

# Food-symptom diaries can generate personalized lifestyle advice for managing gastrointestinal symptoms

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# Food-symptom diaries can generate personalized lifestyle advice for managing gastrointestinal symptoms: A pilot study

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## Abstract

**Background:** Gastrointestinal (GI) symptoms have a heterogeneous pathophysiology. Yet, clinical management uses group-level strategies. There is a need for studies exploring personalized management options in patients with GI symptoms. From diaries of GI symptoms, food intake, and psychological distress, we extracted and validated personalized lifestyle advice. Secondly, we investigated group-level GI symptom triggers using meta-analysis.

**Methods:** We collected 209 diaries of GI symptoms, food intake, and psychological distress, coming from 3 cohorts of patients with GI symptoms ( $n = 20, 26,$  and  $163$ , median lengths  $24, 17,$  and  $38$  days). Diaries were split into training and test data, analyzed, and the triggers emerging from the training data were tested in the test data. In addition, we did a random effects meta-analysis on the full data to establish the most common GI symptom triggers.

**Key Results:** Analysis of the training data allowed us to predict symptom triggers in the test data ( $r = 0.27, P < .001$ ), especially in the subset of patients with a strong global association between lifestyle factors and symptoms ( $r = 0.45, P < .001$ ). Low exposure to these triggers in the test data was associated with symptom reduction ( $P = .043$ ). Meta-analysis showed that caloric intake in the late evening or night predicted an increase in GI symptoms, especially bloating. Several food-symptom associations were found, whereas psychological distress did not clearly lead to more severe GI symptoms.

**Conclusions & Inferences:** Diaries of GI symptoms, food intake, and psychological distress can lead to meaningful personalized lifestyle advice in subsets of patients.

## KEYWORDS

food diary, food record, gastroenterology, gastrointestinal symptoms, IBS

## 1 | INTRODUCTION

Gastrointestinal (GI) symptoms such as abdominal pain, bloating, flatulence, and diarrhea are common in irritable bowel syndrome (IBS) and other functional GI disorders. In these disorders, GI symptoms are influenced, in part, by lifestyle factors such as food

intake,<sup>1</sup> psychological distress,<sup>2</sup> quality of sleep,<sup>3</sup> and exercise.<sup>4</sup> Therefore, the clinical management of disorders such as IBS often involves lifestyle advice including dietary interventions (eg, guidelines of the National Institute of Health and Care Excellence, NICE,<sup>5</sup> diet low in fermentable oligo-, di-, and monosaccharides and polyols, FODMAPs<sup>6</sup>) and/or psychological interventions (eg, cognitive

behavioral therapy<sup>7</sup> and hypnotherapy<sup>8</sup>). Results of these strategies are favorable, with typically around half of patients experiencing adequate symptom relief,<sup>9</sup> although parts of this benefit may be attributable to the placebo effect.<sup>10</sup>

However, treatment responses are heterogeneous, as are the mechanisms underlying symptom onset. For example, dietary intolerances are highly variable and reflect many underlying mechanisms (eg, effects of stimulants on GI motility, changes in osmolarity or volume, or activation of local immune cells by food antigens, leading to visceral hypersensitivity).<sup>11</sup> For some patients, psychological distress or a non-lifestyle factor will be more important than the diet. Finally, some relevant mechanisms will be unknown and are thus currently overlooked when managing GI symptoms based on a priori hypotheses. There is thus a need to go from group-level to person-level management of GI symptoms.

Personalized management of GI symptoms in IBS can be achieved, among others, when a patient keeps a diary of their symptoms as well as lifestyle factors such as food intake, psychological distress, and exercise. Many dietitians routinely request clients with GI symptoms to keep such a diary, although these diaries are then typically assessed “with the bare eye,” raising questions about the accuracy of the advice—besides the accuracy of the diary. Furthermore, diary analysis is rather laborious, especially if one wishes to account for all of various biases, and therefore, it requires computer automation. Several apps exist where one can keep a diary of symptoms and lifestyle factors, but the quality of their advice has not been published. We have developed an automated algorithm<sup>1</sup> to analyze diaries ( $n = 163$ ) kept on the smartphone application *mySymptoms*<sup>12</sup> and found demonstrable food-symptom relations in half to two-thirds of participants depending on the symptom. However, the participants were anonymous, and it was thus unclear whether these had a functional GI disorder. Furthermore, the trigger identification algorithm was not validated in that study.

