# 2020 Vision: A ‘clearer’ view for children and young people

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RHSC Edinburgh
CUK Research Conference March 2020

SSPGHAN

Edinburgh Children's Hospital Charity
Continuing to support the Sick Kids

NHS Lothian

# The coeliac triad? / cocktail

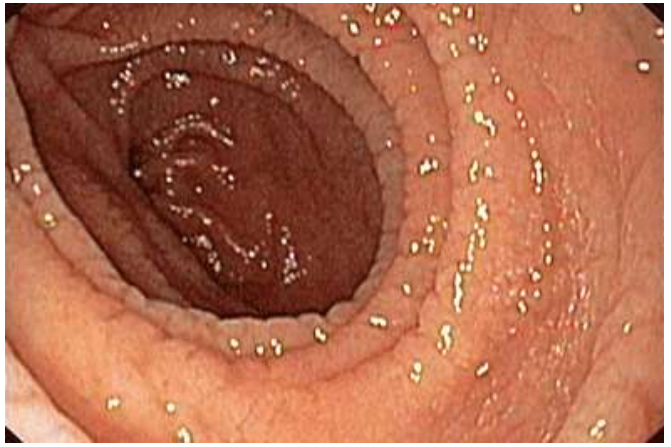
- Serology studies suggest at least 1% of the population is coeliac*
- Genes – importance of DQ2 and 8 - not the whole story
- Gluten – deaminated sequences are 'key'
- Trigger – 'environment'
  - Many postulated
  - No universal trigger
  - Some studies fail to show significant increase in infections
  - Importance of the microbiome* and environment

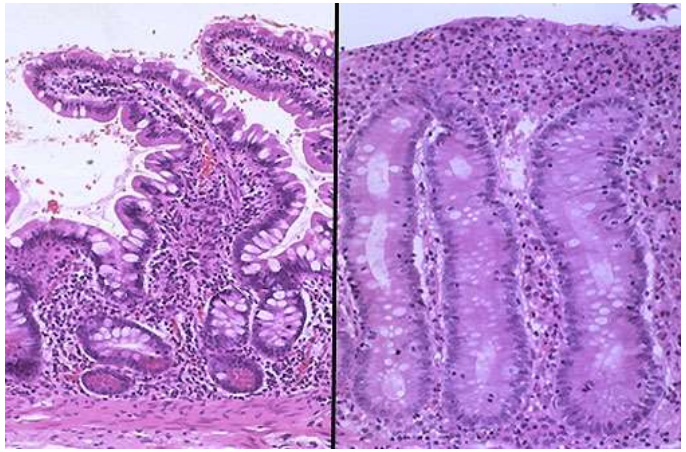

- Overall approx 17% Dx by age 9 ….. Biggest risk factor for being coeliac is being female, with 2 first degree relatives and DQ2.5 homozygote

  Prevent CD Study. More later.

# ESPGHAN pre-1990,1990 – 2012

- Paediatrics takes the lead….
- Three biopsy schedule…..
- Serology, biopsy and follow up
  - Anti-gliadin – rubbish?? - ? IgG Coming back
  - Anti-EmA (1992, Chorzelski)
  - anti tTG (1997, Dieterich, Schuppan)
- Capsule succeeded by endoscopic biopsy
  - D2 and then D1 as standard in addition (BSG 2014)
- All was good with the world……





Since 1997, pathophysiology understanding has exploded…

# Pathophysiology of  Coeliac Disease

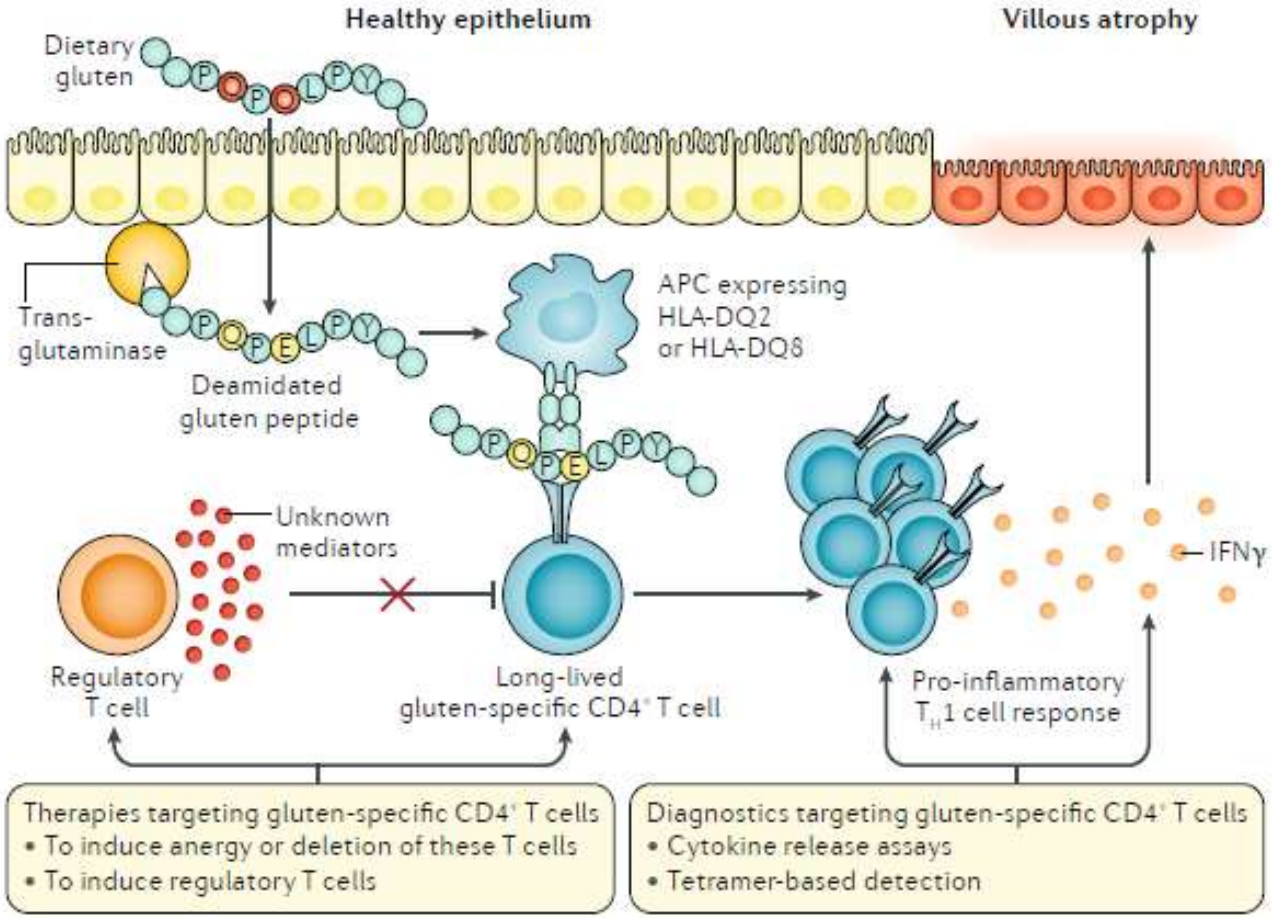
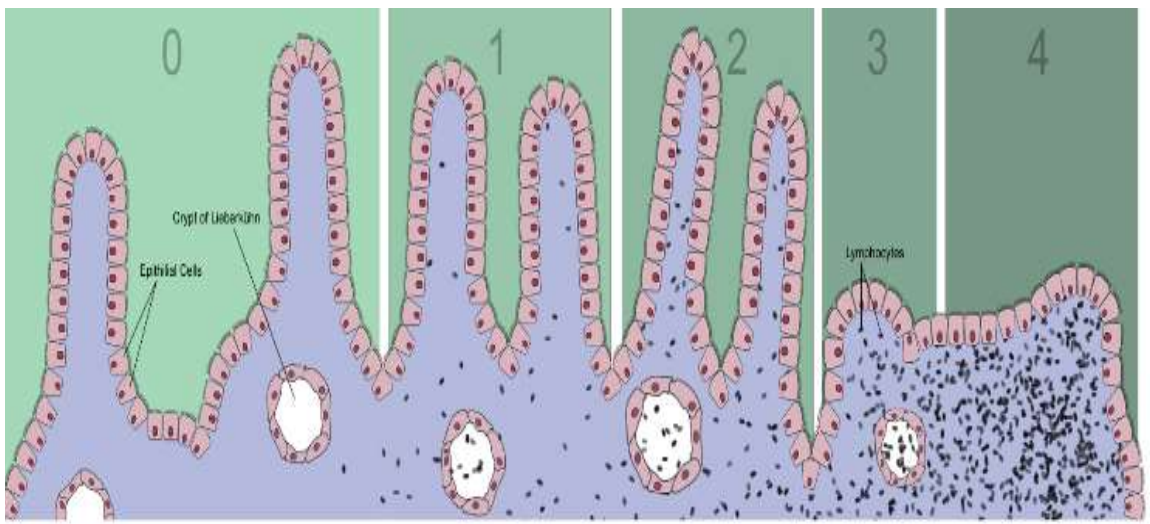
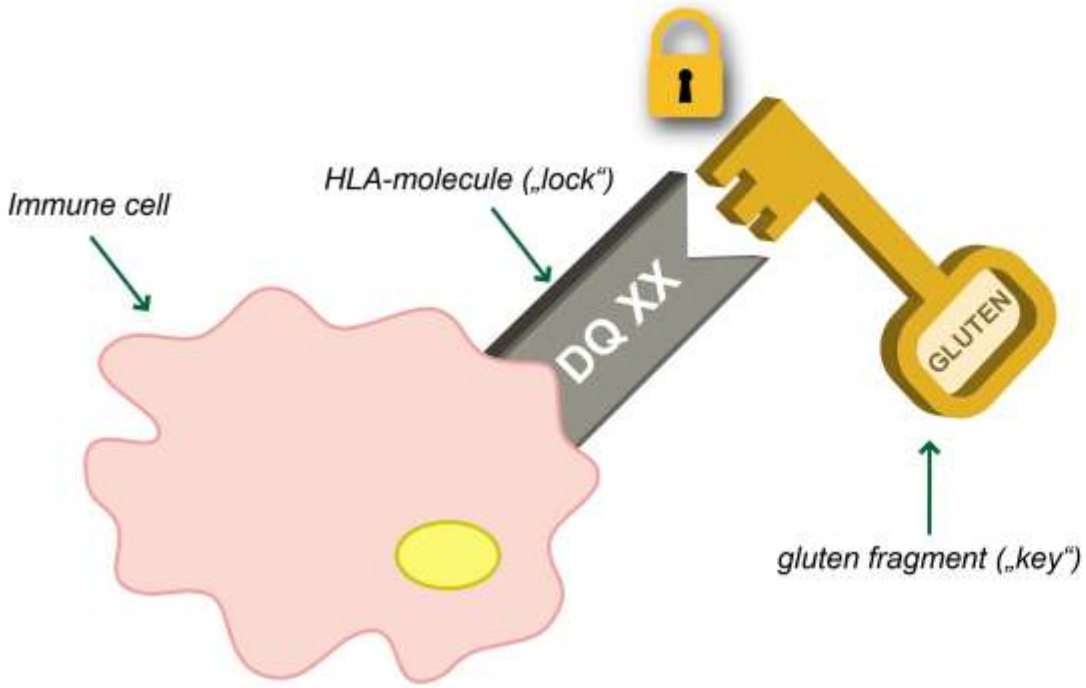



Fig. 1 | **Role and targeting of CD4⁺ T cells in coeliac disease.** Coeliac disease results from a loss of tolerance to dietary gluten in genetically susceptible individuals. A central role of long-lived, pro-inflammatory, gluten-specific CD4⁺ T cells in coeliac disease pathogenesis provides the rationale for potential clinical applications, including diagnostics in the peripheral blood or small intestine and treatments. APC, antigen-presenting cell; IFNγ, interferon-γ; $T_H1$, T helper 1.

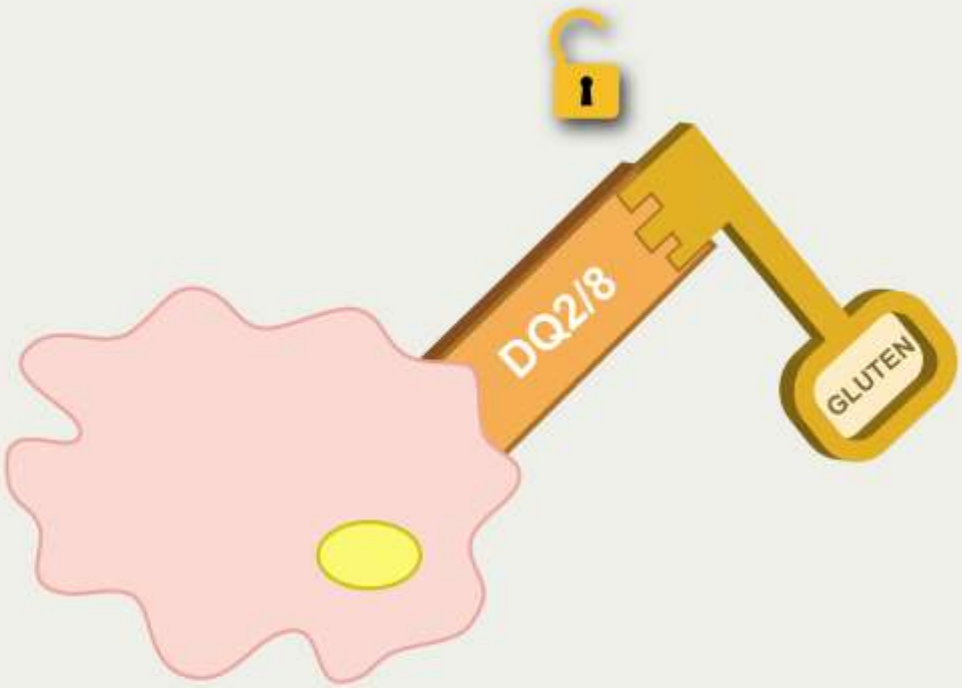


## No risk for celiac disease




**HLA-molecule other than DQ2 or DQ8:**
The key (gluten) does not fit into the lock (HLA-formation)

## Risk for celiac disease




**HLA-molecule is DQ2 or DQ8:**
The key (gluten) perfectly fits into the lock (HLA-formation)

# ESPGHAN 2012


CLINICAL GUIDELINE

## European Society for Pediatric Gastroenterology, Hepatology, and Nutrition Guidelines for the Diagnosis of Coeliac Disease

*S. Husby, †S. Koletzko, ‡I.R. Korponay-Szabó, §M.L. Mearin, ||A. Phillips, ¶R. Shamir, #R. Troncone, **K. Giersiepen, ††D. Branski, ‡‡C. Catassi, §§M. Lelgeman, ||||M. Mäki, ¶¶C. Ribes-Koninckx, ##A. Ventura, and ****K.P. Zimmer, for the ESPGHAN Working Group on Coeliac Disease Diagnosis, on behalf of the ESPGHAN Gastroenterology Committee

**ABSTRACT**

**Objective:** Diagnostic criteria for coeliac disease (CD) from the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) were published in 1990. Since then, the autoantigen in CD, tissue transglutaminase, has been identified; the perception of CD has changed

**Results:** In group 1, the diagnosis of CD is based on symptoms, positive serology, and histology that is consistent with CD. If immunoglobulin A anti-tissue transglutaminase type 2 antibody titers are high (>10 times the upper limit of normal), then the option is to diagnose CD without duodenal biopsies by applying a strict protocol with further laboratory tests. In group

Guidelines

# Joint BSPGHAN and Coeliac UK guidelines for the diagnosis and management of coeliac disease in children

Simon Murch,[1] Huw Jenkins,[2] Marcus Auth,[3] Ronald Bremner,[4] Assad Butt,[5] Stephanie France,[6] Mark Furman,[7] Peter Gillett,[8] Fevronia Kiparissi,[9] Maureen Lawson,[10] Bruce McLain,[11] Mary-Anne Morris,[12] Sarah Sleet,[13] Matthew Thorpe[14]

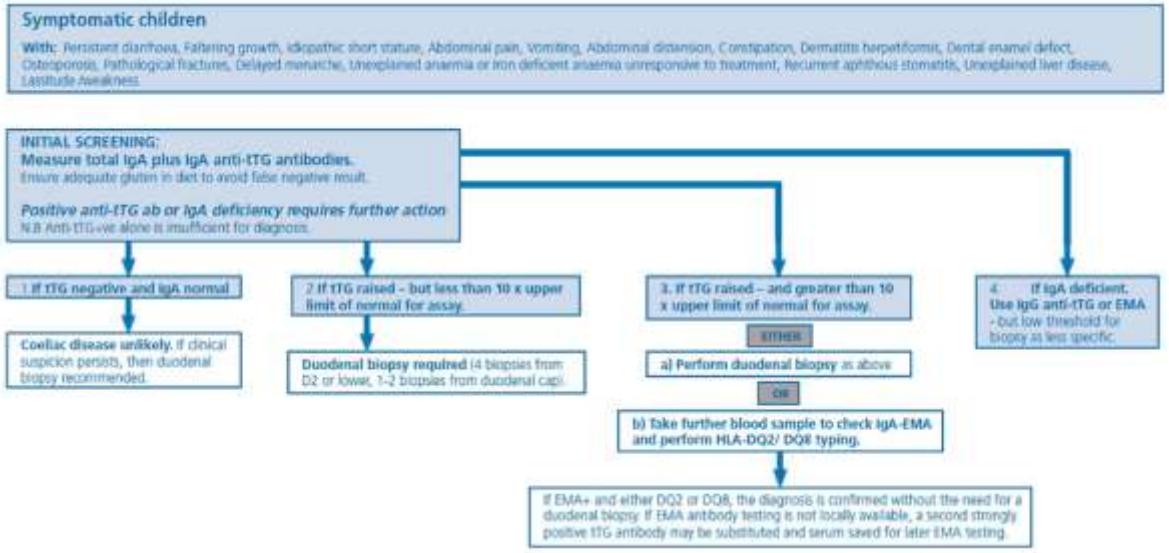
For numbered affiliations see end of article.

