The Impact of Inflammatory Bowel Disease in Canada 2018: Indirect Costs of IBD Care

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Abstract

The indirect cost of illness represents the portion of human capital that is foregone due to lost productivity of patients and their caregivers and out-of-pocket healthcare expenses borne directly by patients. Indirect costs among persons with inflammatory bowel diseases (IBD) may be substantial because disease onset occurs during the teens and 20s for most persons and is lifelong. Thus, most persons with IBD are affected during periods of study or employment. The literature on indirect health-related costs among persons with IBD is limited, particularly with regard to Canadian studies. The greatest burden of indirect costs in this population relates to absenteeism and presenteeism among working individuals and premature retirement. However, costs related to reduced professional development and personal achievement due to illness—as well as caregiver costs—are largely unknown. After being extrapolated from multiple sources, the total indirect health-related cost of IBD in Canada in 2018 is estimated to be $1.29 billion Canadian dollars. Notably, this may be a significant underestimate because costs relating to presenteeism, reduced achievement and caregiver burden could not be estimated and are excluded from this calculation.

Highlights

1. Indirect costs account for a major portion of total healthcare costs among persons with inflammatory bowel disease (IBD) and are higher than indirect costs among persons without IBD.
2. Persons with IBD are more likely to require time off work (absenteeism) and have reduced productivity at work (presenteeism) due to illness as compared with persons without IBD.
3. Premature retirement and long-term disability are major factors contributing to indirect costs among IBD patients.
4. A substantial proportion of individuals with IBD pay out-of-pocket for complementary and alternative medicines.
5. After being extrapolated from multiple sources, the total annual indirect cost of IBD in Canada is estimated to be $1.29 billion CAD in 2018, or $4781 CAD per person with IBD.

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Key Summary Points

1. The total indirect economic burden of IBD in Canada is estimated to be $1.29 billion CAD in 2018, or roughly $4781 CAD per person with IBD. This estimate comprises lost wages related to sick days and disability, premature retirement and premature death, and out-of-pocket costs. Losses from presenteeism, reduced professional development and caregiver burden are not included due to insufficient data on the cost impact of these factors.

2. In a meta-analysis of studies between 1994 and 2014, the annual indirect cost of absenteeism for IBD patients ranged from $515.67 USD (USA) to $14,727 USD (Germany) per patient per annum (pooled estimate $7189 USD), after adjusting for purchasing power disparity.

3. A large US survey found that, on average, IBD patients incurred an extra 4.8 days off of work and $783 USD in excess lost wages annually compared with persons without IBD.

4. A study based on US private insurance claims found that ulcerative colitis patients cost an additional $2164 per person per annum relating to disability days and medically related absenteeism.

5. A prospective study from an IBD centre reported weekly indirect health-related costs of $1133 for IBD patients with active disease, $370.13 for IBD patients in remission, and $191.23 for persons without IBD relating to both presenteeism and absenteeism.

6. In a survey of 744 IBD patients from Manitoba, reduced workplace productivity during the previous 14 days was reported in 37% of individuals, including a reduction of one to two days by 18% of patients, three to nine days by 16% of patients, and on most days by 3% of patients.

7. The estimated average lifetime lost wages due to premature retirement is $1,044,498 CAD per person with Crohn’s disease and $994,760 CAD per person with ulcerative colitis. Aggregated over all IBD retirees, this equates to roughly $629 million CAD in permanent lost wages annually due to premature retirement.

8. The lifetime indirect cost associated with premature death among IBD patients is estimated to be $746,070 CAD per decedent, or roughly $33.6 million aggregated across all IBD decedents of working age.

9. In a US study of caregivers of children, the average unadjusted annual work loss was 214 hours for caregivers of Crohn’s disease patients and 170 hours for caregivers of children without IBD, translating to an additional $1122 in lost productivity for caregivers of persons with Crohn’s disease.

10. Canadian studies have reported complementary and alternative medicines (CAMs) use in 56% to 74% of people with IBD. A US national survey study estimated annual per-person out of pocket costs of $1603 USD for Crohn’s disease patients and $1263 USD for ulcerative colitis patients, which were substantially higher than in persons without IBD.

Gaps in Knowledge and Future Directions

1. Canadian-specific data on indirect health-related costs of IBD is sparse across all domains of indirect costs.

2. In particular, the rates of absenteeism, presenteeism and premature retirement among IBD patients living in Canada require further study to gauge more accurately the indirect health-related costs of IBD in Canada.

