The IDEA Journal
International Digestive Experts Articles

Year IV - N. 1, March 2022

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Microbiota transplantation in metabolic syndrome

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QUARTERLY SCIENTIFIC UPDATE IN GASTROENTEROLOGY

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Editorial

Updates on Literature

In this first number of The IDEA Journal 2022 edition, three new studies and the update on international guidelines from the gastroenterology world are discussed.

In one editorial contribution, Antonelli and Hassan comment on one of their latest publications, discussing the advances in systems using Artificial Intelligence for polyp detection. This is the first clinical study evaluating a new Computer Aided device in polyp detection. The novelty of this device lies in the ability to undergo the diagnostic process in white light and in real time during the endoscopic procedure, virtually bypassing the need to use any kind of chromoendoscopy and integrating in the standard workflow of colonoscopy. Once the polyp is detected, the systems "locks" onto the polyp and, in a few seconds, it displays its prediction. The study highlighted the high potential in meeting the predefined threshold requirements to implement optical diagnosis in clinical practice. The system showed the possibility of implementing a diagnose-and-leave strategy as well as a resect-and-discard strategy for adenomas in the whole colon, which is clinically and financially significant.

In another editorial contribution of this number, Bredenoord discusses a recent article focusing on a very hot topic. Previous evidence, indeed, has showed that gut microbiota transplantation from lean donors to obese recipients can increase insulin resistance. The study discussed here investigated the long-term effects of repeated faecal healthy microbiota transplantation to subjects with obesity and type 2 diabetes who were under lifestyle intervention or not. The results showed not only that the transplantation treatment was effective, as compared to placebo, in increasing the adjustment to the lean-associated microbiota and in increasing the butyrate-producing bacteria, but also that the optimal effect could be achieved when combining this treatment with the lifestyle intervention. This evidence is relevant in light of the global obesity pandemic.

Related to this topic, Bredenoord also discusses another interesting article, this time about gastroesophageal reflux disease, whose incidence has raised in the past 20 years, both in Western countries and in Asia. Two factors that are believed to contribute to it are indeed the increase in body weight as well as changes in eating patterns and lifestyle. Coffee stimulates gastrin release and gastric acid secretion and thus has many effects on the gastrointestinal tract. An artificial dewaxing process is able to extract most of the caffeine, possibly making it more tolerable. The study in object investigated the effects of dewaxed, decaffeinated coffee on reflux symptoms in patients with gastroesophageal reflux disease, consumed daily for two weeks without changing anything else in their habitual diet. The results confirmed the hypothesis that dewaxed coffee triggers significantly less reflux symptoms, both heartburn and regurgitation. Thus, these patients can be recommended to consume dewaxed coffee.

In the fourth editorial contribution are highlighted the main changes in the updated guidelines on diagnosis and treatment of functional dyspepsia of the British Society of Gastroenterology. Based on substantial advances made in understanding the complex pathophysiology of this disease, the guidelines reviewed and summarised the current evidence to inform and guide clinical practice, by providing a practical framework for evidence-based diagnosis and treatment. The approach to investigate the patient on every step and the efficacy of drugs, along with the strength of recommendations and the overall quality of evidence, are reported. Of relevance, the present guidelines have also been reviewed by patients and added their perspective. This point gives additional value to the guidelines, especially in light of the recommendation to clinicians of empathically communicating as well as explaining to the patients their disorder and symptoms, while minimizing unnecessary exams and investigations or therapies. These recommendations are predicted to have an important impact on the patients' quality of life as well as on the healthcare system.

The Editorial Board

Optical diagnosis of colorectal polyps using artificial intelligence: first clinical study on a new device

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Comment to: Hassan, C., Balsamo, G., Lorenzetti, R., Zullo, A., & Antonelli, G. (2022). Artificial Intelligence allows Leaving-in-Situ colorectal polyps. Clinical Gastroenterology and Hepatology. S1542-3565(22)00639-5. https://doi.org/10.1016/j.cgh.2022.04.045

It is well known that colonoscopy and polypectomy reduce colorectal cancer incidence and mortality by removing colorectal cancer precursors (polyps) before they transform in invasive cancer (1). Well established quality parameters, in particular Adenoma Detection Rate (ADR), have been correlated with post-colonoscopy colorectal cancer (2), and a major drive towards improving ADR is still ongoing since recent evidence shows that, even for high detectors, every small improvement in ADR is related to a reduction in CRC risk (3). Artificial Intelligence for polyp detection (CADe) has indeed been one of the most recent breakthroughs in increasing ADR, showing a consistent effect in different Countries, patient populations and variably performing endoscopists (4) (see in-depth Box 1).

On the other hand, when considering the magnitude of colonoscopies performed, covering between 1% and 6% of the target general population per year, the financial and economic burden is relevant. A relevant contribution of such burden is represented by the post-polypectomy histology cost, mostly attributed to diminutive polyps that represent over 90% of all the resected lesions. By predicting in vivo histology, such pathology costs may be averted by the implementation of two cost-saving strategies, namely the 'leave-in-situ' or the 'resect and discard' strategy for <5 mm hyperplastic lesions in the rectosigmoid (5).

This is the first clinical study using a new CADx module integrating the previously commercially available CADe module. The great difference of this system, as compared to all previously studied ones, is the ability to undergo the diagnostic process in white light and in real time during the endoscopic procedure, virtually bypassing the need to use any kind of chromoendoscopy and integrating in the standard workflow of colonoscopy. Once the polyp is detected, the systems "locks" onto the polyp and in a few seconds displays its prediction.

Despite the acceptance by experts, the accuracy of optical diagnosis in the community setting has been unexpectedly poor, preventing the implementation of these cost-saving interventions. Many reasons have been found for this setback, namely fear for medico-legal implications, lack of training and auditing, unavailability of the advanced endoscopic imaging technologies needed to perform a reliable optical diagnosis.

