BMJ Open

What can we learn from top-cited articles in inflammatory bowel disease? A bibliometric analysis and assessment of the level of evidence

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-021233
Article Type:	Research
Date Submitted by the Author:	29-Dec-2017
Complete List of Authors:	Azer, Samy; King Saud University, Medical Education; Australian Professional Teaching, Azer, Sarah; St Vincent Hospital
Keywords:	Inflammatory bowel disease (IBD), Ulcerative colitis (UC), Crohn's disease (CD), Bibliometric analysis, Top-cited articles, Quality of evidence

What can we learn from top-cited articles in inflammatory bowel disease? A bibliometric analysis and assessment of the level of evidence

Samy A. Azer[1] and Sarah Azer[2]

Dr Azer is consultant gastroenterologist and a professor of medical education and the chair of Curriculum Development and Research Unit, College of Medicine, King Saud University, Riyadh, Saudi Arabia[1]

Registrar, St Vincent Hospital, University of Melbourne, Victoria, Australia[2]

Correspondence and requests for reprints should be addressed to Dr Azer:
Curriculum Development and Research Unit,
College of Medicine, King Saud University
P O Box 2925, Riyadh 11461
Saudi Arabia
Telephone: (966) 11-4699178
Fax: (966) 11-4699174

Email:azer2000@optusnet.com.au

SHORT TITLE: Top-cited Inflammatory Bowel Disease

ABSTRACT

Objectives: Our objectives were to identifying the top-cited articles in inflammatory bowel disease (IBD), assessing their characteristics, and identifying the quality of evidence provided by these articles.

Design and outcome measures: The most frequently cited articles in IBD were searched in November 2016 in the Science Citation Index Expanded database. Eligible articles were reviewed for these characteristics- number of years since publication, journal impact factor (JIF), the number of authors, number of females in authorship, number of institutes, countries involved and grants received. The level of evidence was determined using the Oxford Centre for Evidence-Based Medicine guidelines.

Results: The number of citations varied 804 to 3320, total= 65332, median= 1042.50, (IQR= 596). No correlations were found between the number of citations and number of years since publication (p=0.532), JIF (p=0.179), number of authors (p=0.770), females in authorship (p=0.368), number of institutes (p=0.890), number of countries (p=0.959), or number of grants (p=0.464). Countries contributed to the majority of articles were United States, United Kingdom, Germany, France and Canada. The levels of evidence were 10 articles at level 1b, 11 articles at level 3a, and 17 articles at level 3b. The overall agreement between evaluators using Fleiss kappa was 0.8252; 95% CI=0.79-0.85.

Conclusions: research papers represented 68% (basic research 15, 30% and clinical research 19, 38%). Although no article had a level of evidence at 1a, the majority of articles were at reasonable high level of evidence. The study also shows gender gap and the fact that women still compose a minority of authorship in this area.

Key words

Inflammatory bowel disease (IBD), Ulcerative colitis (UC), Crohn's disease (CD), Top-cited articles, Bibliometric analysis, Quality of evidence, Number of authors, Female authors, Grants/funds, Institutes, Countries.

Strengths and limitations of the study

- More than one method was used in searching the Science Citation Index Expanded to maximize the yield of the search.
- The articles represent a historic perspective on key discoveries in the area of inflammatory bowel disease.
- A number of characteristics including number of authors, number of females in authorship, number of institutes, number of countries involved, and grants received have been studied against citations received.
- The level of evidence for each article has been evaluated.
- The search was limited to articles in the English language, raising the possibility of failing to include top-cited articles in other languages.

INTRODUCTION

The number of citations received by an article has been used for several years by universities and grant funding bodies in assessing the quality of research produced by researchers, ranking research performance and in making decisions regarding professional promotion and grant applications [1-4]. Thomson Reuters gather the names of these authors in the Highly Cited Researchers database where they are acknowledged for the quality of their work and the size of their research input in a particular area [5]. However, the number of citations cannot explain why researchers cited a paper nor reflect the quality of the research and the outcomes identified in a manuscript. Recently, three machine learning models were applied to predict the top 10% of articles in terms of number of citations to the article, suggesting that the topic rather than the content may be the reason for the high citations [6]. While one may agree that there is a high correlation between the numbers of papers a researcher has published and the total number of citations received [7] it appears that both indices namely the number of citations and the number of publications are reflective of research performance measurement and both have been represented in the *H-index* [8]. This index has been currently used in quantifying an individual's scientific research output in a much more meaningful way than depending on the number of citations alone.

Another criticism against the number of citations is self-citations, citations because researchers do not agree with the results/the explanations given or they have reached to different conclusions [9]. While this may form an argument, it cannot explain the high citation numbers received, particularly when we talk about top-cited articles. Evidence has shown that the number of self-citation because of disagreement is usually not significant in highly cited

articles [10]. Also it has been shown that journals with lower impact factor tend to have a higher self-citation rate [11].

Therefore, the number of citations and the reputation of contribution to research in a particular field cannot be ignored particularly when there is a pattern of consistency and progressive input into a discipline over years (a life experience), and a demonstration from publication records and citation history of collaboration with other researchers from other institutes at local and international levels. Hence the credits given to an author or a group of authors and the impact of the work in a particular area can be proportionally related to the citation records [12]. The greater the citation history over years, the more influential they are in their specialty [13].

Inflammatory bowel disease comprises ulcerative colitis (UC) and Crohn's disease (CD); both pursue a relapsing and remitting course over years. While the two diseases share several similarities, they have a number of differences in regard to structures involved, pathogenesis, clinical presentation, and management approaches. UC was first reported briefly in mid 1800 [14], while CD was reported in *the Journal of the American Medical Association (JAMA)* later by Crohn, Ginzburg and Oppenheimer in 1932 [15]; describing it as a chronic inflammatory bowel disease of the ilium. Later we learnt that CD can involve any part of the gastrointestinal tract from the lips to the anal margin but the ileocolonic disease represents the common presentation. Since then both diseases have been extensively researched in their different aspects and one would be interested to explore top-cited articles that reflect the topics, aspects, authors, and institutes that were behind our current knowledge and practices of these two diseases.

However, there are no research publications covering top-cited articles in IBD. The identification and analysis of the top-cited articles in inflammatory bowel disease bring a number of educational and research-related issues that we need to consider:

First, these articles can be considered a cornerstone in the field; advanced our knowledge about IBD, and enabled us to make definitive progress in understanding its epidemiology, pathogenesis, diagnostic procedures, and management.

Second, these articles reflect the work of key authors and research teams from particular institutes and countries that have made significant contribution to inflammatory bowel disease over the last 50-60 years or at least their work was the nucleus of hundreds of other research projects.

Third, the analysis of the indicators/parameters related to these articles such as number of authors, number of female authors, number of institutes, number of countries involved, and number of funds/grants received could help in understanding which of these parameters may correlate with higher number of citations and explain key features related to a successful or influential paper.

Therefore, the aims of the present research were: First, identify the top-cited articles in IBD. Second, analyze their characteristics and evaluate any correlations between the number of citations and the number of years since publications, the number of authors, the number of females in authorship, the number of institutes, the number of countries involved and the number of funds/grants received. Because of the assumption that researchers tend to cite recently published articles, it was decided to compare the yearly mean citations received by articles published before the year 2000 compared with the yearly means of those published

after the year 2000. Third, assess the quality of evidence provided by articles. The findings from this study could enable clinicians, pathologists, other allied health professionals, post-graduate students, and researchers to explore key articles behind the progress in this topic over the last few decades and identify areas that need further research. As well as explore the characteristics of these articles and what can be learnt from such analysis.

METHODS

Study Design

The database, the Science Citation Index Expanded (SCI-Expanded) database of the Thomson Reuters Web of Science was searched for the identification of the top-cited articles and tracking the citation records of each publication. Although Scopus and Google Scholar also provide citation records, it was decided to limit the search to SCI-Expanded database. Compared to other databases, SCI-Expanded database is regularly updated and the 2015 Journal Citation Reports (JCRs) included more than 6,500 journals across 150 disciplines. Although Google Scholar database is freely available, it was not used because it is difficult to search, and it cites textbooks, monographs, conference proceedings, as well as non-peer reviewed publications [16]. It is also not possible to track the yearly records of citations attracted by each article since publication. Scopus database was not used because it is not extensive in its coverage and its records only go back to 1996 [17].

To achieve the first two aims of this study we planned to identify the highly cited articles in IBD and assess if there were any correlation between the number of citations and any of the parameters characterizing these highly cited articles- number of authors, percentage of female authors, number of institutes, number of countries involved, and number of grants/funds

received. Regarding the third aim we planned to grade each article against the level of evidence hierarchy as per the Oxford Centre for Evidence-Based Medicine (OCEBM-2011 Levels of Evidence and the accompanying Table of Evidence Glossary) [18, 19].

Searching the Science Citation Index Expanded Database

On 5th to 9th of November 2016, two researchers (the author who is a professor of medical education, consultant gastroenterologist, and a fellow of the American College of Gastroenterology together with a research assistant who has medical background) searched the SCI-Expanded database to retrieve top-cited articles in inflammatory bowel disease. The search words used were the following: "Inflammatory bowel disease", "Ulcerative colitis", "Crohn's disease", 'IBD", "Experimental colitis", "Animal models for Colitis", "Animal models for inflammatory bowel disease", "Pathology IBD", "Pathology UC", Pathology CD", "Pathogenesis IBD", "Pathogenesis UC", "Pathogenesis CD", "Treatment IBD", "Treatment UC", "Treatment CD", "Investigation IBD" and "Regional ileitis". To increase the yield of the search, we used the full terms- inflammatory bowel disease, ulcerative colitis, and Crohn's disease for the abbreviations IBD, UC, and CD, respectively. These search words were identified from the terminology used in gastroenterology journals and the proceedings of major conferences on inflammatory bowel disease and gastroenterology such as the British Society of Gastroenterology (BSG), the American Gastroenterological Association (AGA), American College of Gastroenterology (ACG), Canadian Association of Gastroenterology (CAG), Scottish Society of Gastroenterology (SSG), and Gastroenterological Society of Australia (GESA). For each search word, the results were arranged using a link on the Science Citation Index Expanded database system "sort-by" – "Time Cited- highest to lowest". The

results showed the articles organized in a descending order with the articles most frequently cited on the top. A copy of the results was printed out for further analysis. The findings from each search word were then arranged on one Excel sheet (Microsoft Excel 2010, Microsoft Corp, Redmond, WA) in a descending order based on the number of citations. Duplicate articles and articles not in the English language were excluded. Articles with identical absolute number of citations were identified and were ranked on the basis of average citation per year. The average number of citations per year is the ratio calculated from the number of citations obtained by an article divided by the number of years since published [20]. A copy of all papers included in the list was obtained and read by the two evaluators.

Using the above mentioned search words, we conducted another search of major gastroenterology journals and the 2015-JCR under the category "Gastroenterology and Hepatology". This category comprises 76 journals at the time of conducting the search; of these seven journals were in languages other than English and were not searched. Gastroenterology journals publishing articles not in the English language were excluded because neither the author nor the assistant researchers are competent in the Spanish, Italian or German languages. Since the language recommended by the journal publishing this work is English and its readers are most likely interested in research publications in the English language, we decided not to search these journals.

Interestingly, after identifying the list of top-cited articles in IBD, and again checking these seven non-English journals, none had a paper with a citation higher than the paper ranked number 50 in the list.

Also these key words were used in searching the websites of major general medicine, surgery and research journals including the *New England Journal of Medicine, Lancet, the British*

Medical Journal, the Journal of the American Medical Association, Annals of Internal Medicine, Archives of Medicine, PLOS Medicine, Annals of Surgery, Archives of Surgery, British Journal of Surgery, American Journal of Surgical Pathology, Nature, Science, Nature Reviews Cancer, Nature Genetics, Nature Medicine, Cell, Nature Reviews Microbiology, Immunity, Nature Reviews Immunology, Nature Reviews Molecular Cell Biology, and Journal of Immunology.

A list identifying the 50 top-cited articles was reviewed again and checked regarding authorship, year of publication, title of the article, journal publishing the work, the Journal Impact Factor (JIF) at the time of the search, the number of citations and the institution of the first author (Appendix 1). Two articles shared the same citation number and the average citation per year was used to justify their ranking order. The average citation per year is calculated using this equation= total number of citations obtained/number of years calculated from the year of publication to the time of the research.

==========Add Appendix 1 ==========

Inclusion And Exclusion Criteria

The inclusion criteria were: (i) papers focusing on inflammatory bowel disease (ulcerative colitis or Crohn's disease) in the English language, and (ii) articles, reviews, research papers, reports, meta-analysis on any aspect related to inflammatory bowel disease in the English language (aetiology, contributing factors, incidence, population studies, pathology, pathogenesis, investigations, treatment/management, medications, nutrition, health promotion, patient education, animal studies, clinical studies, *in vitro* or in vivo studies or any related

clinical, healthcare, research issues). The exclusion criteria were: (i) articles on inflammatory bowel disease in languages other than English, (ii) articles that focused on other diseases and inflammatory bowel disease was not the main focus, and (iii) studies that focus on other types of colitis and not inflammatory bowel disease.

Assessing Articles

The full text of the identified 50-top cited articles was obtained and a copy was given to each researcher. The following information was collected for each article: (i) the authors' names, the number of authors, their affiliations, and the number of females contributing to authorship, (ii) the number of institutes involved in the publication, (iii) the city and country of the origin of the publication, (iv) the total number of citations obtained up to the day of searching the database, and the number of yearly citations since publication, (v) the year of publication and the calculated number of years since published, and (vi) the number of funds/grants stated in the publication and the Web of Science.

We have not used the classification provided by the Web of Science regarding study type because we noted that the Web of Science allocates publications that are original research, articles, practical guides and reviews and identified them as articles or reviews. For consistency and the purpose of this study, the system we used groups the top-cited articles into four types - article, review paper/meta-analysis, report, and research. A definition of each type is given in the glossary. Two researchers independently allocated each of the top-cited articles under its type as per the definition given. Any differences between the researchers were discussed in a meeting until a decision was reached.

