ISSN 1948-9366 (online)

World Journal of

Gastrointestinal Surgery

World J Gastrointest Surg 2024 June 27; 16(6): 1485-1955

Published by Baishideng Publishing Group Inc

World Journal of Gastrointestinal Surgery

Contents

Monthly Volume 16 Number 6 June 27, 2024

EDITORIAL

MINIREVIEWS

ORIGINAL ARTICLE

Case Control Study

Retrospective Cohort Study

World Journal of Gastrointestinal Surgery

Monthly Volume 16 Number 6 June 27, 2024

Contents

World Journal of Gastrointestinal Surgery

Monthly Volume 16 Number 6 June 27, 2024

Contents

World Journal of Gastrointestinal Surgery

Monthly Volume 16 Number 6 June 27, 2024

Contents

World Journal of Gastrointestinal Surgery

Monthly Volume 16 Number 6 June 27, 2024

Contents

CASE REPORT

LETTER TO THE EDITOR

ABOUT COVER

Peer Reviewer of *World Journal of Gastrointestinal Surgery*, Deven Juneja, DNB, FNB, EDIC, FCCP, Director, Department of Critical Care Medicine, Max Super Speciality Hospital, New Delhi 110017, India. devenjuneja@gmail.com

AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Surgery* (*WJGS*, *World J Gastrointest Surg*) is to provide scholars and readers from various fields of gastrointestinal surgery with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGS mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal surgery and covering a wide range of topics including biliary tract surgical procedures, biliopancreatic diversion, colectomy, esophagectomy, esophagostomy, pancreas transplantation, and pancreatectomy, *etc*.

INDEXING/ABSTRACTING

The *WJGS* is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports/Science Edition, PubMed, PubMed Central, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2024 Edition of Journal Citation Reports® cites the 2023 journal impact factor (JIF) for *WJGS* as 1.8; JIF without journal self cites: 1.7; 5-year JIF: 1.9; JIF Rank: 123/290 in surgery; JIF Quartile: Q2; and 5-year JIF Quartile: Q3.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Zi-Hang Xu*; **Production Department Director:** *Xiang Li*; **Cover Editor:** *Jia-Ru Fan*.

NAME OF JOURNAL
World Journal of Gastrointestinal Surgery

ISSN
ISSN 1948-9366 (online)

LAUNCH DATE
November 30, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Peter Schemmer

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1948-9366/editorialboard.htm

PUBLICATION DATE
June 27, 2024

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Gastrointestinal Surgery

Submit a Manuscript: https://www.f6publishing.com

World J Gastrointest Surg 2024 June 27; 16(6): 1835-1844

DOI: 10.4240/wjgs.v16.i6.1835

ISSN 1948-9366 (online)

SYSTEMATIC REVIEWS

Global geoepidemiology of gastrointestinal surgery rates in Crohn's disease

Simcha Weissman, Muhammad Aziz, Ayrton Bangolo, Vignesh K Nagesh, Htat Aung, Midhun Mathew, Lino Garcia, Shiva A Chandar, Praveena Karamthoti, Harinder Bawa, Aseel Alshimari, Yabets Kejela, Nazish Mehdi, Chrishanti A Joseph, Athri Kodali, Rohan Kumar, Priya Goyal, Sanya Satheesha, Fnu Nivedita, Nicole Tesoro, Tanni Sethi, Gurpreet Singh, Areej Belal, Alina Intisar, Hirra Khalid, Samuel Cornwell, Suchith B Suresh, Kareem Ahmed, Karabo K Marole, Om P Anand, Rahat B Reshi, Tej I Mehta, Sameh Elias, Joseph D Feuerstein

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification
Scientific Quality: Grade B
Novelty: Grade B
Creativity or Innovation: Grade B
Scientific Significance: Grade B

P-Reviewer: Wang Z, China

Received: December 31, 2023
Revised: April 9, 2024
Accepted: April 24, 2024
Published online: June 27, 2024
Processing time: 182 Days and 5.9 Hours

Simcha Weissman, Ayrton Bangolo, Vignesh K Nagesh, Htat Aung, Midhun Mathew, Lino Garcia, Shiva A Chandar, Praveena Karamthoti, Harinder Bawa, Aseel Alshimari, Yabets Kejela, Nazish Mehdi, Chrishanti A Joseph, Athri Kodali, Rohan Kumar, Priya Goyal, Sanya Satheesha, Fnu Nivedita, Nicole Tesoro, Tanni Sethi, Gurpreet Singh, Areej Belal, Alina Intisar, Hirra Khalid, Samuel Cornwell, Suchith B Suresh, Karabo K Marole, Om P Anand, Rahat B Reshi, Sameh Elias, Department of Medicine, Hackensack Meridian Health Palisades Medical Center, North Bergen, NJ 07047, United States

Muhammad Aziz, Division of Gastroenterology and Hepatology, University of Toledo Medical Center, Toledo, OH 43614, United States

Kareem Ahmed, Department of Medicine, University of Washington, Seattle, WA 98195, United States

Tej I Mehta, Department of Radiology, Johns Hopkins University Hospital, Baltimore, MD 21218, United States

Joseph D Feuerstein, Division of Gastroenterology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02215, United States

Corresponding author: Ayrton Bangolo, Doctor, MD, Doctor, Department of Medicine, Hackensack Meridian Health Palisades Medical Center, 7600 River Road, North Bergen, NJ 07047, United States. ayrtonbangolo0@gmail.com

Abstract

BACKGROUND

Data regarding the worldwide gastrointestinal surgery rates in patients with Crohn's disease (CD) remains limited.

AIM

To systematically review the global variation in the rates of surgery in CD.

METHODS
A comprehensive search analysis was performed using multiple electronic databases from inception through July 1, 2020, to identify all full text, randomized controlled trials and cohort studies pertaining to gastrointestinal surgery rates in adult patients with CD. Outcomes included continent based demographic data, CD surgery rates over time, as well as the geoepidemiologic variation in CD surgery rates. Statistical analyses were conducted using R.

RESULTS
Twenty-three studies spanning four continents were included. The median proportion of persons with CD who underwent gastrointestinal surgery in studies from North America, Europe, Asia, and Oceania were 30% (range: 1.7%-62.0%), 40% (range: 0.6%-74.0%), 17% (range: 16.0%-43.0%), and 38% respectively. No clear association was found regarding the proportion of patients undergoing gastrointestinal surgery over time in North America (R^2 = 0.035) and Europe (R^2 = 0.100). A moderate, negative association was seen regarding the proportion of patients undergoing gastrointestinal surgery over time (R^2 = 0.520) in Asia.

