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

One of the key events in the inflammatory bowel disease (IBD) calendar, Digestive Disease Week (DDW) 2021, was held between 21 and 23 May. This year's virtual congress included a host of speaker sessions and posters with practical and useful information for the fields of gastroenterology, hepatology, endoscopy and gastrointestinal surgery, as well as access to top-tier cutting-edge research in the world of IBD.

Were you too busy to attend this year or to explore all the available content? Read on to find recommendations from **Dr Nick Kennedy** and **Professor Charlie Lees** on what data they found the most impactful at this year's meeting!

Infection and IBD: understanding the risks and predicting adverse outcomes

A prognostic risk factor prediction tool has been developed that is able to predict adverse COVID-19 outcomes with high accuracy in patients with IBD

Using the Surveillance Epidemiology of Coronavirus Under Research Exclusion for IBD (SECURE-IBD) database, Sperger J et al. have developed an individualised prognostic risk factor prediction tool, which predicts the probability of adverse COVID-19 outcomes using demographic, clinical and medication history data from patients with IBD (see **Figure 1**).[1]

The current model uses data from October 2020 to April 2021 (n=3680) and was shown to have a very good discrimination for predicting hospitalisation (area under the curve [AUC] 0.781) and excellent discrimination for intensive care unit (ICU) admission (AUC 0.875) and death (AUC 0.940).

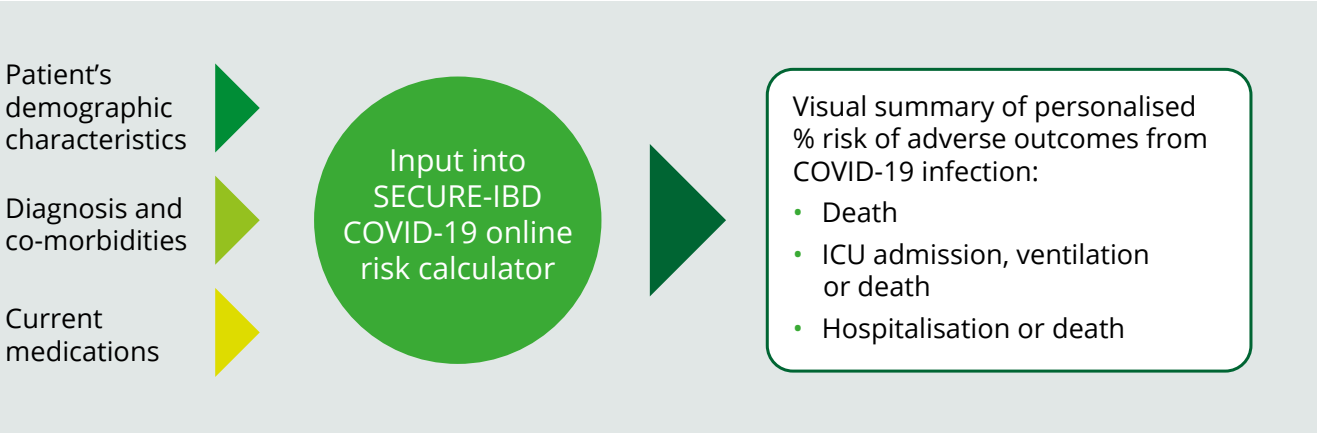
Risk factors for adverse COVID-19 outcomes included older age, male sex, comorbidities and oral corticosteroid use, with oral corticosteroid use being the most important predictor for hospitalisation, ICU admission and death.[1]

The validated risk prediction tool can be accessed here and is free and publicly available for use by healthcare professionals.

Care should be taken to ensure the prediction tool is used within its specified remit: to facilitate discussions about risks due to COVID-19 with their patients with IBD. The tool does not describe causal relationships and so should not be used to answer 'what if' questions (e.g. impacts of medication change).[1]

Limitations of the SECURE-IBD database are important to consider, such as the voluntary, physician-reported nature of the registry[1,2] and the biases this may introduce, as well as the risk of COVID-19 testing bias.[2] Nationwide medico-administrative databases can provide more complete data on patients with IBD and COVID-19, and are expected in the future.[2]

