Rome Foundation Research Institute Annual Report

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Part One: Background and Organization of RFRI

The Rome Foundation Research Institute (RFRI) is a subsidiary organization of the Rome Foundation, an international non-profit academic organization dedicated to improving the lives of patients with Disorders of Gut-Brain Interaction (DGBI) formerly called Functional GI Disorders. The RFRI was created in 2018 to advance the scientific understanding of DGBI through development of a semi-autonomous entity that will promote and support research in the field or DGBI. https://theromefoundation.org/research-institute-rome-foundation/

Vision. To be the global leader in DGBI research

Mission. To improve the lives of patients with DGBI through ground-breaking research

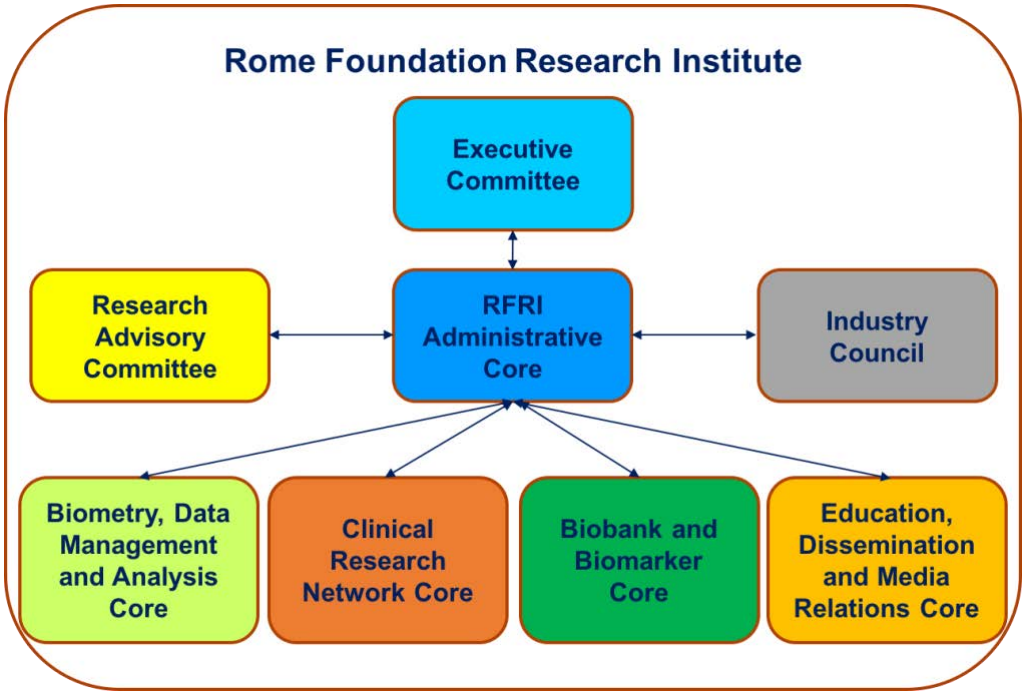
Aim. To increase the knowledge of the causes, identification, treatment and care of patients with DGBI.

Implementation. To establish an international academic research initiative with leading experts, in order to facilitate global DGBI research through collaboration with industry and academic partners, and with the following objectives:

- Develop a centralized data acquisition and research coordinating center.
- Serve as an international clearinghouse for investigators and industry in the development, administration and analysis of clinical research in DGBIs.
- Develop a portfolio of current and future study protocols and an accessible database of knowledge which can be adapted to address specific questions regarding DGBIs pathophysiology, impact, diagnosis and treatment.

Legal Structure and Governance. The RFRI is governed by the Executive Committee consisting: of Magnus Simren MD, PhD (Director and Chair of Executive Committee of RFRI and Board Member of RF), Douglas Drossman MD (RF President Emeritus and COO) and Jan Tack MD, PhD (RF President). It is a Type I supporting organization of the Rome Foundation (RF) under Section 509(a)(3) of the US Internal Revenue Code. The corporate office is located in North Carolina, USA, therefore for legal and tax purposes the RFRI is represented by Douglas Drossman MD (President) and Johannah Ruddy (Secretary/Treasurer).

Organizational Structure. Figure 1 demonstrates the organizational structure.



Executive Committee (EC). The EC (Drossman, Simren - chair, Tack) supports and directs all activities of the RFRI and is ultimately responsible for assuring that the aims and objectives of the program are achieved. The terms for the members are for five years and are renewable with the replacement process staggered to allow for gradual change of leadership.

