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Original Article

A multivariable prediction model to stratify risk of 90-day rehospitalization among adults with ulcerative colitis

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Abstract

Background: Individuals with ulcerative colitis (UC) are frequently re-hospitalized for persistent or recurrent severe disease flares. Accurate prediction of the risk of early re-hospitalization at the time of discharge could promote targeted outpatient interventions to reduce this risk.

Methods: We conducted a retrospective study in adults with UC admitted to The Ottawa Hospital between 2009 and 2016 for an acute UC-related indication. We ascertained candidate demographic, clinical, and health services predictors through medical records and administrative health databases. We derived and bootstrap validated a multivariable logistic regression model of 90-day UC-related re-hospitalization risk. We chose a probability cut point that maximized Youden's index to differentiate high-risk from low-risk individuals and assessed model performance.

Results: Among 248 UC-related hospitalizations, there were 27 (10.9%) re-hospitalizations within 90 days of discharge. Our multivariable model identified gastroenterologist consultation within the prior year (adjusted odds ratio [aOR] 0.11, 95% confidence interval [CI], 0.04-0.39), male sex (aOR 3.27, 95% CI, 1.33-8.05), length of stay (OR 0.94, 95% CI, 0.88-1.01), and narcotic prescription at discharge (OR 1.96, 95% CI, 0.73-5.27) as significant predictors of 90-day re-hospitalization. The optimism-corrected *c*-statistic value was 0.78, and the goodness-of-fit test *P*-value was .09. The chosen probability cut point produced a sensitivity of 77.8%, specificity of 80.9%, positive predictive value (PPV) of 33.0%, and negative predictive value (NPV) of 96.7% in the derivation cohort.

Conclusions: A limited set of variables accessible at the point of hospital discharge can reasonably discriminate re-hospitalization risk among individuals with UC. Future studies are required to validate our findings.

Key words: inflammatory bowel disease; ulcerative colitis; re-hospitalization; risk stratification; predictive model.

Background

Inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are highly morbid conditions associated with high rates of hospitalizations, surgeries and work disability.[1–3] The annual total direct healthcare cost for IBD in Canada in 2023 is estimated at $5.38 billion, which may still be an underestimate of the true cost.[4,5] Rising IBD prevalence and ballooning healthcare costs demand cost-effective strategies to continue to deliver high-quality care.

Close to half of individuals with IBD have UC, and these patients have increased risks of disease-related hospitalizations.[6,7] One in 8 adults with UC is hospitalized annually in Ontario, Canada.[6] Over 20% of UC-related hospitalizations lead to hospital re-admissions within a year, with predictors including extensive colitis, greater comorbidity burden, chronic pain, malnutrition, need for colectomy, and admission to a house staff service.[8–12] Re-admissions are associated with increased length of stay (LOS) and surgical procedures, contributing to further morbidity and costs.[13] Re-hospitalization within 90-days may partly reflect suboptimal inhospital and/or post-discharge care and presents an opportunity for understanding preventable admissions.[14] While previous studies have identified predictors of re-hospitalization, few studies have modelled the cumulative contribution of multiple risk factors and protective factors on re-hospitalization risk in this population.[8–12] Therefore, we

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sought to develop a multivariable model to predict the risk of 90-day re-hospitalization amongst persons with UC admitted to hospital for a UC-related indication. This could identify individuals for targeted outpatient intervention.

Methods

Study cohort and data sources

We conducted a retrospective study of all adults (age ≥ 18 years) with a new or established diagnosis of UC admitted to The Ottawa Hospital for a UC flare or UC-related complication (excluding bowel cancer) between January 1, 2009 and March 31, 2016. The Ottawa Hospital is a tertiary care hospital and IBD referral centre, serving a population of more than 1.2 million people across Eastern Ontario. We identified potential participants through the Ottawa Hospital Data Warehouse, a repository of hospitalizations, emergency department visits, day surgery visits (including endoscopy), and investigations (including laboratory data, pathology, and diagnostic imaging) occurring at The Ottawa Hospital. We queried all adults with 1 or more hospital encounters associated with a discharge diagnosis of CD (International Classification of Diseases (ICD), 10th Version (ICD-10) code K50.x), UC (ICD-10 code K51.x), "noninfective gastroenteritis and colitis, unspecified" (ICD-10 code K52.9) or "indeterminate colitis" (ICD-10 code K52.3). The medical records of these patients were manually reviewed by 2 study investigators (S.G. and S.K.M.) to identify individuals with UC who were admitted to the hospital for a UC-related indication and to collect variables of interest for model building.

