Principal Investigator

First Name: Shane
Last Name: Goodwin
Degree: PhD, BSc
Primary Affiliation: Western University, Ontario, London, Canada
E-mail: shane.goodwin@lhsc.on.ca
State or Province: Ont
Country: Canada

General Information

Key Personnel (other than PI):
First Name: Dhruv
Last name: Ahuja
Degree: MBBS
Primary Affiliation: Indira Gandhi Hospital, New Delhi, India
SCOPUS ID:
Requires Data Access? Yes

First Name: Sudheer
Last name: Kumar
Degree: MBBS, MD, DM
Primary Affiliation: University of Western Ontario
SCOPUS ID:
Requires Data Access? Yes

First Name: Vipul
Last name: Jairath
Degree: BSc, MD, PhD
Primary Affiliation: University of Western Ontario
SCOPUS ID:
Requires Data Access? No

Are external grants or funds being used to support this research?: No external grants or funds are being used to support this research.
How did you learn about the YODA Project?: Scientific Publication

Conflict of Interest

https://yoda.yale.edu/wp-content/uploads/2025/02/YODA-COI-DhruvAhuja.pdf
https://yoda.yale.edu/wp-content/uploads/2025/02/Sudheer-COI-YODA.pdf
https://yoda.yale.edu/wp-content/uploads/2025/02/Jairath-V-COI-YODA.pdf
https://yoda.yale.edu/wp-content/uploads/2025/02/Goodwin_YODA-COI.pdf

Certification

Certification: All information is complete; I (PI) am responsible for the research; data will not be used to support litigious/commercial aims.
Data Use Agreement Training: As the Principal Investigator of this study, I certify that I have completed the YODA Project Data Use Agreement Training

1. NCT01551290 - CR018769; REMICADEUCO3001 - A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy and Safety of Infliximab in Chinese Subjects With Active Ulcerative Colitis
2. NCT00036439 - C0168T37 - A Randomized, Placebo-controlled, Double-blind Trial to Evaluate the Safety and Efficacy of Infliximab in Patients With Active Ulcerative Colitis
3. NCT00096655 - C0168T46 - A Randomized, Placebo-controlled, Double-blind Trial to Evaluate the Safety and Efficacy of Infliximab in Patients With Active Ulcerative Colitis
4. NCT01863771 - CNTO148UCO3001 - A Safety and Effectiveness Study of Golimumab in Japanese Patients With Moderately to Severely Active Ulcerative Colitis
5. NCT00487539 - C0524T17 - A Phase 2/3 Multicenter, Randomized, Placebo-controlled, Double blind Study to Evaluate the Safety and Efficacy of Golimumab Induction Therapy, Administered Subcutaneously, in Subjects with Moderately to Severely Active Ulcerative Colitis
6. NCT00488631 - C0524T18 - A Phase 3 Multicenter, Randomized, Placebo-controlled, Double-blind Study to Evaluate the Safety and Efficacy of Golimumab Maintenance Therapy, Administered Subcutaneously, in Subjects With Moderately to Severely Active Ulcerative Colitis
7. NCT00336492 - C0168T72 - A Phase 3, Randomized, Open-label, Parallel-group, Multicenter Trial to Evaluate the Safety and Efficacy of Infliximab (REMICADE) in Pediatric Subjects With Moderately to Severely Active Ulcerative Colitis
8. NCT00488774 - C0524T16 - A Phase 2/3 Multicenter, Randomized, Placebo-controlled, Double-blind Study to Evaluate the Safety and Efficacy of Golimumab Induction Therapy, Administered Intravenously, in Subjects With Moderately to Severely Active Ulcerative Colitis
9. NCT02407236 - CNTO1275UCO3001 - A Phase 3, Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Protocol to Evaluate the Safety and Efficacy of Ustekinumab Induction and Maintenance Therapy in Subjects With Moderately to Severely Active Ulcerative Colitis

What type of data are you looking for?: Individual Participant-Level Data, which includes Full CSR and all supporting documentation

Research Proposal

Project Title

Impact of disease and patient specific factors on the efficacy and safety of advanced therapies in moderate-to-severe Ulcerative colitis

Narrative Summary:

Ulcerative Colitis (UC) is a chronic life-long condition associated with symptoms of abdominal pain and bloody stools. Our study aims to expand on the factors that impact the intestinal healings and how they can be managed. Some of those factors are modifiable and thus can be controlled. Others which are non-modifiable can help us strategize the treatment plans according to their presence. Therefore, it's crucial to understand how individual factors based on demography, disease activity during the beginning give us a clue about the long-term control of disease. This will help optimize treatment according to patient centered care.

