Abstract Highlights

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The following highlights showcase late-breaking research presented at United European Gastroenterology (UEG) Week 2024, bringing you the most recent developments in the field. Topics covered include the role of statins in the management of inflammatory bowel disease, novel therapeutic targets and predictive biomarkers for Crohn's disease, and updates on the management of constipation.

Statin Use May Reduce Severity of Inflammatory Bowel Disease

NEW research presented at UEG Week 2024 suggests that statins, commonly used to lower cholesterol, may also help ease the severity of inflammatory bowel disease (IBD).

Conducted between 2006–2020, the nationwide cohort study followed nearly 32,000 adults diagnosed with IBD, assessing whether statins, when taken after diagnosis, could reduce disease progression in ulcerative colitis (UC; n=19,788) and Crohn's disease (CD; n=12,582).

Among all participants, 1,733 patients with UC and 962 patients with CD became regular statin users after their diagnosis. Researchers excluded individuals who had been prescribed statins in the 12 months before, or 6 months after, their IBD diagnosis to ensure clear comparisons. After 1:1 propensity score matching, the authors compared statin users with non-users by applying Cox proportional hazards modelling to estimate the risk of IBD-related surgery, hospitalisations, and disease flares.

At start of follow-up, the median age for statin users with UC was 61 years, and 59 years for those with CD. After a median 3.4 years of follow-up, the team found that, in patients with UC, statin use was linked to a significant reduction in the risk of IBD-related surgeries, hospitalisations, and disease flares (marked by the need for additional treatments like corticosteroids, immunomodulators, or anti-TNF treatment). Specifically, statin users with UC had a 45% lower risk of surgery, a 32% lower risk of hospitalisations, and a 14% lower risk of flares.

For patients with CD, the benefits were less broad but still notable. Statin use was associated with a 46% reduced risk of surgery, but did not significantly impact hospitalisations or disease flares. The number of patients needed to treat to prevent one IBD-related surgery was 345 in UC, compared to 161 in CD.

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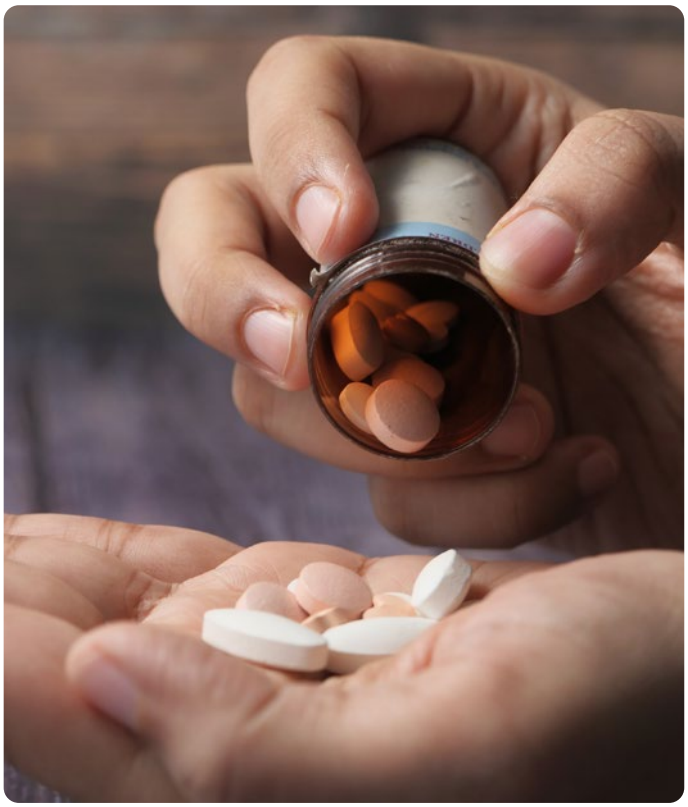
Overall, this study highlights the potential for statins to play a role in managing IBD, especially in patients with UC. These findings open new avenues for IBD management, particularly for reducing the need for surgery.



in the p-FMT

Promising Results from Targeted Faecal Microbiota Transplantation Trial for Patients with Kidney Cancer

A GROUNDBREAKING study from Italy has revealed that targeted faecal microbiota transplantation (FMT) may enhance the effectiveness of combined immune checkpoint inhibitors (ICI) and tyrosine-kinase inhibitors (TKI) in patients with advanced renal cell carcinoma.