Following data collection, we deterministically linked these individuals to province-wide health administrative datasets for Ontario, Canada (held at ICES) to ascertain hospital re-admissions across Ontario for an IBD-related indication with 90 days of index hospitalization and to collect additional variables for model building. ICES is a not-for-profit research institute encompassing a community of research, data and clinical experts, and a secure and accessible array of Ontario's health-related data. Its legal status under Ontario's health information privacy law allows it to collect and analyze healthcare and demographic data, without consent, for health system evaluation and improvement. Administrative, clinical, and demographic information pertaining to hospitalizations across Canada are comprehensively captured in the Canadian Institutes of Health Information Discharge Abstract Database (CIHI-DAD).[15] We defined hospital re-admission for an IBD-related indication in the CIHI-DAD as one that reported a most-responsible, co-morbid, or hospital transfer diagnosis on the discharge abstract that was compatible with an IBD-specific diagnosis (ICD-10 K50.x, K51.x), as per previous studies.[11,16] We included the diagnosis codes for Crohn's disease to avoid excluding hospitalizations with diagnostic misclassification in health administrative data. We excluded individuals who did not have valid and continuous healthcare registration in Ontario for at least 1 year prior to the date of admission or 90 days following the date of discharge, as these time periods were necessary to ascertain several predictor variables and the outcome, respectively. We also excluded any individuals without a valid ICES identification number (an encrypted identifier based on a health card number), which is necessary for the deterministic linkage of individual residents across datasets.

The study protocol was approved by the Research Ethics Boards of the Ottawa Health Sciences Network and Sunnybrook Health Sciences Centre, as well as the ICES Privacy Officer.

Candidate predictors and outcomes

We ascertained candidate predictors for eligible participants through chart review and linkage to province-wide health administrative datasets. We used established macros at ICES to define the Charlson comorbidity score and rural–urban status of residence for each individual at the time of index hospital admission.[17] The candidate predictor list (Supplementary Tables 1 and 2) encompassed demographic, clinical, and healthcare utilization factors occurring prior to or during index hospitalization that could impact UC prognosis and re-hospitalization risk, based on literature review and author consensus.

We defined our outcome as 90-day hospital re-admission for a UC-related indication. As all Canadians are publicly insured to access health services anywhere in the country, hospital re-admissions occurring outside Ontario would not have been captured in ICES datasets; we anticipate that less than 5% of IBD-related re-hospitalizations in this study would have fallen into that category.

Analytic methods

We performed stepwise multivariable logistic regression to model 90-day UC-related hospital re-admission. Each candidate predictor that had a significant bivariate association with the outcome at a *P*-value of <.2 would enter the model (in order of ascending *P*-value) and a variable would be retained in the model if it maintained an independent association with the outcome at a *P*-value of <.1 following entry of other variables.

We assessed model performance based on the discriminatory capacity (*c*-statistic), calibration (Hosmer–Lemeshow goodness-of-fit test) and tests of diagnostic accuracy (sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), negative likelihood ratio (NLR), false positive rate (FPR), and false negative rate (FNR)).[18] We chose the optimal probability cut point in our model (to decide on the need for early post-discharge outpatient intervention) to maximize Youden's index (*J*-index), which provides equal weighting to the sensitivity and specificity of diagnosing the outcome of interest. The FPR is the proportion of individuals who did not undergo re-admission and who were incorrectly predicted to be at high risk of readmission by the model. The FNR is the proportion of individuals who were re-admitted within 90 days and who were incorrectly predicted to be at low risk of readmission by the model. We performed bootstrap internal validation, using 200 bootstrapped samples, to derive the "optimism-corrected" *c*-statistic value (which downgrades model performance to approximate expected discriminatory capacity on external validation).

Results

Of 248 eligible UC-related hospitalizations, 27 (10.9%) were associated with re-hospitalization for a UC-related indication within 90 days of discharge. The baseline and disease characteristics of the study cohort are described in Table 1. The

Table 1. Baseline and disease characteristics for persons with UC relative to the timing of index hospitalization.

