

Development and content validity of a gastroparesis cardinal symptom index daily diary

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SUMMARY

Background

The Gastroparesis Cardinal Symptom Index (GCSI) is a patient-reported outcome for gastroparesis using a two-week recall period. To minimize potential patient recall effects, a daily diary version of the GCSI (GCSI-DD) was developed.

Aims

To evaluate the content validity of GCSI-DD for the symptoms in patients with documented gastroparesis, to capture symptom variability over time and to compare responses of this GCSI-DD to the original GCSI.

Methods

In gastroparesis adults with delayed gastric emptying, cognitive debriefing interviews were conducted to elicit their perspective on relevant symptoms of gastroparesis and relevant recall periods and to evaluate patient understanding of GCSI-DD. Patients completed the GCSI-DD daily over a 2-week period and completed the GCSI at baseline and the 2-week follow-up visit.

Results

Twelve gastroparesis patients, of whom five were diabetic and nine women, reported nausea (100%), vomiting (100%), stomach fullness (75%), bloating (58%) and loss of appetite (50%) were important symptoms. All patients understood diary instructions and item content and reported that the diary captured their gastroparesis symptom experience; 83% considered response scales adequate. There was significant daily variability in GCSI-DD scores. Mean GCSI-DD subscale and total scores over 2 weeks correlated strongly (all $r > 0.90$) with GCSI scores at 2-week follow-up.

Conclusions

The GCSI-DD includes symptoms relevant to patients with gastroparesis, captures daily variability of those symptoms and has psychometric properties consistent with a good patient-reported outcome endpoint for gastroparesis clinical trials.

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INTRODUCTION

Gastroparesis is a condition of delayed gastric emptying with no mechanical obstruction.^{1, 2} Patients experience a variety of symptoms including early satiety, nausea, vomiting and abdominal pain or discomfort. Gastroparesis is frequently associated with diabetes (diabetic gastroparesis); however, gastroparesis of unknown aetiology (idiopathic gastroparesis) accounts for the largest number of cases.^{3, 4}

A patient-reported symptom questionnaire, the Gastroparesis Cardinal Symptom Index (GCSI), was developed in university-based clinical practices for quantifying symptom severity in gastroparesis.^{5, 6} The nine symptom GCSI is based on three subscales (postprandial fullness/early satiety, nausea/vomiting, and bloating). The GCSI represents a subset of the longer Patient Assessment of Upper Gastrointestinal Disorders-Symptoms (PAGI-SYM) that also includes symptoms of gastro-oesophageal reflux and dyspepsia.^{7, 8} The GCSI and PAGI-SYM were designed to assess the severity of patients' symptoms over the last 2 weeks. Both the PAGI-SYM and GCSI have been used in clinical trials for patients with gastroparesis.⁹⁻¹²

The symptom variability described by some patients with gastroparesis suggests that a two-week recall period may not document important changes in symptoms in the short-term. The U.S. Food and Drug Administration (FDA) has indicated a preference for assessing symptoms using daily diaries¹³ on the basis of previous research involving momentary assessments.^{14, 15} Few psychometrically sound, patient-reported symptom scales are available for evaluating treatments for gastroparesis^{5, 16, 17} and none is based on daily recall. To address this, we developed a daily diary version of the CGSI.

The GCSI daily diary (GCSI-DD) includes nausea/vomiting (3 items), postprandial fullness/early satiety (4 items) and bloating (2 items). The diary also asked about symptoms of abdominal pain (2 items), which were not included in the original GCSI. In some patients, abdominal pain and/or discomfort can be an important symptom of gastroparesis¹⁸ and pain has been included in other severity scores for gastroparesis.^{16, 17}

The primary objectives of this study were to: (1) evaluate the content validity of this new GCSI daily diary in patients with gastroparesis, (2) capture symptom variability over time and (3) compare the GCSI-DD subscale and total scores with those of the original GCSI using a two-week recall period.

METHODS

Participants, recruitment and eligibility criteria

Patients with gastroparesis were recruited at Temple University Gastroenterology Section. The site investigator (HP) and clinical staff identified potential participants by reviewing patient records or speaking to patients during their scheduled visit. For patients who agreed to participate in the cognitive debriefing interviews, the site coordinator scheduled an interview date and time.