The preliminary findings from the TACITO trial, led by Gianluca Ianiro and presented at UEG Week 2024, indicate that using faecal matter from donors who respond positively to ICIs could significantly improve patient outcomes.

The randomised, double-blind, placebo-controlled trial involved 50 patients receiving first-line therapy with the ICI, pembrolizumab, and the TKI, axitinib. Participants were divided equally to receive either donor FMT (d-FMT) from a responder or placebo FMT (p-FMT). The study aimed to assess whether d-FMT could improve progression-free survival (PFS) at 12 months, with secondary outcomes including overall survival and objective response rate.

As of August 2024, 44 patients completed the follow-up. Results showed a 12-month PFS rate of 66.7% in the d-FMT group compared to 35.0% in the p-FMT group, a statistically significant difference (p=0.036). The median PFS was 14.2 months for the d-FMT arm versus 9.2 months for the p-FMT arm. Notably, the objective response rate was also higher in the d-FMT group at 54%, compared to 28% in the p-FMT group.

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These promising preliminary results suggest that FMT derived from successful ICI responders may enhance treatment efficacy for advanced renal cell carcinoma, potentially transforming therapeutic strategies for patients facing this challenging cancer. Further investigation and follow-up are needed to confirm these findings and fully understand the implications of this innovative approach.

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Novel Therapeutic Targets in Perianal Fistulising Crohn's Disease

PERIANAL fistulas affect approximately 30–40% of patients with Crohn's disease (CD), significantly impacting their quality of life and presenting substantial management challenges.

These complex lesions are often resistant to standard treatments, underscoring the need for a deeper understanding of their underlying mechanisms. A recent study presented at UEG Week 2024 involved a comprehensive analysis of three patient groups: patients with perianal fistulising CD (PCD; n=25), non-perianal Crohn's disease (NPCD; n=10), and idiopathic perianal fistulas (IPF; n=28). To gain insights into the immune response associated with PCD, biopsies were collected from various sites, including fistula tracts, openings, and rectal mucosa, during examinations under anaesthesia or colonoscopy.

Using mass cytometry and single-cell RNA sequencing, the researchers conducted an in-depth analysis of the mucosal immune cells present in these biopsies. Their findings revealed a notably skewed immune landscape in patients with PCD compared to those with NPCD and IPF. Notably, there was a significant expansion of Th17 cells within the fistula tracts, alongside IL-17-producing CD8 T cells in the rectum of patients with PCD. These observations suggest a potential pathogenic role for these immune cell types in the development and persistence of perianal fistulas.

> **These findings highlight the pathogenic role of hyperactivated IL-17 signalling, suggesting it as a potential therapeutic target for PCD**

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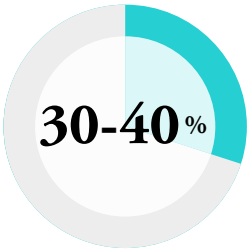


The study also identified altered exhaustion markers, such as CD39 and CD127, in both CD4 and CD8 T cells from patients with PCD, indicating a dysfunctional immune response that may contribute to the chronicity of the condition. Furthermore, regulatory B cells, which are crucial for maintaining immune balance and modulating gut health, were found to be dramatically diminished in PCD compared to IPF. Additionally, the results showed an increased presence of CD172+TREM1+ macrophages in PCD, cells known to be associated with resistance to anti-TNF therapies in luminal CD, suggesting that they may contribute to the treatment challenges faced by patients with PCD.

