: 34/1000 (95% CI 30-117) HLA-DR3 neg: 3/1000 (95% CI 0-27)	**RR according to gender:** Female: 3.34 (95% CI 1.00-10.9) **RR according to ethnicity:** Non-hispanic whites: 3.33 (0.7-12.5) **RR according to genotype** (Compared to HLA DR3 negatives): HLA-DR3/3: 9.1 (95% CI 1.7-48) HLA-DR3/x: 5.6 (95% CI 1.5-21)		

Evidence Table 3 (cont'd). Incidence of CD in the general population

Study, year; country	Group at risk	Case ascertainment	Incidence	Other observations
Ivarsson, 2003, Sweden Duplicate: Ivarsson Acta Paediatrica 2000;89:165	**Region:** Entire Sweden **Period:** 1973-97 prospective and retrospective **Age groups:** Children • 0-2 y • 2-15 y **Size:** 258,683 in 1973; 623,439 in 1991 **Dx Criteria:** ESPGAN	**Institution(s):** Prospective reporting from 9 departments of pediatrics **Register(s):** Sweden's National Child health program; central register of CD cases in children <15; Statistics Sweden **Verification of accuracy:** local registers **% capture:**	**Outcome measures:** Incidence rate: #new cases/100,000 PYs; cumulative incidence: # cases up to age/1000 birth in same cohort **Results:** **# cases of CD:** 2151 (1340F/811M) **Characteristics of cases:** **Crude incidence (/100,000PY):** 1973-84: 0-2: 65 (57-74) 1987-94: 0-2: 198 (186-210) 1997: 0-2: 51 (36-70) **Cumulative incidence at 2 y:** 1995: 1.7 (95% CI 1.3-2.1)/1000 births	**RR according to age:** 0-2 y: 1.0 2-15: 0.031 (0.022-0.043) **RR according to gender:** M: 1.0 F: 1.9 (1.7-2.1) **RR according to period:** 1973-84: 1.0 1985-95 1.7 (1.2-2.5) 1996-97 6.8 (4.5-10)

Evidence Table 3 (cont'd). Incidence of CD in the general population

Study, year; country	Group at risk	Case Ascertainment	Incidence	Other observations
Jansen, 1993 Netherlands	**Region:** Entire country **Period:** 1975-91 retrospective **Age groups:** all ages **Size:** Central Bureau for statistics 14,892,574 in 1990	**Institution(s):** **Register(s):** Dutch Coeliac Disease Society for 1992 **Verification of accuracy:** **Dx criteria:** at least 1 biopsy **% capture:** 97%	**Outcome measures:** Incidence: # new cases/100,000 pop/yr; Prevalence rate: # cases/100,000 **Results:** **# cases:** 1983 **Characteristics of cases:** **Crude incidence (/100,000/yr):** 1981-88: 0.65 1988-90: 0.8 1991-92: 1.0	**Prevalence** 1990: 7.9/100,000 (95% CI 6.7-9.3) 1991: 11.3/100,000 (95% CI 9.5-1.0) 1992: 12.7/100,000 (95% CI 11.0-14.5)

Evidence Table 3 (cont'd). Incidence of CD in the general population

Study, year; country	Group at risk	Case ascertainment	Incidence	Other observations
Lopez Rodriguez, 2003 Spain	**Region:** Caceres, south-west Spain **Period:** 1981-99 retrospective **Age groups:** Children 0-14 y; Spanish National Statistics Institute **Size:** 65 137 children in 1998; 98 641 in 1986 66 496 in 1996	**Institution(s):** San pedro de Alcantara hospital, Province referral center for biopsy **Register(s):** **Verification of accuracy:** clinical records **Dx Criteria:** ESPGAN **% capture:**	**Outcome measures:** crude incidence: # cases/100,000 pop/yr **Results:** **# cases:** 157 (90F/67M) **Characteristics of cases:** **mean age at Dx:** 1981-90: 37.4+/-47.4 mo 1991-99:43.9+/-43.7 mo **Crude incidence (/100,000/yr):** 1981-90: 6.87 (5.26-8.83) 1991-99: 16.04 (12.99-19.59)	**RR according to period:** 1981-90: 1 1991-99: 2.31 (1.61-3.31) **RR according to age:** 4-15 y: 1.0 0-4 y (1981-90): 18.2 0-4 y (1991-99):42.04 **% with typical clinical presentation:** 1981-90: 83.6% 1991-99: 58.3% **Significant positive correlation between age at Dx and age of introduction of gluten:** 1981-90: r=0.296 , p=0.0211 1991-99: r= 0.293, p=0.0037

Evidence Table 3 (cont'd). Incidence of CD in the general population

Study, year; country	Group at risk	Case ascertainment	Incidence	Other observations
Magazzu, 1994 Sicily	**Region:** Entire country **Period:** 1975-89 retrospective **Age groups:** children **Size:** 69,945 births in 1989	**Institution(s):** All 4 Sicilian centers of pediatric GI in Catania, Messina and Palermo **Register(s):** Registrations from all 62 Sicilian health authorities; pt list of each GI pediatric centers; pt list of gluten-free products consumption **Verification of accuracy:** Chart review of cases; personal interviews; contact of family pediatrician **Dx Criteria:** ESPGAN **% capture:** **Exclusion(s):** no proof of remission on GFD; at least subtotal VA on biopsy; pts not traced back (1.5%)	**Outcome measures:** cumulative incidence rate by birth cohort: #new cases/#live birth in same birth cohort (95%CI); incidence density: # cases/(#birth in cohort/#yrs of follow up)/15 y obs period **Results:** **# cases:** 1074 (607F/467M) **Characteristics of cases:** 99.4% Caucasian **Crude incidence:** **Cumulative incidence:** 1980 birth year: 1.19/1000 child.yr, 95% CI 0.96-1.45 1984 birth yr: 1.16/1000 child.yr, 95% CI 0.92-1.42 1989 birth yr: 0.13 /1000 child.yr, 95% CI 0.06-0.23	

Evidence Table 3 (cont'd). Incidence of CD in the general population

Study, year; country	Group at risk	Case ascertainment	Incidence	Other Observations
Maki, 1990 Finland	**Region:** Tampere City **Period:** 1961-84 **Age groups:** Children **Size:** 131,394 live births 1960-84 **Exclusion(s):** Cases not born in a certain strict area around the city	**Institution(s):** Department of Paediatrics, University Central Hospital of Tampere **Register(s):** nil **Verification of accuracy:** Questionnaire to pts and their parents; hospital medical records; Child health center charts **Dx Criteria:** Small bowel biopsy; ESPGAN in 44% **% capture:** NR	**Outcome measures:** Crude incidence: # cases/100,000pop/yr **Results:** **# cases:** 96 **Characteristics of cases:** **Crude incidence:** 1964-73: 10.12/100,000 PYs 1974-83: 3.46/100,000 PYs 1960-84: 2.28/100,000 PYs **Cumulative incidence:**	Significant correlation between the age at Dx and duration of breastfeeding Decreased incidence in 0-2; increased incidence in 2-15; increased subclinical presentation in children

Evidence Table 3 (cont'd). Incidence of CD in the general population

Study, year; country	Group at risk	Case Ascertainment	Incidence	Other Observations
Talley, 1994 US	**Region:** Olmstead County **Period:** 1960-90 retrospective all ages **Age groups:** **Size:**	**Institution(s):** **Register(s):** Rochester Epidemiology Project **Verification of accuracy:** Medical records reviewed; biopsy reviewed **Dx Criteria:** **% capture:** **Exclusion(s):** living outside territory at time dx	**Outcome measures:** **Results:** **# cases:** 28 (19F/9M) **Characteristics of cases:** **Crude incidence:** Overall: 1.2 1960-69: 0.9 1970-79: 0.7 1980-90: 1.7 **Cumulative incidence:**	0-14:0.4/100,000PYs 15-44:0.7 45-64:2.5 >65 2.1 prevalence 1991: 21.8/100 000 **Median age at Dx:** median 50 (interQ range 35-62)

Evidence Table 3 (cont'd). Incidence of CD in the general population

Study, year; country	Group at risk	Case ascertainment	Incidence	Other Observations
Weile, 1993 Denmark	**Region:** Copenhagen County **Period:** 1960-88 retrospective **Age groups:** children **Size:** 1,972,864 live births **Dx criteria:** Biopsy-proven (90%); clinically suspected CD (10%)	**Institution(s):** **Register(s):** National Central register of Diagnosis 1977-87 Local register of pts admitted for SB biopsy Celiac Patient Society **Verification of accuracy:** Data twice thoroughly evaluated **% capture:**	**Outcome measures:** Cumulative incidence: #cases/1000 birth in birth cohort **Results:** **# cases:** 176 (103F/73M) **Characteristics of cases:** **Crude incidence:** 1988: 0.102/1000 births **Cumulative incidence:** median: 0.089/1000 live births (range 0-0.182) age 5: 0.118/1000 births	

Prevalence and Incidence in the General Population—Different Geographic and Racial/Ethnic Populations

Evidence Table 4: Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Borch, 2000 Sweden Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** biopsy; IgA & IgG-AGA; IgA-EMA ME **Biopsy criteria/description:** Alexander Grade **Confirmatory test:** n/r **Checked IgA def.** n/r	**Ethnicity:** 459 Swedish; 17 Northern Europeans; outside of Northern Europe **Patient type/# screened:** n=2,000 healthy adults invited to participate in endoscopy study of relation of H.pylori to duodenitis; 482 agreed to participate **Demographics:** age range: 34-75 y **Incidence:**	first serology: 96 confirmation serology: 7 biopsy proven: 9			Not all systematically biopsied; only those with suggestive endoscopic features

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Carlsson, 2001 Sweden Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** AGA, cut-off at 25AU; indirect IF EMA, cut-off at titre >5; biopsy using Watson capsule **Biopsy criteria/description:** used Waston capsule; revised ESPGAN? for classification: normal, subnormal (villous length/crypt length<2, increased number of inflammatory cells in the muscosa with or without damage to the surface epithelium and the brush border), or total VA (flat mucosa) **Confirmatory test:** biopsy **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** unselected; all children born July 1992 through June 1993 **Demographics:** n=690 (out of 1287/3007 children initially contacted, excluding 22 known CD cases) mean age: 32 mos; range: 27-41 mos **Incidence:**	5.1% (35/690) had either EMA or AGA positive; (13/690) EMA alone: by biopsy: 1.6% (11/35/690) serology positives underwent jejunal biopsies, 11 of them became biopsy-confirmed CDs			

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Catassi, 1996, Italy Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** IgA or IgG-AGA **Biopsy criteria/description:** ESPGAN **Confirmatory test:** EMA and biopsy **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** School age children **Demographics:** n=17,201; age range: 6-15 y **Incidence:**	1289/17201 (7.5%) AGA-IgG or IgA pos; confirmed with EMA=111/17201; biopsy on 98/111 was pos in 75 + 7 who had no biopsy but CD by various investigations			

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Catassi, 2000, Italy Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** IgG-AGA (7 AU); IgA-AGA (15 AU); IgA-EMA indirect IF (1:5 dilution); biopsy **Biopsy criteria/description:** ESPGAN; Marsh; grade I = isolated increase gamma delta IEL count, grade II= increase gamma delta lymphocyte count with shortened villi/crypt hyperplasia, grade III= subtotal VA **Confirmatory test:** biopsy **Checked IgA def.** yes, 6 found	**Ethnicity:** n/a **Patient type/# screened:** general public, students **Demographics:** n=2,096; pedi age range: 11-15 y % F: 49.5 **Incidence:**	0.86% (18/2,096)			

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Collin, 2002 Finland Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** biopsy **Biopsy criteria/description:** ESPGAN **Confirmatory test:** biopsy **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** 1. GERD group: regurgitation or heartburn; 2. dyspepsia group; 3. suspected CD **Demographics:** n=9,971; adolescent and adult median age: 58 y; range: 12-93 y % F: 63.5 **Incidence:**	GERD: 0.61% (18/2974)	dyspepsia: 0.77% (41/5347)	CD: 5.33% (88/1650)	

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Corazza, 1997 Republic of San Marino Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** indirect IF EMA titre >1:5; biopsy **Biopsy criteria/description:** n/r **Confirmatory test:** biopsy **Checked IgA def.** no, but mentioned as such that it could have caused some misclassification of pts, but the effect should be minimal given the powerful sensitivity and specificity of EMA test	**Ethnicity:** n/a **Patient type/# screened:** random sample stratified for age and sex **Demographics:** n=2,237; adult median age: 44 y; range, 20-87 y % F: 53.2 **Incidence:**	by both EMA and biopsy: 1 in 559 pts, or 1.79 per 1,000 (0.18%)			

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Csizmadia 1999 Netherlands Duplicate: no	**Publication type:** Journal (research letter) **Study design:** cross-sectional prevalence **Test/methodology:** IgA-EMA (methodology n/r) **Biopsy criteria/description:** n/r **Confirmatory test:** small bowel biopsy, subset of 27 had HLA typing for DQ2 **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** 6,127 children between ages of 2-4 y general population **Demographics:** 6,127 pediatric pts age: range 2-4 y % F: n/r **Incidence:** Time period: between May 1997-June 1998	1.2% (75/6127) by IgA-EMA, 18/75 refused small bowel biopsy; 0.51% (31/75/6127) VA (CD)			26/27 with VA had the allele HLA-DQ2; prevalence 1:198 in children 2-4 y

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Dickey 1992, Ireland Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** IgA-AGA **Biopsy criteria/description:** no biopsy performed **Confirmatory test:** n/r **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** healthy blood donors **Demographics:** n=443; adults, age range 18-65 y **Incidence:**	By first serology: 5			

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Fasano, 2003, USA Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** EMA-IF; ME or HUC; positive at 1:10; all positive EMA tested with human tTG ELISA positive at 2 SD above mean of healthy controls; HLA DQ2 and DQ8 **Biopsy criteria/description:** **Confirmation test:** htTG; biopsy; also small subset 98 EMA positive and 114 EMA neg had HLA DQ2/8 tested **Checked IgA def.** • n/r	**Ethnicity:** 94% White; 3% Black; 1.5% Hispanic, 1% Asian, 0.5% other **Patient type/# screened:** 9,019 at risk of CD; 4,126 not at risk **Demographics:** at risk: symptoms of CD (1,326 children, 1,909 adults); CD associated disorders; 4,508 1st deg relatives; 1,275 2nd deg relatives; not at risk: 2,000 blood donors (mean age 39 y, range 19-65 y); 1,119 school children (mean age 12.3 y, range 6-18 y); 1,007 adults and children for routine physical (mean age 39 y, and 13.7 y, range 19-71 y and 2-18 y, respectively) **Incidence:**	1) at risk: a) 1st deg relatives-205/4508 (4.55%); children-54/1294 (4.17%); adults-151/3214 (4.70%); b) symptomatic adults-28/1910 (1.47%); children-53/1326 (4.00%) 2) not at risk-1/4126 (0.75%); adults-27/2845 (0.95%); children-4/1281(0.31%); biopsy in EMA pos-Marsh I-0%; II-30/116 (25.9%); IIIa-46/116 (39.7%); IIIb-24/116 (20.7%); IIIc-16/116 (13.8%); HLA DQ2-76/98 (78%); DQ8-16/98 (16%); DQ2 and 8-6/98 (6%); all EMA pos were also tTG pos			116/350 biopsied

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Green, 2000 USA Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** EGD, biopsy **Biopsy criteria/description:** n/r **Confirmatory test:** n/r **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** n=1,749 adults; suggestive endoscopic features of CD while undergoing routine endoscopy **Demographics:** n/r **Incidence:**	Biopsy proven: 9			Not all systematically biopsied; only those with suggestive endoscopic features

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Grodzinsky, 1996 Sweden Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** IgA-AGA; both IgA- and IgG-AGA **Biopsy criteria/description:** n/r **Confirmatory test:** ? **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** healthy adult blood donors **Demographics:** n=1,866; median age 38.5 y, range 18-64 y **Incidence:**	By first serology: 124 by confirmation serology: 11 by biopsy: 7			IgA or IgG-AGA confirmed by having both and by biopsy; prevalence by IgA-EMA n/r

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Hovdenak, 1999 Norway Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** IgA and IgG-AGA, ELISA, cut-off levels: for IgA ≥0.35 and for IgG ≥0.90; IgA-EMA, IF, cut-off n/r **Biopsy criteria/description:** endoscopic biopsy; at least 3 biopsy specimens taken; classification as either normal, partial VA or subtotal VA **Confirmatory test:** biopsy **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** 2,069 healthy blood donors screened for CD; 1st level of screening: measuring of IgA and IgG AGA; 2nd level of screening: measuring IgA-EMA in AGA positives; 3rd level of screening - biopsy in IgA EMA positives **Demographics:** n=2,069; age: median 39 y, range 18-67 y M/F ratio: 1.65 **Incidence:**	Prevalence of CD in the screening group was 1:340 (7/2069); prevalence of test positivity: 83 of 2069 were positive for AGA; EMA was positive in 8 of these 83 pts; biopsy proven CD was diagnosed in 7 of these 8 pts			Biochemical analysis showed iron deficiency in 2 pts, hypocalcemia in 1 pts and low serum zinc in 5 pts; 4 pts had osteoporosis and another 4 had decreased vitamin E serum concentration

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Ivarsson, 1999 Sweden Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA and IgG AGA - ELISA, cut-off n/r; IgA EMA - IF on a ME, cut-off dilution level varied from 1/20 to 1/320; positive if presence of characteristic reticulin-like staining pattern; serum IgA level measurement using routine nephelometric method, level below 0.05 gL was defined as IgA deficient **Biopsy criteria/description:** criteria for the diagnosis of CD was biopsy demonstrating enteropathy grade III to IV according to Alexander **Confirmatory test:** endoscopic biopsy **Checked IgA def.** yes, using routine nephelometric method; 0.2% (4/1892) pts were found to have IgA deficiency	**Ethnicity:** n/a **Patient type/# screened:** 1,894 individuals taken randomly from 1994 WHO MONICA study population and screened for CD **Demographics:** n=1,894 age (y): median 50, range 25-74 % F: 50 **Incidence:**	Prevalence of CD was 5.3 per 1000 (10/1894); prevalence of newly diagnosed CD was at least 4 per 1000 (8/1892) - (1 woman with positive IgA EMA refused biopsy); as for the prevalence of test positivity: IgA and/or IgG AGA - positive in 23% (438/1892); IgA EMA - positive in 0.5% (9/1892); all CD pts had elevated IgA EMA			CD was more common amongst women (7 F and 3 M) and the older age groups, with the highest prevalence in the interval 55-64 y - 50%

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Jager, 2001 Germany Duplicate: no	**Publication type:** Journal **Study design:** Cross-sectional prevalence **Test/methodology:** IDDM-associated antibodies: islet cell antibodies (ICA) - detected by IF, insulin autoantibodies (IAA) - radioimmunoassay, anti-IA-2 antibodies, and anti-GAD65 antibodies (anti-GADA) - both radioligand binding; thyroid disease-associated antibodies: anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-TG) - both ELISA; pernicious anemia-associated antibodies: anti-gastric parietal cell antibodies (anti-GPC) - IF; adrenalitis-associated antibodies: anti-adrenal cortex antibodies - IF; celiac disease-associated antibodies: IgA AGA, IgG AGA, IgA-tTG - all ELISA **Biopsy criteria/description:** n/r **Confirmatory test:** none **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** 197 pts with a new onset of IDDM diagnosed according to WHO criteria; 882 first-degree relatives; 150 healthy controls without a family history of IDDM **Demographics:** 197 pts with IDDM (age (y): median 16, range 5-27, 43% F); 882 first-degree relatives - 485 were parents (age (y): median 43, range 22-59), 382 siblings and 15 offspring of IDDM pts (age (y): median 16, range 2-41) **Incidence:**	Recent-onset IDDM (n=197): IgG AGA - 10.2%; IgA AGA - 7.6%; anti-tTG IgA - 9.7%; at least 1 antibody positive - 16.8%	First-degree relatives (n=882): IgG AGA - 5.6%; IgA AGA - 2.6%; anti-tTG IgA - 3.2%; at least 1 antibody positive- 7.3%	Healthy control subjects (n=150): IgG AGA - 3.2%; IgA AGA - 2.0%; anti-tTG IgA - 2.6%; at least 1 antibody positive- 4.6%	IDDM associated antibodies and thyroid antibodies were significantly more frequent both in recent-onset IDDM group and first-degree relatives, compared to controls (p<0.05); the relevance of IgG/IgA AGA and IgA tTG was significantly higher in the group of recent-onset IDDM compared to first degree relatives and controls (p<0.05), but the difference between first-degree relatives and controls did not reach statistical significance; the overall frequency of GPC and adrenal antibodies did not differ significantly among the groups; as for coexistence of antibodies, recent-onset IDDM pts presented with 27% of the subjects testing antibody-positive-specific for 2 or more the envisaged disorders compared with 3.1% in the group of first-degree relatives and 0% of control population (p<0.05); recent-onset IDDM (n=197): IDDM-associated antibodies: ICA 82.1%; anti-GADA - 76.0%; anti-IA-2 antibodies - 44.4%; IAA - 37.8%; at lease 1 antibody - 93.4%; Thyroid disease-associated antibodies: anti-TPO+-TG antibodies - 18.4%; pernicious anemia-associated antibodies: anti-GPC - 5.6%; adrenalitis-associated antibodies: anti-adrenal cortex antibodies - 1.0%; first-degree relatives (n=882): IDDM-associated antibodies: ICA 4.9%; anti-GADA - 7.6%; anti-IA-2 antibodies - 4.0%; IAA - 3.4%; at lease 1 antibody - 11.6%; Thyroid disease-associated antibodies: anti-TPO+-TG antibodies - 7.8%; pernicious anemia-associated antibodies: anti-GPC -6.0%; adrenalitis-associated antibodies: anti-adrenal cortex antibodies - 1.1%; healthy control subjects (n=150): IDDM-associated antibodies: ICA 1.3%; anti-GADA - 2.6%; anti-IA-2 antibodies - 0.6%; IAA - 0.6%; at lease 1 antibody - 4.0%; Thyroid disease-associated antibodies: anti-TPO+-TG antibodies - 3.2%; pernicious anemia-associated antibodies: anti-GPC -3.2%; adrenalitis-associated antibodies: anti-adrenal cortex antibodies - 0.7%

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Johnston, 1998 UK Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA AGA - ELISA, normal range of 0-99 (97.5th percentile); IgA EMA - IF on a ME, positive was taken at a titre of 1:5 **Biopsy criteria/description:** enteropathy consistent with CD was considered to include severe partial VA, sub-total or total VA **Confirmatory test:** biopsy; Watson-Crosby capsule; biopsy done in 51 out of 87 pts in MONICA 1991 survey pts and in 20 out of 72 pts in MONICA 1983 survey group **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** 1) MONICA 1991 survey study: 89 subjects tested positive for CD serology taken from 1823 subjects randomly tested for CD (2 pts were excluded from further analysis because they had CD diagnosis prior to follow-up of the screening program, but included in the assessment of prevalence); 2) MONICA 1983 survey study: 72 CD pts out of 102 who consented to a follow-up of 11.2 y (range 11.3-11.9) **Demographics:** MONICA 1991: 89 subjects with positive CD serology; age (y): mean 50.9, range n/r, 49.4% F; age- and sex-matched 89 controls: age (y): mean 51.1, range n/r, 49.4% F MONICA 1983: 72 with a known CD; age (y): mean 58.1, range n/r, 53% F; no controls were included in this survey **Incidence:**	MONICA 1991: 0.82% [15 (2 with a CD prior to screening program and 13 - screening revealed CD pts) out of 1823] biopsy proven CD making a prevalence of 1:122	MONICA 1983: the estimated prevalence for CD from this survey is 4/1206, or 1:301; if the 2 deceased subjects are included prevalence raises to 6/1206, or 1:201		MONICA 1991 survey: comparing the untreated CD group with controls, there were no differences between symptom profile or laboratory parameters: attendances at their General Practitioners for diarrhea, fatigue, anemia or weight loss; MONICA 1983 survey: comparison of standardized mortality rates between serology-positive subjects and the general population showed no significant difference (4 deaths observed from cancer during a follow-up, compared to the 4.28% (95% CI 1.09, 10.24) expected cancer deaths, giving a relative risk of cancer deaths as 0.94 (95% CI 0.3, 2.4); 13 deaths in total observed during follow-up, compared to 14.11 (95% CI 6.92, 22.23) expected deaths, giving relative risk of all deaths as 0.92 (95% CI 0.5, 1.6)

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Kolho, 1998 Finland Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** EMA – IF HUC; methodology n/r **Biopsy criteria/description:** capsule or endoscopic biopsy; ESPGAN criterias; CD3-positive T cell calculation (limit for high cell number was 77 cells/mm; limit for a moderate cell number was 63 cells/mm); gamma/delta T-cell receptor-bearing cell calculation (limit for a high cell number was 8.2 cells/mm) **Confirmatory test:** capsule or endoscopic biopsy **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** not at risk: 1,070 adults of Finnish ancestry screened for CD **Demographics:** 1,070 adult population with no clinical signs of CD screened at Helsinki University General Hospital during 1996 **Incidence:**	11 out of 1,070 were positive for IgA EMA; 8 out of these 11 were found to have CD on biopsy, giving the prevalence of CD in this group 1:130			In 7 pts agreeing to start GFD, a 2nd biopsy done after 6 mos, revealed villous structural changes to normal in 6 pts and in 1 to subtotal atrophy

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Maki, 2003 Finland Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA-tTG, Celikey assay with low-cut off of 5U/mL; IgG-tTG, ELISA; IgA- and IgG-EMA, IF; total serum IgA - nephelometerical determination with serum levels of <0.05 g/L indicative of IgA deficiency; HLA- DR; DQ2 and DQ8 **Biopsy criteria/description:** endoscopic biopsy; the ratio of villous height and crypt depth less than 2 was considered to be indicative of CD **Confirmatory test:** biopsy in children with IgA EMA and IgA-tTG positivity (in 2001) **Checked IgA def.** yes	**Ethnicity:** n/a **Patient type/# screened:** 3,654 schoolchildren **Demographics:** asymptomatic schoolchildren median age: 12 y, range 7-16 y at the time of 1st sampling (1994) **Incidence:**	Prevalence of CD was 1:99 (37/3654); prevalence of test positivity for CD was 56/3654; 10 of these were identified by symptoms, and of remaining 46, 27 had abnormal biopsy. all but two (52) of antibody pos pts had either HLA-DQ2 or the HLA-DQ8 haplotype; Prevalence of combination of antibody positivity and CD-associated HLA haplotype was 1 in 67			Unclear if 10 pts screened with serology were biopsied or not (abstract vs result table)

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Mazzeti, 1992 Italy Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** IgA-AGA; biopsy **Biopsy criteria/description:** atrophic or completely absent villi **Confirmatory test:** n/r **Checked IgA def.** n/r	**Ethnicity:** n/r **Patient type/# screened:** n=3,022; Roman school children **Demographics:** age range: 13-15 y olds **Incidence:**	By first AGA-IgA: 19 biopsy proven: 18			Not all systematically biopsied; only those with suggestive endoscopic features

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Not, 1998, USA Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgG and IgA-AGA - ELISA (goat immunoglobulin) cut-off was above mean ± 2 SD; IgA-EMA (IgA-AGA or IgG-AGA) - indirect IF on either ME or HU, cut-off n/r **Biopsy criteria/description:** n/r **Confirmatory test:** no biopsy in the 96 IgA/IgG pos or 8 EMA positive pts; HLA haplotype typed in 4 EMA-positive and 23 EMA-negative donors; all 4 EMA-positives carried CD-associated alleles: 3 had DQA1*0501 and DQB1*0201 haplotype and 1 - DQA1*03 and DQB1*0302 **Checked IgA def.** yes; none of 86 donors with positive IgG AGA and negative IgA AGA/EMA had IgA deficiency	**Ethnicity:** 1,740 Caucasians (87%), 230 African-American (11.5%), and 30 Asians (1.5%) **Patient type/# screened:** 2,000 healthy blood donors **Demographics:** mean age: 39 y % F: 48 **Incidence:**	Prevalence of test positivity: 4.8% (96/2000) for IgA and/or IgG; 0.4% (8/2000) for EMA			No biopsy performed to diagnose CD; Confirmatory test: HLA DQA1& DQB1

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Pittschieler, 1996 Italy Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA- & IgG-AGA; IgA-EMA; biopsy **Biopsy criteria/description:** partial or total VA **Confirmatory test:** ? **Checked IgA def.** n/r	**Ethnicity:** 2,778 German; 1,837 Italian **Patient type/# screened:** healthy consenting adults **Demographics:** n=4,615; median age (y) 36.6; range 18-82 **Incidence:**	By first serology: 140 By confirmation serology: 9 By biopsy: 9			

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Riestra, 2000 Spain Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** IgG/IgA-AGA-ELISA; values above 25 (children) and 34 (adults) AU for IgA or above 46 (children) and 42 (adults) AU for IgG were considered positive; IgA-EMA, IF, sera manifesting fluorescence at a titre of at least 1:5 was considered positive; The study was conducted as a 1) two step (determination of IgA/IgG AGA, if positive measuring IgA-EMA); and a 2) one-step protocol (measuring IgA-EMA) **Biopsy criteria/description:** endoscopic biopsy; Marsh **Confirmatory test:** EMA- indirect IF ME; titre≥1/5; biopsy in IgA and IgG pos/IgG AGA pos with IgA deficiency or isolated EMA positives; HLA DQ2 **Checked IgA def.** yes; none were found to have IgA deficiency	**Ethnicity:** n/a **Patient type/# screened:** 1,170 randomly selected individuals from general population **Demographics:** age (y): mean 44.9+-20.9; range 2-89; 55.3% F **Incidence:**	overall prevalence of CD was 2.6:1000; in two-step screening prevalence rate was 0.8:1000 (1/1170, 95% CI 0-55%); in one-step screening prevalence was 1.7:1000 (2/1170, 95% CI 0-6.9%); as for test positivity: IgA or IgG AGA was positive in 15% (174/1170); 1/174 confirmed with EMA and biopsy; 1 CD biopsy proven CD was confirmed even if AGA and EMA were negative; HLA-DQ2 allele was found in 2/3 new CD pts			

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Rostami, 1999 Netherlands Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** IgA-EMA, IF; IgA-nephelometry; methodology n/r **Biopsy criteria/description:** EPSGAN; Marsh **Confirmatory test:** endoscopic biopsy; endoscopically guided capsule (Fujinon) **Checked IgA def.** yes; none were found to have IgA deficiency	**Ethnicity:** n/a **Patient type/# screened:** 1,000 healthy blood donors **Demographics:** n/r	Prevalence of CD in a healthy donors was 1 in 330 (3/1000); as for the prevalence of test positivity: 3/1000 were positive for EMA; biopsy in all of these 3 confirmed CD: 2/3 Marsh IIIb; 1/3 Marsh II			All 3 EMA positive pts with CD carried the known susceptibility alleles for CD - HLA-DQA1*0501 and HLA-DQB1*0201