CONCLUSION
There appears to be significant inter-continental variation regarding surgery rates in CD. Homogenous evidence-based guidelines accounting for the geographic differences in managing patients with CD is prudent. Moreover, as a paucity of data on surgery rates in CD exists outside the North American and European continents, future studies, particularly in less studied locales, are warranted.

Key Words: Gastrointestinal surgery; Crohn's disease; Geoepidemiology; Inflammatory bowel disease; Prevalence

Core Tip: Surgical intervention in patents with Inflammatory bowel disease and particularly Crohn's disease (CD) to prevent complications remain a controversial subject. Significant inter-continental variation was observed regarding surgery rates in patients with CD. Our study provides insight for future studies targeting pathophysiology, genetics, risk factors, and management based upon the global variations detected. In addition, it serves to encourage the development of homogenous evidence-based guidelines accounting for the geographic differences in managing patients with CD: With an ultimate goal of helping clinicians make informed decisions for their patients independent of the region they practice. Additionally, as a paucity of data on surgery rates in patients with CD exists outside the North American and European continents, future studies, particularly in less studied locales, are warranted.

Citation: Weissman S, Aziz M, Bangolo A, Nagesh VK, Aung H, Mathew M, Garcia L, Chandar SA, Karamthoti P, Bawa H, Alshimari A, Kejela Y, Mehdi N, Joseph CA, Kodali A, Kumar R, Goyal P, Satheesha S, Nivedita F, Tesoro N, Sethi T, Singh G, Belal A, Intisar A, Khalid H, Cornwell S, Suresh SB, Ahmed K, Marole KK, Anand OP, Reshi RB, Mehta TI, Elias S, Feuerstein JD. Global geoepidemiology of gastrointestinal surgery rates in Crohn's disease. *World J Gastrointest Surg* 2024; 16(6): 1835-1844
URL: https://www.wjgnet.com/1948-9366/full/v16/i6/1835.htm
DOI: https://dx.doi.org/10.4240/wjgs.v16.i6.1835

INTRODUCTION

Inflammatory bowel disease (IBD), mainly comprised of Crohn's disease (CD) and ulcerative colitis, is an autoimmune, inflammatory condition marked by periods of clinical remission and disease flares. Unique to CD, it has its transmural inflammatory nature and innate ability to involve any segment along the gastrointestinal tract[1]. Although predominantly seen in industrialized nations, the incidence and prevalence of CD is increasing worldwide[2-4]. While rates in Northern America and Europe have stabilized, studies have shown a significant increase in incidence rates in Eastern European and Asian countries, parallel to their social and economic growth[5-7]. Despite extensive studies, the pathogenesis of this complex disease is still poorly understood; but exposure to environmental risk factors in genetically susceptible individuals is suspected to be one of the primary drivers of inflammation[4]. Differences in diet with subsequent changes in intestinal microbiota, temperature differences, socioeconomic status, and hygiene are some of the environmental factors thought to result in geographical variation and a rising trend with modernization[7-9].

CD can be difficult to manage despite medical expertise, as patients often experience recurrent flares throughout their lifetime, with up to 50% of patients developing an intestinal complication (stricture, abscess, or fistula) within 20 years of diagnosis[10,11]. Despite a dramatic expansion in the therapeutic arsenal for CD and its subsequent ability to be medically managed, surgery remains a crucial option, notably for patients with complications or refractory diseases[12,13]. Although the risk of gastrointestinal surgery in patients with CD has been reported to have decreased in recent years, almost 50% of patients with CD undergo surgery within 10 years of diagnosis[14-16]. GI surgery is defined as any procedure involving bowel resection or strictureplasty. For perianal disease, surgery is defined as requirement of fistulae

resection and/or abscess drainage. Surgery for treatment of perianal disease was also analyzed since it is an important feature in the treatment of penetrating CD affecting the anorectum[17]. Some studies report an estimated 70%-80% of patients with CD may require surgery at some point during their lifetime[18]. However, data regarding the worldwide gastrointestinal surgery rates in patients with CD remains limited.

As the global geographic and ethnic variations noticed in the prevalence rates of CD have inevitably led to a discrepancy in management, in particular surgery rates, a detailed knowledge of the inter-continental differences in surgical rates is paramount[18-39]. This will allow clinicians to evaluate the impact of therapeutic strategies, identify risk factors for disease severity, help facilitate shared decision-making, and potentially guide clinical practice[16]. In this setting, we sought to perform a systematic review to investigate the global variation of gastrointestinal surgery rates in patients with CD. In addition, we attempt to review the inter-continental surgery rates in patients with CD over time.

MATERIALS AND METHODS

Search strategy

A comprehensive search analysis was performed using the electronic databases MEDLINE/PubMed, EMBASE, and Cochrane, through July 1, 2020, to identify all pertinent articles. MeSH terms "Inflammatory bowel disease", "Crohn's disease", "surgery", and "epidemiology" were used in different combinations to generate a comprehensive and up-to-date list of articles. Two individual reviewers (SW and MA) performed the search independently and shortlisted the articles for final review. Any disagreement was resolved through mutual discussion and screening by a third reviewer (JDF) using a modified delphi system[40]. References of the initially identified studies were subsequently reviewed manually to find additional studies that may have been missed on initial search. Articles were initially screened by titles and abstracts. Full text was obtained for final shortlisted studies. We followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) to conduct our systematic review (Figure 1)[41,42].

Inclusion and exclusion criteria

Studies pertaining to adult patients (over age 18) with CD undergoing gastrointestinal surgery were included. We limited our search strategy to include full text, randomized controlled trials and cohort studies. We excluded review articles, case reports, studies with 10 or fewer patients, and letters to the editor. The search strategy was not restricted by language or date.

Outcomes

Outcomes included: (1) Continent based demographic data (gender and age at CD diagnosis); and (2) CD surgery rates over time, as well as iii) the geoepidemiologic variation in CD surgery rates. Figure 1 depicts the screening methodology and inclusion parameters used. The PICO (population, intervention, control group and outcome) description was used as an organizing framework for the study question to ensure *a priori* establishment of the study methodology[42].

Data collection

Demographic data, number of study participants, and surgery rates were extracted from each study. The data collection was performed by 2 individual reviewers (SW and MA) and any discrepancy was resolved by a third reviewer (JDF) using a modified delphi system[40].