Patients were eligible for the study if they were 18 years of age or older, had a diagnosis of gastroparesis with documented delay in gastric emptying of solids during the year prior to participation in this study, were currently receiving care for gastroparesis, were either idiopathic or diabetic aetiology, and were English speakers. Gastric emptying scintigraphy was measured using the method recommended by the consensus report of the Society of Nuclear Medicine and the American Neurogastroenterology and Motility Society,¹⁹ using EggBeaters meal and abdominal imaging conducted intermittently over 4 h. Delayed gastric emptying is defined by >60% retention 2 h postprandially and/or >10% retention 4 h postprandially. Patients were excluded if their gastroparesis arose from postsurgical causes, they were non-English speaking or they had cognitive or other impairment (e.g. visual) that would interfere with completing the study visit.

The study protocol was approved by the Temple University Institutional Review Board, and all patients provided written informed consent.

Study design

Patients participated in cognitive debriefing interviews with research staff trained in qualitative interview methodology. The study was designed to capture symptomatic patients, representative of a range of gastroparesis severity and included patients with and without co-morbid diabetes.

Prior to the cognitive debriefing interview, the site investigator or one of the study coordinators explained the study to the patient and obtained written informed consent. A health-related information form, which included a physician assessment of patient gastroparesis symptoms using an adjective six-point Likert scale (see clinician rated overall gastroparesis severity scale below), was collected after consent was obtained.

Cognitive debriefing interviews. Face-to-face cognitive debriefing interviews were conducted and each interview was approximately 1 h. The interviews followed a semi-structured interview schedule that provided an introduction to the interview session and served as a guide for queries and prompting. The interview was intended to capture information on how the participants describe their symptom experience, on the language they use to describe their condition and symptoms, and how they understood the instructions, individual items and response options on the GCSI-DD. At the conclusion of the interview, participants were asked to complete the PAGI-SYM and demographic questions. All sessions were audio-recorded and later transcribed.

Prior to ending the interview, patients were given a notebook containing 21 copies of the GCSI-DD. The patients were instructed to complete the GCSI-DD each night before bed for 2 weeks (additional copies were provided in case of scheduling conflicts). Patients returned to the clinic for a follow-up visit approximately 2 weeks after the initial visit and completed the PAGI-SYM questionnaire again.

Measures

Gastroparesis cardinal symptom index daily diary. The content of the GCSI-DD was based on the original GCSI.^{5,6} The GCSI-DD consists of nine symptom severity items that cover the following domains: nausea/vomiting (3 items); fullness/early satiety (4 items); and bloating (2 items). In addition, the diary contains two symptom severity items for upper abdominal pain and an overall rating of gastroparesis severity. Symptoms were rated by the patients among the choices none (0), very mild (1), mild (2), moderate (3), severe (4), and very severe (5). The GCSI total score equals the sum of the nausea/vomiting, bloating and fullness/early satiety subscales, divided by 3. The GCSI-DD was completed every day for up to 21 days.

PAGI-SYM questionnaire. The PAGI-SYM was developed to assess gastroparesis, functional dyspepsia and gastro-oesophageal reflux disease.^{7,8} The measure consists of 20 symptom severity items that cover the following domains: nausea/vomiting; fullness/early satiety; bloating; upper abdominal pain; heartburn/regurgitation; and lower abdominal pain. Previous research has demonstrated the reliability and

validity of the PAGI-SYM.^{7,8} The PAGI-SYM was administered at the baseline and two-week visit.

The GCSI is based on a subset of the items within the PAGI-SYM.⁵ The GCSI consists of nine symptom severity items that cover nausea/vomiting, fullness/early satiety and bloating. The GCSI was scored at baseline and week 2, based on the PAGI-SYM items.

Patient rated overall gastroparesis severity. The patients rated the severity of their overall gastroparesis symptoms using the patient rated overall gastroparesis severity (OGS-P). The six-level response scale ranged from none to very severe. The OGS-P was collected daily in the GCSI-DD.

Clinician-rated overall gastroparesis severity. On the day of the interview, physicians rated the severity of the patient's gastroparesis symptoms using the clinician-rated overall gastroparesis severity (OGS-C). The six-level response scale ranged from none to very severe.