3. Indirect costs relating to decreased professional development, caregiver burden and out-of-pocket purchases among IBD patients are largely unknown and require further study.

4. Indirect costs incurred by Canadian children with IBD and their families or caregivers are largely unknown.

Keywords: Costs; Crohn’s disease; Inflammatory bowel disease; Prevalence; Quality of life; Ulcerative colitis

The indirect cost of illness represents the portion of human capital that is foregone due to illness or disability. Indirect costs include lost productivity of patients and their caregivers and out-of-pocket healthcare expenses borne directly by patients, including costs of nonprescription drugs and devices, co-pays or deductibles, public health and preventative care.
Lost productivity due to illness consists of two major components:

1. **Absenteeism**, which reflects absence from paid work due to sick days/leave, unemployment, short-term and long-term disability, early retirement, premature death, and caregiver leave; and,
2. **Presenteeism**, which denotes reduced productivity at work due to illness. An under-recognized aspect of lost productivity relates to reduced professional development and career achievement due to illness.

Most studies of indirect costs in IBD patients use the human capital approach (HCA), which converts the gross income that is not earned by an individual due to illness into real costs from a societal perspective (1). The actual cost impact can be described in a variety of ways, such as in dollar units or as a proportion of the gross domestic product (GDP) per capita (1).

In this report, we summarize older data and present new data on the indirect costs of IBD that have been published since our last report to estimate the indirect costs of IBD in Canada in 2018. A complete overview of the objectives, working committees, and methodology of creating the report can be found in online supplemental file, Technical Document.

**SICK DAYS AND DISABILITY**

A systematic review has summarized studies published between 1992 and 2014 on indirect costs of illness among persons with IBD (1), including nine from North America, one from Canada (2–10), eight from Europe (11–18), and one from New Zealand (19). Importantly, each of these studies included different components in the calculation of absenteeism costs, with some studies incorporating one or more of long-term disability, premature retirement, premature death and caregiver costs, in addition to sick leave and short-term disability. Fifteen studies evaluated indirect costs of absenteeism, and two studies reported indirect costs of presenteeism.

Adjusting for purchasing power disparity, the annual indirect cost estimates relating to absenteeism for IBD patients ranged from $515.67 USD (USA) to $14,727 USD (Germany) per patient, with a pooled estimate of $7189 USD per patient per annum. Standardized to each country’s GDP, the pooled estimate was $9622 USD per patient per annum. Among studies that combined indirect costs relating to absenteeism and presenteeism, the estimates were $2753 USD (Sweden) and $5677 USD (Hungary) after adjusting for purchasing power disparity and $2991.14 USD (Sweden) and $25,194.92 (Hungary) after standardizing to each country’s GDP (15, 16). A literature review from 2007 of eight studies further reported that, on average, 7.2 days per year per patient (range 4.2 to 9.9) are lost due to medical absenteeism secondary to IBD among the IBD-workforce (20).

One Canadian study and three US studies have recently been published on lost productivity among persons with IBD. In a study of more than 90,000 individuals (200 with IBD) from the US Medical Expenditure Panel Survey between 1996 and 2006, 72% of IBD patients and 58.3% of non-IBD patients missed time from work because of illness, with a resultant 3.5 more days off of work (13.4 versus 9.9 days) and $783 USD in excess lost wages per person per annum for IBD patients (21). Patients with IBD were nearly twofold more likely to miss work than controls. After extrapolating IBD prevalence and costs and adjusting for the national employment rate, the incremental IBD absenteeism cost aggregated over the entire US IBD population was estimated to be $249 million USD annually.

Another study used data from a large US private insurance claims database to report on short-term and long-term disability claims among ulcerative colitis patients and matched controls, ages 18 to 64, employed in the United States between 2005 and 2013 (22). A higher proportion of individuals with ulcerative colitis had disability days (10.9% versus 6.7%) and medically related absenteeism days (98.7% versus 80.1%), equating to roughly a twofold greater number of total disability or sick days per person (16.4 versus 8.8 days) as compared with individuals without IBD. Disability days were more frequent among individuals with moderate to severe ulcerative colitis. The adjusted total indirect cost per patient per annum was significantly higher in individuals with ulcerative colitis as compared with those without IBD ($4125 versus $1961) and was even more pronounced in individuals with moderate to severe ulcerative colitis ($5666).

