coeliac uk
live well gluten free

# COELIAC UK'S RESEARCH CONFERENCE 2020

Coeliac disease; from potential to refractory and everything in between

Friday, 20 March 2020

# COELIAC DISEASE; POTENTIAL TO REFRACTORY AND EVERYTHING IN BETWEEN

## ROYAL COLLEGE OF GENERAL PRACTITIONERS

30 Euston Square, London NW1 2FB

Chaired by Professor David Sanders, Royal Hallamshire Hospital and University of Sheffield

10.00 Arrival and networking with refreshments

10.30 Coeliac UK welcome – Chair of Coeliac UK's RSB, Prof Alan Perkins

**Session 1**

10.35 A GP's perspective
Dr Geraint Preest GP

11.00 What is the optimum strategy for identifying adults and children with coeliac disease? An evidence synthesis approach
Dr Penny Whiting

11.25 Potential coeliac disease – Doctor, have I got it or not?
Dr Jeremy Woodward

11.50 Negative blood test; to refer or not to refer? Is that the question?
Prof Federico Biagi

12.15 **Lunch and poster exhibition**

**Session 2**

13.30 Is modern wheat really 'frankenwheat'?
Prof Katharina Scherf

13.55 Hyposplenism and risk of infection
Prof Jonas Ludvigsson

14.20 2020 Vision: a clearer view for children and young people
Dr Peter Gillett

14.45 **Break – refreshments**

**Session 3**

15.05 Persisting symptoms, poly diagnoses, personalised diet – Houston, we have a problem!
Nick Trott RD

15.30 Will the treatment always be just a gluten free diet? What's on the horizon?
Prof Ludvig Sollid

15.55 Refractory coeliac disease – Doctor, should I be worried?
Dr Jeremy Woodward

16.20 Chair's closing remarks and presentation of poster prize

16.25 CLOSE

This event has been kindly sponsored by Dr Schär and Thermo Fisher Scientific and supported by Eat Real.

Dr Schär

ThermoFisher SCIENTIFIC

## PROF ALAN PERKINS

Chair of Coeliac UK's Research Strategy Board

### Welcome

As Chair of Coeliac UK's Research Strategy Board, I would like to welcome you to the 2020 Research Conference. We once again have an excellent programme of presentations and posters, bringing you the very best of research in coeliac disease and gluten related science.

In our 50th anniversary year, 2018, we announced a top ten list of research priorities and since then we have secured over £1M in support of new research into diagnostics, improved long term management of coeliac disease and improved ingredients for better gluten free bread. Yesterday we held a science workshop bringing experts in basic science research to identify key projects that will help us find answers in support of our research priorities. These projects will provide a platform for raising further funds for research.

This conference provides a unique opportunity for clinical and scientific interaction and networking. I hope you have an interesting, informative and enjoyable day.



## PROF DAVID SANDERS

Consultant Gastroenterologist, Royal Hallamshire Hospital, and Professor of Gastroenterology, University of Sheffield, Sheffield UK

Professor David S Sanders is a Professor of Gastroenterology and a Consultant Gastroenterologist at the Royal Hallamshire Hospital & the University of Sheffield. He has published >400 peer reviewed papers (H-score > 60). He is internationally recognised for his work in coeliac disease.

He has received a number of research awards: European Rising Star Award (2010), Cuthbertson Medal (2011) and Silver Medal in 2017 (the latter two awards from the UK Nutrition Society), Swedish Gastroenterology Society Bengt Ihre Medal (2017) and most recently the BSG Hopkins prize for Endoscopy (2019).

He is the current Chair of the Coeliac UK Health Advisory Council & Board member of the European Society for study of Coeliac Disease (ESsCD). Previous roles include President of the International Society for the Study of Celiac Disease 2016-2019 (ISSCD). The Sheffield Unit has recently been recognised as the Rare Disease Collaborative Network for refractory coeliac disease (NHS England).

**www.profdavidsanders.co.uk**

## DR GERAINT PREEST

General Practitioner, Pencoed and Llanharan Medical Centres, South Wales

### Biography

For the past 20 years, Geraint has been a full time GP Principal at Pencoed and Llanharan Medical Centres in South Wales and Primary Care Lead for BMJ OnExamination - the British Medical Journal's flagship online revision resource for doctors sitting postgraduate exams.

Geraint has been a pioneer in the use of the internet to inform patients and educate doctors, having developed one of the very first GP practice and training websites in the country (and winning a national award in the process). He has worked with national and international organisations to develop online learning, needs assessments and testing for primary care clinicians at all stages of their career in the UK, Middle East and Southern Hemisphere.

Geraint is an external examiner for MSc and Diploma courses allied to medicine at the University of South Wales. Geraint is a member of Coeliac UK's Health Advisory Council and a Fellow of the Royal College of General Practitioners.

He is married with four grown up children, one of whom has coeliac disease. Geraint is a lifelong keen cyclist and an appalling, but enthusiastic, guitar player.



## A GP'S PERSPECTIVE

POSTPONED

General practice in 2020 is busier than ever. Finding and managing patients with coeliac disease is a challenge in the primary care setting, particularly when our knowledge of so many different conditions is quickly evolving.

In this brief talk for GPs, Geraint starts with a short historical perspective from 1920 and brings this up to date with a video of patients' experiences. He utilises feedback from doctors and patients via social media, along with his own experience of medical education - and as a father of a daughter with coeliac disease - to bring together a few key points to help GPs diagnose and manage patients who may have coeliac disease.

## DR PENNY WHITING

Associate Professor of Clinical Epidemiology, University of Bristol, Bristol, UK

### Biography

Dr Penny Whiting is Associate Professor at the University of Bristol where she leads the MSc in Epidemiology. She has a BA (Hons) in Human Sciences from the University of Oxford, an MSc in Communicable Disease Epidemiology from the London School of Hygiene and Tropical Medicine, and a PhD in Epidemiology from the University of Amsterdam.

Penny has 20 years' experience in the conduct of systematic reviews across a broad range of topics including both intervention, prognostic and diagnostic test accuracy studies.

During this time, she has also conducted methodological research related to systematic reviews covering all aspects of the review process from literature searching to presentation of results.

She has a particular interest in diagnosis and sources of bias in test accuracy studies. She has expertise in quality assessment, having lead the development of three risk of bias tools, she has also contributed to the development of a further three tools.

Penny also has experience of leading projects based on routine data, including Clinical Practice Research Datalink (CPRD) and of prediction modelling studies through her involvement in the development of the PROBAST tool.

Her son was diagnosed with coeliac disease in May 2018. During his diagnostic workup, she found that there was no robust systematic review of the evidence to help decide whether or not he needed a biopsy or whether to start him on a gluten free diet straight away. This prompted her research interest in coeliac disease.



## WHAT IS THE OPTIMUM STRATEGY FOR IDENTIFYING ADULTS AND CHILDREN WITH COELIAC DISEASE? AN EVIDENCE SYNTHESIS APPROACH

POSTPONED

Guidelines recommend that adults and children "at high risk" of coeliac disease (CD) should be offered testing. However, it is not clear which groups are at sufficiently high risk to justify routine testing, which symptoms should prompt testing, which tests should be offered, and whether confirmatory biopsy is necessary. We are working on an evidence synthesis to address these issues:

### 1. Systematic review on the accuracy of tests for CD

Studies that have evaluated the accuracy of serological tests for the diagnosis of CD were eligible. We have estimated summary measures of accuracy for different serological tests.

### 2. Systematic review of the predictive ability of potential diagnostic indicators for CD

Studies that estimate the association between a potential diagnostic indicator for CD (eg type 1 diabetes, specific symptom) and a confirmed diagnosis of CD will be eligible. Meta-analysis will be used to estimate probability of CD for each indicator.

### 3. Routine data analysis to developing prediction models

We will use routine data to develop prediction models based on indicators identified from the systematic review. We will produce estimates of the probability of CD diagnosis for each combination of indicators available.

### 4. Collaborative work with patients to establish diagnostic thresholds

We will hold focus groups and an online survey with people at risk of CD to identify how confident they want to be in their diagnosis before starting a gluten free diet or accepting a biopsy.

### 5. Cost-effectiveness analysis

We will combine information from the first four components of the projects with data on costs to estimate the cost effectiveness of CD testing of patients.

## DR JEREMY WOODWARD

Consultant Gastroenterologist,
Addenbrooke's Hospital,
Cambridge, UK

### Biography

Dr Jeremy Woodward was appointed as Consultant Gastroenterologist in Addenbrooke's Hospital, Cambridge in 2002.

A PhD in cellular immunology combined with his interest in nutrition led to a career that includes the UK national intestinal and multivisceral transplant service in Cambridge and the recent establishment of Addenbrooke's as one of the two UK centres for refractory coeliac disease.

He leads the Department of Gastroenterology in Cambridge where he has developed an integrated clinical artificial service combining innovative practices in enteral feeding access and parenteral nutrition.

He introduced the Cambridge Coeliac pathway in 2012 and is a keen proponent of patient empowerment through education in this condition.

Jeremy teaches undergraduate physiology and lectures on gastrointestinal pathology and nutrition in Cambridge University Medical School where he is also a Communications Skills Facilitator. He is an Associate Editor of BMJ Nutrition, Prevention & Health.



## POTENTIAL COELIAC DISEASE – DOCTOR, HAVE I GOT IT OR NOT?

WATCH ONLINE

HCP? Watch here for CPD questions.

The diagnosis of coeliac disease is straightforward when indicative antibodies are present on blood tests and mucosal biopsies of the small intestine show characteristic features – regardless of the presence or absence of symptoms.

However, what does it mean when the blood test is positive and the biopsies are entirely normal – or show minor features?

In this session, we will address the difficulties of a diagnosis of 'potential' coeliac disease, how frequently it occurs, its natural history and (hopefully) develop a practical algorithm for the appropriate clinical management of this situation.

## REFRACTORY COELIAC DISEASE – DOCTOR, SHOULD I BE WORRIED?

WATCH ONLINE

HCP? Watch here for CPD questions.

Unlike other European countries where significant advances have been made in our understanding of the progression of coeliac disease to lymphoma, the UK has lagged behind in establishing a national refractory coeliac disease service.

The National Refractory Coeliac Disease Collaborative Network was initiated in 2019 with centres in Sheffield and Cambridge. As well as aiming to define treatment pathways, enrol patients in appropriate therapeutic trials and raise awareness of the condition amongst clinicians, the establishment of a national registry will help to identify the natural history and demographics of this rare condition in the UK.

With increasing patient awareness through Coeliac UK, more patients are now being identified but there is a risk of causing harm through increased anxiety. Enteropathy Associated Lymphoma (EATL) remains extremely rare and patients need easy access to appropriate information and expertise when concerns arise.

**www.coeliac.org.uk/RCD**

## PROF FEDERICO BIAGI

Consultant Gastroenterologist, Coeliac Centre/1st Department of Internal Medicine, University of Pavia, Italy

### Biography

Professor Federico Biagi graduated in Medicine in December 1990 at the University of Bologna. In 1994 he was awarded a diploma as a Specialist in Geriatrics and in 2004 in Gastroenterology. From January 1997 to December 1998 he worked at King's College London, UK.

He joined the University of Pavia in 1999 and he is currently an Associate Professor of Gastroenterology. He has published >100 peer reviewed papers (H-score 32).

He is interested in small bowel diseases, particularly in coeliac disease and its complications, Whipple's disease, and other rare enteropathies characterised by subtotal villous atrophy unrelated to gluten ingestion.



