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The utility of serum zonulin as a marker of gastrointestinal dysfunction

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Background: Dysregulation of the zonulin pathway has been linked to a “leaky gut” due to zonulin’s putative role as a modulator of intestinal epithelial tight junctions. Zonulin is a proposed contributor to the pathogenesis of non-celiac gluten sensitivity/irritable bowel syndrome (NCGS), celiac disease (CD), and inflammatory bowel disease (IBD). However, controversy lies in zonulin’s utility as a serum biomarker of disease and in the assays used for its assessment.

Aims: To characterize serum zonulin levels among individuals with gastrointestinal conditions (NCGS, CD, and IBD) and healthy individuals, and to verify existing commercially available assays for zonulin quantification.

Methods: Serum zonulin was measured in patients with self-reported NCGS ($n = 36$), CD ($n = 37$), and IBD ($n = 20$), as well as healthy participants ($n = 49$) by ELISA (CUSABIO). Zonulin non-producers were determined by western blot-based haptoglobin phenotyping. The commercial assay was spiked with recombinant zonulin for verification. Zonulin levels in selected sera were compared with those determined by another commercially available assay (Immundiagnostik).

Results: Overall, 33 of 36 patients with NCGS, 34 of 37 with untreated CD, 19 of 20 with IBD, and 46 of 49 healthy participants were zonulin producers. Compared with healthy individuals (median, 0.00 ng/mL; interquartile range [IQR], 0.00 ng/mL), patients with NCGS (median, 0.25 ng/mL; IQR, 0.88 ng/mL), CD (median, 0.07 ng/mL; IQR, 1.27 ng/mL), and IBD (median, 1.73 ng/mL; IQR, 2.02 ng/mL; all $P < 0.0001$) had elevated serum zonulin levels (Figure 1). Levels in IBD were higher than those in NCGS ($P = 0.001$) and CD ($P = 0.002$), with no differences between NCGS and CD.

However, recombinant zonulin protein was not detected by the assay. In addition, two of 19 participants who were zonulin non-producers had levels of the protein detected by the assay. There was poor correlation between the results of the two commercially available assays (for levels expressed in ng/mL, $n = 29$; $r = 0.24$; $P = 0.22$).

Conclusion: Serum zonulin levels are elevated in patients with NCGS, CD, and IBD, with the highest levels in IBD when tested using a previously applied commercial ELISA. However, recombinant zonulin protein was not detected by this assay, zonulin non-producers had zonulin detected, and there was no concordance with the results from an alternative assay. Rather than support a role for zonulin in intestinal disease pathogenesis, these results cast doubt on the validity of commercially available zonulin assays.

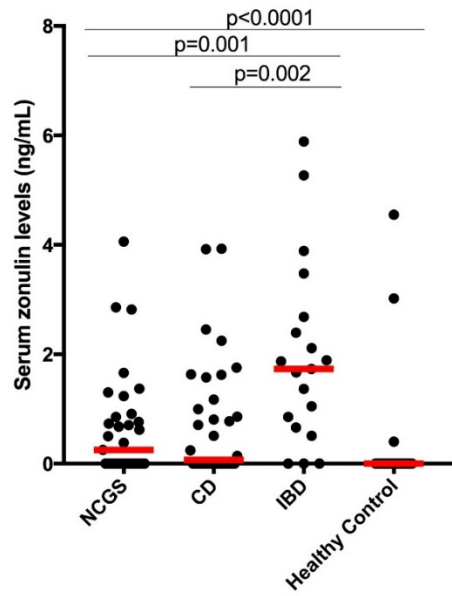


Figure 1. Serum zonulin levels (ng/mL) detected by CUSABIO ELISA assays. Red horizontal bars represent medians.

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Unexpectedly high rates of significant findings at capsule endoscopy in young women with suspected small intestinal bleeding: Don't be ageist

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Background: Capsule endoscopy (CE) is widely used in female patients who present with suspected recurrent small intestine bleeding. However, the yield from CE in young women (aged < 50 years) is low and usually attributed to the effects of menstrual blood loss.¹ We hypothesized that in a carefully selected population of young women where the effects of menstrual blood loss were not considered to contribute to gastrointestinal bleeding, the significant clinical findings would not be different to those found in older women (> 50 years) attending for CE.

Aim: The aim of this study was to analyze the findings at CE in women aged under 50 years compared with women aged over 50 years, and to assess the predictive factors of significant findings at CE in women presenting with iron deficiency anemia (IDA) and/or overt gastrointestinal bleeding (OGIB).

Methods: A retrospective study of a prospectively collected database of CE cases, reported by three gastroenterologists and performed between January 2015 and March 2017, was undertaken. Patient demographics, use of antiplatelets or anticoagulants, and CE quality were documented. A lesion found at CE was considered clinically significant if the reporting physician had concluded this. Data were analyzed by *t*-test and multivariate analysis for associated factors including patient age, CE indication, and antiplatelet or anticoagulant use. Exclusion criteria included indications for CE other than IDA or OGIB.

Results: Of 150 cases, 136 were ultimately analyzed, with a median age of 67 years (17–88 years); 31 patients were under the age of 50 years and 105 over 50 years. Indication for CE in women under the age of 50 compared with over 50 was similar, with OGIB accounting for 16% and 23%, respectively, and IDA for 84% and 77%, respectively. Antiplatelet or anticoagulant drugs were used by 19% of patients over the age of 50 and none under 50. A significant finding was observed in 38% of patients (in 55% of women presenting with OGIB and in 35% with only IDA). Of patients under the age of 50, 23% had a significant finding, compared with 43% of those over 50 ($P = 0.02$). In subgroup analysis of those with significant findings, ulcers were the most common finding in those under the age of 50, compared with arteriovenous malformation in those over 50. In multivariate regression analysis, age was the only predictor of a significant finding ($P = 0.02$).

Conclusion: Our results have shown that women under the age of 50 have a lower likelihood of significant findings at CE compared with older women, despite careful clinical selection of cases where menstrual blood loss was not considered a contributing factor. Age is a predictor of a significant finding.

Nonetheless, one in four women aged under 50 years had a significant finding at CE, suggesting that it should still be considered for the diagnosis of younger women with unexplained IDA or OGIB. Given the majority of these findings were inflammatory lesions, a further study examining the cost benefits of CE compared with other markers of small intestine inflammation, such as magnetic resonance imaging or fecal calprotectin, is warranted.

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Not all pseudomembranes are infectious or ischemic: A case report

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Introduction: We describe a case of pseudomembranous collagenous colitis (PCC) treated with subcutaneous methotrexate.

Case Report: An 81-year-old woman presented with 3 weeks of acute-onset non-bloody diarrhea and weight loss, without abdominal pain. She had no history of inflammatory bowel disease or bowel symptoms, except for intermittent constipation. There were no abnormal findings on physical examination. Blood tests showed an elevated C-reactive protein (CRP) level (137 mg/L; normal, < 2.9). No viral or bacterial pathogen was identified in the stool, and no *Clostridium difficile* toxin was present. Sigmoidoscopy showed diffuse inflammatory changes with pseudomembranes, and histology revealed active colitis with surface pseudomembranes, superficial crypt withering, and lamina propria hyalinisation, raising the possibility of ischemia. She was treated with oral metronidazole without improvement. Magnetic resonance imaging angiography demonstrated normal mesenteric vessels. Prednisolone 25 mg daily was started, with rapid resolution of diarrhea and improvement in CRP (23.4 mg/L after 3 days). Prednisolone was weaned over 6 weeks; however, diarrhea recurred soon after cessation. A repeat colonoscopy was macroscopically normal, but histology showed typical changes of collagenous colitis. Diarrhea worsened after the colonoscopy, associated with a rise in CRP (77 mg/L). Her symptoms settled rapidly with intravenous hydrocortisone and she was transitioned to oral prednisolone. Weekly subcutaneous methotrexate (20 mg/week) was started to allow for prednisolone weaning.

Discussion: PCC is a rare form of microscopic colitis where pseudomembranes occur in the absence of infection or ischemia.¹ Only a few cases have been reported worldwide.² Most patients affected are

middle-aged and female, presenting with chronic watery diarrhea.¹ Diagnosis is based on clinico-endoscopico-pathological correlation,² with the histology of colonic biopsies demonstrating a thickened subepithelial collagen band and a surface pseudomembrane³ (similar to that seen in *C. difficile*-associated pseudomembranous colitis). The pathogenesis of the pseudomembrane in PCC is unclear but may be related to the severity of the underlying mucosal injury.² While the most common approach to first-line treatment of PCC is budesonide,⁴ methotrexate was used in the above case due to its lower cost and reported efficacy.⁴

Conclusion: Our case demonstrates the need to consider this rare form of microscopic colitis in patients presenting with consistent clinical and histological changes where infectious and ischemic causes have been excluded. Our case also lends support to the use of methotrexate in cases where steroid weaning leads to a flare of symptoms.

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Fecal microbiota transplantation for recurrent *Clostridium difficile* infection: When regulatory affairs do not keep pace with evidence-based medicine

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Fecal microbiota transplantation (FMT) is now proven to be the most efficacious therapy for recurrent or refractory *Clostridium difficile* infection (rCDI) and is also cost-effective. When used for rCDI, the cure rate after one or two infusions is 81%–100%, and side effects are few and minor when compared with the risks of severe rCDI. Despite these facts, FMT is not widely available in Australian hospitals.

Healthy donor stool (HDS) currently has an uncertain regulatory status in Australia. The Therapeutic Goods Administration has taken a view that HDS is a “defined therapeutic product” and should thus be regarded as a drug. This is despite the fact that its contents and their concentrations cannot be defined in a standardized fashion, as for drugs. HDS is currently not on the Australian Register of Therapeutic Goods (ARTG). Listing on the ARTG is a costly and detailed process, usually undertaken by a commercial entity with a financial incentive. This is not the case for HDS and thus this represents a major barrier.

Currently in Australia, the law allows a medical practitioner to perform FMT treatment if they have “compounded” the stool aliquot personally. There is no regulation as to the indication for the FMT. This creates a risk of two main problems: avoidance of oversight, which allows FMT to be delivered for non-evidence-based indications; and logistical difficulties in accessing FMT therapy for evidence-based indications, such as rCDI. While a centralized bank of frozen stool would allow rigorous donor testing and safe and efficient “manufacture” of stool aliquots that can be distributed throughout the country, the current Australian legislation would seem to prohibit this.

In some countries, FMT is regarded as analogous to a tissue donation and is regulated as such. This form of regulation has an appropriate emphasis on safety without the requirement for uniformity in chemical composition. In the USA, the US Food and Drug Administration (FDA) placed a moratorium on the practice of FMT in 2013. However, given the clinical need for FMT to treat otherwise intractable cases of *C. difficile* infection, the moratorium was overturned and, in its place, a policy of “enforcement discretion” was adopted. This policy allows the distribution and use of stool for *C. difficile* infection only. To enable oversight, specific written permission from the FDA is required for use in other conditions.

The current situation, whereby FMT is the treatment of choice for rCDI according to high-level evidence but is unsupported—in fact prohibited—by our regulatory bodies, leaves patients without access to treatment or obliges them to seek expensive therapy in private facilities without oversight. This creates an equity-of-access issue and also leaves Australian patients without safe and reliable access to evidence-based effective therapy. This situation must change to allow the distribution of HDS for evidence-based indications and provide more oversight of FMT being performed for other reasons.