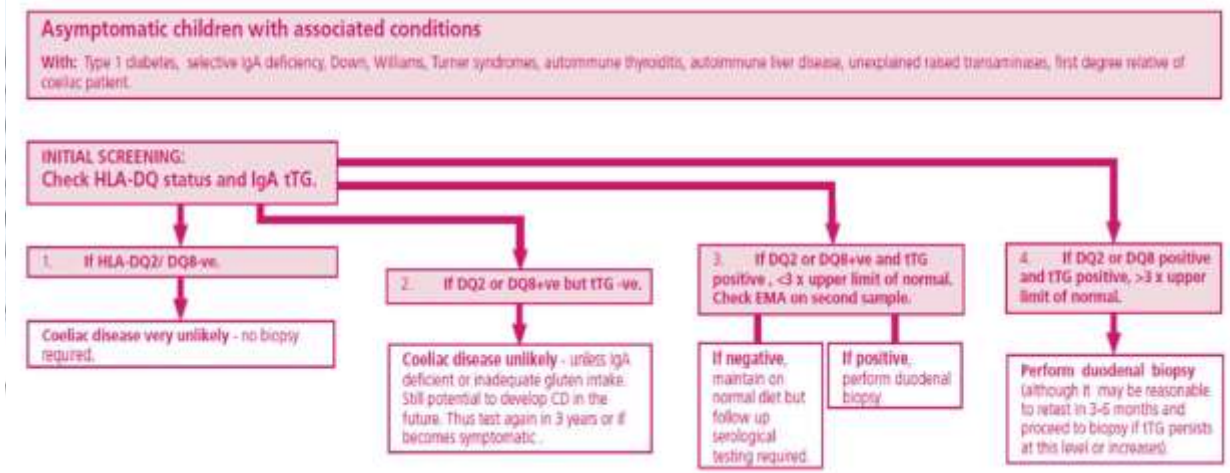
**Correspondence to**
Professor Simon Murch, Division of Metabolic and Vascular Health, Warwick

**ABSTRACT**
The revised BSPGHAN guidelines for the diagnosis and management of coeliac disease represent an important shift in diagnostic strategy, aimed at simplifying and shortening the diagnostic process in selected cases.

**Box 1 Symptomatic children (gastrointestinal tract and non-gastrointestinal tract symptoms)**

- Persistent diarrhoea
- idiopathic short stature
- vomiting, abdominal




# ESPGHAN / BSPGHAN 2012 - 13

# A leap of faith….

# OTHER CANDIDATE GENES HUNNERS !

Importance of other **autoimmune conditions** with shared genetics !

**hunners**

Literally, hundreds. Commonly used to denote "many".

*There was hunners o' polis efter us, but Ah gied thum tha slip, ken! (Many police officers attempted to apprehend me but I was able to elude them.)*

#several #many #lots #scots #vernacular

by RadgeBadger October 23, 2008

# Jonkers I HMG 2017

OXFORD

*Human Molecular Genetics*, 2017, Vol. 26, No. R2 R185–R192

doi: 10.1093/hmg/ddx254
Advance Access Publication Date: 7 July 2017
Invited Review

INVITED REVIEW

## Context-specific effects of genetic variants associated with autoimmune disease

Iris H. Jonkers[1,*] and Cisca Wijmenga[1,2,*]

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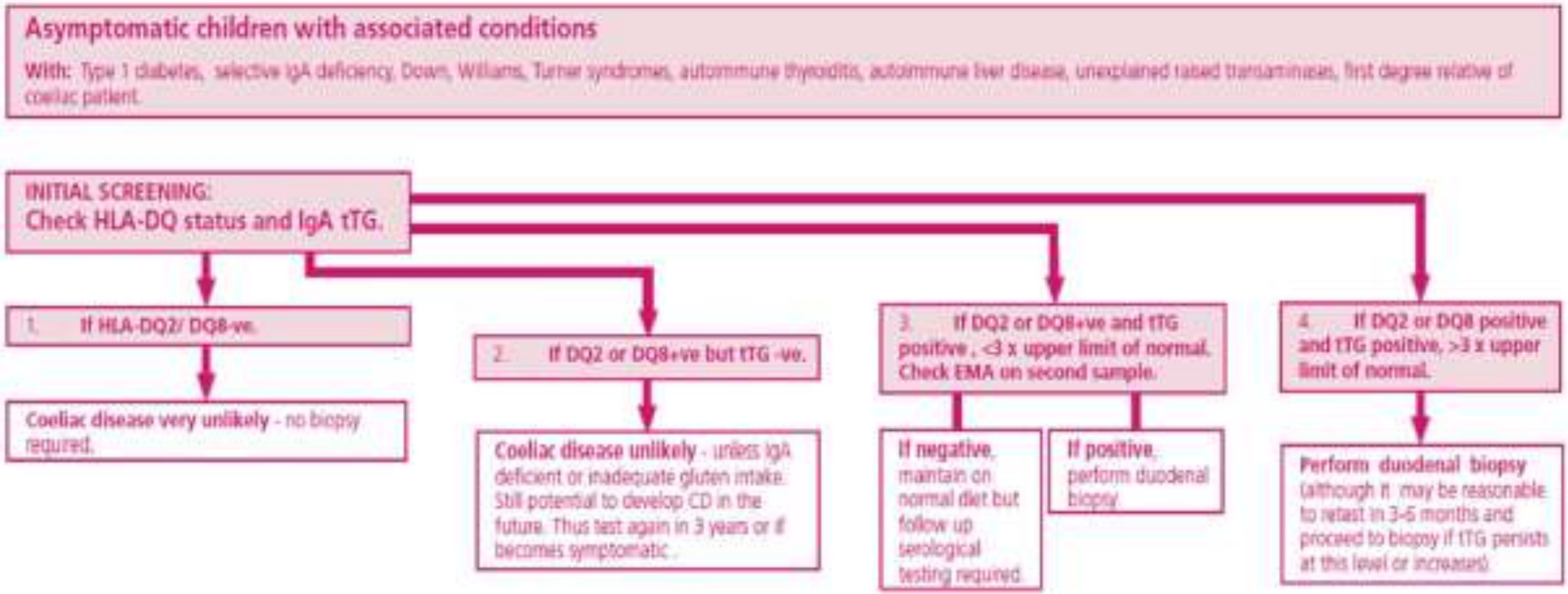
The Netherlands and [2]Department of Immunology, K.G. Jebse
Oslo, 0424 Oslo, Norway

**Table 1** Loci associated with CD development

| Locus | Gene candidate | Function |
|---|---|---|
| 6p21 | HLA | Antigen presentation |
| 3q25-3q26 | IL12A | Subunit of IL12, regulates Th1 differentation |
| 3p21 | CCR1, CCR2, CCR3 and CCR5 | Recruitment of immune cells to the site of inflammation |
| 3q28 | LPP | Possible role in maintaining cell shape |
| 6q23 | TNFAIP3 | Inhibits NFκB activation and TNF-mediated apoptosis |
| 12q24 | SH2B3 | Adaptor molecule involved in signaling in T cells |
| 2q11-2q12 | IL18R1 and IL18RAP | Respectively the α and β-chain of IL18 receptor, IL18 is a pro-inflammatory cytokine |
| 6q25 | TAGAP | Role in modulating cytoskeletal changes |
| 2p16 | REL | Component of NFκB transcription complex |
| 2q33 | CTLA4 | Inhibitory effect on the T cell response |
| | CD28 | Stimulating effect on the T cell response |
| | ICOS | Stimulating effect on the T cell response |
| 1q31 | RGS1 | Acts as GTPase activating protein, thereby regulating cell signating |
| 4q27 | IL2 | Stimulating proliferation of T cells |
| | IL21 | Regulates the function of T and NK cells |

[a] Odds ratios from (Dubois et al. 2010)


Asymptomatic children with associated conditions
With: Type 1 diabetes, selective IgA deficiency, Down, Williams, Turner syndromes, autoimmune thyroiditis, autoimmune liver disease, unexplained raised transaminases, first degree relative of coeliac patient.
INITIAL SCREENING:
Check HLA-DQ status and IgA tTG.
1. If HLA-DQ2/ DQ8-ve.
Coeliac disease very unlikely - no biopsy required.
2. If DQ2 or DQ8+ve but tTG -ve.
Coeliac disease unlikely - unless IgA deficient or inadequate gluten intake. Still potential to develop CD in the future. Thus test again in 3 years or if becomes symptomatic.
3. If DQ2 or DQ8+ve and tTG positive, <3 x upper limit of normal. Check EMA on second sample.
If negative, maintain on normal diet but follow up serological testing required
If positive, perform duodenal biopsy
4. If DQ2 or DQ8 positive and tTG positive, >3 x upper limit of normal.
Perform duodenal biopsy (although it may be reasonable to retest in 3-6 months and proceed to biopsy if tTG persists at this level or increases)

HLA Results

DQB1*02:01; DQB1*05:01; DQA1*01:01/04/05; DQA1*05:01

Method of Testing SSO

Date Test Authorised

07/11/2018

**HLA-DQ2.5 (DQA1*0501/DQB1*0201) DR3 or DR5/7**

**HLA-DQ8 (DQA1*0301/DQB1*0302) DR4**

**HLA DQ-2.2 (DQA1*02:01 and DQB1*02:02) DR7/x**

**Combinations…DQ2.5/8 DQ2.5/2.2 etc**

LL

Comments:

This patient is DQ2.5 positive, heterozygous. This patient is DQ2 positive which is associated with Coeliac Disease.

INTERNAL MEDICINE JOURNAL

*Internal Medicine Journal* **45** (2015)

POSITION PAPER

# Appropriate clinical use of human leukocyte antigen typing for coeliac disease: an Australasian perspective

J. A. Tye-Din,[1,2,3,4] D. J. S. Cameron,[4,5,6] A. J. Daveson,[4,7] A. S. Day,[4,8] P. Dellsperger,[4,9] C. Hogan,[10] E. D. Newnham,[4,11,12] S. J. Shepherd,[4,13] R. H. Steele,[4,14] L. Wienholt[4,15] and M. D. Varney[16]

[1]Immun
of Melb
Gastroe
Clinical
Univers
Gastroe
Wales, I
Otago,

99.6%

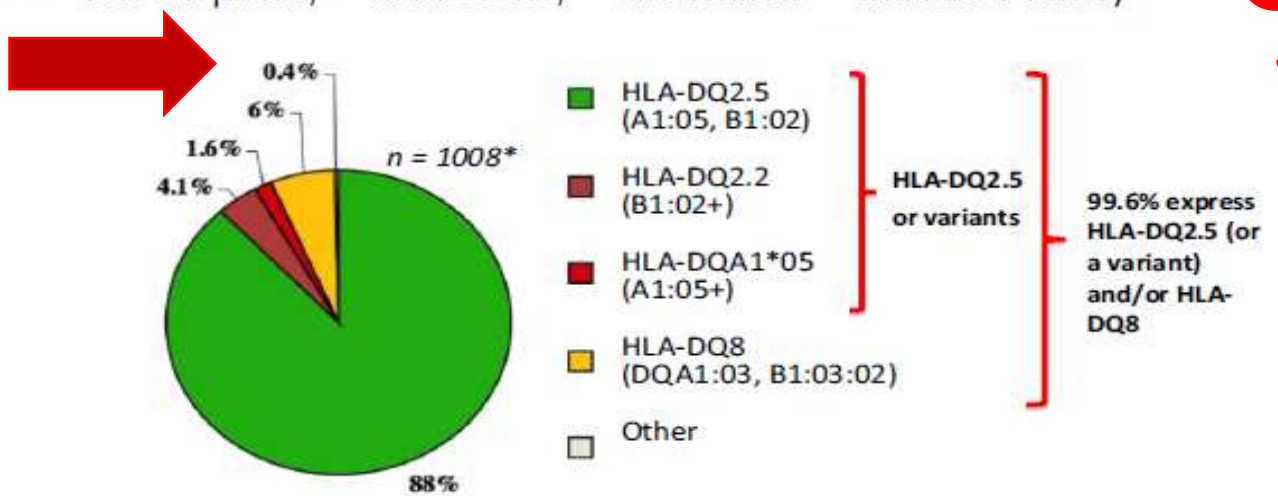
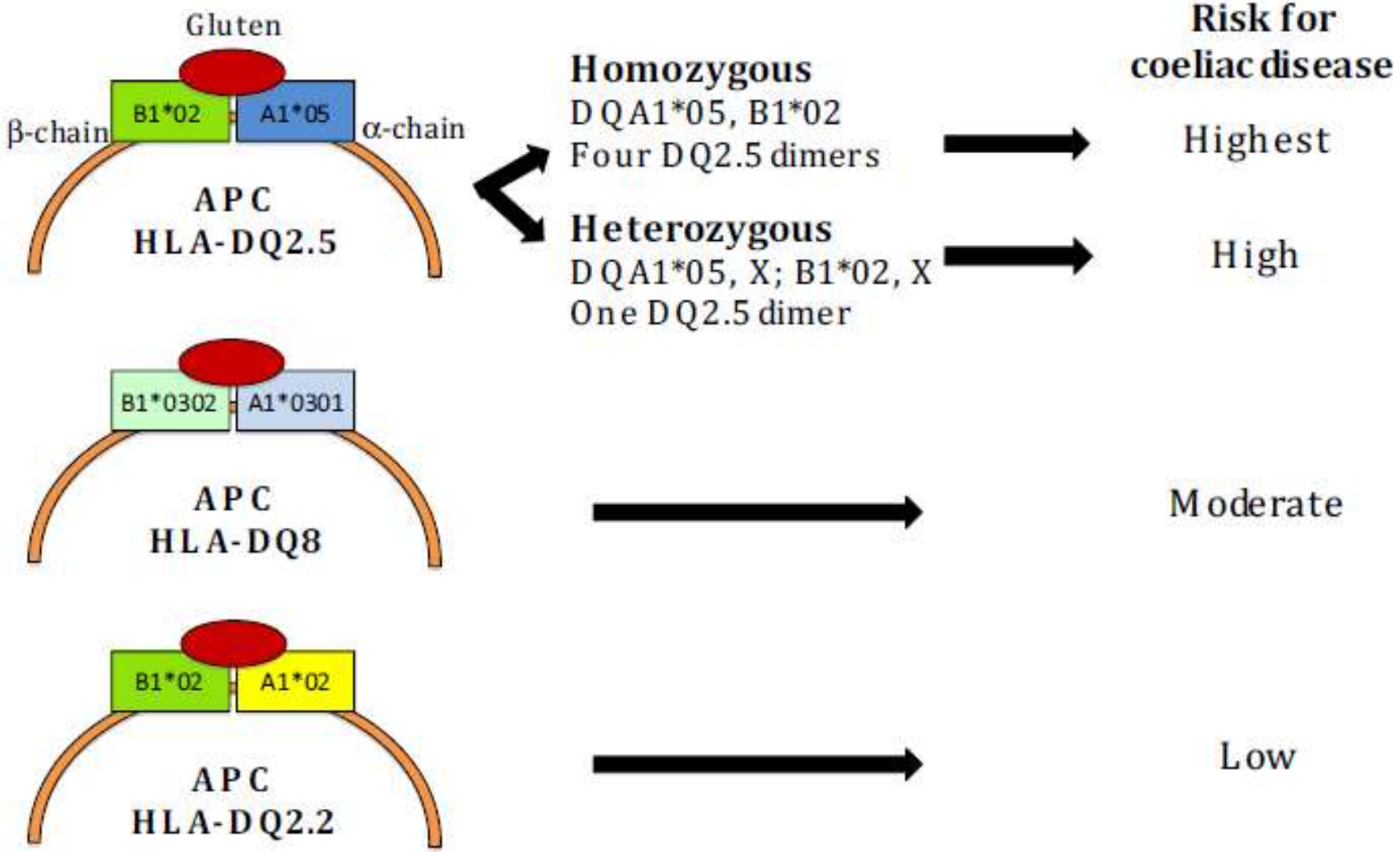
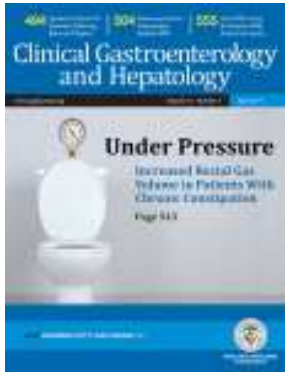



**Figure 2** Human leukocyte antigen (HLA) genotypes associated with coeliac disease (CD). 99.6% of 1008 patients with coeliac disease from Finland, France, Italy, Norway, Sweden and the UK expressed HLA-DQ2.5, a variant of HLA-DQ2.5 and/or HLA-DQ8. Similar proportions have been confirmed in Australia.[11] This exceptionally strong HLA association imparts high negative predictive value for CD when these genotypes are absent. Notably, the high prevalence of these susceptibility genes in the general population (~30–50%) renders HLA typing unhelpful as a stand-alone diagnostic for CD due to poor positive predictive value for CD. Green: HLA-DQ2.5 (A1:05, B1:02); Brown: HLA-DQ2.2 (B1:02+); Red: HLA-DQA1*05 (A1:05+); Yellow: HLA-DQ8 (DQA1:03, B1:03:02). HLA-DQ2.5 and variants are represented by green, brown and red. *Karell *et al.*[22]


Gluten
β-chain
B1*02
A1*05
α-chain
APC
HLA-DQ2.5
Homozygous
DQA1*05, B1*02
Four DQ2.5 dimers
Heterozygous
DQA1*05, X; B1*02, X
One DQ2.5 dimer
Risk for coeliac disease
Highest
High
B1*0302
A1*0301
APC
HLA-DQ8
Moderate
B1*02
A1*02
APC
HLA-DQ2.2
Low




Clinical Gastroenterology and Hepatology 2017;15:594–596

# RESEARCH CORRESPONDENCE

## Systematic Review and Meta-analysis Show 3% of Patients With Celiac Disease in Spain to be Negative for HLA-DQ2.5 and HLA-DQ8

Fernando Fernández-Bañares,[*,‡] Beatriz Arau,[*] Romina Dieli-Crimi,[§] Mercè Rosinach,[*,‡] Concepción Nuñez,[§,b] and Maria Esteve[*,‡,b]

*[*]Department of Gastroenterology, Hospital Universitari Mutua Terrassa, Terrassa (Barcelona), Spain; [§]UGC of Immunology, San Carlos Institute for Health Research (IdISSC), Madrid, Spain; and [‡]Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBEREhd), Terrassa (Barcelona), Spain*

The presence of the *HLA-DQA1*05* and *HLA-DQB1*02* alleles (encoding HLA-DQ2.5) and/or *HLA-DQA1*03* and *HLA-DQB1*03:02* (encoding HLA-DQ8) characterizes celiac disease (CD). Testing negative for both HLA-DQ types makes a diagnosis of CD very unlikely.[1] The majority of non–HLA-DQ2.5/8 patients possess one of the alleles encoding HLA-DQ2.5. According to the European genetic cluster on CD, 6% of CD were non-HLA-DQ2.5/8; 93% of them were encoding just 1 chain of HLA-DQ2.5.[2] However, European countries showed striking differences, with the frequency of being negative for the 2 alleles of HLA-DQ2.5 and HLA-DQ8 among the non-HLA-DQ2.5/8 patients ranging from 0% to 12.5%.

