



## What you may have missed at ECCO 2021: expert-curated digest of hot topics in IBD

The European Crohn's and Colitis Organisation (ECCO) virtual Congress, held between 2–3 and 8–10 July 2021, started off the IBD community's summer with a host of exciting data on a wide variety of topics, ranging from the impact of diet on remission to the unmet needs in IBD-related cancer surveillance.

We caught up with two IBD experts, **Dr Nick Kennedy** and **Professor Ailsa Hart**, to hear about the data they found the most impactful at this year's congress. Check out their insights below, and make sure you head over to our [Hot topics](#) page to listen to their discussion in full.

### Novel diet specifically designed for ulcerative colitis (UC) may improve remission outcomes

*Lessons from the CRAFT UC study: although faecal microbial transplant failed to affect disease activity in patients with refractory mild-to-moderate UC, a novel UC-specific diet alone appeared to increase clinical remission rates*

A novel diet specifically designed for the dysbiosis of UC and to decrease factors that impair goblet cells or mucous production ('UC exclusion diet' [UCED]), has been developed by Levine A et al.<sup>1</sup> In the pilot CRAFT UC blinded randomised controlled trial, the researchers subsequently investigated whether donors and patients with UC following the UCED in addition to receiving a faecal microbial transplantation (FMT) experienced increased rates of FMT remission in UC or whether UCED had an independent impact on remission.<sup>1</sup>

In total, 51 patients with mild-to-moderate refractory UC were randomised to receive either FMT as a solitary intervention, FMT with dietary pre-conditioning of the donors for 14 days and UCED for patients following FMT, or UCED alone without FMT. Patients underwent a repeat endoscopy at Week 8 to determine whether they had achieved clinical steroid-free remission (defined as Simple Clinical Colitis Activity Index [SCCAI] <3), the primary endpoint of the study.<sup>1</sup>

A greater proportion of patients following the UCED alone achieved clinical remission (n=6; **Table 1**) than patients receiving FMT with or without diet, and mucosal healing, defined as Mayo score=0, was achieved by patients in this group only (n=3; p=0.022). Notably, this was a refractory patient population, with 55% having experienced failure of a biologic treatment, and 29% receiving steroids at enrolment.<sup>1</sup>

Although the CRAFT UC study was stopped for futility due to the lack of FMT impact on UC disease activity, its results are a promising early indicator of the possible effectiveness of dietary interventions in IBD treatment. This is in line with the results from the DINE-CD study, reported at Digestive Disease Week (DDW) earlier this year by Lewis JD et al.,<sup>2</sup> whose findings showed that both the specific carbohydrate diet and the Mediterranean diet (**Box 1**) are effective in achieving symptomatic remission at Week 6

**Table 1. Proportion of patients in each treatment group who experienced clinical steroid-free remission,\* endoscopic remission or disease exacerbation at Week 8**

	Clinical steroid-free remission* (%)	Endoscopic remission (%)	Exacerbation of disease (%)
<b>Group 1</b> (n=17) <i>FMT only</i>	11.8	12.0	17.6
<b>Group 2</b> (n=19) <i>FMT and UCED</i>	21.1	16.0	21.1
<b>Group 3</b> (n=15) <i>UCED only</i>	40.0	27.0	6.7

\*Defined as Simple Clinical Colitis Activity Index <3 at Week 8. FMT, faecal microbial transplantation; UCED, ulcerative colitis exclusion diet.

#### Box 1. Dietary definitions

In the **specific carbohydrate diet**, foods such as fresh fruits and vegetables, unprocessed meats, cheeses with minimal lactose and homemade yogurt are allowed; canned fruits, grains, starchy vegetables, such as potatoes, and processed, canned and smoked meats are excluded.<sup>2</sup>

The **Mediterranean diet** is high in fresh fruits, vegetables, nuts, fish and whole grains. Olive oil is used as the predominant fat source.<sup>2</sup>

(defined as short Crohn's disease [CD] Activity Index <150 in the absence of initiation or increase in the dose of any CD medications) in patients with mild-to-moderate CD.<sup>2</sup>

Together, these data suggest that dietary interventions for IBD, such as UCED, should be investigated in further randomised controlled trials specifically designed to assess their efficacy.

