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# COELIAC UK'S RESEARCH CONFERENCE 2019

The gluten free diet; a solution for everyone?

Friday, 29 March 2019

# THE GLUTEN FREE DIET; A SOLUTION FOR EVERYONE?

## ROYAL COLLEGE OF PHYSICIANS

11 St Andrew's Place, Regent's Park, London, NW1 4LE

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

10.00 Arrival and networking – refreshments in the Platt room

10.30 Coeliac UK welcome – Chair of Coeliac UK's Research Strategy Board, Prof Alan Perkins

**Session 1**

10.35 Dietary gluten permanently reconfigures gastrointestinal tissue resident immunity in coeliac disease
Prof David Price

11.00 Doctor I still have symptoms; non responsive and refractory coeliac disease
Prof David Sanders

11.25 To biopsy or not to biopsy? That is the question!
Prof Carolina Ciacci

11.50 Healthcare professionals' and patients' views on the long term follow up of coeliac disease
Dr Manpreet Bains

12.15 **Lunch and poster exhibition – Platt room**

**Session 2**

13.30 Exploring the coeliac 'fermentome' and 'microbiome'
Prof Ramesh Arasaradnam

13.55 Therapeutic advances for coeliac disease
Dr Francisco Leon

14.20 How complex can it be? The bread wheat genome and its implications for wheat intolerance
Dr Manuel Spannagl

14.45 **Break – refreshments – Platt room**

**Session 3**

15.15 Is there a role for gluten in multiple sclerosis?
Lina Moschoula Passali

15.40 What does gluten do to your brain?
Dr Iain Croall

16.05 The latest research; Coeliac UK and Innovate UK awards:
Chris Sale – Nonacus Ltd, Lydia Campbell – Nandi Proteins, Chris Kennelly – Cievert Ltd

16.30 Chair's closing remarks and presentation of poster prize

16.35 CLOSE

This event has been kindly sponsored by BFree, Dr Schär, Regenerus Labs and Thermo Fisher and supported by Neogen Europe Ltd.

## 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 2019 Research Conference. We have an excellent programme of presentations and posters bringing you the very best of research in coeliac disease and gluten related science.

Our 50th anniversary year has been particularly successful for research at Coeliac UK. Following the announcement of our top 10 Research Priorities and the launch of our Research Fund, we carried out a review of our policies and governance for research, ensuring rigorous standards for awarding research grants, protecting intellectual property, data sharing and ethical review. We have established a new Research Awards Panel, chaired by Dr Rick Lones, and secured membership of the Association of Medical Research Charities.

I am especially pleased to inform you that since last year's conference, when we announced our partnership with Innovate UK, we have awarded three major grants to projects totalling £750k in support of new research into less invasive diagnostics, improved long term management of coeliac disease and improved ingredients for better gluten free bread. We are delighted that the grant holders are here today to tell you about their projects. 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

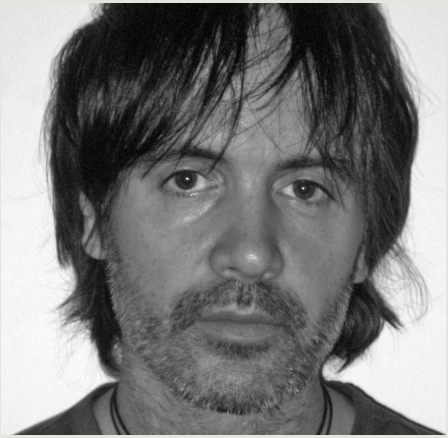
Chair of Coeliac UK's Research Conference and Health Advisory Council

Dear friends and colleagues, thank you for supporting Coeliac UK's 10th annual research conference. At this event we continue to focus on clinically relevant topics and what is new in the world of research.

It is my pleasure to Chair the meeting and in my role as Chair of Coeliac UK's Health Advisory Council (HAC) I invite you too, to consider a role. The HAC currently has vacancies for a dietitian, consultant gastroenterologist and psychologist with specialist knowledge and experience in coeliac disease and gluten related conditions. Please contact Heidi Urwin, Research Manager, at Coeliac UK for further information.

Last year we were delighted to announce the top ten research priorities* for coeliac disease from the priority setting partnership (PSP) involving patients, carers, healthcare professionals and the James Lind Alliance. Thanks again to those of you who took part in the PSP. Coeliac UK continues to explore new funding streams and collaborations to support further research in these areas.

***www.coeliac.org.uk/researchpriorities**



## PROF DAVID PRICE

Division of Infection and Immunity, Cardiff University School of Medicine, Cardiff, UK

### Biography

Professor David A Price MRCP DPhil DTM&H FRSB FLSW graduated with double first class honours in medical sciences and pathology at the University of Cambridge and completed his clinical training at King's College Hospital London. He practised internal medicine, specialising in infectious and tropical diseases, before pursuing a DPhil in immunology at the University of Oxford. After further academic clinical appointments, his research was conducted with fellowship support at the Vaccine Research Center, National Institutes of Health, USA.

He was appointed as Chair of Infection and Immunity at Cardiff University School of Medicine in October 2007. His programme focuses on the development and application of advanced biotechnology to address fundamental and translational issues in adaptive immunobiology.

To date, he has published >350 peer reviewed papers, attracting >20,000 citations in the contemporary literature, with a current H-index of 72 (ISI). In 2009, he was awarded the Graham Bull Prize in Clinical Science by the Royal College of Physicians, UK.

# DIETARY GLUTEN PERMANENTLY RECONFIGURES GASTROINTESTINAL TISSUE RESIDENT IMMUNITY IN COELIAC DISEASE

Tissue resident lymphocytes play a key role in immune surveillance, but it remains unclear how these inherently stable cell populations respond to chronic inflammation. In the setting of coeliac disease (CeD), where exposure to dietary antigen can be controlled, gluten induced inflammation triggered a profound depletion of naturally occurring Vγ4+/Vδ1+ intraepithelial lymphocytes (IELs) with innate cytolytic properties and specificity for the butyrophilin like (BTNL) molecules BTNL3/BTNL8. Creation of a new niche with reduced expression of BTNL8 and loss of Vγ4+/Vδ1+ IELs was accompanied by the expansion of gluten sensitive, interferon-γ-producing Vδ1+ IELs bearing T cell receptors (TCRs) with a shared non germline encoded motif that failed to recognise BTNL3/BTNL8. Exclusion of dietary gluten restored BTNL8 expression but failed to reconstitute the Vγ4+/Vδ1+ 'gut signature' among TCRγδ+ IELs. Collectively, these data show that local antigen driven inflammation dynamically reconfigures the tissue resident TCRγδ+ IEL compartment in genetically susceptible individuals, leading to the acquisition of a proinflammatory immune landscape that underpins the pathogenesis of CeD.

Mayassi T[1,2], Ladell K[3]...Price DA[3],*, Jabri B[1,2,4,*]

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## PROF DAVID SANDERS

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

### Biography

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, percutaneous gastrostomy feeding (PEG) and small bowel endoscopy. His other research interests include pancreatic exocrine insufficiency, irritable bowel syndrome and gastrointestinal bleeding.

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). His clinical work with patients who have coeliac disease has resulted in him being awarded the Coeliac UK Healthcare Professional of the Year Award (2010) and the inaugural Complete Nutrition Coeliac Health Care Professional Award (2013). He is fortunate to work as part of the Sheffield Gastroenterology team which has been recognised for its standards of clinical care. The Small Bowel Endoscopy service won one of the inaugural British Society of Gastroenterology National GI Care awards (2011) and the Medipex award (2013). In 2012 the PEG team won both Health Service Journal primary care and integrated clinical care awards. In 2014 the Sheffield Gastroenterology team, won one of the SAGE (Shire Awards for Gastrointestinal Excellence) awards for its primary care and GI bleed unit services. In 2017 because of his diverse clinical nutrition interests he was voted (by patients and healthcare professionals) the Clinical

Nutrition Health Care Professional of the Year. Professor Sanders has chaired both the British Society of Gastroenterology (BSG) Small Bowel and Nutrition Section (2006-2012) and the BSG Audit Committee (2010-2013).

He is the current Chair of the Coeliac UK Health Advisory Council, BSG Council Member and President of the International Society for the Study of Celiac Disease (ISSCD). The Sheffield Unit has recently been recognised as the Rare Diseases Collaborative Network for refractory coeliac disease (NHS England) in collaboration with Addenbrooke's Hospital, Cambridge.
**www.profdavidsanders.co.uk**

## DOCTOR I STILL HAVE SYMPTOMS; NON RESPONSIVE AND REFRACTORY COELIAC DISEASE

Coeliac disease is a common condition affecting up to 1% of the European adult population. Whilst the majority of patients will respond to a gluten free diet with resolution of symptoms and an improvement in histology, a significant minority have persistent problems. Refractory coeliac disease is a relatively uncommon cause of non-response to a gluten free diet with potentially serious consequences of severe malabsorption and the risk of progression to lymphoma.

This talk will provide a practical approach to the investigation of patients who do not respond to a gluten free diet. I will highlight the differences between the more common non-responsive coeliac disease and the rare entity of refractory coeliac disease and discuss current management and treatment options for both non-responsive coeliac disease and refractory coeliac disease.

## PROF CAROLINA CIACCI

Professor Carolina Ciacci, Celiac Center, University of Salerno, Italy

### Biography

Prof Ciacci is head of the Gastrointestinal Immunology Center for the study of coeliac disease, inflammatory bowel diseases (IBD) and food intolerances at S. Giovanni di Dio e Ruggi D'Aragona Hospital, Salerno, Italy (clinic and laboratory). Prof Ciacci is also head of the tertiary clinic for GI rare diseases and the tertiary IBD clinic, a unique centre that covers an area of about 1 million inhabitants.

She is the coordinator of the Campania Region Celiac Disease Network and responsible for the CeliaDB, a registry of more than 15,000 coeliac patients living in the Campania Region. **www.registrocampaniaceliachia.org/default.aspx.**

Prof Ciacci is Professor of Gastroenterology at Salerno University and has a broad background in clinical and basic research, focusing on coeliac disease, irritable bowel syndrome, IBD and mucosal immunology. As a principle investigator or co-investigator on several university and Italian Ministry of Health funded grants, she has led a number of clinical studies, and has also coordinated the economical research for those studies.

She is a member of the Gender and Diversity task force of United Gastro Week (2017-2021) and a member for the Commission for the qualification of professorship in gastroenterology, infectious disease and dermatology for the Italian Ministry of Education (2018-2020). She was a collaborator for the implementation of the World Gastrointestinal Organisation guidelines for celiac disease.

Prof Ciacci is the author of more than 250 scientific papers, 198 of those are present in Scopus, sum of citations 7532, h-index 43 and Google scholar h-index 47.

## TO BIOPSY OR NOT TO BIOPSY? THAT IS THE QUESTION!

Adult patients with coeliac disease (CeD) will have have duodenal biopsy at diagnosis and in some cases at follow up. However, with the availability of highly specific CeD serum antibodies and markers of gluten intake, as a proxy index of mucosal atrophy, views towards the duodenal biopsy may have changed.