Predicting presence of redundant colon and its impact on quality of life

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Background and Aims: Redundant colon is a surgical, radiological, and endoscopic finding describing an elongated, dilated, or reduplicated colon. The finding is commonly described during colonoscopy, computed tomography, and abdominal x-ray, but held to no clinical accountability. It is a neglected finding for which agreed diagnostic criteria are lacking, and etiology and prognosis are unknown. A body of evidence exists describing an association with chronic constipation, sigmoid volvulus, and the use of antipsychotics and iron tablets. Crossover exists between colonic redundancy and idiopathic megacolon—a condition pertaining to chronically dilated and elongated colon in the absence of organic disease. This study set out to assess the symptoms of patients diagnosed with a redundant colon during colonoscopy and to compare the quality of life of this population with that of the general population.

Methods: In a study of colonoscopy, the presence of redundant colon was recorded. The Talley Bowel Disease Questionnaire, together with medications, aperients, and basic patient demographics were analyzed using multivariate logistic regression to identify variables associated with colonic redundancy. Patients also completed the Short Form-36 (SF36), a standardized and validated quality-of-life questionnaire. One-sample *t*-tests and one-sample Wilcoxon tests were performed on the eight domains of the SF36, comparing differences in mean and median quality of life between the patients with redundant colon and an Australian healthy control population.

Results: Sixteen per cent of patients (31/195) were diagnosed with colonic redundancy during colonoscopy. Among 110 variables evaluated, five variables in the final prediction model had a strong association with presence of colonic redundancy: female sex (odds ratio [OR], 5.6), lack of urgency for defecation (OR, 0.11), less than three bowel movements weekly (OR, 4.9), childhood abdominal pain (OR, 3.7), and abdominal pain in the past year (OR, 3.1). Two look-up tables for the probability of having a redundant colon were constructed based on patient sex. Internal validation of the multivariate model using a receiver operator curve demonstrated an area under the curve of 0.83 ($P = 7.8 \times 10^{-9}$) and Nagelkerke R^2 of 0.32. Patients with colonic redundancy had no statistically significant reductions in quality of life in comparison with the control population.

Conclusions: Two look-up tables were developed as a practical individual risk stratification tool to predict the presence of colonic redundancy. The five variables making up these prediction models are useful in better describing the symptom profile and demographics of patients with a redundant colon.

This study could not link any impairment in quality of life to patients with colonic redundancy. It may be that this colonic finding has no clinical bearing. Alternatively, it may be that only a proportion of these patients experience significant symptoms affecting quality of life. A large-scale study with physically measurable colonic dimensions to allow staging of colonic redundancy is warranted.

Funding: James Cook University Honours Research Department.

Conflict of Interest: None declared.

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Symptoms and diagnostic criteria of acquired megacolon: A systematic literature review

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Background: Acquired megacolon (AMC) is a condition involving persistent dilatation and lengthening of the colon in the absence of organic disease. Diagnosis depends on subjective radiological, endoscopic, or surgical findings in the context of a suggestive clinical presentation. In this review, we set out to investigate diagnostic criteria and symptoms of AMC.

Methods: The literature was searched using the PubMed, Medline via OvidSP, ClinicalKey, Informit, and Cochrane Library databases. Primary studies, published in English, with more than three patients were critically appraised based on study design, methodology, and sample size. Exclusion criteria were studies with the following features: post-operative; megarectum predominant; pediatric; organic megacolon; non-human; and failure to exclude organic causes.

Results: A review of 23 articles found constipation, abdominal pain, distension, and gas distress were predominant symptoms. All ages and both sexes were affected; however, symptoms varied with age. Changes in anorectal manometry, histology, and colonic transit were consistently reported. Studies involved varying patient numbers, demographics, and data acquisition methods.

Conclusions: Outcome data investigating the diagnosis of AMC must be interpreted in light of the limitations of the low-level evidence studies published to date. Proposed diagnostic criteria include: (1) the exclusion of organic disease; (2) a radiological sigmoid diameter of about 10 cm; and (3) constipation, distension, abdominal pain, and/or gas distress. A proportion of patients with AMC may be currently misdiagnosed as having functional gastrointestinal disorders. Our conclusions are inevitably tentative but will hopefully stimulate further research on this enigmatic condition.

Funding: Nil.

Competing interests: Nil.

The correlation between diverticular disease and redundant colon

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Background and Aim: Diverticulosis and redundant colon are colonic conditions for which underlying pathophysiology, management, and prevention are poorly understood, although both pose significant morbidity and mortality risks for those affected. Historical papers suggest an inverse relationship of these two conditions. However, no further attempt has been made to validate this relationship. This study set out to assess the correlation between diverticulosis and colonic redundancy.

Methods: Redundant colon and diverticulosis were recorded as either present or absent during colonoscopy, in addition to basic patient demographics. Multivariate binary logistic regression was performed with the aim of developing a probability nomogram. Redundant colon was used as the dependent variable, and age, sex, and diverticulosis as independent variables. Nagelkerke R^2 and a receiver operator curve (ROC) with area under the curve were calculated to assess goodness of fit and internally validate the multivariate model.

Results: Redundant colon and diverticulosis were diagnosed in 31 and 113 patients, respectively. The probability of redundant colon was increased by female sex (odds ratio [OR], 8.4; 95% CI, 2.7–26; $P = 0.00020$) and increasing age (OR, 1.7; 95% CI, 1.1–2.6; $P = 0.017$). Paradoxically, diverticulosis strongly reduced the probability of redundant colon (OR, 0.12; 95% CI, 0.04–0.32; $P = 0.000039$). The Nagelkerke R^2 for the multivariate model was 0.29 and area under the curve at ROC analysis was 0.81 (95% CI, 0.73–0.90; $P = 3.1 \times 10^{-8}$).

Conclusions: This study found an inverse correlation between redundant colon and diverticulosis, supporting the historical suggestion that the two conditions rarely occur concurrently. The underlying pathology for this relationship remains to be found. However, this study may contribute to the understanding of the etiology and pathophysiology of these colonic conditions.

Funding: James Cook University Honours Research Department.

Conflict of Interest: None declared.

First-line triple therapy for *Helicobacter pylori* eradication in Australia:

Has it stood the test of time?

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Background: Clarithromycin-based triple therapy is the recommended and only listed first-line treatment for *Helicobacter pylori* infection in Australia. Declining efficacy of this therapy has been reported in many but not all parts of the world, associated with rising clarithromycin resistance (CR) rates. However, primary CR in Australia is low.

Aims: To assess the outcome over a 20-year period of standard 1-week therapy of esomeprazole 20 mg, amoxicillin 1000 mg, and clarithromycin 500 mg (EAC7), all twice daily, for treatment-naïve patients in Australia, and to review the available data on primary CR.

Methods: Prospective outcome data were derived from the only multicenter, randomized comparative trial of EAC7 first-line therapy in Australia¹ (2002) and two audits of “real-world” treatment outcomes from a single center in Sydney over two periods: 1996–1998 and 2011–2016. Available national primary CR data (E-test MIC > 2 mg/L) were reviewed.

Results: *H. pylori* eradication rates (Figure 1) did not vary significantly over this period (77.0%–85.7%). Primary CR data were available from the single Sydney center for 1997–2002 and from multiple locations in five states for 2000–2002. CR ranged from 5.5% to 7.9% (Figure 2). There were no recent CR data. The stability of eradication data suggests it remains low.

Conclusions: These Australian data do not show a significant decline in efficacy of first-line therapy over two decades, associated with low primary CR. Eradication rates are reasonable and similar to those from other low CR regions, but are not optimal. The efficacy of a longer duration of therapy should be tested locally, and CR monitored. Similar or better eradication rates have been achieved with other proven but unregistered therapies used as first-line or as salvage therapies locally.

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Figure 1 *H. pylori* eradication with EAC7 over 20 years

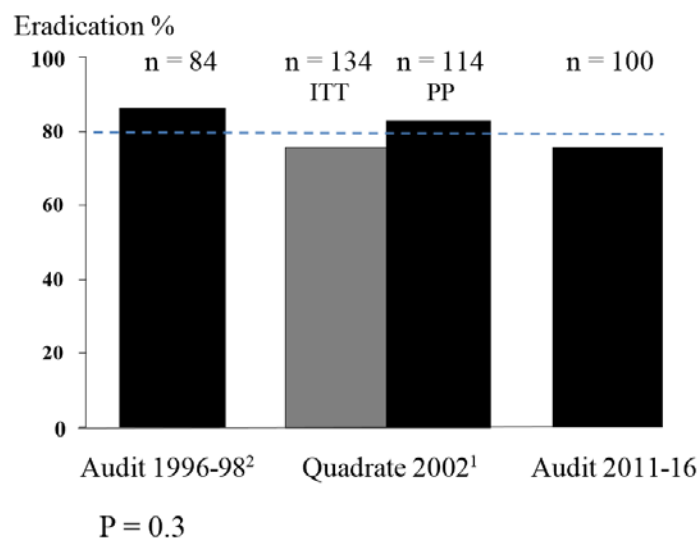
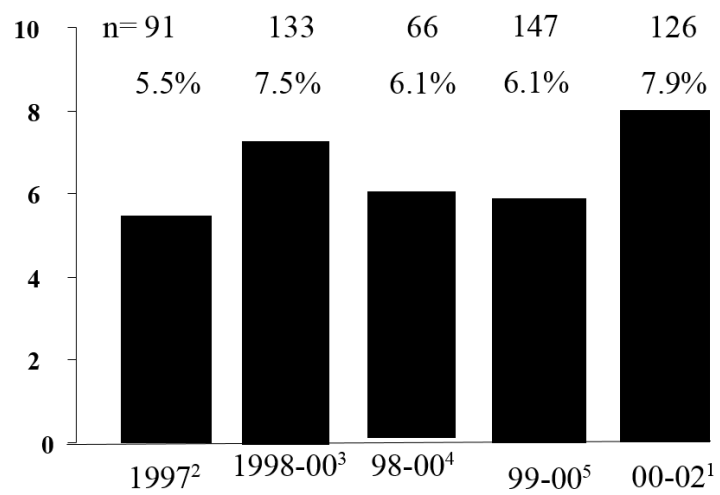


Figure 2 Clarithromycin resistance rates

Clarithromycin resistance rates %



p = NS

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Frailty and AIMS65 score predict mortality in hospitalized patients with gastrointestinal bleeding: A prospective cohort study

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Background: Scoring tools such as AIMS65, as well as patient risk factors, have been demonstrated to predict mortality in patients with gastrointestinal bleeding. Data about the role of frailty and comorbidity as predictors of mortality are limited.

Aim: To identify factors associated with mortality in hospitalized patients with gastrointestinal bleeding, including assessing the role of frailty and major comorbidity.

Methods: A prospective, observational, single-center cohort study at a tertiary referral hospital was performed with data collected over a period of 15 months on all patients experiencing gastrointestinal bleeding during the course of their admission. This included patients presenting initially to the emergency department with gastrointestinal bleeding, as well as patients who were admitted for other reasons and subsequently developed gastrointestinal bleeding as a complication of their admission. The recorded information included patient demographic data, comorbidity scoring using the Canadian Study of Health and Ageing (CSHA) clinical frailty scale and Charleston Comorbidity Index (CCI), laboratory results, endoscopic findings, and outcomes such as mortality up to 30 days after discharge. The data were analyzed using univariate and multivariate analysis to determine associations with mortality.