Figure 1. Flow chart showing process of using online risk tool



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Looking beyond COVID-19, the above findings are consistent with further data published at DDW 2021, which explored risk factors for hospitalisation and death in patients with IBD following **any** infection. A 10-year population-based cohort study by Lyons M et al., described in more detail below, indicated that factors predicting severe infection resulting in ICU admission or death in patients with IBD include age >70 years (p=0.031) and male sex (p=0.034), as well as low body mass index (BMI; p=0.012).[3]

1. Sperger J, et al. DDW 2021. Fr491.
2. Lees CW, et al. *Gut* 2021;70:632–634.
3. Lyons M, et al. DDW 2021. Sa485.

"In general, data so far on inflammatory bowel disease treatments and risk of severe COVID-19 have been reassuring. The SECURE-IBD model confirms that other patient factors including age, sex and comorbidities are important to consider in this context. Not all studies have reported a risk of corticosteroid use, but modern IBD treatment paradigms should, in any case, focus on sustained, corticosteroid-free remission."

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

New insights into vaccine response in patients with IBD

New data show patients with IBD have attenuated immunogenicity to hepatitis B, influenza and pneumonia vaccines. How do these findings fit into the wider context of global health policy regarding COVID-19 vaccination?

Immunosuppressive therapies have revolutionised IBD care; however, prolonged use of these agents leaves patients at higher risk of infectious diseases. Understanding vaccine response in patients with IBD is particularly significant in the context of the global COVID-19 pandemic.

In a meta-analysis of 29 studies (n=3746, including 3539 patients with IBD and 207 healthy controls), Khan S et al. estimated the pooled efficacy rate of various vaccines and quantified the immune response in relation to the immunosuppressive agents the patients were receiving.[1]

Patients with IBD displayed a statistically inferior vaccine response, with pooled odds ratios (ORs) compared with healthy controls of 0.3 for all vaccines combined (95% confidence interval [CI]: 0.1–0.5; p=0.01), 0.13 for the hepatitis B vaccine (95% CI: 0.06–0.32; p=0.01) and 0.43 for the influenza vaccine (95% CI: 0.19–0.98; p=0.04). Subgroup analysis of vaccine responses by the type of treatment patients received showed similar results (**Table 1**).[1]

Table 1. Pooled proportion of HBV, influenza and pneumonia vaccine response by IBD treatment subgroups

Treatment type	Pooled proportion of vaccine response, % (95% CI)
Immune-modifying drugs alone	56.3 (46.9–65.2)
Anti-TNF treatment alone	49.7 (39.0–60.5)
Anti-TNF + immune-modifying drugs	43.7 (34.8–53.0)

CI, confidence interval; HBV, hepatitis B vaccine; IBD, inflammatory bowel disease; TNF, tumour necrosis factor.

These findings prompt discussion regarding the effectiveness of COVID-19 vaccination in patients with IBD. The most recent position statement from the British Society of Gastroenterology IBD Section and IBD Clinical Research Group states that the 'benefits of vaccination, even in patients treated with anti-tumour necrosis factor (TNF) drugs, are likely to outweigh these theoretical concerns' with regard to COVID-19 vaccination.[2]

Further insights into this topic have been provided by the impaCt of bioLogic therApy on saRs-cov-2 Infection and immuniTY (CLARITY) IBD study, a multicentre, UK-wide, prospective, observational cohort study exploring the effect of various immunomodulating therapies on COVID-19 outcomes in patients with IBD.[3] Results from CLARITY IBD, published earlier this year, indicate that patients treated with some systemically acting immune-modifying drugs display attenuated serological response following COVID-19 infection compared with patients treated with gut-specific immune-modifying drugs. These findings suggest that COVID-19 vaccine efficacy may be blunted by some IBD treatments.[3]

However, a second publication from CLARITY IBD, published in April 2021, demonstrated that although immunogenicity following a first vaccine dose is indeed attenuated by some systemic immunomodulatory treatments, seroconversion is detected in the majority of participants after the second dose of vaccine.[4] This finding highlights that patients on some medications may be at greater risk than others during the period between their two doses of COVID-19 vaccine.[4] With a delayed second dosing regimen adopted by many countries,[4] this remains a space to watch.

1. Khan S, et al. DDW 2021. S483.
2. Alexander JL, et al. *Lancet Gastroenterol Hepatol* 2021;6:218–224.
3. Kennedy NA, et al. *Gut* 2021;70:865–875.
4. Kennedy NA, et al. *Gut* 2021; doi:10.1136/gutjnl-2021-324789 [Epub ahead of print].

