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Forecasting the Incidence and Prevalence of Inflammatory Bowel Disease: A Canadian nationwide analysis

Short Title: Forecasting the Incidence and Prevalence of IBD in Canada

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Conflicts of Interest:

Dr. Kaplan has received honoraria for speaking or consultancy from AbbVie, Amgen, Janssen, Pfizer, Sandoz, and Pendophram. Dr. Kaplan received grants for research from Ferring and for educational activities from AbbVie, Bristol Myers Squibb, Ferring, Fresenius-Kabi, Janssen, Pfizer, Takeda. 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.

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Dr. Panaccione has received consulting fees from Abbott, AbbVie, Alimentiv (formerly Robarts), Amgen, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Cosmos Pharmaceuticals, Eisai, Elan, Eli Lilly, Ferring, Galapagos, Fresenius Kabi, Genentech, Gilead Sciences, Glaxo-Smith Kline, JAMP Bio, Janssen, Merck, Mylan, Novartis, Oppilan Pharma, Organon, Pandion Pharma, Pendopharm, Pfizer, Progenity, Protagonist Therapeutics, Roche, Sandoz, Satisfai Health, Shire, Sublimity Therapeutics, Takeda

Dr. Benchimol has acted as a consultant for McKesson Canada and the Dairy Farmers of Ontario for matters unrelated to medications used to treat inflammatory bowel disease. He has also acted as a consultant for the Canadian Agency for Drugs and Technology in Health (CADTH).

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Dr. Frank Hoentjen has served on advisory boards or as speaker for AbbVie, Janssen, MSD, Takeda, Pfizer, Celltrion, Teva, Sandoz, and Pendopharm, and has received independent research funding from Janssen, AbbVie, Pfizer and Takeda.

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All aggregate data reported is provided in an open-access, online interactive map: <u>https://kaplan-gi.shinyapps.io/Canada_inc_prev/</u>

Disclosure

This study is based in part on de-identified data provided by the Saskatchewan Ministry of Health and eHealth Saskatchewan. The interpretation and conclusions contained herein do not necessarily represent those of the Government of Saskatchewan, the Saskatchewan Ministry of Health, or eHealth Saskatchewan. This study is based in part on de-identified data provided by Alberta Health Services, Régie de l'assurance maladie du Québec, Ministry of Health of British Columbia and Population Data BC, Saskatchewan Ministry of Health, Health Data Nova Scotia of Dalhousie University, Manitoba Health, and Newfoundland and Labrador Centre for Health Information. The interpretation and conclusions contained herein are those of the researchers and do not necessarily represent the views of the Government of Alberta, Government of Quebec, Government of British Columbia, Government of Saskatchewan or the Ministry of Health, Health Data Nova Scotia or the Department of Health and Wellness, or the Government of Manitoba, or the Government of Newfoundland & Labrador. Neither the Government of Alberta nor Alberta Health Services expressed any opinion in relation to this study. This study was supported by ICES, which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care. The opinions, results and conclusions reported in this paper are those of the authors and are independent from the funding sources. No endorsement by Institute for Clinical Evaluative Sciences or the Ontario Ministry of Health and Long-Term Care is intended or should be inferred. The interpretation and conclusions contained herein do not necessarily represent those of the Government of Saskatchewan or the Ministry of Health. Although this research and health service assessment analysis is based on data obtained from the Nova Scotia Department of Health and Wellness, the observations and opinions expressed are those of the authors and do not represent those of Health Data Nova Scotia or the Department of Health and Wellness

ICMJE Author Contributions Criteria:

Conception or design of the work: SC, EIB, CNB, AAZ, AB, JLJ, MEK, SKM, ARO, JNPS, LET, GGK

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Reviewing the work critically for important intellectual content: EIB, CNB, AAZ, AB, MWC, YC, FH, LH, KJ, JLJ, JK, MEK, LL, WEM, SKM, ZN, ARO, RP, JNPS, HS, LET, DW, JWW, Final approval of the manuscript: SC, EIB, CNB, AAZ, AB, MWC, YC, FH, LH, KJ, JLJ, JK, MEK, LL, WEM, SKM, ZN, ARO, RP, JNPS, HS, LET, DW, JWW, GGK.

