

Supplement Article

## The Impact of Inflammatory Bowel Disease in Canada 2018: IBD Research Landscape in Canada

Keeley L. Rose MSc, PhD<sup>1</sup>, Philip M. Sherman MD, FRCPC<sup>1</sup>, Jane Cooke-Lauder MBA, DM, CMC<sup>2</sup>, Mina Mawani MHSc, ICD.D<sup>3</sup>, Eric I. Benchimol MD, PhD<sup>4,5,6</sup>, Gilaad G. Kaplan MD, MPH<sup>4,6</sup>, Charles N. Bernstein MD<sup>4,7</sup>, Alain Bitton MD<sup>4,8</sup>, Sanjay K. Murthy MD, MSc<sup>4,9</sup>, Geoffrey C. Nguyen MD, PhD<sup>4,10</sup>, Kate Lee MBA, PhD<sup>3</sup>

<sup>1</sup>Canadian Institutes of Health Research Institute of Nutrition, Metabolism and Diabetes (CIHR-INMD), Toronto, Ontario, Canada; <sup>2</sup>Bataleur Enterprises Inc., Toronto, Ontario, Canada; <sup>3</sup>Crohn's and Colitis Canada, Toronto, Ontario, Canada; <sup>4</sup>Canadian Gastro-Intestinal Epidemiology Consortium, Canada; <sup>5</sup>Children's Hospital of Eastern Ontario IBD Centre, Department of Pediatrics and School of Epidemiology and Public Health, University of Ottawa, Ottawa, Ontario, Canada; <sup>6</sup>Department of Medicine and Community Health Sciences, University of Calgary, Calgary, Alberta, Canada; <sup>7</sup>University of Manitoba IBD Clinical and Research Centre, University of Manitoba, Winnipeg, Manitoba, Canada; <sup>8</sup>McGill University Health Centre (MUHC) IBD Centre, McGill University, Montreal, Quebec, Canada; <sup>9</sup>Ottawa Hospital Research Institute, Department of Medicine and School of Epidemiology and Public Health, University of Ottawa, Ottawa, Ontario, Canada; <sup>10</sup>Mount Sinai Hospital Centre for IBD, Department of Medicine, University of Toronto, Toronto, Ontario, Canada

**Correspondence:** Dr Kate Lee, MBA, PhD, Crohn's and Colitis Canada, 600–60 St. Clair Avenue East, Toronto, Ontario, Canada, M4T 1N5, E-mail: [klee@crohnsandcolitis.ca](mailto:klee@crohnsandcolitis.ca)

### Abstract

**Background:** Health research in Canada is funded by government, health charities, foundations and industry. We investigated levels of IBD research funding and the scientific impact of this research in Canada between 2013 and 2017.

**Methods:** An analysis of global and Canadian funding in IBD research was conducted using the Canadian Institutes of Health Research (CIHR) Funded Research Database and UberResearch's Dimensions platform. Examples of priority-driven and investigator-initiated IBD research in Canada are provided. Bibliometric analysis was used to assess the quality of IBD research output in Canada.

**Results:** Total funding for IBD research Canada between 2013 and 2017 was over \$119 million Canadian dollars (CAD), with CIHR, the largest funder, contributing almost \$66 million CAD, and Crohn's and Colitis Canada, investing more than \$32 million CAD. This ranks Canada fourth internationally. A comparative analysis indicates that publications by Canadian IBD researchers have a greater impact than other Canadian and international comparators. When productivity and impact in IBD research are combined, Canada is among the top three in the world.

**Conclusions:** Investment in IBD research in Canada has resulted in the development of a strong collaborative group of researchers producing impactful, world-class research. On all measures of academic productivity and influence, Canada ranks in the top two or three internationally. The challenges ahead are to continue to fund innovative IBD research and grow the next generation of IBD researchers while moving research findings into changes in health policy and practice in order to benefit affected patients and their families—and ultimately, to find the cause(s) and identify the cure(s).

**Keywords:** *Crohn's and Colitis Canada; CIHR; Gastroenterology; Inflammatory bowel disease, Research capacity*

Health research in Canada is funded by various levels of government, health charities, foundations and industry. Crohn's and Colitis Canada and the Canadian Institutes of Health Research (CIHR), in concert with valued partners, fund the majority of health research in inflammatory bowel diseases (IBD) in Canada. The intent of this section is to provide a historical view of IBD research funding and scientist ratings in Canada between 2013 and 2017, providing international comparisons where possible.

Two perspectives are provided: a look at the amount of funding of IBD research globally over the past five years and then a look at the same time period for Canada.

**GLOBAL FUNDING**

A global funding analysis was conducted using 'UberResearch's Dimensions' platform ([www.uberresearch.com/dimensions-for-funders/](http://www.uberresearch.com/dimensions-for-funders/)). *Dimensions* is a database developed by mining primarily publicly available research funding databases found on the internet. The developers of Dimensions obtain formal permission from all funding bodies included in the platform. A comprehensive list of funders of IBD research for the period 2013 to 2017 included in Dimensions is provided in [Appendix A](#).

[Table 1](#) depicts total global funding for IBD research between 2013 and 2017. During this period, the United States invested the greatest amount: over 75% (\$2.227 billion CAD) of the world's contribution. Canada ranked fourth after Belgium and the United Kingdom, investing 4% (over \$119 million Canadian dollars [CAD]) of the total IBD funding in the world.

**FUNDING IN CANADA**

Within this overview of Canada, the activities of the top two funders, CIHR and Crohn's and Colitis Canada, are presented in more detail, together with an overview of the types of funding mechanisms most frequently used during this period.

**Quantifying Research Funding in Canada**

To determine the extent of IBD funding in Canada, the Dimensions platform was used to identify the major funders (for methodology, see [Appendix A](#)). Once major funders were identified, total funding for the period 2013 to 2017 was confirmed by contacting the funders individually or retrieving data from their websites and manually confirming the information.

