

# Gastrointestinal Experience

*More than 20 staff with experience in GI projects including*

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## A Wealth of Experience

At RTI Health Solutions, we have collaborated with our clients on more than 100 projects researching gastrointestinal (GI) disease, treatment, and complications of GI disease. Our experience includes:

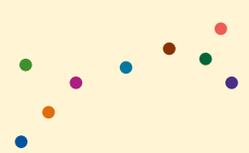
- Celiac disease
- Chronic idiopathic constipation
- Crohn's disease
- Diverticulitis
- Dyspepsia
- Dysphagia
- Gastroesophageal reflux disease (GERD)
- Pediatric GERD
- Gastroparesis
- Gastric cancer
- Irritable bowel syndrome
  - Diarrhea-predominant
  - Constipation-predominant
- Opioid-induced constipation
- Postoperative ileus
- Ulcerative colitis

## Types of Projects

We have implemented studies to help our clients develop strategies in the GI market and to develop and gain market access for products to treat GI disease and complications arising from treatment of GI illnesses. Recent projects have included:

- Clinical trial design and implementation
- Consulting on drug development from preclinical through clinical development
- Patient reported outcomes (PRO) instrument development, evaluation, and validation
- Development of PRO measurement strategies
- Statistical analyses of PRO measures
- Development of PRO dossiers to support label claims
- Exploratory analyses of clinical trial data
- Qualitative physician and patient research
- Health economic models, including
  - Cost-effectiveness models
  - Budget impact models
  - Markov models
- Economic burden of illness studies
- Health care resource utilization studies
- Cohort and case-control studies
- Benefit-risk preference studies
- Risk management programs including development, implementation, and evaluation
- Systematic literature reviews
- Retrospective analyses using longitudinal databases
- Research gap analysis and publication planning
- Development of reimbursement and value communication strategies

*(continued)*



## See How We've Helped Others

### Development of a New PRO Instrument for IBS

We are collaborating with the Critical Path Institute's Patient-Reported Outcome (PRO) Consortium to develop a new PRO instrument for use as a primary endpoint in clinical trials for irritable bowel syndrome (IBS). In cooperation with the FDA and more than 20 pharmaceutical companies, Critical Path Institute (C-Path) formed the PRO Consortium to develop, evaluate, and obtain FDA qualification of PRO instruments for use in clinical trials.

### Phase 3 Clinical Study for Drug Indicated for IBS

We designed and are implementing a phase 3 clinical study for asimadoline, a drug being developed for the treatment of patients with diarrhea-predominant irritable bowel syndrome. As part of this project we developed the study protocol and are managing all aspects of the randomized multicenter clinical study. The study will enroll 600 patients at 150 sites in the United States.

### Benefit-Risk Preference Study in Crohn's Disease

We conducted a benefit-risk analysis using a web-based, choice-format conjoint survey instrument to evaluate patient and gastroenterologist treatment preferences for Crohn's disease. The study found significant variability between gastroenterologists' and patients' tolerance for risk in order to gain benefits of treatment, particularly when patients saw improvement from moderate symptoms to remission. Study results were published in *Journal of Managed Care Pharmacy* 2010;16(8):616-28.

### Prevalence and Impact of Opioid-Induced GI Side Effects

We designed and conducted a web-based survey to assess the prevalence and impact of opioid-induced GI side effects. The survey included responses from more than 2,000 adults in the US who were being treated for chronic pain unrelated to cancer. The study showed that GI side effects, such as nausea and constipation, were common and can be significant, as they can lead to decreased quality of life and increased mortality. The incidence of opioid-related side effects suggests a need for alternative and effective treatments. Study results were published in *Alimentary Pharmacology & Therapeutics* 2008; 27:1224-32.

### Patient Follow-up Survey Assessing Compliance with a Drug Indicated for IBS Risk Management Program

As part of a risk management plan, we conducted a study to measure how well physicians and patients follow the risk management program requirements for prescribing a drug indicated for IBS and to determine how well patients comprehended the information provided to them. Over 4,000 patients enrolled in the study, and the retention rate across multiple follow-up questionnaires was over 95%. As a result of our work, the study sponsor was able to demonstrate high compliance with the risk management program. Results were published in *Alimentary Pharmacology and Therapeutics* 2006;24(5):869-78.

## Selected Recent Publications By Our Staff

**Andrews EB**, Eaton SC, **Hollis KA**, Hopkins JS, Ameen VZ, **Hamm LR**, **Mangel AW**, **Tennis P**, Cook SF. Prevalence and demographics of irritable bowel syndrome: results from a large web-based survey. *Alimentary Pharmacology and Therapeutics* 2005;22:935-42.

Camilleri M, **Mangel AW**, **Fehnel SE**, Drossman DA, Mayer EA, Talley NJ. Primary endpoints for irritable bowel syndrome trials: a review of performance of endpoints. *Clinical Gastroenterology and Hepatology* 2007;5(5):534-40.

Hoyo C, Schildkraut JM, Murphy SK, Chow WH, Vaughan TL, Risch H, Marks JR, Jirtle RL, **Calingaert B**, Mayne S, Fraumeni J Jr., Gammon MD. IGF2R polymorphisms and risk of esophageal and gastric adenocarcinomas. *International Journal of Cancer* 2009;125(11):2673-8.

Johnson FR, **Hauber AB**, **Ozdemir S**, Lynd L. Quantifying women's stated benefit-risk trade-off preferences for IBS treatment outcomes. *Value in Health* 2010;13(4):418-23.

Johnson FR, **Hauber B**, Zdemir S, Siegel CA, Hass S, Sands BE. Are gastroenterologists less tolerant of treatment risks than patients? benefit-risk preferences in Crohn's disease management. *Journal of Managed Care Pharmacy* 2010;16(8):616-28.

**Mangel AW**, **Fehnel SE**. Design of treatment trials in irritable bowel syndrome: opioid agonists and atypical benzodiazepine antagonists. *Neurogastroenterology and Motility* 2008;20(10):1086-93.

**Mangel AW**, **Fehnel SE**. Global endpoints in functional gastrointestinal disease. *Alimentary Pharmacology and Therapeutics* 2005;22(11-12):1162-3.

Spiegel B, Camilleri M, Bolus R, Andresen V, Chey WD, **Fehnel S**, **Mangel A**, Talley NJ, Whitehead WE. Psychometric evaluation of patient-reported outcomes in irritable bowel syndrome randomized controlled trials: a Rome Foundation report. *Gastroenterology* 2009;137(6):1944-53.

**Tennis P**, **Andrews E**, Hickman P, Miller D, **Hollis KA**, **Cook S**. The relationship between dosing of alosetron and discontinuation patterns reported by patients participating in a follow-up programme. *Alimentary Pharmacology and Therapeutics* 2007;25(3):317-22.