Results: A total of 204 patients (66% male; median age, 66 years) were included in the study. Of these, 134 patients (66%) were from a non-English-speaking background and 71% had at least one major comorbidity. The median CSHA and CCI scores were both 4. The most frequent cause of gastrointestinal bleeding was non-variceal upper gastrointestinal hemorrhage (57%), followed by lower gastrointestinal bleeding (10.3%) and variceal bleeding (9.8%). Of the 204 patients, 16 (7.8%) died during admission or within 30 days of discharge. Mortality was predicted on univariate analysis by age > 50 years ($P = 0.04$), CCI (hazard ratio [HR], 1.2; 95% CI, 1–1.42; $P = 0.047$), CSHA (HR, 1.87; 95% CI, 1.33–2.66; $P = 0.001$), Glasgow Blatchford Score (HR, 1.2; 95% CI, 1.03–1.4; $P = 0.017$) and AIMS65 score (HR, 2.6; 95% CI, 1.61–4.19; $P < 0.001$). Need for blood transfusion, intensive care unit admission, time to endoscopy, cause of bleeding, and duration of endoscopic procedure did not predict mortality. In multivariate analysis for independent predictors of mortality, the CSHA score (HR, 1.64; 95% CI, 1.05–2.59; $P = 0.03$) and AIMS65 score (HR, 2.1; 95% CI, 1.16–3.76; $P = 0.014$) were the only statistically significant predictors.

Conclusion: Identification of risk factors in patients hospitalized with gastrointestinal bleeding may help predict patient mortality. The data from this cohort validate the predictive value of AIMS65 for mortality. They also demonstrate a novel association between frailty and gastrointestinal bleeding-related mortality.

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Predictors of length of stay in hospitalized patients presenting with acute gastrointestinal bleeding: A prospective cohort study

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Background: Over 70 000 hospital presentations with gastrointestinal hemorrhage were reported Australia-wide in 2014–15.¹ Resource allocation and utilization is an ever-increasing concern, with length of stay (LOS) benchmarks being used to allocate funding. Identifying predictors for prolonged LOS could aid the targeting of interventions to improve benchmarks.

Aim: To identify factors associated with increased LOS in patients presenting acutely with gastrointestinal bleeding at a large tertiary hospital.

Methods: Data were prospectively collected on all patients presenting to the emergency department with acute gastrointestinal bleeding over a period of 15 months as part of an observational cohort study. The recorded information included baseline patient demographics, LOS data, 30-day readmission status, and investigative results such as laboratory indices and endoscopic findings. Comorbidity and frailty scoring using the Charleston Comorbidity Index (CCI) and the Canadian Study of Health and Ageing (CSHA) clinical frailty scale, respectively, were also recorded. Causal associations with prolonged LOS were investigated using univariate and multivariate analysis. LOS data were compared with the national average benchmark for LOS in major gastrointestinal hemorrhage (4.4 days), as established by the Independent Hospital Pricing Authority.²

Results: A total of 159 patients (mean age, 64.5 years), of whom 67% were male, were included in the study. Of these, 58 patients (36%) were from a non-English-speaking background and 108 patients (67%) had at least one major comorbidity. A total of 100 patients (60.3%) required a blood transfusion (median, 2 units packed red blood cells). Nineteen patients (12%) had an initial systolic blood pressure ≤ 90 mmHg. The most frequent cause of identified gastrointestinal bleeding was non-variceal upper gastrointestinal hemorrhage (56%), followed by lower gastrointestinal bleeding (10%) and variceal bleeding (10%). The median LOS was 4 days (mean, 6.9 days). Prolonged median LOS (≥ 4 days) was predicted on univariate analysis by age > 50 years (median, 5 days; $P = 0.004$), presence of major comorbidities (median, 5 days; $P < 0.001$), and the need for intensive care unit admission (median, 8 days; $P = 0.05$). Increasing LOS was correlated with CCI (correlation coefficient, 0.44; $P < 0.001$), CSHA (correlation coefficient, 0.41; $P < 0.001$), AIMS65 (correlation coefficient, 0.37; $P < 0.001$), red blood cell transfusion (correlation coefficient, 0.36; $P < 0.001$), Glasgow Blatchford score (correlation coefficient, 0.25; $P = 0.002$), and age (correlation coefficient, 0.21; $P = 0.007$). In multivariate analysis using binary logistic regression, the only statistically significant predictor for increased median LOS ≥ 4 days was the need for blood transfusion (hazard ratio, 1.91; 95% CI, 1.3–2.8; $P = 0.001$).

Conclusion: Several factors, including age, comorbidity, frailty, AIMS65 score and Glasgow Blatchford score, predicted increased LOS on univariate analysis; however, only the need for blood transfusion was predictive on multivariate analysis. There remains the possibility of type II error, and further data collection is underway to improve the power of the study.

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Celiac crisis: A rare and profound presentation of celiac disease

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Introduction: Celiac disease is a systemic immune-mediated enteropathy triggered by the ingestion of gluten in genetically susceptible individuals. Celiac crisis is a life-threatening manifestation of celiac disease and is rare in adults. There are currently only a handful of cases of celiac crisis in adults that have been published globally.

Case Report: A profoundly emaciated 43-year-old woman presented with profuse diarrhea, shortness of breath, and left leg swelling with ulceration and immobility (body mass index, 14.7 kg/m²), on a background of biopsy-confirmed celiac disease and non-adherence to a gluten-free diet. The patient was acidotic (pH, 7.16), with persisting hypokalemia, hyponatremia, hypomagnesemia, and hypophosphatemia. Associated thrombocytopenia, profound anemia, and iron, vitamin B12, folate, zinc, copper and selenium deficiency were seen on bloodwork. Due to her chronic hypoalbuminemia, the patient was diagnosed with bilateral massive pulmonary embolism causing pulmonary infarction. Bone marrow suppression was identified, and the immunocompromised patient developed urosepsis. Gastrocolonoscopy was performed, showing severe active celiac disease and lymphocytic colitis (Figures 1 and 2). Anti-transglutaminase antibodies were 608 CU. Poor wound healing was seen when the patient developed a deep foot ulcer. Subacute left distal radius and ulnar fractures were identified during admission due to low-impact trauma and osteopenia. Due to prolonged vitamin B12 deficiency, an imaging-confirmed diagnosis of acute spinal degeneration was made. Treatment included supportive therapies, anticoagulation, antibiotics, optimisation of oral intake (including strict adherence to a gluten-free diet), and extensive inpatient rehabilitation.

Conclusion: Celiac crisis is a rare and potentially life-threatening presentation of celiac disease, with minimal reported literature on its clinical course or manifestations in adults. Its diagnosis should be considered in known celiac patients presenting with acidosis, hypokalemia and profuse diarrhea. Subacute combined degeneration of the spinal cord should be considered in patients with chronic vitamin B12 deficiency presenting with neurological symptoms.

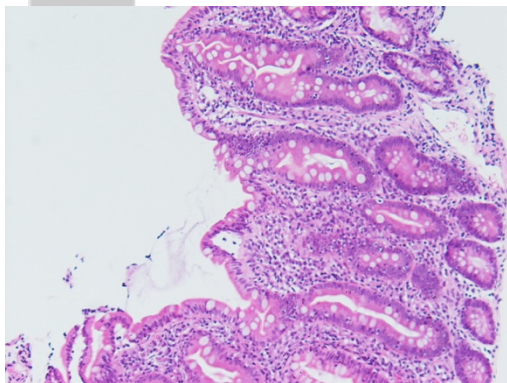


Figure 1 Duodenal biopsy showing villous atrophy

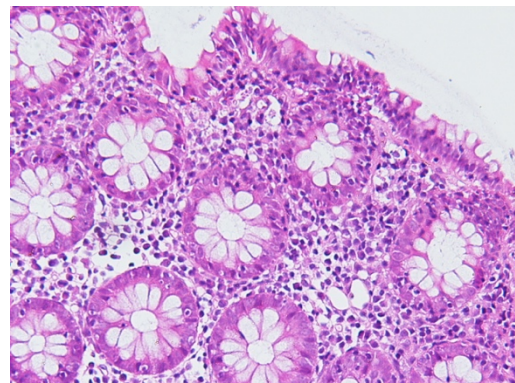


Figure 2 Colonic biopsy showing microscopic features of lymphocytic colitis

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Is fecal elastase-1 a good screening tool to test for exocrine pancreatic insufficiency in patients?

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Introduction: Exocrine insufficiency of the pancreas is an under-recognized complication of pancreatic disease. While those with mild forms of the disease may be asymptomatic, moderate to severe exocrine pancreatic insufficiency (PI) may manifest as maldigestion of fat and protein, and weight loss. Investigation of patients, especially those who are mildly symptomatic, would be useful to detect PI and further investigate its etiology, but also to treat the patient and thus improve their quality of life. Fecal elastase-1 is the most sensitive and specific way to indirectly test pancreatic function. This project was a retrospective study examining patients attending the Prince Charles Hospital (TPCH) gastroenterology outpatient department who had been investigated with fecal elastase between 2013 and 2016.

Aims: The aim was to determine whether measuring fecal elastase levels in patients was an appropriate screening tool for detecting PI. A secondary aim was to determine if the patients who were deemed to have mild, moderate, or severe PI (by their fecal elastase measurements) were treated with a pancreatic enzyme supplement (Creon; AbbVie), and whether there was resolution of their symptoms after commencement of treatment.

Methods: In a total of 173 patients who were investigated for fecal elastase levels between 2013 and 2016 at TPCH (Table 1), we examined for: symptoms leading to presentation; diagnosis of PI; commencement of Creon therapy; and improvement or resolution of symptoms.

Results: Of the 173 patients, 95 (55%) had fecal elastase of $> 500 \mu\text{g/g}$, while 78/173 patients (45%) had mild, moderate, or severe PI. Eighteen of 173 patients (10.4%) commenced Creon therapy. Twelve patients (66%) reported improvement or resolution of their symptoms after treatment (Table 2).

Conclusion: Fecal elastase is a useful non-invasive screening tool to test for PI in patients with malabsorption symptoms. Creon therapy should be trialed in patients with fecal elastase levels of $< 500 \mu\text{g/g}$, and patients monitored for resolution of symptoms.

Table 1 Patients who had fecal elastase levels measured at TPCH gastroenterology outpatient department between 2013 and 2016

Fecal elastase ($\mu\text{g/g}$)	Number of patients	% of total patients
------------------------------------	--------------------	---------------------

Normal, > 500	95	55%
Mild PI, 200–500	59	34%
Moderate PI, 100–200	11	6%
Severe PI, > 100	8	5%
Total	173	

Table 2 Symptom outcome in patients after Creon administration and their fecal elastase measurement

Fecal elastase (µg/g)	No of patients with improved symptoms (%)	No of patients with no improvement in symptoms (%)	Total
> 500	3 (75%)	1* (25%)	4
200–500	2 (50%)	2** (50%)	4
100–200	4 (80%)	1*** (20%)	5
< 100	3 (60%)	2*** (40%)	5
Total	12	6	18

* 1 patient, no discharge letter from subsequent appointments found; **1 patient, non-compliant with Creon; ***2 patients, subsequent elastase levels were normal.

No appointment offered: Does a hard-line approach to triaging work?

