

# Symptoms of Diarrhea-Predominant or Alternating IBS: An Exploratory Analysis

SC Eaton<sup>1</sup>, AW Mangel<sup>1</sup>, KA Hollis<sup>1</sup>, VZ Ameen<sup>2</sup>, LR Hamm<sup>1</sup>, EB Andrews<sup>1</sup>,  
RE Williams<sup>1</sup>, SF Cook<sup>2</sup>

<sup>1</sup>RTI Health Solutions, RTI International, Research Triangle Park (RTP), NC, USA

<sup>2</sup>GlaxoSmithKline, Inc., RTP, NC, USA

## Abstract

**Background:** Irritable bowel syndrome (IBS) is characterized by a constellation of symptoms predominantly affecting the gastrointestinal tract. An understanding of the burden of illness is fundamental to making an assessment of the risk-benefit relationship for existing therapies, as well as for agents in development.

**Objective:** The objective was to explore symptom severity of diarrhea-predominant (dIBS) or alternating IBS (aIBS), using data collected by a novel web-based survey.

**Methods:** A sample of 31,829 individuals was drawn from an online, web-based research panel (surveyed December 2001 to February 2002) consisting of over 150,000 household members. Probability sampling techniques and stratified, random-digit dialing were used to recruit the sample. Panel members received a screener for symptoms of IBS using Rome II criteria. For participants satisfying the Rome II criteria for either dIBS or aIBS, a second questionnaire addressing demographics, resource utilization, and symptoms was administered. Key measures included prevalence, demographic characteristics, health care utilization, and quality of life (SF-36). Five groupings of symptom severity were explored:

1. At least moderate abdominal pain, cramping, or discomfort in combination with diarrhea in the most recent episode and having IBS for  $\geq 1$  year
2. Urgency reported as often or always in the most recent episode and having IBS for  $\geq 1$  year
3. Pain scored as severe in the most recent episode and having IBS for  $\geq 1$  year
4. Urgency scored as often or always and pain as severe in the most recent episode
5. #4 and having IBS for  $\geq 1$  year.

**Results:** The Rome II criteria for IBS were fulfilled for 1,713 participants, yielding a prevalence rate of 6.6% (CI: 6.3, 6.9). Of the 1,354 subjects subtyped as dIBS or aIBS, 1,180 completed the main questionnaire. Almost 70% of participants with dIBS and aIBS reported their most recent IBS episode within 3 months of the survey and 80% within 6 months. During this most recent episode, over 50% of participants had urgency present, 80% had loose or watery stool, and over 80% reported moderate or severe pain. Ten percent (10%) of participants had at least one of the symptom groupings.

**Conclusions:** This web-based method allows for collection of symptoms of episodic conditions such as IBS. The majority of dIBS and aIBS participants had a recent episode of IBS. These episodes are characterized by a substantial level of multiple symptoms. Ten percent had at least one combination of symptom severity groupings.

**NOTE:** For further information on the methods and results of the survey, please see "Prevalence and Demographics of IBS Respondents: Results from a Large Web-Based Survey," Poster #680.

## Background

### Irritable Bowel Syndrome (IBS)

- Functional bowel disorder and, therefore, a diagnosis based on symptom-criteria.
- Three subtypes based on predominant bowel habit:
  - Diarrhea predominant (dIBS)
  - Constipation predominant (cIBS)
  - Alternating diarrhea and constipation (aIBS).
- Evolving symptom criteria for defining IBS in clinical research studies:
  - Manning Criteria
  - Rome I Criteria
  - Rome II Criteria.
- Prevalence has varied across studies using different diagnostic criteria.
- Classifying IBS by severity (e.g., mild, moderate, severe) has not been consistently defined but is important for novel treatments such as alosetron hydrochloride, a 5HT<sub>3</sub> receptor antagonist.
- Alosetron indication upon reintroduction in the U.S. includes the requirements that patients be female, have failed conventional therapy, and have chronic severe IBS, defined as at least one of the following criteria:
  - Frequent and severe abdominal pain/discomfort
  - Frequent bowel urgency or fecal incontinence
  - Disability or restriction of daily activities due to IBS.

## Objective

- To explore symptom severity in dIBS or aIBS using a novel web-based survey in the period prior to the market reintroduction of alosetron hydrochloride.

## Methods

### Recruitment

- Source population was a web-based research panel.
- Over 150,000 household members representative of the U.S. population aged 21–65, recruited through stratified, random-digit dialing (56% response rate).
- Panel members supplied with WebTV Internet service to avoid limiting to current computer or Internet users.
- Conducted between December 2001 and February 2002.

### Questionnaires

Two tiers of questionnaires were used in this study.