Administrative Core (AC). The AC is responsible for the oversight of the day to day activities of the RFRI relating to research administration and program implementation, training, education and dissemination of information, collaboration with sponsors and outside agencies, and quality control of all core programs. The AC consists of the three members of the EC, an administrator (Johannah Ruddy M.Ed., Executive Director of the RF) the research manager of the RFRI (Olafur Palsson Psy.D.), and an external industry consultant who advises the Executive Committee on prospective and ongoing collaborations with commercial organizations within the Life Sciences sector (biopharmaceutical, device, and diagnostics companies) (Doug Levine, MD). The AC is advised by the RAC and the Industry Council (see below)

Research Advisory Committee (RAC). The RAC functions as advisory to the AC as a contributor of ideas, and as a repository to review and revise research proposals. Currently, it is composed of RF Board members who have been selected based on their academic record of scientific achievement, their ability to evaluate, conduct and analyze scientific data related to DGBI, and as well as demographic and geographic diversity issues. RAC members are responsible to participate in the various Cores discussed

below. Current RAC members include: Giovanni Barbara MD, William Chey MD, Lin Chang MD, Laurie Keefer PhD, John Kellow MD, Samuel Nurko MD, MPH, Max Schmulson MD, and Ami Sperber MD, MSPH. In the future, the RAC may include members external to the RF board providing they meet the described guidelines, and their participation will help to serve future needs of RFRI.

Industry Council (IC). The IC is advisory to the AC and is comprised of representatives from pharmaceutical and device companies who share the mission of and sponsor the RFRI. Members of the IC interact with the AC in an advisory capacity and review the activities of the RFRI which may include: discussion of ongoing research studies, exchange of ideas for planned initiatives, review of operations of all cores, evaluation of research data, and participation in bilateral or collaborative research studies with privileged status. The current IC member is Machelle Manuel, Vice President and Head of Global Medical Scientific Affairs at Ironwood Pharmaceuticals. Additional industry members to the IC will be included as additional sponsors come aboard.

Biometry, Data Management and Analysis Core (Biometry Core). The Biometry Core is responsible for providing and/or ensuring the standards for high quality data management systems, quality assurance processes, and statistical analytic aspects for the RFRI. Core members include Olafur Palsson Psy.D. who is the research manager and director of the Core, Shrikant Bangdiwala Ph.D., the statistician (co-director), William Whitehead PhD a former RF Board member, Ami Sperber MD MSPH, and Iram Haq, research coordinator. This core is actively involved with ongoing research proposals currently in effect as discussed below.

Clinical Research Network Core (Research Core). The Research Core is responsible for providing the infrastructure and maintaining the standards for clinical investigative studies involving epidemiological, clinical, outcomes, and treatment studies. It is co-directed by Lin Chang MD and William Chey MD and members include: Laurie Keefer PhD, Samuel Nurko MD, Ami Sperber MD, MSPH and Jan Tack MD, PhD. This Core serves as a clearinghouse for research and is responsible for identification and selection of study centers. This includes: a) responsibility for large scale multicenter studies, b) clinical trials of new and existing treatment interventions, c) organizing and conducting clinical trials of non-pharmacological interventions, d) developing and validating patient reported outcomes (PROs) for DGBI, e) coordinating with the biometry core the development of operations of deep clinical phenotyping including demographic, Rome criteria, psychometric and clinical questionnaires, f) reviewing seed grant and large scale research proposals, and g) maintaining and coordinating, under the direction of the Biometry Core a pool of leading investigators and special population resources.

Biobank and Biomarker Core (Biobank Core). This core is responsible for the coordination of acquisition, storage and processing of biological samples including: blood, stool, urine, biopsy, luminal fluids and breath samples. It also is responsible for data acquisition relating to measurement of motility or sensitivity physiological testing,

peptide hormone assays, assessment of structural and functional alterations in the CNS, pharmacogenomics and other biological data. Finally, in collaboration with the biometry core, the biobank core identifies centers and experts to obtain for analysis biological samples and assist in their processing. The members are Giovanni Barbara MD (Director), Max Schmulson MD (co-director) and Magnus Simren MD, PhD, and additional members will be appointed based on expertise needed.

