Declining Corticosteroid Use for Inflammatory Bowel Disease Across Alberta: A Population-Based Cohort Study

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Abstract

Background and Aims: Corticosteroid-free remission is a primary treatment goal in IBD which may be achieved with greater use of anti-TNF therapy. We defined temporal trends of corticosteroid use, anti-TNF use, hospitalization and surgery in a prevalent IBD cohort within the province of Alberta, Canada.

Methods: Health administrative data were used to identify medication dispensing, hospitalizations and surgery in individuals with IBD from 2010 to 2015. Temporal trends were calculated using log-binomial regression for medications and log-linear models for hospitalization and surgery rates. Analyses were stratified based on geographic location.

Results: Of 28890 individuals with IBD, 50.3% had Crohn’s disease. One in six individuals (15.45%) were dispensed a corticosteroid. Corticosteroid use decreased in both metropolitan areas (AAPC −20.08%, 95% CI: −21.78 to −18.04) and non-metropolitan areas (AAPC −18.14%, 95% CI: −20.78 to −18.04) with a similar pattern for corticosteroid dependence. Corticosteroid dependence was more prevalent in UC vs. CD (P < 0.05), and in the pediatric IBD cohort (13.45) compared to the adult (8.89) and elderly (7.54) cohorts (per 100 prevalent population, P < 0.001). The proportion of individuals dispensed an anti-TNF increased over the study period (AAPC 12.58%, 95% CI: 11.56 to 13.61). Significantly more non-metropolitan versus metropolitan residing individuals were hospitalized for any reason, for an IBD-related, or IBD-specific indication (all P < 0.001) though the proportion requiring IBD surgery was similar between groups.

Conclusions: An increase in anti-TNF use corresponded to a decline in corticosteroid use and dependence in those with IBD. Inequities in IBD care still exist based on location and age.

Key words: Anti-TNF therapy; Corticosteroids; Epidemiology; IBD

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BACKGROUND

Inflammatory bowel disease (IBD), which comprises Crohn’s disease (CD) and ulcerative colitis (UC), affects 0.7% of the Canadian population with Canada having amongst the highest prevalence of IBD in the world (1, 2). The rising incidence along with compounding prevalence of IBD will continue to challenge health care systems as they address the significant impairment of quality of life, excess morbidity and mortality in affected individuals (3–7).

Individuals with IBD commonly require medications or surgical procedures to reduce inflammation or to treat cumulative structural damage. Corticosteroids rapidly induce remission and are readily accessible and inexpensive; however, their lack of long-term efficacy makes them a poor option for maintenance therapy (8–10). Further, chronic corticosteroid use has been associated with increased mortality which is not seen with anti-tumour necrosis alpha (anti-TNF) directed monoclonal antibody therapy (10). Notably, insurance coverage for anti-TNF therapy in Canada mandates a prior trial of corticosteroids (11), yet the International Organization for the Study of Inflammatory Bowel Diseases proposed treatment targets which include clinical remission, endoscopic healing, absence of disability, restoration of quality of life and normal growth in children are predicated on achieving steroid-free remission (12).

As unwarranted corticosteroid use has been listed as a key performance indicator in the management of IBD, it is hoped that increasing use of steroid-sparing agents will result in a reduction in chronic corticosteroid use (13–15). Further, it is anticipated that hospitalization rates and risk of surgery will decrease as a result of anti-TNF therapy but the existing data are equivocal (16–19). Regional differences that reflect Canada’s low population density with divergent access to care may play a role in the disparate health service outcomes, including specialist consultations, hospitalization and emergency department rates, and higher rates of surgery for individuals with IBD living in rural Canada (20–22). We therefore sought to determine patterns of corticosteroid use in relation to use of anti-TNF therapies and to examine factors contributing to corticosteroid use including age, sex, IBD-type and geographic location, in a prevalent IBD cohort in Alberta.