Data synthesis and statistical analysis

All articles were screened for bias using the Newcastle-Ottawa Scale[43]. Individual study data are reported when available and regional rates are reported as weighted averages or median and range. To identify region-specific changes in the proportion of patients undergoing gastrointestinal surgery over time these data were plotted and correlation coefficients were generated. Statistical analysis was conducted using R version 3.6.1.

RESULTS

Literature search

The literature search identified 1397 articles of which 135 were deemed eligible for further assessment. Of these, 112 studies did not report on CD surgery rates and were thus excluded. The remaining 23 studies (examining 24 populations) met inclusion criteria and were deemed eligible for data analysis (Figure 1)[18-39,44]. Table 1 lists the baseline characteristics of the included studies. Meta-analysis was planned for this study, however unaccountable heterogeneity precluded such analysis.

North America

Nine North American studies published between 2004 and 2019 were included (seven in The United States, two in Canada). The median sample size was 400 (range: 99-8985), the median age at CD diagnosis was 27 (range: 15-38), and the median proportion of males was 44% (range: 27%-59%). The median proportion of persons with CD who underwent gastrointestinal surgery was 30.0% (range: 1.7%-62.0%). No clear association was found regarding the proportion of pa-

Table 1 Baseline characteristics of the included studies

Ref.	Region	Total (*N*)	Surgeries (*n*)
Chow *et al*[22], 2009	Asia	132	57
Jeon *et al*[29], 2010	Asia	96	15
Lee *et al*[32], 2017	Asia	165	28
Pandey *et al*[34], 2015	Asia	430	112
Varma *et al*[38], 2019[1]	Asia	103	16
Kariyawasam *et al*[30], 2014	Australia	1035	388
Alvarez-Lobos *et al*[17], 2005	Europe	170	59
Bernell *et al*[19], 2000	Europe	1936	1424
Chhaya *et al*[20], 2015	Europe	5235	32
Chhaya *et al*[21], 2016	Europe	9391	1714
Cosnes *et al*[23], 2005	Europe	2573	1070
Golovics *et al*[28], 2013	Europe	506	204
González-Lama *et al*[44], 2016	Europe	467	210
Szántó *et al*[37], 2018	Europe	428	228
Zaharie *et al*[39], 2016	Europe	478	78
Cushing *et al*[24], 2018	North America	400	198
Dubinsky *et al*[25], 2013	North America	1115	444
Feagan *et al*[26], 2008	North America	778	13
Forcione *et al*[27], 2004	North America	345	69
Kuenzig *et al*[31], 2018	North America	2113	532
Nguyen *et al*[33], 2017	North America	8985	2648
Peyrin-Biroulet *et al*[35], 2012	North America	310	152
Reutemann *et al*[36], 2017	North America	135	84
Varma *et al*[38], 2019[1]	North America	99	16

[1]Data from same study.

tients undergoing gastrointestinal surgery over time (R^2 = 0.035) (Figure 2A).

Europe

Nine European studies published between 2000 and 2018 were included. The median sample size was 506 (range: 170-9391), the median age at CD diagnosis was 32.0 (range: 27.9-38.5), and the median proportion of males was 48% (range: 44%-54%). The median proportion of persons with CD who underwent gastrointestinal surgery was 40.0% (range: 0.6%-74.0%). No clear association was found regarding the proportion of patients undergoing gastrointestinal surgery over time (R^2 = 0.100) (Figure 2B).

Asia

Five Asian studies were included. Median sample size was 132 (range: 96-430). The median proportion of persons with CD who underwent gastrointestinal surgery was 17% (range: 16%-43%). A moderate, negative association was seen regarding the proportion of patients undergoing gastrointestinal surgery over time (R^2 = 0.52) (Figure 2C).

Oceania

Only one study was identified from Oceania. The mean age at CD diagnosis reported by that study was 29; 44% of study participants were male. The study included 1035 patients with CD, of whom 38% (388) underwent gastrointestinal surgery. As only one study, published in 2014, from this region was included, surgery trends over time could not be assessed. See Figure 3 for a summary of the regions reporting studies on CD surgery rates. See Table 2 for the continent-based variation in CD surgery rates. See Table 3 for a summary of included studies based on population basis, time period, follow up period, and journal publication.

Table 2 Continent based variation in Crohn's disease surgery rates

Region	*n* (median, range)	GI surgery (median, range)	Proportion surgery (median, range)
North America	400 (99-8985)	152 (13-2648)	29.0% (1.6%-62.0%)
Europe	506 (170-9391)	210 (32-1714)	40.0% (0.6%-74.0%)
Asia	132 (96-430)	28 (15-112)	17.0% (16.0%-43.0%)
Oceania	1035	388	38.0%

Table 3 Summary of included studies based on population basis, time period, follow up period, and journal publication

Ref.	Population based	Time period	Follow up period	Journal publication
Chow *et al*[22], 2009	No	1987-2007	5.0 yr	*Inflammatory Bowel Diseases Journal*
Jeon *et al*[29], 2010	No	-	36.0 months	*Korean Journal of Gastroenterology*
Lee *et al*[32], 2017	No	2000-2015	6.0 months	*World Journal of Gastroenterology*
Pandey *et al*[34], 2015	Yes	1970-2013	7.3 years	*Inflammatory Bowel Diseases Journal*
Varma *et al*[38], 2019[1]	Yes	2014-2018	-	*Journal of Gastroenterology & Hepatology Foundation*
Kariyawasam *et al*[30], 2014	No	1970-2009	12.0 months	*Inflammatory Bowel Diseases Journal*
Alvarez-Lobos *et al*[17], 2005	No	2002-2004	7.4 yr	*Annals of Surgery*
Bernell *et al*[19], 2000	Yes	1955-1989	14.9 yr	*Annals of Surgery*
Chhaya *et al*[20], 2015	Yes	1995-2009	4.8 yr	*Inflammatory Bowel Diseases Journal*
Chhaya *et al*[21], 2016	Yes	1989-2009	5.8 yr	*European Journal of Gastroenterology & Hepatology*
Cosnes *et al*[23], 2005	No	1978-2002	5.0 yr	*Gut Journal*
Golovics *et al*[28], 2013	Yes	1977-2008	1.0 yr	*World Journal of Gastroenterology*
González-Lama *et al*[44], 2016	No	-	10.7 yr	*Inflammatory Bowel Diseases Journal*
Szántó *et al*[37], 2018	No	2007-2015	3.6 yr	*PLOS One Journal*
Zaharie *et al*[39], 2016	Yes	2006-2014	-	*Journal of Crohn's and Colitis*
Cushing *et al*[24], 2018	No	2014-2016	-	*Inflammatory Bowel Diseases Journal*
Dubinsky *et al*[25], 2013	No	-	60.0 months	*Inflammatory Bowel Diseases Journal*
Feagan *et al*[26], 2008	No	-	12.0 months	*Gastroenterology Journal*
Forcione *et al*[27], 2004	No	1991-1999	3.0 yr	*Gut Journal*
Kuenzig *et al*[31], 2018	Yes	1994-2010	2.0 yr	*American Journal of Gastroenterology*
Nguyen *et al*[33], 2017	Yes	1999-2008	-	*Inflammatory Bowel Diseases Journal*
Peyrin-Biroulet *et al*[35], 2012	Yes	2000-2009	12.0 yr	*American Journal of Gastroenterology*
Reutemann *et al*[36], 2017	No	2006-2014	41.7 months	*Inflammatory Bowel Diseases Journal*
Varma *et al*[38], 2019[1]	No	2014-2018	12.0 months	*Journal of Gastroenterology & Hepatology Foundation*