1. Levine A, et al. ECCO 2021. OP01.
2. Lewis JD, et al. *Gastroenterology* 2021; doi:10.1053/j.gastro.2021.05.047 [Epub ahead of print].



*"The diet is intended to tackle dysbiosis but also have an effect on host mucosal function, and it'll be interesting to explore more, if the diet does indeed work, which of those two is important, or if they actually achieve both of their aims with it as well. I think it'd be good to see this reproduced in larger numbers, certainly before moving towards clinical practice with it."*

**Dr Nick Kennedy, Consultant Gastroenterologist and Honorary Clinical Senior Lecturer, Royal Devon and Exeter NHS Trust**

Would you like to hear about UCED in greater detail? Listen to Professor Ailsa Hart discussing the key CRAFT UC trial results with study author Professor Arie Levine in our data deep-dive video on the [Hot topics](#) page.

Want to find out more about the relationship between diet and disease activity in IBD? Read our digest of hot topics in IBD from DDW, curated by Professor Charlie Lees and Dr Nick Kennedy, on the [Hot topics](#) page.

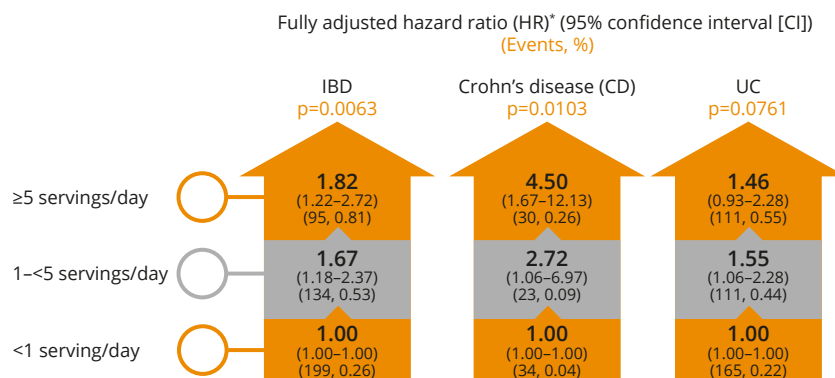
## Is consumption of ultra-processed food linked to IBD?

*Results from the Prospective Urban Rural Epidemiology (PURE) study show a positive association between higher ultra-processed food intake and development of IBD*

In this prospective cohort study, including 21 low-, middle- and high-income countries across seven geographic locations, Narula N et al. evaluated the relationship between ultra-processed food intake and the risk of IBD development. In total, 116,087 participants were followed for a median period of 9.7 years (interquartile range, 8.9–11.2) to monitor the development of IBD. Country-specific validated food frequency questionnaires were used to document baseline dietary intake, with 'ultra-processed foods' defined as all items containing additives, artificial flavourings, colours or other chemical ingredients.<sup>1</sup>

In total, 467 incident cases of IBD were recorded, comprising 377 cases of UC and 90 cases of CD. After adjustment for confounding factors, ultra-processed food consumption was found to be significantly associated with an increased risk of incident IBD (**Figure 1** below). Subgroups of ultra-processed food, such as soft drinks, sweets, salty snacks and processed meats, were each also associated with a higher hazard ratio (HR) for IBD.<sup>1</sup>

**Figure 1. Association between the number of servings of ultra-processed food and the development of IBD**



\*Fully adjusted model includes age, sex, geographic region, education, alcohol intake, smoking status, BMI, total energy intake and location. BMI, body mass index; CI, confidence interval; HR, hazard ratio; IBD, inflammatory bowel disease.