Therefore, the present study had two aims. Firstly, we aimed to test internal validity of the trigger identification algorithm. Secondly, we aimed to report the most common symptom triggers in a better characterized study population.

## 2 | MATERIALS AND METHODS

The present study used three cohorts, in all of which patients kept a diary of GI symptoms, food intake, and, optionally, psychological distress and exercise, either using the app *mySymptoms* (screenshot in Figure S1, a MS Excel template, or a pen & paper template). The sole inclusion criterion was the presence of bothersome GI symptoms more than once a week. Recruitment procedures and study methodology per cohort are given in Table 1. Participants in cohort 1 were required to fill out an online questionnaire with the Rome IV<sup>13</sup> questions that define IBS and functional dyspepsia (FD, epigastric pain syndrome, EPS, and postprandial distress syndrome PDS), as well as the IBS severity scoring system (IBS-SSS, scale: 0-500<sup>14</sup>), the visceral sensitivity index (VSI, scale: 0-75<sup>15</sup>) for GI-specific anxiety,

### Key Points

- Functional gastrointestinal symptoms are often triggered by lifestyle factors such as psychological distress or food items. However, symptom triggers are very person-specific.
- Person-specific symptom triggers may be identified using a diary of food intake, psychological distress, and gastrointestinal symptoms.
- Besides the type of food consumed, eating late in the evening may also lead to gastrointestinal symptoms.

the food subscale of IBS quality of life (IBS-QoL, scale: 0-100<sup>16</sup>), and questions about perceived triggers. We also queried age and sex, and which GI symptoms participants had more than once a week. Participants in cohort 2 had a short oral interview where their GI symptoms and trigger perceptions were discussed. Participants of cohort 3 were not characterized as they were anonymous and opted in to share their data for the present study through the *mySymptoms* app. The reason for launching three cohorts was pragmatic, aiming for a large volume (cohort 3) as well as a well-characterized sample (cohort 1).

The procedure of keeping a diary via *mySymptoms* has been detailed previously.<sup>1</sup> The pen and paper and MS Excel templates had 24 rows per day, that is, one per hour, where participants could write down food intake in free text, and symptoms on a scale from 0 to 10. Data preprocessing was done as described previously,<sup>1</sup> although the minimum number of food reports per day was lifted from 2 to 3 (ie, stricter quality control). Furthermore, reported Bristol stool forms 5, 6, and 7 in the absence of a diarrhea entry were arbitrarily recoded to diarrhea scores 2, 6, and 10 (following the default scale of 0 to 10).

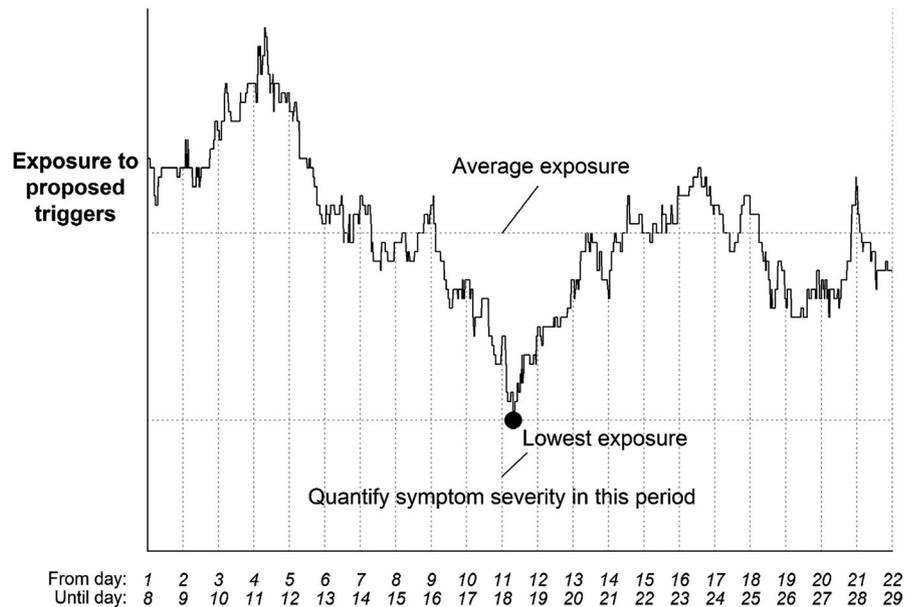
The trigger identification algorithm has been described previously<sup>1</sup> and was run in R version 3.5.3.<sup>17</sup> However, the time to symptom onset was not fixed at 8 hours, but at 2 hours for abdominal pain, belching, and diarrhea, 4 hours for bloating, nausea/vomiting, heartburn, discomfort, headache, and psychological distress, and 8 hours for flatulence and somatic symptoms. These choices were based on food challenge studies (eg, <sup>18,19</sup>), as well as a practical trade-off between capturing most lifestyle-related symptoms while limiting background noise.