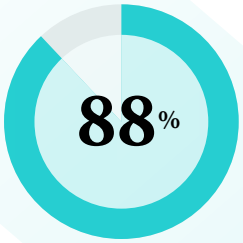
These findings highlight the pathogenic role of hyperactivated IL-17 signalling, suggesting it as a potential therapeutic target for PCD. By identifying these novel targets, this study paves the way for future research aimed at developing more effective treatment strategies for patients with perianal fistulising Crohn's disease.

Tasty & Healthy: A New Diet for Children and Young Adults with Crohn's Disease

NEW data from the Tasty & Healthy (T&H) trial presented at UEG Week 2024 has demonstrated that a flexible exclusion diet is highly effective for inducing remission in children and young adults with mild-to-moderate Crohn's disease (CD).

This showed similar clinical outcomes to exclusive enteral nutrition (EEN) while achieving higher tolerability. EEN is traditionally effective in inducing remission in CD, but due to its structured and restrictive nature, it can be difficult for patients to maintain. The T&H diet, which excludes processed food, gluten, red meat, and dairy (except plain yogurt), offers a more flexible alternative without mandatory ingredients or the need for partial enteral nutrition.

Researchers compared the tolerability and effectiveness of the T&H diet to EEN in children and young adults aged 6–25 years with mild-to-moderate CD. A total of 97 participants were randomised to T&H or EEN for 8 weeks. Both groups received weekly dietary support, and clinical data were collected at baseline and every 2 weeks. The primary outcomes included clinical remission, mucosal inflammation (mucosal healing is defined by mucosal inflammation non-invasive (MINI) index of <8 points), and inflammatory markers such as C-reactive protein, erythrocyte sedimentation rate, and calprotectin. Tolerability was assessed through adherence monitoring, judged by weekly interviews and 24-hour intake diary. Of the 83 patients who completed the trial, 41 were in the T&H group and 42 in the EEN group (mean age 14.5±3.7 years).



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The results showed that the T&H diet had significantly higher tolerability, with 88% of patients adhering to the diet compared to 52% in the EEN group (odds ratio: 6.3; 95% CI: 2.2–22.0; p<0.001). Clinical remission rates at Week 8 were comparable between groups. With intent-to-treat analysis, remission was 56% in the T&H group versus 38% with EEN (p=0.1), and mucosal healing (a MINI index >8) was observed in 54% of patients in the T&H group compared to 41% in the EEN group (odds ratio: 2.6; 95% CI: 1.1–6.3; p=0.026). Both diets significantly improved inflammatory markers, with no major differences in C-reactive protein, erythrocyte sedimentation rate, or calprotectin levels between groups. Three mild adverse events were reported, two in the EEN group (nausea and dizziness), and one in the T&H group (constipation).

The results of the study demonstrate that the T&H diet is a well-tolerated, flexible dietary approach that offers similar clinical benefits to EEN for managing mild-to-moderate CD in paediatric populations, with a higher tolerability. Further research is needed to assess its long-term outcomes and broader applications.

L-carnitine Supplementation Effective for Non-Alcoholic Fatty Liver Disease

NOVEL research presented at UEG Week 2024 has revealed that L-carnitine supplementation significantly improves liver function and reduces fat accumulation in patients with non-alcoholic fatty liver disease (NAFLD), with reductions in liver enzyme levels and improvements in ultrasonographic liver grades.

NAFLD, the hepatic manifestation of metabolic syndrome, is a leading cause of liver failure and transplants worldwide. Currently, the primary treatment for NAFLD involves lifestyle modifications and weight reduction. This study aimed to evaluate the impact of L-carnitine, an amino acid essential for lipid metabolism and the beta-oxidation of long-chain fatty acids, on NAFLD. The multicentre, randomised, clinical trial sought to determine whether L-carnitine could offer an additional therapeutic benefit beyond lifestyle modifications in improving liver health.

