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[Continued on next page]

(54) Title: TOOL FOR ASSESSMENT OF SYMPTOMS OF IRRITABLE BOWEL SYNDROME

Fig. 2

IBS-D Symptom Event Log
The purpose of this Event Log is to collect some information about the symptoms of IBS-D you have experienced. After every bowel movement, please fill out the Date, Time and answer all of the following questions on this form.

Date (MM/DD/YYYY)	Time (HH:MM)	a.m. or p.m.	None at all	Slightly	Moderately	Quite a bit	Extremely	Which best describes what your bowel movement looked like					Did you feel like you completely emptied your bowels?						
								1	2	3	4	5	6	7	8	9	10	Yes	No
(Example) 01/15/2009	1:00							1	2	3	4	5	6	7	8	9	10		
								1	2	3	4	5	6	7	8	9	10		
								1	2	3	4	5	6	7	8	9	10		
								1	2	3	4	5	6	7	8	9	10		
								1	2	3	4	5	6	7	8	9	10		
								1	2	3	4	5	6	7	8	9	10		
								1	2	3	4	5	6	7	8	9	10		
								1	2	3	4	5	6	7	8	9	10		
								1	2	3	4	5	6	7	8	9	10		
								1	2	3	4	5	6	7	8	9	10		
								1	2	3	4	5	6	7	8	9	10		
								1	2	3	4	5	6	7	8	9	10		

(57) Abstract: Methods of treating and/or diagnosing irritable bowel syndrome (IBS) are provided, wherein treatment or diagnosis is undertaken on the basis of the patient's recordation of events associated with IBS in an event log and/or symptom diary.

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TOOL FOR ASSESSMENT OF SYMPTOMS OF IRRITABLE BOWEL SYNDROME

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This patent application claims the benefit of U.S. Provisional Patent Application No. 61/170,059, filed April 16, 2009, and U.S. Provisional Patent Application No. 61/319,656, filed March 31, 2010, each of which is incorporated herein by reference.

BACKGROUND OF THE INVENTION

[0002] About 10% to about 20% of adults and adolescents worldwide suffer from irritable bowel syndrome (IBS). IBS exacts a disproportionate share of the US health care dollar. In US managed-care populations, for example, total direct costs incurred by subjects suffering from IBS have been measured to amount to about 50% higher than those not suffering from IBS. The negative impact of IBS on patients, their families, and their friends can be great, especially in moderate to severe IBS-D, which accounts for extremely high utilization of health care resources and impairment of quality-of-life.

[0003] According to the Rome III criteria, IBS is diagnosed with recurrent abdominal pain or discomfort at least three days per month in the last three months associated with two or more of the following: (1) improvement with defecation, (2) onset associated with a change in frequency of stool, and/or (3) onset associated with a change in form (appearance) of stool. It is also noted that these symptoms typically have had symptom onset at least six months prior to diagnosis. In addition, according to the Rome III criteria, diarrhea-predominant irritable bowel syndrome (IBS-D) is defined as loose mushy stool at least 25% of bowel movements and hard or lumpy stool in less than 25% of bowel movements. However, there currently is no well-validated symptom severity scales for IBS-D.

[0004] Multidisciplinary approaches (including diet changes, over-the-counter (OTC) products, and prescription medications) for treating IBS patients are frequent, and such drugs and remedies are often prescribed by family practitioners. Current treatment is mostly based on pharmacological therapy and is palliative in nature. Only one prescription medication – Alosetron, a selective 5-HT₃ antagonist – has been approved by the US Food and Drug Administration (FDA) for IBS-D, and it is only available under a restricted access program due to risks of severe side effects if taken by patients who suffer from any other form of IBS (e.g., constipation-predominant irritable bowel syndrome (IBS-C) and mixed IBS).

[0005] An instrument (tool) developed and validated for the IBS patient population, ideally to assess symptom severity, would represent an advancement in the treatment of IBS.

BRIEF SUMMARY OF THE INVENTION

[0006] The invention provides a tool for assessment of symptoms of irritable bowel syndrome in a human patient. The tool comprises a diary and/or event log, suitable for psychometric testing of symptoms of IBS. The symptom diary and event log can be used singly or in combination. The symptom diary and/or event log can be used to assess the progress of treatment of IBS in a patient.

[0007] In one aspect, the invention provides a method for diagnosing IBS comprising (a) providing a patient with an event log, wherein the patient is instructed to record in the event log the date and time of each bowel movement together with a description thereof; and/or (b) providing the patient with a symptom diary, wherein the patient is instructed to complete the symptom diary by selecting a characterization from a series of pre-determined characterizations regarding the patient's subjective experience of events associated with IBS; (c) reviewing the event log and/or symptom diary completed by the patient; and (d) determining whether a diagnosis of irritable bowel syndrome is appropriate.

[0008] In another aspect, the invention provides a method for treating IBS comprising (a) administering to a patient having IBS an IBS treatment at a dosage and frequency; (b) providing the patient with an event log, wherein the patient is instructed to record in the event log the date and time of each bowel movement together with a description thereof; and/or (c) providing the patient with a symptom diary, wherein the patient is instructed to complete the symptom diary by selecting a characterization from a series of pre-determined characterizations regarding the patient's subjective experience of events associated with IBS; (d) reviewing the event log and/or symptom diary completed by the patient to assess changes in symptoms; (e) revising the dosage and frequency of the IBS treatment, or, optionally, administering a different IBS treatment; and (f) repeating steps (a)-(e) until the patient achieves a clinically satisfactory improvement in IBS symptoms.