METHODS

Study Cohort and Data Source

This population-based observational cohort study using health administrative data is reported in accordance with “the Reporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement” (23). The province of Alberta, Canada, provides universal publicly administered and funded health care services to all residents. The Alberta Health Care Insurance Plan assigns a unique personal health number (PHN) to residents of Alberta, which can be used to track patients as they access the health care system. De-identified routinely collected health administrative databases maintained by Alberta Health Services and Alberta Health from 2002 were used: the Discharge Abstract Database (DAD), Practitioner Claims data, the Alberta Ambulatory Care Reporting System (AACRS) before the fiscal year (FY) 2010/11 and the National Ambulatory Care Reporting System (NACRS) from FY 2010/11 onwards were utilized to identify a prevalent cohort of individuals with IBD. These databases cover greater than 99% of the Alberta population (4.2 million people in 2015) (24). ICD-9 or ICD-10CA diagnostic codes were used to extract data on inpatient admissions from DAD, whereas the Canadian Classification of Health Intervention (CCI) codes documented in-hospital procedures. Practitioner Claims contains data on physician claims, and AACRS/NACRS contain data on emergency department visits, day surgeries and other ambulatory care services (25, 26).

A previously validated algorithm which identified individuals with IBD with a sensitivity of 78.0%, specificity of 99.8%, positive predictive value of 97.2% and a negative predictive value of 98.0% was utilized. The algorithm identified individuals as having IBD if they had two admissions in DAD, four Practitioner Claims or two contacts in AACRS/NACRS with codes for IBD (ICD-9: 555.X or 556.X; ICD-10 CA K50.X or K51.X) within a 2-year period. This algorithm also defined CD, UC and IBD-U (IBD type that is unclassifiable using data, which may not be reflective of the clinical entity of IBD type unclassified) diagnoses through a scoring system based on CD and UC ICD codes (27).

Records of prescription medications dispensed from community pharmacies were obtained from the Pharmaceutical Information Network (PIN). This does not include parenteral or oral medications that were dispensed in-hospital. Dose, mode of medication delivery, postal code of the patient and date the medication was dispensed are recorded. Complete PIN data were available from FY 2010/11 to 2015/16. The PIN database uses the Anatomical Therapeutic Chemical (ATC) Classification System based on the active ingredient of drugs according to the targeted organ or system (28). Data on oral corticosteroids (prednisone [ATC Codes A07EA03, H02AB07] and prednisolone [ATC Codes A07EA01, H02AB06] are considered corticosteroid equivalents in dosing) and anti-TNF therapies relevant to the treatment of individuals with IBD were obtained (ATC Codes adalimumab L04AB04, infliximab L04AB02, certolizumab L04AB05). Non-systemic corticosteroid preparations including oral budesonide or rectal corticosteroid formulations were excluded.

Corticosteroid use was defined as >650 mg of prednisone being dispensed from a non-hospital based pharmacy over a period of 365 days. This cut off was chosen to exclude patients who may have received prednisone premedication with their infliximab infusions. Corticosteroid dependence was defined by the following criteria: (a) prednisone dispensed on two separate occasions exceeding 500 mg equivalents between 84 and 365 days apart and (b) cumulative prednisone dose exceeding a total of 2000 mg over a 365-day period. Although the indication for the corticosteroid prescription is not recorded specifically in PIN, the dosing criteria above reflect dosing schedules used for the treatment of IBD (vs. other chronic inflammatory disorders such as asthma). A standard corticosteroid taper for IBD would consist of prednisone 40 mg daily which would be tapered over 8–12 weeks (total dose of 1260–1540 mg per course).

Stratified Variables

The predominant focus was on geographic location. Of the five AHS zones, Edmonton and Calgary were defined as metropolitan centres by Statistics Canada, and were serviced by tertiary care hospitals. The other three zones (North, Central
and South) were defined as non-metropolitan zones as they lack either a metropolitan centre and/or a tertiary care hospital (29). Patients were then identified as being within a metropolitan versus non-metropolitan zone based on the reported home postal code. Information from Alberta Health Services (AHS) and Statistics Canada was used to define metropolitan versus non-metropolitan zones by postal code (21, 29, 30) rather than using the more complex definition of rurality (31). Age was stratified as pediatric (<18 years), adult (18–64 years) and elderly (≥65 years) based on when the medication was first dispensed during the study period. Sex was classified as male or female.