A survey study from an IBD referral centre estimated indirect costs relating to absenteeism and presenteeism in their adult IBD population and selected controls (23). Presenteeism was substantially more frequent in patients with Crohn’s disease (61.4%) and ulcerative colitis (64.3%) as compared with non-IBD controls (27.3%), even for IBD patients in remission (54.7%). There was a nonsignificant trend toward higher rates of absenteeism in patients with ulcerative colitis (22.4%) and Crohn’s disease (20%) relative to controls (13.6%), although rates were similar to controls for IBD patients in remission (14.4%). As compared with IBD patients in remission, IBD patients with active disease had much higher rates of absenteeism (46.6% versus 14.4%), presenteeism (94.8% versus 54.7%) and overall activity impairment (98.9% versus 62.7%). Among IBD patients, the most common work limitations were fatigue (41.8%), irritability (12.2%) and decreased motivation (11.7%), and the most frequent reasons for missing work were physician appointments (39%), abdominal discomfort (24.4%) and hospital/ER visits (22.1%). Using a ‘lost wages’ approach (24), this translated to an average indirect cost of $1133 USD per week (55.1% of total weekly compensation) for IBD patients with active disease, $370 USD per week (18% of total weekly compensation) for IBD patients in remission, and
$191 per week (9.3% of total weekly compensation) for controls (see Figures 1 and 2).

In a survey study of 744 individuals living with IBD in Manitoba, reduced workplace productivity during the previous 14 days was reported by 37% of individuals, including a reduction for one to two days by 18% of patients, for three to nine days by 16% of patients, and on most days by 3% of patients (25). In a related study, the authors reported that the most common workplace accommodations required by persons with IBD were for medical appointments (81%), toilet access (71%) and respites (54%). Female sex, more severe symptoms, and a high level of current distress were associated with the need for more accommodations (26).

Overall, working persons with IBD may expect to miss an extra 3.5 to 7.5 days from work annually due to illness compared with non-IBD persons. Based on the average Canadian salary in 2016 from Statistics Canada reports ($956.50 CAD per week or $49,738 CAD per year) (27), the estimated mean annual per patient cost related to medical absenteeism is $752 CAD (range $478 to $1025 CAD). In 2018, it is estimated that there are 97,809 and 80,266 Canadian working-age adults (ages 18–64) with Crohn’s disease and ulcerative colitis, respectively (28). Based on estimated workforce rates of 68% and 63% among persons with Crohn’s disease and ulcerative colitis, respectively, roughly 66,510 and 50,568 (117,078 total) persons with Crohn’s disease and ulcerative colitis in the Canadian IBD workforce, respectively, would be eligible to experience medical absenteeism. The annual cost due to medical absenteeism is estimated to be more than $88 million CAD (range $56 to $120 million CAD) after extrapolating the mean per person absenteeism cost to the entire Canadian IBD workforce. This estimate does not include productivity losses due to presenteeism, which may be 1.5 times greater than absenteeism costs. However, there are limited data to account for presenteeism costs in the Canadian context.

Figure 1. Prevalence of absenteeism, presenteeism and activity impairment in controls and patients with IBD with active and inactive disease. *P < 0.01, **P < 0.01, ***P < 0.01, +P = 0.02 (23) (reprinted with permission)

Figure 2. Indirect costs as a percentage of maximum weekly compensation for employees. *P < 0.01, **P < 0.01, ***P < 0.01, +P = 0.02, ++P < 0.03 (23) (reprinted with permission)
PREMATURE RETIREMENT

Few studies have reported on early retirement in patients with IBD, and only a fraction of these studies have evaluated disease-related early retirement in the postbiologic era. A systematic review was conducted in 2013 to identify studies evaluating the impact of IBD on employment (29). Among two European studies that evaluated retirement among adults younger than age 65, less than 4.4% of people with Crohn’s disease were retired, and 2.6 to 4.5% of people with ulcerative colitis were retired (18, 30). The rates of early retirement among people with IBD were similar to those of people without IBD. Another European study of individuals with IBD, 27% of whom were retired, reported that 6.5% retired because of their IBD (31). A more recent study from Germany reported annual retirement rates of 440 and 226 per 100,000 employees per year for persons retired, and 6.5% retired because of their IBD (31).