[0009] In another aspect, the invention provides calculating an index value based on the patient's score in each category of the symptom diary and/or event log, wherein the index value indicates the relative severity of a patient's IBS symptoms as compared to a healthy individual.

[0010] The IBS can be any type of IBS, such as IBS-D. Also, the tool can be used in conjunction with therapy for IBS (e.g., dietary changes, medication, or both), i.e., in which the patient is undergoing treatment for IBS. In this sense, the event log, symptom diary, or both, can provide meaningful cognitive feedback concerning the severity of the IBS symptoms in response to therapy. In a preferred embodiment, the patient is undergoing treatment with a prescription medication approved for treating IBS or under investigation for such indication.

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S)

[0011] Figure 1A depicts page 1 of an exemplary 10-question symptom diary to be provided to a patient.

[0012] Figure 1B depicts page 2 of an exemplary 10-question symptom diary to be provided to a patient.

[0013] Figure 2 depicts an exemplary event log to be provided to a patient.

[0014] Figure 3A depicts page 1 of an exemplary 15-question symptom diary to be provided to a patient.

[0015] Figure 3B depicts page 2 of an exemplary 15-question symptom diary to be provided to a patient.

[0016] Figure 3C depicts page 3 of an exemplary 15-question symptom diary to be provided to a patient.

[0017] Figure 4 depicts an exemplary event log to be provided to a patient.

[0018] Figure 5A depicts page 1 of an exemplary 17-question symptom diary to be provided to a patient.

[0019] Figure 5B depicts page 2 of an exemplary 17-question symptom diary to be provided to a patient.

[0020] Figure 5C depicts page 3 of an exemplary 17-question symptom diary to be provided to a patient.

[0021] Figure 6 depicts an exemplary event log to be provided to a patient.

DETAILED DESCRIPTION OF THE INVENTION

[0022] The invention provides methods of using the symptom diary and/or event log, such as provided in Figure 1 and Figure 2, respectively, in treating or diagnosing IBS, or in assessing a patient's symptoms or response to IBS treatment.

[0023] In one aspect, the invention provides a method for diagnosing IBS comprising (a) providing a patient with an event log, wherein the patient is instructed to record in the event log the date and time of each bowel movement together with a description thereof; and/or (b) providing the patient with a symptom diary, wherein the patient is instructed to complete the symptom diary by selecting a characterization from a series of pre-determined characterizations regarding the patient's subjective experience of events associated with IBS; (c) reviewing the event log and/or symptom diary completed by the patient; and (d) determining whether a diagnosis of irritable bowel syndrome is appropriate. In preferred embodiments, the patient is provided with both an event log and a symptom diary. However, in some embodiments, the patient can be provided with an event log and not a symptom diary, or a symptom diary and not an event log.

[0024] In another aspect, the invention provides a method for treating IBS comprising (a) administering to a patient having IBS an IBS treatment at a dosage and frequency; (b) providing the patient with an event log, wherein the patient is instructed to record in the event log the date and time of each bowel movement together with a description thereof; and/or (c) providing the patient with a symptom diary, wherein the patient is instructed to complete the symptom diary by selecting a characterization from a series of pre-determined characterizations regarding the patient's subjective experience of events associated with IBS; (d) reviewing the event log and/or symptom diary completed by the patient; (e) revising the dosage and frequency of the IBS treatment, or, optionally, administering a different IBS treatment; and (f) repeating steps (a)-(e) until the patient achieves a clinically satisfactory improvement in IBS symptoms. In preferred embodiments, the patient is provided with both an event log and a symptom diary. However, in some embodiments, the patient can be provided with an event log and not a symptom diary, or a symptom diary and not an event log.

[0025] In embodiments in which the patient is provided with an event log, the patient can be instructed to record bowel movements over a specified time period. For example, the patient can be instructed to record bowel movements over one, two, three, or four weeks. Alternatively, the patient can be instructed to record bowel movements over one or multiple months. In some embodiments, such as when the patient is undergoing investigational drug therapy, it may be preferred that the patient records bowel movements for the full duration of the investigational drug therapy.

[0026] The event log can have any form useful to the clinician. However, in preferred embodiments, the event log includes one or more of the questions provided in Table 4 of Example 1, along with pre-determined characterizations from which the patient can select. In a more preferred embodiment, the event log includes each question provided in Table 4. In a most preferred embodiment, the event log comprises the form of Figure 2.

[0027] In embodiments in which the patient is provided with a symptom diary, the patient can be instructed to select a characterization from a series of pre-determined characterizations regarding the patient's subjective experience of events associated with IBS. The patient can be instructed to complete the symptom diary using characterizations of the patient's experience of events associated with IBS on a single day. Alternatively, the patient can be instructed to complete multiple symptom diaries over a specified time period, wherein each symptom diary is completed using characterizations of the patient's experience of events associated with IBS on a different day. For example, the patient can be instructed to complete symptom diaries each day for one, two, three, or four weeks. Alternatively, the patient can be instructed to complete daily symptom diaries over one or multiple months. In some embodiments, such as when the patient is undergoing investigational drug therapy, it may be preferred that the patient completes daily symptom diaries for the full duration of the investigational drug therapy.

[0028] The symptom diary can have any form useful to the clinician. However, in preferred embodiments, the symptom diary includes one or more of the questions provided in Table 3 of Example 1, along with pre-determined characterizations from which the patient can select. In preferred embodiments, the symptom diary comprises each question provided in Table 3. In a most preferred embodiment, the symptom diary comprises the form provided in Figure 1 (1A and 1B).