### 2.1 | Internal validation of trigger identification algorithm

We aimed to assess the validity of the identified triggers. Ideally, this would be done by the participant excluding the proposed triggers for a few weeks and evaluating the effect on symptoms. However, the present study could not include such a trial, because most participants were anonymous. As an alternative, we performed a validation analysis on the existing diary data, which started by splitting

**TABLE 1** Cohort characteristics

|                         | Cohort 1  | Cohort 2  | Cohort 3                            |
|-------------------------|---|---|-------------------------------------|
| N (enrollment)          | 50  | 28  | 174                                 |
| N (adequate diary)      | 20  | 26  | 163                                 |
| Location                | The Netherlands   | Sweden  | International (app)                 |
| Participating centers   | Maastricht University, KU Leuven, University of Gothenburg            | University of Gothenburg  | KU Leuven, University of Gothenburg |
| Year of data collection | 2019  | 2017  | 2018                                |
| Recruitment             | IBS magazine, Twitter, Facebook, website of patient society           | Flyers in university and healthcare sites, student website            | Opt-in within app                   |
| Diary length criterion  | ≥3 wk   | ≥2 wk   | ≥3 wk                               |
| Diary platform          | <i>mySymptoms</i> app, pen and paper, MS Excel template (free choice) | <i>mySymptoms</i> app, pen and paper, MS Excel template (free choice) | <i>mySymptoms</i> app               |
| Questionnaires          | Rome IV, IBS-SSS, VSI, IBS-QOL, symptoms, trigger perceptions         | Oral interview about symptoms and trigger perceptions                 | None                                |
| Incentive               | Personalized results  | Two cinema tickets  | None (anonymous)                    |
| Informed consent        | At enrollment   | At enrollment   | A posteriori                        |
| Ethics committee        | Maastricht University, the Netherlands                                | Regional ethical review board, Gothenburg, Sweden                     | KU Leuven, Belgium                  |
| Ethics permission       | Exemption granted   | Held  | Deemed unnecessary                  |

**FIGURE 1** Example of the rolling sum of exposure to the top-5 of triggers

each diary into training data (first half) and test data (latter half). We assessed which foods or stress-triggered symptoms in the training data and then tested in the (independent) test data whether the same triggers could be identified. This was done in two ways. Firstly, we computed “trigger scores” (ie, a measure of the likelihood that a certain item is a symptom trigger) in the training and test data, and built a predictive model to predict trigger scores in the test data. Secondly, we extracted the top-5 triggers from the training data, determined the period in the test data in which the exposure to these items was the lowest, and quantified symptom severity in that period (Figure 1). In this way, we mimic the scenario of a lifestyle advice in which proposed triggers would be excluded, yet free from placebo

effects. We compared the personalized triggers of the diary to the food-symptom association of high FODMAP foods as well as for foods part of a processed diet. The foods labeled as high FODMAP or processed are listed in Table S2. Details on the methodology are explained in a technical annex as online supplementary information.

