

# A real-world evidence study evaluating Geffer effervescent granules for the symptomatic relief of digestive symptoms

SAGE Open Medicine

Volume 10: 1–11

© The Author(s) 2022

Article reuse guidelines:

[sagepub.com/journals-permissions](https://sagepub.com/journals-permissions)

DOI: 10.1177/20503121221088815

[journals.sagepub.com/home/smo](https://journals.sagepub.com/home/smo)

Matteo Alemanni<sup>1\*</sup>, Raffaella de Salvo<sup>2\*</sup>, Barbara Moroni<sup>1</sup> and Andreas Ehret<sup>2</sup>

## Abstract

**Objectives:** Geffer effervescent granules (active ingredients: metoclopramide, dimethicone, and sodium bicarbonate) is an established over-the-counter medication available in Italy for the symptomatic treatment of hyperacidity (pain and/or heartburn) when accompanied by slowing of gastric transit, nausea, aerophagia, and bloating, all symptoms that can occur in functional dyspepsia and can negatively impact individuals' quality of life. The aim of this observational study was to explore the perceived benefits of, and consumer experience with, Geffer effervescent granules used for the symptomatic treatment of digestive disorders suggestive of functional dyspepsia under real-life conditions in Italy.

**Methods:** Adults (aged 35–65 years) experiencing symptoms suggestive of functional dyspepsia/indigestion at least once a month and who had used Geffer effervescent granules within the previous 6 months completed an online questionnaire eliciting information on symptom relief (speed of onset and duration) and quality of life.

**Results:** Geffer effervescent granules provided rapid onset of symptom relief, with 21% of respondents perceiving an effect within 10 min and 88% reporting an improvement in overall symptoms within 30 min. A similarly rapid onset of complete resolution of gastric pain/cramps, acidity, bloating, nausea, and bothersome fullness symptoms was reported by 65%–83% of respondents; 50%–59% of respondents were free from such symptoms for more than 3 h or until the next meal. Most participants (92%) reported that their quality of life improved when taking Geffer effervescent granules to treat hyperacidity symptoms. Overall, 95% of the respondents were satisfied with the effectiveness of Geffer effervescent granules on overall symptom relief.

**Conclusions:** In Italian consumers with digestive disorders likely due to functional dyspepsia, Geffer effervescent granules was associated with rapid, complete, and durable relief of symptoms of gastric pain/cramps, acidity, bloating, nausea, and bothersome fullness; an improvement in quality of life; and a high level of consumer satisfaction.

## Keywords

Gastroenterology/hepatology, real world evidence, quality of life, efficacy, functional dyspepsia

Date received: 18 October 2021; accepted: 3 March 2022

## Introduction

Upper gastrointestinal (UGI) symptoms, such as heartburn, acid reflux, indigestion, epigastric pain, and discomfort, are widely prevalent worldwide.<sup>1</sup> A real-world evidence study conducted across 13 European countries indicated an overall prevalence for UGI symptoms of 38%. Prevalence was highest (45%) in Hungary, followed by Poland (44%) and Italy (43%).<sup>1</sup> Meal-related symptoms (discomfort/fullness/bloating, early satiety) and abdominal pain are among the most commonly reported UGI symptoms.<sup>2,3</sup> A recently published cross-sectional survey of Italian community pharmacies found that among 1020 individuals suffering from at least

one common gastrointestinal symptom, 12% reported post-prandial fullness, 10% upper abdominal bloating, and 7% epigastric pain.<sup>4</sup>

<sup>1</sup>Bayer S.p.A., Milano, Italia

<sup>2</sup>Bayer Consumer Care AG, Basel, Switzerland

\*These authors contributed equally to this work.

### Corresponding author:

Matteo Alemanni, Bayer S.p.A., V.le Certosa 130, 20156 Milano (MI), Italia.

Email: [matteo.alemanni@bayer.com](mailto:matteo.alemanni@bayer.com)



Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons

Attribution-NonCommercial 4.0 License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (<https://us.sagepub.com/en-us/nam/open-access-at-sage>).

The most common diagnosis usually assigned to people experiencing such symptoms is functional dyspepsia (FD), characterized by UGI symptoms such as postprandial fullness, early satiation, and epigastric pain/burning in the absence of any evident structural disease; nausea, belching, or abdominal bloating can also occur.<sup>5</sup> Symptoms of FD are strongly linked to the ingestion of food.<sup>6</sup> Causes of FD include stress, diet, delayed gastric (fundic) accommodation/emptying, gastric hypersensitivity to distension, and excess acidity.<sup>6</sup>

Data on the incidence of FD are limited. A systematic review of epidemiological studies reported an estimated global prevalence of FD of 12%–15%.<sup>7</sup> A similar overall prevalence was reported in an endoscopic study conducted in the Italian general population, in which 114 (11%) of 1033 individuals were diagnosed with FD (defined as epigastric pain, postprandial fullness, or early satiation with no concomitant symptoms of reflux or endoscopic evidence of structural disease).<sup>8</sup> A total of 18 (16%) individuals had at least one meal-related symptom (postprandial fullness or early satiation) plus epigastric pain and 8 (7%) exhibited all three symptoms.<sup>8</sup> Italian data suggest that UGI symptoms suggestive of FD appear to be more frequent among individuals aged >35 years than among younger patients.<sup>4,8</sup>

It has been shown that symptoms of epigastric pain, postprandial fullness, and nausea, as well as greater severity of symptoms of FD, impair subjects' quality of life.<sup>9,10</sup>

Gastrointestinal symptoms are often self-treated by patients using over-the-counter (OTC) medications.<sup>11,12</sup> The cross-sectional survey of community pharmacies in Italy considered treatments used by 1020 subjects suffering from UGI symptoms. Of 1609 therapies reported, 36% were proton pump inhibitors, 18% antacids, and 17% alginates. H<sub>2</sub>-blockers, prokinetics, and other types of treatment each comprised fewer than 10% of the therapies used.<sup>4</sup>

Geffer effervescent granules is an established OTC medication available in Italy for the symptomatic treatment of hyperacidity (pain and/or heartburn) when accompanied by slowing of gastric transit, nausea, aerophagia, and bloating.<sup>13</sup> Geffer effervescent granules contain the active ingredients metoclopramide, dimethicone, and sodium bicarbonate. Sodium bicarbonate (also known as sodium hydrogen carbonate or baking soda) is a rapidly acting antacid, quickly reacting with hydrochloric acid in the stomach to produce sodium chloride, carbon dioxide, and water.<sup>14</sup> Despite its long use as a treatment for patients with dyspepsia, evidence of its efficacy in clinical trials is scarce. Confirmation of its efficacy comes from experiments in which symptoms of dyspepsia induced by the endoscopic infusion of HCl in the stomach were relieved following the subsequent infusion of sodium bicarbonate.<sup>15,16</sup>