[0029] It will be understood that the event log and symptom diary are intended to record a patient's experience. Therefore, any suitable format providing any number of pre-determined characterizations can be provided for the patient's answers. In some embodiments, it will be useful to provide pre-determined characterizations for the symptom diary and event log as shown in Tables 3 and 4, respectively. However, in general, the pre-determined characterizations can be based on a 5-point scale (Likert scale), an 11-point scale (0-10), or a positive/negative scale (yes/no). In responding to questions regarding the appearance of the bowel movement, the event log desirably provides visual and/or text

characterizations based on the Adapted Bristol Stool Form Scale, which, for IBS-D, can be modified to include forms relevant to IBS-D (e.g., excluding very hard stool forms).

[0030] In some embodiments, the patient is undergoing a treatment for IBS. The treatment can be any IBS treatment, such as a pharmaceutical or biologic treatment, or a dietary therapy, or other therapy. In some embodiments, the therapy is a prescription medication approved or under investigational use for treatment of IBS.

[0031] In another aspect, the invention provides calculating an index value based on the patient's score in each category of the symptom diary and event log, wherein the index value indicates the relative severity of a patient's IBS symptoms as compared to a healthy individual or to a previous baseline. The index value can also be used to determine whether a patient has achieved clinically satisfactory improvement in IBS symptoms. The index value can be calculated by any method known to one of skill in the art and/or deemed to be useful in applying the methods of the present invention. However, it is not necessary to calculate a single index value in order to determine whether a patient has achieved improvement in IBS symptoms. If the patient shows improvement based on the total score of six or more items of the symptom diary, in general, such improvement will be considered clinically satisfactory improvement in IBS symptoms.

[0032] Additionally, the symptom diary and event log can be used to assess primary and secondary endpoints for diagnosing patients as having IBS or for evaluating the progress of treatment of IBS patients. For IBS-D, diarrhea (stool frequency and stool consistency) and pain are the most frequent and most bothersome symptoms of IBS-D, and these can serve as co-primary endpoints. For example, a patient reporting a weekly average abdominal pain severity over a 24 hour period of a threshold value (e.g., 3 or higher, 4 or higher, 5 or higher, etc. on a 0-10 point scale) and a weekly average stool consistency of a threshold value (for example, 4 or above according to the scale presented in Figure 2) could on that basis be diagnosed as having IBS-D. To assess a patient's response to therapy for IBS-D, a patient can be considered responding if, for example, the patient experiences a threshold decrease (such as, for example, 25% or greater, 30% or greater, 35% or greater) in the weekly average of abdominal pain severity over a 24 hour period. Successful response to IBS-D treatment also can be indicated by a patient who experiences a decreased weekly average stool consistency relative to a baseline measurement, or a weekly average stool consistency below a threshold value (for example, 3 or below according to the scale presented in Figure 2). Preferably, improvement in both abdominal pain severity and stool consistency are

considered. Further, for IBS-D, immediate need to have a bowel movement, bloating, pressure, gas, incomplete evacuation, and rectal symptoms can serve as secondary endpoints, and improvement in these categories can also be employed to assess an IBS-D patient's response to treatment.

[0033] The following examples further illustrate the invention but, of course, should not be construed as in any way limiting its scope.

EXAMPLE 1

[0034] This example demonstrates a method for developing a tool for assessment of symptoms of Irritable Bowel Disease.

[0035] Two sets of concept elicitation focus groups were conducted, with patients in each set meeting the ROME III inclusion and exclusion criteria for IBS-D. In the first (Set 1), 34 patients were interviewed in 8 concept elicitation focus groups having 2-9 subjects per group. In the second (Set 2), 32 patients under 70 years of age were interviewed in four gender-specific concept elicitation focus groups (n=3 female, n=1 male). Demographic and health information for each patient was recorded and is presented in Table 1.

Table 1- Summary of Socio-Demographic and Health Information

Criteria	Set 1	Set 2	Overall
Number	34	32	64
Female (%)	22 (64.71)	24 (75.00)	46 (71.88)
Age Mean $\pm$ SD (Range)	44.65 $\pm$ 15.5 (23, 69)	45 $\pm$ 10.84 (21, 68)	45.02 $\pm$ 13.35 (21, 69)
Ethnicity (%)			
Asian	3 (8.82%)	N/A	3 (4.69%)
Black/African American	4 (11.76%)	4 (12.50%)	8 (12.50%)
Hispanic/Latino (of any race)	1 (2.94%)	1 (3.13%)	2 (3.13%)
White/Caucasian	26 (76.47%)	26 (81.25%)	52 (81.25%)
Multiracial	N/A	1 (3.13%)	1 (1.56%)
Level of education (%)			
High school diploma or GED	5 (14.71%)	6 (18.75%)	11 (17.19%)
Some college	6 (17.65%)	13 (40.63%)	19 (29.69%)
Vocational school or certificate program	2 (5.88%)	5 (15.63%)	7 (10.94%)
College or university degree (2- or 4- year)	16 (47.06%)	6 (18.75%)	22 (34.38%)
Graduate degree	5 (14.71%)	2 (6.25%)	7 (10.94%)
Work status (%)			
Working full-time	15 (44.12)	NE	NE
Working part-time	7 (20.59)	NE	NE
Homemaker	3 (8.82)	NE	NE
Student	2 (5.88)	NE	NE
Retired	8 (23.53)	NE	NE
Unemployed	1 (2.94)	NE	NE
Health in general/health status (%)			
Excellent	4 (11.76%)	N/A	4 (6.25%)