In addition, the clinical relevance of these small lesions has been debated, being mostly represented by either non-advanced adenomas or indolent

hyperplastic polyps. Moreover, the role of pathology as reference standard has been questioned because of possible high interobserver agreement, inadequate orientation or insufficient material, especially when targeting small <5mm lesions that often go lost during the preparation phase. By automatizing the perception phase of colonoscopy, AI may overcome both of these pitfalls in detection and characterization. Based on deep learning, Computer Aided Detection (CADe) can recognize in real-time lesions that are present on the screen and that may have been missed by the endoscopist. Similarly, Computer Aided Characterization (CADx) can predict the histology of the lesion, providing the correct classification to the endoscopist.

Before the publication of this study, only one other clinical study was available studying a commercially available CADx system, showing that the system fell short of required thresholds for the implementation of optical diagnosis in clinical practice, although by very little difference.

The study we are commenting in this edition is the first clinical study of a new CADx module integrating the previously commercially available CADe module of GI Genius (Medtronic, USA). Aim of this study was to assess whether this CADx systems was able to match the predefined thresholds that are required to implement optical diagnosis in clinical practice. The great difference of this system, as compared to all previously studied CADx systems, is the ability to undergo the diagnostic process in white light and in real time during the endoscopic procedure, virtually bypassing the need to use any kind of chromoendoscopy and integrating in the standard workflow of colonoscopy. Once the polyp is detected, the systems "locks" onto the polyp and in a few seconds displays its prediction.

The primary endpoint of this study was to assess whether the system was capable of implementing the Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) diagnose-and-leave strategy for all hyperplastic rectosigmoid polyps. This was possible if the system achieved the required negative predictive value (NVP) of >90% for adenomatous histology in rectosigmoid diminutive polyps.

The secondary endpoint was the agreement in assignment of post-polypectomy surveillance intervals according to established guidelines between the assignment identified according to the combined CADx optical diagnosis for diminutive (≤5 mm) polyps and histology for larger polyps (>6 mm) and the assignment identified according to histology alone, regardless of lesion size. This is the requirement for implementing the PIVI Resect-and-Discard

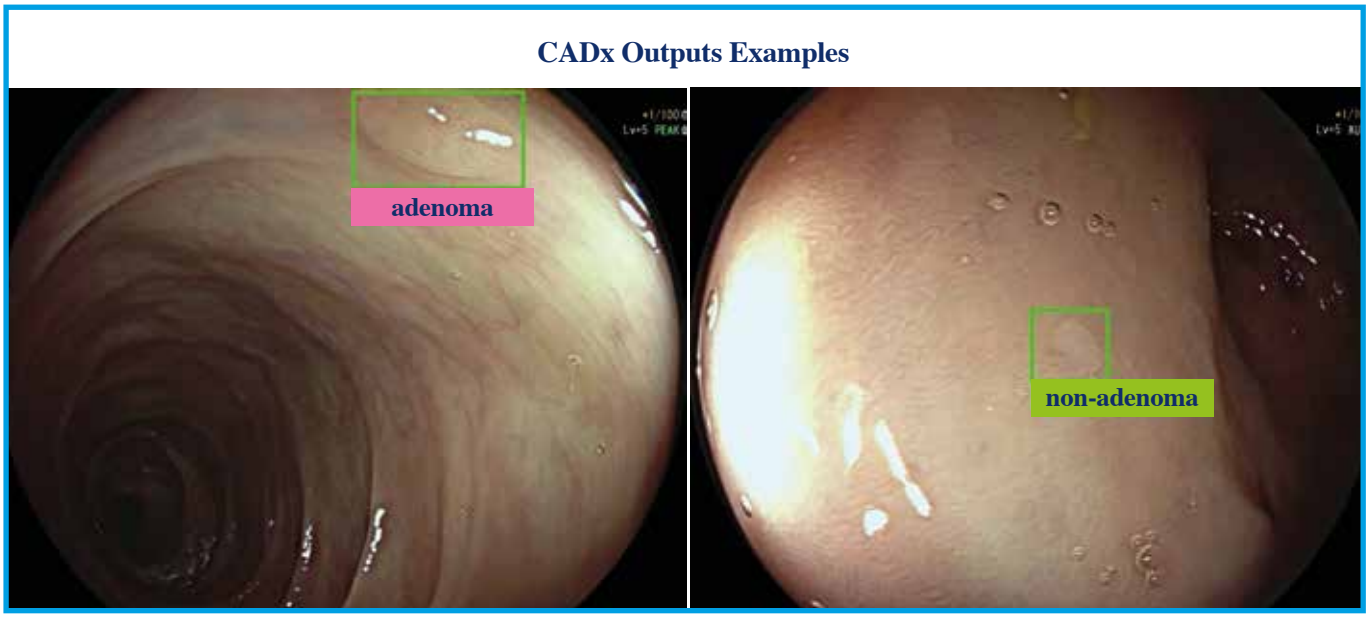

Figure 1

strategy for <5mm adenomas in the whole colon. The results of the study showed, first of all, that the CADx system met the required NPV for implementation of the diagnose-and-leave strategy. This is clinically and financially significant since in the population of the study, implementing diagnose-and-leave would have resulted in a reduction of 44% of pathological analysis. The system also showed the possibility of implementing resect-and-discard strategy for adenomas in the whole colon, bringing the total potential pathology reduction to over 80% (Figure 1). The potential showed by the CADx system is very high, and beyond the great expenses it would save, it would also permit a standardisation and quality control for differently performing endoscopists.

Through a systematic review and meta-analysis, Hassan and colleagues (4) summarised available randomized clinical trials on the performance of computer aided polyp detection (CADe) systems in colorectal neoplasia detection. Deep learning systems with real time CADe have indeed shown high accuracy in artificial settings, and preliminary evidence have indicated favourable outcomes in clinical setting. In conclusion, the authors found that the incorporation of Artificial Intelligence as aid for detection of colorectal neoplasia results in a significant increase of such detection, and this effect is independent from main adenoma characteristics.