Other Outcomes
Hospitalization data were contained in the DAD. Admissions occurring during the prevalent case data set timeframe, i.e., FY 2010/11 to 2015/16, were included and categorized as total hospitalizations (all hospitalizations in the prevalent population), IBD-related hospitalizations (admission with any ICD code for IBD; ICD-9: 555.X or 556.X; ICD-10 CA K50.X or K51.X) and IBD-specific (most responsible diagnosis, as defined in the dataset, is for IBD). With the exception of transfer between hospitals, each discharge abstract was considered a separate admission. The IBD-related hospitalization dataset (FY 2010/11 to 2015/16) was used to identify IBD-related surgery using previously validated codes (32, 33). The following CCI codes for small bowel resections and/or colectomies were included but procedures within the 1-year period from a resection were considered likely complications or part of a multi-stage operation and were not included as separate entities. (1.NK.87, 1.NM.87, 1.NM.89, 1.NM.91, 1.NQ.87, 1.NQ.89 and 1.NQ.90) (32). Patients undergoing perianal surgery in the absence of a bowel resection during an admission were excluded. For UC, the admission for colectomy (1.NM.87, 1.NM.89, 1.NM.91, 1.NQ.89 and 1.NQ.90) was considered the index date and further surgical admissions were not included (33).

Statistical Analysis
The proportion of the IBD prevalent population who were dispensed IBD-related medication between FY 2010/11 and 2015/16 was calculated. Corticosteroid use and corticosteroid dependence were calculated separately. Two-sample tests of proportion were used to compare proportions. Analyses were stratified by metropolitan and non-metropolitan zones, sex (female and male), and age (pediatric [<18 years], adult [18–64 years] and elderly [≥65 years]). Temporal analyses are reported as average annual percentage change (AAPC) with associated 95% confidence intervals (CI)—calculated using log-binomial regression (medications) or Poisson/negative binomial regression (hospitalization and surgery) (34, 35). Statistical analyses were performed in Stata v14. This study was approved by the Conjoint Research Ethics Board at the University of Calgary (REB16-2375).

RESULTS
From 2010 to 2015, 28,890 individuals with IBD were identified in Alberta with 14,527 diagnosed as CD and 10,554 with UC. A total of 3809 individuals were IBD unclassified (Table 1). One-sixth (15.45%) of prevalent IBD individuals (n = 4463) were dispensed a corticosteroid on at least one occasion between 2010 and 2015 of whom 2339 (52.4%) were male. There was a similar proportion of IBD individuals dispensed a corticosteroid in metropolitan vs. non-metropolitan areas (15.64% vs. 15.03%, P = 0.606).

Corticosteroids were dispensed to a lower proportion of adults and the elderly than the pediatric population (15.52% vs. 13.97% vs. 19.28%; P < 0.001). Further, corticosteroids were more commonly dispensed for individuals with UC vs CD (18.58 vs. 15.53%, P = 0.009) and for males vs. females (17.03% vs. 14.01%; P = 0.006).

Dispensing of Corticosteroids Over Time
The proportion of patients (per 100 prevalent population) dispensed a corticosteroid in 2010 compared to 2015 decreased, for both CD (AAPC of −21.35 [95% CI: −23.33 to −19.32]) and UC (AAPC of −17.39 [95% CI: −19.58 to −15.13]). This is represented by an overall AAPC of −19.50% (95% CI: −20.93 to −18.04) for corticosteroid use in IBD. This reduction was identified in individuals residing in metropolitan [AAPC of −20.08% (95% CI: −21.78 to −18.04)] and non-metropolitan areas [AAPC of −18.14% (95% CI: −20.78 to −15.42)]. (Figure 1). The decrease in AAPC was of greater magnitude in those with CD [AAPC of −21.35% (95% CI: −23.33 to −19.32)] compared to those with UC [AAPC of −17.39% (95% CI: −19.58 to −15.13)]. A similar pattern was seen for metropolitan vs. non-metropolitan areas stratified by disease phenotype (CD vs. UC) in Table 2.