Very good	9 (26.47%)	6 (18.75%)	15 (23.44%)
Good	14 (41.18%)	20 (62.50%)	34 (53.13%)
Fair	5 (14.71%)	6 (18.75%)	11 (17.19%)
Poor	2 (5.88%)	N/A	2 (3.13%)
Severity of IBS-D (%)			
Very mild	4 (11.76%)	1 (3.13%)	5 (7.81%)
Mild	8 (23.53%)	4 (12.50%)	12 (18.75%)
Moderate	19 (55.88%)	18 (56.25%)	37 (57.81%)
Severe	3 (8.82%)	8 (25.00%)	11 (17.19%)
Very severe (%)	0	1 (3.13%)	1 (1.56%)

GED: General Educational Development; IBS-D: diarrhea-predominant irritable bowel syndrome ; N/A: not applicable; NE: not evaluated

[0036] Grounded theory data collection and analysis methods were used, including constant comparison of quotations by participants, to determine whether concepts were simple or complex; to determine the grouping of sub-concepts; to determine concepts and domains; to determine the recall period; to determine the response options (e.g., a severity or frequency item); to determine whether the items emphasizing patients' exact words were appropriate; and to develop the conceptual framework.

[0037] In Set 1, thirty-six different concepts were elicited, with 29 concepts saturated. Responses from Set 2 were compared with those of Set 1, and determined to be similar. Ethnicity and other demographic data did not impact the reporting of the symptoms by the patients. In particular, educational level did not impact how the symptoms were reported by patients. For example, all patients tend to describe the occurrence of diarrhea (in relation to eating), and description of diarrhea ("the runs") similarly, as illustrated in Table 2.

Table 2

Level of Education	Sample Quotes
High school diploma or GED	...overeating. Sometimes like a holiday – Thanksgiving...I'll get the diarrhea, got to empty my system. ...I got the runs...
Vocational school or certificate program	...maybe the food that I was eating...the runs. ...I get the runs...
At least some college, college degree or higher	...as soon as you eat something...immediately have to go to the restroom...like every time I eat something. - Just got the runs...had the runs when I drank coffee.

[0038] Concepts elicited that were mentioned spontaneously and that were saturated were included in a draft symptom diary (Figure 5) and a draft event log (Figure 6). However,

some concepts that met these criteria were excluded due to reasons such as a lack of clinical relevance or specificity to IBS-D, such as vomiting, nausea, heartburn, and sweating. More specifically, concepts included in the draft symptom diary and draft event log were limited to lower GI symptoms in accordance with the ROME III Criteria and clinical diagnosis of IBS-D.

[0039] The concepts that were retained for use in the draft symptom diary and event log were: Diarrhea, immediate need (urgency), bloating/pressure, frequency of bowel movement, cramps, abdominal/stomach pain, gas, complete emptying of bowels/incomplete evacuation, accident, bubbling in intestines/bowel sounds, rectal burning, stool consistency, rectal spasm, and pain while wiping.

[0040] The draft symptom diary was developed to capture IBS-D symptoms over a given day while the draft event log was developed to report information regarding individual bowel movements.

[0041] Eleven cognitive interviews were conducted to determine the comprehensiveness, understanding, appropriateness, and readability of the draft symptom diary and draft event log. Patients were asked to complete the 17-item draft symptom diary (Figure 5) and draft event log (Figure 6), and to provide their feedback using the “think aloud” method. Patients were asked to identify words, terms, or concepts that they did not understand or interpreted differently than had been intended. They were also asked if revisions should be made to the 17-item draft symptom diary or event log to make them more appropriate, comprehensive, or interpretable. After the cognitive interviews, two questions based on concepts listed above were deleted from the 17-item draft symptom diary: “In the past 24 hours, how would you rate your immediate need to use the bathroom to have a bowel movement?” and “In the past 24 hours, how often did you feel full before finishing a normal size meal?”

[0042] Five additional questions were deleted from the resulting 15-item symptom diary (Figure 3) in order to avoid redundancy and optimize clarity. The remaining 10 questions of the symptom diary are presented in Table 3. A complete version of the symptom diary is presented in Figure 1.

Table 3 – Symptom Diary

Question	Provided responses
1. In the past 24 hours, on a scale of 0 to 10, how would you rate the severity of your stomach pain?	A range of 0-10, with 0 characterized as “No stomach pain” and 10 characterized as “Worst stomach pain.”
2. In the past 24 hours, on a scale of 0 to 10, how would you rate the severity of the pressure you felt in your abdomen?	A range of 0-10, with 0 characterized as “No abdominal pressure” and 10 characterized as “Worst abdominal pressure.”
3. In the past 24 hours, on a scale of 0 to 10, how bloated did you feel?	A range of 0-10, with 0 characterized as “Not bloated” and 10 characterized as “Extremely bloated.”
4. In the past 24 hours, on a scale of 0 to 10, how would you rate the severity of your abdominal cramps?	A range of 0-10, with 0 characterized as “No abdominal cramps” and 10 characterized as “Worst abdominal cramps.”
5. In the past 24 hours, on a scale of 0 to 10, how would you rate the severity of your rectal spasms?	A range of 0-10, with 0 characterized as “No rectal spasms” and 10 characterized as “Worst rectal spasms.”
6. In the past 24 hours, on a scale of 0 to 10, how would you rate the severity of the burning sensation you experienced after a bowel movement?	A range of 0-10, with 0 characterized as “No burning sensation” and 10 characterized as “Worst burning sensation.”
7. In the past 24 hours, on a scale of 0 to 10, how would you rate the severity of your abdominal pain?	A range of 0-10, with 0 characterized as “No abdominal pain” and 10 characterized as “Worst abdominal pain.”
8. In the past 24 hours, how often did you have gas?	A 5-point Likert scale: (1) None of the time; (2) A little of the time; (3) Some of the time; (4) Most of the time; (5) All of the time.
9. In the past 24 hours, how often were you able to hear sounds coming from your abdomen that signaled that you might have diarrhea?	A 5-point Likert scale: (1) None of the time; (2) A little of the time; (3) Some of the time; (4) Most of the time; (5) All of the time.
10. In the past 24 hours did you have any accidents (lose control of your bowels)?	Yes or No.