"The systematic review and meta-analysis from Khan and colleagues is timely, with our renewed focus on vaccination during the COVID-19 pandemic. CLARITY IBD demonstrates that some systemically acting immune-modifying drugs affect serological responses to COVID-19 infection and vaccination. However, vaccine responses look good following the second dose, and we should encourage our patients to continue their IBD therapies but also to ensure they get their vaccinations in a timely manner."

Dr Nick Kennedy

Global and local analyses give insight into hospitalisation trends in IBD

Results of a global temporal analysis suggest hospitalisation rates among patients with IBD are increasing in over half of the countries analysed

Buie M et al. investigated the global trends in primary and all-cause hospitalisation rates for Crohn's disease (CD) and ulcerative colitis (UC), as well as IBD overall, through a systematic review of papers containing at least 5 years of data over at least three data points. The researchers aimed to review trends in industrialised vs. newly industrialised countries by calculating the average annual percentage change of hospitalisation rates (per 100,000) by year.[1]

The results suggest that over half of all the countries analysed show increasing hospitalisation rates; this trend is particularly evident in newly industrialised countries, which is in keeping with the rapid growth in IBD prevalence in these areas.[1] Notably, these data also show substantial variation in average annual percentage change trends depending on whether studies included unspecified, primary cause and all-cause diagnosis types. This demonstrates the need to identify whether hospitalisation rates are primary or all-cause when interpreting trends in healthcare utilisation.[1]

Analysis of a large Scottish cohort indicates that hospital admission due to infection has remained static in the region over a 10-year period despite increases in the use of immunosuppressive therapies

The link between immunosuppressive agents, individual risk of infection and emergency hospital admission was investigated from 2010 to 2019 in a study based in Lothian, Scotland, using the Lothian IBD registry, a rigorously validated database of all prevalent cases of IBD in Lothian (n=8379 at time of analysis). The study authors concluded that infection is the most common reason for hospitalisation among patients with IBD in this registry.[2] Interestingly, biologic use did not predict poor outcome in this analysis; despite the 10-fold increase in biologic prescription during that 10year period, rates of severe infection remained similar at 2.7 per 100,000 in 2010 and 2 per 100,000 in 2019.

1. Buie M, et al. DDW 2021. Sa506.
2. Lyons M, et al. DDW 2021. Sa485.

"Although IBD incidence rates have now stabilised in industrialised countries, the prevalence has continued to rise through compounding. Hospitalisation rates have increased in line with this. We need to continue to build comprehensive IBD services that offer rapid access to diagnosis and to treatment during flares so that we can minimise the burden of hospitalisation on patients and healthcare systems."

Dr Nick Kennedy

A comprehensive interdisciplinary care programme for recently diagnosed patients with IBD is associated with lower healthcare resource utilisation compared with those receiving usual care

Early interdisciplinary care for IBD has been shown to be successful: the COMPASS-IBD programme was rated excellent by 91% of participants

The Comprehensive Care for the Recently Diagnosed IBD Patient (COMPASS-IBD) programme is composed of a multi-specialist team providing education and a personalised multidisciplinary care plan for patients newly diagnosed with IBD, as well as additional services according to their needs.

In this study, Gold S et al. evaluated the impact of this interdisciplinary care programme on outcomes such as clinical remission (defined as partial Mayo score <2 or Harvey Bradshaw Index <5) and healthcare utilisation (number of hospitalisations and emergency room visits).[1] The programme demonstrated that, compared with a control group of patients receiving usual care, the COMPASS-IBD programme was associated with increased rates of clinical remission and normal BMI after 1 year, and a reduced likelihood of emergency visits or hospitalisation. Moreover, 91% of patients rated the programme as excellent, and 100% stated they would participate again.[1]

The importance of and need for programmes such as this is highlighted by a nationwide Swedish population-based study. Researchers found that adult-onset IBD was associated with an increased risk of psychiatric disorders (1.8 extra morbidity per 100 patients with IBD compared with the general population). Of note, the analysis showed that the first year following IBD diagnosis had the highest risk of overall psychiatric morbidity (hazard ratio 1.4; 95% CI: 1.2–1.6).[2] Together, these data suggest that patients participating in COMPASS-IBD may benefit from psychological follow-up as part of their early care.

1. Gold S, et al. DDW 2021. Sa567.
2. Ludvigsson JF, et al. *J Crohn's Colitis* 2021; doi:10.1093/ecco-jcc/jjab039 [Epub ahead of print].