All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Abbreviations:

AAPC Average Annual Percentage Change AB Alberta ARIMA Autoregressive Integrated Moving Average BC British Columbia CanGIEC Canadian Gastro-Intestinal Epidemiology Consortium CD Crohn's disease CI Confidence Interval IBD Inflammatory bowel disease IBD-U IBD-Unclassifiable MB Manitoba NL Newfoundland ON Ontario PI Predictive Interval QC Quebec NS Nova Scotia SK Saskatchewan UC Ulcerative Colitis

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STUDY HIGHLIGHTS

What is known:

• The incidence and prevalence of IBD in Canada is among the highest in the world.

What is new here:

- Overall incidence of IBD in Canada is projected to remain stable over the next decade.
- Incidence of IBD in children is increasing by 1.27% per year.
- Prevalence of IBD is estimated to rise to 1.1% of the Canadian population by 2035.
- Seniors represent the fastest growing demographic living with IBD.



ABSTRACT

Objective

Canada has a high burden of inflammatory bowel disease (IBD). Historical trends of IBD incidence and prevalence were analyzed to forecast the Canadian burden over the next decade.

Methods

Population-based surveillance cohorts in eight provinces derived from health administrative data assessed the national incidence (2007–2014) and prevalence (2002–2014) of IBD. Autoregressive integrated moving average models were used to forecast incidence and prevalence, stratified by age, with 95% prediction intervals (PIs), to 2035. The average annual percentage change (AAPC), with 95% confidence interval (CI) were calculated for the forecasted incidence and prevalence.

Results

The national incidence of IBD is estimated to be 29.9 per 100,000 (95%PI: 28.3, 31.5) in 2023. With a stable AAPC of 0.36% (95%CI: -0.05, 0.72), the incidence of IBD is forecasted to be 31.2 per 100,000 (95%PI: 28.1, 34.3) in 2035. The incidence in pediatrics (<18 years) is increasing (AAPC:1.27%; 95%CI: 0.82, 1.67), but stable in adults (AAPC: 0.26%; 95%CI: -0.42, 0.82). The prevalence of IBD in Canada was 843 per 100,000 (95%PI: 716, 735) in 2023 and is expected to steadily climb (AAPC: 2.43%; 95%CI: 2.32, 2.54) to 1,098 per 100,000 (95%PI: 1068, 1127) by 2035. The highest prevalence is in seniors with IBD (1174 per 100,000 in 2023; AAPC: 2.78%; 95%CI: 2.75, 2.81).

Conclusion

Over the next decade, the Canadian healthcare systems will contend with the juxtaposition of rising incidence of pediatric IBD and a rising prevalence of overall IBD driven by the aging population.

Keywords: Crohn's disease; ulcerative colitis; epidemiology; population-based

BACKGROUND

Inflammatory bowel disease (IBD), consisting of Crohn's disease and ulcerative colitis, is a global disease.¹ During the latter half of the 20th century, early industrialized regions in North America, Europe, and Oceania experienced rapidly rising incidence.² At the turn of the 21st century, the incidence of IBD stabilized in many regions in the Western world.¹ However, for unexplained reasons, Scandinavia has reported among the highest incidence rates of IBD,^{3,4} and the incidence continues to climb in pediatric-onset IBD.⁵ Elucidating heterogeneity in age and geographic trends of the incidence of IBD across time may provide clues to the environmental drivers of disease pathogenesis.⁶