Education, Dissemination and Media Relations Core (Education Core). The Education Core serves primarily to assure quality control in the dissemination of research knowledge that is accumulated from the RFRI and support its translation into clinical practice. The Core members are Douglas Drossman MD (director), Johannah Ruddy (administrator and Executive Director of the RF), and Mark Schmitter (marketing director of the RF). This core assures that the information provided by the RFRI to external organizations, media and journals and other publications printed and digital, will be scientifically based, unbiased and non-commercial. The core also serves to monitor media, publications and other communications from external sources (e.g., news bureaus, scientific organizations, industry) to be sure the information provided is accurate, scientifically based and unbiased.

Part Two: Activities of the RFRI for 2019

Introduction. Over the past year the RFRI developed and consolidated the infrastructure as follows: further refinement of the biometry and biobank cores, the creation of a database of investigators and the development of the RFRI Investigator Platform (RFRI-IP) to obtain clinical phenotyping data from our research sites. We also engaged in several existing and planned research studies. These include: the development of data analysis of the Rome Foundation Global Epidemiology Study, implementation of two clinical trials: the Domino and ROBOT studies, the development of a research contract with Danone Pharmaceuticals to begin in January 2020, and consultations concerning prospective projects with two pharmaceutical companies. Finally, we are most pleased to have acquired Ironwood Pharmaceuticals under the directorship of Machelle Manuel as a full sponsor for 3 years. What follows is a detailed description of these activities.

Infrastructure Development

Development of the Biobank and Biomarker Core –

In order to be able to perform multinational, multicenter studies with the goal to identify diagnostic and predictive biomarkers of relevance for patients with DGBI, the RFRI spent a considerable amount of time creating this core and determining optimal sampling and storing procedures for biosamples in multicenter settings. This work led by the chair and the co-chair of this committee, in close collaboration with the members of the Executive Committee and the Research Manager. We decided not to create a

central biobank for logistical and regulatory reasons. Instead participating research centers in the multicenter studies will each store their own samples locally according to predefined specifications, and upon request and after agreement ship their samples for analyses. We created detailed Standard Operating Procedures (SOPs) for collection and storage of fecal, urine, blood, and saliva samples, as well as biopsies, where details regarding sampling, equipment needed, storage, and transportation are provided. Regarding biopsies, separate SOPs for esophageal, gastroduodenal and colonic biopsies have been developed. Information about available samples and storage conditions for each subject will be entered into a database and linked with clinical phenotyping data available for that subject in the RFRI Investigator Platform (see below). Hence, the planning in the biobanking and biomarker core done in close collaboration with the biometry core.

Currently the biobank and biomarker core consist of a small group of RFRI members (see above), but additional members based on expertise needed will be appointed during the coming year.

Creation and Application of the RFRI Investigator Platform for Clinical phenotyping

The RFRI is currently developing a secure Internet-based data collection system, the RFRI Investigator Platform (RFRI-IP), that will be used across all the research sites in the Global Research Network (see below) to collect detailed and uniform clinical phenotyping data on large panels of patients with DGBI. At many of the research sites, the patients in the phenotyping database will also have associated biosamples (these will be our ROBOT project sites), and the availability of those samples. This will quickly create an unprecedented large central clinical research database that can be used to (a) rapidly invite large sets of patients with well-known characteristics to participate in specific research studies; (b) conduct analyses for papers by site investigators, individually or in collaboration, and by the RFRI or commissioned by sponsors; and (c) assess feasibility and provide pilot information for grant applications and sponsored projects. Additionally, questionnaire data collected in the unified phenotyping will be instantly scored and will be available in the clinical encounters, and thus clinically useful.

All patient data collection using the RFRI-IP will be strictly de-identified and HIPAA and GDPR compliant. To minimize costs and demands on staff at clinical research sites, data collection will be predominantly self-administered by patients, using easy-to-use web-based assessment that works on any computer device and any web browser. The primary patient evaluation method will be via computer tablets used in the waiting rooms, but the assessment will be fully mobile-device compatible so patients can use their own mobile phones if preferred. Staff-assisted entry and paper questionnaires will only be used in exceptional circumstances if needed.

