

Trends in Corticosteroid Use During the Era of Biologic Therapy: A Population-Based Analysis

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INTRODUCTION: Corticosteroids are effective for inducing clinical remission in inflammatory bowel disease (IBD), but not for maintaining remission. Reducing corticosteroid use and dependence is an important treatment goal since their use is associated with adverse events. The extent to which the improvements in IBD therapy have led to less corticosteroid use in the modern era remains unclear.

METHODS: We used the University of Manitoba Inflammatory Bowel Disease Epidemiologic Database to assess the cumulative annual dosing of corticosteroids on a per-patient basis for all persons with IBD in the province of Manitoba between 1997 and 2017. Joinpoint analysis was used to assess for trends in corticosteroid use and to look at variation in the trends over time.

RESULTS: The mean annual exposure to corticosteroids decreased from 419 mg/yr (1997) to 169 mg/yr (2017) for Crohn's disease (CD) (annual decline: 3.8% per year, 95% confidence interval 3.1–4.6) and from 380 to 240 mg/yr in ulcerative colitis (UC) (annual decline: 2.5% per year, 95% confidence interval 2.1–2.8). In CD, there was an acceleration in the rate of decline after 2007 (pre-2007, 1.9% decline per year; after 2007, 5.7% per year); there was no corresponding acceleration in the rate of decline in UC.

DISCUSSION: Corticosteroid use has decreased in both CD and UC over the past 2 decades, becoming more pronounced after 2007 in CD. Potential explanations include introduction and increasing penetrance of biologic therapy in CD and greater awareness of corticosteroid-related adverse events in IBD. Further work is required understand the drivers of persistent corticosteroid use in IBD and how this can be further reduced.

SUPPLEMENTARY MATERIAL accompanies this paper at <http://links.lww.com/AJG/B932>, <http://links.lww.com/AJG/B933>, <http://links.lww.com/AJG/B934>, <http://links.lww.com/AJG/B935>, <http://links.lww.com/AJG/B936>, <http://links.lww.com/AJG/B937>, <http://links.lww.com/AJG/B938>, <http://links.lww.com/AJG/B939>, <http://links.lww.com/AJG/B940>.

Am J Gastroenterol 2021;116:1284–1293. <https://doi.org/10.14309/ajg.000000000001220>

BACKGROUND

Corticosteroids have been part of the treatment armamentarium for persons with inflammatory bowel disease (IBD) since the middle of the twentieth century (1,2). Although corticosteroids are effective in inducing rapid symptomatic improvement in persons with active Crohn's disease (CD) and ulcerative colitis (UC) (3), they are not an effective or safe maintenance therapy (4). Corticosteroid use is strongly associated with a higher rate of

infectious outcomes (including COVID-19), as well as with overall mortality (5,6). As such, clinicians are advised to limit the use of corticosteroids to situations the need for a rapid response is paramount, such as for persons with severe symptoms. Excessive corticosteroid use is now widely recognized as a marker of poor quality of care (7–9).

With the emergence of effective and well-tolerated biologic therapies for both inducing and maintaining remission for IBD,

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Received July 18, 2020; accepted January 4, 2021; published online March 24, 2021

we should anticipate a decrease in the overall corticosteroid exposure among the IBD population. However, the variability in access to biologic medications and variations in clinical practice and quality of care may impact the reduction in corticosteroid use in the real world. To this effect, we also have previously shown that corticosteroid use is still relatively common among persons with exposure to anti-tumor necrosis factor (anti-TNF) therapies in the short term, especially among persons who have had exposure to corticosteroids before anti-TNF initiation (10). In addition, up to one-fifth of elderly patients with IBD were observed to have exposure to corticosteroids monthly, and this use was consistent across multiple countries (11).

Therefore, we sought to evaluate the trends in corticosteroid use in a populationwide sample of persons with IBD before and during the era of biologic therapy.

METHODS

Data sources

We used the University of Manitoba Inflammatory Bowel Disease Epidemiologic Database (12), which contains routinely collected health care utilization data for nearly 100% of all residents with IBD in the Canadian province of Manitoba (population in 2018: 1.37 million). Manitoba Health maintains several electronic databases which can be linked deterministically using a unique patient identifier which was based on encoded Manitoba Health card number. These databases capture all inpatient hospitalizations as well as physician-patient interactions occurring in a hospital or ambulatory care setting from 1984 onward. Detailed data are also available for all outpatient prescriptions dispensed to Manitobans from 1996 through March 2018. The primary analyst (A.T.) and the lead investigator (L.E.T.) had access to individual level data, and all investigators had access to aggregated data.

Persons with IBD were identified according to a validated administrative definition shown to be 90% sensitive and $\geq 99\%$ specific for identifying persons with IBD and can differentiate between cases of CD and UC with $\sim 90\%$ accuracy. In cases where codes for both CD and UC are present, patients are classified according to the diagnosis in the majority of the 9 most recent health care contacts. Cases were considered to be incident (i.e., new diagnosis of IBD) if they did not have another IBD-related health care contact over an 8-year look-back window within ambulatory or inpatient administrative data sets (13). As only the incident cases can have an identified date of diagnosis, only incident cases are included in analyses evaluating the impact of disease duration.

