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The role of faecal microbiota transplantation in the treatment of inflammatory bowel disease
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Purpose of the review
Faecal microbiota transplantation (FMT) has emerged as a potent form of therapeutic microbial manipulation. There is much interest in exploring its potential in conditions such as inflammatory bowel disease (IBD) where disturbances in the gastrointestinal microbiota play a crucial role in disease pathogenesis. Recent findings
There are 4 randomized controlled trials of FMT as induction therapy in ulcerative colitis, with meta-analyses suggesting significant benefit over placebo. Allied microbial studies have identified potential microbial and metabolic predictors of therapeutic efficacy and highlighted the importance of optimizing future donor and patient selection. Recent literature has evaluated the use of complementary microbial manipulation through pre-antibiotics to improve treatment efficacy. Studies have also assessed the durability of FMT response and its use in maintenance therapy of UC. While data on FMT are more limited in Crohn’s disease and pouchitis, cohort and pilot randomized controlled data are now also emerging in these areas.

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Introduction
Faecal microbiota transplantation (FMT), the introduction of a faecal suspension derived from a healthy donor(s) into the gastro-intestinal (GI) tract of a patient with disease, is a promising therapeutic option for inflammatory bowel disease (IBD). It represents a non-immunosuppressive treatment that attempts to address the microbial disturbances underlying the disease pathogenesis [1]. A key advantage of FMT over other forms of therapeutic microbial manipulation (such as antibiotics, probiotics, prebiotics) is that it provides an entire functional ecosystem comprising the full spectrum of microbial organisms from a healthy individual and can therefore potentially correct as yet uncharacterised dysbiosis and functional disturbances critical to IBD pathogenesis [2]. FMT is becoming more widely recognized and accepted due to increasing use in the management of Clostridiods difficile infection (CDI) [3].

The past few years have seen significant advances in the use of FMT in IBD. Here we will review the key existing and developing evidence in this emerging field.

Faecal microbiota transplantation for the treatment of C. difficile infection in patients with underlying inflammatory bowel disease
FMT has emerged as the most effective treatment for recurrent CDI with a success rate of around 90% [4], and is acknowledged as the standard of care by multiple national and international consensus groups [5,6]. CDI is more prevalent in patients with underlying IBD and is associated with disease recurrence, more severe disease course, longer duration of hospitalisation and higher rates of colectomy and mortality [7]. FMT remains an effective treatment for patients with CDI and underlying IBD, although efficacy may be slightly lower than in patients without IBD [8]. A cohort of CDI patients treated with FMT suggested that the presence of IBD was associated with reduced chance of clinical success (74.4% versus 92.1% p = 0.0018) and a subsequent systematic review showed a pooled initial cure rate of 81% [9,10]. In the setting of IBD, early assessment of response and repeated FMT infusions may be required to increase the overall resolution rate, with severe endoscopic disease being the most useful predictive marker of treatment failure [11].

