

## VIEWPOINT

# Introduction. The Rome Foundation and Rome III

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### INTRODUCTION

It is a great pleasure to introduce the commentaries by Drs Kellow and Quigley on the pros and cons of the new Rome III criteria. Perhaps most of the readership is only familiar with these published diagnostic criteria. However, the Rome Foundation has a larger mission and directive to move the field of functional gastrointestinal (GI) and motility disorders forward through research and education. In this introduction, I will briefly discuss who we are, and offer the rationale and value of its activities and some future challenges.

### MISSION AND GOALS

The Rome Foundation is a non-profit organization which has as its mission: 'To improve the lives of people with functional GI disorders (FGIDs)', and its two goals: 'To promote clinical recognition and legitimization of the FGIDs' and 'To develop a scientific understanding of their pathophysiological mechanisms to achieve optimal treatment'. These directives were developed at the organization's strategic planning meeting in late 2006. To understand how these statements of purpose for the Rome Foundation were reached we need to review how and why this work began.

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### HISTORICAL DEVELOPMENT

The organization began as a small international group of clinical investigators who were charged to develop diagnostic criteria for irritable bowel syndrome (IBS), present these recommendations at the XIII International Congress of Gastroenterology held in Rome in 1988, and publish the results. The origin of the organization's name began with this meeting in Rome. At the time, the need for criteria related to the dilemma that IBS was being studied more and more in clinical trials, yet there were no standards to make this diagnosis. Thus, a heterogeneous group of patients would come into treatment trials up until the 1980s. These trials might include patients with abdominal pain and no bowel dysfunction, constipation or diarrhoea without pain, and even dyspeptic symptoms all in the same recruitment protocol. There was also growing awareness that while most of these patients had motility disturbances that explained their symptoms of diarrhoea and constipation, the research on motility was not sufficient to explain the pain experienced. Furthermore, patients could not be selected based on motility abnormalities. Hence, the need was to identify selection criteria based on the symptoms patients brought to the doctors.

With no 'gold standard' for IBS, the criteria were developed and applied using the so-called 'Delphi' method,<sup>1,2</sup> which involved a preliminary review of the literature and then group discussion to achieve consensus over a 2-day meeting. When possible, evidence was included, at the time based on a few clinical (e.g. the original Manning criteria for IBS)<sup>3</sup> and factor analysis studies.<sup>4,5</sup> The first criteria for IBS resulting from this consensus process was published in 1989<sup>6</sup> and is considered 'pre-Rome' because these criteria were later modified to include pain as a required criterion.

Following this, and with the support of Aldo Torsoli, Professor of the GI division in the University of Rome

and the editor of a publication *Gastroenterology International*, another committee was formed to produce in 1990 a document for this journal that set out a full classification system with criteria for 24 FGIDs from oesophagus to rectum.<sup>7</sup> Further discussions led to support from the journal for a series of working teams that expanded upon this classification system. Each new committee addressed the disorders within a specific GI region (oesophageal, gastroduodenal, biliary, bowel and anorectal) with more specific information about the clinical features, pathophysiology, diagnostic (including criteria) and treatment methods. In addition, committees were set up to address the psychosocial aspects of these disorders and to offer guidelines for the conduct of treatment trials. Between 1992 and 1995 the seven committees published their work in *Gastroenterology International*. In addition, a questionnaire using these criteria was constructed and applied in a population-based national US Householder survey which, for the first time, identified the prevalence of the FGIDs.<sup>8</sup> Finally, the publications were compiled in a book published in 1994 by Little, Brown & Company, and Rome I was launched.<sup>9</sup>

The work also attracted the interest of the FDA and the pharmaceutical industry, as they were looking to more precisely and in a standard fashion target patient populations so new pharmaceuticals could be tested to address these physiological dysfunctions. Eventually, the Rome Foundation acquired sponsorship from the pharmaceutical industry to carry on its work. The Rome organization became incorporated with 501c3 non-profit status in 1996 and work began on Rome II in an effort to update knowledge of these disorders given the explosion of research publications in the late 1990s.