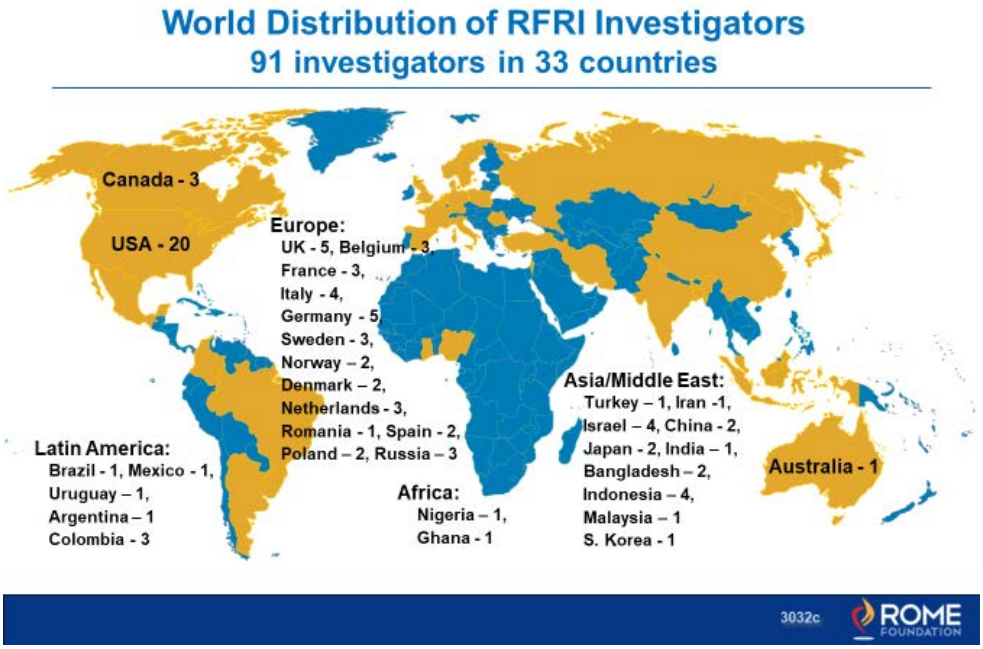
The patient phenotyping assessment will consist of an initial 20-25 min. patient-completed questionnaire, and a shorter assessment (5-10 min.) in return clinic visits, primarily designed to update information on clinical status in the database. These patient-completed assessments will be supplemented with a limited set of information from the medical record, added by the research site staff.

The phenotyping dataset collected on each participating patient, stored and available for queries and research use in the RFRI central database, will include the following: Demographic questions; clinical diagnoses; responses to the Rome IV Diagnostic Questionnaire with scoring for 22 different DGBI diagnoses; characteristics and history of current GI symptoms; co-morbid GI and non-GI medical conditions; history of GI-relevant medical tests, medical procedures and surgeries; psychological symptom scores; quality of life scores; prescription and non-prescription medications used; and self-management methods used by the patient for GI symptoms. The availability and nature of biosamples from each patient (with summary of findings if the samples have been analyzed) will be recorded in the same central RFRI database along with the phenotyping data.

Creation of the Global Research Network. An essential part of carrying out the mission of the RFRI is the establishment of an active Global Research Network of leading and highly productive investigators in the DGBI domain, who will coordinate their research efforts to produce compatible clinical datasets and biosamples on large numbers of DGBI patients, and who operate with sufficiently uniform research methodology to make large multi-center and multi-national research studies quicker and more efficient to implement than previously possible. The first sites in the network will include some of the world's top DGBI centers, and will start systematically collecting data with the RFRI Investigator Platform by the middle of 2020. These will be the following centers:

- KU Leuven, Belgium (PI: Jan Tack, MD, PhD)
- University of California Los Angeles, USA (PI: Lin Chang, MD);
- University of Michigan, USA (PI: Bill Chey, MD);
- Queen's University School of Medicine, Canada (PI: Steve Vanner, MD, MSc)
- Harvard Medical School, USA (PI: Anthony Lembo, MD)
- University of Gothenburg, Sweden (PI: Magnus Simren, MD, PhD)
- Universidad Nacional Autónoma de México (UNAM), Mexico (PI: Max Schmulson, MD)
- University of Bolognia, Italy (PI: Giovanni Barbara, MD, PhD)

These first sites will help to refine and test the unified data collection system and operating procedures of the network. Additional sites will then be invited to join the research network in phases, starting in the second half of 2020, and the number of sites in the network is expected to grow rapidly after that. That expectation is supported by the great interest that DGBI investigators world-wide have shown in joining the RFRI Global Research Network. A preliminary survey among Rome-affiliated researchers in 2018 resulted in 91 investigators in 33 countries expressing strong interest in joining the network (see figure).



