Point of Care Tests in Coeliac Disease- New Emerging Evidence

Dr. Michelle Lau

Clinical Research Fellow in Gastroenterology

- 3 in 4 cases are undiagnosed. West et al. Am J Gastroenterol 2014; 109:757–768
- Poor QoL in those undiagnosed.

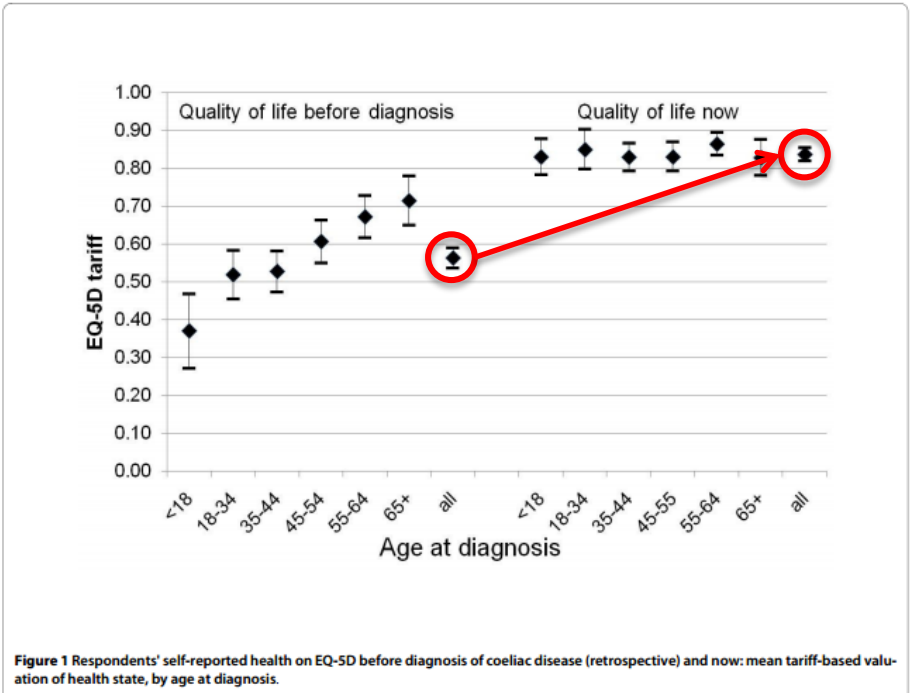


Figure 1 Respondents' self-reported health on EQ-5D before diagnosis of coeliac disease (retrospective) and now: mean tariff-based valuation of health state, by age at diagnosis.

Gray and Papanicolas *BMC Health Services Research* 2010, **10**:105
http://www.biomedcentral.com/1472-6963/10/105

We will cover:

- The commercially available POCTs
- The evidence for POCTs
- The role of POCTs in different settings and clinical presentations

Are we taking biopsies in the right patients?

- N=1423 multicentre study in the UK
- 12.4% new cases had a previous OGD without biopsies in the past 5 years- missed window of opportunity!
- Only 40% adherence to guidelines of taking a minimum of 4 biopsies

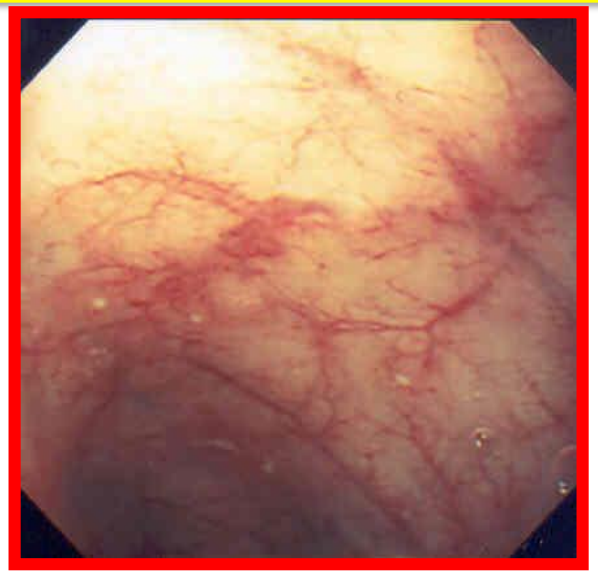
Mooney PD et al *Gut* suppl 2014

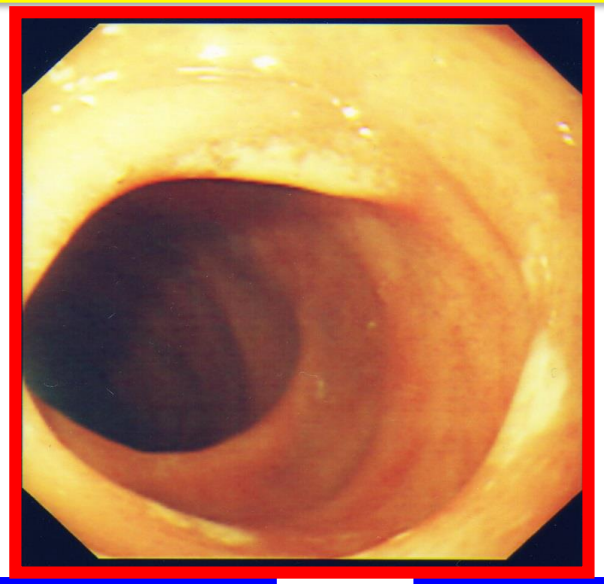
- Nurse endoscopists
  - Median biopsies = 4
  - Diagnostic yield 6.7%
- Physicians
  - Median biopsies = 3
  - Diagnostic yield 7.1%
- Surgeons
  - Median biopsies = 2
  - Diagnostic yield 3%