Rome II was published in 1999 as a supplement in *Gut* and in 2000 as the Rome II book.<sup>10,11</sup> Rome II differed from Rome I by having a more structured method for selecting committee members through a committee process, and by charging each committee to make recommendations based on evidence-based data. Criteria could be changed only if there was a clear rationale for the change based on existing scientific evidence. These publications came at a time of growing awareness of IBS and the FGIDs in part because of the release of new pharmaceutical agents to treat them. Rome II became the standard for providing a compendium of research knowledge on all aspects of these disorders.

With the acceptance of these criteria for research and continued growth of the field, updates were needed. This led to the most recent iteration of this work, Rome III, developed by a new set of committees, and was published in 2006 as a 13th issue in *Gastroenterology* and as a book.<sup>12,13</sup>

## EFFECTS

The development of the criteria has had two notable effects. Firstly, there now was a standardized method for patient selection that could be applied in clinical research. This made it easier to conduct clinical trials and the use of Rome Criteria has become the standard method of patient selection for FDA-approved studies. The criteria also permitted broader based research that eventuated in understanding these painful conditions as related to visceral hypersensitivity, mucosal immune dysfunction and inflammation and brain-gut interactions. The growing rate of publications through 2006 using the Rome criteria is illustrated in Fig. 1.

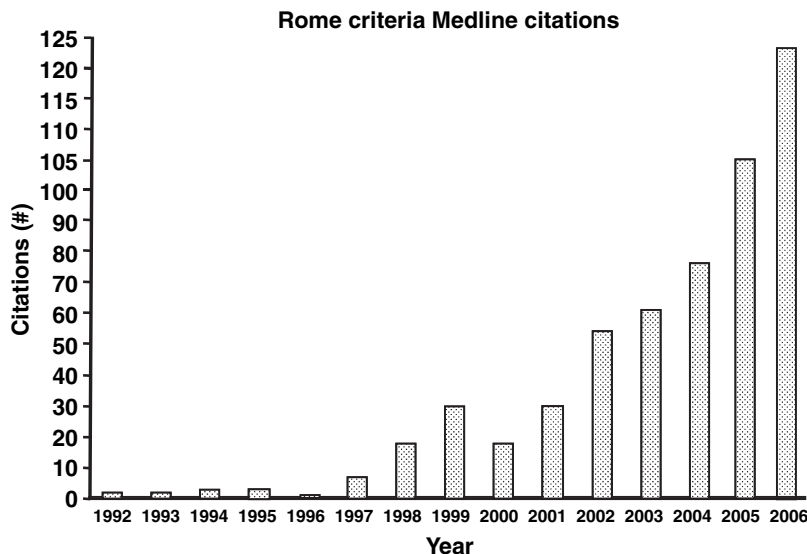


Figure 1 Rome criteria Medline citations.

A second benefit was that by being able to make a positive diagnosis, patients were reassured that they had a 'real' condition, rather than it being unexplained or 'in their head'. Similarly, many doctors started to become more satisfied with not having to do more studies to exclude other diseases. More recently, the organization began to see opportunities to do more for the field than producing criteria, and over the last 3–4 years the scope and direction has expanded.

## CURRENT ACTIVITIES

In 2003, the Rome committee organized into a Foundation with a new directive to help advance the field through a variety of initiatives. By that time, a set of

by-laws were approved, board members were selected, administrative and executive offices were created and new projects began in addition to the symptom criteria and publications. Several areas of interest emerged, to help regulatory agencies on design of treatment trials, to resolve important issues after Rome III on a variety of topics through working teams, to increase education to doctors and to support research. Table 1 highlights all current activities of the Rome Foundation.

## CRITICISMS AND CHALLENGES

In many ways, the Foundation is set up to address needs as they develop. However, over the years several concerns or criticisms have been raised.