Engagement with Industry Consultant. We are pleased to have Doug Levine MD as our external industry consultant. Assistance to the Executive Committee has been provided by advising on pharmaceutical industry perspectives and practices on engagement of external investigators to inform RFRI strategic approaches for establishing research collaborations:

- Supported start-up of Danone project: review of research proposal drafts, budgets, contract, and teleconference minutes
- Supported engagement with prospective research collaborator (Alnylam): reviews of research proposal drafts, company communications, and meeting minutes; provision of rare disease resources for patient-finding for project; participation in teleconferences and on-site protocol planning meeting; review of research protocol and budget drafts

- General activities with Executive Committee: participation in regular meetings; reviews of meeting minutes, reports, and internal planning documents (RFRI infrastructure, sponsorship agreements, ROBOT study proposal)

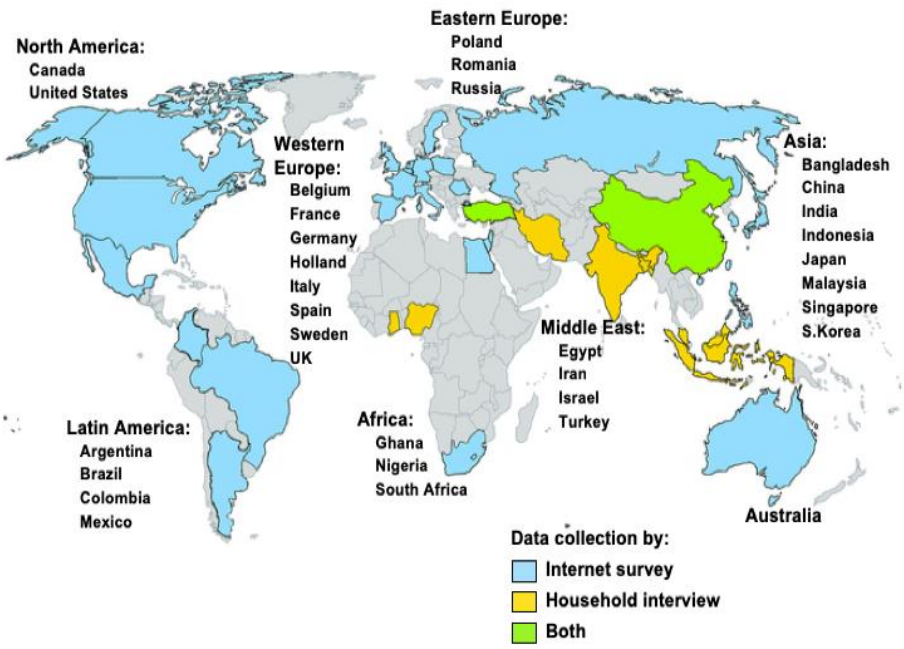
Research Activities

Rome Foundation Global Epidemiology Study Data Analysis and Publication Status. The global study was initiated in 2013 with the establishment of its Executive Committee, a group of 13 leaders in the field who developed the study design and methodology. The primary aims of the global study are to conduct an extensive multinational epidemiological study of all the DGBIs, to obtain reliable regional and local estimates of DGBI prevalence, to evaluate the reasons for differences among regions by collecting data on multiple potentially associated factors, and to generate hypotheses to further advance our understanding of the pathophysiology of IBS and the other DGBIs. Secondary aims are to generate a database that can serve as a source of data mining and be integrated with other similar databases in the future, and to establish a network of FGID experts with a track record of research collaboration on a global scale. A tertiary aim is to establish a repository of translated versions of the Rome IV adult diagnostic questionnaire in multiple languages including linguistic validation (cognitive debriefing) and cultural adaptation.

The planning stage concluded at the beginning of 2016 in advance of the publication of the Rome IV questionnaire. At that time the translation process was begun through a professional translation company (Transperfect Inc.). The questionnaires were translated into 21 languages and localized into an additional 18 versions.

In all, 33 countries participated in the study. Data were collected by Internet survey (Qualtrics, Ltd.) in 26 countries where this was feasible. In 7 countries in which this was not the case we conducted house-to-house personal interviews. In two countries, China and Turkey we conducted both types of survey. The pre-defined demographic parameters were 50% females and 50% males, and an age distribution of 40% for 18-39 years, 40% for 40-64 years, and 20% for 65+ years.

