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Changes in the testing for and incidence of coeliac disease in the UK 2005-2015: a population based cohort study

J West[1,2], H Otete[4], AA Sultan[3], CJ Crooks[1,2]

1 – Division of Epidemiology and Public Health, University of Nottingham; 2 – NIHR Nottingham Biomedical Research Centre (BRC), Nottingham University Hospitals NHS Trust and the University Nottingham, Nottingham, UK; 3 – Research Institute for Primary Care and Health Sciences, Keele University; 4 – School of Pharmacy, University of Nottingham

Figure 1. European age-standardised incidence rates of coeliac disease per 100,000 population

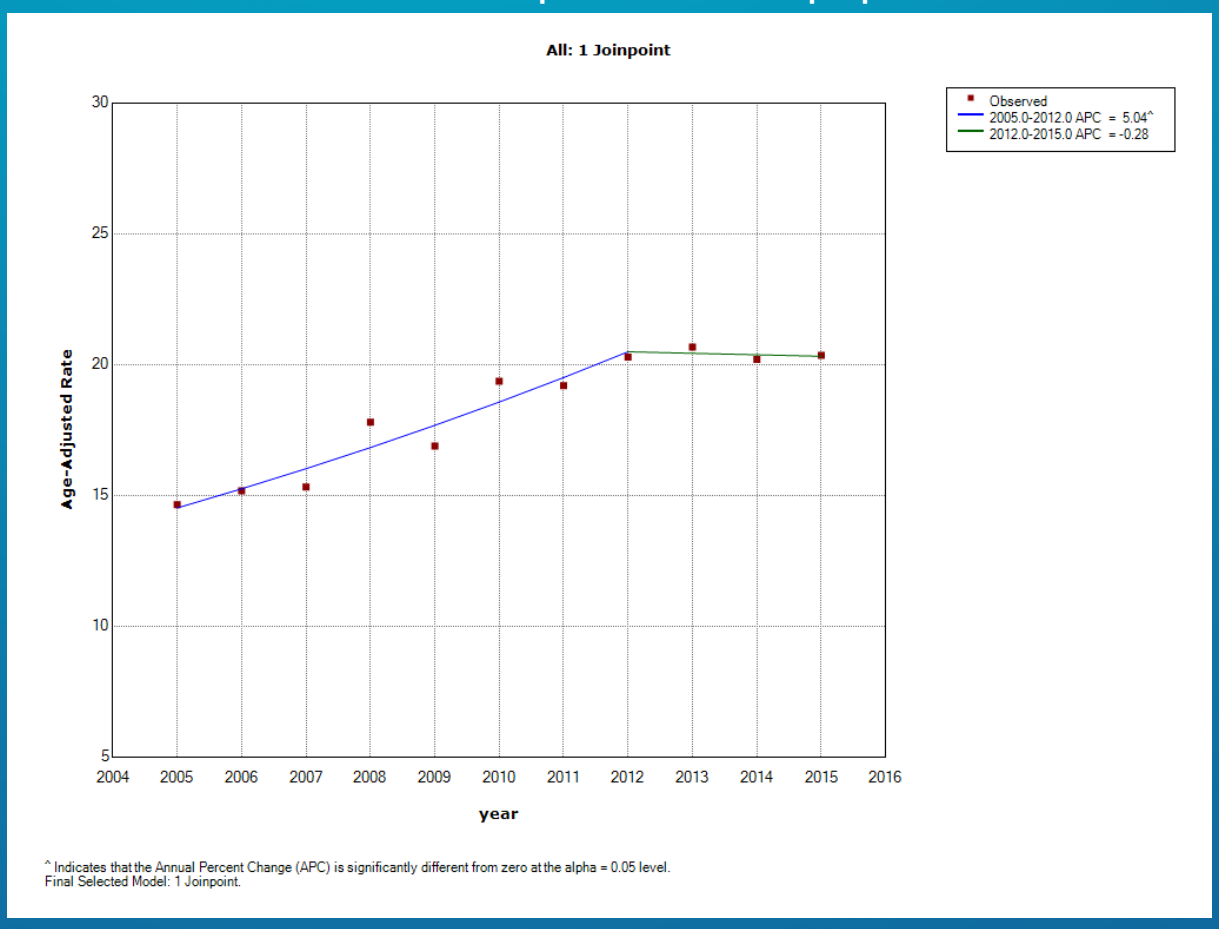
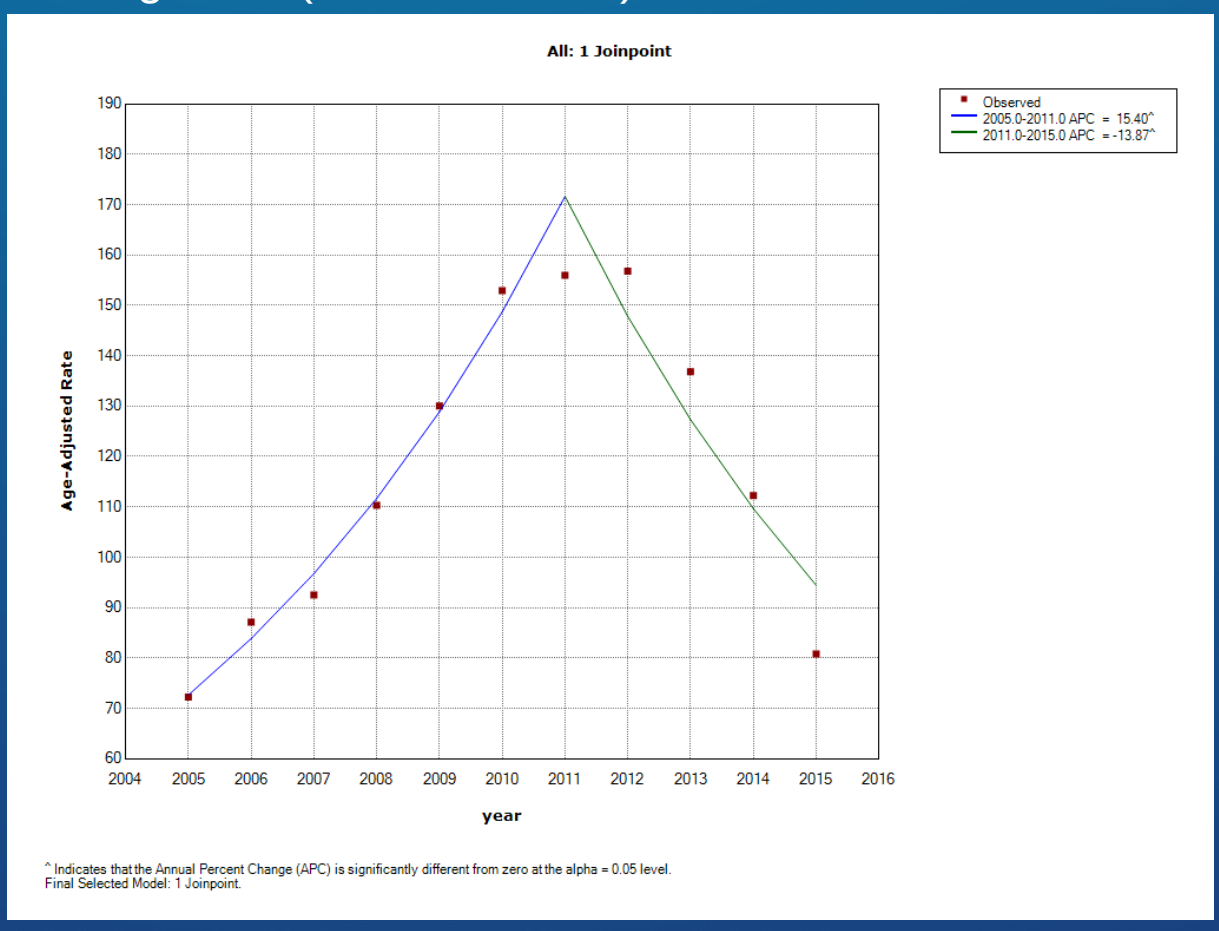


Figure 2. European age-standardised serological testing rates (TTG and EMA) for coeliac disease



[1]West et al. American Journal of Gastroenterology 2014 May; 109(5): 757–768.

Introduction: Over many previous decades the incidence of coeliac disease has been increasing almost everywhere in the world where it has been measured. However there has been a suggestion that in the last 5 years that incidence has plateaued or even declined.

Methods: We used the UK Clinical Practice Research Datalink and examined the electronic health care records therein to estimate the European (2013 population) age-standardised incidence of coeliac disease 2005-2015 and the corresponding rates of serological testing (Anti-Tissue Transglutaminase (TTG) and Endomysial antibody (EMA)) for the disease. We used Joinpoint analysis to examine changes in the rates of diagnosis and testing during this period. We estimated disease prevalence in 2015.

Results: There were 8177 incident cases of coeliac diseases diagnosed among 45,539,216 million population. Over the period 2005-2015 there was an increase in age-standardardised incidence from 2005 (14.6 per 100,000) until 2012 (20.3 per 100,000) and then a plateauing effect (figure 1, $p<0.05$). Serological testing increased and then decreased during the same period (figure 2, $p<0.05$). Prevalence in 2015 was 0.3% compared to 0.24% in 2011[1].

Conclusions: Age-standardised rates of diagnosis of coeliac disease and serological testing have, since 2011, respectively plateaued and declined, while prevalence increased. The plateau in incidence is most likely to be a function of the decline in testing which in turn could be due to lack of resource, more targeted use of testing or that the threshold of clinically identifiable coeliac disease has been reached and a steady-state incidence rate obtained.

Biopsy Avoidance Strategy in Adult Coeliac Disease

Marks L, Lau M, Kurien M, Cross S, Egner W, Hadjivassiliou M, Rees M, Rostrami K, Sargur R, Swallow K, Sanders D

Academic Unit of Gastroenterology, Royal Hallamshire Hospital, Sheffield, UK

Introduction

Paediatric ESPGHAN guidelines support a diagnosis of coeliac disease (CD) when immunoglobulin-A anti-tissue transglutaminase (IgA tTG) antibody titres are >10 times the upper limit of normal (ULN) and combined with supportive criteria. This study examines whether serological testing alone could be sufficient for diagnosis in adult patients, thus avoiding the need for duodenal biopsies.

Method

We performed a prospective analysis of CD patients diagnosed in a University hospital. Symptoms of CD, villous atrophy (VA) on biopsy, IgA-endomysial (IgA-EMA) antibodies, tTG and Human Leukocyte Antigen (HLA) genotype were used for analysis. We then compared the TTG antibody level against small bowel histology.

Results

443 CD patients (66.8% female, median age 41 years, range 15-84 years) were diagnosed between 2008 and 2016. 56.9% (n=252, 95% CI= 52.12-61.53) had a tTG value of greater than 10 times the ULN. 292 fulfilled ESPGHAN guidelines for features of malabsorption (diarrhoea=157, weight loss=45 and anaemia=190). Of these symptomatic patients, 70.4% (n=179, 95% CI= 64.86-76.08) had a tTG value 10 x ULN. The proportion reaching the 10 x tTG threshold was 55.4% (n=87, 95% CI=47.64-63.19) for diarrhoea, 60.0% (n=27, 95% CI=45.69-74.31) for weight loss, and 74.2% (n=141, 95% CI=67.99-80.43) for anaemia. Of the 151 patients who did not experience malabsorptive features, 49.0% met the 10 x ULN tTG level (n=74, 95%CI= 41.03-56.98). The sensitivity of tTG antibodies and EMA antibodies for predicting VA was 93.2% (95% CI=90.89-95.57) and 90.7% respectively (95% CI=88.05-93.44). Combined tTG and EMA was 98.6% (95% CI=97.67-99.72). All patients had compatible HLA typing, thereby failing to add any further diagnostic value.

Discussion

56.9% of patients would have been correctly diagnosed with CD and avoided a duodenal biopsy using an IgA tTG threshold of >10 times the ULN. Symptoms and HLA typing did not add any supportive information. This study provides evidence that a biopsy avoidance strategy may be implemented into adult gastroenterological practice.

Adult Coeliac Disease Remission Assessment: Does a D1 Biopsy Increase The Detection Of Villous Atrophy?

Marks L, Lau M, Kurien M, Hadjivassiliou M, Mooney P, Cross S, Sanders D

Academic Unit of Gastroenterology, Royal Hallamshire Hospital, Sheffield, UK

Introduction

The duodenal bulb (D1) has been shown to be a sensitive site for detecting villous atrophy (VA) in newly diagnosed coeliac disease (CD), however there is a scarcity of data from those with established CD. In patients with established CD, we aim to establish whether D1 biopsies improved the identification of VA compared to biopsies from the second part of the duodenum (D2) alone.

Method

251 patients with established CD were prospectively recruited from the endoscopy department at the Royal Hallamshire Hospital between 2013 and 2017. These patients were undergoing repeat gastroscopy to assess dietary adherence. All patients underwent a gastroscopy, with one biopsy taken from the duodenal bulb and four from D2. Biopsies were classified according to Marsh criteria. We assessed concordance of histology between the D1 and D2 sites, and 95% confidence intervals were calculated for all results using a binominal distribution.