The topics covered by the top-cited articles were identified by each researcher independently and were discussed in a meeting to harmonize the grouping into a logical, simple and practical way. Articles that covered more than one topic were classified on the basis of the aim of the study and the main outcomes. For other evaluations of an article including the number of authors, the number of females represented in authorship, the number of institutes, and countries contributing to the work, and the number of grants/funds received we checked the original article for such details. Regarding the identification of females in the authorship we noted that several journals use abbreviations of the first and second name rather than the full name. In order to identify the females in these articles we tried to search the Google database to find the university, personal website of the author, their Linkedin or ResearchGate accounts. We also tried to identify them by searching the Google Scholar database and identify their account, where we can find other publications under their name and the full first name.

Evaluating the Journals

The publishing journals of the top 50 articles in IBD were identified and evaluated in regard to the following: (i) the 2015-Journal Impact Factor (JIF) of each journal, and (ii) the ranking order of each article in comparison to other articles published in that journal. This was based on the number of citations obtained in comparison to the citation numbers received by other articles published in the journal. For example, an article ranked number one, in its publishing journal, means that the article received the highest number of citations in comparison to all other articles published in that journal. This evaluation aimed at assessing the position order of articles identified among the 50 top-cited articles in IBD in regard to their ranking among other articles published in the journal. Such assessment highlights the significance of the

inflammatory bowel disease articles among other topics published in gastroenterological journals as well as general medicine journals such as *The New England Journal of Medicine, The Lancet, the British Medical Journal, Medicine,* and top research journals such as *Nature, Nature Genetics, Science, Cell,* and top journals in immunology *such as Nature Reviews Immunology, and Immunity* (Appendix 1).

Assessing Level of Evidence

Two researchers independently used the Oxford Centre for Evidence-Based Medicine (OCEBM-2011 Levels of Evidence and the accompanying Table of Evidence Glossary) [18,19] to rank each article regarding level of evidence. In 1998 this hierarchical of evidence was first produced to make the process of finding relevant evidence feasible. Since then the levels have been reviewed and amended, and the version used in this research is the currently available version. [18,19]. This evaluation aimed at identifying the level of evidence of each article and assessing whether the highly cited articles have received higher scores in regard to level of evidence as per the Oxford hierarchy.

Statistical Analysis

Pearson's correlation coefficient (r) was calculated to determine if the high citation numbers obtained was related to the age of the article. Other correlations were between the number of citations and the number of authors, the percentage of females in authorship, the number of institutes, the number of countries involved, the number of grants received, and the Journal Impact Factor (JIF) of the journals in which articles were published. Because of the assumption that researchers usually cite recently published articles, it was decided to compare

the mean yearly citations received of articles published before the year 2000 and compare them with those published after the year 2000. All analyses were conducted using SPSS Software (IBM SPSS Statistics Premium version 22.0 for Mac OS-SPSS Inc., Chicago, IL, USA) and the results were reported at total, mean, median, IQR, and percentage. The inter-rater agreement between evaluators was calculated using the Fleiss kappa scale [21].

RESULTS

Top-Cited Papers Identified

Appendix 1 summarizes the top-cited articles in IBD identified by searching the Science Citation Index Expanded database [22-71]. The articles are listed in a descending order from 1 to 50 with the highest absolute citation number is ranked 1 and the article with the lowest citation ranked 50 as per the day of the search. Articles with the same number of citations were ranked on the basis of average citation per year (the articles ranked 46 and 47 had the same citation number 814, they were allocated to a ranking order based on the calculated citation per year, 50.9 and 30.1, respectively).

Table 1 summarizes the year of publication and article type. The articles were published over 57 years (from 1955 to 2012). During the period from 1955 to 1976, only 3 articles (6%) were published. However, the number increased significantly from 1977 to 1994 making a total of 13 (26%) articles. The number of publications increased significantly to 34 (68%) during the years from1995 to 2012. No correlation was found between the number of citations of these papers and the number of years since published (Pearson correlation (r) = 0.090, p =

0.532). To assess if there were differences between old articles (published before the year 2000) and those published after the year 2000, it was decided to study the mean number of citations received by top-cited articles in each year after their publications. The year 2000 was taken as a midpoint for comparison because the majority of articles identified were published in the period after the year 1986, and hence the year 2000 could represent such point. As shown from Figures 1A and 1B, the mean numbers of citations were higher for articles published after the year 2000 compared to those published before the year 2000.

Approximately one fourth of the top-cited papers were reviews/meta-analysis (n= 13, 26%), two-thirds were research papers (n= 34, 68%), and the remaining were articles (n= 2, 4%) and a report (n=1, 2%).

==========Please Add Table 1 here ========

Table 2 summarizes the distribution of IBD topics covered in the top-cited articles. These can be summarized as follows: Epidemiology and prevalence (n=2, 4%), Crohn's disease genetic susceptibility and NOD2 mutation (n=7, 14%), Animal models (n= 6, 12%), Pathogenesis of IBD (n= 13, 26%), classification and index of disease activity (n= 5, 10%), risk of developing colorectal cancer (n= 2, 4%), extra-intestinal complications (n= 1, 2%), Infliximab in Crohn's disease (n= 6, 12%), corticosteroids in ulcerative colitis (n=1, 2%), drug treatment and cyclosporine in ulcerative colitis (n= 2, 4%), adalimumab in Crohn's disease (n=1, 2%), 5-aminosalicylic acid in ulcerative colitis (n=1, 2%), 6-mercaptopurine in Crohn's disease (n=1, 2%), and monoclonal antibiotics, and anti-tumour necrosis factor in Crohn's disease (n=2,

4%). As shown in Appendix 1, 15 (30%) were basic research and 19 (38%) were clinical research. The level of evidence is discussed later in the results.

======Please Add Table 2 here ==========

The articles were published in the following journals: *New England Journal of Medicine* (n= 12, 24%), *Gastroenterology* (n= 10, 20%), *Nature* (n=4, 8%), *Nature Genetics* (n=4, 8%), *The Lancet* (n= 3, 6%), *Proceedings of the National Academic of Sciences of the United States of America* (n=2, 4%), *Cell* (n= 2, 4%), and *Gut* (n= 2, 4%). See Table 3 for more details about the journals publishing these articles.

======Please Add Table 3 here ==========

Looking at the ranking of the top-cited articles in IBD in the journals they were published in could provide a better picture about the influence of these articles. This influence would be clearly demonstrated when the journal has a relatively higher Journal Impact Factor. The ranking is based on the number of citations received by an article compared to the number of citations received by other articles that were published in that journal. The article by Best et al (1976) [25] is ranked number 4 in the list, and also ranked number 2 among all articles published in *Gastroenterology* (2015-JIF = 18.187). The article by Eaden et al [42] is ranked number 21 in the list and also ranked number 1 among all articles published in *Gut* (2015-JIF=

14.921). The ranking of other articles in List and their rankings in the journals in which they were published are shown in Appendix 1.

The first author of the top-cited articles was from the United States (n= 25, 50%), The United Kingdom (n=6, 12%), Germany (n= 6, 12%), France (n= 4, 8%), Canada (n= 3, 6%), Belgium (n= 2, 4%), Japan (n=2, 4%), Sweden (n=1, 2%), and the Netherlands (n=1, 2%).

Table 4 summarises the 72 authors who have published two papers or more in the top-cited IBD. Of these 19 authors were the first author and coauthors of more than two papers in total, one was only the first author of two papers, all the remaining, 52 were coauthors of more than two papers. Top authors were Rutgeers, P (n=10 papers), Targan, SR (n=8 papers), Schreiber, S (n=8 papers), Cho, JH (n=7 papers), Colombel, JF (n=7 papers), Hanauer, SB (n=7 papers), Duerr, RH (n=6 papers), Silverberg, MS (n=6 papers), and each of the following authors have 5 papers: Podolsky, DK, Rioux, JD, Daly MJ, Steinhart, AH, Rotter, JI, Schumm, LP, van Deventer, SJ, Taylor, KD, Vermeire, S, Mathew, CG, and Regueiro, M**.**

======Please Add Table 4 here ==========

The leadership of universities and institutes that have contributed to the creation of these publications were Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, the United States, Mount Sinai School of Medicine, New York, the United States, Mayo Clinic, Rochester, Minnesota, the United States, Cedars-Sinai Medical Center, Los Angeles, California, the United States, University of Chicago Medical Center, Chicago,

Illinois, the United States, University of Pittsburgh, Pittsburgh, Pennsylvania, the United States, University Hospital of Cleveland Case Western Reserve University School of Medicine, Ohio, the United States, Wellcome Trust Centre for Human Genetics, University of Oxford, Roosevelt Drive, Oxford, the United Kingdom, Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Cambridge, the United Kingdom, and Institute of Virology and Immunobiology, University of Würzburg, Germany. See Appendix 1 for more detail.

Characteristics of the Top-Cited Articles

These articles were created by 673 authors, median 7.0, minimum 1, maximum 106, IQR 12; the females in authorship were 115, median 1.0, minimum 0, maximum 20, IQR 2. It is worth mentioning here that it was difficult to identify the gender of authors in two papers because the full first and middle names were not shown and it was difficult to find more information or clues to make a decision. The number of institutes involved were 431, median 3.0, minimum 1, maximum 88, IQR 9; the countries involved were 139, median 1.0, minimum 1, maximum 16, IQR 2; and the number of grants/funds were 334, median 1.0, minimum 0, maximum 94, IQR 3. No correlations were found between the number of citations and the Journal Impact Factor (JIF) (Pearson correlation (r) = 0.193; p=0.179), the number of authors (r =-0.042; p= 0.770), number of females in authorship (r =-0.125; p= 0.368), the number of institutes involved (r =-0.020; p= 0.890), the number of countries involved (r =0.007; p= 0.959), and the number of grants received (r=-0.106; p=0.464).

Level of Evidence

Table 5 summarizes the grading of articles according to the Oxford Center for evidence-based medicine. The table shows that most articles were graded at levels 1b and 3a and 3b evidence (10 papers had level 1b evidence, 11 papers at level 3a, and 17 papers had level 3b evidence).

Only 5 papers had a level of evidence of 4 and one paper at level 5. No papers were at level 1a. The remaining 3 papers were at level 2b and two papers at level 2c. The overall agreement between the evaluators was acceptable; Fleiss kappa= 0.8252; 95% CI 0.79-0.85.

======Please Add Table 5 here ==========

DISCUSSION

This study aimed at identifying the characteristics of the top 50 most frequently cited papers in IBD and assessing the quality of evidence provided. The papers covered a number of key topics related to IBD including: epidemiology and prevalence, pathogenesis and genetic susceptibility of NOD2 mutation, animal models, clinical classification and indices of disease activity, risks of developing colorectal cancer, extra-intestinal complications, and use of infliximab, adalimumab, monoclonal antibodies and anti-tumour necrosis factor, and 6-mercaptopurine in CD, and use of 5-aminosalicylic acid, corticosteroids, and cyclosporine in treating UC. While these topics cover key issues related to IBD, topics related to molecular biology, surgical management, patient education, nutritional aspects, radiological and other investigations were not represented in the top-cited articles list [72-73].

The assessment of the characteristics of the top 50 highly cited articles identified in this study revels the following:

First, the lack of correlations between the number of citations and the number of years since publication may indicate that the high citation numbers are not caused by ageing of these

articles. In fact, only 16 articles (32%) were published in the period from 1955 to 1994 (39 years), while the majority 34 (68%) were published in the last 17 years. This paper also shows that the mean number of citations of articles published before the year 2000 were much lower than those of articles after the year 2000. This may be related to the tendency of researchers to cite recently published research and new findings [74] and papers that they have read [20, 75]. Also the higher citations have been found to be the strongest predictor of current online availability after long time since publication. Therefore, the higher citation could be a protective mechanism for continued availability of a publication despite aging and hence continuing citation [76].

Second, the lack of a correlation between the number of citations and the Journal Impact Factor (JIF). The JIF has been widely used in ranking and evaluating journals. It stands as a proxy for the relative importance of a journal with its field [77]. Although the top-cited articles identified were published in journals with high impact factors, the impact factors of some journals were not necessarily the highest in their fields. For example, *Human Pathology, Laboratory Investigation, Canadian Journal of Gastroenterology and Hepatology, Medicine (Baltimore), Journal of Immunology, Infection and Immunity, and Scandinavian Journal of Gastroenterology* had JIFs in the range of 2.1 to 4.9. With this information in mind one may postulate that the high JIF is not necessarily related to the higher citation numbers received. Two recent works showed that the JIF is not an accurate indicator of citations an average article receives, articles published in low impact factor journals can still be highly cited and vice versa [78,79].

Third, the study showed negative correlation between the number of citations and the number of authors, the number of female authors, or the number of institutes. The number of authors

and females in authorship varied from one to 106 and from zero to 20, respectively. Also the number of institutes involved varied from one to 88. The question that can be raised in this regards; are we expecting an increase in number of citations as the number of authors or the number institutes involved increased? The work of Garcia-Aroca et al [80] shows that collaboration between authors increases their impact and increases citation rates. However, they showed that publishing in English in certain journals and collaborating with certain authors and institutes increase the visibility of the manuscripts published on the subject. Hence it is the quality of collaboration rather than the absolute number of these parameters. Recently Tanner-Smith and Polanin showed that studies conducted by more established authors (have higher h-indices) and reported in more prestigious journal outlets are more likely to be cited by other scholars, even after controlling for various proxies of study quality [81].

Although the proportion of women in authorship of original research in the United States in general has significantly increased in the last four decades, women still compose a minority of the authors of original research [82]. In the field of gastroenterology, the percentage of the United States female physician authors of original research in the field has relatively increased over time, yet the senior author position remains lower than expected [83,84].

Fourth, the study showed no correlation between the number of citations and the number of funds/grants received. This finding is not surprising. Recently it was shown that too many of the United States authors of most influential papers in science do not receive NH funding [85]. Another group of researchers found no association between grant percentile ranking and grant outcome as assessed by number of top-10% articles per dollar million spent [86].