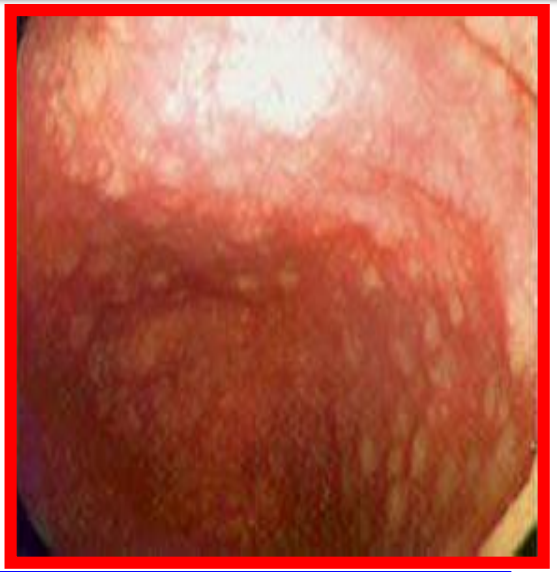
The University Of Sheffield.

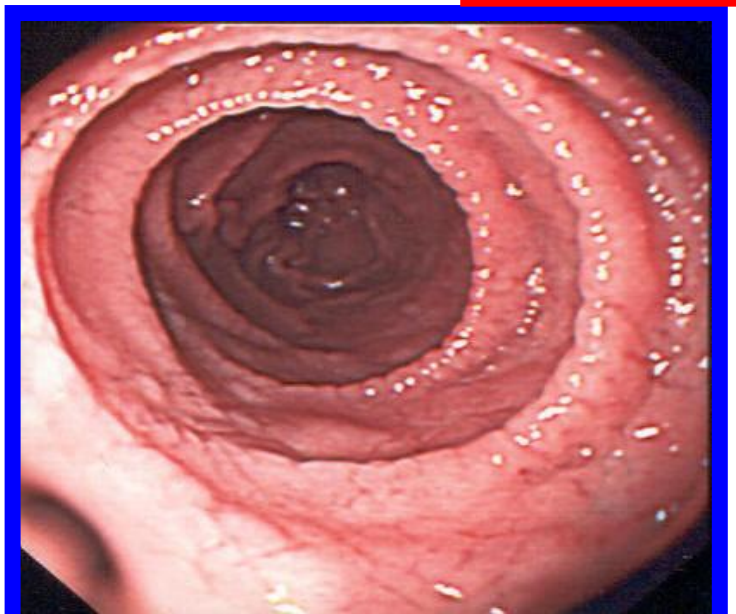
They’re not always this obvious!

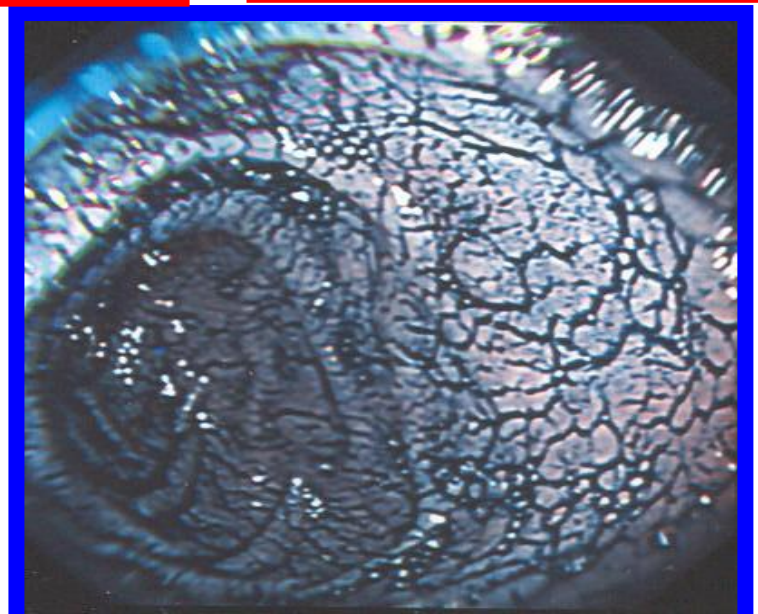
Sheffield Teaching Hospitals NHS
NHS Foundation Trust