In adults, the biopsy is still necessary to confirm the suspicion of CeD based on positive serology but also to avoid missing another diagnosis and/or CeD complications. Moreover, about 20% of patients with positive serology show no mucosal damage (potential CeD) and it is still unclear if and when those patients should start the gluten free diet (GFD). On the other hand, complications are quite rare and never diagnosed at the time of the first endoscopy. Histology can appear to be frequently ambiguous and mucosal damage not appropriately described. Previous observational studies suggest that at least a subgroup of adults (young adults, for example) may not need the biopsy because the risk of an overlapping disease or a serious complication of CeD is very low. An ongoing prospective international study will give a definitive answer as to which adult patients affected with CeD are required to undergo endoscopy and those who are not.

The follow up of patients with CeD can include a second endoscopy and biopsy, especially in the case of symptoms. However, in the absence of any concerns the procedure is often avoided. In addition, fecal and urine gluten immunological peptide tests are being introduced to allow monitoring of compliance to a GFD.


## DR MANPREET BAINS

Assistant Professor, Division of Epidemiology and Public Health, University of Nottingham

### Biography

Dr Manpreet Bains was appointed as Assistant Professor in Qualitative and Mixed Methods Health Research in the Division of Epidemiology and Public Health, University of Nottingham in 2013. She is also part of the UK Centre for Tobacco and Alcohol Studies (UKCTAS). Manpreet is a mixed methods researcher who has forged a respected research career, particularly in qualitative methods spanning a broad variety of topics in public health and health services research.

Manpreet has provided qualitative methods expertise on research funded by the NIHR, MRC, Cancer Research UK and Coeliac UK.
Her work spans purely qualitative studies, feasibility studies, to mixed methods trials in tobacco control, respiratory medicine, gastrointestinal disease, maternal health, alcohol and influenza to name some.

Current projects include preventing smoking uptake among adolescents in India, and the development and feasibility of a novel intervention for active ageing and smoking cessation. Manpreet is also involved in a project exploring the longer term recovery needs among patients affected by community acquired pneumonia.

Manpreet also convenes the Qualitative Methodology and Analysis module on the Masters in Public Health programmes offered by the Division, and is experienced in supervising undergraduate and postgraduate students. Manpreet is also involved in public involvement and jointly coordinates the UKCTAS' tobacco related public involvement activity (https://ukctas.net/public-engagement.html).

# HEALTHCARE PROFESSIONALS' AND PATIENTS' VIEWS ON THE LONG TERM FOLLOW UP OF COELIAC DISEASE


## Abstract

**Introduction**
Recommendations for following up persons with coeliac disease (CD) suggest regular review by a physician or dietitian in secondary or primary care. However, not only is the evidence underpinning these guidelines limited, views of healthcare professionals (HCP) involved in the management of the condition and individuals living with it has scarcely been studied.

**Methods**
Forty three semi structured interviews were conducted with HCPs (gastroenterologists, general practitioners and dietitians) and 50 individuals with CD. Those with CD were purposively sampled to include persons receiving follow up and those who were not (through choice or discontinued). Interviews explored individuals' follow up experiences/ practices, understanding of the purpose of follow up, its perceived importance and if it could be improved. Interviews were digitally audio recorded, transcribed verbatim and analysed using the framework approach.


## Results

*HCP findings*

Some HCPs stated the evidence base for follow up was insufficient. However, others felt follow up was crucial to ensure individuals were adhering to a gluten free diet, and for vulnerable individuals (eg newly diagnosed, elderly, children, pregnant women and those with co-morbidities), than those more proactive in their self management. Non attendance was not seen as particularly problematic by most; those wanting follow up attend and those that did not chose not to. However, several participants inferred that a proportion of those choosing not to attend were likely to be less compliant and thus may not attend due to fear of being judged. Many stressed that an element of patient responsibility and engagement was an important factor in the successful management of coeliac disease. Generally the process for follow up tends to revolve around recap and reassurance for patients whilst the main concerns for HCPs are the deteriorating timelines in which some patients are left without support for a number of years. HCP opinion on and knowledge of current national guidelines on following up individuals with coeliac disease was varied, with most admitting that they were not necessarily adhering to every part of the current standards. Many HCPs noted that a lack of clear guidelines at a local level added to the confusion and disparity in treatment. Improvements at a national level tended to involve a request for clear guidelines based on good evidence that were able to be managed in a resource poor environment.

*Patient findings*

Many participants felt support and the provision of information to manage their condition was lacking soon after diagnosis, when needed most. Follow up was seen as a relatively individualised process with people reporting a wide variation in process from repeat bone scans and endoscopies, to having never been followed up at all. Regularity of follow up also varied with many participants acknowledging that it was rarely in line with the recommended timelines. For some, attendance served to reassure individuals that they were on track, while others felt they needed to attend to 'stay in the system' or in case of any developments. Hence, they seemed to lack understanding on what follow up is meant to achieve. However, for those choosing not to attend, reasons related to not viewing it as worthwhile or useless, particularly if individuals felt they were managing well or because previous negative experiences with unsupportive or unknowledgeable healthcare professionals had deterred them. Most agreed that an annual review at a local location with a consistent person who was knowledgeable about coeliac disease would be a sufficient form of follow up, but that this should be supported by additional services that could deal with more immediate issues. However, some participants were happy not to have follow up as they were managing fine, or were happy to have it offered as needed rather than with prescribed regularity.

Comparing HCP and patient views
HCP and patient views were similar in that follow up provided an opportunity to reaffirm and reinforce compliance, and thus reassured patients that they were managing the condition well. The importance of having a blood test to measure compliance objectively was also relayed by both parties. However, both groups suggested a lack of understanding about the purpose, value and importance of follow up. Moreover, there was some agreement about NHS resources being wasted for cases where follow up was seen as being pointless or during processes, such as ordering repeat prescriptions that were deemed unfit in their current form.

Divergent views were apparent, for instance HCPs believed non attendance was associated with convenience and that patients forgot about appointments; whereas patients stated non attendance related to how worthwhile they deemed it to be, with some admitting that they lacked confidence in HCPs, and instead these individuals felt more knowledgeable themselves. HCPs also underscored the role of patients in the follow up process, in that attendance was their own choice and that it was their responsibility to engage. However, patients did not see attendance as a choice but something that was either encouraged/discouraged by HCPs (e.g. some patients felt the condition was not taken seriously by HCPs), and was influenced by the extent to which they were followed up in accordance with recommended timelines.

**Conclusions**

There was a wide variety of follow up arrangements currently delivered, described by HCPs. Many HCPs seemed to be unconvinced by the quality of the evidence underpinning national guidance for follow up or were unaware of it. Meanwhile, most individuals with coeliac disease expressed a preference for receiving some form of annual follow up, but the reason for having it was unclear to them. Some had a preference for not attending follow up or having it provided only as needed.

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Research funded by Coeliac UK

## PROF RAMESH ARASARADNAM

Consultant Gastroenterologist, University Hospitals Coventry and Warwickshire and Clinical Academic, Universities of Coventry, Leicester and Warwick

### Biography

Professor Ramesh Arasaradnam is a clinical academic/Consultant Gastroenterologist at University Hospitals Coventry & Warwickshire (UHCW) affiliated with University of Coventry, University of Leicester and University of Warwick. He graduated from Queen's in 1996 and is a Fellow of the Royal College of Physicians, London as well as the European Board of Gastroenterology. Currently he is chair of the British Society of Gastroenterology (BSG) research committee. His research interests are in inflammatory conditions within the GI tract and application of non invasive technology for early disease diagnosis. He is a Medical Advisor to BAD-UK (Bile Acid Diarrhoea) charity and Trustee for GUTs UK charity.

# EXPLORING THE COELIAC 'FERMENTOME' AND 'MICROBIOME'

Whilst there is now increasing awareness of coeliac disease (CD), much is left to be understood of disease mechanism and in particular metabolic changes at cellular level. These metabolic changes are altered in the disease state and in response to a gluten free diet (GFD) with resultant changes in the gut bacteria.

We have been exploring the concept of 'fermentome' that is metabolic products or volatile organic compounds (VOCs) that are present in certain inflammatory disease states. VOCs produce a unique chemical fingerprint which can be detected in different biological samples from urine, breath and even sweat. We have previously shown that those with CD produce a unique chemical in urine - cyclooctatetraene. This alkene is thought to be a by product of certain anaerobic bacteria.

We then looked at the VOC chemical print in those with CD (pre-treatment with a GFD) and subsequently at six months and showed that whilst the VOC print does alter it still remains different compared to those without CD. When the microbiome was explored, those with CD had lower diversity and certain species eg *Clos. perfringens* remained at lower levels. This observation persisted at six months despite being on a GFD.

The relevance of these bacteria are unknown and functional aspects need to be explored. Nevertheless, these exploratory findings suggests that certain species in those with CD do not alter to a 'normal' state despite being on a GFD and histological resolution. These changes can potentially be mapped in urine by measuring VOC chemical prints.

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Research funded by Coeliac UK

## DR FRANCISCO LEON

Adjunct Professor, Jefferson Medical College, Philadelphia and Co-founder of Provention Bio, Celimmune and Gultenostics

### Biography

Dr Francisco Leon, MD PhD, is the co-founder of the companies Provention Bio, Celimmune and Glutenostics, developing and commercialising medicines, diagnostics and preventative approaches for people with coeliac disease and other immunological disorders.

Francisco had extensive experience in translational immunology in academia (National Institutes of Health), biotech (Alba Therapeutics, MedImmune) and 'big pharma' (Bristol-Myers Squibb, Johnson & Johnson) before becoming an entrepreneur.

Francisco is a clinical immunologist who received his MD and PhD from Autónoma University in Madrid, Spain. Francisco is also Adjunct Professor at Jefferson Medical College, Philadelphia and has co-authored more than 85 peer reviewed articles, book chapters and patents.

# THERAPEUTIC ADVANCES FOR COELIAC DISEASE

People with coeliac disease are interested in medicines to prevent the symptoms and effects of gluten contamination in the gluten free diet. Multiple 'shots on goal' are needed since most medicines fail to be approved, and it is likely that combinations will be needed for full efficacy. Multiple experimental non-dietary therapies for coeliac disease are being tested in clinical trials and will be reviewed.

One of the most advanced such experimental medications is the anti-IL-15 monoclonal antibody AMG 714, or PRV-015. Interleukin 15 (IL-15) is a driver of intraepithelial lymphocytes in coeliac and refractory coeliac disease Type II (RCD-II), AKA pre-enteropathy associated T cell lymphoma (Pre-EATL). The results of AMG 714/PRV-015 in coeliac disease and RCD-II will be presented.

With the support of coeliac patient support groups, the next round of clinical trials could result in a medication available in the coming years.

## DR MANUEL SPANNAGL

Senior Scientist and Deputy Group Leader, Plant Genome and Systems Biology, Helmholtz Zentrum München, Germany

### Biography

Dr Manuel Spannagl is a Senior Scientist and Deputy Group Leader in the Plant Genome and Systems Biology (PGSB) group at the Helmholtz Zentrum München in Germany. PGSB has been engaged in the development of plant genome bioinformatics for over 15 years and has shaped the field of plant genomics with publications on numerous plant reference genome sequences.