Results

251 patients were recruited (70.5% female, age range 17-81 years, median age 53 years) having been on a gluten-free diet for a median duration of 6 years. Concordant results: 35.1% (n=88, 95% CI = 29.16-40.96) had normal duodenal biopsies in both D1 and D2; 32.3% (n=81, 95% CI= 26.49-38.05) had VA in D1 and D2; 18.3% (n=46, 95% CI= 13.54-23.11) had raised intra-epithelial lymphocytes (IELs) only in both D1 and D2. Disconcordant results: 4.4% (n=11, 95% CI=1.85-6.91) had VA in D1 but not D2; 2.4% (n=6, 95% CI=0.50-4.28) had raised IELs in D1 but normal histology in D2. 2.8% (n=7, 95% CI=0.75-4.83) had VA in D2 but normal histology in D1; 4.8% (n=12, 95% CI=2.14-7.42) had IELs in D2 but normal histology in D1.

Discussion

VA was confined to the duodenal bulb in 4.4% of patients with established CD. Thus a D1 biopsy in addition to distal duodenal biopsies increases the likelihood of detecting VA, although the significance of isolated VA in the bulb in patients on a gluten-free diet is yet to be determined.

Is serology predictive of persisting villous atrophy in patients with established Coeliac Disease (CD)?

Marks L, Lau M, Kurien M, Sanders D, Hadjivassiliou M

Academic Unit of Gastroenterology, Royal Hallamshire Hospital, Sheffield, UK

Introduction

Recent work has suggested that an IgA-tissue transglutaminase (tTG) <1.2 U/mL may predict mucosal healing in those with established CD. This study examines whether a combination of serological markers may be used as a surrogate marker for the detection of villous atrophy (VA) in known CD patients.

Method

We undertook a prospective analysis of known Coeliac disease (CD) patients diagnosed in a University hospital. All patients underwent a gastroscopy, with four biopsies taken from the second part of the duodenum, and one from the duodenal bulb. Serological markers were assessed at the time of endoscopy tTG, IgA-endomysial antibodies (EMA), IgA-antigliadin antibody (IgA AGA) and IgG-anti-gliadin antibody (IgG AGA), and their performances in isolation and in combination compared to histological outcomes.

Results

107 patients (67.3% female, median age 53 years (20-81 years)) that were on a gluten-free diet for a median duration of 6 years were included. The performance of the different serological markers to detect VA, both in isolation and in combination are shown in Table 1. The performance of tTG using the previously used cut-off of <1.2u/ml produced a sensitivity of 38.5%, a specificity of 73.8%, a positive predictive value of 64.9% and a negative predictive value of 43.7% to detect VA.

Discussion

This study is the first study to evaluate the combination of serological markers to detect VA in patients with established CD. Our findings oppose recent work that serology may be used as a surrogate marker of mucosal healing in known CD.

Table 1 - Ability of serological markers to detect VA

	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
tTG	39.0% (CI 29-48%)	97.0% (CI 89-99%)	88.9% (CI 64-98%)	70.8% (CI 61-81%)
EMA	40.5% (CI 26-57%)	96.9% (CI 88-99%)	89.5% (CI 65-98%)	71.6% (CI 61-80%)
IgA AGA	47.5% (CI 32-64%)	95.5% (CI 87-99%)	86.4% (CI 64-96%)	75.3% (CI 65-84%)
IgG AGA	37.5% (CI 23-54%)	90.0% (CI 80-96%)	68.2% (CI 45-85%)	71.6% (CI 61-80%)
EMA + tTG	33.3% (CI 20-50%)	98.5% (CI 91-100%)	93.3% (CI 66-100%)	30.4% (CI 21-41%)
IgA + IgG AGA	28.6% (CI 16-45%)	100% (CI 93-100%)	100% (CI 70-100%)	68.4% (CI 58-77%)
IgA or IgG AGA + EMA	28.6% (CI 16-45%)	100% (CI 93-100%)	100% (CI 70-100%)	68.4% (CI 58-77%)
IgA or IgG AGA + tTG	31.0% (CI 18-47%)	100% (CI 93-100%)	100% (CI (72-100%)	69.1% (CI 59-78%)

THE RISING INCIDENCE OF CHILDHOOD COELIAC DISEASE: A 7 – YEAR REGIONAL COHORT STUDY

Martin Lister[1], Philippa Wood[1], Paul Henderson[2,3], Peter Gillett[2,3]

[1]Victoria Hospital, Hayfield Road, Kirkcaldy
[2]Royal Hospital for Sick Children, Sciennes Road, Edinburgh
[3]Child Life and Health Department, Sylvan Place, University of Edinburgh.

Background

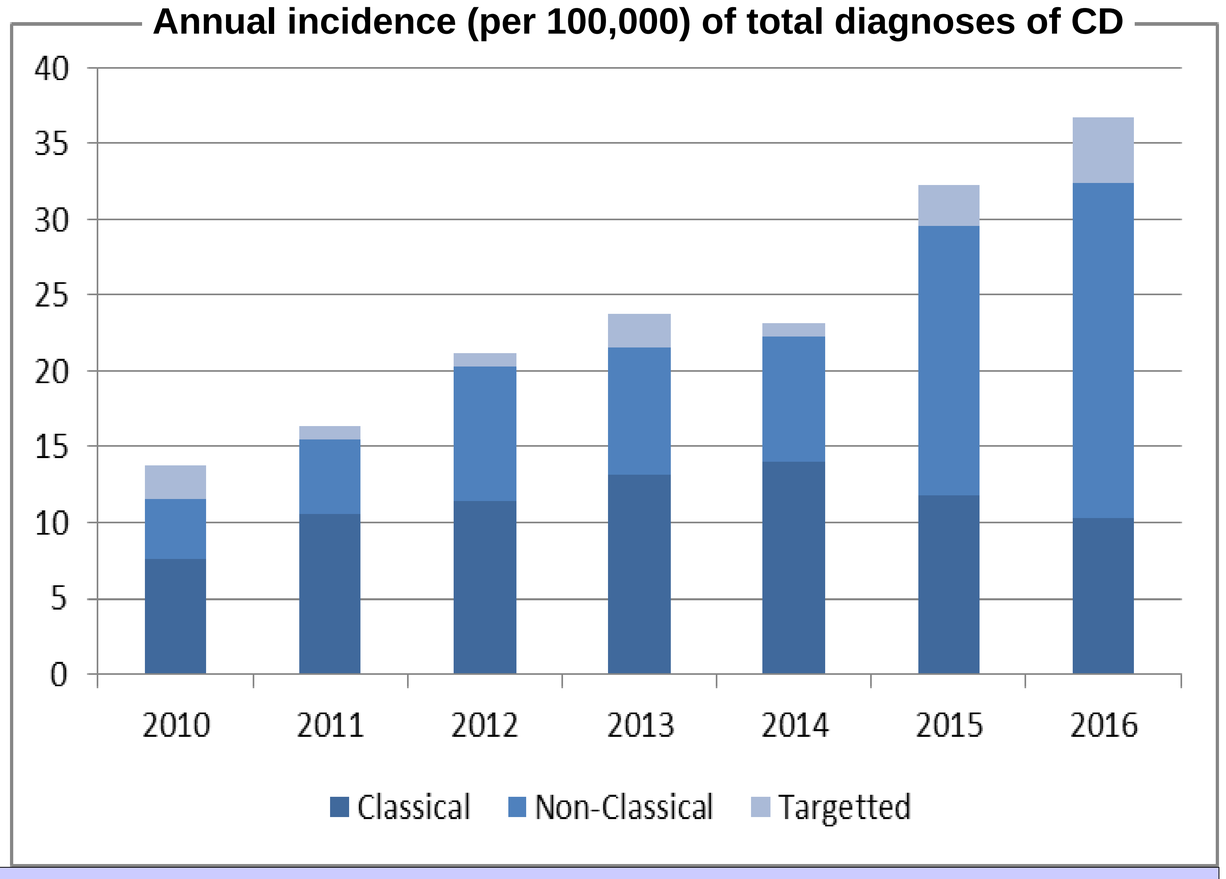
- The incidence of coeliac disease (CD) during childhood is rising in the United Kingdom.
- Prevalence of CD is estimated at ~1% based on serological screening[1]. However, lower rates of diagnosis suggest many patients remain undiagnosed.
- CD may present with classical symptoms, be detected following screening of at-risk populations or be identified during investigation of non-specific symptoms if awareness levels are high.
- Diagnosing CD without biopsy (as per ESPGHAN guidelines[2]) began in South East Scotland in 2012.

Methods

- Retrospective cohort study of all patients <16years diagnosed with CD between 2010 and 2016.
- Direct notification of all positive anti-tTG results via email from laboratory to our clinical lead resulted in full case ascertainment.
- Anti-tTG levels, symptoms (classical vs non-classical, as per Oslo criteria[3]) and demographics were noted.
- Annual incidence was calculated using population figures published by the Scottish government and further classified by mode of presentation (classical/non-classical symptoms, or targeted screening) and method of diagnosis (biopsy/no biopsy).
- The number of anti-tTGs requested was used as a proxy for increasing awareness.

Results

- 382 children and young people were diagnosed with CD (2010-2016).
- Female to male ratio was consistent (2.2:1 throughout period), median age at diagnosis was 8.3 years (IQR 5.1-12.3).
- Incidence rose from 13.8 in 2010 to 36.7 per 100,000 population in 2016.
- There has been a gradual increase in the number of anti-TTG requests but the percentage of positive tests has also risen.
- Since the introduction of ESPGHAN guidelines in 2012, 26% of eligible patients have been diagnosed without biopsy. This has risen to 56% of eligible patients in 2016 as confidence in this strategy grows.



Discussion

- The incidence of coeliac disease in children and young people <16 years of age increased 2.5-fold during the 7 year period from 2010-2016.
- To our knowledge the incidence of 36.7 per 100,000 in 2016 is the highest reported in the UK, whether in childhood or adult studies, and shows no signs of diminishing.
- The proportion of positive anti-tTG results is increasing which confirms a true rise in incidence.
- Diagnosis without biopsy (as per ESPGHAN guidance) is becoming more common in South East Scotland.

References

1. Bingley PJ, Williams AJ et al. Undiagnosed coeliac disease at age seven: population based prospective birth cohort study. BMJ 2004;328:322–3.
2. Husby S, Kolesko S et al. ESPGHAN guidelines for the diagnosis of coeliac disease. JPGN 2012;54:136-160.
3. Ludvigsson JF, Leffler DA et al. The Oslo definitions for coeliac disease and related terms. Gut 2013;62(1):43-52.

COELIAC DISEASE IN THE NO BIOPSY ERA: SCOPE TO DO FEWER SCOPES?

Philippa Wood[1], Martin Lister[1], Paul Henderson[2,3], Peter Gillett[2,3]

[1]Victoria Hospital, Hayfield Road, Kirkcaldy
[2]Royal Hospital for Sick Children, Sciennes Road, Edinburgh
[3]Child Life and Health Department, Sylvan Place, University of Edinburgh.

Background

- 2012 ESPGHAN guidelines[1] simplified the process for diagnosing coeliac disease (CD) in children and young people – biopsy no longer required to secure the diagnosis in **symptomatic** patients with anti-tTG levels **>10 times** the upper limit of normal (ULN).
- We present our incidence data and experience of "no biopsy" diagnosis of childhood CD in the South East Scotland region since that time.

Methods

- Direct notification of all positive anti-tTG results via email from laboratory to our clinical lead = full case ascertainment over the 7 year period studied (2010-2016).
- Anti-tTG levels, symptoms (classical vs non-classical, as per Oslo criteria[2]) and demographics noted.
- Eligibility for diagnosis without biopsy = anti-tTG level > 10xULN in the presence of symptoms attributable to CD.
- An initial care pathway for making a diagnosis without biopsy needed to be developed.

Results

- Total 382 children and young people were diagnosed with CD (2010-2016).
- In retrospect, 219 (57%) of these would have been eligible for no biopsy diagnosis (171 since publication of ESPGHAN guidelines in January 2012).
- 44 diagnoses were made without biopsy (26% of those eligible).