Scientific Abstract:

Background: IBD is a chronic life-long disease affecting the intestines. In the last decade, several

highly efficacious medications have emerged to control the burden of the disease. The treatment effect and safety also depend on factors other than the medication itself and the effect of one medication may be variable depending on factors interacting with its effect. Patient and disease specific characteristics may impact the efficacy and safety of the advanced biological agents for UC. The modifiable factors may be controlled, optimize treatment strategy for those with non-modifiable factors, identify those at risk of poorer outcomes and requirement of regular monitoring.
Objective: The primary objective of this study is to assess if disease and patient specific factors influence efficacy and safety based on of investigational drug in induction trials of Ulcerative Colitis.
Study design: This is a pooled post hoc analysis of multiple phase 3 clinical trials studying advanced therapies in Ulcerative colitis.
Participants: Patients with ulcerative colitis
Main Outcome Measures: The main outcome will be clinical remission. The secondary outcome measures include endoscopic response/remission, infections and serious adverse events.
Statistical Analysis: Individual level data using the modified Poisson regression will be used to quantify drug effect modification by patient and disease characteristics to be studied on the risk ratio scale (Zou 2004). Study-specific estimates and the 95% two-sided confidence intervals will be obtained for outcomes of interest.

Brief Project Background and Statement of Project Significance:

Patient and disease specific characteristics may impact the efficacy and safety of the advanced biological agents for UC. The modifiable factors may be controlled, optimize treatment strategy for those with non-modifiable factors, identify those at risk of poorer outcomes and requirement of regular monitoring.

1. Evidence on impact of patient and disease specific characteristics on treatment efficacy and safety, thereby facilitating positioning of therapies across different disease severity. This will help in optimal management of UC based on patient-centered care.

2. The central hypothesis is that these patient and disease specific characteristics will impact the efficacy and safety of the advanced biological agents for UC. The rationale for this study is to control modifiable factors, optimize treatment strategy for those with non-modifiable factors, identify those at risk of poorer outcomes and requirement of regular monitoring.

Specific Aims of the Project:

The primary objective of this study is to assess if disease and patient specific factors influence efficacy and safety based on of investigational drug in induction trials of Ulcerative Colitis.
Aim #1: assess if disease severity (based on modified Mayo endoscopic score 2 and 3) at baseline has impact on the efficacy and safety of the biological agents.
Aim #2: assess impact of smoking status on the efficacy and safety of biological agents
Aim #3: impact of disease duration on efficacy and safety of the biological agents
Aim #4: assess if geographical location of study makes an impact on both efficacy and safety of the biologics
Aim #5: assess whether differences in efficacy and safety differ based on age, sex and race
Aim #6: assess the impact of baseline corticosteroid use on the efficacy and safety of biological agents
Aim #7: assess how prior exposure to medications affects the efficacy and safety. This will be assessed in patients who have prior non-response, inadequate response or intolerance.
The central hypothesis is that patient and disease characteristics impact the efficacy and safety of the biological agents for UC. The rationale for this study is to control modifiable factors, optimize treatment strategy for those with non-modifiable factors.

Study Design:

Meta-analysis (analysis of multiple trials together)

What is the purpose of the analysis being proposed? Please select all that apply.

New research question to examine treatment effectiveness on secondary endpoints and/or within subgroup populations

New research question to examine treatment safety

Participant-level data meta-analysis

Meta-analysis using data from the YODA Project and other data sources

Research Methods

Data Source and Inclusion/Exclusion Criteria to be used to define the patient sample for your study:

This is an individual participant data (IPD) meta-analysis to assess whether the efficacy and safety differ based on prior clinical history or patient-related characteristics for patients with moderate to severe Ulcerative colitis (UC). Recently published pivotal phase 3 CD trials were identified. IPD (baseline demographics and disease characteristics) will be obtained for induction and maintenance trials.

There are no inclusion or exclusion criteria and all individuals within each requested clinical trial will be included.