After completing his training in bioinformatics Manuel joined PGSB in 2003 and contributed to several high impact publications such as the tomato, Medicago, sorghum, brachypodium, barley and bread wheat genome. With his PhD thesis on the genomic repertoire of complex and polyploid cereal genomes completed in 2015 he became involved in wheat genomics and wheat related diseases.

As a member and team leader in the International Wheat Genome Sequencing Consortium (IWGSC) he coordinated and directed the efforts to generate a high quality gene annotation for the newly generated bread wheat reference genome sequence.

His work on the bread wheat genome sequence also included analyses on gene families/phylogenomics, gene expression, transposable elements and genome structure. In acknowledgment of this work he received an IWGSC leadership award in 2017. His current work focuses on exploring the natural diversity of wheat and cereals in general, using comparative genomics, enabled by the new technologies for sequencing and genome assembly. This work involves a strong interest in understanding and describing the genes, gene families and mechanisms related to wheat sensitivities.

## HOW COMPLEX CAN IT BE? THE BREAD WHEAT GENOME AND ITS IMPLICATIONS FOR WHEAT INTOLERANCE

Wheat is one of the most important crops for human nutrition, but its components are also causative for several human diseases and sensitivities, such as coeliac disease. With the recently published whole genome sequence for bread wheat (IWGSC 2018), an important resource is now available to identify and study gene families related to wheat sensitivities and their products in a genome wide manner. Its complex genetic setup and large genome size of five times the human genome has made the wheat genome impossible to decode for decades.

In 2005, the International Wheat Genome Sequencing Consortium (IWGSC; **www.wheatgenome.org**) had the goal to produce a reference genome sequence for bread wheat by the year 2020. Thanks to novel algorithms and bioinformatics strategies, a reference genome sequence along with gene predictions could now be reported even earlier (IWGSC 2018).

This new resource established the foundation for in depth analyses of gene expression and regulation in the bread wheat genome (Ramirez-Gonzalez et al., 2018) as well as the first genome wide map of genes and gene families encoding immunoresponsive proteins (Juhasz et al., 2018).

This map is a first step to enhancing breeding efforts of wheat lines that are safer for human consumption and provide a higher environmental stability. Ongoing wheat pan-genomics and resequencing efforts such as the 10+ wheat project (www.10wheatgenomes.com) will greatly contribute towards understanding natural variation and the possible impact of different wheat genotypes on the immunoreactive potential of wheat products.

## LINA MOSCHOULA PASSALI

Postgraduate, University of Copenhagen

### Biography

Lina Moschoula Passali has an MSc in Clinical Nutrition from the University of Copenhagen and is currently exploring gluten and multiple sclerosis (MS). During her BSc in Food Science with Nutrition & Health, University of Copenhagen, she was diagnosed with Hashimoto's Thyroiditis, which awakened her interest in autoimmunity.

Claims of gluten free diets being beneficial for patients with autoimmune diseases inspired her to conduct research on the topic with the aim of generating evidence based knowledge on the role of nutrition in autoimmunity.

She wrote her bachelor thesis on non coeliac gluten sensitivity and thereafter she started a collaboration with the Bartholin Institute, leading experts in gluten and type 1 diabetes, as well as researchers from Rigshospitalet, Glostrup working within the fields of MS and MRI. The research group is currently running a clinical trial investigating possible effects of a gluten free diet among patients with early stages of MS. Additionally, the group is studying potential gut brain interactions in MS, trying to understand the role of increased intestinal permeability in MS.

Together with three other members of the research group, Lina has recently published a systematic review on the role of gluten in MS. Her long term research goals include providing clear answers to whether a high gluten intake can increase the risk of autoimmunity and whether gluten free or low gluten diets can be beneficial for patients with multiple sclerosis or other autoimmune disorders in addition to coeliac disease.

# IS THERE A ROLE FOR GLUTEN IN MULTIPLE SCLEROSIS?

Multiple Sclerosis (MS) is a chronic disease affecting the central nervous system. The cause of MS is unknown, and even though medical treatments have been developed, the disease is still not curable.

There is an increasing interest in diet as a modifying factor in MS, but no official dietary guidelines specific for patients with MS have been developed yet. Being on a gluten free or low gluten diet is a current health trend and potential mechanisms through which gluten theoretically could contribute to deteriorating the course of autoimmunity have been suggested.

We conducted a systematic review aiming to evaluate the evidence suggesting a possible role of gluten in MS by addressing the questions:

- Can patients with MS benefit from avoiding gluten?
- Do patients with MS have increased levels of gluten related markers?
- Do patients with coeliac disease (CD) or MS have increased risk of developing MS or CD respectively?

Studies investigating possible beneficial effects of gluten free diets for patients with MS found positive results but have major methodological limitations. Results regarding the presence of gluten related markers in MS patients are inconsistent, whereas current literature does not support a link between MS and CD. The current level of evidence is inadequate to state whether gluten plays a role in MS. Limitations of current evidence have been identified and directions of future research have been suggested.

## DR IAIN CROALL

Cognitive Neuroscientist, Sheffield Institute of Gluten Related Disorders (SIGReD), Sheffield, UK

### Biography

Dr Iain Croall is a cognitive neuroscientist who joined the team at the Sheffield Institute of Gluten Related Disorders (SIGReD) in 2017. He completed his PhD at Newcastle University in 2015, and has previously worked as a research associate at the University of Cambridge.

Iain's career has shaped him into a scientist who specialises in working at the intersection between cognition and the underlying physiology of the brain. His PhD thesis characterised and linked the physical and cognitive effects of traumatic brain injury, while his previous postdoc experience examined different blood pressure treatment regimens in a randomised clinical trial of patients with vascular dementia. This experience has helped him develop an expertise in using "advanced" MR imaging techniques to characterise brain harms and study how these affect patient outcome.

He joined SIGReD as a dedicated image analyst in the research of how the brain is affected across all types of gluten sensitivity. His current projects include imaging work designed to capture "real time" brain changes due to gluten in non coeliac gluten sensitive (NCGS) patients, a survey study examining trends between dietary compliance and quality of life in NCGS, and a large scale MRI experiment utilising UK Biobank data to study the neuro-psychological harms of coeliac disease in greater depth and scope than has been previously achieved.

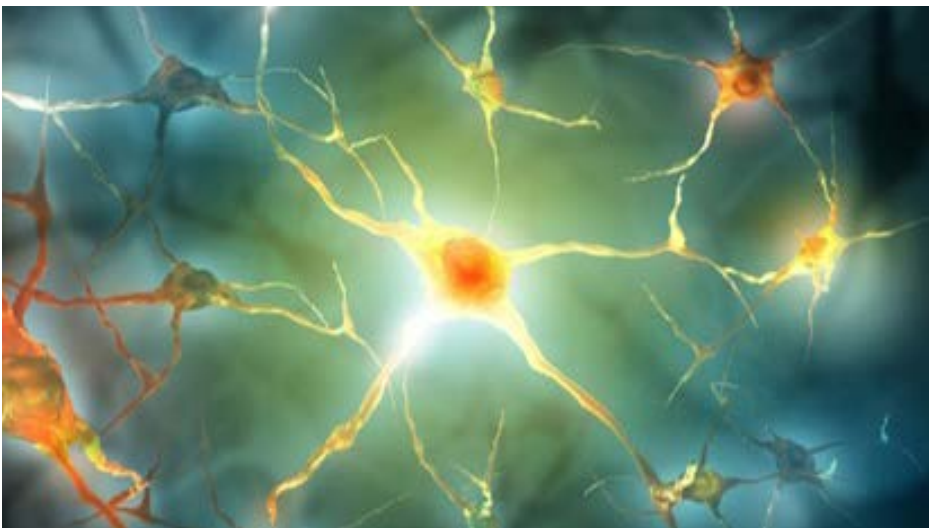
In the future, he hopes to turn his attention to examine the potential role of gluten as a modifiable risk factor for dementia in a subgroup of the general population.

## WHAT DOES GLUTEN DO TO YOUR BRAIN?

Brain harms are recognised to exist across the spectrum of gluten related disorders. However, while the blunt cerebellar atrophy which accompanies a case of Gluten Ataxia may be quickly evident, the presentation and effects of brain damage in coeliac disease (CD) and non coeliac gluten sensitivity (NCGS) can be more subtle and are less well understood. This may lead to uncertainties over to what extent harms exist and how impactful they are on the patient's life.

The last two decades have laid strong foundations in the study of these extra-intestinal effects, but there are many ways this research stands to be expanded. In NCGS, patients (with a gastroenterological presentation) have not yet been imaged to explore for associated brain harms, while investigations like postal surveys can show links which lend credence to how gluten free diet adherence affects their quality of life. "Advanced" imaging techniques can also identify brain damage not immediately evident to the naked eye, helping us better understand the pathology and difficulties which CD patients face.

This talk will give an overview of the neurological focused research being conducted at the Sheffield Institute of Gluten Related Disorders. These experiments are critical in advancing our understanding of brain harms found across gluten sensitivity.



## DR MICHAEL PARKS

Head of Research & Development, Nonacus Ltd

### Project team

At Nonacus our mission is to reduce invasive diagnostic testing by developing robust non invasive alternatives.

Dr Michael Parks leads research and development at Nonacus Limited where he has worked for four years developing novel products and technologies for non invasive genetic testing within prenatal healthcare and oncology.

Before joining Nonacus, Michael worked at the Birmingham Women's Hospital as the lead translational research scientist for the Wellcome Trust, Health Innovation Challenge Fund supported NIPSIGEN project. This project focused around developing, validating and implementing within the NHS new non invasive prenatal diagnostic (NIPD) tests for single gene disorders.

During this time and amongst other developments Michael has developed a novel Targeted Next Generation Sequencing (NGS) assay which can count DNA in a digital way giving an exact read out of the sequences read and quantify them with sensitivity down to 1/1000 while importantly removing PCR and sequencing error and bias.

Nonacus Limited and the University of Cambridge are both enormously grateful to both Coeliac UK and Innovate UK for this opportunity to advance diagnostics in gluten sensitivity. We look forward to combining our expertise to assist coeliac disease patients.

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# DEVELOPMENT AND VALIDATION OF A MINIMALLY INVASIVE COMPREHENSIVE DIAGNOSTIC COELIAC DISEASE TEST

## The Project

Working closely with Dr Elizabeth Soilleux and her team at the University of Cambridge who are joint applicants on this 18 month grant, we intend to develop Nonacus' proprietary, highly sensitive DNA capture methodology for detecting coeliac disease, low frequency DNA sequences and couple it with the computer algorithm developed by the Soilleux group, in order to form the perfect pipeline for a novel minimally invasive coeliac disease diagnostic test.

After initial validation and work up of the Nonacus technology with the Soilleux group's novel algorithm on duodenal biopsy material we will quickly move onto evaluating the technologies applicability to blood samples.

The outcome of this grant is to develop a non invasive coeliac disease diagnostic test which we expect to overcome some of the limitations of existing testing for coeliac disease.