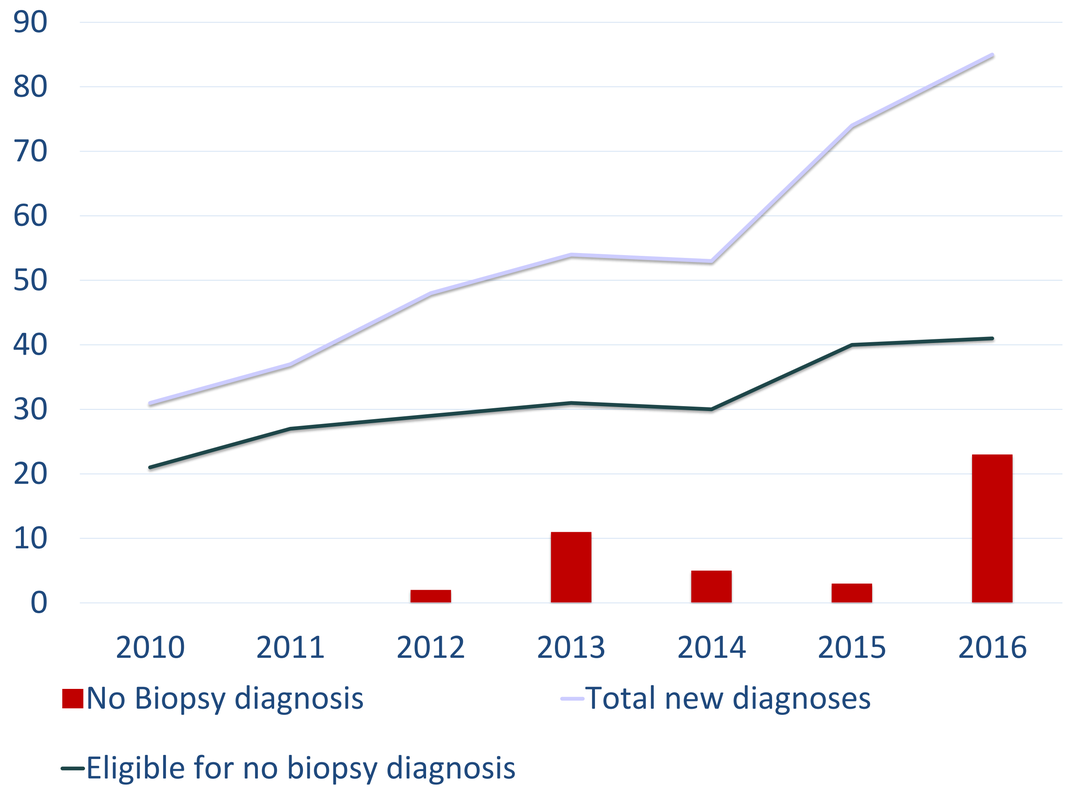
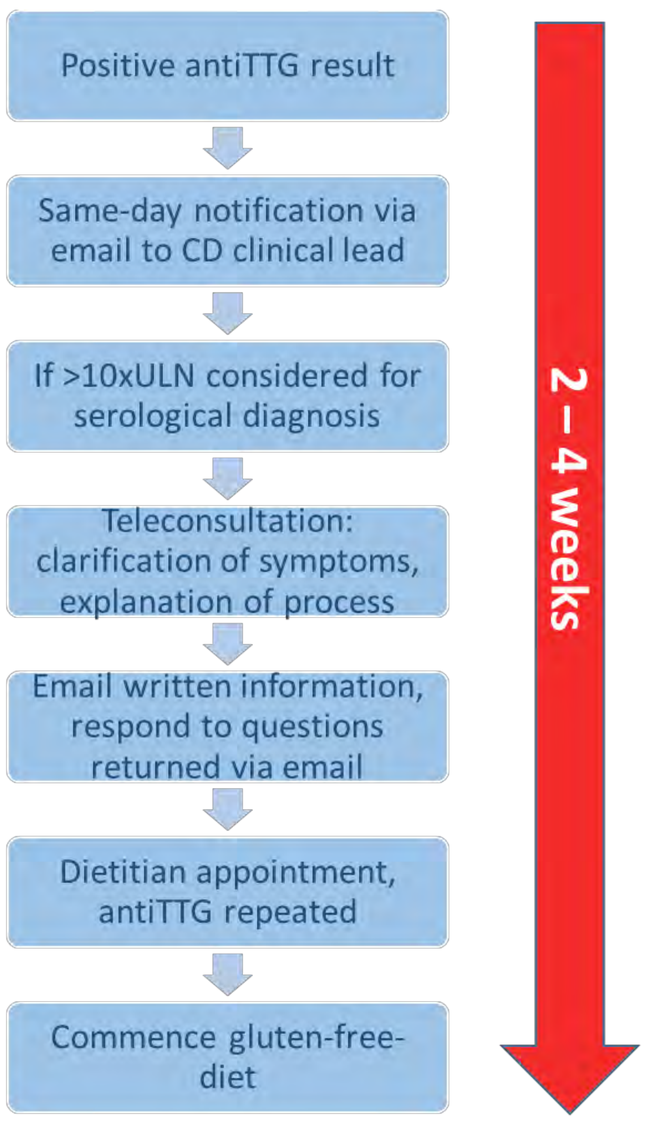


Figure 1 – Annual incidence of total diagnoses of CD, including numbers eligible for no-biopsy diagnoses, and numbers actually made without biopsy

	No biopsy diagnosis (n=44)	Eligible for no Bx diagnosis (n=219)	Not eligible for no Bx diagnosis (n=131)
Age at diagnosis (mean, years)	6.93	7.28	10.12
Female (%)	68.2	70.8	67.2
Classical symptoms[2] (%)	56.8	54.8	45.8

Figure 2 – Features of "no biopsy" group and those eligible/not eligible (excluding patients screened i.e. asymptomatic)

Figure 3 – Diagnostic pathway (modified from ESPGHAN 2012 guideline[1])



Discussion

- A modified ESPGHAN "no biopsy" strategy[1] has been successfully implemented for diagnosis of coeliac disease in children in South East Scotland, and is becoming increasingly popular
- In 2016, 56% of those eligible (symptoms attributable to coeliac disease and anti-tTG >10xULN) were diagnosed without a biopsy
- DQ typing is no longer being performed routinely as per a recent large international study (ProCeDe)[3]
- Diagnosis is confirmed with a second anti-tTG sample (EMA not available in our area)
- Time from initial serology to GFD is less than 4 weeks
- Avoiding biopsy, endoscopy and DQ typing saves the NHS >£1000 per patient
  - 23 patients diagnosed without biopsy in 2016 = 4 endoscopy lists
- Consultation via telephone and supported by email results in high patient and family satisfaction
- As experience increases, we anticipate more diagnoses will be made locally without biopsy
  - Recent literature suggests this may be possible even in asymptomatic high risk patients but this remains controversial

References

1. Husby S, Kolesko S et al. ESPGHAN guidelines for the diagnosis of coeliac disease. JPGN 2012;54:136-160.
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St George's University Hospitals NHS
NHS Foundation Trust

Patient and parent satisfaction with current service for follow-up of paediatric patients with Coeliac Disease

Isobel Connolly, Paediatric Gastroenterology Dietitian

Background

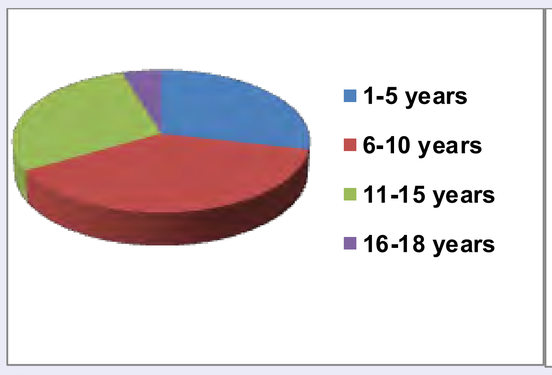
Coeliac disease is a lifelong autoimmune disease caused by a reaction to gluten. One in one hundred people have this condition[1]. There has been a fourfold increase in the UK over a span of 22 years (1990–2011)[2]. Guidelines for the follow-up of paediatric patients with Coeliac Disease are from BSPGHAN[3] and NICE[1], both of which recommend an annual review. BSPGHAN recommends that the follow-up appointments involve a clinical assessment, a review of symptoms, growth, micronutrient status, adherence to GFD, dietary intake of calcium and iron and anti-tTG antibodies[1]. Similarly NICE recommend that weight and height is measured, symptoms are reviewed and an assessment of the diet and adherence to the gluten-free diet is performed at their follow-up appointments[2]. Currently paediatric patients with Coeliac Disease at SGH are followed up annually by the Paediatric Gastroenterologist and the Paediatric Gastroenterology Dietitian at separate time-points. There is an argument that dietitians are the best suited healthcare professional to follow-up patients with Coeliac Disease as voiced in a debate at BSPGHAN conference in 2011[4]. Dietetic-led clinics for paediatric patients with Coeliac Disease have been established in other tertiary paediatric centres within the UK. A study from Addenbrooke's Hospital showed that a high level of patient care can be delivered through a dietetic-led clinic and that the level of care is comparable to a traditional service for Coeliac patients in Norfolk and Norwich University Hospital[5].

Aim To assess the satisfaction of patients and parents with the current service for children with Coeliac Disease at St George's Hospital.

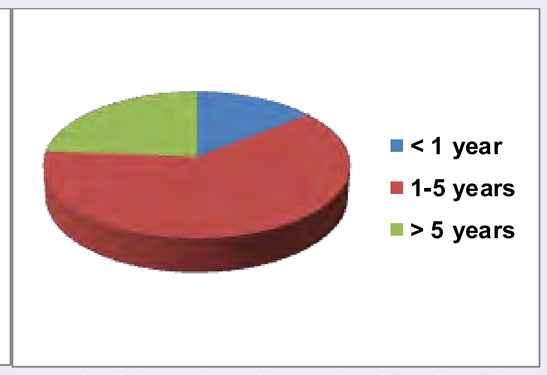
Method The paediatric gastroenterology dietitian developed an online survey. The anonymous online survey asked nine questions about the patient's age, the length of time since diagnosis, how likely they are to recommend the service to friends and family and particular questions in relation to the service. They were given the opportunity to comment in their own words about the current service. Contact was established with 31 parents of patients with Coeliac Disease and they were emailed with the link of the survey.

Results

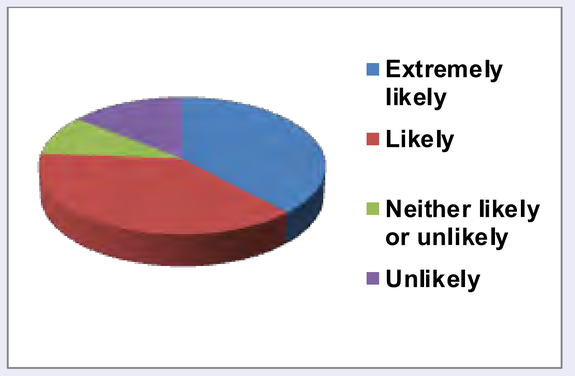
Twenty-one patients or parents of patients with Coeliac Disease completed the survey, a response rate of 67%. The vast majority of patients had been diagnosed with Coeliac disease for over one year. Overall parents of patients were likely or extremely likely to recommend the service to a friend. 10 out of the 21 responders would be receptive to group sessions (e.g. group talks, cookery sessions) with other paediatric patients with Coeliac Disease in addition to their regular clinic reviews.



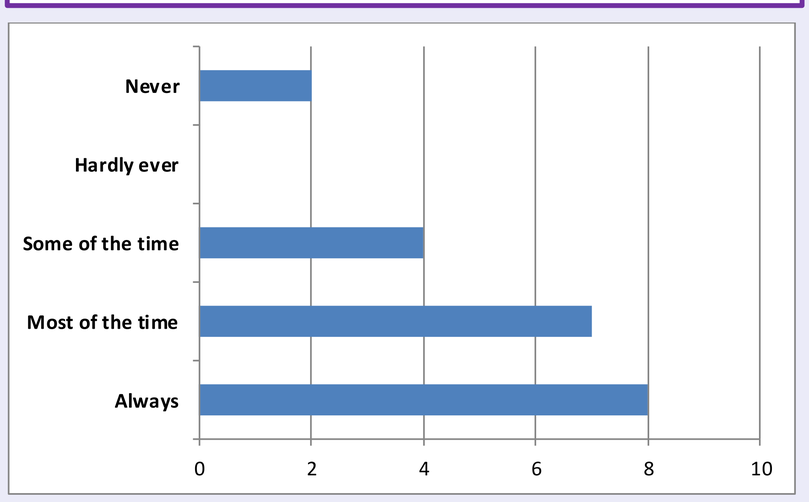
Patient age



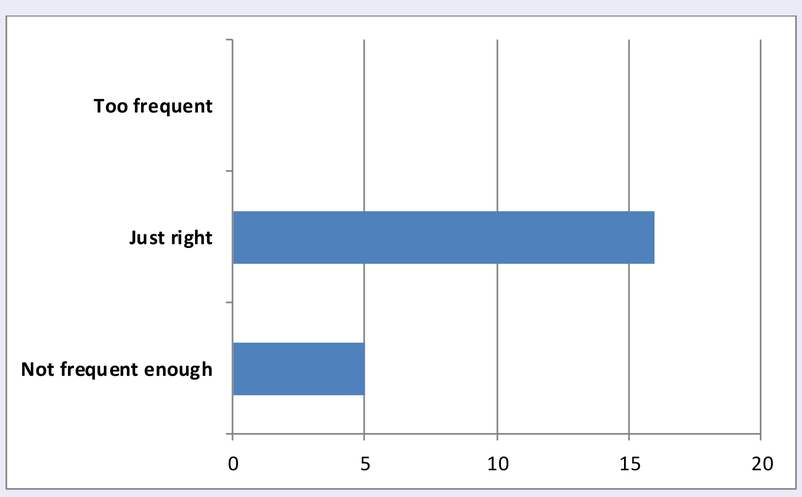
Length of time since diagnosis of Coeliac Disease



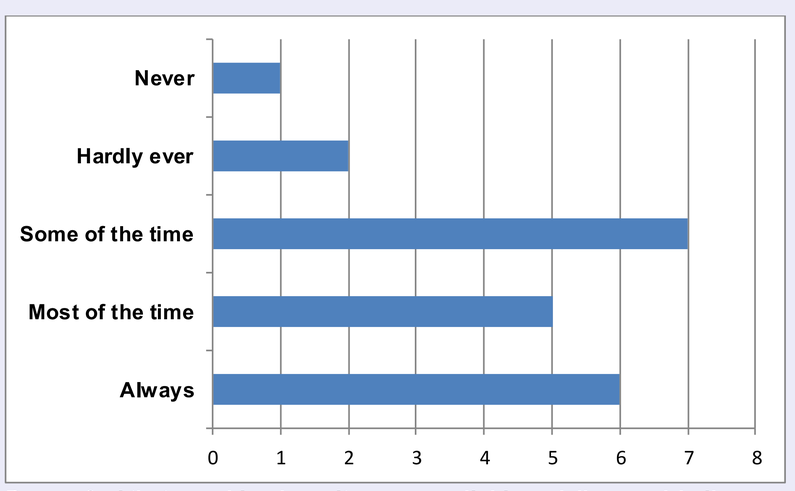
How likely are you to recommend our service to friends and family if they needed similar care



Do you feel that you have adequate access for advice from your dietitian at St George's Hospital?