Determination of corticosteroid dose and cumulative use per calendar year

We identified all prescriptions of oral corticosteroids in the outpatient setting. The list of corticosteroids relevant to the treatment of patients with IBD is shown in Supplementary Table 1 (see Supplementary Digital Content 2, <http://links.lww.com/AJG/B933>). For dispensations other than prednisone, strength was converted to prednisone equivalents using accepted conversion tables (see Supplementary Table 2, Supplementary Digital Content 3, <http://links.lww.com/AJG/B934>). Budesonide use was tracked as well, but was counted separately from conventional corticosteroids, and it cannot be easily converted to prednisone equivalents. We were not able to capture intravenous or oral corticosteroids that were administered during a hospitalization.

The total dose of corticosteroids provided in any pharmacy dispensation was determined by multiplying the number of doses dispensed by the strength of the dose (in milligrams of prednisone equivalents). As corticosteroids are often not prescribed with fixed or exact durations in IBD, we were not able to precisely determine the duration of use. We also assumed that all doses dispensed were taken, recognizing that prescribers may at times provide more prednisone than is needed because of its low cost or to allow patients to have extra doses on hand if needed urgently. For each year that we had complete data (January 1996 to December 2017), we determined the total amount of systemic corticosteroids and budesonide dispensed in a given year and calculated the cumulative dose per person year. We also calculated mean and median cumulative annual doses of corticosteroids solely within the cohort who had received at least 1 prescription for corticosteroids during that calendar year. We assigned each total prescription of corticosteroids to its dispensation date, even if the dispensation potentially covered parts of 2 calendar years. We also calculated the proportion of heavy corticosteroid users, defined as those who were dispensed more than 2000 mg of prednisone equivalents during that year (14). For budesonide, we determined the proportion of persons with CD only who received at least 1 dispensation in any given year.

Statistical analysis

All results pertaining to annual corticosteroid use were reported separately for persons with CD or UC and further stratified by age (<18 , 18–65, and ≥ 65), sex, duration of disease (<1 year, 1–5 years, and >5 years after diagnosis [limited to the inception cohort]), socioeconomic status, and rurality. Socioeconomic status was determined by the Socioeconomic Factor Index, a continuous variable, which determines the degree of deprivation according to known values for unemployment, income, the proportion of single-parent households, and proportion having graduated from high school in that patient's neighborhood of reference (15); rurality was determined according to accepted Statistics Canada definitions which take into account several factors including population density and distance from the closest population center (16). We also assessed corticosteroid use among persons who were recent anti-TNF users (defined as those who were dispensed an anti-TNF in the previous 365 days and those with no recent anti-TNF exposure).

The Joinpoint Regression Program (Information Management Services, Calverton, MD) was used to quantify trends over time and to determine whether there was any inflection point in a given year that represented a significant change in the rate of corticosteroid use. Trends were expressed as the relative annual percentage change. We limited the joinpoint analysis to a maximum of 1 inflection point. All other statistical analysis was performed using SAS 9.4 (Cary, NC). *P* values of 0.05 were assumed to be statistically significant.

RESULTS

The number of people in the cohort with IBD increased from 4,778 (2494 CD, 2284 UC) in 1997 to 8,126 in 2017 (3793 CD, 4433 UC). The characteristics of the patient population in 1997, 2002, 2007, 2012, and 2017 are shown in Table 1. Overall, there is an increase in the mean age of the population over time and increasing frequency of active anti-TNF use and any history of anti-TNF use in both CD and UC. The proportion of total person time in the anti-TNF use categories in 2017 was 21.1% for CD and

Table 1. Baseline characteristics of IBD population

	CD					UC				
	1997	2002	2007	2012	2017	1997	2002	2007	2012	2017
N (overall)	1997	2002	2007	2012	2017	1997	2002	2007	2012	2017
No. of subjects	2,494	2,954	3,303	3,607	3,793	2,284	2,896	3,421	3,971	4,333
Age of diagnosis, mean (SD)	35.47 (15.28)	35.36 (15.28)	35.16 (15.15)	35.04 (15.14)	34.75 (15.13)	39.89 (15.69)	39.92 (15.89)	40.17 (16.02)	39.92 (16.00)	39.35 (16.14)
% Age <18.00	9	10	10	11	12	5	5	5	6	6
% Age 18.00–64.99	86	85	85	85	84	86	86	86	86	86
% Age ≥65.00	5	5	5	4	4	9	9	9	8	8
% Female	58	58	58	57	57	49	50	50	50	51
% Male	42	42	42	43	43	51	50	50	50	49
N (incident cases)	1935	2,345	2,673	2,935	3,103	1876	2,439	2,898	3,373	3,699
Mean disease duration (SD)	8.24 (4.33)	10.50 (5.89)	12.80 (7.35)	15.98 (8.75)	17.59 (10.0)	7.61 (4.18)	9.6 (5.66)	11.74 (7.0)	13.61 (8.36)	15.60 (9.59)
Duration <1.00 yr	8	5	5	4	2	7	6	4	4	2
Duration 1.00–4.99 yr	23	20	16	14	11	30	24	19	17	15
Duration 5.00 yr	69	75	79	82	87	63	70	77	79	83
% Experiencing IBD-related hospitalization	6	4.3	4.3	3.1	1.9	2.7	2.4	1.8	1.8	1.4
% Actively using anti-TNF	—	1.4	3.1	8	13.1	—	0.2	0.7	3	6.4
% Living in rural environment	25.9	26.6	26	26.1	26.2	29.6	29	27.5	27.6	27.3

CD, Crohn's disease; IBD, inflammatory bowel disease; TNF, tumor necrosis factor; UC, ulcerative colitis.