We envisage no ongoing or minimal gluten exposure of patients being required prior to testing and we anticipate endoscopy being unnecessary. Additionally the test outcome will remove some of the subjectivity associated with the current "gold standard" for coeliac disease which involves a pathologist examining a small bowel biopsy taken at endoscopy (Figures 1 and 2), but disagreement between pathologists about the diagnosis is common.

Both the Nonacus and Cambridge University teams are confident that their approach will yield a test that is less likely to miss a diagnosis of coeliac disease and will remove the uncertainty seen with current test methods.

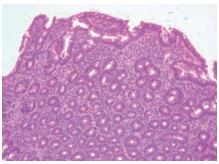

Figure 1 Damaged intestine - Coeliac disease

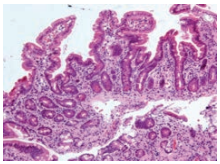

Figure 2 Healthy intestine

## DR LYDIA CAMPBELL

Founder and Chief Technology Officer, Nandi Proteins Ltd

### Project team

The Nandi Proteins led consortium includes Genius Foods which develops and commercialises gluten free baking and breads, an ingredients business AB Mauri, an agronomy firm Agrii and Heriot Watt University (HWU), Edinburgh which will also collaborate with the Scottish Centre for Food Development and Innovation (SCFDI) also in Edinburgh.

The roles of the collaborators in the project will be as follows: Agrii will supply faba beans, oats and rapeseed pressed cakes, Nandi Proteins Ltd and HWU will extract protein, improve functionality using patented technology, test the ingredients for storage stability and nutritional properties and manufacture dried powders on pilot scale. The prototype ingredients will be tested in model gluten free recipes at SCFDI which contains a sensory suite and development kitchens. The optimised ingredients will be tested by AB Mauri and Genius Foods in commercial gluten free recipes.

Dr Lydia Campbell is the founder and Chief Technology Officer of Nandi Proteins Ltd and will lead the project. She is also Associate Professor in the School of Engineering and Physical Science at HWU. She previously held positions for 10 years in product R&D at Nestlé Switzerland and Germany.

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# PROTEIN INGREDIENTS FROM UK CROPS AS SOURCE OF GLUTEN LIKE FUNCTIONALITY

## The Project

Coeliac UK and Innovate UK have together contributed ~£181k towards a £250k research project aimed at developing gluten replacements from UK grown crops.

We plan to design a unique formula of three ingredients consisting of protein extract from rapeseed pressed caked, naked oats and faba bean as a gluten replacer in bread. These crops are currently grown in the UK, but underutilised. The functionality of the ingredients will be tailored by innovative processing technology which will lead to development of gluten free breads with improved nutrient profiles and desired sensory and texture characteristics. New bread formulations and ingredients will be tested by two industrial partners in their gluten free (GF) bread range. This aligns with Coeliac UK's strategy to target food manufacturers to increase the range of foods which are gluten free.

A GF diet is currently the only treatment for coeliac disease. GF foods usually have lower protein concentrations eg GF bread has 30% less protein than standard breads, indicating the need to compensate this loss. Dairy and egg proteins are added for these reasons but are expensive and potentially add to allergenicity. Around 70% of plant proteins are imported into Europe in the form of soy. Replacement by locally sourced plant proteins would address a key dietary need while lowering manufacturing costs and simplifying supply chain management and securing feedstock supply.

Bakery is the largest sector of GF products, which reached sales of €1.5 billion in the past decade. Faba beans (30% protein) are the major beans grown in the UK but are underutilised for human food. Naked oats contain more protein than hulled oats (20% vs 10%) and are a small crop in the UK. Rapeseed pressed cake (RPPC) contains 30-40% protein. The UK produced 2.38 million tonnes of rapeseed in 2017. After the oil has been pressed out, approximately 1.48 million tons of RPPC remains, which is used as animal feed. The development of new markets with protein concentrates from these feedstocks could significantly improve the quality of life of people with coeliac disease whilst adding value to the entire UK (bio) economy.

## DR CHRIS KENNELLY

Managing Director,
Cievert Ltd

### Project team

Cievert is a digital health company based in Newcastle, with offices in London. They specialise in developing innovative software for the health sector, working in partnership with the NHS to develop their solutions.

Established in 2011 by Chris Kennelly, a former NHS radiographer, Cievert software can now be found in NHS Trusts across the UK. In fact, their software has helped manage over 100,000 patients to date. Chris has also previously worked within NHS commissioning leading on regional capacity planning within radiotherapy.

The Penguin Coeliac clinical model will be developed and tested by Dr Matt Kurien, Senior Clinical Lecturer in Gastroenterology and Honorary Consultant Gastroenterologist and Prof Sanders, Consultant Gastroenterologist and Honorary Professor of Gastroenterology.

Matt's research interests are in small bowel disease and clinical nutrition, with outputs predominantly in coeliac disease and gastrostomy feeding.

In coeliac disease Matt's work has focused on detection, using differing endoscopic techniques and point of care tests. Matt Is now examining the autoimmune association between coeliac disease and Type 1 diabetes, and also investigating the overlap with non coeliac gluten sensitivity. In 2016, he was awarded the Julie Wallace Award by the Nutrition Society for his contributions to this field.

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# USING SOFTWARE TO IMPROVE THE LONG TERM MANAGEMENT OF PEOPLE AFFECTED BY COELIAC DISEASE

## The Project

Despite national and international guidelines advocating follow up of coeliac disease, there remains significant differences in how individuals are supported and followed up. For example, some patients have regular follow up consultations with their GPs, others see gastroenterologists or dietitians, and others have no follow up at all.

Ideally, long term care should be tailored to the individual need of the patient. Some patients will adapt well to the dietary modification and require minimal ongoing support or care, whilst others may require significantly greater intervention.

This project has two broad aims. Firstly, to improve how coeliac patients are followed up by using Cievert's software, Penguin, to remotely monitor how patients are living with their coeliac disease and automatically use this information to tailor clinical need to the individual. Secondly, using this improved data collection to help better identify those responding to a gluten free diet, without the need for invasive biopsies of the gut.

The result will be that patients requiring support are identified more quickly and those that are doing fine receive reassurance without unnecessarily consuming finite clinical resource.

If you are a gastroenterologist and interested in being part of this project and trialling the use of this software please contact Chris: **chris.kennelly@cievert.co.uk**

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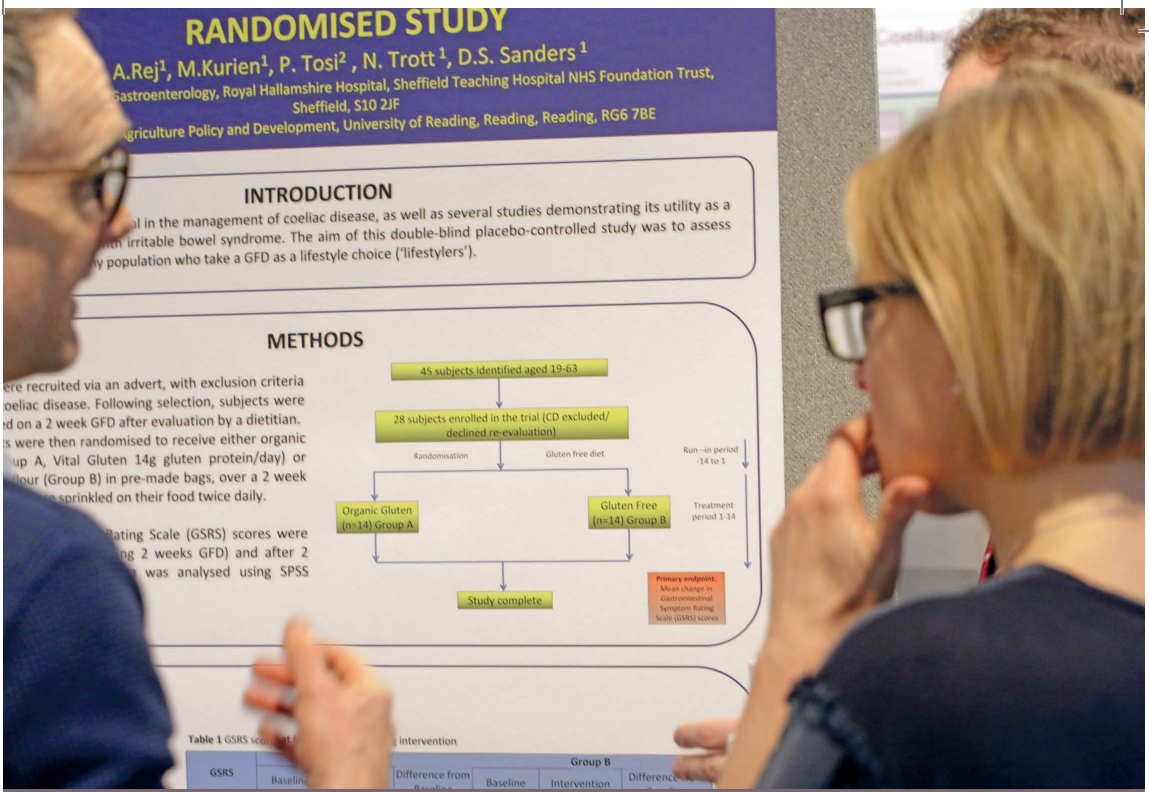


# POSTER COMPETITION

## Entries to the Coeliac UK Research Conference 2019 poster competition.

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. The winner of our poster competition will be announced at the end of the conference.

**£500 PRIZE FOR THE BEST POSTER**

# SHOULD WE BE DIAGNOSING COELIAC DISEASE IN THE ELDERLY?

**Authors**
Marks L[1], Rej A, Kurien M, Rees M, Cross S, Hadjivassiliou M, Sanders DS

**Institution**
University of Sheffield, Sheffield, UK[1]

## Abstract

### Introduction
Coeliac disease (CD) is common, but is underdiagnosed in the elderly due to lack of physician awareness and heterogeneity of presentation. We aimed to establish whether there has been a change in the diagnosis of CD in the elderly (over 65 years old) from 1990 until present day, as well as the clinical and histopathological features of CD in old versus young adults.

### Method
Newly diagnosed CD patients were prospectively recruited from the Coeliac Specialist Clinic at the Royal Hallamshire Hospital, Sheffield, between 2008 and 2017. All patients had villous atrophy on biopsy, positive coeliac serology (IgA tissue transglutaminase and IgA endomysial antibodies) and compatible Human Leukocyte Antigen (HLA) typing. Additionally, patients were retrospectively identified from 1990 to 2008 to determine the trend in elderly CD diagnostic frequency over time.

## Results

1605 patients with CD were recruited (n = 644 prospectively, n = 961 retrospectively). Of these, 208 patients (13.0%) were diagnosed over the age of 65 years between 1990 and 2017. The proportion of elderly CD diagnoses increased from 0% (n = 0/11) in 1990-1991 to 18.7% (n = 41/232) in 2016-2017 ($p < 0.001$). The female to male ratio decreased with increasing diagnostic age from 1.71:1 in the 18 - 34 age group to 1.02:1 in the over 65 age group ($p < 0.001$). Younger patients more commonly presented with fatigue ($p < 0.001$) and gastrointestinal symptoms including diarrhoea ($p = 0.005$), abdominal pain ($p = 0.019$), and IBS type symptoms ($p = 0.008$). Older people more frequently presented with B12 deficiency ($p = 0.037$) and had milder degrees of villous atrophy than younger patients ($p = 0.005$).