[0043] The draft event log (Figure 4) was also modified after additional analysis, although it continued to require patients to note the date and time of each episode, along with the consistency thereof. For example, a question explicitly asking patients to rate the severity of their diarrhea was deleted on the basis that such conclusion is best drawn from the number and type of diarrhea events. Additionally, a new question was added having a positive/negative response: “Did you feel like you completely emptied your bowels?”

[0044] The resulting event log is shown in Figure 2. The questions provided therein are provided in Table 4.

Table 4 – Event Log

Question	Provided responses
Which best describes what your bowel movement looked like?	6 pictures according to the Adapted Bristol Stool Form Scale.
Did you feel like you completely emptied your bowels?	Yes or No
How immediate was your need to have a bowel movement?	A 5-point Likert scale: (1) Not at all; (2) Slightly; (3) Moderately; (4) Quite a bit; (5) Extremely.

[0045] The final event log and symptom diary (Figures 1 and 2) reflect a highly descriptive yet compact tool for assessing a patient's symptoms of IBS-D.

EXAMPLE 2

[0046] This example demonstrates the use of the event diary and symptom log to diagnose IBS-D in a patient.

[0047] A patient suspected of having IBS-D is provided by a clinician with an event log as shown in Figure 2. The patient is instructed to record all bowel movements over a set period, e.g., one week or two weeks, as well as to answer the questions provided regarding urgency, emptying of the bowel, and type of bowel movement according to the Adapted Bristol Stool Form Scale.

[0048] The clinician also provides the patient with a symptom diary as shown in Figure 1. The patient is instructed to complete a copy of the symptom diary each day for a set period, e.g., one week or two weeks.

[0049] Once the patient completes the event log and symptom diaries for the prescribed period, the clinician reviews them. If the patient shows a pattern of response consistent with IBS-D, the patient can be diagnosed with IBS-D.

[0050] Accordingly, the event diary and symptom log can be used to diagnose IBS-D in a patient.

EXAMPLE 3

[0051] This example demonstrates the use of the event diary and symptom log in treating IBS-D in a patient.

[0052] A patient undergoing a treatment for IBS-D is provided by a clinician with an event log as shown in Figure 2. The patient is instructed to record all bowel movements over a set period, e.g., one week or two weeks, as well as to answer the questions provided regarding urgency, emptying of the bowel, and type of bowel movement according to the Adapted Bristol Stool Form Scale.

[0053] The clinician also provides the patient with a symptom diary as shown in Figure 1. The patient is instructed to complete a copy of the symptom diary each day for a set period, e.g., one week or two weeks.

[0054] Once the patient completes the event log and symptom diaries for the prescribed period, the clinician reviews them. If the patient shows improvement based on category score or the total score of six or more items of the symptom diary, then the clinician deems the patient to have improved in IBS symptoms. Alternatively, improvement in the patient's response to two primary endpoints (abdominal pain severity and stool consistency) is considered a favorable response to the IBS-D therapy.

[0055] If the patient does not show adequate improvement in IBS symptoms, the clinician revises the dosage and frequency of the IBS treatment, or, optionally, administers a different IBS treatment.

[0056] The process of recording IBS events and symptoms in the symptom diary and event log, and evaluating such responses may be repeated until the patient achieves a clinically satisfactory improvement in IBS symptoms.

[0057] Accordingly, the event diary and symptom log can be used to evaluate a IBS-D patient's condition and modify treatment accordingly.

[0058] All references, including publications, patent applications, and patents, cited herein are hereby incorporated by reference to the same extent as if each reference were individually and specifically indicated to be incorporated by reference and were set forth in its entirety herein.

[0059] The use of the terms "a" and "an" and "the" and similar referents in the context of describing the invention (especially in the context of the following claims) are to be construed to cover both the singular and the plural, unless otherwise indicated herein or clearly contradicted by context. The terms "comprising," "having," "including," and "containing" are to be construed as open-ended terms (i.e., meaning "including, but not limited to,") unless otherwise noted. Recitation of ranges of values herein are merely intended to serve as a shorthand method of referring individually to each separate value

falling within the range, unless otherwise indicated herein, and each separate value is incorporated into the specification as if it were individually recited herein. All methods described herein can be performed in any suitable order unless otherwise indicated herein or otherwise clearly contradicted by context. The use of any and all examples, or exemplary language (e.g., “such as”) provided herein, is intended merely to better illuminate the invention and does not pose a limitation on the scope of the invention unless otherwise claimed. No language in the specification should be construed as indicating any non-claimed element as essential to the practice of the invention.