7.1% for UC (Figure 1a). We also saw rising rates of immunomodulator use between 1997 and 2017, although the rate of uptake slowed in 2006 relative to the change in rate before 2006 for CD and UC (Figure 1b).

Crohn's disease

There was a substantial decline in the mean rate of corticosteroid utilization in persons with CD (see Supplementary Tables 3, 4, 5, see Supplementary Digital Contents 4, 5, 6, <http://links.lww.com/AJG/B935>, <http://links.lww.com/AJG/B936>, <http://links.lww.com/AJG/B937>). The mean rate of corticosteroid consumption decreased from 419 mg of prednisone equivalents per year in 1997 to 169 mg of prednisone equivalents per year in 2017, corresponding to a decrease in the overall amount of corticosteroid dispensed of 3.8% per year (95% confidence interval [CI] 3.1–4.6) (Figure 2a). The proportion of persons in each year who received any corticosteroid also decreased from 20.0% per year to 13.5% (relative rate of decline: 1.8% per year, 95% CI –1.5 to 2.1) (Figure 2b). Similarly, the proportion of persons who were heavy corticosteroid users in any given year also decreased from 7.2% in 1997 to 2.9% in 2017 (relative annualized rate of decrease 4.5%, 95% CI 3.3%–5.6%) (Figure 2c).

In joinpoint analysis, there seems to be an acceleration in the rate of decline in the total dose of corticosteroid dispensed per year in approximately 2007. Before 2007, the mean dose of corticosteroids was dropping by 1.9% per year (95% CI 0.8–3.1), whereas after 2007, the rate of the annual decrease rose to 5.7% per year (95% CI 4.5%–7.0%). There was also an acceleration in the rate of decline in heavy use in 2007, where the relative change in the use rate was 2.4% before 2007 (95% CI 0.7%–4.1%) and

6.5% after 2007 (95% CI 4.7%–8.3%). There was no inflection point for the overall proportion of corticosteroid dispensed.

Budesonide use remained generally low over the duration of the analysis, with between 3% and 5% of persons using budesonide in any year. In joinpoint analysis, budesonide dispensing was stable between 1997 and 2006 (annual percentage change: –3.9%, 95% CI –8.2 to +0.6), although from 2007 to 2017, the use of budesonide significantly increased (annual percentage change: 3.9%, 95% CI 1.2–6.8) (see Supplementary Figure 1, see Supplementary Digital Content 1, <http://links.lww.com/AJG/B932>).

Ulcerative colitis

As with Crohn's disease (see Supplementary Tables 6, 7, 8, see Supplementary Digital Content 7, 8, 9, <http://links.lww.com/AJG/B938>, <http://links.lww.com/AJG/B939>, <http://links.lww.com/AJG/B940>), there was a substantial decrease in the per person rate of corticosteroid use over the duration of the analysis, with mean annual dose of prednisone equivalents dispensed decreased from 380 mg per patient per year in 1997 to 240 mg per patient per year in 2017 (mean decrease per year of 2.5%, 95% CI 2.1–2.8%) (Figure 3a). However, there was a more modest decline in the proportion of persons with UC dispensed a corticosteroid (17.1% in 1997 to 14.9% in 2017, annualized mean relative rate of decrease 0.7% [95% CI 0.4–1.1]) (Figure 3b), as well as in the proportion of persons who were heavy corticosteroid users in a given year (6.4% in 1997 to 4.2% in 2017, annualized mean relative rate of decrease 2.4% [95% CI 2.0–2.8]) (Figure 3c).

Unlike with CD, there was no evidence of an inflection point corresponding to a change in the rate of change in overall dosing