A key bias in the second approach is the reporting density. For example, it can happen that a participant usually reports 10 times a day, but also has a period with only 5 reports a day, because of distraction or fatigue with the study protocol. In that case, the period of 5 reports a day is likely to be the week of lowest trigger exposure and is also likely to have a reduced symptom severity, simply because the person reported less in general. We adjusted

for this bias by simulation. Food reporting densities (number of food report occasions per day) of the first 28 days were analyzed as latent class mixed model (R-package *lcmm*<sup>20</sup>).

## 2.2 | Meta-analysis of common symptom triggers

We performed a meta-analysis on the full diaries of all participants, in order to establish the most common triggers for GI symptoms. Each symptom of each diary was treated as a separate “study,” for the purpose of meta-analysis. We analyzed for symptom-triggering effects of food items, psychological distress, exercise, and also all other symptoms. The outcome was the prospective increase in symptom severity after exposure to a trigger, adjusted for reverse causation, time of the day, and lifestyle changes as described previously.<sup>1</sup> We performed random effects meta-analyses using the R-package *meta*<sup>21</sup> to allow for heterogeneity of effects. Analysis confined to the four most common symptoms to conserve power (ie, abdominal pain, diarrhea, bloating, and flatulence).

## 3 | RESULTS

Cohort 1 consisted of 50 participants, of whom 74% had IBS according to Rome IV, and 42% had FD. Most had abdominal pain, flatulence, bloating, diarrhea, or discomfort not covered by another symptom term in Table 2. Participants had a median IBS-SSS score of 305, that is, moderate to severe IBS. Descriptive statistics can be viewed in Table 2, and the relations between variables are given in supplementary Figure 2. As for participants' perceptions about triggers, psychological distress topped the list with 64%, followed by food products sweet bakery/confectionery (52%), bread/pasta/rice, milk/cheese, and fats/oils/sauces (all 46%), legumes (44%), fruit (30%), vegetables (22%), meat/fish/eggs (16%), and potatoes (4%). Cohort 2 was a roughly even mix of patients with IBS and subthreshold-IBS GI symptoms, as concluded from oral interviews. Cohort 3 was anonymous and not characterized.

The number of diaries we received was 20, 28, and 174 for the three cohorts, respectively (cohort descriptions in Table 1). Cohort 1 had had 30 individuals drop out of the study (silently, ie, no reasons were given), and 13 diaries (2 from cohort 2, 11 from cohort 3) did not pass quality control, because either food or symptoms were not recorded.

The vast majority of participants reported around 5 times a day, and this was stable over time. Approximately 9% of individuals reported with a larger frequency, but here, too, reporting density was quite stable for most participants (Figure 2).

### 3.1 | Internal validation of trigger identification algorithm

Of the 209 diaries that passed quality control, 163 were long enough to split into training and test data (19, 10, and 134 for the

three cohorts, respectively). We studied a total of 501 symptoms and 12,946 possible triggers. Predicted and observed trigger scores in the test data were correlated ( $r = 0.27$ ,  $P < .001$ ), and this correlation interacted with the strength of the global food/stress/symptom association. Of the 501 symptoms, 42 (8%) had a strong global food/stress/symptom association ( $P < .01$ ), and here trigger scores were best predicted ( $r = 0.45$ ,  $P < .001$ ). Another 42 (8%) had a global association of extent  $.01 \leq P < .05$ , and here the correlation was  $r = 0.38$ ,  $P < .001$ . Weaker food/stress/symptom associations led to smaller correlations between predicted and observed trigger scores in the test data (Figure 3). Trigger confidence was 50% or more for 1 in 28 items, that is, 1 item per symptom per person on average.

We went on to analyze whether, in the test data, in the week of lowest exposure to the top-5 triggers, symptom severity was reduced. This is a prerequisite for the future success of keeping a diary in clinical practice. Symptoms in the week of lowest trigger exposure were reduced in 62% of cases ( $P < .001$ ). After adjustment for reporting density, a statistically significant effect remained ( $P = .043$ ). Symptoms in the week of lowest FODMAP intake were reduced as well, although less strongly so in the adjusted model ( $P = .099$ ). Low consumption of processed foods was not associated with an improved symptom severity after adjustment for reporting density ( $P = .458$ ). Results can be viewed in Figure 4.