Corticosteroid Dependence
Corticosteroid dependence was identified in 8.88 per 100 prevalent IBD population from 2010 to 2015, with a higher proportion observed in those with UC vs. CD (11.16 vs. 8.65 per 100 prevalent population; P = 0.04). Metropolitan usage exceeded that for the non-metropolitan areas overall (9.13 vs. 8.31 per 100 prevalent population, P = 0.02). This was reflected in data for both UC (11.44 vs. 10.40 per 100 prevalent population, P > 0.05) and CD (8.85 vs. 8.23 per 100 prevalent population, P > 0.05), comparing metropolitan vs. non-metropolitan. Age stratified data demonstrated that a greater proportion of the pediatric IBD cohort were corticosteroid dependent than their adult and

Table 1. Baseline demographics of IBD cohort 2010–2015 in Alberta, Canada

| Category                   | IBD (28,890) |
|----------------------------|--------------|
| Total cohort               | 28,890       |
| Corticosteroid dispensed, n (%) | 4463 (15.4)  |
| Sex, n (%)                 |              |
| Male                       | 2339 (52.4)  |
| Female                     | 2124 (47.6)  |
| Age group, n (%)           |              |
| <18 years                  | 225 (5.0)    |
| 18–64 years                | 3653 (81.9)  |
| 65+ years                  | 585 (13.1)   |
| Metropolitan, n (%)        |              |
|                           | 3130 (70.1)  |
| Non-metropolitan, n (%)    |              |
|                           | 1333 (29.9)  |
elderly counterparts (13.45 vs. 8.89 vs. 7.54 per 100 prevalent population; \( P < 0.001 \)). Corticosteroid dependence was more often observed in those with UC than CD in all age groups (pediatric UC vs. CD, 21.07 vs. 11.34; adult UC vs. CD, 11.15 vs. 8.62; elderly UC vs. CD, 8.88 vs. 7.85 per 100 prevalent population).

Corticosteroid dependence significantly decreased over the study period with AAPC of \(-14.6\%\) (95\% CI: \(-16.6\%\) to \(-12.6\%\)) as demonstrated in Figure 2. The difference in corticosteroid dependency in individuals with CD was similar in the metropolitan vs. the non-metropolitan cohort (AAPC of \(-16.86\%\); 95\% CI: \(-20.13\) to \(-13.46\) vs. AAPC of \(16.67\%\); 95\% CI: \(-21.55\) to \(-11.50\)). However, in individuals with UC, the decrease in corticosteroid dependency was more marked in the metropolitan vs. the non-metropolitan areas (AAPC of \(-13.08\%\); 95\% CI: \(-16.45\) to \(-9.58\) vs. AAPC of \(-8.98\%\); 95\% CI: \(-14.95\) to \(-2.59\)).