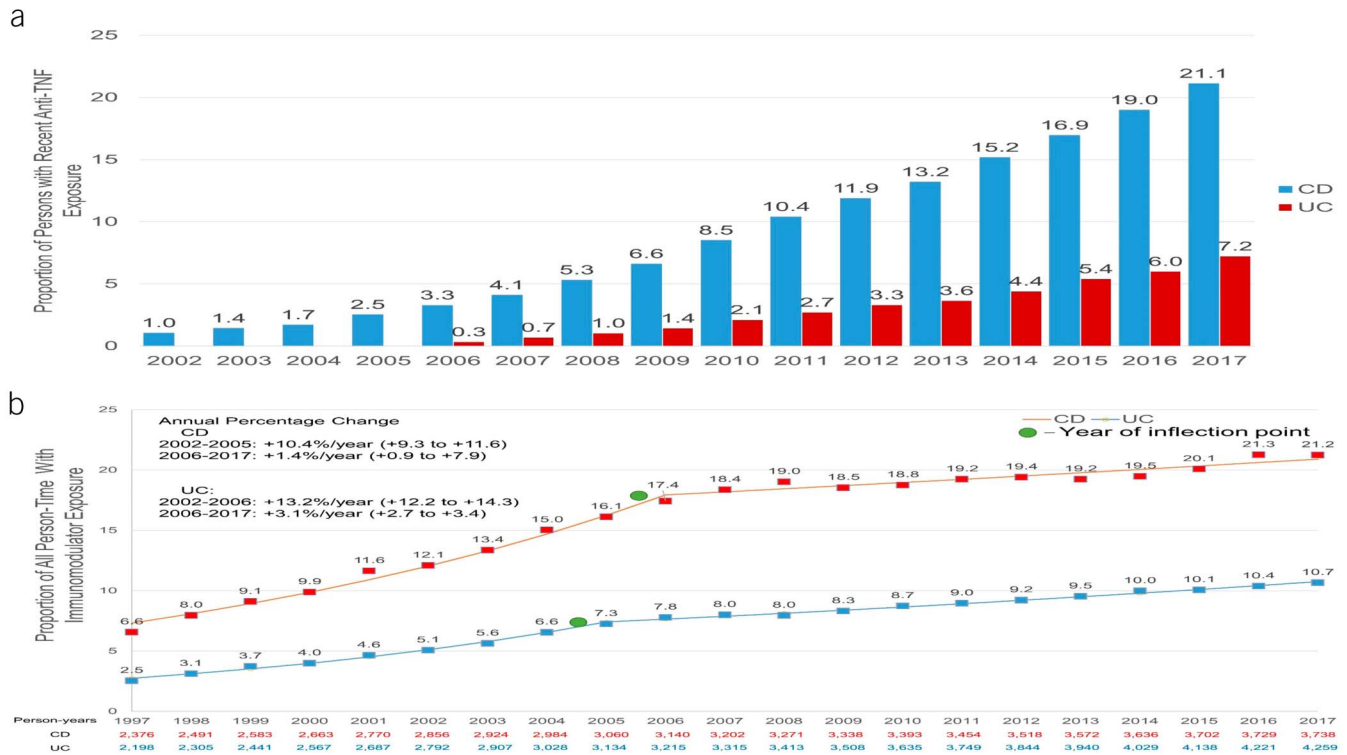


Figure 1. Proportion of person time with recent or current: (a) anti-TNF and (b) immunomodulator use. CD, Crohn's disease; TNF, tumor necrosis factor; UC, ulcerative colitis.

of CS among those with UC. The decrease in the proportion of persons with UC prescribed corticosteroid decreased by 1.6% per year between 1997 and 2005 (95% CI 0.9–2.5), but then remained stable from 2005 onward (rate of change per year -0.1% , 95% CI -0.4 to 0.3). Heavy use of corticosteroid decreased steadily from 1997 to 2017 by a relative rate of 2.4% per year (95% CI 2.0–2.4).

Stratified analysis

In patients with CD and UC, rates of decline in corticosteroid use were similar among men and women (see Supplementary Figure 2a and 2b, see Supplementary Digital Content 1, <http://links.lww.com/AJG/B932>). We also did not see any appreciable impact of socioeconomic status or rurality on the rate of decline of corticosteroid use (data not shown).

By disease duration. During the first year after IBD diagnosis, the cumulative dose of corticosteroids and the likelihood of exposure to corticosteroids did not significantly decrease over time for CD and actually increased slightly over time among persons with UC. However, significant decreases in corticosteroid use were seen in the subset of patients in the second year and beyond after diagnosis (see Supplementary Figure 3a and 3b, see Supplementary Digital Content 1, <http://links.lww.com/AJG/B932>).

By age. Similar rates of decline in corticosteroid use were seen for all age groups; however, the decline was most precipitous among children with CD starting in 2005, after which the annual rate of decline was -16.9% per year (95% CI -13.2 to -20.4) (see Supplementary Figure 4, see Supplementary Digital Content 1, <http://links.lww.com/AJG/B932>). When data from children were removed from the analysis, there remained a significant decline in

the use of corticosteroids, with an acceleration in the rate of decrease occurring in 2010.

By exposure to biologics. Among persons who had been prescribed an anti-TNF in the previous 365 days for CD, the mean annual use of corticosteroids decreased from 1,234 mg of prednisone equivalents per year in 2002 to 248 mg of prednisone equivalent per year, an annual decline of 10.1% per year (95% CI for rate of decline 8.7%–11.4%). Among nonusers of anti-TNFs, the rates have decreased from 336 mg/yr in 2002 to 147 mg/yr in 2017 (5.5% decline per year, 95% CI for rate of decline 4.4%–6.3%) (Figure 4a). Similar trends were seen in UC, where between 2006 and 2017, corticosteroid use decreased from 3,245 mg/yr in 2006 to 617 mg/yr (10.9% decline per year, 95% CI -6.7% to -14.9%) among persons with recent exposure to anti-TNFs and from 319 to 211 mg/yr (3.8% decline per year, 95% CI 3.1%–4.5%) in persons with UC without recent anti-TNF exposure (Figure 4b).