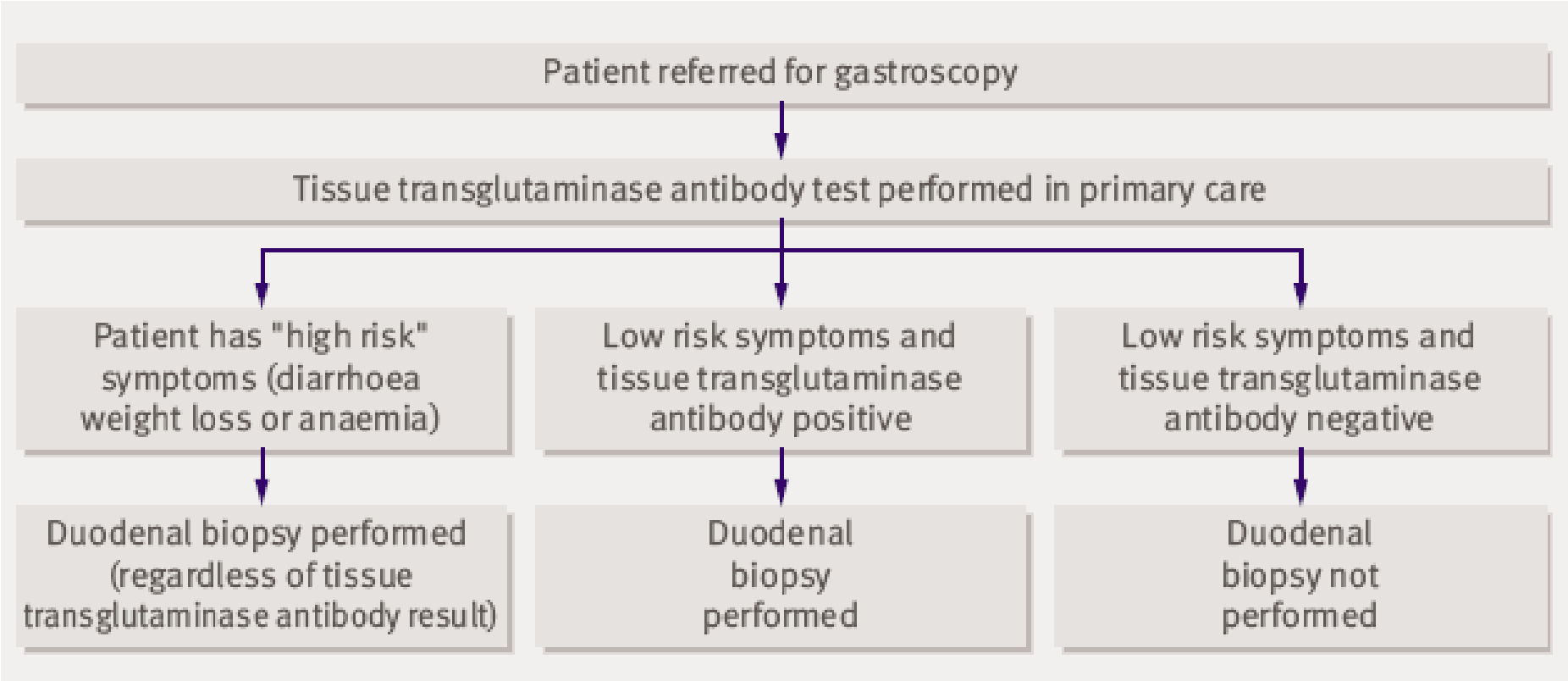








Who needs a duodenal biopsy?



100% sensitivity and NPV in detecting CD!

Hopper AD, et al. BMJ. 2007 7;334(7596):729-33.

But it did not change clinical practice!

Cite this article as: BMJ, doi:10.1136/bmj.39161.587720.BE (published 23 March 2007)

BMJ

RESEARCH

Commentary: Reaching a milestone in diagnosing coeliac disease

Mark L Graber, chief of medical service,[1] Atul Kumar, staff gastroenterologist [1]

Coeliac disease in primary care

Is common, underdiagnosed, and can present with non-specific symptoms

ARS

RESEARCH pp 729, 732

Roger Jones Wolfson professor of general practice
Department of General Practice and Primary Care, KCL School of Medicine, London SE11 6SP
roger.jones@kcl.ac.uk

Competing interests: None declared.
Provenance and peer review: Commissioned; not externally peer reviewed.

BMJ 2007;334:704-5
doi: 10.1136/bmj.39170.410347.80

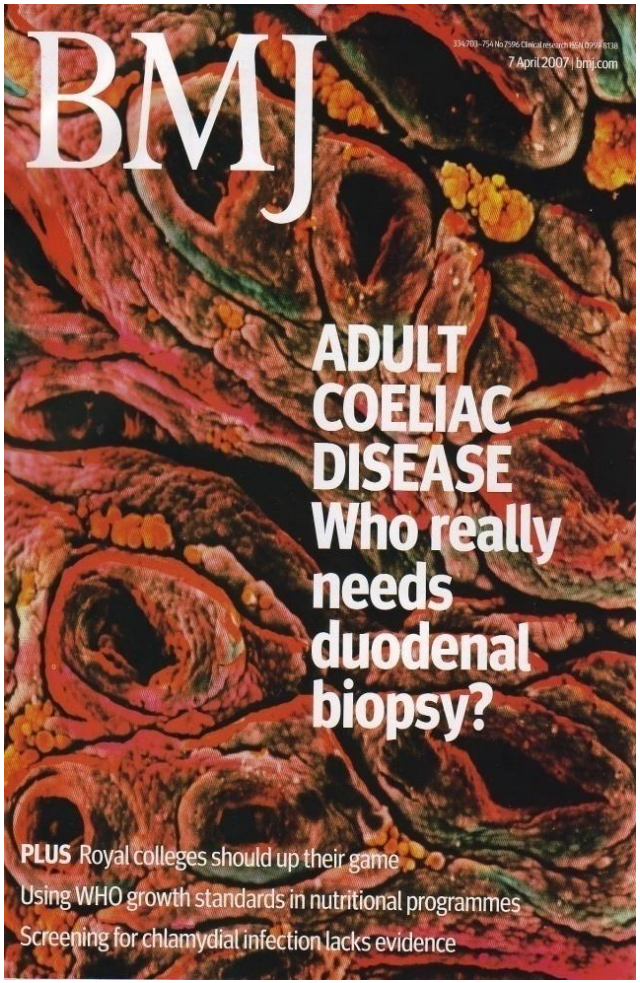
Coeliac disease affects around 1% of the general population, but most cases are unrecognised and diagnosis is often delayed considerably.[1 2] This is surprising, given how common the disease is and how serious its effects can be.[1 3 4] Several possible reasons exist for this delay; the most important is that most patients with coeliac disease do not have typical symptoms of malabsorption. Even if these symptoms are present their non-specific nature may not trigger diagnostic suspicion of coeliac disease. Other atypical presentations can occur, especially in older patients,[5] and the disease may even be seen in obese people.[6]