### Corticosteroid and Anti-TNF Use

The proportion of patients dispensed anti-TNF therapy in Alberta has significantly increased over time (AAPC \(12.58\%\) [95\% CI: 11.56 to 13.61]) whereby 9.96 per 100 persons received anti-TNF therapy in 2010, culminating in 16.70 per 100 persons receiving anti-TNF therapy in 2015. There were similar significant increases in anti-TNF prescriptions in both zones (metropolitan AAPC \(12.25\%\) [95\% CI: 11.04 to 13.47] and non-metropolitan AAPC \(13.33\%\) [95\% CI: 11.47 to 15.23]), in both sexes (male AAPC \(13.65\%\) [95\% CI: 12.18 to 15.14] and female AAPC \(11.53\%\) [10.12 to 12.95]). AAPCs for anti-TNF use for the elderly (AAPC \(21.05\%\) [95\% CI: 16.57 to 25.70]) and pediatric populations (AAPC \(20.22\%\) [95\% CI: 13.78 to 27.02]) exceeded the adult population (AAPC \(12.81\%\) [95\% CI: 11.74 to 13.90]) \( (P < 0.001) \). Figure 3 demonstrates a decrease in AAPC for corticosteroids with a simultaneous increase in AAPC for biologics.
Hospitalizations and Surgery
Of 28,890 individuals in Alberta with IBD, 46.6% had at least one hospitalization; 27.3% had at least one IBD-related hospitalization with an IBD code in any diagnostic position and 15.0% had at least one IBD-specific hospitalization with IBD as the primary diagnostic code. A significantly higher proportion of non-metropolitan versus metropolitan residing individuals with IBD were hospitalized for any indication (51.3% vs. 44.5%, P < 0.001), for an IBD-related (30.1% vs. 26.1%, P < 0.001), and IBD-specific (16.4% vs. 14.4%, P < 0.001) reason. The AAPC of all hospitalizations in AB was −2.08% (95% CI: −2.69 to −1.47) with a significantly larger change in AAPC in the non-metropolitan cohort of −2.97% (95% CI: −3.96 to −1.97) versus metropolitan AAPC of −1.47% (95% CI: −2.25 to −0.70) (P = 0.02). There were non-significant changes in IBD specific hospitalizations for the non-metropolitan cohort with an AAPC of −8.81% (95% CI: −12.87 to −4.56) and a metropolitan AAPC of −6.27% (95% CI: −7.93 to −4.58) as illustrated in Figure 4.

In Alberta, 7.6% had at least one IBD-related surgery from 2010 to 2015. The proportion of non-metropolitan residents requiring IBD surgery (7.7%) was similar to those living in a metropolitan region (7.5%, P = 0.68). The AAPC of IBD-related surgery in Alberta was −8.8% (95% CI: −10.93 to −6.63). Figure 5 demonstrates trends in IBD-related surgery and corticosteroid use over the same time frame.

DISCUSSION
This province-wide study of corticosteroid utilization in individuals with IBD demonstrates the highest baseline use of corticosteroids in males and those with UC and in the pediatric population. Overall, one is six individuals were dispensed a corticosteroid. There has been a decrease in corticosteroid usage across the province of Alberta in recent years. Meanwhile, the proportion of patients dispensed anti-TNF therapy in Alberta significantly increased over time. Regional disparities were apparent and may be a function of the low cost, relative ease of prescription of corticosteroids over other therapies, but may also reflect lack of access to a gastroenterologist (36).

Although most biologic agents have been shown to reduce steroid use in the clinical trial setting, the effect of the more widespread availability of advanced/steroid sparing therapies has been equivocal. Chhaya et al. examined trends in corticosteroid use (1990–2010) predominantly before the widespread use of biologic therapies in the United Kingdom and found decreases in corticosteroid dependency for CD but an increase in individuals with UC despite the use of 5-ASA and thiopurines (37). Medicaid and Medicare data (2001–2013) from the United States reported twice as many individuals with CD and three times as many UC patients received prolonged corticosteroids compared to anti-TNF therapy (10). Investigators from the United Kingdom recorded
corticosteroid prescriptions in 30% of IBD patients within the prior 12 months, with 14.9% qualifying as having steroid dependency or excess, again with a higher prevalence in UC than in CD. The authors deemed dependency or excess was avoidable in almost half of the cohort (49.1%) (38). A lack of decline in corticosteroid use or persistent prolonged corticosteroid usage in those with UC were also documented in other population-based studies from Europe and the United States (39, 40). A Canadian-based study reported that cumulative exposure to corticosteroids did not decrease despite immunomodulator uptake between the years of 1995 and 2010 (41). Data were updated for 2001 to 2014, to capture the impact of biologic therapies; however, corticosteroid use remained prevalent (42). Murthy et al. reported that the introduction of infliximab did not result in a decrease in IBD-related hospitalizations or intestinal resections in Canada’s most populated province, Ontario. The investigators concluded that misguided use or under use of biologic therapy may have accounted for these findings and it should be noted that the end of the study period was a decade ago (19). More recent data demonstrated reductions in corticosteroid use from 1997 to 2017 in Crohn’s disease and the pediatric population in part related to increasing biologic therapy use in these specific cohorts (43). Finally, encouraging data from the Netherlands shows recent decreases in corticosteroid use, which the authors attributed to use of immunomodulators and biologics (39).