[Table 2](#) depicts total funding in Canada between 2013 to 2017 for IBD research by federal and provincial funding agencies and by Crohn's and Colitis Canada. Total funding during this five-year period was over \$119 million, with \$21.4 million to \$27.8 million in annual investments. Funding data for other diseases with similar incidence and prevalence in Canada were obtained from the National Alliance of Provincial Health

**Table 1.** Top 10 countries in the world for IBD funding (2013–2017)

	United States	United Kingdom	Belgium	Canada	Switzerland	Sweden	Norway	Australia	Japan	Poland
Total Funding (millions of CAD)	\$2,227	\$215.3	\$177.5	\$119.5	\$44.80	\$32.24	\$31.82	\$28.71	\$24.78	\$15.83
% of World Funding	75.9%	7.3%	6.1%	4.0%	1.5%	1.1%	1.1%	1.0%	0.8%	0.5%
IBD Prevalence per 100,000 (Study period) <sup>1</sup>	533.0 (2011) <sup>2</sup>	373.0 (2002) <sup>3</sup>	n/a	725.0 (2018) <sup>4</sup>	205.7 (2005) <sup>5</sup>	540.0 (2010) <sup>6</sup>	767.0 (1990–93) <sup>7</sup>	401.8 (2010–05) <sup>8</sup>	75.9 (2003–05) <sup>9</sup>	n/a
2017 Estimated Number of Prevalent Cases of IBD*	1,736,083	246,263	n/a	270,000	17,414	54,365	40,514	98,838	96,230	n/a
Funding per capita of prevalent IBD patients	\$1282.77	\$874.27	n/a	\$426.42	\$2,572.64	\$593.03	\$785.41	\$290.48	\$257.51	n/a

\*Based on country population according to: The World Bank.<sup>10</sup>

Research Organizations (NAPHRO), national health charities and CIHR. Funding for multiple sclerosis, Parkinson's disease and type one diabetes were \$94.5 million, \$61.9 million, \$98.2 million, respectively, compared with \$115.1 million for IBD (Table 3). On a per capita basis, \$426 were invested into IBD research for every patient in Canada. Dollar per patient funding was second to type one diabetes in the least amount of dollars invested among the comparative diseases (Table 3). Funding data for multiple sclerosis, Parkinson's disease and type one diabetes were provided by NAPHRO, Alberta Innovates and 'Fonds de Recherche Santé', which provided their funding information separately. Research funding by the Juvenile Diabetes Research Foundation was included from the Foundation's annual financial reports. The Natural Sciences and Engineering Research Council (NSERC) and Social Sciences and Humanities Research Council (SSHRC) funding databases were queried with the following terms: 'multiple sclerosis', 'type 1 diabetes', 'diabetes', 'T1D', and 'Parkinson'. Other potential sources of funding such as Genome Canada were not included. Inflammatory bowel disease funding was adjusted to include only the previously listed funders.

Canadian Institutes of Health Research is the largest funder, contributing almost \$66 million (55% of the total funding), with Crohn's and Colitis Canada ranking second, investing more than \$32 million (27% of the total funding). National Alliance

of Provincial Health Research Organizations, Genome Canada and the Canadian Foundation for Innovation (CFI) ranked third, fourth and fifth, contributing 13.8%, 2.4% and 0.7% of total funding, respectively. The funded research spans the spectrum from understanding underlying causes and mechanisms of IBD to improving patient care and developing new therapeutic approaches. Investments made by provincial funders have been fairly consistent—and relatively small—within the analysed period (i.e., in the hundreds of thousands of dollars range), with three exceptions: Research Manitoba invested an additional ~\$1.3 million in 2017; a significant reduction in Ontario's investment of ~\$2.5 million from 2013 to 2014, and a reduction by Alberta Innovates of ~\$2.5 million after 2014 (data not shown).

### Funding by the Canadian Institutes of Health Research

Canadian Institutes of Health Research is Canada's federal funding agency for health research. Its mission is to create new scientific knowledge and to enable its translation into improved health, more effective health services and products and strengthened Canadian health care systems. Canadian Institutes of Health Research supports research through investigator-initiated research funding programs (e.g., Project and Foundation Grant Programs) and priority-driven research funding programs (e.g., Programmatic Grants in Environments, Genes and

**Table 2.** IBD research funding in Canada (2013 to 2017)\*

Funder	Year					Total
	2013	2014	2015	2016	2017	
<b>CIHR</b>	\$11,010,425	\$10,897,649	\$12,893,535	\$14,278,583	\$16,867,707	\$65,947,899
<b>CCC</b>	\$5,283,966	\$7,567,053	\$6,002,125	\$6,583,829	\$6,694,961	\$32,131,934
<b>NAPHRO</b>	\$6,842,040	\$4,128,397	\$1,500,941	\$1,413,121	\$2,646,921	\$16,531,420
<b>Genome</b>	\$161,996	\$647,985	\$647,985	\$647,985	\$772,985	\$2,878,935
<b>CFI</b>	\$0	\$0	\$105,033	\$125,000	\$572,960	\$802,993
<b>NSERC</b>	\$43,990	\$90,990	\$106,500	\$162,000	\$102,500	\$505,980
<b>CRS</b>	\$60,000	\$60,000	\$120,000	\$80,000	\$100,000	\$420,000
<b>CCS</b>	\$112,800	\$77,000	\$60,000	\$59,700	\$39,400	\$348,900
<b>SSHRC</b>	\$0	\$0	\$0	\$17,500	\$0	\$17,500
	<b>\$23,515,217</b>	<b>\$23,469,073</b>	<b>\$21,436,119</b>	<b>\$23,367,718</b>	<b>\$27,797,434</b>	<b>\$119,585,561</b>

\* in CAD

**Abbreviations:** CCC: Crohn's and Colitis Canada; CCS: Canadian Cancer Society; CFI: Canada Foundation for Innovation; CRS: Cancer Research Society; Genome: Genome Canada; NAPHRO: National Alliance of Provincial Health Research Organizations; NSERC: Natural Sciences and Engineering Research Council of Canada; SSHRC: Social Sciences and Humanities Research Council

**Table 3.** Research funding in Canada for comparative diseases

	Multiple Sclerosis	Type 1 Diabetes	Parkinson's Disease	IBD
<b>Prevalence</b>	117,976 <sup>11</sup>	300,000 <sup>12</sup>	100,000 <sup>13</sup>	270,000 <sup>4</sup>
<b>Total Funding (CAD)</b>	\$94,497,700	\$98,202,428	\$61,921,948	\$115,134,733
<b>\$ Funding Per Patient (CAD)</b>	\$801	\$327	\$619	\$426

Chronic Disease; Team Grants for Health Challenges in Chronic Inflammation). Canadian Institutes of Health Research also provides various salary awards to train the next generation of researchers and to attract and retain highly qualified scientists in their respective fields (see Box 1: Training the Next Generation of IBD Researchers). Between 2013 and 2017, CIHR funded an average of \$13 million per year in research related to IBD.