The data collection phase was completed in 2018 with a final database of 73,076 respondents: 36,148 women (49·47%) and 36,928 men (50·53%). Equal sex distribution and the pre-planned age ranges were successfully achieved with both surveying methods. The participating countries and the data collection method in each country are depicted in this map.



In the 26 Internet countries we achieved excellent national geographic representation with close approximation to official census figures in these countries. The household studies were not designed to be nationally representative, but rather to be representative samples of the general population in the communities in which they were conducted. This was accomplished.

We formulated a protocol for Policy and Procedures for Access to the Database, Conduct of Data Analyses, and Publications; in parallel we established a Database Committee, a Statistical Analysis Committee, and a Publications Committee. Initial statistical analyses were conducted by the Central statistical analysis core headed by Dr. Shrikant Bangdiwala at McMasters, Canada. We also vetted candidates for global study statisticians and established regional and local statistical analysis cores. A one and one-half day Global Study Statistical Worshop was held in Barcelona Spain in October 2019 for individuals who will serve as analysts of data for regional and local manuscripts and investigators who intend to be lead authors of manuscripts from the study. The workshop was led by Drs. Sperber, Palsson, and Bangdiwala and was attended by close to 40 participants from around the world.

We completed data analysis for the first global paper and the first manuscript, summarizing the major findings, will be submitted shortly to Gastroenterology. We also submitted two abstracts to DDW 2020 based on the initial study results. Once the first paper is published, the embargo on study results will be lifted and we will begin the process of multiple publications on global, inter-regional, intra-regional, and country levels.

We are in the process of opening a submission website to submit proposal for abstracts or papers based on the study databases. These will be submitted on official online submission forms and all proposals will undergo a review process (including the statistical analysis plan) similar to editorial reviews in medical journals.

We are also in the process of establishing a closed online forum for study investigators and statisticians (consistent with a “chat room”) where free interchange of ideas, questions, and information related to the study will be shared.

Domino Trial

The DOMINO trial (Diet Or Medication in Irritable bowel syNdrOme) is a randomized trial to evaluate the short-term efficacy and long-term health economic impact of a dietary intervention compared to pharmacotherapy with a musculotropic spasmolytic agent for newly diagnosed or newly treated irritable bowel syndrome in primary care. This trial is funded by Belgian Government Money, is pragmatic and aims at optimizing primary care. It uses questionnaires that were developed for the Rome IV Global Epidemiology study in Belgium and also serves as an opportunity to collect biobank material from primary care IBS patients. Patients are randomized to treatment with OB 60 mg t.i.d., the traditional first-line medical therapy, or by a FODMAP lowering diet, provided via a smartphone application. Before and after 8 weeks of treatment, patients completed questionnaires evaluating demographics, stool types, Rome IV criteria, IBS-Symptom Severity (IBS-SSS), anxiety (GAD), depression (PHQ9) and somatization (PHQ15).

As of December 4th, 2019 a total of 466 of the targeted 470 patients were enrolled and 95% of the subjects provided biobanking samples for genetics, serum and stool analysis. Patients with an improvement of at least 50 points on IBS-SSS were considered as a responder. The following paragraphs summarize abstracts regarding this study, which were submitted to FNM 2020 and to DDW 2020.

At baseline, 70 % of these primary care-diagnosed IBS patients fulfill the Rome 4 criteria. (74% female, mean age 42±0.9 years, and mean BMI of 24±0.3). The following IBS-SSS distribution was found: 4, 16, 41, 39 % for normal, mild, moderate, and severe IBS-SSS respectively. Patients were characterized according to the stool pattern: diarrhea (27%), constipation (23%), mixed stool type (38%) and normal (12%).

Respectively 59% and 70% of patients treated with OB and diet were IBS-SSS responders. In the OB group, responders had significantly higher somatization scores compared to non-responders (10.5±0.5 vs 9.0±0.4, p=0.01), but both groups had comparable demographic and other clinical characteristics. Responders to the diet were significantly younger than non-responders (mean age 39±1 vs 44.6±2 (p=0.03). Diet

response was not determined by the stool pattern subtype, but Rome+ patients were significantly more likely to respond to the diet compared to Rome- (p=0.002).

Last patient enrollment is expected around December 10th, 2019. The primary endpoint analysis is anticipated in early February 2020.