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Background: Public hospital outpatient clinics frequently work at or near capacity. A proportion of clinical referrals can be considered not necessary for several reasons, including no need for specialist opinion, a pre-existing guideline or pathway to manage a condition, or multiple specialty referrals for a single issue. These referrals can overburden clinical workload, which leads to an increase in waiting time for urgent cases. In response to yearly outpatient referrals doubling from 2000 to more than 4000 over 7 years, our local gastroenterology service introduced a triaging roster in which a single clinician triages all referrals for a 7-day period before handing the role over for the next week, and triaging is performed with clear and consistent criteria. We reviewed the results of this approach 7 months after its introduction.

Methods: Referrals for outpatient gastroenterology appointments are processed through a locally developed electronic referral management system. Data regarding the volume and outcome of all referrals triaged by a consultant gastroenterologist from January 2016 to March 2017 were extracted from this system. Triage decisions were trichotomized as “urgent” (requiring a clinic appointment within 30 days), “routine” (requiring an appointment, but not within 30 days), or “no appointment offered”. The volume and proportion of triaged referrals were contrasted before and after the introduction of standardized triaging practices that commenced in October 2016.

Results: Following the introduction of standardized triage practices, the overall rate of “no appointment offered” increased by 4.8% (95% CI, 2.9%–6.9%, $P < 0.01$). As illustrated in Figure 1, however, there has been a downward trend in the proportion of referrals with a “no appointment offered” outcome in the months subsequent to the introduction of standardized triaging.

Discussion: Rostered triaging using a locally developed standardized practice resulted in an initial increase in “no appointment offered” triage outcomes, which appears to have regressed towards the mean over a 7-month period. This may be explained by an increase in quality and appropriateness of referrals with referrer adherence to local health pathways in response to “no appointment offered” correspondence. Further work will review the total number of referrals over a 12-month period before and after standardized triaging.

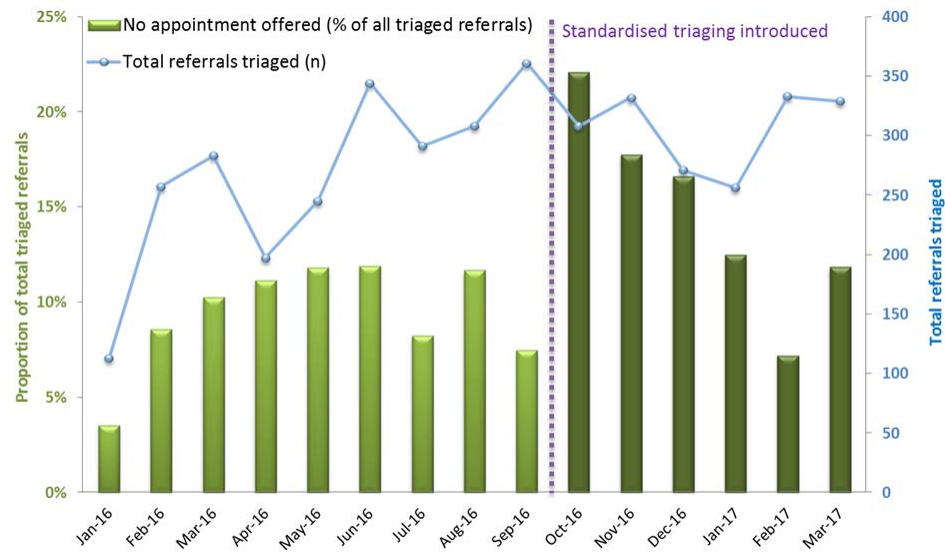


Figure 1 Proportion of “no appointment offered” referral outcomes from clinical triage. Standardized triaging was introduced in October 2016.

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A single-entry model for clinical triaging reduces wait time and improves key performance indicators of service delivery

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Background: Individual gastroenterologists vary in practice style and clinical interest. In a tertiary center, this can lead to significant heterogeneity in clinic referral load, triage protocols, and subsequent wait time. Recent population increases and a shift in demographics have led to a near doubling of gastroenterology referrals to our center, and time from referral to appointment allocation varied broadly. A single-entry model (SEM) wait time management strategy was developed for gastroenterology referrals with five core components:

- A pooled waitlist
- Centralized intake and triage with a “week on” roster for staff specialists and standardized triage guidelines
- Simplification of triage categories to “urgent” and “routine”
- Patients are allocated to the next available provider
- Establishment of a rapid access clinic for urgent cases.

This process was audited to determine whether an SEM improved access to specialist care for urgent cases and reduced variation in triaging.

Methods: Referrals for outpatient gastroenterology appointments were processed through a locally developed electronic referral management system. Data regarding the volume and outcome of all referrals triaged by a consultant gastroenterologist from October 2015 to April 2016 (pre-SEM) and from October 2016 to April 2017 (post-SEM) were extracted from this system. Triage decisions were trichotomized as “urgent” (requiring a clinic appointment within 30 days), “routine” (requiring an appointment, but not within 30 days), or “no appointment offered”. The volume and proportion of triaged referrals were contrasted before and after the introduction of standardized triaging practices that commenced in October 2016.

Results: Following the introduction of standardized triage practices, the number of initial urgent appointments offered to patients increased from 680 to 1118 over a 7-month period. During the same period, the median wait time for an urgent clinic appointment decreased from 78 days to 58 days ($P < 0.01$). Introduction of an SEM made a substantial difference to triage processes, with a more standardized approach (Figure 1).

Discussion: An SEM improved resource allocation, with a scheduled staff specialist allocated to triage every week, with scheduled work time allowances. Median access for urgent referrals was improved by 3 weeks with the introduction of standardized triaging and a rapid access clinic. Identification of appropriate and inappropriate referrals has improved and become more consistent using an SEM.

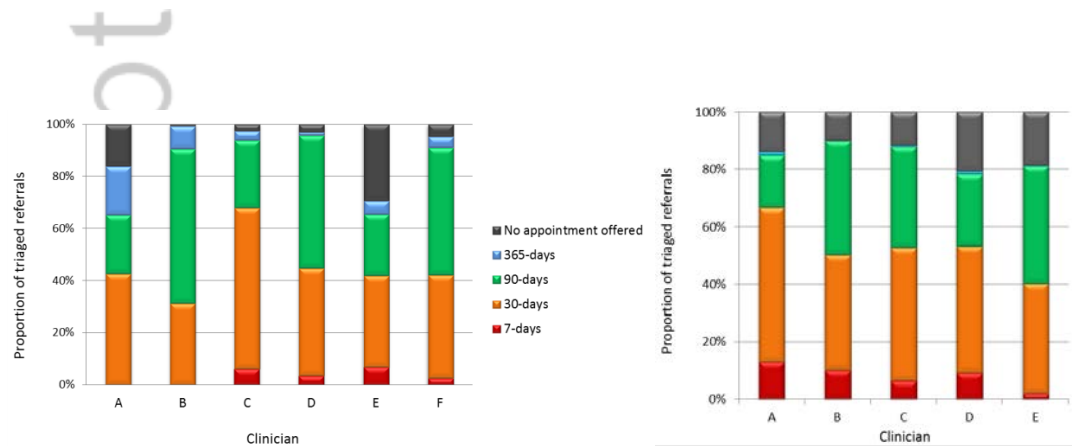


Figure 1 Proportion of clinical triage categories by individual gastroenterologist before and after introduction of a single-entry model with standardized triage guidelines

Compliance of gluten-free food provided in Melbourne food outlets

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Introduction: Effective treatment of celiac disease is contingent on a strict gluten-free diet, but remission is often incomplete.¹ Inadvertent or accidental gluten exposure is considered an important cause of this problem. Patient reports of symptoms triggered by gluten relate mostly to dining out;² however, the compliance of food outlets providing gluten-free food has never been formally assessed. This study aimed to investigate the likelihood of gluten exposure in outlets providing gluten-free food by analyzing samples of food declared gluten-free for gluten content and assessing knowledge of food service staff.

Methods: Food outlets within the City of Melbourne that declared at least one gluten-free item on their menus were randomly selected for inclusion. City of Melbourne environmental health officers (EHOs) conducted unannounced site inspections during October–December 2016. Each inspection involved: sampling of at least one gluten-free food item for independent qualitative and quantitative analysis of gluten content (Ridascreen R5 Elisa); and completion of a questionnaire assessing knowledge and implementation of gluten-free standards by the manager or most appropriate onsite employee. Gluten-free was defined as “no detectable gluten”, as per the Food Standards Australia New Zealand code. Data were compared with retrospectively obtained compliance rates of gluten-free food samples tested within a 2-month period in both 2015 and 2014 in an overlapping sample of outlets.

Results: From the 127 food outlets included in the 2016 audit, 158 food samples were analyzed, and 14 (9%) had detectable levels of gluten. Of these samples, five had < 20 parts per million (ppm), four had 20–80 ppm, and three had gluten content above the measurable limit of 80 ppm (two were from gluten-containing foods mistakenly provided to the EHO as gluten-free). Non-compliance rates had improved, being 28/138 (20%) in 2014 ($P = 0.005$ compared with 2016; chi-squared analysis) and 22/151 (15%) in 2015 ($P = 0.118$). About one-third of the outlets assessed in 2016 had been previously assessed, and follow-up from EHOs in previous years seemed to prevent repeat non-compliance. Knowledge and practice regarding gluten-free food was generally poor, with survey results indicating that 110/123 survey responders (89%) could not correctly identify gluten-containing and gluten-free grains, including 12 not identifying wheat as gluten-containing. The only factor associated with non-compliance was a lack of staff training (11/118 compliant vs 2/5 non-compliant, $P = 0.029$; chi-squared analysis) (Table 1). Interestingly, of the five outlets that did not provide any training to staff, two were repeatedly non-compliant and the third repeat non-compliant outlet received informal training from other staff.

Table 1 Associations with outlets being non-compliant in providing gluten-free food

Variable	Non-compliance (%)	P	Odds ratio
Knowledge questions all correct	1/12 (8)	0.791	1.33
Knowledge questions not all correct	12/111 (11)		
No staff training	2/5 (40)	0.029	0.154
Staff training	11/118 (9)		
Prohibited claims used	2/16 (13)	0.788	0.802
Prohibited claims not used	11/107 (10)		
Contamination disclaimer used	5/51 (10)	0.909	1.07
Contamination disclaimer not used	7/67 (10)		

Conclusions: Despite improving rates of compliance to provide gluten-free menu items, knowledge of gluten and food standards among food service staff is inadequate, and not training staff on gluten-free handling practices is associated with gluten contamination. Training food service staff would likely further improve the safe provision of gluten-free food.

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Thunderstorm food bolus impaction?

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Background: Specific environmental conditions can occasionally precipitate acute exposure to highly antigenic small particulate aeroallergens, such as those implicated in “thunderstorm asthma”. Given aeroallergens *may* exacerbate eosinophilic oesophagitis (EoE), we similarly sought to determine if there was a corresponding increase in emergency department (ED) presentations with acute food bolus obstruction (FBO) and associated EoE following the recent thunderstorm asthma epidemic on 21 November 2016 in Melbourne, Australia.¹

Methods: Medical records at Eastern Health were interrogated to identify all ED presentations with FBO between 10 October and 31 December during both 2015 and 2016. Data were further subdivided into two 6-week blocks to reflect the periods immediately preceding (Period 1: 10 October – 20 November) and immediately following (Period 2: 21 November – 31 December) the documented thunderstorm event. Patient demographics, atopic history, prior FBO, admission rates, peripheral eosinophilia, endoscopic findings, and rates of EoE were recorded. Definitive EoE was defined histologically, while possible EoE was defined as characteristic endoscopic appearance without oesophageal biopsy. “N-1” chi-squared test was performed, with a significant *P* value < 0.05 used.