Data analysis

Cognitive debriefing transcripts were reviewed and analysed using ATLAS.ti version 5.0, a qualitative analysis software program. Transcripts were reviewed to obtain key concepts and themes regarding gastroparesis symptoms, as well as specific issues related to the GCSI-DD instructions, response options, and items. Using ATLAS.ti, qualitative data (patient quotes from interviews) can be systematically analysed, coded and compared. First, 'open coding' was performed. This involves technically fracturing the data (i.e. passages from transcripts and notes) into smaller units and identifying concepts, themes or recurring regularities that appear within each interview. Second, axial coding was used to connect categories and subcategories of the data. Specifically, each of the detailed codes or categories in open coding was connected based on their emergent theoretical linkages so that they represent specific instances of more general and abstract phenomena.

Saturation is reached once no new terms or concepts are being identified from the patient interview data.^{20,21} According to Willis,²¹ saturation is often reached after seven to eight interviews. Qualitative coding of data and concepts play a key role in determining whether saturation has been reached. A saturation grid

was used to track symptoms after each individual interview. A record of symptoms and impact of symptoms elicited was entered in the saturation grid after each interview.

The second objective was to examine the day-to-day variability of symptoms in patients with gastroparesis. This was assessed two ways. First, the GCSI-DD item responses were evaluated for variability of symptoms over the two-week period. This was performed initially by visual analysis of the descriptive statistics for the GCSI-DD symptom, subscale and total scores over time for each patient. In addition, the standard deviation of the daily symptom scores was calculated and compared among the different patients. Second, an average GCSI-DD subscale and total scores were calculated for each patient for one to 14 days and for the 7 days before the two-week follow-up visit. GCSI-DD scores were correlated to the patient's assessment of symptoms over the past 2 weeks based on the PAGI-SYM (i.e. GCSI subscale and total GCSI scores).

RESULTS

Demographic and clinical characteristics

Twelve patients with gastroparesis were recruited for this study. Five (42%) of the 12 participants had a concurrent diagnosis of diabetes (two of these diabetic patients were on insulin pumps). Participants were, on average, 43.9 (s.d. = 10.6) years old (range 26 to 62), predominantly female (75%) and Caucasian (100%). Many patients had a college degree (33%) or had completed some training beyond high school (25%) and 66.7% were married. The majority of patients (66.7%) were currently employed.

Clinical characteristics for the sample are summarized in Table 1. On average, patients began experiencing gastroparesis symptoms when they were 35.9 years old and were diagnosed with gastroparesis at 40.9 years. Four patients (33.3%) reported visits to the emergency department because of their gastroparesis symptoms in the past year and two patients (16.7%) reported an inpatient hospitalization in the past year. Seven of the patients currently had gastric electric stimulators (GES) and three had previously received botulinum toxin injections into the pylorus, indicating that their symptoms have been severe, at least in the past. Current medical treatments for their gastroparesis included seven patients (58.3%) with the GES, four patients (33.3%) receiving prokinetic medications and

Table 1. Clinical characteristics

	(N = 12)
Age started having symptoms of gastroparesis, mean (s.d.) [range]	35.9 (13.9) [15.0–57.0]
Age diagnosed with gastroparesis, mean (s.d.) [range]	40.9 (10.9) [23.0–59.0]
Gastroparesis symptom experience, n (%)	
Chronic symptoms, but stable	9 (75.0%)
Chronic, but progressive worsening of symptoms	0 (0.0%)
Chronic, with periodic exacerbations	3 (25.0%)
Cyclic pattern of exacerbations with feeling well in between	0 (0.0%)
Diabetes, n (%)	5 (41.7%)
Most recent gastric emptying test results, mean (s.d.)*	
2 h % retention	65.1 (18.4)
4 h % retention	40.2 (23.6)
Current medications†, n (%)	
Prokinetic agent	4 (33.3%)
Antiemetic agent	4 (33.3%)
Gastric antisecretory agent	7 (58.3%)
Pain medications	4 (33.3%)
Psychotropic agent	5 (41.7%)
Diabetes treatment	4 (33.3%)
Gastric electric stimulation (pacemaker)	7 (58.3%)
Other medical conditions, n (%)	11 (91.7%)
Prior surgery, n (%)	10 (83.3%)
Physician-rating of gastroparesis severity, n (%)	
None	2 (16.7%)
Very mild	1 (8.3%)
Mild	4 (33.3%)
Moderate	5 (41.7%)
Severe	0 (0.0%)
Very severe	0 (0.0%)

* Two patients' test results were missing.