As such, the role of corticosteroids in the modern management of IBD should be re-examined worldwide. Coupled with an unwarranted fear of other therapies and an abundance of short-, medium-, and long-term corticosteroid-related adverse effects, patients may seek short-term intermittent corticosteroid therapy due to rapid resolution or reduction in symptoms, familiarity with use and ease of prescription rather than appropriate maintenance therapy (44). In children, biologic therapies can circumvent negative effects on growth potential related to disease activity or corticosteroids; however, biologic approval in this cohort has been delayed awaiting dedicated pediatric randomized control trials in IBD (45). Although EEN is favoured for its benefit on inflammation, nutrition status as well as absence of side effects in comparison to corticosteroids, our pediatric IBD population comprised both children with CD and UC. EEN is only indicated for CD; therefore, the impact of EEN on corticosteroid use may be difficult to elicit in this combined population. Although clinicians caring for children with IBD have moved towards early immunomodulator and/or anti-TNF therapy, the era during which this study was conducted (2010–2015) reflects a period of time during which the adoption of anti-TNF therapy into clinical practice was in its early stages; the first

Figure 3. Proportions (per 100 prevalent population) of corticosteroids and anti-TNFs dispensed and corticosteroid dependent from 2010 to 2015 stratified by metropolitan and non-metropolitan zones in Alberta.
anti-TNF therapy for pediatric CD received Health Canada approval in 2006, and while anti-TNF use for pediatric UC was only approved in 2011. Therefore, corticosteroids would have been a part of routine clinical practice for moderate to severe pediatric CD and UC during the study period. In addition, children frequently present with more severe disease that requires corticosteroids for induction. In the international multi-center ImproveCareNow Network of 27,321 children with IBD (65% Crohn’s disease, 28% ulcerative colitis and 7% indeterminate colitis), 37% of children received corticosteroids between 2007 and 2018 (46). Meanwhile, in the elderly population, comorbid conditions and a predisposition to infective and metabolic complications make corticosteroid use particularly concerning (47).

Education needs to be readily available to health care providers and patients, reiterating that anti-TNF therapies are associated with lower morbidity and mortality compared to high dose corticosteroid use (10, 48). The impact of biosimilars, newer biologic therapies (e.g., vedolizumab and ustekinumab which were approved by Health Canada in 2015 and 2017, respectively) and the introduction of oral small molecule therapy, on corticosteroid prescribing practices are awaited.

Ongoing optimal management of IBD has to be framed within the Canadian context. The Canada Health Act was created with the intent to provide Canadians with universal, transportable and accessible health care (49). Due to the geography of the country, this creates significant challenges for health care administration given the population density of Canada was 4.2/km² in 2011 (50). The large landmass and low population density of Canada increase travel time to tertiary care centers and decrease access to specialists for patients living in non-metropolitan areas which results in a disparity in health care outcomes (51). This is not an inconsequential problem with the prevalence of IBD in Canada amongst the highest in the world. Approximately 270,000 Canadians live with IBD, and this number is expected to increase to 403,000 by 2030 (2, 6, 52, 53). Although patients cared for by gastroenterologists have better outcomes including lower risk of surgery and hospitalization, the converse is that poorer outcomes have been identified for those in rural or non-metropolitan areas who receive a higher proportion of their care by non-specialists (21). Abundant Canadian data support this. Benchimol et al. demonstrated that rural IBD patients had lower rates of gastroenterologist physician visits, more hospitalizations and greater rates of ER visits, the latter reflecting easier access to ERs than family physicians or specialist care (21, 22). Al-Darmarki et al. demonstrated that UC patients hospitalized for an acute flare outside the metropolitan health zone were significantly more likely (OR
2.81 [95% CI, 1.49–5.29]) to undergo early colectomy (20). The reduced penetration of anti-TNF therapy may be a potential explanation for the worse outcomes among rural IBD patients but reassuringly, our data demonstrate similar upward trends in anti-TNF use both within and outside metropolitan population centres. Updated temporal analyses are required as non-metropolitan patients may now have better access to metropolitan care given the increasing accessibility and uptake of virtual consultations (highlighted during the COVID pandemic) which may blunt the apparent differences between metropolitan and non-metropolitan care (54, 55).