Box 1

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Microbiota transplantation in metabolic syndrome

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Comment to: Ng SC et al. Microbiota engraftment after faecal microbiota transplantation in obese subjects with type 2 diabetes: a 24-week, double-blind, randomised controlled trial. Gut. 2022 Apr;71(4):716-723. doi: 10.1136/gutjnl-2020-323617. Epub 2021 Mar 30. PMID: 33785557.

INTRODUCTION

The metabolic syndrome, typically characterized by hypertension, obesity, hypercholesterolaemia, liver steatosis, and type 2 diabetes mellitus is increasing rapidly in incidence in many countries. It results in substantial morbidity and mortality. The first line management consists of lifestyle measures, such as diet and physical exercise, but this is usually not very effective in reducing body weight and the consequences of the metabolic syndrome. Effective pharmacological treatments are lacking either and new breakthrough drugs are not expected soon. The only truly high success approach is bariatric surgery, but this is very invasive, irreversible, and accompanied by substantial peri-operative complications and long-term risks.

It is thus essential to better understand the pathogenesis of obesity-related insulin resistance and type 2 diabetes and subsequently, the lifestyle refractory nature of obesity. This could lead to more effective interventions in the future.

It has been suggested that changes in gut microbiota are important in the pathophysiology of obesity and the metabolic syndrome. Studies have reported that obese individuals had abnormal gut microbiota and humanised mouse models suggest that the gut microbiota may be a causative factor in obesity (1). An abnormal microbiome with a decrease in butyrate-producing bacteria and enrichment of microbial functions conferring sulphate reduction and oxidative stress resistance has been found in patients with diabetes. The microbiome of the obese subject seems to be more effective in retrieving energy from the consumed foods.

> The relevance of this study lies especially in the fact that it shows that for an optimal effect in reducing markers of the metabolic syndrome, not only repeated faecal microbiota transplantation is required, but also its combination with lifestyle interventions.

The microbiome can be changed actively by faecal microbiota transplantation (FMT). With this technique the processed faeces of a donor are instilled via a naso-jejunal catheter in the small bowel of the recipient, with the objective of replacing or altering the recipient unhealthy microbiome. Alternatively, capsules containing microbiome extracts are taken orally. The use of FMT for treatment of the metabolic syndrome is a hot scientific topic. Unconfirmed data in patients with metabolic syndrome suggest that FMT can indeed improve insulin sensitivity and increases gut microbial diversity, showing increases in butyrate-producing bacteria (2). Two randomised trials with a small sample size showed that the use of oral capsules containing healthy microbiota grafts to obese subjects resulted in short-term adoption

of the new microbiota. A randomised trial in type 1 diabetes mellitus showed that FMT could temporarily halt the decline in endogenous insulin production and certain gut microbiota were linked to preserved beta-cell function in humans (3) (see in-depth Box 1). The question remains whether the change in the microbiome is long-lasting or whether maintenance administration of the new microbiome will be required.

Also, if FMT would be efficacious for metabolic syndrome and type 2 diabetes, what would be the role of lifestyle adjustments? Could lifestyle measures themselves have added value, have a direct effect on the microbiome itself by reducing obesity and drivers of the abnormal obese microbiome? FMT of microbiome of previously obese subjects that lost weight after adopting lifestyle measures has shown to reduce weight again if given to these same subjects after they gained weight again, suggesting that the effects should be searched for in the microbiome itself.

The objective of the study was to assess the long-term effects of repeated FMT of healthy microbiome to subjects with obesity and type 2 diabetes, who were adopting lifestyle modifications or not. This allowed the investigators to study the effects of concurrent lifestyle measures on FMT in this patient population.

The study was performed in a double-blind, randomised, placebo-controlled manner with three arms: FMT plus lifestyle intervention, FMT alone, or sham transplantation plus lifestyle intervention. FMT was repeated every 4 weeks up to week 12, and patients were followed up until 24 weeks. FMT was prepared from six healthy lean donors. Faecal metagenomic sequencing was performed at different time points throughout the study and results show that at week 24 all subjects receiving FMT and lifestyle measures acquired ≥20% of lean-associated microbiota, 88.2% of the subjects receiving only FMT acquired ≥20% of lean-associated microbiota and only 22% of the patients receiving sham FMT plus lifestyle interventions. The differences between these groups were statistically significant.

It was also shown that multiple FMTs increased the adjustment to lean-associated microbiota. FMT increased butyrate-producing bacteria, even if not combined with lifestyle interventions; however, combining FMT and lifestyle interventions also led to an increase in *Bifidobacterium and Lactobacillus*. The combination of FMT plus lifestyle intervention also had beneficial effects on markers of the metabolic syndrome such as reduced total and low-density lipoprotein cholesterol and reduced liver