Results: There were more ED presentations with FBO in 2016 than in 2015 (30 vs 23, Table 1). Although there were a similar number of ED presentations across both years during Period 1 (11 vs 10), there was a trend towards more ED presentations during Period 2 relative to Period 1 across both years (overall, 32 vs 21). There was also a trend towards more ED presentations with FBO during Period 2 in 2016 (63% vs 57%, *P* = 0.66) relative to 2015. Patients who presented with FBO following the thunderstorm event in Period 2 of 2016 tended to be younger, with a greater proportion reporting a prior history of FBO (8 vs 2, *P* = 0.23) compared with 2015. Endoscopy was performed following 49% of ED presentations (26/53), with 38% (10/26) having oesophageal biopsies. The period following the thunderstorm event in 2016 yielded the greatest number of FBOs attributable to EoE (*n* = 4).

Conclusions: There was a trend toward an increased frequency of ED presentations with FBO in the period following the thunderstorm event in 2016. This suggests that fine particulate aeroallergens may exacerbate EoE and contribute towards FBO. We plan to further collate results from other centers to assess the strength of this association.

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Table 1: Patient characteristics and outcomes

2016	2015	<i>P</i>
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	Period 1 <i>n</i> (%)	Period 2[*] <i>n</i> (%)	Period 1 <i>n</i> (%)	Period 2 <i>n</i> (%)	Period 2 2016 vs Period 2 2015
ED presentations	11 (37)	19 (63)	10 (43)	13 (57)	0.66
Admissions	5 (33)	10 (67)	4 (36)	7 (64)	0.82
Endoscopy	5 (33)	10 (67)	4 (36)	7 (64)	0.82
EoE diagnosis	2 (33)	4 (67)	1 ^{**} (33)	2 (67)	1.00
Prior FBO	4 (33)	8 (67)	2 (50)	2 (50)	0.23
Atopic history	1 (20)	4 (80)	3 (37)	5 (63)	0.17
Male	7 (41)	10 (59)	7 (58)	5 (42)	0.22
Median age (years)	56.3	49.9	52.4	57.3	

* Period 2 2016 includes the documented period of “thunderstorm asthma” on 21 November 2016.

** Possible EoE diagnosis.

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Acute food bolus presentation to emergency department and follow-up endoscopy: Are we missing potential pathology?

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Background: Food bolus obstruction (FBO) is a common emergency department (ED) presentation in Australia and has been documented as the third most common gastrointestinal ED presentation in other countries.¹ Given that >50% of patients presenting with FBO who undergo endoscopic assessment display oesophageal abnormalities (usually reflux oesophagitis or eosinophilic oesophagitis [EoE]), and because FBO is often recurrent, the need for careful follow-up is apparent.² However, 50% of FBOs resolve spontaneously before endoscopic intervention, and patients may be discharged home directly from the ED.³ We therefore aimed to determine the extent of follow-up in current practice for patients with FBO discharged from the ED.

Methods: Cases of FBO were identified by a retrospective search of the electronic medical record using ICD-9/10 codes (foreign body or oesophageal obstruction) over two separate periods (7 October 2015 – 31 December 2015 and 1 October 2016 – 31 December 2016) at three hospitals across the Eastern Health network. Foreign body (non-food-related) or bone impactions were excluded from the analysis. Patient demographics, smoking status, medical history including co-existing atopic conditions, prior history of food bolus, type of food bolus, ED management, rates of admission, and performance of inpatient or outpatient endoscopy were recorded.

Results: A total of 53 patients presented to the ED with FBO over the study period. Of these, 25/53 (47%) required admission and 28/53 (53%) had their FBO resolve in the ED and were discharged home. Three of the 28 patients (11%) who were discharged from the ED subsequently underwent either gastroenterology follow-up or outpatient gastroscopy, with two of the three (33%) having abnormality (EoE and benign stricture) identified. In comparison to those admitted, patients discharged directly from the ED were of similar age (median, 52 vs 55 years; $P = 0.72$) and sex (50% vs 60% male; $P = 0.47$) but were less like to have a prior history of FBO (18% vs 44%; $P = 0.04$). Most patients who underwent gastroscopy (19/27, 66%) had an abnormality identified, most commonly EoE (10/19, 53%).

Conclusions: Patients who have spontaneous resolution of FBO in the ED will frequently be discharged home without a plan that includes follow-up with a gastroenterologist or endoscopy. This represents a significant departure from ideal practice, and important pathology may be overlooked. Improvement in education or referral pathways should be considered for ED management of these patients, given the frequent finding of treatable abnormalities.

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Does irritable bowel syndrome increase symptomatic response to inulin ingestion?

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Background and Aim: Visceral hypersensitivity is now widely regarded as an important factor in irritable bowel syndrome (IBS) pathogenesis. Multiple studies have shown no significant difference in objective malabsorption-related gastrointestinal changes;¹⁻³ however, patients with IBS experience greater subjective symptoms in response to these changes. Symptoms are therefore believed to arise from an increased awareness of internal stimuli due to over-amplification of signals between the gut and the brain. The success of the low-FODMAP diet, which minimizes consumption of fermentable oligo-, di-, mono-saccharides and polyols, is likely attributable to the reduction in symptom-provoking luminal distension in those IBS patients for whom hypersensitivity is an important pathogenic factor. There is, however, currently no practical test to detect visceral sensitivity. Inulin is suggested as an appropriate substrate for detection of visceral hypersensitivity using hydrogen breath testing. As inulin (long-chain fructan) is completely malabsorbed in humans, hydrogen should be produced in all participants with hydrogen-producing gut microbiota, regardless of IBS status. Patients with visceral hypersensitivity are expected to experience greater symptoms in response to this gas production than controls. This pilot study aims to determine if ingestion of inulin causes an increased symptomatic response in participants with IBS compared with healthy controls, despite equable breath hydrogen excretion.

Methods: Participants underwent a 3-hour hydrogen breath test after consuming 10 g of inulin in 100 mL of water. Adherence to a low-FODMAP diet for 1 day before testing and an overnight fast were required. Breath samples were recorded before inulin consumption and every 30 minutes thereafter. Severity of abdominal pain, bloating, flatulence, and diarrhea were documented with each breath sample.

Results: Twenty-three participants (14 IBS, nine control) took part in the study. Three IBS participants were excluded from symptom analysis due to incomplete data. No differences in breath hydrogen or symptoms were found between groups at baseline. Total breath hydrogen production did not differ between the two study groups (67 [-3.5 to 178] control vs 56 [10 to 113] IBS; $P = 0.516$). IBS participants had significantly more flatulence than controls (4 [2–5] vs 1 [0–1]; $P = 0.006$). The two groups did not differ in severity of abdominal pain, bloating, or diarrhea. IBS participants showed a higher combined symptom score; however, this increase did not reach statistical significance (5 [3–13] vs 2 [0–7]; $P = 0.095$).

Conclusion: This study demonstrates significantly increased flatulence in IBS participants; however, the increase in total symptoms did not reach significance. Breath hydrogen excretion was comparable between groups, but peak hydrogen concentrations were not reached during the study duration for

most participants. The optimal dose of inulin to allow differentiation is also not known. It is therefore recommended that further studies be completed with increased test duration, greater study power, and multiple inulin doses.

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“Keep calm and spare the surgeon”: An Australian single-center experience with over-the-scope clips for iatrogenic gastrointestinal perforations

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Introduction: Perforation during upper and lower gastrointestinal endoscopy is relatively rare; however, its occurrence conveys significant morbidity and potential mortality for the affected patient. Endoscopic management of gastrointestinal perforation is increasingly being thought of as a first-line treatment for a condition that has traditionally been managed surgically. The aim of this study was to determine the outcome of the management of iatrogenic gastrointestinal perforations treated by over-the-scope clip (OTSC) placement in our patient cohort.

Methods: We conducted a retrospective review of patients with upper or lower iatrogenic gastrointestinal perforation treated with OTSC placement in a single tertiary referral center between April 2014 and April 2017.

Results: Ten patients were included in our study (eight female, two male). The mean age of our patient cohort was 74 years. Three different endoscopists were involved in the use of OTSCs in these patients. Five of the cases (50%) involved iatrogenic perforations detected immediately during an endoscopic intervention (two following endoscopic mucosal resections [EMRs] in the stomach, one following an oesophageal dilatation, and two following EMRs in the rectum and descending colon, respectively). The other five cases (50%) involved iatrogenic perforations detected during a diagnostic endoscopy (three colonoscopies, one gastroscopy, and one attempted endoscopic retrograde cholangiopancreatography during duodenal intubation with a duodenoscope). Immediate technical success of defect closure was possible in all cases (100%). Adjunct therapy with through-the-scope-clips was required for complete defect closure only in one case (10%). Eight of the patients (80%) were discharged without further clinical deterioration or need for surgical intervention after the OTSC placement. Two patients (20%) went on to require surgical intervention for ongoing complications from the primary perforation event. One of the two patients (10%) died, despite timely surgical intervention.

Conclusion: This study highlights the emerging role and success of OTSCs as an endoscopic tool for primary closure of iatrogenic gastrointestinal perforations. It also highlights the paradigm shift in the new era of managing iatrogenic gastrointestinal perforations; where the skillset of OTSC placement is available, one can truly keep calm and call upon this first, instead of the surgeon. It would be prudent for all endoscopists and trainees to incorporate the use of OTSCs in their armamentarium.

A local focus on *Helicobacter pylori* antibiotic resistance: Experience in a single Australian hospital

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Introduction: *Helicobacter pylori* is a common cause of gastrointestinal presentations, with remarkably increasing antibiotic resistance rates observed in many countries. Recent recommendations emphasise the importance of knowledge of local antibiotic resistance patterns in selecting therapies for *H. pylori*.^{1,2} Maastricht recommendations state that susceptibility testing should be performed before therapy in regions with high clarithromycin resistance rates.³

Methods: Patients with proven *H. pylori* infection and documented failure of first-line therapy were referred for endoscopic examination. We determined the antibiotic resistance patterns of *H. pylori* based on cultures of gastric tissue biopsies. Concomitant biopsies were also taken for histology.

Results: A total of 300 patients with documented symptomatic *H. pylori* infection in whom first-line clarithromycin-based therapy failed underwent endoscopic evaluation. Of these, the success rate of attempted culture and susceptibility testing was 33%. Data were available for complete analysis on 98 patients (32 male and 66 female; mean age, 49 years [range, 22–76 years]). Fifteen patients were current smokers, 23 consumed regular alcohol, and seven had diabetes. Twenty-eight were taking long-term acid suppression therapy and two were on regular NSAIDs. Thirteen patients reported an allergy to penicillin, two to sulphur and two to cephalosporin. Patients reported a total of 31 countries as their place of birth; 21 patients were born in Australia and 12 in China, with other countries including Vietnam, Iran, Afghanistan, and Korea. Clarithromycin resistance was observed in 65%, and metronidazole resistance in 54%. Overall, 80% were sensitive to amoxicillin. Thirteen patients had significant histological findings, including 10 with intestinal metaplasia, two with MALT, and one with adenocarcinoma.

Conclusion: Our reported *H. pylori* antimicrobial resistance profiles are consistent with data in current literature, but show exceptionally high resistance rates to clarithromycin. Amoxicillin remains an appropriate antibiotic of choice for first-line therapy in most *H. pylori* infections.