Over the past several decades, the prevalence of IBD has steadily climbed due to the incidence of IBD greatly exceeding the mortality rate among persons with IBD.⁷ The compounding prevalence of IBD has been demonstrated in several early industrialized regions including the USA,⁸ Canada,⁹ Scotland,¹⁰ and Denmark.^{3,4} A general increase in life expectancy is contributing to the increasing prevalence of older adults with IBD. As a result, gastroenterology clinics must contend with a rising volume of patients with greater complexity, while society bears the high cost of IBD care.¹¹ Forecasting the change in epidemiologic trends of IBD over the next decade allows healthcare systems to prepare for the rising burden of IBD.¹²

To understand the potential future burden of IBD in Canada, we conducted a nationwide epidemiologic study to explore historical trends in the incidence and prevalence of IBD, including the estimated incidence and prevalence in 2023, and then forecasted the changing epidemiologic patterns out to 2035.

METHODS

Data Sources and Study Populations

The Canadian Gastro-Intestinal Epidemiology Consortium (CanGIEC) is a national research collaboration of gastroenterologists and epidemiologists. Population-based health administrative data with validated algorithms are used to identify people living with IBD.¹³⁻¹⁵ IBD prevalent cohorts were created from the following provinces (representing over 95% of the Canadian population): Alberta (AB), British Columbia (BC), Manitoba (MB), Newfoundland (NL), Nova Scotia (NS), Quebec (QC), Ontario (ON), and Saskatchewan (SK). Based on these prevalent cohorts, incident cohorts were created using validated five-year washout periods for adults and a three-year washout for those <18 years old.^{15,16} Annual estimates for incidence and prevalence of IBD were provided for each province and stratified by disease type (Crohn's disease and ulcerative colitis including IBD-Unclassifiable using administrative data codes, hereafter referred to as IBD-U, but not representing the clinical entity IBD-Unclassified), age groups, and sex. Supplemental Table 1 provides the administrative healthcare database sources, algorithm used to identify the study population, data availability, and population estimates for each of the eight provinces. All provinces received ethics approval in accordance with their appropriate governing bodies.

Patient Involvement

There was no direct patient or public involvement in the creation, execution, or review of this study. Crohn's and Colitis Canada, a national patient advocacy organization, works in partnership with CanGIEC to outline the needs of people living with IBD in terms of research and advocacy—our study was a result of that advocacy. Patients and the public have access to our findings through a shiny app (<u>https://kaplan-gi.shinyapps.io/Canada_inc_prev/)</u>.

Provincial and National Data

Age- and sex-specific annual rates of IBD, Crohn's disease, and ulcerative colitis were provided from each individual province from the available healthcare databases as follows: AB [2002–2018], BC [1999–2019], MB [1987–2014], NL [1995–2014], NS [2001–2018], QC [1996–2014], ON [1999–2016], and SK [1998–2018]. Overlapping years of provincial incidence (2005–2014) and prevalence (2002–2014) data, numerators, and denominators were combined to create a national Canadian model. Data from Statistics Canada were used to calculate the annual age-and sex-standardized incidence and prevalence rates, both provincially and nationally, using the age- and sex-matched Canadian population for a given year. Age- and sex-stratified analyses were undertaken using the following categories: male, female, pediatric (<18 years old), adults (18–64 years old), and seniors (≥65 years old). As the pediatric age group used a three-year washout for incidence instead of the five-year used for adult and elderly populations, their data extend from 2005–2014 instead of 2007–2014.

Statistical Analysis

Primary forecasting analyses of standardized incidence and prevalence were performed using autoregressive integrated moving average (ARIMA) models, which is a type of time series analysis that can analyze data at a specific time period relative to data contained in prior periods while addressing dependence in yearly prevalence or incidence data.¹⁷ A comprehensive description of the rationale, development, and assumptions of ARIMA models has been previously published.^{9,10} Once the appropriate ARIMA model was chosen for the data, the incidence and prevalence (per 100,000 persons) were then forecast from 2014 to 2035 with associated 95% prediction intervals (PI).⁹ The average annual percentage change (AAPC), with associated 95% confidence interval (CI), of forecast incidence was calculated using Poisson

regression, and log binomial regression was used for forecasted prevalence. A sensitivity analysis restricting to only those provinces that had available IBD incidence and prevalence data to 2018 (AB, BC, SK NS) to validate the forecast using a longer timeframe. The study was reported in accordance with the Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) statement (Supplemental File).