A more recent study from Germany reported annual retirement rates of 440 and 226 per 100,000 employees per year for persons with Crohn’s disease and ulcerative colitis, respectively, with average annual retirement ages of 41.7 and 43.5 for women, respectively, and 43.6 and 44.0, respectively, for men (32). Although we are unaware of the age at which Canadians with IBD retire, the retirement age for the general population in Canada is similar to that of Germany (roughly 64 years of age) (33–35).

In 2018, it is estimated that there are 97,809 and 80,266 Canadian working-age adults (18 to 64) with Crohn’s disease and ulcerative colitis, respectively (28). After we extrapolated annual retirement rates from the German study to working-age Canadians with IBD (32), 430 persons with Crohn’s disease and 181 persons with ulcerative colitis may be expected to retire each year in Canada, assuming that all working-age persons with IBD would otherwise be employed. Using the mean retirement rates from the German study of roughly 43 and 44 among Crohn’s disease and ulcerative colitis patients, respectively (32), and the average earnings for Canadians in 2016 ($956.50 CAD per week or $49,738 CAD per year) (27), the average lifetime lost wages from premature retirement among IBD persons in the workforce are calculated to be $1,044,498 CAD per person with Crohn’s disease and $994,760 CAD per person with ulcerative colitis (based on an average retirement age among working Canadians of 64). Aggregated across all IBD retirees each year, this equates to roughly $449 million CAD among persons with Crohn’s disease and $180 million CAD among persons with ulcerative colitis (total $629 million CAD) in permanent lost wages annually, assuming that there is a similar wage distribution among IBD retirees and nonretirees.

PREMATURE MORTALITY

Premature mortality (before the age of 65) also contributes to lost productivity among persons with IBD. Population-based studies from Ontario and Manitoba report higher mortality rates among patients with Crohn’s disease compared with the general population, particularly among young and middle-aged individuals (36, 37). In comparison, people with ulcerative colitis are not at an increased risk of death compared with people without IBD. Almost one-quarter (88 of 379) of all deaths among patients with Crohn's disease in Manitoba occurred in those who were younger than 50, and 5% (20 of 379) of Crohn's disease-related deaths occurred in patients younger than 30 (data spanning 1984 to 2010) (36). In Ontario, there are 5.66 and 1.0 Crohn’s disease-related deaths and 1.33 and 1.0 ulcerative colitis-related deaths per 10,000 person-years among middle-aged (41 to 64) and young adults (18 to 40), respectively (37).

According to Statistics Canada data from 2010 to 2014, there is an average of 33 deaths directly resulting from Crohn’s disease per year and 12 deaths directly attributable to ulcerative colitis per year among individuals under the age of 65 (38). The average age of Canadians with IBD who die before the age of 65 has been previously estimated as 49, corresponding to an average of 15 years of lost employment per individual that dies prematurely (based on the average retirement age of 64 in Canada) (39). Based on the average earnings for Canadians in 2016 ($956.50 CAD per week or $49,738 CAD per year) (27), the 45 IBD-specific premature deaths would result in 675 lost years of productivity and roughly $33 million CAD in permanent lost wages ($746,070 CAD per decedent) accrued annually across all working-age IBD persons (over and above lost wages due to premature mortality from non-IBD related causes), assuming there is a similar distribution of wages among employed IBD persons.

In 2012, the cost of premature death among IBD persons in Canada was estimated to be just $9.4 million CAD. The rise in estimated indirect costs of premature mortality in people with IBD over the past five years is the result of higher wages and a higher number of deaths due to IBD, likely because of the increasing prevalence of IBD in Canada.

PROFESSIONAL DEVELOPMENT

As a chronic disease that is often diagnosed during childhood and adolescence, IBD may negatively impact academic performance and subsequent professional development. There are limited data on the impact of IBD on academic success. A large population-based study from Manitoba compared 337 IBD patients in grade 12 with 3093 healthy grade 12 controls (40). There were no differences in academic outcomes between the two groups.

In a small survey study of undergraduate students at the University of Michigan, IBD disease activity was inversely associated with adjustment to college life (41). Poor college adjustment has been associated with worse academic outcomes, lower graduation rates, and impairments in career development.

Inflammatory bowel disease is also associated with a high rate of unemployment, with one study reporting unemployment in up to 39% of patients with moderate-severe Crohn’s disease.
Among those patients who are employed, IBD can impact salary growth. Loftus et al. demonstrated that while annual salary did not differ among patients with moderate-severe Crohn’s disease and healthy controls in the first year of study, salary growth rate was 31% lower in those with Crohn’s disease spanning up to a 7-year period (43). Whether earlier and more aggressive medical therapy can potentially improve academic and professional development and income potential warrants further study.