### 3.2 | Meta-analysis of common symptom triggers

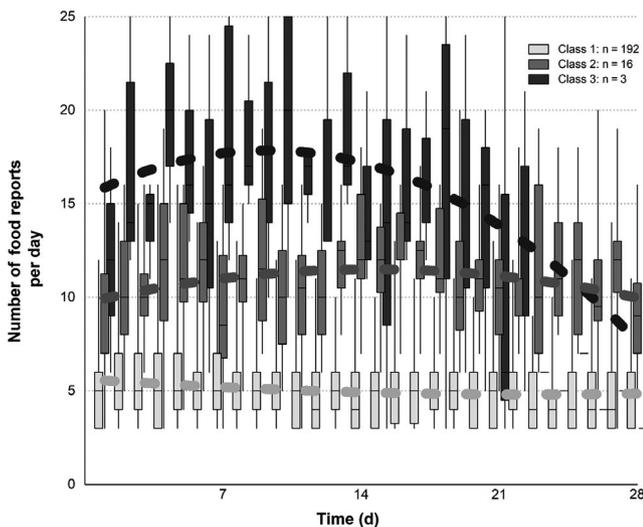
Figure 5 shows, for each symptom, meta-analytic estimates for the top-5 (group-level) triggers, the bottom-3 (negative association), and some selected items. Caloric intake late in the evening or at night seemed to be an important trigger for bloating ( $P < .001$ ), abdominal pain ( $P < .001$ ), and flatulence ( $P = .006$ ). Rice and bread triggered abdominal pain ( $P = .006$  and  $0.02$ ). Diarrhea was predicted by the intake of confectionery, coffee, and spices in particular (all  $P < .001$ ), whereas flatulence was often triggered by the intake of fruits ( $P = .008$ ), onions, and bread (both  $P = .009$ ). Psychological distress was not predictive of an increase in GI symptoms, at least not after adjusting for reverse causation (GI symptoms may increase psychological distress). Exercise weakly predicted a decrease in abdominal pain ( $P = .027$ ). An event of diarrhea predicted a decrease in other GI symptoms, especially flatulence, whereas flatulence often preceded diarrhea (both  $P < .001$ ). Other associations of interest were that coffee reduced discomfort and fatigue whereas onions increased both of these, and alcohol reduced psychological distress but increased heartburn (all  $P < .05$ ).

## 4 | DISCUSSION

This study shows that keeping a diary of food intake, psychological distress, and GI symptoms can identify personal GI symptom triggers, especially when a global association between food, stress, and GI symptoms is established. Furthermore, in the period when the participant naïvely had low exposure to the triggers, symptom

**TABLE 2** Descriptive statistics of cohort 1. Values are percentages or medians (interquartile range). NOS: not otherwise specified

| Descriptive         | n = 50        | Symptom > 1/wk     | n = 50 |
|---------------------|---------------|--------------------|--------|
| Female              | 98%           | Abdominal pain     | 88%    |
| Rome IV - IBS       | 74%           | Flatulence         | 80%    |
| Rome IV - FD        | 42%           | Bloating           | 74%    |
| PDS                 | 34%           | Discomfort NOS     | 56%    |
| EPS                 | 20%           | Diarrhea           | 54%    |
| Age (years)         | 45 (32-54)    | Nausea             | 36%    |
| IBS-SSS             | 305 (240-330) | Excessive belching | 24%    |
| GI-specific anxiety | 42 (31-49)    | Heartburn          | 20%    |
| IBS-QoL food        | 58 (42-83)    | Vomiting           | 6%     |



**FIGURE 2** Food reporting density shown as latent class mixed model

severity was reduced. Finally, we show in a meta-analysis that caloric intake late in the evening or at night may be an important trigger for bloating and other GI symptoms. Furthermore, specific food-symptom associations were found, for example, for abdominal pain (rice, bread), diarrhea (confectionery, coffee, spices), flatulence (onions, fruits), and bloating (vegetables).