RESULTS

Incidence

In 2014, the age- and sex-standardized incidence between provinces was lowest in QC at 21.9 per 100,000 persons (95%CI: 20.9, 22.9) and highest in the Atlantic provinces (NL: 44.7 per 100,000; 95%CI: 39.0, 50.4; NS: 41.6 per 100,000; 95%CI: 37.5, 45.8) (Figure 1A and Supplemental Table 2). Figure 1A shows the provincial temporal trends of historical and forecasted incidence with significantly decreasing rates in MB, NS, and SK; stable in AB and ON; and significantly increasing in BC, NL, and QC (Supplemental Table 2).

In 2023, the national incidence rate of IBD is estimated to be 29.9 per 100,000 (95%PI: 28.3, 31.5) equating to 11,708 (95%PI: 11,079, 12,336) people that will be newly diagnosed with IBD in Canada this year (Table 1 and Figure 2A). The forecasted incidence of IBD in Canada was stable from 2014 to 2035 with an AAPC of 0.36% (95%CI: -0.05, 0.72) (Table 1 and Figure 2A) and forecast to be 31.2 per 100,000 (95%PI: 28.1, 34.3) in 2035 (Table 1 and Figure 2A). The incidence of Crohn's disease (2023: 12.7 per 100,000; 95%PI: 11.5, 13.9) is forecast to remain stable, whereas for ulcerative colitis combined with IBD-U (2023: 17.2 per 100,000; 95%PI: 16.4, 18.1), the incidence is forecast to increase (AAPC: 0.99%; 95%CI: 0.69, 1.26) (Table 1).

Whereas the incidence rates of IBD, Crohn's disease, and ulcerative colitis in the adult and senior groups and Crohn's disease in pediatrics were forecast to remain stable, the incidence of pediatric-onset IBD and ulcerative colitis were forecast to significantly increase with an AAPC of 1.27% (95%CI: 0.82, 1.67) and 1.98% (95%CI: 0.80, 2.84), respectively (Table 1 and Figure 2A). The incidence of IBD in pediatrics was 14.4 per 100,000 (95%CI: 13.5, 15.3) in 2014 and is forecast to rise to 18.5 per 100,000 (95%PI: 16.3, 20.8) in 2035, which equates to an increase from an estimated 1000 new pediatric cases in 2014 to 1479 new pediatric cases in 2035 (Table 1 and Figure 2A).

Prevalence

The estimated prevalence of IBD in 2023 ranged from 720 per 100,000 (95%PI: 688, 751) in MB to 1239 per 100,000 (95%PI: 1182, 1296) in NS. Figure 1B shows historical and forecasted prevalence rates for the individual provinces. The prevalence of IBD in all provinces is forecast to continue to significantly increase with positive AAPCs ranging from 1.84% (95%CI: 1.47, 2.17) in MB to 3.03% (95%CI: 2.39, 3.55) in QC (Supplemental Table 2 and Figure 1B).

The national prevalence of IBD in 2023 is estimated to be 843 per 100,000 (95% PI: 828, 859), which represents 329,688 (95% PI: 323,629, 335,746) Canadians living with IBD (Table 1 and Figure 2B). The prevalence in Canada is forecast to significantly increase with an AAPC of 2.43% (95% CI: 2.32, 2.54) (Table 1 and Figure 2B). In 2035, the forecasted prevalence is 1,098 per 100,000 (95% PI: 1068, 1127), representing 480,294 (95% PI: 467,321, 493, 268) individuals living with IBD (Table 1 and Figure 2B). The prevalence of Crohn's disease (2023: 423 per 100,000; 95% PI: 412, 435) and ulcerative colitis with IBD-U (2023: 420 per 100,000; 95% PI: 414, 426) are forecast to increase significantly by 2.33% and 2.54%, respectively (Table 1).