CAREGIVER COSTS
Caregivers are people who provide informal and unpaid care to others who may need assistance for health reasons and may take time off work to provide this care. Caregivers are needed for the most severely affected people with IBD and for children (where parents are usually the caregivers) and seniors (where children are usually the caregivers) with IBD. However, there are very few data available on the economic impact of IBD caregivers.

There are minimal data available on caregiver costs internationally and even less in a Canadian context. In a US study of pediatric IBD patients using health insurance databases, 200 patients with Crohn’s disease and their caregivers were compared with age-matched controls without IBD and their caregivers. Unadjusted annual hours of work loss were 214.4 ± 171.5 and 169.6 ± 157.5 for caregivers of Crohn’s disease patients and controls, translating to annual lost productivity costs of $5243 and 169.6 ± 157.5 for caregivers of Crohn’s disease patients and their caregivers. Whether earlier and more aggressive medical therapy can potentially improve academic and professional development and income potential warrants further study.

OUT-OF-POCKET COSTS
Literature on the out-of-pocket expenses among individuals living with IBD is limited. These expenses include complementary and alternative medicines (CAMs), ostomy supplies, travel to attend appointments and dietary/nutritional therapy. A US study estimated annual per-person out of pocket costs of $1603 USD for persons with Crohn’s disease and $1263 USD for persons with ulcerative colitis (45). Per-person out-of-pocket expenses were higher in persons with IBD as compared with persons without IBD. Out-of-pocket costs in pediatric IBD patients have been reported to be even higher than those in adults (46).

Complementary and alternative medicines are generally defined as a therapy that falls beyond the realm of conventional medicine (i.e., herbal therapy, homeopathy, massage therapy, chiropractor, prayer) (47, 48) and are not based on rigorous scientific evidence for a particular indication (49). Most CAMs are not covered under public or private drug plans. Canadian studies have reported CAMs use in 56% to 74% of people with IBD (48, 50, 51). European and Asian studies have reported the use of CAMs in about one-half of people with IBD (52–54). Notably, many physician providers are unaware that their patients are using CAMs, and only about one-third of patients consult with their gastroenterologist before starting CAMs (51). A recent Crohn’s and Colitis Canada survey identified access to information and research on CAMs as priority areas for Canadians with IBD (55).

The cost of travel to attend appointments is likely a significant expense for many IBD patients, although no specific Canadian data exist. Among pediatric IBD patients living in California, 25% spend $500 USD annually to see their providers (56).

Diet may be another source of considerable expense for IBD patients. Among families living in California that have a child with IBD, 34.3% spend less than $200 USD per year, 31.3% spend $200 to 400 USD per year, and 11.4% spend more than $1000 USD per year on diet (56). In the pediatric IBD population, exclusive enteral nutrition has been shown to be an effective therapy for inducing clinical remission and is a contributor to dietary costs (57). The costs of various popular elimination diets, such as the specific carbohydrate diet (SCD), have not been well explored in IBD.

There are no data on comprehensive out-of-pocket expenses for IBD patients living in Canada. If the data from the US study (45) are extrapolated to Canadians with IBD, then the annual out-of-pocket expenses for the 146,000 Canadians living with Crohn’s disease and 124,000 Canadians living with ulcerative colitis in Canada in 2018 could be as high as $324 and $217 million CAD, respectively, for a total of $541 million CAD (28).

SUMMARY AND CONCLUSIONS
The total indirect health economic burden of IBD on patients, the healthcare system and society is significant. Based on the aforementioned cost estimates for sick days and short-term disability, premature retirement, premature death and out-of-pocket expenses, the total indirect health-related cost to the Canadian economy due to IBD is estimated to be close to $1.29 billion CAD in 2018, or roughly $4781 CAD per person with IBD. The largest component of this cost is related to lost productivity, particularly premature retirement ($629 million CAD). Importantly, this estimate does not consider presenteeism costs, caregiver costs and the costs of reduced professional development, which may be substantial but could not be accurately estimated due to insufficient data. Applying the pooled estimate of $7189 USD per patient per year ($9231 CAD) in absenteeism costs from the 2014 meta-analysis to working-age Canadians with IBD (1), the estimated annual cost due to medical absenteeism may be as high as $1.57 billion CAD.