### Funding by Crohn's and Colitis Canada

Crohn's and Colitis Canada is one of the largest nongovernment funders of Crohn's disease and ulcerative colitis in the world. Founded in 1974, the promise of Crohn's and Colitis Canada is to cure Crohn's disease and ulcerative colitis and to improve the lives of children and adults affected by these chronic diseases. In fulfilling this promise, Crohn's and Colitis Canada invests in research to increase understanding of, improve and expand treatment options for, and ultimately find the cure(s) for these life-long diseases.

During the past five years (2013 to 2017), Crohn's and Colitis Canada invested an average of \$6.4 million per year to support investigator-led research projects, targeted research initiatives, and fellowships and studentships to train the next generation of IBD researchers in Canada. In addition, Crohn's and Colitis Canada has held annual research conferences as part of the Meeting of the Minds education event to bring together scientists and health care providers to discuss the latest topics in research and IBD care.

## FUNDING MECHANISMS

### Priority-Driven IBD Research Funding in Canada

Priority-driven funding opportunities are supported by CIHR, Crohn's and Colitis Canada and their partners to address specific

gaps or opportunities related to IBD research. The purpose of focusing on a specific disease, theme or discipline is to address a research gap or develop Canadian research strength. A number of different priority-driven funding mechanisms have been used over the last decade, including research networks and team grants, examples of which are shared later on. Where relevant, leadership of Nominated Principal Investigators and Principal Investigators is acknowledged as indicated in the CIHR Funding Decisions Database. An example of priority-driven research is profiled in Box 2: Project Profile: IBD Genomic Medicine (iGenoMed) Consortium.

### Examples of Priority-Driven Research Networks

- *The Canadian children inflammatory bowel disease network: A joint partnership of CIHR and the CHILD foundation (CIDCaNN).* This network is led by Anne Griffiths, David Mack, Eric Benchimol, Kevan Jacobson, Gilaad Kaplan, David Mack, Aleixo Muise, Anthony Otley, Ernest Seidman, Bruce Vallance, Thomas Walters, Christopher Waterhouse, Eytan Wine and a team of clinical leads representing each participating centre. CIDCaNN brings together medical doctors and scientists working across Canada with the common goals of understanding why IBD affects so many children in Canada and determining the best treatment strategies to heal bowel inflammation and allow children to grow and enjoy life normally (\$5 million; 2013 to 2018).
- *The IMAGINE (Inflammation, Microbiome, and Alimentation: Gastro-Intestinal and Neuropsychiatric Effects) Chronic Disease Network (IMAGINE SPOR).* This network is led by Paul Moayyedi, Douglas Howse, Premysl Bercik, Charles Bernstein, Stephen Collins, Johannes A. Eksteen, Richard Fedorak, Gilaad Kaplan, Paul Kubes, Glenda Macqueen, Anthony Otley, John Rioux, Michael Surette, and Stephen Vanner. IMAGINE SPOR aims to transform the management of IBD, irritable bowel syndrome (IBS) and associated mental health issues.

### Box 1. Training the Next Generation of IBD Researchers

The CIHR/CCC/CAG Partners Program is an ongoing grants and awards program funded by CIHR and Crohn's and Colitis Canada, and administered by the Canadian Association of Gastroenterology. Originally launched in 1992, this program has funded research fellowships, new investigator awards, career transition awards and operating grants to support gastroenterology research, including a subset in the area of IBD. A 2012 review of this program demonstrated the impact of long-term and collaborative investments in training and capacity building, with recipients of funding producing research publications that had greater scientific impact than publications by peers both in Canada and around the world.<sup>14</sup> The CIHR/CCC/CAG Partners Program demonstrates the effectiveness of organizations collaborating across sectors to support world-class research that will ultimately improve the lives of patients with IBD.

Other examples of collaborative approaches to training the next generation of IBD researchers include partnerships between members of National Alliance of Provincial Health Research Organizations (NAPHRO) and charities such as Crohn's and Colitis Canada, which have resulted in the funding of provincial fellowships, scholarships and other capacity building opportunities.

### Box 2. Project Profile: IBD Genomic Medicine (iGenoMed) Consortium

Funded jointly by CIHR, Genome Canada, Crohn's and Colitis Canada and Genome Quebec (\$9.97 million), the objectives of the iGenoMed Consortium were to identify biomarkers of response to therapy and to develop predictive tests to help guide patients and their physicians in their treatment decisions. As part of the iGenoMed research project, Professors John D. Rioux and Alain Bitton, along with their colleagues across Canada and international collaborators, have produced high-impact findings. These include a high-resolution map that was used to investigate which genetic variants have a causal role in IBD<sup>15</sup> and an integrative approach to the development of multi-omic biomarkers of response to therapy<sup>16</sup>. In order to improve the chances of success of this new generation of predictive tests, the iGenoMed Consortium identified potential socioeconomic barriers to acceptance and strategies to address these challenges<sup>17-20</sup>. These findings will help researchers identify both which genes are involved in playing a role in IBD and which medications might be successful in which patients.

IMAGINE SPOR involves 17 hospitals/universities and 75 researchers across Canada who will study interactions between inflammation, the microbiome, diet and mental health in patients with IBD and IBS (\$12.45 million; 2016 to 2021).