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Comparing the eradication rate of *Helicobacter pylori* among tailored, sequential, and concomitant therapy

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Aim: The *Helicobacter pylori* eradication rate of clarithromycin-based triple therapy has decreased to an unacceptably low level, and novel therapeutic strategies are necessary. The aim of this study is to compare the efficacy of concomitant, sequential, and tailored therapy as the first-line therapy for *H. pylori* eradication.

Methods: A total of 1290 patients infected with *H. pylori* were divided into three groups, and each group was treated with a different eradication therapy. The first group was simultaneously treated with rabeprazole, amoxicillin, clarithromycin, and metronidazole (concomitant therapy group). The second group was treated with rabeprazole and amoxicillin, followed by rabeprazole, clarithromycin, and metronidazole (sequential group). In the final group, amoxicillin, rabeprazole, and clarithromycin were given in the absence of a mutation in a 23S rRNA, while clarithromycin was replaced by metronidazole when the mutation was detected (tailored group). In the case of a failure to eradicate *H. pylori*, second-line quadruple and third-line eradication therapies were administered. Six weeks after the treatment period, the patients underwent ¹³C-urea breath tests to confirm *H. pylori* eradication.

Results: The eradication rates were 92.0% (312/339) in the concomitant group, 85.1% (285/335) in the sequential group, and 91.2% (176/193) in the tailored group ($P = 0.135$). The second-line therapy was applied to 94 patients, and the eradication rate was 79.8% (71/89). The eradication rate for the third-line therapy was 47.1% (8/17).

Conclusion: No statistical difference was found in eradication rates among the three groups. However, in areas where resistance of clarithromycin is high, concomitant and tailored therapy may be more effective than sequential therapy for *H. pylori* eradication.

Divit D: A prospective study on predictors and risk factors for acute severe and recurrent diverticulitis

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Introduction: Diverticular disease is among the most prevalent diseases of Western society, particularly in older populations but with an increasing trend among the younger generation. The risk factors associated with clinically significant diverticulitis requiring hospital admission and predictors of recurrent diverticulitis have not been fully established. The aim of this study is to determine the specific risk factors that can predict recurrent episodes and patients at higher risk of requiring surgical management.

Methods: This is a prospective, observational (cross-sectional) study of patients admitted to our health service with diagnosed diverticulitis. A consecutive series of patients who were identified on admission with acute diverticulitis, as confirmed by computed tomography scan, were included in this study. Subsequent chart review was conducted to assess for suspected risk factors, including demographics, biochemistry (vitamin D), C-reactive protein (CRP) and evidence of complicated disease (perforation, abscess or fistula). Patients were then followed up 4-monthly for 12 months with either clinic review or phone consultation to assess whether they required readmission to hospital with diverticulitis or surgery within the follow-up period. A statistical analysis was performed on pilot data available for the first year of recruitment.

Results: A total of 43 patients presented with acute diverticulitis in the first year of recruitment, with 39 patients completing follow-up over the next 12 months. Four patients were excluded because they were lost to follow-up. The median age of the group was 56.9 years, with only two patients younger than 45 years of age. Forty-six percent of patients had had a previous episode of diverticulitis, and 64% were a current or previous smoker. Vitamin D deficiency was present in 19% of patients tested but was not clinically significant in predicting further admission to hospital ($P = 0.75$) or requiring surgical intervention ($P = 0.99$). A trend in the difference of the means of CRP at hospital presentation was noted between those with further admissions (140.6 mg/L) and those without (101.8 mg/L). This trend was also present in those requiring and not requiring surgical intervention (136.8 mg/L vs 105.4 mg/L). However, neither comparison achieved statistical significance ($P = 0.321$, $P = 0.513$, respectively). A similar trend was noted in those patients with a smoking history, with 62.5% of smokers required surgical management in the follow-up period ($P = 0.099$). Among those patients diagnosed with uncomplicated diverticulitis, 71.4% had no further episodes. In the cohort of patients with complicated diverticulitis, 62.5% went on to surgical management.

Conclusion: Risk factors of high CRP at admission, history of smoking and complicated diverticulitis at presentation are suggestive of a trend towards more severe and recurrent disease. However, our data are limited by the small sample size at present. Of note, vitamin D deficiency was not associated with future surgery or recurrent episodes of acute diverticulitis in our patient cohort. Our ongoing study will

look to analyse a larger patient group into the future to assess if these trends prove to be clinically significant.

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Does addition of Movicol to standard bowel preparation improve the quality of bowel preparation in patients undergoing routine colonoscopy?

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Introduction: Adequate bowel preparation is vital for the efficacy and safety of colonoscopy. Studies have demonstrated that inadequate bowel preparation may affect up to 30% of patients undergoing colonoscopy and is associated with reduced polyp detection, higher rates of incomplete colonoscopy, and need for repeat procedures or shorter surveillance intervals. Efficacy of standard bowel preparation may be improved by addition of osmotic laxatives such as Movicol (Norgine).

Aim: This study aimed to evaluate the efficacy and tolerability of standard bowel preparation (SBP) compared with augmented bowel preparation (M-BP), where osmotic laxatives were used before bowel preparation.

Methods: This was a single-center, randomized, single (proceduralist)-blinded study. Adults undergoing outpatient colonoscopy were randomized to receive either SBP (split dose Prep Kit-C: one sachet of GlycoPrep-C plus two sachets of PicoPrep) or M-BP (one sachet of Movicol twice daily for eight doses before split dose Prep Kit-C). Bowel cleansing was assessed using the Ottawa bowel preparation scale. Successful cleansing was defined by a score of 2 or less in each colonic segment and a score of 2 or less for fluid content. Patient satisfaction, risk factors for poor bowel preparation, and preparation-related symptoms were recorded.

Results: A total of 172 patients were randomized (89 to SBP and 83 to M-BP). Patients had a median age of 62 years, and 51% were male. Preparation was adequate in 70.7% of SBP patients compared with 73.5% of M-BP patients ($P = 0.69$). The majority of patients in both groups complained of adverse symptoms with Prep Kit-C (68%), but Movicol was well tolerated, with only 0.7% of patients reporting adverse symptoms with Movicol. Both groups of patients had a similar polyp detection rate (44.5% vs 44.9%, $P = 0.96$). Higher proportions of patients in the M-BP arm were taking opioids (19% vs 15%, $P = 0.44$) and regular laxatives (12% vs 8%, $P = 0.51$) and had a known history of previous incomplete colonoscopy due to poor bowel preparation (24% vs 16%, $P = 0.23$).

Conclusion: This study suggests Movicol-augmented bowel preparation is not superior to standard bowel preparation in achieving adequate bowel cleansing. Movicol was well tolerated, causing very few adverse symptoms. However, there was a trend to a higher proportion of patients in the Movicol arm having risk factors for suboptimal bowel preparation, which did not reach statistical significance.

Adjunctive induction therapy with oral effervescent budesonide in newly diagnosed celiac disease:
Results of a pilot, randomized, double-blind, placebo-controlled trial

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Background: Traditional treatment paradigms in celiac disease (CD) have relied upon the commencement of a gluten-free diet (GFD) as the sole therapy. Using this approach, complete histological response is seen in less than 40% of patients after 1 year of treatment. Ongoing mucosal inflammation in CD is associated with an increased risk of malignancy and other associated complications of CD.

Aims: To address the hypothesis that addition of induction therapy with oral, topically acting budesonide to the GFD would lead to (i) more frequent and faster healing of the intestinal lesion; and (ii) greater improvement in symptoms and functional capability in patients with newly diagnosed CD. It also aimed to determine the frequency of early (8-week) healing.

Methods: Participants with newly diagnosed CD (defined by at least Marsh 3A histology, elevated celiac antibodies, and commencement of a GFD < 4 weeks before randomization) were randomized to 10 weeks of daily effervescent budesonide or placebo (9 mg budesonide or placebo for 8 weeks followed by 6 mg for 1 week and 3 mg for 1 week). Participants were eligible if they were aged between 16 and 75 years, if endoscopy had been performed within 6 weeks of enrolment, and if they had been treated with a GFD for < 4 weeks. Participants were excluded if they had Marsh 1–2 histology. All participants underwent follow-up endoscopy at Weeks 8 and 52. The primary outcome was the proportion of participants achieving mucosal response (Marsh 1 or better) at Week 8. Secondary outcomes included: mucosal response at Week 52; mucosal remission (Marsh 0) at Weeks 8 and 52; improvement in villous height to crypt depth ratio (Vh:Cd) at Weeks 8 and 52; improvement in symptoms; change in bone mineral density; and change in fatigue and depression. Assessment of compliance to therapy included tablet count and dietitian-led food diary assessment.

Results: A total of 37 participants (73% female; mean age, 36 ± 16 [SD] years; Marsh 3C, 62%; Marsh 3B, 24%; Marsh 3A, 13%) were randomized to budesonide ($n = 19$) or placebo ($n = 18$). Compliance to the study treatment was good or excellent in 34 participants (84%) and compliance to a GFD was excellent in 36 (97%), being good in the remainder. In the total cohort, mucosal response and remission were noted in 12 (32%) and nine (24%), respectively, at Week 8, and 20 (53%) and 14 (38%), respectively, at Week 52. Regarding the primary outcome, mucosal healing was seen in six (37%) receiving budesonide

and five (28%) receiving placebo ($P = 0.73$; Fisher's exact test). Mucosal remission was more common in those receiving budesonide ($n = 12$, 32%) than placebo ($n = 3$, 17%; $P = 0.45$). A similar non-significant trend was noted at Week 52 ($n = 8$, 42% vs $n = 6$, 33%; $P = 0.74$). Change in Vh:Cd was non-significantly higher in the budesonide group at Week 8 (1.64 ± 1.07 vs 1.31 ± 0.87) and at Week 52 (2.39 ± 1.02 vs 2.01 ± 1.03). Change in bone mineral density, and levels of fatigue, anxiety, depression and gastrointestinal symptoms were similar between groups. The safety profile of oral effervescent budesonide was acceptable, with no significant differences in treatment-related adverse events.

Conclusions: Within 8 weeks, complete normalization of histology was seen in one in four participants, suggesting that, in some, disease response can be rapid and complete. When used in conjunction with a GFD, treatment with budesonide in newly diagnosed CD showed a non-significant trend toward improved mucosal healing rates and was well tolerated. The small sample size in this study limits robust conclusions but permits planning of future well-powered randomized controlled trials of oral formulations of budesonide.

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Endoscopic treatment of patients with intramucosal carcinoma in Barrett's oesophagus: Outcomes and long-term follow-up

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Background: Barrett's oesophagus is the most important risk factor for the development of oesophageal adenocarcinoma. Endoscopic treatment has brought a paradigm shift in the management of patients with Barrett's oesophagus with intramucosal carcinoma (IMC), from oesophagectomy to endoscopic mucosal resection (EMR) and HALO radiofrequency ablation (RFA). IMC has a 1%–3% risk of lymph node (LN) metastasis, which would be missed and not treated when Barrett's with IMC is treated endoscopically.

Aim: To assess the long-term outcomes of patients with Barrett's with IMC receiving endoscopic treatment; in particular, the number of EMR and HALO treatments required, complications, progression to adenocarcinoma, complete remission of dysplasia (CRD) and intestinal metaplasia (CRIM), LN metastasis, and survival.