Prokinetic agents included: domperidone. Antiemetic agents included: prochlorperazine and ondansetron. Gastric antisecretory agents included: omeprazole, pantoprazole, lansoprazole, famotidine, esomeprazole, ranitidine, and rabeprazole. Pain medications included: ibuprofen, hydromorphone, and oxycodone with acetaminophen. Psychotropic agents included: pregabalin, levetiracetam, nortriptyline, and amitriptyline.

four patients (33.3%) receiving antiemetic medications (ondansetron or prochlorperazine). a majority of patients (75.0%) indicated that their gastroparesis symptoms were now chronic but stable, and three patients (25.0%) reported chronic symptoms with

periodic exacerbations. Based on physician-rated gastroparesis severity at study entry, five patients (41.7%) were rated as moderate; four patients (33.3%) as mild; one patient (8.3%) as very mild and two patients (16.7%) as having no current gastroparesis symptoms as a result of their ongoing treatment.

The majority of patients (91.7%) reported at least one other medical condition and 10 patients (83.3%) reported having previous non-gastric surgery. The most recent gastric emptying results in this group of patients were: 2 h % retention 65.1 (s.d. = 18.4) and 4 h % retention mean of 40.2 (s.d. = 23.6).

Qualitative research findings

Gastroparesis symptom experience. Initially, the participants were asked about their gastroparesis symptom experience in general and to describe their symptoms of gastroparesis. Then they were asked to complete the GCSI-DD and asked whether the GCSI symptoms covered the relevant and important symptoms of gastroparesis. Participants reported that nausea (100%), vomiting (100%), stomach fullness (75%), bloating (58%) and loss of appetite (50%) were important symptoms of gastroparesis. Overall, all the participants stated that the questionnaire covered the majority of their symptoms and experience with gastroparesis. There were no substantive differences between idiopathic and diabetic gastroparesis patients related to their symptom experience. One participant suggested adding 'at what point in the meal process' to all of the items, as this participant linked every symptom to whether or not food had been/could be consumed.

Cognitive debriefing of GCSI daily diary. Seven participants (58%) reported that all of their gastroparesis symptoms were included in the GCSI-DD and suggested that no additional symptom items were needed. One participant stated that items on belching, whether or not food was being digested, should be included if food was coming up into the mouth suddenly without force and it was associated with weight loss. Another participant stated an item on belching was needed.

No one or two items were identified by all or a majority of participants as best describing their current experience with gastroparesis. Symptoms identified by more than one participant included: stomach fullness (42%); nausea (33%); vomiting (25%); loss of appetite (25%); discomfort in upper abdomen (25%); not able

to finish a normal-sized meal (17%); and pain in upper abdomen (17%).

All 12 participants reported that the GCSI daily diary was short and easy to complete. None of the participants had difficulty with the number of questions that were asked or the time it took to complete the questionnaire. All the participants reported understanding the instructions. One participant suggested making the phrase 'in the past 24 h' bold to help focus patients on that timeframe. None of the participants suggested re-phrasing the instructions or reported that any part of the instructions was confusing.

There was great symptom variability among all 12 of the participants and they reported that changes in symptom experience ranged from hourly, daily, to weekly or monthly. All participants reported that they were able to think about their symptoms in terms of the last 24 h. Five participants reported that the easiest timeframe to think back on was 24 h and four reported preferring weekly, while others varied from daily to monthly preferences. The majority of participants experienced some symptoms daily and thought that daily collection of symptom severity was needed to capture changes in symptom severity.

On the basis of cognitive debriefing of the GCSI-DD items, most, if not all of the participants, understood the item content and thought that the symptoms captured the key features of their gastroparesis experience. The Appendix S1 provides information about each item in the GCSI-DD and the saturation grid. The results of the cognitive debriefing interviews demonstrated that these gastroparesis patients understood the item content for the nausea (92%), retching (100%), vomiting (100%), stomach fullness (83%), not able to finish a full-sized meal (100%), feeling excessively full after meals (100%), loss of appetite (100%), bloating (100%), stomach or belly visibly larger (100%), upper abdominal pain (83%) and upper abdominal discomfort (92%). Although some similarity in item content was noted by the patients, none suggested eliminating any of the GCSI-DD items. For the most part, the severity response scale was understood and considered adequate by all the participants for each item, except for nausea and upper abdominal pain, which were understood and thought adequate in 10 of 12 participants each.