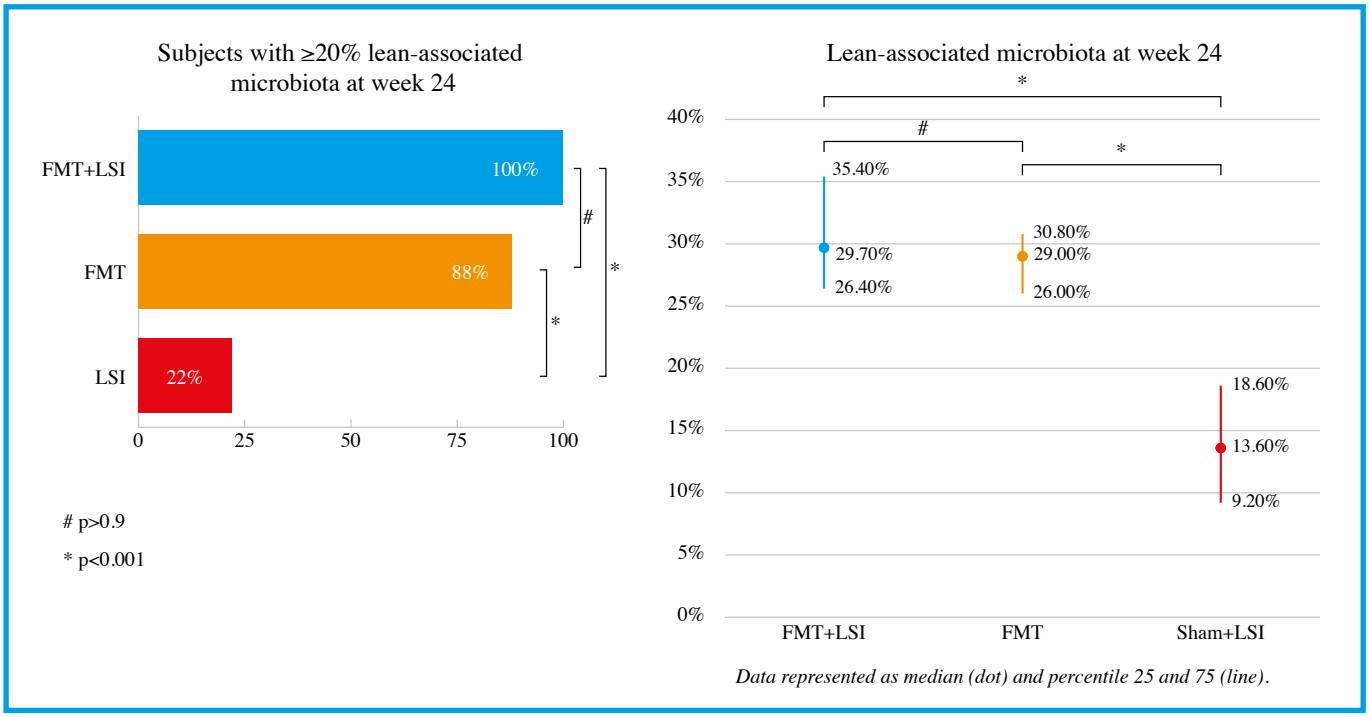

Figure 1

stiffness at week 24 compared with study onset. The present study is important as it shows that for the optimal effect, repeated FMT will be required and there is a larger effect of FMT when this is combined with lifestyle interventions. The results are encouraging for scientists working in this field, for clinicians treating patients with metabolic syndrome, for patients, and for society as the phenomenon of metabolic syndrome has become a huge burden.

Vrieze and colleagues (3) studied the effects of infusing intestinal microbiota from lean donors to male recipients with metabolic syndrome (body mass index > 30 kg/m^2 or waist circumference > 102 cm and a fasting plasma glucose level > 5.6 mmol/L) on the recipients' microbiota composition and glucose metabolism. Patients were assigned randomly to groups that were given small intestinal infusions of allogenic or autologous microbiota. Six weeks later, insulin sensitivity of obese recipients increased (median rate of glucose disappearance changed from 26.2 to 45.3 μmol/kg/min; $p < 0.05$) along with levels of butyrate-producing intestinal microbiota. These results suggest that intestinal microbiota might be developed as therapeutic agents to increase insulin sensitivity in humans.

Box 1

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The updated British Society of Gastroenterology guidelines on diagnosis and treatment of functional dyspepsia: on the patient's side in primary care

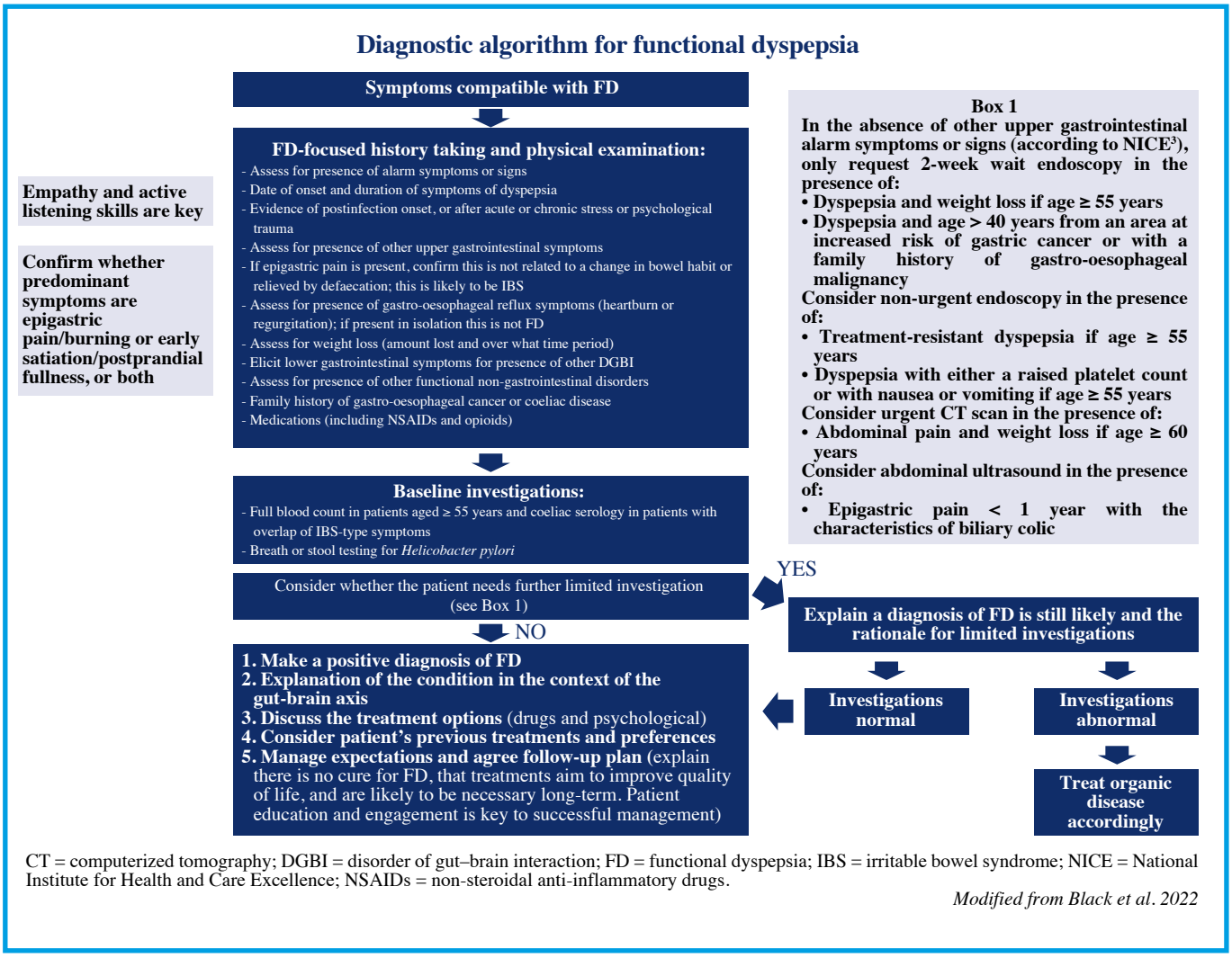
Comment to: Black, C. J., Paine, P. A., Agrawal, A., Aziz, I., Eugenicos, M. P., Houghton, L. A., Hungin, P., Overshott, R., Vasant, D. H., Rudd, S., Winning, R. C., Corsetti, M., & Ford, A. C. (2022). British Society of Gastroenterology guidelines on the management of functional dyspepsia. Gut, 71(9), 1697–1723. https://doi.org/10.1136/gutjnl-2022-327737