DISCUSSION

In our analysis of more than 2 decades of population-based data on medication use in IBD, we detected significant declines in the overall use of corticosteroids, resulting in an overall decline of 60% between 1997 and 2017 for CD, and an overall drop of approximately 40% for UC. Moreover, the rate of decline in CD was greater in the more recent decade under evaluation, although there was no detectable acceleration in the rate of decline for persons with UC. However, when evaluated more closely, the most rapid deceleration in corticosteroid use after 2007 was restricted to the under 18 cohort in CD, which comprised less than 10% of the overall cohort. Among persons with CD, decreases in

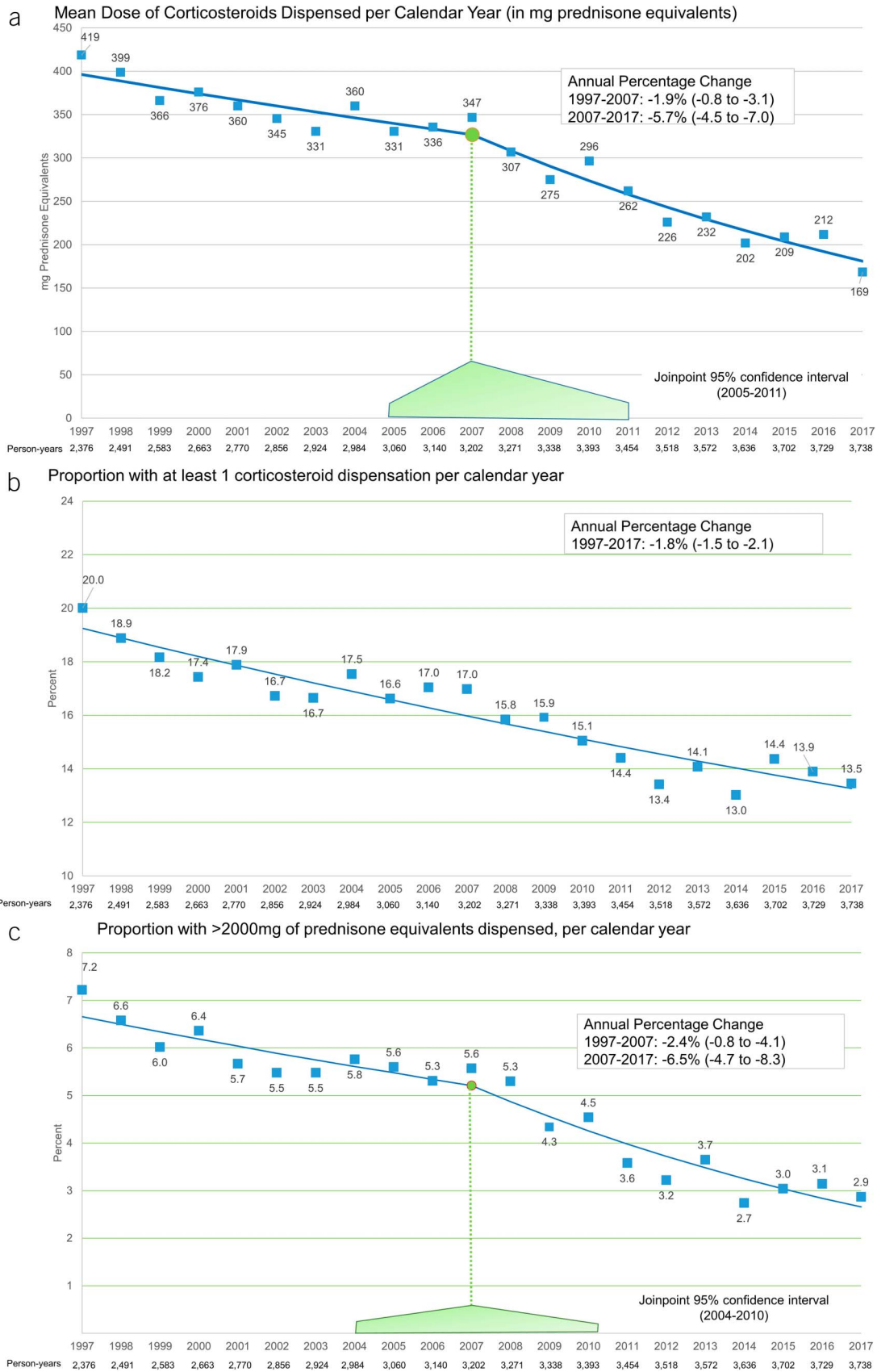


Figure 2. (a-c) Corticosteroid dosing by year for Crohn's disease.



Figure 3. (a-c) Corticosteroid dosing by year for ulcerative colitis.