#### 4.1 | Personalized management of GI symptoms

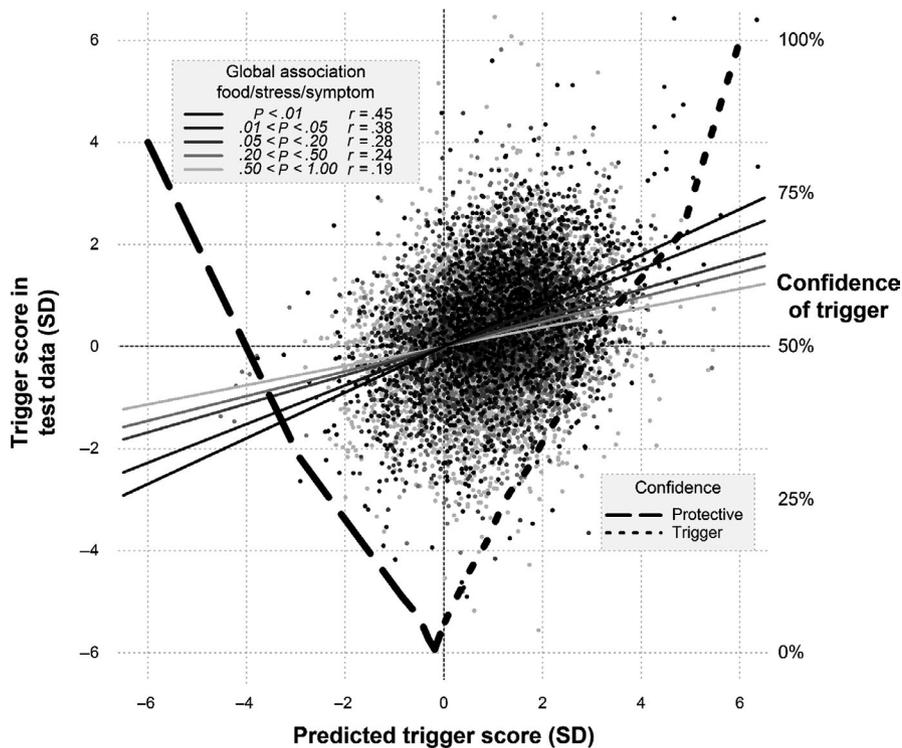
A conceivably important goal in the management of GI symptoms, a health problem with heterogeneous underlying pathophysiology, is to personalize the advice given to patients. When done properly, this can resolve the problem of between-person heterogeneity of mechanisms and treatment responses, and it is also an additional resource on top of the current strategies. Personalized management can be achieved in several ways. One of these is to keep a diary on a smartphone. Many digital applications exist for GI purposes,<sup>22</sup> but the quality of their output is typically not verified and/or not published. The present validation study highlights that the advice can be repeatable and meaningful. Moreover, the period when exposure

to the top-5 triggers was low tended to coincide with a period of reduced symptom severity. Our diary analysis service can therefore be considered to be capable of giving meaningful personalized lifestyle advice to at least subsets of patients. At the same time, much unexplained variance persists, which will be largely due to reporting inaccuracy, response shift, and unreported factors relevant for GI symptoms. Some participants commented that their internal standards had changed throughout the study and wanted to restart the diary anew. A fantastic opportunity to improve reporting accuracy and consistency is to use microelectronics/ smart devices to track changes in physiology, as these measure objectively and with accurate timestamps. A first step in their application would be to select physiologic outcomes most reflective of symptoms or disturbed homeostasis. Candidates would be GI motility, pressure, acidity, heart rate, continuous measurement of abdominal girth as direct measure of abdominal distension, or interactions of these. The second step would then be to dynamically assess the person-specific effects of different food items/ stress conditions on physiology, which could serve as the basis for personalized lifestyle advice in IBS. We hope that the present study can inspire such efforts.

All of that said, other roads to personalized management of GI symptoms have been paved. Fritscher-Ravens *et al*<sup>23</sup> injected food allergens in controlled conditions and used confocal laser endomicroscopy to record losses of epithelial integrity and infiltration by immune cells. Such adverse reactions were seen in 61% of IBS patients but 0% of non-IBS controls. Replication is warranted, especially through studies that subsequently give personalized advice to exclude the identified allergens. Responses to the low FODMAP diet can be predicted using volatile organic compounds in faeces<sup>24</sup> or the microbiota.<sup>25</sup> It would be interesting to see whether biomarkers can also predict specific food intolerances as identified by a diary or endomicroscopy.

