

# DIGEST



UNC  
SCHOOL OF MEDICINE

*Our mission is to advance the biopsychosocial understanding and care of patients with functional GI & motility disorders through research, training and education.*

## IN THIS ISSUE:



POEM AND G-POEM

DR. VAN TILBURG LEAVES UNC CFGIMD

DDW 2017 PUBLICATIONS AND RESEARCH FORUMS

## POEM AND G-POEM: NEW APPROACHES TO TREATMENT OF ESOPHAGEAL MOTILITY DISORDERS AND GASTROPARESIS



*Dr. Ian Grimm has served as Director of the GI Procedures unit at UNC Memorial Hospital since 2000 and has been a faculty member of the Division of Gastroenterology and Hepatology at UNC for 24 years. Accomplished in a wide range of advanced endoscopic procedures, Dr. Grimm has had a longstanding clinical specialty in*

*removal of very large and difficult polyps of the colon and duodenum, principally using endoscopic mucosal resection (EMR) as a minimally invasive solution for patients who are otherwise often referred for surgery.*

*More recently, Dr. Grimm has focused his attention on training in endoscopic submucosal dissection (ESD). ESD is a technically demanding and meticulous form of endoscopic microsurgery initially developed in the 1990s in Japan as a minimally invasive method for treating early gastric cancer. Although ESD can effectively eliminate the need for surgery in selected patients with early cancers of the digestive tract, it is only available at very few centers in the US. After*

*18 months of developing his skills in ESD, Dr. Grimm undertook intensive training during a sabbatical in Japan, where he was able to study with many of the pioneers of ESD and POEM. Since returning from Japan, he has been routinely performing both ESD and POEM procedures on patients from throughout North Carolina and the Southeast.*

Achalasia is a rare condition that develops in about 1.6 of every 100,000 individuals per year. The underlying cause is unknown, but the symptoms of achalasia result from a degeneration of the nerves that regulate muscle coordination in the esophagus. This leads to a failure of relaxation of the lower esophageal sphincter, and persistent difficulty swallowing, or dysphagia. Achalasia can affect people of almost any age, gender, or ethnicity, with a peak incidence between the ages of 30 and 60. The dominant symptoms include difficulty swallowing both liquids and solids, regurgitation, weight loss, and occasionally chest pain.

Peroral endoscopic myotomy, also known as POEM, is a promising new method for treating achalasia and other primary motility disorders of the esophagus

[Continued on Pg 4](#)

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*DIGEST* is a quarterly publication of the UNC Center for Functional GI & Motility Disorders, a center of excellence within the Division of Gastroenterology and Hepatology, School of Medicine, University of North Carolina at Chapel Hill.

Over the past decade, the UNC Center for Functional GI and Motility Disorders has enjoyed significant grant support from a number of private foundations and corporations. These grants have ranged from sponsorships of specific events (symposia or CME courses) to unrestricted grants in support of fellowships and the Center's education and training effort.

The Center's director is **William E. Whitehead, PhD**, Professor of Medicine and Gynecology.

HAVE A QUESTION?

ASK THE CENTER PERSONNEL A QUESTION!

# DIGEST

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Printed on 30% post-consumer  
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## DR. IAN GRIMM; CONTINUED FROM COVER

that is now available at UNC. Initially developed in Tokyo in 2008 by Dr. Haruhiro Inoue, the procedure has been rapidly adopted around the world as a less invasive means of performing a surgical myotomy for relief of motility disorders of the esophagus, especially achalasia. POEM combines the durability of a time-honored surgical operation – the Heller myotomy - with the simplicity and non-invasiveness of an endoscopic procedure.

POEM is performed entirely through the mouth, under general anesthesia, without the need for any external incisions or scars. A recent meta-analysis of 36 studies regarding POEM found that the procedure is both safe and effective, with an initial clinical success rate of 98%. The authors concluded that POEM “warrants consideration as a first-line therapy when an expert operator is available”.[1]

The diagnosis of achalasia usually requires a combination of studies, often including upper endoscopy, radiography (barium swallow), and esophageal manometry. Most patients can be treated successfully with balloon dilation, a surgical Heller myotomy, and now, with POEM. There are pros and cons to each approach, and some patients may ultimately require more than one method of treatment over their lifetime. After any of these treatments, most people find that they can resume a normal diet. Swallowing function will not return to normal, however, because the achalasia esophagus cannot regain normal peristaltic contractions that propel the passage of food. Therefore, following treatment, patients should eat slowly, chew carefully, and remain in an upright posture whenever swallowing, as the esophagus can only empty by gravity. Long-term follow-up is recommended for all achalasia patients, as a risk of symptom recurrence and potential problems caused by acid reflux will remain a concern over time.