By contrast, consumption of non-processed foods, including, but not limited to, white and red meat, dairy, fruits and vegetables, were not associated with incident IBD.<sup>1</sup>

Although these results highlight an increased risk of IBD development associated with high consumption of ultra-processed food, further studies are needed to identify the specific ingredients within ultra-processed foods that contribute to this risk.<sup>1</sup>

1. Narula N, et al. ECCO 2021. OP05.



*"I was fascinated by this one because of course it's one of the most common questions we get asked as clinicians. Any patient, if they've got IBD, is wondering what they can do to mitigate the risk in their children, for example, and we're always slightly stuck as to what to say they could do. So this is rather a helpful study, because it means at least we can start to have a conversation with patients, and patients like to think they're doing something and they like to be able to take some control over the dietary aspects in particular."*

**Professor Ailsa Hart, Consultant Gastroenterologist and Sub-Dean, St Mark's Hospital and Academic Institute, London North West University Healthcare NHS Trust**

## Data from the SECURE-IBD database provide new insights on treatment impact in patients with IBD and COVID-19

*5-aminosalicylates (5-ASAs) are not associated with adverse outcomes in patients with IBD and severe COVID-19*

Using the data from the Surveillance Epidemiology of Coronavirus Under Research Exclusion for Inflammatory Bowel Disease (SECURE-IBD) registry, Ungaro R et al. evaluated the association between 5-ASA use and severe COVID-19, with the primary outcome being intensive care unit admission, ventilator use and/or death.<sup>1</sup>

Included in the analysis were 5174 patients with IBD and confirmed COVID-19; 212 severe COVID-19 events (4.1%) were reported. Three populations were analysed: all patients (N=5174), patients on any biologic (n=3325) and patients on tumour necrosis factor (TNF) antagonists (n=2216). At the time of COVID-19 infection, 1504 patients were receiving 5-ASAs.<sup>1</sup>

The study demonstrated no significant association between 5-ASA use and severe COVID-19 in any of the groups analysed (**Table 2**).<sup>1</sup>

**Table 2. Association between 5-ASA use and severe COVID-19 outcomes or COVID-19-related hospitalisation in all patients, patients receiving any biologic and patients receiving TNF antagonists only**

Model*	Adjusted odds ratio (aOR) severe COVID-19 (95% CI)	aOR hospitalisation (95% CI)
5-ASA use in all patients (ref=none)	1.14 (0.86–1.52)	1.18 (0.93–1.50)
5-ASA use among all patients on biologics (ref=none)	0.76 (0.38–1.50)	0.96 (0.70–1.33)
5-ASA use among all patients on TNF antagonists (ref=none)	0.99 (0.43–2.32)	0.96 (0.69–1.32)

\*All models adjusted for age, sex, race, disease phenotype (CD or UC/IBD-u), corticosteroid use, azathioprine/6-mercaptopurine use, TNF antagonist use, disease activity by physician global assessment, number of comorbidities and days from SECURE-IBD inception to reporting. 5-ASA, 5-aminosalicylate; aOR, adjusted odds ratio; CD, Crohn's disease; CI, confidence interval; IBD-u, inflammatory bowel disease unclassified; TNF, tumour necrosis factor; UC, ulcerative colitis.

These reassuring results suggest that 5-ASA use is not associated with severe outcomes in patients with IBD who have contracted COVID-19.

1. Ungaro R, et al. ECCO 2021. OP06.



*"I thought it was very reassuring, and I think it shows the importance of using large-scale studies adequately controlling for confounders, particularly those that we know to be important, like age and comorbidity. The message remains that patients with IBD should continue effective therapies to treat their disease and try and keep themselves in remission as much as possible."*

**Dr Nick Kennedy, Consultant Gastroenterologist and Honorary Clinical Senior Lecturer, Royal Devon and Exeter NHS Trust**

Interested in further information on predicting adverse COVID-19 outcomes in patients with IBD or in the latest data on COVID-19 vaccine responses in patients with IBD? Explore our digest of hot topics in IBD from DDW, curated by Professor Charlie Lees and Dr Nick Kennedy, on our [Hot topics](#) page.

Keen for more detail on the management of IBD during the COVID-19 pandemic? Browse the guidance from the British Society of Gastroenterology, along with a host of other consensus recommendations, in the IBD guidance library on our [Resources](#) page.