## NEGATIVE BLOOD TEST; TO REFER OR NOT TO REFER? IS THAT THE QUESTION?

WATCH ONLINE

HCP? Watch here for CPD questions.

Duodenal villous atrophy is mainly related to coeliac disease (CD), whose diagnosis is based on positive endomysial/tissue transglutaminase antibodies while on a gluten containing diet.

Although this is the case for the vast majority of patients, CD can also occur without coeliac antibodies and is defined "seronegative CD". However, since villous atrophy can occur also in other conditions unrelated to gluten consumption, the diagnosis of these forms of villous atrophy is a challenging one.

We recently reviewed the data of all n=274 patients with villous atrophy diagnosed in Pavia. A seronegative form of villous atrophy (SNVA) was found in n=14 patients (5.1%): n=5 suffered from common variable immunodeficiency, n=3 dermatitis herpetiformis, n=2 IgA deficiency associated with CD, n=1 abdominal lymphoma, n=1 idiopathic villous atrophy, n=1 olmesartan associated enteropathy, n=1 true seronegative CD.

The remaining n=260 were affected by "seropositive CD". Mortality was 6.0 deaths per 100 persons/year in patients with SNVA, while only 0.2 deaths per 100 persons/year occurred in patients with coeliac disease. Although patients with SNVA are rare, these forms of villous atrophy identify specific causes that must be recognised because of a very high mortality.

## PROF KATHARINA SCHERF

Department of Bioactive and Functional Food Chemistry, Institute of Applied Biosciences, Karlsruhe Institute of Technology (KIT), Karlsruhe, Germany

### Biography

Prof Katharina Scherf leads the Department of Bioactive and Functional Food Chemistry at the Institute of Applied Biosciences, Karlsruhe Institute of Technology (KIT), Karlsruhe, Germany. Together with her team, she studies the complex interplay between structure, functionality and bioactivity of food biopolymers in a multidisciplinary way and uses these fundamental insights to improve food security, food quality and food safety.

One of her main research interests is analytical, immunological and biochemical aspects of coeliac disease, non-coeliac gluten sensitivity and wheat allergy. Having studied food chemistry at the Technical University of Munich (TUM), Katharina obtained her PhD degree from the TUM. From 2012 to 2019 she worked at the Leibniz-Institute for Food Systems Biology at the Technical University of Munich and has led the research group Functional Biopolymer Chemistry since 2017.

Her research was awarded with several prestigious scientific prizes, including the Research Award of the German Coeliac Society (2019 and 2014), the Young Scientist Research Award of the Cereals & Grains Association (2018) and the Gerhard-Billek-Prize of the German Chemical Society (2015).



## IS MODERN WHEAT REALLY 'FRANKENWHEAT'?

WATCH ONLINE

HCP? Watch here for CPD questions.

Next to maize and rice, wheat is one of the most important crops for human nutrition, but a growing number of individuals are affected by wheat related disorders. In search for the underlying causes, one hypothesis is that wheat breeding to increase grain yield and plant resistance to abiotic and biotic stress factors may have inadvertently increased its immunoreactive potential.

To verify or refute this hypothesis, we studied the five most widely grown German wheat cultivars per decade from 1890 until 2010. The 60 selected cultivars were grown in Gatersleben in the years 2015, 2016 and 2017 and agronomic characteristics as well as protein content and composition were analysed.

Wheat protein contents and compositions were highly variable over all 60 cultivars irrespective of the harvest year. The harvest year had a greater influence on protein contents and compositions than the cultivar, with significant interaction between both factors. The median of five cultivars per decade showed no clear change for albumins/globulins and gluten over the 100 years, but a slight decreasing trend for contents of gliadins and crude protein and a slight increasing trend for glutenins.

From our study, we conclude that wheat breeding did contribute to changes in gluten protein composition, but whether this may have an effect on the immunoreactivity of wheat remains unclear due to the significant environmental effect on wheat protein expression. Further work will focus on studying known specific coeliac disease active and other immunoreactive protein sequences.

## PROF JONAS LUDVIGSSON

Karolinska Institutet and
Paediatrician at Örebro University
Hospital, Sweden

### Biography

Dr Ludvigsson is one of the world's leading experts in gastrointestinal epidemiology and former Chair of the Swedish Society of Epidemiology (2011-14). He is a professor of Clinical Epidemiology at the Karolinska Institutet, Sweden, but also holds positions as Adjunct Professor in Medicine at Columbia University (US), and Honorary Professor at Nottingham University (UK).

Ludvigsson was the lead author of the latest British Society of Gastroenterology guidelines on diagnosis and management of adult coeliac disease, published in the journal, Gut in 2014. He also initiated the so called Oslo classification of coeliac disease. He has so far published more than 200 papers about coeliac disease.



## HYPOSPLENISM AND RISK OF INFECTION

POSTPONED

Coeliac disease has been linked to a number of complications.

In this talk, Prof Ludvigsson will first give an overview of mortality in general in patients with coeliac disease, and then focus on the risk of infections.

He will also comment on vaccinations in coeliac disease.

## DR PETER GILLETT

Consultant Paediatric Gastroenterologist, Royal Hospital for Sick Children, Edinburgh

### Biography

Peter Gillett is a Consultant Gastroenterologist at the Royal Hospital for Sick Children, Edinburgh, Scotland since 2001. His paediatric training was in Newcastle and Edinburgh and his GI fellowship at the Children's Hospital in Vancouver. His interests are coeliac disease, upper GI and small bowel disorders, endoscopy, functional GI disorders, constipation and its improved management, informatics, education and engagement across multi-disciplinary teams with patients and families, to make holistic management more consistent and responsive.

He helped set up the SE Scotland regional paediatric coeliac service in 2001, is a member of Coeliac UK's Health Advisory Council, providing support to the charity for over 10 years. He was a member of the Scottish Government Group, developing the Gluten Free Food Service and was a member of the NICE Coeliac Disease NG20 group. He chairs the BSPGHAN coeliac disease working group and co-leads the Scottish Government new coeliac strategy which aims to provide optimal diagnostics and ongoing management for patients with CD as part of the Modern Outpatient Programme, with dietitians playing a key role in primary management in all age groups.

He is a member of the ESPGHAN Coeliac SiG group and is a co-author of the new ESPGHAN 2019/20 guidelines. The group's key new strategies are including ongoing pragmatic/evidence based guidance to reduce unnecessary testing and enabling self-care. Coeliac UK's Awareness Week 2020, focusing on children, will prove to be an exciting one for 'coeliac-ologists'.



## 2020 VISION: A CLEARER VIEW FOR CHILDREN AND YOUNG PEOPLE

WATCH ONLINE

HCP? Watch here for CPD questions.

In this presentation, Dr Gillett will provide an update of the new ESPGHAN 2020 guidelines, the latest information on screening strategies using DQ typing, the approach to management in children, how we do it differently and how we should be doing it differently, aiming to be more personalised and pragmatic.

He'll also discuss how guidelines can be misinterpreted, highlighting the need for these to be managed better.

He will share work from Scotland in children and adult management of coeliac disease, putting dietitians at the forefront of the 'coeliac service' and how networks can and should work together to provide evidence; the suspicion is it's not quite there yet!

With Coeliac UK's Awareness Week this year focusing on children, 2020 heralds a great year for Dr Gillett and his paediatric GI and dietetic colleagues.

There are also some challenges; increased prevalence of anxiety and psychological issues, concern in view of recent evidence that health related inequalities have resulted in greater morbidity and reduced quality of life, whether NHS policies might reflect soon on adherence and ultimately morbidity and finally, how we empower young people and those leaving home to keep managing their condition optimally.

## NICK TROTT RD

Gastroenterology Dietitian, Royal Hallamshire Hospital, Sheffield, UK

### Biography

Nick Trott studied at the University of Wales Institute, Cardiff where he obtained an Honours degree in Nutrition and Dietetics and in 2017 he completed a Post Graduate Master's degree in Clinical Research.

Nick has worked in a variety of clinical areas within the NHS including Critical Care, Oncology and Haematology.

Currently Nick works as a Gastroenterology Dietitian, covering the specialist coeliac clinic at the Royal Hallamshire Hospital, Sheffield.

His areas of particular clinical interest include coeliac disease, gluten ataxia, non-coeliac wheat sensitivity and the Low FODMAPs approach to functional bowel disorders.

Nick is a member of Coeliac UK's Health Advisory Network as well as a Board member of the International Society for the Study of Celiac Disease (ISSCD).

In 2016 Nick was presented with the Complete Nutrition Coeliac Professional of the year award.



## PERSISTING SYMPTOMS, POLY DIAGNOSES AND PERSONALISED DIET – HOUSTON WE HAVE A PROBLEM!

WATCH ONLINE

HCP? Watch here for CPD questions.

International clinical practice guidelines for the management and treatment of people with coeliac disease all emphasise the central role of the dietitian in their management and follow on care. Research also indicates that patients have a preference for dietetic follow up.

Despite this recognition, recent surveys have highlighted the lack of dietetic support both at diagnosis and in the follow up of people with coeliac disease.

In reality many patients have no access to any dietetic support.

Unfortunately, the lack of specialist dietitians has been coupled with a rise in the incidence of patients being referred with increasingly complex nutritional needs. The majority of these cases could be broadly categorised into two groups:

Those who continue to have, or re-present, with persistent ongoing symptoms despite apparent adherence to a gluten free diet (GFD). The second category includes patients who are referred for a GFD with (or develop) a comorbidity that requires additional dietary intervention and management; such as diabetes, food allergy and eating disorders.

This talk will explore these issues with reference to the current literature and clinical examples to generate debate on how we can manage such cases within the current level of dietetic provision.

## PROF LUDVIG SOLLID

KG Jebsen Coeliac Disease Research Centre and Department of Immunology, University of Oslo and Oslo University Hospital, Oslo, Norway

### Biography

Ludvig M. Sollid (MD, PhD) is a Professor at the University of Oslo and a Senior Consultant at the Oslo University Hospital - Rikshospitalet. He is also the Director of the KG Jebsen Coeliac Disease Research Centre and UiO FOCIS Centre of Excellence.

His research interests are focused around genetics and immunology of autoimmune diseases. His group has made important contributions to the understanding of the molecular basis of coeliac disease, in particular the role of HLA genes, the existence of gluten reactive (HLA-DQ restricted) T cells in the coeliac intestinal lesion, and the functional involvement of the primary autoantigen, transglutaminase 2.

His group is currently working on the characterisation of the antigen receptors of T cells and B cells that recognise the coeliac disease relevant antigens gluten and transglutaminase 2.



## WILL THE TREATMENT ALWAYS BE JUST A GLUTEN FREE DIET? WHAT'S ON THE HORIZON?

WATCH ONLINE

HCP? Watch here for CPD questions.

Our insight into the disease mechanism of coeliac disease has made huge advances in the last couple of decades. This progress has paved the road for development of new therapies as alternatives to the gluten free diet.

Prof Sollid will review the rationales behind the new therapeutic approaches. He will also give an overview of the state of play in coeliac disease drug development.

Currently, patient reported outcomes are considered the most important endpoints for evaluation of clinical trials.

Given his detailed knowledge of the pathogenesis of coeliac disease, he will make the case that in the future, monitoring of drug effects by good surrogate markers might be more productive for drug evaluation.