[1]Data from same study.

DISCUSSION

Our systematic review pertaining to global CD surgery rates and rates over time yielded considerable inter-continental differences. The median proportion of persons with CD who underwent gastrointestinal surgery in studies from North America, Europe, Asia, and Oceania were 30% (range: 1.7%-62.0%), 40% (range: 0.6%-74.0%), 17% (range: 16.0%-43.0%), and 38% respectively. While no clear association was found regarding the proportion of patients undergoing gastrointestinal surgery over time in North America (R^2 = 0.035) and Europe (R^2 = 0.100), a moderate, negative association was seen (R^2 = 0.520) in Asia. In addition, studies emerging from Asia had the greatest median proportion of males, namely 68% (with a range of 59% to 76%).

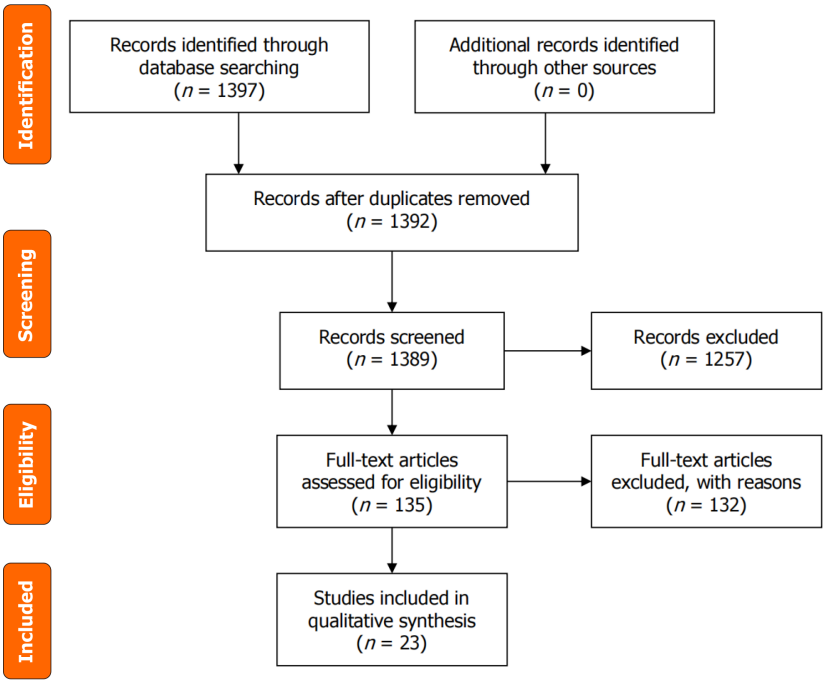

Figure 1 Preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement diagram delineating the process by which articles were screened and ultimately included.

The complexity of CD is multifactorial: Variable disease presentations, progression, complications, and therapeutic options (medical, surgical). The therapeutic options themselves are varied in terms of type of therapy, administration, patient adherence, and follow-up[45]. As the understanding of the risk/benefits for each option continues to evolve, clinicians face an arduous task of selecting the appropriate management for their patients[46]. The utility of an appropriate therapeutic/management strategy is paramount and needs to be individualized, *i.e.*, based upon patient factors. In the age of biologics, the rate of surgical interventions has dropped, nonetheless, it still remains as a viable alternative option for certain complications of CD such as strictures, fistulas, perforations, abscess, and malignancy and for patients who do not tolerate medical therapy[1,3]. The types of surgery include small bowel or ileocecal resection, small bowel strictureplasty, colorectal resection, perianal surgery, and combined procedures for any combination of the previous stated procedures[14].

As illustrated within, we observed marked variation in the inter-regional surgery rates according to region with proportions ranging from as low as 17% to as high as a staggering 40%. This is likely due to several factors including socioeconomic status, healthcare delivery model, regional difference in practices, type of surgery, and patient factors. The variation was also noted within the region, for example in North America, Feagan *et al*[26] noted a surgical rate of 1.7% while Reutemann *et al*[36] noted rate of 62.2%. In addition to the factors described above, these variations can also reflect the uncertainty in best clinical practice, hence suggesting a need for updated, and perhaps more global, evidence-based guidelines for the management of patients with CD.

The variation in patient demographics and surgical rates are perhaps also due to the lower incidence of CD in certain geographical regions such as Asia[2]. Indeed, the incidence and prevalence of CD in Asia is somewhat lower compared to rest of the world, however, this trend has changed in the last few years. Some of the disease characteristics are also different such as higher male proportions, older age of onset, lower rates of family history, extra-intestinal manifestations, and surgery. Despite the lack of strong family history, the postulated mechanisms for increasing IBD prevalence in Asian countries are attributable to a host of factors including vaccinations, antibiotics, western diet, contact with west, and alteration in gut microbiota[47]. Future research targeted to understanding the differences in these factors in the various populations (and variations in disease manifestations) are important to develop improved health care models and guidelines to cater to different populations more appropriately.