Similarly, all age groups are forecast to have significantly increasing prevalence rates, with the largest AAPC occurring in seniors (AAPC: 2.78%; 95%CI: 2.75, 2.81) (Table 1 and Figure 2B). In 2023, the prevalence of IBD is highest in seniors (1174 per 100,000; 95%PI: 1164, 1184) and lowest in pediatrics (82 per 100,000; 95%PI: 77, 88) (Table 1 and Figure 2B).

The sensitivity analysis restricting to 4 provinces with data ending in 2018 demonstrated a forecasted AAPC for incidence was -0.30% (95%CI: -0.97, 0.27) and the 2035 value was 31.8 per 100,000 (95%PI: 27.5, 36.1) (Supplemental Table 4). For prevalence, the forecasted AAPC was 2.30 (95%CI: 1.94, 2.63) and the prevalence per 100,000 in 2035 was 1160 (95%PI: 1086, 1236) (Supplemental Table 4). All aggregate data on incidence and prevalence is provided in an open-access, online interactive map: https://kaplan-gi.shinyapps.io/Canada_inc_prev/.

DISCUSSION

This study demonstrates that Canada is entrenched in the third epidemiologic stage of IBD evolution: Compounding prevalence, where incidence stabilizes while prevalence steadily climbs.⁷ Historical data from eight population-based provincial IBD surveillance cohorts were used to forecast incidence and prevalence of IBD to 2035. The incidence of IBD is estimated to remain at approximately 30 per 100,000 over the next decade. In 2023, 11,000 Canadians are expected to be newly diagnosed with Crohn's disease or ulcerative colitis. The prevalence of IBD in 2023 is estimated to be 843 per 100,000 and, with the forecasted rise in prevalence of 2.4% per year, it is anticipated to climb to 1.1% of the population by 2035. Today roughly 330,000 individuals are living with IBD in Canada, and this number will grow to nearly half a million Canadians by 2035. Regions throughout the early-industrialized world need to prepare their healthcare systems to care for the rising burden of IBD.¹²

Our study is consistent with global trends demonstrating that the incidence of pediatriconset IBD is climbing,⁵ whereas rates in adults and seniors remain stable or decline.¹ Incidence rates are influenced by a number of factors including genetic susceptibility, ethnicity, demography, and environmental exposures such as diet.⁶ Determinates of disease development differ across the continuum of age at diagnosis, which may result in differential incidence rates across ages.¹⁸ For example, children diagnosed with IBD under the age of 16 years have a high frequency of NOD2 mutations and virtually none smoked tobacco cigarettes prior to diagnosis, whereas a history of smoking is more common in adults diagnosed with Crohn's disease after the age of 40 years when the frequency of carrying NOD2 alleles is low.¹⁹ Consequently, population-level environmental risk factor modifications, such as lower occurrence of smoking over the past generation in Canada, may influence the incidence of adult-onset IBD without impacting rates in children with IBD.²⁰

As with historical reports, trends in incidence rates varied between provinces. Historical data from Nova Scotia previously demonstrated the highest incidence of IBD in Canada²¹ and new data reported in our study from Newfoundland confirm these trends in the Atlantic provinces. Similarly, on the other side of the Atlantic, Northern Scandinavian countries such as Denmark report among the highest incidence of IBD in the world.^{3,4} In contrast, the incidence of IBD was low in Quebec, which may be explained by genetic, cultural, and dietary differences between regions in Canada. Immigrants to Canada from low-prevalence areas have a lower risk of IBD and thus, differing immigration patterns may lead to heterogeneity in incidence of IBD across provinces.²² It is also important to consider the population distribution of Indigenous peoples across Canada (including First Nations, Inuit, and Métis), as well the epidemiology of IBD among Indigenous peoples. For example, lower numbers of IBD have been reported among

First Nations individuals in comparison to the general population; however, a considerable increasing prevalence along with a stable incidence trend of IBD has been documented among First Nations individuals in one of the Western Canadian provinces.^{23,24} Future studies are needed to explore the multifaceted differences of the Canadian population that explain the heterogeneity in incidence across provinces.

