

ADVANCES IN IBS

Current Developments in the Treatment of Irritable Bowel Syndrome

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Highlights of the Findings From the Rome Foundation Global Epidemiology Study



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G&H What is the Rome Foundation Global Epidemiology Study, and what are its goals?

AS The problem, and reason for the study, was the lack of good epidemiologic information on the prevalence of irritable bowel syndrome (IBS) and similar conditions. Although there have been many studies on IBS prevalence, their methodologies, diagnostic criteria, and populations have varied. Most prevalence estimates were based on the pooling of data from heterogeneous studies, usually with inappropriate pooling methods, seriously limiting the relevance of the results. In a literature review in which we calculated pooled prevalence rates from 83 studies, including 288,103 participants in 41 countries, we concluded that a single pooled global prevalence rate would not be appropriate because the data we reviewed were so heterogeneous. We decided that the only way to understand the global prevalence of IBS is to perform a single uniform—as much as possible—study with as much of a global reach as we can achieve, which is basically what the Rome Foundation Global Epidemiology Study was.

The overall aim was to study the epidemiology of 22 disorders of gut-brain interaction (DGBIs)—not only IBS—using the Rome IV diagnostic criteria in 33 countries around the world to obtain adequate global distribution. We had already worked out the methodology in terms of how to perform cross-cultural, multinational studies in this area. Data were obtained through a survey using a single questionnaire that was administered at the same time to all countries. The questionnaire had 89 diagnostic questions for the disorders and 80 supplemental

questions looking at, for example, social issues, psychological issues, medication use, other diagnoses, and diet. So, the aim was to collect data on not only the prevalence rates of DGBIs but also factors that might explain their pathophysiology. Two forms of data collection were used: an Internet survey, which enabled us to obtain a national representation for each of the 26 countries with Internet access; and in-person interviews, which were conducted

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in 7 countries where, for different reasons, we could not do an Internet survey. The 7 countries either lacked the Internet infrastructure or, for example, in the case of Iran, the company providing the Internet survey did not have access to a population in that country. It turned out that the survey methods were so different that we could not pool the results together. We ended up with 2 separate sets of results, one for the Internet survey countries, which

included about 54,000 people, and the other for the in-person interviews, which totaled about 21,000 people. Including the planning and design stage, identification of principal investigators for the 33 countries, formulating the questionnaire, translating it into the participating country languages, data collection, quality control and analyses, and paper preparation, the study was conducted over a period of 10 to 11 years from start to finish and its first publication.

G&H What did the main analysis of the Rome IV Internet survey reveal about the prevalence of DGBIs and IBS and their global burden?

AS I think the most important result may be that 40.3% of the approximately 54,000 people who completed the Internet survey met the diagnostic criteria for at least one DGBI. In other words, 2 of every 5 people surveyed in 26 different countries had a DGBI, and it was not necessarily IBS that was the most prevalent; other DGBIs were more prevalent, for example, functional constipation and functional dyspepsia. However, the results gave us a very broad picture of the absolute burden of these disorders, which, when considering the larger population and all that entails (eg, in terms of use of the health care system), was rather astounding.

G&H What was the prevalence of IBS by Rome IV compared with Rome III criteria, and what are the reasons for the differences?

AS Although this was a Rome IV questionnaire, we also included, for 14 of the 26 Internet-surveyed countries, the questions to diagnose IBS by the Rome III criteria. The difference between them was very large—and this has been shown in other studies as well but not on the scale of this study—to the point where the proportion of persons with IBS was higher when the Rome III criteria were used and lower when the Rome IV criteria were used (10.1% vs 4.1%). This shows that the Rome IV criteria are more rigid. The Rome IV criteria select out a population that has more severe disease and consequently has lower quality of life, higher psychological distress, somatization, as well as other psychosocial impairments. Having a more stringent criteria leads to all kinds of advantages and some disadvantages. One advantage is, for example, when conducting a clinical drug trial, there is a much more homogeneous population. On the other hand, some experts may say this excludes patients whom a clinician would consider as having IBS even if they do not meet the diagnostic criteria.

