MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

**Division of Gastroenterology & Hepatology**
3912 Taubman Center
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Dear Candidate,

Thank you for your interest in our NIH T32 Training Program in Gastrointestinal Epidemiology.

Gastroenterologists and hepatologists trained in clinical research are needed to translate new discoveries in basic science into better patient care, sustain future generations of scientists, and advance scientific innovation. **The purpose of our Training Program is to fulfill these critical needs by providing selected 1st year GI fellows with:** (1) core methodological skills in the design and execution of clinical research; and, (2) a structured, mentored research experience under the guidance of our world-class Core Faculty. With this training, fellows leave GI fellowship poised to compete for tenure-track faculty positions and secure external funding for further career development. Ultimately, we expect our trainees to become independent, NIH-funded researchers who spend at least 75% of their time conducting clinical, outcomes, or health services research.

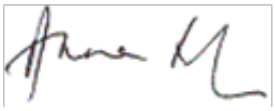
**The goals of the T32 Program are:** (1) completion of a Master's degree focused on the design and execution of clinical research; (2) completion of a focused GI clinical research seminar series and a comprehensive epidemiology/health policy seminar series; (3) successful design, execution, and publication of multiple research projects under the guidance of a team of mentors, including content experts (e.g., gastroenterologists) and methodologists (e.g., epidemiologists); and, (4) preparation of a career development award or other grant application. **Each trainee focuses on a specific topic and completes 3 interrelated projects: (1) a systematic review or meta-analysis; (2) a secondary data analysis; and, (3) design of a prospective study.** These projects provide the foundation and preliminary data for an **NIH K-award application, to be submitted in 3rd year of fellowship.**

**Our training program is greatly enhanced by the rich, collaborative environment of the University of Michigan,** with its vast resources, centers, and research institutes, including: (1) the CTSA-supported Michigan Institute of Clinical and Health Research (MICHR); (2) the Institute for Healthcare Policy and Innovation; and, (3) the VA Center for Clinical Management Research (a VA HSR&D Center of Innovation). Our multi-disciplinary Core Faculty includes expert biostatisticians, epidemiologists, behavioral economists, policy-makers, and translational, clinical, and outcomes researchers from not only the Division of Gastroenterology and Hepatology, but also the Division of General Internal Medicine and the School of Public Health. Most faculty are federally-funded for their ongoing research and offer a broad spectrum of research expertise with multiple levels of established collaboration and many years of experience mentoring trainees.

We look forward to reviewing your application and hope to see you in Ann Arbor in the coming year!

Sincerely,

Sameer D. Saini, MD, MS
Associate Professor of Medicine
Director, GI Faculty Mentoring Program (JF2K)
Michigan Medicine



Anna Lok, MD
Alice Lohrman Andrews Professor
Director, Clinical Hepatology
Assistant Dean for Clinical Research
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Peter D. Higgins, MD, PhD, MSc
Associate Professor of Medicine
Director, Inflammatory Bowel Disease Program
Michigan Medicine

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# T32 TRAINING PROGRAM IN GASTROINTESTINAL EPIDEMIOLOGY
# APPLICATION

## APPLICATION INSTRUCTIONS

The application for our T32 Training Program in Gastrointestinal Epidemiology has three components:

1. Identification of **up to three potential research mentors**: please see the attached list of faculty mentors to help you identify which individuals may be the best fit for your research interests. You can also find more information about each faculty member online, at PubMed, and by searching experts.umich.edu.

2. A one-page overview of your proposed research. This "one-pager" should include a brief introduction to the topic area followed by three proposed projects:
   (a) a systematic review
   (b) a secondary data analysis
   (c) a prospective study

   References are not required. Two examples have been provided to help you as you put together your application.

3. Completion of a "Research Design" task and a "Research Interpretation" task to assess your critical thinking about basic study design and interpretation of data.

**Please keep in mind that you will not be required to work on the projects that you propose in your one-pager.** Rather, this is an exercise to assess your suitability and readiness for the T32 curriculum. Additionally, you will have the option of ranking the T32 track and the clinical track separately.

You should feel free to work with your local mentors as you put together your application materials. Should you have any questions, please feel free to reach out to Melissa Gabriel, our GI Fellowship Program Manager - missrick@med.umich.edu.