GCSI daily diary assessment. All of the patients (100%) completed the GCSI daily diary for at least

14 days; seven (58.3%) completed the diary through Day 15. The mean number of days between baseline and week 2 visits was 16.50 (± 2.20 , range 15–21) days.

Over the course of the study, only Item 2 (Retching) and Item 3 (Vomiting) had floor effects (i.e. lowest possible score) >80% indicating no symptom severity. No other items had floor effects >80%. No ceiling effects (i.e. highest possible score) were observed for any of the items suggesting that worsening symptom scores could be assessed. Response options for each item ranged from 0 to 4 or from 0 to 5 with higher scores indicating greater symptom severity. Although the entire range of response options were not used each day for each item, all response options were utilized for almost all items over the 14-day study period (data not shown).

Mean GCSI-DD subscale and total scores by day are summarized in Figures 1 and 2, respectively. Daily variability of symptoms was seen in half the patients, and for the other six patients, their symptoms were relatively stable over the two-week period (data not shown). Although these data are based on a small sample, the results suggest that the daily diary is capturing day-to-day variations in symptom experience. Patient daily rating of overall gastroparesis severity item over the course of the study is depicted in Figure 3.

Association of major clinical categories on symptoms. We also examined the pattern of daily symptoms between those with and without a gastric electrical stimulator (GES) and between diabetic and idiopathic gastropare-

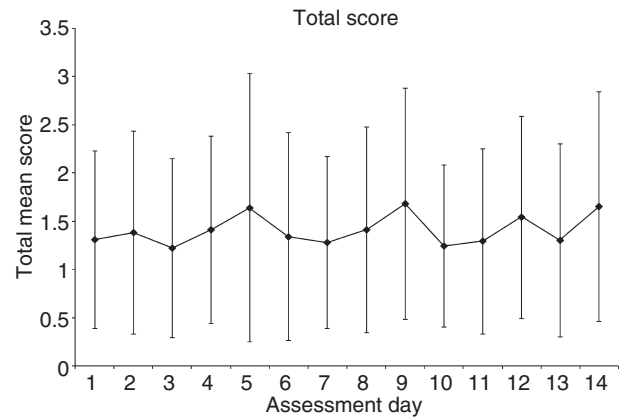


Figure 2. Mean (s.d.) GCSI-DD total scores over 14 days for patients with gastroparesis ($n = 12$).

sis patients (data not shown). The daily symptoms experience was comparable between those with and without a GES and for diabetic vs. idiopathic patients. The patients with a GES reported less nausea than the non-GES patients and diabetic patients reported less abdominal pain and discomfort than the idiopathic patients.

Relationship of mean GCSI-DD scores and overall patient severity rating. Mean GCSI, Pagi-SYM and OGS scores by the patients are summarized in Table 2. Subscale and the total score decreased slightly between the baseline and week 2 visit and showed that overall, patients reported mild to moderate symptoms.

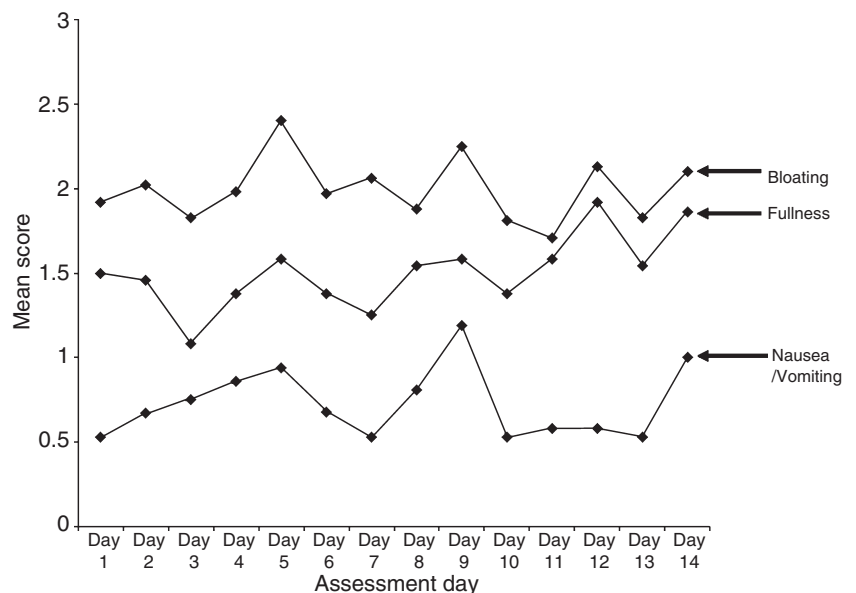


Figure 1. Mean GCSI-DD subscale scores over 14 days for patients with gastroparesis ($n = 12$).