- *Genetic, Environmental, Microbial (GEM)*. This study is led by Kenneth Croitoru. Funded by Crohn's and Colitis Canada and the Leona M. Helmsley Charitable Trust, GEM is a prospective study started in 2008 to recruit healthy first-degree relatives of Crohn's patients and follow them, expecting that a proportion would develop the disease in time. An international collaboration with over 100 recruitment sites worldwide, which reached recruitment milestones, GEM is now developing predictive biomarkers of disease (\$15.4 million; 2008 to present).
- *Promoting Access and Care through Centres of Excellence (PACE)*. This network is led by Geoffrey Nguyen. A Crohn's and Colitis Canada initiative with cofunding from industry, PACE aims to address gaps in care to increase the quality of life of those living with Crohn's disease or ulcerative colitis. PACE involves five centres of excellence working together (Remo Panaccione & Cynthia Seow, University of Calgary; Richard Fedorak, University of Alberta; John Marshall & Neeraj Narula, McMaster University; Alain Bitton & Waqqas Afif, McGill University) (\$2.5 million; 2016 to present).
- *Canadian IBD Research Consortium (CIRC)*. This consortium is led by Brian Bressler, Vipul Jairath, Geoffrey Nguyen, Neeraj Narula and Laura Targownik. Although Canada has one of the highest prevalence values of Crohn's disease and ulcerative colitis in the world and excellent clinician scientists, Canada is not thought of as a primary choice for industry-sponsored clinical studies to test novel therapies. With the support of industry partners, Crohn's and Colitis Canada is addressing this gap with CIRC in bringing together a pan-Canadian, multi-investigator network designed to increase clinical research activity in Canada (~\$300,000 per year; 2017 to present).
- *Nod-like receptors: linking innate immunity and inflammation to chronic disease*. Leads: Dana Philpott and Daniel Muruve. Team Grant: Health Challenges in Chronic Inflammation Initiative (with CIHR and Crohn's and Colitis Canada; \$2.4 million; 2014 to 2019).
- *The diet-microbiota-gut axis in pediatric IBD*. Leads: Alain Stintzi, Daniel Figeys, David Mack, Kieran O'Doherty and Bruce Vallance. Programmatic Grants in Environments, Genes and Chronic Disease (with CIHR and Crohn's and Colitis Canada; \$1.9 million; 2015 to 2020).
- *Elucidating the gene-environment interactions that drive auto-immune disease among South Asian Canadians: The GEMINI Program*. Leads: Jennifer Gommerman and Kenneth Croitoru. Programmatic Grants in Environments, Genes and Chronic Disease (with CIHR and Crohn's and Colitis Canada; \$2.0 million; 2015 to 2020).

### Investigator-Initiated IBD Research in Canada

Investigator-initiated research refers to funding competitions where the focus of the project is proposed by individual researchers and their teams. Selected projects funded by CIHR, Crohn's and Colitis Canada and partners through investigator-initiated funding that demonstrate local and Canadian leadership in international collaborations are listed in this section. Also listed are examples of other investigator-initiated programs demonstrating the collaborative nature of the Canadian IBD research sector:

#### *Canadian Gastro-Intestinal Epidemiology Consortium (CanGIEC)*

Led by Eric Benchimol at the Children's Hospital of Eastern Ontario and University of Ottawa; this pan-Canadian network of clinicians, researchers and methodologists has been working together to provide the evidence required to improve outcomes and health care services for Canadians with IBD using population-level studies

#### *The International Early Onset Paediatric IBD Cohort Study (NEOPICS)*

Led by Aleixo Muise at the Hospital for Sick Children and University of Toronto; NEOPICS brings together international pediatric gastroenterologists and scientists from academic centres around the world to work together on identifying causes of IBD in very young children (those under 6 years of age). The goals of NEOPICS are to investigate and identify the causes of IBD in young children and infants, and to develop new treatments and cures for IBD in these patients.

#### *The Canadian IBD Network for Research and Growth in Quality Improvement (CINERGI)*

Led by Geoffrey Nguyen at the Mount Sinai Hospital and University of Toronto; CINERGI is a research network of 14 IBD specialists representing 12 Canadian academic institutions spanning seven provinces with expertise in epidemiology, clinical trials, health services research, economic analysis and quality improvement. CINERGI is committed to improving health care delivery in IBD. Recent CINERGI projects include Choosing

### Examples of Priority-Driven Research Grants

- *Influences of host genome on the human gut microbiome: Studies in a healthy cohort carrying Crohn's disease risk alleles*. Leads: Kenneth Croitoru, Denis Krause and Mark Silverberg. Emerging Team Grant: Canadian Microbiome Initiative (with CIHR and Crohn's and Colitis Canada; \$2.4 million; 2010 to 2015).
- *Influence of the microbiome on epigenetic mechanisms in inflammatory bowel disease (IBD)*. Lead: Cheryl Arrowsmith. Team Grant: Canadian Epigenetics, Environment and Health Research Consortium (CEEHRC) (with CIHR and Genome British Columbia; \$1.5 million; 2013 to 2018).
- *NADPH oxidase function in the pathogenesis of pediatric IBD and JIA*. Lead: John Brumell. Team Grant: Health Challenges in Chronic Inflammation Initiative (with CIHR, Crohn's and Colitis Canada and The Arthritis Society; \$2.2 million; 2013 to 2018).

Wisely Canada for IBD and developing measures of inpatient quality indicators for inflammatory bowel disease.

## OUTPUT AND QUALITY OF IBD RESEARCH IN CANADA

### Overview

The collaborative efforts of CIHR, Crohn's and Colitis Canada and other Canadian research funders have supported the development of a strong cadre of Canadian health researchers who have worldwide impact. Inflammatory bowel disease researchers in Canada are among the most internationally collaborative in the world,<sup>21</sup> and Canadian researchers are among those identified as authors of the top 100 cited research manuscripts in IBD worldwide.<sup>22</sup> An example of impactful Canadian IBD Research is detailed in Box 3: International Recognition of Canadian Research Strength in IBD.

