Aims To identify the predictors of CD when presented with LD.
Methods 215 LD patients had undergone prospective and systematic evaluation for CD and other recognised associations.

The gold-standard diagnosis of CD was based upon the presence of HLA-DQ2 and/or DQ8, persistence or progression of LD following a gluten challenge, symptomatic improvement on a gluten-free diet, and no alternate cause found.

Binary logistic regression models, adjusting for age and gender, were subsequently performed to compare presenting variables between CD and non-CD cases, and to determine their sensitivity, specificity, positive and negative predictive values (PPV and NPV).

Results CD was diagnosed in 47 cases (22%) and non-CD in 168 cases (78%). There was no statistical difference in demographics, clinical symptoms (i.e. diarrhoea, weight loss, abdominal pain), anaemia or haematinics between the CD and non-CD group.

Patients with CD, in comparison to non-CD, were significantly more likely to have a positive family history of CD (21.3% vs. 3.6%, OR 6.81; PPV 62.5%, NPV 81.4%, specificity 96.4%), positive HLA-DQ status (100% vs. 49.4%; PPV 36.2%, NPV 100%, specificity 50.6%), and presence of endomysial antibody [EMA] (49% vs. 0.6%, OR 159; PPV 96%, NPV 87%, specificity 99.4%); all $p \leq 0.001$.

A normal tissue transglutaminase antibody (TTG) level was seen in 29.8% CD and 82.7% non-CD cases (OR 0.086, $p < 0.001$; PPV 9.1%). There was no difference in the prevalence of TTG levels 1–2 x upper limit of normal (ULN) between the groups (29.8% CD vs. 14.3% non-CD; PPV 38%). However, TTG levels between 3–20 x ULN were significantly more prevalent in the CD group (31.9% vs. 3%; PPV 66.6% >87.5%), whilst a TTG > 20 x ULN was exclusive to CD (8.5%, $p < 0.001$, PPV 100%).

Conclusion At the outset, only the presence of positive EMA or TTG > 20 x ULN are highly predictive and specific for CD. However, as they have limited sensitivities, most patients with LD require further work-up prior to diagnostic confirmation.

Disclosure of Interest None Declared.

PTU-152 PEPSIN IN SALIVA FOR THE DIAGNOSIS OF GASTRO-ESOPHAGEAL REFLUX DISEASE

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Introduction Current diagnostic tests for GORD have moderate sensitivity/specificity and can be invasive and expensive. Pepsin detection in saliva has been proposed as an “office-based” method for GORD diagnosis. The aims of this study were to establish normal values of salivary pepsin in a large cohort of healthy asymptomatic subjects and to determine its value to discriminate patients with reflux-related symptoms (GORD, hypersensitive oesophagus) from functional heartburn.

Methods 100 asymptomatic controls and 111 patients with heartburn underwent MII-pH monitoring and simultaneous salivary pepsin determination on waking, after lunch and dinner. Cut off value for pepsin positivity was 16 ng/ml. Patients were divided into GORD (increased acid exposure time (AET) $n = 58$); Hypersensitive Oesophagus (HO) (normal AET and + SAP), $n = 26$ and Functional Heartburn (FH) (normal AET and –

SAP, $n = 27$). Multiple group comparisons were performed using one-way ANOVA followed by with Tukey's Test for Gaussian distributed data and the Kruskal-Wallis Test with Dunns comparison for non-Gaussian data. Receiver Operator Characteristic curves were constructed to determine and compare the sensitivity and specificity of different pepsin cut-off concentrations.

Results 1/3 of asymptomatic subjects had pepsin in saliva at low concentration (0(0–59) ng/ml). Patients with reflux-related symptoms (GORD and HO) had higher prevalence (77–89%) and pepsin concentration than controls (HO, 237(52–311) ng/ml and GORD, 121(29–252) ng/ml) ($p < 0.05$). Patients with FH had low prevalence (33%) and concentration of pepsin in saliva (0 (0–40) ng/ml). The area under the receiver operating characteristic curve had a value of 0.8034 $\pm$ 0.04 (95% confidence interval 0.719 to 0.8873, $p < 0.0001$). A positive test had 77.6% sensitivity and 63.2% specificity for diagnosis of GORD/HO. When all saliva samples were negative, there was 80% probability that symptoms were not due to reflux (FH). One positive sample with >210 ng/ml pepsin suggested the presence of GORD/HO with 95% probability.

Conclusion In patients with symptoms suggestive of GORD, salivary pepsin can be used to confirm or reject the diagnosis before empirical PPI treatment. This may lessen the use of unnecessary anti-reflux therapy and the need for further invasive and expensive diagnostic methods.

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PTU-153 THE TIMING OF ONCOGENIC EVENTS IN THE EVOLUTION OF THE OESOPHAGEAL ADENOCARCINOMA GENOME AND IMPLICATIONS FOR CLINICAL DIAGNOSTICS

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Introduction A series of clonal expansions are thought to underlie the progression of Barrett's oesophagus (BE) to oesophageal adenocarcinoma (OAC). Each expansion carries with it somatic driver mutation (s) fixing it within a larger population and therefore increasing the likelihood of acquiring a second mutation. However, the precise order in which somatic variants occur remains unknown.

Methods We performed whole genome sequencing in 25 cases of OAC and 3 matched cases of BE. Findings were validated in a larger cohort of OACs ($n = 90$), metaplastic never-dysplastic BE (NDBE, $n = 66$ with a median follow-up of 58 months) and high-grade dysplasia ($n = 43$) using amplicon resequencing. Mutational signatures and gene-centric somatic mutations were determined using an in-house pipeline incorporating standard statistical methods and the publically available EMu pipeline.