In this week's *BMJ*, Hopper and colleagues report a validated clinical prediction rule to determine an effective diagnostic method of detecting all cases of coeliac disease in people referred for gastroscopy. People with positive tissue transglutaminase antibodies and "low risk symptoms," as well as those with the high risk symptoms of diarrhoea, weight loss, and anaemia, were investigated with duodenal biopsy, while those with a negative antibody result and low risk symptoms were not biopsied.[7] They found that pre-endoscopy serological testing combined with biopsy of people with high risk symptoms

this issue by Graber and Kumar discusses the potential application of the decision rule to clinical practice.[8]

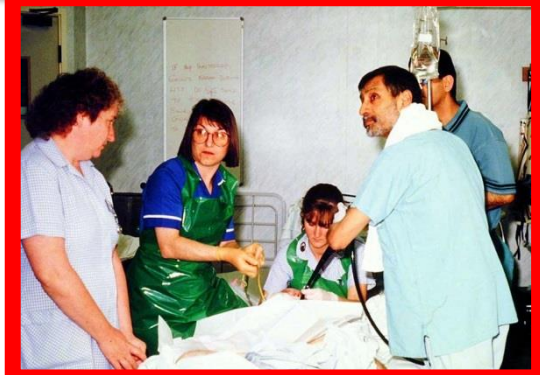
Coeliac disease is characterised by a lifelong intolerance to certain storage proteins contained in wheat, rye, and barley, collectively known as gluten, and it is an unusual combination of food intolerance and autoimmunity. Chronic inflammation of proximal small intestinal mucosa, with atrophy of small intestinal villi, is associated with impaired absorption of nutrients and increased secretion of water and solids because of abnormal intestinal permeability. The disease has been classified into four phenotypes.[2] In classic coeliac disease, patients have intestinal malabsorption and gastrointestinal symptoms, whereas the atypical (most common) form of the disease has few or no gastrointestinal symptoms. Atypical disease has other problems, however, including iron deficiency anaemia, osteoporosis, short stature, infertility, and unfavourable outcomes of pregnancy.[9] In silent coeliac disease, asymptomatic patients are found to have gluten induced villous atrophy, and in latent disease, patients may have normal mucosa or may show villous atrophy, which improves after gluten withdrawal.

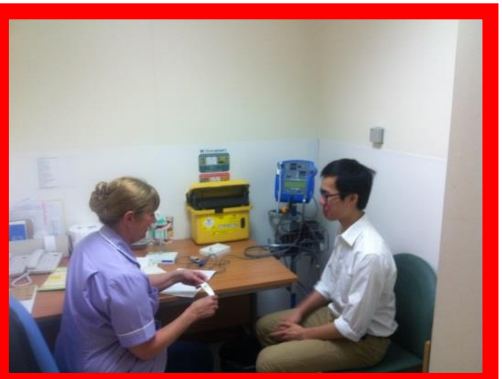
The gold standard for the diagnosis of coeliac disease