**Applications are due by 5 pm EST on October 30, 2020**

## RESEARCH DESIGN TASK

You are seeing an increasing number of patients on call with food impactions due to eosinophilic esophagitis (EoE). Often, these are patients who have already been diagnosed and treated with effective medications, but have simply stopped taking these medications. They usually come in at night after eating multiple pieces of meat at dinner time. The emergency department tries a dose of IV glucagon, which rarely helps, and you end up performing an endoscopy in the middle of the night.

After one of these late-night scoping sessions, you hypothesize that EoE-related food impaction might respond to IV steroids to treat the causative inflammation, followed by IV glucagon, which relaxes the esophagus and allows food to pass. When you wake up in the morning, you decide to outline a randomized controlled trial.

**Please answer the questions below to the best of your ability.** There may not be a good answer to every question. Be sure to justify your choices.

1) What will your intervention and control arms be?

2) How will you select subjects (important inclusion & exclusion criteria)?

3) What endpoint (outcome) data will you collect?

**4) What covariates that could influence the outcome will you collect?**

**5) How will you measure and stratify for baseline severity?**

**6) How would you estimate the sample size?**

## RESEARCH INTERPRETATION TASK

You notice that your interns have become very fond of a newfangled, expensive test for stool infections. They are using it for all inflammatory bowel disease (IBD) admissions to your service. The panel tests for 22 infections in the stool, and results are reported within two hours. You want to determine whether the detected infectious agents are actually impacting the clinical course of IBD, or whether they represent colonization that is clinically irrelevant. You review the test results and clinical data for 400 patients, shown below. The most commonly identified infectious agents across study groups are Clostridium difficile, assorted E. coli, and Norovirus.

**Interpret the results below and discuss the implications.** Escalation of therapy is defined as step-up in intensity of treatment for IBD (to thiopurine or anti-TNF) or IBS (increased use of antispasmodics and/or anti-diarrheals) within 90 days of hospitalization.

| Study Group | N | # With Infectious Agent (%) | Need for Escalation in Patients with Infectious Agent | Need for Escalation in Patients without Infectious Agent |
|---|---|---|---|---|
| Symptomatic CD* | 104 | 37 (36%) | 4/37 | 44/67 |
| Asymptomatic CD | 52 | 12 (23%) | 2/12 | 3/40 |
| Symptomatic UC* | 112 | 42 (39%) | 6/42 | 48/70 |
| Asymptomatic UC | 51 | 5 (9%) | 1/5 | 1/46 |
| Acutely symptomatic IBS-D* | 27 | 17 (57%) | 14/17 | 1/10 |
| Chronic baseline IBS-D | 25 | 4 (16%) | 0/6 | 1/19 |
| Healthy Controls | 52 | 3 (6%) | -- | -- |

*CD = Crohn's disease | UC = ulcerative colitis | IBS-D = irritable bowel syndrome with diarrhea

1) In which group(s) of patients is the presence of an infectious agent associated with a need for escalation of therapy?

2) If you were writing up an abstract for DDW, what main points would make in your results section?

3) What are the limitations of this study?

4) What conclusions would you draw? What are the implications for clinical care?

| LIST OF POTENTIAL MENTORS | | |
|---|---|---|
| **Name** | **Clinical and Research Interests** | **Other Interests** |
| Allen, John | GI healthcare policy, quality of care | Leadership |
| Chey, William | Functional bowel disorders | H. pylori, fecal incontinence, pelvic floor disorders |
| DiMagno, Matt | Acute pancreatitis, chronic pancreatitis, exocrine pancreatic insufficiency | |
| De Vries, Raymond | Mixed-methods research, deliberative methods, intervention design | |
| Fontana, Robert | Liver transplant, acute liver failure | |
| Hayward, Rodney | Execution and interpretation of clinical trials, quality of care | |
| Higgins, Peter | Inflammatory bowel disease, advanced data science | Statistical modeling |
| Lok, Anna | Viral hepatitis | Clinical research in hepatology, research administration and |
| McMahon, Laurence | Delivery of cancer screening services, health care administration | |
| Menees, Stacy | Colorectal cancer screening and quality, functional bowel disorders | |
| Parikh, Neehar | Liver cancer, liver transplant, cirrhosis outcomes | Econometrics, quality of life |
| Rubenstein, Joel | Esophageal disorders | Health services, simulation modeling |
| Saini, Sameer | Colorectal cancer prevention, quality of care, performance measurement | Informed decision making, simulation modeling |
| Sharma, Pratima | Health services research, epidemiology, risk prediction, observational studies | |
| Speliotes, Elizabeth | NAFLD, obesity, bioinformatics | Personalized medicine, genetics |
| Stidham, Ryan | Inflammatory bowel disease, analysis of imaging and other unstructured data | |
| Stoffel, Elena | Hereditary cancers, colorectal cancer risk stratification | |
| Su, Grace | Analytic morphomics in the care of patients with chronic liver disease | Subspecialty care access |
| Vijan, Sandeep | Simulation modeling and economic analysis | |
| Waljee, Akbar | Inflammatory bowel disease, machine learning, predictive modeling | |
| Zikmund-Fisher, Brian | Medical decision-making, risk communication, survey design | Behavioral economics |