The high negative predictive value (>99%) of HLA-DQ2.5/8 is regarded as valuable in cases of equivocal diagnosis,[3–5] but because of the differences described, it is necessary to learn the frequency of non–HLA-DQ2.5/8 CD in different geographical areas. This will provide true diagnostic value to HLA genotyping and allow for appropriate changes in the local diagnostic protocols. We aimed to systematically review and perform a meta-analysis of the presence of non–HLA-DQ2.5/8 CD in Spain.

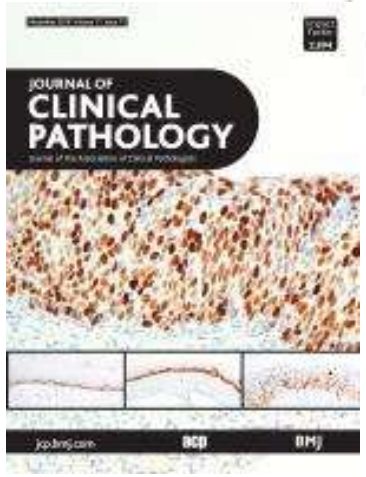
The frequency of negative HLA-DQ2.5/8 CD and being negative for the 2 alleles encoding HLA-DQ2.5 and for HLA-DQ8 in CD patients was analyzed by using StatsDirect v3.0.179 (http://www.statsdirect.com). Subanalyses were conducted by pooling studies from the same geographical region.

### Results

The search strategy yielded 199 publications; of these, 155 were excluded after examining title/abstract, and 34 were excluded because of duplicate information, lack of description of HLA-DQ2.5/8, or doubts about diagnosis or genotyping. Two documents were retrieved from national congresses. Finally, 12 studies comprising 2963 patients were included.

The frequency of non–HLA-DQ2.5/8 CD was 3% (95% confidence interval [CI], 2%–5%; 2963 patients; $I^2 = 84\%$) (Figure 1*A*). Subanalysis by geographical areas showed a frequency of 4% (95% CI, 2%–7%; 2450 patients; $I^2 = 88\%$), which returned to 3% with low heterogeneity (95% CI, 2%–4%; 2212 patients; $I^2 = 26\%$) after excluding the study from Asturias.

# 2018




Original article

## High rates of variation in HLA-DQ2/DQ8 testing for coeliac disease: results from an RCPAQAP pilot program

Martin Patrick Horan,[1] Sze Yee Chai,[1] Nalishia Munusamy,[1] Kwang Hong Tay,[1] Louise Wienholt,[1] Jason A Tye-Din,[2,3] James Daveson,[4,5,6] Michael Varney,[7] Tony Badrick[1]

**ABSTRACT**

**Aim** Coeliac disease(CD) is a highly prevalent, gluten-dependent, autoimmune enteropathy. While the diagnosis is based on serological and histological criteria, genotyping of the human leucocyte antigens (HLA) DQ2 and DQ8 has been shown to have substantial clinical utility, especially in excluding the diagnosis in patients who do not carry either antigen. As a result, HLA genotyping is now being performed by more laboratories and has recently become one of the most frequently requested genetic tests in Australia. To date, there has been little scrutiny on the accuracy and reporting of results by laboratories new to HLA typing. In response to clinician feedback that identified potentially clinically significant discrepancies in HLA typing results, the Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP) undertook a pilot study to assess laboratory performance in the detection of HLA-DQ2/DQ8 and their associated *HLA-DQA1* and *HLA-DQB1* alleles.

**Methods** DNA was extracted from 5 patients and sent to 10 laboratories for external quality assurance (EQA) testing. Laboratories were assessed for reporting in genotyping, interpretation and methodology.

**Results** Our findings showed that at least 80% of laboratories underperform with respect to recommended guidelines for HLA typing and reporting for CD, with 40% of laboratories failing to provide any clinical interpretation or full genotyping data. This suboptimal level of reporting may lead to ambiguities for downstream clinical interpretation that may compromise patient management.

**Conclusions** These findings highlight the importance of adherence to standardised guidelines for optimal performance and reporting of HLA results and substantiate the need for EQA and proficiency testing for laboratories providing this service.

# ‘At riskers’- DQ Still relevant ??

# COELIAC SCREENING IN TYPE 1 DIABETES – IS HLA GENOTYPING THE WAY FORWARD?

**Rod Mitchell*[1], Amaila Mayo[2], Angela Sun[3], Maureen Forgan[4], Alan Comrie[4], Peter Gillett[1]**

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[4]BTS Tissue Typing, Dundee, United Kingdom

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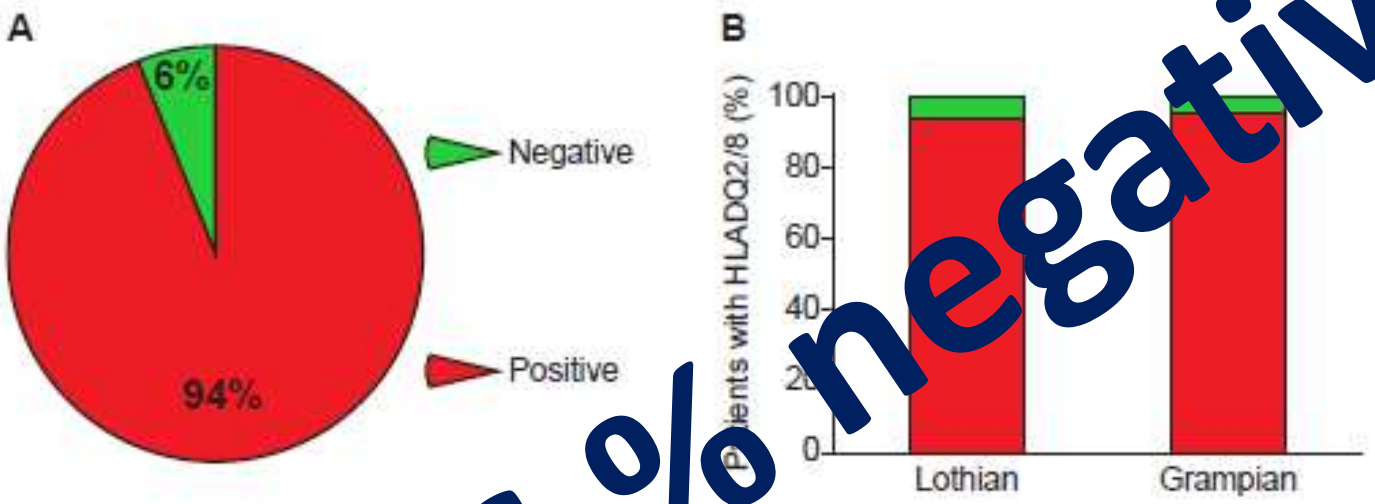
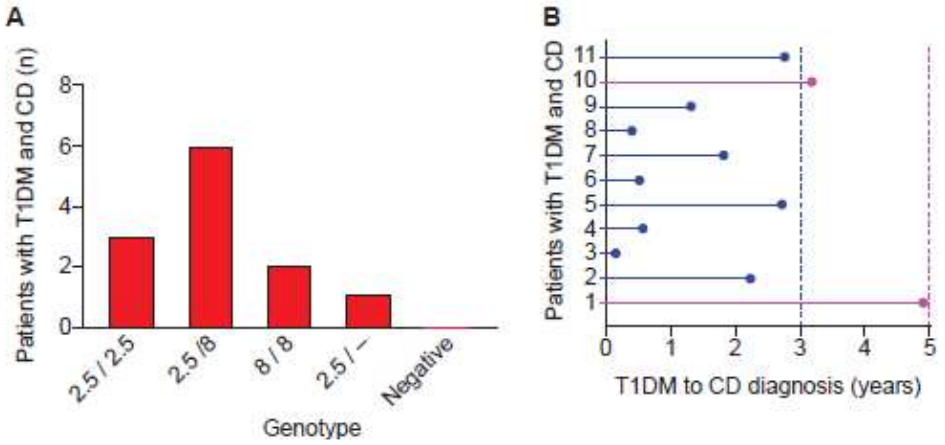
MRC Centre for Reproductive Health




6 % negative

**Figure 1 - A)** Frequency of CD–predisposing HLA (DQ2 and/or DQ8) genotypes in children with T1DM. **B)** Frequency of HLADQ2 and/or DQ8 by region.



JGH Journal of Gastroenterology and Hepatology

JGHF

doi:10.1111/j.1440-1746.2009.06044.x

GASTROENTEROLOGY

# Prevalence, human leukocyte antigen typing and strategy for screening among Asian first-degree relatives of children with celiac disease

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**Key words**
celiac, first-degree relati[illegible]hology, HLA, screeni[illegible]ology

Accepte[illegible]ation 29[illegible]uly 2009.

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## Abs[illegible]ract

**ackground and Aim:** Data on prevalence, human leukocyte antigen (HLA) typing and small bowel histology among first-degree relatives of subjects with celiac disease (CD) is scarce. This prospective study evaluated the prevalence and role of HLA DQ2/8 testing in screening of first-degree relatives of children with CD.

**Methods:** Thirty confirmed children with CD and 91/94 first-degree relatives (parents and siblings) were enrolled. HLA DQ2/8 testing was carried out in all index CD cases. Clinical evaluation with a questionnaire, total serum immunoglobulin A (IgA), human IgA-tissue transglutaminase (IgA-tTGA) and HLA DQ2/8 testing was carried out in all first-degree relatives. Subjects who were positive for IgA-tTGA were recommended endoscopic duodenal biopsy to document histological changes of CD.

**Results:** Nine first-degree relatives were positive for IgA-tTGA, seven underwent duodenal biopsy and four subjects had Marsh IIIa changes suggestive of CD. The prevalence of histologically confirmed CD in first-degree relatives was 4.4%. The prevalence of potential CD was 9.8%. IgA-tTGA-positive subjects (4/9) were significantly more often symptomatic than IgA-tTGA-negative first-degree relatives (2/82). Twenty-nine (96.6%) index cases of CD and all IgA-tTGA-positive first-degree relatives were positive for HLA DQ2. None of the index CD cases or first-degree relatives were HLA DQ8-positive. A total of 85% of the first-degree relatives were positive for HLA DQ2 and thus at risk of developing CD.

**Conclusions:** In this first Asian study on a limited number of families of children with CD, 4.4% of the first-degree relatives had CD. Only 15% of the first-degree relatives were negative for HLA DQ2/DQ8. Initial evaluation with HLA and serology followed by only serial serology in HLA-positive relatives is recommended.

# DQ TYPING IS EFFECTIVE IN COELIAC DISEASE SCREENING IN DOWN SYNDROME IN SOUTHEAST SCOTLAND

Claire Sumner[1], Geetha Veerasamy[1], Sarah Clegg[1], Helen Barlow[2], Maureen Forgan[3], Alan Comrie[3], Rod Mitchell[1,4], Peter Gillett[1]

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[2]Victoria Hospital, Kirkcaldy, Fife
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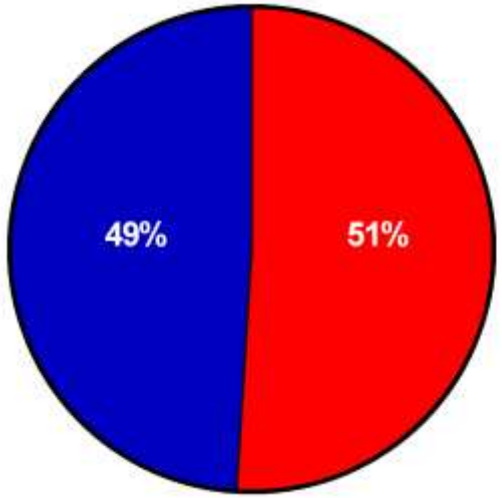
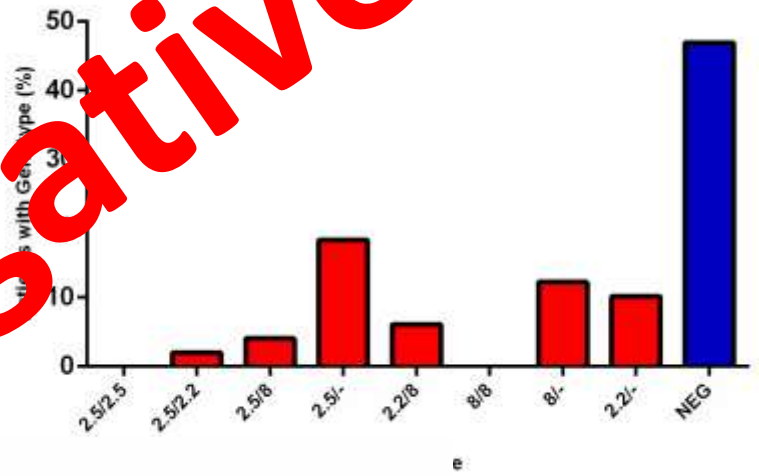
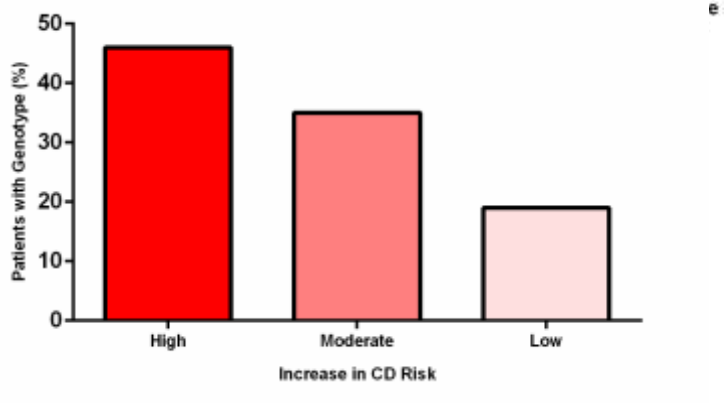



NEGATIVE
POSITIVE

40 % negative



# Screening and PreventCD


Eur J Pediatr. 2018 Nov;177(11):1585-1592. doi: 10.1007/s00431-018-3199-6. Epub 2018 Jul 4.

# Towards an individual screening strategy for first-degree relatives of celiac patients.

Wessels MMS[1,2], de Rooij N[3], Roovers L[4], Verhage J[3], de Vries W[3], Mearin ML[5].

Author information

## Abstract

Celiac disease (CD) is known to be more prevalent in first-degree relatives of patients. In this retrospective cohort study of 609 relatives between 1994 and 2016, we investigated the effect of sex, HLA type, and age at time of index celiac diagnosis. Pearson's chi-square test and Kaplan-Meier survival analysis were used as statistical analyses. CD screening was carried out for 427 relatives (70%), resulting in a prevalence of 15%. HLA typing in 335 relatives showed HLA-DQ2/DQ8 positivity in 87.5%. In 63% of children and all parents, celiac disease was diagnosed at first screening. It was diagnosed significantly more often in females, HLA-DQ2 homozygosity, and children (all $p < 0.05$). In children aged 0-1 year at time of index diagnosis, celiac disease was diagnosed after consecutive screening in 58%, after $3.9 \pm 2.5$ (max 10) years ($p < 0.001$).Conclusion: Future screening policies for relatives of celiac patients should include retesting, especially in HLA-positive relatives younger than 10 years of age. In addition, one-time celiac-specific antibody testing alone could be sufficient to rule out the disease in adolescent siblings and parents of newly diagnosed celiac patients. What is Known: • Celiac disease is more prevalent in first-degree relatives of celiac patients (risk 3-12%). • HLA-DQ2 homozygous sisters/daughters are at highest risk (25%). What is New: • If younger than 10 years of age, repeated testing is necessary in HLA-DQ2/DQ8-positive first-degree relatives when celiac disease is diagnosed in a family. • One-time celiac-specific antibody testing alone could be sufficient to rule out the disease in adolescent siblings and parents of newly diagnosed celiac patients.