All procedures that provide durable symptom relief to patients with achalasia do so by disrupting the lower esophageal sphincter, which normally acts as a barrier to reflux of stomach contents into the esophagus – gastroesophageal reflux (or GER). Therefore, the potential for postoperative heartburn, regurgitation, and other consequences of gastroesophageal reflux need to be considered when discussing all of the various

treatment options for achalasia. The most commonly employed surgical approach to achalasia, laparoscopic Heller myotomy, is usually combined with an anti-reflux operation (fundoplication) which is intended to reduce problems with postoperative GERD. Acid reflux and heartburn sometimes occur following POEM. In the recent meta-analysis, the rate of symptomatic reflux after POEM was only 8.5%, whereas signs of reflux esophagitis were seen on endoscopy in 13% and abnormal acid exposure in the esophagus was detected in 47% of patients at an average of 8 months following the procedure. Whether postoperative GERD is likely to be more problematic after POEM than after a laparoscopic Heller myotomy with fundoplication is an important question for future research. However this condition has generally been easily controlled with acid suppression medications, i.e., proton pump inhibitors (PPIs). Some patients will likely need to continue these medications indefinitely.

In addition to treating achalasia, POEM is often effective in managing other swallowing disorders that are characterized by difficulty swallowing and chest pain due to esophageal spasm (Jackhammer esophagus, diffuse esophageal spasm). A similar procedure can also be performed in the stomach (G-POEM), which involves cutting the pyloric muscle (pyloromyotomy) in order to treat symptoms caused by a failure of the pyloric sphincter to relax (gastroparesis). This approach has been particularly effective in patients who have sustained an injury to the vagal nerve.

Following the POEM procedure, patients are generally observed overnight in the hospital. A barium swallow is typically performed before oral intake can resume. Then a soft diet is started, which is continued for two weeks before progression to a normal diet. Serious complications from POEM have been rare - under 3%, and the need for surgery to treat complications from POEM has been under 1%. [1]

### References

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## DR. VAN TILBURG TAKES NEW POSITION AT CAMPBELL UNIVERSITY



Dr. Miranda A.L. van Tilburg, Ph.D. has worked at the University of North Carolina as an Associate Professor of Medicine since November of 2002. She recently took a position within the Department of Clinical Research at Campbell University in December, 2016.

Dr. van Tilburg has contributed to multiple scientific discoveries while working as a UNC faculty member as well as collaborations involving national and international institutions. She holds committee seats in the American Neurogastroenterology and Motility Society and North American Society for Pediatric Gastroenterology, Hepatology and Nutrition.

Her academic career and interest in psychological medicine started in the Netherlands where she defended her dissertation on homesickness in adults. Through examination of the symptoms associated with this phenomena, she noticed a correlation between emotions, behavior, and the manifestation of physical conditions, such as headaches, fatigue, and gastrointestinal complaints.[3] She picked up on the connections between cognitive factors and physical symptoms and continued her academic career and training in Medical Psychology at Duke University and the University of North Carolina at Chapel Hill.

In the past few years, her research primarily involved the pediatric population; however, her expertise in the field of functional gastrointestinal disorders, specifically functional abdominal pain, allowed her to cross between adult and pediatric populations. The most recognizable areas of research that Dr. van Tilburg has contributed to include mitochondrial DNA in Irritable Bowel Syndrome (IBS) patients and her work on guided imagery for the treatment of gastrointestinal disorders.[1-2]

Dr. van Tilburg has contributed to many important scientific publications, including the development and publication of the Rome IV FGID diagnostic questionnaire and the development and validation of Rome III diagnostic questionnaire for infants and toddlers.[4,5]

Though she is currently a professor at Campbell University, she is still an adjunct professor at UNC and will continue collaborating on current and future research projects.

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1. Van Tilburg MA, Zaki EA, Venkatesan T, Boles RG. Irritable bowel syndrome may be associated with maternal inheritance and mitochondrial DNA control region sequence variants. *Dig Dis Sci.* 2014; 59(7): 1392-7.
2. Palsson OS, van Tilburg M. Hypnosis and Guided Imagery Treatment for Gastrointestinal Disorders: Experience With Scripted Protocols Developed at the University of North Carolina. *Am J Clin Hypn.* 2015; 58(1): 5-21.
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5. van Tilburg MA, Rouster A, Silver D, Pellegrini G, Gao J, Hyman PE. Development and Validation of a Rome III Functional Gastrointestinal Disorders Questionnaire for Infants and Toddlers. *J Pediatr Gastroenterol Nutr.* 2016 Mar;62(3):384-6.