The underlying disease course of IBD is variable following FMT with a few uncontrolled studies suggesting worsening of disease in some patients; [9] however, it remains unclear whether this is attributable to the FMT, or rather reflects that CDI co-infection is a poor prognostic marker of underlying IBD disease course. In the largest cohort of 67 IBD patients co-infected with...
| Author          | Patients | Patient selection | Dosage | Treatment regimen [route of administration, frequency and interval] | Primary endpoint | Clinical remission | Endoscopic remission | Controlled follow up; final follow up (if reported) |
|-----------------|----------|-------------------|--------|-------------------------------------------------|------------------|-------------------|---------------------|-------------------------------------------------|
| **UC remission induction** |          |                   |        |                                                 |                  |                   |                     |                                                 |
| Rossen et al. [16] | 48: 23 FMT, 25 control autologous stool | Mild-moderate UC [SCCAI 4–11] | 60 g stool in 500 ml | 2 nasoduodenal infusions 3 weeks apart | Clinical remission and endoscopic improvement at week 12; 7/23 [30%] versus 5/25 [20%] \( p = 0.51 \) | 7/23 [30%] versus 8/25 [32%] \( p = NS \) | NR                  | 12 weeks                          |
| Moayeddi et al. [15] | 75: 38 FMT, 37 Placebo controls | Mild to severe UC [Mayo 4–12] | 50 g stool in 50 ml infusion | Weekly enemas for 6 weeks | Clinical and endoscopic remission at week 7; 9/38 [24%] versus 2/37 [5%] \( p = 0.03 \) | 9/38 [24%] versus 2/37 [5%] \( p = 0.03 \) | 7 weeks; 52 weeks |                     |
| Paramsothy et al. [17] | 81: 41 FMT, 40 Placebo controls | Mild to moderate UC [Mayo 4–10] | 37.5 g stool in 150 ml saline | Colonoscopic infusion followed by enemas 5× per week for 8 weeks | Steroid-free clinical remission and endoscopic improvement at week 8; 11/41 [27%] versus 3/40 [8%] \( p = 0.02 \) | 18/41 [44%] versus 8/40 [20%] \( p = 0.02 \) | 5/41 [12%] versus 3/40 [8%] \( p = NS \) | 16 weeks                          |
| Costello et al. [18] | 73: 38 FMT, 35 control autologous stools | Mild to moderate [Mayo 3–10] | 50 g stool in 200 ml for colonoscopy then 25 g stool in 100 ml for enema | Colonoscopic infusion followed by 2 enemas in 1 week | Steroid-free clinical and endoscopic improvement at week 8; 12/38 [32%] versus 3/35 [9%] \( p = 0.03 \) | 18/38 [55%] versus 8/35 [23%] \( p = 0.007 \) | 4/38 [11%] versus 0/35 [0%] \( p = 0.12 \) | 8 weeks; 52 weeks |
| Crothers et al. [23] | 15: 7 FMT, 8 placebo control | Mild to moderate [Mayo 4–10] | 50 g stool in infusion 0.375 g in each capsule. | Colonoscopy followed by 1× capsule daily for 1 week | NR | 2/7 [29%] versus 1.8 [13%] \( p = NS \) | NR | 12 weeks                          |
| **UC remission maintenance** |          |                   |        |                                                 |                  |                   |                     |                                                 |
| Sood et al. [34] | 61: 31 FMT, 30 placebo | UC in clinical remission following induction FMT | 100 g in 200 ml saline | Colonoscopic infusion every 8 weeks for 48 | Steroid free clinical remission at week 48; 27/31 [87.1%] versus 20/30 [66.7%] \( p = 0.111 \) | 27/31 [87.1%] versus 20/30 [66.7%] \( p = 0.111 \) | 18/31 [58.1%] versus 8/30 [26.7%] \( p = 0.026 \) | 48 weeks                          |
| Sokol et al. [42] | 21: 11 FMT, 10 placebo | CD in clinical remission [HBI <5] within 3 weeks of oral corticosteroids | 50–100 g in 250–350 ml | Single colonoscopic infusion | Successful colonisation of donor microbiota at week 6 [Sorensen’s index >0.6]; 0/11 [0%] versus 0/10 [0%] | 7/8 [87.5%] versus 4/9 [44%] \( p = 0.23 \) | NR | 24 weeks                          |
| Herfarth et al. [46] | 6: 4 FMT, 2 placebo | Antibiotic dependant proctitis | 24 g of stool in 2× 30 ml enema; 4.2 g stool in 6 capsule | 2× enemas followed by 6 capsules daily for 14 days | Safety, NR | 0/4 [0%] versus 0/2 [0%] \( p = NS \) | NR | 16 weeks                          |

NR, not recorded; SCCAI, simple Clinical Colitis Activity Index; HBI, Harvey Bradshaw Index; NS, not significant; NR, not reported.
CDI, after FMT IBD disease activity was reported as improved in 25 (37%), no change in 20 (30%), and worse in 9 (13%) patients through a combination of clinical assessments and biomarkers of disease activity [12\(^*\)]. Reassuringly, any potential disease worsening is usually transient and should not impact the decision to use FMT in this cohort [5\(^*\),11,12\(^*\),13,14].

**Faecal microbiota transplantation for the treatment of ulcerative colitis**

**Induction of remission**

There is substantial evidence for the use of FMT in the induction of remission of mild to moderate UC, including multiple cohort studies and four randomised controlled trials (RCT) incorporating strict steroid-free clinical and endoscopic endpoints, three of which demonstrated significant benefit over placebo (Table 1) [15,16,17\(^*\),18\(^*\)]. Meta-analyses of the 140 FMT treated patients included in the RCTs showed that FMT was significantly associated with clinical remission in these patients [OR = 2.89, 95% CI 1.36–6.13, \(p = 0.006\)] with a number needed to treat of 5 [19\(^*\)]. There are many factors that are known or suspected to influence FMT efficacy (Figure 1).