# Barriers to implementing the revised ESPGHAN guidelines for coeliac disease in children: a cross-sectional survey of coeliac screen reporting in laboratories in England

Siba Prosad Paul,[1] Sophie Louise Harries,[2] Dharamveer Basude[1,2]

**Results** Responses were available from 134 (96.4%) laboratories. Anti-tTG titres are performed by 83/134 (62.6%) laboratories and 68/83 (81.4%) of those also offered EMA testing. Four different anti-tTG assays are available in England, but there are 10 different ULN values. The range for ULN varies widely from 4 to 30 IU/mL. Automatic reporting of total IgA concentration for a coeliac serology request occurs in only 24/83 laboratories.

**Conclusions** Significant heterogeneity exists for serological tests for CD in particular anti-tTG titre reporting even within the same regions. This potentially affects the interpretation of the results by clinicians diagnosing CD and hence harbouring diagnostic inconsistencies in their practice. Standardisation especially of the anti-tTG assays and routine reporting of IgA concentration nationally should be strongly considered to support the current diagnostic process for CD.

APMIS JOURNAL OF PATHOLOGY, MICROBIOLOGY AND IMMUNOLOGY

APMIS 126: 208–214



DOI 10.1111/apm.12812

# Histopathological evaluation of duodenal biopsy in the PreventCD project. An observational interobserver agreement study

Villanacci V, Lorenzi L, Donato F, Auricchio R, Dziechciarz P, Gyimesi J, Koletzko S, Mišak Z, Laguna VM, Polanco I, Ramos D, Shamir R, Troncone R, Vriezinga SL, Mearin ML. Histopathological evaluation of duodenal biopsy in the PreventCD project. An observational interobserver agreement study. APMIS 2018; 126: 208–214.

Aim of the current study was to evaluate the inter-observer agreement between pathologists in the diagnosis of celiac disease (CD), in the qualified context of a multicenter study. Biopsies from the "PreventCD" study, a multinational-prospective- randomized study in children with at least one-first-degree relative with CD and positive for HLA-DQ2/HLA-DQ8. Ninety-eight biopsies were evaluated. Considering diagnostic samples with villous atrophy (VA), the agreement was satisfactory ($\kappa = 0.84$), but much less when assessing the severity of these lesions. The use of the recently proposed Corazza-Villanacci classification showed a moderately higher level of agreement ($\kappa = 0.39$) than using the Marsh-Oberhuber system ($\kappa = 0.31$). 57.1% of cases were considered correctly oriented. A number of >4 samples per patient was statistically associated to a better agreement; orientation did not impact on $\kappa$ values. Agreement results in this study appear more satisfactory than in previous papers and this is justified by the involvement of centers with experience in CD diagnosis and by the well-controlled setting. Despite this, the reproducibility was far from optimal with a poor agreement in grading the severity of VA. Our results stress the need of a minimum of four samples to be assessed by the pathologist.

Key words: Histopathology; children; $\kappa$ value; villous atrophy; coeliac disease.

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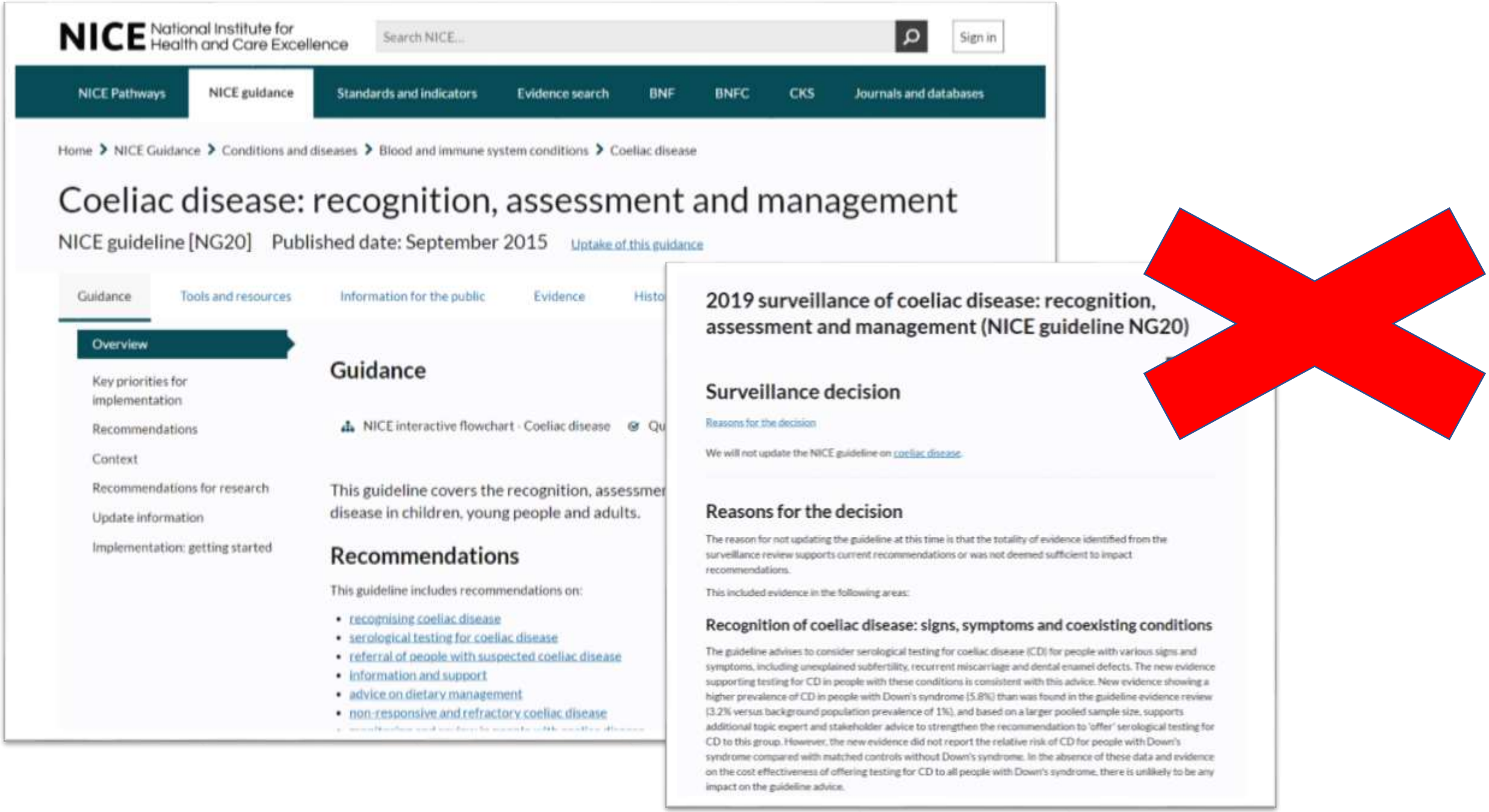
# NICE 2015 NG20 update….


NICE National Institute for Health and Care Excellence
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NICE guidance
Standards and indicators
Evidence search
BNF
BNFC
CKS
Journals and databases
Home > NICE Guidance > Conditions and diseases > Blood and immune system conditions > Coeliac disease
Coeliac disease: recognition, assessment and management
NICE guideline [NG20] Published date: September 2015
Uptake of this guidance
Guidance
Tools and resources
Information for the public
Evidence
Overview
Key priorities for implementation
Recommendations
Context
Recommendations for research
Update information
Implementation: getting started
Guidance
NICE interactive flowchart - Coeliac disease
This guideline covers the recognition, assessmer
disease in children, young people and adults.
Recommendations
This guideline includes recommendations on:
recognising coeliac disease
serological testing for coeliac disease
referral of people with suspected coeliac disease
information and support
advice on dietary management
non-responsive and refractory coeliac disease
2019 surveillance of coeliac disease: recognition, assessment and management (NICE guideline NG20)
Surveillance decision
Reasons for the decision
We will not update the NICE guideline on coeliac disease.
Reasons for the decision
The reason for not updating the guideline at this time is that the totality of evidence identified from the surveillance review supports current recommendations or was not deemed sufficient to impact recommendations.
This included evidence in the following areas:
Recognition of coeliac disease: signs, symptoms and coexisting conditions
The guideline advises to consider serological testing for coeliac disease (CD) for people with various signs and symptoms, including unexplained subfertility, recurrent miscarriage and dental enamel defects. The new evidence supporting testing for CD in people with these conditions is consistent with this advice. New evidence showing a higher prevalence of CD in people with Down's syndrome (5.8%) than was found in the guideline evidence review (3.2% versus background population prevalence of 1%), and based on a larger pooled sample size, supports additional topic expert and stakeholder advice to strengthen the recommendation to 'offer' serological testing for CD to this group. However, the new evidence did not report the relative risk of CD for people with Down's syndrome compared with matched controls without Down's syndrome. In the absence of these data and evidence on the cost effectiveness of offering testing for CD to all people with Down's syndrome, there is unlikely to be any impact on the guideline advice.

# ESPGHAN 2020


SOCIETY PAPER

CME

# European Society Paediatric Gastroenterology, Hepatology and Nutrition Guidelines for Diagnosing Coeliac Disease 2020

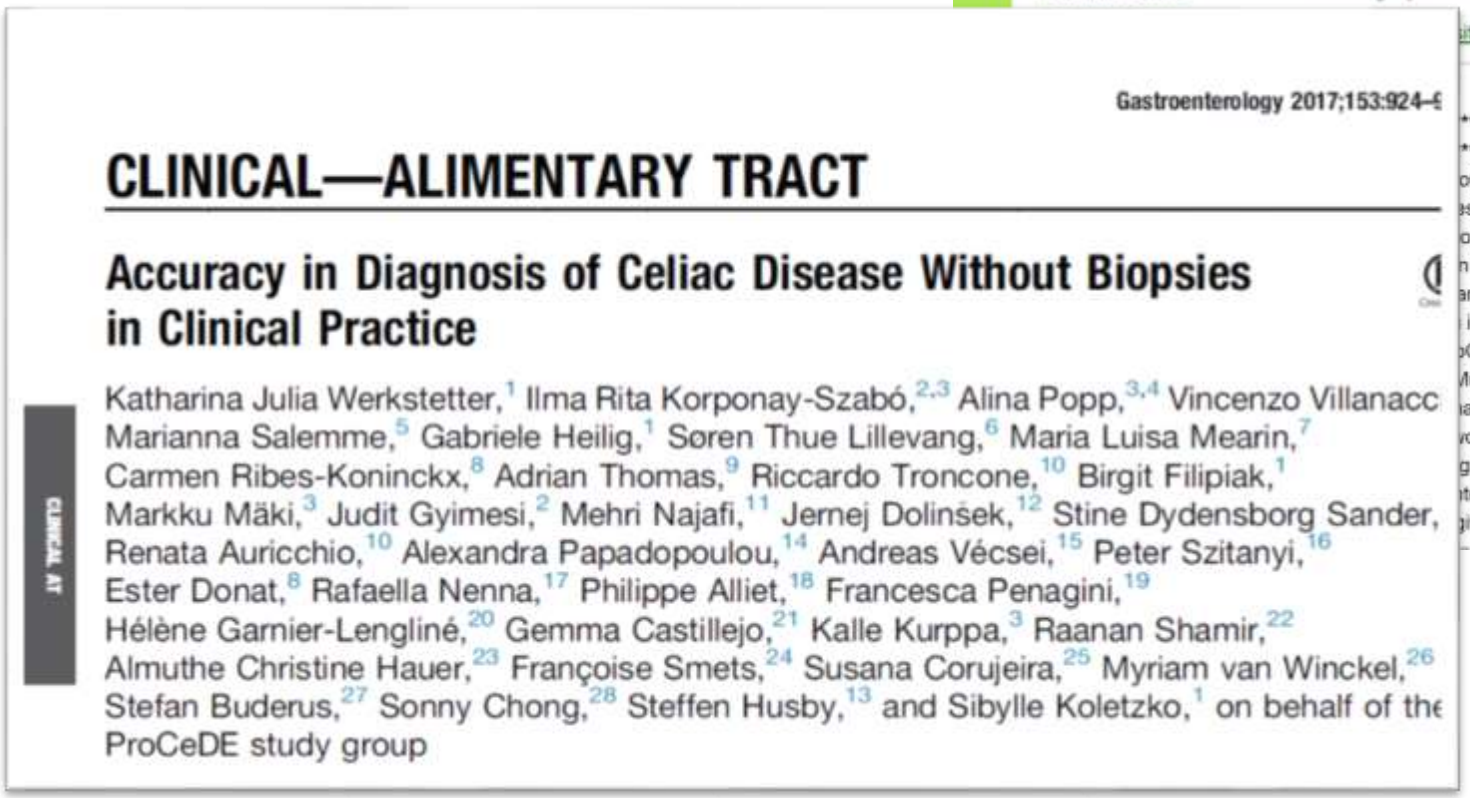
*Steffen Husby, †Sibylle Koletzko, ‡Ilma Korponay-Szabó, §Kalle Kurppa, ‖M. Luisa Mearin, ¶Carmen Ribes-Koninckx, #Raanan Shamir, **Riccardo Troncone, **Renata Auricchio, ††Gemma Castillejo, ‡‡Robin Christensen, §§Jernej Dolinsek, ‖‖Peter Gillett, ¶¶Ásbjørn Hróbjartsson, ##Tunde Koltai, §Markku Maki, ‡‡Sabrina Mai Nielsen, ***Alina Popp, †††Ketil Størdal, †Katharina Werkstetter, and ‡‡‡Margreet Wessels

**What Is Known**

- Coeliac disease is underdiagnosed because of the heterogeneous presentation of clinical signs and symptoms.
- To diagnose coeliac disease, different approaches are applied (history, clinical examination, serology, HLA testing, histopathology), but neither 1 of them has been considered sufficient alone to make a reliable diagnosis.
- For the first time, the European Society of Paediatric …y and Nutrition 2012 …ased diagnosis, omitting … in selected cases, but the …trospective studies.

…ation of total IgA and IgA …sglutaminase 2 is more …binations.
…liac disease diagnosis is safe … class antibody concentra… …alues (≥10 times the upper …te tests and positive endo… …a second serum sample.
…class antibodies against … titers (<10 times upper …rgo biopsies to decrease …nosis.
…nptoms are not obligatory criteria for a serology-based diagnosis without biopsies.

# 2017 Wolf & Werkstetter

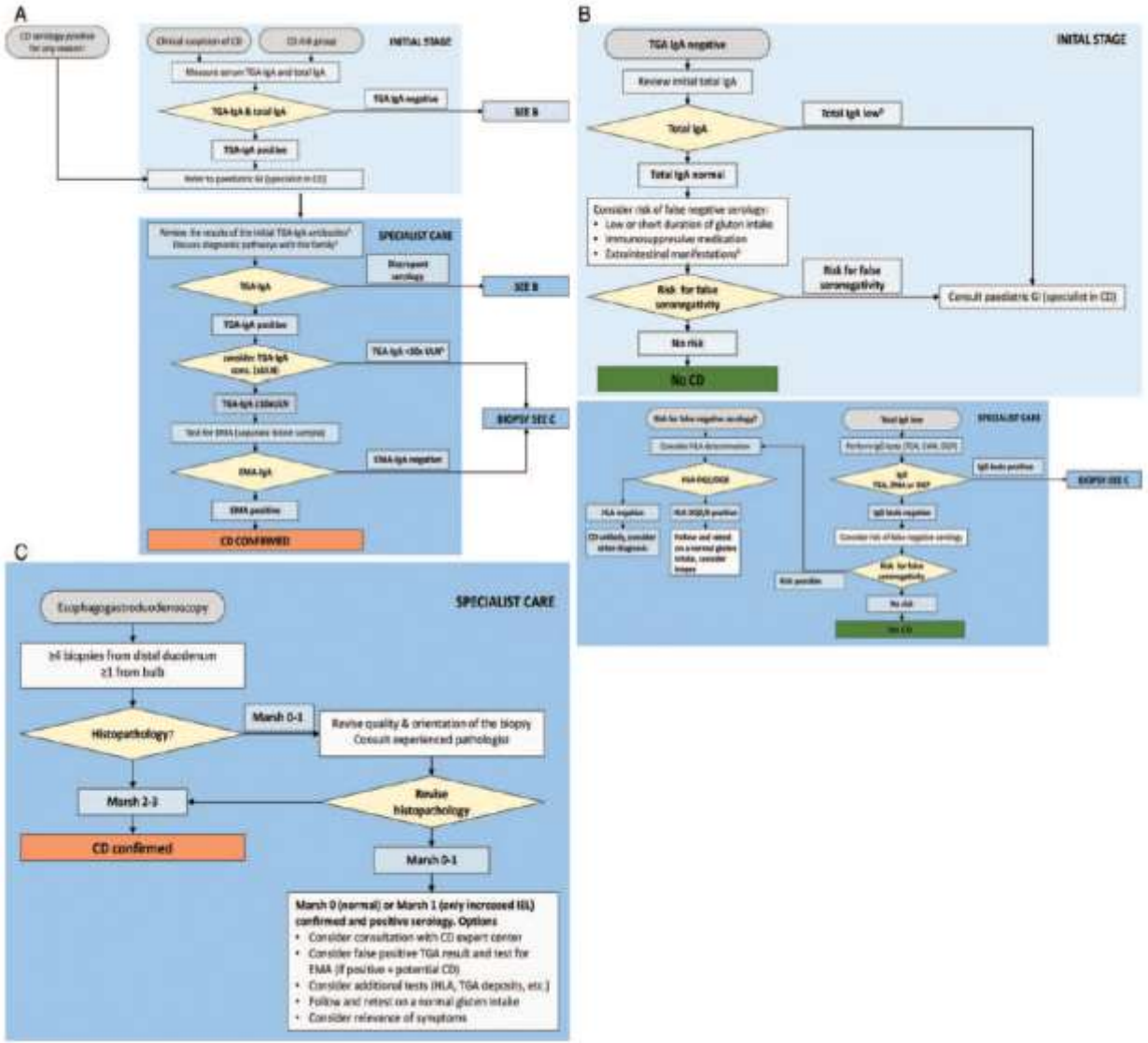



# P 143&153

TABLE 1. Questions for the 2019 European Society Paediatric Gastroenterology, Hepatology and Nutrition criteria for the diagnosis of coeliac disease