## Semi-automated benchmarking system may help improve quality of care across IBD centres

*Study successfully implements web-based benchmarking system in three Belgian centres*

Bossuyt P et al. have created a platform that automatically captures key outcome quality indicators and provides a benchmarking output. They investigated the feasibility of implementing this platform across multiple IBD centres to improve the quality of care.<sup>1</sup>

Following the selection of 12 quality indicators, a web-based interface was built in three large-volume IBD centres in Belgium. Data were collected from 265 patients in three ways:<sup>1</sup>



**Patients** completed PRO questionnaires and answered disease-specific questions when attending the outpatient and/or day clinic (data on clinical remission, fatigue and work productivity were collected this way)



**Software** automatically extracted data from electronic medical files, including biochemical and endoscopic reports (data on anaemia and deep remission were extracted this way)



**HCPs** completed baseline medical characteristics and outcome indicators for each patient at inclusion and then on a yearly basis (data on CRC status, steroid use [topical or systemic], severe infection, hospital admission, perianal surgery and IBD-related surgery information were extracted this way)

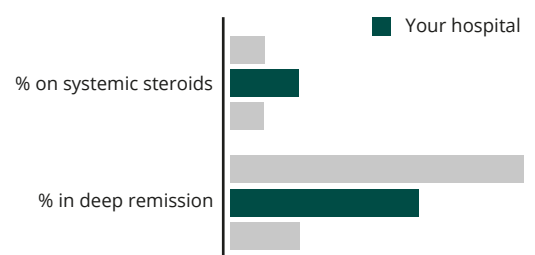
CRC, colorectal cancer; HCP, healthcare professional; IBD, inflammatory bowel disease; PRO, patient-reported outcome.

All items were benchmarked with reference to baseline data (e.g. IBD type, severity, demographics), anonymised and presented on a dashboard, with each centre only able to view data pertaining to their patients (**Figure 2**). The interface was successfully implemented across the three IBD centres.<sup>1</sup>

These results indicate that multicentre benchmarking, allowing for an objective assessment and comparison of the IBD-related quality of care in different centres, is feasible. However, further evaluation is necessary to confirm whether benchmarking implementation improves the quality of IBD care.<sup>1</sup>

1. Bossuyt P, et al. ECCO 2021. DOP81.

**Figure 2. Example output of a report benchmarking a centre against other centres on the platform**





"I really like the fact that they had some of the patient aspects, the patient-reported parts, embedded in it, such as fatigue and work productivity. [...] It would be nice to see even more patient aspects in this. Because patients' perception of their quality of care is often really very different, I think, from how we see it. And I think to see even more of the patient angle coming into these sorts of tools would be fantastic in the future."

**Professor Ailsa Hart, Consultant Gastroenterologist and Sub-Dean, St Mark's Hospital and Academic Institute, London North West University Healthcare NHS Trust**

## Developing a cost-effective genomic biomarker of cancer risk in UC

*Chromosomal copy-number alteration (CNA) analysis effectively discriminates between colorectal cancer (CRC) cases and non-neoplastic control biopsies*

Patients with UC are enrolled into surveillance programmes for the early detection of CRC. Although most patients under surveillance will never progress to CRC, identifying potential genomic CRC biomarkers, such as the CNA burden in biopsies taken at surveillance colonoscopies using low-pass whole genome sequencing (lpWGS), may offer an appealing approach for CRC risk stratification and timely identification of any developing pathology in the colon tissue (**Box 2**).<sup>1</sup>

To test the efficacy of this method in distinguishing CRC cases from controls, Al Bakir I et al. conducted a retrospective case-control study using lpWGS to analyse the CNA burden in four unselected non-neoplastic left-sided colorectal biopsies. Samples collected at CRC surveillance colonoscopies from patients with UC 1–5 years prior to their diagnosis with high-grade dysplasia (HGD) or CRC (cases) were compared with biopsies collected from patients who had remained HGD/CRC-free for at least 5 years following their biopsy (controls). The analysis included 476 biopsies, derived from 42 cases and 77 controls.<sup>1</sup>