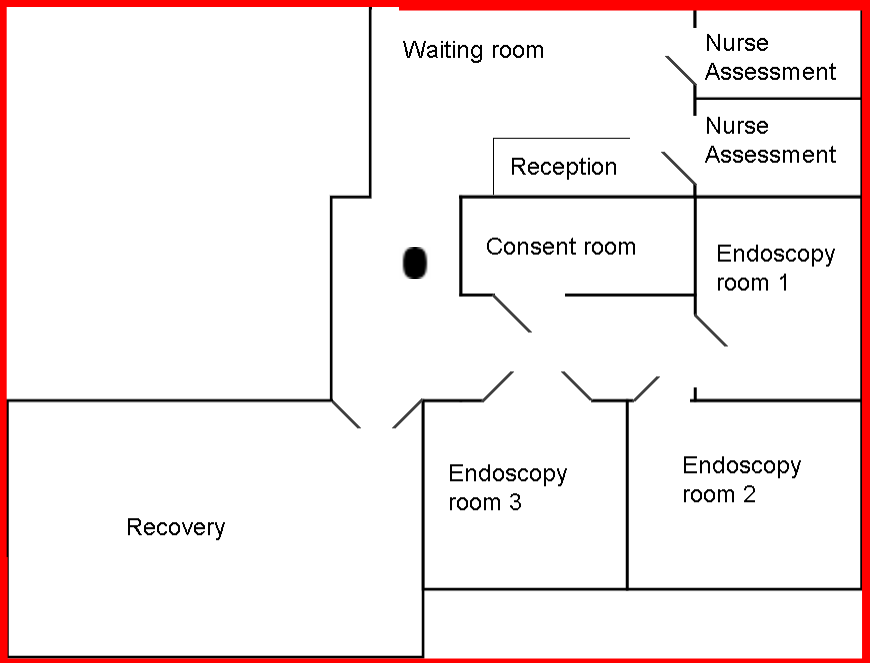


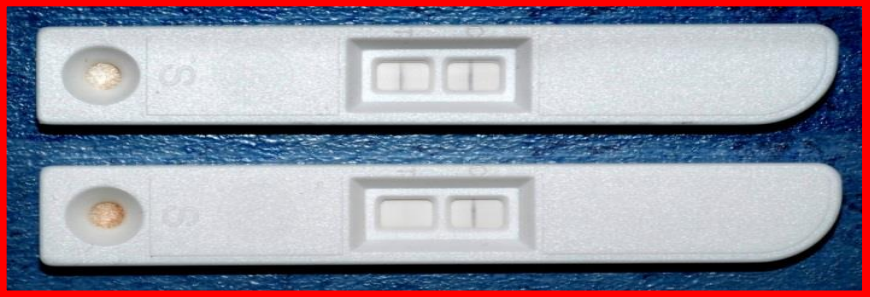
The University Of Sheffield.

Sheffield Teaching Hospitals NHS
NHS Foundation Trust









Commercially available POCTs

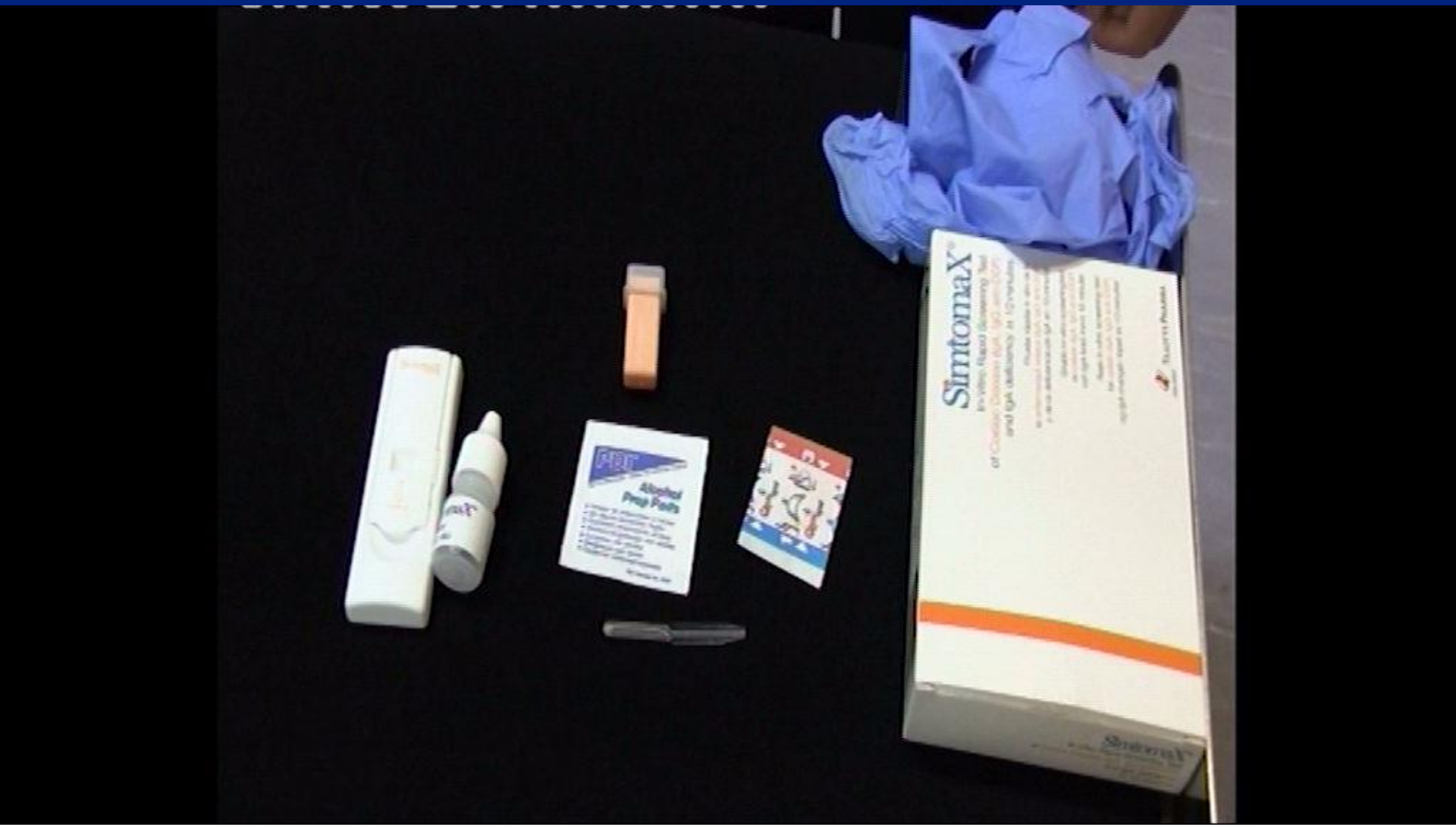
Biocard: IgA-TTG (ANI Biotech)