**Route of administration and optimal dosing intensity**

The optimal route of administration and dosing regimen is still unknown with each RCT utilizing different FMT production methods and treatment protocols with varying dosing intensity. The one RCT that did not meet its primary endpoint was the only to utilize upper GI infusions [16], with a subsequent meta-analysis suggesting the superiority of lower GI administration [19\(^*\)]. The largest RCT to date is the FOCUS study which used an intensive protocol of initial colonoscopic FMT followed by enema therapy 5 times per week for 8 weeks [17\(^*\)]. More recently, Costello et al. used a significantly less intensive regimen with initial colonoscopic infusion followed by only two enemas with similar efficacy [18\(^*\)].

FMT encapsulation through liquefying, freezing or lyophilisation has more recently emerged, enabling oral administration which can provide a safe, consistent, and more widely accessible treatment that may also suitable for maintenance therapy. Oral encapsulated FMT has proven clinical efficacy in recurrent CDI [20–22]. Data using oral FMT in UC are limited but a recent small pilot study was presented of 15 UC patients using colonoscopic FMT followed by oral lyophilized FMT capsules for 12 weeks was associated with increased rates of clinical response (29% versus 0%) and endoscopic response (43% versus 0%) when compared with placebo [23].

**Donor selection and multi-donor FMT**

Unlike CDI, where high treatment efficacy makes donor selection less important, individual donor characteristics likely play a significant role in FMT treatment outcomes in UC. While not formally assessed, there may be a theoretical advantage in using unrelated rather than related donors in IBD to avoid potential shared genetic and environmental determinants of the gastrointestinal microbiota. In the RCT by Moayeddi et al. post-hoc analyses showed that FMT from a particular donor was associated with a non-significant trend (\(p = 0.06\)) towards higher response rates compared to FMT derived from the other donors [15].

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*Factors that may influence FMT efficacy in IBD.*
There is considerable interest in determining what makes a ‘good’ donor, although recent analyses have suggested the concept of a universal ‘super donor’ should not be overstated [24]. Phenotypic donor characteristics including age and diet may play a role. More importantly, donor microbial profile is likely key with some studies identifying improved FMT outcomes with increased donor microbial diversity [24]. The FOCUS study [17**] and then the trial by Costello et al. [18**] utilised a novel multi-donor approach to increase microbial and associated functional diversity as well as to minimise the potential detrimental impact of any individual ‘suboptimal’ donor. Indeed, microbial analyses from the FOCUS study showed that UC patients receiving multi-donor FMT attained and sustained microbial alpha diversity levels equivalent to that of the individual healthy donors, though less than that of the multi-donor batch itself.

**Fresh versus frozen FMT and the role of anaerobic processing**

There are no data in IBD comparing fresh versus frozen FMT but data in CDI patients did not identify a difference in efficacy or safety [25]. Many colonic bacteria shown to be associated with improved outcomes in IBD such as Faecalibacterium prausnitzii are obligate anaerobes that may be reduced with aerobic FMT processing [26]. It has, therefore, been suggested that producing FMT using an anaerobic technique could further enhance clinical efficacy in UC. This technique was employed by Costello et al. in a low intensity FMT regimen, which may explain the similar results seen compared with the more intensive regimens used previously [18**]. However, other donor and patient confounders cannot be excluded so controlled research assessing anaerobic versus traditional FMT processing is required to determine whether using this technique leads to improved outcomes.

**Complementary microbial manipulation**

Complementary microbial manipulation with pre-treatment antibiotics is hypothesized to improve clinical efficacy of FMT in UC by reducing the host dysbiotic bacterial load, thus creating an ecological niche for donor microbiota engraftment and subsequent colonisation. A meta-analysis specifically investigating antibiotics before FMT for treatment of UC suggested that antibiotics were associated with higher rates of clinical remission (54% versus 25% \( p = 0.03 \)); however, there were significant limitations due to the lack of RCT evidence and heterogeneity in study design [27].