Metoclopramide, a prokinetic (increases the gastric emptying rate) with antiemetic properties,<sup>17</sup> has been shown to reduce symptoms of nausea and vomiting in randomized

placebo-controlled trials and to exhibit a good tolerability profile.<sup>18–20</sup> As a prokinetic, it is considered a valid treatment for FD.<sup>21</sup> Dimethicone is a silicon polymer similar to simethicone, a medication used in the management and treatment of flatulence.<sup>22</sup> In controlled trials, dimethicone in combination with an antacid has been shown to improve gastric symptoms (including heartburn, acid regurgitation, flatulence, pain, epigastric distention, nausea, and vomiting) and to reduce endoscopically assessed esophageal inflammation over time.<sup>23,24</sup>

The aim of this observational study was to explore the perceived benefits of, and consumer experience with, Geffer effervescent granules used for the symptomatic treatment of digestive disorders suggestive of FD under real-life conditions in Italy. This real-world evidence study specifically focused on outcomes that are of importance to the consumer, which are the speed of symptom relief onset, the duration of symptom relief, and the impact of Geffer effervescent granules on the consumers' quality of life.

## Methodology

### Study design

This real-world evidence study was a retrospective observational study with primary data collection using a computer-aided web quantitative interview (maximum duration of about 20 min). A protocol for the collection of the retrospective data was agreed upon, with input from medical, clinical, and pharmacovigilance from Bayer Consumer Health and IQVIA Inc., an independent agency. The study protocol was designed to collect information on adult Italian consumers using Geffer effervescent granules for the symptomatic treatment of digestive disorders likely due to FD. Subjects were recruited from a panel in which they had been previously profiled for digestive disorders likely due to FD (with or without heartburn). Panel subjects were self-diagnosed; prior assessment by a physician was not a requirement. Consumers were informed electronically about the study; those consenting to take part were asked to complete an online questionnaire. Those meeting the inclusion criteria (assessed using a short screening section) were then asked to complete the full online survey. Recruitment in Italy was conducted by IQVIA, Inc. (C. Juan Esplandiú, 11, 28007 Madrid, Spain). Due to the observational character of this retrospective study, only an abbreviated consent to participate was required. All participants provided written informed consent before the study. According to the "Governance arrangements for research ethics committees: 2020 edition" document published by the NHS Health Resource Authority, UK, Section 2.3.15,

Market research may be undertaken by professional market researchers, e.g. for public health research or on behalf of pharmaceutical or medical device companies. Where such research is conducted by professional market researchers in

accordance with the principles set out in the Market Research Society Code of Conduct or with the Legal and Ethical Guidelines issued by the British Healthcare Business Intelligence Association (BHBIA), it does not require REC review, except where otherwise required by law, e.g. if it requires approval under the Mental Capacity Acts.

In line with the British Healthcare Business Intelligence Association (BHBIA) guidelines, in this study, participants were informed about the objective and the use of the study prior to completing the questionnaire.

As this is a retrospective observational study with no involvement of health care providers and no information was being collected from medical records, as well as no proactive safety signal collection, there was no need for a review and approval of this study by an Ethics Committee (EC). Due to this, also a waiver for EC review was not needed and not asked for. Participants received no incentives.

### *Survey development*

The survey comprised 31 questions in total. Questions were worded in a consumer-friendly manner and were self-exploratory and non-technical. Content, phrasing, and order of the questions were standardized and were based on previous extensive experience with a similar real-world study. The questionnaire posed questions on respondents' demographics; digestive symptoms of hyperacidity (excessive production of gastric acid by the stomach), heartburn (burning pain in the lower chest), gastric pain/cramps, bloating (swollen and uncomfortable sensation), aerophagia (excessive air swallowing), nausea (sensation of an urge to vomit), bothersome fullness and/or early satiety (slowed gastric transit), and their severity; Geffer effervescent granules usage patterns; and the consumer's experience with Geffer effervescent granules with regard to symptom relief, onset, and duration of action; impact on quality of life; and consumer benefits and satisfaction. Questions relevant to the data presented are provided in Supplementary Figure 1.

Respondents selected answers to questions from a pre-defined list. There were no free text options provided, and pre-defined answers were phrased in a consumer-friendly, self-explanatory, non-technical way. For the question "How satisfied are you with effectiveness of Geffer effervescent tablets for the treatment of your symptoms?" respondents were asked to rate their answer using a 7-point Likert-type scale (1 = strongly dissatisfied, 2 = dissatisfied, 3 = slightly dissatisfied, 4 = neither satisfied nor dissatisfied, 5 = slightly satisfied, 6 = satisfied, 7 = strongly satisfied). For a number of other questions (mainly exploring the impact of Geffer effervescent granules on quality of life and product attributes), respondents were asked to rate their answers using the following 7-point rating scale (1 = strongly disagree, 2 = disagree, 3 = slightly disagree, 4 = neither agree

nor disagree, 5 = slightly agree, 6 = agree, 7 = strongly agree).

### *Survey population*

The key inclusion criteria for subject participation in the study were an age of 35–65 years, experience of symptoms suggestive of FD/indigestion at least once a month, use of Geffer effervescent granules within the previous 6 months, and the ability to read and understand the online survey. Participants had to provide written informed consent for voluntary participation in the study as well as use of pseudo-anonymized data for research, marketing purposes, and/or talking to authorities and could not be currently employed by a pharmaceutical and health care company or currently be participating in any other research studies including, but not limited to, a clinical study.

In line with real-world evidence methodology, no exclusion criteria were specified.

On entry into this real-world evidence study, participants were informed of the objective and use of the study.

### *Data collection and analysis*

The survey was conducted in Italy over the period 4–18 December 2020. Each survey respondent was assigned a Subject ID that was used throughout the study (to maintain the anonymity of the participant). IQVIA handled all study participant liaison, retrieved participant written informed consent for participation, collected participant survey responses, and conducted data management and aggregated statistical analyses.