Do you feel that your doctor or dietetic reviews for coeliac disease at St George's are:



Do you feel that your blood results were available and discussed in line with your clinic appointments?

Discussion

Paediatric patients with Coeliac Disease require annual follow-up as recommended by BSPGHAN (2013)[3] and NICE (2015)[1]. The results of this study show that the satisfaction rates with the current service are high. Areas which require improvement are that blood results are available and discussed in line with the clinic appointments and that the reason for annual review appointments was clearly explained. Additionally 23% of responders reported that their doctor or dietetic reviews were not frequent enough and 10% did not feel that they had adequate access for advice from the dietitian.

Positive comments

- Good annual follow up. Offer of dietitian services
- Dr Mitton was fantastic and the dietician team are always very helpful and full of advice.
- Initial diagnosis and care amazing. Ongoing care good but occasionally a bit chaotic – but that's ok...
- Both dieticians and gastro paeds have been helpful and knowledgable

Comments for improvement

- To date I think every single appointment we have had booked with a gastroenterologist has been postponed for months.....
- Very difficult to access blood tests
- It would be good if the team could communicate more via e-mail.
- The annual meetings/ check ins are unclear in purpose other than weight and height check to feel valueless. Being asked the open question of "is everything all right" is unhelpful.....
- Plenty of useful information on websites and patient forums, coeliac society etc. Dietitians did not really add value. They also ignored the real issue which was that our daughter was a c fussy eater and with the gf diet this made the situation worse.....

Conclusion

The results of this survey provides us details of patient and parent satisfaction rates with the current service for paediatric patients with Coeliac Disease and highlights areas for improvement. Through a service change to a dietetic-led clinic for the management of Coeliac Disease these areas for improvement should be addressed. A dietetic-led clinic will allow for adequate access to the dietitian, bloods tests will be arranged prior to their appointment so that they can be discussed at the appointment and the frequency of follow-up can be more frequent if clinically indicated. A referral back to the Paediatric Gastroenterologist can be made if clinical input is required.

Service change to a Dietetic-Led Clinic

A dietetic-led clinic for the follow-up of paediatric patients with Coeliac Disease commenced in SGH in May 2017. This clinic will run once a month in an established gastroenterology dietetic clinic. A protocol including a referral criteria which indicates that a referral back to the Paediatric Gastroenterologist is necessary has been agreed with the Paediatric Gastroenterology team. This survey will be re-distributed to patients and parents after the dietetic-led clinic has been running for a year to assess the satisfaction rates with the new service. Results of the survey will be compared to the current results and used to continually improve the service provided for this patient group.

References: 1. National Institute for Health and Clinical Excellence (2015) Recognition and assessment of coeliac disease in children and adults: summary of NICE guidance. Clinical Guideline 86. London: NICE. 2. West J., Fleming KM., Tata LJ., Card TR., Crooks CJ. Incidence and Prevalence of Celiac Disease and Dermatitis Herpetiformis in the UK Over Two Decades: Population-Based Study Am J Gastroenterol. 2014; 109:757–768; doi:10.1038/ajg.2014.55. 3. Murch, S., Jenkins, H., Auth, M., Bremner, R., Butt, A., France, S., Furman, M., Gillett, P., Kiparissi, F., Lawson, M., McLain, B., Morris, M., Sleet, S. and Thorpe, M. (2013). Joint BSPGHAN and Coeliac UK guidelines for the diagnosis and management of coeliac disease in children. Archives of Disease in Childhood, 98(10), pp.806-811. 4. 5. Ross A, Shelley H, Novell K, et al. Assessing Quality Outcome Measures in Children with Coeliac Disease—Experience from Two UK Centres. *Nutrients*. 2013;5(11):4605-4613. doi:10.3390/nu5114605.

Seeing the right clinician first time:
designing a modern outpatient coeliac disease service for Scotland

Jacqueline Walker RD[1], Dr. Alan Clarke[2], Pauline Fyfe, Fiona Bernardis, Anna Milsom, David Pratt

Aim/The Challenge

- Around 1 in 100 people in Scotland have Coeliac Disease (CD), but there is an average of **13 years** from first presentation to diagnosis[i], a reported point prevalence of 0.27 (95% Confidence Interval 0.26 to 0.29)[ii], and variation in access to the right clinicians to support the gluten-free diet treatment – dietitians[iii].
- Clinicians agreed that there was a need to **transform** CD services to provide a standard approach to the diagnosis, treatment and review of CD in Scotland.
- The challenge was to deliver an improved and comparable, clinically appropriate, cost effective, safe and sustainable quality CD service on a 'once for Scotland' basis.
- This transformation of the service is particularly relevant to the 2020 vision, in terms of services being provided to the highest standards of quality and safety, with the person at the centre of all decisions and is supported to self-manage.

"Coeliac UK welcomes the introduction of a dedicated pathway for Scotland focused on providing a more consistent and joined up service, aimed at delivering better outcomes for patients with coeliac disease."

Myles Fitt,
Coeliac UK

Key transformation areas:

1. Diagnosis

- Increase awareness
- Prevent unwarranted variation
- Reduce time to diagnosis.

2. Treatment

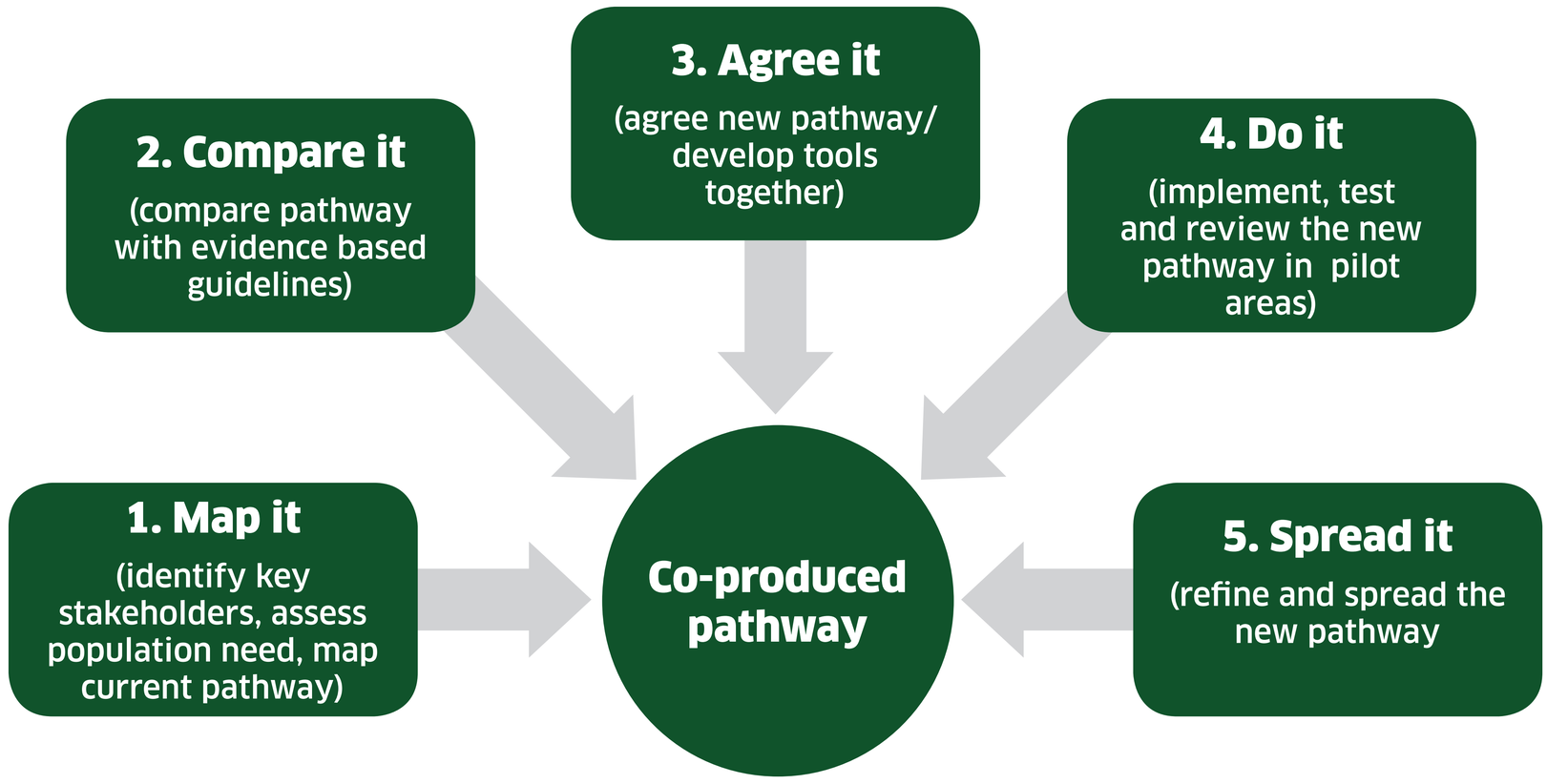
- Optimise dietetic leadership.

3. Review

- Prevent delay and create community capacity

Methods

- We co-produced a new standard CD pathway with all stakeholders (Gastroenterology (GI) **consultants**, **GPs**, **dietitians**, **GI nurses**, **community pharmacy**, **immunologists**, **patient representatives** and **Coeliac UK**).
- The Modern Outpatient Programme core principles of strengthening self-management, accessing decision support and care in the community, using the Consultant resource only for the most complex cases, enhancing the role of the wider multi-disciplinary team in the community, optimising e-health and digital technology and reducing variation in practice are incorporated into the new CD pathway.



2016/17
Co-produce change/co-develop pathway and support tools

2017/18
Implement changes/test pathway/measure outcomes including person experience

2018/19
Refine and spread pathway, share learning

Fig. 1: Diagram showing key stages in process of redesigning new pathway

"I am very enthusiastic about this new pathway as I believe it would have made a real difference to my own diagnosis in terms of speed but also in follow-up care by providing an expert point of contact to support me make the transition to managing a lifelong condition."

Kelly Taylor,
Person with diagnosis of coeliac disease

Results

Key Transformation Area activities - in progress	Anticipated Outcomes
• Once for Scotland pathway • Digital patient management/clinical decision making app to support clinicians manage diagnosis, treatment and review • Clinician and public coeliac disease awareness raising activities • Improved information on diet during investigations for public • Development of a coeliac disease co-ordinator role	• Improved diagnosis rates • Agreed diagnosis pathway • New GI Consultant out-patient only for complex clinical cases • Routine diagnosis with virtual GI Consultant involvement • Reduction in average length of time to diagnosis from presentation
• E-consultation video call web-based management systems, telephone reviews which enable consultation in the persons home • Simple tele health mobile phone based person support and monitoring tools which assists in self-management and virtual review • Planned return treatment list which ensures the person is seen by the dietitian at the right interval time • Standardisation of gluten-free formulary development to ensure best value and maximum choice • Dietetic led care	• Co-ordination of treatment and review which ensures person sees the right clinician at the right time • Virtual consultation and person initiated reviews • Person is better supported and can be monitored remotely at home • Triage of return based on person's need • Extended scope of dietetic practice around coeliac care management • GI Consultant managed only the most complex coeliac disease cases • Dietitians manage GFFS registrations freeing up valuable GP time • Gluten free food online ordering direct to community pharmacy
• Training and e-learning for community pharmacy on annual adult coeliac disease health check • Implementation of Scottish Coeliac Disease pathway to ensure person sees the right clinician first time • Health economic assessment of old and new pathways	• Maximisation of the community pharmacy health check • Fast track back to the right clinician as required • Reduced delay in access to right clinician • More efficient use of resources and better value pathway • Improved short and long term clinical outcomes and person experience

Conclusion

- The method used to transform the CD service is based on public health population needs assessment, co-production, clinical leadership and health quality improvement methodology is transferable for use in the transformation of other services/pathways.
- Transforming services with clinicians, third sector and people using the service are achievable if the correct methods are employed. Stakeholders enjoyed the opportunity to come together and reflect on current practice, identify the issues, agree a future state and co-produce a better pathway for CD in Scotland.