[0060] Preferred embodiments of this invention are described herein, including the best mode known to the inventors for carrying out the invention. Variations of those preferred embodiments may become apparent to those of ordinary skill in the art upon reading the foregoing description. The inventors expect skilled artisans to employ such variations as appropriate, and the inventors intend for the invention to be practiced otherwise than as specifically described herein. Accordingly, this invention includes all modifications and equivalents of the subject matter recited in the claims appended hereto as permitted by applicable law. Moreover, any combination of the above-described elements in all possible variations thereof is encompassed by the invention unless otherwise indicated herein or otherwise clearly contradicted by context.

CLAIM(S):

1. A method of diagnosing irritable bowel syndrome (IBS) comprising:
 - (a) providing a patient with an event log, wherein the patient is instructed to record in the event log the date and time of each bowel movement together with a description thereof;
 - (b) reviewing the event log completed by the patient; and
 - (c) determining whether a diagnosis of irritable bowel syndrome is appropriate.
2. A method of diagnosing irritable bowel syndrome (IBS) comprising:
 - (a) providing the patient with a symptom diary, wherein the patient is instructed to complete the symptom diary by selecting a characterization from a series of pre-determined characterizations regarding the patient's subjective experience of events associated with IBS;
 - (b) reviewing the symptom diary completed by the patient; and
 - (c) determining whether a diagnosis of irritable bowel syndrome is appropriate.
3. A method of diagnosing irritable bowel syndrome (IBS) comprising:
 - (a) providing a patient with an event log, wherein the patient is instructed to record in the event log the date and time of each bowel movement together with a description thereof;
 - (b) providing the patient with a symptom diary, wherein the patient is instructed to complete the symptom diary by selecting a characterization from a series of pre-determined characterizations regarding the patient's subjective experience of events associated with IBS;
 - (c) reviewing the event log and symptom diary completed by the patient; and
 - (d) determining whether a diagnosis of irritable bowel syndrome is appropriate.
4. A method of treating irritable bowel syndrome (IBS) comprising:
 - (a) administering to a patient having IBS an IBS treatment at a dosage and frequency;

- (b) providing the patient with an event log, wherein the patient is instructed to record in the event log the date and time of each bowel movement together with a description thereof;
- (c) reviewing the event log completed by the patient;
- (d) revising the dosage and frequency of the IBS treatment, or, optionally, administering a different IBS treatment; and
- (e) repeating steps (a)-(d) until the patient achieves a clinically satisfactory improvement in IBS symptoms.

5. A method of treating irritable bowel syndrome (IBS) comprising:

- (a) administering to a patient having IBS an IBS treatment at a dosage and frequency;
- (b) providing the patient with a symptom diary, wherein the patient is instructed to complete the symptom diary by selecting a characterization from a series of pre-determined characterizations regarding the patient's subjective experience of events associated with IBS;
- (c) reviewing the symptom diary completed by the patient;
- (d) revising the dosage and frequency of the IBS treatment, or, optionally, administering a different IBS treatment; and
- (e) repeating steps (a)-(d) until the patient achieves a clinically satisfactory improvement in IBS symptoms.

6. A method of treating irritable bowel syndrome (IBS) comprising:

- (a) administering to a patient having IBS an IBS treatment at a dosage and frequency;
- (b) providing the patient with an event log, wherein the patient is instructed to record in the event log the date and time of each bowel movement together with a description thereof;
- (c) providing the patient with a symptom diary, wherein the patient is instructed to complete the symptom diary by selecting a characterization from a series of pre-determined characterizations regarding the patient's subjective experience of events associated with IBS;
- (d) reviewing the event log and symptom diary completed by the patient;

(e) revising the dosage and frequency of the IBS treatment, or, optionally, administering a different IBS treatment; and

(f) repeating steps (a)-(e) until the patient achieves a clinically satisfactory improvement in IBS symptoms.

7. The method of any of claims 1-6, wherein the pre-determined characterizations are selected from the group consisting of a 5-point scale (Likert scale), an 11-point scale (0-10), and a positive/negative scale (yes/no).

8. The method of claim 1, 3, 4, or 6, wherein the patient is instructed to record bowel movements of one or more weeks in the event log.

9. The method of claim 1, 3, 4, or 6, wherein the patient is instructed to record bowel movements of one or more months in the event log.

10. The method of 1, 3, 4, or 6, wherein the event log further comprises one or more of the following questions:

- (a) "How immediate was your need?";
- (b) "Did you feel like you completely emptied your bowels?";
- (c) "Which best describes what your bowel movement looked like?";

wherein the event log further comprises pre-determined characterizations from which the patient can choose in answering each question.

11. The method of claim 10, wherein 5 different pre-determined characterizations are provided for question (a).

12. The method of claim 10, wherein the pre-determined characterizations for question (b) are positive and negative, or yes and no.

13. The method of claim 10, wherein the pre-determined characterizations for question (c) are based on the Adapted Bristol Stool Form Scale.

14. The method of claim 10, wherein the event log comprises each of questions (a)-(c).

15. The method of claim 2, 3, 5, or 6, wherein the patient is instructed to complete the symptom diary using characterizations of the patient's experience of events associated with IBS on a single day.

16. The method of claim 2, 3, 5, or 6, wherein the patient is instructed to complete multiple symptom diaries, wherein each symptom diary is completed using characterizations of the patient's experience of events associated with IBS on a different day.