### Recognition of Canadian Research Strength in IBD

A bibliometric data analysis (see [Appendix B](#) for methodology) conducted in 2018 demonstrates the quality of IBD

research in Canada. This analysis showed that Canada ranks sixth worldwide in terms of number of IBD scientific papers published (which is equal to Canada's ranking when taking into account all scientific papers published). When productivity and impact in IBD research are combined, Canada is among the top three in the world. [Table 4](#) summarizes the top five countries with the highest bibliometric indices for IBD research between 2012 and 2016. Canada consistently ranked within the top three for each of the three bibliometric measures outlined:

#### *Average Relative Impact Factor (ARIF)*

This indicator is a measure of the expected impact of the research portfolio. To account for different citation patterns across fields and subfields, a Relative Impact Factor (RIF) is calculated by dividing the impact factor of the journal that the paper is published in by the mean impact factor of all papers in a particular subfield. The ARIF of a country is then calculated by computing the mean of the RIF of all published papers in a particular discipline for the country. An ARIF value greater than one indicates that the country publishes in journals cited more often than the world average.

Canada's ARIF (1.53) places Canada third internationally in IBD research after the Netherlands and the United Kingdom, with no statistical significance between the results of the top five countries. In terms of all scientific publications, Canada's ARIF is 1.22, which is lower than the ARIF achieved by Canadian IBD-focused researchers.

#### *Average of Relative Citations (ARC)*

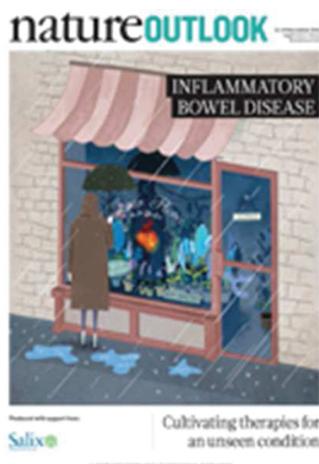
This indicator measures the observed impact of the research portfolio. It is based on the number of citations received by a published paper over a three-year period following the publication year. The number of citations received by each paper is normalized by the average number of citations received by all papers of the same subfield.

Canada's ARC value in all scientific research for the period measured was 1.42, with IBD research being 2.19. This is well above the IBD world average (1.27) and second only to the Netherlands (2.37), with the difference in score not being statistically significant. This finding means that, on average, papers dealing with IBD topics are cited 1.27 times more often than the average papers of their respective disciplinary field. For example, an IBD paper published in a journal of gastroenterology would be cited more frequently than other papers in gastroenterology. In terms of Canadian IBD papers, these are cited 2.19 times more frequently than other papers in their respective disciplines and 1.72 times more often than the world average of IBD papers. It is also important to note that Canada's ARC is significantly higher than its ARIF, indicating that the IBD research portfolio outperformed expectations over this period.

### Box 3. International Recognition of Canadian Research Strength in IBD

The incidence of IBD is now increasing not only in North America and Europe but also in parts of Asia, such as India and China. The increasing incidence of IBD around the world is thought to be linked not only to genetics but also to lifestyle and environmental changes. Canadian researchers are leading the way in identifying how changes in environment such as sanitation, air quality and diet may contribute to the development of IBD.

Two Canadian research networks, The Canadian Children Inflammatory Bowel Disease Network (CIDsCaNN) and Generational Differences in Environmental Exposure Caused by Migration: Impact on Incidence of Inflammatory Disease (GEMINI) were profiled as worldwide leaders in a *Nature Outlook* article.<sup>23</sup> These research networks are among the Canadian resources that are helping us understand how environmental exposures can impact the composition of bacteria in the gut (the microbiome) and how we can treat these changes to reduce inflammation.



**Table 4.** Bibliometric data analysis: top five countries with the greatest impact

Nations	Total Papers	Proportion of Country's Publications in Top 10% Impact (RC) Papers	Average of Relative Citations (ARC)	Average Relative Impact Factor (ARIF)
<b>Netherlands</b>	562	27%	2.37	1.56
<b>Canada</b>	<b>902</b>	<b>25%</b>	<b>2.19</b>	<b>1.53</b>
<b>France</b>	730	25%	2.14	1.53
<b>United Kingdom</b>	1,050	25%	2.14	1.55
<b>United States</b>	3,865	21%	1.78	1.52
<b>World</b>	12,750	14%	1.27	1.15

*Top 10% impact: based on the Relative Citations (RC) measure*

From 2012 to 2016, 25% of Canada's published IBD papers were within the top 10% of all IBD published papers, placing Canada second in the world (behind the Netherlands) on this measure.

Although there is a time lag between research funding and publication of data, we assumed relative productivity within plus or minus a three-year time period within a country would not vary significantly. Using this assumption, we created an average dollar investment per published paper by determining the number of published papers in the Dimensions platform that were found in the top 10 bibliometric analysis and then dividing by the research investment. With these limitations, we compared Canada, the United Kingdom and the United States: Canadian funders invested \$132,578 for every paper published in the top 10% impact listing. In comparison, the United Kingdom and United States invested \$205,053 and \$576,316, respectively. Comparative funding data are not available for the Netherlands and France in the Dimensions platform, precluding our ability to include these countries in this comparative analysis.

## CONCLUSIONS

Investment in IBD research in Canada has resulted in the development of a strong collaborative group of researchers producing impactful, world-class research. Relatively high levels of investment in all forms of research—including cure, treatment, prevention, health services and policy and quality of life—are likely a response to the prevalence and impact on quality of life of these diseases in Canada. Historically, Canada has been the fourth largest IBD research funder in the world, investing over \$119 million from 2013 to 2017. With this investment, the research community has delivered an extraordinary performance. On all measures of academic productivity and influence, Canada ranks in the top two or three internationally.

Against a backdrop of generally constrained resources, the challenge ahead is twofold: to continue to fund innovative, relevant IBD research and grow the next generation of IBD researchers while at the same time moving research findings ever more quickly into changes in health policy and practice in order to benefit affected patients and their families and, ultimately, identify the cause(s) and find the cure(s).