Acknowledgements

Developed in partnership with [1]NHS Tayside, [2]NHS Greater Glasgow and Clyde, Coeliac UK, Kelly Taylor.

Contact: jwalker6@nhs.net

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RAPID URINE HOME TEST FOR GLUTEN FREE DIET MONITORING

M. Remedios Domínguez-Flores[1], Verónica Segura[1], Ángela Ruíz-Carnicer[2], Isabel Comino[2], Carolina Sousa[2] and Ángel Cebolla[1].

[1]Biomedal S.L., Sevilla, Spain.
[2]Departamento de Microbiología y Parasitología, Facultad de Farmacia, Universidad de Sevilla, Sevilla, Spain.
Email: remedios.dominguez@biomedal.com

Introduction

To date, the only effective management of celiac disease is adherence to a strict gluten free diet (GFD). However, there has been no reliable method to confirm adherence to a GFD or to ascertain whether the origin of acute symptoms in a celiac patient may be related to gluten exposure. There is poor or no correlation of celiac serology and dietary questionnaires with gut mucosa recovery.

To address this need, we developed a lateral flow immunoassay (LFIA) to detect gluten immunogenic peptides (GIP) in urine samples, excreted after gluten consumption. Our study demonstrated that about 50% of celiac patients following a GFD have GIP in urine and that there is a high correlation between GIP detection and gut mucosal damage (Moreno et al., 2017).

Our goal was to simplify the LFIA method so that it could be used at home (Figure 1), and to validate the test, establishing its performance characteristics.

Figure 1. LFIA home test procedure

Methods

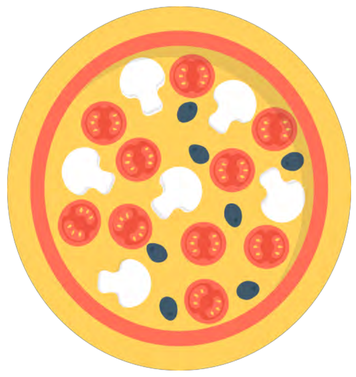
Urine samples (n=254) from volunteers under different gluten exposure conditions were analyzed with the simplified urine GIP LFIA. The samples included:

•**Positive-control** first morning urine samples from healthy volunteers following a non-standardized gluten-containing diet (GCD) who reported gluten ingestion in the previous 16 hours (n=25).

•**Negative-control** random samples from celiac patients on a strictly supervised GFD (n=180).

•First morning samples from healthy subjects on a GFD after the administration of 0.5g of gluten a day (2.5-5% of the gluten content of the average Western diet, Figures 2 and 3) -i.e., a moderate **gluten challenge-** (n=49).

Daily gluten content of the average Western diet



10-20g of gluten

0.5g of gluten

Figure 2. Example of the amount of food that contains 10-20 g or 0.5g of gluten

Simulated transgression of a Gluten Free Diet

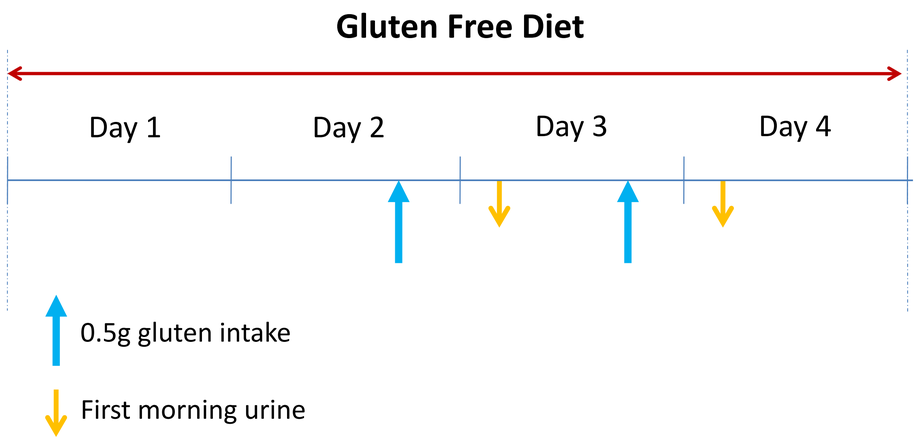


Figure 3. 0.5g gluten challenge study design

Results

GIP were detected in all samples of volunteers on a GCD whereas no GIP were detected in 179 out of 180 samples from patients on a strict GFD. GIP were detected in 44 of the 49 samples collected from volunteers ingesting 0.5g of gluten. The diagnostic sensitivity of the test was 100% and the specificity 99%. The positive and negative predictive values were 96% and 100% respectively. The sensitivity for the detection of the ingestion of 0.5g of gluten was 90%.

		Control samples		0.5g gluten challenge
		Positive	Negative	
Urine GIP LFIA	Positive	25	1	44
	Negative	0	179	5
	Total	25	180	49

Discussion

The rapid urine gluten test is highly specific and sensitive to assess adherence to GFD and gluten exposure in celiac and gluten-sensitive patients.

IS THERE A ROLE FOR A GLUTEN FREE DIET IN 'LIFESTYLERS'? THE FIRST DOUBLE-BLIND RANDOMISED STUDY

A.Rej[1], M.Kurien[1], P. Tosi[2] , N. Trott [1], D.S. Sanders [1]

[1]Academic Unit of Gastroenterology, Royal Hallamshire Hospital, Sheffield Teaching Hospital NHS Foundation Trust, Sheffield, S10 2JF

[2] School of Agriculture Policy and Development, University of Reading, Reading, Reading, RG6 7BE

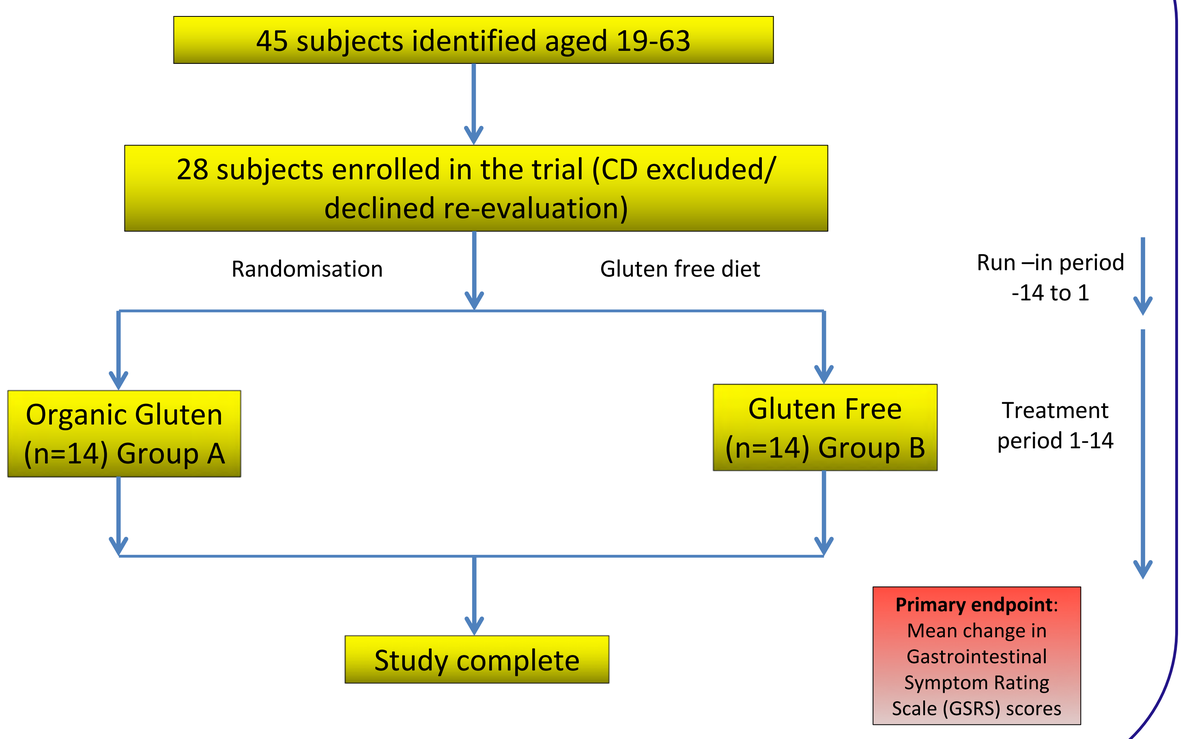
INTRODUCTION

A gluten free diet (GFD) is essential in the management of coeliac disease, as well as several studies demonstrating its utility as a dietary therapy in patients with irritable bowel syndrome. The aim of this double-blind placebo-controlled study was to assess the role of a GFD in a healthy population who take a GFD as a lifestyle choice ('lifestylers').

METHODS

Subjects were recruited via an advert, with exclusion criteria including coeliac disease. Following selection, subjects were commenced on a 2 week GFD after evaluation by a dietitian. Participants were then randomised to receive either organic gluten (Group A, Vital Gluten 14g gluten protein/day) or gluten free flour (Group B) in pre-made bags, over a 2 week period. These were sprinkled on their food twice daily.

Gastrointestinal Symptom Rating Scale (GSRS) scores were assessed at baseline (following 2 weeks GFD) and after 2 weeks of randomisation. Data was analysed using SPSS version 22.



RESULTS

45 subjects were identified with 28 participants recruited into the trial (Group A; n=14, Group B; n=14) following exclusion criteria. Median age was 36.5 years (range: 19-63) and 21 (75%) were female.

There was no significant difference in baseline demographics between both groups (p=0.54). Over a 2 week period there was no significant difference in gastrointestinal symptoms or fatigue in either group, as seen in Table 1.

Table 1 GSRS scores at baseline and following intervention

GSRS	Group A			Group B		
	Baseline	Intervention	Difference from Baseline	Baseline	Intervention	Difference from Baseline
	Mean +/- SD	Mean +/- SD	Paired T-test, p-value	Mean +/- SD	Mean +/- SD	Paired T-test, p-value
Abdo Pain	2.50 +/- 1.40	2.14 +/- 1.70	0.50	2.35+/- 1.33	2.07+/- 0.99	0.49
Reflux	1.71 +/- 1.13	1.64 +/- 1.15	0.72	2.50 +/- 2.20	2.57 +/- 1.95	0.90
Indigestion	2.14 +/- 1.35	2.07 +/- 1.32	0.88	2.14 +/- 1.35	1.79 +/- 0.97	0.34
Diarrhoea	2.71 +/- 1.93	1.64 +/- 0.92	0.03	1.85 +/- 1.46	1.86 +/- 1.35	1.00
Constipation	2.50 +/- 1.82	2.46 +/- 1.81	0.70	1.92 +/- 1.54	2.50 +/- 1.65	0.18
Fatigue Score	6.61 +/- 2.36	6.00 +/-2.98	0.59	6.57 +/-2.44	5.36 +/-2.27	0.23

DISCUSSION

This study demonstrates that gluten is unlikely to be the culprit agent for gastrointestinal symptoms or fatigue in healthy individuals. A GFD has no evidence base in individuals who do not have coeliac disease or IBS. The public should be discouraged from considering a GFD of their own volition.

Developing a nutrient database of gluten free foods for the Coeliac Diet and Nutrition Survey

Nathalie Wolf[1], Ruth Passmore[2], Heidi Urwin[2]
[1]Bern University of Applied Sciences, Switzerland, [2]Coeliac UK

Introduction

Coeliac disease is a lifelong autoimmune disease cause by an adverse reaction to gluten. The only available treatment is strict adherence to a gluten free diet for life.

In the UK, the National Diet and Nutrition Survey (NDNS) is carried out to provide detailed food consumption data. The NDNS does not identify people following a gluten free diet within the analysis and there is an evidence gap with regard to the nutritional adequacy of a gluten free diet.

The Coeliac Diet and Nutrition Survey (CDNS) aims to improve our understanding of the gluten free diet and the nutritional adequacy of the gluten free diet. Participants of the CDNS will complete four 24h recalls of their food and drink intake using the online platform Intake24 (www.intake24.co.uk), during four times throughout the year to capture seasonal variations.

National nutrient databases such as McCance and Widdowson[1] and the NDNS[2] do not contain information about gluten free foods. Intake24 has a nutrient database, which includes over 1500 foods, but it required additional nutritional information for gluten free foods.

