Gastroenterology Research Review™

Making Education Easy

Issue 121 - 2025

In this issue:

Abbreviations used in this issue:

CRC = colorectal cancer; **FMT** = faecal microbiota transplant; **GI** = gastrointestinal; **IBD** = inflammatory bowel disease; **PPI** = proton-pump inhibitor; **UC** = ulcerative colitis.

Welcome to issue 121 of Gastroenterology Research Review.

We begin this issue with a systematic review and network meta-analysis of randomised controlled trials of therapies for *Clostridioides difficile* infections and their prevention. There are also two audits of local interest – one compared functional GI disorder management in South Australia against current guidelines, and the other reported on the characteristics and management of Australasian children with eosinophilic oesophagitis. We have also included results from a phase 2 trial of a novel system for medication delivery to the oesophagus, in this case steroids for eosinophilic oesophagitis. The issue concludes with a retrospective cohort study reporting that patients with IBD not only have higher rates of herpes zoster, but are also at increased risk of its complications.

We hope you enjoy this update in gastroenterology research, and we look forward to comments and feedback.

Kind Regards,

Dr Andrew Buckle
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Comparative effectiveness of different therapies for *Clostridioides difficile* infection in adults

Authors: Bednárik DS et al.

Summary: This was a systematic review with network meta-analysis of data from 73 randomised controlled trials (low-to-high risk of bias, with heterogeneity evident in terms of doses, treatment durations and doses, and follow-up times) assessing 28 interventions for *C. difficile* infection treatment or prevention in 27,959 individuals aged >16 years. The most effective treatment for achieving cure, including for *C. difficile* infection recurrence, was found to be FMT. For recurrent *C. difficile* infection, fidaxomicin showed superiority over vancomycin and tolevamer, whereas for nonrecurrent infections, equal efficacy was seen among FMT, ridinilazole, fidaxomicin and nitazoxanide. For prevention of recurrence, ridinilazole and fidaxomicin were found to be most effective, and although there was no significant difference detected between probiotics and placebo overall, subgroups pairwise meta-analyses identified *Lactobacillaceae* to be significantly better than placebo. For FMT effectiveness, there was no significant difference between oral and colonoscopic administration.

Comment: Our combined experience using FMT for *C. difficile* infection is growing, and by now we have all had excellent patient outcomes. Thankfully the process has been streamlined significantly with the availability of commercial FMT preparations, and long gone are the days of being a registrar blending and straining donor stool in a begged and borrowed fume hood in the microbiology department. Complications are somewhat uncommon but include sepsis, and the long-term risks, if any, are still to be determined. Understanding of what we are actually doing with FMT is also still in its infancy, with large-scale microbiome projects underway to determine if targeted approaches with select bacterial species can be successful. This paper is a systematic review and meta-analysis comparing treatment modalities for *C. difficile* infection, with FMT coming out on top, irrespective of delivery method.

Reference: Lancet Reg Health Eur 2025;49:101151

Abstract

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Faecal microbiota transplantation for patients with diabetes type 1 and severe gastrointestinal neuropathy (FADIGAS)

Authors: Høyer KL et al.

Summary: Twenty adults with type 1 diabetes and moderate-to-severe GI symptoms were evenly randomised to receive a single administration of 25 FMT or placebo capsules in this trial. There was no significant difference between the FMT and placebo arms for the primary endpoint of grade ≥2 adverse events, with four FMT recipients experiencing seven such events and five placebo recipients experiencing 19. Of the reported adverse events, none were serious and the most frequent were diarrhoea, bloating and abdominal pain. Compared with placebo, FMT was associated with significant improvements in median Gastrointestinal Symptom Rating Scale – Irritable Bowel Syndrome, Irritable Bowel Syndrome Impact Scale and Patient Assessment of Gastrointestinal Symptom Severity Index scores (p≤0.03).

Comment: Diabetic gastroenteropathy is an under-recognised condition; however, it is one we come across regularly as gastroenterologists. I tend to approach management similarly to complex irritable bowel syndrome, given a presumed microvascular neurogenic aetiology. This is an interesting Danish study taking a different approach with FMT, for presumed underlying dysbiosis. This was a pilot phase 2/phase 3 randomised trial, with the primary outcome safety and secondary outcome of symptom improvement. Although only a small pilot, the results are encouraging.