Methods: We performed a retrospective analysis of patients who underwent endoscopic treatment of Barrett's with IMC at our institute over an 8-year period. Patients who had visible mucosal nodularity underwent EMR. Patients were treated with a maximum of two circumferential HALO 360 and four focal HALO ablations, 2–6 months apart. First follow-up gastroscopy was performed at 2 months, and subsequent gastroscopies were performed based on findings. Patients with IMC underwent staging endoscopic ultrasound (EUS), computed tomography (CT) scans and fluorodeoxyglucose-positron emission tomography (FDG-PET) scans, and follow-up scans as clinically indicated. Further recurrence of Barrett's was treated with repeat EMR and/or HALO ablation.

Results: A total of 14 patients with Barrett's oesophagus with IMC (either on referral biopsies or EMR at our institute) were treated; 71% of patients (10/14) were male, with a mean age of 67 years. Barrett's segment median length was C4 M6 (range of circumferential extent, 0.5–19 cm). EMR at baseline was performed in 86% of patients ($n = 12$), and 21% ($n = 3$) and 14% ($n = 2$) of patients required two and three EMRs, respectively, for focal nodular lesions at follow-up gastroscopies. Pinch biopsies on initial referral histology were suggestive of IMC in 42% of patients ($n = 6$). Of these patients, EMR upgraded histology in two patients, downgraded in two patients, and confirmed IMC in two patients. The other patients ($n = 8$) in this cohort were referred as Barrett's with low-grade or high-grade dysplasia on initial referral pinch biopsies and were upgraded to IMC on EMR.

EUS was performed before index HALO ablation in 86% of patients ($n = 12$) and PET scan in 14% ($n = 2$). Among patients who underwent EUS ($n = 12$), five were also investigated with a whole-body CT scan and one patient had a PET scan. No pathological LN involvement was found in any of these patients before HALO ablation. A total of 30 HALO ablations were performed, with an average of 2.1 ablations

per patient. A total of 10 circumferential HALO 360 ablations were performed. Patients were followed up for a mean of 53 months (range, 31–78 months). Two patients have been lost to follow-up. Twelve patients (100%) had CRD and 11 (92%) had CRIM at their last follow-up gastroscopy. The patient who has not achieved CRIM is still undergoing HALO RFA treatment.

Two patients with IMC on pinch biopsies were upgraded to invasive adenocarcinoma by EMR. They were both poor surgical candidates and underwent endoscopic treatment. Both these patients achieved CRIM and are doing well with follow-up at 41 and 67 months, respectively. No patients had positive LNs during follow-up on PET or CT. Follow-up PET scan detected incidental lesions in two patients—a parotid lesion and a base of tongue lesion. Complications after HALO ablation include bleeding requiring blood transfusion (7%, $n = 1$) and mild stricturing not requiring dilatation (14%, $n = 2$). The survival rate of patients with Barrett's and IMC is 100% at a mean follow-up of 53 months at our institution.

Conclusion: Patients with Barrett's oesophagus and IMC who were treated endoscopically with a combination of EMR and HALO RFA had excellent outcomes in terms of survival, CRD and CRIM, with a low complication rate. No LN metastasis was detected at long-term follow-up.

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Solid organ transplantation is not a risk factor for eosinophilic oesophagitis: A review of 13 792 transplants performed in a predominantly adult population in North Carolina

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Background: Case reports in the pediatric literature suggest that solid organ transplantation, medications used to treat potential rejection (such as calcineurin inhibitors), or post-transplant lymphoproliferative disease (PTLD) may be a risk factor for eosinophilic oesophagitis (EoE).^{1,2} This association has not yet been examined in an adult cohort.

Aim: To determine the prevalence of EoE in patients who have received a solid organ transplantation.

Methods: We performed a retrospective search of the Carolina Data Warehouse (a central data repository of clinical, research, and administrative data for a tertiary health system) for all patients (adult and pediatric) receiving solid organ transplantation (heart, kidney, liver, lung, pancreas, single or in combination) at the University of North Carolina between 1 January 2009 and 1 April 2017. Cases of EoE and solid organ transplantation were identified using ICD-9 and -10 coding, and comorbidities were identified using electronic data extraction tools. EoE cases were compared with a pre-established research database to confirm complete case identification. The electronic medical records of patients were interrogated. Age, sex, pre-transplant diagnosis leading to organ transplantation, date of solid organ transplantation, date of diagnosis of EoE, type of solid organ transplantation, medications, and substance use were recorded.

Results: Of 13 792 individuals who received a solid organ transplant, five were found to have EoE (estimated period prevalence equivalent to 36.25/100 000 people). Only adult cases of EoE were noted. The current mean age of the five patients with EoE was 42.8 years (range, 21–60 years), three were male (60%), and three (60%) had comorbid atopic illness. Renal, combined renal and pancreas, combined renal and liver, liver, and heart transplantations (respectively) were received by the five patients. Post-transplant lymphoproliferative disorder was not diagnosed. All five patients received the solid organ transplantation before the diagnosis of EoE (mean, 11.8 years; range, 4–18 years). All five patients used some form of immunosuppression (tacrolimus monotherapy, two patients [40%]; tacrolimus with mycophenolate, two patients [40%]; sirolimus monotherapy, one patient [20%]).

Conclusion: The prevalence of EoE was not more common in a mainly adult cohort of solid organ transplant recipients. The use of tacrolimus was predominant in this cohort, and may be of significance.¹ Further research could focus on why EoE could develop on concomitant immunosuppression.

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Video capsule endoscopy for obscure gastrointestinal bleeding: Diagnostic effectiveness and factors associated with a positive study

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Introduction: Video capsule endoscopy (VCE) allows for complete visualization of the small intestine and is the first-line investigation for obscure gastrointestinal bleeding (OGIB). There is large variability in the diagnostic yield of VCE reported in the literature. Data from Australian cohorts are very limited.

Aims: We aimed to establish the effectiveness of VCE (rate of completion, complications, and diagnostic yield) in a large Australian cohort; and to identify factors associated with a positive capsule study.

Methods: We performed a retrospective cohort study of all patients who underwent VCE for obscure bleeding between January 2010 and December 2016. All patients had a negative oesophagogastroduodenoscopy and colonoscopy, performed before VCE. Patient sociodemographics, characteristics of occult bleeding, and VCE findings were obtained from electronic records. Multivariate logistic regression analysis was performed to identify factors associated with a positive study.

Results: A total of 501 patients (average age, 62.5 years; 52.5% male) underwent VCE for obscure bleeding. A causative lesion was identified in 231 studies, resulting in an overall diagnostic yield of 46.1%. Lesions identified are outlined in Table 1. Seventy of 231 patients (30.3%) proceeded to further treatment for the identified lesion. The mean gastric transit time was 35.5 ± 25.1 minutes, and small bowel transit time was 251.7 ± 54.9 minutes. The capsule study was incomplete (did not reach the colon) in 50 patients (10%), and capsule retention occurred in four patients (1%). On multivariate analysis, advanced age (> 60 years) (odds ratio [OR], 1.73; $P = 0.006$), overt as opposed to occult bleeding (OR, 1.9; $P = 0.005$), and prolonged small bowel transit time (> 240 minutes) (OR, 2.51; $P = 0.001$) were all independently associated with the identification of a causative lesion. Inpatient status was a significant factor in univariate but not multivariate analysis.

Conclusion: VCE is effective for the investigation of OGIB, with a low rate of complications and overall diagnostic yield of 46.1%. The most common lesions identified were small bowel erosions or ulceration and angioectasias. Advanced age, overt bleeding, and prolonged small bowel transit were all independent predictors of a positive capsule study.

Table 1 Types of lesions identified on VCE

Erosion or ulceration	96 (41.6%)
Angioectasia	89 (38.5%)

Mass	13 (5.6%)
Diverticula	7 (3.0%)
Other*	26 (11.3%)

* Includes blood or clot, Dieulafoy lesion, ulcerated polyp, celiac disease.

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Susceptibility for celiac disease based on tissue transglutaminase seroprevalence and HLA genotype in a community study

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Background and Aim: Celiac disease (CD) is common, with a prevalence of about 1 in 100 adults worldwide. Variations in prevalence are related to ethnicity and geographical location. In Australia, the prevalence has been estimated to be as high as one in 70.¹ CD is associated with specific HLA genotypes: HLA DQ2 and HLA DQ8 alleles (95% and 5%, respectively). However, these alleles are present in up to 55% of the Australian population and are therefore unhelpful in screening.² The aim of this study was to combine HLA susceptible genotype and tissue transglutaminase (tTG) antibody levels to estimate the prevalence of CD in the Hunter region of New South Wales, Australia.

Methods: The Hunter Community Study has collected data (2004–2007), including tTG titers and HLA genotypes, from over 2500 individuals aged 55–85 years. Individuals were excluded from analysis if they had an immunological disease that affected known auto-antibody titers, such as rheumatoid arthritis, or if the data were incomplete. Our hospital laboratory reports a combined tTG IgA/IgG result. Positive tTG serology was defined as a level of 30 U/mL or above.³ HLA genotyping was performed using an Affymetrix Kaiser Axiom array to locate single nucleotide polymorphisms (SNPs) on chromosome 6. Single SNPs were used to locate HLA DQ2.5 and DQ8. Three SNPs were selected for tagging the HLA DQ2.2 haplotype, and haplotype phasing for the three DQ2.2 tag SNPs was performed using SHAPEIT software. Those who were HLA DQ2- or DQ8-negative were classified as not having an at-risk genotype.

Results: Complete results were obtained from 2076 patients. Of these, 60.3% (95% CI, 58.3%–62.5%) had a susceptible genotype, testing positive for HLA DQ2.2, 2.5, or DQ8 (alone or in combination), and 6.02% (95% CI, 5.00%–7.04%) had positive tTG serology. Of those with an at-risk genotype, 4.34% (95% CI, 3.46%–5.21%) had positive serology for CD.

Conclusions: We report a prevalence of at-risk cases of CD in the Hunter region of Australia of 4.34% based on positive serology and HLA genotype. Our reported prevalence of positive tTG serology of 6.02% is significantly higher than previous local studies, which have reported positive tTG serology in only 1.56% of the population.¹ Using a tTG cut-off of 30 U/mL has been shown to have a positive predictive value of 80% at endoscopy for the diagnosis of CD.⁴ This suggests that the prevalence of CD may be one in 29 in a representative sample of older Australian adults. This prevalence estimate is significantly higher than that previously reported in Australia and elsewhere in the world, and suggests

that the incidence of CD is increasing. Cases should be actively sought to prevent long-term complications such as osteoporosis, particularly in an elderly population subject to falls.

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Does stress ulcer prophylaxis in critically ill patients reduce gastrointestinal bleeding? A meta-analysis of randomized controlled trials

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Introduction: Stress ulcer prophylaxis (SUP) using a proton pump inhibitor (PPI) or H2-receptor blocker (H2RA) is widely used in critical care settings all over the world. Several randomized controlled trials testing the efficacy of SUP have measured gastrointestinal bleeding as an outcome, and we wanted to obtain collective evidence of whether SUP, leading to reduced gastric acid secretion, has a protective effect on gastrointestinal bleeding.

Methods: The literature search was done using electronic databases including PubMed, Cochrane Library, and Embase from inception until March 2017. We isolated 23 randomized controlled trials that measured gastrointestinal bleeding as an outcome and extracted relevant data. Statistical analysis was done using Rev Man 5.3.