Objectives

- To determine if there are differences in the nutrient content of different brands of gluten free foods within the same food group eg bread, pasta, flour, cereals.
- To compare the macronutrient content of gluten free and gluten containing foods to identify if gluten containing foods are nutritionally similar enough to use in place of gluten free
- Estimating the theoretical macro- and micronutrient content of gluten free foods based on their ingredients

Methodology

The macronutrient composition of gluten free substitute foods within the same food group were compared across brands and with their gluten containing equivalents:

1. There were significant differences ($p < 0.05$) for some macronutrient contents within the same food group across different brands. Therefore it was necessary to include within the database, several different brands from the same food group, rather than using an average for the category.
2. Significant differences ($p < 0.05$) also existed between some macronutrient contents of gluten free foods and their gluten containing equivalents. Therefore nutrient data for gluten containing foods could not always be used as a proxy for gluten free foods. Figure 1, provides an example with the comparison of gluten containing and gluten free fresh white bread.

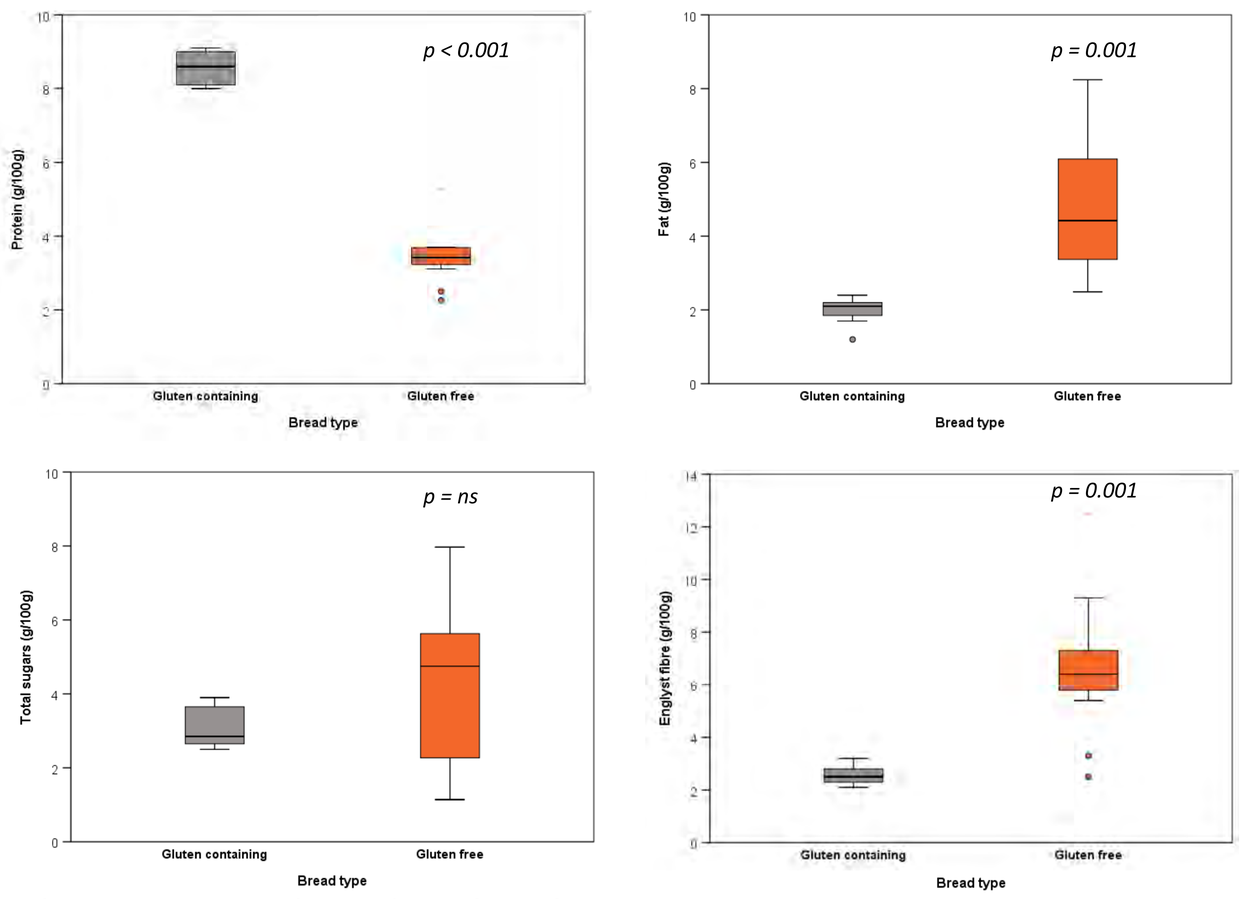


Figure 1. Comparison of nutrient data and energy between gluten containing and gluten free fresh white bread

The information provided on back of pack labelling is limited to macronutrients, unless manufacturers voluntarily provide additional information. In order to obtain information about the content of 53 additional nutrients, without costly lab analysis, the nutrient content of more than 200 gluten free foods was theoretically estimated using a process previously reported by Missbach et al[3]. Ingredient lists were obtained from food labels found online and in store. Subsequently a stepwise approximation process was used to match the amount of each ingredient to the macronutrient content within set precision margins. Detailed micronutrient composition of the ingredients within the products was obtained from nutrient databases[1,4].

Steps for estimating nutritional composition

1. Ingredient lists and macronutrient information for gluten free products obtained from food labels in store and online
2. Nutrient data for ingredients sourced from nutrient databases
3. Ingredient proportions estimated to match macronutrient profile within set margins
4. Laboratory analysis to validate methodology (to be carried out in the future)

Results

The final database provides an estimation of 59 macro- and micronutrients contained in more than 200 gluten free products available in the UK, matched within limits shown in Table 1.

Table 1. Difference between the calculated macronutrient content and food label macronutrient value

Nutrient	Mean % difference (95% CI)
Protein	0.18 (-3.54, 3.90)
Carbohydrate	0.17 (-2.53, 2.87)
Fat	0.01 (-2.99, 3.01)

Discussion

Theoretical analysis is less costly than carrying out lab analysis of all products and can be performed rapidly with information that is readily available. There are disadvantages with calculating the theoretical nutrient composition of a food product compared to using lab analysis. It is for example not possible to determine micronutrient losses during the cooking process for certain foods. Nevertheless, the difference between the calculated macronutrient content and food label values was within ± 4% for each macronutrient.

To validate our data, lab analysis of a selection of gluten free food products will be carried out.

The nutrient database for Intake24 has been updated to include gluten free foods and the first phase of the CDNS has been launched, March 2018. As the project progresses, participants are able to report missing foods which can be added to the database.

Acknowledgments

We would like to thank Maisie Rowland and Dr Emma Foster, Newcastle University, for their support with this project and providing access to Intake24.

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Cost, availability and nutritional composition comparison between gluten free and gluten containing food staples provided by food outlets and internet food delivery services between two areas of London with differing UK deprivation indices

Hanci, O[1] and Jeanes, YM[2]

[1]Consultant Paediatrician, Royal Surrey County Hospital, Guildford, [2]Dietitian, Principal Lecturer in Clinical Nutrition, University of Roehampton, London

Introduction

Coeliac disease affects approximately 1% of the UK population, it is managed by adhering to a strict gluten free (GF) diet. However, barriers to adherence with this diet include amplified cost and limited availability of gluten free products, especially in light of the diminishing availability of GF foods on prescription.

Study Aim

To compare the cost, availability and nutritional composition of manufactured GF products with their gluten-containing (GC) counterparts, provided by food retailers (physical stores and online) between two areas of London with distinctly contrasting deprivation indices.

Methods

- A cross-sectional survey of 26 food categories was conducted in May 2017, data was collected on the cost, availability and nutritional composition of GF and GC foods. The allocated UK Deprivation Index (based on a multifactorial scale of poverty, ranking all postcodes in England with 1 being the most deprived) for Richmond CCG is 24730, making it one of the best ranked in London, whereas Enfield CCG is ranked 12795, one of the worst in rankings within the M25.
- Fifty physical stores were surveyed (10 in each category); premium, regular and budget supermarkets, convenience stores and health food stores. Online retailers of manufactured GF products which offered a delivery service to the areas under study were also included.
- Food categories included traditionally wheat based (listed within table 2) and eleven everyday foods usually containing gluten (for example sauces, sausages, battered fish, ready meals).
- The mean value from the cheapest and most expensive GF and GC food for each category were compared.

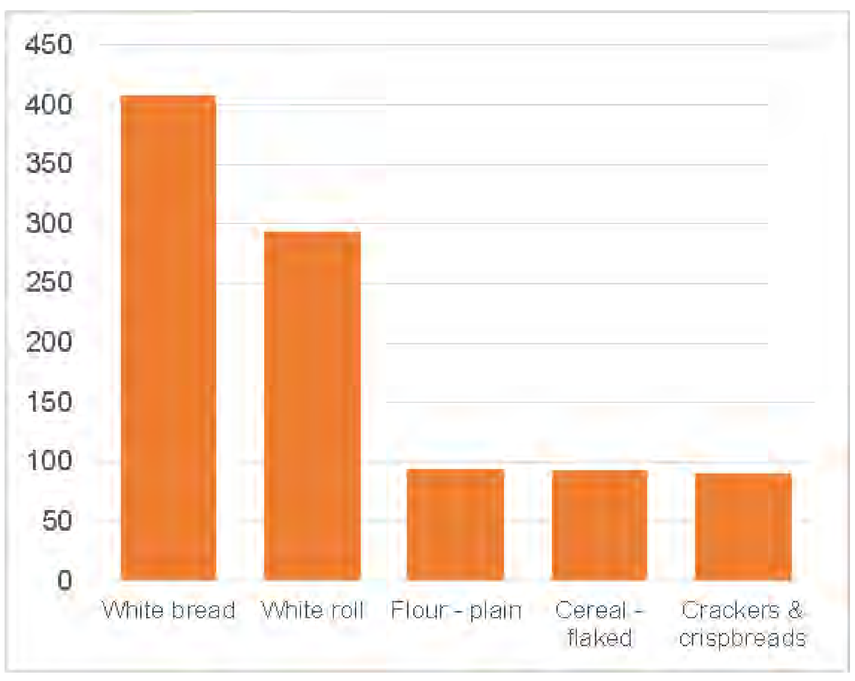
Results

No convenience stores and only one budget supermarket, out of ten surveyed, stocked any traditionally wheat based manufactured GF items (Table 1). The availability of GF foods across the two regions were similar. Premium and regular supermarkets stocked significantly more GF breads than Health food stores (Table 2).

The online GF food suppliers superseded all of the physical stores in the number of manufactured GF items available (Table 1). However, over half of the GF items were more expensive in online stores than in regular supermarkets.

Seventy four percent of GF foods surveyed were more expensive than their GC counterparts; GF white bread had the greatest cost excess of 408% compared to GC white bread (Figure 1).

Figure 1. Percentage greater cost of GF foods compared with GC foods (p/100g)



Sixty percent of surveyed GF foods contained higher energy, 73% contained more fat and 60% had more saturated fat compared with published values for GC foods (all per 100g).

Acknowledgements:
Sponsored dissertation award from Coeliac UK

Table 1. Percentage of manufactured GF products available according to store type (values expressed as median (IQR)).

Premium Supermarkets	Regular Supermarkets	Budget Supermarkets	Convenience/ corner stores	Health Food Stores	Online Food Retailers
58 (54-69)	73 (71-81)	0 (0)	0 (0)	39 (38-48)	85 (75-93)

Table 2. Number of different brands available of each GF surveyed item in stores (5 in each category) within the Enfield CCG geographical area (values expressed as median (IQR)).

Gluten Free product	Premium Supermarkets	Regular Supermarkets	Budget Supermarkets	Convenience/ corner stores	Health Food Stores	p-value*
White bread	4 (3-4)[c,d,e]	4 (3-4)[c,d, e]	0	0	1 (0-1)	<0.001
Brown bread	7 (6.5-8)[b,c,d,e]	4 (3-5)[c,d,e]	0	0	1 (0-1)	<0.001
White rolls	1 (1)[c,d]	1 (1-1.5)[c,d]	0	0	1 (0-1)	0.001
Brown rolls	1 (1)[c,d]	1 (1)[c,d]	0	0	1 (0-1)	0.001
Cereal bars	5 (0-5.5)	8 (5.5-14)[c,d]	0	0	8 (5.5-8.5)[c,d]	0.001
Cereal – flaked	3 (1-3)[c,d]	4 (4-6.5)[a,c,d]	0	0	1 (1-4.5)[c,d]	<0.001
Cereal – other	10 (1-12.5)[c,d]	8 (6.5-11.5)[c,d]	0	0	8 (7-12)[c,d]	0.001
Pasta	4 (2.5-4)[c,d]	5 (3.5-6)[c,d]	0	0	4 (3.5-9)[c,d]	0.001
Flour – plain	1 (1)[c,d]	2 (1.5-3)[a,c,d]	0	0	0 (0-5.5)	0.004
Flour – other	2 (1-2)[c,d]	3 (0.5-5)[c,d]	0	0	0 (0-11.5)	0.015
Crackers & crispbreads	9 (6-12)[c,d]	12 (7-15.5)[c,d]	0	0	10 (7.5-12)[c,d]	0.001
Pizza bases	1 (0-1)	0 (0-0.5)	0	0	0 (0)	0.046
Biscuits	9 (3.5-12.5)[c,d]	17 (13.5-26)[a,c,d,e]	0	0	9 (3.5-10)[c,d]	<0.001
Cake – sponge	0 (0-3.5)	3 (2-5)[c,d,e]	0	0	0 (0-1.5)	0.007
Sandwiches and wraps	0 (0)	0 (0)	0	0	0 (0)	NS

*** Kruskal-Wallis H test [a] Significantly more than premium supermarkets [b] Significantly more than regular supermarkets [c] Significantly more than budget supermarkets [d] Significantly more than Convenience stores [e] Significantly more than health food stores (all p<0.05, following Mann-Whitney tests)**

Conclusion

Availability of manufactured GF products remains poor, especially in convenience stores and budget supermarkets, serving those from poor socio-economic cohorts, the elderly and physically disabled. The stores where availability has improved from previous published findings are associated with the greatest additional cost.