**Table 1** Association between clinical features at presentation and age of coeliac disease diagnosis

| | Prevalence in overall prospective cohort % (n = 644) | Age (years) | | | *p* value |
|---|---|---|---|---|---|
| | | 18-34 % (n = 258) | 35-64 % (n = 287) | >65 % (n = 99) | |
| Fatigue | 24.9 (160) | 31.8 (82) | 23.0 (66) | 12.1 (12) | <0.001 |
| Diarrhoea | 30.4 (196) | 35.7 (92) | 30.0 (86) | 18.2 (18) | 0.005 |
| Abdominal pain | 23.2 (149) | 29.1 (75) | 20.2 (58) | 16.2 (16) | 0.019 |
| IBS type symptoms | 18.0 (116) | 24.4 (63) | 15.0 (43) | 10.1 (10) | 0.008 |
| B12 deficiency | 12.1 (78) | 10.5 (27) | 10.8 (31) | 20.2 (20) | 0.037 |

## Discussion

Coeliac disease is common in elderly patients but gastrointestinal symptoms occur less frequently than in younger individuals. Elderly patients tend to present with a milder degree of villous atrophy. This questions the utility of active case finding in this age group, as a gluten free diet may not be the most appropriate management in this cohort.

# COELIAC DISEASE - OLDER PATIENTS HAVE THE MOST EXTENSIVE SMALL BOWEL INVOLVEMENT ON CAPSULE ENDOSCOPY

**Authors**
Chetcuti Zammit S[1], Sanders DS, Sidhu R

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## Abstract

**Introduction**
The relationship between symptomatology, serology and findings on small bowel capsule endoscopy (SBCE) in patients with coeliac disease (CD) remains unclear. Clarifying such associations will help determine if symptoms and serology can predict severity and extent of disease on SBCE.

**Method**
Patients with newly diagnosed CD (villous atrophy on duodenal histology and positive CD serology) were recruited. Patients underwent a SBCE at the time of diagnosis. Information on SBCE was recorded. Signs and symptoms at presentation, serological markers, histological classification of disease in the duodenum were noted.

**Results**
Sixty patients with newly diagnosed CD (mean age 44.9 years SD ± 17.4, 17 - 76) were included in this study. Older patients ($p$ = 0.025) and patients presenting with iron deficiency anaemia ($p$ = 0.026) had more extensive small bowel (SB) involvement. Patients presenting with weight loss were more likely to have SB involvement beyond the duodenum ($p$ = 0.027). Patients presenting with iron deficiency anaemia ($p$ = 0.038) and weight loss ($p$ = 0.009) were significantly older at diagnosis. Serum albumin was lower in those patients diagnosed later on in life ($p$ = 0.007).

There was no significant association between anti-tissue transglutaminase antibody ($p$ = 0.396) and extent of affected SB mucosa.

Patients with more severe Marsh classification of disease on histology from the duodenal bulb had more extensive SB involvement ($p$ = 0.017).

**Discussion**
This is the largest study on newly diagnosed CD and SBCE. Older patients are likely to have more extensive disease on SBCE at diagnosis. Symptoms and serology had no impact on the findings on SBCE apart from weight loss and iron deficiency anaemia.

# CAPSULE ENDOSCOPY IN COELIAC DISEASE: THE ROLE OF FLEXIBLE SPECTRAL IMAGING COLOUR ENHANCEMENT

**Authors**
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## Abstract

### Introduction
Flexible spectral imaging colour enhancement (FICE) is a form of virtual chromoendoscopy that is incorporated in the capsule reading software and that can be used by reviewers to enhance the delineation of lesions in the small bowel. This has been shown to be useful in the detection of pigmented (ulcers, angioectasias) lesions. However, its application to coeliac disease (CD) images from small bowel capsule endoscopies (SBCE) has rarely been studied.

### Method
This was a European, multicentre study that included five expert capsule reviewers who were asked to evaluate a number of normal and abnormal de-identified images from SBCE of patients with CD to determine whether the use of FICE and blue light can improve the detection of CD related changes.

**Results**
Sensitivity and specificity of conventional white light in the delineation of CD related changes were 100%. The next best image modification was FICE 1 with a sensitivity of 88% and a specificity of 96%. There was no difference between conventional white light, FICE and blue light for the identification of CD related changes. There was a low agreement (Fleiss Kappa 0.107; $p = 0.147$) between expert reviewers in selecting the best image modification that detected CD related changes.

**Discussion**
FICE and blue light were not found to be superior to conventional white light in the delineation of macroscopic changes related to CD on SBCE.

# THE ASSOCIATION OF SMALL CAPSULE ENDOSCOPY AND BONE MINERAL DENSITY IN PATIENTS WITH COELIAC DISEASE

**Authors**
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**Institution**
Sheffield Teaching Hospitals, Sheffield, UK[1]

## Abstract

### Introduction
Osteoporosis is an established complication of coeliac disease (CD). Adherence to a gluten free diet is important for the small bowel (SB) to heal and to improve calcium and vitamin D absorption, both of which are important in bone formation and repair.

### Method
Patients with histologically proven CD were recruited. Small bowel capsule endoscopy (SBCE) was carried out within two months of obtaining duodenal histology. BMD was carried out within 12 months of SBCE.

### Results
A total of 80 patients (68.8% females, 56.3% newly diagnosed) with CD were included. Mean age of the patients was 48.3 years ±17.3.

Mean anti-tissue transglutaminase antibody was 53.9 ± 65.4 at the time of SBCE. Anti-endomysial antibody was positive in 49 patients (61.3%) at SBCE. Patients had a mean calcium of 2.35 ± 0.079 mmol/l and mean vitamin D of 58.1 ± 26.0 nmol/l. A significant number of patients had deficient (44%) and insufficient (32%) vitamin D levels.

Patients had the following BMD results: 42 patients (53.2%) normal, 28 patients (35.4%) osteopenia, 9 patients (11.4%) osteoporosis.

In patients with newly diagnosed CD, age at SBCE correlated inversely with BMD (T score lumbar spine $p = 0.022$, T score total hip $p < 0.001$, overall score $p < 0.001$). This was also true in patients with established CD (T score lumbar spine $p = 0.013$, T score total hipp = 0.048, overall score $p = 0.019$).

Extent of abnormal SB mucosa on SBCE correlated with BMD parameters. Percentage of abnormal SB mucosa correlated with BMD at the lumbar spine and T score at the spine (Table 1).

**Table 1** Association between clinical features at presentation and age of coeliac disease diagnosis

| | Total SB transit | | % length of abnormal SB | | % time without villi | |
|---|---|---|---|---|---|---|
| | Pearson correlation | *p* value | Pearson correlation | *p* value | Pearson correlation | *p* value |
| BMD lumbar spine g/cm2 | 0.150 | 0.214 | -0.239 | 0.044 | / | < 0.001 |
| BMD total hip g/cm2 | -0.155 | 0.183 | -0.202 | 0.080 | -0.168 | 0.226 |
| T score lumbar spine | 0.150 | 0.223 | -0.254 | 0.035 | / | < 0.001 |
| T score total hip | -0.186 | 0.115 | -0.197 | 0.093 | -0.169 | 0.237 |
| Normal/osteopenia/ osteoporosis | | 0.809 | | 0.376 | | 0.378 |
| Calcium mmol/L | 0.082 | 0.491 | -0.064 | 0.589 | 0.088 | 0.540 |
| Vitamin D nmol/L | -0.004 | 0.977 | -0.138 | 0.269 | 0.361 | 0.014 |

## Discussion

This is the first study that demonstrates that extent of SB involvement on SBCE corresponds to increased severity of BMD particularly in the elderly. They should be treated aggressively to improve BMD and should be monitored closely with regular repeat BMD.

# CAPSULE ENDOSCOPY IN ESTABLISHED COELIAC DISEASE: CLINICAL SYMPTOMS, EXTENT OF DISEASE AND SMALL BOWEL TRANSIT

**Authors**
Chetcuti Zammit S[1], Kurien M, Sanders DS, Sidhu R

**Institution**
Sheffield Teaching Hospitals, Sheffield, UK[1]

## Abstract

**Introduction**
Patients with established coeliac disease (CD) can present with recurrent symptoms requiring further investigations including small bowel capsule endoscopy (SBCE). There is paucity of data on the relationship between the extent, severity of disease and small bowel transit (SBT) on capsule endoscopy in relation to histology, clinical and serological parameters.

**Method**
One hundred patients with CD and 200 controls were recruited. All of these patients underwent a SBCE because of symptoms, abnormal serology or a suspicion of complications. Extent of disease SBCE and SBT were studied in relation to symptomatology, serology and severity of histology from the duodenum.

**Results**

In patients with CD, n = 30 (30.0%) had a normal SBCE, n = 56 patients (56.0%) had proximal small bowel (SB) involvement, n = 7 patients (7.0%) had proximal and mid SB involvement and n = 7 patients (7.0%) had diffuse disease.

SBT was shortest in controls (275.0; range 60.0 – 981.0 minutes), followed by those with established CD and a normal SBCE (260.0; range 104.0 – 467.0 minutes) and those with established CD and macroscopic evidence of CD on SBCE (286.0; range 60.0 - 981.0 minutes) ($p < 0.001$). Age at time of SBCE ($p < 0.006$), serum albumin ($p = 0.004$) and haemoglobin ($p < 0.001$), Marsh score of histology from the duodenal bulb (D1) ($p < 0.001$) and the second part of the duodenum ($p < 0.001$), the presence of RCD features on histology correlated significantly with the percentage of affected mucosa on SBCE on univariate analysis. On multiple regression analysis, serum albumin level ($p = 0.036$) and Marsh score of histology taken from the duodenal bulb (D1) ($p = 0.019$), serum vitamin B12 ($p = 0.001$) and folic acid levels ($p = 0.008$) were statistically significant.

**Discussion**

Patients with CD have a persistently prolonged SB transit even if there is no evidence of disease on SBCE. This is the first study showing correlation between extent of disease and severity of duodenal histology according to the Marsh classification.

# TYPE I DIABETES: SCREENING FOR COELIAC DISEASE AND QUALITY STANDARDS AUDIT


## Authors
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## Institution
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## Abstract

### Introduction
Type 1 diabetes patients are at risk of coeliac disease. The NICE guideline recommends screening for coeliac disease at Type 1 diagnosis and the NICE Quality Standard for coeliac disease has five statements that should be met.

### Audit aims:
1) To identify the screening level (IgA tissue transglutaminase antibodies tTGA) for current Type 1 patients attending the hospital diabetes service (East and North Hertfordshire NHS Trust).
2) To review screening for 19 - 50 year olds with Type 1 for up to ten years from diagnosis; and for all patients newly diagnosed in 2015 - 2016.
3) To determine whether the NICE quality standard for coeliac disease was met in new Type 1 diabetes patients (2015 - 2016) with raised tTGA levels.