Results There were 7 distinct mutational signatures present in both early (BE) and late disease (OAC). Fifteen genes were determined to be potential novel drivers of OAC development.

Surprisingly in 53% of NDBE tissue samples we identified clonal expansion of cells (>10% mutant fraction) harbouring mutations in one or more of 13/15 of these putative driver genes. No difference in the frequency of mutation of these genes was observed between any of the disease stages studied. *TP53* mutations clearly delineate between HGD/OAC and benign NDBE ($p < 0.001$). Whilst *SMAD4* mutations are only observed in OAC ($p < 0.001$) demonstrating for the first time a clear genetic difference between the two.

Conclusion Mutagenic processes active in OAC are also active in the earliest stages of BE. Recurrent driver mutations identified in cancer may be acquired very early in the disease and may provide little or no progression advantage. Molecular diagnostic approaches must account for this.

Disclosure of Interest None Declared.

PTU-154 DIFFERENCES IN COELIAC SEROLOGY OUTCOMES APPEAR DEPENDANT UPON THE ORIGIN OF THE REQUEST: A SEVEN YEAR REVIEW OF ANTI-TISSUE TRANSGLUTAMINASE TESTING

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Introduction Coeliac disease is the most common genetically based food intolerance worldwide with a UK prevalence of 1 in 150. The condition poses a diagnostic difficulty due to the often non-specific symptoms at presentation and a sub-group who will be asymptomatic. Successful diagnosis is based upon a high degree of suspicion, correct screening and a subsequent confirmatory test with an intestinal biopsy. Serological testing via anti-endomysial antibody (AEA) and anti-tissue transglutaminase (ATTG) is a simple, highly accurate method of screening, with a sensitivity and specificity in the region of 95–98% and 95–97%, respectively. Due to these attributes, serological screening accounts for a significant proportion of laboratory workloads nationwide.

Methods All ATTG coeliac serology requests made in a busy district general hospital over a 7 year period between 2007 and 2013 were reviewed, with a particular focus upon the positive results. A further assessment of case records and in particular the origin of requester was conducted. A positive result was issued by the laboratory if the ATTG was greater than or equal to 4.

Results Overall, a total of 29795 ATTG requests were made to the biochemistry department, of which results were obtained from 28819. Of this number, 1005 were performed in inpatients, 7140 in outpatients and 20674 were from primary care. In the GP cohort, 785/20674 (3.8%) proved to be positive. In comparison 37/1005 (3.7%) were positive from the inpatient group, and 371/7140 (5.2%) were positive from the outpatient cohort. The deficit in results gained was primarily due to the rejection of samples by the laboratory as being “not indicated” in 402 inpatient cases (27%) and 4 outpatient cases. No GP requests were rejected. The overall numbers of ATTG requests also increased year on year with 913 being performed in 2008 and 6483 in 2013.

Conclusion It is clear the demand for coeliac serology is increasing with its use becoming more widespread in a variety of clinical settings. The mere fact that patients are presenting to hospitals for outpatient appointments or inpatient assessments, places them in a self selecting group where one would expect to see a higher frequency of positive coeliac serology. This was duly

noted in our outpatient cohort, but the inpatients had a similar positive pick up rate to the GP cohort. It is possible this result was slightly skewed by the high rejection rate seen with inpatient requests. The high positive pick up rate from specialist outpatient clinics emphasises the importance of having a high degree of clinical suspicion in order to make an appropriate diagnosis.

Disclosure of Interest None Declared.

PTU-155 PROGRESSION OF LOW GRADE DYSPLASIA TO HIGH GRADE DYSPLASIA IN BARRETT'S OESOPHAGUS IN A SINGLE CENTRE

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Introduction Barrett's oesophagus is a common condition found in 4% of patients undergoing upper gastrointestinal endoscopy.⁽¹⁾ The association between Barrett's oesophagus and oesophageal adenocarcinoma has been well established. Scotland has a particularly high incidence of both Barrett's and adenocarcinoma of the oesophagus.

The risk of progression from high grade dysplasia (HGD) to oesophageal adenocarcinoma (OAC) has been reported at approximately 10% per year.¹ However the risk of progression from low grade dysplasia (LGD) is harder to quantify with studies showing progression to OAC from 0.6–1.69% per year, not dissimilar to that of non-dysplastic Barrett's.² More recently the SURF trial reported a 25% (17/68) progression from LGD to HGD/OAC in a surveillance group with LGD versus radiofrequency ablation.³

Methods In 2009 a clinical database of Barrett's patients was developed in Forth Valley Hospital to ensure appropriate surveillance as per BSG guidelines. All patients diagnosed with Barrett's were cared for by one responsible team, a dedicated Barrett's endoscopy list was developed, and the use of narrow band imaging was introduced. At the end of 2012 the database was interrogated to assess the progress of all patients who had been diagnosed with LGD within the previous three years.

Results There were 915 patients with Barrett's on the database, of which 829 were under follow up. 85 (10%) had LGD and of this patient cohort 19 had progressed to HGD. The progression rate from LGD to HGD was 22% (19/85). The median follow up of patients with LGD was 29 months (range 12–34 months). All patients who progressed from LGD to HGD had endoscopic therapy with endoscopic mucosal resection and/or ablative therapies. There are no recorded cases of progression of LGD to OAC.

Conclusion The progression rate from LGD to HGD is similar to reported rates found in the SURF trial. This suggests that LGD carries a greater risk of progression, and therefore worse prognosis than previously reported. This is a potential group of patients in whom to consider early intervention rather than adopt the standard surveillance strategy. Further studies to evaluate the effectiveness of treatment rather than surveillance in this group should be considered.

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