The survey aimed primarily to collect data regarding the efficacy of Geffer effervescent granules. Subjects were asked to report details of any adverse events or any non-efficacy experienced via the Bayer tool dedicated to spontaneous reporting of events from the market. Information and guidance on how to handle spontaneous reporting were provided to all participants as part of the subject information and consenting.

### *Sample size and power*

Assuming an error margin of 5%, a standard deviation (SD) of 0.5, and a confidence level of 95%, a sample size of approximately 400 was considered sufficient for a study of this type.<sup>25</sup> Due to the real-world nature of the study, however, no limit was placed on the number of participants who could be enrolled.

### *Statistical methods*

Due to the observational nature of this study, results are presented in the form of summary statistics with numbers and

**Table 1.** Respondent demographics (N=409).

Parameter	n (%)
Gender	
Male	210 (51)
Female	198 (48)
Intersex	1 (<1)
Age group	
35–40 years	126 (31)
41–45 years	80 (20)
46–50 years	90 (22)
51–55 years	57 (14)
56–60 years	36 (9)
61–65 years	20 (5)
Hyperacidity symptom episodes in past 6 months	
1 per month	63 (15)
2 per month	71 (17)
3 per month	80 (20)
4 per month	68 (17)
>4 per month	127 (31)
Severity of usual disease	
Mild (presence of symptoms, but easy to tolerate)	71 (17)
Moderate (discomfort enough to cause interference with normal activities)	318 (78)
Severe (severe enough to unable to perform activities of daily living)	20 (5)

Percentages do not total 100% in all cases due to rounding.

percentages of respondents based on the total number of respondents, unless otherwise stated.

## Results

A total of 409 subjects aged 35–65 years who had used Geffer effervescent granules in the past 6 months were enrolled from a panel of 15,000 consumers with digestive disorders in Italy and consented to participate. Of the 409 subjects enrolled, there was an almost equal split between males and females, most (296, 72%) were aged between 35 and 50 years (Table 1), and nearly half (195, 48%) were experiencing four or more episodes of hyperacidity symptoms (stomachache and/or heartburn) per month (Table 1).

Respondents were using Geffer effervescent granules for the symptomatic relief of a range of digestive symptoms, most frequently hyperacidity (80% of respondents), heartburn (72%), and bloating (66%) (Table 2). Gastric pain/cramps, aerophagia, nausea, and bothersome fullness and/or early satiety were also common symptoms prompting the use of Geffer effervescent granules in 30%–46% of respondents (Table 2). Nearly half (201, 49%) of respondents reported experiencing four or more of these symptoms (Table 2).

When asked about the severity of their symptoms, respondents were able to select from three options: mild (presence of symptoms, but easy to tolerate), moderate (discomfort enough to cause interference with normal activities),

**Table 2.** Symptoms treated using Geffer effervescent granules (N=409).

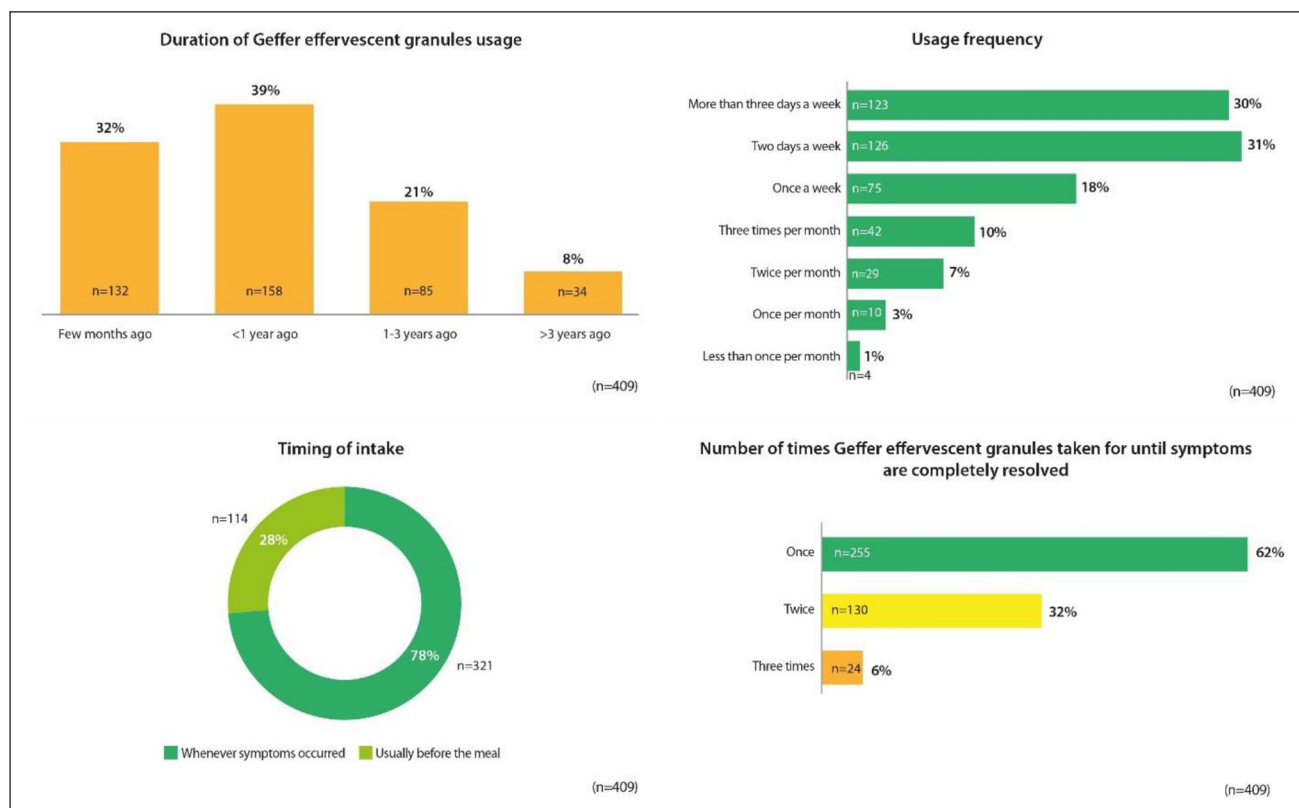
Parameter	n (%)
Symptoms treated using Geffer effervescent granules <sup>a</sup>	
Hyperacidity (excessive production of gastric acid by the stomach)	328 (80)
Heartburn (burning pain in the lower chest)	296 (72)
Bloating (swollen and uncomfortable sensation)	271 (66)
Aerophagia (excessive air swallowing)	188 (46)
Gastric pain/cramps	150 (37)
Nausea (sensation of an urge to vomit)	140 (34)
Bothersome fullness and/or early satiety	121 (30)
Proportion of patients experiencing symptoms being treated with Geffer effervescent granules	
1 of the above symptoms	25 (6)
2 of the above symptoms	66 (16)
3 of the above symptoms	117 (29)
4 of the above symptoms	95 (23)
5 of the above symptoms	61 (15)
6 of the above symptoms	45 (11)
Duration symptoms <sup>b</sup> have been experienced	
Few weeks/<1 month	10 (2)
Few months	56 (14)
<1 year	70 (17)
1–3 years	151 (37)
>3 years	122 (30)

<sup>a</sup>Multiple answers allowed.