## THE CASE FOR FUNDING FGID RESEARCH

The human gastrointestinal (GI) tract is a complex network of tissues, organs, nerves, fluids, bacteria, hormones, and invariably, something will happen to throw a wrench into our GI homeostasis. Some problems resolve relatively quickly, as in acute gastroenteritis, and sometimes, GI issues can develop and last a lifetime. Medical research in the field of gastroenterology has progressed in leaps and bounds in the past thirty years. New diagnostic criteria and devices, increased understanding of disorders and diseases, and development of new medicines, therapies, and devices has provided a more in depth understanding of why, what, and when things go wrong.

Research conducted through the National Institutes of Health (NIH) and private industry have aided tremendously to our understanding of organic and functional gastrointestinal disorders. However, research funding varies between disease cohorts and can be influenced by legislative lobbying, disease severity, and patient impact. Celiac disease is a genetic disorder where if gluten is ingested, an inflammatory response in the GI tract damages the intestinal mucosa, and can lead to diarrhea, abdominal pain, and weight loss.[1] Inflammatory bowel disease (IBD) is an umbrella term used to identify Crohn's disease and ulcerative colitis and are described as longstanding inflammation within the GI tract, but what causes IBD is still unknown.[2] There are also disease crossovers, where IBD patients are also diagnosed with IBS.[5]

Estimated population prevalence of celiac disease in the United States is 0.40% to 0.95% (400 to 950 people per 100,000) [1], Crohn's Disease at 0.24% (241 per 100,000), and Ulcerative Colitis at 0.26% (263 per 100,000).[2] It is estimated that the prevalence of IBS is 10-15% (10,000 to 15,000 people per 100,000).[3] In 2015, the NIH allocated \$128 million dollars towards funding inflammatory bowel disease research, \$66 million for Crohn's Disease research, and separately an additional 1.68 billion dollars for all other research involving digestive disorders.[4] It is difficult to easily quantify how much money was earmarked specifically for irritable bowel syndrome (IBS), as there is not a

specific category listed, as is the case with IBD and Celiac funding, within the NIH.

In a recent research study of 6,309 Crohn's Disease and Ulcerative Colitis patients, 20.3% (one in five patients) reported also having a diagnosis of IBS. [5] Those who had IBD-IBS diagnosis were more likely to use narcotics and to have a lower quality of life score when compared to patients who only had a diagnosis of IBD. Using the NIH's Federal RePORTER tool [6] to look up studies funded in 2015 containing the text term "irritable bowel syndrome," 80 studies were funded for an approximate cumulative fiscal year award of \$27.19 million dollars. This does not include funding provided by private interests, such as pharmaceutical companies and research development companies.

Herein lies the elephant in the room. Though serious complications can arise from IBD and celiac disease, there is a large population of individuals diagnosed with IBS who experience a wide range of similar painful and debilitating symptoms, health care burdens, work absenteeism, and impairment to quality of life. With a larger population of IBS patients impacted, additional funding and attention is needed for IBS research, similar to IBD and celiac disease.

In 2012, functional GI and motility disorders made up the highest proportion of emergency department visits, with over 941,000 visits compared to Crohn's disease and ulcerative colitis, which when combined, only accounted for an estimated 47,700 visits.[7] Though, from the Peery et. al. article, the overall median hospital admissions cost for IBD is more than IBS by about \$10,000, the higher number of health care visits encumbered by IBS patients has a larger weight over total patient burden.

Studies involving IBS, IBD, and celiac disease have identified patient reported work absenteeism, productivity, health-related quality of life, and increased health care utilization.[1,2,3,5] Patients who have IBS-IBD diagnosis reported significantly higher scores for anxiety, depression, fatigue, pain, and

sleep disturbances than non-IBS IBD patients. [5] IBS patient's indirect costs associated with absenteeism and lost productivity at work account for an estimated \$20 billion annually.[3]

IBD, Celiac disease, and IBS are debilitating and life altering disorders. The symptoms impact almost every aspect of a patient's life. It is time for funding agencies like the NIH and private industry to invest in research for IBS similarly to that of organic GI disorders. If not, the health care, financial, and quality of life burdens will continue to mount, at a disadvantage for IBS patients, health care insurers, and Medicare/Medicaid.

Written by Stefanie Twist

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## RESEARCH SUBJECTS NEEDED

### Accidental Bowel Leakage Self Help Website (FISH)

The UNC Center for Functional GI and Motility Disorders is looking for eligible subjects to participate in the FISH Study/

Researchers in the UNC Center for Functional GI & Motility Disorders are finishing development of a complete 6 week online self-help program designed to enable individuals to reduce or get rid of accidental bowel leakage (fecal incontinence) on their own.