The present guidelines of the British Society of Gastroenterology − an update of the previous document published in 1996 (1) − provide new evidence-based clinical guidance for doctor-patient communication and diagnosis, management, and further investigation of functional dyspepsia (FD). FD, a common disorder of gut-brain interaction, is the main underlying cause of symptoms in patients with dyspepsia, often referred by them as indigestion. Based on the Rome IV criteria (2), FD is classified into two distinct subtypes: postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS). Clinically, although PDS and EPS can overlap, the EPS subtype separates those with epigastric pain or burning, which is often present regardless of meals, from those with PDS who report early satiation and postprandial fullness, mainly triggered by meals.

Importantly, the present guidelines have also been reviewed by patients and added their perspective. This point gives additional value to the guidelines, especially in light of the recommendation to the doctors of empathically communicating as well as explaining to the patients their disorder and symptoms, while minimizing unnecessary exams and investigations or therapies. These recommendations are predicted to have an important impact on the patients' quality of life as well as on the healthcare system.

> A multidisciplinary approach with a special eye on the patient is what constitutes the updated British Society of Gastroenterology guidelines on diagnosis and treatment of functional dyspepsia in primary care.

Among the most relevant recommendations concerning symptoms investigation and diagnosis, based on the epidemiology and the pathophysiology of FD, the guidelines highlight that clinicians in primary care should be aware that the 80% of people with dyspepsia are diagnosed with FD following endoscopy. Moreover, the guidelines recommend that, in the absence of upper gastrointestinal alarm symptoms or signs, FD should be diagnosed when bothersome epigastric pain or burning, early satiation, and/or postprandial fullness of length greater than 8 weeks are present. Also of relevance is that the guidelines recommend using a full blood count in patients ≥ 55 years with dyspepsia; coeliac serology in all patients with FD and overlapping irritable



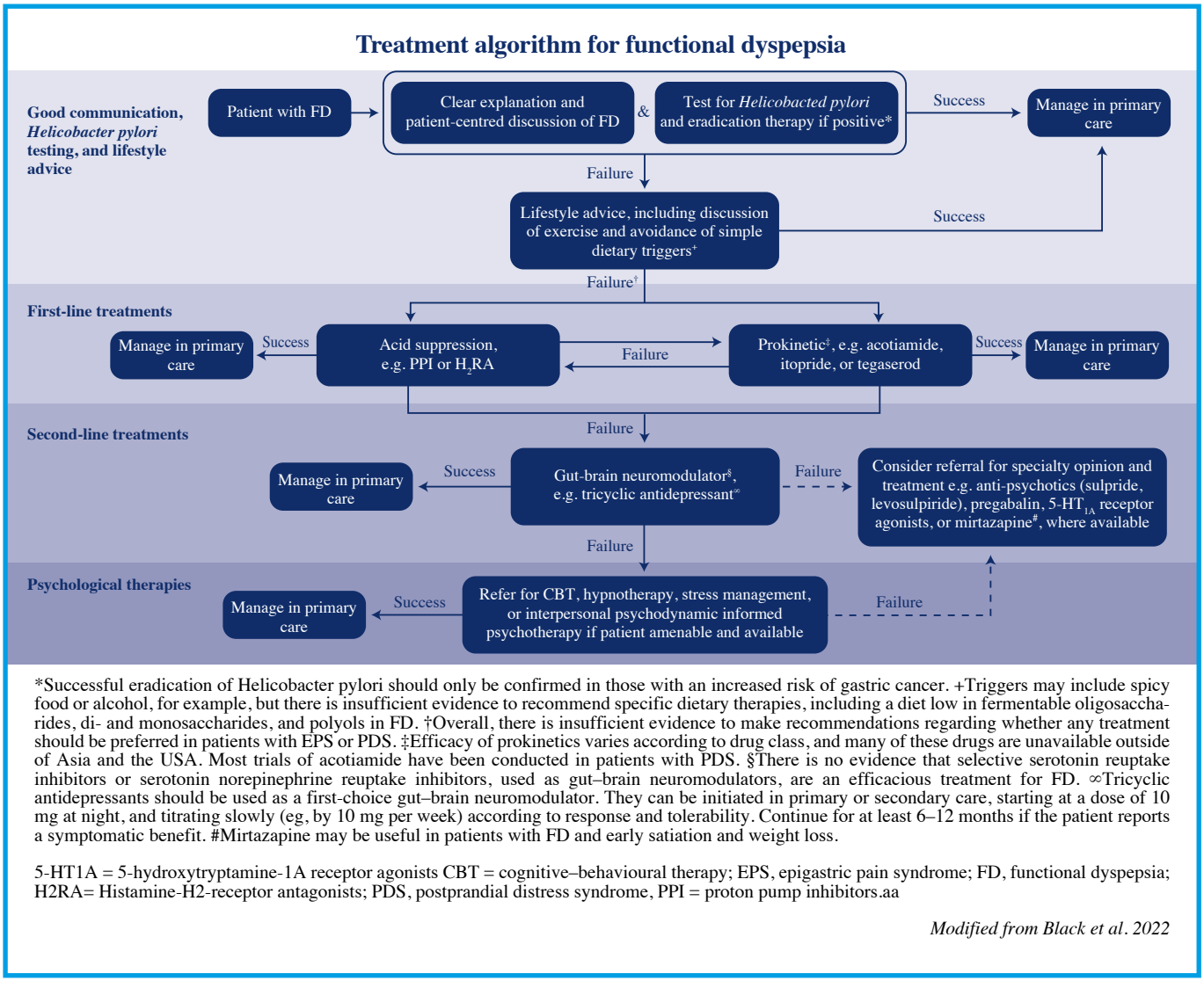
CT = computerized tomography; DGBI = disorder of gut–brain interaction; FD = functional dyspepsia; IBS = irritable bowel syndrome; NICE = National Institute for Health and Care Excellence; NSAIDs = non-steroidal anti-inflammatory drugs.