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Rutz, 2002 Switzerland Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** IgA-EMA, indirect IF on ME; IgA-tTG- ELISA with lower threshold value 0.2 g/L; IgG-AGA and IgA-AGA **Biopsy criteria/description:** Marsh criteria; endoscopic biopsy **Confirmatory test:** endoscopic biopsy **Checked IgA def.** yes (0/1450)	**Ethnicity:** n/a **Patient type/# screened:** 1,450 students **Demographics:** age range 12-18 y; 871 (60.1%) F	Prevalence of CD was 1 in 132 (0.75%; 11/1450); as for the prevalence of test positivity: 11/1450 EMA/tTG positive; 10/11 (1refusal) EMA/TTG/AGA/AGG positive (second level of screening); 9/10 (1 refusal) biopsied: 8/9 Marsh III			Assessing prevalence of CD authors included 2 pts who were EMA and TTG positive but refused biopsy as well as 1 pts with positive tests and a normal mucosal histology, calling it latent CD; biopsy proven CD was diagnosed in 8 pts, but prevalence was calculated taking into account 11 pts

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Sanders, 2003 UK Duplicate: no	**Publication type:** Journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgG and IgA - ELISA; EMA-indirect IF of ME; methodology n/r **Biopsy criteria/description:** Revised Marsh **Confirmatory test:** biopsy **Checked IgA def.** yes	**Ethnicity:** n/a **Patient type/# screened:** 1,200 randomly selected individuals divided in 2 groups: visitors and pts: 1) 609 pts with a non CD-related symptoms in 338; 2) visitor group 591 individuals with a non-CD associated symptoms found in 409 (69.2%) **Demographics:** 1) pts group: age (y): median 48, range 16-91; 64.4% F; 2) visitors group: age (y): median 45, range 18-85; 61.1% F **Incidence:**	Prevalence of CD in primary care population was 1% (12/1200; 95% CI 0.4-1.3%); as for the prevalence of test positivity: 13.5% (162/1200) were antibody positives: 139 - IgG AGA positive, 10 - IgA AGA positive; 4 both IgA/IgG AGA positive, 3 - only EMA positive, 4 - EMA and IgG AGA positive; 2 all antibody positive; 23 pts were eligible for biopsy; out of 22 biopsies (1 pts refused) CD was confirmed in 12 pts			In the whole group of 1,200 screened individuals there were 3 subgroups of pts suffering from: 1) IDA - n=64 (5.3%); 2) IBS - n=123 (10.25%); and 3) fatigue - n=92 (7.7%); prevalence of CD in IDA group was 4.7% (3/64, 95% CI 0-9.8%); prevalence of CD in IBS group was 3.3% (4/123, 95% CI 0.1-0.6%); prevalence of CD in the fatigue group was 3.3% (3/92, 95% CI 0-7%)

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Sjoberg, 1994 Sweden Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgG AGA- ELISA, cut-off 330; IgA AGA- cut-off 8.5; (arbitrary cut-off values adopted based on normal samples) **Biopsy criteria/description:** Marsh; Watson Capsules **Confirmatory test:** biopsy **Checked IgA def.** n/a	**Ethnicity:** n/a **Patient type/# screened:** 1) 1,537 consecutive healthy blood donors; 2) 384 school children; 3) 944 women **Demographics:** 1) age (y): mean 38, range 19-70; 27.3% F; 2) 12 y; 51% F; 3) 57 y women only **Incidence:**	Prevalence of CD in blood donors was at least 1 in 1,500; as for test positivity: 22/1537 (1.43%) pts were positive for IgG and IgA AGA; 13 of these 22 pts were biopsied and 1 of 13 had biopsy confirmed CD	12 y old children- 15/384 (3.9%) were positive for IgG and/or IgA AGA	57 y old women- 11/944 (1.17%) were positive for IgG and/or IgA AGA;	No biopsy results for IgA IgG positive school children and middle aged women was reported

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Sjoberg, 1999 Sweden Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA-AGA, ELISA values above 8.5 arbitrary units were considered positive; IgG-AGA, ELISA values above 330 arbitrary units were considered positive; EMA, IF ME **Biopsy criteria/description:** subtotal and total VA considered diagnostic of CD. Infiltrative lesions, i.e., increased level of IELs were also considered as CD **Confirmatory test:** small bowel biopsy **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** 1,970 blood donors **Demographics:** 685 women 1,285 men (adults) mean age: 41.2 y, range 18-70 y % F: 35 **Incidence:** Time period: between Oct. 1996-Feb.1997 (4 mos)	Positive results from 1970 pts IgG AGA- 60/1970 (3%) IgA AGA- 150/1970 (7.6%); both IgA and IgG- were 25/210 for a total of 185/1970 (9.4%) who had either IgA or IgG. Those 185 serum samples were analysed for EMA 3/185 positive 3 had small bowel Bx, 2 subtotal VA, 1- total VA. One had classic CD and 2 had infiltrative lesions and were on GFD with improvement. Thus prevalence rate for confirmed CD 4:1970 (0.20%) if infiltrative lesions regarded as CD prevalence 6:1970 (0.30%)			

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Trevisol, 1999 Italy Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA-EMA; biopsy **Biopsy criteria/description:** subtotal or total VA **Confirmatory test:** ? **Checked IgA def.** n/r	**Ethnicity:** White Caucasians **Patient type/# screened:** healthy adult blood donors **Demographics:** n=4,000; mean age 35 y; range 18-60 **Incidence:**	By first serology: 10 By biopsy: 10			

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence				Comments
			Group 1	Group 2	Group 3	Group 4	
Ventura, 2001 Italy Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA-EMA , indirect IF using HU **Biopsy criteria/description:** ESPGAN a single specimen from the duodenal junction with a Watson capsule **Confirmatory test:** intestinal biopsy **Checked IgA def.** yes	**Ethnicity:** n/a **Patient type/# screened:** 19,791 children visiting family pediatrician over a 2 y period. Inclusion criteria "at risk": short stature; recurrent abdominal pain; IDA; enamel hypoplasia; recurrent aphthous stomatitis; autoimmune disease (such as IDDM, juvenile arthritis, autoimmune thyroiditis), occult hypertransaminasemia, IgA deficiency Down syndrome or CD in a first degree relative 240 met criteria; first-degree relatives of newly diagnosed CDs of this study (n=17?) **Demographics:** 240 (103 male 43%) mean age 4.8 y **Incidence:** Time period: Oct. 31, 1995- Oct. 31, 1997	Overall at risk 18/240 were EMA positive and confirmed positive with intestinal biopsy (7.5%)	Stature growth defect 8:105 (7.6%)	Recurrent abdominal pain 3:45 (6.6%)	Sideropenic anemia 4:17 (23.5%)	
			Group 5	**Group 6**	**Group 7**	**Group 8**	
			Autoimmune disease 1:19 (5.2%)	Down syndrome 1:11 (9.0%)	CD first-degree relative 1:14 (7.1%)		

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Volta, 2001 Italy Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA-EMA-HU **Biopsy criteria/description:** Roy-Choudhry; Subtotal villous strophy **Confirmatory test:** ? **Checked IgA def.** n/r	**Ethnicity:** Northern Italians **Patient type/# screened:** 3,483 general population **Demographics:** n=3,483; 12-65 y, only 784 in 12-25 group **Incidence:**	By EMA: 0.57% (20/3483); by biopsy: 0.49% (17/3483)			Prevalence of 0.57% (20/3483) if included three pts with normal villous but with increased IELs

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Weile, 2001 Denmark & Sweden Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** serum IgA; IgG-AGA; IgA-AGA, cut-off >40 units; EMA; in cases of IgA <0.07g/L, IgG-AGA was analyzed **Biopsy criteria/description:** n/a **Confirmatory test:** biopsy in the Swedish sample only **Checked IgA def.** yes; prevalence in both population of blood donors was 0.3%	**Ethnicity:** n/a **Patient type/# screened:** blood donors **Demographics:** Denmark: n=1,573 adults mean age: 41.4 y, range >18 y % F 40.9 Sweden: n=1,866 adults mean age = 37.6 y, range >18 y % F: 31.7 **Incidence:**	Denmark: by IgA-AGA 4% (61/1573), by EMA 0.25% (4/1573)	Sweden: by IgA-AGA 3.2% (60/1866), by EMA 0.27% (5/1866); by biopsy 0.27% (5/1866)		

Evidence Table 4 (cont'd): Prevalence/incidence of CD in the general population

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
West, 2003 UK Duplicate: no	**Publication type:** Journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA EMA, indirect IF on commercial ME using 1:10 dilution; tTGA, ELISA >3 U/mL considered positive **Biopsy criteria/description:** no biopsy done **Confirmatory test:** tTGA (no confirmatory test conducted i.e. biopsy) **Checked IgA def.** yes	**Ethnicity:** n/a **Patient type/# screened:** 7,550 general practice unselected **Demographics:** 7,527 adults aged 45-76 y not previously diagnosed with CD, mean age 59 y; 4,444 (59% F) **Incidence:** Time interval: 1990-1995	EMA positive 87/7527 (1.2%); EMA pos and abnormal tTGA 77/87 (89%)			In the whole group of 1,200 screened individuals there were 3 subgroups of pts suffering from: 1) IDA, n=64 (5.3%); 2) IBS, n=123 (10.25%); and 3) fatigue, n=92 (7.7%); prevalence of CD in IDA group was 4.7% (3/64, 95% CI 0-9.8); prevalence of CD in IBS group was 3.3% (4/123, 95% CI 0.1-0.6); prevalence of CD in the fatigue group was 3.3% (3/92, 95% CI 0-7)

Prevalence of CD in Associated Clinical Conditions—Patients with Suspected CD

Evidence Table 5: Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Agardh, 2001 Sweden Duplicate: yes, Celiac 1 (Carlsson et al., Pediatrics 1999;103: 1248)	**Publication type:** journal **Study design:** retrospective cross-sectional prevalence **Test/methodology:** tTG; HLA DQB1; AGA ≥25 AU; EMA titres ≥1:5, biopsies **Biopsy criteria/description:** as described in Carlsson et al., 1999 (Pediatrics 103:1248) **Confirmatory test:** biopsy **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** Group 1: IDDM (three were known and treated CD cases) Group 2: generally healthy subjects **Demographics:** IDDM group: (n=165) with CD: median age 7 y, age range=1-13 y; 64% F Without CD: median age=10 y, age range 2-19 y, 44% F control group: (n=277) age range 11-16 y, 53% F **Incidence:** n/a	IDDM group: by AGA: 6.8% (11/162); by EMA: 4.9% (8/162); by biopsy: 3.7% (6/162); by IgA-tTG: 5.6% (9/162); by IgG-tTG: 6/162 (3.7%)	control group: by AGA: 8.7% (24/277); by EMA: 0% (0/277); by IgA-tTG: 0% (0/277); by IgG-tTG: 0% (0/277)		Type 1 diabetics having either DQB1*02 or DQB1*0302 had higher IgA-tTG levels than those not having these alleles (p=0.023)

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Annibale, 2003 Italy Duplicate: no	**Publication type:** journal **Study design:** prospective prevalence **Test/methodology:** IgA-tTG, ELISA normal values were < 7UA/mL **Biopsy criteria/description:** Marsh **Confirmatory test:** Biopsy, antral, gastric body, and duodenal biopsy collected **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** IDA in premenopausal women **Demographics:** n=59 premenopausal women; age range 22-54 y with IDA Hb<12g/dLF **Incidence:** Time period: March-July 2000	7/59 (11.9%) had positive anti-tTG antibodies titre; biopsy-confirmed: 8.5% (5/59)			40/59 subjects tested positive for various tests including tTG for CD detection and progressed to have upper endoscopy with biopsy

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Bardella 1991 Italy Duplicate: no	**Publication type:** journal **Study design:** prevalence **Test/methodology:** IgA-AGA **Biopsy criteria/description:** n/r **Confirmatory test:** **Checked IgA def.**	**Ethnicity:** n/r **Patient type/# screened:** suspected CD: iron-deficient, bowel disturbances, chronic intermittent diarrhea, severe malabsorption, tiredness and wt loss, mineral metabolism deficiencies, gluten-intolerance in childhood not further investigated **Demographics:** n=60; median age 28 (range 15-69); 41 F/19 M **Incidence:**	26			

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Bardella 2001 Italy	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** IgA-tTG >10 AU/mL using GP liver; AGA >12 AU/mL; indirect IF EMA titre>1:10; biopsy **Biopsy criteria/description:** n/a? didn't mentioned the biopsy results, not used for case diagnosis **Confirmatory test:** none **Checked IgA def.** yes, one found	**Ethnicity:** n/a **Patient type/# screened:** suspected CD, confirmed and treated CD pts (to be excluded), disease control group (to be excluded) **Demographics:** n=80 suspected CD; adult; mean age 39 y; age range 17-79 y; 70% F **Incidence:**	50% (40/80)			

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Bode 1993 Denmark Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** AGA, IgG, IgA **Biopsy criteria/description:** all biopsied **Confirmatory test:** all biopsied criteria not stated **Checked IgA def.** no	**Ethnicity:** n/r **Patient type/# screened:** suspected CD; all children **Demographics:** n=191; 74 F/117 M; median age: 2.75 y (range 0.33-15.5 y) **Incidence:**	14 cases (7.3%)			

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Carroccio, 2002 Italy Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** serum EMA; serum anti-GP-tTG; serum anti-human-tTG **Biopsy criteria/description:** ESPGAN? Three groups: normal, partial VA or subtotal/total VA; positive for CD if partial or total VA **Confirmatory test:** biopsy **Checked IgA def.** Yes, none found	**Ethnicity:** n/a **Patient type/# screened:** adult pts with suspected CD **Demographics:** n=207; adult; median age 42 y; age range 17-84 y; 52.3% F **Incidence:**	By GP-tTG: 18.8% (39/207); by h-tTG: 14.5% (30/207); by biopsy: 11.6% (24/207)			

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Chan, 2001 Canada Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** GP-tTG; EMA; biopsy **Biopsy criteria/description:** Carey capsule, or 4-6 duodenal biopsies at time of endoscopy; no grade provided, a diagnosed case=increased number of IELs with associated subtotal or total VA **Confirmatory test:** biopsy **Checked IgA def.** Yes, two found	**Ethnicity:** n/a **Patient type/# screened:** 77 pediatric pts with suspected CD; 16 type I diabetes **Demographics:** n=93; mean age: n/r; range 2 mos to 18 y; % F: n/r **Incidence:**	GI group: 12% (9/77)	DM group: 75% (12/16)		

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Chartrand, 1997 Canada Duplicate: no	**Publication type:** journal **Study design:** prevalence **Test/methodology:** biopsy **Biopsy criteria/description:** ESPGAN **Confirmatory test:** **Checked IgA def.**	**Ethnicity:** n/r **Patient type/# screened:** suspected CD; n=179 **Demographics:** all children; mean age 5.2 y, range 0.5-18.1 y **Incidence:**	30 (17%); mean age 3.7 y (range 0.6-11.2); 17 F/13 M			

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Csizmadia 1999, Netherlands Duplicate: no	**Publication type:** journal (research letter) **Study design:** cross-sectional Prevalence **Test/methodology:** IgA-EMA (methodology n/r) **Biopsy criteria/description:** n/r **Confirmatory test:** Small bowel biopsy, subset of 27 had HLA typing for DQ2 **Checked IgA def.** n/r	**Ethnicity:** n/r **Patient type/# screened:** 6,127 children between ages of 2-4 y general population **Demographics:** 6,127 pediatric pts between 2-4 y; gender:n/r **Incidence:** Time period: between May 1997-June, 1998	1.2% (75/6127) by IgA-EMA, 18/75 refused small bowel biopsy; 0.51% (31/75/6127) VA			26/27 with VA had the allele HLA-DQ2; prevalence 1:198 in children 2-4 y

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Day, 2000 New Zealand Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** IgA, IgG-AGA, EMA **Biopsy criteria/description:** single pathologist, Marsh **Confirmatory test:** biopsy on EMA pos **Checked IgA def.** yes	**Ethnicity:** n/r **Patient type/# screened:** pediatric input or output; single center; suspected CD: failure to thrive, short stature, chronic GI symptoms; DM; histological findings of CD; 6 mos-15 y **Demographics:** mean age: 63 mos (range 6 mos-15 y); % M: 58 **Incidence:**	27/36 EMA+; 5/11 biopsy confirmed			

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Fasano, 2003 USA Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** EMA-IF; ME or HU; positive at 1:10 ; all positive EMA tested with human tTG ELISA positive at 2 SD above mean of healthy controls; HLA DQ2 and DQ8 **Biopsy criteria/description:** single pathologist, Marsh **Confirmatory test:** htTG; biopsy; also small subset 98 EMA positive and 114 EMA neg had HLA DQ2/8 tested **Checked IgA def.** n/r	**Ethnicity:** 94% White; 3% Black; 1.5% Hispanic, 1% Asian, 0.5% other **Patient type/# screened:** 9,019 at risk of CD; 4,126 not at risk **Demographics:** at risk: symptoms of CD (1,326 children, 1,909 adults); CD associated disorders; 4,508 1st deg relatives; 1,275 2nd deg relatives; not at risk: 2,000 blood donors (mean age 39 y range 19-65 y); 1,119 school children (mean age 12.3 y, range 6-18 y); 1,007 adults and children for routine physical (mean age: 39 y, and 13.7 y; range: 19-71 y, and 2-18 y, respectively) **Incidence:**	1) At risk: a) 1st deg relatives-205/4,508 (4.55%); children-54/1,294 (4.17%); adults-151/3,214 (4.70%); b) symptomatic adults: 28/1,910 (1.47%); children: 53/1326 (4.00%) 2) Not at risk: 1/4,126 (0.75%); adults-27/2,845 (0.95%); children-4/1281(0.31%); biopsy in EMA+ Marsh I-0%; Marsh II-30/116 (25.9%); IIIa-46/116 (39.7%); IIIb-24/116 (20.7%); IIIc-16/116 (13.8%); HLA DQ2-76/98 (78%); DQ8-16/98 (16%); DQ2 and 8-6/98 (6%); all EMA pos were also tTG pos			

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Fitzpatrick 2001 Canada Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence; authors state that the study is a case-control (doubtful) **Test/methodology:** IgA-EMA-IF using ME; positive when characteristic fluorescence pattern was produced **Biopsy criteria/description:** not performed **Confirmatory test:** None **Checked IgA def.** n/r	**Ethnicity:** n/r **Patient type/# screened:** 92 pts with recurrent abdominal pain screened for EMA positivity; 81 healthy children also screened for EMA positivity **Demographics:** 92 pts with recurrent abdominal pain; age: n/r; 62% F; 81 healthy controls; age: n/r; 42% F **Incidence:**	The prevalence of IgA-EMA positivity in children with recurrent abdominal pain was 1 in 92 (1%, 95% CI 0-6)	The prevalence of IgA-EMA positivity in controls was 1 in 81 (1%, 95% CI 0-7)		

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Hill 2000 USA Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** IgA-EMA, IF on ME, methodology n/r; IgA and IgG-AGA, ELISA, methodology n/r **Biopsy criteria/description:** Marsh **Confirmatory test:** biopsy **Checked IgA def.** yes	**Ethnicity:** n/r **Patient type/# screened:** 1,200 pediatric group of individuals at risk of CD; pts were assigned to one of 7 groups: 1) chronic diarrhea (n=182); 2) abdominal pain (n=316); 3) IDDM (n=81); 4) short stature (n=259); 5) failure to thrive (n=123); 6) miscellaneous (Down's syndrome, thyroiditis, anemia, unexplained elevation of liver enzymes) (n=47); 7) asymptomatic relatives (n=192) **Demographics:** 1,200 pediatric group of individuals at risk of CD; age: mean n/r; range: 6 mos-20 y; % F n/r **Incidence:**	Prevalence of CD in pts at risk was 1 in 57 (21/1200); prevalence of test positivity: 2.8% (34/1200) was both EMA and AGA positive; 26 of pts (19 EMA positive) underwent biopsy and 21 were diagnosed with CD			15 pts out of 34 EMA positives refused biopsy; thus prevalence of biopsy proven CD in pts at risk was at least 1 in 57; if considered above mentioned 15 pts, prevalence of CD could have been 1 in 33 (36/1200)

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Hin 1999 UK Duplicate: no	**Publication type:** journal **Study design:** cross-sectional Prevalence **Test/methodology:** EMA (ME); biopsy of positives; IgA levels, IgG-AGA for IgA deficient **Biopsy criteria/description:** Crosby capsule, EGD distal duod in 2 cases **Confirmatory test:** biopsy; 100% positive; IEL: 1/30; mild VA: 1/30; partial VA: 1/30; subtotal VA: 14/30; total VA: 13/30 **Checked IgA def.** yes	**Ethnicity:** n/a **Patient type/# screened:** entry criteria: IBS, anemia, histological findings of CD, malabsorption symptoms, diarrhea, fatigue, thyroid disease, DM, wt loss, short stature, failure to thrive, epilepsy, infertility, arthralgia, eczema; 1,000 screened **Demographics:** n=271 M, mean age: 49.9 y (range 1-84); n=729 F, mean age: 45.2 y, range 6 mos-85 y); 5.3% <10 y, 3.1% aged 80-90 y; % F: 73 **Incidence:** # New cases: 30 pts (8 M:22 F) +ve EMA and +ve biopsy Time period: 30/1 y Control popn: 7 /preceding 1 y in absence of case finding	Prevalence of CD in pts at risk was 1 in 57 (21/1200); prevalence of test positivity: 2.8% (34/1200) was both EMA and AGA positive; 26 of pts (19 EMA positive) underwent biopsy and 21 were diagnosed with CD			126 cases tested for anemia: 21 positive

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Hoffenberg 2003 USA Duplicate: no	**Publication type:** journal **Study design:** prospective stratified cohort study **Test/methodology:** IgA tTG **Biopsy criteria/description:** Marsh score of 2 (enlarged crypts and increased numbers of intraepithelial lymphocytes) or 3 (any degree of VA) was considered evidence of CD **Confirmatory test:** TG autoantibody seropositivity on two separate occasions at least 6 mos apart; biopsy **Checked IgA def.** yes	**Ethnicity:** non-Hispanic white 56%, Hispanic 30%, African-American 7%, Asian-American 2%, or biracial/other 5% **Patient type/# screened:** 987 infants with high-risk genotypes: HLA DR3-3; DR3/4, DQB1*0302; DR4, DQ8 DR5/7 (since 2000) **Demographics:** 987 infants (tested over 5 y span) gender n/r **Incidence:** Time period: newborns between Dec 1993-Sept 1999		40/987 tested positive for tTG; 19/40 met criteria for CD (10 with intestinal biopsy and 9 with persistent tTG autoantibody seropositivity)		By the age of 5 y, the adjusted risk estimate of the frequency of evidence of CD in general Denver population is 0.9%(95% CI, 0.4-2.0) or 1 in 104 (1:49 to 1:221).

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Hogberg, 2003 Sweden Duplicate: no	**Publication type:** journal **Study design:** longitudinal follow-up, incidence & prevalence **Test/methodology:** IgA-AGA, ELISA cut-off for a positive outcome 42.5 units; IgA-EMA, indirect IF using ME, antibody titre defined as the highest serum dilution yielding positive fluorescence; IgA-TGA, commercially available ELISA, highest cut-off value for positive results >30 units. **Biopsy criteria/description:** revised ESPGAN. Grade 1 normal; Grade 2 mild; Grade 3 moderate, Grade 4 total VA **Confirmatory test:** Small bowel biopsy **Checked IgA def.** yes, 5 cases found	**Ethnicity:** n/a **Patient type/# screened:** 120 first degree relatives of CD pts **Demographics:** n=56 parents (adults), mean age 53.6 y, range 43-78 y; n=44 siblings (ped and adult), mean age 27.4 y, range 15-49 y; n=20 offspring, mean age 6.5 y, range 1-16 y; gender n/r **Incidence:** Time period: 20 y follow-up study. Original study period Sept 1975-Feb 1981	10/120 (8.3%) prevalence, 2 were diagnosed in the original study 20 y prior, 8 new cases from the present follow-up study group. (biopsy confirmed); serum results: IgA-AGA 8/120 pos; IgA-EMA 0.5% (6/120) pos; IgA-TGA 3.8% (4/104) pos (3 pts with positive biopsy were not tested for IgA TGA)			IgA deficient pt, IgG antibodies positive. Biopsy findings were in serologically positive relatives IgA-TGA was performed in sera of n=104 when access to assay became available 1 yr later.

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Pittschieler, 2003 Italy Duplicate: no	**Publication type:** journal **Study design:** prospective prevalence **Test/methodology:** EMA, HUC examined by fluorescence. Absence of binding was considered a negative test; HLA typing was done exclusively once diagnosis of CD was confirmed (micro-lymphocytotoxic technique) **Biopsy criteria/description:** Small intestinal biopsy of first jejunal loop. Ferraris Watson capsule. Normal values being <3.2 cells/mm γ/δ T-cell receptors by immuno-histology **Confirmatory test:** biopsy, HLA typing **Checked IgA def.** yes, none found	**Ethnicity:** n/a **Patient type/# screened:** 92 first-degree relatives of CD pts. Yearly testing over 12 y period **Demographics:** n=92 at risk (first-degree relatives; 18 offspring and 74 siblings); aged 2-18 y **Incidence:** Time period: 12 y time period Jan 1990-Dec 2001	6.5% (6/92) confirmed CD by both serology & biopsy within a few months of CD diagnosis in one of their relatives. 5 total VA and 1 partial VA; over 2-5 y a further 5.8% (5/86) confirmed positive with both HUC EMA-IgA and biopsy 1 partial VA and 4 total VA; combined prevalence=12% (11/92); 11/11 were carriers of HLA DQ2/ heterodimers			all 11 were clinically silent for CD

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Thomas, 1992 England Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** biopsy **Biopsy criteria/description:** normal histology; mild enteropathy; moderate enteropathy; severe enteropathy; response to GFD **Confirmatory test:** n/r **Checked IgA def.** yes	**Ethnicity:** n/r **Patient type/# screened:** pediatric pts presenting with chronic diarrhea **Demographics:** n=381; 64% <2 y; 20% 2-5 y; 16% 5-15 y; % F: 41.5 **Incidence:**	2/97 mild enteropathy; 1/38 moderate enteropathy; 27/34 severe enteropathy=7.9%			

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Tursi, 2003 Italy Duplicate: no	**Publication type:** journal **Study design:** prevalence **Test/methodology:** IgA IgG, ELISA lower limit of positivity of IgA 0.2 EU/mL and IgG 10.0 EU/mL; IgA-EMA, indirect IF on ME; IgA-tTG, ELISA using GP liver substrate, lower limit of positivity was 7 UA/mL **Biopsy criteria/description:** Marsh criteria 6 biopsies from small bowel from the second part of duodenum. Marsh Type I -'infiltrative' lesions with >30 lymphocytes/100 epithelial cells; Type II-'infiltrative/hyperplastic' lesions; Type III-'partial (sub)total VA; partial VA Marsh IIIa); subtotal VA Marsh IIIb); and total VA as Marsh IIIc) **Confirmatory test:** Biopsy **Checked IgA def.** yes	**Ethnicity:** n/r **Patient type/# screened:** 111 first-degree relatives of pts with CD **Demographics:** at risk n=111 first-degree relatives: mean age 28.7 y, range (10-65 y); 38 M, 73 F **Incidence:** n/r	CD diagnosed in 49/11 screened relatives (44.14%) prevalence; Prevalence AGA 36.73%; EMA 38.78% ; anti-tTG 44.89%			Prevalence of antibodies was higher in severe histological lesions (Marsh IIIb-c) than in not so severe lesions (Marsh I-IIIa). Note: prevalence of AGA was higher than that of EMA/anti-tTG in less severe histological lesions

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
van Mook, 2001 Netherlands Duplicate: no	**Publication type:** journal **Study design:** retrospective prevalence **Test/methodology:** EGD; upper digestive tract endoscopy in 10/35; duodenal biopsies taken in 15/35 **Biopsy criteria/description:** Marsh **Confirmatory test:** biopsy **Checked IgA def.** no	**Ethnicity:** n/r **Patient type/# screened:** 35 pts with IDA, anaemia defined as Hb <8.0 mmol/L in men or < 7.4 mmol/L in women. Iron deficiency defined as a serum ferritin level ≤20 µg/L for men or ≤10 µg/L in women; or serum iron concentration ≤45 µg/dL with a transferrin saturation of 10% or less, or the absence of iron stores in bone marrow biopsy specimens. **Demographics:** n=35 pts: median age 71 y, range 22-89 y; 22 F (63%) and 13 M (37%), **Incidence:** n/r	2.9% (1/35) Marsh IIIc on both biopsy and endoscopy			

Evidence Table 5 (cont'd): Prevalence of CD in patients with suspected CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Ventura, 2001 Italy Duplicate: no	**Publication type:** journal **Study design:** cross-sectional Prevalence **Test/methodology:** IgA EMA, indirect IF using HUC **Biopsy criteria/description:** ESPGAN a single specimen from the duodenal junction with a Watson capsule **Confirmatory test:** intestinal biopsy **Checked IgA def.** yes	**Ethnicity:** n/r **Patient type/# screened:** 19,791 children visiting family pediatrician over a 2 y period. Inclusion criteria "at risk": short stature; recurrent abdominal pain; IDA; enamel hypoplasia; recurrent aphthous stomatitis; autoimmune disease (such as IDDM, juvenile arthritis, autoimmune thyroiditis),occult hypertransaminasemia, IgA deficiency Down's syndrome or CD in a first degree relative; 240 met criteria; first-degree relatives of newly diagnosed CDs of this study (n=17?) **Demographics:** n=240: mean age 4.8 y; 103 M (43%) **Incidence:** Time period: Oct. 31, 1995-Oct. 31, 1997	Overall at risk 18/240 were EMA positive and confirmed positive with intestinal biopsy (7.5%);	Stature growth defect 8/105 (7.6%)	Recurrent abdominal pain 3/45 (6.6%)	
			Group 4	**Group 5**	**Group 6**	
			Sideropenic anemia 4/17 (23.5%)	Autoimmune disease 1/19 (5.2%)	Down syndrome 1/11 (9.0%)	
			Group 7			
			CD first degree relative 1/14 (7.1%)			

Prevalence of CD in High-Risk Patients—Type I Diabetes

Evidence Table 6: Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Agardh, 2001 Sweden Duplicate: yes, Celiac 1 – Carlsson et al., Pediatrics 1999;103: 1248	**Publication type:** journal **Study design:** retrospective cross-sectional prevalence **Test/methodology:** tTG; HLA-DQB1; AGA≥25 AU; EMA titres≥ 1:5, biopsies **Biopsy criteria/description:** as described in Carlsson et al., 1999 Pediatrics 103:1248 **Confirmatory test:** biopsy **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** 1. IDDM (3 were known and treated CD cases); 2. generally healthy subjects **Demographics:** ped; 1. IDDM group (n=165)- with CD: median age 7 y, age range 1-13 y, 64% F; without CD: median age 10 y, age range 2-19 y, 44% F. 2. control group (n=277)- age range 11-16 y, 53% F **Incidence:**	IDDM group: by AGA: 6.8% (11/162); by EMA: 4.9% (8/162); by biopsy: 3.7% (6/162); by IgA-tTG: 5.6% (9/162); by IgG-tTG: 6/162 (3.7%)	Control group: by AGA: 8.7% (24/277); by EMA: 0% (0/277); by IgA-tTG: 0% (0/277); by IgG-tTG: 0% (0/277)		Type 1 diabetics having either DQB1*02 or DQB1*0302 had higher IgA-tTG levels than those not having these alleles (p=0.023)

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Arato, 2002 Hungary Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** EMA, indirect IF; serum IgA measured to avoid false-negative IgA-EMA tests in cases of IgA deficiency (serum IgA<0.2g/L); jejunal biopsy using Crosby capsule for EMA positives; intraepithelial gamma/delta T-cells elevated if >7 cells/mm (95% CI) **Biopsy criteria/description:** other: not described **Confirmatory test:** jejunal biopsy **Checked IgA def.** yes; none found	**Ethnicity:** n/a **Patient type/# screened:** type I diabetes **Demographics:** n=205; randomly selected ped pts with IDDM; mean age 11.6 y; age range 2.0-17.0 y; 42.9% F **Incidence:** n/a	By EMA: 11.7% (24/205); by biopsy: 8.3% (17/205)			Randomly selected subject pool, considered more representative of the population than in the other studies. No significant difference among EMA positive children with or without jejunal VA

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Bao, 1999 USA Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** tTG (ELISA) >0.05=positive; IgA-EMA using indirect IF; HLA genotype DQ B1 typing of peripheral WBCs with PCR amplification and hybridization; DQ alpha-typing performed with ampliType; DQ2, DQ8 **Biopsy criteria/description:** Other: not described **Confirmatory test:** *consent to biopsies in only 20 of the 98 tTG positives **Checked IgA def.** no, not mentioned	**Ethnicity:** n/a **Patient type/# screened:** type I diabetes **Demographics:** n=847; children and adult; mean age 14.5 y; range 0.7-77.7 y; % F? **Incidence:** n/a	By tTG only: 11.6% (98/847); by tTG & EMA: 5.8% (49/847); by biopsy: 1.8% (15/20/98/847)			Levels of tTG IgA and IgA-EMA were correlated: r=0.44, p=0.002. Prevalence of tTG was higher in diabetics with HLA DQ2 or DQ8.