## Acknowledgements

We thank NAPPHRO, in particular the Nova Scotia Health Authority and Alberta Innovates for providing data from Dimensions. We thank Shabnaz Siddiq for her assistance in obtaining publication permissions and for acting as a coordinator for this work, and Joseph Windsor and Fox Underwood who edited the articles. EB, GK and GN were supported by New Investigator Awards from CIHR, Crohn's and Colitis Canada, and the Canadian Association of Gastroenterology. EB was also supported by the Career Enhancement Program from the Canadian Child Health Clinician Scientist Program. CB was supported in part by the Bingham Chair in Gastroenterology. GN and GK were CIHR Embedded Clinician Research Chairs.

**Supplement sponsorship.** This article appears as part of the supplement "The Impact of Inflammatory Bowel Disease in Canada 2018," sponsored by AbbVie Corporation and co-sponsored by Crohn's and Colitis Canada.

## References

- Ng SC, Shi HY, Hamidi N, et al. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: A systematic review of population-based studies. *Lancet* 2017;390(10114):2769–78.
- Shivashankar R, Tremaine WJ, Harmsen WS, Loftus EV Jr. Incidence and prevalence of Crohn's disease and ulcerative colitis in Olmsted County, Minnesota from 1970 through 2010. *Clin Gastroenterol Hepatol* 2017;15(6):857–63.
- Stone MA, Mayberry JF, Baker R. Prevalence and management of inflammatory bowel disease: A cross-sectional study from central England. *Eur J Gastroenterol Hepatol* 2003;15(12):1275–80.
- Coward S, Clement F, Benchimol EI, et al. The rising prevalence of inflammatory bowel disease in Canada: Analyzing the past to predict the future (abstract). *J Can Assoc Gastroenterol* 2018;1(Suppl 2):47–8.
- Juillerat P, Pittet V, Bulliard JL, et al. Prevalence of Inflammatory Bowel Disease in the Canton of Vaud (Switzerland): A population-based cohort study. *J Crohns Colitis* 2008;2(2):131–41.
- Busch K, Ludvigsson JF, Ekstrom-Smedby K, et al. Nationwide prevalence of inflammatory bowel disease in Sweden: A population-based register study. *Aliment Pharmacol Ther* 2014;39(1):57–68.
- Bengtson MB, Solberg C, Aamodt G, et al. Familial aggregation in Crohn's disease and ulcerative colitis in a Norwegian population-based cohort followed for ten years. *J Crohns Colitis* 2009;3(2):92–9.
- Studd C, Cameron G, Beswick L, et al. Never underestimate inflammatory bowel disease: High prevalence rates and confirmation of high incidence rates in Australia. *J Gastroenterol Hepatol* 2016;31(1):81–6.
- Asakura K, Nishiwaki Y, Inoue N, et al. Prevalence of ulcerative colitis and Crohn's disease in Japan. *J Gastroenterol* 2009;44(7):659–65.
- World Bank Data- Total Population. 2018. <https://data.worldbank.org/indicator/SP.POPTOTL> (Accessed September 29, 2018).
- Amankwah N, Marrie RA, Bancej C, et al. Multiple sclerosis in Canada 2011 to 2031: Results of a microsimulation modelling study of epidemiological and economic impacts. *Health Promot Chronic Dis Prev Can* 2017;37(2):37–48.
- Type 1 Diabetes. 2018. <https://www.jdf.ca/who-we-are/type-1-diabetes/> (Accessed September 29, 2018).

13. Parkinson's: The Facts. 2017. <[http://www.parkinson.ca/wp-content/uploads/2017\\_Brochure\\_The\\_Facts\\_En.pdf](http://www.parkinson.ca/wp-content/uploads/2017_Brochure_The_Facts_En.pdf)> (Accessed August 28, 2018).
14. Sherman PM, Banks Hart K, Rose KL, et al. Evaluation of funding gastroenterology research in Canada illustrates the beneficial role of partnerships. *Can J Gastroenterol* 2013;27(12):717–20.
15. Huang H, Fang M, Jostins L, et al. Fine-mapping inflammatory bowel disease loci to single-variant resolution. *Nature* 2017;547(7662):173–8.
16. Ivison S, Des Rosiers C, Lesage S, et al. Biomarker-guided stratification of autoimmune patients for biologic therapy. *Curr Opin Immunol* 2017;49:56–63.
17. Jean L, Audrey M, Beauchemin C, et al. Economic evaluations of treatments for inflammatory bowel diseases: A literature review. *Can J Gastroenterol Hepatol* 2018;2018:7439730.
18. Veilleux S, Noiseux I, Lachapelle N, et al. Patients' perception of their involvement in shared treatment decision making: Key factors in the treatment of inflammatory bowel disease. *Patient Educ Couns* 2018;101(2):331–9.
19. Veilleux S, Villeneuve M, Lachapelle N, et al. Exploring the use of a participative design in the early development of a predictive test: The importance of physician involvement. *Public Health Genomics* 2017;20(3):174–87.
20. Veilleux S, Villeneuve M, Belanger M, et al. Factors leading to acceptance of and willingness to pay for predictive testing among chronically ill patients. *JABE* 2016;16(4):35–46.
21. Schoffel N, Bendels MH, Groneberg DA. Ulcerative colitis: A scientometric approach to the global research output and network. *Eur J Intern Med* 2016;34:e41–3.
22. Connelly TM, Devane L, Kelly JC, et al. The 100 classic papers in ulcerative colitis: a bibliometric analysis. *Expert Rev Gastroenterol Hepatol* 2016;10(10):1–9.
23. Chi KR. Epidemiology: Rising in the East. *Nature* 2016;540(7634):S100–2.
24. Gingras Y. Performance Indicators: Keeping the Black Box Open. Proceedings of the second International Symposium on Research Funding, Ottawa, 1995:45–49.
25. Gingras Y. *Bibliometrics and Research Evaluation: Uses and Abuses*. Cambridge, MA: The MIT Press, 2016.
26. Sugimoto CR, Lariviere V. *Measuring Research: What Everyone Needs to Know*. New York: Oxford University Press, 2018.