Celiac Quick Test: IgA/G/M-TTG (Biohit)

Simtomax: IgA/G-DGP (Augurix/Tillotts)

XeliacTest Pro: IgA/G-TTG (Eurospital)

Simtomax- IgA/IgG DGP POCT



Biocard studies

Test	Ref	Country	Year	n	Population	Sensitivity	Specificity	Study Limitations
Biocard	Korponay-Szabo	Hungary and Finland	2005	165*	Paediatric	97.4%	97.6%	Antibody neg. without GI symptoms not biopsied
Biocard	Nemec	Italy	2006	151	Adult / Paediatric	90.2%	100.0%	Only positive POCT biopsied
Biocard	Raivio	Hungary and Finland	2006	150	Paediatric	95.5%	97.1%	Compared to serology only
Biocard	Korponay-Szabo	Hungary	2007	2676	Paediatric	78.1%	100.0%	Only positive POCT biopsied
Biocard	Raivio	Finland	2007	43	Adult	91.7%	78.9%	High pre-test probability (CD 56%)
Biocard	Kotze	Brazil	2009	254	Adult / Paediatric	No data given		Only positive POCT biopsied
Biocard	Pichler	UK	2011	196	Adult / Paediatric	No data given		Only positive POCT biopsied
Biocard	Alarida	Libya	2011	2920	Paediatric	19/ 50 +POCT patients had biopsy confirmed CD. 4 –POCT patients had CD		Not all patients tested with standard serology. Only positive POCT/serology biopsied
Biocard	Popp	Romania	2013	148	Adult/ Paediatric	92.3%	100.0%	Compared to EMA only
Biocard	Singh	India	2015		Paediatric	83.6%	90%	Large number of negative serology patients were not biopsied

Biocard sensitivity: 70%!

ORIGINAL ARTICLE: Clinical Endoscopy

Point-of-care testing for celiac disease has a low sensitivity in endoscopy

Peter D. Mooney, MRCP,[1] Matthew Kurien, MRCP,[1] Kate E. Evans, MRCP,[1] Ioannis Chalkiadakis, MD,[1] Melissa F. Hale, MRCP,[1] Mohamad Z. Kannan, MRCP,[1] Victoria Courtice,[1] Alexander J. Johnston,[1] Andrew J. Irvine,[1] Marios Hadjivassiliou, FRCP,[2] David S. Sanders, FACG[1]

Sheffield, South Yorkshire, United Kingdom

Measure	Sensitivity%, (CI)	Specificity %, (CI)	PPV % (CI)	NPV % (CI)
Biocard	70.1	96.6	85.4	91.8
EMA	83.3	97.5	90.7	95.4
TTG	91.0	83.5	61.3	96.8

Head to head trial of POCTs

Clinical Gastroenterology and Hepatology 2015;13:1278–1284

Increased Detection of Celiac Disease With Measurement of Deamidated Gliadin Peptide Antibody Before Endoscopy

Peter D. Mooney,[*,‡] Simon H. Wong,[‡] Alexander J. Johnston,[‡] Matthew Kurien,[*,‡] Anastasios Avgerinos,[*] and David S. Sanders[*,‡]

Table 1. Analysis of the Point-of-Care Tests in Group 1: Sensitivity for Detecting Villous Atrophy and Agreement of the Available Tests With Serum tTG and EMA

Test	Sensitivity, % (95% CI)	Agreement with EMA	κ (95% CI)	Agreement with tTG	κ (95% CI)
Serum tTG	97.2 (83.8–99.9)	90.9%	0.652 (0.371–0.933)	—	—
Biocard	72.2 (54.6–85.2)	70.9%	0.346 (0.128–0.565)	69.1%	0.346 (0.128–0.565)
Celiac Quick Test	77.8 (60.4–89.3)	76.4%	0.384 (0.130–0.639)	78.2%	0.384 (0.130–0.639)
Simtomax	94.4 (80.0–99.0)	87.3%	0.513 (0.199–0.827)	89.1%	0.561 (0.248–0.874)

CI, confidence interval.

Table 3. Analysis of the Point-of-Care Test to Standard Serology

Test	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
Simtomax	92.7 (83.0–97.3)	85.2 (81.5–88.3)	49.2 (40.3–58.2)	98.7 (96.8–99.5)
tTG	91.2 (81.1–96.4)	87.5 (84.0–90.4)	53.0 (43.6–62.2)	98.5 (96.5–99.4)
EMA	89.7 (79.3–95.4)	96.6 (94.3–98.0)	80.3 (69.2–88.2)	98.4 (96.5–99.3)

CI, confidence interval.