Reference: eClinicalMedicine 2025;79:103000
Abstract

Adenoma detection rates by physicians and subsequent colorectal cancer risk

Authors: Pilonis ND et al.

Summary: Associations of improved physician adenoma detection rates with patient CRC incidence were explored in 789 physicians from Poland who collectively treated 485,615 patients, among whom there were 1873 CRC diagnoses and 474 CRC-related deaths over a median 10.2 years of follow-up. The physicians' baseline median and maximum adenoma detection rates were 21.8% and 63.0%, respectively. A change in CRC incidence trends was evident at an adenoma detection rate of 26%, corresponding to a CRC incidence of 27.1 per 100,000 person-years. When physicians whose adenoma detection rate was <26% at baseline but improved during follow-up were compared with those with no improvement, their patients had a lower postcolonoscopy CRC incidence (31.8 vs. 40.7 per 100,000 person-years [p<0.001]), whereas there was no such difference for patients of physicians whose adenoma detection rate was >26% at baseline (23.4 vs. 22.5 per 100,000 person-years [p=0.80]).

Comment: This Polish study is intriguing, and suggests another potential quality indicator, or more accurately a quality-improvement indicator, for colonoscopy. GESA's conjoint colonoscopy recertification program allows us regular audit of our work, enabling comparison of adenoma detection rates to a minimum performance threshold and mean. Our epoch-to-epoch performance is not something that is emphasised in this program however. From this study an adenoma detection rate improvement over time appears to be important in reducing postcolonoscopy CRC rates, especially for underperforming proceduralists with low adenoma detection rates.

Reference: JAMA 2025;333:400–7
Abstract

Patients with functional gastrointestinal disorders spend less time in tertiary care when managed by a single clinician

Author: Mathias RM et al.

Summary: This multicentre audit from South Australia examined concordance of functional GI disorder management with current guidelines for 275 patients reviewed for the condition at one of two tertiary gastroenterology services during the 12 months beginning Jun 2021. Patients were diagnosed with a functional GI disorder in a median of 70 days and over a median of four outpatient encounters, and the overall in-service time was 182 days. The likelihood of an early diagnosis was increased when care was delivered by a single clinician rather than multiple clinicians (hazard ratio 1.6 [95% CI 1.25–2.04]), as was the likelihood of an earlier discharge (1.83 [1.44–2.33]); there was also a trend for less harmful investigations (odds ratio 1.79 [0.96–3.58]).

Comment: Care for complex functional gut patients can be challenging in the public system. Often there is no guarantee of seeing the same clinician clinic to clinic, leading to the same ground and investigations being covered time and time again. This can be frustrating for patients and at worse dangerous with repeated invasive procedures. Diagnoses can be missed or delayed, and this of course puts more pressure on an under-resourced system. This multicentre audit from South Australia demonstrated that single-clinician co-ordinated care improved time to diagnosis and discharge from hospital; however, there was no statistically significant decrease in harmful investigations.

Reference: Intern Med J 2025;55:260–9
Abstract

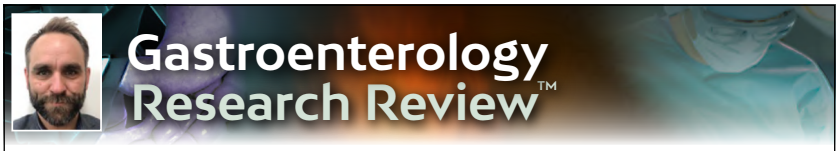
Characteristics and management of eosinophilic esophagitis in Australasian children

Authors: Philpott H et al.

Summary: This retrospective audit for the 10-year period starting Jan 2008 explored eosinophilic oesophagitis among paediatric patients from Australia and New Zealand. Across tertiary paediatric hospitals in seven Australasian cities, the prevalence of eosinophilic oesophagitis ranged from 15 to 54 per 100,000 children, with the cases greatest in Adelaide. There were significant increases in incidence over the 10 years seen at all sites, again with Adelaide having the greatest (6.4 per 100,000 children in 2017). There were three males with eosinophilic oesophagitis for every female, and >90% of the patients were white Caucasian, with Polynesians in Auckland and Middle Eastern race in Sydney the next most frequent, both at 10%. There was variation across sites in terms of treatment choice, and endoscopy was not performed to assess initial treatment success in >30% of patients.