An important, and as yet unanswered, question is which antibiotic combination to use. Microbiome analysis from clinical trials of FMT in UC has provided further insight into certain detrimental bacterial groups that may inform antibiotic selection. In the FOCUS study, the presence of Fusobacterium in the recipient was strongly associated with non-response to FMT therapy [28**]. The pathogenic role of these bacteria has previously been suggested. In one study, twenty patients with UC and antibodies to Fusobacterium varius were treated with a combination of antibiotics (amoxicillin, metronidazole and fosfomycin) targeted towards Fusobacteria and had improvement in endoscopic and histological disease activity scores compared to the control group, with prolonged remission out to 14 months even after therapy cessation [29]. More recently, a combination of antibiotics with similar spectrum of activity was assessed before FMT in a cohort study of 21 patients with UC with an antibiotic only control group. Antibiotic pre-treatment reduced the abundance of pro-inflammatory bacteria and was associated with high rates of clinical response (82.3%) and clinical remission (52%) [30*].

**Paediatric UC**

Some have postulated that paediatric patients could be more suitable for FMT as their GI microbiome may be more susceptible to engraftment than adults with longstanding disease and ‘resilient dysbiosis’. However, despite the first cohort study of FMT in IBD involving a paediatric cohort [31], data on FMT in the paediatric setting are limited. The results of the first pilot RCT in paediatric UC were recently presented [32*]. Twenty-five patients with UC were randomized to twice weekly enema therapy or placebo for 6 weeks and showed improved biochemical markers (CRP, faecal calprotectin) at six weeks with trends towards improved clinical response. Additional larger studies are required to definitively determine the role of FMT for UC in children.

**Durability and maintenance of remission**

The durability of a response following FMT therapy in UC is unclear with only a few publications reporting uncontrolled long-term outcomes.

Two of the RCT’s assessing the induction of remission in UC reported one-year outcomes of those patients who met the week 8 primary outcome. Costello et al. reported that 5 of the 12 (42%) patients who achieved steroid-free clinical and endoscopic remission following donor FMT maintained remission at 12 months [18**]. Moayyedi et al. reported that 8 out of 9 patients maintained clinical remission at 9–12 months, although some patients did receive interval monthly FMT therapy [15].

A subgroup analysis of a Japanese cohort study of UC patients treated with FMT following pre-antibiotics showed that 33% (\( n = 10 \)) had clinical durability of initial response out to 24 months and suggested that recipients of donors who were of a similar age may have higher durability rates [33].

With reference to available data, it is evident that some form of maintenance microbial therapy will be required to
sustain remission, whether that could be achieved through diet or further FMT. There is only a single RCT on the use of FMT for maintenance of remission in UC, assessing 61 patients who achieved clinical remission following intensive FMT induction. Patients were then randomized to receive either 8 weekly colonoscopic FMT or placebo infusions for 48 weeks. The primary outcome of clinical remission was numerically higher in the FMT group, however, did not meet statistical significance (58.1% versus 26.7%, p = 0.11). Secondary endpoints including endoscopic and histological remission were significantly greater in the FMT group (p = 0.026 and p = 0.033 respectively), suggesting maintenance FMT may be efficacious in sustaining remission [34**]. While an interesting proof of concept, regular colonoscopic FMT is resource intensive and not a feasible option for routine clinical use, so larger maintenance studies utilizing other more practical long-term routes of administration (especially oral administration) are required.

**Microbial impacts on disease response**

Microbial analysis of samples from clinical studies of FMT provides valuable insights on the impact of FMT on the microbiome and potential mechanisms of action. Studies have consistently shown that microbial diversity increases following FMT, and some suggest that greater recipient microbial diversity levels (pre and post FMT) are associated with response [17**]. More important, however, is developing an understanding of microbial associated metabolic and functional profiles that determine therapeutic outcomes. In the FOCUS Study, on metagenomic and metabolomic analyses patients in remission after FMT had enrichment of *Eubacterium hallii* and *Roseburia inulicorns* and had increased levels of short-chain fatty acid biosynthesis and secondary bile acids. Meanwhile, patients who did not achieve remission had enrichment of *Fusobacterium, Sutterella* and *Escherichia* species and increased levels of heme and lipopolysaccharide biosynthesis [28**]. While the specific microorganisms varied, analysis of the Rossen *et al.* trial cohort found that sustained remission was also associated with restoration of butyrate production capacity [35]. It is likely that the resultant functional changes are more important in determining outcome than the precise microbial shifts, given inter-individual microbial variation and inherent microbial metabolic redundancy.