Importantly, the calculation of indirect costs in this report makes multiple assumptions, including the generalizability of non-Canadian estimates relating to lost productivity and out-of-pocket expenses to the Canadian context and the projection of the mean wage of Canadian workers to IBD persons in the workforce. More data, specifically in the Canadian context, are
needed to gauge the indirect health economic impact of IBD to Canadian society accurately.

Our gross estimate for total indirect cost differs from the estimate of $1.6 billion CAD reported in 2012 (39), reflecting new data and slightly different methodology and assumptions used to calculate indirect costs in this report. Notably, estimates of productivity losses are 40% lower in this report than in the previous report. The previous report also used a hypothetical scenario to estimate caregiver cost, which we chose to exclude from our cost estimate in favour of using only estimates substantiated by some real-world data. This further demonstrates that estimates of indirect costs are crude at this point and will undoubtedly be refined over time as more data become available.

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References

1. Kawalec P, Malinowski KP. Indirect health costs in ulcerative colitis and Crohn's disease: A systematic review and meta-analysis. Expert Rev Pharmacoecon Outcomes Res 2015;15(2):253–66.
2. Cohen R, Rizzo J, Yang M, et al. Direct and indirect utilization and costs associated with ulcerative colitis. Am J Gastroenterol 2012;107.
3. Gibson TB, Ng E, Orminkowski BJ, et al. The direct and indirect cost burden of Crohn's disease and ulcerative colitis. J Occup Environ Med 2008;50(11):1261–72.
4. Hay JW, Hay AR. Inflammatory bowel disease: Costs-of-illness. J Clin Gastroenterol 1992;14(4):309–17.
5. Lofland J, Naim A, Rizzo J, et al. The indirect costs of inflammatory bowel disease: Evidence from United States National Data Survey. J Occup Environ Med 2015;57(4):393–401.
6. Cohen R, Skup M, Olsoby AB, et al. Direct and indirect healthcare resource utilization and costs associated with ulcerative colitis in a privately-insured employed population in the US. J Med Econ 2015;18(6):447–56.
7. Zand A, van Deen W, Inserre E, et al. Presenteeism in Inflammatory Bowel Diseases: A hidden problem with significant economic impact. Inflamm Bowel Dis 2015;21(7):1623–30.
8. Berger M, Murray J, Xu J, et al. Alternative valuations of work loss and productivity. J Occup Environ Med 2003;45(1):18–24.
9. Shafer LA, Walker JR, Restall G, et al. Association between IBD disability and reduced work productivity (Presenteeism): A population-based study in Manitoba, Canada. Inflamm Bowel Dis 2018.
10. Chibbisa T, Walker JR, Sexton K, et al. Workplace accommodation for persons with IBD: What is needed and what is accessed. Clin Gastroenterol H 2017;15(10):1589–95.
11. Statistics Canada. Average weekly earnings (including overtime), by province and territory. 2017.
12. Coward S, Clement F, Bemicheml Eric, I, et al. The rising prevalence of inflammatory bowel disease in Canada: Analyzing the past to predict the future. JCAG 2018;1(Suppl 2):A-29.
13. Busch K, da Silva SA, Bolton M, et al. Sick leave and disability pension in inflammatory bowel disease: A systematic review. J Crohns Colitis 2014;8(11):1366–72.
14. Boonen A, Dagnelie PC, Feleux A, et al. The impact of inflammatory bowel disease on labor force participation: Results of a population sampled case-control study. Inflamm Bowel Dis 2002;6(6):382–9.
15. Nurmi E, Haapamaki J, Pavilainen E, et al. The burden of inflammatory bowel disease on health care utilization and quality of life. Scand J Gastroenterol 2013;48(1):31–7.
16. Stallmach A, Denaler U, Marschall U, et al. Patient-relevant endpoints in inflammatory bowel diseases—have changes occurred in Germany over the past twelve years? J Crohns Colitis 2015;9(5):390–7.
17. Statistics Canada. Table 282-0051: Labour Force Survey Estimates, Retirement Age by Class of Worker and Sex. 2018.