<sup>b</sup>Hyperacidity accompanied by bothersome fullness and/or early satiety, nausea, aerophagia, and bloating.

and severe (severe enough to make the subject unable to perform the activities of daily living). Most respondents (318, 78%) usually experienced symptoms of moderate severity (Table 1), and 67% (n=273) of them reported that they had experienced hyperacidity symptoms accompanied by bothersome fullness, nausea, aerophagia, and bloating for more than 1 year (Table 2). Most of the respondents (339, 83%) reported that their daily activities were impacted by the symptoms they were treating with Geffer effervescent granules, whereas only 1 (<1%) respondent reported symptoms to have no impact, and 69 (17%) experienced only a little impact. The life aspects most commonly impacted by symptoms were respondents' emotional life (e.g. frustration, bad mood, anxiety, irritability; n=221, 54%), respondents' sleep (n=203, 50%), aesthetic aspects (mainly due to abdominal swelling; n=149, 36%), and social life (n=133, 33%).

The most common (reported by >30% of respondents) perceived reasons for the symptoms being treated with Geffer effervescent granules included stress (e.g. heavy workload, too many responsibilities; n=244, 60%), eating heavy food (e.g. meat, pizza, burgers, etc; n=214, 52%), unhealthy behaviors (e.g. sedentary lifestyle; n=188, 46%), anxiety (n=167, 41%), eating too much (n=133, 33%), and consuming large amounts of caffeine (n=128, 31%) (Supplementary Figure 2).



**Figure 1.** Geffer effervescent granules usage patterns: duration of use, usage frequency, usage time, and number of times taken until resolution of symptoms, as reported by respondents (N = 409).

To treat their symptoms, most respondents reported that they took Geffer effervescent granules on 2 or more days per week (249, 61%) and when symptoms occurred (321, 79%) rather than regularly before a meal. When suffering a hyperacidity episode, most respondents (255, 62%) reported that their symptoms usually resolved after a single administration of Geffer effervescent granules, with only 24 (6%) of respondents having to take the product three times (Figure 1).

### Speed and duration of symptom relief after taking Geffer effervescent granules

Respondents were asked how rapidly after having taken Geffer effervescent granules they started to experience an effect and for how long they were symptom free. Eighty-seven respondents (21%) reported that they experienced an effect within 10 min after product intake and more than half (218, 53%) experienced an overall effect within the initial 15 min (Figure 2(a)). The majority of respondents (359, 88%) stated that they experienced symptom relief within 30 min (Figure 2(a)). Half of the respondents (204, 50%) reported that they were symptom free for more than 3 h or until their next meal (Figure 2(b)). Similar percentages were reported by respondents for onset of complete relief and the

time being symptom free on the individual symptoms of gastric pain/cramps, acidity, bloating, nausea, and sense of fullness (Figure 2(b)–(f)).

### Impact on quality of life

Nearly all (375, 92%) respondents agreed that their quality of life improved while they were taking Geffer effervescent granules to treat hyperacidity symptoms, with only 3 (<1%) stating they disagreed (8% of respondents were neutral).

More than two thirds (283, 69%) of the respondents had previously used other medications to treat their hyperacidity symptoms, of whom 121 (43%) reported that they switched to Geffer effervescent granules because it was more effective than their previous medication. Other reasons for switching to Geffer effervescent granules included faster symptom relief (79/283, 28%) and a broader range of action on symptoms (77/283, 27%) than their previous product.

When asked why they had selected to use Geffer effervescent granules to treat their digestive symptoms, 340 (83%) reported that the product had been recommended to them by a health care professional. Other reasons included recommendations by friends or relatives (37, 9%), searches on the Internet or on social media (11, 3%), or having seen an advertisement (6, 2%).