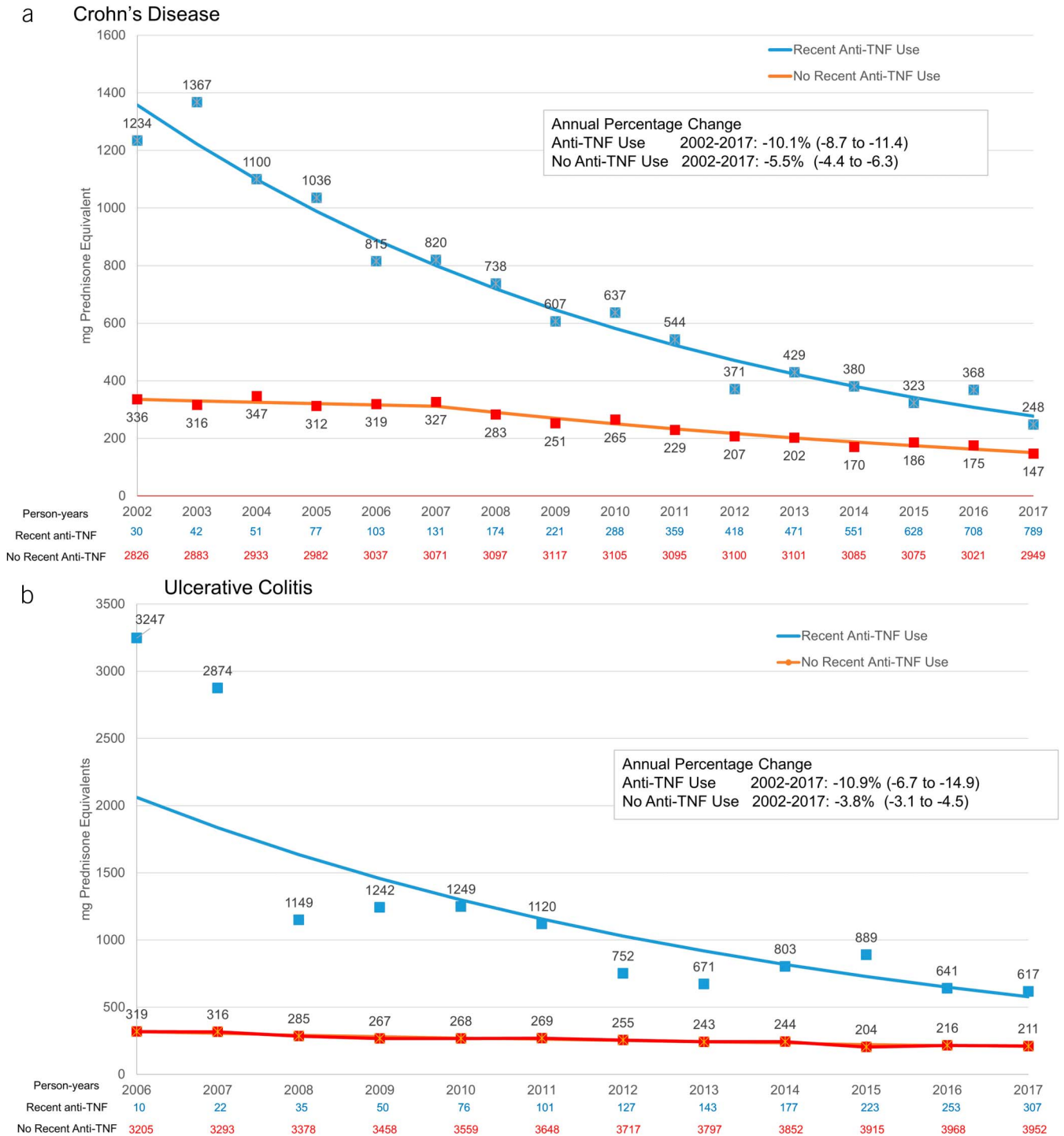


Figure 4. Cumulative annual dose of corticosteroids, by recent anti-TNF use. TNF, tumor necrosis factor.

overall corticosteroid consumption were most notable among persons with longer durations of disease (at least 1 year or more), particularly after 2007. However, 1 in 7 persons with IBD still had a prescription for a corticosteroid in 2017, and 2%–4% were receiving more than 2000 mg of corticosteroids annually. Among recent users of anti-TNF medications, the mean dosage of corticosteroids used has decreased by 80%

This analysis raises several questions that are deserving of further explanation. First, what is responsible for the overall

decline in corticosteroid use over the past 2 decades? Second, what happened on or around 2007 which led to a further acceleration in the decline in corticosteroid use among persons with CD? Last, why was a similar acceleration in the rate of decline not seen in persons with UC?

Among persons with CD, there was a modest reduction (2% annual relative decrease) in the mean corticosteroid dose per person between 1997 and 2007, as well as in the proportion of people who became heavy users. This trend largely predates the

introduction of continuous anti-TNF therapy into the treatment armamentarium because maintenance infliximab was not approved in the Manitoba formulary until 2005. This modest initial decline could be related to several factors. First, this may have been the continuation of a conscious reduction in the use of corticosteroids for milder symptoms of IBD in recognition of the known complications of corticosteroid use. Second, oral budesonide was introduced around 1996 (17), which may have been substituted for some prednisone prescriptions. As is shown in Supplementary Figure 1 (see Supplementary Digital Content 1, <http://links.lww.com/AJG/B932>), the rate of increase in budesonide use is relatively small in comparison with the decline in CS use rates in CD. In addition, the rates of surgical intervention have been relatively stable in the past decade or persons with CD at approximately 0.85% of persons with CD per year undergoing an intestinal resection. Therefore, it would be unlikely that the decline in corticosteroid use can be ascribed to changes in the rate of surgical intervention (18). Last, use of immunomodulators such as thiopurines and methotrexate was increasing before the introduction of anti-TNF agents (19); although these therapies are less effective than biologics in their corticosteroid sparing effects (20,21), they are still superior to placebo (22). Therefore, it is more likely on the preponderance of the evidence that the declining rates of CS use in CD were more related to an increasing uptake of anti-TNFs.