The study involved 393 patients with NAFLD (55.2% male; average age: 44.8 years; 76.7% of Middle Eastern/North African ethnicity) from five referral centres across three countries. Participants were randomly assigned to either the L-carnitine supplementation group (Group A) or the control group (Group B).

Group A received 1,000 mg of L-carnitine twice daily for 12 weeks, while Group B was advised on lifestyle modifications only. The baseline metabolic profile, including liver enzyme levels, was recorded for all participants. After 12 weeks, hepatic fat status was reassessed using ultrasound, and the biophysical parameters were compared between the groups.

The analysis revealed that alanine aminotransferase levels in Group A decreased significantly from 65.6 to 40.9, but only reduced from 62.8 to 50.7 in Group B ($p=0.0029$). Similarly, there was a significant difference in the reductions of aspartate aminotransferase levels between groups, with a decrease from 50.9 to 35.7 in Group A, compared to a decrease from 54.7 to 44.85 in Group B ($p=0.046$). Additionally, ultrasonographic evaluation revealed that the proportion of patients with Grade 3 NAFLD in Group A decreased from 37.9% to 12.6%, whereas in Group B it declined from 36.6% to 22.7% ($p<0.05$).

In conclusion, L-carnitine supplementation appears to be an effective adjunct therapy for managing NAFLD, with significant improvements in liver function markers and reduction of fat accumulation in the liver. Given these results, L-carnitine could be considered for inclusion in clinical practice to enhance NAFLD management, though further long-term studies are needed to assess its sustained efficacy and safety.

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Partially Hydrolysed Guar Gum: New Treatment for Constipation?

PARTIALLY hydrolysed guar gum (PHGG), a water-soluble fibre, can significantly improve bowel movement frequency in adults with chronic constipation, according to new research presented at UEG Week 2024.

Constipation is commonly treated with non-absorbable fibre supplements, but evidence supporting their effectiveness is inconsistent. Previous studies have indicated that PHGG, a water-soluble fibre derived from the endosperm of *Cyamopsis tetragonolobus* L. seeds, may help relieve constipation, with benefits observed as early as 1 week into treatment.

The study aimed to provide more robust data by extending the treatment duration to 6 weeks and using a larger sample size, including 160 adults with chronic functional constipation or constipation related to irritable bowel syndrome. PHGG was compared to a placebo to assess its effectiveness and safety.

In this double-blind, randomised, placebo-controlled trial, participants were divided into two groups, with 80 receiving 10 g of PHGG and 80 receiving a placebo. Outcomes were measured through daily diaries, tracking bowel movement frequency, stool characteristics (using the Bristol Stool Scale), and symptom severity (using the PAC-SYM questionnaire). The primary goal was to see how PHGG affected the frequency of spontaneous bowel movements (SBM).

> **By the end of the study, 50% of participants in the PHGG group had three or more SBMs per week, compared to 32.5% in the placebo group**

Results showed that PHGG significantly increased SBM frequency compared to the placebo group. By the end of the study, 50% of participants in the PHGG group had three or more SBMs per week, compared to 32.5% in the placebo group. Additionally, 34.2% of PHGG users met the pre-defined responder criteria of ≥3 SBM/week and an increase of ≥1 SBM from baseline for at least 4 of the 6 weeks of treatment, achieving a significant improvement in their bowel movement frequency. This was compared to only 17.7% of placebo users.

PHGG was generally well tolerated, with no serious adverse events reported and no treatment discontinuations due to side effects. The study concluded that PHGG effectively increased bowel movement frequency without increasing gastrointestinal symptoms, making it a promising option for individuals with chronic constipation or irritable bowel syndrome-related constipation.

Limited Value of Colonoscopy for Evaluating Constipation in Young Women

A LARGE-SCALE, multi-centre study presented at UEG Week 2024 has shed new light on the effectiveness of colonoscopy as a diagnostic tool for young women with constipation.