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Barera, 1991 Italy Duplicate: no	**Publication type:** journal **Study design:** **Test/methodology:** AGA IgA then if negative, IgG AGA **Biopsy criteria/description:** subtotal VA **Confirmatory test:** none **Checked IgA def.**	**Ethnicity:** n/a **Patient type/# screened:** type I diabetes **Demographics:** n=498; children **Incidence:** n/a	By first AGA-IgA: 30 Biopsy proven: 16			Levels of tTG IgA and IgA-EMA were correlated: r=0.44, p=0.002. Prevalence of tTG was higher in diabetics with HLA DQ2 or DQ8.

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Barera, 2002 Italy Duplicate: no	**Publication type:** journal **Study design:** prospective cohort; 6 years follow-up [did not give incidence measures, only prevalence] **Test/methodology:** EMA, indirect IF; serum IgA <0.05 g/L in the presence of normal IgG and IgM were regarded as selective IgA deficiency; duodenojejunal biopsy in >8 y children with positive EMA; upper endoscopy for younger children, mucosal histology **Biopsy criteria/description:** Marsh; three types of lesions: 1. Infiltrative lesion normal mucosa, 2. Hyperplastic lesion with enlarged crypts infiltrated by IELs, 3. Some degree of VA with inflammation and hyperplastic crypts; diagnosis considered positive with demonstration of type 2 or 3 lesion **Confirmatory test:** biopsy **Checked IgA def.** yes, 2 selective IgA deficiency	**Ethnicity:** n/a **Patient type/# screened:** type I diabetes **Demographics:** n=273; children; mean age 8.28 y, age range 0.6-18.7 y; 42.5% F **Incidence:** n/a	By 1 EMA only: 5.5% (15/273); after second EMA: 3.7% (10/273); by biopsy: 3.3% (9/10/273); if add the 1 excluded case (because diagnosed CD before developed IDDM): 3.6% (10/274)			Levels of tTG IgA and IgA-EMA were correlated: r=0.44, p=0.002. Prevalence of tTG was higher in diabetics with HLA DQ2 or DQ8.

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Calero, 1996 Spain Duplicate: no	**Publication type:** journal **Study design:** **Test/methodology:** IgA-AGA if positive on two occasions **Biopsy criteria/description:** subtotal VA **Confirmatory test:** none **Checked IgA def.**	**Ethnicity:** n/a **Patient type/# screened:** type I diabetes **Demographics:** n=141; children **Incidence:** n/a	By first AGA-IgA: 12 Biopsy proven: 4			

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Cronin, 1997 Ireland Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** EMA; biopsy **Biopsy criteria/description:** other: not mentioned **Confirmatory test:** biopsy **Checked IgA def.** no, not mentioned	**Ethnicity:** n/a **Patient type/# screened:** IDDM pts **Demographics:** n=101 diabetic pts and n=51 controls; adolescent and adult; age range for diabetic pt 15-59 y. Other info n/a **Incidence:** n/a	By EMA: 7.9% (8/101) By biopsy: 5.0% (5/101)			

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
De Block, 2001 Belgium Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional Prevalence] **Test/methodology:** islet cell antibodies (ICA) - IF, cut-off level was >12 JDF; antibodies to glutamic acid decarboxilase-65 (GADA) - radiobinding assay, cut-off level was >2.6% tracer bound GADA; tyrosine phosphate antibodies (IA2A) - radiobinding assay, cut-off level was >0.5% tracer bound IA2A; thyroid peroxidase antibodies (aTPO) - radiobinding assay, cut-off was >100 U/mL; parietal cell antibodies (PCA) - IF, positivity at >1:20 dilution; antibodies to intrinsic factor (AIF) - radiobinding assay; anti-adrenal antibodies (AAA) - IF; anti-EMA - IF on a ME, positivity at >1:10 dilution; HLA DQ **Biopsy criteria/description:** no biopsy performed **Confirmatory test:** none **Checked IgA def.** n/r	**Ethnicity:** all Caucasians **Patient type/# screened:** 399 pts with IDDM screened for different autoimmune diseases (176 children <18 y; 223 adults) **Demographics:** 399 pts with IDDM screened for different autoimmune diseases; age (y): mean 26±16, range n/r; 53% F **Incidence:** n/a	Prevalence of CD in 399 pts with IDDM was 0.75% (3/399); prevalence of test positivity: 1) ICA - 39% (157/399); GADA - 70% (278/399); IA2A - 44% (177/399); aTPO - 22% (87/399); PCA - 18% (73/399); AAA - 1% (5/399); IgA EMA - 2% (9/399)			IgA-EMA was detected in 2.3% of IDDM pts particularly in HLA-DQA1*0501-DQB1*0201 subjects

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
De Vitis, 1996 Italy Duplicate: no	**Publication type:** journal **Study design:** **Test/methodology:** IgA, IgG then IgA EMA **Biopsy criteria/description:** Marsh VA **Confirmatory test:** biopsy **Checked IgA def.**	**Ethnicity:** n/a **Patient type/# screened:** type I diabetes **Demographics:** n=1,114; children & adults **Incidence:** n/a	By first IgA: 121 Biopsy proven: 63			78/121 biopsied

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Fasano, 2003 USA Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** EMA, IF ME or HU; positive at 1:10 ; all positive EMA tested with human tTG ELISA positive at 2 SD above mean of healthy contols; HLA DQ2 and DQ8 **Biopsy criteria/description:** single pathologist, Marsh **Confirmatory test:** htTG; biopsy; also small subset 98 EMA-positive and 114 EMA-neg had HLA DQ2/8 tested **Checked IgA def.** n/r	**Ethnicity:** 94% White; 3% Black; 1.5% Hispanic, 1% Asian, 0.5% other **Patient type/# screened:** 9,019 at risk of CD; 4,126 not at risk **Demographics:** at risk: symptoms of CD (1,326 children, 1,909 adults); CD-associated disorders; 4,508 1st deg relatives; 1,275 2nd deg relatives; not at risk: 2,000 blood donors (mean age 39 y range 19-65 y); 1,119 school children (mean age 12.3 y, range 6-18 y); 1,007 adults and children for routine physical (mean age 39 y, and 13.7 y, range, 19-71 y, and 2-18 y) **Incidence:**	1) At risk - a) 1st deg relatives - 205/4,508 (4.55%); children - 54/1,294 (4.17%); adults - 151/3,214 (4.70%); b) symptomatic adults - 28/1,910 (1.47%); children - 53/1,326 (4.00%); 2) Not at risk - 1/4126 (0.75%); adults - 27/2,845 (0.95%); children - 4/1281(0.31%); biopsy in EMA pos - Marsh 1- 0%; 2 - 30/116 (25.9%); 3a - 46/116 (39.7%); 3b - 24/116 (20.7%); 3c - 16/116 (13.8%); HLA DQ2-76/98 (78%); DQ8 - 16/98 (16%); DQ2 and 8 - 6/98 (6%); all EMA pos were also tTG pos			

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Frazer-Reynolds, 1998 Canada Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA EMA - IF using ME, positive if staining at a dilution of 1:10; total serum IgA, measured using rate nephelometry **Biopsy criteria/description:** Carey capsule; Marsh criteria **Confirmatory test:** biopsy **Checked IgA def.** yes; none of IDDM pts had IgA deficiency; 3 pts in suspected malabsorption group were found to have IgA deficiency	**Ethnicity:** 94% white; 3% Black; 1.5% Hispanic, 1% Asian, 0.5% other **Patient type/# screened:** 236 pts with IDDM screened for CD; 56 pts who underwent intestinal biopsy for suspected malabsorption **Demographics:** 236 pts with IDDM; age (y): mean n/r, range 1-18; 50% F; 56 pts with GI complaints; age (y): mean n/r, range n/r; 43% F **Incidence:**	Estimated prevalence of CD in 236 pts with IDDM was 5.1% (12/236; 95% CI 2.7-8.8); as for test positivity: none were IgA deficient; 19 pts were IgA EMA positive; 2 refused biopsy; of 17 pts with IgA EMA, 12 had CD on biopsy	Estimated prevalence of CD in 56 pts with suspected malabsorption was 9% (5/56); as for test positivity: 3 pts were EMA positive and all had biopsy proven CD; 3 pts were IgA deficient and EMA negative and 1 of them was found to have CD on biopsy; 1 of 50 IgA-sufficient and EMA negative pts had biopsy proven CD		Sensitivity and specificity of IgA EMA for the detection of CD in all 73 biopsied pts (both IDDM and GI pts) were 88.2% (15/17; 95% CI 63.6-98.5), respectively; when the 3 IgA deficient pts were excluded, sensitivity increased to 93.7% (15/16; 95% CI 69.8-99.8) and specificity remained unchanged (49/54, or 90.7%; 95% CI 79.7-96.9)

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Gillett, 2001 Canada Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA EMA, IF on HU, starting dilution 1:5; positive sample were tested at increased dilutions until fluorescence disappeared; IgA tTG, ELISA; reference range of 140 AU/mL or less was calculated to include 3 SD above the mean (99% confidence limit) **Biopsy criteria/description:** endoscopic biopsy; ESPGAN criteria; 4 biopsy specimens from distal duodenum; elevated IEL count was defined as more than 40 IELs per 100 enterocytes **Confirmatory test:** biopsy **Checked IgA def.** yes; using Nor-Partigen Total IgA Kit; 1 pt was found to be IgA-deficient	**Ethnicity:** 209 White, 12 East Indian, 7 Asian, 4 First Nation, 1 African **Patient type/# screened:** 233 pts with IDDM screened for CD **Demographics:** 233 pts with IDDM screened for CD; age (y): median 12.9, range 1.3-19.2; 46% F **Incidence:**	Prevalence of CD in IDDM pts was 7.7% (18/233); prevalence of test positivity: 8.2% (19/233) was both EMA and AGA positive and all were white; 18 of these 19 pts underwent biopsy (1 was previously diagnosed with CD and was not offered biopsy); CD was confirmed in 14 of these 18 pts			

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Hansen, 2001 Denmark Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA AGA - ELISA, cut-off n/r; IgA EMA - IF on a ME; IgA tTG - ELISA; thyroid antibodies: thyroid peroxidase (TPO) and thyroglobulin (TG), using radioimmunoassay **Biopsy criteria/description:** endoscopic biopsy; CD was diagnosed when mucosa showed partial or total VA, crypt hyperplasia and IEL infiltration **Confirmatory test:** endoscopic biopsy **Checked IgA def.** yes; none was IgA deficient	**Ethnicity:** n/a **Patient type/# screened:** 106 pts with IDDM screened for CD; 106 aged-, and sex-matched healthy controls **Demographics:** 106 pts with IDDM screened for CD; 2 had been previously diagnosed with CD; age (y): median 12.8, range 2.3-18.2; 47% F; median duration of IDDM 4.8 y, range 0.2-13.3 y; 1 pt had a second-degree relative with CD; 106 aged-, and sex-matched healthy controls; age (y): median 12.9, range 1.3-18.3; 47% F; none had relatives with CD **Incidence:**	Screening revealed 9 biopsy proven CD in the 104 pts with IDDM, giving a prevalence of CD 10.4% (95% CI 4.6-16.2%), (11/106 - 2 pts had CD prior to screening); as for test positivity: of 104 tested pts 7 had IgA AGA, 19 - IgG AGA, and 10 - IgA EMA+ IgA tTG; 9 out of 10 EMA+tTG positive pts underwent biopsy (1 refused) and were found all of them to have CD	Control: none had been diagnosed with CD; as for test positivity: 1 had IgA AGA, 9 - IgG AGA, none - EMA or tTG		Screening revealed IDDM pts with CD were significantly younger than the group of IDDM without CD (p=0.017); IDDM+CD group also had an earlier onset of diabetes: median 3.2 y (range 0.7-9.3 y), compared with 7.4 y (range 1.3-16.6 y) in pts without CD (p=0.005); in pts with IDDM+CD the height standard deviation score (SDS) was significantly lower compared with diabetics without CD (p=0.019); no statistically significant difference with regards of weight SDS and body mass index SDS; thyroid antibodies were significantly more frequent in IDDM+CD (36% - 4/12), whereas 12/94 (13%) of IDDM without CD and 2/106 (2%) of controls had detectable thyroid antibodies (p=0.04)

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Jager, 2001 Germany Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** DDM-associated antibodies: islet cell antibodies (ICA) - detected by IF, insulin autoantibodies (IAA) - radioimmunoassay, anti-IA-2 antibodies, and anti-GAD65 antibodies (anti-GADA) - both radioligand binding; thyroid disease-associated antibodies: anti-TPO and anti-TG - both ELISA; pernicious anemia-associated antibodies: anti-gastric parietal cell antibodies (anti-GPC) - IF; adrenalitis-associated antibodies: anti-adrenal cortex antibodies - IF; CD-associated antibodies: IgA AGA, IgG AGA, IgA-tTG - all ELISA **Biopsy criteria/description:** n/r **Confirmatory test:** none **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** 197 pts with a new onset of IDDM diagnosed according to WHO criteria; 882 first-degree relatives; 150 healthy controls without a family history of IDDM; **Demographics:** 197 pts with IDDM (age (y): median 16, range 5-27, 43% F); 882 first-degree relatives - 485 were parents (age (y): median 43, range 22-59), 382 siblings and 15 offsprings of IDDM pts (age (y): median 16, range 2-41) **Incidence:**	Recent-onset IDDM (n=197): IgG AGA - 10.2%; IgA AGA - 7.6%; anti-tTG IgA - 9.7%; at least 1 antibody positive - 16.8%	First-degree relatives (n=882): IgG AGA - 5.6%; IgA AGA - 2.6%; anti-tTG IgA - 3.2%; at least 1 antibody positive- 7.3%	Healthy control subjects (n=150): IgG AGA - 3.2%; IgA AGA -2.0%; anti-tTG IgA - 2.6%; at least 1 antibody positive- 4.6%	

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Kaukinen, 1999 Finland Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA EMA - IF, screening dilution of 1:5 was considered as a positive; IgA and IgG AGA - ELISA, for IgA AGA lower limit of positivity was 0.2 EU/mL and for IgG AGA - 10.0 EU/mL **Biopsy criteria/description:** endoscopic biopsy; ESPGAN criteria; 7 forceps biopsy specimens; histological classification as 1) normal; 2) mild partial VA; 3) severe partial VA; 4) subtotal VA; 3 and 4 were considered as CD **Confirmatory test:** endoscopical biopsy; performed in 6 (10%) previously diagnosed CD and in 28 pts without the diagnosis of CD; (23 refused biopsy, 3 - lost to follow-up, 2 - died); HLA DR and HLA DQ alleles in a dilution of 1:1500 using PCR/RFLP method **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** 62 adult pts with more than one autoimmune endocrinologic disorder **Demographics:** 67% F); ATD+addison's disease - 4 (age (y): median 52, range 34-53; 50% F); APECED - 4 (age (y): median 26, range 17-51; 25% F); IDDM+alopecia areata - 3 (age (y): median 20, range 17-30; 67% F); ATD+alopecia areata - 3 (age (y): median 48, range 33-57; 100% F); ATD+addison's disease+alopecia areata - 1 (age (y): median 42; 0% F); IDDM+addison's disease - 1 (age (y): median 32; 100% F) **Incidence:**	In total 7 (11%) out of 62 pts were diagnosed to have biopsy-proved CD; 6 (10%) were previously diagnosed with CD, and 1 (3.6%) of the 28 pts undergoing biopsy also was diagnosed with CD; EMA was positive in 1 (3.6%) pts with a newly diagnosed CD; IgA AGA - in 7 (25%), and IgG AGA - in 1 (3.6%); 14 of 26 subjects were HLA-DQ2 positive, in addition 4 had a celiac-type DQ8 haplotype; thus, 18 (69%) had celiac-type and 8 (31%) - a non-celiac genetic background;			IDDM - insulin dependent diabetes mellitus; ATD - autoimmune thyroid disorder (including autoimmune thyroiditis or Graves' disease); APECED - autoimmune polyendocrinopathy-candidosis-cetodermal dystrophy; 11% prevalence does not necessarily depict the true frequency of CD in pts with more than one autoimmune disorder; all 62 pts were treated in endocrinological clinic, which can lead to referral bias

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Kordonouri, 2000 Germany Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA anti-tTG - ELISA antibody titers above 15 were considered positive; EMA - IF, fluorescence at 1:5 dilution was considered as a positive; IgA and IgG AGA - ELISA, for both methods a level above 35 AU were considered as a positive **Biopsy criteria/description:** endoscopical biopsy; Marsh criteria **Confirmatory test:** endoscopical biopsy; Marsh criteria (stated as a reference 9); done in 13 CD pts out of 23 suspected CD pts (7 lost to follow-up, 3 - refused biopsy); 9 were found to have biopsy proven CD; IEL per 100 enterocytes counted after immunohistochemical staining for CD8+ cells (normal values in children up to 26 IEL per 100 enterocytes) **Checked IgA def.** yes; 9 pts out of initial 529 had below normal IgA levels and were excluded from further analysis	**Ethnicity:** n/a **Patient type/# screened:** 520 pts with IDDM and no clinical signs of CD **Demographics:** 520 pts with IDDM; age (y): median 14.2, range 1.6-27.3; 47% F; medium duration of IDDM 4.0 y, range 0-23.6 y **Incidence:**	23 (4.4%) of the 520 pts with IDDM were found to be positive for IgA anti-tTG; 18 (3.5%) - for EMA; and 18 (3.5%) - for IgA AGA; prevalence of biopsy proven CD in the whole group of IDDM pts was at least 1.7% (9/520), because in 10 pts with increased IgA anti-tTG levels biopsy was not performed; all 9 pts with biopsy confirmed CD were positive for anti-tTG, and 8 - for EMA			Study demonstrates that elevated IgA anti-tTG, especially when present on more than one occasion, may be more sensitive than EMA for detecting a silent form of CD; while prevalence of positive IgA anti-tTG was 4.4%, the incomplete prospective histological assessment by biopsy precludes a final calculation of the prevalence of biopsy-proven CD in this pts group

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Lampasona, 1999 Italy Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional Prevalence **Test/methodology:** human tissue transglutaminase C - TGCA IgA and TGC IgG; the threshold for positivity was the upper first percentile of normal controls, respectively 0.9 AU for IgG TGCA and 0.3 for the IgA TGCA; typing of HLA for 128 pts with IDDM either using the standard microcytotoxicity test on lymphocytes isolated by immuno-magnetic beads or by sequence specific PCR on DNA extracted from blood mononuclear cells; subjects grouped as DR3/X, DR4/Y, DR3/4, or DRX/Y **Biopsy criteria/description:** endoscopical biopsy; Marsh criteria **Confirmatory test:** n/r **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** 287 pts with a new onset IDDM; 119 pts with NIDDM; 213 pediatric controls with no family history of diabetes **Demographics:** 287 pts with IDDM; age (y): median 10, range 0.8-33; 41% F; 119 pts with NIDDM; age (y): median 65, range 42-87; 45% F; 213 controls; age (y): median 4.4, range 0.1-11.2; 49% F **Incidence:**	Increased levels of TGCA were detected in 122 of 287 pts with IDDM (43%; CI 37-48%); of the pts 25 (9%; CI 6-13%) had raised levels of IgA TGCA and 121 (42%; CI 36-48%) - IgG TGCA; in 24 pts (8%; CI 5-12%) both IgA and IgG TGCA were found	In the NIDDM group 2 pts had low levels of IgG TGCA only; as for HLA typing, 34 had DR3/4 genotype, 41 - DR3/X, 38 - DR4/Y and 15 - DRX/Y; increased TGCA were found in 22 (65% CI 46-80%) with the DR3/4 genotype, 19 of those with DR4/Y (50%; CI 33-67%), 16 with DR3/X (39%; CI 24-55%) and in 3 with DRX/Y (20%; CI 4-48%)		Almost 10% of pts have autoimmunity typical of CD and another 30% have low level TGCA antibody binding; this high prevalence suggests either involvement of the gut in the pathogenesis of IDDM or that transglutaminase is a secondary autoantigen resulting from beta-cell destruction

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Li Voon Chong, 2002 UK Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA EMA - IF; IgA AGA - ELISA; total serum IgA **Biopsy criteria/description:** n/r **Confirmatory test:** biopsy **Checked IgA def.** yes	**Ethnicity:** n/a **Patient type/# screened:** 509 pts with IDDM assessed during 1998; treated autoimmune thyroid disease - AITD - present in 28 (5.5%); 7 (1.4%) out of 509 had known CD; 38 pts with coexisting IDDM and AITD, but without known CD studied during 1999; and 112 pts with IDDM alone and without known CD assessed during 1999 **Demographics:** age (y): mean 29.4, range 16-45; 41% F; 38pts with coexisting IDDM and AITD screened for CD: age (y): mean 35.6, range 17-53; 66% F; 112 pts with IDDM alone screened for CD: age (y): mean 30.6+-9, range 16-57; 43% F **Incidence:**	1) prevalence of known CD in 509 IDDM pts was 1.4% (7/509); 2 of these 7 pts later on developed AITD	2) in the 38 pts with coexisting IDDM and AITD screening revealed 1 pts with increased IgA EMA, but normal IgA AGA levels; none were diagnosed with biopsy proven CD, making a prevalence of CD 0% in this group	3) in the 112 pts with IDDM alone screening for CD revealed 2 pts with increased IgA EMA and normal IgA AGA, 1 of whom had biopsy confirmed CD, making a prevalence of CD in this group 0.9%	Undiagnosed CD in pts with both IDDM and AITD is not increased compared with pts with IDDM alone; because 2 of 7 pts with known CD subsequently developed hypothyroidism, authors suggest that pts with known CD and IDDM be annually screened for AITD

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Lorini, 1996 Italy Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA and IgG AGA: ELISA; levels more than 2 SD were considered abnormal - for IgA >10 AU; for IgG - >7500 AU; R1-ARA: IF on rat kidney and liver; IgA EMA: IF on a distal ME; HLA-DR3, HLA-DR4, HLA-DR7 **Biopsy criteria/description:** n/r **Confirmatory test:** intestinal biopsy in 6 pts with constantly elevated IgA AGA during a follow-up **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** 133 pts with IDDM; 45 age-matched, apparently normal controls **Demographics:** 133 IDDM - age (y): mean 14.1, range 1.4-28.4; 47.3% F; 53 pts were considered at the onset of IDDM and 49 of them were also investigated for a 1-10 y follow-up; 45 aged-matched controls (CO); age: mean, range n/r **Incidence:**	IDDM pts: 3.75% (5/133)	IDDM pts: 3.75% (5/133)		At the diagnosis of IDDM IgA AGA were elevated in 32% (17/53), and during a follow-up it decreased within a normal limits in 13 pts; out of 32 pts with IgA AGA normal levels at the diagnosis of IDDM, 2 developed IgA AGA increased levels during a follow-up; in all pts with IgA AGA positivity during a follow-up, R1-ARA and EMA levels were also increased; high IgA AGA levels at the onset of IDDM are a transient abnormal immunological response and do not predict the occurrence of CD; they should not be considered a primary indication for performing a diagnostic intestinal biopsy unless R1-ARA and EMA are present too; HLA-Dr3 and/or DR4 were present in all 5 pts with AGA, R1-ARA and EMA positive

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Not, 1998, USA Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgG and IgA-AGA - ELISA (goat immunoglobulin) cut-off was above mean ± 2 SD; IgA-EMA (IgA AGA or IgG AGA) - indirect IF on either ME or HU, cut-off n/r **Biopsy criteria/description:** n/r **Confirmatory test:** no biopsy in the 96 IgA/IgG pos or 8 EMA positive pts; HLA haplotype typed in 4 EMA-positive and 23 EMA-negative donors; all 4 EMA-positives carried CD-associated alleles: 3 had DQA1*0501 and DQB1*0201 haplotype and 1 - DQA1*03 and DQB1*0302 **Checked IgA def.** yes; none of 86 donors with positive IgG AGA and negative IgA AGA/EMA had IgA deficiency	**Ethnicity:** 1,740 Caucasians (87%), 230 African-American (11.5%), and 30 Asians (1.5%) **Patient type/# screened:** 2,000 healthy blood donors **Demographics:** mean age: 39 y % F: 48 **Incidence:**	Prevalence of test positivity: 4.8% (96/2,000) for IgA and/or IgG; 0.4% (8/2,000) for EMA			No biopsy performed to diagnose CD; Confirmatory test: HLA DQA1& DQB1

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Page, 1994, UK	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA-AGA-in-house ELISA; titers of >90 U/L were considered abnormal **Biopsy criteria/description:** n/a **Confirmatory test:** Biopsy **Checked IgA def.** yes (8 pts had IgA deficiency and 1 was found to have CD)	**Ethnicity:** n/a **Patient type/# screened:** 1,785 diabetic pts (43% with IDDM and 57% with NIDDM) **Demographics:** n/r **Incidence:**	Prevalence of test positivity: IGA-AGA was positive in 4.1% (73/1785); 49 of these 73 pts were biopsied; CD was diagnosed in 13 of 49 biopsied pts; in 8 out of 1,765 pts IgA and 1 pt was diagnosed with CD; in general, prevalence of newly diagnosed CD was at least 0.78% (14/1785); the overall prevalence of CD in the whole group (4 pts were previously diagnosed with CD) was at least 1% (18/1789); 0.4% (8/2000) for EMA			Prevalence of CD in IDDM pts group was at least 1:50 compared with 1:340 in pts with NIDDM

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Rensch, 1996 USA Duplicate: no	**Publication type:** journal **Study design:** **Test/methodology:** EMA **Biopsy criteria/description:** Loss of villous architecture, crypt hyperplasia, and increased IELs **Confirmatory test:** none **Checked IgA def.**	**Ethnicity:** n/a **Patient type/# screened:** type I diabetes **Demographics:** n=47; adults **Incidence:** n/a	By first EMA: 3 Biopsy proven: 3			

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Roldan, 1998 Spain Duplicate: no	**Publication type:** journal **Study design:** **Test/methodology:** IgA, IgG AGA (and known cases, and some tested with EMA) **Biopsy criteria/description:** ESPGAN **Confirmatory test:** none **Checked IgA def.**	**Ethnicity:** n/a **Patient type/# screened:** type I diabetes **Demographics:** n=117; children **Incidence:** n/a	By first IgA: 19 Biopsy proven: 7			Mixed group diagnosed by different means

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Rossi, 1993, USA Duplicate: no	**Publication type:** journal **Study design:** **Test/methodology:** EMA **Biopsy criteria/description:** ESPGAN **Confirmatory test:** none **Checked IgA def.**	**Ethnicity:** **Patient type/# screened:** type I diabetes **Demographics:** n=211; children **Incidence:**	By first EMA: 10 Biopsy proven: 3			Only 3/10 biopsied

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Sategna-Guidetti, 1994 Italy Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA EMA - IF ME **Biopsy criteria/description:** Roy-Choudhury capsule from upper jejunum; criteria of Roy-Choudhury **Confirmatory test:** endoscopic biopsy and Roy-Choudhury capsule **Checked IgA def.** no	**Ethnicity:** n/a **Patient type/# screened:** 383 consecutive IDDM adults; 151 CD pts (as true positives) and 250 healthy and diseased controls (as true negatives) to assess IgA EMA test sensitivity and specificity **Demographics:** IDDM - age (y): mean 39, range 16-84; 43.9% F **Incidence:**	Prevalence of test positivity: CD pts -145/151 (96%) EMA positive(1:50-1:>2000); sensitivity of IgA EMA was 96%	Prevalence of biopsy proven CD in IDDM group was at least 2.6% (10/383): 2 pts out of 12 IgA EMA positives refused biopsy; prevalence of IgA EMA positivity was 3% (12/383)	Controls-0/437 EMA positive; specificity of IgA AGA was 100%	Prevalence of CD in IDDM pts group was at least 1:50 compared with 1:340 in pts with NIDDM