One possible reason for the rate of decline in the latter half of our study period among persons with CD is the introduction and increasing penetrance of anti-TNF therapies into practice. Although infliximab was first listed in Manitoba in 2001 for use as an induction therapy for CD, maintenance infliximab was not approved until 2005, and patients could only receive recurrent doses of infliximab if symptoms recurred. In 2005, adalimumab was also approved for induction and maintenance of CD. Therefore, the bending of the curve would not be expected to take place immediately on introduction of biologic agents, but only after there was clearance with using agents as maintenance agents (when their corticosteroid-sparing effects can be more completely realized). It is also possible that clinicians developed sufficient comfort with anti-TNFs to substitute the use of anti-TNFs instead of corticosteroids for acutely ill patients. Concurrent with increasing penetrance of biologic therapies into the CD population, there was an acceleration in rates of decline (averaging 6% per year up until at least 2017). The decline was especially evident in the pediatric population, where CS use rates declined by 16.7% per year from 2004 onward, after steadily increasing before 2004, leading to a 90% absolute decline in the modeled mean amount of corticosteroid dispensed from the peak in 2004 of nearly 2.5 g/yr to 250 mg/yr in 2017. We have also previously shown that anti-TNF use was more prevalent in our pediatric population than in our adult population, with 43% of children diagnosed with CD being prescribed an anti-TNF within the 1st year after diagnosis (23). In addition, a better understanding over the past decade on the importance of targeting and maintaining mucosal healing in CD for preventing future disease activity and complications may be also be responsible for the continuing declines in corticosteroid use. One further explanation for the increasing rate of decline in the most recent decade is that clinicians became more aware of serious adverse effects of corticosteroids especially in relation to serious infections.

Although corticosteroid use has declined in UC, we have not seen a further increase in the rate of decline in the era of

biologic therapy. The initial studies supporting the efficacy of anti-TNF therapy in UC were first published in 2005 (24), and utilization rates of biologics for UC have lagged behind that for CD. We had previously published data which showed that in 2007 roughly 5% of persons with CD were using an anti-TNF, but it was not until 2015 that 5% of patients with UC were using anti-TNFs (10). This trend of higher utilization of biologic therapy in CD vs UC has also been shown in many other patient cohorts. Moreover, we do show that despite similar proportions of persons with CD and UC having being prescribed corticosteroids over time, the rates of use exceeding 2,000 mg/yr are higher among persons with UC. This may imply that persons who are being treated with UC have greater difficulty with completing a corticosteroid taper or may be more likely to reinstate corticosteroids after an apparently successful taper. Alternatively, it may be that clinicians find UC to be more corticosteroid-responsive than CD, especially since corticosteroids are generally ineffective in penetrating CD. Last, the availability of aminosaliculates as alternative therapy for UC may lead to these agents being used in persons who should instead be on biologic therapy. As aminosaliculates are less effective in persons with moderate-to-severe disease, inappropriate persistence on aminosaliculates may lead to a greater need for rescue therapy with corticosteroids. Although our data only go to 2017, it remains to be seen whether further refinements in the care of persons with IBD, such as the increasing use of therapeutic drug level monitoring, regular use of disease activity markers such as fecal calprotectin and earlier use of biological therapies will promote the lower utilization of corticosteroids in years to come.

Approximately 1 in 7 persons is still receiving a corticosteroid dispensation in a calendar year, and each of those persons on average is exposed to 1,200–1,600 mg of corticosteroid per year. Although there is likely some corticosteroid use that is unavoidable because of lack of response to noncorticosteroid therapies, rapid responses seen in acutely inflamed disease such as acute severe colitis, or exhaustion of other available treatment options, it is undeniable that some proportion of the ongoing corticosteroid use is unnecessary (25). Selinger et al. (26) have recently reported on excess corticosteroid use among 11 IBD specialty practices in the United Kingdom and found that 30% of patients with IBD used corticosteroids in a given year, and approximately 15% were deemed to have corticosteroid dependence or excessive use of corticosteroids. Of those with excessive use, approximately 50% on review were felt to be avoidable or inappropriate. This would suggest that in a defined population of patients with IBD, no more than 5%–7% of patients should be exposed to corticosteroids annually if high quality care is provided. This threshold may have potential for being used as a quality metric; i.e., clinicians should be striving to ensure no more than 5%–7% of patients are exposed to corticosteroids in any given year, and that patient cohorts with higher rates may represent opportunities for improvement in the process of care.

This same group later showed that a multipronged intervention aimed at auditing practices and identifying opportunities to avoid corticosteroid use was able to reduce excess corticosteroid use compared with centers where this intervention was not implemented (11.5% vs 17.1%, $P < 0.001$) (27). In addition to the intervention, the other factor which was most strongly associated with a reduction in excessive

corticosteroid use was a patient being associated with IBD clinics where a multidisciplinary team approach was used to manage IBD care. These studies highlight the organizational approaches which may have to be adopted to result in further decreases in corticosteroid use, especially among persons with UC.