### Method
Interrogation of the hospital diabetes database (CIPTS). Analysis of patient records to determine whether the NICE quality standard was met.

**Results**

There were n = 1,100 Type 1 diabetes patients registered with the East and North Hertfordshire NHS Trust of which n = 227 were under 19 years and n = 873 were 19 years and over. Those under 19 years had all been screened for coeliac disease but only 53.5% of those 19 years and over had been screened for the condition.

In n = 240 patients with Type 1 diabetes aged 19 – 50 years, over a period of ten years from diagnosis, 64.6% had been screened for coeliac disease.

In 2015 - 16, n = 109 patients were newly diagnosed with Type 1 diabetes, n = 57 were under 19 years and 100% were screened for coeliac disease, n = 52 patients were 19 years and over and only 63% had been screened for coeliac disease. During 2015 - 16, n = 5 (4.6%) of patients diagnosed with Type 1 diabetes had raised tTGA; four paediatric and one adult patient.

The extent to which the Quality Standard for coeliac disease had been met:

- People at increased risk of CD offered serological screening – Yes for paediatrics (100%); No for adults (63%)
- Positive serology, referred to specialist - Not recorded
- Biopsy within six weeks of referral - Not recorded
- Specialist advice on a gluten free diet - Yes (paediatric patients), No (adult)
- Annual review offered – pending

**Discussion**

Coeliac screening in Type 1 adults in East and North Hertfordshire Trust is suboptimal. A pop up screen has been developed to remind clinicians to screen for coeliac disease on diagnosis and every three years thereafter. Greater efforts are needed to meet the Quality Standard for coeliac disease.

# PHENOTYPIC AND GENETIC CHARACTERISTICS OF THOSE FOLLOWING A GLUTEN FREE DIET IN THE UK BIOBANK

**Author**
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**Institution**
University of Oxford[1]

## Abstract

**Introduction**
The gluten free (GF) diet in those not diagnosed with coeliac disease (CD) has increased in popularity in recent years; however, there is limited information on the characteristics of these individuals. To address this, we investigated the association between a variety of sociodemographic and health related characteristics in those who follow a GF diet in a large UK based study. We also explored whether the prevalence of human leukocyte antigen DQ2/8 haplotypes, a necessary factor in CD, are higher in those who follow a GF diet compared to non GF participants.

**Method**
Participants were selected from UK Biobank, a population based cohort of half a million women and men aged 40 - 69 years at recruitment between 2006 and 2010. Adherence to a GF diet was determined through 24 hour dietary questionnaires which were completed by a subset at the end of baseline assessment (n = 70,714; 2009 - 2010) or online thereafter (n = 175,990; 2011 - 2012). Participants were excluded if they completed fewer than two dietary questionnaires (n = 84,167), reported following a GF diet on only one questionnaire (n = 1,547) or had self reported or had a hospital inpatient diagnosis of CD (n = 791), resulting in a sample size of 124,519. Multivariate logistic regression models were used to investigate the association of a range of characteristics in GF compared with non GF participants.

## Results

1,789 (1.4%) participants reported following a GF diet on at least two questionnaires. The presence of one or more DQ2/8 haplotypes was similar between GF and non GF participants (58.2% and 57.6%, respectively; $p = 0.6$). Men were 71% less likely to follow a GF diet than women (OR = 0.29, 95% confidence interval 0.25 - 0.33). Participants who were more highly educated, of non white ethnic origin, lived in more socioeconomically deprived areas, had a lower alcohol intake, had a lower BMI, had lower blood pressure, former smokers, rated their health as poor or reported having a long standing illness were more likely to follow a GF diet. Associations with selected conditions are shown in Table 1. There was no significant association with age.

**Table 1** Logistic regression models investigating the associations between following a gluten free diet and selected prevalent self reported conditions

| Condition | Total Cases % | Gluten free cases % | OR (95% CI)[a] |
|---|---|---|---|
| Stroke | 1.2 | 1.1 | 1.02 (0.65-1.62) |
| Heart disease | 4.6 | 3.5 | 1.02 (0.79-1.32) |
| Hypertension | 22.3 | 15.7 | 0.75 (0.65-0.85) |
| Type 2 diabetes | 3.7 | 2.1 | 0.67 (0.48-0.93) |
| Cancer[b] | 6.8 | 6.9 | 0.90 (0.75-1.08) |
| Irritable bowel syndrome | 2.1 | 8.8 | 3.79 (3.19-4.49) |
| Irritable bowel disorder | 0.8 | 1.9 | 2.42 (1.71-3.43) |
| Asthma | 11.5 | 15.5 | 1.36 (1.19-1.54) |
| Allergies | 8.3 | 14.7 | 1.91 (1.67-2.18) |
| Eczema/dermatitis/psoriasis | 3.8 | 5.6 | 1.56 (1.27-1.91) |
| Chronic fatigue syndrome | 0.5 | 4.0 | 6.74 (5.20-8.73) |

CI, Confidence Interval, OR, Odds Ratio
[a]Adjusted for age, sex, ethnicity, education, Townsend deprivation score, body mass index, smoking and alcohol intake
[b]Excluding nonmelanoma skin cancers

## Discussion

These results provide an interesting insight into the characteristics of individuals who follow a GF diet, an area which has been understudied. Following a GF diet is positively associated with a range of healthy lifestyle factors and in turn a lower prevalence of hypertension and Type 2 diabetes. However, it is also positively associated with a poorer perception of health and a range of non cardiovascular conditions. This warrants further investigation.

# NO ASSOCIATION BETWEEN HLA-DQA1*05 AND -DQB1*02 GENE DOSAGE AND CLINICAL PHENOTYPE OF COELIAC DISEASE


## Authors
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## Institution
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## Abstract

### Introduction
Coeliac disease is a common gluten sensitive enteropathy. Disease susceptibility is strongly associated with specific Human Leukocyte Antigen (HLA)-DQA1 and -DQB1 loci. Individuals with the HLA-DQA1*05:HLA-DQB1*02 heterodimer (referred to as HLA-DQ2.5) have the highest risk of developing coeliac disease, particularly if two copies of HLA-DQB1*02 are present. Understanding whether differences in the frequency of DQA1*05 and DQB1*02 accounts for differences in the clinical phenotype of coeliac disease is important for the development of personalised medicine for patients and was addressed in the following study.

### Method
Demographic, clinical and laboratory data was retrospectively collected from adult patients attending the specialist coeliac disease clinic, Royal Hallamshire Hospital between 2008 to 2016 and correlated with the number of DQA1*05:DQB1*02 combinations forming the DQ2.5 heterodimer (DQ2.5 gene dose), as well as the frequency of DQB1*02.

**Results**

N = 490 patients had biopsy proven coeliac disease and HLA genotype information. Individuals who were positive for the DQ2.5 heterodimer were more likely to be EMA positive than those who were DQ2.5 negative ($p$ = 0.013). There were no linear associations between the DQ2.5 gene dosage and clinical or laboratory parameters assessed. 190/490 (39%) patients carried two copies of DQB1*02, 278/490 (57%) patients had a single copy and DQB1*02 was absent in 22/490 (4%) patients. The prevalence of folate deficiency was higher and mean haemoglobin levels lower, in individuals carrying two copies of DQB1*02 than those with a single copy of DQB1*02 ($p$ < 0.001 and $p$ = 0.002, respectively), but neither were different in DQB1*02 negative individuals ($p$ > 0.05). The carriage of two copies of DQB1*02 did not correlate with any other parameters.

**Discussion**

The presence of DQA1*05 and DQB1*02 is well documented to correlate with risk of developing coeliac disease. Our results suggest that there is no association between homozygosity/heterozygosity for DQA1*05 and DQB1*02 and the clinical phenotype of active disease. These results provide an important insight into the interpretation of HLA-DQ data in the setting of coeliac disease.

# USE OF T CELL SPECIFIC RNA IN SITU HYBRIDISATION AS A NOVEL TEST TO DISTINGUISH MALIGNANT (LYMPHOMATOUS) AND BENIGN (INFLAMMATORY) T CELL INFILTRATES: A POSSIBLE NEW APPROACH IN THE DIAGNOSIS OF REFRACTORY COELIAC DISEASE

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## Abstract

### Introduction

A small proportion of people with coeliac disease develop refractory coeliac disease (RCD), with type I RCD showing features akin to active coeliac disease and type II RCD showing features similar to an early T cell lymphoma. Differentiating between these two types of RCD is very clinically important, but is difficult with common histopathological, flow cytometric and PCR based clonality testing. We present here our recently developed approach to distinguishing between T cell lymphoma and benign T cell lymphoid infiltrates, which we believe could provide a clear distinction between RCD types I and II. Our approach to T cell infiltrates is similar to that used for B cell infiltrates, which relies on kappa/lambda immunoglobulin light chain staining. If all the lymphoid cells are of the same light chain type, they are malignant (lymphomatous), while a mixture indicates they are benign (inflammatory). For T cells, using the same principles, we have identified two T cell specific, mutually exclusively expressed, RNA sequences (TRBC1 and TRBC2), corresponding to the two, alternatively employed, T cell receptor beta constant regions.

**Method**
We analysed the TRBC1/2 gene segments using standard bioinformatic tools, undertook Q-PCR to investigate relative expression levels and developed single and duplex TRBC1/TRC2 segment specific probes for chromogenic in situ hybridisation (CISH), which we validated on FFPE sections of T cell lymphoma/ leukaemia lines, T cell lymphoma (n = 100) and corresponding benign tissue (n = 100).

**Results**
The coding regions of TRBC1/2 are very similar at amino acid level, making development of highly specific TRBC1/2 monoclonal antibodies difficult. However, the 3' untranslated regions differ substantially and Q-PCR demonstrated the TRBC1: TRBC2 transcript ratio in peripheral blood mononuclear cells to be very close to 1:1. This was confirmed by single and duplex TRBC1/2 CISH staining of benign T cell infiltrates. CISH staining of T cell lymphoma/ leukaemia lines and FFPE sections of T cell lymphoma demonstrated clear TRBC1/2 restriction (monotypia for TCR), correlating with Q-PCR results. Double (duplex) CISH staining can distinguish between benign (inflammatory) and malignant (lymphomatous) lymphocyte populations in a wide range of tissues.

**Discussion**
This is the basis of a novel diagnostic test for T cell lymphoma, applicable to FFPE sections. In a manner analogous to the way kappa/ lambda staining has transformed the diagnosis of B cell lymphoma, we believe that our TRBC1/2 CISH test has the potential to transform both the diagnosis of T cell lymphoma and the distinction between type I and type II RCD. We wish to build a collaborative consortium to collect RCD cases for further validation of T cell testing strategy.