## THANK YOU TO OUR SPONSORS

Dr Schär

ThermoFisher SCIENTIFIC

## AND OUR SUPPORTER

Eat Real® Healthier Snacking




## POSTER COMPETITION

Entries to the Coeliac UK Research Conference 2020 poster competition are now closed

There is a £500 prize for the best poster. The lead author may use the prize money to help pay towards attendance at an international event to increase dissemination of their research.

**£500 PRIZE FOR THE BEST POSTER**

# THE SOCIODEMOGRAPHIC, LIFESTYLE AND HEALTH RELATED CHARACTERISTICS OF INDIVIDUALS WITH COELIAC DISEASE IN THE UK BIOBANK: A LARGE POPULATION BASED COHORT


## Authors
Littlejohns T[1], Tong T, Bradbury K, Conroy M, Allen N, Soilleux E

## Institution
University of Oxford, Oxford[1]



## Abstract

### Introduction
Coeliac disease (CD) is associated with a range of non-gastrointestinal conditions and complications throughout the life course. However, much of the evidence base is informed by medical or population registry records, as there is a lack of large, detailed, prospective population based cohort studies which contain information on individuals diagnosed with CD. An exception is the UK Biobank (UKB), a large cohort which contains enough information to identify people with CD and is well set up to explore exposure outcome associations. Here, we investigate CD in association with a range of characteristics in UKB, a cohort of half a million middle aged women and men.

### Methods
At baseline, participants provided lifestyle and sociodemographic information through a touchscreen questionnaire and verbal interview, underwent a physical examination and provided non-fasting blood samples. Haematological assays and genome wide genotyping were performed on all samples. CD was ascertained through either self report at baseline or a hospital inpatient diagnosis before baseline. Multivariate multinomial logistic regression models were used to investigate the association between CD and a range of lifestyle, sociodemographic and health related characteristics.

### Results
Of 502,506 participants, 2,267 (0.5%) participants had CD at baseline. Of these, 153 (6.7%) participants without human leucocyte antigen DQ2/8 haplotypes, a necessary cause of CD, were excluded. Compared to non-CD participants, those with CD were more likely to be older, women, of white ethnic background, have fewer educational qualifications, non-smokers and had lower alcohol intake, physical activity levels and body mass index. There was no association between CD and area level deprivation. When investigating the haematological data, CD was associated with a higher likelihood of anaemia (Relative Risk Ratio = 1.61, 95% Confidence Interval 1.36 - 1.91), with 7% and 4.3% of CD and non-CD participants having anaemia, respectively. The associations remained similar after excluding participants who reported using vitamin B, folate, iron and/or multivitamin supplementation. Only 45% of CD participants with anaemia reported using at least one of these forms of supplementation. Age and sex adjusted means with other haematological parameters are provided in **Table 1**.

**Table 1** Age and sex adjusted means of haematological parameters by coeliac disease status

| Haematological parameter | No coeliac disease Mean (95% CI) | Coeliac disease Mean (95% CI) |
|---|---|---|
| Red blood cell count | 4.52 (4.52-4.52) | 4.46 (4.44-4.47) |
| Haemoglobin | 141.8 (141.7-141.8) | 140.2 (139.8-140.7) |
| Reticulocyte, % | 1.35 (1.35-1.35) | 1.21 (1.17-1.25) |
| Immature reticulocyte fraction | 0.29 (0.29-0.29) | 0.28 (0.28-0.28) |
| White blood cell count | 6.89 (6.88-6.89) | 6.85 (6.76-6.95) |
| Basophils | 0.039 (0.039-0.039) | 0.041 (0.039-0.043) |
| Eosinophils | 0.17 (0.17-0.17) | 0.19 (0.19-0.20) |
| Lymphocytes | 1.97 (1.96-1.97) | 1.93 (1.88-1.98) |
| Monocytes | 0.48 (0.47-0.48) | 0.55 (0.54-0.56) |
| Neutrophils | 4.23 (4.22-4.23) | 4.14 (4.08-4.20) |
| Platelet count | 253.0 (252.8-253.1) | 258.3 (255.8-260.9) |
| Platelet volume | 9.33 (9.33-9.34) | 9.37 (9.33-9.42) |

### Discussion
These results provide an insight into the characteristics of participants with CD in the UKB. Although causality cannot be inferred, certain associations might be a consequence of having CD, for example consuming less alcohol, not smoking and exercising less. Anaemia, which is typically treatable, was significantly higher in those with CD. In the UKB, further research investigating CD in association with incident disease, whilst considering the role of these characteristics, is warranted.

# DUODENAL BULB BIOPSIES INCREASE THE DETECTION OF VILLOUS ATROPHY WHEN ASSESSING ADHERENCE IN COELIAC DISEASE


## Authors
Coleman S[1], Rej A, Baggus E, Marks L, Lau M, Sanders D

## Institution
Academic Unit of Gastroenterology, Royal Hallamshire Hospital, Sheffield Teaching Hospital NHS Foundation Trust, Sheffield[1]



## Abstract

### Introduction
Duodenal bulb biopsies have been demonstrated to increase the diagnostic rate of newly diagnosed coeliac disease (CD) by 10%. The aim of this study was to assess the utility of duodenal bulb biopsies for the assessment of established CD for the first time in the literature.

### Methods
A prospective study of n=375 established CD patients (mean age 51.0 years; 69.9% female) who underwent endoscopy for assessment of persisting symptoms or remission at Sheffield Teaching Hospitals was performed, between 2013 - 2019. Quadrant biopsies were taken from D2 in addition to duodenal bulb biopsies.

### Results
Sixty three percent of patients (n=237) had ongoing villous atrophy (VA). **Table 1**, outlines the histological appearance of D1 and D2 biopsies. Among those with VA (n=237), this was confined to D1 in 10.2% (n=14) and to D2 in 8.0% (n=11). There was no significant difference in number of patients with VA confined to D1 versus D2 (p=0.69). There was no difference in age (p=0.18) or gender (p=0.10) between patients with VA confined to D1 compared to the remaining cohort. As time from diagnosis increased, the proportion of individuals with complete duodenal mucosal healing (defined as Marsh 0 in both D1 and D2 biopsies) also increased. Timings of biopsies were available for n=225 patients; two years after diagnosis 4.9% (n=11) of patients had complete healing, increasing to 10.7% (n=24) after 4 years, 17.3% (n=39) after 6 years, 20.9% (n=47) after 8 years and 24.0% (n = 54) after ten years. A further 11.1% (n=25) of patients achieved complete healing after more than 10 years since diagnosis, but 64.8% (n=146) did not have complete mucosal healing at the end of the study.


**Table 1** Histological appearance of D1 and D2 biopsies

| | | D1 histology | | |
|---|---|---|---|---|
| | | Marsh 0 (normal) % (n) | Marsh 1-2 % (n) | Marsh 3 a-c % (n) |
| D2 histology | Marsh 0 (normal) | 36.8 (138) | 3.2 (12) | 0.5 (2) |
| | Marsh 1-2 | 5.6 (21) | 17.9 (67) | 3.2 (12) |
| | Marsh 3 a-c | 1.3 (5) | 1.6 (6) | 29.9 (112) |

### Discussion
Duodenal bulb biopsies increased the detection of VA by 10% in established CD, highlighting the importance of bulbar biopsies in established CD for the first time in the literature.

# DEVELOPMENT OF AN ARTIFICIAL INTELLIGENCE SOLUTION FOR DIAGNOSIS AND ASSESSMENT OF SEVERITY OF PATHOLOGY IN SMALL INTESTINAL BIOPSIES IN SUSPECTED OR KNOWN COELIAC DISEASE


## Authors
Schreiber B, Sharma A, Crook O, Schönlieb CB, Soilleux E[1]

## Institution
Department of Pathology, University of Cambridge[1]



## Abstract

**Introduction**
The UK prevalence of coeliac disease is increasing and as few as 1/9 cases may be detected. Average time from symptoms to diagnosis is 13 years. Assessing whether a patient has coeliac disease (CD), or features of gluten exposure in a clinical trial, relies primarily on “gold standard” small intestinal biopsy examination by a pathologist; an unavoidably subjective process with poor inter-observer concordance (in up to 25% cases), variable concordance with serology and a high rate of “equivocal” biopsies. There is a clear unmet need for a more sensitive, objective and reproducible test.

**Methods**
Based on histopathological, serological and other laboratory criteria, we assembled a carefully clinicopathologically annotated, high resolution cohort of digitised images of n=500 small intestinal biopsy samples, n=250 CD of at least Marsh grade 3a, n=200 normal, n=50 from the intermediate grey zone between CD and normal. Informed by data from our recent pilot study, we included a haematoxylin and eosin stained image, a CD8 immunostained image and a mib-1 (proliferation marker) immunostained image. In order to minimise costs, biopsies from three separate patients were stained and scanned per glass microscope slide.

**Results**
As a first step towards developing an artificial intelligence (AI) solution for CD diagnosis, we developed colour thresholding followed by Sobel edge detection as an automated methodology for separating the three different patient biopsies per slide. The individual 3-5 tissue fragments per patient biopsy were similarly separated, giving a total set of >1500 digital images suitable for algorithm training. As one of the major features impacting upon diagnosis is poor biopsy orientation, we assigned all images an orientation score on a three point scale. We then investigated various methods for the identification of lymphocytes within samples, concluding that a k-means algorithm combined with a Gaussian mixture method provides a powerful methodology. We also concluded that lymphocyte identification needs to be undertaken prior to spatial segmentation of the image, because of the importance of lymphocyte position for diagnosis. Taking a broader range of features into account, neural network based approaches have given the most promising results.

**Discussion**
We have assembled a training and testing dataset and a multi disciplinary team to undertake this timely project; building on contemporary progress in neural networks. We intend to use convolutional neural networks to produce a classifier for small intestinal biopsies that can distinguish CD from healthy controls and all other relevant pathology, eg close mimics of CD, that can occur in the small intestine.

# ARTIFICIAL INTELLIGENCE MEDIATED ANALYSIS OF TCR RECEPTOR CAN DIAGNOSE COELIAC DISEASE ON DUODENAL BIOPSIES REGARDLESS OF DIETARY GLUTEN STATUS


## Authors
Shoukat S[1], FitzPatrick M, Foers A, Welsh O, Donovan K, Petry R, Evans, Klenerman P, Fowler A, Soilleux E

## Institution
Department of Pathology, University of Cambridge[1]


## Abstract


**Introduction**
Current testing strategies in coeliac disease (CD) (serology and histopathological examination of small intestinal endoscopic biopsies) require patients to eat adequate gluten prior to testing, meaning that significant numbers of likely undiagnosed gluten sensitive patients choose not to seek testing. Tests often give equivocal results, meaning that, even after endoscopy, patients may remain unsure about whether they are gluten sensitive. We aimed to develop a more robust and objective test that could identify CD in patients regardless of whether they are consuming gluten.

**Methods**
DNA was extracted from n=44 formalin fixed paraffin embedded (FFPE) biopsy proven cases of CD (histologically Marsh 3B/C) and n=33 control cases (with no histological features of CD, no history of anaemia or abdominal bloating, biopsy taken for suspected gastro-oesophageal reflux disease). Bulk amplification of the T-cell receptor gamma and delta repertoires was undertaken with Lymphotrack and Biomed-2 kits (Invivoscribe) followed by next generation sequencing (Illumina). N=33 CD and n=21 control biopsies were used in analysis of the T-cell receptor gamma repertoire (TRG), while n=11 CD and n=12 control biopsies were used in analysis of the T-cell receptor delta repertoire (TRD). Novel methods for bioinformatic analysis were constructed in Python and R, using the IMGT database as a reference.