Our study does have some limitations impacting our ability to draw high-level inferences. Determining the precise cause of changes in prevalence over time is always speculative, given that these changes take place in a real-world environment where individual factors are all changing in unison. We are performing a separate analysis to specifically evaluate the impact of anti-TNF use on subsequent corticosteroid use in individual patients which suggests that biologic use is associated with a significant reduction in corticosteroid use for up to 5 years after anti-TNF initiation (28). Although we were not able to identify inpatient use of corticosteroids, we believe that most inpatient use would be in either persons who had been previously prescribed corticosteroids in the outpatient setting or would have been prescribed oral corticosteroids after discharge. Moreover, our database does not contain information on underlying disease severity or phenotype, and therefore, we are not able to identify with precision whether the decline in corticosteroid use over time was more or less pronounced among different patient profiles. There have been no systemwide initiatives in the province to optimize the care of individuals with IBD, and hence, these results, particularly in the most recent years, may not be applicable to jurisdictions/institutions undertaking such efforts. It is also uncertain how generalizable our findings are to non-anti-TNF biologics because there was only minimal use of these agents in this population before 2017. In conclusion, we have shown that there has been a substantive decline in corticosteroid use in persons with IBD over the past 2 decades, which at least in persons in CD have been accelerated during a time when anti-TNF use became more prevalent. We have also shown that the rates of corticosteroid use in our population still remain too high. Further exploration of the precise impact of anti-TNF use, particularly in regards to whether wider adoption of more aggressive monitoring of disease activity and treating to target, promotes further reduction in corticosteroid use in the years to come. Given that reduction in corticosteroid use is an important indicator of quality of care, our work highlights the importance of defining a threshold of “acceptable” corticosteroid use that clinicians should strive for in their IBD population.

CONFLICTS OF INTEREST

Guarantor of the article: Laura E. Targownik, MD, MSHS, FRCPC.

Specific author contributions: L.E.T., E.I.B., G.G.K., C.N.B., and H.S.: study concept and design. L.E.T., C.N.B., A.T., and Z.N.: acquisition of data. L.E.T., E.I.B., G.G.K., C.N.B., H.S., S.B.C., M.E.K., and S.K.M.: analysis and interpretation of data. L.E.T.: drafting of the manuscript. L.E.T., E.I.B., G.G.K., C.N.B., H.S., S.B.C., M.E.K., and S.K.M.: critical revision of the manuscript for important intellectual content. L.E.T., A.T., and Z.N.: statistical analysis. L.E.T.: obtained funding.

Financial support: None to report.

Potential competing interests: L.E.T. has received investigator initiated funding from Janssen Canada and served on advisory boards for AbbVie Canada, Takeda Canada, Merck Canada, Pfizer

Canada, Janssen Canada, and Roche Canada. C.N.B. has served on advisory Boards for AbbVie Canada, Ferring Canada, Janssen Canada, Shire Canada, Takeda Canada, and Pfizer Canada; consultant for Mylan Pharmaceuticals; educational grants from AbbVie Canada, Shire Canada, Takeda Canada, and Janssen Canada; speaker's panel for AbbVie Canada, Ferring Canada, Medtronic Canada, and Shire Canada; and received research funding from AbbVie Canada. E.I.B. was supported by a New Investigator Award from the Canadian Institutes of Health Research, Crohn's and Colitis Canada, and Canadian Association of Gastroenterology; also supported by the Career Enhancement Program of the Canadian Child Health Clinician Scientist Program. G.G.K. has received speaking or consultancy honoraria from AbbVie, Janssen, Pfizer, Takeda, and Shire; he has received a grant from AbbVie, Janssen, Merck, and Shire. H.S. has been on advisory board of Pendopharm, Ferring, Takeda, and Merck Canada and received educational grant from Ferring and investigator initiated research funding from Merck Canada. S.K.M. has received honoraria for speaking or consultancy from AbbVie, Janssen, Takeda, Pfizer, Shire, and Ferring. This study is based in part on deidentified data Manitoba Health, obtained with the permission of the Manitoba Health Information Privacy Committee. The interpretation and conclusions contained herein are those of the researchers and do not necessarily represent the views of the Government of Manitoba.

Study Highlights

WHAT IS KNOWN

- ✓ Anti-TNFs therapy has been shown to reduce the use of corticosteroids among persons with moderate-to-severe IBD in randomized controlled trials and in closely observed cohorts.
- ✓ It is less certain the impact of anti-TNF therapy on corticosteroid use in the diverse real-world practice setting.

WHAT IS NEW HERE

- ✓ Corticosteroid use has dramatically decreased among persons with Crohn's disease (CD) and ulcerative colitis (UC) from the prebiologic era to the current day.
- ✓ Although the rate of decline accelerated after the introduction of anti-TNF therapy in CD, a similar acceleration was not seen among persons with UC.
- ✓ Reductions in corticosteroid use have further decreased among anti-TNF users, suggesting improving timing and dosing of biologic therapy over time.
- ✓ The rate of acceleration was greatest among persons younger than 18 years, who also have the greatest prevalence of anti-TNF use.

TRANSLATIONAL IMPACT

- ✓ Showing a benefit in the real world for biologic use in reducing corticosteroid use in IBD provides further impetus for relaxing restrictions on the use of these agents in clinical practice.

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