While there is a growing appreciation of the importance of the non-bacterial components of the microbiome, such as viruses and fungi, in health and disease, their role in UC pathogenesis and FMT outcomes are less well understood. Leonardi *et al.* suggested fungal trans-kingdom dynamics may be of importance in FMT outcomes in UC. In particular, they found that pre-FMT *Candida* associated with bacterial diversity and genera linked to responsiveness and demonstrated a fall in *Candida* species in responders post FMT [36*]. With respect to the virome, analyses from a small cohort study of 9 UC patients suggested that while no difference was identified in the phageome, low eukaryotic viral richness associated with FMT success [37*].

**Faecal microbiota transplantation for the treatment of Crohn's disease**

The literature on FMT in Crohn’s disease (CD) is limited and varied. Patients with CD demonstrate marked differences in disease distribution and clinical phenotypes, each with likely differing responsiveness to FMT. To date, there have been no powered RCTs of FMT in CD. Clinical remission rates in uncontrolled cohort studies and case series have varied greatly from 0 to 76% [24,38–40]. A meta-analysis of 6 cohort studies (71 patients) determined the pooled proportion of CD patients achieving clinical remission with FMT was 52% (95% CI 31–72%) with significant heterogeneity and publication bias [19].

Durability and maintenance of response in CD has been assessed in 2 recent pilot studies. An uncontrolled prospective cohort study showed a median clinical response time of 125 days following a single colonoscopic FMT infusion, at which point 63% of patients were able to maintain clinical response for a further 125 days with a second FMT treatment [41]. A pilot RCT of 17 CD patients used FMT (*n* = 8) or placebo (*n* = 9) to maintain remission after recent CD flare treated with corticosteroids. Clinical remission rate at 10 and 24 weeks in the FMT arm was 87.5% (7/8) and 50% (4/8) respectively, while endoscopic disease activity decreased following FMT (*p* = 0.03) [42*]. However, no patients met the primary endpoint of donor microbial engraftment with a Sorensen index >0.6.

**Faecal microbiota transplantation for the treatment of pouchitis**

Despite pouchitis being extremely responsive to microbial manipulation therapy with antibiotics, the data for the use of FMT in this condition are limited [43]. A few small cohort studies have been conducted, all utilising different treatment regimens with significant variation in response rates. In the most promising cohort study that delivered multiple FMT infusions via the upper gastrointestinal system, 4/5 patients achieved clinical remission and the remaining patient had a clinical response [44]. However, in the largest study of 19 patients treated with 1–2 FMT infusions delivered via pouchoscopy (7 pre-treated with rifaximin), only 1 patient achieved a clinically meaningful reduction in PDAI [45].

A single RCT has been published delivering FMT via enema followed by two weeks of daily oral capsules; however, this was stopped early after 6 patients were enrolled due to low response rates with only 1 achieving clinical remission [46]. In this study, low donor
engraftment was noted, potentially contributing to the lack of efficacy.

**Safety of FMT in IBD**

Common adverse events deemed related to FMT in the IBD literature are transient minor gastrointestinal complications such as bloating, diarrhoea and flatulence [19]. Serious adverse events related to route of administration have been reported including aspiration [24] and a suspected small bowel perforation related to upper GI route of administration [16]. There have also been reports of colectomies and death due to toxic megacolon following FMT, though these appear to be related more to the underlying IBD disease process than FMT itself [19]. While some cohort studies have suggested FMT for CDI may result in underlying IBD disease flare, these studies were uncontrolled and did not provide confirmatory endoscopic data [9]. The RCTs to date have not demonstrated a difference between FMT and control arms in terms of disease worsening or attributable minor or serious adverse events, though it must be noted that these studies were not powered to specifically assess for safety [19]. There are no published long-term safety data on FMT in IBD patients.

The safety of FMT in general has recently come to the forefront due to reports of morbidity and mortality related to preventable transmission of extended-spectrum beta-lactamase (ESBL)–producing *Escherichia coli*, [47] enteropathogenic *E. coli* (EPEC) and Shiga toxin-producing *E. coli* (STEC) causing subsequent bacteraemia in the recipient [48]. Such reports highlight the need for appropriate informed consent for known and unknown disease transmission with FMT and the need for robust and adaptable donor screening.

There is uncertainty regarding the impact of COVID-19 on the donor pool and future FMT production. The SARS-CoV-2 virus has been shown to continue to shed in the faeces after nasopharyngeal swabs have been negative for viral RNA [49,50]. To avoid potential spreading of the virus, it is recommended to review screening practices and exclude donors with recent symptoms or travel and consider viral testing based on local epidemiology [51].