Modified from Black et al. 2022

Figure 1

bowel syndrome; urgent endoscopy only in dyspeptic patients ≥ 55 years old with weight loss and no other upper gastrointestinal symptoms, or in those > 40 years old when in high risk of gastric cancer or with a family history of gastro-oesophageal cancer. Non-urgent endoscopy is, on the other hand, recommended in patients ≥ 55 years old with treatment-resistant dyspepsia or dyspepsia with either raised platelet count or nausea or vomiting. Urgent abdominal computed tomography scanning is recommended in patients ≥ 60 years old with abdominal pain and weight loss, whereas for all other patients with dyspepsia is recommended Helicobacter pylori non-invasive testing (recommendation: "strong"; quality of evidence: "high"). Relatedly, the guidelines report a visual diagnostic algorithm, useful as a memorandum in "busy clinical practice" (Figure 1).

In the case of treatment too, the present guidelines offer a visual algorithm (Figure 2). Once again, good communication and suggestions for a better life style (i.e. regular aerobic exercise in light of scarce evidence about dietary solutions) have a prominent as well as primary role. Recommendations on how to treat patients in case they are positive for Helicobacter pylori infection (i.e. eradication; recommendation: "strong"; quality of evidence: "high"), or not (i.e. empirical acid suppression therapy) are offered. Confirmation of successful treatment is recommended only in patients at increased risk of gastric cancer. Referral of patients with FD to gastroenterology in secondary care is deemed appropriate where there is diagnostic doubt, severe symptoms, or when they are refractory to first-line treatments or when they specifically request



*Successful eradication of Helicobacter pylori should only be confirmed in those with an increased risk of gastric cancer. +Triggers may include spicy food or alcohol, for example, but there is insufficient evidence to recommend specific dietary therapies, including a diet low in fermentable oligosaccharides, di- and monosaccharides, and polyols in FD. †Overall, there is insufficient evidence to make recommendations regarding whether any treatment should be preferred in patients with EPS or PDS. ‡Efficacy of prokinetics varies according to drug class, and many of these drugs are unavailable outside of Asia and the USA. Most trials of acotiamide have been conducted in patients with PDS. §There is no evidence that selective serotonin reuptake inhibitors or serotonin norepinephrine reuptake inhibitors, used as gut–brain neuromodulators, are an efficacious treatment for FD. ∞Tricyclic antidepressants should be used as a first-choice gut–brain neuromodulator. They can be initiated in primary or secondary care, starting at a dose of 10 mg at night, and titrating slowly (eg, by 10 mg per week) according to response and tolerability. Continue for at least 6–12 months if the patient reports a symptomatic benefit. #Mirtazapine may be useful in patients with FD and early satiation and weight loss.

5-HT1A = 5-hydroxytryptamine-1A receptor agonists CBT = cognitive–behavioural therapy; EPS, epigastric pain syndrome; FD, functional dyspepsia; H2RA= Histamine-H2-receptor antagonists; PDS, postprandial distress syndrome, PPI = proton pump inhibitors.aa

Modified from Black et al. 2022

Figure 2

a specialist opinion. It is also recommended that gastric emptying testing or 24-hour pH monitoring should not be undertaken routinely in patients with typical symptoms of FD. Moreover, patients with FD referred to secondary care should be managed in a specialist clinic that offers dietetic and lifestyle support as well as with access to effective drugs and gut–brain cognitive-behavioural therapies.

Furthermore, the guidelines provide a detailed overview of different drugs used in primary and secondary care of FD along with their efficacy, with a quick look at drugs and therapies to date under development (see in-depth Box 1). In first-line FD treatment, besides the Helicobacter pylori eradication, also Histamine-H2-receptors, Proton pump inhibitors (recommendation: "strong"; quality of evidence: "high"), and prokinetics are discussed. In second-line FD treatment, tricyclic antidepressants, antipsychotics, selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors, and others are discussed. Of note, most of these drugs are used as gut-brain neuromodulators, highlighting the role of disordered brain processing in this pathology.

To sum up, a multidisciplinary approach with a special eye on the patient is what constitutes the updated British Society of Gastroenterology guidelines on diagnosis and treatment of functional dyspepsia in primary care.