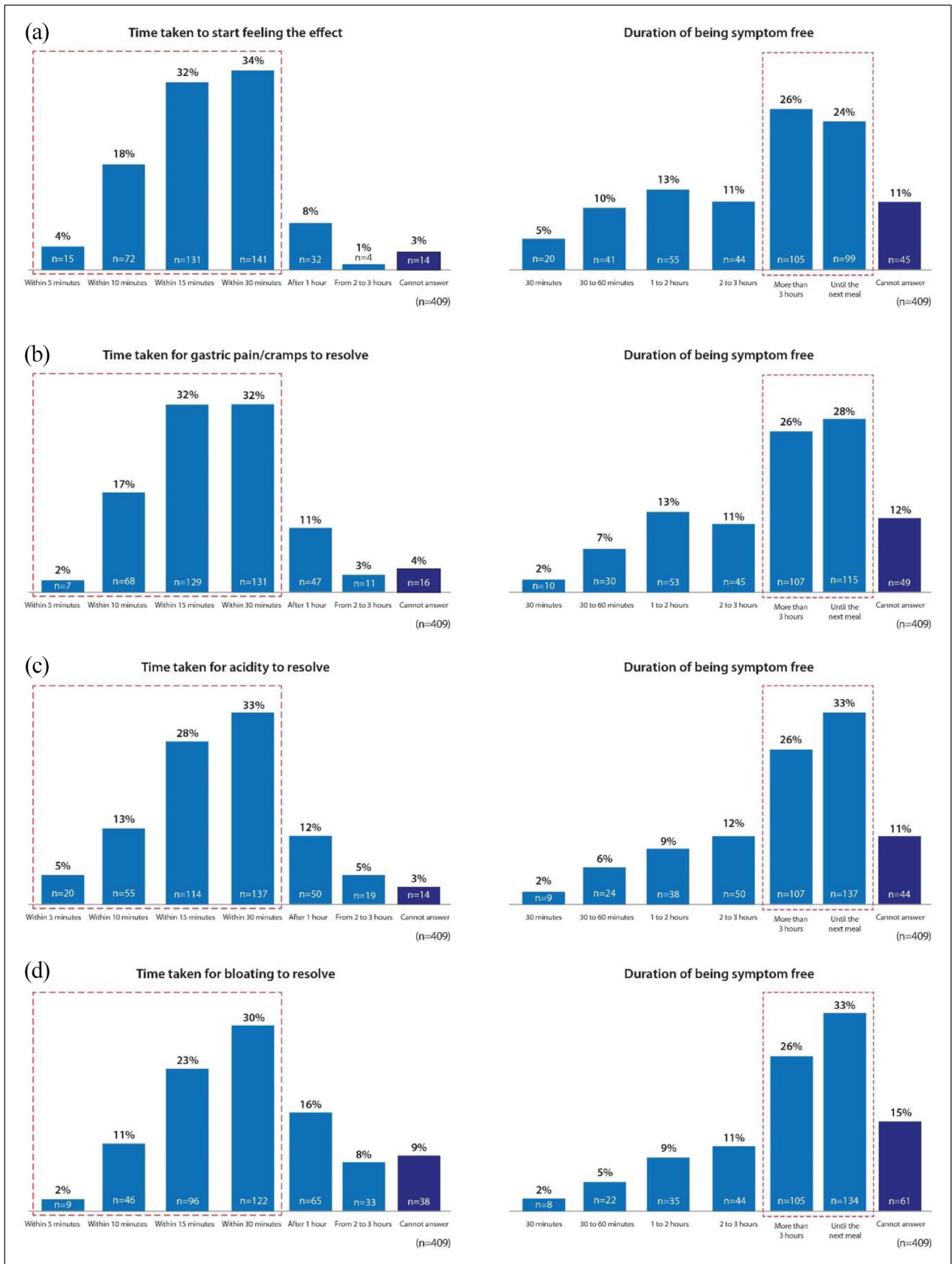
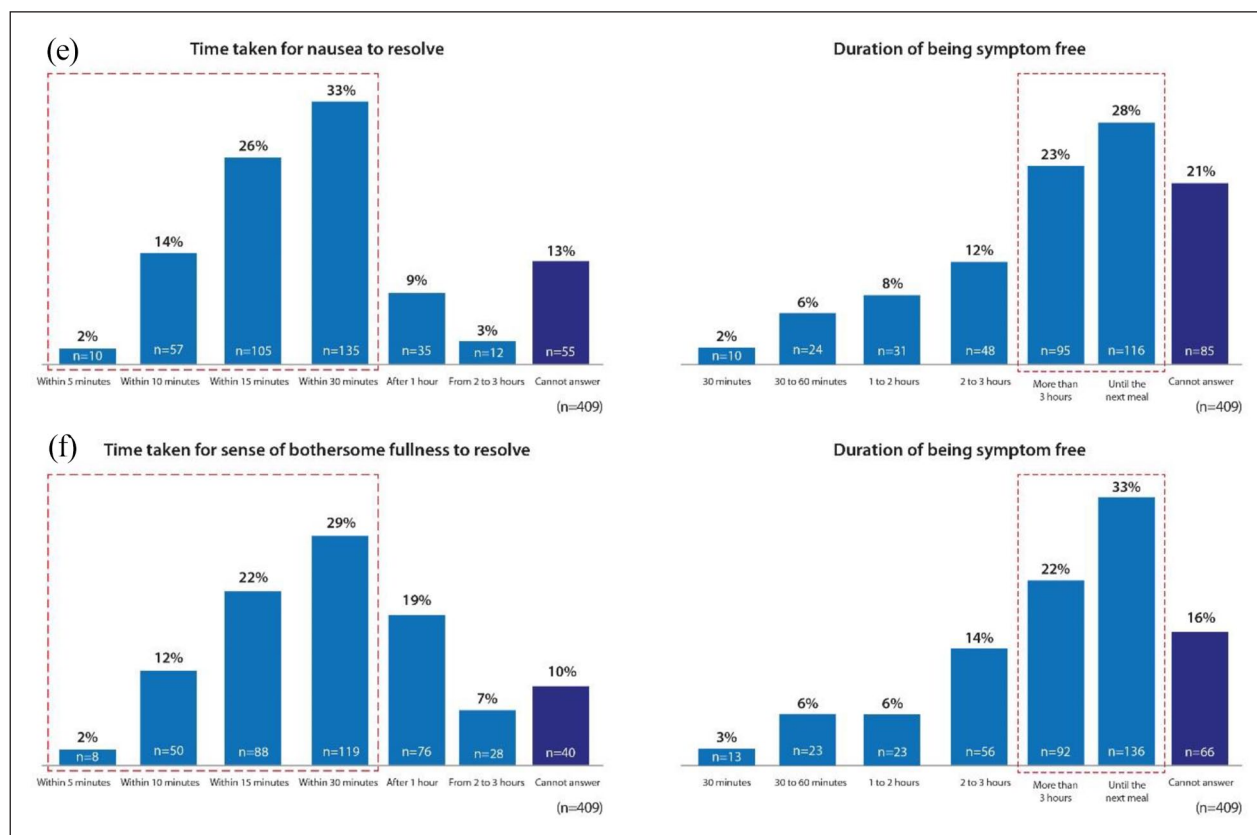


Figure 2. (Continued)



**Figure 2.** Time from Geffer effervescent granules intake to provision of symptom relief and duration of complete symptom relief for (a) overall symptoms, (b) gastric pain/cramps, (c) acidity, (d) bloating, (e) nausea, and (f) sense of fullness (N = 409).

Overall, 95% of the respondents were satisfied with the effectiveness of Geffer effervescent granules on overall symptom relief; percentages varied between 82% and 95% for the individual symptoms of gastric pain/cramps, acidity and acid reflux, bloating, nausea, and bothersome fullness (Figure 3).

Over 85% of the respondents agreed that their entire experience with taking Geffer effervescent granules was easy/very easy (364, 89%); they liked the effervescent formulation (352, 86%); the product was good value for their money (370, 90%); and they would recommend Geffer effervescent granules to family and friends (385, 94%) (Figure 4).

## Discussion

Meal-related digestive symptoms can differ from individual to individual, ranging from epigastric pain and burning to nausea and bloating.<sup>2,3</sup> Accordingly, FD, the most common form of meal-induced digestive disorder, has been divided into two sub-types, postprandial distress syndrome and epigastric pain syndrome, to account for the different presentations the disease can have in patients.<sup>5</sup> Treatments able to combine multiple pharmacological actions are therefore relevant to address the array of symptoms patients can face with meal-related digestive disorders.