**Table 1** Rome foundation activities

Activity	Purpose	Product and year
Rome III committee work	Provided a standard for medical information and new criteria for the FGIDs	Rome III issue in <i>Gastroenterology</i> and the Rome III book (2006)
CD slide set committees	Creation of a PowerPoint slides set of updated Rome III data for presentations an self-learning	CD slide set (2008)
Research support	Support for pilot studies to validate criteria and provide epidemiological data using criteria	5 pilot studies funded in 2004 and new research funding to begin in 2008
AGA lectureship	State-of-the-art lecture by a prominent authority to cover broader areas of health care or the FGIDs	To be held annually at DDW beginning in 2008
Working teams	To provide new data for publication by experts that addresses current needs using the Rome III committee process	Severity for IBS and FGIDs (2008) Outcomes in clinical trials (2008) Brain imaging standardization (2008)
Clinical algorithms	To provide algorithms for clinicians to diagnose functional GI and also motility disorders and to exclude other diseases	Publications on clinical algorithms to simplify diagnosis – for primary care doctors and gastroenterologists (2009)
Sponsorship of National and International Meetings	To provide support for educational programmes at symposia covering the FGIDs and motility disorders	NASPGHAN (2007) DDW (2008) Combined Neurogastroenterology Meetings in Lucerne (2008)
Media	To provide ongoing information about activities and opportunities of the Rome Foundation	Updated website: <a href="http://www.romecriteria.org">http://www.romecriteria.org</a> (2007) Rome Foundation Reporter Newsletter (2007)
Book for general public and primary care providers	Easy to read book that reviews FGIDs based on Rome III	To be published early 2008
Rome III questionnaire and Rome III book translations	To permit global education and research opportunities	Translations underway: Spanish Portuguese Italian Chinese Japanese
Outcome conference	To provide a state-of-the-art symposium to bring together thought leaders from academia, industry and regulatory agencies to develop guidelines for outcomes in treatment trials	Meeting planning underway. Symposium scheduled for April 2009

Perhaps the first one, which may be less of an issue these days, was the concern about the first set of criteria being 'etched in stone', i.e. not changing with new scientific developments. I think this has been addressed through the ongoing process of refining the Rome criteria. Changes in criteria are not made unless there is new evidence to do so.

A second issue relates to the perceived schism between FGIDs, defined by symptoms (e.g. functional dyspepsia), and motility disorders, defined by physiological dysfunction (e.g. gastroparesis). While these disorders can overlap, we chose the symptom-based classification for pragmatic reasons, to address clinical needs, and now have begun to remedy this issue by developing a means for clinicians to sort out when motility assessment may be of value in treatment. A committee has been set up that includes motility experts and those involved in FGIDs to produce over the next year a set of clinical algorithms.

After Rome II, there was concern that developing countries were not represented. Accordingly for Rome III, each committee included experts in the area of interest from Asia or South America.

Another criticism is that the criteria, being designed primarily for research, are not practical for clinicians. Accordingly, the Rome III criteria have been simplified and the use of clinical algorithms may help it to achieve greater application in practice.

Finally, there have been concerns that involvement in the Rome process is not open to membership. Indeed, it is not a membership organization as that would be inconsistent with our goals. Much like the Institute of Medicine or the American Board of Internal Medicine in the US, the effort is to produce educational products. Thus, a rigorous committee process identifies people with records of research and publication in the areas where particular questions need to be addressed and clarified. All who are identified are required to devote considerable time in Rome Foundation projects. They are not paid for their work or they receive modest honorariums at the completion of the work. Yet over the years, we have been able to include increasing numbers of investigators to accomplish these tasks.

## THE FUTURE

For the future there is still much work to be done. To move the field forward, we need to 'legitimize' these disorders in a way that will encourage investigators to do the research and clinicians to find the value in caring for our patients. This can be accomplished with education not only to doctors, investigators and our

patients, but also to research funding and regulatory agencies. Establishing standards to conduct this research in many areas, from brain imaging to mucosal immune assessment, is also of great importance. Looking onto Rome IV we hope to include new knowledge relating to genetics, biomarkers in diagnosis and work in pharmacogenomics. In the end, to achieve our mission, we hope that our patients will ultimately benefit.

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