Variable	Total cohort (*n* = 248)	Not re-hospitalized (*n* = 221)	Re-hospitalized (*n* = 27)
Pre-admission characteristics			
Sex, *n* (%)			
Male	125 (50.4%)	118 (53.4%)	7 (25.9%)
Female	123 (49.6%)	103 (46.6%)	20 (74.1%)
Age at UC diagnosis (years; mean ± SD)	35.3 ± 18.3	35.7 ± 17.9	32.1 ± 21.5
Disease duration (years; mean ± SD)	6.26 ± 8.49	6.11 ± 8.38	7.48 ± 9.39
History of extra-intestinal Manifestations, *n* (%)			
No	223 (89.9%)	–	–
Yes	25 (10.1%)		
Past exposure to steroids, *n* (%)			
No	96 (38.7%)	87 (39.4%)	9 (33.3%)
Yes	152 (61.3%)	134 (60.6%)	18 (66.7%)
Past exposure to immunomodulator, *n* (%)			
No	169 (68.1%)	155 (70.1%)	14 (51.9%)
Yes	79 (31.9%)	66 (29.9%)	13 (48.1%)
Past exposure to biologic, *n* (%)			
No	202 (81.5%)	182 (82.4%)	20 (74.1%)
Yes	46 (18.5%)	39 (17.6%)	7 (25.9%)
Previous UC hospitalization within prior year, *n* (%)			
No	207 (83.5%)	186 (84.2%)	21 (77.8%)
Yes	41 (16.5%)	35 (15.8%)	6 (22.2%)
Gastroenterologist visit within prior year, *n* (%)			
No	110 (44.4%)	–	–
Yes	138 (55.6%)		
Admission characteristics			
Age at index hospitalization (years; mean ± SD)	41.8 ± 19.2	42.0 ± 18.9	40.3 ± 22.0
New UC diagnosis during index hospitalization, *n* (%)			
No	206 (83.1%)	–	–
Yes	42 (16.9%)		
Admitting service, *n* (%)			
Gastroenterology	126 (50.8%)	–	–
Medicine	92 (37.1%)		
Surgery	21 (8.5%)		
Other	9 (3.6%)		
Length of stay (days; mean ± SD)	9.97 ± 9.25	10.3 ± 9.37	7.18 ± 7.77
Intra-abdominal catastrophe, *n* (%)			
No	233 (94.0%)	–	–
Yes	15 (6.0%)		
Intra-abdominal surgery, *n* (%)			
No	223 (89.9%)	–	–
Yes	25 (10.1%)		
Discharge characteristics			
Discharge with biologic, *n* (%)			
No	156 (62.9%)	139 (62.9%)	17 (63.0%)
Yes	92 (37.1%)	82 (37.1%)	10 (37.0%)
Discharge with narcotics, *n* (%)			
Missing	1 (0.4%)	1 (0.5%)	0 (0.0%)
No	213 (85.9%)	192 (86.9%)	21 (77.8%)
Yes	34 (13.7%)	28 (12.7%)	6 (22.2%)

Exposure to steroids, biologics, or immunomodulators is defined as previous use at any time prior to index hospitalization. Intra-abdominal catastrophe is defined as either abdominal perforation, toxic megacolon, fulminant colitis, or intra-abdominal sepsis. Small cells (values < 6, excluding missing values) were suppressed.
Abbreviations: EIM, extra-intestinal manifestations; ICU, intensive care unit; TPN, total parenteral nutrition; WBC, white blood cell counts.