#### 4.2 | Lifestyle triggers on the group level

We present evidence for several food items and eating habits as triggers for GI symptoms. Caloric intake late in the evening and at night was associated with bloating in particular. This is in line with a study by Gill *et al*,<sup>26</sup> who restricted daily eating intervals

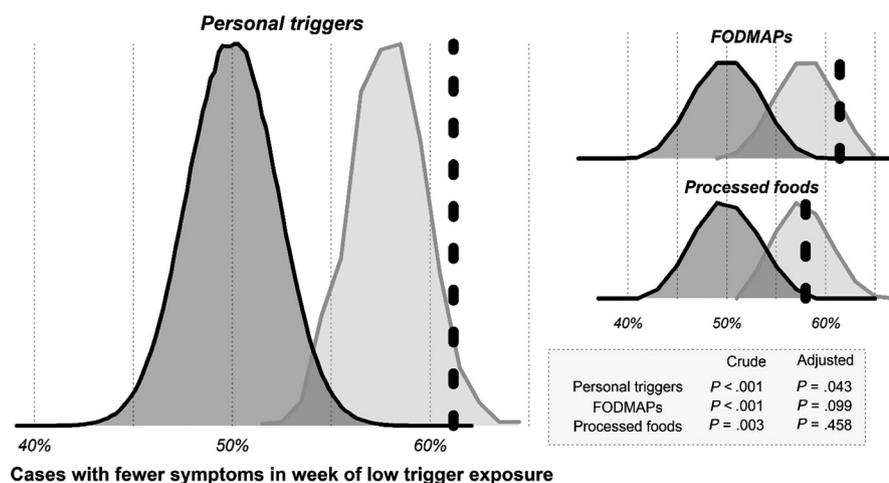


**FIGURE 3** Correlation between predicted and observed trigger scores in test data, stratified by the global food/stress/symptom association (primary y-axis). Dotted/dashed lines: confidence that an item is a trigger (secondary y-axis)

of participants from >14 hours to 10–11 hours and reported beneficial effects on general health at 16 weeks. However, studies specific to GI symptoms are missing, and it remains unclear what part of circadian metabolism might be at play in GI symptom generation. Coffee, spices, and confectionery, among others, were associated with a subsequent diarrheal event. This is in agreement with the NICE guidelines for IBS, which recommend limited consumption of (caffeinated) coffee, spices, and (artificially sweetened) confectionery.<sup>5</sup> In our study, though, we lacked the information to consistently distinguish between caffeinated and non-caffeinated coffee, or between sugar-sweetened and artificially sweetened items. Psychological distress was not meta-analytically associated with a subsequent increase in GI symptoms in our cohorts, because the reverse association was as strong or