ROBOT Project

During this year, the RFRI has planned the **RO**me foundation **B**i**O**marker and phenotyping projec**T** (ROBOT) in detail, to support the launch of this multinational project in early 2020 at a small number of sites, with the aim to expand this project to more sites in the coming years. The aim of ROBOT is to develop a state-of-the-art biobank and database of patients with DGBI, supported by an international network of top international research sites. Patients in the database will be thoroughly characterized as follows: clinical phenotype and associated demographic, medical history, psychosocial and lifestyle factors will be established, fecal, blood and urine samples will be collected and stored in a standardized fashion, and in select sites biopsies from the upper and/or lower GI tract will be collected depending on the predominant symptom profile. The collection of biosamples and data will enable evaluation of different biomarkers in large groups of very well-characterized individuals in different parts of the world and assessment of their validity for use as diagnostic and /or predictive tools. A centralized electronic database will enable development of profiles of available clinical phenotypes and biosamples at any time to assess the feasibility of new studies.

ROBOT will involve leading DGBI research sites that recruit patients in different parts of the world. In the first phase of ROBOT each center will recruit ≥100 patients who fulfill diagnostic criteria (Rome IV) for at least one DGBI, with the aim of having a 50:50 split between predominantly upper, i.e. esophageal and gastroduodenal, and lower, i.e. bowel and anorectal DGBI (to be separately negotiated with each site, depending on their expertise and research focus, with the aim to have an overall 50:50 split across sites). Each site will ideally also include 20-50 healthy controls without current GI symptoms. All patients will complete questionnaires and provide information for the RFRI clinical phenotyping tool (see below). In most patients, blood, fecal and urine samples will also be collected, as well as GI biopsies in some of the sites where this is possible, and the samples will be stored at the individual sites in a local biobank. In select centers, a small number of patients will also undergo physiologic testing. Thus, based on site capabilities, patient characterization / data collection in ROBOT will vary and yield different levels of integrated information from individual sites:

1. RFRI clinical phenotyping tool alone
2. RFRI clinical phenotyping tool and collection of biosamples.

3. RFRI clinical phenotyping tool, collection of biosamples, and performance of physiologic testing.

Each investigator will “own” the samples from his/her patients, and will be included as an author in publications / projects in which his/her samples are used. After discussions with participating investigators, a study management committee will make decisions about prioritization of proposals for sample analyses from individual investigators and/or external collaborators, e.g. RFRI sponsors / academic collaborators. Specifically, if approved, samples will be shipped to analytical centers from the local biobanks; after the analyses are completed, the remainder of the samples will be shipped back to the local biobanks at the sites for continued storage.

The current goal is to start this ambitious project in 6-8 centers during 2020, and expand to more sites in the coming years.

RFRI-Danone Survey

This study focuses on symptoms of bloating and distention in the general population and is currently in final stages of preparation. Data will be acquired via a nationwide population-based Internet survey of adults in three countries: United States, Mexico and United Kingdom. The project research protocol is designed collaboratively by the RFRI and Danone, is subsidized by Danone, and is scheduled to be initiated in 2020.

The study is designed to serve a number of different descriptive and hypothesis-driven aims. The a priori hypotheses to be evaluated are: (a) different personal factors and symptoms characterize the subset of individuals who report bloating or distention compared to those without these symptoms; (b) certain personal factors and symptoms distinguish bloating from distension that may reflect different pathophysiologic mechanisms; and (c) subgroups of individuals meeting Rome IV diagnostic criteria for Functional Abdominal Bloating/Distention will report only bloating or only distention and have different associated characteristics. Evaluation of data pertinent to the last hypothesis may yield identification of characteristic clinical features warranting subtyping of patients that may be amenable to different, more specific forms of treatment. Descriptive aims include: (a) characterizing prevalence, frequency and severity of current (last 24 hours) and chronic bloating and/or distention in the adult population; (b) overlap of these symptoms with other related GI symptoms and Rome IV diagnoses (IBS, functional dyspepsia, functional constipation and functional diarrhea); and (c) quantification of the quality of life impairment and health care utilization effects of having these symptoms. Additionally, a sub-study will address the relationship of bloating and/or distention symptoms with dietary factors in detail.