## ONE-PAGER EXAMPLE #1

**Title:** Understanding Variation in Use of Monitored Anesthesia Care for Gastrointestinal Endoscopy
**Potential Mentors:** Joel Rubenstein, Eve Kerr

**Background:** I intend to focus on evaluating the factors underlying the marked increase in utilization of monitored anesthesia care (MAC) for endoscopic procedures and designing interventions to decrease overutilization of MAC. MAC is increasingly being utilized for uncertain indications, such as in patients with chronic narcotic and/or alcohol use, and to enhance endoscopy unit efficiency or perceived patient comfort. This has resulted in increased costs and complications. To date, the majority of studies in this area have evaluated MAC usage in the Medicare population. Surprisingly, the VA population represents uncharted territory in studying MAC utilization in endoscopy. The VA represents a unique forum in which to study whether financial incentives represent the primary driving force behind increased utilization of MAC, as VA providers should be less susceptible to these financial incentives in making endoscopic sedation decisions. If significantly increased use of MAC for endoscopy also exists in the VA population, it would strongly suggest that factors other than financial incentives are important drivers of MAC overutilization. This issue has important public health implications, both in terms of promoting more cost-conscious, value-based utilization, and optimizing patient safety and quality of care.

**Project 1 (systematic review):** A comprehensive evaluation of the factors driving increased MAC utilization for endoscopy requires not only a synthesis of the medical literature, but also an examination of the political/regulatory landscape, societal factors (increased use of narcotics, patient intolerance with discomfort), economic factors (endoscopy-unit efficiency, financial incentives for overuse, etc.), and other contributors. This type of critical analysis may not be well suited for a traditional meta-analysis or systematic review. Therefore, for Practicum 1, I intend to prepare a narrative review/"policy brief' in order to better understand the influence that each of these factors has had on increased utilization of anesthesia services for endoscopic sedation. This may include construction of an influence diagram to provide a conceptual framework for understanding the interplay between the above factors. Through this critical synthesis, gaps in our existing understanding of the issue will become apparent, providing opportunities for future research, including in Projects 2 and 3.

**Project 2 (secondary data analysis):** For Project 2, I will perform a retrospective cohort analysis using national VA data to assess changes in utilization of MAC for endoscopy over time in the VA, both nationally and also regionally. My hypothesis is that utilization rates in the VA will have also markedly increased over the past two decades, despite the presence of fewer financial incentives within the VA to drive this overuse. My cohort will consist of Veterans who underwent outpatient endoscopy from 1993-2013. I will use CPT codes 00810 (anesthesia assistance for lower endoscopy) and 00740 (anesthesia assistance for upper GI endoscopy), medication administration records, and/or endoscopy reports to identify cases done with anesthesia assistance. Patient demographics, health status/comorbidities, and other data will be analyzed to identify patient and provider characteristics that may predict use of MAC. We will also assess for variation by region and individual VA facilities, hypothesizing that MAC utilization is more prevalent in the VA in regions where MAC utilization is more prevalent in non-VA facilities (i.e., New York, New Jersey, Nevada).

**Project 3 (design of a prospective study):** While there are a number of economic, social, and regulatory factors that are theoretical drivers of the increased use of anesthesia services for endoscopy, little is known about the relative impact of these factors and their role in provider decision-making, which is often discretionary. A literature review reveals no existing qualitative studies examining this issue. Project 3 would draw from the findings of Project 2 (which we predict will show regional variation in MAC utilization rates at VA facilities). For Project 3, I will design a qualitative study using semi-structured interviews with a cohort of providers (including GI, PCPs, anesthesiologists, and others) from high utilization and low utilization VA regions/facilities to determine, through thematic content analysis, the extent to which various factors influence physician decision-making and attitudes regarding when to recommend MAC for endoscopy. If no regional variation is found among VA facilities, I will design an identical study using non-VA facilities/providers. Understanding provider motivations is key to devising incentive programs to promote appropriate utilization of anesthesia services for endoscopic procedures only in patients for whom its benefits outweigh the increased costs and risk of adverse events associated with its use.