The study, conducted across seven endoscopy departments between 2016–2021, analysed colonoscopy findings in a cohort of women aged 40 years and younger to assess the procedure's diagnostic value in cases of isolated constipation.

Constipation is one of the most common gastrointestinal disorders affecting women, with a variety of potential causes. The research team aimed to determine whether colonoscopy, a common procedure used to diagnose gastrointestinal conditions, is necessary or beneficial for younger women presenting with constipation.

The study included a total of 377,795 patients, of which 198,629 (52.6%) were female. Of these women, 7,872 underwent colonoscopies for constipation and other symptoms (Cohort 1), while 6,852 underwent colonoscopy specifically for constipation (Cohort 2). The findings in younger women under 40 years of age were compared to those in older women.

Results revealed that colonoscopies performed on women under 40 years old had a limited diagnostic yield. In both cohorts, approximately 75% of colonoscopies in this age group returned normal results.

However, the study did highlight a higher prevalence of inflammatory bowel diseases, such as ulcerative colitis (UC) and Crohn's disease, amongst younger women compared to older women. In Cohort 1, UC was found in 1.2% and Crohn's disease in 0.7% of women under 40 years of age. In Cohort 2, UC was present in 0.7% and Crohn's disease in 0.2%.

In contrast, the prevalence of conditions like diverticulosis and polyps increased significantly with age, with a notable rise in women over 40 years old. Among women younger than 40, the rate of diverticulosis was only 0.5%, and the rate of polyps was 7.4%. Only one case of colorectal cancer was identified in women under 40 years.

The study also compared findings between genders and found no significant difference in the prevalence of inflammatory bowel diseases, diverticulosis, polyps, or colorectal cancer between men and women under 40 years.

Ultimately, the study concluded that colonoscopy has limited diagnostic value for isolated constipation in young women, suggesting that clinicians should consider other, less invasive diagnostic tools before recommending colonoscopy in such cases.

In Cohort 1:

UC was found in **1.2%**

Crohn's disease in **0.7%**

of women under 40 years of age

In Cohort 2:

UC was found in **0.7%**

Crohn's disease in **0.2%**

of women under 40 years of age

New Study Identifies Predictive Biomarkers for Inflammatory Bowel Disease Treatments

A NEW study from Spain has advanced the search for predictive biomarkers that could enhance personalised medicine for patients with inflammatory bowel disease (IBD).

The research, presented at UEG Week 2024, highlights the importance of understanding the diverse biological factors that influence treatment responses in conditions like Crohn's disease (CD) and ulcerative colitis (UC).

Inflammatory bowel diseases are characterised by significant heterogeneity, making it challenging to predict which patients will respond to therapies, particularly biologics and JAK inhibitors. The study involved a multiomic analysis of 53 patients with active CD and 50 with active UC, assessing their responses to treatments over 14 weeks. By employing techniques such as RNA sequencing, liquid chromatography-mass spectrometry, and 16S rRNA gene sequencing, researchers aimed to identify specific biomarkers associated with treatment responses.

Results revealed several promising indicators. Differential gene expression analyses in intestinal tissues highlighted key differences between responders and non-responders among patients with UC treated with anti-TNF, vedolizumab, and tofacitinib.

Proteomic analyses identified various proteins that could differentiate responders from non-responders, particularly for anti-TNF treatment, with predictive values indicated by area under the curve scores of 0.81 and 0.96 for CD and UC, respectively.

Metabolomic findings showed an up-regulation of 21 lipoproteins in serum from CD responders to ustekinumab, while metabolic pathways linked to ketone and butyrate metabolism were enriched. Additionally, significant differences in miczrobial composition were noted in patients with UC, depending on their treatment response.

The findings from this study represent a significant step toward personalised treatment strategies for patients with IBD, suggesting that biomarkers in gene expression, protein levels, metabolites, and gut microbiota composition could guide therapy selection. Further research is essential to validate these biomarkers and their potential clinical applications, paving the way for more effective and individualised treatment options for those with IBD.

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