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Saukkonen, 1996 Finland Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** gA- reticulin-indirect IF goat anti-human antiserum; IgA and IgG AGA - ELISA cut-off >30% of an intralaboratory standard (intra and inter-assay CV of 5.6% and 10.5% for IgA, and 6.9% and 16.1% - for IgG, respectively) **Biopsy criteria/description:** n/r **Confirmatory test:** Biopsy for all pts with abnormally high levels of antibodies but not for those with initially (diagnosis of IDDM) positive antibodies but negative at follow-up (6, 12, 18, 24 and 36 mos) **Checked IgA def.** no	**Ethnicity:** n/a **Patient type/# screened:** 776 IDDM children **Demographics:** children less than 16 y **Incidence:**	Prevalence of CD in IDDM pts was at least 2.4% (19/776); prevalence of test positivity: at the diagnosis of IDDM and or at 24/36 months follow-up 76/775 positive for IgA-ARA and or IgA-AGA; 35 of these 76 pts were biopsied; in 17 of 35 pts biopsy confirmed CD was found; 2 pts out of 76 pts with a negative antibodies/symptomatic/ were diagnosed by biopsy; overall, 19/776 biopsy confirmed cases; 19/19 positive IgA-ARA; 14/18 genotyped for HLA DR positive for DR3 and 10 (56%) positive for DR4; DQB2 present in 17/18 (94%)			The observed prevalence of CD is an underestimate, because biopsy was not performed in 17 pts who screened positive for IgA ARA or AGA in the follow-up sample

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Schober, 2000 Austria Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** EMA - indirect IF of ME, any positive reading at a dilution of 1:10 was considered as a positive; IgG-AGA and IgA-AGA - ELISA; cut-off for IgG AGA was ->30 AU; for IgA-AGA - >25 AU **Biopsy criteria/description:** Modified Marsh and Crowe; Watson-type capsule **Confirmatory test:** Biopsy **Checked IgA def.** yes	**Ethnicity:** n/a **Patient type/# screened:** 403 children and adolescents with type I diabetes **Demographics:** age (y): mean 12.4, range 1-22; 47.9% F **Incidence:**	Overall prevalence of biopsy proven CD was 1.49% (6/403); as for prevalence of test positivity: 12 pts had increased IgA EMA; 11 of these 12 were biopsied (1 refusal); on biopsy: 3 (0.74%) had Marsh I; 2 (0.49%) - Marsh 0; 1 - Marsh IIIa/c and 5 Marsh IIIc (1.49%)			

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Sigurs, 1993 Sweden Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA- AGA - ELISA, cut off level at least 25 AU; IgA and IgG ARA - IF; titers equal to or diluted more than 1:5 were considered positive **Biopsy criteria/description:** Watson Capsule **Confirmatory test:** Biopsy **Checked IgA def.** yes (3 cases)	**Ethnicity:** n/a **Patient type/# screened:** 436 children with IDDM **Demographics:** age (y): mean 13.6+-4.1, range 2-21 y, 46.3% F **Incidence:**	Minimum prevalence of CD in IDDM pts was 4.6% (21/459); prevalence of newly diagnosed CD was 3.4% (15/436); as for prevalence of test positivity: 4.3% (19/436) were IgA AGA positive; 18 of these 19 pts were biopsied; minimum PPV for IgA ARA was 77% (13 of 17)			

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Sjoberg, 1998 Germany Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA-AGA - ELISA, titre > 8.5 AU was considered positive; IgG-AGA - ELISA, titre > 330 AU was considered positive **Biopsy criteria/description:** Marsh; Watson Capsule or gastroscopy and biopsy **Confirmatory test:** EMA-indirect IF of ME- titre ≥ 5; biopsy **Checked IgA def.** no	**Ethnicity:** n/a **Patient type/# screened:** 1,664 diabetes pts (848 IDDM; 745 NIDDM; 71 secondary diabetes) **Demographics:** IDDM - age (y): mean 46.1, range 17-86; 52.8% F; NIDDM - age (y): mean 61.7, range 24-92; 47.3 F; secondary diabetes - age (y): mean 53.9, range 33-77, 9.8% F **Incidence:**	Prevalence of biopsy proven CD was 1.8% (15/848): 8 out of 848 were previously diagnosed with CD; as for prevalence of test positivity: 258/848 were positive for IgA and/or IgG-AGA; 22/258 were positive for EMA giving a prevalence of 2.6%; 7/20 were biopsy positive (14/20 potential CD:4 death; 3 refused biopsy)	NIDDM- 1/745 previously diagnosed CD; 1/745 EMA positive; prevalence in total 0.27%	Secondary diabetes group- 3/71 IgG-AGA positive; no EMA positives; no previously diagnosed CD; prevalence of CD was 0%	Pts with previously known CD had more symptoms, more deficiency states and more autoimmune diseases than those identified by screening (p<0.001); IDDM pts with a diabetes duration of 31-40 y were characterised by a higher prevalence of CD than pts with a duration of less than 30 y (6.7% vs. 1.7%; p<0.02)

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Spiekerkoetter, 2002 Germany Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** human tTG: IgA/IgG assay cut-off of 9.0 units, IgG-tTGA cut-off 7.0 units, IgA-tTGA cut-off 8.3 units **Biopsy criteria/description:** Marsh **Confirmatory test:** biopsy **Checked IgA def.** no, not mentioned	**Ethnicity:** n/a **Patient type/# screened:** ped IDDM pts **Demographics:** n=205; ped; median age=12 y 7 mos; age range=3-19.5 y; 47.3% F **Incidence:**	By IgA/IgG-tTG: 6.3% (13/205); by IgG-tTG: 5.4% (11/205); by biopsy 2.9% (6/8/13/205) [only 8 of the 13 with elevated tTGA levels agreed to biopsy]			

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Talal, 1997 USA Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** EMA, cut-off at dilution ≥ 1:10; biopsy **Biopsy criteria/description:** ESPGAN **Confirmatory test:** small bowel biopsy **Checked IgA def.** yes	**Ethnicity:** n/a **Patient type/# screened:** adult diabetic pts **Demographics:** n=185; adult; other info n/a **Incidence:**	By EMA: 4.9% (9/185); by biopsy 2.2% (4/5/9/185) [only 5 of the 9 EMA positives underwent biopsy]			

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Valerio, 2002 Italy Duplicate: Yes (see Celiac 1)	**Publication type:** journal **Study design:** Prevalence **Test/methodology:** IgA AGA, ELISA; IgG AGA, ELISA; IgA EMA, indirect IF (substrate n/r) **Biopsy criteria/description:** ESPGAN **Confirmatory test:** small bowel biopsy **Checked IgA def.** yes	**Ethnicity:** n/a **Patient type/# screened:** 383 type 1 diabetes pts **Demographics:** 383 Type 1 diabetics (194 M, 189 F, 49% F) age < 18 y **Incidence:** Time period: from January 1992 to December 2000	Type 1 diabetics 32/383 (8.3%); 2 out of 32 had IgA deficiency			

Evidence Table 6 (cont'd): Prevalence/incidence of CD in patients with diabetes

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Vitoria, 1998 Spain Duplicate: no	**Publication type:** journal **Study design:** Prevalence **Test/methodology:** AGA; EMA; intestinal biopsy; IAA, GAD65, IA2, ICA tests to assess IDDM-related pancreatic autoimmunity among CD pts **Biopsy criteria/description:** ESPGAN **Confirmatory test:** biopsy **Checked IgA def.** yes, none found	**Ethnicity:** n/a **Patient type/# screened:** confirmed CD pts and IDDM pts; exclude confirmed CD pts for data extraction, irrelevant data **Demographics:** 93 IDDM: pedi; mean age=10.5 y; ?% F **Incidence:**	IDDM group: by AGA 17.2% (16/93); by EMA 7.25% (7/93); by biopsy 6.5% (6/93)			IDDM could develop in pts with silent, non-treated CD through gluten-mediated immune activation

Prevalence of CD in High-Risk Patients—Relatives

Evidence Table 7: Prevalence of CD in relatives of patients with CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Book, 2003 USA Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** IgA-EMA; tTG-ELIZA; HLA DQA1, DQB1 **Biopsy criteria/description:** n/a **Confirmatory test:** biopsy; diagnosis based on positive biopsy or had positive EMA and tTG serologies **Checked IgA def.** n/a	**Ethnicity:** n/a; but all families were Caucasian **Patient type/# screened:** Relatives of CD pts **Demographics:** n=163 first-degree relatives, n=82 second-degree relatives, n=47 first cousins; ped & adult; mean age=?; age range=2-78 y; % F? **Incidence:**	Parents: 14.7%	Siblings: 21.3%	Offspring: 14.7%	HLA DQ available in 34/37 of the seropositives, all but one was DQ2 or DQ8
			Group 4	**Group 5**		
			Second-degree relatives: 19.5%	First cousins: 17.0%		

Evidence Table 7 (cont'd): Prevalence of CD in relatives of patients with CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Corazza, 1997 Italy Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** AGA **Biopsy criteria/description:** Some VA **Confirmatory test:** n/a **Checked IgA def.** n/a	**Ethnicity:** n/a **Patient type/# screened:** Relatives of CD pts **Demographics:** n=328 first-degree relatives **Incidence:**	4%			

Evidence Table 7 (cont'd): Prevalence of CD in relatives of patients with CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Farre, 1999 Spain Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA EMA - IF either on a ME (n=550), or HU (n=119); positive ab 1:5 dilution and characteristic honeycomb staining pattern; IgA AGA - ELISA; values over 40 AU were considered positive; HLA-DQ2 (DQA1*0501 and DQB1*0201 alleles) were assayed in 169 pts; typing performed by PCR amplification **Biopsy criteria/description:** Watson-Crosby capsule; classification: 1) total VA; 2) severe partial VA with crypt hyperplasia; 3) minor non-specific abnormalities; 4) morphologically normal; 1 and 2 were diagnostic criterias for CD **Confirmatory test:** Watson-Crosby capsule; HLA-DQ2 typing performed in 169 first-degree relatives of CD pts, in 60 CD pts and in 50 ethnically matched controls from the general population **Checked IgA def.** yes, results were not explicitly given in the text. Presumably there was no case of IgA deficiency found because the alternative IgG test for such pts were not used or mentioned in the results section	**Ethnicity:** n/a **Patient type/# screened:** 675 first-degree relatives in 227 families of CD probands (149 pediatric and 78 adult pts) **Demographics:** 669 first-degree relatives in 227 families of CD probands (149 pediatric and 78 adult pts) screened for CD (6 were diagnosed with CD prior to screening and excluded from the study, but accounted for overall prevalence); out of 669 relatives: 331 were parents (163 fathers, 168 mothers), 260 siblings (123 brothers and 137 sisters), and 78 children (42 sons and 36 daughters) **Incidence:**	The prevalence of unrecognised CD in first-degree relatives of CD pts was 4.6% (31/669); the overall prevalence of CD in this group is 5.5% (37/675 - 6 relatives of CD pts were diagnosed with CD prior to the study); as for test positivity: IgA EMA was positive in 39/669 (5.8%) and IgA-AGA - in 13/669 (1.9%) relatives; simultaneous positivity occurred in 12 of 669 relatives (1.8%); of 39 EMA-positive relatives, biopsy has been done in 32 pts (7 refused) and CD were found in 31 individuals			HLA-DQ2 was typed in 12 of the 32 EMA-positive relatives who underwent biopsy and was positive in all cases; HLA-DQ2 haplotype was also present in 64% (108/169) of relatives, 93% (56/60) CD pts and 18% (9/50) of controls; all unrecognised CD relatives detected by screening were DQ2 positive

Evidence Table 7 (cont'd): Prevalence of CD in relatives of patients with CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Fasano, 2003 USA Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** EMA - IF; ME or HU; positive at 1:10; all positive EMA tested with human tTG ELISA positive at 2 SD above mean of healthy controls; HLA DQ2 and DQ8 **Biopsy criteria/description:** single pathologist, Marsh **Confirmatory test:** htTG; biopsy; also small subset 98 EMA positive and 114 EMA neg had HLA DQ2/8 tested **Checked IgA def.** n/a	**Ethnicity:** 94% white; 3% black; 1.5% Hispanic, 1% Asian, 0.5% other **Patient type/# screened:** 9,019 at risk of CD; 4,126 not at risk **Demographics:** at risk - symptoms of celiac (1326 children, 1909 adults); CD associated disorders; 4,508 1st deg relatives; 1,275 2nd deg relatives; Not at risk – 2,000 blood donors (mean age 39 range 19-65); 1,119 school children (mean age 12.3, range 6-18); 1,007 adults and children for routine physical (mean age 39, and 13.7, range, 19-71, and 2-18) **Incidence:**	1) At risk - a) 1st deg relatives - 205/4,508 (4.55%); children - 54/1,294 (4.17%); adults - 151/3,214 (4.70%); b)symptomatic adults - 28/1,910 (1.47%); children - 53/1,326 (4.00%); 2) Not at risk - 1/4126 (0.75%); adults - 27/2,845 (0.95%); children - 4/1,281(0.31%); biopsy in EMA pos - Marsh 1- 0%; 2 - 30/116 (25.9%); 3a - 46/116 (39.7%); 3b - 24/116 (20.7%); 3c - 16/116 (13.8%); HLA DQ2-76/98 (78%); DQ8 - 16/98 (16%); DQ2 and 8 - 6/98 (6%); all EMA pos were also tTG pos			

Evidence Table 7 (cont'd): Prevalence of CD in relatives of patients with CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Hill 2000 USA Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA-EMA - IF on ME, methodology n/a; IgA and IgG-AGA - ELISA, methodology n/a **Biopsy criteria/description:** Marsh **Confirmatory test:** Biopsy **Checked IgA def.** yes	**Ethnicity:** n/a **Patient type/# screened:** 1,200 pediatric group of individuals at risk of CD; pts were assigned to one of 7 groups: 1) chronic diarrhea (n=182); 2) abdominal pain (n=316); 3) IDDM (n=81); 4) short stature (n=259); 5) failure to thrive (n=123); 6) miscellaneous (down's syndrome, thyroiditis, anemia, unexplained elevation of liver enzymes) (n=47); 7) asymptomatic relatives (n=192) **Demographics:** 1,200 pediatric group of individuals at risk of CD; age (y): mean n/a, range 6 mos - 20 y; % F n/a **Incidence:**	Prevalence of CD in pts at risk was 1 in 57 (21/1200); prevalence of test positivity: 2.8% (34/1200) was both EMA and AGA positive; 26 of pts (19 EMA positive) underwent biopsy and 21 were diagnosed with CD			15 pts out of 34 EMA positives refused biopsy; thus prevalence of biopsy proven CD in pts at risk was at least 1 in 57; if considered above mentioned 15 pts prevalence of CD could have been 1 in 33 (36/1200)

Evidence Table 7 (cont'd): Prevalence of CD in relatives of patients with CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Hogberg, 2003 Sweden Duplicate: no	**Publication type:** journal **Study design:** longitudinal follow-up, incidence & prevalence **Test/methodology:** IgA-AGA, ELISA cut off for a positive outcome 42.5 units; IgA-EMA, indirect IF using ME the antibody titre was defined as the highest serum dilution yielding positive fluorescence; IgA-TGA, commercially available ELISA, highest cut-off value for positive results >30 units. **Biopsy criteria/description:** revised ESPGAN. Grade 1 normal; Grade 2 mild; Grade 3 moderate, Grade 4 total VA **Confirmatory test:** Small bowel biopsy **Checked IgA def.** yes, 5 cases found	**Ethnicity:** n/a **Patient type/# screened:** 120 first degree relatives of CD pts **Demographics:** 56 parents (adults) mean age 53.6 range (43-78); 44 siblings (ped and adult) mean age 27.4 y age range (15-49); offspring 20 mean age 6.5 y age range (1-16). Gender not reported **Incidence:** Time period: 20 y follow-up study. Original study period Sept. 1975- Feb. 1981	10/120 (8.3%) prevalence, 2 were diagnosed in the original study 20 y prior, 8 new cases from the present follow-up study group. (biopsy confirmed); Serum results; IgA AGA 8/120 pos; IgA EMA 0.5% (6/120) pos; IgA TGA 3.8% (4/104) pos (3 pts with positive biopsy were not tested for IgA TGA)			IgA deficient pt, IgG antibodies positive. Biopsy findings were in serologically positive relatives IgA TGA was performed in sera of n=104 when access to assay became available 1 y later.

Evidence Table 7 (cont'd): Prevalence of CD in relatives of patients with CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Holm, 1993 Finland Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** biopsy **Biopsy criteria/description:** Some VA **Confirmatory test:** n/a **Checked IgA def.** n/a	**Ethnicity:** n/a **Patient type/# screened:** Relatives of celiac pts **Demographics:** n=121 first-degree relatives **Incidence:**	10.7%			

Evidence Table 7 (cont'd): Prevalence of CD in relatives of patients with CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Korponay-Szabo, 1998 Hungary Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional Prevalence **Test/methodology:** IgA EMA - IF using ME and human duodenum as substrate; serum total IgA, deficiency was defined as total serum IgA<0.1 g/L **Biopsy criteria/description:** Watson capsule; histological evaluation according to the grading of Fontaine and Navarro; ESPGAN criteria for CD **Confirmatory test:** biopsy; Watson-Crosby capsule; biopsy done in 77 out of 81 pts with positive IgA EMA **Checked IgA def.** yes; 2.1% (21/997) of all family members studied were IgA deficient; among CD diagnosed pts 10.8% (9/83) were IgA deficient	**Ethnicity:** n/a **Patient type/# screened:** 997 family members of 396 pts with CD screened for CD **Demographics:** 997 family members of 396 pts with CD screened for CD (521 parents, 368 siblings, 54 children and 54 second-degree relatives); age: mean/median, range n/a **Incidence:** # New cases: 75 new cases of CD; incidence of CD was 7.6% (75/989)	Prevalence of CD in the whole screened population was 8.3% (83/997); prevalence for first-degree relatives in total: 8.6% (80/943)	parents: 4.2% (22/521)	siblings: 13.8% (51/368)	Screening revealed 75 new CD cases (in 71 IgA EMA were positive and in 4 - negative); 8 pts had been previously diagnosed with CD and were on a GFD and thus EMA negative; the total number of CD in the family members was 83; in 55 families two, in 10 families 3, in 1 family 4 and in 1 more family 6 members were affected by CD
			Group 4	**Group 5**		
			children: 12.9% (7/54);	second-degree relatives: 5.6% (3/54)		

Evidence Table 7 (cont'd): Prevalence of CD in relatives of patients with CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Kotze, 2001 Brazil Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** EMA **Biopsy criteria/description:** n/a **Confirmatory test:** n/a **Checked IgA def.** n/a	**Ethnicity:** n/a **Patient type/# screened:** Relatives of celiac pts **Demographics:** n=115 first-degree relatives **Incidence:**	3.5%			Negative serology; EMA titre =1/5

Evidence Table 7 (cont'd): Prevalence of CD in relatives of patients with CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Mustalahti, 2002 Finland Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional Prevalence **Test/methodology:** IgA-EMA- indirect IF on a HU, serum dilution of at least 1:5 was considered positive; IgA and IgG AGA - ELISA, level of AGA was considered positive when mean+-2 SD of healthy controls; IgA-tTG-ELISA, values at least 20 AU were considered positive **Biopsy criteria/description:** Small-bowel biopsies with pediatric or adult Watson capsule or forceps from the distal duodenum **Confirmatory test:** Biopsy; DQ2 and DQ8 typing on PCR **Checked IgA def.** n/a	**Ethnicity:** n/a **Patient type/# screened:** 466 healthy first-degree family members of CD pts **Demographics:** 466 healthy first-degree family members of CD pts; age (y): median 41, range 2-90 **Incidence:**	Prevalence of CD in healthy, first-degree relatives of CD pts was 6.2% (29/466); as for test positivity: 72/466 pts (44 EMA pos 9.4% and 48 IgA pos 10.3%) were positive for EMA and IgA; IgA-tTG was positive in 12.9% (60/466) pts; IgA-EMA detected 97% of CD (28/29) and IgA-AGA detected - 51% (15/29); all 44 IgA EMA and 19/28 AGA positive pts were positive for DQ2; all 29 newly diagnosed CD pts were DQ2 positive			15 pts out of 34 EMA positives refused biopsy; thus prevalence of biopsy proven CD in pts at risk was at least 1 in 57; if considered above mentioned 15 pts prevalence of CD could have been 1 in 33 (36/1,200)

Evidence Table 7 (cont'd): Prevalence of CD in relatives of patients with CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Pittschieler, 2003 Italy Duplicate: no	**Publication type:** journal **Study design:** Prospective prevalence **Test/methodology:** EMA, HUC examined by fluorescence. Absence of binding was considered a negative test; HLA typing was done exclusively once diagnosis of CD was confirmed= micro-lymphocytotoxic technique **Biopsy criteria/description:** Small intestinal biopsy of first jejunal loop. Ferraris Watson capsule. Normal values being less than 3.2 cells/mm γ/δ T-cell receptors by immunohistology **Confirmatory test:** biopsy, HLA typing **Checked IgA def.** yes, none found	**Ethnicity:** n/a **Patient type/# screened:** 92 first-degree relatives of CD pts. Yearly testing over 12 year period **Demographics:** 92 at risk (first-degree relatives; 18 offspring and 74 siblings) aged 2-18 y **Incidence:** Time period: 12 year time period January 1990-December 2001	6.5% (6/92) confirmed CD by both serology & biopsy within a few months of CD diagnosis in one of their relatives; 5 total VA and 1 partial VA; over 2-5 y a further 5.8% (5/86) confirmed positive with both HU EMA IgA and biopsy 1 partial VA and 4 total VA; combined prevalence=12% (11/92); 11/11 were carriers of HLA DQ2/ heterodimers			All 11 were clinically silent for CD

Evidence Table 7 (cont'd): Prevalence of CD in relatives of patients with CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Polvi, 1996 Finland Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional Prevalence **Test/methodology:** DQA1*0501 and DQB1*0201 **Biopsy criteria/description:** n/a **Confirmatory test:** n/a **Checked IgA def.** n/a	**Ethnicity:** n/a **Patient type/# screened:** 31 CD index pts; 14 silent CD pts; 29 healthy siblings of CD index pts; 32 controls; **Demographics:** n/a **Incidence:**	Prevalence of DQA1*0501 and DQB1*0201 positivity in CD index group: 100% (31/31) CD index pts were positive; relative risk for having at least two alleles 156 **Group 4** prevalence of DQA1*0501 + DQB1*0201 in cadaver organ donors: 28% (9/32) controls	Prevalence of DQA1*0501 and DQB1*0201 positivity in silent CD group: 100% (14/14) silent CDs	Prevalence of DQA1*0501 and DQB1*0201 positivity in siblings of index CD pts: 48% (14/29) healthy sibs	There was a very strong association of DRA1*0501 and DQB1*0201 alleles positivity with CD; the RR for an individual having at least 2 susceptibility alleles suffering from CD was as high as 156 ($p<0.001$); RR was also high (67; $p<0.001$) when the index cases were compared with their siblings. The etiologic fraction in both cases was 0.99

Evidence Table 7 (cont'd): Prevalence of CD in relatives of patients with CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Robinson, 1971 UK	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** small bowel biopsy, Crosby capsule **Biopsy criteria/description:** Other: normal, convoluted, and flat; either partial or subtotal VA represents confirmed CD **Confirmatory test:** biopsy **Checked IgA def.** n/a	**Ethnicity:** n/a **Patient type/# screened:** relatives of celiac pts **Demographics:** 1) n=68, first-degree relatives=parents & siblings; 2) n=164, second-degree relatives=uncles & aunts, 50.6% F; 3) n=238, third-degree relatives=cousins, 52.1% F **Incidence:**	First-degree: 4.4% (3/68)	Second-degree: 0% (0/164)	Third-degree: 0% (0/238)	

Evidence Table 7 (cont'd): Prevalence of CD in relatives of patients with CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Rolles, 1974 UK Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** biopsy **Biopsy criteria/description:** n/r **Confirmatory test:** n/a **Checked IgA def.** n/a	**Ethnicity:** n/a **Patient type/# screened:** Relatives of CD pts-CD child in family **Demographics:** n=72 first-degree relatives **Incidence:**	5.6%			

Evidence Table 7 (cont'd): Prevalence of CD in relatives of patients with CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Rostami, 2000 Netherlands	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** IgA-EMA- indirect IF on a primate ileum; min 1:5 and 1:100; IgA-AGA- ELISA, >25 AU/mL was considered positive; IgA by nephelometry **Biopsy criteria/description:** EPSGAN; Marsh 1992 **Confirmatory test:** biopsy in all pts with positivity of symptoms and/or serology tests **Checked IgA def.** yes; 3 individuals were found to have IgA deficiency	**Ethnicity:** n/a **Patient type/# screened:** 388 first-degree relatives of CD pts **Demographics:** age (y): mean 39, range 1-80; 60% F **Incidence:** # New cases: 17 new cases of CD; incidence of 5% (17/338)	Overall prevalence of CD in the first-degree relatives of CD pts was 11% (37/338); there were 17 new and 20 previously diagnosed CD cases; as for the prevalence of test positivity: 28% (96/338) were positive for clinical complaints + lab tests (4 pts) and serology screening; 17/96 (18%) biopsy positive; 6/17 Marsh IIIc; 5/17 Marsh IIIa; 6/17 strongly positive EMA and AGA			

Evidence Table 7 (cont'd): Prevalence of CD in relatives of patients with CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	**Group 2**	**Group 3**	
Stokes, 1976 UK Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional Prevalence **Test/methodology:** biopsy **Biopsy criteria/description:** biopsy result must be grade III to be considered confirmed CD: subtotal VA **Confirmatory test:** biopsy **Checked IgA def.** n/a; no serology done; not mentioned	**Ethnicity:** n/a **Patient type/# screened:** Relatives of CD pts **Demographics:** n=326; children and adult; other info n/a **Incidence:** # New cases: 17 new cases of CD; incidence of 5% (17/338)	Fathers: 10.3% (4/39)	Mothers: 2.3% (1/43)	Brothers: 7.4% (5/68)	
			Group 4	**Group 5**	**Group 6**	
			Sisters: 17.3% (13/75)	Sons: 8.3% (5/60)	Daughters: 17.1% (7/41)	
			Group 7			
			19.2% (35/182 total biopsied)			

Evidence Table 7 (cont'd): Prevalence of CD in relatives of patients with CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Tursi, 2003 Italy Duplicate: no	**Publication type:** journal **Study design:** Prevalence **Test/methodology:** IgA IgG AGA, ELISA lower limit of positivity of IgA 0.2 EU/mL and IgG 10.0 EU/mL; IgA EMA, indirect IF on ME; IgA tTG, ELISA using GP liver substrate lower limit of positivity of these antibodies was 7 UA/mL **Biopsy criteria/description:** Marsh criteria 6 biopsies from small bowel from the second part of duodenum. Marsh Type I -'infiltrative' lesions with >30 lymphocytes/100 epithelial cells; Type II-'infiltrative/hyperplastic' lesions; Type III-'partial (sub)total VA; partial VA Marsh IIIa); subtotal VA Marsh IIIb); and total VA as Marsh IIIc) **Confirmatory test:** Biopsy **Checked IgA def.** yes	**Ethnicity:** n/a **Patient type/# screened:** 111 first-degree relatives of pts with CD **Demographics:** at risk 111 first degree relatives 38 M, 73 F, mean age 28.7 y, range (10-65 y); 65.8% F **Incidence:** n/a	CD diagnosed in 49/11 screened relatives (44.14%) prevalence; prevalence AGA 36.73%; EMA 38.78% ; anti-tTG 44.89%			Prevalence of antibodies was higher in severe histological lesions (Marsh IIIb-c) than in not so severe lesions (Marsh I-IIIa). Noteworthy, prevalence of AGA was higher than that of EMA/anti-tTG in less severe histological lesions

Evidence Table 7 (cont'd): Prevalence of CD in relatives of patients with CD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Vitoria, 1994 Spain Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional Prevalence **Test/methodology:** IgA-AGA>0.085 AU in children, >0.128 AU in adults; IgG-AGA>0.45 AU in children, >0.317 AU in adults; EMA titre≥1:5 **Biopsy criteria/description:** ESPGAN **Confirmatory test:** biopsy **Checked IgA def.** n/a	**Ethnicity:** n/a **Patient type/# screened:** first degree relatives of celiac pts **Demographics:** n=642 (380 parents, 249 siblings, 13 offspring); ped and adult; mean age= 27 y; age range=1-64 y; 52.3% F **Incidence:**	Fathers: by IgA-AGA: 11.7% (21/180), by IgG-AGA: 13.9% (25/180), by EMA: 0% (0/180), by biopsy: 0.56% (1/180)	Mothers: by IgA-AGA: 9% (18/200), by IgG-AGA: 8.5% (17/200), by EMA: 2.5% (5/200), by biopsy: 2.5% (5/200))	Brothers: by IgA-AGA: 8.3% (10/120), by IgG-AGA: 9.2% (11/120), by EMA: 3.3% (4/120), by biopsy: 2.5% (3/120)	
			Group 4	**Group 5**		
			Sisters: by IgA-AGA: 12.4% (16/129), by IgG-AGA: 15.5% (20/129), by EMA: 5.4% (7/129), by biopsy: 6.2% (8/129)	Offspring: by IgA-AGA: 15.4% (2/13), by IgG-AGA: 23.1% (3/13), by EMA: 7.7% (1/13), by biopsy: 7.7% (1/13)		

Prevalence of CD in Associated Clinical Conditions—Anemia

Evidence Table 8. Prevalence of CD in patients with anemia

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Akerman, 1996 Israel Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** EGD/Biopsy **Biopsy criteria/description:** subtotal or greater VA **Confirmatory test:** n/a **Checked IgA def.** n/a	**Ethnicity:** n/a **Patient type/# screened:** out pts with IDA (50% symptomatic) **Demographics:** 93 pts; mostly adults although some teens **Incidence:**	By biopsy: 13			

Evidence Table 8 (cont'd): Prevalence of CD in patients with anemia

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Annibale, 2001 Italy Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** antral (n=3 per pt)/body(n=3)/duodenal(n=2) biopsies; assessment of gastritis according to Sydney system; March classification for CD; colonoscopy for suspicious lesions; refusal of colonoscopy led to double-contrast barium enema; NOTE: no serology done **Biopsy criteria/description:** n/a **Confirmatory test:** Biopsies **Checked IgA def.** no, not mentioned	**Ethnicity:** n/a **Patient type/# screened:** iron deficiency **Demographics:** 81 pts; adult; median age 54; range 23-87; 74% F **Incidence:**	By biopsy: 6% (4/71); 71 pts formed the final sample of completely examined subjects. Note: no serology done			The celiac pts are younger compare to the rest of the sample

Evidence Table 8 (cont'd): Prevalence of CD in patients with anemia

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Annibale, 2003 Italy Duplicate: no	**Publication type:** journal **Study design:** Prospective prevalence **Test/methodology:** IgA tTG, ELISA normal values were <7 UA/mL **Biopsy criteria/description:** Marsh **Confirmatory test:** Biopsy - antral, gastric body, and duodenal biopsy collected **Checked IgA def.** n/a	**Ethnicity:** n/a **Patient type/# screened:** IDA in premenopausal women **Demographics:** 59 premenopausal women age range 22-54 y with IDA Hb < 12g/dLF **Incidence:** Time period: March-July 2000	7/59 (11.9%) had positive tTG antibodies titre; biopsy-confirmed: 8.5% (5/59)			40/59 subjects tested positive for various tests including tTG for CD detection and progressed to have upper endoscopy with biopsy