Geffer effervescent granules is sold in Italy as an OTC medication able to treat hyperacidity (pain and/or heartburn) when accompanied by slowing of gastric transit, nausea, aerophagia, and bloating, all symptoms that can occur in FD. It combines the prokinetic action of metoclopramide, whose utility in FD is recognized,<sup>6,21</sup> with the antacid activity of sodium bicarbonate and the anti-bloating action of dimethicone. The combination of dimethicone with an antacid, in particular, has already been shown to improve gastric symptoms, including heartburn, pain, and flatulence.<sup>23,24</sup> However, the impact of this combination in a real-life setting and on patients' quality of life has not previously been investigated.

Real-world evidence studies investigate the performance of medicinal products and treatments in everyday use, complementing the evidence from controlled clinical trials, to better understand patient health, compliance, and the effects and attributes of products when used outside the context of a controlled setting. Unlike controlled clinical trials, real-world evidence studies are observational in nature and usually, in the case of prescription medicines, use data already available from electronic health records, insurance claims, product/disease registries, and patient surveys designed to generate evidence. What is possible for prescription medicines, however, does not always apply to self-care products, such as Geffer effervescent granules, since such sources

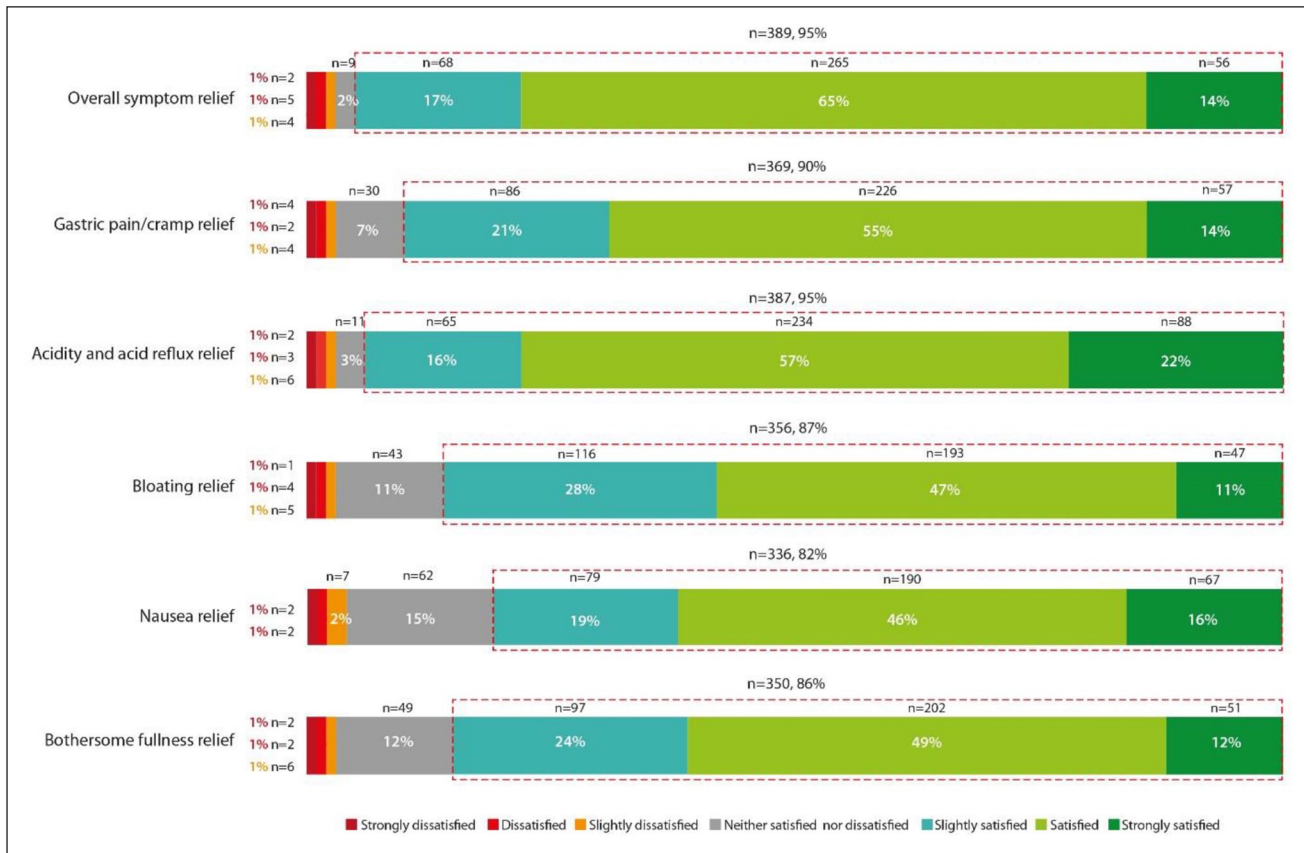


Figure 3. Respondent satisfaction with overall symptom relief and relief of gastric pain/cramps, acidity and acid reflux, bloating, nausea, and bothersome fullness (N = 409).



Figure 4. Consumer ratings of satisfaction with Geffer effervescent granules.



rarely provide information on their use and performance under real-world conditions. Therefore, real-world evidence on self-care products needs to be generated via prospective or retrospective observational studies involving subjects who are current or past users of the product. For this retrospective real-world data study, subjects who had used Geffer effervescent granules within the previous 6 months were recruited from an existing panel of 15,000 Italian consumers with digestive disorders suggestive of FD.

The aim of the study was to assess the experience of consumers taking Geffer effervescent granules for the symptomatic relief of digestive symptoms suggestive of FD (i.e. hyperacidity, heartburn, gastric pain/cramps, aerophagia, nausea, and meal-related symptoms such as bloating and bothersome fullness/early satiety) in a real-life, routine, self-care setting. The population recruited into this study was equally split between males and females (51% vs 48%, respectively), with 72% of respondents being between 35 and 50 years. Most respondents reported experiencing multiple digestive symptoms for more than 1 year, with stress and anxiety being among the main perceived causes of symptoms, together with meal-related factors (e.g. eating heavy or too much food), which is in line with the known causes of FD,<sup>16</sup> as well as recent findings that show a direct interaction between mood and diet.<sup>26</sup>

There is growing recognition of the value of assessing the experience of patients when evaluating symptomatic diseases and the effectiveness of treatments.<sup>27</sup> Clinical trials evaluating therapies for people with FD and other digestive disorders largely focus on the improvement of symptoms and, to a lesser extent, quality of life, assessed using a range of global, generic, and disease-specific instruments.<sup>27,28</sup> Other outcomes, such as the perceived speed of symptom relief and duration of symptom relief under everyday use conditions, which are considered important to consumers/patients, are usually not assessed in clinical trials.