**Results**
We developed a novel algorithm to analyse T-cell receptor repertoires (TCRR), based on semi supervised nearest neighbour classification (eg clustering), grouping together cases with similar TCRR. By modifying the parameters, we could train/ supervise the algorithm to ensure that new cases were correctly clustered. Importantly, biopsies with normal histology from CD patients on a gluten free diet for at least six months were classified as having CD.

**Discussion**
We demonstrated that analysis of TRG and TRD repertoires from duodenal biopsies permitted accurate classification of biopsies from patients with active CD and those who had followed a strict gluten free diet for at least six months, who would be misclassified as unaffected by CD by all current tests. Our methodology has the potential to revolutionise the diagnosis of CD, so that it no longer relies on either the rather subjective opinion of a histopathologist or on sufficient gluten consumption by the patient. It is also applicable to FFPE biopsies and may, in future, be modified for use as a blood test.

# THE PHENOTYPE AND TCR REPERTOIRE OF INTESTINAL CD8+ T CELLS IS ALTERED IN COELIAC DISEASE


## Authors
FitzPatrick M[1], Antanavicuite A, Provine N, Garner L, Soilleux E, Klenerman P

## Institution
Translational Gastroenterology Unit, University Of Oxford[1]



## Abstract

**Introduction**
Coeliac disease (CD) is a common immune mediated condition driven by aberrant adaptive CD4+ T cell responses to gluten. The cytotoxic CD8+ and γδ+ T cell response in the epithelium is thought to be predominantly cytokine driven and T cell receptor (TCR) independent, however recent work has challenged this. We investigated the wider role of intestinal CD8+ and γδ+ T cells in CD using RNA sequencing (RNAseq), single cell RNAseq, and TCR repertoire sequencing (TCRseq).

**Methods**
Intestinal CD8+ and γδ+ T cells were isolated from duodenal biopsies from paediatric and adult patients collected at endoscopy. RNAseq, TCRseq, and single cell RNAseq were performed on FACS sorted T cells using the Smartseq2, iRepertoire, and 10x genomics protocols respectively. Flow cytometry was performed on intestinal T cells and peripheral blood mononuclear cells (PBMCs) from subjects with and without CD.

**Results**
Bulk RNAseq of intestinal CD8+ and γδ+ T cells from n=12 subjects with and without CD were analysed. There were 236 differentially expressed genes (DEGs) between health and active CD in the CD8+ T cells, and 451 DEGs in the γδ+ T cells. Common pathways upregulated in coeliac disease included those involved in the regulation of cell activation and adhesion, and T cell costimulation. Expression of key immune checkpoint molecules differed between CD8+ and γδ+ T cells.

TCRseq of sorted intestinal CD8+ T cells from n=20 subjects showed perturbations in the TCR repertoire between health and CD, with particular V-region genes used more frequently in CD. These changes were also seen in the RNAseq dataset, providing validation in a second cohort. The proportion of CD8+ T cells expressing these TCRs was increased in peripheral memory and gut homing populations in subjects with CD.

Single cell RNAseq of intestinal CD8+ and γδ+ T cells revealed two transcriptionally distinct clusters of CD8+ T cells that were increased in coeliac disease. These had an activated, cytotoxic transcriptional profile, with high expression of immune checkpoint molecules and associated transcription factors, consistent with a highly-regulated phenotype. Similar TCR V-region genes were enriched and clonally expanded in these clusters, suggesting a pathogenic, potentially antigen driven, role for these cells in coeliac disease.

**Conclusions**
This multimodal analysis of cytotoxic T cells in coeliac disease has revealed a population of activated, cytotoxic, and highly regulated CD8+ T cells with clonally expanded and biased TCR repertoires in the intestinal mucosa in CD. These populations may have a previously unappreciated role in CD pathogenesis.

# AUDIT OF CLONALITY TESTING IN SUSPECTED REFRACTORY COELIAC DISEASE TO DETERMINE FREQUENCY OF MONOCLONAL RESULTS AS FUNCTION OF TEST METHODOLOGY AND TO UNDERSTAND THE PREDICTIVE VALUE OF A MONOCLONAL RESULT


## Authors
Davies K[1], Foers A, Woodward J, Du MQ, Liu H, Soilleux E

## Institution
Department of Pathology, University of Cambridge[1]


## Abstract


**Introduction**
Despite treatment with a gluten free diet, severe symptoms persist in 2-5% of patients with coeliac disease (CD), a condition known as refractory coeliac disease (RCD). RCDI is relatively indolent and is most likely caused by ongoing inadvertent exposure to gluten in highly sensitive individuals. RCDII harbours a clonal population of intra-epithelial lymphocytes (IELs) and has a poor prognosis, with a 5-year survival rate of 44-58%, largely due to progression to an aggressive lymphoma, known as enteropathy associated T cell lymphoma (EATL).

Clonality studies are frequently used in an effort to distinguish between RCDI and II, using DNA extracted from small intestinal biopsy specimens. Clonality studies aim to determine whether many of the T cells in the sample have identical T cell receptor (TCR) sequences (ie they are monoclonal), indicating origin from a common neoplastic progenitor cell (as seen in RCDII/ EATL). Samples with a polyclonal TCR (ie many different receptor sequences) represent either active coeliac disease or RCDI. The current gold standard clonality test, performed by polymerase chain reaction (PCR) is analysed either with a bioanalyzer, to investigate amplicon length, or by heteroduplex gel to look for clonal bands.

Here we investigate the frequency of monoclonal results with each method and correlate this with patient outcome.

**Methods**
We identified all CD biopsies that had undergone clonality testing in our centre in the last 16 years, following persistent symptoms. For each, we recorded (a) TCR clonal status, (b) analytical method (bioanalyzer or heteroduplex gel), (c) patient diagnosis following the clonality results and (d) whether they progressed to RCDII/ EATL.

**Results**
Overall 31/111 (27.9%) cases gave monoclonal results. 36.4% cases (16/44) appeared monoclonal on the bioanalyzer and 22.4% (15/67) by heteroduplex gel analysis. Of the samples designated as monoclonal using the bioanalyzer, 3/16 (18.8%) showed progression to RCDII/ EATL, whereas for heteroduplex gel analysis, 5/15 (33.3%) progressed.

**Discussion**
PCR based clonality testing, when analysing amplicon length with a bioanalyzer, may give a false impression of monoclonality because many non identical TCR sequences may be the same length. While heteroduplex gel analysis is a more specific method for assessing clonal status, relying on monoclonality by either method appears to overestimate the risk of progression to RCD/EATL. Our results underline the need for a more specific test that enables accurate prediction of progression to EATL/ RCDII. Such a test would need to undertake next generation sequencing of either TCR PCR products or TCR sequences obtained by hybrid capture, in order to determine whether a sample was genuinely monoclonal.

# REDEFINING THE DIAGNOSIS OF TYPE I REFRACTORY COELIAC DISEASE USING GLUTEN IMMUNOGENIC PEPTIDES


## Authors
Coleman S[1], Rej A, Penny H, Wild G, Sanders D

## Institution
Academic Unit of Gastroenterology, Royal Hallamshire Hospital, Sheffield Teaching Hospital NHS Foundation Trust, Sheffield[1]



## Abstract

### Introduction
Refractory Coeliac Disease (RCD) is defined as ongoing symptoms or signs of malabsorption with associated villous atrophy (VA) despite strict adherence to a gluten free diet (GFD). However, assessment of dietary adherence is challenging. The utility of urine gluten immunogenic peptides (GIP) in patients with RCD1 was assessed for the first time in the literature.

### Methods
N=2553 patients with coeliac disease (CD) were reviewed at Sheffield Teaching NHS Foundation Trust between 1998 and 2019. There were n=103 (4.0%) patients with RCD, of which n=66 (64.1%) were classified as RCD1, and n=37 (35.9%) classified as RCD2/complicated coeliac disease (CCD). From the RCD1 cohort, n=22 patients (33.3%) were successfully treated with budesonide, with n=44 patients (66.7%) having ongoing VA. All of these patients had a dietetic review suggestive of good GFD adherence. RCD1 patients with ongoing VA (n=44) were invited to complete three gluten immunogenic peptides (GIP) tests, using rapid immunochromatographic testing, following the collection of mid-stream urine samples. Ongoing gluten ingestion was defined as having at least one weak positive/positive urine GIP sample.

### Results
At diagnosis, RCD 1 patients were significantly younger than RCD2/CCD patients (p=0.002). RCD1 patients with ongoing VA (n=38) were recruited (71.1% female [n=27], median age 60 years). There were n=20 (52.6%) of patients with RCD1 who had three negative GIP tests, suggestive of strict GFD adherence. However, n=18 (47.4%) had at least one positive GIP result, suggestive of possible ongoing gluten exposure.

### Discussion
A high proportion of individuals with RCD1 appear to have ongoing gluten exposure, as assessed by urine GIP, despite reported strict GFD adherence. Urine GIP may re-define and enable the accurate diagnosis of RCD1 in the future.

# ESPGHAN GUIDELINES ON COELIAC DISEASE LEADING THE WAY – IS THE NO-BIOPSY PATHWAY APPLICABLE TO THE ADULT POPULATION?


## Authors
Paul S[1], Chan Y J, Bailey J, Johnston R

## Institution
Torbay Hospital, Torquay[1]



## Abstract

**Introduction**
The ESPGHAN 2012 guidelines for paediatric coeliac disease (CD) suggested a no-biopsy pathway (NBP) in symptomatic children who fulfilled the triple criteria (IgA-TGA >10x upper limit of normal; ULN, IgA-EMA positive and who had a positive HLA-DQ2/8 haplotype).

This has recently been changed in the revised 2020 ESPGHAN guidelines. A NBP has been successfully implemented in the paediatric population in the UK. There has been increasing interest as to whether this approach is also applicable for adults with various clinical presentations. A NBP has now been adopted in Finland as a standard approach in adults. Aims of this study were:

1) To evaluate accuracy of serology based criteria in adults with suspected CD whose IgA-TGA >10x ULN

2) To understand the extent of the population with positive IgA-TGA who have no histological assessment

**Methods**
Adult patients aged ≥18 years were identified from the laboratory database of Torbay Hospital from May 2012 – May 2019. Those who had repeat IgA-TGA for CD monitoring, all children and adults with negative serology were excluded.

A retrospective case note study and Marsh histological classification of intestinal biopsies compared to serological titres was performed in 2019. Cases where no biopsy records were identified were cross-checked with our endoscopy database.

**Results**
A total of n=544 new samples with positive IgA–TGA were identified. There were 111/544 samples from individuals <18 years, leaving 433 adult samples. Of the adult samples n=23 had normal biopsy histology, n=150 (34.6%) had positive serology but had not been referred for endoscopy to the GI service, and of these, 25/150 (16.7%) had IgA-TGA >10x ULN.

CD was established in 210/260 adults (80.8%), 50/260 (19.2%) were not diagnosed with CD. IgA-TGA >10x ULN was seen in 73/260 adults and of these 69/73 had CD (94.6%). The rate of positive histology results, 69/73 (IgA-TGA >10x ULN) vs 141/187 (IgA-TGA <10x ULN) was statistically significant ($p<0.01$). There was a comment of poorly oriented biopsies in 3/4 samples with IgA-TGA >10x ULN and Marsh 0 classification.