The most important difference between the Rome IV and Rome III criteria proved to be the frequency of

symptoms. Rome III says a patient must have a symptom (eg, abdominal pain) 2 or 3 times a month. Rome IV says a patient must have the symptom once a week. Although this difference may seem negligible, it was significant, accounting for about 4% to 5% of the entire 6% difference. So, then, the next question to ask is whether frequency is the most important factor or whether there are other factors in the clinical setting to consider. For

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example, which is more important, if the symptom is bothersome or if it is frequent? A symptom may occur only 2 times a month, but it may be so bothersome that it is ruining a person's life, whereas somebody else has the symptom once a week and it is not that bothersome. How is it impacting them? As a result of the study, we are beginning to understand different perspectives, and hopefully, we will be able to address a lot of the issues that trouble doctors.

G&H What was the most important thing learned in your opinion?

AS If I could pick two, first would be the overall burden, which I mentioned earlier, and second, the global consistency. We found that the results were consistently similar regardless of what part of the world we looked at: North America; Western Europe; Eastern Europe, where we surveyed Romania, Russia, and Poland; Latin America, where we surveyed Argentina, Colombia, Brazil, and Mexico; Asia, where we surveyed China, Japan, South Korea, and Singapore; and the other countries where we did in-person surveys. For all countries surveyed by the Internet, the relative prevalence among the various DGBIs was consistent, so IBS and the other DGBIs are indeed a global problem.

G&H Can knowledge of the overlap of Rome IV disorders with DGBIs improve care of patients with IBS?

AS My answer would be, yes, to start with. When discussing overlap, it is helpful to divide the gastrointestinal tract into anatomic regions, and there are 4 primary ones for which we had results in this study: the esophagus, gastroduodenal, bowel, and anorectal. So, a person can have a disorder in any one of those regions, and may have, for example, functional dyspepsia in the gastroduodenal region and IBS in the bowel, which would be 2 overlapping conditions.

Theoretically, a patient could have up to 4 overlapping conditions. We found that the more overlapping conditions a person has, the more severe the symptoms and the greater the impact on quality of life and functional ability—the more anxiety, depression, somatization, and so forth. One reason I think this is important beyond the fact of understanding overlap is that clinicians are not aware of overlap enough. Clinicians who have a patient with IBS may not check to see if there is something else; they may attribute every symptom to the irritable bowel. However, when the patient has an overlapping condition, the clinician must approach that patient, in terms of therapeutics and treatment, as a person with more severe illness. That patient must be managed in more of a multimodality way, not just by reassurance, education, or other measures provided for a person with a less severe disorder.

G&H What were the limitations of the Rome Foundation Global Epidemiology Study?

AS First, although it was quite global with 33 countries, there were still some areas that were not well represented. One such area was the Middle East, where we conducted the survey in Israel, Turkey, and Iran only. Also, Latin America and Eastern Europe were not covered as much as other regions. This depended somewhat on funding but even more on finding the person who could be the investigator in a particular country.

The second limitation is the fact that we could not do Internet surveys everywhere. For example, in countries where in-person surveys were done, including Nigeria, Ghana, India, Bangladesh, Indonesia, and Malaysia, a national representation was not obtainable. This is because in-person interviews take place in a particular community, village, or urban neighborhood, covering a small section of the population, whereas Internet surveys can be distributed over a larger area and have quotas. In the United States, looking at the census population in the 50 states and the percentage of people surveyed in each of those states, they are essentially the same, which means there was excellent representation. It is not known whether the population surveyed by in-person interview was representative.

Finally, regarding the questionnaire, we left out

some potentially important questions. There are 1 or 2 questions that we regret not having put in, but I guess we cannot think of it all. Although the questionnaire was long, people were able to answer the questions in a period of about 20 to 25 minutes because there were a lot of skipped questions. For example, for the survey question “Do you have abdominal pain?” if the answer is “No,” then the person skips 13 questions from 41 to 54. So, it was not as burdensome as it might seem.