If you have been experiencing accidental bowel leakage, then the researchers would like your help to evaluate their new program in a research study that you can participate in entirely through your own computer.

You may be able to take part in this research study if you;

- Have experienced accidental bowel leakage at least once a week in the past 6 months.
- Are able and willing to log into a website and complete the learning tasks and answer diary questions for a few minutes each night for a six week period.
- Live in North Carolina or Virginia.
- Speak and write fluent English.

No study visits will be required. You will be reimbursed up to \$200 for completing the 6 week online self-help program.

For more information or to enroll in the study, click here to go to the online consent form: <http://bit.ly/1PFbV18> (The link is case sensitive)

## TREATMENT STUDIES

**Principal Investigator**  
**Dr. William E. Whitehead**

### Contact Information

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# DIGESTIVE DISEASE WEEK: ACCEPTED PUBLICATIONS AND PRESENTATIONS

## DDW 2017

Center faculty and investigators will be well represented in presentations and posters at Digestive Diseases Week 2017 May 5-9, located in Chicago, Illinois.

DDW is the premier research and clinical forum for scientists and clinicians within digestive diseases which includes gastroenterology, liver disease and gastrointestinal surgery. The American Gastroenterology Association (AGA) represents gastroenterologists. The UNC Center plays an important role that is spanning this decade in developing programs that focus on research and education for those with functional gastrointestinal disorders.

Saturday, May 6

**Abstract Title:** ESOPHAGEAL SYMPTOMS ARE COMMON AND RELATED TO OTHER FUNCTIONAL GASTROINTESTINAL DISORDERS (FGIDS) IN A WESTERN POPULATION

**Session Type:** Poster

**Authors:** Olafur S. Palsson, Magnus Simren, Ami D. Sperber, Hans Törnblom, William E. Whitehead

**Time:** 12:00pm - 2:00pm

**Location:** South Hall McCormick Place

Saturday, May 6

**Abstract Title:** WHAT DETERMINES WHETHER INDIVIDUALS WITH IRRITABLE BOWEL SYNDROME (IBS) IN THE GENERAL POPULATION SEEK MEDICAL CARE FOR THEIR DISORDER?

**Session Type:** Research Forum

**Authors:** Magnus Simren, Ami D. Sperber, Imran Aziz, William E. Whitehead, Olafur S. Palsson, Hans Törnblom

**Time:** 5:00pm - 5:12pm

**Location:** Session #2435, McCormick Place S406a

Sunday, May 7

**Abstract Title:** SERUM CYTOKINES ARE ELEVATED IN PATIENTS WITH IRRITABLE BOWEL SYNDROME (IBS) BUT LARGELY UNRELATED TO SYMPTOM CHARACTERISTICS

**Session Type:** Research Forum

**Authors:** Olafur S. Palsson, William E. Whitehead, David A. Barrow, Hans Törnblom, Lena Ohman, Magnus Simren, Miranda A.L. van Tilburg

**Time:** 8:30aam - 8:45am

**Location:** Session #3185, McCormick Place S103

Sunday, May 7

**Abstract Title:** HEALTH CARE UTILIZATION FOR ROME IV IRRITABLE BOWEL SYNDROME; A THREE-COUNTRY SURVEY IN THE GENERAL POPULATION

**Session Type:** Research Forum

**Authors:** Magnus Simren, Ami D. Sperber, Imran Aziz, William E. Whitehead, Hans Törnblom, Olafur S. Palsson

**Time:** 8:15am - 8:30am

**Location:** Session #3185, McCormick Place S103

Sunday, May 7

**Abstract Title:** PREVALENCE OF FUNCTIONAL GASTROINTESTINAL DISORDERS IN INFANTS AND TODDLERS ACCORDING TO THE ROME IV CRITERIA

**Session Type:** Poster

**Authors:** Samantha Robin, Catherine Keller, Paul E. Hyman, Samuel Nurko, Miguel Saps, Carlo Di Lorenzo, Robert J. Shulman, Jeffrey Samuel Hyams, Olafur S. Palsson, Miranda A.L. van Tilburg

**Time:** 12:00pm - 2:00pm

**Location:** South Hall, McCormick Place

Sunday May 7

**Abstract Title:** PREVALENCE OF ROME IV FUNCTIONAL GASTROINTESTINAL DISORDERS IN CHILDREN AND ADOLESCENTS IN THE UNITED STATES