The United States, the United Kingdom, Germany, France, and Canada contributed to the majority of these articles. The leadership of universities from these countries in gastrointestinal research particularly IBD is no surprise, top universities identified from this study were Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, the United States, Mount Sinai School of Medicine, New York, the United States, Mayo Clinic, Rochester, Minnesota, the United States, Cedars-Sinai Medical Center, Los Angeles, California, the United States, University of Chicago Medical Center, Chicago, Illinois, the United States, University of Pittsburgh, Pittsburgh, Pennsylvania, the United States, University Hospital of Cleveland Case Western Reserve University School of Medicine, Ohio, the United States, Wellcome Trust Centre for Human Genetics, University of Oxford, Roosevelt Drive, Oxford, the United Kingdom, Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Cambridge, the United Kingdom, Institute of Virology and Immunobiology, University of Würzburg, Germany, Institute of Clinical Molecular Biology, Christian-Albrechts-University Kiel, Kiel, Germany, Hôpital Claude Huriez and Centre d'Investigation Clinique, Centre Hospitalier Universitaire de Lill, Université Lille Nord de France, Lille, France, Foundation Jean Dausset CEPH, France, University of Toronto, Toronto, Ontario, Canada, and University of Montreal, Research Center, Montreal, Quebec, Canada

All articles were published in the English language. The most productive journals were the *New England Journal of Medicin*e, and *Gastroenterology* with a total of 22 articles. Others were *Nature, Nature Genetics, the Lancet, and Proceedings of the National Academy of Sciences of the United States of America, Cell, Gut, British Medical Journal, Science, Nature Reviews Immunology, and Immunity,* making a total of 21 articles. While these journals have a

relatively high JIF, other journals published one article each and had a relatively low JIF compared to journals included in their categories. For example, *Human Pathology* listed number 22 under the category of Pathology, *Canadian Journal of Gastroenterology and Hepatology*, listed number 74 under the category Gastroenterology and Hepatology, *Scandinavian Journal of Gastroenterology*, listed number 77 under the category Gastroenterology and Hepatology, and *Infection and Immunity* listed number 67 under the category Immunology. The high level of evidence as outlined in the top-cited articles could be an important contributing factor to the higher number of citations received by these articles [87].

CONCLUSIONS

The top 50 top-cited articles in inflammatory bowel disease were identified by searching the Science Citation Index Expanded database; the citation analysis revealed that these articles were published between 1955 and 2012 with the years from 1995 to 2012 representing the best productive period. The citations varied from 804 to 3320 and the yearly mean numbers of citations for papers published after the year 2000 were relatively higher compared to those published before the year 2000. Over two thirds of these papers were research (30% basic research and 38% clinical research), and the remaining were mainly reviews and meta-analysis. Only three were articles and reports. The top-cited articles focused on: epidemiology and prevalence of IBD, pathogenesis and genetic susceptibility of NOD2 mutation, animal models, clinical classification and indices of disease activity, risks of developing colorectal cancer, extra-intestinal complications, and use of infliximab, adalimumab, monoclonal

antibodies and anti-tumour necrosis factor, and 6- mercaptopurine in CD, and use of 5-aminosalicylic acid, corticosteroids, and cyclosporine in treating UC. The journals that published top-cited articles were not limited to gastroenterology journals; top general medicine journals such as the *New England Journal of Medicine*, *the Lancet, British Medical Journal,* and *Medicine (Baltimore),* as well as top research journals such as *Nature, Nature Genetics, Science and Nature Reviews Immunology* contributed to the publication of these papers. On assessing the evidence level, ten articles were at level 1b, eleven articles were at level 3a, and seventeen articles were at level 3b. Countries that contributed to the majority of articles were the United States, the United Kingdom, Germany, France and Canada. There was no significant correlation between the number of citations and the number of years since publication, the Journal Impact Factor (JIF), the number of authors, the number of female authors, the number of institutes, the number of countries involved, or the number of grants received. These findings may be consistent with the concept that it is not the absolute number of collaboration that will make an impact on the citation number or the influence of a publication but rather the quality of such collaboration in regard to the researchers involved, their institutes, and the ongoing contribution to the advances of a particular area in research. The relatively small number of females in the authorship reflects the gender gap and the fact that women still compose a minority of the authors of original research and reviews in gastroenterology. The higher level of evidence demonstrated in most top-cited articles may have contributed to the higher number of citations received by these articles.

Acknowledgement: The author would like to thank Diana Sanad for her assistance and reviewing the manuscript. Also thank Dr Lily Scott for her assistance in this work.

Funding support: This work was funded by the College of Medicine, Research Center Deanship of Scientific Research, King Saud University, Riyadh, Saudi Arabia.

Ethical approval: Not applicable to this study.

Contributors SAA and SA shared equally the different roles and responsibilities to complete the submitted article including, the research idea, the search of databases, the evaluation of data collected, the statistical analysis, the interpretation of findings, the creation of tables and figures, writing the manuscript and the approved the final version of the manuscript.

Competing interests: Both authors (SAA and SA) declare that they have no competing interests and have completed the International Committee of Medical Journal Editors (ICMJE) form

Provenance and peer review: Not commissioned; externally peer reviewed

Data sharing statement: No further data available to share

REFERENCES

1. MacMaster FP, Swansburg R, Rittenbach K. Academic Productivity in Psychiatry: Benchmarks for the H-Index. Acad Psychiatry. 2017 Apr 18. [Epub ahead of print]

2. Susarla HK, Dhar V, Karimbux NY, Tinanoff N. Do Standard Bibliometric Measures Correlate with Academic Rank of Full-Time Pediatric Dentistry Faculty Members? J Dent Educ. 2017 Apr;81(4):427-432.

3. Milone MT, Bernstein J. On Track to Professorship? A Bibliometric Analysis of Early Scholarly Output. Am J Orthop (Belle Mead NJ). 2016 Mar-Apr;45(3):E119-23.

4. Azer SA, Holen A, Wilson I, Skokauskas N. Impact factor of medical education journals and recently developed indices: Can any of them support academic promotion criteria? J Postgrad Med. 2016 Jan-Mar;62(1):32-39. doi: 10.4103/0022-3859.173202.

5. Jones AW. Impact of JAT publications 1981-2003: the most prolific authors and the most highlycited articles. J Anal Toxicol. 2004 Oct;28(7):541-545.

6. Rosenkrantz AB, Doshi AM, Ginocchio LA, Aphinyanaphongs Y. Use of a Machine-learning Method for Predicting Highly Cited Articles Within General Radiology Journals. Acad Radiol. 2016 Dec;23(12):1573-1581. doi: 10.1016/j.acra.2016.08.011. Epub 2016 Sep 28.

7. Bosquet C, Combes PP. Are academics who publish more also more cited? Individual determinants of publication and citation records Scientometrics 97 (3), 831-857

8. Hirsch JE. An index to quantify an individual's scientific research output. Proc Natl Acad Sci U S A. 2005 Nov 15;102(46):16569-72.

9. Miyamoto S. Self-citation rate and impact factor in the field of plastic and reconstructive surgery. J Plast Surg Hand Surg. 2017 May 9:1-7. doi: 10.1080/2000656X.2017.1319847. [Epub ahead of print]

10. Ioannidis JP, Klavans R, Boyack KW. Multiple Citation Indicators and Their Composite across Scientific Disciplines. PLoS Biol. 2016 Jul 1;14(7):e1002501. doi: 10.1371/journal.pbio.1002501. eCollection 2016 Jul.

11. Reiter O, Mimouni M, Mimouni D. Analysis of self-citation and impact factor in dermatology journals. Int J Dermatol. 2016 Sep;55(9):995-9. doi: 10.1111/ijd.13193. Epub 2015 Dec 23.

12. Patsopoulos NA, Ioannidis JP, Analatos AA. Origin and funding of the most frequently cited papers in medicine: database analysis. BMJ 2006;332:1061–4.

13. Garfield E. Fortnightly review: how can impact factors be improved? BMJ 1996;313:411–413.

14. Wilks S. Morbid appearances in the in- testines of Miss Bankes. Med Times Gazette 1859;2:264-265.

15. Crohn BB, Ginzburg L, Oppenheimer GD. Regional ileitis: a pathologic and clinical entity. JAMA 1932;99:1323-1329.

16. Van Noorden R, Maher B, Nuzzo R. The top 100 papers. Nature. 2014;514(7524):550.

17. Kulkarni AV, Aziz B, Shams I, Busse JW. Comparisons of citations in Web of Science, Scopus, and Google Scholar for articles published in general medical journals. JAMA. 2009 Sep 9;302(10):1092-1096.

18. Azer SA. Top-Cited Articles in Problem-Based Learning: A Bibliometric Analysis and Quality of Evidence Assessment. J Dent Educ. 2017 Apr;81(4):458-478.

19. Oxford Centre for Evidence-based Medicine – Levels of Evidence (March 2009). Available at: http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009 [Accessed 20 May 2017].

20. Azer SA. The top-cited articles in medical education: a bibliometric analysis. Acad Med 2015;90(8):1147-1161.

21. D'Antiga L, Betalli P, De Angelis P, et al. Interobserver agreement on endoscopic classification of oesophageal varices in children. J Pediatr Gastroenterol Nutr 2015;61(2):176-181.

22. Hugot JP, Chamaillard M, Zouali H, Lesage S, Cézard JP, Belaiche J, Almer S, Tysk C, O'Morain CA, Gassull M, Binder V, Finkel Y, Cortot A, Modigliani R, Laurent-Puig P, Gower-Rousseau C, Macry J, Colombel JF, Sahbatou M, Thomas G. Association of NOD2 leucine-rich repeat variants with susceptibility to Crohn's disease. Nature. 2001 May 31;411(6837):599-603.

23. Ogura Y, Bonen DK, Inohara N, Nicolae DL, Chen FF, Ramos R, Britton H, Moran T, Karaliuskas R, Duerr RH, Achkar JP, Brant SR, Bayless TM, Kirschner BS, Hanauer SB, Nuñez G, Cho JH. A frameshift mutation in NOD2 associated with susceptibility to Crohn's disease. Nature. 2001 May 31;411(6837):603-6.

24. Kühn R, Löhler J, Rennick D, Rajewsky K, Müller W.Interleukin-10-deficient mice develop chronic enterocolitis. Cell. 1993 Oct 22;75(2):263-74

25. Best WR, Becktel JM, Singleton JW, Kern F Jr. Development of a Crohn's disease activity index. National Cooperative Crohn's Disease Study. Gastroenterology. 1976 Mar;70(3):439-44.

26. Podolsky DK. Inflammatory bowel disease. N Engl J Med. 2002 Aug 8;347(6):417-429.

27. Targan SR, Hanauer SB, van Deventer SJ, Mayer L, Present DH, Braakman T, DeWoody KL, Schaible TF, Rutgeerts PJ. A short-term study of chimeric monoclonal antibody cA2 to tumor necrosis factor alpha for Crohn's disease. Crohn's Disease cA2 Study Group. N Engl J Med. 1997 Oct 9;337(15):1029-35.

28. Hanauer SB, Feagan BG, Lichtenstein GR, Mayer LF, Schreiber S, Colombel JF, Rachmilewitz D, Wolf DC, Olson A, Bao W, Rutgeerts P; ACCENT I Study Group. Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial. Lancet. 2002 May 4;359(9317):1541-1549.

29. Truelove SC and Witts LJ. Cortisone in ulcerative colitis; final report on a therapeutic trial. Br Med J. 1955 Oct 29;2(4947):1041-1048.

30. Xavier RJ, Podolsky DK. Unravelling the pathogenesis of inflammatory bowel disease. Nature. 2007 Jul 26;448(7152):427-434.

31. Duerr RH, Taylor KD, Brant SR, Rioux JD, Silverberg MS, Daly MJ, Steinhart AH, Abraham C, Regueiro M, Griffiths A, Dassopoulos T, Bitton A, Yang H, Targan S, Datta LW, Kistner EO, Schumm LP, Lee AT, Gregersen PK, Barmada MM, Rotter JI, Nicolae DL, Cho JH. A genome-wide association study identifies IL23R as an inflammatory bowel disease

gene. Science. 2006 Dec 1;314(5804):1461-1463.

32. Present DH, Rutgeerts P, Targan S, Hanauer SB, Mayer L, van Hogezand RA, Podolsky DK, Sands BE, Braakman T, DeWoody KL, Schaible TF, van Deventer SJ. Infliximab for the treatment of fistulas in patients with Crohn's disease. N Engl J Med. 1999 May 6;340(18):1398-405.

33. Rutgeerts P, Sandborn WJ, Feagan BG, Reinisch W, Olson A, Johanns J, Travers S, Rachmilewitz D, Hanauer SB, Lichtenstein GR, de Villiers WJ, Present D, Sands BE, Colombel JF. Infliximab for induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2005 Dec 8;353(23):2462-76.

34. Fiocchi C. Inflammatory bowel disease: etiology and pathogenesis. Gastroenterology. 1998 Jul;115(1):182-205.

35. Barrett JC, Hansoul S, Nicolae DL, Cho JH, Duerr RH, Rioux JD, Brant SR, Silverberg MS, Taylor KD, Barmada MM, Bitton A, Dassopoulos T, Datta LW, Green T, Griffiths AM, Kistner EO, Murtha MT, Regueiro MD, Rotter JI, Schumm LP, Steinhart AH, Targan SR, Xavier RJ; NIDDK IBD Genetics Consortium, Libioulle C, Sandor C, Lathrop M, Belaiche J, Dewit O, Gut I, Heath S, Laukens D, Mni M, Rutgeerts P, Van Gossum A, Zelenika D, Franchimont D, Hugot JP, de Vos M, Vermeire S, Louis E; Belgian-French IBD Consortium; Wellcome Trust Case Control Consortium, Cardon LR, Anderson CA, Drummond H, Nimmo E, Ahmad T, Prescott NJ, Onnie CM, Fisher SA, Marchini J, Ghori J, Bumpstead S, Gwilliam R, Tremelling M, Deloukas P, Mansfield J, Jewell D, Satsangi J, Mathew CG, Parkes M, Georges M, Daly MJ. Genome-wide association defines more than 30 distinct susceptibility loci for Crohn's disease. Nat Genet. 2008 Aug;40(8):955-962.