The inferior comparative nutritional quality of manufactured GF products emphasizes the need for those on a medically indicated GF diet to be advised and monitored by adequately trained health professionals, such as dietitians.

Subjective experiences of post-diagnosis weight change in adults with coeliac disease: Relationships with BMI, weight loss intentions, and body image

E Hogg[1], S Tulip[1], E Evans[1], K Sainsbury[2]

[1]School of Psychology, Faculty of Medical Sciences, Newcastle University

[2]Institute of Health and Society, Faculty of Medical Sciences, Newcastle University

Introduction

- Although weight loss pre-diagnosis and weight gain post-diagnosis are common in individuals diagnosed with coeliac disease (CD) during adulthood[1,2] little research has focused on the subjective experiences of weight change or their relationship with body mass index (BMI), weight loss intentions, and body image in this population[3].
- For those attempting weight loss, little is known about the strategies used, or barriers encountered, while balancing weight loss with a gluten free diet (GFD).

Aims

To explore:

- objective and subjective experiences of weight changes following CD diagnosis;
- the relationship between weight changes post-diagnosis, current BMI, weight loss intentions and body image;
- the predictors of current BMI in adults with CD;
- the weight loss intentions of adults with CD, strategies used and barriers to weight loss.

Methods

- Online cross-sectional survey
- 447 adults with CD (diagnosed in adulthood) completed measures of BMI before diagnosis, direction of any weight change following diagnosis, weight change interpretation (positive or negative), current BMI, body image, and weight loss intentions, strategies, and barriers.
- Analyses: descriptives and a hierarchical multiple linear regression to predict current BMI.

Results

- Most adults underweight at diagnosis gained weight post-diagnosis (72%) and were currently healthy (60%) or overweight (23%).
- 52% of those with a healthy BMI pre-diagnosis gained weight.
- Initial BMI and post-diagnosis weight change were related to current BMI in the expected directions, $F(7, 1239.29)=66.526$, $p<.001$.
- A more negative interpretation of weight change and poorer body image were related to higher BMI, although their influence was reduced when weight history was accounted for.
- 50% of adults were currently trying to lose weight.
- A higher current BMI, weight gain following diagnosis, a more negative interpretation of post-diagnosis weight change, and poorer body image were all related to current weight loss intentions.
- Weight loss strategies were consistent with those reported by the general population (see figure 1 for the six most commonly used).
- Barriers unique to the GFD are provided in table 1.

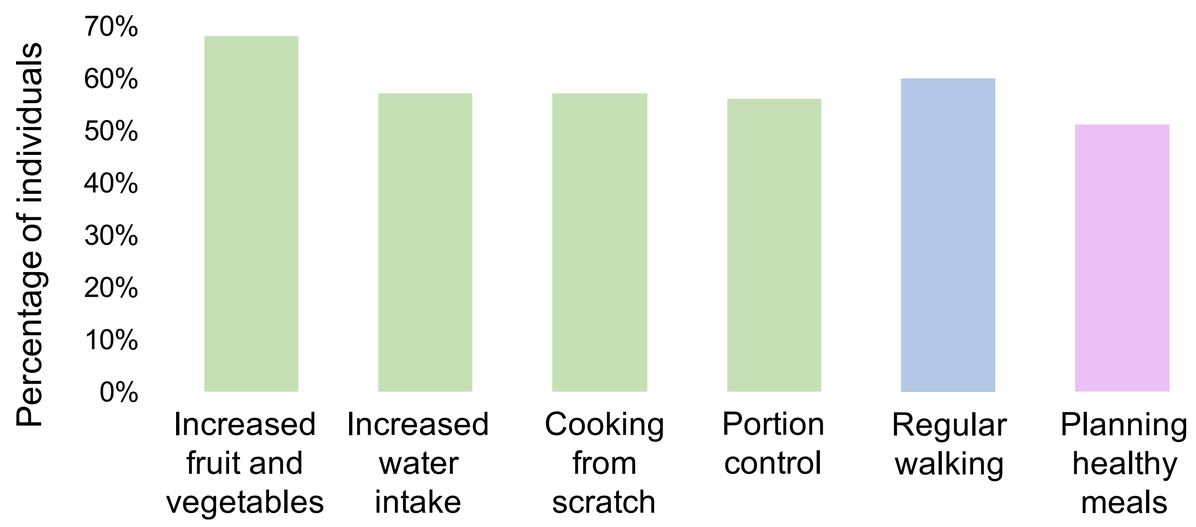


Figure 1. The percentage of individuals currently using each weight loss method.

Table 1. The percentage of individuals who strongly agreed/agreed with each barrier to weight loss.

Weight Loss Barrier	Strongly Agree/ Agree (%)
GF replacement foods are higher in fat and sugar than regular foods	72.3
GF foods are not as nutritionally balanced as regular foods	53.2
I feel tempted to try new GF products when I see them	49.7
Weight loss programmes/diets are hard to adapt to a GFD	22.6
To stay strictly GF, I sometimes have no option but to eat unhealthily	19.9
Having to monitor my food intake conflicts with my weight loss goals	15.6

Conclusion

- Weight changes prior to, and following, diagnosis (commencing the GFD) are important determinants of later weight status in adults with CD, and interpretations of post-diagnosis weight changes impact upon body image and weight loss intentions.
- Current weight loss intentions were common. Consequently, continued dietary and weight support from the point of diagnosis, including ways to ensure success of any weight loss efforts while maintaining GFD adherence, are of paramount importance to ensure the achievement and maintenance of a healthy BMI.

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The Body Image of Females with Coeliac Disease

S Tulip[1], E Hogg[1], E Evans[1], K Sainsbury[2]

[1] School of Psychology, Faculty of Medical Sciences, Newcastle University
[2] Institute of Health & Society, Faculty of Medical Sciences, Newcastle University

Introduction

- Body image is a person's perception of the appearance and function of their body, and can be separated into positive and negative body image, which are related but distinct constructs (positive body image is not just the absence of negative characteristics).[1]
- Positive and negative body image have not been directly researched in the context of coeliac disease (CD), but may be relevant from two perspectives:

1
- **Weight gain** following gluten-free diet (GFD) commencement is common.[2]
- Qualitative research indicates that weight gain may be unexpected and **interpreted negatively** by adults with CD, provoking body image concerns and disordered eating.[3]

2
- Negative body image is high in inflammatory bowel disease, a similar **gastrointestinal illness**, and is associated with **poorer physical and psychological health**.[4,5]
- Comparable relationships may exist in adults with CD.

Aim: Determine whether these variables, along with GFD adherence, are associated with body image in CD.

Hypotheses:

1. Negative interpretation of weight gain (controlled for BMI) will be associated with higher negative body image & lower positive body image.
2. Higher BMI, poorer GFD adherence, increased CD symptoms, increased depression & anxiety, and poorer quality of life will be associated with higher negative body image & lower positive body image.

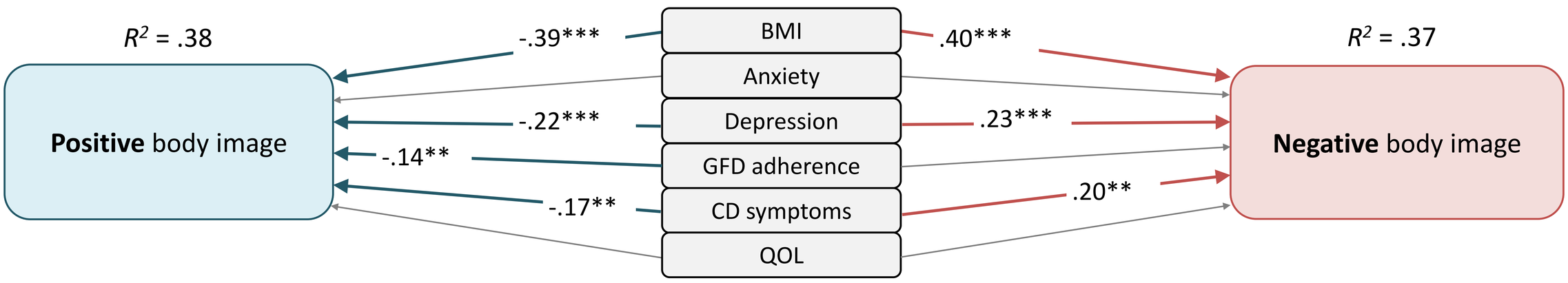
Methods

- **Participants:** 471 females ≥ 18 years with a self-reported medical diagnosis of CD. Recruited online via Facebook support groups and Coeliac UK.
- **Questionnaires (online):**
  - Demographics; Disease & weight characteristics; GFD adherence (CDAT); CD symptoms (CSI); Quality of life; Positive body image; Negative body image; Depression (DASS-21); Anxiety (DASS-21).
- **Analyses:** T-test, correlations, and multiple regression analyses to determine associations between the hypothesised predictors and both positive and negative body image.

Results

1. **Characteristics:** 51% gained weight after the GFD; 17% lost weight. Weight gain was interpreted significantly more negatively than weight loss; $t(274) = 8.38$, $p < .001$.
2. **Weight variables:** More negative interpretation of weight change after a GFD & higher BMI predicted lower positive body image & higher negative body image. Direction of weight change was not significant.
3. **Disease & psychological variables:** Lower BMI, decreased depression, better GFD adherence & decreased CD symptoms predicted higher positive body image. Higher BMI, increased depression & increased CD symptoms predicted higher negative body image.

Figure 1 Regression analyses predicting body image
Standardised beta coefficients shown for significant predictors: * $p = < .05$, ** $p = < .01$, *** $p = < .001$



Discussion

- Negative interpretation of weight changes, irrespective of weight change direction, is associated with high negative body image. This appears to be a bigger issue for those who gain weight (majority gain weight; weight gain interpreted more negatively than weight loss).
- Education about possible weight changes following a GFD may help patients interpret weight gain as healthy, positively impacting body image and reducing disordered eating.
- As in similar illnesses[3,4], disease symptoms and depression significantly predicted body image, indicating body image may be an additional psychological comorbidity to screen for in adults with CD and ongoing symptoms.
- Anxiety and quality of life were not significant when other predictors were in the model. This is likely due to overlap in constructs (e.g., quality of life measures include physical and psychological symptoms).
- Positive body image was associated with GFD adherence; negative body image was not. The relationship between positive body image and GFD adherence is likely to be reciprocal (good adherence increases positive body image; higher positive body image improves adherence).
- Interventions promoting positive body image at diagnosis may be a unique way of improving GFD adherence and overall health.
- **Limitations:** Cross-sectional design means the direction of causation is unclear; longitudinal research is needed to determine causation**.**

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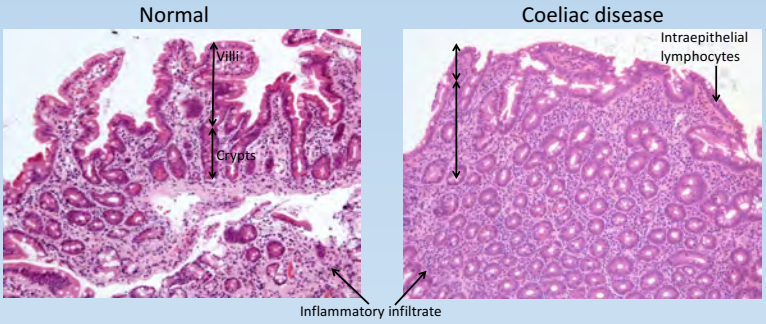
Identification of optimal immunohistochemical parameters to separate coeliac disease from normal duodenal biopsies, with implications for digital image analysis development

Melisa Arias[1] and Elizabeth J. Soilleux[2, 3]

1 Department of Cellular Pathology, Oxford University Hospitals NHS Foundation Trust
2 Department of Pathology, University of Cambridge
3 Work funded by the Pathological Society of Great Britain and Ireland

INTRODUCTION: Coeliac disease (CD) has around 1% prevalence and is due to an immune response to gluten that damages the small intestine. Manifestations range from no symptoms, through anaemia to severe intestinal symptoms, with complications (bone thinning, infertility, lymphoma and duodenal cancer). Other gluten-sensitive conditions, including non-coeliac gluten sensitivity, irritable bowel syndrome and wheat allergy, fail to fulfil CD criteria, but are up to 12 times as common. The exact relationship between these conditions remains unclear. Treatment of CD is a lifelong gluten-free diet, but the importance of a gluten-free diet is unclear in other gluten-sensitive conditions.