| Question | Text | Recommendation | Grading (strength) |
|---|---|---|---|
| 1 | Is there a difference in the prevalence of CD in children with constipation, abdominal pain, signs of irritable bowel syndrome (IBS), dyspepsia, malabsorption, iron deficiency anaemia, oral aphthae as compared with the general population? | We recommend considering testing for CD in children and adolescents with symptoms, signs and conditions shown in Table 2. | ↑ |
| 2 | What will HLA-DQ2 and DQ8 determination add to the diagnostic certainty of CD-diagnosis? | We recommend that HLA-DQ2 and DQ8 typing is not required in patients with positive TGA-IgA, if they qualify for CD diagnosis with biopsies or have high-serum TGA-IgA (≥10× ULN) and EMA-IgA positivity. If a patient tests negative for HLA DQ2 and DQ8, the risk of CD is very low, whereas a positive result does not confirm the diagnosis | ↑↑ |
| 3 | How does the algorithm proposed to avoid biopsies in symptomatic patients work in asymptomatic subjects? | We give a conditional recommendation that, taking available evidence into account, CD can be diagnosed without duodenal biopsies in asymptomatic children, using the same criteria as in patients with symptoms. We recommend that the decision whether or not to perform diagnostic duodenal biopsies should be made during a shared decision-making process together with the parent(s) and, if appropriate, with the child | ↑ |
| 4 | Which serological test is the most appropriate to diagnose CD? | We recommend that in subjects with normal serum IgA values for age, TGA-IgA should be used as the initial serological test regardless of age | ↑↑ |
| 5 | Should more than 1 serological test be used and, if so, what should be the sequence of testing? | We recommend testing for total IgA and TGA-IgA as initial screening in children with suspected CD. In patients with low total IgA concentrations, an IgG-based test (DGP, EMA or TGA) should be performed as a second step. Testing for EMA, DGP or AGA antibodies (IgG and IgA) as initial screening in clinical practice is not recommended | ↑↑ |
| 6 | A diagnosis of CD may be safely done (positive-predictive value >95%) with omission of biopsy, at which cutoff for TGA-IgA (ULN ×10, ×7, ×5)? | We recommend that for CD diagnosis without biopsies, TGA- IgA serum concentration of at least 10× ULN should be obligatory. Only antibody tests with proper calibrator curve-based calculation, and having the 10× ULN value within their measurement range, should be used. Omitting biopsies in IgA-deficient cases with positive IgG-based serological tests is not recommended | ↑↑ |
| 7 | Is endomysial antibody test (EMA) testing necessary in every case to diagnose CD with omission of biopsy? | We recommend that in children with TGA ≥10× ULN, and parents' patient agreement to the no-biopsy approach, the CD diagnosis should be confirmed by a positive EMA-IgA test in a second blood sample | ↑↑ |
| 8 | What is the inter- and intra-observer variability regarding CD diagnosis of histopathology results of duodenal and bulb biopsies? What degree of lesion is considered to be untreated CD? Do duodenal bulb biopsies increase the detection rate of CD? Is a reference pathologist needed in clinical practice? | At least 4 biopsies from the distal duodenum and at least 1 from the duodenal bulb should be taken for histology assessment during a gluten-containing diet. Reading of biopsies should be performed on optimally orientated biopsies. A villous to crypt ratio of <2 indicates mucosal lesions. In cases of discordant results between TGA-results and histopathology, re-cutting of biopsies and/or second opinion from an experienced pathologist should be requested | ↑↑ |
| 9 | Does Marsh 0 or 1 (increased IEL count>only) compared with Marsh 0 have a different long-term outcome regarding diagnosis of CD in children with coeliac autoimmunity (positive TGA or EMA)? | We recommend before diagnosing potential CD to check the gluten content of the diet and the correct orientation of biopsies. Once confirmed, potential CD requires clinical and laboratory surveillance (serology, further biopsies) to monitor possible evolution to villous atrophy. For follow-up, it is important to refer the patient to tertiary care centres with expertise in CD | ↑ |
| 10 | How often are other clinically relevant diagnoses missed if upper (oesophageal-gastroduodenal) endoscopy is not performed in patients diagnosed by the no-biopsy approach? | We recommend that the decision to omit upper endoscopy with biopsies can be taken without the consideration of missing other pathologies or diagnoses | ↑↑ |

Two arrows (↑↑) indicate a strong recommendation in favour, 1 arrow (↑) indicates a weak conditional recommendation, and similarly for strong and weak conditional recommendations against (↓↓ or ↓) as suggested by the GRADE Working Group (11).
Statements and recommendations from the 2012 Guidelines not investigated in the frame of these 10 questions remain in force (see supplementary file S 23, http://links.lww.com/MPG/B719). CD = coeliac disease.

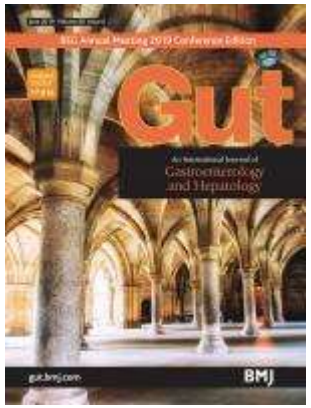


# Main take home messages…

- Main symptoms just as we expected * (see Table 2 p 145)
- No need for DQ to make positive diagnosis – adds nothing to certainty
- Asymptomatic ≥ 10 x ULN are ‘fair game’ but a **serious conversation reqd**!
- PPV best with Phadia and Immco assays but all pretty robust*
- Two separate tests - TGA-IgA then EMA-IgA*
- ≥ 10 x ULN is a safe and robust cut off for kids
- Significant interobserver variability in histology reporting -2$^{nd}$ opinion may be required and biopsying D1 adds to diagnostics
- Marsh 0 and 1 and natural evolution to CD – see later re potentials
- Other relevant diagnoses – anything missed ? Not really
- Everyone with IgA deficiency should be biopsied – ‘no Bx Dx’ doesn’t apply

# Key pragmatic questions and trends….what have we taken from adult guidance 2014 ?

# Adult GI guidelines BSG Gut 2014




OPEN ACCESS

## Diagnosis and management of adult coeliac disease: guidelines from the British Society of Gastroenterology

Jonas F Ludvigsson,[1,2] Julio C Bai,[3] Federico Biagi,[4] Timothy R Card,[5] Carolina Ciacci,[6] Paul J Ciclitira,[7] Peter H R Green,[8] Marios Hadjivassiliou,[9] Anne Holdoway,[10] David A van Heel,[11] Katri Kaukinen,[12,13,14] Daniel A Leffler,[15] Jonathan N Leonard,[16] Knut E A Lundin,[17] Norma McGough,[18] Mike Davidson,[19] Joseph A Murray,[20] Gillian L Swift,[21] Marjorie M Walker,[22] Fabiana Zingone,[23] David S Sanders,[24] Authors of the BSG Coeliac Disease Guidelines Development Group

For numbered affiliations see end of article.

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Received 12 December 2013
Revised 23 April 2014
Accepted 25 April 2014

**ABSTRACT**
A multidisciplinary panel of 18 physicians and 3 non-physicians from eight countries (Sweden, UK, Argentina, Australia, Italy, Finland, Norway and the USA) reviewed the literature on diagnosis and management of adult coeliac disease (CD). This paper presents the recommendations of the British Society of Gastroenterology. Areas of controversies were explored through phone meetings and web surveys. Nine working groups examined the following areas of CD diagnosis and management: classification of CD; genetics and immunology; diagnostics; serology and endoscopy; follow-up; gluten-free diet; refractory CD and malignancies; quality of life; novel treatments; patient support; and screening for CD.

last 8 years). As a result, the Clinical Services and Standards Committee of the BSG commissioned these guidelines, subject to rigorous peer review and based on a comprehensive review of the recent literature, including data from any available randomised controlled trials, systematic reviews, meta-analyses, cohort studies, prospective and retrospective studies.

A multidisciplinary panel of 18 physicians from eight countries (Sweden, UK, Argentina, Australia, Italy, Finland, Norway and the USA), a dietitian and a representative and a patient advocate from Coeliac UK reviewed the literature on the management of CD. These individuals were involved in the original stakeholder meetings and with revision of the manuscript.

# Oats from the start?

Yep!

ORIGINAL ARTICLES

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## Safety of Oats in Children with Celiac Disease: A Double-Blind, Randomized, Placebo-Controlled Trial

Elena Lionetti, PhD[1], Simona Gatti, MD[1], Tiziana Galeazzi, PhD[1], Nicole Caporelli, MD[1], Ruggiero Francavilla, PhD[2], Salvatore Cucchiara, MPH[3], Paola Roggero, MD[4], Basilio Malamisura, MD[5], Giuseppe Iacono, MD[6], Stefania Tomarchio, MD[7], Wolfgang Kleon, MD[8], Patrizia Restani, PhD[9], Ignazio Brusca, MD[10], Andrea Budelli, PhD[11], Rosaria Gesuita, MPH[12], Flavia Carle, MPH[12], and Carlo Catassi, MPH[1]

**Objective** To evaluate the long-term validity and safety of pure oats in the treatment of children with celiac disease.

**Study design** This noninferiority clinical trial used a double-blind, placebo-controlled, crossover design extended over 15 months. Three hundred six children with a biopsy-proven diagnosis of celiac disease on a gluten-free diet for ≥2 years were randomly assigned to eat specifically prepared gluten-free food containing an age-dependent amount (15-40 g) of either placebo or purified nonreactive varieties of oats for 2 consecutive 6-month periods separated by washout standard gluten-free diet for 3 months. Clinical (body mass index, Gastrointestinal Symptoms Rating Scale score), serologic (IgA antitransglutaminase antibodies, and IgA anti-avenin antibodies), and intestinal permeability data were measured at baseline, and after 6, 9, and 15 months. Direct treatment effect was evaluated by a nonparametric approach using medians (95% CI) as summary statistic.

**Results** After the exclusion of 129 patients who dropped out, the cohort included 177 children (79 in the oats–placebo and 98 in the placebo–oats group; median, 0.004; 95% CI, –0.0002 to 0.0089). Direct treatment effect was not statistically significant for clinical, serologic, and intestinal permeability variables (body mass index: median, –0.5; 95% CI, –0.12 to 0.00; Gastrointestinal Symptoms Rating Scale score: median, 0; 95% CI, –2.5 to 0.00; IgA antitransglutaminase antibodies: median, –0.02; 95% CI, –0.25 to 0.23; IgA anti-avenin antibodies: median, –0.0002; 95% CI, –0.0007 to 0.0003; intestinal permeability test: median, 0.004; 95% CI, –0.0002 to 0.0089).

**Conclusions** Pure nonreactive oat products are a safe dietary choice in the treatment of children with celiac disease. *(J Pediatr 2018;194:116-22).*

**Trial registration** ClinicalTrials.gov: NCT00808301.

# Other guidance 2019 and 2020– non-responsive and refractory CD helpful literature from adult colleagues*….




REVIEW

# How to manage adult coeliac disease: perspective from the NHS England Rare Diseases Collaborative Network for Non-Responsive and Refractory Coeliac Disease

Elisabeth Megan Rose Baggus,[1] Marios Hadjivassiliou,[1] Simon Cross,[1] Hugo Penny,[1] Heidi Urwin,[2] Sarah Watson,[3] Jeremy Mark Woodward,[4] David S Sanders[5]

## Significance of this study

- Historically, in the UK, serology has been used as a marker for adherence, but growing evidence in the published literature does not support this.
- Reported histological remission rates range from 34% to 65% at 2 years after diagnosis, and 66% to 85% at 5 years, with some patients never achieving complete resolution.
- We propose a contemporary treatment algorithm for patients with persisting symptoms, with a starting point of repeat gastroscopy and duodenal biopsy.
- We provide a contemporary perspective of adherence and refractory coeliac disease (RCD1; gluten contamination elimination, elemental diets) and of functional symptoms (alternative diets, low fermentable oligosaccharide disaccharide monosaccharide and polyols).
- In any patient in whom RCD is suspected, we recommend early contact with the National Health Service England's Rare Diseases Collaborative Network for Non-Responsive and Refractory Coeliac Disease.

*nutrients*

MDPI

*Review*

# Non-Responsive Coeliac Disease: A Comprehensive Review from the NHS England National Centre for Refractory Coeliac Disease

Hugo A. Penny [1,2], Elisabeth M. R. Baggus [1], Anupam Rej [1], John A. Snowden [3] and David S. Sanders [1,*]

[1] Academic Unit of Gastroenterology, University of Sheffield, Sheffield S10 2TN, UK; h.penny@sheffield.ac.uk (H.A.P.); emrbaggus1@sheffield.ac.uk (E.M.R.B.); anupam.rej@nhs.net (A.R.)

**Table 1.** Conditions associated with coeliac disease that should be considered as a cause for persisting symptoms in coeliac patients [5,19–22].

| |
|---|
| Pancreatic insufficiency |
| Inflammatory bowel disease |
| Lactose and/or fructose intolerance |
| Small intestinal bacterial overgrowth |
| Microscopic colitis |
| Irritable bowel syndrome |
| Functional dysmotility |

inflammation. These individuals can be classified as having non-responsive coeliac disease (NRCD), which may be associated with dietary indiscretion, slow healing, refractory coeliac disease, and/or an alternative condition. The purpose of this review is to provide an overview of the causes of NRCD in adults, highlight a systematic approach to investigate these patients, and appraise the latest management aspects of this subset of coeliac disease.

# What about the Children who are ‘potentials’- normal biopsies with positive serology ?


# The Effect of Gluten-free Diet on Clinical Symptoms and the Intestinal Mucosa of Patients With Potential Celiac Disease

*Roberta Mandile, Valentina Discepolo, Serena Scapaticci, Maria Rosaria Del Vecchio, Maria Antonia Maglio, Luigi Greco, Riccardo Troncone, and Renata Auricchio*

## ABSTRACT

In this prospective study, we evaluated the effect of gluten-free diet (GFD) in a cohort of 65 children with potential celiac disease. Patients received GFD for signs/symptoms (N = 47) or parents' choice (N = 18). Most frequent signs/symptoms were low body mass index (36%), recurrent abdominal pain (34%), and diarrhea (19%). Of the 35/47 patients followed-up on GFD, only 54% (19/35) showed a complete clinical response. In 9 of 65 patients an intestinal biopsy was also performed after at least 1 year of GFD. No significant differences were observed in terms of Marsh grade ($P = 0.33$), lamina propria CD25+ cells ($P = 0.80$), CD3+ ($P = 0.9$), and $\gamma\delta$+ ($P = 0.59$) intraepithelial lymphocytes density and intestinal anti-TG2 deposits ($P = 0.60$). In conclusion, caution is necessary before attributing all symptoms to gluten in this condition.

**Key Words:** gluten-free diet, intestinal biopsies, intraepithelial lymphocytes, potential celiac disease

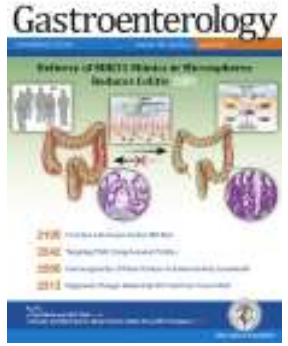
(*JPGN* 2018;66: 654–656)

### What Is Known

- Potential celiac disease is a clinical condition characterized by the presence of anti-tissue tranglutaminase antibodies in the blood, but with a preserved intestinal villi architecture.
- Patients with potential celiac disease can present or not clinical symptoms and/or signs.
- Whether patients with potential celiac disease should or should not receive a gluten-free diet has not been well established yet.

### What Is New

- Symptoms after gluten-free diet improve in only about half of the cases.
- The intestinal inflammation and infiltration does not always improve after gluten-free diet in potential celiac disease.




Gastroenterology. 2019 Apr 9. pii: S0016-5085(19)35671-9. doi: 10.1053/j.gastro.2019.04.004. [Epub ahead of print]

# Progression of Celiac Disease in Children With Antibodies Against Tissue Transglutaminase and Normal Duodenal Architecture.

Auricchio R[1], Mandile R[2], Del Vecchio MR[2], Scapaticci S[2], Galatola M[2], Maglio MA[2], Discepolo V[3], Miele E[2], Cielo D[2], Troncone R[2], Greco L[2].

Author information

## Abstract

**BACKGROUND & AIMS:** Potential celiac disease is characterized by positive results from serologic tests for tissue transglutaminase antibodies (anti-TG2) but normal duodenal architecture (Marsh stages 0-1). There is controversy over the best way to manage these patients. We investigated risk factors associated with the development of villous atrophy in children with potential celiac disease.