The data from the YODA platform will be combined with studies from the Vivli platform. The external studies included in the analysis are as follows:
NCT00853099
NCT02065622
NCT01550965
NCT00385736
NCT00408629
NCT03524092
NCT03518086
NCT01458951
NCT01465763
NCT00783718
NCT02039505
NCT02497469
NCT00790933
NCT02611830

Primary and Secondary Outcome Measure(s) and how they will be categorized/defined for your study:

Different definitions of efficacy outcomes:

1. The definition of clinical remission in UC will be based on Mayo Clinic score: stool frequency sub-score (SF) <= 1, rectal bleeding sub-score of 0 and endoscopic sub-score <= 1

2. Endoscopic remission will be defined as endoscopic sub-score of 0

3. Endoscopic improvement will be reported when endoscopic sub-score of 0/1 will be achieved

4. PRO2 remission will be described as SF <= 1 and RB = 0 (SF = stool frequency sub score and RB = rectal bleeding sub score)

Different definitions of safety outcomes:

1. Infections -- any infections as recorded in the data

2. Serious adverse events -- as recorded and described in the data

Secondary : Change in CRP/FCP, Change in total MCS score and change in each subcomponent of MCS

Main Predictor/Independent Variable and how it will be categorized/defined for your study:

The following outcomes will be assessed:

- Prior exposure to biologics
- Prior failure to biologics
- Prior intolerance to biologics
- Duration of disease (in years)
- Smoking status -- Ever smoked vs Never smoked
- Baseline corticosteroids use yes/no
- Baseline disease activity- modified mayo endoscopic score 2/3

Other Variables of Interest that will be used in your analysis and how they will be categorized/defined for your study:

Covariates of interest: We will adjust for multiple confounding variables during the baseline period including baseline demographics and disease characteristics. Key patient related factors include age, sex, BMI, race and smoking. Laboratory findings will include baseline hemoglobin, albumin, C-reactive protein and fecal calprotectin. Disease specific factors include medical history, UC disease history (extent, severity, activity), endoscopic findings, other comorbid conditions, disease activity indices, self-reported measures of health and medication history. From all these available data, we will review all clinically relevant variables collected in the trial (<= 10% missingness), remove highly collinear variables, and impute any missing information using chained random forests with predictive mean matching.

Statistical Analysis Plan:

Appropriate descriptive statistics will be presented for demographic and baseline characteristics for both the entire study sample and according to each variable of interest. In order to assess our primary outcome (clinical/endoscopic remission), we will analyze individual level data using the modified Poisson regression to quantify modification of new drug effects by race/ethnicity on the risk ratio scale (Zou 2004). Study-specific estimates and the 95% two-sided confidence intervals will be obtained for outcomes of interest (clinical and endoscopic remission). To obtain overall estimates and 95% confidence intervals of all studies, we will apply the extended modified Poisson regression model (Zou et al., 2013) with studies being considered as clusters. The same analysis will be performed for the other efficacy outcomes (including endoscopic improvement and PRO2 remission) and safety outcomes (infections and serious adverse events).

To assess the additional endpoints for the UC trials, appropriate regression methods for continuous data will be used. All analyses will be adjusted for other patient characteristics including age, sex, and disease duration. Results will be reported in terms of treatment effects (mean differences in scores) for patients in non-White race/ethnicity and non-Hispanic whites. Two-sided 95% confidence intervals and associated p-values will be presented. The focus of this project is the coefficient estimation for the interaction term.

Software Used:

R

Project Timeline:

Project start date: June 1, 2025
Analysis completion date: November 1, 2025
Abstract and manuscript drafted: January 1, 2026
Submission to journal: February 1, 2026

Dissemination Plan:

We anticipate that analysis will result in manuscript in a specialty gastrointestinal or Inflammatory Bowel Disease journal such as: Alimentary Pharmacology and Therapeutics, Gut, Gastroenterology or Clinical Gastroenterology and Hepatology. We also anticipate the sharing of results through presentations at national gastroenterology conferences like Digestive Disease Week (DDW) or American College of Gastroenterology (ACG).