36. Riddell RH, Goldman H, Ransohoff DF, Appelman HD, Fenoglio CM, Haggitt RC, Ahren C, Correa P, Hamilton SR, Morson BC, et al. Dysplasia in inflammatory bowel disease: standardized classification with provisional clinical applications. Hum Pathol. 1983 Nov;14(11):931-968.

37. Sadlack B, Merz H, Schorle H, Schimpl A, Feller AC, Horak I. Ulcerative colitis-like disease in mice with a disrupted interleukin-2 gene. Cell. 1993 Oct 22;75(2):253-261.

38. Loftus EV Jr. Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. Gastroenterology. 2004 May;126(6):1504-1517.

39. Okayasu I, Hatakeyama S, Yamada M, Ohkusa T, Inagaki Y, Nakaya R A novel method in the induction of reliable experimental acute and chronic ulcerative colitis in mice. Gastroenterology. 1990 Mar;98(3):694-702.

40. Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. Lancet. 1980 Mar 8;1(8167):514.

41. Frank DN, St Amand AL, Feldman RA, Boedeker EC, Harpaz N, Pace NR. Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. Proc Natl Acad Sci U S A. 2007 Aug 21;104(34):13780-13785

42. Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut. 2001 Apr;48(4):526-535.

43. Baert F, Noman M, Vermeire S, Van Assche G, D' Haens G, Carbonez A, Rutgeerts P. Influence of immunogenicity on the long-term efficacy of infliximab in Crohn's disease. N Engl J Med. 2003 Feb 13;348(7):601-608.

44. Cooper HS, Murthy SN, Shah RS, Sedergran DJ. Clinicopathologic study of dextran sulfate sodium experimental murine colitis. Lab Invest. 1993 Aug;69(2):238-249.

45. Ekbom A, Helmick C, Zack M, Adami HO. Ulcerative colitis and colorectal cancer. A population-based study. N Engl J Med. 1990 Nov 1;323(18):1228-1233.

46. Silverberg MS, Satsangi J, Ahmad T, Arnott ID, Bernstein CN, Brant SR, Caprilli R, Colombel JF, Gasche C, Geboes K, Jewell DP, Karban A, Loftus EV Jr, Peña AS, Riddell RH, Sachar DB, Schreiber S, Steinhart AH, Targan SR, Vermeire S, Warren BF. Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. Can J Gastroenterol. 2005 Sep;19 Suppl A:5A-36A

47. Rioux JD, Xavier RJ, Taylor KD, Silverberg MS, Goyette P, Huett A, Green T, Kuballa P, Barmada MM, Datta LW, Shugart YY, Griffiths AM, Targan SR, Ippoliti AF, Bernard EJ, Mei L, Nicolae DL, Regueiro M, Schumm LP, Steinhart AH, Rotter JI, Duerr RH, Cho JH, Daly MJ, Brant SR. Genome-wide association study identifies new susceptibility loci for Crohn disease and implicates autophagy in disease pathogenesis. Nat Genet. 2007 May;39(5):596-604.

48. Bouma G, Strober W. The immunological and genetic basis of inflammatory bowel disease. Nat Rev Immunol. 2003 Jul;3(7):521-533.

49. Lichtiger S, Present DH, Kornbluth A, Gelernt I, Bauer J, Galler G, Michelassi F, Hanauer S. Cyclosporine in severe ulcerative colitis refractory to steroid therapy. N Engl J Med. 1994

Jun 30;330(26):1841-1845.

50. Summers RW, Switz DM, Sessions JT Jr, Becktel JM, Best WR, Kern F Jr, Singleton JW. National Cooperative Crohn's Disease Study: results of drug treatment. Gastroenterology. 1979 Oct;77(4 Pt 2):847-869

51. Franke A, McGovern DP, Barrett JC, Wang K, Radford-Smith GL, Ahmad T, Lees CW, Balschun T, Lee J, Roberts R, Anderson CA, Bis JC, Bumpstead S, Ellinghaus D, Festen EM, Georges M, Green T, Haritunians T, Jostins L, Latiano A, Mathew CG, Montgomery GW, Prescott NJ, Raychaudhuri S, Rotter JI, Schumm P, Sharma Y, Simms LA, Taylor KD, Whiteman D, Wijmenga C, Baldassano RN, Barclay M, Bayless TM, Brand S, Büning C, Cohen A, Colombel JF, Cottone M, Stronati L, Denson T, De Vos M, D'Inca R, Dubinsky M, Edwards C, Florin T, Franchimont D, Gearry R, Glas J, Van Gossum A, Guthery SL, Halfvarson J, Verspaget HW, Hugot JP, Karban A, Laukens D, Lawrance I, Lemann M, Levine A, Libioulle C, Louis E, Mowat C, Newman W, Panés J, Phillips A, Proctor DD, Regueiro M, Russell R, Rutgeerts P, Sanderson J, Sans M, Seibold F, Steinhart AH, Stokkers PC, Torkvist L, Kullak-Ublick G, Wilson D, Walters T, Targan SR, Brant SR, Rioux JD, D'Amato M, Weersma RK, Kugathasan S, Griffiths AM, Mansfield JC, Vermeire S, Duerr RH, Silverberg MS, Satsangi J, Schreiber S, Cho JH, Annese V, Hakonarson H, Daly MJ, Parkes M. Genome-wide meta-analysis increases to 71 the number of confirmed Crohn's disease susceptibility loci. Nat Genet. 2010 Dec;42(12):1118-1125.

52. Sands BE, Anderson FH, Bernstein CN, Chey WY, Feagan BG, Fedorak RN, Kamm MA, Korzenik JR, Lashner BA, Onken JE, Rachmilewitz D, Rutgeerts P, Wild G, Wolf DC, Marsters PA, Travers SB, Blank MA, van Deventer SJ. Infliximab maintenance therapy for fistulizing Crohn's disease. N Engl J Med. 2004 Feb 26;350(9):876-85.

53. Jostins L, Ripke S, Weersma RK, Duerr RH, McGovern DP, Hui KY, Lee JC, Schumm LP, Sharma Y, Anderson CA, Essers J, Mitrovic M, Ning K, Cleynen I, Theatre E, Spain SL, Raychaudhuri S, Goyette P, Wei Z, Abraham C, Achkar JP, Ahmad T, Amininejad L, Ananthakrishnan AN, Andersen V, Andrews JM, Baidoo L, Balschun T, Bampton PA, Bitton A, Boucher G, Brand S, Büning C, Cohain A, Cichon S, D'Amato M, De Jong D, Devaney KL, Dubinsky M, Edwards C, Ellinghaus D, Ferguson LR, Franchimont D, Fransen K, Gearry R, Georges M, Gieger C, Glas J, Haritunians T, Hart A, Hawkey C, Hedl M, Hu X, Karlsen TH, Kupcinskas L, Kugathasan S, Latiano A, Laukens D, Lawrance IC, Lees CW, Louis E, Mahy G, Mansfield J, Morgan AR, Mowat C, Newman W, Palmieri O, Ponsioen CY, Potocnik U, Prescott NJ, Regueiro M, Rotter JI, Russell RK, Sanderson JD, Sans M, Satsangi J, Schreiber S, Simms LA, Sventoraityte J, Targan SR, Taylor KD, Tremelling M, Verspaget HW, De Vos M, Wijmenga C, Wilson DC, Winkelmann J, Xavier RJ, Zeissig S, Zhang B, Zhang CK, Zhao H; International IBD Genetics Consortium (IIBDGC)., Silverberg MS, Annese V, Hakonarson H, Brant SR, Radford-Smith G, Mathew CG, Rioux JD, Schadt EE, Daly MJ, Franke A, Parkes M, Vermeire S, Barrett JC, Cho JH. Host-microbe interactions have shaped the genetic architecture of inflammatory bowel disease. Nature. 2012 Nov 1;491(7422):119-24.

54. Sokol H, Pigneur B, Watterlot L, Lakhdari O, Bermúdez-Humarán LG, Gratadoux JJ, Blugeon S, Bridonneau C, Furet JP, Corthier G, Grangette C, Vasquez N, Pochart P, Trugnan G, Thomas G, Blottière HM, Doré J, Marteau P, Seksik P, Langella P. Faecalibacterium prausnitzii is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. Proc Natl Acad Sci U S A. 2008 Oct 28;105(43):16731-16736.

55. Hampe J, Franke A, Rosenstiel P, Till A, Teuber M, Huse K, Albrecht M, Mayr G, De La Vega FM, Briggs J, Günther S, Prescott NJ, Onnie CM, Häsler R, Sipos B, Fölsch UR, Lengauer T, Platzer M, Mathew CG, Krawczak M, Schreiber S. A genome-wide association scan of nonsynonymous SNPs identifies a susceptibility variant for Crohn disease in ATG16L1. Nat Genet. 2007 Feb;39(2):207-211.

56. Colombel JF, Sandborn WJ, Reinisch W, Mantzaris GJ, Kornbluth A, Rachmilewitz D, Lichtiger S, D'Haens G, Diamond RH, Broussard DL, Tang KL, van der Woude CJ, Rutgeerts P; SONIC Study Group. Infliximab, azathioprine, or combination therapy for Crohn's disease. N Engl J Med. 2010 Apr 15;362(15):1383-1395.

57. Elson CO, Sartor RB, Tennyson GS, Riddell RH. Experimental models of inflammatory bowel disease. Gastroenterology. 1995 Oct;109(4):1344-1367.

58. Colombel JF, Sandborn WJ, Rutgeerts P, Enns R, Hanauer SB, Panaccione R, Schreiber S, Byczkowski D, Li J, Kent JD, Pollack PF. Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: the CHARM trial. Gastroenterology. 2007 Jan;132(1):52-65.

59. Greenstein AJ, Janowitz HD, Sachar DB. The extra-intestinal complications of Crohn's disease and ulcerative colitis: a study of 700 patients. Medicine (Baltimore). 1976 Sep;55(5):401-412.

60. Schroeder KW, Tremaine WJ, Ilstrup DM. Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study. N Engl J Med. 1987 Dec 24;317(26):1625-1629.

61. Fujino S, Andoh A, Bamba S, Ogawa A, Hata K, Araki Y, Bamba T, Fujiyama Y. Increased expression of interleukin 17 in inflammatory bowel disease. Gut. 2003 Jan;52(1):65-70.

62. van Dullemen HM, van Deventer SJ, Hommes DW, Bijl HA, Jansen J, Tytgat GN, Woody J. Treatment of Crohn's disease with anti-tumor necrosis factor chimeric monoclonal antibody

(cA2). Gastroenterology. 1995 Jul;109(1):129-135.

63. Fuss IJ, Neurath M, Boirivant M, Klein JS, de la Motte C, Strong SA, Fiocchi C, Strober W. Disparate CD4+ lamina propria (LP) lymphokine secretion profiles in inflammatory bowel disease. Crohn's disease LP cells manifest increased secretion of IFN-gamma, whereas ulcerative colitis LP cells manifest increased secretion of IL-5. J Immunol. 1996 Aug 1;157(3):1261-1270.

64. Hampe J, Cuthbert A, Croucher PJ, Mirza MM, Mascheretti S, Fisher S, Frenzel H, King K, Hasselmeyer A, MacPherson AJ, Bridger S, van Deventer S, Forbes A, Nikolaus S, Lennard-Jones JE, Foelsch UR, Krawczak M, Lewis C, Schreiber S, Mathew CG. Association between insertion mutation in NOD2 gene and Crohn's disease in German and British populations. Lancet. 2001 Jun 16;357(9272):1925-1928.

65. Present DH, Korelitz BI, Wisch N, Glass JL, Sachar DB, Pasternack BS. Treatment of Crohn's disease with 6-mercaptopurine. A long-term, randomized, double-blind study. N Engl J Med. 1980 May 1;302(18):981-987.

66. Abraham C, Cho JH. Inflammatory bowel disease. N Engl J Med. 2009 Nov 19;361(21):2066-2078.

67. Cario E, Podolsky DK.Differential alteration in intestinal epithelial cell expression of toll-like receptor 3 (TLR3) and TLR4 in inflammatory bowel disease. Infect Immun. 2000 Dec;68(12):7010-7017.

68. Lennard-Jones JE. Classification of inflammatory bowel disease. Scand J Gastroenterol Suppl. 1989;170:2-6.

69. 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 Jan;142(1):46-54.

70. Swidsinski A, Ladhoff A, Pernthaler A, Swidsinski S, Loening-Baucke V, Ortner M, Weber J, Hoffmann U, Schreiber S, Dietel M, Lochs H. Mucosal flora in inflammatory bowel disease. Gastroenterology. 2002 Jan;122(1):44-54.

71. Powrie F, Leach MW, Mauze S, Menon S, Caddle LB, Coffman RL. Inhibition of Th1

responses prevents inflammatory bowel disease in scid mice reconstituted with CD45RBhi CD4+ T cells. Immunity. 1994 Oct;1(7):553-562.

72. Azer SA. Overview of molecular pathways in inflammatory bowel disease associated with colorectal cancer development. Eur J Gastroenterol Hepatol. 2013 Mar;25(3):271-281.

73. Azer SA, AlOlayan TI, AlGhamdi MA, AlSanea MA. Inflammatory bowel disease: An evaluation of health information on the internet. World J Gastroenterol. 2017 Mar 7;23(9):1676-1696.

74. Börner K, Maru JT, Goldstone RL. The simultaneous evolution of author and paper networks. Proc Natl Acad Sci U S A. 2004 Apr 6;101 Suppl 1:5266-73.

75. Azer SA. Exploring the Top-Cited and Most Influential Articles in Medical Education. J Contin Educ Health Prof. 2016 Summer;36 Suppl 1:S32-S41.

76. Wren JD, Georgescu C, Giles CB, Hennessey J. Use it or lose it: citations predict the continued online availability of published bioinformatics resources. Nucleic Acids Res. 2017 Apr 20;45(7):3627-3633.