**Discussion**
CD can reliably and safely be diagnosed via a NBP in adults fulfilling the "triple criteria". Of those with IgA-TGA >10x ULN, 94.6% were diagnosed with CD and those non-diagnosed commonly had sampling issues. Of all the IgA-TGA positive patients, 35% weren't referred for endoscopy. Patient reluctance for an endoscopic biopsy is likely to be a massive factor. Yet without this patients do not get access to specialist secondary care services for coeliac disease. An adult NBP with IgA-TGA >10x ULN would reduce endoscopy requirements and activity by 25% and therefore improve patient care, experience and endoscopy service pressures.

# NOT JUST ANOTHER COELIAC!!


## Authors
Paul S[1], Singhal N

## Institution
Torbay Hospital, Torquay[1]



## Abstract

### Introduction
ESPGHAN 2012 guidelines for paediatric coeliac disease (CD) recommended a serology based no-biopsy pathway (NBP) for symptomatic children with very high IgA anti-tissue transglutaminase titres, 10 times the upper limit of normal (IgA-TGA 10x ULN) alongside need for biopsy for all suspected cases of CD. While CD is managed with a gluten free diet (GFD), there are many facets to managing patients which often present with challenges in the clinic and in the community. This study highlights five such challenging cases and the need for an individualised approach for managing these cases.

### Methods
Cases were identified through a search of the single consultant led CD clinic database, kept for four years.

### Results
Case 1: 15 year old female with known CD diagnosed 12 years ago presenting with delayed onset of menarche. Skeletal age was 13.5 years, family wanted to adopt wait and watch approach. Optimisation of CD management through improved nutrition and four monthly clinic follow-up.

Case 2: 14 year old female with chest pain and incidental diagnosis of CD. Multi-disciplinary team approach became necessary to manage biopsychosocial issues and musculoskeletal chest pain.

Case 3: 8 year old female started on a GFD by the dietitian based on a single raised IgA-TGA without HLA-DQ2/8 confirmation. Issues complicated by a difference in guidelines at the tertiary centre compared with what was being followed in the District General Hospitals.

Case 4: 13 year old female with abdominal pain, family history of IBS, referred with slightly raised IgA-TGA and dietitian planning to commence GFD as HLA-DQ2 was positive. Detailed counselling followed by endoscopic assessment on a gluten containing diet returned with normal biopsies. Case had to be managed as non-coeliac gluten sensitivity.

Case 5: 16 year old female with IgA-TGA >20x ULN, diagnosed via a NBP with normalisation of IgA-TGA within one year. Patient found the GFD very restrictive and requested a gluten challenge to see if there was a recurrence of symptoms and an endoscopy with biopsy without general anaesthesia.

### Discussion
CD is not just about ensuring adherence to a GFD and monitoring of IgA-TGA titres but more of managing individual expectations and early recognition of issues arising out of a chronic condition. Allied health professionals conducting CD clinics are an innovative way of workforce utilisation, however clear patient pathways are necessary to deal with the uncertainties and ensuring clear accountability. The 2020 revision of the ESPGHAN guidelines will help confirm and harmonise recommendations from previous iterations, allow a secure NBP diagnosis for asymptomatic children and remove HLA-DQ2/8 testing from routine diagnosis.

# VARIATION IN COELIAC DISEASE MANAGEMENT IN SPECIALIST PAEDIATRIC GASTROENTEROLOGY CENTRES ACROSS THE UNITED KINGDOM - A 2019 SERVICE SNAPSHOT


## Authors
Paul S[1], Balakumar V, Gillett P

## Institution
Torbay Hospital, Torquay[1]



## Abstract

**Introduction**
ESPGHAN 2012 guidelines on coeliac disease (CD) recommended a no biopsy pathway (NBP) for symptomatic children with IgA anti-tissue transglutaminase titres (IgA-TGA) >10X the upper limit of normal (ULN) and with positive IgA anti-endomysial antibody (IgA-EMA) and HLA-DQ2/8 positivity. A survey in Southwest England highlighted the need for greater awareness of the NBP and the utility of HLA-DQ2/8 amongst paediatricians. Aims of this survey were:

1) To assess the implementation of the 2012 ESPGHAN guidelines and

2) To understand variation in practice in CD management across the UK in specialist GI centres

**Methods**
We sent all specialist gastroenterology centres (n=29) providing endoscopy services for CD diagnosis across the UK an email survey in August 2019. This included 20 questions under four main headings:

- Pre-diagnosis
- Post-diagnosis
- Annual review
- Transition

**Results**
All n=29 (100%) centres responded. A NBP was fully implemented in 28/29 centres, 22/28 centres started in the two years post publication of the ESPGHAN 2012 guidelines. HLA-DQ2/8 testing had stopped in 5/29 for a NBP diagnosis. A NBP diagnosis in asymptomatic children from high risk groups had been offered in 2/29 centres. IgG-TGA or IgG-EMA were mainly used in IgA deficient children as initial screening. Diagnosis of CD was initially discussed by a doctor in 65% centres (n=19). Most centres (n=21) waited at least six months post diagnosis to start gluten free oats. DEXA was offered as routine in 4/29 centres. Routine vitamin D supplementation was suggested by 25% centres, and all centres would repeat IgA-TGA to assess normalisation. Annual follow-up was with a combination of doctors/dietitians (n=26). Transition was mainly to primary care between 16-18 years, with 3/29 exclusively transferring to adult gastroenterology services.

**Discussion**
Our survey highlighted excellent uptake of a NBP. HLA-DQ2/8 remained an important test in 83% centres and there remain other considerable differences in ongoing management. Most do not use the NBP for asymptomatic children. The new ESPGHAN guidelines will help confirm and harmonise recommendations from previous iterations, allow a secure NBP diagnosis for asymptomatic children and remove HLA-DQ2/8 testing from routine diagnosis.

# IS IT USEFUL TO INCLUDE HbA1c IN THE ANNUAL BLOOD MONITORING FOR CHILDREN WITH COELIAC DISEASE?


## Authors
Paul S[1], Akpobire W

## Institution
Torbay Hospital, Torquay[1]



## Abstract

**Introduction**
Coeliac disease (CD) is an autoimmune condition, a lifelong gluten free diet being the only treatment option currently available. Other autoimmune conditions such as Type 1 diabetes mellitus (T1DM), autoimmune hypothyroidism, are known to be associated with an increased prevalence of CD. A national survey in the UK has highlighted variation in practice as regards to the list of blood investigations to be included in the annual monitoring for CD. This aim of this study was to determine whether including HbA1c in the annual monitoring blood investigations would be useful to detect T1DM earlier than it would present clinically.

**Methods**
Cases (n=74) were identified through a search of the CD clinic database kept for four years (2016-19). Data were collected on IgA-based anti-tissue transglutaminase (IgA-TGA) and HbA1c done at annual monitoring. Children with T1DM preceding the diagnosis of CD (n=6) and those children with CD who never had a HbA1c tested at annual reviews (n=21) were excluded.

**Results**
A total n=47 patients were included in the study, female 27/47 (57%). Mean age at diagnosis was 8.8 years. Modality of diagnosis; n=18 were diagnosed via the biopsy pathway and n=29 were via the serology based, no-biopsy pathway. An average of two HbA1c were done for each patient. Two patients, both female, had developed T1DM during the study period, neither reported any of the 4Ts (Thirsty, Toilet, Tired, Thinner) at screening blood tests.

Patient characteristics are described below:

Case 1: Diagnosed with CD in 2014 and developed T1DM five years later, HbA1c on screening was 91 mmol/mol and IgA-TGA, which was negative at the previous annual review, was reported as positive at the time of diagnosis of T1DM.

Case 2: Diagnosed with CD in 2019 and developed T1DM four months later, HbA1c on screening was 81 mmol/mol.

**Discussion**
We have presented our single centre experience wherein we identified two sub-clinical cases of T1DM through HbA1c screening along with other blood tests. A number of children (n=21) didn't have HbA1c checked as they were primarily managed by a different clinician or were diagnosed in 2019. Screening for T1DM through HbA1c in children with CD is not currently recommended in the ESPGHAN/NICE guidelines. We are in the process of collaborating with other centres in England, identified through the BSPGHAN CD working group, who have been doing HbA1c monitoring along with their annual blood tests. Although there may be a cost implication (£0.50/test locally), this may be a useful tool in detection of sub-clinical cases of T1DM in patients with CD.

# A QUALITATIVE REVIEW: THE PSYCHOSOCIAL AND EMOTIONAL EXPERIENCES OF CHILDREN AND ADOLESCENTS WITH COELIAC DISEASE


## Authors
Harvey M[1], Velleman S, Dinning A, McVeigh L

## Institution
University Hospitals Bristol NHS Foundation Trust, Bristol Royal Hospital for Children[1]



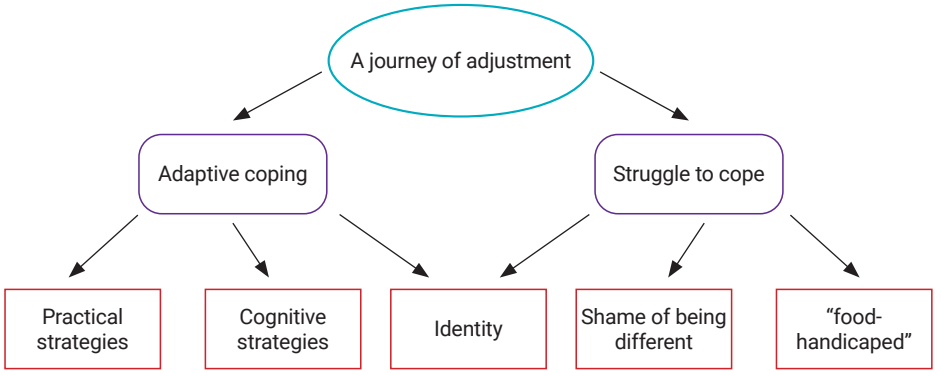
## Abstract

**Introduction**
A recently published quantitative systematic review suggests that young people with coeliac disease (CD) have increased symptoms of anxiety and depression and a lower quality of life. Despite these findings, there is limited knowledge about the subjective experiences of young people with CD and the impact of having CD. Therefore, the present review aimed to identify and synthesise the themes across qualitative studies to develop an integrated understanding of the psychosocial and emotional experiences of children and adolescents with CD.

**Methods**
EMBASE, Medline and PsycINFO databases were searched for studies using exclusively qualitative methodology up to September 2019. Thematic synthesis was used to analyse the data from across studies.

**Results**
Seven studies from four countries were included. An overarching theme emerged: ***A Journey of Adjustment***, and two subordinate themes, each with three subcategories: ***Adaptive coping*** (practical strategies, cognitive strategies, identity) and ***Struggle to cope*** (shame of being different, "food-handicapped", identity), **Figure 1**. Identity was found to be an influential pattern across experiences of young people with CD and therefore fits under both of the subordinate themes.

**Figure 1** The themes identified from across qualitative studies capturing the psychosocial and emotional experiences of children and adolescents with CD.




**Discussion**
Children and adolescents with CD have a diverse range of psychosocial and emotional experiences. Some young people make use of coping strategies and personal identity positively influences adjustment and adherence to the gluten free diet (GFD), whereas others struggle to integrate the diagnosis into their identity. Young people with CD also experience shame around being different and feel limited by the need to follow a GFD. These findings highlight the need to consider the young person's individual situation and personal outlook when providing support with managing their condition. Additionally, strategies which aim to increase a sense of belonging and reduce feelings of constraint may be useful for this population. Further research is required to understand the experiences of children and adolescents with CD within different cultures and healthcare services. In particular, this review found no qualitative studies from the UK.