## Appendix A: UberResearch Methodology and List of Funding Organizations

### Overview of Methodology

Dimensions was the core database used, and it is one of the service offerings provided by Digital Science; it was developed in collaboration with over 100 leading research organizations around the world and links 128 million formerly siloed documents, including \$1.3 trillion in research funding, 94 million publications, 35 million patents and 399,000 clinical trials and identifies almost 4 billion connections between them. This database also makes over 986 million academic citations available for appraisal.

Grants data in Dimensions are provided directly by either funders or from public sources (Table 5). Funding data often comes directly from the funder organization, especially when funders are Dimensions partners, and this is provided in a variety of different ways depending on the funder's preference. New grant sources are added on a regular basis, and existing funder sources are updated when new data are available.

To obtain data for this analysis, the database was searched using the key words: 'Crohn's disease', 'colitis' and 'ulcerative colitis'. A full database search was conducted initially to identify all grants made internationally and then filtered for the five-year period from 2013 to 17. Funding amounts are listed in Canadian dollars.

### Appendix B: Bibliometric Data

The bibliometric data used in this study are drawn from the Canadian Bibliometric Database (CBD<sup>TM</sup>) built by the

**Table 5.** List of funders in the Dimensions platform who funded IBD research in 2013 to 17

Country	Funder
<b>Australia</b>	Australian Research Council National Health and Medical Research Council
<b>Austria</b>	FWF Austrian Science Fund
<b>Belgium</b>	Belgian Federal Science Policy Office European Commission European Research Council Fund for Scientific Research - FNRS
<b>Brazil</b>	National Council for Scientific and Technological Development São Paulo Research Foundation
<b>Canada</b>	Alberta Innovates – Health Solutions Canada Foundation for Innovation Canadian Cancer Society Canadian Institutes of Health Research Cancer Research Society Fonds de Recherche du Québec Genome Canada Michael Smith Foundation for Health Research Ministry of Research and Innovation Natural Sciences and Engineering Research Council Nova Scotia Health Research Foundation Research Manitoba Saskatchewan Health Research Foundation Social Sciences and Humanities Research Council
<b>China</b>	National Natural Science Foundation of China Zhejiang Provincial Natural Science Foundation
<b>Croatia</b>	Croatian Science Foundation
<b>Czechia</b>	Czech Science Foundation Ministry of Education Youth and Sports Ministry of Health
<b>Estonia</b>	Estonian Research Council
<b>Finland</b>	Academy of Finland
<b>France</b>	Human Frontier Science Program National Agency for Research
<b>Germany</b>	German Research Foundation
<b>Hong Kong</b>	University Grants Committee
<b>Hungary</b>	Hungarian Scientific Research Fund
<b>Ireland</b>	Science Foundation Ireland
<b>Israel</b>	Israel Science Foundation

Table 5. Continued

Country	Funder
<b>Italy</b>	Ministry of Education, Universities and Research
<b>Japan</b>	Japan Society for the Promotion of Science
<b>Luxembourg</b>	National Research Fund Luxembourg
<b>Netherlands</b>	Netherlands Organisation for Scientific Research
<b>New Zealand</b>	Health Research Council of New Zealand
<b>Norway</b>	NordForsk The Research Council of Norway
<b>Poland</b>	Ministry of Science and Higher Education National Centre for Research and Development National Science Center
<b>Portugal</b>	Foundation for Science and Technology
<b>Russia</b>	Russian Foundation for Basic Research Russian Science Foundation
<b>Slovakia</b>	Ministry of Education, Science, Research and Sport of the Slovak Republic Slovak Research and Development Agency
<b>Slovenia</b>	Slovenian Research Agency
<b>Sweden</b>	Swedish Foundation for Strategic Research Swedish Research Council Swedish Research Council for Environment Agricultural Sciences and Spatial Planning Swedish Research Council for Health Working Life and Welfare VINNOVA
<b>Switzerland</b>	Swiss National Science Foundation
<b>United Kingdom</b>	Academy of Medical Sciences Biotechnology and Biological Sciences Research Council Cancer Research UK Department for Environment Food and Rural Affairs Engineering and Physical Sciences Research Council Innovate UK Medical Research Council National Centre for the Replacement Refinement and Reduction of Animals in Research

Table 5. Continued

Country	Funder
	Natural Environment Research Council NIHR Central Commissioning Facility NIHR Evaluation, Trials and Studies Coordinating Centre NIHR Trainees Coordinating Centre Royal Society Scottish Government Health and Social Care Directorates Wellcome Trust
<b>United States</b>	Agency for Health Care Research and Quality Agricultural Research Service Alzheimer's Drug Discovery Foundation Arnold and Mabel Beckman Foundation Arthritis Foundation Autism Speaks California HIV/AIDS Research Program California Institute for Regenerative Medicine Cancer Prevention and Research Institute of Texas Centers for Disease Control and Prevention Congressional Direct Medical Research Program Crohn's and Colitis Foundation of America Directorate for Biological Sciences Directorate for Computer & Information Science & Engineering Directorate for Engineering Directorate for Mathematical & Physical Sciences Directorate for Social, Behavioral & Economic Sciences Health Resources and Services Administration Juvenile Diabetes Research Foundation National Aeronautics and Space Administration National Cancer Institute National Center for Advancing Translational Sciences National Center for Complementary and Integrative Health National Eye Institute National Heart Lung and Blood Institute National Human Genome Research Institute

**Table 5.** *Continued*

Country	Funder
	National Institute of Allergy and Infectious Diseases
	National Institute of Arthritis and Musculoskeletal and Skin Diseases
	National Institute of Biomedical Imaging and Bioengineering
	National Institute of Child Health and Human Development
	National Institute of Dental and Craniofacial Research
	National Institute of Diabetes and Digestive and Kidney Diseases
	National Institute of Environmental Health Sciences
	National Institute of Food and Agriculture
	National Institute of General Medical Sciences
	National Institute of Mental Health
	National Institute of Neurological Disorders and Stroke
	National Institute of Nursing Research
	National Institute on Aging
	National Institute On Alcohol Abuse and Alcoholism
	National Institute on Drug Abuse
	National Institutes of Health Clinical Center
	National Psoriasis Foundation
	Office of the Director
	Patient Centered Outcomes Research Institute
	Shriners Hospitals for Children
	United States Army
	United States Department of the Navy
	United States Department of Veterans Affairs
	United States National Library of Medicine
	University of California: Cancer Research Coordinating Committee

'Observatoire des sciences et des technologies' (OST) by using Clarivate Analytic's Web of Science (WoS). The WoS includes three databases (the Science Citation Index Expanded™, the Social Sciences Citation Index™, and the Arts & Humanities Citation Index™) covering more than 12,000 journals from all fields of knowledge in 2016.