Bibliography:

1. Zou G. A modified poisson regression approach to prospective studies with binary data. Am J Epidemiol. 2004 Apr 1;159(7):702-6. doi: 10.1093/aje/kwh090. PMID: 15033648.
2. Zou GY, Donner A. Extension of the modified Poisson regression model to prospective studies with correlated binary data. Stat Methods Med Res. 2013 Dec;22(6):661-70. doi: 10.1177/0962280211427759. Epub 2011 Nov 8. PMID: 22072596.
3. Nguyen NH, Kurnool S, Dulai PS, Boland BS, Sandborn WJ, Singh S. Short Disease Duration Is Associated With Increased Risk of Treatment Failure in Biologic-Treated Patients With Ulcerative Colitis. Inflamm Bowel Dis. 2020 Aug 20;26(9):1429-1435. doi: 10.1093/ibd/izz276. PMID: 31748806; PMCID: PMC7441095.
4. Iril Lovise Monstad, Inger Camilla Solberg, Milada Cvancarova, Oistein Hovde, Magne Henriksen, Gert Huppertz-Hauss, Eva Gunther, Bjørn Allan Moum, Njaal Stray, Morten Vatn, Ole Hoie, Jørgen Jahnsen, Outcome of Ulcerative Colitis 20 Years after Diagnosis in a Prospective Population-based Inception Cohort from South-Eastern Norway, the IBSEN Study, *Journal of Crohn's and Colitis*, Volume 15, Issue 6, June 2021, Pages 969--979, https://doi.org/10.1093/ecco-jcc/jjaa232
5. Fumery M, Singh S, Dulai PS, Gower-Rousseau C, Peyrin-Biroulet L, Sandborn WJ. Natural History of Adult Ulcerative Colitis in Population-based Cohorts: A Systematic Review. Clin Gastroenterol Hepatol. 2018 Mar;16(3):343-356.e3. doi: 10.1016/j.cgh.2017.06.016. Epub 2017 Jun 16. PMID: 28625817; PMCID: PMC6658168.
6. Safroneeva E, Vavricka SR, Fournier N, Straumann A, Rogler G, Schoepfer AM. Prevalence and Risk Factors for Therapy Escalation in Ulcerative Colitis in the Swiss IBD Cohort Study. Inflamm Bowel Dis. 2015 Jun;21(6):1348-58. doi: 10.1097/MIB.0000000000000368. PMID: 25806845; PMCID: PMC4450965.
7. Bernstein CN, Ng SC, Lakatos PL, Moum B, Loftus EV Jr; Epidemiology and Natural History Task Force of the International Organization of the Study of Inflammatory Bowel Disease. A review of mortality and surgery in ulcerative colitis: milestones of the seriousness of the disease. Inflamm Bowel Dis. 2013 Aug;19(9):2001-10. doi: 10.1097/MIB.0b013e318281f3bb. PMID: 23624887.
8. Feagan, B. G., Rubin, D. T., Danese, S., Vermeire, S., Abhyankar, B., Sankoh, S., ... & Smyth, M. (2017). Efficacy of vedolizumab induction and maintenance therapy in patients with ulcerative colitis, regardless of prior exposure to tumor necrosis factor antagonists. *Clinical Gastroenterology and Hepatology*, *15*(2), 229-239.
9. Singh, S., George, J., Boland, B. S., Vande Casteele, N., & Sandborn, W. J. (2018). Primary non-response to tumor necrosis factor antagonists is associated with inferior response to second-line biologics in patients with inflammatory bowel diseases: a systematic review and meta-analysis. *Journal of Crohn's and Colitis*, *12*(6), 635-643.
10. Gisbert, J. P., & Chaparro, M. (2021). Primary failure to an anti-TNF agent in inflammatory bowel disease: switch (to a second anti-TNF agent) or swap (for another mechanism of

action)?. *Journal of Clinical Medicine*, *10*(22), 5318.
11. Casanova, M. J., Chaparro, M., Mínguez, M., Ricart, E., Taxonera, C., García-López, S., ... & Gisbert, J. P. (2020). Effectiveness and safety of the sequential use of a second and third anti-TNF agent in patients with inflammatory bowel disease: results from the Eneida registry. *Inflammatory Bowel Diseases*, *26*(4), 606-616.

Supplementary Material:

https://yoda.yale.edu/wp-content/uploads/2025/02/Supplementary-Material-2025_0096_medDRA-training-confirmation.pdf
https://yoda.yale.edu/wp-content/uploads/2025/03/2025_0096_Supplementary.docx