"I was pleased to see the COMPASS study reporting positive outcomes. These findings fit with an evolving concept of holistic remission, which takes us beyond clinical remission and mucosal healing to consider psychosocial factors affecting the patient as a whole, including anxiety, depression and fatigue."

Prof. Charlie Lees, Consultant Gastroenterologist, Edinburgh IBD Unit, Professor of Gastroenterology, University of Edinburgh

To learn more about holistically approaching remission, don't miss the Galapagos-sponsored ECCO symposium 'We see what UC: time for a holistic approach to remission' on Thursday 8 July, 16:55–17:55 BST.

BST, British summer time. This programme is not affiliated with ECCO.

Exploring the relationship between diet and disease activity in patients with IBD

The specific carbohydrate diet (SCD) was shown not to be superior to the Mediterranean diet as treatment for patients with mild-to-moderate CD

Dietary definitions

In the **SCD**, 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.[1]

The **Mediterranean diet** is high in fresh fruits, vegetables, nuts, fish and whole grains. Olive oil is used as the predominant fat source.[1]

DINE-CD is a multicentre, randomised, comparative effectiveness trial comparing the SCD and Mediterranean diet, both of which have been associated with an improvement in symptoms of CD.

In total, 194 patients with mild-to-moderate CD were randomised 1:1 to follow either the Mediterranean diet or the SCD for 12 weeks.[1]

Table 2 (below) shows the primary and secondary endpoints in DINE-CD. The primary endpoint of symptomatic remission at Week 6 was achieved in ≥40% of patients following both diets (43.5% with the Mediterranean diet and 46.5% with the SCD). No superiority with SCD vs. Mediterranean diet was observed for any endpoint (p=0.22–0.92), regardless of the inflammation status at screening.

These results suggest that the SCD was not superior to the Mediterranean diet in achieving symptomatic remission; given the ease of following the Mediterranean diet and additional health benefits associated with it, the authors suggested that the Mediterranean diet may be preferred over the SCD as treatment for patients with mild-to-moderate CD.

Dietary changes are more likely to be reported as causes of flares by patients with CD compared with patients with UC

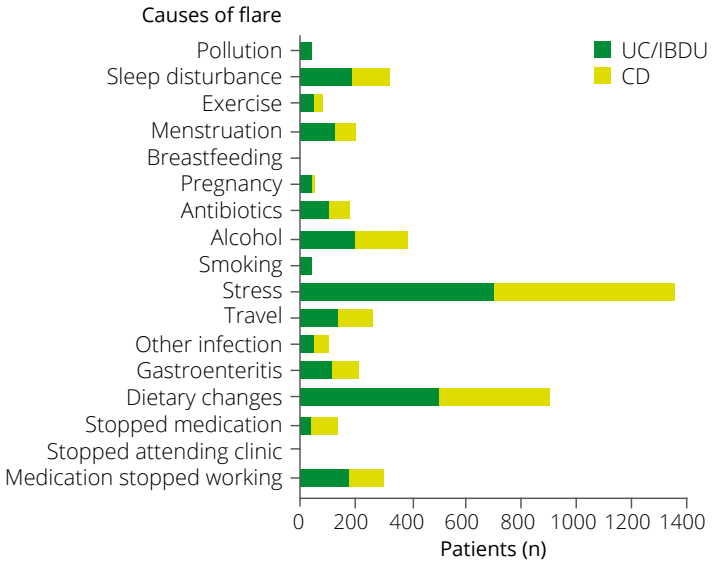
Table 2. Endpoints in DINE-CD

Primary endpoint
Symptomatic remission at Week 6, defined as short CD Activity Index <150 in the absence of initiation or increase in the dose of any CD medications
Secondary endpoints
Faecal calprotectin response
C-reactive protein*

*C-reactive protein response was uncommon in both treatment arms.
CD, Crohn's disease.

Uncovering the impact of factors like diet on IBD is a key area of research interest. The PRognostic effect of Environmental factors in Crohn's and Colitis (PREdiCCt) study is a large, prospective, multicentre UK study exploring potential predictors of disease outcomes in IBD. In the study, patients with IBD who are in clinical remission are followed up for 2 years, using monthly questionnaires to identify predictors of disease flare, focussing on genetic factors, environment, diet and gut microbiota.