77. Shanahan DR. Auto-correlation of journal impact factor for consensus research reporting statements: a cohort study. PeerJ. 2016 Mar 31;4:e1887.

78. Royle P, Kandala NB, Barnard K, Waugh N. Bibliometrics of systematic reviews: analysis of citation rates and journal impact factors. Syst Rev. 2013 Sep 12;2:74.

79. Falagas ME, Kouranos VD, Michalopoulos A, Rodopoulou SP, Batsiou MA, Karageorgopoulos DE. Comparison of the distribution of citations received by articles published in high, moderate, and low impact factor journals in clinical medicine. Intern Med J. 2010 Aug;40(8):587-591.

80. García-Aroca MÁ, Pandiella-Dominique A, Navarro-Suay R, Alonso-Arroyo A, Granda-Orive JI, Anguita-Rodríguez F, López-García A. Analysis of Production, Impact, and Scientific Collaboration on Difficult Airway Through the Web of Science and Scopus (1981-2013). Anesth Analg. 2017 Jun;124(6):1886-1896.

81. Tanner-Smith EE, Polanin JR. Brief alcohol intervention trials conducted by higher prestige authors and published in higher impact factor journals are cited more frequently. J Clin Epidemiol. 2016 Feb 6.

82. Jagsi R, Guancial EA, Worobey CC, Henault LE, Chang Y, Starr R, Tarbell NJ, Hylek EM. The "gender gap" in authorship of academic medical literature--a 35-year perspective. N Engl J Med. 2006 Jul 20;355(3):281-287.

83. Long MT, Leszczynski A, Thompson KD, Wasan SK, Calderwood AH. Female authorship in major academic gastroenterology journals: a look over 20 years. Gastrointest Endosc. 2015;81(6):1440-1447.

84. Diamond SJ, Thomas CR Jr, Desai S, Holliday EB, Jagsi R, Schmitt C, Enestvedt BK. Gender Differences in Publication Productivity, Academic Rank, and Career Duration Among U.S. Academic Gastroenterology Faculty. Acad Med. 2016 Aug;91(8):1158-1163.

85. Nicholson JM, Ioannidis JP. Research grants: Conform and be funded. Nature. 2012 Dec 6;492(7427):34-36.

86. Lauer MS, Danthi NS, Kaltman J, Wu C. Predicting Productivity Returns on Investment: Thirty Years of Peer Review, Grant Funding, and Publication of Highly Cited Papers at the National Heart, Lung, and Blood Institute. Circ Res. 2015 Jul 17;117(3):239-243.

87. Cheng K, Dodson TB, Egbert MA, Susarla SM. Which Factors Affect Citation Rates in the Oral and Maxillofacial Surgery Literature? J Oral Maxillofac Surg. 2017 Apr 1. pii: S0278-2391(17)30361-0.

Glossary

Articles are scientific written composition representing a substantial advance in the understanding of a topic or problem. They raise questions, provide thoughtful, critical analysis and aim at establishing new directions.

Basic research is defined as fundamental research, which aims at improving scientific theories and our understanding of a phenomenon. Basic research may use animal models and include in vivo and in-vitro studies that target advances of fundamental knowledge.

Clinical research is defined as research applied to a clinical condition/disease with the aim to test an intervention or make a change to a phenomenon. Basic research usually fuels clinical research.

Reports are defined as brief articles with conclusions, results, and recommendations. They report on a substantial advance in an area/topic or a problem and aim at reporting findings and standardization of practice.

Review and meta-analysis are defined as an article reviewing the progress of knowledge in a particular topic, critically analysing the current status of knowledge and presenting an understanding of the subject by discussing related literature. A review should identify gaps in the literature and highlight future directions for further research. **A meta-analysis** is defined as a statistical analysis that combines the results from different scientific studies to provide conclusive evidence.

Figure Legend

Figure 1A: Number of citations of papers published before the year 2000 (mean±SD)

Figure 1B: Number of citations of papers published after the year 2000 (mean±SD)

Table 1 Top cited papers in inflammatory bowel disease identified by searching the Web of Knowledge, summarized by year of publication and category

Article type	Year of publication: no of articles [References]							
	1950-1958	1959-1967	1968-1976	1977-1985	1986-1994	1995-2003	2004-2012	Total (%)
Article				1 [36]	1 [68]			2 [4%]
Review/Meta-analysis			1 [59]			5 [26,34,42,48,57]	7 [30,35,38,51,53,66,69]	13 [26%]
Report							1 [46]	1 [2%]
Research	1 [29]		1 [25]	3 [40,50,65]	8 [24,37,39,44,45,49,60,71]	12 [22,23,27,28,32,43,61,62,63,64,67,70]	9 [31,33,41,47,52,54,55,56,58]	34 [68%]
Total (%)	1 [2%	0 [0%]	2 [4%]	4 [8%]	9 [18%]	17 [34%]	17 [34%]	50 [100%]

Table 2 Top-cited papers in inflammatory bowel disease (IBD) identified by searching the Web of Knowledge, summarized by category and topic

Topics on IBD	Category: no of articles [References]				
	Article	Review/ Meta-analysis	Report	Research	Total (%)
Epidemiology, prevalence		2 [38,69]			2 [4%]
CD genetic susceptibility and NOD2 mutation		2 [35,51]		5 [22,23,47,55,64]	7 [14%]
Animal models for IBD		1 [57]		5 [24,37,39,44,71]	6 [12%]
Pathogenesis of IBD		6 [26,30,34,48,53,66]		7 [31,41,54,61,63,67,70]	13 [26%]
Classification, index of disease activity	2 [36,68]		1 [46]	2 [25,40]	5 [10%]
Risk of developing colorectal cancer		1 [42]		1 [45]	2 [4%]
Extra-intestinal complications		1 [59]			1 [2%]
Infliximab in CD				6 [28,32,33,43,52,56]	6 [12%]
Corticosteroids in UC				1 [29]	1 [2%]
Drug treatment and cyclosporine in UC				2 [49,50]	2 [4%]
Adalimumab in CD				1 [58]	1 [2%]
5-aminosalicylic acid in UC				1 [60]	1 [2%]
6-mercaptopurine in CD				1 [65]	1 [2%]

Monoclonal antibodies, anti-tumor necrosis factor in CD				2 [27,62]	2 [4%]
Total (%)	2 [4%]	13 [26%]	1 [2%]	34 [68%]	50 [100%]

Table 3. The journals that published the top-cited inflammatory bowel disease (IBD) articles included in the study, the journal impact factor, and the number of papers published and reference number.

Journal*	2015-Journal Impact Factor (JIF)	Number of papers published [References]
New England Journal of Medicine	59.558	12 [26,27,32,33,43,45,49,52,56,60,65,66]
Gastroenterology	18.187	10 [25,34,38,39,50,57,58,62,69,70]
Nature	38.138	4 [22,23,30,53]
Nature Genetics	31.616	4 [35,47,51,55]
The Lancet	44.002	3 [28,40,64]
Proceedings of the National Academy of Sciences of the United States of America	9.423	2 [41,54]
Cell	28.710	2 [24,37]
Gut	14.921	2 [42,61]
British Medical Journal	19.697	1 [29]
Science	34.661	1 [31]
Human Pathology	2.791	1 [36]
Laboratory Investigation	4.202	1 [44]
Canadian Journal of Gastroenterology and Hepatology	2.307	1 [46]
Nature Reviews Immunology	39.416	1 [48]
Medicine (Baltimore)	2.133	1 [59]
Journal of Immunology	4.985	1 [63]
Infection and Immunity	3.603	1 [67]
Scandinavian Journal of Gastroenterology	2.199	1 [68]
Immunity	24.082	1 [71]

- Gastroenterology related journals (Gastroenterology, Gut, and the Scandinavian Journal of Gastroenterology) only published 13 articles out of the top highly cited 50 articles (26%)

Table 4 Authors and co-authors of two or more articles of the top-cited articles in inflammatory bowel disease identified by searching the Web of Science

Author's name**	Number [References]		Author's Name**	Number [References]	
	First author	Coauthor		First author	Coauthor
Hugot, JP	1 [22]	2 [35,51]	Daly,MJ	-	5[31,35,47,51,53]
Podolsky, DK	1 [26]	4 [29,30,32,67]	Steinhart,AH	-	5[31,35,46,47,51]
Targan, SR	1 [27]	7 [31,32,35,46,47,51,53]	Griffiths,A	-	4[31,35,47,51]
Hanauer,SB	1 [28]	6 [23,27,32,33,49,58]	Dassopoulos,T	-	2[31,35]
Xavier,RJ	1 [30]	3 [35,47,53]	Bitton,A	-	3[31,35,53]
Duerr,RH	1 [31]	5 [23,35,51,53]	Datta,LW	-	3[31,35,47]
Present,DH	2 [32,65]	3 [27,33,49]	Kistner,EO	-	2[31,35]
Rutgeerts, P	1 [33]	9 [27,28,32,35,43,51,52,56,58]	Rotter,JI	-	5[31,35,47,51,53]
Fiocchi,C	1 [34]	1 [63]	Schumm,LP	-	5[31,35,47,51,52]
Barrett,JC	1 [35]	2 [51,53]	Lee,J	-	2[51,53]
Riddell,RH	1 [36]	2 [46,57]	Lees,CW	-	2[51,53]
Loftus,EV Jr	1 [38]	1 [46]	Sandborn,WJ	-	3[33,56,58]
Franke,A	1 [51]	2 [53,55]	Barmada,MM	-	3[31,35,47]
Silverberg,MS	1 [46]	5 [31,35,47,51,53]	Nicolae,DL	-	4[23,31,35,47]
Rioux,JD	1 [47]	4 [31,35,51,53]	Sands,BE	-	3[32,33,52]
Lichtiger,S	1 [49]	1 [56]	Belaiche,J	-	2[22,35]
Colombel,JF	2 [56,58]	5 [22,28,33,46,51]	Laukens,D	-	3[35,51,53]
Hampe,J	2 [55,64]	-	Lawrance,I	-	2[51,53]
Abraham,C	1 [66]	2 [31,53]	Louis,E	-	3[35,53,51]

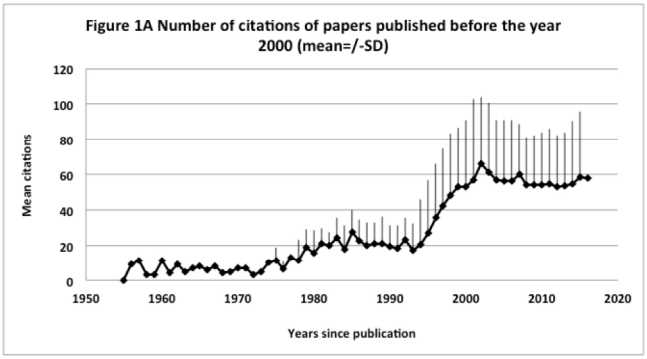
Lennard-Jones,JE	1 [68]	1 [64]	Vos,M	-	3[35,51,53]
Becktel,JM	-	2 [25,50]	Vermeire,S	-	5[35,43,46,51,53]
Singleton,JW	-	2 [25,50]	Satsangi,J	-	4[35,46,51,53]
Kern,F Jr	-	2 [25,50]	Bernstein,CN	-	2[46,52]
Van Deventer,SJ	-	5 [27,32,52,62,64]	Tremelling,M	-	2[35,53]
Mayer,L	-	3 [27,28,32]	Mansfield,J	-	3[35,51,53]
Braakman,T	-	2 [27,32]	Jewell,D	-	2[35,46]
DeWoody,KL	-	2 [27,32]	Mathew,CG	-	5[35,51,53,55,64]
Schaible,TF	-	2 [27,32]	Parkes,M	-	3[35,51,53]
Feagan,BG	-	3 [28,33,52]	Georges,M	-	3[35,51,53]
Lichtenstein,GR	-	2 [28,33]	Karban,A	-	2[46,51]
Schreiber,S	-	8 [28,46,51,53,55,58,64,70]	Gossum,A	-	2[35,51]
Rachmilewitz,D	-	4 [28,33,52,56]	Franchimont,D	-	3[35,51,53]
Wolf,DC	-	2 [28,52]	Newman,W	-	2[51,53]
Olson,A	-	2 [28,33]	Regueiro,M	-	5[31,35,47,51,53]
Taylor,KD	-	5 [31,35,47,51,53]	Kornbluth,A	-	2[49,56]
Bayless,TM	-	2 [23,51]			
Cho,JH	-	7 [23,31,35,47,51,53,66]			

*The table is limited to authors and coauthors of two or more articles regardless to the category of the article.

**Author's name= family name, abbreviations of first or first and second names.

Table 5 Grading the top-cited articles in inflammatory bowel disease according to the Oxford Centre for Evidence-based Medicine – Levels of Evidence.

Level	Characteristics and description	Articles number [References]
1a	Systematic reviews of RCTs (with consistent results from individual studies)	-
1b	Individual RCT (with narrow confidence intervals)	10 [27,28,33,49,50,52,56,58,60,65]
2a	Systematic review of cohort studies (with consistent results from individual studies)	1 [35]
2b	Individual cohort study (including low quality RCT; e.g., <80% follow-up)	3 [32,43,45]
2c	Outcome studies (analysis of large registries)	2 [59,69]
3a	Systemic reviews of case-control studies (with consistent results from individual studies)	11 [26,30,34,38,42,46,48,51,52,56,66]
3b	Individual case-control study	17 [22,23,24,29,31,37,39,41,47,54,55,61,63,64,67,70,71]
4	Case series (studies without control group, including poor quality cohort studies)	5 [25,36,40,44,62]
5	Expert opinion without explicit critical appraisal or based on research evidence.	1 [68]



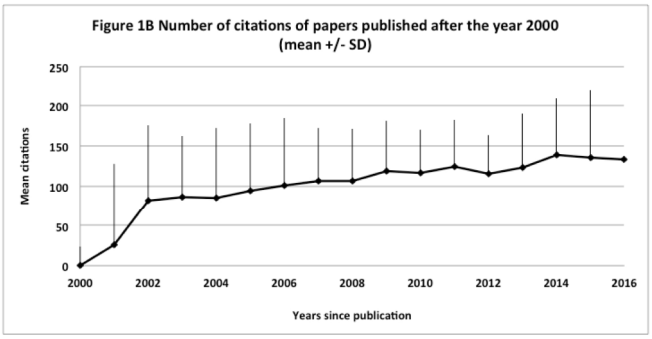


Figure 1A and 1B

209x296mm (300 x 300 DPI)

Appendix 1.