The most common CNA events were losses of up to 30 megabases in the sub-telomeric regions of chromosomes 5–9 and 22, and these were found in similar proportions in both case and control biopsies. Losses extending beyond the sub-telomeric region and copy number gains, however, were found in a greater proportion of case biopsies compared with controls ( $p < 0.0001$ ). The presence of these more extensive losses in any of a patient's four biopsies was the most discriminating CNA event, with a high specificity of 0.96 (**Figure 3**).<sup>1</sup>

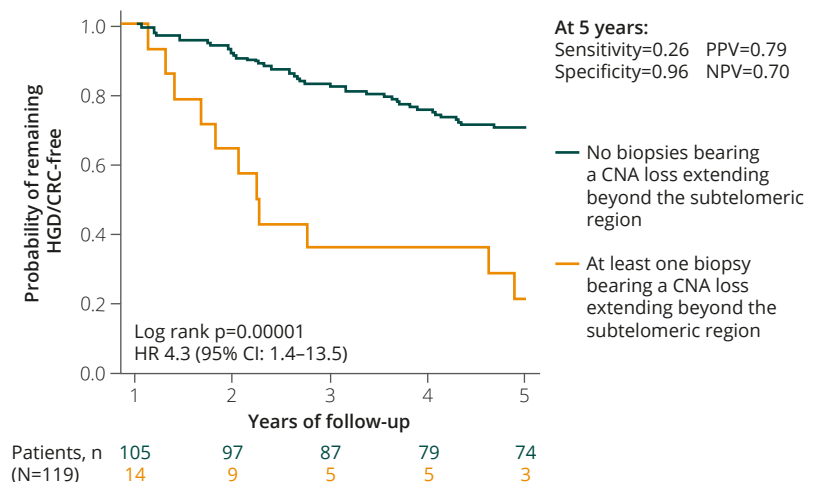
A significant proportion of CRCs develop in patients with UC who have no prior confirmed diagnosis of dysplasia, and non-dysplastic colitic epithelium can bear a significant burden of CNAs without displaying either a dysplastic or neoplastic phenotypic transformation. However, the exciting results of this study show that CNA burden analysis allows for a significant discrimination between control samples and cases of HGD/CRC and may thus have applications in CRC risk stratification during surveillance.<sup>1</sup>

### Box 2. Additional study background

Chromosomal CNAs comprise deletions or amplifications of fragments of genomic material. A hallmark of IBD-associated carcinogenesis, they are associated with CRC development and progression.

lpWGS is an accurate, versatile, robust (2% failure rate on samples over 20 years old) and cost-effective method for measuring genome-wide genetic variation and, as such, offers a potential approach for CRC stratification by detecting early CNA events prior to neoplastic formation.

**Figure 3. Probability of remaining HGD/CRC-free based on CNA losses extending past the sub-telomeric region**



CNA, copy-number alteration; CRC, colorectal cancer; HGD, high-grade dysplasia; HR, hazard ratio; NPV, negative predictive value; PPV, positive predictive value.

1. Al Bakir I, et al. ECCO 2021. OP38.





*"I think it looks like a really nice technique, and it obviously helps, and it's one that doesn't require a lot of additional, or any additional, equipment in the endoscopy room. [...] Perhaps when combined with other clinical factors, and perhaps other biomarkers in time as well, this would be a really nice way of improving our accuracy at determining which patients to survey and how frequently."*

**Dr Nick Kennedy, Consultant Gastroenterologist and Honorary Clinical Senior Lecturer, Royal Devon and Exeter NHS Trust**

Interested in additional expert insights on how to discuss IBD-related cancer and other challenging topics with your patients? Listen to our 'Managing difficult conversations' podcast series on our [Expert insights](#) page.