## ONE-PAGER EXAMPLE #2

**Title:** Improving Appropriate Use of Gastroprotection in Patients on Anticoagulation
**Potential Mentors:** Sameer Saini, Rod Hayward

**Background:** Gastrointestinal (GI) bleeding is a common and morbid medical condition, resulting in nearly 600,000 hospitalizations each year. Use of proton-pump inhibitors (PPIs) and, to a lesser degree, H2 receptor antagonists (H2RAs), reduces the risk of upper GI bleeding (UGIB) compared with no therapy, and experts recommend that PPIs be used in patients at high risk for GI bleeding. But few patients on NSAIDs receive concomitant treatment with gastroprotective agents (GPAs). Given the underuse of GPAs in patients at increased risk for UGIB, we are in need of adaptable and effective interventions to promote appropriate use.

**Project 1: Systematic review:** Currently, multiple risk models exist for the prediction of morbidity and mortality associated with UGIB and the prediction of bleeding from any source in the setting of anticoagulation. However, to our knowledge, no risk model has been developed to predict risk specifically of a future UGIB. The purpose of this systematic review will be to define the summary relative risks of established clinical factors for predicting UGIB and to perform a narrative review of existing predictive scoring systems. We will systematically search PubMed, Web of Science, Medline, and Embase using the MESH headings "gastrointestinal hemorrhage," "risk assessment," and "risk factors" for relevant articles or abstracts. We will calculate hazard ratios separately for each risk factor identified. We will summarize the performance characteristics of the selected scoring systems. The results of this meta-analysis can guide the future development of risk models for the prediction of UGIB based on patient factors, and the assessment of UGIB risk among the study sample for the retrospective study described in Project 2.

**Project 2: Secondary data analysis:** While previous studies have documented suboptimal rates of adherence to GPAs in various clinical settings, no studies have evaluated the use of GPAs in the setting of an anticoagulation clinic. The Michigan Anticoagulation Quality Improvement Initiative (MAQI2) is an ongoing regional collaborative involving five healthcare systems in Michigan. The MAQI2 collaborative collects data from each patient visit on a variety of relevant variables, including demographics, comorbidities, indication for and type of anticoagulation, use of other medications, and laboratory studies such as CBC and INR. The primary goal of the secondary data analysis will be to quantify the use of GPAs among patients on anticoagulation, stratified according to bleeding risk. We will test for statistically significant differences across groups using chisquared tests and perform multivariable analysis to identify independent predictors of GPA use. Secondary aims are to quantify changes in prescription of GPAs since 2009 (the first year of controversy over drug interactions between PPIs and thienopyridines), stratified by indication; and to determine how the class and specific agent used for gastroprotection have changed since 2009. Our hypotheses are that: (1) the use of GPAs is <50% across subgroups; and, (2) the use of omeprazole specifically has decreased relative to other PPIs. This project has been approved by the MAQI2 scientific board, which expressed interest in the possibility of future interventions to improve adherence.

**Project 3: Prospective study:** Assuming Project 2 demonstrates a need; we will conduct a formative evaluation of the MAQI2 sites to inform the development of a multifaceted intervention to increase the appropriate use of GPAs. We will investigate system-, clinic-, provider-, and patient-level factors, including capabilities of the medical record systems, means of communication with primary care, knowledge and attitudes of patients and providers surrounding use of GPAs, patient demographics and prescription insurance coverage mix. Some clinical sites have previously managed dosing of anticoagulants prescribed by other providers but have not routinely initiated new drugs. Clinic policies and scope of practice of the staff will also therefore be relevant. We anticipate that this project will be funded by Blue Cross Blue Shield of Michigan, which also funds MAQI2.

Ultimately, this project can guide implementation of a multifaceted, evidence-based intervention, for example educational outreach to patients and providers, computerized decision support and performance feedback, and delegation of prescribing responsibility to pharmacists.