Top-cited articles on inflammatory bowel disease identified by searching the Science Citation Index Expanded database[a]

Rank	Authors, Year [Reference]	Article (*Journal*)	2015-JIF	Category	Number of citations, Web of Knowledge	Average citation per year[b]	Rank of the article in the journal publishing it[c]	Origin: First author's organization, location (country)
1	Hugot et al, 2001[22]	Association of NOD2 leucine-rich repeat variants with susceptibility to Crohn's disease. (*NATURE).*	38.138	Basic research	3,320	221.3	128	Fondation Jean Dausset CEPH (France)
2	Ogura et al, 2001[23]	A frameshift mutation in NOD2 associated with susceptibility to Crohn's disease. (*NATURE*).	38.138	Basic research	3,105	207.0	151	The University of Michigan Medical School, Michigan (United States).
3	Kuhn et al, 1993[24]	Interleukin-10-deficient mice develop chronic enterocolitis. (*CELL*)	28.710	Basic research	2,804	121.9	62	Institute for Genetics, University of Cologne, (Germany)
4	Best et al, 1976[25]	Development of a Crohns-disease activity index-National cooperative Chrons-disease study (*Gastroenterology*).	18.187	Clinical research	2,362	59.0	2	Hines Veterans Administration Cooperative Studies Support Center, University of Colorado Medical Center, Denver, Colorado, (United States).
5	Podolsky, 2002[26]	Inflammatory bowel disease. (*New England Journal of Medicine)*	59.558	Review	2,261	161.5	151	Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts (United States).
6	Targan et al, 1997[27]	A short-term study of chimeric monoclonal antibody cA2 to tumor necrosis factor alpha for Crohn's disease (*New England Journal of*	59.558	Clinical research	2,242	118.0	153	Cedars-Sinai Medical Center, Los Angeles, California (United States)

		Medicine)						
7	Hanauer et al, 2002[28]	Maintenance infliximab for Crohn's disease: the ACCENT I randomized trial (*Lancet*)	44.002	Clinical research	2,126	151.8	47	University of Chicago Medical Center, Chicago, IL (United States).
8	Truelove and Witts, 1955[29]	Cortisone in ulcerative colitis- Final report on a therapeutic trial (*British Medical Journal*).	19.697	Clinical research	1,756	28.8	17	Nuffield Department of Clinical Medicine, Oxford (United Kingdom)
9	Xavier and Podolsky, 2007[30]	Unravelling the pathogenesis of inflammatory bowel disease (*NATURE*)	38.138	Review	1,693	188.1	501	Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts (United States).
10	Duerr et al, 2006[31]	A genome-wide association study identifies IL23R as an inflammatory bowel disease gene. **(***SCIENCE*).	34.661	Clinical research	1,683	168.3	554	Department of Medicine, School of Medicine, University of Pittsburgh, Pittsburgh, PA (United States).
11	Present et al, 1999[32]	Infliximab for treatment of fistulas in patients with Crohn's disease (*New England Journal of Medicine*)	59.558	Clinical research	1,615	95	315	Mount Sinai Medical Center, New York, NY, (United States)
12	Rutgeerts et al, 2005[33]	Infliximab for induction and maintenance therapy for ulcerative colitis (*New England Journal of Medicine*)	59.558	Clinical research	1,506	136.9	318	University Hospital Gasthuisberg, Leuven, (Belgium).
13	Fiocchi, 1998[34]	Inflammatory bowel disease: Etiology and pathogenesis (*Gastroenterology*)	18.187	Review	1,490	82.8	8	University Hospitals of Cleveland Case Western Reserve University School of Medicine, Ohio (United States)

14	Barrett et al, 2008[35]	Genome-wide association defines more than 30 distinct susceptibility loci for Crohn's disease. *(Nature Genetics*)	31.616	Review Meta-analysis	1,440	180	28	Wellcome Trust Centre for Human Genetics, University of Oxford, Roosevelt Drive, Oxford (United Kingdom)
15	Riddell et al, 1983[36]	Dysplasia in inflammatory bowel disease- Standardized classification with provisional clinical applications (*Human Pathology)*	2.791	Article	1,335	40.4	2	National Foundation for Ileitis and Colitis, New York, (United States).
16	Sadlack et al, 1993[37]	Ulcerative colitis-like disease in mice with a disrupted interleukin-2 gene (*CELL*)	28.710	Basic research	1,328	57.7	370	Institute of Virology and Immunobiology, University of Würzburg, (Germany)
17	Loftus, 2004[38]	Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences (*Gastroenterology*)	18.187	Review	1,295	107.9	15	Mayo Clinic, Rochester, Minnesota, (United States)
18	Okayasu et al, 1990[39]	A novel method in the induction of reliable experimental acute and chronic ulcerative-colitis in mice (*Gastroenterology)*	18.187	Basic research	1,266	48.7	19	School of Medicine, Tokyo Medical and Dental University, (Japan).
19	Harvey and Bradshaw, 1980[40]	A simple index of Crohns-disease activity (*Lancet*)	44.002	Clinical research	1,239	34.4	173	Bristol Royal Infirmary and Frenchay Hospital, Bristol (United Kingdom)
20	Frank et al, 2007[41]	Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. (*Proceedings of the National Academy of Sciences of the United States of America*)	9.423	Basic research	1,231	136.8	221	University of Colorado, Boulder, CO (United States)
21	Eaden et al, 2001[42]	The risk of colorectal cancer in ulcerative colitis: a meta-analysis. (*Gut)*.	14.921	Review Meta-analysis	1,178	78.5	1	Leicester General Hospital, Gwendolen Road, Leicester (United Kingdom)

22	Baert et al, 2003[43]	Influence of immunogenicity on the long-term efficacy of infliximab in Crohn's disease. *(New England Journal of Medicine*)	59.558	Clinical research	1,112	85.5	584	University Hospital Gasthuisberg, Leuven, (Belgium).
23	Cooper et al, 1993[44]	Clinicopathologic study of dextran sulfate sodium experimental murine colitis. *(Laboratory Investigation*)	4.202	Basic research	1,088	47.3	4	Hahnemann University, Philadelphia, Pennsylvania. (United States)
24	Ekbom et al, 1990[45]	Ulcerative colitis and colorectal cancer. A population-based study. (*New England Journal of Medicine)*	59.558	Clinical research	1,061	40.8	651	University Hospital, Uppsala, (Sweden).
25	Siliverberg et al, 2005[46]	Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. *(Canadian Journal of Gastroenterology and Hepatology)*	2.307	Report	1,043	94.8	1	Mount Sinai Hospital IBD Centre, University of Tronto, Toronto, Ontario (Canada)
26	Rioux et al, 2007[47]	Genome-wide association study identifies new susceptibility loci for Crohn disease and implicates autophagy in disease pathogenesis. (*Nature Genetics*)	31.616	Basic research	1,042	115.8	90	Université de Montréal and the Montreal Heart Institute, Research Center, Montreal, Quebec (Canada).
27	Bouma and Strober, 2003[48]	The immunological and genetic basis of inflammatory bowel disease. *(Nature Reviews Immunology)*	39.416	Review	1,028	79.1	32	National Institutes of Health, and National Institutes of Allergy and Infectious Diseases, Bethesda, Maryland (United States)

28	Lichtiger et al, 1994[49]	Cyclosporine in severe ulcerative colitis refractory to steroid therapy. *(New England Journal of Medicine*)	59.558	Clinical research	1,026	46.6	714	Mount Sinai School of Medicine, New York (United States).
29	Summers et al, 1979[50]	National Cooperative Crohn's Disease Study: results of drug treatment (*Gastroenterology*)	18.187	Clinical research	1,020	27.6	33	Division of gastroenterology, University of Iowa Medical Center, Iowa City, Virginia, (United States).
30	Frank et al, 2010[51]	Genome-wide meta-analysis increases to 71 the number of confirmed Crohn's disease susceptibility loci. *(Nature Genetics*)	31.616	Review Meta-analysis	1,019	169.8	91	Institute of Clinical Molecular Biology, Christian-Albrechts-University Kiel, Kiel, (Germany).
31	Sands et al, 2004[52]	Infliximab maintenance therapy for fistulizing Crohn's disease. *(New England Journal of Medicine)*	59.558	Clinical research	1,004	83.7	737	Massachusetts General Hospital, and Harvard Medical School, Boston (United States)
32	Jostins et al, 2012[53]	Host-microbe interactions have shaped the genetic architecture of inflammatory bowel disease. (*Nature*)	38.138	Review Meta-analysis	997	249.2	938	Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, (*United Kingdom)*
33	Sokol et al, 2008[54]	Faecalibacterium prausnitzii is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. *Proceedings of the National Academy of Sciences of the United*	9.423	Basic research	994	124.2	318	Institut National de la Recherche Agronomique U910, Domaine de Vilvert, Jouy-en-Josas, (France).

		States of America)						
34	Hampe et al, 2007[55]	A genome-wide association scan of nonsynonymous SNPs identifies a susceptibility variant for Crohn disease in ATG16L1. *(Nature Genetics)*	31.616	Basic research	989	109.9	95	Institute for Clinical Molecular Biology, Christian-Albrechts University Kiel, University Hospital Schleswig-Holstein, (Germany).
35	Colombel et al, 2010[56]	Infliximab, azathioprine, or combination therapy for Crohn's disease (*New England Journal of Medicine*)	59.558	Clinical research	955	159.2	738	Hôpital Claude Huriez and Centre d'Investigation Clinique, Centre Hospitalier Universitaire de Lille, Université Lille Nord de France, Lille, (France).
36	Elson CO et al, 1995[57]	Experimental models of inflammatory bowel disease. (*Gastroenterology*).	18.187	Review	913	43.5	35	Department of Medicine, University of Alabama Hospital at Birmingham, AL, (United States).
37	Colombel et al, 2007[58]	Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: the CHARM trial. (*Gastroenterology*).	18.187	Clinical research	900	100	36	Hôpital Claude Huriez, Centre Hospitalier Universitaire de Lille, Rue Michel Polonovski, Lille, (France)
38	Greenstein et al, 1976[59]	The extra-intestinal complications of Crohn's disease and ulcerative colitis: a study of 700 patients. *Medicine (Baltimore).*	2.133	Review	899	22.5	10	Department of Surgery, Mount Sinai School of Medicine and the City University of New York, New York, (United States.)

39	Schroeder et al, 1987[60]	Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study *(New England Journal of Medicine*)	59.558	Clinical research	897	30.9	775	Mayo Clinic, Rochester, MN (United States)
40	Fujino et al, 2003[61]	Increased expression of interleukin 17 in inflammatory bowel disease. (*Gut*).	14.921	Basic research	850	65.4	13	Shiga University of Medical Science, Seta-Tukinowa, Otsu, (Japan).
41	Vandullemen et al, 1995[62]	Treatment of Crohn's disease with anti-tumor necrosis factor chimeric monoclonal antibody (cA2). **(***Gastroenterology*).	18.187	Clinical research	845	40.2	44	Academic Medical Center, Amsterdam, (The Netherlands).
42	Fuss et al 1996[63]	Disparate CD4+ lamina propria (LP) lymphokine secretion profiles in inflammatory bowel disease. Crohn's disease LP cells manifest increased secretion of IFN-gamma, whereas ulcerative colitis LP cells manifest increased secretion of IL-5. *(Journal of Immunology*)	4.985	Basic research	842	42.1	69	National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, (United States)
43	Hampe et al, 2001[64]	Association between insertion mutation in NOD2 gene and Crohn's disease in German and British populations. **(***Lancet)*.	44.002	Clinical research	835	55.7	444	Christian-Albrechts-University, Kiel, (Germany).
44	Present et al, 1980[65]	Treatment of Crohn's disease with 6-mercaptopurine. A long-term, randomized, double-blind study. *(New England Journal of Medicine)*	59.558	Clinical research	834	23.2	1054	Lenox Hill Hospital and the Mount Sinai School of Medicine of City University of New York (United States)

45	Abraham et al, 2009[66]	Inflammatory bowel disease. *(New England Journal of Medicine)*	59.558	Review	817	116.7	1099	Yale University School of Medicine, New Haven, CT (United States)
46	Cario and Podolsky, 2000[67]	Differential alteration in intestinal epithelial cell expression of toll-like receptor 3 (TLR3) and TLR4 in inflammatory bowel disease. *(Infection and Immunity*)	3.603	Basic research	814	50.9	6	Massachusetts General Hospital, and Harvard Medical School, Center for the Study of Inflammatory Bowel Disease, Boston, Massachusetts (United States)
47	Lennard-Jones, 1989[68]	Classification of inflammatory bowel disease. *(Scandinavian Journal of Gastroenterology)*	2.199	Article	814	30.1	2	St Mark's Hospital, London, (United Kingdom)
48	Molodecky et al, 2012[69]	Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. (*Gastroenterology*).	18.187	Review	809	202.2	45	University of Calgary, Calgary, Alberta, (Canada).
49	Swidsinski et al, 2002[70]	Mucosal flora in inflammatory bowel disease. (*Gastroenterology*).	18.187	Basic research	806	57.6	49	Charité Humboldt Universität, Berlin, (Germany).
50	Powrie et al, 1994[71]	Inhibition of Th1 responses prevents inflammatory bowel disease in scid mice reconstituted with CD45RBhi CD4+ T cells. (*Immunity*).	24.082	Basic research	804	36.5	41	DNAX Research Institute of Molecular and Cellular Biology Incorporated, Palo Alto, California (United States).