G&H What has been published from the global study, and how can its findings enhance our understanding of DGBIs or IBS specifically?

AS Overall, 27 papers have been published to date, including the first one, which presents the study and its main findings, and a special issue of *Neurogastroenterology and Motility* with 15 papers. About 25 more papers are in the process of being written—some have already been submitted—for a total over 50 papers published, under review, or in preparation so far. These papers cover the data from various perspectives. For instance, the data may be from a global analysis of all 33 countries, an inter-regional comparison of East and West, a regional evaluation of all the countries in Western Europe, or country-specific statistics.

The Rome Foundation Global Epidemiology Study dataset provides copious reference material that is being used for research and is an important contribution to the literature. The study has, first, provided a lot of information; second, we have established a protocol for submitting proposals for future publications using the dataset. The database can be mined for future studies on specific disorders—IBS, for example—and on specific issues such as sexual differences, quality of life, meal-related symptoms, and factor analyses. Because it is such a large database, I think it has the potential to enhance our perspective in multiple directions and further our understanding of IBS and the other DGBIs.

G&H How will the global study findings impact the future diagnosis and management of IBS?

AS As I mentioned earlier, one view is that having stringent criteria may exclude some patients who may be considered in clinical practice to have IBS. This is an area where I think the global study can inform the process to develop the next iteration of diagnostic criteria, Rome V. Committees are in the process of developing the Rome V criteria. Previous iterations, beginning with Rome I to Rome IV, which was completed in 2016, were predominantly based on expert opinion. Over time, the criteria have become more evidence-based to the point now

where the committees for Rome V have the database from Rome IV to work from and use as evidence for changes to future criteria. The main use of the criteria to date has been for epidemiologic studies and clinical drug trials. Their use has been more limited in clinical practice, so another way the global study can have an impact is on the development of clinical criteria, which have been lacking and which may help us understand the relative importance of frequency of symptoms compared with other factors. How bothersome symptoms are, how they impact quality of life, and when would they make a patient go to a doctor—these are types of questions that this study is helping to understand better.

G&H What aspects of IBS will the Rome Foundation look at next?

AS I think the most important aspect is trying to understand why there is such a big gap between the Rome III and Rome IV criteria. Are we getting something wrong? Are the criteria too rigid or too lenient? How should we define the criteria so that they are more applicable, first, in the research setting; second, in the clinical trial setting; and third, in the clinical setting? If we can answer those

questions correctly as a result of data that we now have from Rome IV, then I think we will be on much firmer ground in the future.

Disclosures

Dr Sperber has no relevant conflicts of interest to disclose.

Suggested Reading

Knowles SR, Skvarc D, Ford AC, et al. Negative impact of disorders of gut-brain interactions on health-related quality of life: results from the Rome Foundation Global Epidemiology Study. *Gastroenterology*. 2023;164(4):655-668.e10.

Sperber AD. The Rome Foundation Global Epidemiology Study: conception, implementation, results, and future potential. *Neurogastroenterol Motil*. 2023;35(6):e14567.

Sperber AD, Bangdiwala SI, Drossman DA, et al. Worldwide prevalence and burden of functional gastrointestinal disorders, results of Rome Foundation Global Study. *Gastroenterology*. 2021;160(1):99-114.e3.

Sperber AD, Dumitrascu D, Fukudo S, et al. The global prevalence of IBS in adults remains elusive due to the heterogeneity of studies: a Rome Foundation working team literature review. *Gut*. 2017;66(6):1075-1082.

Sperber AD, Freud T, Abu-Freha N, et al. Epidemiology of disorders of gut-brain interaction in Israel: results from the Rome Foundation Global Epidemiology Study. *Neurogastroenterol Motil*. 2022;34(8):e14323.

Sperber AD, Freud T, Aziz I, et al. Greater overlap of Rome IV disorders of gut-brain interactions leads to increased disease severity and poorer quality of life. *Clin Gastroenterol Hepatol*. 2022;20(5):e945-e956.