Postprandial worsening of symptoms, as well as adverse reactions to one or more foods are common in patients with irritable bowel syndrome (IBS), and self-reported food intolerance in IBS is associated with high symptom burden and reduced quality of life. In line with this, approximately two thirds of IBS patients exclude food items from their diet to improve symptoms. Despite this, there is no evidence suggesting inadequate nutrient intake in the majority of patients with IBS. For patients, identifying the food item/s they do not tolerate is often central when consulting for their symptoms, and in general guidelines for management of IBS, dietary advice is proposed to be of major importance. However, there are currently no available evidence-based guidelines for dietetic practice in IBS, as very few randomized, controlled trials exist on dietary treatment of IBS patients. Instead, the current recommendations are primarily based on studies assessing physiologic function in relation to dietary components, and to a lesser degree on research based on randomized, controlled trials examining the role of dietary components in the therapeutic management of IBS patients. Therefore, the article by Halmos et al published in this issue of Gastroenterology is a welcome addition to the existing literature. In a randomized, controlled trial, they demonstrate that reducing the intake of poorly absorbed short-chain carbohydrates, or fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs), substantially improves the severity of the key symptoms of IBS.

The hypothesis that reducing intake of FODMAPs can improve gastrointestinal (GI) symptoms stems from the clinical observation that a proportion of patients with IBS tolerate intake of certain short-chain carbohydrates poorly. Moreover, these carbohydrates can be incompletely absorbed in the small intestine due to absent hydrolyzation (eg, lactose maldigestion, and nondigestible oligosaccharides), dependence on simultaneous intake of glucose for adequate absorption (fructose), or passive diffusion (certain monosaccharides and polyols). Therefore, the absorption of short-chain carbohydrates in the small intestine varies depending on different factors such as presence/absence of enzymes to digest disaccharides (eg, lactase), intestinal transit time, dose of the carbohydrate, meal composition, and also on the presence of mucosal disease. If a proportion of the FODMAPs pass unabsorbed through the small intestine, this increases intestinal luminal water content through osmosis, and increases gas production via fermentation by gut bacteria, leading to intestinal distension, which may cause symptoms in susceptible individuals. Moreover, fermentation products such as short-chain fatty acids may also be involved in symptom generation. However, incomplete absorption of carbohydrates in the small intestine is not enough to cause symptoms, because not all subjects with, for example, lactose maldigestion and fructose malabsorption report symptoms. Therefore, other factors implicated in the pathophysiology of IBS such as alterations in gut microbiota composition, visceral hypersensitivity, GI barrier defects, and abnormal immune function, may serve as factors in symptom generation after intake of an excess of FODMAPs in the diet. Further, symptom experience after intake of short-chain carbohydrates is also likely to be affected by central nervous system factors, and therefore directly or indirectly influenced by anxiety, depression, and stress, but potentially also by classical conditioning and expectations (Figure 1). An important research task is to address the ability of these factors to predict the response to dietary interventions in general, and low-FODMAP diet in particular, as few predictors for a positive symptomatic response to this diet exist.

The scientific evidence supporting a clinically relevant positive effect of reducing FODMAPs in IBS has so far been relatively limited, but gradually accumulating over the last couple of years, and has, besides observational reports, mainly been based on a randomized single-blinded FODMAP challenge study, a nonrandomized, comparative study, and a randomized, controlled trial comparing a low FODMAP diet with the habitual diet in IBS. Moreover, a recent study also demonstrated that a general reduction of FODMAPs in the diet was effective in patients with suspected nonceliac gluten sensitivity, and no gluten-specific effect beyond that of the effect of the general FODMAP reduction could be demonstrated. Because few clinical trials in this area exist, the current study by Halmos et al is very important, because it provides high-quality evidence supporting the effectiveness of a low-FODMAP diet in IBS. By using a randomized, cross-over design, the authors were able to demonstrate a convincing reduction of the reported severity of all the key symptoms of IBS—abdominal pain, bloating, and bowel habit dissatisfaction—when the patients were on a low-FODMAP diet compared with when they received a standard Australian diet. Both diets had a similar nutritional composition, except for a difference in the FODMAP content. Moreover, the low FODMAP diet was well tolerated and the nutritional composition met current nutritional recommendations. The dietary intake was also strictly controlled as almost all food was provided to the subjects during the study, which further strengthens the reliability of the findings, but also begs for future studies to evaluate how this diet works in clinical practice when the patient is given dietary advice in an outpatient clinic setting, without receiving all food from a study center. The clinical experience is that a substantial proportion of patients find it difficult to follow strict diets for other than short periods of