Alternate therapies such as herbal medications in India/Pakistan and Chinese medications in China can lead to a delayed presentation to conventional medical practitioners. The mechanism of action, drug interactions, and adverse events are not clear for these medications[48]. The use of these medications needs to be regulated after establishing safety and efficacy using the appropriate process (research, marketing surveillance, and FDA approval, *etc*). Awareness should be created in patients regarding the potential adverse outcomes of using inappropriate therapies for CD. A delayed presentation can potentially lead to higher surgical complications necessitating surgical corrections.

European countries were observed to have higher surgical rates amongst patients with CD (approximately 40%). The higher surgical rate, particularly from centers in Northern Europe, is thought to be secondary to aggressive disease phenotype, higher prevalence, attitude towards surgery, and/or genetics[49]. The surgery rates in Europe were higher likely because of the public insurance system in majority of the countries compared to the private insurance in United States. Studies have showed people with IBD had thrice the direct cost of treatment for IBD compared to a non-IBD

Figure 2 Gastrointestinal surgery rates in Crohn's disease. A: Gastrointestinal surgery rates in Crohn's disease (CD) in North America over time as reported by the included studies; B: Gastrointestinal surgery rates in CD in Europe over time as reported by the included studies; C: Gastrointestinal surgery rates in CD in Asia over time as reported by the included studies.

patient and twice the out-of-pocket expenses[50]. In Asia, the surgery rates for IBD were likely lower because of the low socio-economic status and limited access to surgical care[51].

Our systematic review has some limitations. First, data was gathered primarily from observational studies which have significant bias (recall, information, selection, subjective *etc.*). Second, there was significant variation in the reporting of data and follow-ups. Studies with longer follow-up/study duration period tended to have increased proportions of surgical rates. Third, we were not able to account for the type of surgery that CD patients underwent. Further, surgery based on urgency (elective, urgent, and emergent) was also not accounted for. Lastly, we were also not able to account residual

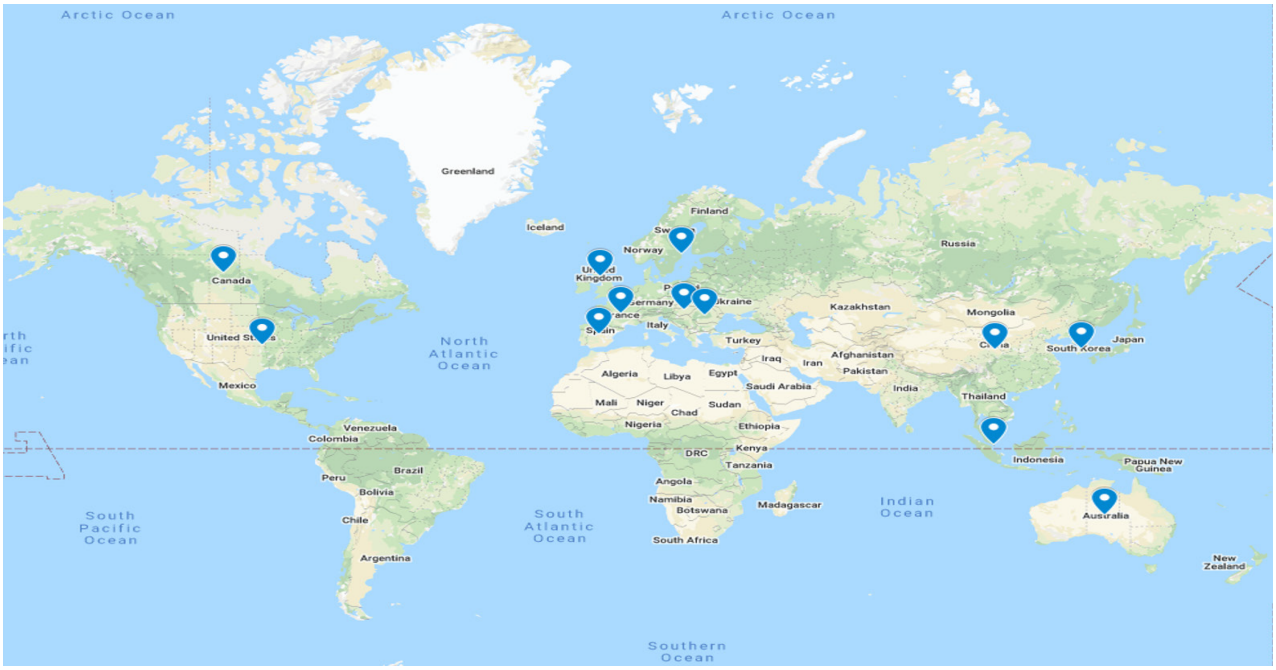

Figure 3 Map summary of the epidemiology of Crohn's disease surgery rates based upon study region.

confounders such as concomitant IBD medications (particularly biologics), co-morbidities, and disease flares. Despite the limitations, we included a large number of studies with a diverse and robust number of patients. Moreover, this is the first study reporting the geoepidemiological variations in the rate of surgery for CD patients.

CONCLUSION

In summary, significant inter-continental variation was observed regarding surgery rates in patients with CD. Our study provides insight for future studies targeting pathophysiology, genetics, risk factors, and management based upon the global variations detected. In addition, it serves to encourage the development of homogenous evidence-based guidelines accounting for the geographic differences in managing patients with CD, with an ultimate goal of helping clinicians make informed decisions for their patients independent of the region they practice. Additionally, as a paucity of data on surgery rates in patients with CD exists outside the North American and European continents, future studies—particularly in less studied locales, are warranted.

FOOTNOTES

Author contributions: Weissman S, Aziz M, and Bangolo A searched the literature, wrote, and revised the manuscript; Aung H, Mathew M, Garcia L, Chandar SA, Karamthoti P, Bawa H, Alshimari A, Kejela Y, Mehdi N, Joseph CA, Kodali A, Kumar R, Goyal P, Satheesha S, Nivedita F, Nagesh VK, Tesoro N, Sethi T, Singh G, Belal A, Intisar A, Khalid H, Cornwell S, Suresh SB, Ahmed K, Marole KK, Anand OP, and Reshi RB revised and edited the manuscript; Mehta TI, Elias S, and Feuerstein JD revised and approved the final version and are the article's guarantors; and all authors certify that they contributed sufficiently to the intellectual content and data analysis, and have reviewed the final version of the manuscript and approves it for publication.

Conflict-of-interest statement: The authors have no conflict of interest to disclose.

PRISMA 2009 Checklist statement: The authors have read the PRISMA 2009 Checklist, and the manuscript was prepared and revised according to the PRISMA 2009 Checklist.