Evidence Table 8 (cont'd): Prevalence of CD in patients with anemia

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Corazza, 1997 Republic of San Marino Duplicate: no	**Publication type:** journal **Study design:** Cross-sectional prevalence **Test/methodology:** indirect IF EMA titre >1:5; biopsy **Biopsy criteria/description:** n/a **Confirmatory test:** biopsy **Checked IgA def.** no, but mentioned as such that it could have caused some misclassification of pts, but the effect should be minimal given the powerful sensitivity and specificity of EMA test	**Ethnicity:** n/a **Patient type/# screened:** random sample stratified for age and sex **Demographics:** n=2,237; adult median age: 44 y; range: 20-87 y % F: 53.2 **Incidence:**	By both EMA and biopsy: 1 in 559 pts, or 1.79 per 1000 [0.18%]			

Evidence Table 8 (cont'd): Prevalence of CD in patients with anemia

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Dickey, 1997 UK Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** EMA; AGA; methodology and cut-off levels n/a **Biopsy criteria/description:** endoscopic biopsy; criteria n/a; finding of VA and IELs in duodenal biopsy **Confirmatory test:** Biopsy **Checked IgA def.** n/a	**Ethnicity:** n/a **Patient type/# screened:** 41 pts with IDA and no specific GI symptoms or evidence of a bleeding on FOBT or upper GI and colonic endoscopy screened for achlorhydric gastric atrophy and CD **Demographics:** 41 pts with IDA screened for achlorhydric gastric atrophy and CD; age (y): mean 59, range 15-84; 61% F **Incidence:**	prevalence of CD in IDA pts was 10% (4/41); EMA was positive in 3 (75%) of 4 these pts; prevalence of EMA and/or AGA being positive was 10% (4/41)			The celiac pts are younger compared to the rest of the sample

Evidence Table 8 (cont'd): Prevalence of CD in patients with anemia

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Howard, 2002 UK Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** IgA/IgG-AGA and EMA then biopsy **Biopsy criteria/description:** n/a **Confirmatory test:** n/a **Checked IgA def.** n/a	**Ethnicity:** n/a **Patient type/# screened:** IDA identified through lab **Demographics:** 258 adult pts with IDA, folate **Incidence:**	By first serology: 28 by biopsy: 12			24/28 biopsied

Evidence Table 8 (cont'd): Prevalence of CD in patients with anemia

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Kepczyk, 1995 USA Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** EGD/biopsy **Biopsy criteria/description:** VA, crypt hyperplasia, inflammatory infiltrate **Confirmatory test:** n/a **Checked IgA def.** n/a	**Ethnicity:** n/a **Patient type/# screened:** Mostly symptomatic out pts with IDA **Demographics:** 39 adult pts with IDA **Incidence:**	By biopsy: 4			

Evidence Table 8 (cont'd): Prevalence of CD in patients with anemia

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
McIntyre, 1993 UK Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** duodenal biopsy performed in 50 pts; upper GI endoscopy performed in 108 pts **Biopsy criteria/description:** n/a **Confirmatory test:** prevalence of biopsy proven CD was at least 6% (3/50) **Checked IgA def.** No serology tests done. Results based on clinical findings of upper & lower GI symptoms. Prevalence was calculated only in biopsy-performed group of pts that consisted of 50 individuals.	**Ethnicity:** n/a **Patient type/# screened:** 111 pts with IDA **Demographics:** 111 pts with IDA; age (y): mean 63+-17.3, range 20-86; 61.3% F **Incidence:**	Prevalence of biopsy proven CD was at least 6% (3/50)			The celiac pts are younger compare to the rest of the sample

Evidence Table 8 (cont'd): Prevalence of CD in patients with anemia

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Oxentenko, 2002 USA Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** endoscopic biopsy of second and third parts of duodenum **Biopsy criteria/description:** CD was defined as total or partial VA with IELs **Confirmatory test:** Biopsy **Checked IgA def.** NA	**Ethnicity:** n/a **Patient type/# screened:** 113 pts with IDA **Demographics:** age (y): mean 55.6+-15.3, median 54, range 20-86; 71.7% F **Incidence:**	Prevalence of CD was 15% (17/113); 10 of these 17 pts had positive endoscopic markers suggestive of CD; 8 pts with endoscopic markers present did not have CD on biopsy			Only biopsy/no serology tests performed

Evidence Table 8 (cont'd): Prevalence of CD in patients with anemia

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Ransford, 2002 UK Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** IgA-EMA-ME, titers> 1:5 was considered positive; IgA tTG- ELISA, cut-off n/a **Biopsy criteria/description:** revised ESPGAN; duodenal histologic changes were graded according to Marsh criteria **Confirmatory test:** Biopsy **Checked IgA def.** No	**Ethnicity:** n/a **Patient type/# screened:** 484 anemic pts; 498 age and sex matched controls **Demographics:** n/a **Incidence:**	Prevalence of newly diagnosed CD in anemic pts was at least 2.2% (11/484)prevalence of CD in "EMA positive pts" was 1 in 28; prevalence of CD in "definite celiac + ↑IELs alone+not biopsied group" was 1 in 30; prevalence of CD in "definite celiac and ↑IELs alone group" was 1 in 35; prevalence of CD in "definite celiac group" was 1 in 44	Prevalence of newly diagnosed CD in age & sex matched non-anemic pts was 0.2% (1/484); prevalence of CD in "EMA positive group" was 1 in 83; prevalence of CD in "definite celiac +↑IELs alone+ not biopsied group" was 1 in 100; prevalence of CD in "definite celiac & ↑IELs alone group" was 1 in 166; prevalence of CD in "definite celiac group" was 1 in 498		Prevalence of newly diagnosed CD in anemic pts was at least 2.2% (11/484) compared with 0.2% (1/484) that of non-anemic pts (p<0.01)

Evidence Table 8 (cont'd): Prevalence of CD in patients with anemia

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Unsworth, 2000 UK Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** plasma diluted 1:5 IgA EMA using HU as substrate. Seropositives tested for IgA and IgG AGA ELISA and tTG ELISA using GP liver tTG **Biopsy criteria/description:** n/a **Confirmatory test:** small bowel biopsy **Checked IgA def.** n/a	**Ethnicity:** n/a **Patient type/# screened:** 110,937 blood donors, 1,380 anaemic donors, 483 with haemaglobin(<11 g/dL for women; <13.5 g/dL for men) **Demographics:** 1,380 anemic adult blood donors 87% women (age range n/a) 483 anemic pts meeting criteria 84% women **Incidence:**	IgA EMA positive 32/483 (6.6%); 25/32 had small bowel biopsy (4 pts lost to follow-up and 3 refused further testing) 22/25 had positive small bowel biopsy(88%) Subsequent results 22/32 cases IgA AGA positive; 26/32 cases were either IgA or IgG AGA pos; 31/32 cases pos using ME as substrate rather than HU; 31/32 were IgA tTG antibody pos	Prevalence of newly diagnosed CD in age & sex matched non-anemic pts was 0.2% (1/484); prevalence of CD in "EMA positive group" was 1 in 83; prevalence of CD in "definite celiac +↑IELs alone+ not biopsied group" was 1 in 100; prevalence of CD in "definite celiac & ↑IELs alone group" was 1 in 166; prevalence of CD in "definite celiac group" was 1 in 498		Prevalence of newly diagnosed CD in anemic pts was at least 2.2% (11/484) compared with 0.2% (1/484) that of non-anemic pts (p<0.01)

Evidence Table 8 (cont'd): Prevalence of CD in patients with anemia

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
van Mook, 2001 Netherlands Duplicate: no	**Publication type:** journal **Study design:** retrospective prevalence **Test/methodology:** EGD; upper digestive tract endoscopy in 10/35; duodenal biopsies taken in 15/35 **Biopsy criteria/description:** Marsh **Confirmatory test:** biopsy **Checked IgA def.** no	**Ethnicity:** n/a **Patient type/# screened:** 35 pts with IDA, anaemia defined as Hb below 8.0 mmol/L in men or below 7.4 mmol/L in women. Iron deficiency defined as a serum ferritin level equal to or below 20 ug/L for men equal to or below 10 ug/L ; or serum iron concentration equal to or below 45 ug/dl with a transferrin saturation of 10% or less, or the absence of iron stores in bone marrow biopsy specimens. **Demographics:** 35 pts, 22 F (63%) and 13 M (37%), median age 71 y range (22-89 y) **Incidence:** n/a	2.9% (1/35) Marsh III(C) on both biopsy and endoscopy			

Prevalence of CD in Associated Clinical Conditions—Low Bone Mineral Density (BMD)

Evidence Table 9: Prevalence of CD in patients with low BMD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Gonzalez, 2002 Argentina Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** IgA and IgG-AGA, ELISA; cut-off levels: for IgA, 15 AU/mL; for IgG, 20 AU/mL; IgA-EMA, IF on ME; positive if fluorescence at 1:5 dilution; 1st level of screening: measuring of IgA and IgG-AGA; 2nd level of screening: measuring of IgA and IgG-EMA and total serum IgA if AGA positive; 3rd level of screening: biopsy in EMA positives **Biopsy criteria/description:** endoscopic biopsy; CD was diagnosed when mucosa showed VA, crypt hyperplasia and intraepithelial lymphocytic infiltration (>30%) **Confirmatory test:** EMA; biopsy **Checked IgA def.** yes; 2 controls were found to have very low IgA level	**Ethnicity:** n/a **Patient type/# screened:** 127 consecutive postmenopausal pts with verified osteoporosis screened for CD; 747 controls screened for CD taken from a population-based study aiming to determine the prevalence of CD in Argentina **Demographics:** n=127 postmenopausal pts with osteoporosis; age: mean 68 y, range 50-82 y; n=747 controls; age: mean 29 y, range 16-79 y **Incidence:** <u>Time period</u>: prevalence of CD in 127 postmenopausal pts with osteoporosis was 1/127, or 7.9x1000 (95% CI 0.2-43.1); as for test positivity: AGA was found in 8 of 127 pts on level 1; 1 of these 8 pts was EMA-positive on the 2nd level and eligible for biopsy which established a diagnosis of CD <u>Control popn</u>: estimated prevalence of CD in control women population was 6/747, or 8x1000 (95% CI 3.3-18.3); as for test positivity: AGA was found in 96 of 747 (12.8%) pts on level 1; 4 pts were EMA-positive and 2 other pts had very low serum IgA on the 2nd level and all 6 were eligible for biopsy which established a diagnosis of CD in all cases	Prevalence of CD in 127 postmenopausal pts with osteoporosis was 1/127, or 7.9x1000 (95% CI 0.2-43.1); as for test positivity: AGA was found in 8 of 127 pts on level 1; 1 of these 8 pts was EMA-positive on the 2nd level and eligible for biopsy which established a diagnosis of CD			Prevalence of CD in postmenopausal osteoporotic women was similar to that of the general population

Evidence Table 9 (cont'd): Prevalence of CD in patients with low BMD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Lindh, 1992 Sweden Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** IgA-AGA, micro ELISA method; cut-off point was selected to be a 2 SD above the mean in a healthy population of blood donors **Biopsy criteria/description:** endoscopic biopsy; methodology and criteria of CD diagnosis n/r **Confirmatory test:** endoscopic biopsy **Checked IgA def.** n/r	**Ethnicity:** n/a **Patient type/# screened:** 92 consecutive pts with idiopathic osteoporosis screened for CD **Demographics:** n=92 consecutive pts with idiopathic osteoporosis screened for CD; 91% F (mean age 66±12 y)/ 9% M (mean age 50±12 y); **Incidence:** prevalence of CD was 3% (3/92); IgA-AGA was positive in 11 of 92 pts and biopsy was performed in 6 pts	Prevalence of CD was 3% (3/92)			

Evidence Table 9 (cont'd): Prevalence of CD in patients with low BMD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Mather, 2001 Canada Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** IgA-EMA, IF of ME **Biopsy criteria/description:** increased number of IELs with associated subtotal or total VA **Confirmatory test:** biopsy **Checked IgA def.** yes	**Ethnicity:** n/a **Patient type/# screened:** 96 consecutive idiopathic low BMD pts **Demographics:** n=96: mean age 57 y; range 18-86 y; 81.3% (78) F, 18.7% M (18) **Incidence:** n/a	7 (7.3%) of 96 pts were EMA pos at titers of ≥1:10; all biopsies were negative; prevalence of 0%			

Evidence Table 9 (cont'd): Prevalence of CD in patients with low BMD

Author, Year, Location	Study Design	Patient Characteristics	Prevalence			Comments
			Group 1	Group 2	Group 3	
Nuti, 2001 Italy Duplicate: no	**Publication type:** journal **Study design:** cross-sectional prevalence **Test/methodology:** IgA-AGA, ELISA cut-off level of 10 U/mL-1 **Biopsy criteria/description:** intestinal biopsy criteria n/r **Confirmatory test:** TG-ab-ELISA with cut-off 22 AU; intestinal biopsy **Checked IgA def.** no	**Ethnicity:** n/a **Patient type/# screened:** 255 females with osteoporosis **Demographics:** mean age 66.6 y, range 36-65 y **Incidence:** n/a	53/255 pos IgG-AGA; 24/53 pos TG-ab (9.4%); intestinal biopsy in 10/24 resulted in 6 confirmed CDs			

Celiac 3: Risk of Lymphoma in CD

Evidence Table 10: Risk of lymphoma in patients with CD

Author, year, country	Methods	Participants	Outcomes	Measures of risk (lymphoma)	Measures of risk (mortality)
Askling, 2002, Sweden Other reports of same cohort: Peters et al., Arch Int Med 2003;163:1566	Retrospective Cohort Study Study Dates: 1964-1994 **Group selection** Pts with CD: All individuals discharged at least once with a Dx CD (ICD 7-9) Controls: (5-y)Age/sex and (1 y) calendar period matched cancer incidence rate and mortality rate for the entire Swedish population **Institution:** All hospitals in Sweden (Swedish input register) **Ascertainment of outcome** Cancer register, register of causes of death, population register, register of population changes. Pathology report from Cancer Registry for lymphomas Dx'ed 1990 or after **Blinding** n/r **Follow-up** See ascertainment of outcome. 3.4% excluded with incomplete/non matching ID numbers	**CD pts**: n = 11,019 Mean age at CD Dx: 17.4 (range 0->70) Mean follow-up: 9.8 y (range 0-32) 97236 PYs Proportion of females: 59% Proportion on GFD: n/r % refractory CD: n/r Clinical presentation: symptomatic (admission to hospital)	**Lymphoma** # lymphomas 38 Lymphoma types: NHLs **Dead patients** Mean age at death: 68.6 Time from CD Dx: n/r **Death from NHL** #Ls in celiacs: 33 # expected lymphomas:2.9 **Death from all causes** # deaths 828 # expected 419.3 **Exclusions** Were lymphomas occurring prior to CD Dx included? NO Were lymphomas occurring within 12 months of CD Dx included? NO Were incidental lymphomas found at autopsy included? NO	**SIR NHL** 6.3 95% CI 4.2-125 **SIR 1-4 y Dx**: 9.7 95% CI 6.3-14 **SIR >5 y Dx**: 3.8 95% CI 2.2-6 **SIR age 0-59:** 6.0 95% CI 3.7-9.5 **SIR age >60:** 5.8 95% CI 3.7-8.5 **SIR childhood Dx (age 0-19):** 1.9 95% CI 0.4-5.5 **SIR adult Dx (age 20-59):** 7.7 95% CI 4.9-12 **SIR late Dx (age >60):** 6.3 95% CI 3.8-9.8 SIR 1970-79: 12 (3.8-28) SIR 1980-89: 8.5 (5.5-13) SIR 1990-95: 3.4 (1.9-5.7) P (linear trend) 1964-95 0.025	**SMR all causes** 2 95% CI 1.8-2.1 **SMR 1-4 y Dx:** 2.2 (1.9-2.4) **SMR 5-9 y Dx:** 2.0 (1.8-2.2) **SMR >10 y Dx:** 1.7 (1.5-2.0) P(trend) 0.12 **SMR from NHL** 11.4 (7.8-16)

Evidence Table 10 (cont'd): Risk of lymphoma in patients with CD

Author, year, country	Methods	Participants	Outcomes	Measures of risk (lymphoma)	Measures of risk (mortality)
Collin, 1996, Finland Other reports of same cohort: Collin et al. Gut 1994;35:1215	Prospective cohort study (Collin et al. Gut 1996;38:528) Study dates: 1970-1993 Case-control study (Collin et al. Gut 1994;35:1215) **Group selection** Pts with CD: All consecutive biopsy-proven CD (ESPGAN criteria) Controls: age/sex matched for Finnish population (database not stated) Controls(2): age/sex and year matched outputs for upper endoscopy **Institution:** single tertiary care institution **Ascertainment of outcome** Finnish cancer registry, Statistics Finland **Blinding** n/r **Follow-up** See ascertainment of outcome. 290 pts available for biopsy 6-12 mos post Dx	**CD pts**: n = 383 Mean age at CD Dx: 41.8 (range 16-78) Mean follow-up: 8.1 y 3107 PYs Mean follow-up (case-control) 3.1 (range 0.5-11) Proportion of females: 73% Proportion on GFD: Strict GFD 75% Partial GFD 8% Normal diet 6% Unknown 11% Compliance monitoring: control bx and dietary assessment 6-12 mos after Dx Clinical presentation: 82% symptomatic 18% serology Dx	**Lymphoma** # lymphomas 1 Lymphoma types: # expected lymphomas 0.4 **Death from all causes** # deaths: 31 (8.1%) # expected: see graph p1217 of Collin et al. Gut 1994;35:1215 **Exclusions** Were lymphomas occurring prior to CD Dx? NO Were lymphomas occurring within 12 months of CD Dx? YES Were incidental lymphomas found at autopsy included? PROBABLY NOT	**SIR NH** 2.66 95% CI 0.07-14.8	10 and 15 y survival rates of pts with CD did not differ significantly from the rates seen in general population

Evidence Table 10 (cont'd): Risk of lymphoma in patients with CD

Author, year, country	Methods	Participants	Outcomes	Measures of risk (lymphoma)	Measures of risk (mortality)
Corrao, 2001 Italy Other reports of same cohort: none	Prospective Cohort Study Dates: 1962-1994 **Group selection** Pts with CD: All consecutive biopsy-proven CD (ESPGAN criteria) Controls: (5-y) age/sex and calendar year matched national life tables and regional mortality rates **Institution:** 11 GI units throughout Italy selected for quality of record keeping; mostly tertiary **Ascertainment of outcome** phone interview (pts, relatives); death certificates, Italian National Institute of Statistics **Blinding** n/r **Follow-up** see ascertainment of outcome. 8 pts or their relative not tracked down; excluded. 50 pts lost to follow-up	**CD pts**: n = 1,072 Mean age at CD Dx: 35.7 (range 18->50) Median Dx delay 17 months Mean follow-up: 6.0 y 6444 PYs Proportion of females: 76% Proportion on GFD: 59% Strict GFD: 59% Not likely: 15% Unknown: 27% Compliance monitoring: control biopsy and phone interview 1999 % refractory CD: none Clinical presentation: 55% symptomatic 39% mild symptoms 6% serology Dx	**Death from NHL** # lymphomas: 16 lymphoma types: # expected lymphomas 0.2 **Death from all causes** # deaths 53 # expected 25.9 **Exclusions** Were lymphomas occurring prior to CD Dx included? NO Were lymphomas occurring within 12 months of CD Dx included? YES Were incidental lymphomas found at autopsy included? PROBABLY NOT	**SIR NHL**	**SMR from NHL:** 69.3 95% CI 40.7-112.6 **SMR all causes:** 2.0 95% CI 1.5-2.7 SMR 0-3 y Dx: 0.98 (0.97-0.98) SMR >3 y Dx: 0.98 (0.96-0.99) SMR age 18-29 at Dx: 2.5 (0.5-7.3) SMR age 30-49 at Dx: 2.4 (1.3-4.0) SMR age >50 at Dx: 1.9 (1.3-2.6) SMR 1962-74: 3.2 (1.4-6.3) SMR 1975-84: 1.8 (1.0-3.1) SMR >1985: 2.0 (1.3-2.8) SMR Dx delay <1 y: 1.5 (0.9-2.3) SMR Dx delay 1-10 y: 2.6 (1.6-4.1) SMR Dx delay >10 y: 3.8 (2.2-6.4) SMR symptoms: 2.5(1.8-3.4) SMR mild symptoms: 1.1 (0.5-2.2) SMR asymptomatic: 1.2 (0.1-7.0) SMR GFD: 0.5 (0.2-1.1) SMR unlikely: 6.0 (4.0-8.8) SMR uncertain: 2.0 (1.2-3.0)

Evidence Table 10 (cont'd): Risk of lymphoma in patients with CD

Author, year, country	Methods	Participants	Outcomes	Measures of risk (lymphoma)	Measures of risk (mortality)
Cottone, 1999, Sicily Other reports of same cohort: none	Retrospective cohort study Study dates: 1980-1997 **Group selection** CD pts: All biopsy-proven CD Controls: Age and sex-matched reported mortality from same period and region; cancer registry of the city of Ragusa in Sicily 1983-1987 **Institution:** Single institution; referral basis for all of Sicily **Ascertainment of outcome** Hospital medical records were reviewed; pathology specimen reviewed **Blinding** n/r **Follow up** 5% incomplete records	**CD pts**: n = 228 Mean age at CD Dx: 34.7 adult Dx: 98% Range of age: n/r Mean follow-up: 73 mos (range 1-204) #PYs: n/r Proportion of females: 76% Proportion on GFD: 100% Compliance monitoring: serial EMA % refractory CD: n/r Clinical presentation: Anemia 60% Malabsorbtion 20% Other 10% Asymptomatic 10% % inputs: 29% Marsh grade: n/r	**Lymphoma** #NHLs in celiacs: 7 Lymphoma types: ETCL (4), B-cell (2), other NHL(1) # expected lymphomas: 1.824 % silent: n/r % Dx'ed during childhood : 0 **Lymphoma patients** Mean age: 59.4 Time from CD Dx: 78 mos % compliant to diet: 100 incidence NHL: 3% expected incidence: 0.8 **Death from lymphoma** # death from lymphoma in celiacs: 5 # expected death from lymphomas: n/r **Death from all causes** # death CD: 12 # expected deaths: 3.12 # deaths within 4 y of Dx: 8 # expected: 1.48 **Exclusions** Were lymphomas occurring prior to Dx of CD included? NO Were lymphomas occurring within 6 months of CD Dx included? NO Were incidental lymphomas found at autopsy included? No such cases	SIR NHL **3.75** P<0.01	**SMR from NHL** n/r **SMR all causes** 3.8 95% CI 1.9-6.7 **SMR 4 y from:** 5.8 **95% CI 2.5-11.5**

Evidence Table 10 (cont'd): Risk of lymphoma in patients with CD

Author, year, country	Methods	Participants	Outcomes	Measures of risk (lymphoma)	Measures of risk (mortality)
Delco, 1999 US Other reports of same cohort: none	Case-control study Study Dates: 1986-1995 **Group selection** Pts with CD: all consecutive pts discharged with CD Dx (ICD 579.0) Controls: 5 randomly selected controls from same annual data file per case **Institution:** All US VA hospitals **Ascertainment of outcome** Pt Treatment File of the VA. Validity of records checked with 7 pt files **Blinding** n/r **Follow-up** See ascertainment of outcome.	**CD pts**: n = 458 **Controls:** n=2692 Mean age: celiacs: 63.8 +/- 12.4 controls: 59.7 +/- 14.8 p< 0.0001 Proportion of females: celiacs 4% controls 2% p=0.105 Race: celiacs: 93% whites controls: 74% p<0.0001 Proportion on GFD: n/r Compliance monitoring: n/a % refractory celiac: n/r Clinical presentation: 100% symptomatic (all discharged Dx)	**Lymphoma** # lymphomas n/r Lymphoma types: n/r # expected lymphomas n/r **Death from all causes** # deaths: n/r **Exclusions** Were lymphomas occurring prior to CD Dx included? NO Were lymphomas occurring within 12 mos of CD Dx included? LIKELY Were incidental lymphomas found at autopsy included? LIKELY Pts with repeated admission within 1 y were excluded	**OR NHL** 4.53 95% CI 2.01-10.23	

Evidence Table 10 (cont'd): Risk of lymphoma in patients with CD

Author, year, country	Methods	Participants	Outcomes	Measures of risk (lymphoma)	Measures of risk (mortality)
Green, 2003, US (New York) Other reports of same cohort: none	Prospective Cohort Study Dates: 1981-2000 **Group selection** Pts with CD: All consecutive biopsy-proven CD (ESPGAN criteria) Controls: (5-y) age/sex and calendar year matched site-specific incidence rates from the National Cancer Institute's Surveillance, Epidemiology and End Results Program for whites **Institution:** single tertiary care institution **Ascertainment of outcome** pt interview, review of pathology records **Blinding** n/r **Follow-up** pts not followed-up excluded; # n/r	**CD pts**: n = 381 Mean age at CD Dx: 44 +/- 18 y Duration of CD symptoms prior to Dx: 5y +/- 8 Mean follow-up: 6 +/- 11 y 1977 PYs Proportion of females: 64% Proportion on GFD: 100% of NHLs after Dx Compliance monitoring: clinical interview, yearly AGA and EMA after 1993 % refractory celiac: n/r Clinical presentation: n/r	**NHL 1 mos after CD Dx** # lymphomas 5 # expected lymphomas n/r Age at Dx cancer 62+/- 8 y Mean duration from celiac Dx 5+/- 4 y Mean follow-up 16+/- 17 y **NHL before/1 mos after CD Dx*** # NHLs: 4 # expected: 0.7 **NHL any time before/after Dx celiac*** # NHLs: 9 # expected: 1 Lymphoma types: B-cell(3), T-cell (4 – ETCL 3), large cell (2) **Exclusions** Were lymphomas occurring prior to Dx of celiac included? YES* Were lymphomas occurring within 1 months of celiac Dx included? YES* Were incidental lymphomas found at autopsy included? n/r *separate analysis	**SIR NHL** 6.2 95% CI 2.9-14 **SIR NHL before/1 mos after Dx celiac:*** 5.3 (2.3-13) incidence NHL 135/100 000 PYs expected 14.8/100 000 PYs **SIR NHL any time before/after Dx celiac:*** 9.1 (4.7-13)	

Evidence Table 10 (cont'd): Risk of lymphoma in patients with CD

Author, year, country	Methods	Participants	Outcomes	Measures of risk
Holmes, 1989, England Other reports of same cohort: Holmes et al. Gut 1976;17:612; Harris et al, Am J Med 1967;42:899	Prospective cohort study Study Dates: 1941-1985 **Group selection** Pts with CD: All biopsy-proven CD Controls: Age/sex matched incidence for 2 calendar periods standardized to ICD 8,200 and 202, in West Midlands region **Institution:** Single institution **Ascertainment of outcome** Direct pt interview, case notes, GP, Birmingham and West Midlands cancer registry, autopsy results, death certificates, pathology specimen reviewed **Blinding** n/r **Follow-up** Use of the family Practitioner Committee records and National Health Service Central Register at Southport; 2% drop outs	**CD pts**: n = 210 Mean age at CD Dx: n/r Adult Dx: 80%* (*from Harris et al, Am J Med 1967;42:899) Mean follow-up: 17.4 PYs for men, 19.4 PYs for women; minimum 13 y Proportion of females: 55.2% Proportion on GFD: 51% strict GFD 51% reduced gluten 27% normal diet 22% Compliance monitoring: direct interview; repeat biopsy in 86 pts % refractory CD: 17 poor response to GFD Clinical presentation: n/r	**Lymphoma** #NHLs in celiacs: 9 lymphoma types: n/r # expected lymphomas: 0.21 **Lymphoma patients** Mean age: n/r Time from CD Dx: n/r % compliant to diet: 2 NHL in strict GFD 7 NHL in gluten diet **Death from lymphoma** Not calculated **Death from all causes** Not calculated **Exclusions** Were lymphomas occurring prior to Dx of CD included? NO Were lymphomas occurring within 12 months of CD Dx included? NO Were incidental lymphomas found at autopsy included? No such cases	SIR NHL **42.7** 95% CI 19.6-81.4 **SMR from NHL** n/r **SMR all causes** Not calculated **SMR 4 y from Dx** n/r **SIR NHL** **Strict gluten-free diet** 44.4 **Gluten diet** 100

Evidence Table 10 (cont'd): Risk of lymphoma in patients with CD

Study	Methods	Participants	Outcomes	Measures of risk
Logan, 1989, Scotland Other reports of same cohort: Celiac 2; Logan et al. Gastroenterol 1986;90:334 Celiac 2; Logan et al. BMJ (Clinical research ed) 1983;286:95	Prospective cohort study Study dates: 1979-1986 **Group selection** Pts with CD: All biopsy-proven CD entered in register for Edinburgh and the Lothians Controls: Age/sex matched mortality for Scotland and corresponding person-years over 5 calendar periods standardized to ICD 8 200-203, in Scotland **Institution:** All hospitals in Edinburgh and the Lothian region, postal survey of all GPs, Scottish in-pt Statistics 1961-1977, local branch of Celiac Society **Ascertainment of outcome** Death certificates **Blinding** n/r **Follow-up** National Health Service Central Record, death certificates, Scottish national death records. 6% lost to follow-up	**CD pts**: n = 653 Mean age at CD Dx: n/r Mean follow-up: 13.5 y 8823 PYs Proportion of females: 60% Proportion on GFD: n/r % refractory CD: n/r Clinical presentation: n/r	**Lymphoma** # lymphomas: n/r Lymphoma types: most lymphosarcomas or reticulum-cell sarcomas, 2 Hodgkins **Dead patients** Mean age at death: 60.8 Time from CD Dx: n/r **Death from lymphoma** #s in celiacs: 17 #expected lymphomas: 0.55 **Death from all causes** # deaths 115 # expected 61.8 **Exclusions** Were lymphomas occurring prior to CD Dx included? NO Were lymphomas occurring within 12 months of CD Dx included? YES Were incidental lymphomas found at autopsy included? NO	**SIR NHL:** n/r **SMR from lymphoma** 31 p<0.001 **SMR(L) 0-1 y Dx**: 108 **SMR(L) 2-4 y Dx**: 9 **SMR (L) 5-49 y Dx**: 22 **SMR all causes** 1.9 95% CI 1.5-2.2 **SMR <1 y from Dx:** 4.1 **SMR 1-2 y from Dx:** 3.2 **SMR 3-4 y from Dx:** 2.2 **SMR 5-9 y from Dx:** 1.5 **SMR 10-14 y from Dx:** 1.5 **SMR childhood Dx:** 1.4 95% CI 0.4-3.7 **SMR adult Dx:** 1.9 95% CI 1.5-2.3 **SMR late Dx:*** 1.7 95% CI 0.02-4.8 *obvious CD symptoms during childhood