time, and as can be expected adherence to the low-FODMAP
diet has been found to be an important predictor for the
outcome. The authors also assessed the effect on stool
parameters objectively, by collection of feces, and here the
effect of the diet was modest, despite the fact that the effect
on bowel habit dissatisfaction was striking, further high-
lighting the complex nature of symptom reporting in IBS
patients.

As the authors rightfully acknowledge in their discus-
sion, there were of course some limitations with the present
study. Due to the logistic complexity of the study a relatively
limited number of patients (n = 30) was included, which
limits the possibility of finding predictors for a favorable
response, which is a clinically important question, as not all
patients respond favorably to this treatment alternative.
Further, a relatively short treatment period (3 weeks) was
used and currently no scientific guidance exists on how this
diet works in the long run or if gradual reintroduction of
excluded food items can be done without worsening of
symptoms. Moreover, the use of a cross-over design carries
a risk of carry-over effects, but the authors used a relatively
long wash-out period to reduce this risk, and also performed
several additional analyses to secure the absence of a rele-
vant carry-over effect. In the present study, no further
mechanistic insight into the mechanism behind symptom
improvement was provided, as for instance the results from
breath testing or stool parameters did not predict symptom
response. However, based on the current convincing data,
clearly demonstrating an excellent short-term response of
low-FODMAP diet in a substantial proportion of IBS
patients, future studies can address the remaining research
questions, such as how to identify the right patients for this
therapy and also to determine how strict the diet needs to be to
yield a sufficiently favorable long-term response. Moreover, so
far no study has demonstrated that this diet therapy is supe-
rior to the dietetic practice that has been used for patients with
IBS before a low-FODMAP diet was suggested as a treatment
alternative for IBS, that is, to encourage a regular meal pattern
and a “healthy eating,” to avoid large meals, reduce intake of
fat, discourage excessive fiber intake (especially soluble fi-
bers), reduce caffeine, and avoid gas-producing foods, such as
beans, cabbage, and onions. To conclude, with the study from Halmos et al, we now
have solid scientific data supporting that a low-FODMAP
diet is efficient in reducing GI symptoms in IBS, at least in
the short term. Long-term studies are now needed, as well
as investigations finding clinically useful predictors that can
help clinicians in selecting patients who are likely to
respond to this relatively cumbersome form of therapy, for
which access to expert dieticians are needed. Moreover,
high-quality, head-to-head comparisons with other dietary
strategies used in the management of patients with IBS will
be helpful for practicing dieticians and gastroenterologists,
as well as evaluation of ways to facilitate dissemination of
dietary information to large groups of patients, such as
group education and web-based tools. For the benefit of our
patients, some progress has been made finally regarding
diet as a therapy for IBS, but as always, a nice study always
raises further questions that need to be addressed in future
studies!
References


Reprint requests
Address requests for reprints to: Professor Magnus Simrén, Department of Internal Medicine & Clinical Nutrition, Sahlgrenska Academy, University of Gothenburg, 41345 Gothenburg, Sweden. e-mail: magnus.simren@medicine.gu.se.

Conflicts of interest
The author discloses the following: Magnus Simrén has received unrestricted research grants from Danone and AstraZeneca, served as a Consultant/Advisory Board member for Danone, Novartis, Almirall, Albireo, and Shire, and been on the Speaker’s bureau for Almirall, Danone, Shire, Menarini, Abbvie, MSD, Tillotts and Vifor Pharma.

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