POCT in the community

Location	No. of POCT undertaken	No. of + POCT
BSG 2014	245	9 (3.7%)

Location	No. of POCT undertaken	No. of + POCT
London	67	16 (24%)
Leeds	66	10 (15%)
Cardiff	101	19 (19%)

Case finding in primary care

Target population with symptoms and risk factors:
Irritable bowel syndrome
Anaemia
Family history of coeliac disease
Malabsorption or diarrhoea
Fatigue
Thyroid or diabetes
Weight loss, short stature, failure to thrive
Other (epilepsy, infertility, abnormal blood test, arthralgia)

Study	Year	n=	Studied population	CD prevalence
Hin	1999	1000	Central England	3%
Sanders	2003	1200	S. Yorkshire, UK	3%
Berti	2006	1041	Italy	2.08%
Catassi	2007	976	North America	2.3%

Increased case detection

Using POCT in pharmacies

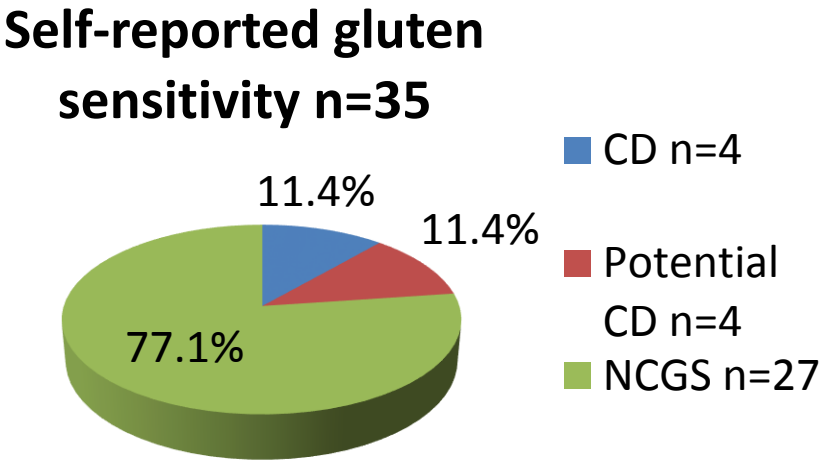
Simtomax sensitivity comparable to serology in low prevalence population

Measure	Sensitivity%, (CI)	Specificity %, (CI)	PPV % (CI)	NPV % (CI)
Simtomax	78.8 (78.3-79.2)	85.0 (84.9-85.1)	21.5 (21.3-21.7)	98.7 (98.69-98.75)
EMA	72.7 (72.2-73.2)	99.5 (99.51-99.54)	88.9 (88.5-89.3)	98.6 (98.57-98.62)
TTG	75.8 (75.3-76.2)	93.1 (93.0-93.1)	36.2 (35.9-36.6)	98.7 (98.6-98.7)

- GI symptoms = 667
- Exclusion criteria: referred with +EMA, previous VA, known CD, on a GFD, self-reported gluten sensitivity
- CD prevalence 4.95%

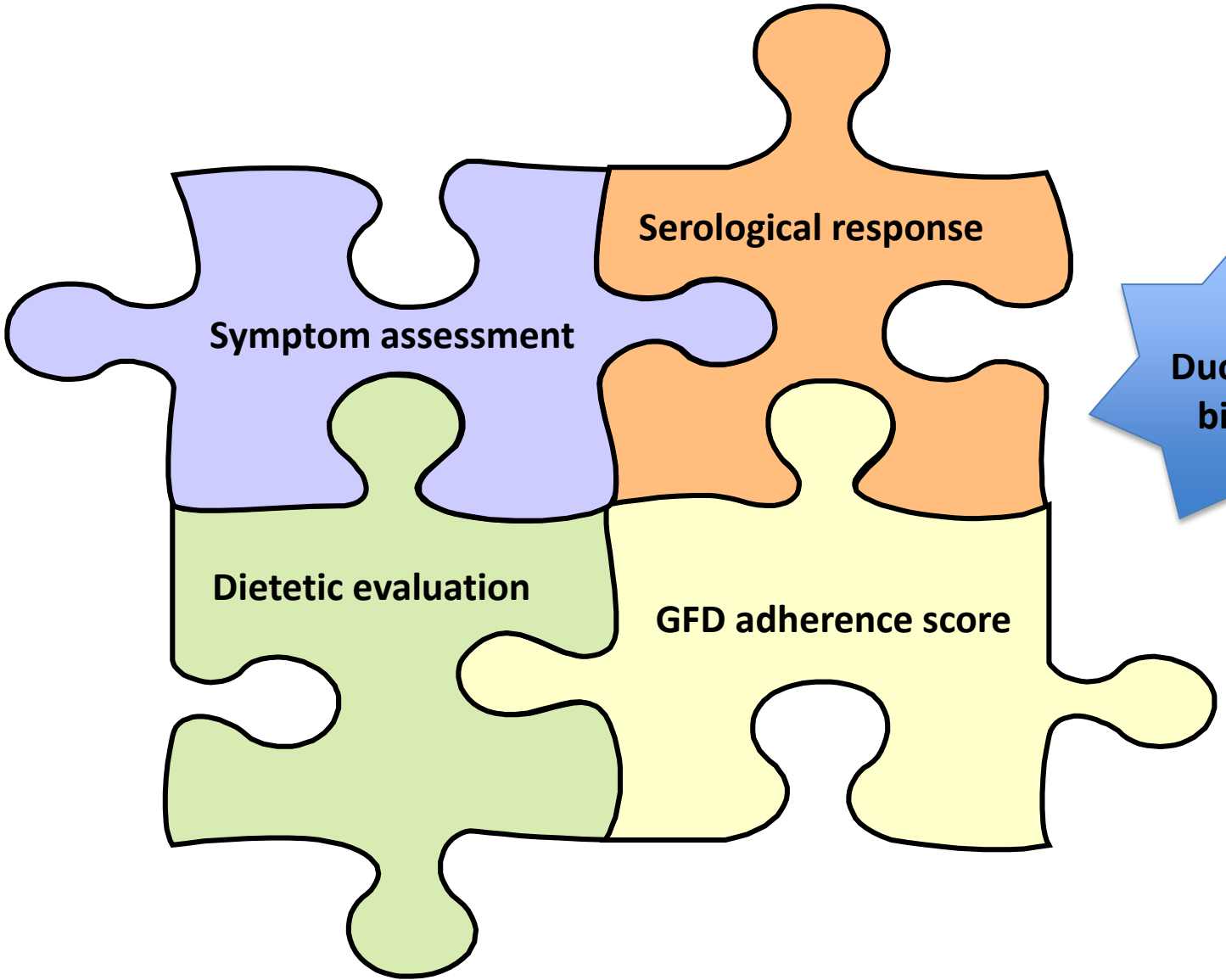
Simtomax for differentiating between NCGS and CD