[a] The search was conducted in November 2016 by searching the Web of Knowledge (1900 to 2016).
[b]Because the article by Cario and Podolsky (2000) and the article by Lennard-Jones (1989) had the same absolute number of citations, the paper with higher average citation per year was ranked higher. The average citation per year for Cario and Podolsky was 50.9 (ranked 46) and the paper by Lennard-Jones had an average citation per year of 30.1 (ranked 47).
[c]This ranking was identified by searching each journal for a top-cited article and identifying its ranking based on the number of citations received in comparison to the number of citations received by other articles published in that journal.

BMJ Open

What can we learn from top-cited articles in inflammatory bowel disease? A bibliometric analysis and assessment of the level of evidence

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-021233.R1
Article Type:	Research
Date Submitted by the Author:	01-May-2018
Complete List of Authors:	Azer, Samy; King Saud University, Medical Education; Australian Professional Teaching, Azer, Sarah; St Vincent Hospital
Primary Subject Heading:	Gastroenterology and hepatology
Secondary Subject Heading:	Gastroenterology and hepatology, Medical education and training, Medical publishing and peer review
Keywords:	Inflammatory bowel disease (IBD), Ulcerative colitis (UC), Crohn's disease (CD), Bibliometric analysis, Top-cited articles, Quality of evidence

Amended version

What can we learn from top-cited articles in inflammatory bowel disease? A bibliometric analysis and assessment of the level of evidence

Samy A. Azer[1] and Sarah Azer[2]

Dr Azer is a Consultant Gastroenterologist and Professor of Medical Education and the chair of Curriculum Development and Research Unit, College of Medicine, King Saud University, Riyadh, Saudi Arabia[1]

Registrar, St Vincent Hospital, University of Melbourne, Victoria, Australia[2]

Correspondence and requests for reprints should be addressed to:
Professor Samy Azer
Curriculum Development and Research Unit,
College of Medicine, King Saud University
P O Box 2925, Riyadh 11461
Saudi Arabia
Telephone: (966) 11-4699178
Fax: (966) 11-4699174

Email:azer2000@optusnet.com.au

SHORT TITLE: Top-cited Inflammatory Bowel Disease

ABSTRACT

Background and Objectives: Despite increasing number of publications in inflammatory bowel disease (IBD) no bibliometric analysis has been conducted to evaluate the significance of highly-cited articles. Our objectives were to identify the top-cited articles in IBD, assessing their characteristics, and determining the quality of evidence provided by these articles.

Design and outcome measures: IBD and related terms were used in searching the Web of Science to identify English language articles. The 50 top-cited articles were analyzed by year, journal impact factor (JIF), authorship, females in authorship, institute, country, and grants received. The level of evidence was determined using the Oxford Centre for Evidence-Based Medicine guidelines.

Results: The number of citations varied from 871 to 3555 with a total of 74638, and a median 1339.50, (IQR= 587). No correlations were found between the number of citations and number of years since publication (r=0.042, p=0.771), JIF (r= 0.186, p=0.196), number of authors (r= 0.061, p=0.674), females in authorship (r=0.064, p=0.661), number of institutes (r= 0.076, p=0.602), number of countries (r= 0.101, p=0.483), or number of grants (r= - 0.015, p=0.915). The first authors were from the United States (n= 24), United Kingdom (n= 6), Germany (n=5), France (n=5), Belgium (n=3), and Canada (n=3). The levels of evidence were 12 articles at level 1b, 9 articles at level 3a, and 15 articles at level 3b and fewer were at other levels.

Conclusions: Research papers represented 66% of articles. The majority of items have reasonably high levels of evidence; which may have contributed to the higher number of citations. The study also shows a gender gap in authorship in this area.

Key words

Inflammatory bowel disease (IBD), Ulcerative colitis (UC), Crohn's disease (CD), Top-cited articles, Bibliometric analysis, Quality of evidence, Number of authors, Female authors, Grants/funds, Institutes, Countries.

Strengths and limitations of the study

- More than one method was used in searching the Web of Science to maximize the yield of the search.
- The articles represent a historic perspective on key discoveries in the area of inflammatory bowel disease.
- A number of characteristics including journal impact factor, number of authors, number of females in authorship, number of institutes, number of countries involved, and grants received have been studied against citations received.
- The level of evidence for each article has been evaluated.
- The search was limited to articles in the English language, raising the possibility of failing to include top-cited articles in other languages.

INTRODUCTION

The number of citations received by an article has been used for several years by universities and grant funding bodies in assessing the quality of research produced by researchers, ranking research performance and in making decisions regarding professional promotion and grant applications [1-4]. Thomson Reuters gather the names of these authors in the Highly Cited Researchers database where they are acknowledged for the quality of their work and the size of their research input in a particular area [5]. Although the number of citations cannot explain why researchers cited a particular paper nor reflect the quality of the research and the outcomes identified in a manuscript, the number of citations and the reputation of contribution to research in a particular field cannot be ignored. This is particularly important when there is a pattern of consistency and progressive input into a discipline over years (a life experience), and a demonstration from publication records and citation history of collaboration with other researchers from other institutes at local and international levels. Hence the credits given to an author or a group of authors and the impact of the work in a particular area can be proportionally related to the citation records [6]. The greater the citation history over years, the more influential they are in their specialty [7]. In this study, we hypothesized that examining the most cited in IBD may provide more insight into the significance of these articles and the level of evidence they present [8]. Considering the fact that there are over 91,000 articles on IBD in the literature as per our preliminary search of Web of Science, it is important to consider the characteristics of highly cited articles.

Inflammatory bowel disease comprises ulcerative colitis (UC) and Crohn's disease (CD); both pursue a relapsing and remitting course over years. While the two diseases share several similarities, they have a number of differences with regard to structures involved, pathogenesis, clinical presentation, and management approaches. UC was first reported briefly in mid 1800 [9], while CD was reported in *the Journal of the American Medical Association (JAMA)* later by Crohn, Ginzburg and Oppenheimer in 1932 [10]; describing it as a chronic inflammatory bowel disease of the ileum. Later, it was discovered that CD can involve any part of the gastrointestinal tract from the lips to the anal margin but the ileocolonic disease represents the common presentation. Since then both diseases have been extensively researched in their different aspects.

We assumed that these articles may be a cornerstone in IBD, and may enable researchers in understanding a range of aspects related to IBD. Therefore, the bibliometric analysis of these articles including journal impact factor, authorship, females in authorship, institute, country and grants received may explain key features of a successful or influential article in IBD. The aims of the present research were (1) identify the top-cited articles in IBD, and analyze their characteristics and (2) assess the quality of evidence provided by articles.

METHODS

Study Design

The Web of Science database was searched for the identification of the top-cited articles and tracking the citation records of each publication. Although Scopus and

Google Scholar also provide citation records, it was decided to limit the search to Web of Science database. Compared to other databases, the Web of Science is regularly updated and the 2015 Journal Citation Reports (JCRs) included more than 6,500 journals across 150 disciplines. Although Google Scholar database is freely available, it was not used because it is difficult to search, and it cites textbooks, monographs, conference proceedings, as well as non-peer reviewed publications [11]. It is also not possible to track the yearly records of citations attracted by each article since publication. Scopus database was not used because it is not extensive in its coverage and its records only go back to 1996 [12]. Furthermore, several other researchers have used Web of Science to identify top-cited articles [13,14,15]

To achieve the aims of this study we planned to identify the highly cited articles in IBD and assess if there were any correlation between the number of citations and any of the parameters characterizing these highly cited articles. We also aim to grade each article against the level of evidence hierarchy as per the Oxford Centre for Evidence-Based Medicine (OCEBM-2011 Levels of Evidence and the accompanying Table of Evidence Glossary) [16,17].

Searching the Web of Science database

On 15 and 16 April 2018,the authors searched the Web of Science database to retrieve top-cited articles in inflammatory bowel disease. The search words used were the following: “Inflammatory bowel disease”, “Ulcerative colitis”, “Crohn’s disease”, ‘IBD”, “Experimental colitis”, “Animal models for Colitis”, “Animal models for inflammatory bowel disease”, “Pathology IBD”, “Pathology UC”, Pathology CD”,

"Pathogenesis IBD", "Pathogenesis UC", "Pathogenesis CD", "Treatment IBD", "Treatment UC", "Treatment CD", "Investigation IBD" and "Regional ileitis". To increase the yield of the search, we used the full terms- inflammatory bowel disease, ulcerative colitis, and Crohn's disease for the abbreviations IBD, UC, and CD, respectively. These search words were identified from the terminology used in gastroenterology journals and the proceedings of major conferences on inflammatory bowel disease and gastroenterology such as the British Society of Gastroenterology (BSG), the American Gastroenterological Association (AGA), American College of Gastroenterology (ACG), Canadian Association of Gastroenterology (CAG), Scottish Society of Gastroenterology (SSG), and Gastroenterological Society of Australia (GESA). For each search word, the results were arranged using a link on the Web of Science system, "sort-by" – "Time Cited- highest to lowest". The results showed the articles organized in a descending order with the articles most frequently cited at the top. A copy of the results was printed out for further analysis. The findings from each search word were then arranged on one Excel sheet (Microsoft Excel 2010, Microsoft Corp, Redmond, WA) in descending order based on the number of citations. Duplicate articles and articles not in the English language were excluded. In addition to the absolute number of citations, we calculated the average citations per year for each article. The average number of citations per year is the ratio calculated from the number of citations obtained by an article divided by the number of years since publication [18].

Using the above mentioned search words, we conducted another search of major gastroenterology journals and the 2016-JCR under the category "Gastroenterology

and Hepatology". This category comprises 76 journals at the time of conducting the search; of these seven journals were in languages other than English and were not searched. Gastroenterology journals publishing articles not in the English language were excluded because neither the author nor the assistant researchers are competent in the Spanish, Italian or German languages. Since the language recommended by the journal publishing this work is English and its readers are most likely interested in research publications in the English language, we decided not to search these journals.

Interestingly, after identifying the list of top-cited articles in IBD, and again checking these seven non-English journals, none had a paper with a citation higher than the paper ranked number 50 on the list.

These key words were also used in searching the websites of major general medicine, surgery and research journals including the *New England Journal of Medicine, Lancet, the British Medical Journal, the Journal of the American Medical Association, Annals of Internal Medicine, Archives of Medicine, PLOS Medicine, Annals of Surgery, Archives of Surgery, British Journal of Surgery, American Journal of Surgical Pathology, Nature, Science, Nature Reviews Cancer, Nature Genetics, Nature Medicine, Cell, Nature Reviews Microbiology, Immunity, Nature Reviews Immunology, Nature Reviews Molecular Cell Biology, and Journal of Immunology.*

A list identifying the 50 top-cited articles was reviewed again and checked regarding authorship, year of publication, title of the article, journal publishing the work, the Journal Impact Factor (JIF) at the time of the search, the number of citations and the institution of the first author (Appendix 1).

==========Add Appendix 1 ==========

Inclusion And Exclusion Criteria

The inclusion criteria were: papers focusing on IBD (ulcerative colitis or Crohn's disease) written in the English language. The exclusion criteria were: (i) articles on inflammatory bowel disease in languages other than English, (ii) articles that focused on other diseases and inflammatory bowel disease was not the main focus, and (iii) studies that focus on other types of colitis and not inflammatory bowel disease.

Assessing Articles

The full text of the identified 50-top cited articles was obtained and a copy was given to each researcher. The following information was collected for each article: (i) the authors' names, the number of authors, their affiliations, and the number of females contributing to authorship, (ii) the number of institutes involved in the publication, (iii) the city and country of the origin of the publication, (iv) the total number of citations obtained up to the day of searching the database, and the number of yearly citations since publication, (v) the year of publication and the calculated number of years since publication, and (vi) the number of funds/grants stated in the publication and the Web of Science.

We have not used the classification provided by the Web of Science regarding study type because we noted that the Web of Science groups publications as original research, articles, practical guides and reviews and identifies them as articles or reviews. For consistency and the purpose of this study, the top-cited articles were grouped into four types - article, review paper/meta-analysis, report, and research. A

definition of each type is given in the glossary. Two researchers independently allocated each of the top-cited articles under its type as per the definition given. Any differences between the researchers were discussed in a meeting until a decision was reached.

The topics covered by the top-cited articles were identified by each researcher independently and were discussed in a meeting to harmonize the grouping into a logical, simple and practical way. Articles that covered more than one topic were classified on the basis of the aim of the study and the main outcomes. For other evaluations of an article including the number of authors, the number of females represented in authorship, the number of institutes, and countries contributing to the work, and the number of grants/funds received we checked the original article for such details. Institute was defined as the university where an author belonged. If an author belonged to two universities, this was considered to be two different institutes. Regarding the identification of females in the authorship we noted that several journals use abbreviations of the first and second name rather than the full name. In order to identify the females in these articles we tried to search the Google database to find the university, personal website of the author, their LinkedIn or ResearchGate accounts. We also tried to identify them by searching the Google Scholar database and identify their account, where we can find other publications under their name and the full first name. In two papers, despite our efforts, we failed to identify the gender of five authors and we contacted the corresponding authors. We received a response from one correspondence, making us unable to identify the gender of three authors in the second paper.

Evaluating the Journals

The publishing journals of the top 50 articles in IBD were identified and evaluated in regard to the following: (i) the 2016-Journal Impact Factor (JIF) of each journal, and (ii) the ranking order of each article in comparison to other articles published in that journal. This was based on the number of citations obtained in comparison to the citation numbers received by other articles published in the journal. For example, an article ranked number one, in its publishing journal, means that the article received the highest number of citations in comparison to all other articles published in that journal. This evaluation aimed at assessing the position order of articles identified among the 50 top-cited articles in IBD in regard to their ranking among other articles published in the journal. Such assessment highlights the significance of the inflammatory bowel disease articles among other topics published in gastroenterological journals as well as general medicine journals such as *The New England Journal of Medicine, The Lancet, the British Medical Journal, Medicine,* and top research journals such as *Nature, Nature Genetics, Science, Cell,* and top journals in immunology *such as Nature Reviews Immunology* (Appendix 1).