Figure 2. Analysis by diagnosis



Using baseline questionnaire data from the PREdiCCt cohort (n=2629), Siakavellas S et al. reported the factors that patients believed precipitated a disease flare. The findings showed that patients with CD are more likely to identify dietary changes as a main cause of flare than patients with UC or unspecified IBD (50% vs. 43%, p<0.001; see **Figure 2**); other key perceived precipitators of flare were stress, alcohol consumption and sleep disturbances.[2]

Further data from the PREdiCCt study should help to shed light on how factors such as diet affect IBD flares.[2]

1. Lewis JD, et al. *Gastroenterology* 2021; doi:10.1053/j.gastro.2021.05.047 [Epub ahead of print].
2. Siakavellas S, et al. DDW 2021. Sa577.

"I was excited to see some great new data at DDW 2021 looking beyond drug therapy for IBD. In particular, we saw a presentation from the first randomised intervention study in Crohn's disease of a dietary therapy other than enteral nutrition. Although neither the Mediterranean diet nor the specific carbohydrate diet was shown to be superior to one another, this trial yielded many useful insights and shows that controlled diet studies are feasible. On a similar theme, patients in our PREdiCCt study identified diet along with stress as the major cause of disease flare in IBD."

Prof. Charlie Lees

New data highlight the emerging relationship between fat and IBD

Among patients with non-alcoholic fatty liver disease (NAFLD), patients with CD were found to be more likely to have advanced fibrosis than patients with UC and patients without an IBD diagnosis

NAFLD is seen in 40–50% of patients with IBD and ranges from steatosis to advanced fibrosis (AF), with AF being the most important determinant of death due to NAFLD. In their recent study, Aggarwal M et al. evaluated the histopathological spectrum of NAFLD in a pool of 1022 patients with this condition. Patients among this cohort with a comorbid diagnosis of IBD were matched to non-IBD controls by propensity scores for potential covariates, including age, BMI and type 2 diabetes.[1]

AF was significantly more common in patients with IBD compared with the non-IBD group (30.0% vs. 16.6%, p=0.03). Subgroup analysis showed that patients with CD were significantly more likely to have AF (OR 2.82; 95% CI: 1.3–6.2; p=0.01) compared with the non-IBD group. Conversely, rates of AF in patients with UC were lower than those observed in the CD and non-IBD groups. The authors concluded that CD predisposes patients to liver fibrosis. However, this study was limited by its relatively small IBD population (n=40); therefore, these data need to be confirmed in a larger IBD cohort.[1]

This finding was one of several studies at DDW 2021 exploring the impact of fat on IBD. In a second notable poster, Noorian S et al. reported data from a nationwide admissions database of >10,000 hospitalised patients with IBD, showing that comorbid NAFLD was associated with an increased risk of readmission, and greater length of stay and cost of care, compared with matched patients with IBD and no diagnosis of NAFLD.[2]

In addition to NAFLD, the impact of visceral fat is also an area of interest in IBD. A recent study by Gu P et al., published at the 2021 Crohn's & Colitis Congress in January, evaluated the effect of visceral fat index (VFI) on treatment response and the risk of surgery in 181 patients with IBD initiating anti-TNF agents between 2009 and 2019, who were stratified by their VFI scores. Results showed that although no differences were observed between patient groups in the achievement of corticosteroid-free response at 6 and 12 months, patients with VFI >0.67 were significantly more likely to undergo surgery at 6 and 12 months (adjusted OR 41.92 [95% CI: 5.09–345.59] and 15.55 [95% CI: 2.85–80.56]).[3]

Although additional research involving larger patient cohorts is needed, together these results suggest that patients with IBD may benefit from intensive NAFLD and VFI screening programmes.[1]

1. Aggarwal M, et al. *DDW* 2021. Sa496.
2. Noorian S, et al. *DDW* 2021. Sa547.
3. Gu P, et al. *Inflam Bowel Dis* 2021;27:S47–S48.

'It is interesting to see the various different roles fat plays in IBD. NAFLD looks to be a bigger issue than we thought, and we should possibly be actively screening for this. Other recent data have looked at visceral fat, suggesting that it affects surgical outcomes. Given the recent paper by Suzanne Devkota in Cell describing the role of creeping fat in Crohn's disease,[1] this merits further exploration."

Prof. Charlie Lees

1. Ha CWY, et al. *Cell* 2020;183:666–683.