# CAN DIGITAL TECHNOLOGY BE USED TO IMPROVE THE FOLLOW-UP CARE PROVIDED FOR PEOPLE LIVING WITH COELIAC DISEASE?


## Authors
Cooper R[1], Kurien M, Bell-Williams R, Whittamore K, Hall N, West J, Kennelly C, Bains M

## Institution
University Hospitals of Derby and Burton NHS Trust, University of Nottingham Division of Epidemiology & Public Health, Nottingham[1]



## Abstract

**Introduction**
Around 1% of people in the UK are estimated to have coeliac disease (CD). The National Institute for Health and Care Excellence guidelines for CD, 2015, suggest regular review in either primary or secondary care. However, these guidelines are based on relatively weak evidence.

This abstract describes current research undertaken to explore the opinions of patients and relevant healthcare professionals on CD follow up and outlines a research proposal to evaluate whether digital technology can be used to enhance follow up provision.

**Methods**
CD patients n=50 and healthcare professionals n=43 (Dietitians, GPs and Gastroenterologists) were interviewed to understand their follow up practices, experiences and perception of importance. Interviews were transcribed verbatim and analysed using the framework approach.

**Results**
Our research found that follow up practice varied, resulting in some patients being discharged soon after diagnosis whereas others received ongoing regular appointments. Patients' reflections on support after diagnosis varied from feeling isolated to feeling well supported.

Healthcare professionals largely felt that patients needed to be both engaged and hold responsibility for their own health in order for CD to be successfully managed. As such, many felt that there was no benefit to chasing patients who did not engage with services.

**Discussion**
Following the above research, digital software is being developed and trialled in Sheffield to change the current follow up approaches being employed in primary and secondary care. This software will evaluate using clinic targets, which means that clinical resources will be able to be targeted at those who require additional support. There is therefore huge potential that this may target inequalities. To determine whether those who don't traditionally engage with services may be more likely to engage with a digital service, and if so how they may engage and under what circumstances, this study will be evaluated using a realist evaluation. It is hopeful that the results of this may enable improved follow up of CD patients nationally, ensuring that those who most need follow up are able to access it.

# A DIETETIC LED PATHWAY – TRANSFORMING THE MANAGEMENT OF PATIENTS WITH COELIAC DISEASE IN SCOTLAND


## Authors
Yuill R[1], Headridge F, Oddy T, Richardson S, Gillet P, Walker J

## Institution
NHS Lothian, Edinburgh[1]


## Abstract


**Introduction**
The Scottish Government's Modern Patient Pathways Programme provided 18 months funding to four health boards in Scotland (NHS Lothian, NHS Lanarkshire, NHS Greater Glasgow and Clyde and NHS Tayside) to localise and test a new national pathway for adults diagnosed with coeliac disease (CD) that meets evidence based care. The pathway aims to deliver early diagnosis, early intervention via dietetic led care and support people to better self manage to ensure life long living well with monitoring via community pharmacy.

**Objectives**
- To implement and test the new Scottish CD pathway.
- To move from consultant led secondary care approaches to a dietetic model focusing on self management in the community setting
- To reduce time from first presentation to treatment
- To reducing GI consultant appointments
- To improve people's experience of CD care

**Methodology**
Improvement methods were used to track key outcomes.

Key areas for improvement were:

***Diagnosis*** - staff were made aware of the new pathway and current practice was changed where necessary. Changes made within GP, GI Consultant laboratory, endoscopy and pathology services.

***Treatment*** - community based dietetic led packages of care were developed and delivered via group education (1:1 were available if necessary) with emphasis on self management. The education package was co-designed by project dietitians in collaboration with GI Consultants, Coeliac UK and people with CD. GI consultants saw only complex cases. Dietitians tested new review processes such as virtual consultations and telehealth.

***Monitoring*** - Seamless transition from dietetic led to annual community pharmacy monitoring via the Gluten Free Food Service (GFFS).

**Results**
- Reduction in the number of acute GI appointments by more than 75%
- Reduction in time from diagnosis to treatment
- Positive person experience of care by 98% of patients
- Improved uptake of prescribable products from 78% at baseline to 90%
- Shift to community based care targeting areas of deprivation

**Discussion**
Each health board has seen positive results. GI consultant time has been reduced and dietetic led care has increased self management of the gluten free diet. Challenges identified include monitoring of CD blood tests within the community setting and management of bone health long term. Pressures on endoscopy services continue to be the main issue affecting wait time to diagnosis.

The new pathway demonstrates a standardised safe person centred approach to care which supports self management, ensures efficient use of resources, delivers improved experience for people living with coeliac disease and is delivering an improved pathway of care compared to traditional models.

# PREVALENCE OF LACTOSE MALABSORPTION IN COELIAC DISEASE AND SYMPTOM CORRELATION


## Authors
Coleman S[1], Rej A, Baggus E, Sanders D

## Institution
Academic Unit of Gastroenterology, Royal Hallamshire Hospital, Sheffield Teaching Hospital NHS Foundation Trust, Sheffield[1]



## Abstract

### Introduction
Coeliac disease (CD) is a frequent cause of secondary lactose malabsorption. Many methods are available for the diagnosis of lactose malabsorption. The aim of this study was to assess the prevalence of lactose malabsorption in individuals with CD, as well as symptom correlation with test results.

### Methods
Patients were prospectively recruited between February 2018 and October 2019. Individuals with a potential new diagnosis of CD (positive IgA-EMA/IgA-TGA) or established CD had a duodenal biopsy to assess for lactose malabsorption (Lactose Intolerance Quick Test [LIQT], BIOHIT Oyj, Helsinki, Finland) at time of gastroscopy. Subsequent to this, individuals had a lactose hydrogen breath test (LHBT). Symptoms around the time of gastroscopy were assessed, to allow assessment of symptom correlation with lactose malabsorption (eg abdominal pain, bloating, diarrhoea, borborygmi).

### Results
Patients (n=97) were prospectively recruited; out of these n=24 had a LHBT suggestive of small intestinal bacterial overgrowth (SIBO) and were excluded. Of the remaining n=73 patients (n=54 female, median age 47 years), n=50 patients had a potential new diagnosis of CD and n=23 had established CD. The total prevalence of a positive duodenal lactase test was 43.8%, compared to 15.1% for a positive LHBT. The prevalence of lactose malabsorption was significantly higher in individuals with villous atrophy compared to those without, when using the duodenal lactase test ($p<0.01$). **Table 1** highlights the prevalence of lactose malabsorption in each group. There was no significant correlation between symptoms compatible with lactose intolerance detected by either LHBT or duodenal lactase test ($p=1.00$).

**Table 1** Prevalence of lactose malabsorption

| | Villous Atrophy (Marsh 3a or above) | | | No villous atrophy (Marsh 0-II) | | | Villous atrophy vs no villous atrophy | |
|---|---|---|---|---|---|---|---|---|
| | Negative % (n) | Positive LHBT % (n) | Positive Lactase test % (n) | Negative % (n) | Positive LHBT % (n) | Positive Lactase test % (n) | Positive LHBT *p* | Positive Lactase test *p* |
| **Potential new diagnosis of CD (n=39/ n=11)** | 28.2 (11) | 17.9 (7) | 53.8 (21) | 54.5 (6) | 0.0 (0) | 45.5 (5) | 0.32 | 0.74 |
| **Established CD (n=4/ n=19)** | 25.0 (1) | 0.0 (0) | 75.0 (3) | 68.4 (13) | 21.1 (4) | 10.5 (2) | 1.00 | 0.02 |
| **Total (n=43/ n=30)** | 27.9 (12) | 16.3 (7) | 55.8 (24) | 63.3 (19) | 13.3 (4) | 23.3 (7) | 1.00 | <0.01 |

### Discussion
The prevalence of lactose malabsorption in individuals with CD was higher using the lactase test compared to the LHBT. The prevalence of lactose malabsorption was significantly higher in those with villous atrophy (VA) compared to those without. Although symptom correlation was poor there may be value in using LIQT when assessing CD patients with persisting symptoms.

# ARE DIETARY ADHERENCE QUESTIONNAIRES AN EFFECTIVE TOOL TO ASSESS ADHERENCE TO A GFD IN COELIAC DISEASE?


## Authors
Coleman S[1], Rej A, Baggus E, Lau M, Marks L, Hadjivassiliou M, Sanders D

## Institution
Academic Unit of Gastroenterology, Royal Hallamshire Hospital, Sheffield Teaching Hospital NHS Foundation Trust, Sheffield[1]



## Abstract

### Introduction
Adherence to a gluten free diet (GFD) in coeliac disease (CD) is challenging, with adherence being reported as 42-91% in the literature. The Coeliac Disease Adherence Test (CDAT) questionnaire is the favoured adherence questionnaire but has never been compared with the gold standard of duodenal biopsy (for the presence or absence of villous atrophy).

### Methods
Patients with established CD who were referred for histological assessment of persisting symptoms were prospectively recruited between December 2015 and December 2019. Participants were invited to complete CDAT and Biagi questionnaires and serology at the time of endoscopy. Quadrant biopsies were taken from D2 in addition to duodenal bulb biopsies. Sensitivities of CDAT, Biagi score and coeliac serology were determined by using the presence (Marsh 3a or above) or absence (Marsh 0-2) of villous atrophy on duodenal biopsy.

### Results
Patients (n=207) were prospectively recruited (67.1% female, n=139). The median duration on a GFD (n=200) was 66 months (range 0 - 840 months). In total, 31.9% of patients (n=66) had ongoing villous atrophy (VA). Of the patients with VA, 48.5% were Marsh grade 3a (n=32), 27.3% were Marsh grade 3b (n=18) and 24.2% were Marsh grade 3c (n=16). There was no significant difference in sensitivities between CDAT or Biagi scores and coeliac serology, however CDAT had a significantly greater sensitivity than Biagi score ($p<0.05$). CDAT had a significantly lower specificity than both Biagi score and coeliac serology ($p<0.05$). **Table 1** outlines the sensitivities and specificities of these tests.

**Table 1** Comparison of tools used to assess adherence

| | Sensitivity % (CI) | Specificity % (CI) | Positive Predictive Value % (CI) | Negative Predictive Value % (CI) |
|---|---|---|---|---|
| **CDAT** | 56.1 (43.3 – 68.3) | 51.8 (43.2 - 60.3) | 35.2 (29.3 – 41.7) | 71.6 (64.7 – 77.5) |
| **Biagi** | 19.7 (14.1 – 26.9) | 94.3 (90.5 – 96.7) | 61.9 (41.5 – 78.9) | 71.5 (68.9 – 74.0) |
| **CDAT & Biagi** | 29.7 (15.9 – 47.0) | 91.1 (82.6 – 96.4) | 61.1 (39.9 – 78.8) | 73.5 (69.0 – 77.5) |
| **IgA-EMA** | 36.4 (24.9 – 49.1) | 96.5 (91.9 – 98.8) | 82.8 (65.7 – 92.3) | 76.4 (72.9 – 79.6) |
| **IgA-tTG** | 37.9 (26.2 – 50.7) | 94.3 (89.1 – 97.5) | 75.8 (59.8 – 86.8) | 76.4 (72.8 – 79.7) |

### Discussion
The CDAT questionnaire appears to be a poor marker of villous atrophy, with a similar sensitivity and lower specificity than coeliac serology. Duodenal biopsy remains the gold standard for assessment of adherence in CD, with development of further non-invasive markers required.