Country of origin: United States

ORCID number: Ayrton Bangolo 0000-0002-2133-2480.

S-Editor: Chen YL
L-Editor: A
P-Editor: Xu ZH

REFERENCES

1 **Torres J**, Mehandru S, Colombel JF, Peyrin-Biroulet L. Crohn's disease. *Lancet* 2017; **389**: 1741-1755 [PMID: 27914655 DOI: 10.1016/S0140-6736(16)31711-1]
2 **Han M**, Jung YS, Cheon JH, Park S. Regional variations in the use of biologics and immunomodulators among Korean patients with inflammatory bowel diseases. *J Gastroenterol Hepatol* 2019; **34**: 1166-1174 [PMID: 30672608 DOI: 10.1111/jgh.14609]
3 **Wong DJ**, Roth EM, Feuerstein JD, Poylin VY. Surgery in the age of biologics. *Gastroenterol Rep (Oxf)* 2019; **7**: 77-90 [PMID: 30976420 DOI: 10.1093/gastro/goz004]
4 **Molodecky NA**, Soon IS, Rabi DM, Ghali WA, Ferris M, Chernoff G, Benchimol EI, Panaccione R, Ghosh S, Barkema HW, Kaplan GG. Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. *Gastroenterology* 2012; **142**: 46-54.e42; quiz e30 [PMID: 22001864 DOI: 10.1053/j.gastro.2011.10.001]
5 **Vegh Z**, Kurti Z, Lakatos PL. Epidemiology of inflammatory bowel diseases from west to east. *J Dig Dis* 2017; **18**: 92-98 [PMID: 28102560 DOI: 10.1111/1751-2980.12449]
6 **Park SJ**, Kim WH, Cheon JH. Clinical characteristics and treatment of inflammatory bowel disease: a comparison of Eastern and Western perspectives. *World J Gastroenterol* 2014; **20**: 11525-11537 [PMID: 25206259 DOI: 10.3748/wjg.v20.i33.11525]
7 **Ng SC**, Bernstein CN, Vatn MH, Lakatos PL, Loftus EV Jr, Tysk C, O'Morain C, Moum B, Colombel JF; Epidemiology and Natural History Task Force of the International Organization of Inflammatory Bowel Disease (IOIBD). Geographical variability and environmental risk factors in inflammatory bowel disease. *Gut* 2013; **62**: 630-649 [PMID: 23335431 DOI: 10.1136/gutjnl-2012-303661]
8 **Loftus EV Jr**. Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. *Gastroenterology* 2004; **126**: 1504-1517 [PMID: 15168363 DOI: 10.1053/j.gastro.2004.01.063]
9 **Baumgart DC**, Sandborn WJ. Crohn's disease. *Lancet* 2012; **380**: 1590-1605 [PMID: 22914295 DOI: 10.1016/S0140-6736(12)60026-9]
10 **Fichera A**, McCormack R, Rubin MA, Hurst RD, Michelassi F. Long-term outcome of surgically treated Crohn's colitis: a prospective study. *Dis Colon Rectum* 2005; **48**: 963-969 [PMID: 15785882 DOI: 10.1007/s10350-004-0906-3]
11 **Lichtenstein GR**, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults. *Am J Gastroenterol* 2018; **113**: 481-517 [PMID: 29610508 DOI: 10.1038/ajg.2018.27]
12 **Ma C**, Moran GW, Benchimol EI, Targownik LE, Heitman SJ, Hubbard JN, Seow CH, Novak KL, Ghosh S, Panaccione R, Kaplan GG. Surgical Rates for Crohn's Disease are Decreasing: A Population-Based Time Trend Analysis and Validation Study. *Am J Gastroenterol* 2017; **112**: 1840-1848 [PMID: 29087396 DOI: 10.1038/ajg.2017.394]
13 **Hazlewood GS**, Rezaie A, Borman M, Panaccione R, Ghosh S, Seow CH, Kuenzig E, Tomlinson G, Siegel CA, Melmed GY, Kaplan GG. Comparative effectiveness of immunosuppressants and biologics for inducing and maintaining remission in Crohn's disease: a network meta-analysis. *Gastroenterology* 2015; **148**: 344-54.e5; quiz e14 [PMID: 25448924 DOI: 10.1053/j.gastro.2014.10.011]
14 **Frolkis AD**, Dykeman J, Negrón ME, Debruyn J, Jette N, Fiest KM, Frolkis T, Barkema HW, Rioux KP, Panaccione R, Ghosh S, Wiebe S, Kaplan GG. Risk of surgery for inflammatory bowel diseases has decreased over time: a systematic review and meta-analysis of population-based studies. *Gastroenterology* 2013; **145**: 996-1006 [PMID: 23896172 DOI: 10.1053/j.gastro.2013.07.041]
15 **Gomollón F**, Dignass A, Annese V, Tilg H, Van Assche G, Lindsay JO, Peyrin-Biroulet L, Cullen GJ, Daperno M, Kucharzik T, Rieder F, Almer S, Armuzzi A, Harbord M, Langhorst J, Sans M, Chowers Y, Fiorino G, Juillerat P, Mantzaris GJ, Rizzello F, Vavricka S, Gionchetti P; ECCO. 3rd European Evidence-based Consensus on the Diagnosis and Management of Crohn's Disease 2016: Part 1: Diagnosis and Medical Management. *J Crohns Colitis* 2017; **11**: 3-25 [PMID: 27660341 DOI: 10.1093/ecco-jcc/jjw168]
16 **Rieder F**, Fiocchi C, Rogler G. Mechanisms, Management, and Treatment of Fibrosis in Patients With Inflammatory Bowel Diseases. *Gastroenterology* 2017; **152**: 340-350.e6 [PMID: 27720839 DOI: 10.1053/j.gastro.2016.09.047]
17 **Alvarez-Lobos M**, Arostegui JI, Sans M, Tassies D, Plaza S, Delgado S, Lacy AM, Pique JM, Yagüe J, Panés J. Crohn's disease patients carrying Nod2/CARD15 gene variants have an increased and early need for first surgery due to stricturing disease and higher rate of surgical recurrence. *Ann Surg* 2005; **242**: 693-700 [PMID: 16244543 DOI: 10.1097/01.sla.0000186173.14696.ea]
18 **Larson DW**, Pemberton JH. Current concepts and controversies in surgery for IBD. *Gastroenterology* 2004; **126**: 1611-1619 [PMID: 15168371 DOI: 10.1053/j.gastro.2004.03.063]
19 **Bernell O**, Lapidus A, Hellers G. Risk factors for surgery and postoperative recurrence in Crohn's disease. *Ann Surg* 2000; **231**: 38-45 [PMID: 10636100 DOI: 10.1097/00000658-200001000-00006]
20 **Chhaya V**, Saxena S, Cecil E, Subramanian V, Curcin V, Majeed A, Pollok RC. Impact of timing and duration of thiopurine treatment on first perianal surgery in Crohn's disease: UK population-based study (1995-2009). *Inflamm Bowel Dis* 2015; **21**: 385-391 [PMID: 25569740 DOI: 10.1097/MIB.0000000000000290]
21 **Chhaya V**, Saxena S, Cecil E, Subramanian V, Curcin V, Majeed A, Pollok RC. Emerging trends and risk factors for perianal surgery in Crohn's disease: a 20-year national population-based cohort study. *Eur J Gastroenterol Hepatol* 2016; **28**: 890-895 [PMID: 27128719 DOI: 10.1097/MEG.0000000000000651]
22 **Chow DK**, Sung JJ, Wu JC, Tsoi KK, Leong RW, Chan FK. Upper gastrointestinal tract phenotype of Crohn's disease is associated with early surgery and further hospitalization. *Inflamm Bowel Dis* 2009; **15**: 551-557 [PMID: 19067420 DOI: 10.1002/ibd.20804]
23 **Cosnes J**, Nion-Larmurier I, Beaugerie L, Afchain P, Tiret E, Gendre JP. Impact of the increasing use of immunosuppressants in Crohn's disease on the need for intestinal surgery. *Gut* 2005; **54**: 237-241 [PMID: 15647188 DOI: 10.1136/gut.2004.045294]
24 **Cushing KC**, Chiplunker A, Li A, Sung YJ, Geisman T, Chen LS, Cresci S, Gutierrez AM. Smoking Interacts With CHRNA5, a Nicotinic Acetylcholine Receptor Subunit Gene, to Influence the Risk of IBD-Related Surgery. *Inflamm Bowel Dis* 2018; **24**: 1057-1064 [PMID: 29688464 DOI: 10.1093/ibd/izx094]
25 **Dubinsky MC**, Kugathasan S, Kwon S, Haritunians T, Wrobel I, Wahbeh G, Quiros A, Bahar R, Silber G, Farrior S, Stephens M, Teleten N,