These databases do not include all documents likely to have been published by Canadian or foreign researchers, since some works are disseminated through other scientific media not indexed by the WoS (for instance, highly specialized journals, national journals, grey literature and conference proceedings not published in journals). However, the WoS databases include the researchers' scientific output most visible to Canadian and worldwide scientific communities and, therefore, is most likely to be cited.

Given that the WoS subject classification is applied to journals and not individual papers, in order to more specifically identify papers focused on Crohn's disease and colitis, OST used the US National Library of Medicine's Medical Subject Headings (MeSH), which relies on a controlled vocabulary to assign a medical topic to each paper indexed in PubMed. Table 6 presents the MeSH queries selected for this study and the number of papers retrieved in PubMed.

Taken together, these three queries retrieved 22,647 papers in PubMed over the 2009 to 2016 period. Due to the structure of the MeSH classification, these queries also cover the following concepts and MeSH terms:

Query #1 includes papers dealing with idiopathic proctocolitis and ulcerative colitis.

Query #2 retrieves papers dealing with Crohn's disease, Crohn's enteritis, granulomatous colitis, granulomatous enteritis, ileocolitis, regional enteritis and terminal ileitis.

It should also be noted that a given paper can bear more than one of these terms, which is why the sum of papers retrieved by each selected query is greater than the total number of distinct papers retrieved by the whole retrieval strategy.

Using authors' names, article titles, publication year, journal volume, journal number and page numbers, these PubMed papers were matched to corresponding items in the WoS to populate the bibliometric dataset from which the measurement areas identified were calculated.

It should be noted that PubMed records do not necessarily have a corresponding item in the WoS. Among the 22,647 papers retrieved from PubMed, 20,245 were published in a journal indexed in the WoS. Among these, 18,967 were matched to a record bearing at least one institutional address and corresponding to the document types used in the bibliometric analysis: articles, research notes and review articles because they are all considered as vehicles of new knowledge).

Details about the methodology have been published over the years.<sup>24-26</sup> What follows is a synopsis of the key elements.

### Indicators

For the 10 most productive countries in IBD research, the following indicators were produced at the level of each country and each priority area.

**Table 6.** IBD keywords and MeSH queries

Search	Query	Items Found
#1	Search (Colitis Gravis [MeSH terms] AND (Review[ptyp] OR Journal Article[ptyp])) AND (“2009/01/01”[PDat]: “2016/12/31”[PDat]))	7188
#2	Search (crohns disease [MeSH terms] AND (Review[ptyp] OR Journal Article[ptyp])) AND (“2009/01/01”[PDat]: “2016/12/31”[PDat]))	9356
#3	Search (inflammatory bowel[MeSH Terms] AND (Review[ptyp] OR Journal Article[ptyp])) AND (“2009/01/01”[PDat]: “2016/12/31”[PDat]))	10914
#4	Search #1 OR #2 OR #3	22647

Source: PubMed. Data retrieved on November 24, 2017

#### *Number of publications*

The number of scientific papers with authors from a country, as identified in the authors' addresses, were counted. Although OST's database includes several types of documents, only articles, research notes and review papers are included as described previously because these are the primary means of disseminating new knowledge. This indicator is also presented as a percentage of world papers in which at least one institutional address is from the country. These numbers of publications are also compiled for Canadian institutions and sectors (university, hospitals, industries, federal government, provincial government and others).

#### *Specialization index (SI)*

This is an indicator of the relative intensity of publication of a country in the priority areas identified relative to the intensity of the world in the same areas. An SI value above one means that a country is specialized in the priority area compared with the world average, whereas an index value below one means the opposite.

#### *Average relative impact factor (ARIF)*

This indicator provides a measure of the scientific impact of the journals in which a group of researchers publish. Each journal has an impact factor (IF), which is calculated annually based on the average number of citations received by the papers it published during the two previous years. The value of a journal's IF is assigned to each paper it publishes. In order to account for different citation patterns across fields and subfields (e.g., there are more citations in biomedical research than mathematics), each paper's IF is then divided by the average IF of the papers in its particular subfield in order to obtain a Relative Impact Factor (RIF). The ARIF of a given

institution (or group of researchers) is computed using the average RIF of all papers belonging to it. When the ARIF is greater than one, it means that this institution (or group of researchers) publishes in journals cited more often than the world average; when it is below one, the institution (or group of researchers) publishes in journals that are not cited as often as the world average. This indicator is set to nonsignificant when the number of publications involved is below 30.

#### *Average of Relative Citations (ARC)*

This indicator is based on the number of citations received by a published paper over a three-year period following the publication year. Thus, for papers published in 2000, citations received between 2000 and 2003 are counted. Author self-citations are included. The number of citations received by each paper is normalized by the average number of citations received by all papers of the same subfield, taking into account the fact that citation practices are different for each specialty. When the ARC is greater than one, it means that a paper or a group of papers scores better than the world average of its specialty; when it is below one, those publications are not cited as often as the world average. It should also be noted that this indicator is set to nonsignificant when the number of publications involved is below 30.

#### *Top 10% impact (RC)*

This indicator is based on the value of the relative citation (RC). Each paper has a RC that is the number of citations it receives normalized (divided) by the average number of citations received by all papers published the same year in the same specialty. The top 10% impact (RC) are the papers with the RC value in the top 10% of all papers published in the same year in the same specialty.