Strengths and Limitations
Strengths of this study include the use of administrative data, which provides details on approximately 99% of individuals in the province, mitigating selection bias and providing real-world evidence of health services use and treatment selection. The use of the PIN database allows for verification of medications that are dispensed, not just prescribed. These findings can be extrapolated to other Canadian regions and potentially other health systems with universal access to health care.

Limitations of administrative data research include the risk of misclassification bias. However, validated algorithms were used to identify patients with IBD, specifically CD or UC, and IBD surgical procedures. Hospitalization and emergency department data were collected by hospital coders trained by CIHI and whose data entry is subject to quality-control measures. Dispensing of medications may not be representative of adherence to therapy. In-hospital dosing and compassionate dosing provided by pharmaceutical companies are not contained within our datasets. A small number of individuals live on the provincial geographical border may attend specialist care in neighbouring provinces. Variation exists in corticosteroid prescribing in addition to definitions of corticosteroid use and dependence. Corticosteroid dependency in young children who receive weight-based dosing may be underestimated, due to lack of anthropometric data. Data on smoking, disease severity and details on disease phenotype, all which are important covariates, could not be reliably obtained from administrative databases resulting in a small risk of unmeasured confounding. Finally, our data are only able to demonstrate associations and the use of anti-TNF therapy must be interpreted as such, and is not necessarily causal.

Future Directions and Knowledge Translation
To avoid over-utilization of corticosteroids for the management of IBD, provincial-based clinical care pathways have been developed through Alberta Health Services...
collaborative multidisciplinary ‘Digestive Health Strategic Clinical Network’ (DHSCN) (56, 57). Further, links to clinical practice guidelines, patient-oriented literature and patient support organizations including Crohn’s and Colitis Canada, along with alerts to those prescribing corticosteroids will be embedded in the provincial clinical information system designed to provide a single access point to health information for health care professionals and patients (58). This combination of patient and physician education, and timely use of health technologies may achieve the goal of reducing disparity in IBD care within, and later, across provinces.

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Study concept and design: C.S., S.C., K.L., K.D., G.K. and R.P. Acquisition of data: S.C., L.T., G.N., E.B. and G.K. Analysis and interpretation of data: C.S., S.C., G.K. and R.P. Drafting of the manuscript: C.S., S.C., K.L., J.S., K.D., G.K. and R.P. Critical revision of the manuscript for important intellectual content: C.S., S.C., J.K., K.D., L.T., G.N., C.M., J.D., M.C., F.P., D.B., J.R., S.V., E.B., G.K. and R.P. Obtained funding: C.S., K.K., G.K. and R.P.