## PREdiCCting factors for fatigue in IBD: what are the culprits?

Fatigue is one of the most common symptoms in IBD, but little is known of its aetiology. Here, the baseline data set of the PREdiCCt study was used to identify its putative causes

**The PRognostic effect of Environmental factors in Crohn's and Colitis (PREdiCCt) study** is a large, ongoing study evaluating the causes of IBD flare in 2629 patients in clinical remission recruited from 48 UK sites. In this analysis, Derikx L et al. evaluated the baseline prevalence of fatigue in the PREdiCCt data set using a single item from the IBD-Control questionnaire to identify demographic, biochemical, environmental and psychosocial factors independently associated with fatigue in IBD.<sup>1</sup>

Despite being in clinical remission, 759 out of 1919 patients (39.6%) included in the analysis reported fatigue in the preceding 2 weeks. Patients reporting fatigue were more likely to be female ( $p < 0.001$ ), smokers ( $p = 0.002$ ) and diagnosed with CD ( $p < 0.001$ ) compared with those who did not report fatigue in the preceding 2 weeks. Subsequent univariable and multivariable analyses also identified elevated C-reactive protein levels ( $> 5$  mg/L), poor sleep quality, anxiety and depression as independent factors associated with fatigue (Table 3).<sup>1</sup>

**Table 3. Independent factors associated with fatigue in multivariable analysis**

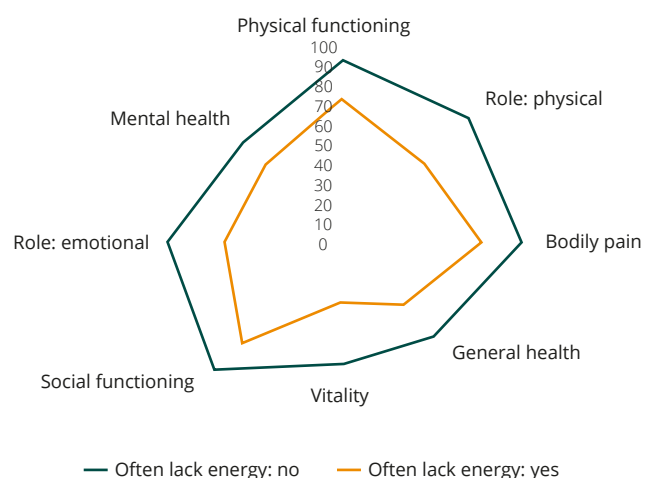
Variable	OR	95% CI	p-value
Female sex	2.4	1.3–8.8	<0.001
C-reactive protein (CRP) >5 mg/L	2.1	1.3–3.5	0.004
Depression (HADS >9)	6.2	2.9–13.3	<0.001
Anxiety (HADS >9)	1.8	1.1–3.0	0.031
Sleep quality (PSQI >5)	2.5	1.5–4.6	0.002

CI, confidence interval; CRP, C-reactive protein; HADS, Hamilton Anxiety and Depression Scale; OR, odds ratio; PSQI, Pittsburgh Sleep Quality Index.

In addition, comparison of responses to the 12-Item Short-Form Health Survey demonstrated a significantly reduced quality of life (QoL;  $p < 0.001$ ) in patients who reported fatigue compared with those who did not (Figure 4).<sup>1</sup>

Overall, these findings indicate a relationship between residual gut inflammation, fatigue and psychological well-being in patients with IBD in clinical remission. This relationship may help to identify possible factors that can be addressed to reduce fatigue and improve the QoL of patients with IBD.

**Figure 4. Impact of fatigue on patients' QoL**



1. Derikx L, et al. ECCO 2021. OP22.



*"If there's a clinical message that comes out of it, it's make sure that we ask about fatigue, and then think about depression, anxiety. We're not doing a good enough job, I don't think, at asking patients about it, screening for these things, and then try to find, whatever healthcare system we work in, some form of support for these patients, which of course can be completely different levels, depending on the system you work in."*

**Professor Ailsa Hart, Consultant Gastroenterologist and Sub-Dean, St Mark's Hospital and Academic Institute, London North West University Healthcare NHS Trust**

Interested in an in-depth discussion on patients' expectations for their QoL and treatment, and the importance of considering their holistic needs when setting remission goals in IBD? At Galapagos, we're collaborating with experts in IBD to champion the concept of Holistically Approaching Remission (HAPPI-R) – head over to our [Hot topics](#) page to find out more!