Comment: This is a timely multicentre observational study of the trend in eosinophilic oesophagitis in children across Australia and New Zealand, impressive in its scope. The worldwide prevalence of eosinophilic oesophagitis is increasing, with data predominantly available from the northern hemisphere. This study showed a similar trend mirrored here. Demographics of those with the disease are not surprising, with Caucasian males making up the vast majority of patients. What is interesting is the heterogeneity of treatment choices across sites, as well as the relatively low rates of repeat endoscopy to check macroscopic and histological improvement with treatment, with clinicians presumably being guided by clinical symptoms.

Reference: Intern Med J 2025;55:284–9
Abstract



Independent commentary by Dr Andrew Buckle

Andrew Buckle is a Gastroenterologist and Hepatologist with the Launceston General Hospital. His clinical interest is gastro-oncology, with a specific focus on the management of gastroenterological hereditary syndromes, prevention of GI cancer and management of the complications of cancer therapy. He has a PhD in cell and molecular biology and a research interest in GI immunology.

Cost-effectiveness of Vibrant System vs. linaclotide in chronic idiopathic constipation

Authors: Voigt JD & Frissora CL

Summary: These researchers used Markov models to compare total costs and quality of life for vibrating capsules (Vibrant System) versus the standard-of-care pharmacological therapy, namely linaclotide, over 1–3 years of treatment for chronic idiopathic constipation. It was found that compared with linaclotide use, vibrating capsules were associated with lower direct costs and improved QALYs (quality-adjusted life-years) during years 1–3, and direct plus indirect cost savings of USD345–3866 and improved effectiveness during years 2–3.

Comment: Chronic idiopathic constipation is a common reason for referral to gastroenterologists, with females carrying the predominant burden. Options such as prucalopride are not covered by the PBS, and in combination with fibre and aperients can be expensive, onerous and intrusive on lifestyle. I've commented on the Vibrant vibrating capsule system trials in previous issues of Gastroenterology Research Review, which has been shown to be safe and effective in improving spontaneous bowel actions. Most importantly, it appears safe and well tolerated. It is expensive, however, and a source of e-waste. This paper shows the cost effectiveness in the US system, arguing for it to be covered by insurers. If it becomes available locally, I suspect it will have a niche but important role to play for patients.

Reference: Adv Ther 2025;42:310–21
Abstract

Management of patients with refractory reflux-like symptoms despite proton pump inhibitor therapy

Authors: Armstrong D et al., the International Working Group for the Classification of Oesophagitis (IWGCO)

Summary: This article reported on evidence-based consensus statements from the International Working Group for the Classification of Oesophagitis for guiding the care of patients with refractory reflux-like symptoms or refractory gastro-oesophageal reflux disease. Of 17 statements on diagnosis and management, consensus was reached for 13. Suggested strategies for diagnosing refractory reflux-like symptoms included endoscopy, ambulatory reflux testing and oesophageal manometry. Consensus could not be reached on the role of oesophageal biopsies or reflux-symptom association use in patients undergoing reflux testing. There was consensus against increasing PPI doses in patients who had already received 8 weeks of a PPI twice daily, with adjunctive alginate or antacid therapy suggested. No consensus was reached on the role of adjunctive prokinetics, and the roles for adjunctive transient lower oesophageal sphincter relaxation inhibitors and bile acid sequestrants were considered to be small. It was agreed that for patients with refractory reflux-like symptoms but without an objectively confirmed gastro-oesophageal reflux disease diagnosis, neither endoscopic nor surgical antireflux procedures should be performed.

Comment: This paper covers Canadian consensus guidelines for managing refractory reflux symptoms. They are largely what one would expect, recommending the use of PPIs, PPI adjuncts such as histamine-2 receptor antagonists and alginates, along with the use of endoscopy, ambulatory pH testing and manometry prior to consideration of gastric surgery. I certainly think guidelines such as these are important, as anecdotally, I commonly see large heterogeneity in how patients are managed and considered for surgery. This appears highly dependent on the managing clinician, and most discordant between upper GI surgeons and gastroenterologists.

Reference: Aliment Pharmacol Ther 2025;61:636–50
Abstract

Clinical trial: safety and efficacy of a novel oesophageal delivery system for topical corticosteroids versus placebo in the treatment of eosinophilic oesophagitis

Authors: Lucendo AJ et al.