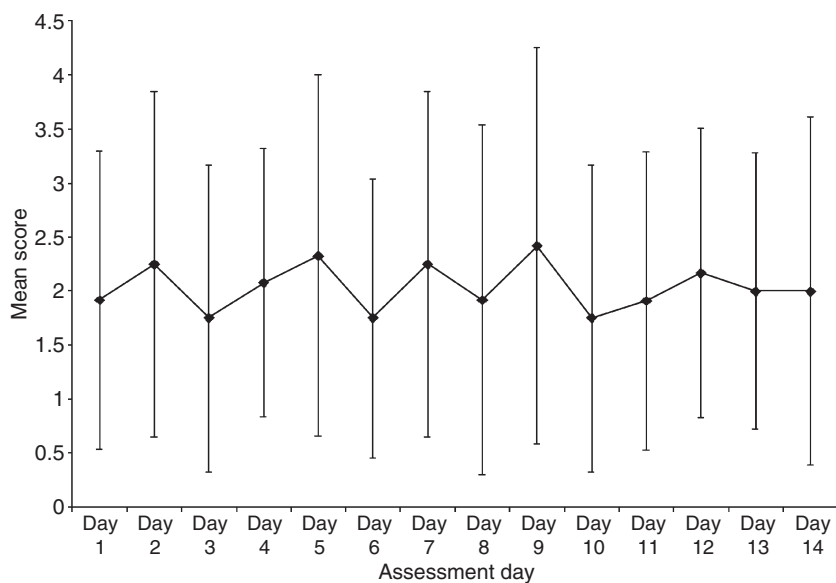


Figure 3. Mean (s.d.) overall gastroparesis symptom severity ratings over 14 days for patients with gastroparesis ($n = 12$).

Fullness/early satiety was the most severe symptom reported at baseline and the week 2 visit. Mean OGS-P baseline and week 2 visit scores were comparable.

Construct validity. Correlations between GCSI total and GCSI subscale scores and average GCSI-DD subscale and total GCSI-DD scores are summarized in Table 3. The GCSI total score at week 2 (based on a 2-week recall) was correlated 0.93 with the average GCSI-DD total scores for days one to 14. For the GCSI-DD subscale scores, most correlations were greater than 0.90 with their respective GCSI subscale score.

The correlation between the GCSI total score assessing patient recall over 2 weeks was only minimally greater if compared with average GCSI-DD over the 7 days rather than 14 days prior to the day of assess-

ing the GCSI. The correlation was 0.96 between the GCSI total score and the GCSI-DD total scores for the 7 days before the follow-up visit and the correlations for the GCSI-DD subscales (based on 7 days prior to the follow-up visit) and corresponding GCSI subscales were all greater than 0.90 (data not shown).

Spearman coefficient correlations between the OGS-P rated at the two-week visit and GCSI-DD scores were low to moderate for days one to 14 (see Table 3). The highest correlations were observed for the GCSI-DD Total and Bloating scores and OGS-P for all time points ($P < 0.01$). Diary-based upper abdominal pain scores were also correlated with OGS-P scores ($P < 0.05$). Comparable correlations were observed between the GCSI-DD scores averaged over the 7 days prior to the follow-up visit and OGS-P scores (data not shown).

Instrument/Subscale	Baseline mean (s.d.)	Week 2 mean (s.d.)
GCSI		
Fullness/early satiety	2.77 (1.27)	2.04 (1.29)
Nausea/vomiting	1.22 (1.37)	0.97 (1.01)
Bloating	2.29 (1.42)	1.75 (1.47)
Total score	2.09 (0.97)	1.59 (1.02)
PAGI-SYM		
Upper abdominal pain	2.83 (1.71)	1.83 (1.50)
Heartburn/regurgitation	1.40 (1.60)	1.30 (1.50)
Lower abdominal pain	2.08 (1.46)	1.29 (1.25)
Overall Gastroparesis	2.33 (1.4)	2.33 (1.30)
Severity-Physician assessment		
Overall Gastroparesis Severity-Clinician	2.00 (1.13)	N/A