**Session Type:** Poster

**Authors:** Catherine Keller, Samantha Robin, Paul E. Hyman, Olafur S. Palsson, Miguel Saps, Carlo Di Lorenzo, Robert J. Shulman, Jeffrey Samuel Hyams, Samuel Nurko, Miranda A.L. van Tilburg

**Time:** 12:00pm - 2:00pm

**Location:** South Hall, McCormick Place



Monday, May 8

**Abstract Title:** THE PREVALENCE AND IMPACT OF OVERLAPPING ROME IV FUNCTIONAL GASTROINTESTINAL DISORDERS ON SOMATISATION, QUALITY OF LIFE, AND HEALTHCARE UTILISATION: RESULTS FROM A THREE-COUNTRY GENERAL POPULATION STUDY

**Session Type:** Research Forum

**Authors:** Olafur S. Palsson, Hans Törnblom, Ami D. Sperber, William E. Whitehead, Magnus Simren

**Time:** 8:15am - 8:30pm

**Location:** Session #4155, McCormick Place S503

Monday, May 8

**Abstract Title:** FUNCTIONAL ABDOMINAL PAIN DISORDERS AMONG CHILDREN AT HIGH RISK FOR AUTISM: A PILOT STUDY TO EXAMINE THE ROLE OF SENSORY HYPERSENSITIVITY AND ANXIETY

**Session Type:** Poster

**Authors:** Sallie W. Nowell, Linda R. Watson, Miranda A.L. van Tilburg

**Time:** 12:00pm - 2:00pm

**Location:** South Hall, McCormick

## MAGNUS SIMREN RETURNS TO UNC



Magnus Simren, MD returned to UNC Center for Functional GI and Motility Disorders in April, 2017. Dr. Simren is a Professor of Medicine at the University of Gothenburg. Dr. Simren continues to play an important role in collaborative research with the Center faculty, presenting at GI Grand Rounds, Fellows GI Epidemiological Conferences, and Fellow Core Curriculum Conferences.

During his collaborative visit, he was appointed as an adjunct faculty member within the Center for Gastrointestinal Biology and Disease at UNC.

Dr. Simren is anticipated to return to UNC in September, 2017 to continue collaborations on ongoing research projects with Drs. Whitehead and Palsson.

## LEGISLATIVE SUPPORT NEEDED TO HELP ADVANCE FUNCTIONAL GI HEALTH RESEARCH BILL

Did you know there is legislation pending in the U.S. House of Representatives that could help aid research efforts into the treatment of functional gastrointestinal disorders? H.R. 1187 “Functional Gastrointestinal and Motility Disorders Research Enhancement Act of 2015” was introduced into the 2017-2018 115th Congress.

This legislation is budget neutral, which means it does not ask for additional money in the budget.

- Expanding basic and clinical research into FGIMDs by implementing the research recommendations of the National Commission on Digestive Diseases,
- Providing support for the establishment of centers of excellence on FGIMDs,
- Supporting innovative approaches to educating health care providers and patients regarding strategies that improve patient-provider relationships and care,
- Directing the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) to provide the necessary funding for the continued expansion and advancement of the FGIMDs research portfolio, and
- Directing NIDDK and the Eunice Kennedy Shriver National Institute of Child Health and Human Development to expand research into FGIMDs that impact children.

Eleven representatives cosponsored this important piece of legislation last year. However, only one representative has cosponsored so far in 2017. This legislation has the potential to help many patients, including active duty military personnel and veterans, who developed a chronic multisymptom illness (which includes IBS) or other functional gastrointestinal disorder due to deployments and stress. (<http://www.dha.org/advocate-change/veterans-issues>)

Rep Sensenbrenner, F. James Jr. [R-WI-5] has and continues to be the sponsor of this legislation.

Senator Thom Tillis (R) from North Carolina has written Stefanie Twist, Center Coordinator for UNC’s Center for Functional GI and Motility Disorders, directly and stated “If HR 2311 comes before the Senate floor, I will carefully consider everything you have stated in making a decision on what is best for North Carolina and the country.”

We need your help as patients, advocates, and health care providers to make this legislation pass the House of Representatives and continue onto the Senate floor. If your representative isn’t listed, contact them today and ask them to cosponsor this important legislation now!

More information about the bill can be found at <https://www.congress.gov/bill/115th-congress/house-bill/1187>



## OPPORTUNITY TO SUPPORT

To donate to the Center, simply print this form, fill in the blanks, and mail to the address

below with your donation. Please be sure to let us know if you are making your contribution to the Alan Wayne Ducoff Memorial Research Fund or directly to the Center, and let us know if you DO NOT wish to be publicly acknowledged.

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