The compounding prevalence of IBD was consistently observed in each province. As long as incidence exceeds mortality, the prevalence of IBD will continue to steadily climb.^{7,25} CanGIEC previously used provincial surveillance cohorts to demonstrate a prevalence of IBD at 0.51% in 2008,⁹ which our current study has shown to rise to 0.65% in 2014. Previously we forecast that the prevalence of IBD in 2014 would be 640 per 100,000, a value replicated in our current study that measured a prevalence of 651 per 100,000 (Supplemental Table 3). The accuracy of replicating previously forecasted data strengthens the confidence of our current forecasted estimates of 843 per 100,000 in 2023. In 2032, at the one hundred year anniversary of Crohn, Ginzburg, and Oppenheimer's landmark paper of eight cases of regional ileitis,²⁶ the prevalence of IBD in Canada may exceed 1.1% of the population. Forecasting models in Canada have been replicated in Scotland.²⁷ Consequently, early-industrialised regions in North America, Europe, and Oceania need to prepare healthcare infrastructure for the rising burden of IBD.¹²

Over the next decade, gastroenterology clinics and primary healthcare providers will need to handle a rising number of people with IBD and more complex care as their IBD population ages. Seniors with IBD represent the fastest growing demographic with IBD. One in 85 individuals over the age of 65 are estimated to be living with IBD in 2023, which has nearly doubled as compared to 2008 when 1 in 154 seniors had IBD.⁹ While new diagnoses in seniors contributes to the prevalence, the major driver of the rising prevalence is an aging IBD population that is living longer.⁷ For example, people diagnosed with IBD in their 30s in 1993 are in their 60s in 2023. IBD in seniors introduces complexity as gastroenterologists and primary healthcare providers contend with management decisions that account for age-related comorbidities, such as cardiovascular disease and cancer.²⁸ Over the next decade, the shifting demographics will expand the number octogenarians, raising challenges associated with caring for people with IBD who have dementia.²⁸ Consequently, partnership of geriatricians and primary healthcare providers will be necessary for the multidisciplinary gastroenterology clinics of the future.

Several limitations should be considered. The data sources are population-based administrative healthcare databases across eight separate provinces with heterogeneity between database characteristics (Supplemental Table 1). The administrative process to acquire provincial data and then share aggregate-level data across provinces is lengthy leading to a gap between last year of data availability and publication year. However, our sensitivity analysis restricting to fewer provinces with longer span of data yielded similar forecasting of incidence and prevalence. Algorithms to identify the IBD populations are subject to misclassification bias; however most of our identification algorithms were validated in the local provincial contexts, minimizing the bias.²⁹ Washout periods are used to establish inception cohorts recognizing the trade-off between sensitivity of the study population and mixing prevalent with incidence cases.³⁰ Forecasting relies on analysis of historical trends that do not account for unexpected future events that may influence incidence or prevalence. Moreover, our study period ended prior to the onset of the pandemic in March 2020, and would not account for excess mortality associated with COVID-19. The overall mortality attributable to COVID-19 in those with IBD was low, but highest among octogenarians,³¹ which may have influenced forecasting estimates among seniors with

IBD. While our past forecasting models in the prevalence of IBD closely approximated updated data in the current study (Supplementary Table 3),⁹ future studies are necessary to assess whether the global pandemic influenced the trajectory of the epidemiology of IBD.³²