Conflict of Interest
C.H.S.: Advisory Boards: Janssen, Abbvie, Takeda, Ferring, Shire, Pfizer, Sanpodo, Pharmascience. Speaker: Janssen, Abbvie, Takeda, Ferring, Shire, Pfizer, Pharmascience. Research support: Takeda. K.I.K.: Advisory Boards: Abbvie, Janssen, Takeda. J.S.: Advisory Boards: Abbvie, Pfizer. K.S.D.: This work was supported by Crohn’s and Colitis Canada. K.S.D. is paid a salary from Crohn’s and Colitis Canada. L.E.T.: L.E.T. has received investigator initiated funding from Janssen Canada, and has received support for database infrastructure from Abbvie, Pfizer, Takeda, Merck, Sanpodo, Roche, and Gilead. served on advisory boards for AbbVie Canada, Takeda Canada, Merck Canada, Pfizer Canada, Janssen Canada, Roche Canada, Celtrion Canada, JAMP Canada, and Sandoz Canada. G.C.N.: G.C.N. is supported by a CIHR Embedded Clinician Researcher Award. C.M.: Consulting fees from AbbVie, Alimentiv, Amgen, AVIR Pharma Inc, BioJAMP, Bristol Myers Squibb, Celtrion, Ferring, Fresenius Kabi, Janssen, McKesson, Mylan, Takeda, Pendopharm, Pfizer, Roche; speaker’s fees from AbbVie, Amgen, AVIR Pharma Inc, Alimentiv, Ferring, Janssen, Takeda, and Pfizer; research support from Ferring, Pfizer. J.C.D.: Advisory Board Member: Mylan, Abbvie, Amgen. F.P.: Advisory Boards: Janssen, AbbVie, Takeda, Ferring, Pfizer, Pharmascience. Speaker: Janssen, AbbVie, Takeda, Pfizer. D.C.B.: Advisory boards for: 4d Pharma, Abbott, AbbVie, Allergan, Amgen, Astra Zeneca, Bayer, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb (BMS), Canon, Celgene, Cellerix, ChemOCentrinx, CSL Behring, Dr. Falk, Elan, Eli Lilly, Essex Pharma, Ferring, Forward, Genetech, Gilead, GSK, Hitachi, Janssen, Johnson & Johnson, Merck, Merck Serono, Merck Sharp Dohme (MSD), Millenium, Novartis, Novo Nordisk, Ocera, Otsuka, PDL Biopharma, Pfizer, Prometheus, Recordati, Roche, Sandoz, Sanofi Aventis, Schering, Schering-Plough, Shield, Shire, Takeda, Theravance, TriGenix, Thiilotti Pharma AG, Toshiba, UCB Pharma, Vifor. S.V.: Consultant: Paladin. E.I.B.: Legal consultant for Hoffman La-Roche Limited and Peabody & Arnold LLP for matters unrelated to a medication used to treat inflammatory bowel disease. Consulting for the Dairy Farmers of Ontario for matters unrelated to inflammatory bowel disease. Consultant for McKesson Canada. G.G.K.: Speaking or consultancy: Abbvie, Janssen, Pfizer, and Takeda. Research support: Ferring, Janssen, Abbvie, GlaxoSmith Kline, Merck, and Shire. He has been a consultant for Gilead. He shares ownership of a patent: TREATMENT OF INFLAMMATORY DISORDERS, AUTOIMMUNE DISEASE, AND PBC. UTI Limited Partnership, assignee. Patent WO2019046959A1. PCT/CA2018/051098. 7 Sept. 2018. R.P.: Grants: Abbvie, Janssen, Pfizer, Takeda Pharmaceuticals. Consulting Fees: AbbVie, Abbott, Alimentiv (formerly Robarts), Amgen, Arena Pharmaceuticals, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim Celgene, Celtrion, Cosmos Pharmaceuticals, Eisai, Elan, Eli Lilly, Ferring, Galapagos, Genentech, Gilead Sciences, Glaxo-Smith Kline, JAMP biopharma, Janssen, Merck, Mylan, Oppilan Pandion, Pharma, Pandion Pharma, Pfizer, Progenity, Protagonist Therapeutics, Roche, Satisfi Health, Sandoz, Schering-Plough, Shire, Sublimity Therapeutics, Theravance Biopharma, UCB, Takeda Pharmaceuticals Speaker Fees: Abbvie, Arena Pharmaceuticals, Celgene, Eli Lilly, Ferring, Gilead Sciences, Janssen, Merck, Pfizer, Roche, Sandoz, Shire, Takeda Pharmaceuticals, Viatris Advisory Boards: Abbvie, Amgen, Arena Pharmaceuticals, Bristol-Myers Squibb, Celgene, Cellertron, Eli Lilly, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead Sciences, Glaxo-Smith Kline, JAMP biopharma, Janssen, Merck, Mylan, Oppilan, Organon, Pandion Pharma, Pfizer, Sandoz, Shire, Sublimity Therapeutics, Theravance Biopharma, Takeda Pharmaceuticals. Research/Educational Support: Abbvie, Ferring, Janssen, Pfizer, Takeda. The other authors declared no conflict of interest.

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