17. The method of claim 2, 3, 5, or 6, wherein the symptom diary comprises one or more of the following questions:

- (a) "In the past 24 hours, how would you rate the severity of your stomach pain?";
- (b) "In the past 24 hours, how would you rate the severity of the pressure you felt in your abdomen?";
- (c) "In the past 24 hours, how bloated did you feel?";
- (d) "In the past 24 hours, how would you rate the severity of your abdominal cramps?";
- (e) "In the past 24 hours, how would you rate the severity of your rectal spasms?";
- (f) "In the past 24 hours, how would you rate the severity of the burning sensation you experienced after a bowel movement?";
- (g) "In the past 24 hours, how would you rate the severity of your abdominal pain?";
- (h) "In the past 24 hours, how often did you have gas?";
- (i) "In the past 24 hours, how often were you able to hear sounds coming from your abdomen that signaled that you might have diarrhea?"; and
- (j) "In the past 24 hours, did you have any accidents (lose control of your bowels)?".

18. The method of claim 17, wherein at least 5 different pre-determined characterizations are provided for each of questions (a)-(i).

19. The method of claim 17, wherein 11 different pre-determined characterizations are provided for each of questions (a)-(g).

20. The method of claim 17, wherein the event log comprises each of questions (a)-(j).
21. The method of claim 20, wherein 11 different pre-determined characterizations are provided for each of questions (a)-(g); 5 different pre-determined characterizations are provided for each of questions (h)-(i); and a positive/negative selection is provided for question (j).
22. The method of any of claims 4-6, wherein the treatment comprises a prescription medication approved or under investigational use for treatment of IBS.
23. The method of any of claims 1-6, further comprising calculating an index value based on the patient's score in each category of the symptom diary and event log.
24. The method of claim 23, wherein the index value indicates the relative severity of a patient's IBS symptoms as compared to a healthy individual.
25. A method of assessing the symptoms of irritable bowel syndrome (IBS) in a patient comprising providing a human patient suffering from IBS with an event log to record the date and time of events associated with IBS together with a description of the event.
26. The method of claim 25, wherein the event log comprises substantially the form identified in Figure 2.
27. A method of assessing the symptoms of IBS in a patient comprising providing a human patient suffering from IBS with symptom diary to select a characterization from a series of pre-determined characterizations regarding the patient's subjective experience of events associated with IBS;
28. The method of claim 27, wherein the symptom diary comprises substantially the form identified in Figure 1.
29. The method of any of claims 25-28, wherein the patient is undergoing therapy for treatment of IBS.
30. The method of any preceding claim, wherein the IBS is IBS-D.

Fig. 1B

6. In the past 24 hours, on a scale of 0-10, how would you rate the severity of the burning sensation you experienced after a bowel movement?										
0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
No burning sensation										Worst burning sensation

7. In the past 24 hours, on a scale of 0-10, how would you rate the severity of your abdominal pain?										
0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
No abdominal pain										Worst abdominal pain

8. In the past 24 hours, how often how often did you have gas?				
1	2	3	4	5
☐	☐	☐	☐	☐
None of the time		A little of the time		All of the time

9. In the past 24 hours, how often were you able to hear sounds coming from your abdomen that signaled you that you might have diarrhea?				
1	2	3	4	5
☐	☐	☐	☐	☐
None of the time		Some of the time		All of the time

10. In the past 24 hours, did you have any accidents (lose control of your bowels)?

Yes	No
☐	☐

Fig. 2

IBS-D Symptom Event Log

The purpose of this Event Log is to collect some information about the symptoms of IBS-D you have experienced. **After every bowel movement, please fill out the Date, Time and answer all of the following questions on that row.**

[illegible]

Fig. 3A

IBS-D DAILY SYMPTOM DIARY

The purpose of this diary is to collect some information about the symptoms of IBS-D you have experienced. Please read each question carefully, answering as openly as you can and without help from anyone.

Please answer the following questions to describe the IBS-D symptoms you have experienced **within the past 24 hours**. For each question, please mark (✓ or ✕) the **one** answer most appropriate for that bowel movement.

1. In the past 24 hours, on a scale of 0-10, how would you rate the severity of your diarrhea?										
0	1	2	3	4	5	6	7	8	9	10
☐ No diarrhea	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ Worst diarrhea

2. In the past 24 hours, on a scale of 0-10, how often did you have diarrhea?										
0	1	2	3	4	5	6	7	8	9	10
☐ Never	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ All of the time

3. In the past 24 hours, how often did you feel an immediate need to use the bathroom because you had to have a bowel movement?										
0	1	2	3	4	5	6	7	8	9	10
☐ No diarrhea	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ All of the time

4. In the past 24 hours, how many times did you have an accident (lose control of your bowels)?										
0	1	2	3	4	5	6	7	8	9	10
☐ Never	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ All of the time

5. In the past 24 hours, on a scale of 0-10, how would you rate the severity of your stomach pain?										
0	1	2	3	4	5	6	7	8	9	10
☐ No stomach pain	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ Worst stomach pain

6. In the past 24 hours, on a scale of 0-10, how would you rate the severity of your abdominal pain?										
0	1	2	3	4	5	6	7	8	9	10
☐ No abdominal pain	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ Worst abdominal pain

Fig. 3B

7. In the past 24 hours, on a scale of 0-10, how would you rate the severity of the pressure you felt in your abdomen?										
0	1	2	3	4	5	6	7	8	9	10
☐ No abdominal pressure	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ Worst abdominal pressure

8. In the past 24 hours, on a scale of 0-10, how would you rate the severity of your abdominal cramps?										
0	1	2	3	4	5	6	7	8	9	10
☐ No abdominal cramps	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ Worst abdominal cramps