- **Screening Questionnaire** was used to confirm that participants fulfilled Rome II criteria for dIBS and aIBS.
- **Main Questionnaire** included the following categories relating to severity:

- Duration of symptoms
- Time since last episode
- SF-36
- Symptoms and severity of most recent IBS episode
  - Urgency
  - Consistency
  - Frequency
  - Pain

- Five exploratory definitions of symptom severity were retrospectively constructed. With the exception of definition #4, all definitions required the duration of symptoms to be  $\geq 1$  year combined with information about symptoms experienced in the most recent episode.

- Definitions:
  1. At least moderate abdominal pain, cramping or discomfort with diarrhea
  2. Urgency reported as often or always
  3. Pain scored as severe
  4. Urgency scored as often or always and pain as severe
  5. #4 and duration of symptoms for  $\geq 1$  year.

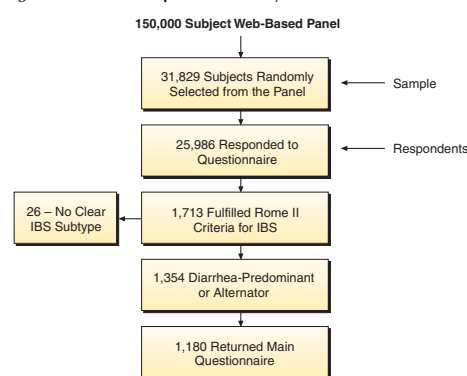
### Analysis

- Continuous data: mean + standard deviation (sd)
- Categorical data: proportions
- Prevalence rates and 95% confidence intervals: per 100 respondents
- Univariable analyses conducted to compare demographic profiles of dIBS and aIBS respondents
- Group differences:
  - Categorical variables via Chi-square test
  - Continuous variables via two-sample independent t-test
- Mean scores for SF-36 domains compared between groups by the two-sample independent t-test; Bonferroni correction for the level of significance of  $\alpha=0.05/8=.00625$  used as a correction for multiple domain scores between groups
- All analyses performed using SAS<sup>®</sup> for Windows<sup>®</sup> (version 8.2).

## Results

The Screening Questionnaire was sent to 31,829 participants, of which 25,986 (82%) completed the questionnaire. The flow of participants through the study is shown in Figure 1.

Figure 1. Flow of Participants in the Study



Characteristics of the sample population were:

- Reflective of the U.S. population (see Figure 2).
- Notable difference between respondents and US population:
  - Fewer younger individuals (ages 21–29)
  - Fewer individuals reporting lesser amounts of formal education

The main questionnaire was sent to the 1,354 dIBS and aIBS participants, and 1,180 of these (87%) satisfactorily completed the survey.

**Demographics:** Analysis of the 1,180 participants completing the main questionnaire showed that 66% (n=782) had symptoms consistent with dIBS and 34% (n=398) had symptoms consistent with aIBS.

**Symptoms:** More than 60% of participants reported experiencing their most recent episode within the 3 months prior to the survey. The responses to questions about urgency, frequency, consistency, and pain are presented in Figures 2, 3, 4, and 5, respectively.

- Levels of urgency (rarely or never), frequency (<1/day), and consistency (very hard, hard) associated with constipation were more frequent reportedly in participants assigned to aIBS.
- Males (n=437)—particularly those with aIBS symptoms—reported less urgency, frequency, and severity of pain than females.
- Individuals assigned to dIBS more frequently reported loose or watery consistency of stools, more urgency (always or often), and increased frequency (4–5/day) of bowel movements in their most recent episode.
- Moderate or worse pain was reported by more than 70% of participants regardless of gender or subtype.

Figure 2. Urgency

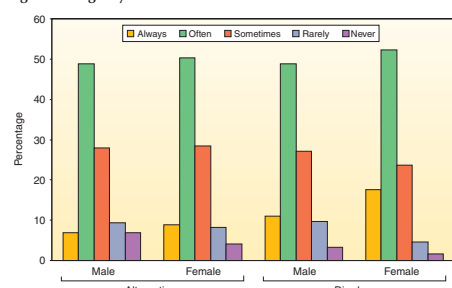


Figure 3. Frequency

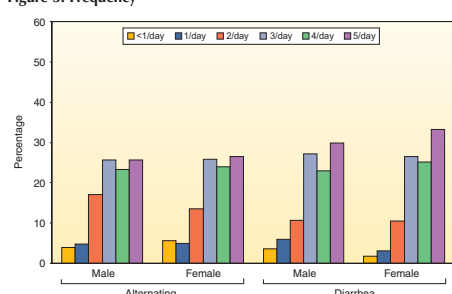


Figure 4. Consistency

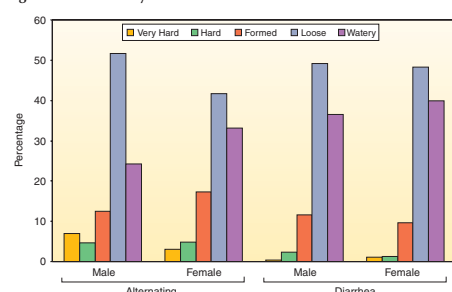
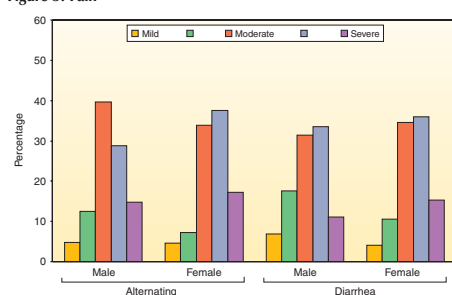