Results: A total of 23 randomized controlled trials measuring gastrointestinal bleeding as an outcome were included. There were a total of 1802 patients in the intervention group and 1665 in the control group, with 112 patients developing gastrointestinal bleeding in the study group and 235 in the control group. Overall, SUP did significantly reduce the occurrence of gastrointestinal bleeding in critically ill patients (odds ratio, 0.36; 95% CI, 0.28–0.46; $P < 0.00001$; $I^2 = 49\%$) compared with the control group. Due to the increase in the use of PPI in recent times, we did a subgroup analysis separating patients who received H2RA alone and those who received PPI alone or in combination with H2RA, which showed 81 of 1367 and 183 of 1365 gastrointestinal bleeding events in the H2RA and control groups, and 30 of 390 and 31 of 243 in the PPI+H2RA and control groups, respectively.

Conclusion: Our large meta-analysis demonstrates a significant reduction in the occurrence of gastrointestinal bleeding in critically ill patients with the use of SUP. Hence, we strongly recommend the use of SUP in critically ill patients with appropriate clinical indications. Though the study results are statistically significant, there are some limitations to this study: the definition of gastrointestinal bleeding was different in different randomized controlled trials; and head-to-head trials were not included. More high-powered trials with PPI need to be done to identify the efficacy of newer PPI, which are now widely used.

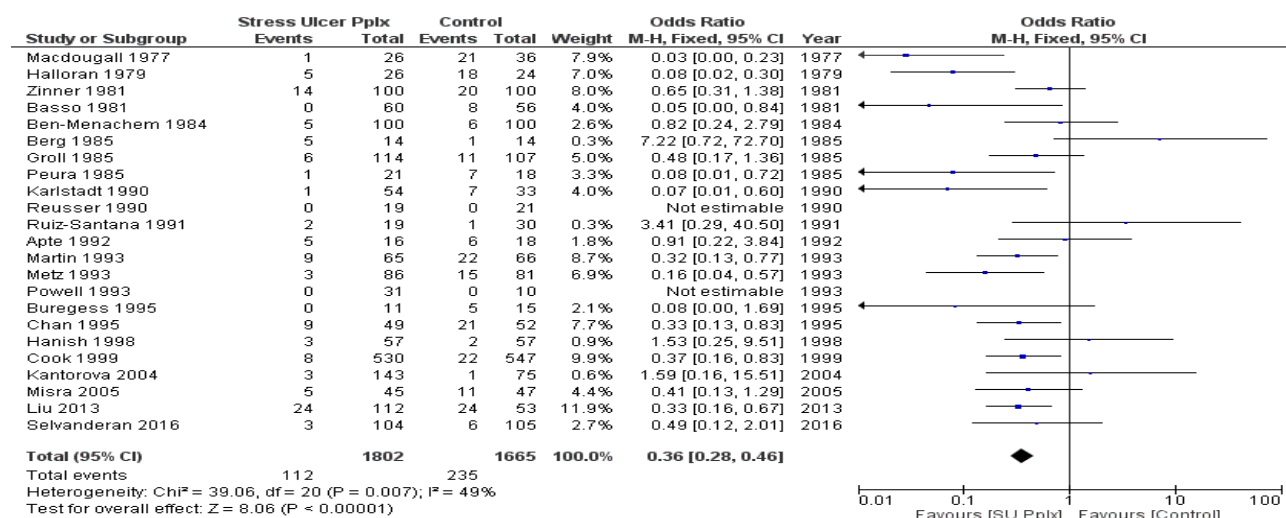


Figure 1 Forest plot showing effects of stress ulcer prophylaxis on gastrointestinal bleeding in critically ill patients

Mucosal bridge from small intestinal amyloid

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Introduction: Amyloidosis is characterized by the extracellular deposition of an abnormal fibrillar protein (AA and AL), which disrupts tissue structure and function. It can be hereditary or acquired, and amyloid deposition can be localized or systemic, which will ultimately determine the phenotypical manifestations within an individual. The diagnosis of gastrointestinal amyloidosis is difficult because of the variable clinical manifestations and the non-specific nature of endoscopic findings. This is a case report of a 55-year-old man with chronic anemia who presented with massive bleeding due to gastrointestinal amyloidosis, with balloon enteroscopy revealing an unusual finding.

Case Report: Our patient was a 55-year-old man who presented with iron deficiency anemia and intermittent melena. His past medical history included a cholecystectomy in 1997, with ongoing low-grade persistent right upper quadrant and epigastric pain. Gastroscopy revealed a small peri-ampullary submucosal nodule. Colonoscopy was non-contributory, and capsule endoscopy showed possible submucosal deposits in the ileum. Biopsy of the peri-ampullary nodule was strongly positive for amyloid P, and immunohistochemistry revealed strong staining for lambda light chain, with only patchy positivity for kappa light chain, suggesting AL amyloid. Investigations for systemic amyloidosis were negative. He was treated with five cycles of melphalan; however, chemotherapy was ceased early due to the increased frequency of gastrointestinal bleeding. He was maintained on regular parenteral iron infusions and tranexamic acid for the next 3 years.

Subsequently, he presented with a large gastrointestinal bleed (hemoglobin, 75 g/L) and underwent an emergent antegrade double balloon enteroscopy (DBE). At about 2.8 m past the pylorus, there was a large submucosal 2 cm lesion with an actively bleeding ulcer on its surface, which was treated endoscopically. There were multiple ulcerated polypoid lesions (ranging from 5 to 20 mm long) throughout the jejunum. An unusual appearing mucosal bridge was also noted (Figure 1). Histological confirmation of amyloid deposition in the submucosa and within vascular channels in these jejunal lesions was made on biopsies.

Conclusion: Mucosal bridges have most often been observed in the colon, associated with inflammatory bowel disease, and in the oesophagus, associated with reflux oesophagitis.^{1,2} Our case of a mucosal bridge in the jejunum due to amyloidosis is a rare finding that has not been previously reported in the literature. Its formation likely represents the attachment of the free end of a polyp to the adjacent mucosa; however, the pathogenesis of mucosal bridges remains unclear.

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Figure 1.

Author

Baseline characteristics and clinical response to teduglutide in patients with short bowel syndrome based on residual bowel anatomy

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Introduction: Intestinal failure associated with short bowel syndrome (SBS–IF) arises from different etiologies, resulting in a heterogeneous population. This is a post hoc analysis of patients with SBS–IF based on residual bowel anatomy.

Method: STEPS (NCT00798967; EudraCT 2008-006193-15) was a 24-week, placebo-controlled study of teduglutide (TED) 0.05 mg/kg/day in patients with SBS–IF. Three groups were evaluated: Group 1 (no colon/stoma present/no colon-in-continuity), Group 2 ($\geq 50\%$ colon/no stoma/colon-in-continuity), and Group 3 (other bowel anatomies). Clinical response was defined as $\geq 20\%$ reduction from baseline in weekly parenteral support (PS) volume at Weeks 20–24. Data are presented as mean (SD).

Results: Baseline patient details are shown in Table 1. TED-induced PS volume reduction (change in litres/week) took longer to be realized in Group 2 (Week 12: -0.9 [1.2], Week 24: -2.5 [2.1]) *versus* Group 1 (Week 12: -5.5 [3.8], Week 24: -6.4 [4.5]) or Group 3 (Week 12: -2.7 [1.2], Week 24: -5.1 [3.7]). Response rates were higher with TED *versus* placebo in all groups, but the difference was significant only in Group 1 (76% vs 19%, $P = 0.001$; Group 2: 56% vs 40%, $P = 0.36$; Group 3: 57% vs 29%, $P = 0.33$). Adverse events were reported by 94% (Group 1), 72% (Group 2), and 86% (Group 3) of TED patients.

Conclusion: Patients with SBS–IF in Group 1 had the highest baseline PS volume needs and responded most and fastest to TED with PS volume reductions compared with patients in Group 2 or Group 3.

Conflict of interest: This research was funded by Shire International GmbH, Zug, Switzerland.

Table 1 Baseline patient characteristics

	Group 1		Group 2		Group 3	
	TED ($n = 17$)	Placebo ($n = 16$)	TED ($n = 18$)	Placebo ($n = 20$)	TED ($n = 7$)	Placebo ($n = 7$)
Cause of SBS–IF, %						
Crohn's disease	53	44	0	0	14	14
Vascular complications	12	13	50	65	29	14
Other	35	44	50	35	57	71
Colon-in-continuity, %	0	0	100	100	100	100

Stoma present, %	100	100	0	0	57	14
Ileocecal valve present, %	0	0	17	40	0	14
Mean (SD) estimated remaining small bowel length, cm	137.7 (70.9)*	113.7 (79.8)*	52.2 (27.4)	39.2 (30.4) [†]	59.3 (44.4) [‡]	49.3 (30.0) [‡]
Mean (SD) PS volume, L/week	14.5 (9.6)	18.8 (7.9)	10.6 (5.8)	10.5 (5.3)	12.4 (7.1)	9.1 (3.9)

* $n = 15$; [†] $n = 19$; [‡] $n = 6$.

No role for routine duodenal biopsy in the evaluation of patients with unexplained anemia

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Background: Gastroscopy is frequently performed for investigation of unexplained anemia, and small bowel biopsy (SBBx) is routinely recommended to exclude celiac disease. This approach may not be cost-effective, given increasing evidence that celiac serology and advanced endoscopic imaging may be sufficiently sensitive to exclude celiac disease.¹⁻⁵

Aims: To determine the yield of routine duodenal biopsies in a large cohort of patients who had endoscopy for investigation of anemia.

Methods: Data of consecutive patients who underwent gastroscopy for investigation of anemia in a tertiary hospital, from January 2008 to December 2011, were prospectively collected. Patients' demographics, complete blood count, celiac antibody status, iron studies, endoscopic findings and small bowel histology were recorded. Measured outcomes were the incidence of celiac disease, the yield of duodenal biopsies, and the correlation between celiac serology and diagnosis.

Results: Over 4 years, 987 patients (385 male, 602 female; aged 48 ± 15 years) underwent endoscopy for investigation of anemia, of whom 534 had proven iron deficiency anaemia (IDA) and 453 had non-IDA. Abnormal SBBx consistent with celiac disease was found in 2% ($n = 22$) of the cohort, with significantly higher prevalence in the IDA (19/534; 3.7%) than non-IDA group (3/453; 0.6%), $P = 0.002$). Multivariate analyses indicate that female patients under the age of 50 years had the highest incidence of celiac disease (5%), and no male patients with non-IDA had abnormal SBBx. Of the 178 patients who had concurrent celiac serology, transglutaminase antibody had the highest sensitivity (80%) and specificity (99%), compared with anti-gliadin (sensitivity, 67%; specificity, 96%) and anti-endomysial (sensitivity, 64%; specificity, 100%) antibodies. Combined serology was associated with a sensitivity of 86% and a negative predictive value of 98% (95% CI, 95%–100%). Endoscopic abnormalities suggestive

of celiac disease were more frequently found in patients with celiac disease (13/22; 59%) than those without (63/965; 6%) ($P < 0.001$). Of the nine celiac patients with normal endoscopic findings, six had positive celiac serology. The use of combined serology and endoscopic findings would identify 19 of 22 patients (87%) with celiac disease.

Conclusion: Only 2% of patients with unexplained anemia had abnormal SBBx consistent with celiac disease, and even fewer (0.6%) if the anemia was not related to iron deficiency. Given the 87% sensitivity of serology combined with endoscopic appearance, SBBx should be limited to patients who present with IDA, positive celiac serology and/or abnormal endoscopic appearance.

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