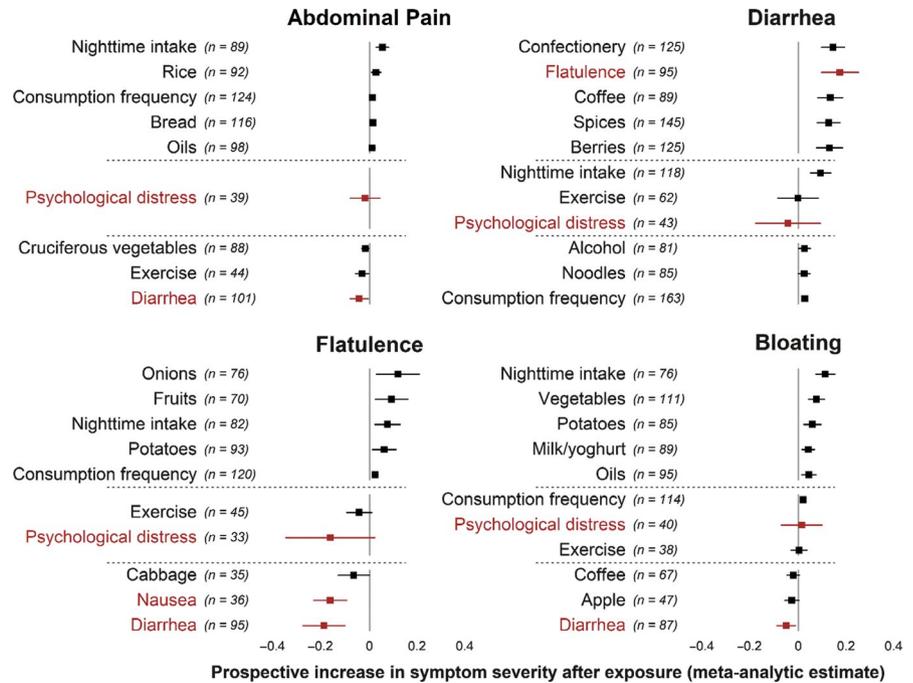
stronger (flatulence). In some individuals, psychological distress had a larger trigger score than any food item. While mechanistic studies suggest that psychological distress is capable of changing GI physiology (eg, disruption of the intestinal barrier<sup>27</sup>), other studies found only a weak influence of daily stress or state anxiety on GI symptoms.<sup>28,29</sup> Possible explanations for this discrepancy are a difference in definition of psychological distress, or that self-reports differ from psychological distress as induced in controlled designs and measured through markers such as cortisol. Finally, we show that diarrhea improves abdominal pain in the subsequent 2 hours, which supports the Rome conceptualization of abdominal pain related to (and usually improved by) defecation.<sup>30</sup>

This study presents an objective quantification of relations between food intake, psychological distress, and GI symptoms. This was done in



**FIGURE 4** Percentage of cases with improved symptoms in the week of low exposure to the top-5 of triggers (thick dashed line), and its relation to the null-hypothesis adjusted (light gray curve) and unadjusted (dark gray curve) for reporting density. The same is shown for the weeks of low intake of FODMAPs and processed foods respectively

**FIGURE 5** Meta-analysis of triggers for four common GI symptoms. The top-5 is sorted by the lower confidence limit; the bottom-3 is sorted by the upper confidence limit. N-values are the number of participants who reported the respective item and the respective symptom



three cohorts, of which one was well-characterized. A strength of our analysis algorithm is that it is highly flexible (can process multilingual free text, any diary length, can toggle between food items and food groups, and does not require portion sizes), and that it adjusts for important confounders: reverse causation, time of the day, lifestyle changes,<sup>1</sup> and, to some degree, response shift. A strength of the validation analysis is that we tested symptom severity in a period of low exposure to the triggers, which mimics an intervention while remaining clear of placebo effects. Limitations of our study include reporting inaccuracy and residual response shift. Besides, the incentive of personalized results in cohort 1 did not prevent a high dropout rate (60%), while, apparently, monetary or tangible incentives such as in cohort 2 are needed. A follow-up phase with trigger exclusions was not in scope of the present study, but could be a next step. We lack the power and patient characterization to state whether demonstrable food-symptom associations are more common in IBS patients or people with another functional GI disorder. Finally, our study would have been stronger with broader characterization of participants, and if we had included objective biomarkers in the design. These limitations should be addressed in follow-up studies.

In conclusion, keeping a diary of food intake, psychological distress, and GI symptoms can identify personal GI symptom triggers for at least some patients. Common triggers for GI symptoms are in line with the NICE guidelines<sup>5</sup> and add that caloric intake in the late evening and at night may increase GI symptoms. The diary approach of the present study can help pave the way toward personalized management of GI symptoms in patients with IBS and other functional GI disorders.

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#### CONFLICT OF INTEREST

The authors have no conflicts of interest.

#### AUTHOR CONTRIBUTIONS

EC designed the research, collected all data, analyzed the data, and wrote the manuscript. AN collected data (cohort 2). EC, AN, DK, AM, and MS aided in the ethics procedures. HT, JT, LVO, AM, DK, and MS gave critical feedback at various points during the research.

All authors have revised and approved of the final draft submitted.

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#### SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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