# NCGS PATIENTS ARE LESS LIKELY TO ADHERE TO A GFD THAN PATIENTS WITH COELIAC DISEASE


## Authors
Hallam R[1], Webster G, Rej A, Croall I, Coleman S, Key T, Goodwin J, Aziz I, Sanders D

## Institution
Academic Unit of Gastroenterology, Royal Hallamshire Hospital, Sheffield Teaching Hospital NHS Foundation Trust, Sheffield[1]



## Abstract

### Introduction
Adherence to a gluten free diet (GFD) can be challenging, reported between 42-91% in individuals with coeliac disease (CD). However, little is known about the adherence to a GFD in patients with non coeliac gluten sensitivity (NCGS). A previous study demonstrated that 58% of patients with NCGS reported that they were on a strict GFD, although no objective marker to assess GFD adherence was used. The aim of this study was to use an objective marker to assess adherence in individuals with NCGS and compare with those who have CD.

### Methods
Individuals diagnosed with NCGS or CD at a specialist centre for gluten related disorders were prospectively recruited and invited to complete a validated dietary adherence questionnaire (Coeliac Disease Adherence Test; CDAT). A CDAT score of <13 indicated excellent adherence, with a score of >17 indicating non adherence to a GFD. Individuals with CD were age and sex matched to individuals with NCGS for data analysis.

### Results
NCGS patients (n=111) were compared against (n=111) age and sex matched controls with CD (mean age 47 years, 87% female). The mean duration of disease for NCGS was 5.3 years and for CD was 10.5 years. Individuals with NCGS had a significantly higher CDAT score (mean 16.7 ±4.7) versus individuals with CD (mean 13.8 ±4.5) p<0.01, indicating poorer adherence to a GFD. Excellent adherence was observed in 44.1% of patients with CD versus 19.8% of NCGS patients, **Table 1**.

**Table 1** Adherence to a gluten free diet (GFD) in coeliac disease (CD) and non coeliac gluten sensitivity (NCGS)

| Adherence to a GFD | CD (n=111) % (n) | NCGS (n=111) % (n) |
|---|---|---|
| Excellent | 44.1 (49) | 19.8 (22) |
| Moderate | 37.8 (42) | 37.8 (42) |
| Poor | 18.0 (20) | 42.3 (47) |

### Discussion
This is the first study to objectively assess GFD adherence in NCGS. The data suggests lower levels of adherence to a GFD in NCGS compared with CD.

# INTERVENTION IMPROVES KNOWLEDGE OF GLUTEN FREE FOODS AND DIETARY ADHERENCE IN ADULTS WITH COELIAC DISEASE; 3 MONTHS FOLLOW UP DATA


## Authors
Jeanes Y[1], Muhammad H, Ishaq S, Reeves S

## Institution
University of Roehampton[1]



## Abstract

**Introduction**
Coeliac disease (CD) affects 1% of the population globally, with no cure, the only treatment is a lifelong gluten free diet (GFD). Adherence to a GFD can be challenging, it requires knowledge, skills and modified behaviours to undertake substantial changes to dietary habits, including within cultural and social set up. The study aimed to determine whether a healthcare professional led intervention impacts gluten free (GF) knowledge and dietary adherence.

**Methods**
Adults diagnosed with CD were recruited from a hospital database. All participants completed a GF knowledge questionnaire and the validated Coeliac Dietary Adherence Test (CDAT) at baseline and at three months; where a score <13 indicates dietary adherence. The intervention group received a CD information leaflet and a healthcare professional led telephone clinic which aimed to improve participants' knowledge of CD and GF foods, as well as discussing behaviour change. The control group received no intervention. Data is presented as mean and standard deviation, and median and interquartile range (IQR) where appropriate.

**Results**
The intervention group consisted of n=30 adults not adhering to the GFD (CDAT score;16, 14-17), mean age 50.5 ±17.7 years, 77% female and 100% Caucasians. The control group consisted of n=86 adults adhering to the GFD (CDAT score; 9, 8-10), mean age 51.3 ±17.6 years, 77% female, 76% Caucasians. At baseline the knowledge of GF foods score was significantly lower in the intervention group compared with the control group (13.5 (12.0-14.0) and 15.0 (14.0-16.0) respectively; $p<0.01$). GF knowledge significantly improved at three months in the intervention group (15.0 (14.0-16.0); $p<0.01$) and to a lesser extent in the control group (16.0 (15.0-16.0; $p<0.01$). Dietary adherence score remained similar in the control group (9 (8-10) and 9 (8-11); NS), whereas there was a significant improvement in the intervention group (16 (14-17) and 13 (12-14); $p<0.001$). The component scores for 'how important are accidental gluten exposures' and 'how many times have you eaten gluten containing foods on purpose' significantly improved (both $p<0.001$) in the intervention group only.

**Discussion**
This is the first study to report how a healthcare professional led telephone clinic can improve gluten free dietary adherence in adults with coeliac disease. This evidence also suggests follow up via remote access to patients is effective.

# THE ABSENCE OF GLUTEN IMMUNOGENIC PEPTIDES IN URINE STRONGLY CORRELATES TO DUODENAL MUCOSAL HEALING IN COELIAC PATIENTS


## Authors
Pizarro A[1], Ruiz-Carnicer A, Garzón-Benavides M, Fombuena B, Sequra V, Sousa C, Comino I, Cebolla A, Azkoaga I M

## Institution
Unidad Clínica Aparato Digestivo, Hospital Universitario Virgen del Rocío, Sevilla, Spain[1]



## Abstract

### Introduction
A lifelong gluten free diet (GFD) is the only treatment for coeliac disease (CD). Available methods such as dietary questionnaire or serology are insufficiently sensitive to detect dietary transgressions and duodenal biopsies are invasive, expensive and not a practical method for monitoring. This study aimed to determine the clinical usefulness of urine gluten immunogenic peptides (GIP) as a biomarker to monitor GFD adherence in patients with CD and to evaluate its correlation to mucosal damage.

### Methods
A prospective observational study involving n=23 de novo CD patients and n=80 patients with CD on a GFD was performed. Three days a week (two at the weekend) urine samples were collected, and GIP were studied. Anti-tissue transglutaminase antibodies, the Celiac Dietary Adherence Test (CDAT), clinical manifestations and small bowel histology were analysed simultaneously.

### Results
Among the 25% (20/79) patients with CD on a GFD who showed Marsh II-III mucosal atrophy, 95% had detectable urine GIP in at least one sample, nonetheless, 80% of them were asymptomatic, 65% showed negative serology and 60% a good GFD adherence according to CDAT.

In contrast, 97% of patients with CD with no duodenal atrophy had no detectable GIP in any sample. These results demonstrated a high sensitivity (95%) and negative predictive value (NPV, 97%) of GIP measurement with respect to the results of duodenal biopsy, **Table 1**.


**Table 1** Comparison of predictor methods of the intestinal mucosa damage in terms sensitivity, specificity, positive predictive value (PPV) and negative (NPV).

| Methodology | Samples | Day of collection | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|---|---|---|---|---|---|---|
| **Serology** | | | 35 | 97 | 78 | 81 |
| **Symptomatology** | | | 20 | 71 | 21 | 73 |
| **Adherence GFD Test** | | | 40 | 83 | 43 | 82 |
| **GIP** | One urine sample | Saturday | 65 | 83 | 57 | 87 |
| | | Sunday | 60 | 71 | 41 | 84 |
| | | visit day | 40 | 84 | 47 | 80 |
| | Two urine samples | Saturday-Sunday | 75 | 61 | 39 | 88 |
| | | Saturday-visit day | 85 | 69 | 49 | 93 |
| | | Sunday-visit day | 80 | 59 | 40 | 90 |
| | Three urine samples | Saturday-Sunday-visit day | 95 | 53 | 40 | 97 |

### Discussion
In this study, the detection of GIP in the urine of patients with CD on a GFD correlated with histological lesions. In turn, the repeated absence of GIP in urine correlated with mucosal healing, thus suggesting the testing of GIP in urine could potentially avoid the need for invasive techniques.

# NATIONAL SURVEY EVALUATING THE PROVISION OF GASTROENTEROLOGY DIETETIC SERVICES IN ENGLAND


## Authors
Rej A[1], Buckle R, Shaw C, Trott N, Urwin H, McGough N, Aziz I, Sanders D

## Institution
Academic Unit of Gastroenterology, Royal Hallamshire Hospital, Sheffield Teaching Hospital NHS Foundation Trust, Sheffield[1]



## Abstract

### Introduction
The aim of this study was to assess the current provision of dietetic services for coeliac disease (CD), irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD) in England.

### Methods
Hospitals within all NHS trusts in England were approached (n=209). A custom designed web based questionnaire was circulated via email, post or telephone. Individuals/teams with knowledge of gastrointestinal (GI) dietetic services within their trust were invited to complete the questionnaire.

### Results
GI dietetic services were provided in 76% of trusts (n=158), with responses received from 78% of these trusts (n=123). The median number of dietitians per 100,000 population was 3.64 (range 0.15-16.60), which differed significantly between regions (p=0.03). The commonest individual consultation time for patients with CD, IBS and IBD was 15-30 mins (43%, 44% and 54% respectively). GI dietetic services were delivered both via individual and group counselling, with individual counselling being the more frequent delivery method available (93% individual vs 34% group). A significant proportion of trusts did not deliver any specialist dietetic clinics for CD, IBS and IBD (49%; n=60, 50%; n=61 and 72%; n=88 respectively).

### Discussion
There is a variable number of dietitians per head of population across the UK. Allocated time for clinics appears to be insufficient compared to time advocated in the literature. Many trusts do not deliver specialist dietetic clinics, impacting on the optimal delivery of dietary therapies. Group clinics are becoming a more common method of dietetic service delivery (in order to cope with demand). National guidelines are required to ensure equity of dietetic services across England.

# GLUTEN FREE BREADS ARE NOT EQUAL: A FOCUS ON CALCIUM


## Authors
Jeanes Y[1], Spitale A, Nicolini G, Bergmann V, Fagbemi L, Rasheid R, Hovland C, Dalton D, Costabile A

## Institution
University of Roehampton[1]



## Abstract

**Introduction**
Calcium is particularly relevant for people with coeliac disease, as there is an increased prevalence of osteoporosis associated with coeliac disease. UK adults and adolescents get 31% and 39% of their dietary calcium from cereals and cereal products. The micronutrient content of gluten free (GF) breads is often not reported on the food labels and very few studies have used laboratory methods to measure micronutrient content of GF food products. There is a paucity of GF foods with known calcium content leading to reduced accuracy when analysing the nutrient intake from the population with coeliac disease. This study aimed to determine the calcium content of GF breads.

**Methods**
N=55 GF bread samples and n=11 wraps were analysed. Calcium was extracted from samples with lithium acetate solution and analysed directly by flame emission photometry. The micronutrient values of wheat based foods were sourced from the McCance and Widdowson's The Composition of Foods Integrated Dataset.