Evidence Table 10 (cont'd): Risk of lymphoma in patients with CD

Author, year, country	Methods	Participants	Outcomes	Measures of risk (lymphoma)	Measures of risk (mortality)
Selby, 1979 Australia Other reports of same cohort: none	Retrospective cohort study dates: 1959-1978 **Group selection** Pts with CD: All consecutive biopsy-proven CD (ESPGAN criteria) Controls: ?age/sex and period matched incidence New South Wales Central cancer Registry **Institution:** Single tertiary care institution **Ascertainment of outcome** direct call or via medical officer **Blinding** n/r **Follow-up** Direct call or via medical officer. 21% lost to follow-up	**CD pts**: n = 93 Mean age at diagnosis celiac: 40 (range 14-70) Duration of Sx of celiac prior to Dx: 3yrs (range 2 wks to 26 y) Mean follow-up: 6 y (max 9 y) Proportion of females: 67% Proportion on GFD: 100% of NHLs after Dx Compliance monitoring: n/r % refractory CD: none of the lymphoma pts Clinical presentation: 100% malabsorption: 18% malabsorption during childhood	**Lymphomas** # lymphomas 4 # expected lymphomas 0.081 Age at cancer Dx: 47.5 Mean duration from CD symptoms: 11 y (range 2-26 y) Mean follow-up: n/r Lymphoma types: ETCL (2), lymphosarcoma (1), histiocytic medullary reticulosis (1) **Exclusions** Were lymphomas occurring prior to Dx of celiac included? NO Were lymphomas occurring concomitantly with celiac Dx included? NO Were incidental lymphomas found at autopsy included? n/r	**SIR NHL 4.94** p< 0.0005 symptom duration (cancer vs none): not significant age Dx (cancer vs none): not significant	

Celiac 4: Consequences of Testing for CD

Evidence Table 11: Consequences of testing for CD

Study, Year Country	Methods	Participants	Outcomes	Results	Limitations
Addolorato, 2001 Italy	Study type - 1996-1998 Population-group selection Celiacs – newly diagnosed CD selected from outpatient clinic of 234 adult CD Controls - healthy asymptomatic controls - matched for age, sex and SES Loss to follow-up -8 Setting - Tertiary	Celiac - n=43 enrolled Controls - n=59 Proportion F – 60% Mean follow-up - 1 y Mean age: 29.8 ± 7.4	Before/after GFD Anxiety State and Trait Anxiety Inventory test Depression SDS self rating depression scale	Before – CD 71.4% showed high levels of state anxiety, 25.7% showed anxiety as a trait and 57.1% positive for depression compared to 23.7%, 15.2% and 9.6% of controls Post GFD – 25.7% still affected by state anxiety, 17% trait anxiety, and 45.7% depressed Significant decrease in state anxiety ($p<0.001$) No significant changes in trait anxiety or depression - anxiety in CD predominantly reactive	Small sample, loss to 8 pts to follow-up Relatively short follow-up

Evidence Table 11 (cont'd): Consequences of testing for CD

Author, Year Country	Methods	Participants	Outcomes	Results	Limitations
Amin, 2002 UK	Study type - case controlled longitudinal 1994-1998 Population-group selection Celiacs – 11 pts, EMA + and biopsy diagnosed CD out of 230 pts screened from diabetic clinic Controls – 22 matched for age, sex and duration of diabetes, with negative serology Institution – diabetic clinic – tertiary care hospital	Celiacs: n=11 (6 had repeat small bowel Bx on GFD) Controls: n=22 Age: 8.1 (1.2-16.1) cases, 7.4 (1.3-14.8) controls Proportion of females: 54.5% Duration of type 1 diabetes: 4.2 y Mean follow-up - 4 y BMISDS -1.2 ± 0.1 (SEM) vs -0.1 ± 0.1 WtSDS - 0.7 vs 0.5 HbgA1c – 8.3 cases 9.8 controls Insulin units – 0.8	BMI Hgba1c Insulin regimens	Cases: 1.1 ± 0.1 Controls: 1 ± 0.1 Cases: 8.3 ± 0.2 Controls: 10 ± 0.2 Insulin regimens increased but did not differ significantly between Insulin units 1.0 All reverted to antibody negative	Small sample Selection of controls

Evidence Table 11 (cont'd): Consequences of testing for CD

Study, Year Country	Methods	Participants	Outcomes	Results	Results after treatment
Annibale, 2001 Italy	Study type - prospective 1994- May 1997 Population-group selection Celiacs- 190 consecutive adults with iron deficiency anemia, 26 pts were diagnosed with CD after duodenal biopsy	Celiac n= 26 of 190 pts with IDA Proportion F - 92% Mean age - 31.3 Mean follow-up – 24 mos 77% had total VA, 23% had subtotal atrophy 11 did not have symptoms apart from anemia 42% BMI	Iron Deficiency (Hgb<14 for men and 12 for women, MCV <80, low serum iron and low serum ferritin Ferritin Nutritional parameters Repeat endoscopy – 6 mos	6 mos 77.8% recovered IDA, but only 5 of 18 (27.8%) developed normal ferritin levels 12 mos – 94.4% recovered from anemia and 50% from iron deficiency – all pts had normal RDW 24 mos, 55% recovered from iron deficiency	Recovery from IDA occurs within the initial 6-12 mos but only 50% recover from iron deficiency In subgroup of pts (n=7) who had repeat biopsies at 6 and 12 mos – inverse correlation between histological grade and increase in Hgb

Evidence Table 11 (cont'd): Consequences of testing for CD

Author, Year Country	Methods	Participants	Outcomes	Results		Limitations
Arato, 2002 Hungary	Study type – longitudinal – own controls Population-group selection Celiacs selected from 205 children with type 1 diabetes randomly selected, screened with EMA and then confirmed with biopsy Controls – no controls	Celiacs: n=17 % Females -59% Mean follow-up – 3 mos BMI 14.2 vs 16.3 for controls 11 had silent CD, 6 had mild GI symptoms	BMI HbA1c Insulin requirements	Before 16.8 <0.05 7.82 NS 0.48	After GFD 0.64 <0.05	Short follow-up small sample size No controls

Evidence Table 11 (cont'd): Consequences of testing for CD

Author, Year Country	Methods	Participants	Outcomes	Results	Limitations
Bardella, 1985 Italy	Study type - prospective Population-group selection Celiacs- adults with biopsy confirmed disease (Grade II or IV – Scott/Losowsky) and malabsorption Controls ---none	Celiacs - n=26 Proportion F - 81% Mean age - 42.2 Mean follow-up– 55.4 mos on GFD (range 13-137 mos)	Clinical Symptoms CBC, biochemical parameters Repeat biopsy (17/26)	8 pts good health and normal blood tests and 18 had some clinical or biochemical abnormalities, 4 pts had recurrent abd pain, meteorism and diarrhea, 2 isolated episodes of diarrhea and 5 meteorism alone present, 11 pts had one more of anemia, moderate abnormal of calcium, alkaline phosphatase, phosphorus 13 showed grade II, and 4 grade III – all improved by 1 or 2 grades but none returned to normal	

Evidence Table 11 (cont'd): Consequences of testing for CD

Author, Year Country	Methods	Participants	Outcomes	Results	Limitations
Bardella, 2000 Italy	Study type - case control 1962-1994 Population-group selection Celiacs not clear how selected 33.4% asymptomatic Controls – 2/pt matched for age and sex	Cases 71 out of 212 43 diagnosed as children, 28 as adults Control - n=142 Proportion F - 72%	Weight BMI Fat mass Lean mass	Lower than controls 55.5 vs 58.7 kg (p=0.004) 20.9 vs 22.4, p=0.03 22.9 vs 27.5, p<0.05 38.8 vs 40.5 (p<0.03)	

Evidence Table 11 (cont'd): Consequences of testing for CD

Author, Year Country	Methods	Participants	Outcomes	Results	Limitations
Barera, 2000 Italy	Study type - case control prospective Population-group selection Celiacs – biopsy confirmed CD, 4 classic symptoms, remainder atypical Controls - age and sex matched healthy controls	Celiac cases - n=29 Control - n=29 Age - 9.54 + 3.42 Proportion F: 51.7% Mean follow-up – 1.20 ± 0.15 Compliance – EMA ab	Body composition - DEXA Weight (kg) Height (cm) BMI (kg/m2) Lean Mass	At baseline, weight, fat mass, BMD, lean mass of limbs all lower in the pts versus controls, after 1 y no significant differences in body composition between pts and controls Untreated / Treated 30.3 + 11.5kg / 34.7 + 12.3 134.9 + 19 / 140.9 + 18.4 16.7 +4.5 / 17.3 + 3.1 166.8 / 179.9 +42	

Evidence Table 11 (cont'd): Consequences of testing for CD

Author, Year Country	Methods	Participants	Outcomes	Results	Limitations
Boersma, Netherlands 2002	Study type - 1994-1995 prospective study Population-group selection Celiacs-children with newly diagnosed celiac (symptoms and biopsy confirmed) CD patients acted as own controls	Celiacs - 28 Proportion F - 68% Mean follow-up - 3 y BMI	BMI BMI-SDS Height SDS	BMI - SDS for CD improved significantly after a GFD over 1st half year. (P<0.001) Height for SDS for CD showed a continuous significant increment over the first 3 y of GFD (p<0.001)	With institution of GFD also noted increased sensitivity to GH, and levels of IGF-1, IGF-2, and IGFBP-3 rise

Evidence Table 11 (cont'd): Consequences of testing for CD

Study, Year Country	Methods	Participants	Outcomes	Results	Risk estimates
Ciacci, 1996 Italy	Study type - case control Before after Population-group selection Celiacs Untreated CD had a least one pregnancy when symptoms leading to diagnostic workup for CD were present Controls (treated) had at least one pregnancy after 1 y of GFD Setting- Tertiary clinic	Celiac - n=94 Controls - n= 31 12 separate women acted as own control for before after study to assess impact of the GFD (not included in other analysis). Mean age at diagnosis of untreated older than treated (37.3 vs 22.4) Mean follow-up of treated celiacs 9.2 ± 1.4 Mean weight of treated 50.6 vs 50 Mean BMI 20.1 vs 19.4 Clinical symptoms of untreated group 33% did not have diarrhea, 24.5% did not have anemia	Number of pregnancies/woman Number of abortions/woman Abortion to pregnancy ratio Low birth weight baby to pregnancy ratio	2.72 in untreated vs 1.36 in controls 0.489 ± 0.08 untreated vs 0.032 ± 0.032 treated (17.8% vs 2.4%) 0.153 ± 0.027 vs 0.024 ± 0.024 0.126 ± 0.037 vs 0.024 ± 0.024 (prevalence 12.7% vs 2.4% in treated) *controls not age matched – cases significantly older	RR of abortion 8.9 (95% CI 1.19, 31.9) RR of low birth weight baby 5.84 (95% CI 1.07, 31.9) 12.7% vs2.4% Did not have external control group or control for confounders.

Evidence Table 11 (cont'd): Consequences of testing for CD

Author, Year Country	Methods	Participants	Outcomes	Results	Limitations
Fabiani, 1996 Italy	Study type - longitudinal Population-group selection Celiacs – biopsy proven CD from screening of adolescents (n = 6,315) Controls - none Loss to follow-up – 5	Celiacs – n=28 adolescents (age 11-14) Proportion F -74% Mean F/U 23 ± 7 mos	Compliance	52% on strict GFD 47% partial adherence weight gain 12/23 (52%), height gain (11/25)	

Evidence Table 11 (cont'd): Consequences of testing for CD

Author, Year Country	Methods	Participants	Outcomes	Results	Limitations
Fabiani, 2000 Italy	Study Type – case control 1992-1994 Population-group selection Celiacs – selected from screening program for CD ages 11-14, Group A and second group B from pts diagnosed due to typical symptoms (biopsy proven ESPGAN) Loss to follow-up: Group A 5 pts, Group B 2 pts	Celiacs Group A n = 22 pts, asymptomatic Group B n = 22 pts symptomatic Mean follow-up – 5 y Age at diagnosis of CD: Group A 13 y, Group B 4.3 y	Compliance – FFQ conducted by dietician Anthropometric assessment	Adherence to treatment lower in Group A (23%) asymptomatic versus Group B (68%) p value sig BMI no differences between groups	*Difference in adherence could be related to age at diagnosis

Evidence Table 11 (cont'd): Consequences of testing for CD

Author, Year, Country	Methods	Participants	Outcomes	Measures of risk	Limitations
Fickling, 2001, UK	Retrospective case-control study **Group selection** CD pts: All individuals with CD who attended gastroenterology output depart and those with CD who were member of local celiac society Controls: Age/sex matched controls/ one per case selected from database of normal adults who had a bone densitometry performed with the same machine **Institution:** District general hospital **Ascertainment of outcome:** By questionnaire on fracture history with attempt to verify by case notes **Blinding:** n/r **Follow-up:**	**CD pts:** n=75; 15 with metabolic bone disease and CD **Controls:** n=75 **Mean age of CD pts:** 52 y **Proportion on GFD:** full details n/r **Median duration of GFD:** 3.4 y **Proportion of females:** 80% **Clinical presentation:** n/r **BMI:** n/r	**Fractures:** CD pts: 16/75 (21%), 10 before Dx, 6 after Dx Controls: 2/74 (3%) **BMD-DXA** 6 pts had histomorphometry- 3 pts had osteomalacia	RR: 7.0 (95% CI 4.2-125) Increased history of past fractures in subjects with CD. ($p<0.001$) No difference in BMD in those with and without fractures, but pts who had a fracture were older (56.3 vs 50.3)	Not population-based Selection bias No mention that CD was confirmed by biopsy

Evidence Table 11 (cont'd): Consequences of testing for CD

Author, Year Country	Methods	Participants	Outcomes	Results	Limitations
Greco, 1997 Italy	Study type- cohort Population- Celiac – biopsy confirmed pts (92.8%) consecutively recruited from a celiac clinic, 22 pts diagnosed on basis of immunological and clinical findings	Celiac - 306 adolescent/young adults Cases of CD Mean age – 15.9 (range 10-27) Proportion F - 60.8% Mean follow-up BMI	Compliance – one month retrospective questionnaire	Three groups 1. Strict GFD 73% 2. Occasional relapse 15% 3. Full gluten containing 12% Females more compliant (80% vs 64% of males)	88.4% of younger teenagers on a strict diet vs 68.8% of older patients >18 y Avg monthly cost GFD 242,000 Italian Lire, 3 million per year 11.32 kg/month

Evidence Table 11 (cont'd): Consequences of testing for CD

Study, Year Country	Methods	Participants	Outcomes	Results	Risk estimates
Johnston, 1998 N. Ireland	Study type-case control Longitudinal follow-up of cases 1983-1998 Population-Group Selection- population survey Celiacs -screening detected CD of 1823 subjects with serology (n=113)- 3% also had inflammatory bowel disease Controls – 89 age and sex matched randomly selected from survey – antibody negative Ascertainment of outcome – death certificates	Celiac n= 89 (72 followed) – 20 biopsied and 13 untreated detected Controls 89 Proportion F – 53 % Mean follow-up – 11.6 y	Mortality- overall and cancer Number of deaths compared to Registrar General's reports 1983-1994	13 subjects with positive serology died, 4 with malignant disease No increase in all-cause mortality or number of cancer-related deaths in screening detected cases of CD	Cancer death RR 0.94 (95% CI 0.3-2.4) All deaths RR 0.92 (95% CI 0.5, 1.6) Limitations Incomplete follow-up Response rate for biopsy (20/72 is low)

Evidence Table 11 (cont'd): Consequences of testing for CD

Author Year Country	Methods	Participants	Outcomes	Results	Limitations
Kemppainen, 1998 Finland	Study type - cohort Duration: 1988-1990 Population-group selection Celiacs: newly diagnosed biopsy confirmed, symptomatic, all started on GFD Partial (8), subtotal (17) and total VA (15) Controls –none Institution – Tertiary care Kuopio University Hospital Follow-up – 6 pts lost to follow-up	Celiacs – 40 pts Age – 47 for men and 44 for women Proportion F - 70% Proportion on GFD -100% Mean follow-up: 1 y Duration of CD symptoms – males 15.8, women 13.1 BMI 25 in men, and 24 in women	Nutritional status examined by food records, and BMI Ferritin/biochemical values Biopsy	BMI increased after GFD, decreased intakes of fibre, thiamine Most of abnormal biochemical values improved, in 1 pt with subtotal atrophy – low Hgb, in pts with subtotal VA – 7 pts had low Hgb and 5 low ferritin After GFD – VA improved in all patients 29 pts had partial VA, 2 subtotal, 3 normal villi	Baseline - serum ferritin lower in pts with total VA, also had low RBC folate, and ferritin

Evidence Table 11 (cont'd): Consequences of testing for CD

Study, year, location	Methods	Participants	Outcomes	Measures of risk	Limitations
Moreno, 2004, Argentina	Case-control, cross sectional **Group selection** CD pts: unselected 53% classic symptoms, 36% subclinical, 11% silent by screening Controls**:** 296 age and sex matched diagnosed with functional disorders **Institution:** 2 different tertiary referral centres **Ascertainment of fracture**: in-person interview	**CD pts:** n=148 unselected CD **Controls:** n=296 (2:1) **Mean age CD pts:** Classic: 44 y Subclinical/silent: 38 y **Age at diagnosis:** Classic: 42 y Subclinical/silent: 36 y **BMI:** 22/22.1 **Proportion females:** 79 % **Clinical presentation:** 53% classical CD; 35% subclinical, and 11% silent	**Fractures:** classic symptoms vs subclinical overall -51pts **Fractures-peripheral** 47% symptomatic CD vs 15% controls 20% subclinical/silent CD vs 14% controls Mean BMD femoral neck	OR 3.6 (95% CI 1.7-7.5) OR for symptomatic pts 5.2 (95% CI 2.8-9.8) OR 1.7 (0.7-4.4) Fractures not any greater in subclinical cases of CD vs controls Higher for subclinical/silent cases vs classical p<0.05 (T score -0.6 vs -1.5) Pts with CD–sig more fractures in 5th/6th decade; also sig more low trauma fractures than controls	Choice of controls–functional disorders/cases Fractures not verified by X-ray report

Evidence Table 11 (cont'd): Consequences of testing for CD

Study, Year Country	Methods	Participants	Outcomes	Measures of risk - mortality	Measure of risk
Nielsen, 1985 Denmark	Study type - retrospective cohort Study dates 1964-82 Population-group selection Celiacs – histologic diagnosis of CD - 100 Ascertainment of outcome-Central person register, cancer registry Tertiary hospital	Celiac pts - 98 Proportion F - 61 % Median age at diagnosis – 41 (F) and 42 (M) Mean follow-up - 18 y % refractory CD - 24% treated with prednisone since did not respond to GFD Compliance – not described how assessed	Mortality	5-y survival 88%, 10-y survival 68.5% (23 deaths, 4 deaths attributed to malignancy) 8 pts developed cancer Responders to GFD – 2.2 extra mortality factor Non-responders to GFD - 5.8 Compliance with diet – 3.2 Non compliant – 4.5	SMR 3.4

Evidence Table 11 (cont'd): Consequences of testing for CD

Author, Year Country	Methods	Participants	Outcomes	Results	Limitations
Poddar, 2002 India	Study type – case control longitudinal Period – 09/1997 – 12/1998 Population-group selection Celiacs-104 children with clinical symptoms evaluated for celiac disease, 57 biopsy confirmed. Excluded those who did not have good response to diet Controls –Those who did not have celiac on biopsy of the initial 104	Celiacs - n= 57 Controls - n=47 Proportion F - Mean follow-up - 19.6 ± 8 mos 17% poor compliance	Height Weight gain Symptoms	Height 88 ± 5% of expected vs 94 ± 5% of expected baseline and follow-up (p=ns) 66% ± 14 vs 86% ± 11 of expected (p<0.001) Improved in 16 ± 9.8 days 34% had poor compliance to diet	Did not analyze on basis of compliance Selection of cases

Evidence Table 11 (cont'd): Consequences of testing for CD

Author, Year Country	Methods	Participants	Outcomes	Results	Limitations
Rea, 1996 Italy	Study type - case control longitudinal Study dates 1992-1994 Population-group selection Celiacs - newly diagnosed children, biopsy confirmed Controls-age and sex matched healthy controls	Celiacs: n= 23 Controls: n=23 Proportion of F - 65.2% Mean age 4.7 ± 0.76 Mean follow-up - 1 y Co-interventions All patients received vitamin D 1000 IU If iron was low, received iron supplementation	Height, BMI Weight, fat area index Triceps subscapular skin fold Biochemical values	Height. BMI, triceps skinfold, fat area index, and weight for height index all improved significantly. Hgb, iron, protein, albumin, triglycerides, calcium and zinc significantly improved Transferring, cholesterol, phosphorus and alk phos were not different	Compared to controls height still significantly lower

Evidence Table 11 (cont'd): Consequences of testing for CD

Study, Year Country	Methods	Participants	Outcomes	Results	Results after treatment
Sategna-Guidetti, 2001 Italy	Study type - longitudinal case control 1996-1998 Population-group selection Celiacs consecutive newly diagnosed CD patients, biopsy proven Controls – age, sex matched healthy volunteers recruited among medical and nursing staff, blood donors or pts affected by COPD, peptic ulcer disease, no past history of thyroid dysfunction Excluded conditions that could affect thyroid function, excluded CD by means of EMA or biopsy Setting- 5 Italian centres	Celiac - 241 Proportion F – 73% Controls – 212 Mean follow-up- 1 y Clinical presentation Typical in 49%, atypical in 44% and silent in 16%	BMI Thyroid function (serum fT3 and fT4 by RIA, TSH by IRA and thyroid microsomal antibodies	Similar in patients with and without thyroid disease Thyroid dysfunction in 73/241 (30.3%) vs 11.3% (p<0.0005) Thyroid disease 3 X higher than controls Hypothyroidism diagnosed in 12.9% vs 4.2% of controls (p<0.003) 128 pts reassessed at 1 y 91 had normal thyroid, 37 some impairment Subclinical hypothyroidism improved in 71% patients with nonautoimmune thyroid disease	Improvements in BMI, nutritional indices, albumin and serum iron with GFD Gluten withdrawal (confirmed by biopsy recovery) seemed to normalize nonautoimmune thyroid disease 5.5% of pts with normal thyroid function while untreated developed thyroid dysfunction one y later

Evidence Table 11 (cont'd): Consequences of testing for CD

Author, Year Country	Methods	Participants	Outcomes	Results	Limitations
Saukkonen, 2002 Finland	Study type - longitudinal Population-group selection Celiacs, screened 776 children with type 1 diabetes with serology/biopsy (over 2.7 y period) – own controls Controls - none	Celiacs/type 1 diabetes n = 18 Mean onset of diabetes – 8.0 ± 4.5 y Proportion F – 50% Mean follow-up – 1 y	HbA1c GI symptoms	No change in HbA1c levels with GFD Symptoms which were reported in a retrospective questionnaire resolved in all but 2 pts	Significant increase in weight for height after diagnosis No changes in Ht SDS

Evidence Table 11 (cont'd): Consequences of testing for CD

Author, Year Country	Methods	Participants	Outcomes	Results	Limitations
Smecuol, 1997 Argentina	Study type - longitudinal Dates – 1991-1993 Population-group selection Celiacs unselected consecutive patients with newly diagnosed CD, all were symptomatic, and biopsy confirmed acted as own controls	Celiac – 47 and 25 pts re-evaluated in 1995 Proportion F - Mean follow-up - 37 mos Compliance- 15 pts – strict GFD, 10 partial GFD BMI	Fat and bone mass Lean tissue mass Weight and tricep skin fold thickness Mid arm circumference and muscle mass	Significant increase in fat/bone mass No change in lean tissue mass Increases in body weight/triceps skinfold thickness	

Evidence Table 11 (cont'd): Consequences of testing for CD

Study, year, location	Methods	Participants	Outcomes	Measures of risk	Limitations
Thomason, 2003, UK	Case-control study Self-report data from questionnaire. **Group selection:** CD pts: all biopsy-proven CD (also clinical/serology) from population based registers for Derby and Nottingham (less than 7% did not have a bx) Only pts born prior to 1950 included. Controls: age/sex matched random sample from Nottingham family health services. **Ascertainment of fractures:** Self-report of low trauma and non low trauma fractures **Blinding:** Investigator who categorized fractures as low trauma or not was blinded to whether case or control	**CD pts:** n = 244 (70% females) **Controls** n=161 **Mean age:** CD: 60.2 y (10.1) Controls: 61.2 y **Mean BMI:** CD: 23.9 Controls: 25.8 **Proportion of females:** 70% **Proportion on GFD**: n/r **Clinical presentation:** n/r **Dx of osteoporosis:** 7.4% of cases versus 3.1% of controls **Smokers:** CD: 52.5% Controls: 43.3% **Cointerventions:** 4% of CD pts reported taking calcium **HRT:** 31% vs 21% of controls (significant), adjusted for HRT use in analysis	**Fractures – low trauma** (fall from a standing height or less) **Any fracture:** CD: 82 (34.5%) Control: 53 (33.3%) **Forearm/wrist:** CD: 39 (16.4) Control: 22 (13.8) **Low trauma fracture:** CD: 37 (15.7%) Control: 21 (13.8%) (20 reported first fracture before diagnosis of CD and 10 pts reported first fracture after diagnosis) Logistic regression to estimate odds ratio for fracture – adjusted for sex and age group Cox's proportional Hazard model was used and only first low trauma fracture was included.	OR 1.05 (0.68-1.02) OR1.21 (0.66-2.25) OR 1.16 (0.65-2.10) When adjusted age, sex, BMD and smoking the OR 1.13 (95% CI 0.6-2.12) Before Dx: HR 1.24 (95% CI 0.65 – 2.39) Small but statistically-significant increase in risk of fractures	Retrospective Self- report data Response rate to questionnaire was 72% in controls, 89% in celiacs Inadequate power to detect fractures

Evidence Table 11 (cont'd): Consequences of testing for CD

Study, year, location	Methods	Participants	Outcomes	Measures of risk	Limitations
Vasquez, 2000, Argentina	Cross-sectional case-control study Retrospective historical review **Group selection** CD pts: All biopsy-proven celiac disease, and clinical picture, excluded those with secondary osteoporosis other than celiac Controls: 165 subjects selected from output clinic and selected if their final diagnosis was a functional disorder. Excluded cases with known metabolic bone disorders **Institution:** Single institution Buenos Aires –tertiary hospital **Ascertainment of fracture** Pt interview, case report Vertebral fractures –X-ray of lumbar spine (not thoracic) in all CD and 62% of controls Did not have medical records of trauma events **Blinding**: n/r	**CD pts**: n=165 **Median Age:** CD: 40 (16-74) y; 23% over 50 y **Mean age of controls:** 41 y **Median time from symptoms to diagnosis**: 7 y **Proportion of females:** 86.6% **Proportion on GFD:** 69% Strict GFD: 44.8% Reduced gluten: 24% Untreated: 31% **Mean BMI:** 21.4 **Clinical presentation:** malabsorption or subclinical **Post-treatment biopsy:** histological improvement in 38 pts **Serology:** negative or reduced titres in all with positive serology	**Fractures** Peripheral: Cases: 41 (25%) Controls: 14 (8%) Total number of fractures: 51 in celiacs/15 in controls **BMD:** Lower in those with fractures (non-significant) **Exclusions:** Only lumbar spine X-rays from 68 pts and 78 controls were considered to be of adequate quality	**OR: Peripheral fractures** (25%) of CD pts and (8%) of controls; 3.5 (95% CI 1.8-7.2) p<0.0001, wrist most common **Vertebral fractures** 4/78 (5%) of controls versus 9/68 (13%); OR 2.8 (0.7, 1.15) incomplete ascertainment X-rays: 68 pts and 78 controls were adequate quality Most fractures observed pre-diagnosis Only 7% of pt developed fractures after starting GFD	Cases were from a malabsorption clinic and therefore may have included subjects with more severe disease

Evidence Table 11 (cont'd): Consequences of testing for CD

Study, Year, Location	Methods	Participants	Outcomes	Measures of risk	Limitations
Vestergard, 2002, Denmark	Retrospective cohort study, population based Study dates: 1983-1996 **Group selection** CD pts: All individuals admitted/ discharged with a CD Dx (ICD -8) Controls: 3 controls per case population age and sex matched **Institution:** Danish hospitals **Ascertainment of fracture** National pt discharge register–any fracture registered during hospitalization **Confounders:** not examined **Blinding:** n/r Comorbidity examined by assessing hospital admissions for conditions that may alter risk of fractures. (2.8% in CD vs 2.6% in controls)	**CD pts:** n=1,021; 7,774 PY **Controls:** n=23; 316 PY **Mean age at diagnosis:** 31.5 y (24.7) **Mean follow-up:** 7,774 PYs cases; 23,316 controls **Proportion of females:** 58% **Proportion on GFD:** n/r **Compliance:** n/r **Clinical presentation:** symptomatic (admission to hospital) **BMI:** n/r **Age at first fracture after diagnosis:** 40.2 y **Exclusions** ? output diagnosis of CD	**All Fractures: CD vs control** Before diagnosis: 24/7774 PY vs 103/23,316 PY After diagnosis: 65/6,675 vs 223/21,468 PY **Spine Rib Pelvis Osteoporosis**	**Incidence rate ratio (ALL)** Before Dx: 0.70 (0.45,1.09) After Dx: 0.94 (0.71, 1.24**)** (spine, rib, pelvis) IRR 2.14 (0.70, 6.57) pre IRR 1.07 (0.39, 2.95) post IRR 3.00 (0.21,41.9) pre IRR 1.29 (0.4, 4.09) post	Used only hospital-based discharge data therefore could miss output fractures (wrist, rib) Based on assumption that majority of pts pre 1996 hospitalized early in course of disease Validity of diagnosis verified in random sample and was low (78%) n=9 therefore potential for misclassification Selection of controls Some of controls had diseases that may have increased fracture risk

Evidence Table 11: Consequences of testing for CD

Study, Year, Location	Methods	Participants	Outcomes	Measures of risk	Limitations
West, 2003, UK	Retrospective matched cohort study Study dates: 1987-2002 **Group selection** Pts with CD: All recorded Dx of CD recorded 1-yr after beginning of the GPRD record; no biopsy data Controls: matched by age, sex, general practice and follow-up time, excluded any who had record of a gluten-free prescription **Primary care database:** GPRD established in 1987 **Ascertainment of fracture:** Admin database **Blinding:** n/r **Examined potential confounders**	**CD pts**: n=4,732 observ. time (27,116) **Controls:** n=23,620 (149,896 y of risk) **Mean age at diagnosis celiac**: 43.5 y Range of age: n/r **Proportion of females:** 67% **Proportion smoke:** 13% (controls 15.4%) **Mean follow-up:** 5.7 y, # PYs: 27,116 10% of cohort did not receive a prescription for GFD, 36% 0-10 and 54≥10 **BMI:** Celiacs: <25 – 47% Controls: <25: 30.6% ≤18.5; 4.2% vs 1.2% of controls	**Fracture: CD vs control** **Any fracture:** 356/4732 vs 1524/23616 137.9/10,000 PYs vs 105.9/10,000 in controls **Hip:** 8.9/10,000 PY versus 4.7/10,000 PY **Ulna/radius fracture:** 24.9/10,000 versus 14.1/10,000 No difference in risk of fracture in period after diagnosis compared to before diagnosis	HR: 1.30 (95% CI, 1.16,1.46) (report prevalent and incident) HR 1.9 (1.20,3.02) HR 1.77 (1.35,2.34) Absolute diff in overall fracture rate was 3.2/1000 person y 0.97/1000 for hip fracture in those >45 y	Celiacs more frequent attenders, ?overestimate rate of some fractures relative to controls Misclassification – accuracy of diagnosis of CD ? Less likely in UK, since GPs not likely to write prescription for GFD