Panikkath D, Ippoliti A, Vasiliauskas E, Fleshner P, Williams C, Landers C, Rotter JI, Targan SR, Taylor KD, McGovern DP. Multidimensional prognostic risk assessment identifies association between IL12B variation and surgery in Crohn's disease. *Inflamm Bowel Dis* 2013; **19**: 1662-1670 [PMID: 23665963 DOI: 10.1097/MIB.0b013e318281f275]

26 **Feagan BG**, Panaccione R, Sandborn WJ, D'Haens GR, Schreiber S, Rutgeerts PJ, Loftus EV Jr, Lomax KG, Yu AP, Wu EQ, Chao J, Mulani P. Effects of adalimumab therapy on incidence of hospitalization and surgery in Crohn's disease: results from the CHARM study. *Gastroenterology* 2008; **135**: 1493-1499 [PMID: 18848553 DOI: 10.1053/j.gastro.2008.07.069]

27 **Forcione DG**, Rosen MJ, Kisiel JB, Sands BE. Anti-Saccharomyces cerevisiae antibody (ASCA) positivity is associated with increased risk for early surgery in Crohn's disease. *Gut* 2004; **53**: 1117-1122 [PMID: 15247177 DOI: 10.1136/gut.2003.030734]

28 **Golovics PA**, Lakatos L, Nagy A, Pandur T, Szita I, Balogh M, Molnar C, Komaromi E, Lovasz BD, Mandel M, Veres G, Kiss LS, Vegh Z, Lakatos PL. Is early limited surgery associated with a more benign disease course in Crohn's disease? *World J Gastroenterol* 2013; **19**: 7701-7710 [PMID: 24282358 DOI: 10.3748/wjg.v19.i43.7701]

29 **Jeon SJ**, Lee KJ, Lee MH, Lim SK, Kang CJ, Kim JH. Rates of early surgery and associated risk factors in Crohn's disease. *Korean J Gastroenterol* 2010; **56**: 236-241 [PMID: 20962559 DOI: 10.4166/kjg.2010.56.4.236]

30 **Kariyawasam VC**, Selinger CP, Katelaris PH, Jones DB, McDonald C, Barr G, Chapman G, Colliwshaw J, Lunney PC, Middleton K, Wang RR, Huang T, Andrews J, Leong RW. Early use of thiopurines or methotrexate reduces major abdominal and perianal surgery in Crohn's disease. *Inflamm Bowel Dis* 2014; **20**: 1382-1390 [PMID: 24991785 DOI: 10.1097/MIB.0000000000000119]

31 **Kuenzig ME**, Sadatsafavi M, Aviña-Zubieta JA, Burne RM, Abrahamowicz M, Beauchamp ME, Kaplan GG, Benchimol EI. Asthma is not associated with the need for surgery in Crohn's disease when controlling for smoking status: a population-based cohort study. *Clin Epidemiol* 2018; **10**: 831-840 [PMID: 30038523 DOI: 10.2147/CLEP.S156772]

32 **Lee DW**, Koo JS, Choe JW, Suh SJ, Kim SY, Hyun JJ, Jung SW, Jung YK, Yim HJ, Lee SW. Diagnostic delay in inflammatory bowel disease increases the risk of intestinal surgery. *World J Gastroenterol* 2017; **23**: 6474-6481 [PMID: 29085197 DOI: 10.3748/wjg.v23.i35.6474]

33 **Nguyen GC**, Bernstein CN, Benchimol EI. Risk of Surgery and Mortality in Elderly-onset Inflammatory Bowel Disease: A Population-based Cohort Study. *Inflamm Bowel Dis* 2017; **23**: 218-223 [PMID: 27997435 DOI: 10.1097/MIB.0000000000000993]

34 **Pandey A**, Salazar E, Kong CS, Lim WC, Ong J, Ong DE, Ong C, Aw M, Wee E, Chuah SW, Tan V, Tay WL, Nadkarni N, Ling KL. Risk of Major Abdominal Surgery in an Asian Population-based Crohn's Disease Cohort. *Inflamm Bowel Dis* 2015; **21**: 2625-2633 [PMID: 26240999 DOI: 10.1097/MIB.0000000000000525]