**Results**
The majority of GF bread products were not fortified with micronutrients, only 33% were fortified with calcium. Only 27% of white loaves and rolls were fortified with calcium (6/18), this contrasts with mandatory fortification in 100% of wheat based white breads in the UK. The calcium content of wheat based white loaves (177 mg/100g) was significantly greater than all GF white loaves (99 ±29 mg/100g, n=12; $p<0.01$), those fortified with calcium (122 ±11 mg/100g, n=5; $p<0.01$) and those not fortified with calcium (83 ±28 mg/100g, n=7; $p<0.01$). The GF wraps encompassed a broad range of flours inclusive of sorghum, rice, tapioca, corn, buckwheat, sweet potato, millet and teff flours. The mean calcium content of wheat based wraps (148 mg/100g) was significantly higher than GF wraps (109 ±17 mg/100g, n=11; $p<0.01$), none of the GF wraps were fortified with calcium.

**Discussion**
These calcium values provide a valuable addition in enabling more accurate nutrient intake analysis for the population with coeliac disease. The use of quinoa and buckwheat flours with a higher calcium content will have a small impact on calcium content, compared with rice flour and maize starch. However, the biggest impact on calcium content is whether the product has been fortified with calcium. We recommend mandatory calcium fortification of all GF breads to promote adequate dietary calcium intake in a population with an increased risk of fractures.

# PHASE II, RANDOMISED, PLACEBO CONTROLLED CROSSOVER TRIAL USING ANTI GLIADIN ANTIBODY (AGY) FOR PATIENTS WITH SYMPTOMATIC COELIAC DISEASE


## Authors
Sample D[1], Turner J, Dieleman L

## Institution
University of Alberta, Canada[1]



## Abstract

**Introduction**
Coeliac disease (CD) is an immune mediated disorder triggered by ingested gluten in genetically predisposed individuals. At present, the only approved treatment for coeliac disease is a life long, strict gluten free diet, and non adherence is associated with increased morbidity and mortality. However, gluten is present in many products, making elimination of all gluten extremely difficult. New treatment options are needed.

Anti Gliadin Antibody (AGY) is an encapsulated oral anti gliadin antibody made from the yolks of immunised laying hens. The amount of AGY in a single dose (2 capsules) is designed to neutralise 5 g of gliadin (10 g of gluten). An open label pilot study was previously completed with n=10 adults with CD, to determine safety of AGY (2 capsules per meal) for four weeks, and to explore potential efficacy related to symptoms, anti tissue transglutaminase antibody (tTGA) levels, and lactulose/mannitol excretion ratios (LMER) at baseline and after treatment. No safety concerns were identified, and some participants had improvements in symptoms, tTGA, and LMER.
We now outline the plan for a phase II efficacy study.

**Methods**
We are currently conducting a 16 week, double blind, placebo controlled crossover trial, for individuals age 10 - 65 years, with symptomatic CD at least one year post diagnosis. The primary objective is to determine the efficacy of AGY as measured by the Daily Coeliac Symptom Index (CSI). Secondary objectives include safety, quality of life assessment, monthly symptom scores, tTGA, and LMER. Because AGY has not yet been tested in paediatric patients, we have incorporated an innovative strategy to mimic the previous pilot study, but added a pilot paediatric cohort imbedded in a larger trial. Total enrolment in the study will be n=149 patients, allowing 80% power and 5% alpha. Participants will be stratified by age and screening tTGA levels at study entry.

**Results**
Enrolment began in late 2019 and is expected to run through mid 2021.

**Discussion**
A non toxic, food source based natural health product that could neutralise remnant gliadin in food, thus preventing gliadin absorption and subsequent gliadin induced pathogenesis, could dramatically improve the quality of life for people with coeliac disease who are symptomatic despite a gluten free diet.

# IS THE LOW FODMAP DIET EFFECTIVE IN THE LONG TERM? THE LARGEST MULTICENTRE PROSPECTIVE STUDY


## Authors
Rej A[1], Buckle R, Shaw C, Trott N, Adu-Tei S, Agrawal A, Mosey J, Sanders K, Allen R, Martin S, Newton A, Robinson K, Elphick D, Aziz I, Sanders D

## Institution
Academic Unit of Gastroenterology, Royal Hallamshire Hospital, Sheffield Teaching Hospital NHS Foundation Trust, Sheffield[1]



## Abstract

**Introduction**
The low FODMAP diet (LFD) has been demonstrated to be effective in managing the symptoms of irritable bowel syndrome (IBS) in the short term. However, data remains limited on the long term effects of this dietary therapy. The aim of this study was to assess the long term effect of the LFD on symptom management and adherence.

**Methods**
Patients with IBS who had received LFD advice between 2012-2019 were prospectively recruited at seven centres in the United Kingdom. Participants were invited to complete dietary questionnaires assessing the LFD at long term follow up (> 6 months). Symptoms were assessed using a modified gastrointestinal symptom rating scale (0, none; 1, mild; 2, moderate; 3, severe).

**Results**
Patients (n=589) were approached, with n=154 participants completing the study (76% female, mean age 51 ±15 years). The mean duration of follow up, following initiation of the LFD was 42 ±28 months.

A statistically significant improvement in abdominal pain (2.3 ±0.8 vs 1.2 ±0.9, p<0.001), abdominal bloating/distention (2.3 ±0.8 vs 1.4 ±1.0, p<0.001) and bowel urgency (2.0 ±1.1 vs 1.3 ±1.0, p<0.001) was noted following the LFD at long term versus baseline.

Individuals (n=120), 78%, reported following an adapted LFD at long term follow up. The remaining 7% (n=11) were on a normal diet, 6% (n=10) on a strict LFD, 4% (n=6) on a gluten free/wheat free diet, 1% on a lactose free diet (n=2) and 3% (n=5) on another diet at long term follow up.

The grains (wheat, rye, barley) were reported as a trigger for symptoms by 60% participants (n=92), with 64% (n=98) purchasing gluten or wheat free products in the long term.

**Discussion**
This is the largest study demonstrating the efficacy of the LFD in the long term for individuals with IBS. Adherence to an adapted LFD appears to be good in the long term, with the majority of individuals reporting grains as a trigger and purchasing gluten or wheat free products to manage their symptoms.

# THE FIRST CASE CONTROL STUDY COMPARING DIAGNOSTIC OUTCOMES IN IRRITABLE BOWEL SYNDROME AND SELF REPORTED GLUTEN SENSITIVITY


## Authors
Webster G[1], Hallam R, Rej A, Croall I, Coleman S, Key T, Goodwin J, Aziz Imran, Sanders D

## Institution
Academic Unit of Gastroenterology, Royal Hallamshire Hospital, Sheffield Teaching Hospital NHS Foundation Trust, Sheffield[1]



## Abstract

**Introduction**
Irritable bowel syndrome (IBS) and self reported gluten sensitivity (SRGS) are common, with a prevalence reported at approximately 10%. Little is known on the diagnostic outcomes comparing both IBS and SRGS, with the aim of this study to explore this.

**Methods**
Individuals with SRGS, or suspected IBS were prospectively investigated at a tertiary centre. Patients were characterised according to demographics as well as final diagnosis.

**Results**
Patients with SRGS n=264 and patients with suspected IBS n=75 were reviewed. There was no significant difference between SRGS and suspected IBS with regards to mean age at presentation (41 vs 38 years, respectively, p=0.17), with the majority of individuals being female in both groups (83% vs 63%). The most frequent presenting symptoms for SRGS were abdominal pain (76%) and diarrhoea (70%), with 13% of patients presenting with neurological symptoms of fatigue, headaches or sensory disturbance. After investigation, 83% (n=219) did not have an organic gastrointestinal pathology and were diagnosed as self reported non coeliac gluten sensitivity. The remaining 17% (n=45) of patients with SRGS had an organic gastrointestinal pathology, with coeliac disease being the most common diagnosis (7%, n=19). In comparison, 17% (n=13) of suspected IBS patients were identified to have an organic gastrointestinal diagnosis, with bile acid diarrhoea being the most common (13%, n=10). There was no significant difference in the proportion of organic gastrointestinal diagnoses between IBS and SRGS (p=0.95).

**Discussion**
The presenting demographics of SRGS and suspected IBS are similar, comprising mainly of young to middle aged women. Following investigations, around one in six have an organic gastrointestinal disease to explain their symptoms, notably coeliac disease in SRGS and bile acid diarrhoea in suspected IBS. Our study highlights the importance of excluding organic pathology in these cohorts.

# JOIN COELIAC UK AS A HEALTHCARE PROFESSIONAL MEMBER

Coeliac UK really appreciates all the work you do to support people living with coeliac disease and wants to make sure that you have the resources and tools you need to do so. As a Healthcare Professional (HCP) member of Coeliac UK you will have access to:

- Research updates into coeliac disease and the gluten free diet, including access to our Research Conferences and videos.
- Information updates on coeliac disease and the gluten free diet on our website and email newsletters to support your patients with their condition and diet, reading labels, eating out and cooking.
- Personalised online account where you can save all downloadable documents including information leaflets, our gluten free checklist, booklets and information for parents and carers.

Don't forget, your HCP membership gives you access to the most up to date information and training to support your patients from diagnosis through to managing the gluten free diet. This information includes:

- Food and Drink Guide and monthly updates.
- Online Food and Drink Information listing over 150,000 gluten free products.
- Our award winning Gluten Free Food Checker app providing on the go access to our Food and Drink Information.
- Support for eating out on a gluten free diet including our Gluten Free on the Move app and Venue Guide of over 7,000 venues recommended by our members and/or accredited with our Gluten Free standard.
- Our Home of Gluten Free Recipes to search over 1,000 recipes for inspiration for any occasion.
- Live Well Gluten Free magazine.
- Helpline support.

**Join Coeliac UK for free at**
**www.coeliac.org.uk/joinushcp**



# MEET THE RESEARCHERS

Periodically throughout the year, we will focus on key research centres from around the globe bringing you their latest research into coeliac disease and gluten related conditions. At the end of each week, the researchers will answer questions from the community.

We began this new initiative with the super enthusiastic team, headed by Iris Jonkers and Sebo Withoff, in the Genetics Department of the University Hospital in Groningen. The team is exploring the genetics behind coeliac disease and using Gut-on-Chip technology to study potential environmental factors in coeliac disease, such as the gut microbiome.

We then moved on to the KG Jebsen Coeliac Disease Research Centre (JCoDiRC), Norway, where the super talented scientists are led by Prof Ludvig Sollid. Their research is aimed at finding better diagnostics and identifying targets for new therapeutics.

Visit our website to read more about the researchers' projects and visit regularly for further introductions: **www.coeliac.org.uk/MTR**

PLEASE USE THESE PAGES FOR ANY NOTES YOU WOULD LIKE TO TAKE:

Coeliac UK is the charity for people who need to live without gluten. For 50 years, we've been helping people with coeliac disease and other gluten related conditions live happier, healthier lives.

We do this by striving for better gluten free food in more places, providing independent, trustworthy advice and support and funding crucial research to manage the impacts of gluten and find answers to coeliac disease. And we do it all so that one day no one's life will be limited by gluten.

coeliac uk
live well gluten free

Registered office: Coeliac UK
3rd Floor Apollo Centre Desborough Road
High Wycombe Bucks HP11 2QW
Tel: 01494 437278

Registered with FUNDRAISING REGULATOR

Phone: 0333 332 2033
Facebook: Coeliac UK
Twitter: @Coeliac_UK
Instagram: @CoelaicUK

A Registered Charity and Company Limited by Guarantee and Registered in England. Registered Number 3068044. Registered Charity Number in England and Wales 1048167. Registered Charity Number in Scotland SC039804.