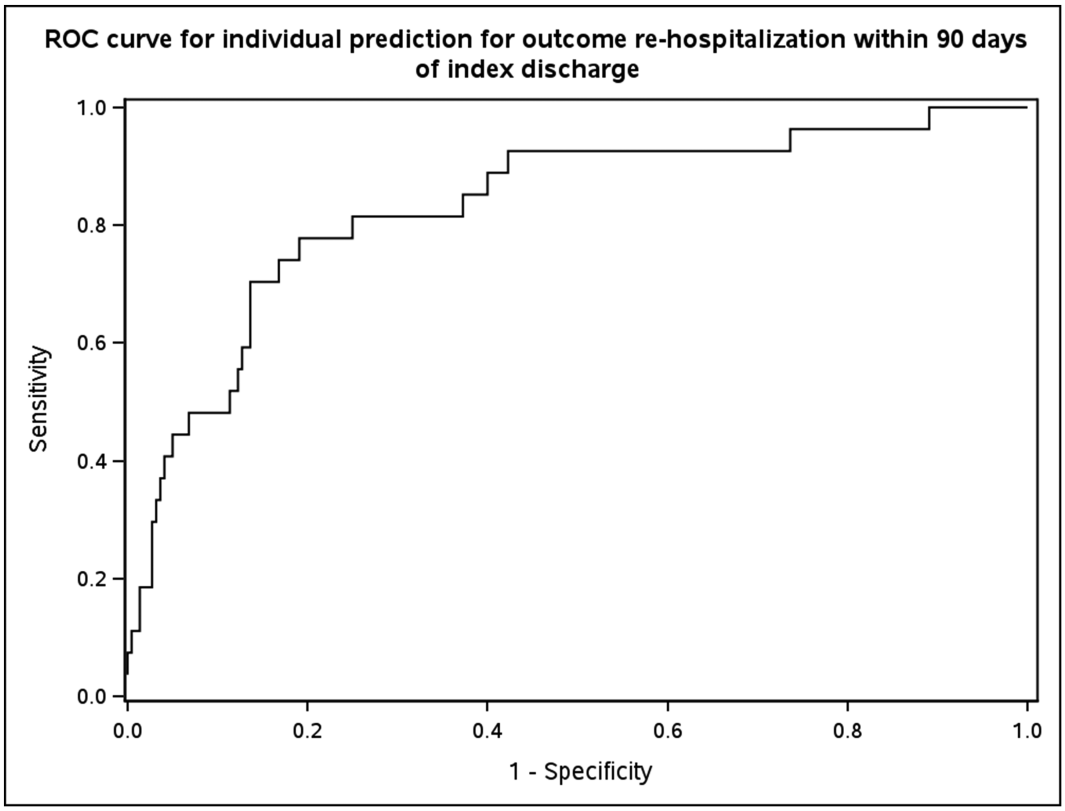

Figure 1. Receiver operating curve for patients with UC with 90-day re-hospitalization.Notes: ROC=receiver operator curve.

mean age at UC diagnosis was 35.3 ± 18.3 years, and 50.4% of the cohort was male. In the year prior to index hospitalization, 138 (55.6%) had a gastroenterologist visit, while only 41 (16.5%) persons were hospitalized. During index hospitalization, 42 (16.9%) persons were newly diagnosed with UC and 25 (10.1%) persons underwent intra-abdominal surgery. At discharge, 34 (13.7%) individuals were prescribed an outpatient narcotic. The mean length of hospital stay was 9.97 ± 9.25 days.

A comprehensive list of the 35 candidate predictors that were tested in the multivariable models, stratified by 90-day hospital re-admission status, is presented in Supplementary Table 1. The results of the univariable logistic regression analysis for each variable are presented in Supplementary Table 2. Based on the criteria for bivariate association with the outcome at $P < .2$, 8 candidate predictors met the criteria for further testing during model building. Those with the highest strength of association included: previous gastroenterologist visit (odds ratio [OR] 0.11, 95% confidence interval [CI] 0.038-0.34), male sex (OR 3.27, 95% CI 1.33-8.05), previous immunomodulator exposure (OR 2.01, 95% CI 0.90-4.50), current use of narcotics (3.82, 95% CI 0.93-15.8), length of stay (OR 0.94, 95% CI 0.88-1.01), and discharge with narcotics (OR 1.96, 95% CI 0.73-5.27).

Variables that were retained in the final multivariable logistic regression model included gastroenterologist consultation within the prior year (adjusted odds ratio [aOR] 0.09, 95% confidence interval [CI], 0.03-0.29), male sex, (aOR 3.77, 95% CI 1.42-10.0), length of hospital stay (aOR 0.93, 95% CI 0.86-1.00), and discharge with narcotics prescription (aOR 5.94, 95% CI 1.64-21.5). The optimism-corrected *c*-statistic value for the model was 0.78, and the goodness-of-fit test *P*-value was .09. The receiver operator curve (ROC) is displayed in Figure 1.

The optimal probability cut point was found to be 0.14, corresponding to a *J*-index of 0.59. At this cut point, 25.5% of the cohort was predicted to have a high probability of hospital re-admission, giving a model sensitivity of 77.8% (95% CI 57.7%-91.4%), specificity of 80.9% (95% CI 75.1%-85.9%), PPV of 33.0% (95% CI 26.3%-41.2%), NPV of 96.7% (95 % CI 93.6%-98.4%), PLR of 4.07 and NLR of 0.27, for predicting high vs. low risk of 90-day hospital readmission.