9. In the past 24 hours, on a scale of 0-10, how often did you have gas?										
0	1	2	3	4	5	6	7	8	9	10
☐ Never	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ All of the time

10. In the past 24 hours, on a scale of 0-10, how bloated did you feel?										
0	1	2	3	4	5	6	7	8	9	10
☐ Not bloated	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ Extremely bloated

11. In the past 24 hours, how often were you able to hear sounds coming from your abdomen that signaled you that you might have diarrhea?										
0	1	2	3	4	5	6	7	8	9	10
☐ Never	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ All of the time

12. In the past 24 hours, when you had a bowel movement, how often did you feel like you completely emptied your bowels?										
0	1	2	3	4	5	6	7	8	9	10
☐ Never	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ All of the time

13. In the past 24 hours, how would you rate the severity of your rectal spasms?										
0	1	2	3	4	5	6	7	8	9	10
☐ No rectal spasms	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ Worst rectal spasms

Fig. 3C

14. In the past 24 hours, on a scale of 0-10, how would you rate the severity of the burning sensation you experienced after a bowel movement?										
0	1	2	3	4	5	6	7	8	9	10
☐ No burning sensation	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ Worst burning sensation

[illegible]

Fig. 5A

IBS-D DAILY SYMPTOM DIARY

The purpose of this diary is to collect some information about the symptoms of IBS-D you have experienced. Please read each question carefully, answering as openly as you can and without help from anyone.

Please answer the following questions to describe the IBS-D symptoms you have experienced **within the past 24 hours**. For each question, please mark (✓ or ✕) the **one** answer most appropriate for that bowel movement.

1. In the past 24 hours, on a scale of 0-10, how would you rate the severity of your diarrhea?										
0	1	2	3	4	5	6	7	8	9	10
☐ No diarrhea	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ Worst diarrhea

2. In the past 24 hours, on a scale of 0-10, how often did you have diarrhea?										
0	1	2	3	4	5	6	7	8	9	10
☐ Never	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ All the time

3. In the past 24 hours, how often did you feel an immediate need to use the bathroom because you had to have a bowel movement?										
0	1	2	3	4	5	6	7	8	9	10
☐ Never	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ All the time

4. In the past 24 hours, on a scale of 0-10, how would rate your immediate need to use the bathroom to have a bowel movement?										
0	1	2	3	4	5	6	7	8	9	10
☐ No need	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ Extreme need

5. In the past 24 hours, how many times did you have an accident (lose control of your bowels)?										
0	1	2	3	4	5	6	7	8	9	10
☐ Never	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ All the time

6. In the past 24 hours, on a scale of 0-10, how would you rate the severity of your stomach pain?										
0	1	2	3	4	5	6	7	8	9	10
☐ No stomach pain	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ Worst stomach pain

Fig. 5B

7. In the past 24 hours, on a scale of 0-10, how would you rate the severity of your abdominal pain?										
0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
No abdominal pain										Worst abdominal pain

8. In the past 24 hours, on a scale of 0-10, how would you rate the severity of the pressure you felt in your abdomen?										
0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
No abdominal pressure										Worst abdominal pressure

9. In the past 24 hours, on a scale of 0-10, how would you rate the severity of your abdominal cramps?										
0	1	2	3	4	5	6	7	8	9	10
☐ No abdomin al cramps	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐ Worst abdominal cramps

[illegible][illegible][illegible][illegible]

IBS-D Symptom Event Log

[illegible]

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 10/31502

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - G06F 17/40 (2010.01)

USPC - 702/187

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC(8)- G06F 17/40 (2010.01);

USPC- 702/187

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Patents and NPLElectronic data base consulted during the international search (name of data base and, where practicable, search terms used)
USPTO PubWest (USPT, PG PUB, EPAB, JPAB: class, keyword); DialogClassic (Derwent, EPO, JPO, USPTO, WIPO: keyword),
GoogleScholar;
search terms: ibs, irritable, spasm, bowel, colon, syndrome, diagnose, treat, record, log, diary

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	WO 2006/091903 A1 (CARAS) 31 August 2006 (31.08.2006), para [00140], [00147], [00262], [00307], [00312]-[00317], [00369], [00382], [00525], [00532]	4, 5, 7-9, 15, 16, 22-24 ----- 6, 10-14, 17-21, 25-29
Y	WO 2008/028976 A1 (BALLEGAARD, et al.) 13 March 2008 (13.03.2008), pg 7, ln 7 to pg 8, ln 27; pg 25, ln 20-27; pg 26, ln 1-13; pg 36, ln 16-21; pg 38, ln 15-16	1-3
Y	MANNING, et al. Towards Positive Diagnosis of the Irritable Bowel. British Medical Journal, 1976; Vol. 2, pp 653-654; Table 1; pg 563, col 2, para 3 to pg 654, col 2, para 2.	1-3, 6, 10-14, 17-21, 25-29
A	MAXTON, et al. More Accurate Diagnosis of Irritable Bowel Syndrome By the Use Of 'Non-Colonic' Symptomatology. Gut. 1991, Vol. 32, pp 784-786.	1-29
A	WO 00/75748 A2 (DOUGLAS, et al.) 14 December 2000 (14.12.2000), entire document	1-29

☐ Further documents are listed in the continuation of Box C.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

02 June 2010 (02.06.2010)

Date of mailing of the international search report

30 JUN 2010

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
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Facsimile No. 571-273-3201

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PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 10/31502

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 30
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.