In the current real-world data study, Geffer effervescent granules provided rapid onset of symptom relief, with 21% of respondents experiencing an effect within 10 min and 88% reporting an improvement in overall symptoms within 30 min. This was also reflected in the similarly rapid onset of complete resolution of gastric pain/cramps, acidity, bloating, nausea, and bothersome fullness symptoms, reported by 65%–83% of respondents.

Data from this study show that beside the rapid onset of perceived symptom relief by Geffer effervescent granules, respondents also reported the action of the product to be long-lasting, with 50%–59% of respondents being free from their overall symptoms and from symptoms of gastric pain/cramps, acidity, bloating, nausea, and fullness for more than 3 h or until the next meal.

The majority of respondents (83%) reported that before using Geffer effervescent granules, their digestive symptoms affected their everyday activities, a finding that is in line with the observed impairment of quality of life by symptoms

of epigastric pain, postprandial fullness, and nausea.<sup>9,10</sup> Most of the individuals who participated in this real-world data study (92% of respondents) were of the opinion that their quality of life improved when taking Geffer effervescent granules to treat hyperacidity symptoms.

Consumer satisfaction with Geffer effervescent granules was high: 89% or more of respondents described their entire experience with taking Geffer effervescent granules to be easy/very easy, agreed that they would recommend the product to family or friends for the treatment of hyperacidity, and considered Geffer effervescent granules good value for their money.

Strengths of this study include the large sample size and the fact that it provides a real-world snapshot of how Geffer effervescent granules are used and perform in everyday routine self-care in Italy, providing data on patient-important outcomes not usually assessed in clinical trials and putting patients and their health journey at the heart of the investigation. The study focused on consumers taking Geffer effervescent granules for the symptomatic relief of digestive symptoms suggestive of FD (i.e. hyperacidity, heartburn, gastric pain/cramps, aerophagia, nausea, and meal-related symptoms, such as bloating and bothersome fullness/early satiety). All participants were recruited from a panel in which they had been previously profiled for self-reported digestive disorders likely due to FD. FD is a clinical diagnosis that can be made only after excluding all other causes of dyspepsia;<sup>6</sup> hence, whether participants had FD cannot be confirmed. As respondents in this real-world data study were people who had purchased and used Geffer effervescent granules in the past 6 months (with no incentives offered for participation), the self-reported results of this study may be considered neutral. Limitation of real-world data studies such as this one, in which retrospective data are collected via an electronic questionnaire, is that they cannot be monitored and therefore may be subject to recall bias.<sup>29</sup> The impact of this limitation was reduced through use of inclusion criteria limiting participants to those aged 35–65 years who had used Geffer effervescent granules in the 6 months prior to the study (i.e. those with the highest probability of recent use of Geffer effervescent granules). This is in line with previous investigations, which have shown that the time between an event and the time of its assessment is an important factor, with ~20% of critical details of an event irretrievably lost after 1 year and ~50% after 5 years.<sup>30</sup> Therefore, a period of 6 months in a repetitively occurring indication was considered adequate to reduce recall bias and generate reliable and precise data. In addition, the age inclusion criterion of 35–65 years enabled us to target those most likely to experience symptoms suggestive of FD.<sup>4,8</sup> The survey questions were not formally validated. However, the way questions were asked, including the provision of categorical answer options to respondents, has been used and tested for robustness and stability in several other similar studies conducted by Bayer within the past 2 years. In addition, similar questions and Likert-type

scales have been used to assess digestive symptoms in other real-world studies assessing treatments for gastrointestinal disorders.<sup>31</sup> Finally, consumers were selected from a panel comprising people with digestive disorders likely to be due to FD (with or without heartburn) who were willing to take part in online surveys, and data may not, therefore, be generalizable to all such people in the Italian general population.

## Conclusion

This real-world study in Italian consumers who used Geffer effervescent granules for the symptomatic treatment of digestive disorders likely due to FD demonstrated the perceived benefits of a combination of metoclopramide, sodium bicarbonate, and dimethicone with regard to the rapid, complete, and durable relief of symptoms of gastric pain/cramps, acidity, bloating, nausea, and bothersome fullness; an improvement in quality of life; and a high level of consumer satisfaction.

## Acknowledgements

The authors thank the study participants, Göran Patrick Fernström and Ankita Baru from IQVIA who helped develop and manage the study, and Shruti Saxena and Aditi Saxena from IQVIA who provided and implemented the online platform for the screening questionnaire and questionnaire. Gillian Gummer, Proactive Editorial Services Ltd, assisted with the writing of this manuscript.

## Declaration of conflicting interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Matteo Alemanni and Barbara Moroni are employees of Bayer S.p.A., Italy. Raffaella de Salvo and Andreas Ehret are employees of Bayer Consumer Care AG, Switzerland. All authors were responsible for the study concept and/or design, acquisition/analysis/interpretation of the data, drafting/revising/reviewing the manuscript critically, and approval of the final version of the manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The study was fully funded by Bayer S.p.A., Italy.

## Ethics approval

According to the “Governance arrangements for research ethics committees: 2020 edition” document published by the NHS Health Resource Authority, UK, Section 2.3.15, “Market research may be undertaken by professional market researchers, e.g. for public health research or on behalf of pharmaceutical or medical device companies. Where such research is conducted by professional market researchers in accordance with the principles set out in the Market Research Society Code of Conduct or with the Legal and Ethical Guidelines issued by the British Healthcare Business

Intelligence Association (BHBIA), it does not require REC review, except where otherwise required by law, e.g. if it requires approval under the Mental Capacity Acts.” In line with BHBIA guidelines, in this study, participants were informed about the objective and use of the study prior to completing the questionnaire. As this is a retrospective observational study with no involvement of health care providers and no information was being collected from medical records, as well as no proactive safety signal collection, there was no need for a review and approval of this study by an Ethics Committee (EC). Due to this, also a waiver for EC review was not needed and not asked for.

## Informed consent

Written informed consent was obtained from all subjects before the study.

## ORCID iD

Matteo Alemanni  <https://orcid.org/0000-0002-5335-0907>

## Primary data

Data generated and analyzed during the current study are available from the corresponding author on reasonable request.