Intervention	Recommendation	Quality of Evidence
Helicobacter pylori eradication therapy is effective in FD	Strong	High
Histamine-H2-receptor antagonists may be effective in FD	Weak	Low
Proton pump inhibitors are effective in FD • Any dose • High dose • Standard dose • Low dose	 Strong Strong Strong Strong	 High High High High
Prokinetics may be effective in FD • Acotiamide • Itopride • Mosapride • Tegaserod	 Weak Weak Weak Strong	 Low Low Low Moderate
Antipsychotic drugs (sulpiride and levosulpiride) may be effective in FD	Weak	Low
Tricyclic antidepressants are effective in FD	Strong	Moderate
Selective serotonin reuptake inhibitors are not effective in FD	Weak	Moderate
Serotonin norepinephrine reuptake inhibitors are not effective in FD	Weak	Low
Tandospirone may be effective in FD	Weak	Low
Buspirone is not effective in FD	Weak	Low
Modified from Black et al. 2022		

Box 1. Recommendation and Quality of Evidence for Drugs used in the treatment of Functional Dysplasia (FD)

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Dewaxed coffee is better if you suffer from heartburn

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Comment to: Effect of Dewaxed Coffee on Gastroesophageal Symptoms in Patients with GERD: A Randomized Pilot Study. Polese B, Izzo L, Mancino N, Pesce M, Rurgo S, Tricarico MC, Lombardi S, De Conno B, Sarnelli G, Ritieni A. Nutrients. 2022 Jun 16;14(12):2510.

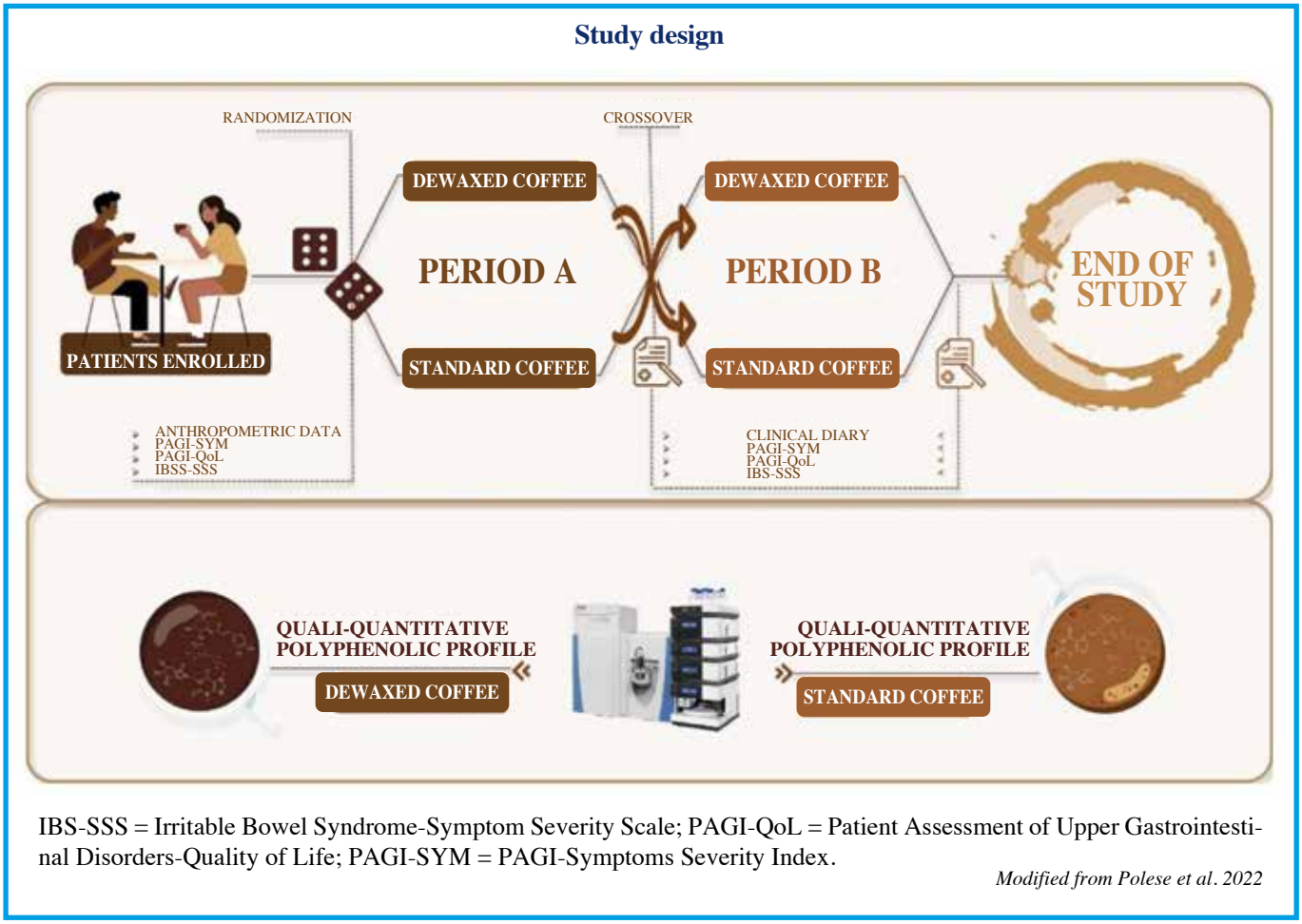
Gastroesophageal reflux disease (GERD) is characterized by symptoms of heartburn and regurgitation due to the retrograde flow of gastric contents into the esophagus. There has been a strong increase in incidence of GERD is the past 20 years, both in Western countries and in Asia. It is believed that changes in lifestyle play a role here. Both increasing body weight and obesity as well as changes in eating patterns contribute to this.

In the medical specialist practice, treatment of GERD consists of proton pump inhibitors or even surgery, but it is estimated that 80-90% of the GERD patients never consult a doctor for their symptoms (1). Instead, they use over-the-counter solutions such as mucosal protectants and antacids or find relief from changes in lifestyle patterns. Weight loss can result in symptoms' reduction, but it is notoriously difficult to obtain and persistent; instead, many patients avoid foods and drinks that they feel trigger their symptoms. Products that are often reported to trigger GERD symptoms are orange juice, high-fat meals, chocolate, red wine, and coffee (2).