**Next generation faecal microbiota transplantation**

Donor-derived FMT is highly variable on an inter-donor and even intra-donor level, which limits standardisation and impacts efficacy, safety and regulation. Manufactured or cultured microbial-based therapies including defined bacteria strains, spores, microbial small molecules and/or metabolites to treat disease are a logical next step in the development of microbial manipulation therapy (MMT) [52]. However, the mechanism of action of FMT in IBD is as yet unclear and there is no guarantee that narrow spectrum MMT will be as effective as ‘conventional’ donor-derived FMT.

Results of a phase 1b study of SER-287, a first-in-class oral ecobiotic comprising of Firmicutes spores, in 58 mild-moderate UC patients were recently presented. SER-287 demonstrated no safety signal and was found to be significantly more effective in inducing clinical remission than placebo in UC patients when dosed daily following vancomycin pre-treatment (*p* = 0.024) [53].

**The role of FMT in current IBD clinical practice**

Previous European, American and British guidelines have not supported the use of FMT outside of CDI, including for IBD, except in the context of clinical trials [6,54,55]. The more recently published Australian guidelines meanwhile acknowledge the clinical efficacy of FMT in the induction of remission of ulcerative colitis, while at the same time recognising that its optimal place in the therapeutic algorithm remains unclear and that more long term efficacy and safety data are required [57]. Regulations regarding the use of FMT in IBD also vary considerably around the world, limiting its application. Along with the lack of phase 3 RCT evidence, additional hurdles to implementation of FMT in routine clinical practice for UC include issues developing a sustainable delivery mechanism and the subsequent lack of maintenance therapy data. Encapsulated FMT may increase acceptability and address these issues.

While we do not recommend FMT in routine clinical practice outside of clinical trials, it may be of value in certain carefully selected patients at centres with appropriate IBD expertise. This includes adequately informed patients who strongly object to, or are intolerant of, immune based therapies with an interest in non-pharmacologic approaches. Our anecdotal experience, supported in part with trial data, is that FMT is best suited for UC patients with mild to moderate disease as a pre-biologic therapy, either before or after commencement of immunomodulator therapy/thiopurines, or as an adjunct therapy to existing medications. It is also our opinion that FMT may be more effective in those with shorter disease duration than those with longstanding disease. We hypothesise this may relate in part to a less resistant dysbiosis, more amenable to therapeutic microbial manipulation. Following FMT, there should be an early assessment of response and escalation to conventional medical and surgical therapies if inadequate clinical response based on objective clinical, biochemical and endoscopic markers. Treatment ideally should occur through a tertiary referral IBD center with the resources to analyse, report and publish clinical and microbiological outcomes following FMT.

**Conclusion**

The role of FMT and more refined forms of therapeutic microbial manipulation in IBD is an exciting and rapidly
evolving field. The use of FMT in IBD patients co-infected with CDI is established and supported by multiple guidelines. Furthermore, the evidence for FMT as remission induction therapy in UC is very encouraging with ongoing research efforts focusing on optimising accessibility and efficacy through numerous strategies including harnessing emerging data on microbial and metabolic predictors of therapeutic outcome. Data remain scant on FMT as maintenance therapy in UC, or its role in CD and pouchitis with rigorously designed and appropriately powered studies required coupled with comprehensive allied longitudinal microbial, metabolic and immunological analyses. Future research priorities include improved understanding of the mechanism of action of FMT in IBD to enable personalisation of therapy and development of next generation defined narrow-spectrum microbial manipulation therapy.

Conflict of interest statement
CH has received speaker fees and educational support from Janssen, Pfizer, Takeda, Ferring and Abbvie; and received a research grant through the Royal Australasian College of Physicians. RWL reports advisory board fees from AbbVie, Aspen, Celgene, Ferring, Gilead, Hospira, Janssen, MSD, Novartis, Pfizer, and Takeda; research fees from Gastrointestinal Society of Australia (GESA), Endochoice, Janssen, National Health and Medical Research Council of Australia, Shire, and Takeda; and speaker fees from Emerge Health, Ferring, Janssen, Shire, and Takeda. SP has served as a consultant for Finch Therapeutics and has received speaker fees from Ferring, Janssen and Takeda.

CRediT authorship contribution statement
Craig Haifer: Conceptualization, Writing - review & editing. Rupert W Leong: Conceptualization, Writing - review & editing. Sudarshan Paramsothy: Conceptualization, Writing - review & editing.

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• of special interest
**• of outstanding interest**

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