## Supplemental material

Supplemental material for this article is available online.

## References

1. Haag S, Andrews JM, Gapasin J, et al. A 13-nation population survey of upper gastrointestinal symptoms: prevalence of symptoms and socioeconomic factors. *Aliment Pharmacol Ther* 2011; 33(6): 722–729.
2. Camilleri M, Dubois D, Coulie B, et al. Prevalence and socio-economic impact of upper gastrointestinal disorders in the United States: results of the US Upper Gastrointestinal Study. *Clin Gastroenterol Hepatol* 2005; 3(6): 543–552.
3. van Kerkhoven LA, Eikendal T, Laheij RJ, et al. Gastrointestinal symptoms are still common in a general Western population. *Neth J Med* 2008; 66(1): 18–22.
4. Keber E, Rocco P, Musazzi UM, et al. The management of upper gastrointestinal symptoms: a study on community pharmacies in Italy. *Pharmacia* 2021; 68(2): 401–409.
5. Stanghellini V, Chan FK, Hasler WL, et al. Gastrointestinal disorders. *Gastroenterology* 2016; 150(6): 1380–1392.
6. Talley NJ. Functional dyspepsia: new insights into pathogenesis and therapy. *Korean J Intern Med* 2016; 31(3): 444–456.
7. El-Serag HB and Talley NJ. Systemic review: the prevalence and clinical course of functional dyspepsia. *Aliment Pharmacol Ther* 2004; 19(6): 643–654.
8. Zagari RM, Law GR, Fuccio L, et al. Epidemiology of functional dyspepsia and subgroups in the Italian general population: an endoscopic study. *Gastroenterology* 2010; 138(4): 1302–1311.
9. Talley NJ, Locke GR 3rd, Lahr BD, et al. Functional dyspepsia, delayed gastric emptying, and impaired quality of life. *Gut* 2006; 55(7): 933–939.

10. Hantoro IF, Syam AF, Mudjaddid E, et al. Factors associated with health-related quality of life in patients with functional dyspepsia. *Health Qual Life Outcomes* 2018; 16(1): 83.
11. Sheen CL and Colin-Jones DG. Over-the-counter drugs and the gastrointestinal tract. *Aliment Pharmacol Ther* 2001; 15(9): 1263–1270.
12. Sihvo S and Hemminki E. Self-medication of dyspepsia: how appropriate is it? *Scand J Gastroenterol* 1997; 32(9): 855–861.
13. L'Informatore Farmaceutico. Geffer, <https://www.codifa.it/farmaci/g/geffer-metoclopramide-e-dimeticone-e-potassio-citrato-e-acido-tartarico-e-acido-citrico-anidro-e-sodio-bicarbonato-procinetici> (accessed 1 October 2021).
14. Maton PN and Burton ME. Antacids revisited: a review of their clinical pharmacology and recommended therapeutic use. *Drugs* 1999; 57(6): 855–870.
15. Misra SP and Broor SL. Is gastric acid responsible for the pain in patients with essential dyspepsia? *J Clin Gastroenterol* 1990; 12(6): 624–627.
16. Joffe SN and Primrose JN. Pain provocation test in peptic duodenitis. *Gastrointest Endosc* 1983; 29(4): 282–284.
17. PubChem. Metoclopramide, <https://pubchem.ncbi.nlm.nih.gov/compound/Metoclopramide> (accessed 1 October 2021).
18. Jahromi HE, Gholami M and Rezaei F. A randomized double-blinded placebo controlled study of four interventions for the prevention of postoperative nausea and vomiting in maxillofacial trauma surgery. *J Craniofac Surg* 2013; 24(6): e623–e627.
19. Hardy J, Daly S, McQuade B, et al. A double-blind, randomised, parallel group, multinational, multicentre study comparing a single dose of ondansetron 24 mg p.o. with placebo and metoclopramide 10 mg t.d.s. p.o. in the treatment of opioid-induced nausea and emesis in cancer patients. *Support Care Cancer* 2002; 10(3): 231–236.
20. Ragan RE, Rock RW and Buck HW. Metoclopramide pretreatment attenuates emergency contraceptive-associated nausea. *Am J Obstet Gynecol* 2003; 188(2): 330–333.
21. Yang YJ, Bang CS, Baik GH, et al. Prokinetics for the treatment of functional dyspepsia: Bayesian network meta-analysis. *BMC Gastroenterol* 2017; 17: 83.
22. Ingold CJ and Akhondi H. Simethicone. In: *StatPearls* (Internet). Treasure Island, FL: StatPearls Publishing, 2021 (PMID: 32310457), <https://pubmed.ncbi.nlm.nih.gov/32310457/>
23. Smart HL and Atkinson M. Comparison of a dimethicone/antacid (Asilone gel) with an alginate/antacid (Gaviscon liquid) in the management of reflux oesophagitis. *J R Soc Med* 1990; 83(9): 554–556.
24. Cobden I, McMahon MJ, Dixon MF, et al. Double-blind clinical, endoscopic and histological comparison of hydrotalcite/dimethicone suspension and magnesium hydroxide/aluminum hydroxide suspension in the treatment of symptomatic gastritis. *Pharmatherapeutica* 1981; 2(9): 607–612.
25. Cochran WG. *Sampling techniques*. 2nd ed. New York: John Wiley & Sons, Inc, 1963.
26. Gibson EL. Emotional influences on food choice: sensory, physiological and psychological pathways. *Physiol Behav* 2006; 89(1): 53–61.
27. Vakil NB, Halling K, Becher A, et al. Systematic review of patient-reported outcome instruments for gastroesophageal reflux disease symptoms. *Eur J Gastroenterol Hepatol* 2013; 25(1): 2–14.
28. Ang D, Talley NJ, Simren M, et al. Review article: endpoints used in functional dyspepsia drug therapy trials. *Aliment Pharmacol Ther* 2011; 33(6): 634–649.
29. Blome C and Augustin M. Measuring change in quality of life: bias in prospective and retrospective evaluation. *Value Health* 2015; 18(1): 110–115.
30. Wagenaar WA. My memory: a study of autobiographical memory over six years. *Cogn Psychol* 1986; 18(2): 225–252.
31. Wegener T and Heimuller E. Treatment of mild gastrointestinal disorders with a herbal combination: results of a non-interventional study with Gastritol® Liquid. *Phytother Res* 2016; 30(1): 72–77.