Discussion

In our cohort of UC patients hospitalized at a tertiary referral centre, a multivariable prediction model comprising just 4 variables that are easily attainable at the point of care reasonably discriminated individuals at high vs. low risk of 90-day hospital re-admission. At the chosen probability cut-point, our model demonstrated sensitivity and specificity of close to 80% when applied to our cohort. Although the PPV of the model was low, only 22% of individuals who were destined for early re-admission (FNR), and less than 20% of individuals who were not destined for early re-admission (FPR), were misclassified. Importantly, only about a quarter of admitted UC patients were classified as high-risk and potentially in need of early outpatient intervention, which captured close to 80% of individuals who are destined for early re-admission. This demonstrates a potentially good trade-off between high-risk case ascertainment and minimizing unnecessary resource allocation if such individuals were prioritized for early outpatient intervention. Furthermore, the PLR of our model was

more than 4, while the NLR was 0.27 when applied to our cohort. As our model was only internally validated, confirmation of these model attributes is required in other cohorts before this model is applied to clinical practice.

To our knowledge, this is the first study to develop a model that accurately discriminates 90-day hospital re-admission risk among individuals with UC and holds promise to help target early outpatient interventions following hospital discharge to reduce this risk. We selected 90-day readmission as our outcome as it would provide a window to identify individuals who experience early disease recurrence who might benefit from early or intensive post-discharge outpatient monitoring and/or intervention. Previous single-centre US studies have modelled bowel obstruction,[8] malnutrition,[8] surgical admission,[8] narcotic use at discharge,[19] benzodiazepines,[19] and discharge to homecare or assisted living[19] as predictors of 30-day re-admission in this population. However, such a short window between discharge and re-hospitalization may, in fact, reflect inadequate management during index admission as opposed to recurrence of symptoms or complications and leaves little opportunity to implement strategies to prevent re-admission.[8,19] Identifying individuals at less immediate risk of re-admission is more useful to guide strategies that could reduce recurrence of severe disease and target preventable re-hospitalizations for intensive outpatient monitoring.

Gastroenterologist visits within the prior year were strongly protective against hospital re-admission and the only potentially modifiable factor included in our final model. Previous studies have reported that a lack of scheduled follow-up with a gastroenterologist after hospital discharge increases the risk of re-admission in IBD.[20,21] Other studies have shown that gastroenterologist care is associated with a reduced risk of complications in both ambulatory CD patients[22] and admitted UC patients.[23] The value of pre-admission gastroenterologist care in preventing hospital re-admission in our study may reflect the availability and impact of timely and regular outpatient monitoring and/or treatment optimization by an appropriate specialist either prior to hospitalization or following hospital discharge. Alternatively, outpatient gastroenterologist contact could simply be a marker of better access to healthcare services or else a greater propensity for a patient to use advanced healthcare services, both of which could also be associated with better disease prognosis.[6] Factors associated with outpatient gastroenterologist care as well as optimal timing of post-discharge care should be elucidated in future studies, as this may be a modifiable factor that could reduce hospital re-admission rates in this population.

Increased length of hospital stay (LOHS) was marginally protective against hospital re-admission in our study, possibly reflecting more comprehensive management during hospital admission or better organization of outpatient services prior to discharge. Notably, other studies have demonstrated that a longer LOS is a risk factor for re-hospitalization in patients with IBD.[11,13] This may be due to greater disease severity or complexity among those requiring longer admission. As multiple factors, both medical and non-medical, can dictate LOHS, this variable may not be a particularly useful predictor in isolation and its true impact on rehospitalization risk in Canada requires further study.

Narcotic prescription at discharge was strongly predictive of 90-day re-admission in our study. The literature on narcotic use and prescriptions has been quite inconsistent. One study identified opioid dependence as a predictor of 30-day re-admission,[8] while another study identified narcotic prescription at discharge as protective against re-admission.[19] Conversely, a recent meta-analysis did not show any association.[24] Discharging an individual with UC on narcotics may suggest increased symptom burden as a result of greater disease activity, although a previous study suggested use of narcotic pain medications was not associated with disease severity.[25] Chronic pain, which is often treated with narcotics, has been previously shown to be associated with UC re-admission.[11] Therefore, in addition to possible greater UC burden, narcotic prescription at discharge may be a surrogate measure for greater symptom burden, such as having a lower pain threshold, undermanaged pain, or greater anxiety in relation to pain. This may lead some patients to re-present to the hospital for pain control if they are not able to easily find help to manage their symptoms in the outpatient setting.