A total of 6000 adults will be surveyed in the U.S., U.K., and Mexico (2000 survey completers in each country) via a secure Internet survey, using Qualtrics Research Suite survey software. Quota-based sampling will be applied to obtain survey samples with the

same age and sex groups composition in each country: 50% females and 50% males; 40% individuals of ages 18-39 years, 40% of ages 40-64 years, and 20% ages 65 and older. The subject sample in each country will also have nationwide geographic distribution.

The contents of the survey include demographic variables, Rome IV diagnostic questionnaire modules for gastroduodenal disorders and functional bowel disorders, questions about bloating and distention rated separately for the previous 3 months (as opposed to the question on a combination asked in Rome IV), the Intestinal Gas Questionnaire, questions about association of bloating/distension to meals, the PHQ-12 non-GI physical symptom questionnaire, selected medical and health history, questions about medications used regularly (at least once a week), and questions about anxiety and depression symptoms, stress, sleep, exercise, diet, quality of life, height and weight, and healthcare utilization.

A subset of 1500 subjects (500 from each country) of the 6000 who complete the main survey in each of the three countries will be selectively invited to also complete a follow-up sub-study survey two weeks later to retrospectively assess their total diet over the past 3 months. This will be done via the validated 25-minute online VioScreen food frequency questionnaire assessment provided by Viocare Technologies.

This will be the first study to examine both current and chronic presence of bloating/distention and numerous potential associated factors in the same population-based sample. The large and demographically balanced multi-national sample will allow presentation of a comprehensive picture of the scope of these symptoms and their impact in the population, as well as the relative prevalence and overlap of bloating vs. distention. It is anticipated that this project will result in multiple influential scientific publications that will significantly advance the state of knowledge about the nature of these symptoms in the general population. The findings are also likely to help guide future refinement of the Rome diagnostic criteria for functional bloating and distention.

Education Core: Rome-DrossmanCare Communications Program Analyses.

Over the last year the Rome Foundation in collaboration with the Center for Education and Practice of Biopsychosocial Care (DrossmanCare) conducted several workshops, symposia and train the trainer sessions to help clinicians improve their communication skills. The RFRI took on the responsibility to study the value of these programs. Thus, we embedded online questionnaires in all programs to obtain feedback. We also undertook a survey of over 300 patients seeking health care from GI faculty members who underwent a communication workshop at Johns Hopkins medical center. This was done in part to determine the value of the clinician training with regard to patient satisfaction. This involves two validated questionnaires developed by Dr. Drossman: the satisfaction with care scale, and the patient provider relationship (PPR) scale. These questionnaires, in addition to patient general symptoms and anxiety scores will

be used to evaluate patient perceptions both before and after their faculty providers attend the communication workshop. We are currently looking at predictors of patient satisfaction and perception of the PPR through multivariate analysis and will include in these models based on the contribution of the faculty that attended the workshop along with other predictor variables. We will then revise our program based on some of these responses and continue to evaluate all communication programs in future activities.

Consultations with Industry. Over the past year the RFRI consulted with two companies.

- **Transparency and Rose Pharmaceuticals**. Drs. Drossman, Chang and Chey consulted on the protocol of a Phase IIb study evaluating the efficacy and safety of the GLP-1 analogue ROSE- 010 in reducing moderate to severe acute abdominal pain in IBS. The RFRI received $20,000 for this effort.
- **Alnylam Pharmaceuticals**. Upon the request of the company, Dr. Drossman initiated a study proposal that was further modified by Drs. Tack, Simren, Palsson and Bangdiwala to identify hepatic type porphyria (primarily AIP) at multiple sites globally. Dr. Doug Levine served as external industry consultant to the Executive Committee. The initial proposal was approved by the company. Subsequently a full day meeting with the above consultants was held in June of 2019 to finalize the proposal which was submitted to the company. Unfortunately, several months ago a change of senior leadership and a shift in research priorities led the company to inform us that this study was dropped.

Conclusion

For 2019, the RFRI advanced in its position to become a global leader in DGBI research. With the support of Ironwood Pharmaceuticals, we established an efficient infrastructure consisting of an Executive Committee, academic and industry advisory boards and five cores. To date, we consulted with two pharmaceutical companies on their programs, designed and implemented our own epidemiological studies and clinical trials, initiated the ROBOT and Domino programs, established the ability to collect biosamples, and are beginning to analyze and publish the results. The RFRI continues several international studies and is building a global research network to expand our research capability. We believe that these activities will continue to grow over the next year and fulfill our mission: To improve the lives of patients with DGBI through ground-breaking research.