Table 2. Descriptive characteristics of GCSI, PAGI-SYM and OGS scores at baseline and week 2

Table 3. Correlation between GCSI and PAGA-SYM subscale and total scores and average GCSI-DD subscale and total scores†

Visit 2 score	Mean GCSI-DD scores (Days 1–14)				
	Fullness/ Early satiety	Nausea/Vomiting	Bloating	Upper abdominal pain	Total score
GCSI total	0.68*	0.75**	0.76**	0.83***	0.93****
GCSI - Nausea/vomiting	0.59*	0.96****	0.51	0.66*	0.81**
GCSI - Fullness/early satiety	0.91****	0.58*	0.32	0.78**	0.71**
GCSI - Bloating	0.20	0.38	0.91****	0.45	0.71**
PAGA-SYM - Upper abdominal pain	0.73**	0.67*	0.70*	0.93****	0.92****
PAGA-SYM - Lower abdominal pain	0.47	0.35	0.66*	0.54	0.66*
PAGA-SYM - Heartburn/regurgitation	0.10	0.42	0.63*	0.23	0.47
Patient-rated overall gastroparesis severity (OGS-P)	0.34	0.57	0.75**	0.61*	0.76**

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, **** $P < 0.0001$. † Spearman rank-order correlations.

DISCUSSION

This cognitive debriefing study assessed symptoms of gastroparesis from patients with documented diabetic or idiopathic gastroparesis. The study examined the content validity of the GCSI-DD developed to capture daily symptoms of gastroparesis and evaluated whether diabetic and idiopathic gastroparesis patients understood the instructions, item content, and response scales in the daily diary. As a secondary objective, we explored the variation and construct validity of the GCSI-DD scores. The findings from the cognitive debriefing interviews supported the content validity of the GCSI-DD and confirmed that the instrument covered the most important and relevant symptoms of gastroparesis from the patients' perspective. The significant day-to-day variation is illustrated in Figures 2 and 3, and justifies the recommendation from regulatory agencies to acquire data with a daily diary.

The qualitative findings further support the original instrument development work completed for the GCSI.^{5, 6} In addition, on the basis of interviews, all of the patients fully understood the instructions, content of the items and the response scales. There were only a few instances where participants expressed concerns about the items or response scales in the GCSI-DD, again confirming the systematic development of the GCSI and PAGA-SYM instruments.^{5–8} The analysis of the 2 weeks of GCSI-DD data demonstrated that the instrument assessed variations in gastroparesis

symptoms and provided evidence supporting construct validity. The average GCSI-DD total and subscale scores were strongly correlated with two-week recall GCSI total and subscale scores.

The change to a 24-h recall period (from 2 weeks) for the GCSI-DD was well accepted and also suggested by the patients. Furthermore, the symptom variability described by patients, both severity and frequency, suggests that a longer recall period may fail to capture important and variable symptom change, potentially minimizing the detection of effects of new treatments. All participants thought that they would be capable of answering these questions on a daily basis without problem. Based on the analyses of 2 weeks of daily diary data, we observed no missing data despite the use of a paper diary form, which further supports ease of use for gastroparesis patients.

When the participants were asked to indicate their most important and troublesome symptom of gastroparesis, the symptoms most frequently mentioned were stomach fullness (42%), nausea (33%), vomiting (25%), and loss of appetite (25%). These reports reflect the varied symptom experience and variable nature of gastroparesis and are consistent with current clinical understanding of the disorder.^{1–3} For most patients, nausea, vomiting, postprandial fullness, and bloating were the main symptoms that led them to contact physicians. Of note, the most important and troublesome symptoms reported by these participants as well as the main symptoms that led them to contact physicians are all included in the GCSI-DD.

Despite the overlap in some symptoms, the majority of participants did not suggest removing any items from the GCSI-DD. In addition, participants generally expressed their satisfaction that the questionnaire captured their experience with gastroparesis symptoms. The suggestions participants made regarding additional symptoms were often symptoms related to comorbid conditions, such as gastro-oesophageal reflux disease or diabetes, and did not suggest that any additional items need to be added to the GCSI-DD. Two (17%) participants suggested adding the symptom belching. However, belching of food (digested or undigested) coming up into the mouth suddenly, without force and association with weight loss is more suggestive of the characteristic symptoms of rumination syndrome in adolescents and adults,²² and it would be erroneous to include this among the symptoms of gastroparesis. The GCSI-DD included two exploratory items on upper abdominal pain. However, only 33% of participants indicated that these symptoms were an important part of their gastroparesis symptom experience. Therefore, we have decided not to include these two items in computing the GCSI-DD total score. However, future research will examine upper abdominal pain and discomfort in gastroparesis patients.