After decades of rising incidence of IBD during the latter half of the 20th century,² Canada experienced a paradigm shift in the epidemiology of IBD over the last two decades.¹ Incidence is modestly rising in children, but stabilized in adults. Today, the prevalence is 0.84% of the population and will surpass 1.1% over the next decade. Data from Canada is analogous to most early-industrialized regions in North America, Europe, and Oceania, which will need to prepare their healthcare systems for the rising burden of IBD and the changing demographics of the IBD population.¹²

TABLES

Table 1: Age and Sex Stratified Incidence and Prevalence

		Incidence ⁰ Data: 2007 to 2014			Prevalence Data: 2002 to 2014			
	Forecasted	Rate (per 100.00 Per	rsons)	Forecasted Rate (per 100.00 Persons)			ersons)
	AAPC	2014*	2023**	2035**	AAPC	2014*	2023**	2035**
	(95%CI)	(95%CI)	(95%PI)	(95%PI)	(95%CI)	(95%CI)	(95%PI)	(95%PI)
AGE GROUPS (IBD)								
All Ages	0.36	29.0	29.9	31.2	2.43	651	843	1098
	(-0.05, 0.72)	(28.5, 29.6)	(28.3, 31.5)	(28.1, 34.3)	(2.32, 2.54)	(648, 653)	(828, 859)	(1068, 1127)
Pediatric	1.27	14.4	16.1	18.5	1.91	67	82	101
(<18)	(0.82, 1.67)	(13.5, 15.3)	(14.9, 17.2)	(16.3, 20.8)	(1.46, 2.31)	(65, 69)	(77, 88)	(91, 112)
Adult	0.26	33.7	34.7	35.7	2.25	776	981	1253
(18–64)	(-0.42, 0.82)	(32.9, 34.5)	(31.5, 37.8)	(29.9, 41.6)	(2.06, 2.42)	(772, 780)	(922, 1040)	(1172, 1334)
Elderly	0.39	28.1	28.8	30.2	2.78	865	1174	1585
(65+)	(-1.11, 1.38)	(26.7, 29.5)	(23.6, 34.1)	(20.5, 39.9)	(2.75, 2.81)	(857, 873)	(1164, 1184)	(1567, 1603)
AGE GROUPS (CD)								
All Ages	-0.52	13.5	12.7	11.9	2.33	331	423	545
	(-1.44, 0.21)	(13.1, 13.9)	(11.5, 13.9)	(9.5, 14.3)	(2.18, 2.47)	(329, 333)	(412, 435)	(524, 566)
Pediatric	0.75	8.3	9.2	10.0	1.50	41.4	47.6	55.9
(<18)	(-0.88, 1.75)	(7.6, 9.0)	(7.2, 11.0)	(6.4, 13.6)	(0.53, 2.19)	(39.8, 42.9)	(40.3, 54.8)	(43.0, 68.8)
Adult	-0.56	15.6	14.8	13.9	2.15	411	513	649
(18–64)	(-1.71, 0.32)	(15.1, 16.1)	(13.1, 16.6)	(10.5, 17.2)	(1.85, 2.41)	(408, 413)	(481, 545)	(598, 699)
Elderly	-0.08	11.2	10.3	10.2	2.88	365	501	684
(65+)	(-1.74, 1.02)	(10.3, 12.1)	(8.5, 12.1)	(6.7, 13.6)	(2.87, 2.90)	(359, 370)	(498, 505)	(678, 690)
AGE GROUPS (UC [¥])								
All Ages	0.99	15.5	17.2	19.3	2.54	320	420	553
	(0.69, 1.26)	(15.1, 16.0)	(16.4, 18.1)	(17.8, 20.9)	(2.48, 2.60)	(318, 322)	(414, 426)	(543, 563)
Pediatric	1.98	6.0	6.9	8.5	2.29	25.7	32.4	41.6
(< 18) ^β	(0.80, 2.84)	(5.4, 6.6)	(5.8, 7.9)	(6.4, 10.7)	(2.15, 2.42)	(24.5, 26.9)	(31.1, 33.7)	(39.3, 43.9
Adult	0.86	18.1	19.8	21.9	2.36	365	468	605
(18–64)	(-0.08, 1.55)	(17.5, 18.7)	(17.1, 22.5)	(16.9, 26.9)	(2.21, 2.49)	(363, 368)	(455, 482)	(581, 628)
Elderly	0.65	16.9	18.6	20.0	2.70	501	673	901