Current diagnostic parameters used for evaluation of duodenal biopsies

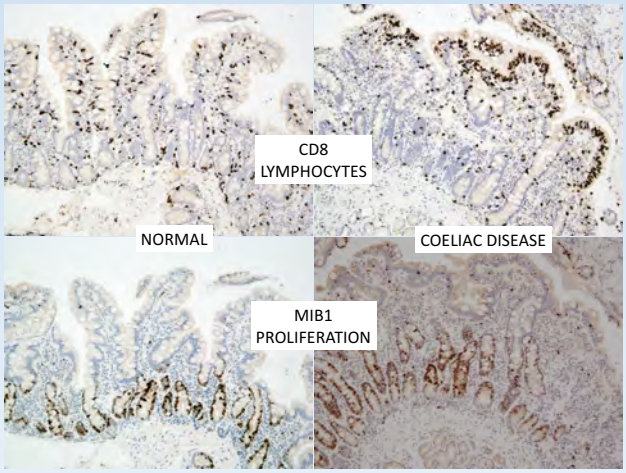


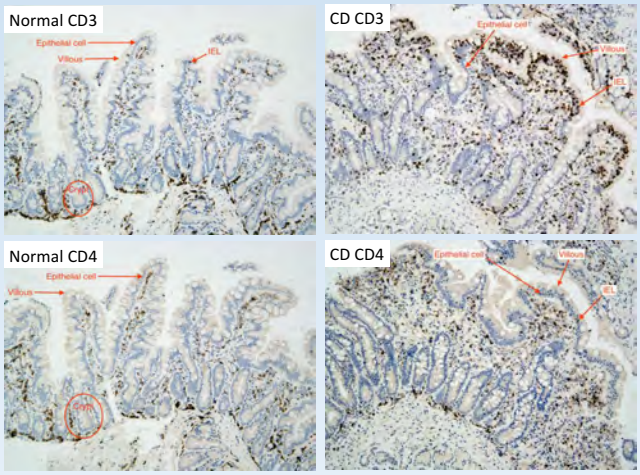
HYPOTHESIS: There is significant underdiagnosis of CD on duodenal biopsy. More objective and accurate CD diagnosis might be achieved by digital image analysis, either alone, or as part of multiparameter clinical and laboratory analysis.

AIM: We set out to determine which two routine immunohistochemical (IHC) stains best separate CD and normal duodenal biopsies.

METHODS: Under ethical/ HRA approval, we obtained 20 duodenal biopsies, including 10 definitive cases of CD (Modified Marsh Score grade 3a, 3b or 3c) and 10 control (normal) biopsies. Sections were immunostained and parameters evaluated manually, with subsequent statistical analysis (student's T-test).

RESULTS: Representative examples of candidate immunostains





Statistical analysis of manually evaluated immunostains

Immunostain/ location	Intra-epithelial lymphocyte	Basal (lamina propria)
CD3+ lymphocytes	$p = 2.097 \times 10^{-6}$ ▲	$p = 0.154$ ▲
CD4+ lymphocytes	$p = 0.264$ ▼	$P = 0.0125$ ▲
CD8+ lymphocytes	$p = 1.383 \times 10^{-7}$ ▲	$p = 0.00126$ ▼
Mib1+ epithelial cells in lowest 50 epithelial cells each side of crypts	Not applicable	$p = 0.00167$ ▲

Key to table: ▲Higher in CD than normal; ▼Higher in normal than CD

CONCLUSION: When developing a deep learning analytical algorithm for digital image analysis, provided that our algorithm is able adequately to segment villous epithelium, lamina propria and crypt bases, the optimal IHC stains to accompany H&E are CD8 and mib1.

Gluten Sensitivity and Epilepsy
A Systematic Review of the Current Literature.

Julian T[1], Zis P[2], Hadjivassiliou M[2].

1. Sheffield Institute of Translational Neurology (SITrAN), The University of Sheffield.
2. Academic Department of Neurosciences, Sheffield Teaching Hospitals NHS Foundation Trust.

Introduction:

Gluten-related disorders (GRDs) represent a spectrum of diverse clinical manifestations sharing a common trigger: The ingestion of gluten.

The most widely recognized and best characterised disease within this spectrum is coeliac disease (CD).Non-coeliac gluten sensitivity (NCGS) refers to patients with primarily gastrointestinal symptoms, often with positive serology (i.e. gliadin, transglutaminase and/or endomysial antibodies) but without enteropathy that symptomatically benefit from being on a gluten-free diet (GFD). Both CD and NCGS can present with neurological dysfunction, with gluten ataxia being the commonest.

Aim:

To systematically review the current literature in order to establish the prevalence of idiopathic epilepsy in patients with CD and NCGS, the prevalence of CD and NCGS in patients with idiopathic epilepsy and characterise the phenomenology of the epileptic syndromes that these patients present with.

Methodology:

A systematic PubMed search was conducted on 14/12/2017. Out of 236 papers identified, 79 met our inclusion criteria and were considered for analysis. Information regarding prevalence, demographics and CD, NCGS and epilepsy phenomenology was extracted. **Figure 1** summarizes the selection process.

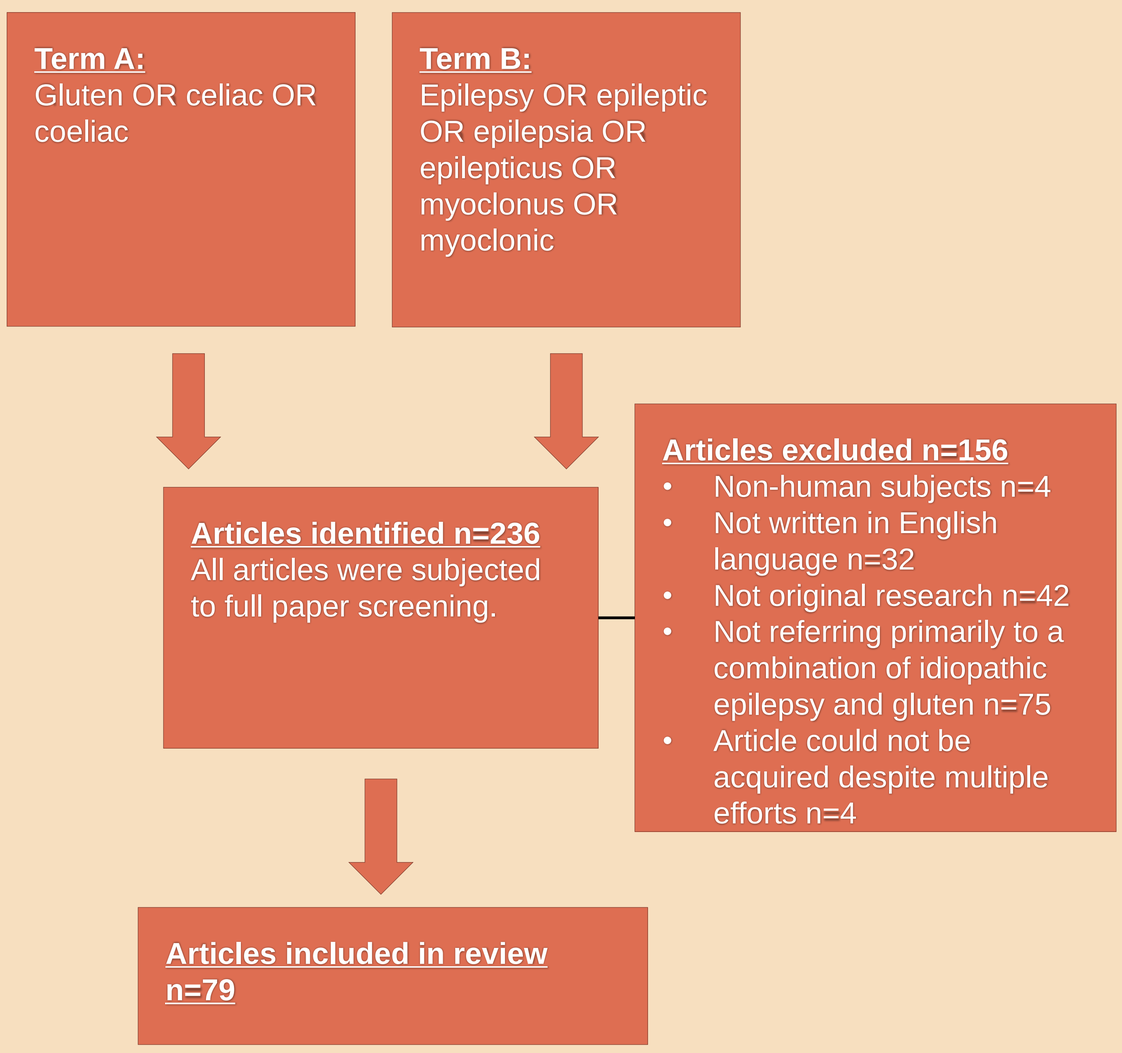


Figure 1: PRISMA chart detailing study inclusion/exclusion.

Results:

Out of 79 papers, 27 were case reports, 45 case series and 7 case-controlled studies. These papers were published between 1970 and 2017.

Epidemiology:

Fourteen studies detailed the prevalence of CD amongst those suffering idiopathic epilepsy. The total pooled prevalence was 2.11% (n=3465). Amongst exclusively paediatric populations the prevalence was 1.86% (n=1880). Amongst exclusively adult populations the prevalence was 2.27% (n=1280). This compares to the prevalence of 1% of CD in the general population. Interestingly up to 40% of patients with CD and epilepsy have no gastrointestinal symptoms.

Eight studies detailed prevalence of serologically confirmed NCGS amongst patients with idiopathic epilepsy. The pooled prevalence was 4.28% (n=841).

Fifteen studies detailed prevalence of idiopathic epilepsy amongst CD sufferers. The pooled prevalence was 1.17% (n=35102). This compares to the active point prevalence of 0.64% of epilepsy in the general population.

A single study detailed prevalence of epilepsy amongst serologically confirmed NCGS. The pooled prevalence was 0.48% (n=835)

The role of gluten free diet:

29 studies commented on the effectiveness of GFD in the management of seizures as an add-on intervention in patients with CD. Out of 105 patients, already receiving anti-epileptic drugs (AED) 61 (58%) reported a reduction or cessation of the seizures. Interestingly some patients managed to reduce or even stop their AED as a result of GFD.

GFD seems to become less effective the longer the duration of epilepsy. This demonstrates an inverse relationship between onset of seizure to GFD and effective seizure control with GFD.

CD, epilepsy and cerebral calcification syndrome:

A well-defined syndrome where epilepsy is comorbid with CD is the CD, epilepsy and cerebral calcification syndrome. Patients with this syndrome often do not respond well to AEDs, however up to 50% will benefit from being on a GFD. **Figure 2** shows a characteristic CT and MRI scan of a patient with this syndrome.

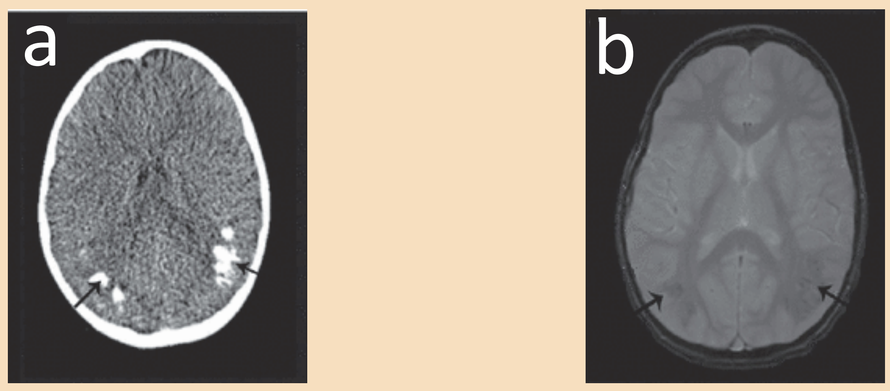


Figure 2: CT (**a**) and MRI (**b**) scans demonstrating occipital CCs.

Discussion:

Epilepsy is 2 times more prevalent in CD, compared to the general population. CD is also 2 times more prevalent in epilepsy compared to the general population. Further studies are required to assess the prevalence of NCGS in epilepsy. Patients with idiopathic epilepsy should be investigated for CD and/or NCGS as such patients may benefit from a GFD.

The University Of Sheffield.

Sheffield Teaching Hospitals NHS
NHS Foundation Trust