Summary: Adults with eosinophilic oesophagitis were randomised to a thin mucoadhesive film designed to target the oesophageal mucosa, named 'EsoCap', either loaded with mometasone furoate 800µg ('ESO101'; n=28) or placebo (n=15) once daily for 28 days in this phase 2 proof-of-concept trial. Compared with placebo EsoCaps, use of ESO-101 resulted in greater reduction in mean eosinophils per high-power field from baseline (primary outcome; 49.1 vs. 6.6 [p=0.03]) with greater proportions of participants achieving <15 and <6 eosinophils per high-power field (48% vs. 0% and 44% vs. 0%, respectively), as well as a significant reduction in EREFS endoscopic reference score for eosinophilic esophagitis. There was no significant between-group difference for decreases in dysphagia or odynophagia severity. Mean serum cortisol levels did not change significantly and there were no serious treatment-emergent adverse events during the trial; however, there were cases of oropharyngeal or oesophageal candidiasis.

Comment: This paper outlines the use of an interesting novel technology for the delivery of topical medications to the oesophagus. EsoCap is a thin film that adheres to the oesophagus, which can be impregnated with target drug for direct topical therapy. It is ingested in a capsule and unfurls as it passes down the oesophagus. In the context of this phase 2 study, EsoCap with mometasone was investigated for the treatment of eosinophilic oesophagitis. This is an interesting delivery mechanism, and one could see how this could be used for other medications to target the oesophageal mucosa.

Reference: Aliment Pharmacol Ther 2025;61:444–55
Abstract

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Risk factors and clinical characteristics of *Clostridium difficile* colonization and infection in patients with inflammatory bowel disease exposed to vedolizumab

Authors: Li Q et al.

Summary: This retrospective study reported on the incidence of and risk factors for the emergence of *C. difficile* colonisation or infection in 454 real-world patients with IBD treated with vedolizumab and followed for a median of 12.9 months. *C. difficile* colonisation occurred in 6.2% of the patients, including 11.4% with UC, consisting of 18 who were asymptomatic carriers and five with symptomatic infection, and 2.0% of patients with Crohn's disease, all five of whom were asymptomatic carriers. Independent risk factors for the emergence of *C. difficile* colonisation after vedolizumab initiation were age >40 years old and having UC. Regarding infection with *C. difficile*, this occurred in 1.1% of the patients (none severe), all of whom continued vedolizumab therapy after receiving antibiotics; there were no risk factors significantly associated with the development of *C. difficile* infection.

Comment: Patients with IBD are at higher risk of *C. difficile* infection, and in the vedolizumab GEMINI long-term safety cohort, *C. difficile* infection was the most common opportunistic infection. This study looked at *C. difficile* colonisation rates in individuals with IBD following vedolizumab exposure, which was fairly high at 6.2%, and more common in individuals greater than 40 years of age and with UC. This of course raises questions if high rates of colonisation are due to a direct effect of vedolizumab exposure and altered mucosal immunological function, or simply secondary to regularly attending healthcare centres for infusions. It will be interesting if *C. difficile* colonisation rates fall as subcutaneous vedolizumab use increases.

Reference: Therap Adv Gastroenterol 2025;18:doi:10.1177/17562848251321707
Abstract

Patients with inflammatory bowel disease are at increased risk for complications of herpes zoster

Authors: Caldera F et al.

Summary: The frequency of herpes zoster complications in 4756 patients with IBD versus the same number of matched individuals without IBD was evaluated in this retrospective cohort study. Compared with controls, patients with IBD were more likely to experience herpes zoster complications (15.52% vs. 12.51% [p<0.0001]), particularly those with higher comorbidity scores, those aged >50 years and those receiving tumour necrosis factor inhibitors or corticosteroids.

Comment: It is well established that patients with IBD are at higher risk of herpes zoster, with IBD treatments further compounding the issue. We know the risk from corticosteroids, and more recently zoster has been at the forefront of our minds with the PBS inclusion and growing use of Janus kinase inhibitors. For patients with IBD who unfortunately develop herpes zoster, this study showed that they are also at increased risk of complications such as postherpetic neuralgia, disseminated disease and hospitalisation compared with matched controls. I'm sure we are all prescribing it regularly now, but this serves as a good reminder of the importance of the recombinant zoster vaccine.

Reference: Clin Gastroenterol Hepatol 2025;23:331–40.e2
Abstract

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