Figure 5. Pain

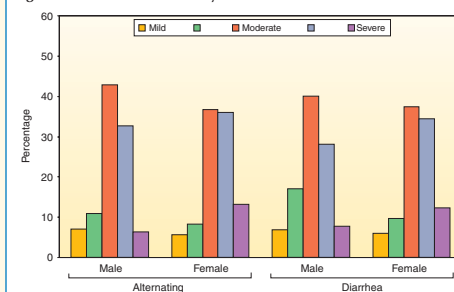


## Results (continued)

Figure 6 presents self-assessed severity results. As with pain, more than 70% of participants rated their most recent episode as severe. A higher proportion of those rating their most recent episode as severe were women (75%) compared to those rating their episode as not severe (61%). Other measures were consistent with a self-assessed rating of severe for the most recent episode, including

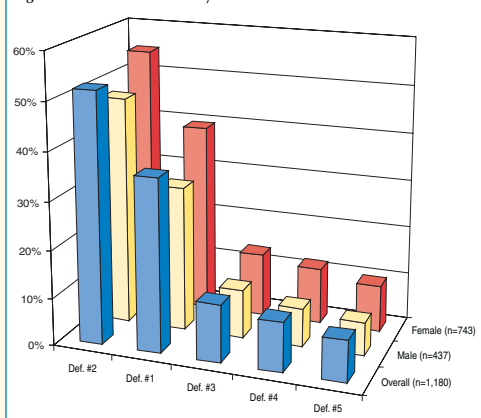
- Lower scores on all domains of the SF-36
- Visiting a physician (71% vs. 50%)
- Having a physician diagnosis of IBS (47% vs. 33%).

Figure 6. Self-Assessed Severity



**Severity Definitions:** Figure 7 presents the proportion of participants meeting each of the retrospectively constructed severity definitions. Definition #5 was the most restrictive, with 8.6% of participants. No meaningful differences were noted between subtypes.

Figure 7. Constructed Severity Definitions



## Discussion

- More than 60% of participants reported an episode in the 3 months prior to the survey.
- Males—particularly those with aIBS symptoms—reported less urgency, frequency, and severity of pain (5-point Likert scale) than females.
- Individual assessments of symptoms were consistent with the Rome II subtype.
- A higher proportion of males rated the severity of their most recent episode to be mild to moderate.
- Self-reported severity was highly correlated with other variables, suggesting greater impact of IBS.
- Five exploratory definitions of severity were constructed, three requiring severe pain:
  - ~10% of participants met the three more restrictive definitions.
  - 36% of participants rated their most recent episode at more than moderate severity.
  - Results varied slightly by gender as a greater proportion of women met each of the definitions.
  - No significant variation by subtype.
- Use of the web-enabled panel constituted a new, rapid tool for assessment of epidemiologic information.
  - Advantages
    - Speed of data collection (data collection in less than 2 months)
    - U.S. population-based sample
    - Participants not restricted to those seeking medical care
    - Patient-reported rather than physician evaluation, symptom history, prior health care utilization, or functional status.
  - Disadvantages
    - No clinical confirmation of self-reported clinical information on IBS severity
    - Potential technology bias in overall web-based panel.

## Conclusion

- Web-based methodology allows for collection of symptoms of episodic conditions, such as IBS.
- Majority of dIBS and aIBS participants reported a recent episode of IBS.
- Episodes were characterized by a substantial level of multiple symptoms.
- Approximately 10% met at least one combination of symptom severity. Using different definitions, 8–52% of patients with IBSa or IBSd could be considered to have "severe" IBS.
- One limitation:
  - Clinical definitions of IBS severity have not previously been developed, so no benchmarks are available for comparisons due to cyclic and variable nature of the disorder.
- Patient-reported data about symptoms can help in the evolving characterization of IBS severity and understanding of the prevalence and burden of IBS.

## Disclosure

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## Presenter

**Susan Eaton**  
Director, Epidemiology Research  
RTI Health Solutions, RTI International  
3040 Cornwallis Road, PO Box 12194  
Research Triangle Park, NC 27709-2194  
Phone: 919.541.6986 Fax: 919.541.7222  
E-mail: seaton@rti.org www.rtihs.org

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