**METHODS:** We performed a prospective study of 280 children (ages 2-18 years) in Italy with suspected celiac disease, followed for up to 12 years (range, 18-150 months; median 60 months). The subjects had 2 consecutive positive results from tests for anti-TG2, tested positive for the endomysial antibody (anti-EMA), had total serum levels of IgA in the normal range, normal duodenal architecture (Marsh stages 0-1) in 5 biopsies, and HLA DQ2- or DQ8-positive haplotypes. The children underwent serologic tests and clinical analyses every 6 months and a small bowel biopsy was taken every 2 years. Two hundred ten patients of the original cohort were assessed at the 9-year follow-up evaluation. We performed multivariate analyses of clinical, genetic, and histologic data to identify factors associated with progression to villous atrophy.

**RESULTS:** During the follow-up period, 42 of 280 children (15%) developed villous atrophy whereas 89 children (32%) no longer tested positive for anti-TG2 or anti-EMA. The cumulative incidence of progression to villous atrophy was 43% at 12 years. In multivariate analysis, the baseline factors most strongly associated with development of villous atrophy were numbers of γδ intraepithelial lymphocyte cells followed by age and homozygosity for the HLA DQB1*02. In discriminant analysis, these baseline factors identified 80% of the children who developed baseline atrophy.

**CONCLUSIONS:** In a long-term study of 280 children with suspected celiac disease (based on anti-TG2 and anti-EMA) on gluten-containing diets, the cumulative incidence of progression to villous atrophy was 43% over a 12-year period. We identified factors that can be used to identify children at highest risk for villous atrophy. This approach might be used to determine whether children with suspected celiac disease should immediately start a gluten-free diet or be monitored on their regular diet.

# Increasing awareness of neurology and psychological / psychiatric issues……


J Clin Psychol Med Settings. 2019 Oct 31. doi: 10.1007/s10880-019-09673-9. [Epub ahead of print]

# Psychological Needs and Services in a Pediatric Multidisciplinary Celiac Disease Clinic.

Coburn S[1,2,3], Rose M[4], Streisand R[4,5], Sady M[4,5], Parker M[4], Suslovic W[4], Weisbrod V[4], Kerzner B[4,5], Kahn I[4,5].

Author information

## Abstract

This study aims to describe the psychological needs in children with celiac disease (CD) and to examine the feasibility of psychological consultation in a multidisciplinary clinic. Participants (N = 69) included children with CD and their parents who completed a pre-clinic mental health survey and a 30-min psychological consultation as part of a multidisciplinary clinic (including gastroenterology, nutrition, education, neurology, and neuropsychology). Quantitative and qualitative analyses examined psychological needs, experiences, and satisfaction. The psychologist identified clinically significant symptoms and provided referrals in 49% of children. There were no significant differences by time since CD diagnosis. During the psychology consultation, families discussed emotional adjustment, impact on life and physical well-being, and management of the gluten-free diet. Parents reported high levels of satisfaction from the clinic visit. We identified frequent psychological needs in pediatric CD. The multidisciplinary approach may be a feasible model for specialized, optimal treatment in this population.

**KEYWORDS:** Celiac; Child; Coeliac; Gluten-free; Multidisciplinary; Pediatric; Psychological

*nutrients*

MDPI

*Review*

# Psychiatric Manifestations of Coeliac Disease, a Systematic Review and Meta-Analysis

**Emma Clappison [1,*], Marios Hadjivassiliou [2] and Panagiotis Zis [2,*,†]**

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† Current address: Medi

Received: 9 December 201

**Abstract:** Background: Coeliac disease (CD) is increasingly prevalent and is associated with both gastrointestinal (GI) and extra-intestinal manifestations. Psychiatric disorders are amongst extra-intestinal manifestations proposed. The relationship between CD and such psychiatric disorders is not well recognised or understood. Aim: The aim of this systematic review and meta-analysis was to provide a greater understanding of the existing evidence and theories surrounding psychiatric manifestations of CD. Methodology: An online literature search using PubMed was conducted, the prevalence data for both CD and psychiatric disorders was extracted from eligible articles. Meta analyses on odds ratios were also performed. Results: A total of 37 articles were included in this review. A significant increase in risk was detected for autistic spectrum disorder (OR 1.53, 95% CI 1.24–1.88, $p < 0.0001$), attention deficit hyperactivity disorder (OR 1.39, 95% CI 1.18–1.63, $p < 0.0001$), depression (OR 2.17, 95% CI 2.17–11.15, $p < 0.0001$), anxiety (OR 6.03, 95% CI 2.22–16.35, $p < 0.0001$), and eating disorders (OR 1.62, 95% CI 1.37–1.91, $p < 0.00001$) amongst the CD population compared to healthy controls. No significant differences were found for bipolar disorder (OR 2.35, 95% CI 2.29–19.21, $p = 0.43$) or schizophrenia (OR 0.46, 95% CI 0.02–10.18, $p = 0.62$). Conclusion: CD is associated with an increased risk of depression, anxiety, eating disorders as well as ASD and ADHD. More research is required to investigate specific biological explanations as well as any effect of gluten free diet.

# Coeliac disease now topped out, despite the 1 in 100 mantra….

*Table 2: Incidence Rates of NHS Boards for 2018*

| Board | Board Population | Number of Incidences Per Year | Incidence Rate per year |
|---|---|---|---|
| NHS Western Trust | 300,000 | 75 | 0.025 % |
| NHS Tayside | 415470 | 121 | 0.029% |
| NHS Lothian | 800000 | 362 | 0.045% |

# Changes in Testing for and Incidence of Celiac Disease in the United Kingdom

## *A Population-based Cohort Study*

***To the Editor:***

The diagnosis rates of celiac disease differ substantially between countries.[1] Intriguingly, there has been recent evidence from Olmstead County, United States, and Finland that in the last 5–10 years incidence has leveled off or even declined.[2,3] In most populations, the prevalence also varies widely with serologic prevalence from 0% to 1.87% and clinical prevalence from 0.9 to 12.9 per 100,000.[1] Understanding of why this variation exists is minimal, yet one of the key aspects governing incidence rates of any disease are factors related to the health system, such as the availability and use of diagnostic tests. We previously reported rising incidence rates of celiac disease[4] from 1990 to 2011 with differences related to socioeconomic

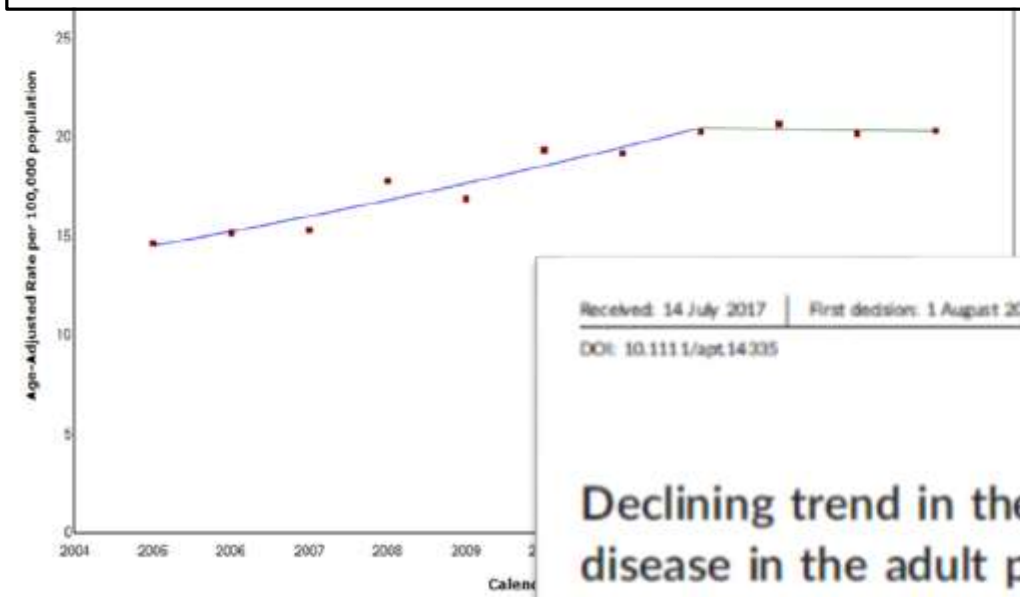



FIGURE 1. European age-standardized inc
person-years.

Received: 14 July 2017 | First decision: 1 August 2017 | Accepted: 29 August 2017
DOI: 10.1111/apt.14335

WILEY APT Alimentary Pharmacology & Therapeutics

## Declining trend in the incidence of biopsy-verified coeliac disease in the adult population of Finland, 2005-2014

L. J. Virta[1] | M. M. Saarinen[2] | K.-L. Kolho[3]

# Exciting new diagnostics and treatments??

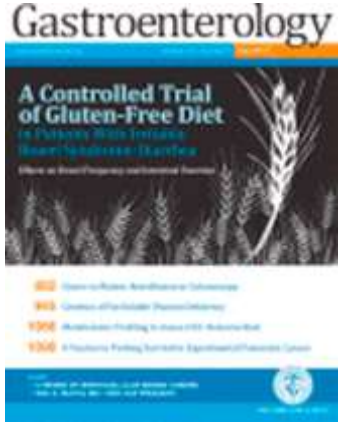
# The future- non gluten dependent testing…

Gastroenterology 2018;154:886–896

## HLA-DQ–Gluten Tetramer Blood Test Accurately Identifies Patients With and Without Celiac Disease in Absence of Gluten Consumption

Vikas K. Sarna,[1,2] Knut E. A. Lundin,[2,3] Lars Mørkrid,[4] Shuo-Wang Qiao,[1,2,5] Ludvig M. Sollid,[1,2,5] and Asbjørn Christophersen[1,2]

*[1]Department of Immunology, Oslo University Hospital–Rikshospitalet; [2]KG Jebsen Coeliac Disease Research C of Oslo; [3]Department of Gastroenterology, Oslo University Hospital–Rikshospitalet; [4]Department of Medical Bi University Hospital–Rikshospitalet; and [5]Centre for Immune Regulation, Oslo University Hospital–Rikshospitak of Oslo, Oslo, Norway*




**EDITOR'S NOTES**

BACKGROUND AND CONTEXT

Diagnosis of celiac disease is difficult when patients do not consume gluten. Detection of gluten-specific cells has shown promise as a diagnostic test, even in subjects on a gluten-free diet.

NEW FINDINGS

An HLA-DQ–gluten tetramer based assay that detects gluten-specific T cells accurately identifies patients with and without celiac disease, regardless of whether the individuals are on a gluten-free diet.

LIMITATIONS

The performance of the test is yet not validated in a multi-center study, and the test is currently not commercially available.

IMPACT

The test may replace gluten-challenge and duodenal biopsy to exclude celiac disease in subjects on gluten-free diet.

Digestive and Liver Disease 52 (2020) 130–137

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

Review Article

# Therapeutic options for coeliac disease: What else beyond gluten-free diet?

Giacomo Caio[a,1], Rachele Ciccocioppo[b], Giorgio Zoli[c], Roberto De Giorgio[a,*], Umberto Volta[d]

[a] Department of Medical Sciences, University of Ferrara, Italy
[b] Gastroenterology Unit, Department of Medicine, A.O.U.I. Policlinico G. B
[c] Department of Morphology, Surgery and Experimental Medicine, Univer
[d] Department of Medical and Surgical Scieces, University of Bologna, Italy

A B S T R A C T

Coeliac disease is a chronic and systemic autoimmune condition triggered by gluten ingestion in genetically predisposed subjects. Currently, the only effective treatment available is a strict, lifelong gluten-free diet. However, patients perceive gluten withdrawal as an unsustainable burden in their life and some of them can exhibit persistent symptoms despite a strict diet. Thus, gluten-free diet represents a challenge, leading scientists to look for alternative or complementary treatments. This review will focus on non-dietary therapies for coeliac disease highlighting six therapeutic strategies: (1) decreasing gluten immunogenic content before it reaches the intestine; (2) sequestering gluten in the gut lumen before absorption; (3) blocking the passage of gluten through a leaky intestinal barrier; (4) preventing the enhancement of immune response against gliadin; (5) dampening the downstream immune activation; (6) inducing immune tolerance to gluten. Most developing therapies are only in the pre-clinical phase with only a few being tested in phase 2b or 3 trials. Although new approaches raise the hope for coeliacs giving them a chance to come back to gluten, for the time being a cautionary appraisal of new therapies suggests that they may have a complementary role to gluten withdrawal, mainly to prevent inadvertent gluten contamination.



Caio G DLD 2020

# The role of GIP…..where does it fit in assessment?

ORIGINAL ARTICLE: GASTROENTEROLOGY: CELIAC DISEASE

OPEN

# Comparison of Clinical Methods With the Faecal Gluten Immunogenic Peptide to Assess Gluten Intake in Coeliac Disease

*Konstantinos Gerasimidis, *Konstantina Zafeiropoulou, *Mary Mackinder, †Umer Z Ijaz, ‡Hazel Duncan, ‡Elaine Buchanan, ‡Tracey Cardigan, *Christine A. Edwards, ‡Paraic McGrogan, and ‡Richard K. Russell

**What Is Known**

- Strict adherence to gluten-free diet is the only treatment of coeliac disease.
- The precision of current clinical methods to ascertain gluten-free diet compliance in coeliac disease remains unclear.
- Gluten immunogenic peptides in faeces have been proposed as a biomarker of gluten intake.

**What Is New**

- Gluten immunogenic peptide was detected in 16% of coeliac disease patients on recommendation to adhere to gluten-free diet.
- Using current clinical methods, almost 4 out of 5 children who do not comply with gluten-free diet will be potentially missed.
- Inclusion of gluten immunogenic peptide in routine practice may improve objective health professional judgment and management of coeliac disease.

# What’s now……guideline misinterpretation?

# Variation in coeliac disease management in specialist paediatric gastroenterology centres across the United Kingdom - a 2019 service snapshot

Poster ID: 14

**Siba Paul[1], Varathagini Balakumar[1,2], Peter Gillett[3].**

[1]Torbay Hospital, Torquay; [1,2]Medical School, University of Cardiff; [3]Royal Hospital for Sick Children, Edinburgh

## Background and Objectives

- The ESPGHAN guidelines (2012)[1] recommended the no-biopsy pathway [NBP] for symptomatic children who fulfill the three criteria:
  - IgA anti-tissue transglutaminase antibodies (TGA-IgA) titre ≥10 times upper-limit-of-normal (10×ULN) and are IgA sufficient.
  - Positive IgA anti-endomysial antibodies (EMA).
  - Positive HLA-DQ2/DQ8 haplotype
- Endoscopy and duodenal biopsies remained mandatory for diagnosing all other children with suspected CD while on a gluten-containing diet
- Studies demonstrated that serology-based CD diagnosis is possible in asymptomatic children from high-risk groups with TGA-IgA ≥10xULN.[2,3]
- Previous survey and audit from SW England highlighted need for greater awareness of the NBP and HLA-DQ2/8 testing.[4,5]

Aims and objectives:

1. To assess the implementation of the 2012 ESPGHAN guidelines across the UK in specialist GI Centres [SGIC].
2. Understand variation in practice in CD management across SGIC


## Subjects and Methods

- A short survey [20 questions] was sent to all SGIC [n=29] providing a paediatric endoscopy service for diagnosis of CD across the UK.
- Response rate was 100%
- The survey questionnaire was divided into 4 main subgroups:
  - Diag
  - Imm
  - Patie
  - Tran
- A maxin
- Data wa