35 **Peyrin-Biroulet L**, Harmsen WS, Tremaine WJ, Zinsmeister AR, Sandborn WJ, Loftus EV Jr. Surgery in a population-based cohort of Crohn's disease from Olmsted County, Minnesota (1970-2004). *Am J Gastroenterol* 2012; **107**: 1693-1701 [PMID: 22945286 DOI: 10.1038/ajg.2012.298]

36 **Reutemann BA**, Turkeltaub JA, Al-Hawary M, Waljee AK, Higgins PDR, Stidham RW. Endoscopic Balloon Dilation Size and Avoidance of Surgery in Stricturing Crohn's Disease. *Inflamm Bowel Dis* 2017; **23**: 1803-1809 [PMID: 28691940 DOI: 10.1097/MIB.0000000000001181]

37 **Szántó K**, Nyári T, Bálint A, Bor R, Milassin Á, Rutka M, Fábián A, Szepes Z, Nagy F, Molnár T, Farkas K. Biological therapy and surgery rates in inflammatory bowel diseases-Data analysis of almost 1000 patients from a Hungarian tertiary IBD center. *PLoS One* 2018; **13**: e0200824 [PMID: 30059523 DOI: 10.1371/journal.pone.0200824]

38 **Varma S**, Hu J, Mehta A, Song Y, Park A, Zhi M, Hutfless S. Initial medical and surgical management of inflammatory bowel disease in the biologic era: A comparison between the United States and China. *JGH Open* 2019; **3**: 234-241 [PMID: 31276042 DOI: 10.1002/jgh3.12146]

39 **Zaharie R**, Tantau A, Zaharie F, Tantau M, Gheorghe L, Gheorghe C, Gologan S, Cijevschi C, Trifan A, Dobru D, Goldis A, Constantinescu G, Iacob R, Diculescu M; IBDPROSPECT Study Group. Diagnostic Delay in Romanian Patients with Inflammatory Bowel Disease: Risk Factors and Impact on the Disease Course and Need for Surgery. *J Crohns Colitis* 2016; **10**: 306-314 [PMID: 26589956 DOI: 10.1093/ecco-jcc/jjv215]

40 **Eubank BH**, Mohtadi NG, Lafave MR, Wiley JP, Bois AJ, Boorman RS, Sheps DM. Using the modified Delphi method to establish clinical consensus for the diagnosis and treatment of patients with rotator cuff pathology. *BMC Med Res Methodol* 2016; **16**: 56 [PMID: 27206853 DOI: 10.1186/s12874-016-0165-8]

41 **Moher D**, Altman DG, Liberati A, Tetzlaff J. PRISMA statement. *Epidemiology* 2011; **22**: 128; author reply 128 [PMID: 21150360 DOI: 10.1097/EDE.0b013e3181fe7825]

42 **Shea BJ**, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, Moher D, Tugwell P, Welch V, Kristjansson E, Henry DA. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ* 2017; **358**: j4008 [PMID: 28935701 DOI: 10.1136/bmj.j4008]

43 **Wells G**, Shea B, O'Connell D, Peterson J, Losos WM, Tugwell P, Ga SW, Zello G, Petersen J. Newcastle-Ottawa Scale for assessing the quality of studies in the meta-analysis. 2014. [cited 20 March 2024]. Available from: https://api.semanticscholar.org/CorpusID:79550924

44 **González-Lama Y**, Suárez C, González-Partida I, Calvo M, Matallana V, de la Revilla J, Magaz M, Bernardo C, Agudo B, Ibarrola P, Relea L, Arévalo J, Vera MI, Abreu L. Timing of Thiopurine or Anti-TNF Initiation Is Associated with the Risk of Major Abdominal Surgery in Crohn's Disease: A Retrospective Cohort Study. *J Crohns Colitis* 2016; **10**: 55-60 [PMID: 26520164 DOI: 10.1093/ecco-jcc/jjv187]

45 **Ananthakrishnan AN**, Kwon J, Raffals L, Sands B, Stenson WF, McGovern D, Kwon JH, Rheaume RL, Sandler RS. Variation in treatment of patients with inflammatory bowel diseases at major referral centers in the United States. *Clin Gastroenterol Hepatol* 2015; **13**: 1197-1200 [PMID: 25460565 DOI: 10.1016/j.cgh.2014.11.020]

46 **Kane S**. If variety is the spice of life, we need to rethink our recipe: variation in inflammatory bowel disease practice among tertiary centers. *Clin Gastroenterol Hepatol* 2015; **13**: 1201-1203 [PMID: 25638587 DOI: 10.1016/j.cgh.2015.01.020]

47 **Prideaux L**, Kamm MA, De Cruz PP, Chan FK, Ng SC. Inflammatory bowel disease in Asia: a systematic review. *J Gastroenterol Hepatol* 2012; **27**: 1266-1280 [PMID: 22497584 DOI: 10.1111/j.1440-1746.2012.07150.x]

48 **Ke F**, Yadav PK, Ju LZ. Herbal medicine in the treatment of ulcerative colitis. *Saudi J Gastroenterol* 2012; **18**: 3-10 [PMID: 22249085 DOI: 10.4103/1319-3767.91726]

49 **Burisch J**, Jess T, Martinato M, Lakatos PL; ECCO -EpiCom. The burden of inflammatory bowel disease in Europe. *J Crohns Colitis* 2013; **7**: 322-337 [PMID: 23395397 DOI: 10.1016/j.crohns.2013.01.010]

50 **Park KT**, Ehrlich OG, Allen JI, Meadows P, Szigethy EM, Henrichsen K, Kim SC, Lawton RC, Murphy SM, Regueiro M, Rubin DT, Engel-Nitz NM, Heller CA. Corrigendum to The Cost of Inflammatory Bowel Disease: An Initiative From the Crohn's & Colitis Foundation. *Inflamm Bowel Dis* 2020; **26**: 1118 [PMID: 32374862 DOI: 10.1093/ibd/izaa081]

51 **Sewell JL**, Velayos FS. Systematic review: The role of race and socioeconomic factors on IBD healthcare delivery and effectiveness. *Inflamm Bowel Dis* 2013; **19**: 627-643 [PMID: 22623078 DOI: 10.1002/ibd.22986]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com