With few exceptions, participants responded positively to the response options overall and could differentiate between the six-symptom severity response options. Based on these findings, no alterations to the response options are needed. Recommendations to change the response options were limited to only one or two participants, who made the same recommendations about simplifying the response options by, for example removing 'very mild' as a response option. All participants understood the instructions and content of the diary symptom items, and all participants thought that the response scales captured their symptom experience and were simple and straightforward to use. All participants thought that the diary items captured the essence of their symptom experience with gastroparesis. Both diabetic and nondiabetic gastroparesis participants reported comparable understanding and comprehension of the GCSI-DD, indicating that the set of symptom items was relevant across different gastroparesis etiologies.

Although based on the small sample size ($n = 12$), the analysis of the 2-week GCSI-DD data provided insight into the variation in symptoms in gastroparesis patients. Over the 2-week period, we observed that participants used the entire or nearly the entire

response scale range for all symptoms, except for nausea and retching, reflecting this variability. The average symptom experience overall was mild-to-moderate in severity indicating that the current medical treatment for these patients was largely successful.

We found evidence supporting the construct validity of the GCSI-DD subscale and total scores. The subscale scores were moderately correlated with the total score at baseline and at week 2. The GCSI-DD subscale scores, collected over the 2-week period, were strongly correlated with the week 2 subscale scores for the GCSI and PAGI-SYM (with 2-week recall). In addition, both the GCSI-DD total scores were significantly associated with patient overall ratings of gastroparesis severity and health care use. At week 2, patient ratings of overall severity of gastroparesis were moderately correlated with GCSI nausea/vomiting, bloating and total scores and upper abdominal pain/discomfort scores.

Mean GCSI-DD subscale and total scores (over 14 days) were correlated >0.90 with the relevant subscale scores collected at week 2 (based on 2-week recall). These findings suggest that the GCSI-DD scores are very comparable to GCSI scores with a two-week recall period. The evidence supporting construct validity of the GCSI-DD scores is encouraging and needs to be confirmed with additional psychometric analyses based on larger samples of gastroparesis patients. However, these findings and support the existing research on the reliability and validity of the original GCSI.^{5, 6}

The study involved patients followed up for gastroparesis in a tertiary centre, generally referred for refractory symptoms of gastroparesis. The patients were currently receiving active treatment for their symptoms which is reflected in their mild-to-moderate symptom severity. Many of the patients were undergoing treatment with gastric electric stimulation and some had undergone botulinum toxin injection of the pylorus, indicating that their symptoms, at least in the past, had been relatively severe. We found similar patterns of daily symptom experience between those patients with and without a gastric electric stimulator, although these with a gastric electric stimulator reported less nausea related symptoms. No differences in pattern of daily symptom experience were seen between diabetic and idiopathic patients.

Caution needs to be exercised in interpreting these findings as they are based on small samples recruited from a single centre. No information is available about the responsiveness of the GCSI-DD and further research is needed to evaluate sensitivity to change

and to develop interpretation guidelines. Further assessment of the GCSI-DD is warranted in patients with relatively severe symptoms and those from community gastroenterologist practices. This additional research will help confirm the generalizability of the current findings and the usefulness of the GCSI-DD for evaluating treatments for gastroparesis.

This study confirms the content validity and gastroparesis patients' understanding of the GCSI-DD. We found that diabetic and idiopathic gastroparesis patients had comparable perspectives on the gastroparesis symptom experience and all participants thought that the GCSI-DD captured the most important and relevant symptoms of gastroparesis. All patients understood the instrument instructions, item stems and response scales, further confirming the utility of the GCSI-DD (and original GCSI) as a useful patient-reported endpoint for clinical trials comparing different treatments for gastroparesis. The evidence of construct validity and strong association between GCSI-DD and GCSI (2-week recall) scores further supports the use of the GCSI-DD in clinical trials. Given the previous systematic development and psychometric characteristics of the GCSI and the current research, the GCSI-DD appears to be a useful outcome endpoint for gastroparesis clinical trials.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Detailed cognitive debriefing results

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