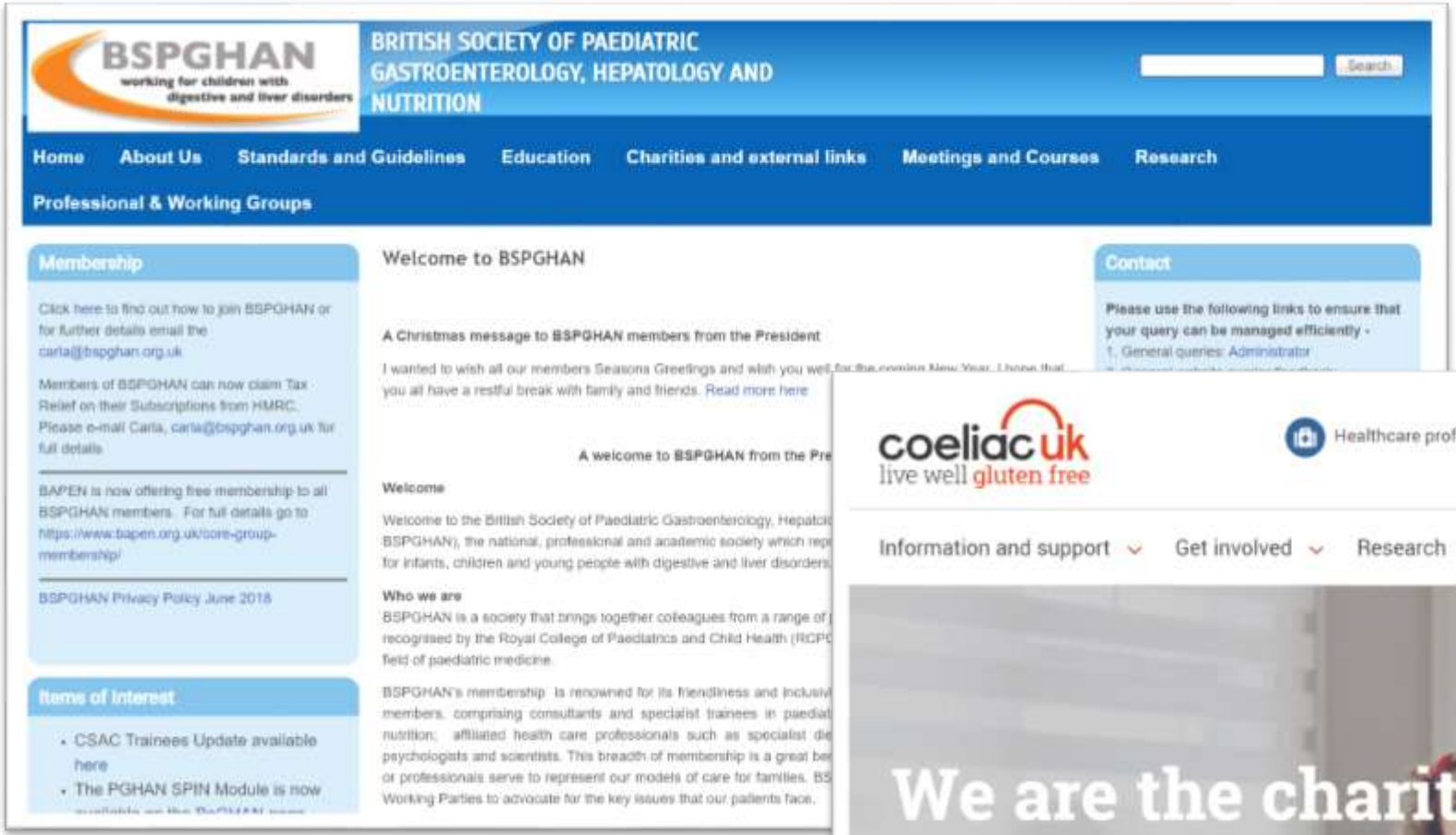
## Conclusions

- Our survey highlighted the excellent uptake of NBP from ESPGHAN 2012.
- HLA-DQ2/8 remained an important test in 83% centres and there remain other considerable differences in ongoing management.
- Most SGIC do not use the NBP for asymptomatic children.
- The new ESPGHAN guidelines[6] will help confirm and harmonise recommendations from previous iterations, allow an option for a secure NBP diagnosis for asymptomatic children and remove HLA-DQ2/8 testing from routine diagnosis.
- All IgA deficient patients must be biopsied, irrespective of the titres - the ESPGHAN guideline[6] for NBP only applies to TGA-IgA

Paul S et al
BSPGHAN 2020

# 2020 BSPGHAN / CUK iteration of ESPGHAN.....but with personalised care considerations in follow up advice

# In progress


BSPGHAN
working for children with digestive and liver disorders
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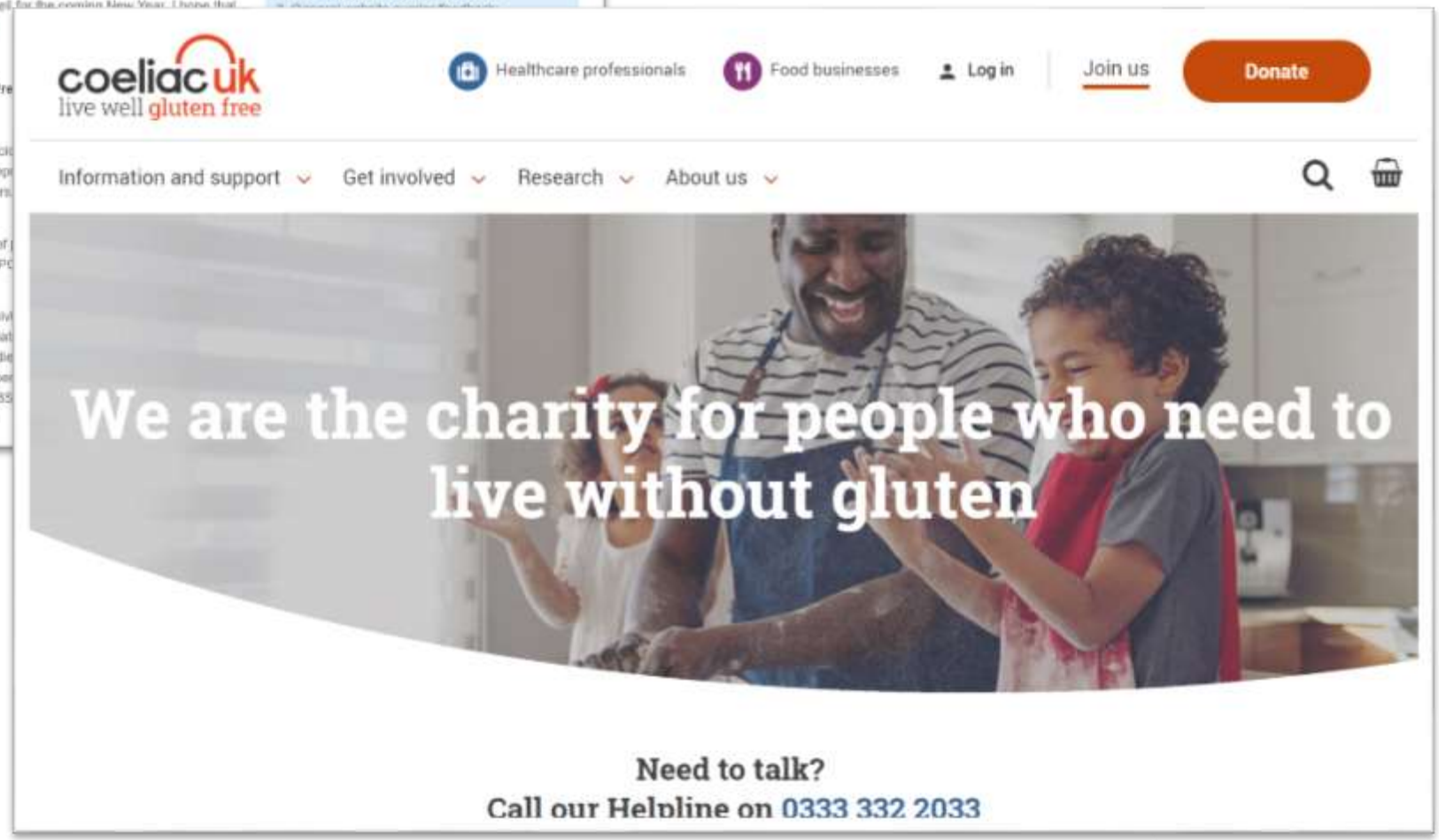
BAPEN is now offering free membership to all BSPGHAN members. For full details go to https://www.bapen.org.uk/core-group-membership/
BSPGHAN Privacy Policy June 2018
Items of Interest
CSAC Trainees Update available here
The PGHAN SPIN Module is now
Welcome to BSPGHAN
A Christmas message to BSPGHAN members from the President
I wanted to wish all our members Seasons Greetings and wish you well
you all have a restful break with family and friends. Read more here
A welcome to BSPGHAN from the Pre
Welcome
Welcome to the British Society of Paediatric Gastroenterology, Hepatol
BSPGHAN), the national, professional and academic society which rep
for infants, children and young people with digestive and liver disorders
Who we are
BSPGHAN is a society that brings together colleagues from a range of
recognised by the Royal College of Paediatrics and Child Health (RCP
field of paediatric medicine
BSPGHAN's membership is renowned for its friendliness and inclusiv
members, comprising consultants and specialist trainees in paediat
nutrition; affiliated health care professionals such as specialist die
psychologists and scientists. This breadth of membership is a great be
or professionals serve to represent our models of care for families. BS
Working Parties to advocate for the key issues that our patients face.
Contact
Please use the following links to ensure that your query can be managed efficiently -
1. General queries: Administrator


coeliac uk
live well gluten free
Healthcare professionals
Food businesses
Log in
Join us
Donate
Information and support
Get involved
Research
About us
We are the charity for people who need to live without gluten
Need to talk?
Call our Helpline on 0333 332 2033

# A children’s and YP agenda ?

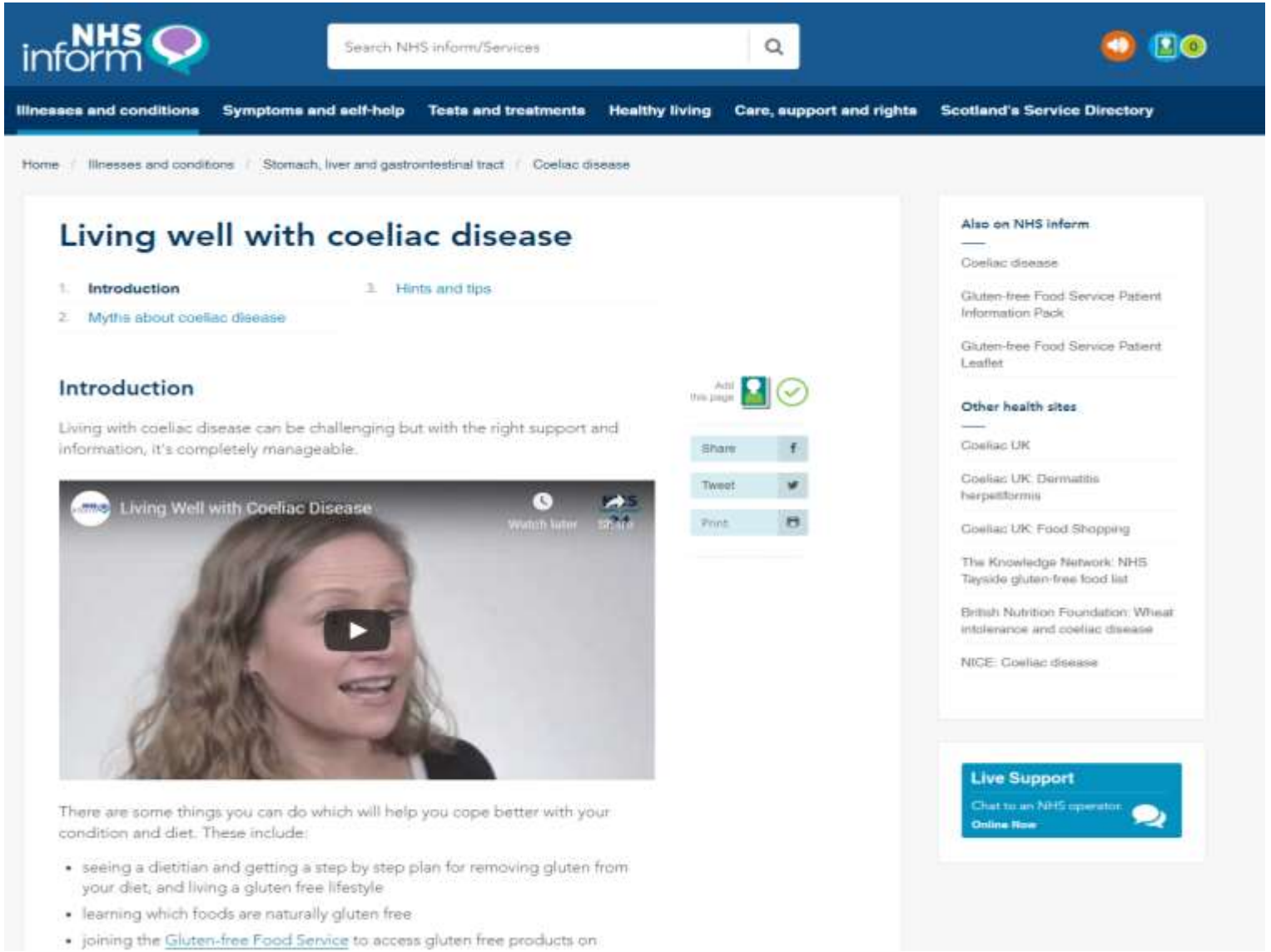
# CDWG -What can we agree on pragmatically?

- Bloods at baseline and follow up – only TGA, all or targeted to what wasn't right at the start ie. has Fe Def An resolved, B12 , etc…..
- Pragmatic Vitamin D and Calcium advice
- Who is for DEXA – anyone?
- Who is for further follow up – dietetically
- Who is for further follow up – medically in primary or secondary care?
- Psychology- increasingly aware of support required
- 'Goodbye' Advice - Folate and pre- peri-pregnancy
- Pneumococcal vaccination – also who is actually hyposplenic?
- Advice for patients , GPs and other HCPs about what other conditions need to be thought of when it doesn't go right and GFD is 100%

# More challenges…..

# New innovations/ informatics…..helping coeliac families self care?

https://www.nhsinform.scot/illnesses-and-conditions/stomach-liver-and-gastrointestinal-tract/coeliac-disease/living-well-with-coeliac-disease



INTERREG CENTRAL EUROPE

PRIORITY: INNOVATION AND KNOWLEDGE DEVELOPMENT

Interreg CENTRAL EUROPE
Focus IN CD
European Union
European Regional Development Fund

# Focus IN CD

NEWS | EVENTS | PILOTS | PUBLICATIONS | FACTS | CONTACTS

# PROJECT DOCUMENTS

## OUTPUTS

- Assessment of celiac disease management practices (pdf 0.4 MB)


## E-GUIDELINES

- Focus-on-CD-A5-SLO (pdf 1.9 MB)
- E-guidelines protocol of celiac disease treatment (pdf 1.9 MB)


## E-BROCHURE FOR NEWLY DIAGNOSED PATIENTS

- Focus on CD brochure for patients ENG (pdf 4.9 MB)
- Focus on CD brochure for patients SLO (pdf 5.4 MB)
- Focus on CD brochure-CRO (pdf 4.0 MB)

# Coeliac Passport

Logo of relevant National CD society

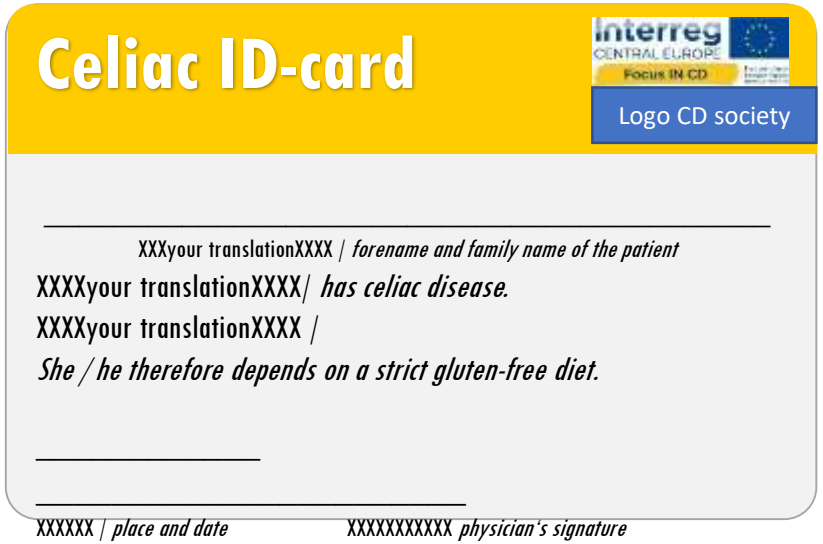
Interreg CENTRAL EUROPE

Focus IN CD

European Union European Regional Development Fund

# Coeliac ID-card

In addition to the detailed coeliac passport, the HCP making the diagnosis can also give you the bilingual Celiac ID-card in a handy credit-card format :




On the reverse of the card, you will find a summary of the most important information on gluten-free diet and can be shown in restaurants, hotels, cafeterias, hospital etc.

# Coming to your adult services…your chance to influence No Bx Dx ….already happening in Finland

33%
across all
pre-test
probabilities

Received: 5 October 2018 | First decision: 25 October 2018 | Accepted: 2 December 2018
DOI: 10.1111/apt.15109

WILEY AP&T Alimentary Pharmacology & Therapeutics

# Serology-based criteria for adult coeliac disease have excellent accuracy across the range of pre-test probabilities

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Email: kalle.kurppa@uta.fi

**Funding information** This study was supported by the Academy of Finland, the Sigrid Juselius Foundation, the Päivikki and Sakari Sohlberg Foundation, the Competitive State Research Financing of the Expert Area of Tampere University Hospital, the Finnish Medical Foundation, and the Foundation for Paediatric Research.

**Summary**

**Background:** The revised paediatric criteria for coeliac disease allow omission of duodenal biopsies in symptomatic children who have specific serology and coeliac disease-associated genetics. It remains unclear whether this approach is also applicable for adults with various clinical presentations.

**Aim:** To evaluate the accuracy of serology-based criteria in adults with variable pre-test probabilities for coeliac disease.

**Methods:** Three study cohorts comprised adults with high-risk clinical coeliac disease suspicion (n = 421), moderate-risk family members of coeliac disease patients (n = 2357), and low-risk subjects from the general population (n = 2722). Serological and clinical data were collected, and "triple criteria" for coeliac disease comprised transglutaminase 2 antibodies >10× the upper limit of normal, positive endomysium antibodies, and appropriate genetics without requirement of symptoms. The diagnosis was based on intestinal biopsy.

**Results:** The diagnosis of coeliac disease was established in 274 subjects. Of these, 59 high-risk subjects, 17 moderate-risk subjects, and 14 low-risk subjects fulfilled the "triple criteria". All had histologically proven coeliac disease, giving the criteria a positive predictive value of 100%. Altogether, 90 (33%) of all 274 newly diagnosed patients could have avoided biopsy, including 37% among high-risk, 20% among moderate-risk, and 48% among low-risk patients. No histological findings other than coeliac disease were found in the biopsies of "triple positive" subjects.