# NON RESPONSIVE AND REFRACTORY COELIAC DISEASE: THE LARGEST UK EXPERIENCE FROM THE NHS ENGLAND RARE DISEASES COLLABORATIVE NETWORK

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## Abstract

### Introduction
Non responsive coeliac disease (NRCD) is defined by persisting symptoms or laboratory abnormalities in patients with coeliac disease (CD) despite a gluten free diet (GFD). Causes of NRCD are heterogeneous, with refractory CD (RCD) being associated with poor prognosis. The aims of this study are to identify the aetiologies for persisting symptoms in patients with NRCD referred to a national UK centre for CD, and to assess mortality rates in each group.

### Method
Data on all CD patients, including those with persisting symptoms and tertiary referrals, were collected prospectively from 1998 - 2018. Patients were systematically investigated to establish the aetiology of their continued symptoms. They were also referred to a specialist coeliac dietitian to identify any lapses in GFD adherence or gluten cross contamination.

A repeat duodenal biopsy was performed and compared to previous biopsies where possible to check for histological remission. Colonoscopy, lactose hydrogen breath test, glucose hydrogen breath test, SeHCAT scan, CLO testing, faecal elastase, immunohistochemistry and γ-TCR clonality were performed.

**Results**

N = 2,356 patients with suspected CD were seen in this time period (121 were tertiary referrals). N = 157 were excluded from analysis due to unconfirmed diagnosis. Of the remaining 2,199 patients with confirmed CD, n = 2,123 had both villous atrophy and positive IgA-EMA/TTG, and n = 76 had seronegative CD. Of the 2,199 patients with CD (67% female, mean age at diagnosis 42.8 years ± 18.5), n = 292 (13%) had persisting symptoms. The leading causes for persisting symptoms in patients without RCD (73% female, mean age at diagnosis 35.7 years ± 19.2) were: gluten contamination (22%), functional/irritable bowel syndrome (20%), pancreatic exocrine insufficiency (7%), reflux dysmotility (5%), and microscopic colitis (5%). Of a total of 74 patients who were identified with RCD, n = 56 had RCD I (71% female, mean age at CD diagnosis 41.8 years ± 19.0) and n = 18 had RCD II (33% female, mean age at CD diagnosis 55.4 years ± 13.3). After a median follow up of 40.5 months (IQR 21.8 - 73.3), mortality was 7% in the RCD I group, compared to 39% in the RCD II group ($p$ = 0.019). Higher age at diagnosis of CD is a predictor for having RCD in patients with persisting symptoms ($p$ < 0.001).

**Discussion**

This is the largest UK study of NRCD and RCD. The contemporary mortality data in RCD II remains poor. Patients with suspected RCD should be referred to the National Centre for consideration of novel therapies such as IL-15 and stem cell transplant.

# QUALITATIVE INTERVIEWS TO EXPLORE PATIENT PREFERENCE FOR HEALTHCARE LED INTERVENTIONS TO PROMOTE GLUTEN FREE DIETARY ADHERENCE

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## Abstract

**Introduction**
A proportion of people (53 to 76%) with coeliac disease (CD) are not adhering to a strict gluten free diet and reasons for this are multifactorial. Promoting dietary adherence is a key role for healthcare professionals and has beneficial effects on the activity and associated complications of CD. This study aimed to explore patient preference for a healthcare professional led intervention to promote gluten free dietary adherence in patients with coeliac disease.

**Method**
Patients diagnosed with histology confirmed CD were contacted via a hospital database. N = 37 patients with coeliac disease underwent an individual qualitative telephone interview with the researcher to explore the acceptability of a broad range of intervention to promote gluten free dietary adherence. Ethical approval was granted by the procedures of the University of Roehampton Ethics Committee (LCS 15/130) and by the NHS Research and Ethics Committee (Ref: 15/YH/0289).

**Results**

Participants included 28 Caucasians and 9 South Asians (29 females and 8 males). N = 30 patients were classified as non adherent as they scored >13 on the CDAT questionnaire. Participants reported they considered physical clinics with a doctor or dietitian to be as useful as a telephone clinic to help them improve gluten free dietary adherence. Participants predominately perceived telephone clinics as easy (n = 33), flexible (n = 29) and convenient (n = 19). Participants reported high costs incurred to attend clinic visits or group education sessions, due to parking. Telephone clinic, a leaflet, text messages, home visit and internet based interventions were considered low cost to the patients. However, home visits and internet based interventions were rated poorly for their acceptability and usefulness to promote dietary change.

**Discussion**

This study has given a unique view of a multi ethnic population to inform interventions aimed at increasing adherence to a gluten free diet. Whilst acknowledging its limitations, this study has strengthened the viewpoint that patients are crucial in all aspects of the treatment and management of chronic diseases, including the design of interventions and service development. An intervention to establish if a telephone clinic can increase dietary adherence is required.

# A STUDY TO EXAMINE THE DIETARY AND SYMPTOM ADVICE PROVIDED TO COELIAC PATIENTS DURING THEIR ANNUAL COELIAC REVIEW AT HAMPSHIRE HOSPITALS FOUNDATION TRUST JULY - OCTOBER 2018

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## Abstract

### Introduction

NICE (2016) recommends patients with coeliac disease are offered an annual review to assess adherence to a gluten free diet, review symptoms and provide advice about coeliac disease/diet. The British Society of Gastroenterology (2014) recommends patients with coeliac disease should be reviewed by a dietitian and/or a clinician with an interest/expertise in coeliac disease.

The coeliac team at Hampshire Hospitals Foundation Trust comprises of two gastrointestinal dietitians and one certified nutrition specialist and offers patients with coeliac disease within their CCG an annual appointment. Prior to their appointment patient bloods are checked for tTG antibodies, folate, vitamin B12, ferritin, vitamin D, haemoglobin and liver function.

As standard during an appointment, adherence to a gluten free diet, symptoms, weight and dietary intake are discussed. The aim of this short study was to identify what additional advice the team was providing to patients at their annual coeliac review.

**Method**
A proforma was used in clinic to collect the data. This data was then inputted onto a spreadsheet and analysed.

**Results**
The study took place between July - October 2018. During this period 139 coeliac reviews were undertaken. Patients required advice regarding vitamin D supplementation (37%), increasing their calcium intake (35%) and low ferritin levels (25%). Advice was also provided to patients regarding their folate (4%) and vitamin B12 levels (3%), gastrointestinal symptoms including bloating (7%), constipation (5%) and diarrhoea (4%), gluten free prescriptions (12%) and eating out (9%).

Concerns were raised by individual patients that you would not typically expect to be discussed at a coeliac review including advice regarding:

- Healthy eating
- Low sulphite diet
- Cholesterol reducing diet
- Introducing fibre after surgery
- Dietary advice for thyroxine
- Low FODMAP diet
- Urgency of stools
- Raised alanine aminotransferase (ALT)

**Discussion**
The results of the study demonstrate that a coeliac review is not just there to discuss adherence to a gluten free diet, as patients have additional nutritional concerns and gastrointestinal symptoms that need to be addressed. In addition the study demonstrates that non coeliac related concerns can be raised and therefore justifies the rationale for a specialist dietetic team to provide the annual reviews.

# A RETROSPECTIVE STUDY TO MEASURE VITAMIN D LEVELS IN PATIENTS WITH COELIAC DISEASE ATTENDING ANNUAL REVIEW CLINICS DURING JANUARY - MARCH 2018

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## Abstract

### Introduction
Bone health is an important consideration in the management of coeliac disease but vitamin D testing has not been routinely undertaken within our Trust. Following British Society of Gastroenterology guidance that vitamin D levels should be measured at diagnosis and supplemented as necessary, vitamin D testing was introduced in January 2018 for patients in annual review clinics.

Patients with coeliac disease are at greater risk of fragility fractures, are recommended to have a higher calcium intake than the general population and may have persisting vitamin D deficiency despite a gluten free diet.

In the UK, vitamin D deficiency in adults (< 25 nmol/L) is estimated to be 30-40% during winter. National Institute for Clinical Excellence (NICE) guidelines state levels of < 30 nmol/L should be treated.

### Method
The aim of this study was to explore the prevalence of vitamin D deficiency in adult (> 18 years) coeliac patients attending an annual review clinic during the winter months and establish if routine monitoring is justified in this cohort of patients.

Patients booked into annual review clinics between 1 January and 31 March 2018 had their demographic information, IgA tissue transglutaminase antibodies (tTGA) and vitamin D levels reviewed retrospectively. Deficiency was defined as levels < 30 nmol/L and insufficiency as 30 - 50 nmol/L as per the NICE guideline 2016.

**Results**

During the period studied, n = 122 patients were booked into an annual review clinic. The mean age of people attending was 48 years. 77% of patients were female, 82.5% identified as white British, 6% any other ethnicity, 2% any other white ethnicity and 2% Indian. Ethnicity information was not available for 7.5% of the cohort. tTGA was negative for 97 of 106 patients (91.5%). Vitamin D levels were tested in n = 106; 33% were deficient in vitamin D and 24% had insufficient vitamin D.

**Discussion**

Deficiency levels in our cohort are in line with national population estimates which would be expected in a cohort of patients that are following a strict gluten free diet. Moving forward we will continue to measure vitamin D levels in both newly diagnosed and established coeliac patients and recommend supplementation to:

- All patients in the deficiency range
- All patients in the insufficiency range with demonstrated reduced bone density or who are likely to experience malabsorption due to raised tTGA.

As we repeat this data collection in winter 2018/9 we hope to see a reduction in the rate of deficiency for patients previously measured and treated.

# ASSESSING GLUTEN FREE DIET ADHERENCE USING CDAT AND BIAGI QUESTIONNAIRES IN PATIENTS WITH COELIAC DISEASE


## Authors

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## Abstract

### Introduction

The current gold standard for assessing dietary adherence in individuals with coeliac disease is via duodenal biopsies, which is invasive and costly. In view of this, we assessed the utility of the CDAT and Biagi questionnaires for non invasive assessment of gluten free adherence.

### Method

Patients with an established diagnosis of coeliac disease, referred for further evaluation of dietary adherence and disease remission were assessed between January 2016 to December 2018. Patients were prospectively recruited, and completed CDAT and Biagi questionnaires, with at least four duodenal biopsies taken from D2 in addition to at least one biopsy from the duodenal bulb. The presence (Marsh 3a or above) or absence (Marsh 0-II) of villous atrophy was used to determine the sensitivities of the tests.

## Results

Patients n = 151 were recruited, n = 101 females (66.9%), median age 55.0 years, median duration on a gluten free diet 72.0 months. Table 1 outlines the sensitivity and specificity of the CDAT questionnaire, Biagi questionnaire, immunoglobulin A tissue transglutaminase antibodies (IgA tTGA) and IgA endomysial antibodies (EMA).