Coffee has many effects on the gastrointestinal tract, it indeed promotes the occurrence of gastroesophageal reflux and subsequent heartburn (3). Coffee stimulates gastrin release and gastric acid secretion, but studies on the effect on lower esophageal sphincter pressure yielded conflicting results. Coffee also prolongs the adaptive relaxation of the proximal stomach, suggesting that it might slow gastric emptying. However, other studies indicate that coffee does not affect gastric emptying or small bowel transit. Coffee induces cholecystokinin release and gallbladder contraction, which may explain why patients with symptomatic gallstones often avoid drinking coffee. Coffee increases rectosigmoid motor activity within a few minutes after consumption. Since coffee contains no calories, and its effects on the gastrointestinal tract cannot be ascribed to its volume load, acidity, or osmolality, it must have pharmacological effects but caffeine alone cannot explain all these gastrointestinal effects.

This study results are in line with the idea that dewaxed coffee triggers less reflux symptoms in patients with gastroesophageal reflux disease. Patients in which coffee is associated with their symptoms can thus be recommended to consume dewaxed coffee.

In coffee beans, waxes are present on the surface. These waxes represent 0.2% - 0.3% of the lipids on green coffee and they are difficult to absorb and barely digestible, and it has been suggested that these waxes can trigger symptoms. Using a process with dichloromethane, the waxes can be separated from the beans and dewaxed coffee can be made. In this process, also the majority of caffeine is extracted. It is claimed that this dewaxed, decaffeinated coffee is better tolerable to patients with GERD symptoms, but this has not been proven so far.



IBS-SSS = Irritable Bowel Syndrome-Symptom Severity Scale; PAGI-QoL = Patient Assessment of Upper Gastrointestinal Disorders-Quality of Life; PAGI-SYM = PAGI-Symptoms Severity Index.

Modified from Polese et al. 2022

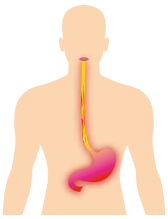
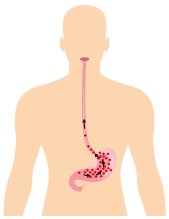
Figure 1

Therefore, Polese and colleagues have performed a randomized crossover clinical trial to investigate the effects of dewaxed coffee on reflux symptoms. The study was performed in 40 patients with GERD, in which the diagnosis was previously made in their clinic. The study design consisted of a four-week randomized, cross-over period consisting of two weeks of standard coffee consumption and two weeks of dewaxed coffee consumption, separated by a two-week washout period (Figure 1). Randomization was performed in blocks of four using a computer-generated list, and subjects were blinded to their allocation. Patients were asked to continue their habitual diet during the whole study period. Patients received the assigned coffee on the first day and they were advised to consume a maximum of four cups/pods a day. After two weeks, patients returned and received the second type of coffee, which they started after the wash-out period. Number of consumed coffee pods, presence of the GERD symptoms heartburn and regurgitation, and antacid assumption were assessed by patient entries into a tick-box diary for the two study periods (see in-depth Box 1).

The results of the study confirmed the hypothesis. The assessment of patient diaries highlighted a significant reduction of symptoms frequency when consuming dewaxed coffee and a significant increase in both heartburn-free and regurgitation-free days. Consequentially, patients had a significant increase of antacid-free days during the two weeks they consumed dewaxed coffee.

The content and polyphenolic profile of the coffee pods was also ascertained in an in vitro analysis using UHPLC-Q-Orbitrap HRMS analysis. Chlorogenic acids were the most abundant investigated compounds. Caffeine was quantified at a concentration level of 5.6 mg/g in dewaxed coffee and 11.091 in standard coffee.

The data from this study thus confirm the hypothesis that dewaxed coffee triggers less reflux symptoms in patients with GERD. Patients in which coffee is associated with their symptoms can thus be recommended to consume dewaxed coffee.

	 Heartburn	 Regurgitation		 Need to taken antacids	 Number coffee
DAY 1	YES ☐ NO ☐	YES ☐ NO ☐	DAY 1	YES ☐ NO ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐
DAY 2	YES ☐ NO ☐	YES ☐ NO ☐	DAY 2	YES ☐ NO ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐
DAY 3	YES ☐ NO ☐	YES ☐ NO ☐	DAY 3	YES ☐ NO ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐
DAY 4	YES ☐ NO ☐	YES ☐ NO ☐	DAY 4	YES ☐ NO ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐
DAY 5	YES ☐ NO ☐	YES ☐ NO ☐	DAY 5	YES ☐ NO ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐
DAY 6	YES ☐ NO ☐	YES ☐ NO ☐	DAY 6	YES ☐ NO ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐
DAY 7	YES ☐ NO ☐	YES ☐ NO ☐	DAY 7	YES ☐ NO ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐
DAY 8	YES ☐ NO ☐	YES ☐ NO ☐	DAY 8	YES ☐ NO ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐
DAY 9	YES ☐ NO ☐	YES ☐ NO ☐	DAY 9	YES ☐ NO ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐
DAY 10	YES ☐ NO ☐	YES ☐ NO ☐	DAY 10	YES ☐ NO ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐
DAY 11	YES ☐ NO ☐	YES ☐ NO ☐	DAY 11	YES ☐ NO ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐
DAY 12	YES ☐ NO ☐	YES ☐ NO ☐	DAY 12	YES ☐ NO ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐
DAY 13	YES ☐ NO ☐	YES ☐ NO ☐	DAY 13	YES ☐ NO ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐
DAY 14	YES ☐ NO ☐	YES ☐ NO ☐	DAY 14	YES ☐ NO ☐	0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐

Box 1. Example of patient diary during the 14-day treatment adapted from Polese et al. 2022. Annotation for heatburn, regurgitation symptoms, and need to take antacids correlated to coffee intake.

References

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