Measure	Sensitivity%, (CI)	Specificity %, (CI)	PPV % (CI)	NPV % (CI)
Simtomax	100	80.6 (80.2-81.1)	40.0 (39.0-41.0)	100
EMA	75.0 (73.6-76.4)	96.8 (96.6-97.0)	75.0 (73.6-76.4)	96.8 (96.6-97.0)
TTG	75.0 (73.6-76.4)	87.1 (86.7-87.5)	42.9 (41.7-44.0)	96.4 (96.2-96.6)



CD prevalence 11.4%

Assessing for remission



Simtomax for predicting histological remission

Surrogate marker	Sensitivity%, (CI)	Specificity %, (CI)	PPV % (CI)	NPV % (CI)
Simtomax	78.8 (78.5-79.2)	55.9 (55.6-56.2)	50 (49.7-50.3)	82.5 (82.2-82.8)
TTG	51.9 (51.5-52.4)	80.6 (80.4-80.9)	60 (59.5-60.5)	75 (74.7-75.2)
EMA	36.5 (36.1-37.0)	83.9 (83.6-84.1)	55.9 (55.3-56.4)	70.3 (70.0-70.5)
GFD adherence score	23.1 (22.7-23.4)	82.8 (82.6-83.0)	42.9 (42.3-43.4)	65.8 (65.5-66.1)

- Known CD on a GFD= 145
- Persistent VA =52 (36%)

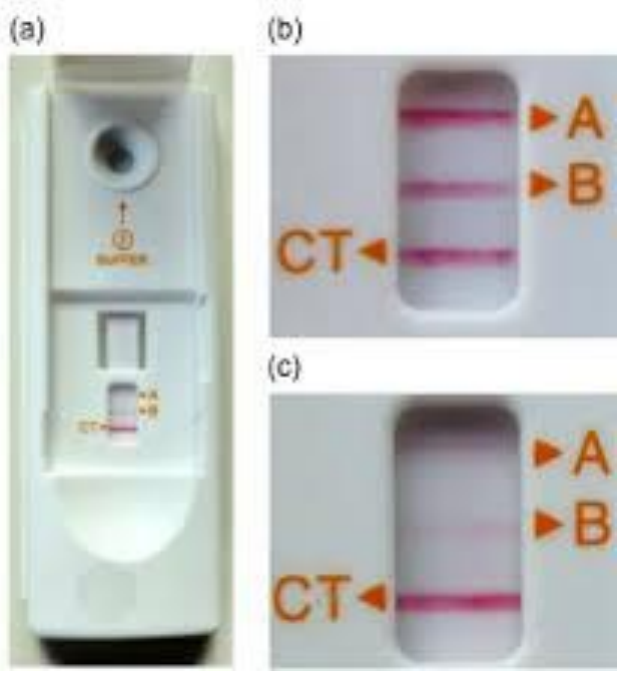
POCT cost saving in IDA

	Sensitivity%, (CI)	Specificity %, (CI)	PPV % (CI)	NPV % (CI)
Simtomax	100	82.2 (82.0-82.5)	57.8 (57.3-58.2)	100
TTG	96.2 (95.9-96.4)	91.5 (91.3-91.7)	73.5 (73.1-74.0)	99.0 (98.9-99.0)
EMA	84.6 (84.2-85.1)	99.1 (99.0-99.1)	95.7 (95.4-95.9)	96.4 (96.3-96.5)

Multicentre 934 IDA patients: serology available in 33.8% only

N=133 patients with iron deficiency attending endoscopy

Departmental cost saving of £3690 /100 gastroscopies



Conclusion

- POCTs: promising role to increase CD detection
- The most sensitive POCT: Simtomax
- Case finding tool in primary and secondary care
- Cost saving in endoscopy

Royal Hallamshire Hospital
Academic Unit of Gastroenterology

Research

BSG Hopkins Endoscopy Prize 2012
Small Bowel Endoscopy

Cuthbertson Medal 2011
Nutrition Society & BAPEN
(British Association of Parenteral & Enteral Nutrition)

European Rising Star Award 2010
Association of National European & Mediterranean Societies of Gastroenterology

Clinical

BSG Clinical Care Award
2011 Small Bowel Endoscopy
2014 Primary Care Services & GI Bleed Unit

Health Service Journal Awards 2012
Gastrostomy/PEG Feeding Service

Coeliac UK 2010 Patient Healthcare Award

Complete Nutrition 2013 Coeliac Healthcare Award

Medipex Award 2013 Small Bowel Endoscopy