**Conclusions:** Coeliac disease can reliably and safely be diagnosed without biopsy in adults fulfilling the "triple criteria" regardless of the pre-test probability. Revised criteria would enable the number of endoscopies to be reduced by one-third.

# Scottish collaboration post TOC pathway…

- Enthusiasm to work collaboratively – SSG and MOP
- Part of the TOC Coeliac pathway
- 5 boards in Scotland reviewing pathways and serology vs histology (3 different assays)
  - GI and dietitians and pathologists
- Who needs biopsy? What else would we miss?
- What investigations do we really need to do?
  - What are the outcomes at 1 year +?
- How do we educate and offer ongoing support?

# The ‘’three Ds’’ of coeliac disease (Sanders)

- DIAGNOSE
- DIETITIAN
- DISCHARGE

British Journal of General Practice
bringing research to clinical practice



# Coeliac disease - a forgotten condition

Alasdair Carter, Locum GP, Retired GP principal, Clitheroe, Lancashire

6 August 2018

Your recent editorial is a timely reminder of the absurd inequities in the NHS prescribing system and of coeliac disease, a poorly understood Cinderella disease with significant morbidity and potential mortality. A 13 year delay in diagnosis is a scandal and I can't think of another disease which could match this delay, let alone have it tolerated. The mainstay of management is adherence to a gluten free diet. The catering industry, although improving, has remarkably poor knowledge and worse still attitude in making a gluten free option available to ever increasing numbers of people eating out. This is across the board from so called good restaurants to a corner cafe. It is easy to find a vegetarian option. Yet this is a lifestyle choice not a medical necessity. A coeliac who entrusts their well being to a restaurant without a thorough interrogation of the staff is both brave and foolhardy. The toxic proliferation of gluten free diets, promoted by film stars, sports people and the like, who both should know better and be advised better, makes it even harder for coeliacs. A gluten free diet for a non coeliac is not a healthy option, but for a coeliac it is life changing. Coeliac disease is a soft target for governments. Perhaps the government should stop free prescriptions for diabetics and see how they get on. It would of course again be the wrong decision on health grounds. Allowing gluten free foods on prescription acknowledges the existence of coeliac disease as a significant disease, still vastly under diagnosed. Just as treating diabetes is cost effective in preventing long term morbidity, treating coeliac disease is the same.

Digestion

Original Paper

# Pediatric Celiac Disease Patients Who Are Lost to Follow-Up Have a Poorly Controlled Disease

Barnea L.[a] · Mozer-Glassberg Y.[a] · Hojsak I.[b] · Hartman C.[a] · Shamir R.[a]

Author affiliations

## Abstract

***Background:*** Follow-up of celiac disease (CD) patients is recommended for gluten-free diet (GFD) adherence monitoring and complication detection. We recently showed that 35% of children with CD were lost to follow-up (LTFU). We aimed to characterize LTFU population, and thus identify compliance barriers to GFD and follow-up. ***Methods:*** 50 LTFU patients were investigated using a telephone questionnaire, regarding frequency of follow-up, serology testing, and adherence to GFD (using the validated Biagi score). Fifty two regular follow-up patients served as controls. ***Results:*** LTFU patients had poor adherence to GFD (average Biagi score of 2.0 ± 1.4) compared to controls (3.0 ± 1.0, $p < 0.001$). Only 22% of LTFU performed periodic celiac serology testing compared to 82% of controls ($p < 0.001$). LTFU had higher prevalence of positive celiac serology tests (50% compared to 25% of controls, $p = 0.01$). Fewer LTFU were National Celiac Association members (24%) compared with controls (44%, $p = 0.05$). Regression analysis showed positive relationships between LTFU and poor adherence to GFD ($R^2 = 0.26737$, $p = 0.001$), older age at diagnosis ($R^2 = 0.30046$, $p = 0.03$), and non-membership in a celiac association ($R^2 = 0.18591$, $p = 0.0001$). ***Conclusion:*** LTFU is associated with non-adherence to GFD and positive serology. Risk factors for LFTU should be identified and addressed in order to improve patient care.

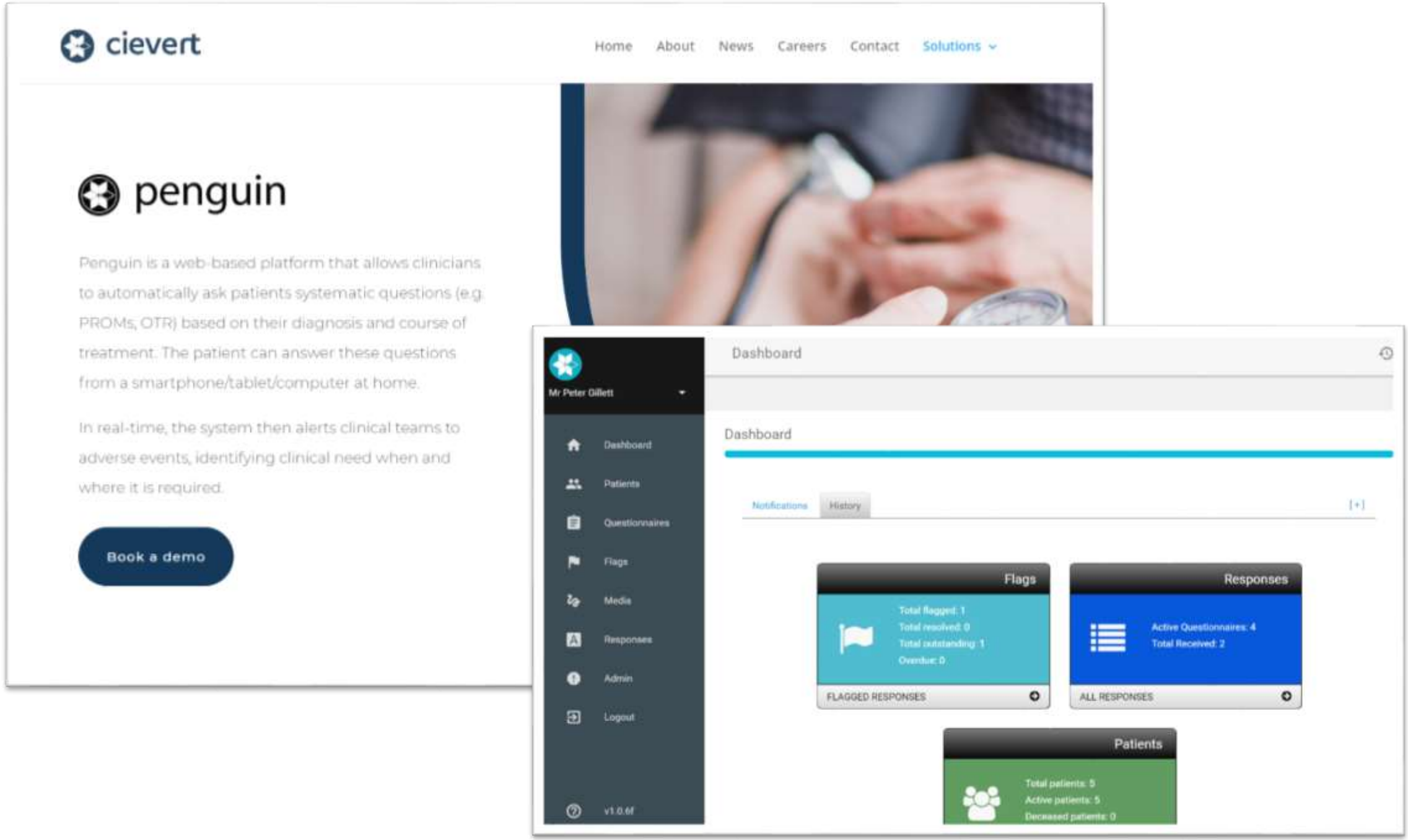
# Bringing it all together?

- Reimagination of ESPGHAN 2020 guidance
- BSPGHAN / CUK 2020…watch this space
- Educational material – video education – with people living gluten free
- ESPGHAN SIG
  - Incidence and prevalence across ESPGHAN, towards a helpful international view of practice
  - Optimal dietetic guidance
  - Management of children and young people – who and what level of support, pragmatism in investigative follow up…..
- Working together with adult colleagues….

# Solutions ? maybe things to ponder?

- Paediatrics traditionally F2F
- The role of a doctor – primary or the ‘go to’ for medical issues – and which doctor?
- The role of the expert dietitian and hubs / networks
  - Regional networks offering support
- With the current situation do we need to think differently?
  - Group clinics*
  - Video / telephone clinics – carbon footprint – save the planet !
  - Email
  - PIFU but with a way back if required

# Follow up, other ways of doing it and collaborative research…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Contact
Solutions
penguin
Penguin is a web-based platform that allows clinicians to automatically ask patients systematic questions (e.g. PROMs, OTR) based on their diagnosis and course of treatment. The patient can answer these questions from a smartphone/tablet/computer at home.
In real-time, the system then alerts clinical teams to adverse events, identifying clinical need when and where it is required.
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Mr Peter Gillett
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Questionnaires
Flags
Media
Responses
Admin
Logout
v1.0.6f
Dashboard
Dashboard
Notifications
History
Flags
Total flagged: 1
Total resolved: 0
Total outstanding: 1
Overdue: 0
FLAGGED RESPONSES
Responses
Active Questionnaires: 4
Total Received: 2
ALL RESPONSES
Patients
Total patients: 5
Active patients: 5
Deceased patients: 0

# Follow up?


## NHS Near Me?

new service which aims to provide consultations as close as possible to patients' homes: either at home or at a local NHS Near Me clinic.

### How do NHS Near Me appointments work?

**Patient at home**
- Uses computer with webcam, smartphone or tablet (own device)
- Needs a reliable internet connection

**Patient at local clinic**
- Patient does not have own video calling device at home
- Patient wants staff to help with call
- Clinical support is needed in the call (eg, a blood test)

Single point of entry website: **https://nhsh.scot/nhsnearme**

Receptionist appears on screen, greets patient and transfers to the clinical service

Each clinical service has its own virtual waiting area: consultant connects secure video call to patient

# The promotion of the dietitian in management and involvement in research…

# Repeating in 2020 – join us !

Original article

## Childhood coeliac disease diagnoses in Scotland 2009–2010: the SPSU project

Lois E White,[1] Elaine Bannerman,[1] Paraic McGrogan,[2] Dagmar Kastner-Cole,[3] Elsie Carnegie,[4] Peter M Gillett[5]

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[2]Department of Paediatric Gastroenterology, RHSC, Glasgow, UK
[3]Department of Paediatrics, Ninewells Hospital and Medical School, Dundee, UK
[4]Department of Paediatric Dietetics, RACH, Aberdeen
[5]Department of Paediatric Gastroenterology, RHSC, Edinburgh, UK

**ABSTRACT**

**Objectives** To establish the incidence of childhood coeliac disease (CD) in Scotland between 1 September 2009 and 31 August 2010, to determine clinical features at presentation and reasons for diagnosis, and to identify any differences in incidence and practice between regions.

**Design** Prospective data collection through the Scottish Paediatric Surveillance Unit (SPSU). Strategic contacts in each tertiary gastrointestinal region (East, West and North) were emailed monthly to report new cases of CD (<16 years). A clinical questionnaire was completed for each case. Additionally, regional laboratories were asked to report the number of diagnostic antibody tests for CD

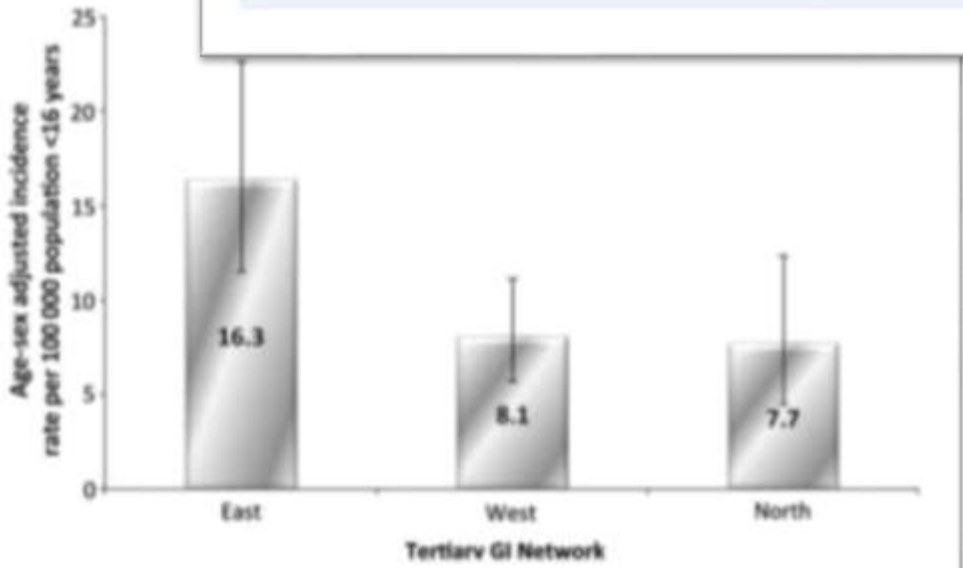
Corres

### What is already known on this topic

- Just two countries to da
  on 'real world' incidenc
  coeliac disease, but UK
- Sweden has demonstrat
  case ascertainment nati
  variation was not obser
- Increased detection of c
  years is assumed to be
  education, awareness ar
  'at risk' groups.

### What this study adds

- The yearly incidence of paediatric coeliac disease in Scotland is higher than that previously recorded in smaller Scottish retrospective studies.
- Significant geographical differences exist, even within a genetically stable population, and may relate to the threshold to test—a proxy for awareness?
- Additional exogenous factors may partly explain the variation observed, highlighting the need for a national longitudinal prospective study from birth.




SSPGHAN

‘Development and testing of an intervention to improve Gluten Free Diet Adherence, Health Related Quality of Life, Patient Reported Outcome Measures, Nutritional Adequacy and Readiness for Transition to Adult Health Care in Young People with Coeliac Disease’

Goversby@qmu.ac.uk

# What do you find out what's important to CD patients in a pandemic, let alone post Brexit?

**Information and support**

- Coeliac disease and coronavirus (COVID-19) →
- Coeliac disease and coronavirus (COVID-19) FAQs
- Your gluten free hub
- Living gluten free
- Coeliac disease
- Competitions
- Living gluten free FAQs

# Coeliac disease and coronavirus (COVID-19)

New governmen roups now includes criteria with coeliac disease.

We should all be ng measures, but a especially stringent in follc ancing aims to reduce s een people. This is different olation for people with corc ch as a persistent cougl

## What is the risk for adults with coeliac disease?

As coronavirus is a new illness, there is no specific research on the risk to people with coeliac disease

# 25

# Pneumococcal



**Pneumococcal meningitis** **NOTIFIABLE**

## The disease

Pneumococcal disease is the term used to describe infections caused by the bacterium *Streptococcus pneumoniae* (also known as the pneumococcus).



| Clinical risk group | Examples (decision based on clinical judgement) |
|---|---|
| Asplenia or dysfunction of the spleen | This also includes conditions that may lead to splenic dysfunc homozygous sickle cell disease and coeliac syndrome. |



# 7

# Immunisation of individuals with underlying medical conditions



## Introduction

Some medical conditions increase the risk of complications from infectious diseases, and children and adults with such conditions should be immunised as a matter of priority. These groups may also require additional vaccinations or additional doses of vaccines to provide adequate protection.

## Asplenia (absent or dysfunctional spleen)

Individuals with an absent or dysfunctional spleen are at increased risk of severe infection, particularly those caused by encapsulated bacteria. The commonest organism associated with severe infection in these patients is the pneumococcus (*Streptococcus pneumoniae*) but other organisms also appear to be a more common cause of overwhelming infection in these patients, including *Haemophilus influenzae* type b (Hib) and *Neisseria meningitidis*. In addition to surgical splenectomy, certain conditions, such as sickle cell disease and other haemoglobinopathies, are accompanied by functional hyposplenism. Around 30% of adults with coeliac disease have defective splenic function.

All patients with absent or dysfunctional spleens should be fully vaccinated according to the national schedule. Because of the high risk of overwhelming infection, additional vaccination against pneumococcal infection is recommended for all individuals who have or are at high risk of developing splenic dysfunction in the future, including those with coeliac disease and sickle cell disease (see Chapter 25: Pneumococcal). Given the high risk of secondary bacterial infection, annual influenza vaccine is also recommended for these patients. Data on long-term antibody levels in asplenic patients are limited. Additional booster doses of pneumococcal polysaccharide vaccine (PPV) are recommended every five years for this patient group.

Additional vaccination against meningococcal groups A, C, W, Y and B should be offered to patients with absent or dysfunctional spleens, at appropriate opportunities. Hyposplenism in coeliac disease is uncommon in children, and the prevalence correlates with the duration of exposure to gluten (Di Sabatino A, 2013). Therefore, patients diagnosed with coeliac disease early in life and well managed are unlikely to require additional doses of these vaccines beyond those given in the routine immunisation schedule. Only those with known splenic dysfunction should receive additional vaccination against meningococcal infection (see Chapter 22: Meningococcal). Although additional vaccination against *Haemophilus influenzae* type b (Hib) used to be recommended for asplenic patients, current control of Hib is excellent because of a long-standing successful vaccination programme in children and the risk of Hib disease is extremely low. Therefore, additional Hib vaccination is no longer recommended.

# Coeliac UK Awareness Week 2020

- Save the date: 11 – 17 May 2020
- Focus on diagnosis of children aged 5 – 11 years
- Update to online assessment isitcoeliacdisease.org.uk
- Epidemiology research
  - Preliminary results by May

# Questions and comments?

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