**Table 1** Comparison of tools used for adherence

| | Sensitivity % (CI) | Specificity % (CI) | Positive predictive value % (CI) | Negative predictive value % (CI) |
|---|---|---|---|---|
| **CDAT** | **52.0** (37.6–66.1) | **69.8** (60.9-77.5) | **40.6** (28.8–53.6) | **78.6** (69.6–85.5) |
| **Biagi** | **22.4** (12.2-37.0) | **93.1** (85.6–97.0) | **61.1** (36.1–81.7) | **71.4** (62.8–78.8) |
| **CDAT & Biagi** | **61.2** (46.2-74.8) | **69.3** (60.5-77.2) | **43.5** (35.3-52.0) | **82.2** (76.2-87.0) |
| **IgA tTGA** | **30.6** (18.7–45.6) | **91.6** (83.6–96.0) | **65.2** (42.8–82.8) | **71.9** (62.8–79.5) |
| **IgA EMA** | **34.3** (26.7–42.7) | **92.5** (84.8–96.7) | **68.2** (45.1–85.2) | **71.9** (62.9–79.5) |

## Discussion

The sensitivity of the CDAT questionnaire was not superior to IgA tTGA for predicting villous atrophy in patients with coeliac disease. However, the use of a combination of both Biagi and CDAT had a greater sensitivity than IgA tTGA and IgA EMA ($p < 0.05$), but lower specificity ($p < 0.05$). Duodenal biopsy remains the gold standard, although these scores remain useful tools in the assessment of dietary adherence.

# ASSESSING GFD ADHERENCE USING URINE GLUTEN IMMUNOGENIC PEPTIDES IN COELIAC DISEASE: FIRST UK PILOT STUDY

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## Abstract

### Introduction
Adherence to a gluten free diet (GFD) is essential, as poor adherence can lead to persistent villous atrophy and subsequent complications of coeliac disease (CD). We have previously shown that non invasive markers of adherence have a poor sensitivity in comparison to the gold standard of duodenal biopsy. As a result of this, we assessed the novel technique of gluten immunogenic peptides (GIP) in urine.

### Method
Patients with coeliac disease, both newly diagnosed and those referred to secondary care for further evaluation of dietary adherence/disease remission were assessed from September 2018 to December 2018. Patients were tested for GIP using a rapid immunochromatographic test, following the collection of mid-stream urine samples. All patients were also tested for tissue transglutaminase antibodies IgA tTGA and endomysial antibodies IgA EMA via blood tests. At least four duodenal biopsies were taken from D2 and at least one biopsy from the duodenal bulb, with the presence/absence of villous atrophy used to determine the sensitivities of the tests.

## Results

Seventeen patients were recruited (n = 12 female, 71%), median age 52 years (range 25 - 74 years), median duration on a GFD 96 months (range 0 - 840 months). Two patients were newly diagnosed with CD, n = 15 patients had an established diagnosis of CD. Table 1 outlines the sensitivity and specificity of GIP, IgA tTGA and IgA EMA.

**Table 1** Comparison of GIP, tTGA and EMA

| | **Sensitivity % (CI)** | **Specificity % (CI)** | **Positive predictive value % (CI)** | **Negative predictive value % (CI)** |
|---|---|---|---|---|
| **GIP** | **66.7** (24.1–94.0) | **63.6** (24.1–94.0) | **50.0** (17.4–82.5) | **77.7** (40.1–96.1) |
| **IgA tTGA** | **40.0** (7.3–83.0) | **100.0** (67.9–100.0) | **100.0** (19.8–100.0) | **78.6** (48.8–94.3) |
| **IgA EMA** | **40.0** (7.3–83.0) | **100.0** (67.9–100.0) | **100.0** (19.8–100.0) | **78.6** (48.8–94.3) |

## Discussion

Urine GIP testing was not superior to IgA tTGA or IgA EMA. Further data is required to assess this modality as a predictor of villous atrophy and adherence before this can be used in clinical practice.

# THE IMPACT OF COELIAC DISEASE ON FAMILIES PSYCHOSOCIAL WELLBEING AND QUALITY OF LIFE: A MIXED METHODS SYSTEMATIC REVIEW

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## Abstract

**Introduction**
A diagnosis of coeliac disease (CD) requires individuals to adopt a strict gluten free diet (GFD). Naturally, younger patients must rely on their families for instruction, support and daily help with navigating the GFD. Therefore, CD may challenge the entire family's emotional and social wellbeing. This mixed methods systematic review provides insight into the challenges that families of children with CD may face.

**Method**
Five databases were systematically searched from 1990 - 2018, to identify qualitative and quantitative studies that assessed the psychosocial wellbeing and quality of life of caregivers of children (0 - 18 years) with CD. All papers were quality assessed before being included in the review. Qualitative and quantitative data were extracted separately, before being integrated to explore key themes across the papers.

**Results**
Twelve papers were included in the review reporting across 615 caregivers, three using qualitative and nine using quantitative methodologies. The presence of CD contributed to economic hardship, family conflict and disrupted family routines. Families often adopted a GFD to support their children, and reported avoidance of travelling and dining at restaurants, to accommodate their child's dietary restrictions. Maternal quality of life was impaired and concerns around the child's GFD management and future were common.

**Discussion**
Further research is needed to explore whether the impact of a child's CD on the family affects adherence to the GFD by impairing family management of the disease, and by impacting CD through stress related pathways. The family unit must be considered when providing education and support for children with CD.

# DELUSION LIKE BELIEFS IN COELIAC DISEASE: A QUALITATIVE INVESTIGATION

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## Abstract

### Introduction
For individuals with coeliac disease, management of the gluten free diet (GFD) is associated with improved physical and psychosocial health. However, hypervigilance characterised by food preoccupation, avoidance of food related events and controlling behaviour around food, arises in some patients and is associated with impaired quality of life. This study aims to understand the beliefs of individuals who take a hypervigilant approach to managing CD and the consequences of holding such beliefs.

### Method
Secondary analysis of qualitative data was conducted on 12 adults with CD (18 - 69 years), following the GFD for at least one year. All participants were classified as using hypervigilant approaches to manage the GFD based on the following criteria defined by Cadenhead et al. (in press): food rigidity (ie unable to eat outside the home), avoidance of food settings, controlling behaviour and preoccupation with management of a GFD (as opposed to awareness). Transcripts were analysed using interpretive phenological analysis in order to identify important aspects of the lived experience of managing their diagnosis and diet.

**Results**
All participants reported confidence in GFD management in their own home, as they could control cross contamination risk ("I can eat gluten free at home, because I'm in control. Everywhere else is a danger zone"). Beliefs around cross contamination suggested delusion like ideation. Individuals had sensible concerns about food related cross contamination but also described irrational concerns focused on implausible cross contamination from non food products ("I found out there was flour in my car air bag… so I don't drive anymore / My husband put the wallpaper up but he forgot that the wallpaper paste has gluten in it… I was so upset he forgot"). This resulted in individuals refusing attendance at food related social activities ("I couldn't go to my cousin's wedding because of all the food... staying at home keeps me safe") and completing food shopping online ("I only buy food online from gluten free sites that I know well… supermarkets are dangerous"), resulting in anxiety and social isolation ("Coeliac has destroyed me and my friends. I can't see them anymore, it's too hard").

**Discussion**
These findings suggest that cognitions related to coeliac disease management can take a delusional quality. Although strict management of the GFD is essential for those with CD, this needs to be balanced with the individual's wellbeing. As per recommendations we recommend ongoing follow up, and psychosocial support referrals, as needed.

# LIVING WELL WITH COELIAC DISEASE


## Authors
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## Abstract

### Introduction
The Scottish Government has led the co-production of a new coeliac disease pathway for Scotland which aims to improve the experience people with coeliac disease receive, it meets both Modern Outpatient Programme and Scottish Access Collaborative core principles, reduces health inequalities and provides best value for the NHS. During the co-assessment phase, greater access to online digital self management support was identified.

### Method
Working with key stakeholders the Scottish Government, NHS 24, Coeliac UK, gastrointestinal consultants, dietitians, and people living with coeliac disease, identified key messages people newly diagnosed would find helpful. Coeliac UK specifically worked with its members to develop the material. This included top tips and myth busting messages. Self management materials were drafted and a film script was created. The film was delivered by a person living with and having experience of coeliac disease personally and as a parent. The material now forms part of a refreshed coeliac disease NHS Inform website which aims to give vital information to people at the treatment stage of the new Scottish coeliac disease pathway but will be especially useful for newly diagnosed people transitioning from gluten to gluten free living.

**Results**
The digital resource[a] was created. Feedback on the resource captured in the NHS Inform site will be collected over the next few months to ascertain the usefulness of this resource to both clinicians and people living with coeliac disease. The film link has been incorporated into the 'once for Scotland' dietetic coeliac disease intervention currently under development. The site went live on 7 February 2019, no data is available yet.

**Discussion**
Co-production has resulted in key stakeholders delivering quality self management information to citizens in a unique digital setting and on a 'once for Scotland' basis. The resource should encourage people living with coeliac disease to live well with their condition and provides positive advice for the newly diagnosed, on living with coeliac disease and managing a gluten free lifestyle.

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

# WHY CAN'T WE HAVE WHAT WE NEED? : EXPLORING THE IMPACT OF PRESCRIBING CHANGES FOR GLUTEN FREE FOODS IN COELIAC DISEASE

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## Abstract

**Introduction**
Historically, the English National Health Service has supported people with coeliac disease by providing prescriptions for gluten free foods. In recent years, as the availability of gluten free foods has increased, some Clinical Commissioning Groups (CCGs) have restricted or stopped this support, leading to inconsistencies in access across England. Therefore, the aim of this research was to explore the impact of changes to prescribing policies on adults with coeliac disease.

**Method**
In depth, semi structured interviews were conducted to explore the impact of prescribing policy changes. Interview participants were recruited from a pool of respondents to a related survey (reported elsewhere) who indicated their willingness to participate in an interview. While a maximum variation sample was sought, those from more deprived backgrounds or who no longer had access to prescriptions were oversampled, as the main aim of the study was to understand the impact of changes to prescribing policy. Interviews were conducted face to face (n = 16) or over the telephone (n = 8), audio recorded with the participant's consent, and transcribed verbatim. A thematic analysis was conducted in NVivo.

**Results**

N = 24 (13 female, 11 male) adults with coeliac disease participated in an interview, of which 17 lived in CCG areas that were no longer prescribing gluten free foods. Participants were aged between 18 and 84 years old, had been diagnosed for between six months and 44 years, and had household incomes ranging from less than £10,000 to £60,000. Participants discussed three main aspects of prescriptions: (1) frustrations about prescribing changes; (2) coping and adapting to the changes; and (3) future access to prescriptions.

Many participants acknowledged the financial challenges faced by the NHS, but some questioned the inequity of support between health conditions. Despite these frustrations, the majority of participants had adapted to prescribing changes, adopting coping strategies to obtain the food they need to follow a gluten free diet. However, three less mobile participants faced financial and accessibility barriers to obtain gluten free substitute foods from elsewhere. All participants thought that gluten free foods should be available on prescription in some form.

**Discussion**

While the majority of participants were no longer able to access prescriptions for gluten free foods, most had developed coping strategies and adapted to prescribing changes. However, the impact of these changes was much greater for participants with mobility issues. When reviewing prescribing policies, CCGs should consider retaining access to prescriptions for gluten free foods. This would in particular benefit adults from more vulnerable groups who are disproportionately affected by the complete removal of prescriptions.

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- Information updates on coeliac disease and the gluten free diet in our email newsletters and on our website to support your patients with their diet, including reading labels, eating out and delicious gluten free recipes
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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.

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