Evidence Table 11 (cont'd): Consequences of testing for CD

Author, Year Country	Methods	Participants	Outcomes	Results	Limitations
Westman 1999 Australia	Study type- Population-coexisting type 1 diabetics and CD identified from database of Diabetes Center-biopsy proven Controls- 40 matched for age and sex and duration of IDDM	Cases 20 Control 40 Duration of diabetes: 7.2 vs 7.3 y controls % F - 75% Mean follow-up Compliance with FFQ	Height SDS Weight SDS BMI SDS HbA1c Compliance	No difference in height SDS, weight SDS or BMI SDS 8.48 ± 0.98% for CD vs 8.87 ± 1.46 for controls 30% strict GF, 30% trace gluten and 40% significant amt of gluten	

Celiac 5: Promoting or Monitoring Adherence to a GFD

Evidence Table 12: Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Anson, 1990, Israel	**Publication type:** journal **Study design:** Parental questionnaire **Ethnicity:** n/r **Population type:** Jewish children with CD **Biopsy criteria:** n/r **Checked IgA def.** no **Serologic tests:** Test name: n/a Methodology: n/a Cut-off: n/a	**Celiac Group 1** •31 children judged GFD compliant based on symptoms and/or serology and/or biopsy •age: n/r •%F: n/r **Celiac Group 2** • 12 children judged non-compliant with GFD • age: n/r • %F: n/r	Baseline				Compliance correlated with father being professional/parental education/parental ability to choose GF items from menu.
			Biopsy				
			AGA				
			EMA				
			tTG				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Bardella, 2001, Italy	**Publication type:** journal **Study design:** case-control **Ethnicity:** n/r **Population type:** CD: details of diagnosis n/r **Biopsy criteria:** Marsh **Checked IgA def.** Yes, excluded **Serologic tests:** Test name: IgA-AGA; IgA-EMA; IgA-tTG Methodology: n/r; ME; GP liver Cut-off: 12 AU/mL; 1:10; 10 AU/mL	**Celiac Group 1** • 40 pts, untreated CD • mean age: 38 y (range 16-77 y) **Celiac Group 2** • 25 CD; poor GFD compliance • age: n/r • gender: n/r **Celiac Group 3** • 22 CD. Compliant GFD<2 y • age: n/r • gender: n/r **Celiac Group 4** • 148 CD. Compliant GFD >2 y • age: n/r gender: n/r Control • 110 non-CD controls • age: nr • gender: n/r	Baseline				Serology falls with increasing length of compliance with GFD. No biopsy to correlate serology with in this study.
			Biopsy				
			AGA Group 1 95%; Group 2 100%; Group 3 40.9%; Group 4 16.2%; Control 10.9%				
			EMA 100%; 100%; 54.5%; 9.5%; 2.7%				
			tTG 100%; 100% 63.6%; 14.2% 1.8%				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Bartholomeus, 1990, Australia	**Publication type:** journal **Study design:** cohort **Ethnicity:** n/r **Population type:** CD: details of diagnosis n/r **Biopsy criteria:** Adults partial VA, subtotal VA, total VA; children ESPGAN **Checked IgA def.** No **Serologic tests:** Test name: IgA-AGA Methodology: n/r Cut-off: n/r	**Celiac Group 1** • 17 CD. GFD >6 mos adults and children • age: n/r • gender: n/r **Celiac Group 2** • 12 adults and children with CD on gluten • age: n/r • gender: n/r	Baseline				PPV of IgA AGA for non-compliance 78.5% for pts on GFD > 6 mos. How compliance ascertained not described.
			Biopsy				
			AGA Group 1 3 (17%); Group 2 11 (92%)				
			EMA				
			tTG				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Burgin-Wolff, 1991, Switzerland	**Publication type:** journal **Study design:** case-control **Ethnicity:** n/r **Population type:** Classic CD **Biopsy criteria:** CD if subtotal VA, total VA **Checked IgA def.** no **Serologic tests:** Test name: IgA-AGA ; IgA-EMA Methodology: n/r; ME Cut-off: n/r; 1:10	**Celiac Group 1** • 134 children CD on GFD • mean age: n/r (range 3-18 y) • gender: n/r	Baseline	GC 36 to 90 d	GC 3 to 12 mos	GC > 3 y	With gluten challenge IgA AGA and EMA seroconversion. AGA rises faster but positivity wanes with time.
			Biopsy				
			AGA 23% IgA-AGA	97%	5%	49%	
			EMA 13% EMA	65%	84%	93%	
			tTG				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Dickey, 2000, Northern Ireland	**Publication type:** journal **Study design:** prospective cohort **Ethnicity:** n/r **Population type:** Adults with classic CD **Biopsy criteria:** Marsh **Checked IgA def.** Yes. Excluded **Serologic tests:** Test name: IgA EMA Methodology: ME Cut-off: >1:5	**Celiac Group 1** • 53 pts • mean age: 55; range 16-80 y • 74% F	Baseline	GFD 3 mos	GFD 6 mos	GFD 12 mos	EMA failed to detect VA in a significant number. These cases were felt to have VA due to non-compliance.
			Biopsy 12 partial VA; 21 subtotal VA; 21 total VA			20 normal;1 Marsh 1 (high IEL); 22 partial VA; 10 total VA or subtotal VA	
			AGA				
			EMA 100%	42%	25%	0% normal; 0% Marsh 1; 2 (9%) partial VA; 3 (30%) subtotal/total VA	
			tTG				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Fabiani, 1996, Italy	**Publication type:** journal **Study design:** retrospective cohort **Ethnicity:** n/r **Population type:** CD identified by screen **Biopsy criteria:** no description **Checked IgA def.** No **Serologic tests:** Test name: IgA AGA; IgA EMA Methodology: n/r Cut-off: n/r	**Celiac Group 1** • 12 children reporting strict GFD • age: n/r • gender: n/r **Celiac Group 2** • 11 children reporting non-compliance • age: n/r • gender: n/r	Baseline				Among pts reporting dietary transgressions 9 of 11 (81%) had normal AGA and EMA.
			Biopsy				
			AGA				
			EMA				
			tTG				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Fabiani, 2000, Italy	**Publication type:** journal **Study design:** case-control **Ethnicity:** n/r **Population type:** CD identified in a mass screen **Biopsy criteria:** ESPGAN **Checked IgA def.** No **Serologic tests:** Test name: n/a Methodology: n/a Cut-off: n/a	**Celiac Group 1** • 22 children CD identified by screen • mean age: 17.9 y; range: n/r • 59% F **Control** • 22 children with classic CD on GFD • mean age: 16 y; range: n/r • 59% F	Baseline				5 (23%) identified by screen reporting strict GFD. 15 (68%) of controls reporting strict GFD? Less compliant if screened CD.
			Biopsy				
			AGA				
			EMA				
			tTG				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Fabiani, 2001, Italy	**Publication type:** journal **Study design:** case-control **Ethnicity:** n/r **Population type:** Classic CD **Biopsy criteria:** Marsh **Checked IgA def.** Yes. Excluded **Serologic tests:** Test name: IgA-tTG Methodology: GP liver Cut-off: 7 AU	**Celiac Group 1** • 176 pt new diagnosis CD • mean age: 16.4 y; range 0.3-87.4 y • 65% F **Celiac Group 2** • 172 CD on GFD > 1 • mean age: 17.6 y; range 0.3 - 89.8 y • 66% F **Control** • 206 healthy and non-CD • mean age: 15.6 y; range 0.4-78 y • 50% F	Baseline				tTG value higher in higher Marsh lesions. Values tend to be higher in pts admitting dietary transgressions.
			Biopsy Group 1: 0 Marsh 1, 29 (16%) Marsh 2, 145 (84%) Marsh 3 Group 2: n/a Control: n/a				
			AGA				
			EMA				
			tTG Group 1: mean tTG Marsh 2 16 AU, Marsh 3 22 AU Group 2: strict GFD 4.2 AU, GFD transgressions 9.9 AU Control: 2.7 AU				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Fotoulaki, 1999, Greece	**Publication type:** journal **Study design:** prospective cohort **Ethnicity:** n/r **Population type:** Classic and atypical CD **Biopsy criteria:** ESPGAN **Checked IgA def.** yes **Serologic tests:** Test name: IgG AGA; IgG AGA; IgA EMA Methodology: n/r; ME Cut-off: 0.3 control; 0.3 control; 1:2.5	**Celiac Group 1** • 30 CD • mean age: n/r; range 1-24 y • 57% F **Celiac Group 2** • median age: (range:) • % F:	Baseline	GFD 12 mos	GC 6 mos		Study suggests that after 1 y GFD, AGA and EMA predict Marsh 0 or 1 lesion. Significance of Marsh 1 unclear.
			Biopsy n/r	100% Marsh 0 or 1 (breakdown not given)	All Marsh 2 or 3 (breakdown not given)		
			AGA IgG AGA 100%; 90% IgA AGA	40% IgG AGA; 0% IgA AGA	100% IgG: 90% IgA		
			EMA 100%	0%	90%		
			tTG				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Hogberg, 2003, Sweden	**Publication type:** journal **Study design:** retrospective cohort **Ethnicity:** n/r **Population type:** Classic CD **Biopsy criteria:** ESPGAN **Checked IgA def.** no **Serologic tests:** Test name: IgG-EMA; IgA-EMA; tTG Methodology: ME; GP Cut-off: 1:10;1:10;>25 AU	**Celiac Group 1** • 29 adults diagnosed as a child • mean age: 26 y; range 19-34 y • 69% F	Baseline				12/15 (80%) diagnosed before age 4 judged GFD compliant (serology/questionnaire) vs. only 5/14 (36%) diagnosed after age 4.
			Biopsy				
			AGA				
			EMA				
			tTG				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Jackson, 1985, Ireland	**Publication type:** journal **Study design:** questionnaire **Ethnicity:** n/r **Population type:** Classic CD **Biopsy criteria:** CD if severe VA and gluten response **Checked IgA def.** no **Serologic tests:** Test name: n/a Methodology: n/a Cut-off: n/a	**Celiac Group 1** • 50 children CD • median age: 9.9 y; range 1.5-19 y • 58% F	Baseline				GFD judged by parental questionnaire correlated with parental membership in Celiac society, parental knowledge of CD.
			Biopsy				
			AGA				
			EMA				
			tTG				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Kaukinen, 2002, Finland	**Publication type:** journal **Study design:** prospective cohort **Ethnicity:** n/r **Population type:** Classic CD **Biopsy criteria:** Marsh **Checked IgA def.** Yes. Excluded **Serologic tests:** Test name: IgA-EMA; IgA-tTG Methodology: HU; GP liver Cut-off: 1:5; 1:20	**Celiac Group 1** • 87 pts on GFD • mean age: 49 y; range 22-73 y • 72% F	Baseline GFD median 1 y				tTG sens 41% spec 88% PPV 61% NPV 77% EMA sens 26% spec 93% PPV 63% NPV 74%
			Biopsy 60 (69%) Marsh 0-II; 27 (31%) Marsh III				
			AGA				
			EMA 7 (26%) in Marsh III				
			tTG 11 (41%) in Marsh III				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Lamontagne, 2001, Canada	**Publication type:** journal **Study design:** questionnaire **Ethnicity:** n/r **Population type:** **Biopsy criteria:** **Checked IgA def.** **Serologic tests:** Test name: n/a Methodology: n/a Cut-off: n/a	**Celiac Group 1** • 234 CD. Members of Quebec Celiac Foundation • mean age: 49 y; range 18-84 y • 75% F	Baseline				Older age (p<.05) & high level of confidence in treatment information from gastroenterologists & dieticians (p<.005) assoc. compliance.
			Biopsy				
			AGA				
			EMA				
			tTG				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Lee, 2003, USA	**Publication type:** journal **Study design:** retrospective cohort **Ethnicity:** n/r **Population type:** Classic CD **Biopsy criteria:** Normal, partial VA or total VA **Checked IgA def.** n/r **Serologic tests:** Test name: IgG AGA; IgA AGA; IgA AMA Methodology: n/r Cut-off: n/r	**Celiac Group 1** • n=39 pts on GFD • mean age: 52 y; range 20-74 y • 60% F	Baseline	1-14 y after initial Dx: only 12 pts re-biopsied; 31/39 had serology			Persistent abnormal biopsy on GFD. Only 21% had normal duodenal biopsy; serology was negative despite some VA in most.
			Biopsy Normal 8 (21%); partial VA 27 (69%); total VA 4 (10%); IEL/epithelial cells 61	IEL/100 epithelial cells-38; villous height to crypt ratio improved in all but one; none normalized			
			AGA	7; IgG only 4; IgG and IgA in 3			
			EMA	1 of 31			
			tTG				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Ljungman, 1993, Sweden	**Publication type:** journal **Study design:** questionnaire **Ethnicity:** n/r **Population type:** Classic CD **Biopsy criteria:** ESPGAN **Checked IgA def.** n/r **Serologic tests:** Test name: n/a Methodology: n/a Cut-off: n/a	**Celiac Group 1** • 47 children born between 1973-78 • mean age: n/r • gender: n/r	Baseline				Self-assessed GFD compliance correlated with knowledge as scored on a test and with a feeling of being well informed.
			Biopsy				
			AGA				
			EMA				
			tTG				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Martini, 2002 Italy	**Publication type:** journal **Study design:** prospective cohort **Ethnicity:** n/r **Population Type:** Classic CD **Biopsy criteria:** Marsh **Checked IgA def.** n/r **Serologic tests:** Test name: IgA-EMA; IgA-tTG-1; tTG-2, tTG-3, tTG4, tTG-GP Methodology: ME; HU; HU; HU; HU; GP Cut-off: 1:5; n/r	**Celiac Group 1** • 109 CD on GFD 1 y • median age: 37 y; range 21-72 y • 78% F	Baseline (at diagnosis)	GFD 1 y +/- 1mos			Poor concordance between biopsy and serology after GFD for one year. GFD led to a significant decrease in majority.
			Biopsy 6 (6%) Marsh 2; 95 (95%) Marsh3	12 (12%) normal; 51 (50%) Marsh 1; 38 (38%) Marsh 2 or 3			
			AGA n/a	n/a			
			EMA n/a	Concordance (both biopsy/EMA + or both) 48%			
			tTG n/a	Concordance 29%; 65%;14%; 16%; 19%			

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
McNichol, 1976, Ireland	**Publication type:** journal **Study design:** cohort **Ethnicity:** n/r **Population type:** Classic CD **Biopsy criteria:** Normal, slight, moderate, severe mucosal damage **Checked IgA def.** n/r **Serologic tests:** Test name: n/a Methodology: n/a Cut-off: n/a	**Celiac Group 1** • 36 children on GFD (mean 6 y) • mean age: n/r; range 2.75-11 y • gender: n/r **Control** • 25 normal siblings • mean age: 9.9; range: 4-18 • gender: n/r	Baseline				IEL count higher in CD with slight damage than no damage (p<.005) or controls (p<.001)
			Biopsy Group 1- 16 (44%) normal. 20 (56%) slight mucosal damage; controls all normal				
			AGA				
			EMA				
			tTG				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, Year, Location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Pacht 1995, Israel	**Publication type:** journal **Study design:** retrospective cohort **Ethnicity:** n/r **Population Type:** Classic CD **Biopsy criteria:** ESPGAN **Checked IgA def.** n/r **Serologic tests:** Test name: IgA EMA Methodology: ME Cut-off: >1:2.5	**Celiac Group 1** • 39 CD, 22 GCD and 17 GFD • mean age: 10 y; range: n/r • % F: 46% **Celiac Group 2** • median age: (range:) • % F:	Baseline 22 GCD;17 GFD				EMA titre monitored longitudinally in 10 pts correlated with gluten intake. EMA correlated with investigator gluten assessment.
			Biopsy n/r; histology available on 5 on GFD - all normal				
			AGA				
			EMA 22/22 GCD EMA+; 0/17 GFD EMA+				
			tTG				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Sategna-Guidetti, 1996, Italy	**Publication type:** journal **Study design:** prospective cohort **Ethnicity:** n/r **Population Type:** CD: details of diagnosis not reported **Biopsy criteria:** Normal, partial VA, subtotal VA, total VA **Checked IgA def.** Yes, excluded **Serologic tests:** Test name: total AGA; IgA EMA Methodology: n/r; ME Cut-off: n/r	**Celiac Group 1** • 47 pts • mean age: n/r; range: 18-68 y • 55% F	Baseline	GFD 8-30 mos			EMA PPV for abnormal histology 100%, NPV 23%; AGA (total) PPV for abnormal histology 93.8%, NPV 25%
			Biopsy 0 normal; 1 (2.1%) partial VA; 11 (23%) subtotal VA; 35 (74%) total VA	9 (19%) normal ; 23 (49%) partial VA; 13 (28%) subtotal VA ;2 (4%) total VA			
			AGA 39 (83%)	AGA measured in 39; Bx normal: 1/7 AGA+; partial VA: 7/20; subtotal VA: 5/10; total VA: 2/2			
			EMA 47 (100%)	Bx normal: 0 EMA+; partial VA: 5/23; subtotal VA: 3/13; total VA: 1/2			
			tTG n/a				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Scalici, 2003, Italy	**Publication type:** journal **Study design:** prospective cohort **Ethnicity:** n/r **Population type:** Classic CD **Biopsy criteria:** ESPGAN **Checked IgA def.** n/r **Serologic tests:** Test name: IgA EMA Methodology: n/r Cut-off: n/r	**Celiac Group 1** • 61 CD pts • mean age: n/r; age range 2-27 y • %F: n/r **Celiac Group 2** • median age: (range:) • % F:	Baseline (at diagnosis)	GFD for 6 mos			Only 11.1% EMA + if 1 dietary transgression/ mos (after 6 mos GFD). 19% EMA + if 1 or more dietary transgressions per week
			Biopsy n/r	n/a			
			AGA				
			EMA 0 EMA+	2/16 (12.5%) reporting strict GFD EMA+; 5/45 (11.1%) admitting dietary mistakes EMA+			
			tTG				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, Year, Location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Selby, 1999 Australia	**Publication type:** journal **Study design:** cross sectional **Ethnicity:** n/r **Population Type:** Classic CD **Biopsy criteria:** Normal, partial VA, subtotal VA, total VA **Checked IgA def.** n/r **Serologic tests:** Test name: n/a Methodology: n/a Cut-off: n/a	**Celiac Group 1** • 89 pts CD on GFD mean 8.3 y • mean age: 47 y; range: 20-75 • 82% F	Baseline 39 Codex diet; 50 no detectable gluten				VA persisted at high rates after prolonged GFD (whether Codex diet allowing .03% protein from gluten or on no detectable GFD)
			Biopsy 18/39 (46%) VA; 20/50 (40%) VA				
			AGA				
			EMA				
			tTG				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, Year, Location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Troncone, 1995 Italy	**Publication type:** journal **Study design:** cohort **Ethnicity:** n/r **Population Type:** CD : details of diagnosis not reported **Biopsy criteria:** Normal, partial VA, subtotal VA, total VA **Checked IgA def.** n/r **Serologic tests:** Test name: IgA EMA Methodology: ME Cut-off: >1:5	**Celiac Group 1** • 4 CD on strict GFD (23 in overall study • mean age: 14.5 y; range 10-19 y • 35% F) **Celiac Group 2** • 6 pts <0.5 g/d gluten • median age: n/r; range: n/r • % F: n/r **Celiac Group 3** • 6 pts 0.5-1.0 g/d gluten • median age: n/r; range: n/r • % F: n/r **Celiac Group 4** • 7 pts>2 g/d gluten • median age: n/r; range: n/r • % F: n/r	Baseline				EMA often did not pick up mild dietary transgressions despite mucosal abnormalities including VA.
			Biopsy Group 1 4/4 normal; Group 2 3/6 high IEL, 1/6 VA; Group 3 5/6 high IEL 3/6 VA; Group 4 7/7 VA				
			AGA				
			EMA Group1 0/4; Group 2 1/6; Group 3 3/6; Group 4 7/7				
			tTG				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, Year, Location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Vahedi, 2000 France	**Publication type:** abstract **Study design:** cross sectional **Ethnicity:** n/r **Population type:** CD: details of diagnosis not reported **Biopsy criteria:** no description **Checked IgA def.** Yes. Excluded **Serologic tests:** Test name: IgA EMA; IgA tTG Methodology: n/r Cut-off: 1:5; n/r	**Celiac Group 1** • 137 CD on GFD>1 y - median 75 mos • median age: 46 y; range 18-74 y • 76% F	Baseline (39% strict GFD)				EMA and tTG often negative despite dietary transgression. EMA 37% sensitive for minor transgression. tTG 31% sensitive.
			Biopsy n/a				
			AGA				
			EMA 2.5% strict GFD; 37% minor transgression; 86% major transgression				
			tTG 3% strict GFD; 31% minor transgression; 77% major transgression				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Valentini, 1994, Italy	**Publication type:** journal **Study design:** prospective cohort **Ethnicity:** n/r **Population Type:** Classic and atypical CD **Biopsy criteria:** Normal, partial VA, subtotal VA **Checked IgA def.** n/r **Serologic tests:** Test name: IgA EMA Methodology: ME Cut-off: >1:5	**Celiac Group 1** • 33 CD pts on GFD >6 mos- mean 9 mos • mean age: n/r; range: n/r • % F: n/r	Baseline GFD > 6 mos				17/24 EMA negative after 6 mos on a GFD despite VA on biopsy
			Biopsy 8 normal; 21 partial VA; 4 subtotal VA				
			AGA				
			EMA 9 (27%). Of 73% EMA negative, 7 normal,14 partial VA,3 subtotal VA				
			tTG				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, Year, Location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Valetta, 1990 Italy	**Publication type:** journal **Study design:** prospective cohort **Ethnicity:** n/r **Population type:** CD: details of diagnosis not reported **Biopsy criteria:** N,slight VA, moderate VA, severe VA **Checked IgA def.** n/r **Serologic tests:** Test name: IgA AGA Methodology: n/r Cut-off: >3 SD controls	**Celiac Group 1** • 17 pts given gluten challenge • mean age: n/r; range 3 – 11 y • 59% F	Baseline				With GC, most AGA+ which prompted Bx showing VA in all. Does not necessarily mean compliance could be monitored.
			Biopsy at 20-45 d, all had moderate or severe VA				
			AGA 16/17 (94%) after 15 - 35 d gluten challenge				
			EMA				
			tTG				

Evidence Table 12 (cont'd): Promoting or monitoring adherence to a GFD

Author, year, location	Study Design	Study Population	Outcomes				Comments
			Time 1	Time 2	Time 3	Time 4	
Wahab, 2002, unknown	**Publication type:** journal **Study design:** retrospectve cohort **Ethnicity:** n/r **Population type:** Classic CD **Biopsy criteria:** Marsh **Checked IgA def.** No **Serologic tests:** Test name: n/a Methodology: n/a Cut-off: n/a	**Celiac Group 1** • 158 pts • mean age: 44 y; range 0 – 74 y • 91% F **Celiac Group 2** • median age: (range: n/r) • % F:	Baseline	GFD <2 years	GFD 2-5 years	GFD >5 years	Overall, only 65% recovery within 2 y. 10% with no recovery after 5 y. Recovery defined as no VA (Marsh 0-2).
			Biopsy 59 (37%) Marsh 3a; 59 (37%) 3b; 40 (25%) 3c	88% 3a recovery to 0-2; 58% 3b recovery ; 81% 3c recovery	98% 3a recovery to 0-2; 78% 3b recovery; 81% 3c recovery	98% 3a recovery to 0-2; 88% 3b recovery; 86% 3c recovery	
			AGA				
			EMA				
			tTG				

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Appendix J. Quality Assessment

Table 1: Celiac 1 diagnostic studies (QUADAS)

Author (Year)	Item 1: spectrum of patients	Item 2: selection criteria	Item 3: reference standard	Item 4: time period	Item 5: sampling	Item 6: test result	Item 7: sampling independence	Item 8a: index test description	Item 8b: reference standard description	Item 9a: reference standard results(1)	Item 9b: reference standard results (2)	Item 10: interpretation	Item 11: uninterpretable/ intermediate test result	Item 12: withdrawal explanation	Total No. of Items = 14	
Altuntas (1998)	yes	yes	yes	yes	yes	yes	yes	yes	yes	no	unclear	yes	yes	yes	**12**	(+) reported
Artan (1998)	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	yes	yes	yes	**13**	(+) reported
Ascher (1996)	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	unclear	yes	yes	yes	**12**	(+) reported
Ascher (1990)	yes	yes	yes	yes	yes	yes	yes	unclear	yes	unclear	unclear	yes	yes	yes	**11**	(+) reported
Bahia (2001))	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	unclear	yes	no	no	**10**	(+) reported
Bardella (2001)	yes	yes	yes	yes	yes	yes	yes	unclear	yes	unclear	unclear	yes	yes	yes	**11**	(+) reported
Berger (1996)	no	yes	yes	unclear	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	**12**	(+) reported
Biagi (2001)	no	unclear	yes	no	yes	yes	yes	yes	yes	no	unclear	yes	yes	yes	**9**	(+) reported
Bode (1993)	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	unclear	yes	yes	yes	**12**	(+) reported
Bonamico (2001)	no	unclear	yes	no	yes	yes	yes	yes	unclear	no	unclear	yes	yes	yes	**8**	(+) reported

Table 1: Celiac 1 diagnostic studies (QUADAS) (cont'd)

Author (Year)	Item 1: spectrum of patients	Item 2: selection criteria	Item 3: reference standard	Item 4: time period	Item 5: sampling	Item 6: test result	Item 7: sampling independence	Item 8a: index test description	Item 8b: reference standard description	Item 9a: reference standard results(1)	Item 9b: reference standard results (2)	Item 10: interpretation	Item 11: uninterpretable/ intermediate test result	Item 12: withdrawal explanation	Total No. of Items = 14	
Bottaro (1997)	no	no	yes	no	yes	yes	yes	unclear	yes	yes	unclear	yes	yes	yes	**9**	(+) reported
Carroccio (2002)	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	yes	yes	yes	**13**	(+) reported
Carroccio (1993)	no	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	yes	yes	yes	**12**	(+) reported
Carroccio (2002)	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	yes	yes	yes	**13**	(+) reported
Cataldo (2000)	no	yes	yes	unclear	yes	yes	yes	yes	yes	no	unclear	yes	yes	yes	**10**	(+) reported
Chan (2001)	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	yes	yes	yes	**13**	(+) reported
Chartrand (1997)	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	yes	yes	yes	**13**	(+) reported
Chirdo (1999)	yes	unclear	yes	yes	yes	yes	yes	yes	yes	no	unclear	yes	yes	yes	**11**	(+) reported
Chirdo (2000)	no	no	yes	yes	unclear	yes	yes	yes	yes	unclear	unclear	yes	yes	yes	**9**	(+) reported
Dahele (2001)	no	no	yes	yes	yes	yes	yes	yes	yes	yes	unclear	yes	yes	yes	**11**	(+) reported
Di Leo (1999)	no	unclear	yes	unclear	yes	yes	yes	yes	no	no	unclear	yes	yes	yes	**8**	(+) reported
Dickey (2001)	no	unclear	yes	yes	yes	yes	yes	yes	yes	yes	unclear	yes	yes	yes	**11**	(+) reported

Table 1: Celiac 1 diagnostic studies (QUADAS) (cont'd)

Author (Year)	Item 1: spectrum of patients	Item 2: selection criteria	Item 3: reference standard	Item 4: time period	Item 5: sampling	Item 6: test result	Item 7: sampling independence	Item 8a: index test description	Item 8b: reference standard description	Item 9a: reference standard results(1)	Item 9b: reference standard results (2)	Item 10: interpretation	Item 11: uninterpretable/ intermediate test result	Item 12: withdrawal explanation	Total No. of Items = 14	
Falth-Magnus-son (1994)	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	unclear	yes	yes	no	**11**	(+) reported
Gillett (2000)	no	no	yes	yes	yes	no	yes	yes	yes	unclear	unclear	yes	yes	yes	**9**	(+) reported
Gonczi (1991)	yes	yes	yes	yes	no	yes	yes	yes	yes	no	unclear	yes	yes	yes	**11**	(+) reported
Hallstrom (1989)	no	no	yes	unclear	yes	yes	yes	yes	yes	unclear	unclear	yes	yes	yes	**9**	(+) reported
Hansson (2000)	no	no	yes	yes	yes	yes	yes	yes	yes	unclear	unclear	yes	yes	yes	**10**	(+) reported
Iltanen (1999)	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	unclear	yes	yes	yes	**12**	(+) reported
Kaukinen (2000)	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	yes	yes	yes	**13**	(+) reported
Kolho (1997)	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	**14**	(+) reported
Kumar (1989)	yes	yes	yes	yes	unclear	yes	yes	yes	yes	unclear	unclear	yes	yes	yes	**11**	(+) reported
Ladinser (1994)	no	no	yes	unclear	unclear	unclear	yes	yes	yes	unclear	unclear	yes	unclear	unclear	**5**	(+) reported

Table 1: Celiac 1 diagnostic studies (QUADAS) (cont'd)

Author (Year)	Item 1: spectrum of patients	Item 2: selection criteria	Item 3: reference standard	Item 4: time period	Item 5: sampling	Item 6: test result	Item 7: sampling independence	Item 8a: index test description	Item 8b: reference standard description	Item 9a: reference standard results(1)	Item 9b: reference standard results (2)	Item 10: interpretation	Item 11: uninterpretable/ intermediate test result	Item 12: withdrawal explanation	Total No. of Items = 14	
Lerner (1994)	no	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	**13**	(+) reported
Lindberg (1985)	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	unclear	yes	yes	yes	**12**	(+) reported
Lindquist (1994)	yes	yes	yes	yes	yes	yes	yes	yes	yes	no	unclear	yes	yes	yes	**12**	(+) reported
Maki (1991)	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	yes	yes	yes	**13**	(+) reported
McMillan (1991)	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	**14**	(+) reported
Meini (1996)	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	unclear	yes	yes	yes	**12**	(+) reported
Pacht (1995)	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	yes	yes	yes	**13**	(+) reported
Picarelli (2000)	yes	unclear	yes	yes	yes	yes	yes	yes	yes	no	unclear	yes	yes	no	**10**	(+) reported
Poddar (2002)	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	yes	yes	unclear	**12**	(+) reported
Rich (1990)	yes	yes	yes	yes	yes	yes	yes	yes	yes	no	unclear	yes	yes	yes	**12**	(+) reported
Russo (1999)	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	yes	yes	yes	**13**	(+) reported