18.Trading Economics. Germany retirement age—men. 2018.
19. Trading Economics. Germany retirement age—women. 2018.
20. Bernstein CN, Nougent Z, Targownik LE, et al. Predictors and risks for death in a population-based study of persons with IBD in Manitoba. Gut 2015;64(9):1403–11.
21. Nguyen GC, Bernstein CN, Benchmark EL. Risk of surgery and mortality in elderly-onset inflammatory bowel disease: a population-based cohort study. Inflamm Bowel Dis 2017;23(2):218–23.
22. Statistics Canada. Table 102–0531--Deaths, by cause, Chapter XI: Diseases of the digestive system (K00 to K93), age group and sex, Canada, Annual. 2017.
23. Rocchi A, Benchmark EL, Bernstein CN, et al. Inflammatory bowel disease: A Canadian burden of illness review. Can J Gastroenterol 2012;26(11):811–7.
24. Singh H, Nougent Z, Brownell M, et al. Academic performance among children with inflammatory bowel disease: A population-based study. J Pediatr 2015;166(3):1128–33.
25. Adler J, Rau J, Beveridge AS, et al. College adjustment in University of Michigan students with Crohn's and colitis. Inflamm Bowel Dis 2008;14(9):1281–6.
42. Feagan BG, Bala M, Yan S, et al. Unemployment and disability in patients with moderately to severely active Crohn’s disease. J Clin Gastroenterol 2005;39(5):390–5.
43. Loftus EV Jr, Skip M, Ozbay AB, et al. The impact of moderate-to-severe Crohn’s disease on employees’ salary growth. Inflamm Bowel Dis 2014;20(10):1734–8.
44. Kahn SA, Lin CW, Ozbay R, et al. Indirect costs and family burden of pediatric Crohn’s disease in the United States. Inflamm Bowel Dis 2017;23(12):2089–96.
45. Gunnarsdottir C, Chen J, Rizzo JA, et al. Direct health care insurer and out-of-pocket expenditures of inflammatory bowel disease: Evidence from a US national survey. Dig Dis Sci 2012;57(12):3080–91.
46. Kappelman MD, Rifas-Shiman SL, Porter CQ, et al. Direct health care costs of Crohn’s disease and ulcerative colitis in US children and adults. Gastroenterology 2006;135(6):1907–13.
47. Hilsden RJ, Verhoef MJ, Rasmussen H, et al. Use of complementary and alternative medicine by patients with inflammatory bowel disease. Inflamm Bowel Dis 2011;17(2):655–62.
48. Rawsthorne P, Clara I, Graff LA, et al. The Manitoba Inflammatory Bowel Disease Cohort Study: A prospective longitudinal evaluation of the use of complementary and alternative medicine services and products. Gut 2012;61(4):521–7.
49. Zollman C, Vickers A. What is complementary medicine? BMJ 1999;319(7211):693–6.
50. Nguyen G, Creoitoru K, Silverberg MS, et al. Use of complementary and alternative medicine for inflammatory bowel disease is associated with worse adherence to conventional therapy: The COMPLIANT study. Inflamm Bowel Dis 2016;22(6):1412–7.
51. Weizman AV, Ahn E, Thanabal R, et al. Characterisation of complementary and alternative medicine use and its impact on medication adherence in inflammatory bowel disease. Aliment Pharmacol Ther 2012;35(3):542–9.
52. Abtibol V, Lahmek P, Busis A, et al. Impact of complementary and alternative medicine on the quality of life in inflammatory bowel disease: Results from a French national survey. Eur J Gastroenterol Hepatol 2014;26(3):288–94.
53. Opheim R, Bernklau T, Fagermoen MS, et al. Use of complementary and alternative medicine in patients with inflammatory bowel disease: Results of a cross-sectional study in Norway. Scand J Gastroenterol 2012;47(12):1436–47.
54. Park D, Cha J, Kim H, et al. Predictive factors of complementary and alternative medicine use for patients with inflammatory bowel disease in Korea. Complement Ther Med 2013;21(1):87–93.
55. Becker HM, Griog D, Ghosh S, et al. Living with inflammatory bowel disease: A Crohn’s and Colitis Canada survey. Can J Gastroenterol Hepatol 2015;29(2):77–84.
56. Sin A, Damman J, Ziring D, et al. Out-of-pocket cost burden in pediatric inflammatory bowel disease: A cross-sectional cohort analysis. Inflamm Bowel Dis 2015;21(6):1368–77.
57. Mrzeczka P, Horvath A, Shamir R, et al. Meta-analysis: Enteral nutrition in active Crohn’s disease in children. Aliment Pharmacol Ther 2007;26(6):795–806.