SEX (IBD) Female 0.07 29.6 29.5 29.7 2.40 687 886 1149 (-0.06, 0.20) (28.8, 30.4) (28.9, 30.0) (28.6, 30.8) (2.27, 2.51) (683, 690) (866, 905) (1112, 112)	, 909)	(894, 90	(669, 677)	(495, 507)	(2.68, 2.72)	(15.5, 24.5)	(16.2, 20.9)	(15.8, 18.0)	(-0.35, 1.39)	(65+)
Female 0.07 29.6 29.5 29.7 2.40 687 886 1149 (-0.06, 0.20) (28.8, 30.4) (28.9, 30.0) (28.6, 30.8) (2.27, 2.51) (683, 690) (866, 905) (1112, 112, 112, 112, 112, 112, 112, 112	SEX (IBD)									
(-0.06, 0.20) (28.8, 30.4) (28.9, 30.0) (28.6, 30.8) (2.27, 2.51) (683, 690) (866, 905) (1112, 1	149	1149	886	687	2.40	29.7	29.5	29.6	0.07	Female
	, 1185)	(1112, 11	(866, 905)	(683, 690)	(2.27, 2.51)	(28.6, 30.8)	(28.9, 30.0)	(28.8, 30.4)	(-0.06, 0.20)	
Male 0.71 28.4 30.6 33.3 2.47 614 800 1046)46	1046	800	614	2.47	33.3	30.6	28.4	0.71	Male
(-0.16, 1.38) (27.6, 29.2) (26.9, 34.4) (26.3, 40.2) (2.40, 2.54) (610, 618) (789, 811) (1026, 19)	, 1066)	(1026, 10	(789, 811)	(610, 618)	(2.40, 2.54)	(26.3, 40.2)	(26.9, 34.4)	(27.6, 29.2)	(-0.16, 1.38)	

⁰ Five-year washout for Adult (Data: 2007–2014); Three-year washout for Pediatrics (Data: 2005–2014)

¥ Includes IBD-U

BOLD: Significantly increasing/decreasing AAPC

*Estimates based data derived from administrative healthcare databases in the year 2014.

**Forecasted estimated for the years 2023 and 2035.

FIGURE LEGEND

Figure 1: Actual and forecasted incidence (Figure 1A) and prevalence (Figure 1B) of IBD in Canada by province. Actual incidence and prevalence, standardized for age and sex, is denoted by the solid line. Forecasted incidence and prevalence, analyzed with an ARIMA model and then forecasted until 2035, is indicated by a dashed line with the prediction intervals highlighted. All aggregate data reported is provided in an open-access, online interactive map: https://kaplan-gi.shinyapps.io/Canada_inc_prev/





Figure 2: Actual and forecasted national estimates for incidence (Figure 2A) and prevalence (Figure 2B) for all ages and stratified by pediatric-onset, adult-onset, and senior-onset IBD. Actual incidence and prevalence, standardized for age and sex, is denoted by the solid line. Forecasted incidence and prevalence, analyzed with an ARIMA model and then forecasted until 2035, is indicated by a dashed line with the prediction intervals highlighted. All aggregate data reported is provided in an open-access, online interactive map: <u>https://kaplan-gi.shinyapps.io/Canada_inc_prev/</u>



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