Male sex has been previously identified as a risk factor for re-admission for patients with IBD,[8,12,26] as well as a higher rate of IBD-related complications as compared to females.[27,28] Potential explanations for this finding include poorer response to therapy or increased medication non-compliance among males, although findings across studies have been inconsistent.[29–31] A detailed inquiry into gender-based differences in IBD care was beyond the scope of our study but will be an important consideration for future research in this area.

Interestingly, multiple variables that have either been previously identified as risk factors or were anticipated to be risk factors for re-admission risk among individuals with IBD did not associate with 90-day re-admission risk in our cohort, including disease duration or treatment at admission,[20] increased comorbidities,[20] previous hospital admission,[27] in-hospital intra-abdominal catastrophe (sepsis, peritonitis, perforation, and megacolon) or surgery,[8,12] admitting service,[9] or discharge IBD medications.[26] The predictive value of some of these variables may have been captured in other variables in the model. Association with pre-admission gastroenterologist care or narcotic prescription at discharge may have acted as surrogates for more severe or complex diseases in our study. Alternatively, event rates may have been too low for some variables to have sufficient statistical power to detect a significant association with the outcome, such as for ICU admission, intra-abdominal surgery, and in-hospital receipt of total parental nutrition, for which the point estimates were imprecise. Additionally, as the data were collected retrospectively, the accuracy of the clinical variables used as candidate predictors is uncertain. Notably, as virtually all hospitalized UC patients in our study had severe extensive colitis at admission, disease activity and extent were not formally tested in our models.

There are several limitations to our study. Firstly, our study cohort was relatively small, which limits the statistical power for model building and identifying variable associations with the outcome. We also conducted our study in a single tertiary care centre, which limits its generalizability, particularly with respect to applying our models to community and rural hospitals. As we relied on retrospective data for model derivation, inaccuracies or incompleteness in the source data could have impacted the accuracy and/or precision of our estimates. We were also unable to acquire accurate data on some variables that could influence the propensity for early re-admission, such as historical disease burden smoking

status, chronic pain, and mental health,[8,32] nor could we adequately evaluate factors in the immediate post-discharge setting that could impact readmission risk, such as medication compliance, outpatient specialist care, or social supports. Importantly, our model will require external validation before it can be broadly applied to clinical practice settings.

Despite these limitations, this is the first study of 90-day rehospitalization risk in this population, which has intuitive advantages for managing post-discharge care in the Canadian context as compared to 30-day re-admission risk. Our study provides a foundation for future studies on this question as well as insights into potentially relevant factors dictating re-hospitalization risk among individuals with UC. While our model performed reasonably well in discriminating 90-day readmission risk in our cohort, larger prospective studies in other centres, including both academic and community centres, will be important to validate and/or improve upon our findings. Future research should focus efforts on identifying modifiable factors of hospital re-admission in this setting.

Supplementary material

Supplementary material is available at *Journal of the Canadian Association of Gastroenterology* online.

Author contributions

Sanjay K. Murthy (Formal Analysis, Writing—review & editing). Claudia Dziegielewski (Data curation, Writing—original draft). Sarang Gupta and Sanjay K. Murthy (Data curation). Tim Ramsay and Michael Pugliese (Formal Analysis). Jahanara Begum (Formal Analysis). All authors involved in writing—review & editing.

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Conflicts of interest

E.B. serves as the editor-in-chief of the Journal of the Canadian Association of Gastroenterology (JCAG), however, was not involved in the peer review process or editorial decision for this manuscript. Conflict of interest disclosure forms (ICMJE) have been collected for all co-authors and can be accessed as Supplementary material here. The authors do not declare any other relevant competing interests.

Ethics approval and consent to participate

ICES is a prescribed entity under Ontario's Personal Health Information Protection Act (PHIPA). Section 45 of PHIPA authorizes ICES to collect personal health information, without consent, for the purpose of analysis or compiling statistical information with respect to the management of, evaluation or monitoring of, the allocation of resources to or planning for all or part of the health system. Projects that use data collected by ICES under Section 45 of PHIPA, and use no other data, are exempt from REB review. The use of the data in this project is authorized under Section 45 and approved by ICES' Privacy and Legal Office.

Data availability

The data underlying this article are available in the article and in its online supplementary material. The dataset from this study is held securely in coded form at ICES. While legal data sharing agreements between ICES and data providers (e.g., healthcare organizations and government) prohibit ICES from making the dataset publicly available, access may be granted to those who meet pre-specified criteria for confidential access, available at www.ices.on.ca/DAS (email: das@ices.on.ca). The full dataset creation plan and underlying analytic code are available from the authors upon request, understanding that the computer programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.

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