Table 1: Celiac 1 diagnostic studies (QUADAS) (cont'd)

Author (Year)	Item 1: spectrum of patients	Item 2: selection criteria	Item 3: reference standard	Item 4: time period	Item 5: sampling	Item 6: test result	Item 7: sampling independence	Item 8a: index test description	Item 8b: reference standard description	Item 9a: reference standard results(1)	Item 9b: reference standard results (2)	Item 10: interpretation	Item 11: uninterpretable/ intermediate test result	Item 12: withdrawal explanation	Total No. of Items = 14	
Salmaso (2001)	no	unclear	yes	unclear	unclear	unclear	yes	yes	no	unclear	unclear	yes	yes	yes	**6**	(+) reported
Sategna-Guidetti (1995)	no	unclear	yes	unclear	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	**11**	(+) reported
Sblattero (2000)	no	yes	yes	no	yes	no	yes	yes	yes	yes	unclear	yes	yes	yes	**10**	(+) reported
Sulkanen (1998)	no	yes	yes	yes	yes	yes	yes	yes	yes	unclear	unclear	yes	yes	yes	**11**	(+) reported
Tesei (2003)	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	yes	yes	yes	**13**	(+) reported
Troncone (1999)	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	unclear	yes	yes	yes	**12**	(+) reported
Valdimars-son (1996)	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	unclear	yes	yes	yes	**13**	(+) reported
Valentini (1994)	no	no	yes	yes	yes	yes	yes	yes	yes	unclear	unclear	yes	yes	yes	**10**	(+) reported
Vitoria (2001)	no	no	yes	no	yes	yes	yes	yes	no	no	unclear	yes	yes	yes	**8**	(+) reported
Vogelsang (1995)	yes	yes	yes	yes	yes	yes	yes	yes	yes	no	unclear	yes	yes	yes	**12**	(+) reported

Table 1: Celiac 1 diagnostic studies (QUADAS) (cont'd)

Author (Year)	Item 1: spectrum of patients	Item 2: selection criteria	Item 3: reference standard	Item 4: time period	Item 5: sampling	Item 6: test result	Item 7: sampling independence	Item 8a: index test description	Item 8b: reference standard description	Item 9a: reference standard results(1)	Item 9b: reference standard results (2)	Item 10: interpretation	Item 11: uninterpretable/ intermediate test result	Item 12: withdrawal explanation	Total No. of Items = 14	
Volta (1995)	no	unclear	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	**12**	(+) reported
Whelan (1996)	no	unclear	yes	unclear	yes	yes	yes	yes	unclear	unclear	unclear	yes	yes	yes	**8**	(+) reported
Wolters (2002)	yes	no	yes	unclear	yes	yes	yes	yes	yes	no	unclear	yes	yes	yes	**10**	(+) reported
Item % (+) reported	**59%**	**64%**	**100%**	**75%**	**91%**	**93%**	**100%**	**95%**	**91%**	**41%**	**11%**	**100%**	**96%**	**91%**		

NOTE: (+) reported = postively reported; yes = reported; no = not reported

Table 2: Celiac 2 prevalence & incidence studies (cross-sectional checklist)

Author (Year)	Item 1: Source of Information	Item 2: Inclusion/Exclusion Criteria	Item 3: Time Period for Identity	Item 4: Subjects consecutive	Item 5: Evaluators Masked	Item 6: Quality Assurance Assessments	Item 7: Patient Exclusions	Item 8: Confounding assessed/controlled	Item 9: Missing Data	Item 10: Response Rates	Item 11: Follow-up	Total Items Reported (Max. 11)	
Acerini (1998)	yes	no	yes	no	can't tell	no	no	no	yes	yes	yes	**5**	(+) reported
Ackerman (1996)	can't tell	no	yes	can't tell	no	no	no	no	no	yes	yes	**3**	(+) reported
Agardh (2001)	yes	can't tell	no	can't tell	no	no	yes	no	yes	can't tell	no	**3**	(+) reported
Aktay (2001)	yes	no	yes	no	no	no	no	no	no	no	no	**2**	(+) reported
Annibale (2001)	yes	yes	yes	yes	can't tell	can't tell	yes	no	no	yes	no	**6**	(+) reported
Annibale (2003)	yes	yes	yes	yes	no	no	yes	can't tell	no	yes	no	**6**	(+) reported
Arato (2002)	yes	yes	yes	yes	no	no	no	can't tell	no	can't tell	no	**4**	(+) reported
Bao (1999)	yes	no	no	can't tell	no	no	no	no	no	can't tell	no	**1**	(+) reported
Bardella (1991)	yes	no	no	yes	can't tell	yes	no	no	no	yes	no	**4**	(+) reported
Bardella (2001)	yes	no	yes	yes	no	no	no	no	no	yes	no	**4**	(+) reported
Barera (1991)	can't tell	no	yes	can't tell	no	no	no	no	no	yes	no	**2**	(+) reported
Barera (2002)	no	no	yes	yes	no	no	yes	no	no	can't tell	yes	**4**	(+) reported
Bode (1996)	yes	yes	yes	no	can't tell	no	yes	no	no	yes	no	**5**	(+) reported
Bode (1993)	yes	yes	yes	yes	no	yes	can't tell	yes	can't tell	yes	yes	**8**	(+) reported
Book (2003)	yes	can't tell	no	no	no	no	can't tell	no	no	no	can't tell	**1**	(+) reported
Borch (2000)	yes	no	no	no	no	no	yes	can't tell	no	yes	can't tell	**3**	(+) reported
Calero (1996)	yes	no	yes	yes	no	yes	yes	yes	no	no	no	**6**	(+) reported
Carlsson (2001)	yes	yes	yes	no	no	no	no	yes	no	yes	yes	**6**	(+) reported
Carroccio (2002)	can't tell	no	yes	yes	yes	no	yes	yes	no	yes	no	**6**	(+) reported
Catassi (1996)	yes	no	yes	can't tell	no	yes	no	yes	no	yes	no	**5**	(+) reported
Catassi (2000)	yes	yes	yes	no	no	no	yes	yes	no	yes	no	**6**	(+) reported

Table 2: Celiac 2 prevalence & incidence studies (cross-sectional checklist) (cont'd)

Author (Year)	Item 1: Source of Information	Item 2: Inclusion/Exclusion Criteria	Item 3: Time Period for Identity	Item 4: Subjects consecutive	Item 5: Evaluators Masked	Item 6: Quality Assurance Assessments	Item 7: Patient Exclusions	Item 8: Confounding assessed/controlled	Item 9: Missing Data	Item 10: Response Rates	Item 11: Follow-up	Total Items Reported (Max. 11)	
Chan (2001)	yes	yes	yes	can't tell	yes	no	can't tell	no	no	can't tell	no	**4**	(+) reported
Chartrand (1997)	yes	can't tell	yes	can't tell	no	can't tell	no	no	no	yes	no	**3**	(+) reported
Collin (2002)	yes	can't tell	yes	can't tell	no	no	yes	yes	no	can't tell	no	**4**	(+) reported
Collin (1997)	yes	yes	yes	no	no	no	no	yes	no	can't tell	no	**4**	(+) reported
Corazza (1997)	no	no	no	no	no	no	no	no	no	can't tell	no	**0**	(+) reported
Corazza (1995)	no	no	no	yes	no	no	no	no	no	yes	no	**2**	(+) reported
Corazza (1992)	no	no	no	can't tell	no	no	no	no	no	yes	no	**1**	(+) reported
Corrao (1996)	yes	can't tell	yes	no	can't tell	yes	yes	no	no	yes	no	**5**	(+) reported
Cronin (1997)	yes	no	no	yes	no	no	no	no	no	yes	no	**3**	(+) reported
Csizmadia (1999)	yes	can't tell	yes	no	can't tell	no	can't tell	no	no	yes	yes	**4**	(+) reported
Day (2000)	yes	yes	yes	no	can't tell	no	yes	no	no	no	no	**4**	(+) reported
De Block (2001)	yes	no	no	can't tell	no	no	no	no	no	can't tell	no	**1**	(+) reported
De, Vitis (1996)	no	no	no	no	no	no	no	no	no	yes	no	**1**	(+) reported
Dickey (1997)	no	can't tell	no	can't tell	no	no	no	can't tell	no	yes	no	**1**	(+) reported
Dickey (1992)	yes	yes	no	can't tell	no	no	no	no	yes	no	no	**3**	(+) reported
Farre (1999)	yes	yes	yes	can't tell	no	no	no	yes	no	yes	no	**5**	(+) reported
Fasano (2003)	yes	yes	yes	can't tell	no	no	no	yes	no	yes	yes	**6**	(+) reported
Fitzpatrick (2001)	yes	can't tell	no	can't tell	no	no	yes	no	no	yes	no	**3**	(+) reported
Fraser-Rey0lds (1998)	can't tell	can't tell	yes	no	no	no	no	yes	no	yes	yes	**4**	(+) reported
Gillett (2001)	yes	can't tell	yes	no	yes	no	no	yes	no	yes	no	**5**	(+) reported
Gonzalez (2002)	can't tell	can't tell	no	yes	yes	no	can't tell	yes	no	yes	no	**4**	(+) reported
Green (2000)	yes	no	yes	yes	yes	yes	no	can't tell	no	yes	yes	**7**	(+) reported
Grodzinsky (1996)	yes	no	yes	no	no	yes	no	no	no	no	no	**3**	(+) reported

Table 2: Celiac 2 prevalence & incidence studies (cross-sectional checklist) (cont'd)

Author (Year)	Item 1: Source of Information	Item 2: Inclusion/Exclusion Criteria	Item 3: Time Period for Identity	Item 4: Subjects consecutive	Item 5: Evaluators Masked	Item 6: Quality Assurance Assessments	Item 7: Patient Exclusions	Item 8: Confounding assessed/controlled	Item 9: Missing Data	Item 10: Response Rates	Item 11: Follow-up	Total Items Reported (Max. 11)	
Hansen (2001)	no	can't tell	no	yes	no	no	no	no	no	no	no	**1**	(+) reported
Hawkes (2000)	yes	can't tell	yes	no	no	no	no	no	no	no	no	**2**	(+) reported
Hill (2000)	yes	no	no	no	no	no	no	yes	no	yes	yes	**4**	(+) reported
Hin (1999)	yes	yes	yes	yes	can't tell	yes	no	can't tell	no	yes	no	**6**	(+) reported
Hoffenberg (2003)	yes	yes	yes	can't tell	yes	no	can't tell	yes	no	yes	yes	**7**	(+) reported
Hogberg (2003)	yes	no	yes	no	no	no	can't tell	no	no	yes	yes	**4**	(+) reported
Holm (1993)	can't tell	no	no	can't tell	no	no	no	can't tell	no	yes	no	**1**	(+) reported
Hovdenak (1999)	no	no	no	no	no	no	no	no	no	yes	no	**1**	(+) reported
Howard (2002)	yes	yes	yes	can't tell	can't tell	no	yes	no	no	yes	no	**5**	(+) reported
Ivarsson (1999)	yes	can't tell	yes	yes	no	no	no	yes	no	yes	no	**5**	(+) reported
Ivarsson (2003)	yes	yes	yes	yes	no	no	no	yes	no	yes	no	**6**	(+) reported
Jaeger (2001)	no	can't tell	no	no	no	no	no	can't tell	no	yes	no	**1**	(+) reported
Jansen Th (1993)	yes	yes	yes	no	no	can't tell	no	no	no	yes	no	**4**	(+) reported
Johnston (1998)	yes	can't tell	can't tell	can't tell	yes	no	yes	no	can't tell	yes	yes	**5**	(+) reported
Kaukinen (1999)	can't tell	no	yes	can't tell	no	no	no	no	no	yes	no	**2**	(+) reported
Kepczyk (1995)	yes	yes	yes	yes	can't tell	yes	no	can't tell	no	yes	yes	**7**	(+) reported
Kolho (1998)	yes	can't tell	yes	can't tell	no	no	no	no	no	yes	yes	**4**	(+) reported
Kordo0uri (2000)	no	no	no	no	no	no	yes	no	no	yes	no	**2**	(+) reported
Kotze (2001)	yes	no	no	no	can't tell	no	no	can't tell	can't tell	yes	no	**2**	(+) reported
Lampasona (1999)	no	no	no	no	no	no	no	no	no	can't tell	no	**0**	(+) reported
Li Voon Chong (2002)	no	no	yes	no	no	no	no	yes	no	can't tell	no	**2**	(+) reported
Lindh (1992)	no	no	no	yes	no	no	no	no	no	yes	no	**2**	(+) reported

Table 2: Celiac 2 prevalence & incidence studies (cross-sectional checklist) (cont'd)

Author (Year)	Item 1: Source of Information	Item 2: Inclusion/Exclusion Criteria	Item 3: Time Period for Identity	Item 4: Subjects consecutive	Item 5: Evaluators Masked	Item 6: Quality Assurance Assessments	Item 7: Patient Exclusions	Item 8: Confounding assessed/controlled	Item 9: Missing Data	Item 10: Response Rates	Item 11: Follow-up	Total Items Reported (Max. 11)	
Lopez-Rodriguez (2003)	yes	can't tell	yes	yes	no	yes	no	no	no	yes	no	**5**	(+) reported
Lorini (1996)	no	no	no	no	no	yes	no	no	no	yes	no	**2**	(+) reported
Magazzu (1994)	yes	can't tell	yes	no	can't tell	no	no	no	no	yes	no	**3**	(+) reported
Maki (1988)	yes	no	yes	yes	can't tell	no	no	no	no	no	no	**3**	(+) reported
Maki (2003)	yes	can't tell	yes	can't tell	no	no	yes	yes	no	yes	no	**5**	(+) reported
Mather (2001)	no	no	no	yes	no	no	can't tell	no	yes	yes	no	**3**	(+) reported
Mazzetti (1992)	yes	yes	no	no	no	no	no	no	no	no	no	**2**	(+) reported
McIntyre (1993)	yes	no	yes	yes	no	no	yes	no	no	yes	yes	**6**	(+) reported
Mustalahti (2002)	no	can't tell	no	can't tell	no	yes	yes	no	no	yes	no	**3**	(+) reported
Ot (1998)	can't tell	no	no	no	can't tell	no	no	yes	no	can't tell	no	**1**	(+) reported
Ot (2001)	yes	no	yes	yes	no	no	no	no	no	yes	no	**4**	(+) reported
Nuti (2001)	yes	yes	yes	yes	can't tell	yes	can't tell	no	can't tell	yes	yes	**7**	(+) reported
Oxentenko (2002)	yes	can't tell	yes	no	no	no	yes	can't tell	no	yes	no	**4**	(+) reported
Page (1994)	yes	yes	yes	yes	yes	no	yes	yes	no	no	yes	**8**	(+) reported
Pittschieler (1996)	yes	no	no	no	no	no	no	no	no	no	no	**1**	(+) reported
Pittschieler (2003)	yes	can't tell	yes	can't tell	no	no	can't tell	can't tell	no	can't tell	yes	**3**	(+) reported
Polvi (1996)	yes	yes	no	yes	no	no	yes	no	yes	yes	yes	**7**	(+) reported
Ransford (2002)	no	no	no	yes	no	no	yes	no	no	yes	no	**3**	(+) reported
Rensch (1996)	yes	yes	yes	yes	can't tell	yes	yes	no	yes	yes	no	**8**	(+) reported
Riestra (2000)	can't tell	can't tell	yes	no	no	yes	no	yes	no	yes	no	**4**	(+) reported
Robinson (1971)	yes	no	no	yes	no	no	no	no	no	no	no	**2**	(+) reported
Roldan (1998)	yes	no	yes	no	no	yes	no	no	no	no	no	**3**	(+) reported

Table 2: Celiac 2 prevalence & incidence studies (cross-sectional checklist) (cont'd)

Author (Year)	Item 1: Source of Information	Item 2: Inclusion/Exclusion Criteria	Item 3: Time Period for Identity	Item 4: Subjects consecutive	Item 5: Evaluators Masked	Item 6: Quality Assurance Assessments	Item 7: Patient Exclusions	Item 8: Confounding assessed/controlled	Item 9: Missing Data	Item 10: Response Rates	Item 11: Follow-up	Total Items Reported (Max. 11)	
Rolles (1974)	yes	yes	no	no	no	no	no	no	no	yes	can't tell	**3**	(+) reported
Rossi (1993)	yes	can't tell	yes	no	no	no	no	no	no	yes	no	**3**	(+) reported
Rostami (2000)	no	no	no	no	yes	no	no	no	no	yes	no	**2**	(+) reported
Rostami (1999)	yes	no	yes	no	no	no	no	no	no	yes	no	**3**	(+) reported
Rutz (2002)	can't tell	no	no	no	no	yes	no	yes	no	yes	yes	**4**	(+) reported
Sanders (2003)	yes	no	yes	no	no	no	no	yes	no	yes	yes	**5**	(+) reported
Sategna-Guidetti (1994)	yes	no	no	no	no	no	no	no	no	yes	no	**2**	(+) reported
Saukkonen (1996)	yes	no	yes	yes	no	yes	yes	can't tell	no	yes	yes	**7**	(+) reported
Schober (2000)	yes	no	no	no	no	no	no	yes	no	no	no	**2**	(+) reported
Sigurs (1993)	yes	yes	yes	no	no	no	yes	no	no	yes	no	**5**	(+) reported
Sjoberg (1999)	yes	can't tell	yes	yes	can't tell	no	can't tell	yes	no	yes	no	**5**	(+) reported
Sjoberg (1994)	yes	can't tell	yes	yes	no	no	yes	no	no	yes	no	**5**	(+) reported
Sjoberg (1998)	yes	no	yes	no	no	yes	yes	no	no	yes	no	**5**	(+) reported
Spiekerkoetter (2002)	no	no	yes	can't tell	can't tell	no	no	no	no	yes	yes	**3**	(+) reported
Stokes (1976)	yes	no	no	can't tell	no	no	can't tell	yes	no	yes	yes	**4**	(+) reported
Talal (1997)	no	yes	no	can't tell	no	no	yes	yes	no	yes	yes	**5**	(+) reported
Talley (1994)	yes	yes	yes	no	no	can't tell	yes	yes	no	yes	no	**6**	(+) reported
Thomas (1992)	yes	no	yes	can't tell	can't tell	can't tell	no	no	no	yes	no	**3**	(+) reported
Trevisiol (1999)	yes	can't tell	yes	can't tell	no	no	no	no	no	no	yes	**3**	(+) reported
Tursi (2003)	no	no	no	can't tell	yes	no	no	no	no	no	no	**1**	(+) reported

Table 2: Celiac 2 prevalence & incidence studies (cross-sectional checklist) (cont'd)

Author (Year)	Item 1: Source of Information	Item 2: Inclusion/Exclusion Criteria	Item 3: Time Period for Identity	Item 4: Subjects consecutive	Item 5: Evaluators Masked	Item 6: Quality Assurance Assessments	Item 7: Patient Exclusions	Item 8: Confounding assessed/controlled	Item 9: Missing Data	Item 10: Response Rates	Item 11: Follow-up	Total Items Reported (Max. 11)	
Unsworth (2000)	yes	can't tell	yes	can't tell	no	no	no	yes	no	yes	yes	**5**	(+) reported
Valerio (2002)	yes	can't tell	yes	can't tell	no	no	no	no	no	yes	no	**3**	(+) reported
Van Mook (2001)	yes	yes	no	no	can't tell	no	yes	no	no	yes	no	**4**	(+) reported
Ventura (2001)	can't tell	yes	can't tell	can't tell	no	no	yes	can't tell	no	yes	no	**3**	(+) reported
Vitoria (1994)	no	can't tell	no	can't tell	no	no	can't tell	no	no	can't tell	no	**0**	(+) reported
Vitoria (1998)	yes	no	no	no	no	no	no	no	no	no	yes	**2**	(+) reported
Volta (2001)	can't tell	yes	yes	no	no	no	no	no	no	yes	no	**3**	(+) reported
Weile (1993)	yes	yes	yes	no	no	no	no	no	no	yes	no	**4**	(+) reported
Weile (2001)	yes	no	no	yes	no	no	no	yes	no	yes	no	**4**	(+) reported
West (2003)	yes	can't tell	yes	no	no	no	yes	yes	no	yes	no	**5**	(+) reported
% Items (+) reported:	**71%**	**27%**	**60%**	**29%**	**8%**	**16%**	**28%**	**27%**	**5%**	**73%**	**25%**		

Table 3. Celiac 3 cohort studies (Ottawa-Newcastle Scale)

Author (Year)	Item 1: selection of exposed	Item 2: selection of non-exposed	Item 3: ascertainment of exposure	Item 4: outcome missing data at initiation	Item 5: control factors (2*'s)	Item 6: assessment of outcome	Item 7: adequacy of follow-up length	Item 8: accountability for follow-up	
Askling (2002)	1	1	1	1	2	1	1	1	9 (*) awarded
Collin (1996)	1	1	1	1	2	1	1	0	8 (*) awarded
Corrao (2001)	1	1	1	0	2	1	1	1	8 (*) awarded
Cottone (1999)	1	1	1	1	2	1	1	1	9 (*) awarded
Green (2003)	1	1	1	1	2	1	1	0	8 (*) awarded
Holmes (1989)	1	1	1	1	2	1	1	1	9 (*) awarded
Logan (1989)	1	1	1	0	2	1	1	1	8 (*) awarded
Nielsen (1985)	1	1	1	1	2	1	1	0	8 (*) awarded
Selby (1979)	1	1	1	1	2	1	1	0	8 (*) awarded
Item % (+) reported	**100%**	**100%**	**100%**	**78%**	**100%**	**100%**	**100%**	**56%**	

NOTE: a maximum of 9 stars* may be awarded per study

Table 4: Celiac 3 case-control study (Ottawa-Newcastle Scale)

Author (Year)	Item 1: case definition	Item 2: representativeness of cases	Item 3: selection of controls	Item 4: definition of controls	Item 5: control factors	Item 6: ascertainment of exposure	Item 7: method of ascertainment for cases and controls	Item 8: non-response rate	
Delco (1999)	1	1	1	1	2	0	1	0	7 (*) awarded

NOTE: a maximum of 9 stars* may be awarded per study

Table 5. Celiac 4 cohort studies (Ottawa-Newcastle Scale)

Author (Year)	Item 1: selection of exposed	Item 2: selection of non-exposed	Item 3: ascertainment of exposure	Item 4: outcome missing data at initiation	Item 5: control factors (2*s)	Item 6: assessment of outcome	Item 7: adequacy of follow-up length	Item 8: accountability for follow-up	
Amin (2002)	1	1	1	0	1	0	1	0	5 (*) awarded
Greco (1997)	1	1	0	0	1	1	1	0	5 (*) awarded
Harewood (2001)	1	1	0	0	1	0	1	1	5 (*) awarded
Holmes (1976)	1	1	1	1	1	0	1	0	6 (*) awarded
Johnston (1998)	1	1	1	1	2	1	0	1	8 (*) awarded
Poddar (2002)	1	1	1	1	0	0	1	0	5 (*) awarded
Item % (+) reported	100%	100%	70%	50%	50%	33%	83%	33%	

NOTE: a maximum of 9 stars* may be awarded per study

Table 6. Celiac 4 case-control study (Ottawa-Newcastle Scale)

Author (Year)	Item 1: case definition	Item 2: representativeness of cases	Item 3: selection of controls	Item 4: definition of controls	Item 5: control factors (2*'s)	Item 6: ascertainment of exposure	Item 7: method of ascertainment for cases and controls	Item 8: non-response rate	
Ciacci (1996)	1	0	1	1	0	1	1	0	4 (*) awarded
Fabiani (1996)	1	1	1	1	1	1	1	0	7 (*) awarded
Thomason (2003)	1	0	1	1	2	0	1	1	6 (*) awarded
Westman (1999)	1	0	1	1	2	0	1	0	5 (*) awarded
Item % (+) reported	100%	25%	100%	100%	62.5%	50%	100%	25%	

NOTE: a maximum of 9 stars* may be awarded per study

Table 7: Celiac 4—Quality assessment not applicable to those studies identified as 'Other' in design

Author (Year)
Annibale (2001)
Arato (2002)
Atkinson (1997)
Bai (1997)
Bardella (2000)
Bardella (1985)
Barera (2000)
Boersma (2002)
Corrao (2001)
Fabiani (2000)
Kemppainen (1999)
Kemppainen(1998)
Mora (2001)
Mustalahti (1999)
Rea (1996)
Sategna-Guidetti (2000)
Sategna-Guidetti (2001)
Saukkonen (2002)
Valdimarsson (2000)
Zaccari (1996)

Table 8: Celiac 4—Quality assessment pending

Author (Year)
Smecuol (1997)
Valdimarsson (1996)

Table 9: Celiac 5 case-control studies (Ottawa-Newcastle Scale)

Author (Year)	Item 1: case definition	Item 2: representativeness of cases	Item 3: selection of controls	Item 4: definition of controls	Item 5: control factors (2*'s)	Item 6: ascertainment of exposure	Item 7: method of ascertainment for cases and controls	Item 8: Non-response rate	
Bardella (2001)	1	1	1	1	1	1	1	1	8 (*) awarded
Fabiani (2001)	1	1	1	0	1	0	1	1	6 (*) awarded
Anson (1990)	1	1	1	0	1	0	1	1	6 (*) awarded
Fabiani (2000)	1	1	1	1	1	0	1	1	7 (*) awarded
Item % (+) reported	100%	100%	100%	50%	50%	25%	100%	100%	

NOTE: a maximum of 9 stars* may be awarded per study

Table 10. Celiac 5 cohort studies (Ottawa-Newcastle Scale)

Author (Year)	Item 1: Selection of exposed	Item 2: selection of non-exposed	Item 3: ascertainment of exposure	Item 4: outcome missing data at initiation	Item 5: control factors (2*'s)	Item 6: assessment of outcome	Item 7: adequacy of follow-up length	Item 8: accountability for follow-up	
McNicholl (1976)	0	1	1	0	1	1	1	1	6 (*) awarded
Pacht (1995)	1	1	0	0	1	1	1	1	6 (*) awarded
Sategna-Guidetti (1996)	1	1	1	1	0	1	1	1	7 (*) awarded
Troncone (1995)	1	1	1	0	0	1	1	1	6 (*) awarded
Hogberg (2003)	1	1	1	1	1	1	1	1	8 (*) awarded
Fabiani (1996)	1	1	1	1	1	0	1	1	7 (*) awarded
Item % (+) reported	83%	100%	83%	50%	33%	83%	100%	100%	

NOTE: a maximum of 9 stars* may be awarded per study

Table 11. Celiac 5 non-comparative case series checklist

Author (Year)	Item 1: Intervention	Item 2: Inclusion/exclusion criteria	Item 3: follow-up as an inclusion	Item 4: sample size determination	Irem 5: sample size calculations	Item 6: method & length/accumulation of cases	Item 7: sources of participants	Item 8: method of outcome assessments	Item: 9: blinding	Item 9: primary and secondary measures	Item 11: timing of outcome assessment	Item 12: follow-up schedule	Item 13: maintaining follow-up	Item 14: compliance with follow-up	Item 15: method of data collection	Item 16: exclusions	Item 17: statistical approach for analysis	Item 18: missing data	Item 19: adverse events	Total # of Items = 19	
Burgin-Wolff (1991)	yes	yes	no	can't tell	no	no	yes	yes	no	yes	can't tell	can't tell	yes	yes	yes	can't tell	yes	no	no	9	(+) reported
Burgin-Wolff (2002)	yes	yes	can't tell	can't tell	no	no	yes	yes	no	yes	yes	yes	no	no	yes	no	yes	can't tell	no	9	(+) reported
Dickey (2000)	yes	yes	no	yes	no	yes	yes	yes	no	yes	yes	yes	can't tell	yes	yes	yes	yes	yes	no	14	(+) reported
Fotoulaki (1999)	yes	yes	no	yes	no	yes	yes	yes	no	yes	yes	yes	no	no	yes	no	yes	no	no	11	(+) reported
Kaukinen (2002)	yes	yes	no	yes	no	no	no	yes	no	yes	yes	yes	no	no	yes	no	yes	no	no	9	(+) reported
Lee (2003)	yes	yes	no	yes	no	yes	yes	yes	no	yes	yes	yes	can't tell	yes	yes	yes	yes	yes	no	14	(+) reported
Martini (2002)	yes	yes	no	yes	no	yes	yes	yes	no	yes	yes	yes	can't tell	no	yes	no	yes	no	no	11	(+) reported
Scalici (2003)	yes	yes	can't tell	can't tell	no	no	can't tell	can't tell	yes	yes	yes	yes	can't tell	can't tell	yes	can't tell	yes	no	no	8	(+) reported
Selby (1999)	yes	yes	no	yes	no	yes	yes	yes	no	yes	yes	yes	can't tell	yes	yes	can't tell	yes	no	no	12	(+) reported

Table 11. Celiac 5 non-comparative case Series checklist (cont'd)

Author (Year)	Item 1: Intervention	Item 2: Inclusion/exclusion criteria	Item 3: follow-up as an inclusion	Item 4: sample size determination	Irem 5: sample size calculations	Item 6: method & length/accumulation of cases	Item 7: sources of participants	Item 8: method of outcome assessments	Item: 9: blinding	Item 9: primary and secondary measures	Item 11: timing of outcome assessment	Item 12: follow-up schedule	Item 13: maintaining follow-up	Item 14: compliance with follow-up	Item 15: method of data collection	Item 16: exclusions	Item 17: statistical approach for analysis	Item 18: missing data	Item 19: adverse events	Total # of Items = 19	
Valentini (1994)	yes	yes	no	no	no	no	can't tell	yes	no	yes	yes	yes	no	no	yes	no	yes	no	no	7	(+) reported
Valletta (1990)	yes	yes	no	no	no	no	no	yes	no	yes	yes	yes	can't tell	no	yes	no	yes	no	no	8	(+) reported
% of items (+) reported	**100%**	**100%**	**0%**	**55%**	**0%**	**45%**	**64%**	**91%**	**9%**	**100%**	**91%**	**91%**	**9%**	**36%**	**100%**	**18%**	**100%**	**18%**	**0%**		

NOTE: yes = reported; no = not reported

Table 12: Celiac 5—Quality assessment not applicable to the following study designs

Author (Year)	Study type	
Jackson (1985)	questionnaire	
Lamontagne (2001)	questionnaire	
Ljungman (1993)	questionnaire	
Vahedi (2000)	abstract	

Table 13: Celiac 5—Quality assessment pending

Author (Year)
Baker (1975)
Bartholomeusz (1990)
Ciacci (2002)
Ciacci (2002)
Fabiani (1996)
Hogberg (2003)
Johnston (1998)
Kotze (2001)
Mayer (1991)
Skerritt (1991)
Vahedi (2003)
Volta (1990)

Appendix K. Additional Acknowledgements

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