Assessing Level of Evidence

Two researchers independently used the Oxford Centre for Evidence-Based Medicine (OCEBM-2011 Levels of Evidence and the accompanying Table of Evidence Glossary) [16,17] to rank each article regarding level of evidence. In 1998 this hierarchical of evidence was first produced to make the process of finding relevant evidence feasible. Since then the levels have been reviewed and amended, and the

version used in this research is the currently available version. This evaluation aimed at identifying the level of evidence of each article and assessing whether the highly cited articles have received higher scores in regard to level of evidence as per the Oxford hierarchy. The assessment required extensive review of each article since quality descriptors exist for different types of studies and level of evidence vary depending on therapeutic, prevention, prognostic, diagnostic, or prevalence design [13,14].

Statistical Analysis

Pearson's correlation coefficient (r) was calculated to determine if the high citation numbers obtained was related to the age of the article. Other correlations were between the number of citations and the number of authors, the percentage of females in authorship, the number of institutes, the number of countries involved, the number of grants received, and the Journal Impact Factor (JIF) of the journals in which articles were published. Because of the assumption that researchers usually cite recently published articles, it was decided to compare the mean yearly citations received of articles published before the year 2000 and compare them with those published after the year 2000. All analyses were conducted using SPSS Software (IBM SPSS Statistics Premium version 22.0 for Mac OS-SPSS Inc., Chicago, IL, USA) and the results were reported at total, mean, median, IQR, and percentage. The inter-rater agreement between evaluators was calculated using the Fleiss kappa scale [19].

Patient and Public involvement

This study did not involve patients or the public.

RESULTS

Top-Cited Papers Identified

Appendix 1 summarizes the top-cited articles in IBD identified by searching the Web of Science [20-69]. The articles are listed in a descending order from 1 to 50 with the highest absolute citation number is ranked 1 and the article with the lowest citation ranked 50 as per the day of the search.

Table 1 summarizes the year of publication and article type. The articles were published over 57 years (from 1955 to 2012). During the period from 1955 to 1976, only 3 articles (6%) were published. However, the number increased significantly from 1977 to 1994 making a total of 12 (24%) articles. The number of publications increased significantly to 35 (70%) during the years from1995 to 2012. No correlation was found between the number of citations of these papers and the number of years since published (Pearson correlation (r) = 0.042, p = 0.771). To assess if there were differences between old articles (published before the year 2000) and those published after the year 2000, it was decided to study the mean number of citations received by top-cited articles in each year after their publications. The year 2000 was taken as a midpoint for comparison because the majority of articles identified were published in the period after the year 1986, and hence the year 2000 could represent such point. As shown from Figures 1A and 1B, the mean numbers of citations were higher for articles published after the year 2000 compared to those published before

the year 2000. Approximately one fourth of the top-cited papers were reviews/meta-analysis (n= 14, 28%), two-thirds were research papers (n= 33, 66%), and the remaining were an article (n= 1, 2%) and two reports (n=2, 4%).

==========Please Add Table 1 here ========

Table 2 summarizes the distribution of IBD topics covered in the top-cited articles. These can be summarized as follows: epidemiology and prevalence (n=2, 4%), Crohn's disease genetic susceptibility and NOD2 mutation (n=6, 12%), Animal models (n= 5, 10%), Pathogenesis of IBD (n= 15, 30%), classification and index of disease activity (n= 5, 10%), risk of developing colorectal cancer (n= 2, 4%), extra-intestinal complications (n= 1, 2%), Infliximab in Crohn's disease (n= 6, 12%), corticosteroids in ulcerative colitis (n=1, 2%), drug treatment and cyclosporine in ulcerative colitis (n= 2, 4%), adalimumab in Crohn's disease (n=1, 2%), 5-aminosalicylic acid in ulcerative colitis (n=1, 2%), 6-mercaptopurine in Crohn's disease (n=1, 2%), and monoclonal antibiotics, and anti-tumour necrosis factor in Crohn's disease (n=2, 4%). As shown in Appendix 1, 14 (28%) were basic research and 19 (38%) were clinical research. The level of evidence is discussed later in the results.

======Please Add Table 2 here ==========

The articles were published in the following journals: *New England Journal of Medicine* (n= 12, 24%), *Gastroenterology* (n= 12, 24%), *Nature* (n=4, 8%), *Nature Genetics* (n=4, 8%), *The Lancet* (n= 2, 4%), *Proceedings of the National Academic of*

Sciences of the United States of America (n=2, 4%), *Cell* (n= 2, 4%), and *Gut* (n= 4, 8%). See Table 3 for more details about the journals publishing these articles.

======Please Add Table 3 here ==========

Looking at the ranking of the top-cited articles in IBD in the journals they were published in could provide a better picture about the influence of these articles. This influence would be clearly demonstrated when the journal has a relatively higher Journal Impact Factor. The ranking is based on the number of citations received by an article compared to the number of citations received by other articles that were published in that journal. The article by Best et al (1976) [23] is ranked number 4 in the list, and also ranked number 2 among all articles published in *Gastroenterology* (2016-JIF = 18.392). The article by Eaden et al [41] is ranked number 22 in the list and also ranked number 1 among all articles published in *Gut* (2016-JIF= 16.658). The ranking of other articles in List and their rankings in the journals in which they were published are shown in Appendix 1.

The first authors of the top-cited articles were from the United States (n= 24, 48%), the United Kingdom (n=6, 12%), Germany (n= 5, 10%), France (n= 5, 10%), Belgium (n= 3, 6%), Canada (n= 3, 6%), Japan (n=2, 4%), Sweden (n=1, 2%), and the Netherlands (n=1, 2%).

Table 4 summarises the 70 authors who have published two papers or more in the top-cited IBD. Of these 18 authors were the first author and coauthors of more than two papers in total, all the remaining, 52 were coauthors of more than two papers.

Top authors were Rutgeers, P (n=10 papers), Targan, SR (n=8 papers), Schreiber, S (n=7 papers), Cho, JH (n=7 papers), Colombel, JF (n=7 papers), Hanauer, SB (n=7 papers), Silverberg, MS (n=6 papers), and each of the following authors have 5 papers: Podolsky, DK, Rioux, JD, Daly MJ, Steinhart, AH, Rotter, JI, Schumm, LP, Taylor, KD, Vermeire, S, Duerr, RH, and Regueiro, M**.**

======Please Add Table 4 here ==========

The leadership of universities and institutes that have contributed to the creation of these publications were Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, the United States, Mount Sinai School of Medicine, New York, the United States, Mayo Clinic, Rochester, Minnesota, the United States, Cedars-Sinai Medical Center, Los Angeles, California, the United States, University of Chicago Medical Center, Chicago, Illinois, the United States, University of Pittsburgh, Pittsburgh, Pennsylvania, the United States, University Hospital of Cleveland Case Western Reserve University School of Medicine, Ohio, the United States, Wellcome Trust Centre for Human Genetics, University of Oxford, Roosevelt Drive, Oxford, the United Kingdom, Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Cambridge, the United Kingdom, and Institute of Virology and Immunobiology, University of Würzburg, Germany. See Appendix 1 for more detail.

Characteristics of the Top-Cited Articles

These articles were created by 667 authors, median 7.0, minimum 1, maximum 106, IQR 9.5; the females in authorship were 111, median 1.0, minimum 0, maximum 20, IQR 2. It is worth mentioning here that it was difficult to identify the gender of some

authors in two papers because the full first and middle names were not shown and it was difficult to find more information or clues to make a decision. We contacted the corresponding authors of these two articles; we received information for one article but we had no response from the corresponding author of the second article. Thus the gender of three authors could not be identified. The number of institutes involved were 436, median 3.0, minimum 1, maximum 88, IQR 9; the countries involved were 141, median 1.0, minimum 1, maximum 16, IQR 2.75; and the number of grants/funds were 328, median 1.0, minimum 0, maximum 94, IQR 2.75. No correlations were found between the number of citations and the Journal Impact Factor (JIF) (Pearson correlation (r) = 0.186; p=0.196), the number of authors (r =0.061; p= 0.674), number of females in authorship (r =0.064; p= 0.661), the number of institutes involved (r =0.076; p= 0.602), the number of countries involved (r =0.101; p= 0.483), and the number of grants received (r= - 0.015; p=0.915).

Level of Evidence

Table 5 summarizes the grading of articles according to the Oxford Center for evidence-based medicine. The table shows that most articles were graded at levels 1b and 3a and 3b evidence (12 papers had level 1b evidence, 9 papers at level 3a, and 15 papers had level 3b evidence). Five articles had a level of evidence of 4 and no article at level 5. The remaining articles were at levels 1a, 2a, 2b and 2c. The overall agreement between the evaluators was acceptable; Fleiss kappa= 0.8252; 95% CI 0.79-0.85.

======Please Add Table 5 here ==========

DISCUSSION

This study aimed at identifying the characteristics of the top 50 most frequently cited papers in IBD and assessing the quality of evidence provided. The papers covered a number of key topics related to IBD including: epidemiology and prevalence, pathogenesis and genetic susceptibility, animal models, clinical classification and indices of disease activity, risks of developing colorectal cancer, extra-intestinal complications, and use of infliximab, adalimumab, monoclonal antibodies and anti-tumour necrosis factor, and 6- mercaptopurine in CD, and use of 5-aminosalicylic acid, corticosteroids, and cyclosporine in treating UC. While these topics cover key issues related to IBD, topics related to molecular biology, surgical management, patient education, nutritional aspects, radiological and other investigations were not represented in the top-cited articles list [70,71].

The assessment of the characteristics of the top 50 highly cited articles identified in this study reveals the following:

First, the lack of correlations between the number of citations and the number of years since publication may indicate that the high-citations is not caused by ageing of these articles. In fact, only 15 articles (30%) were published in the period from 1955 to 1994 (39 years), while the majority, 35 (70%) were published in the last 17 years. No papers were published after 2012. This article also shows that the mean number of citations of articles published before the year 2000 were much lower than those of

articles after the year 2000. This may be related to the tendency of researchers to cite recently published research and new findings [72] and papers that they have read [18]. Also the number of citations and the papers' age might be attributed to the changes in citation behaviour over time. For example, in the 50s and 60s, the authors used to cite fewer papers compared to what was practiced over the last 20 years [73]. The higher citations have been found to be the strongest predictor of current online availability after a long time since publication. Therefore, the higher citation could be a protective mechanism for continued availability of a publication despite aging and hence continuing citation [74].

Second, the lack of a correlation between the number of citations and the Journal Impact Factor (JIF). The JIF has been widely used in ranking and evaluating journals. It stands as a proxy for the relative importance of a journal with its field [75]. Although the top-cited articles identified were published in journals with high impact factors, the impact factors of some journals were not necessarily the highest in their fields. For example, *Laboratory Investigation, Canadian Journal of Gastroenterology and Hepatology, Medicine (Baltimore), and Journal of Immunology* had JIFs in the range of 1.804 to 4.857. With this information in mind one may postulate that the high JIF is not necessarily related to the higher citation numbers received. Two recent works showed that the JIF is not an accurate indicator of citations an average article receives, articles published in low impact factor journals can still be highly cited and vice versa [76,77].

Third, the study showed negative correlation between the number of citations and the number of authors, the number of female authors, or the number of institutes. The

number of authors and females in authorship varied from one to 106 and from zero to 20, respectively. Also the number of institutes involved varied from one to 88. The question that can be raised in this regards; are we expecting an increase in number of citations as the number of authors or the number institutes involved increased? The work of Garcia-Aroca et al [78] shows that collaboration between authors increases their impact and increases citation rates. However, they showed that publishing in English in certain journals and collaborating with certain authors and institutes increase the visibility of the manuscripts published on the subject. Hence it is the quality of collaboration rather than the absolute number of these parameters. Recently Tanner-Smith and Polanin showed that studies conducted by more established authors (have higher h-indices) and reported in more prestigious journal outlets are more likely to be cited by other scholars, even after controlling for various proxies of study quality [79].

Although the proportion of women in authorship of original research in the United States in general has significantly increased in the last four decades, women still compose a minority of the authors of original research [80]. In the field of gastroenterology, the percentage of the United States female physician authors of original research in the field has relatively increased over time, yet the senior author position remains lower than expected [81,82].

Fourth, the study showed no correlation between the number of citations and the number of funds/grants received. This finding is not surprising. Recently it was shown that too many of the United States authors of most influential papers in science do not receive NH funding [83]. Another group of researchers found no association between

grant percentile ranking and grant outcome as assessed by number of top-10% articles per dollar million spent [84].

The United States, the United Kingdom, Germany, France, Belgium, and Canada contributed to the majority of these articles. The leadership of universities from these countries in gastrointestinal research particularly IBD is no surprise, top universities identified from this study were Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, the United States, Mount Sinai School of Medicine, New York, the United States, Mayo Clinic, Rochester, Minnesota, the United States, Cedars-Sinai Medical Center, Los Angeles, California, the United States, University of Chicago Medical Center, Chicago, Illinois, the United States. Other institutes and research centres that had lead these studies are shown in Appendix 1.

All articles were published in the English language. The most productive journals were the *New England Journal of Medicine*, and *Gastroenterology* with a total of 24 articles. Others were *Nature, Nature Genetics, the Lancet, and Proceedings of the National Academy of Sciences of the United States of America, Cell, Gut, British Medical Journal, Science*, and *Nature Reviews Immunology* making a total of 20 articles. While these journals have a relatively high JIF, other journals published one article each and had a relatively low JIF compared to journals included in their categories. For example*, Human Pathology* listed number 22 under the category of Pathology, and *Canadian Journal of Gastroenterology and Hepatology*, listed number 74 under the category Gastroenterology and Hepatology. The high level of evidence as outlined in the top-cited articles could be an important contributing factor to the higher number of citations received by these articles [85].

After the submission of our study we came across the study by Connelly et al [86] on top 100 articles on IBD. While they indicated that their findings covered the period between 1955-2012 which is consistent with our findings, our study has examined a range of parameters including correlation of citation numbers with JIF, number of years since publication, number of authors, females in authorship, institutes, and number of countries and grants, which were not addressed by Connelly's work. Also we have examined the level of evidence of highly cited articles.

CONCLUSIONS

Our list of top-cited articles in IBD highlights key contributions that based the foundation of research and examination of different aspects of the disease over 57 years. This scholarly contribution came from universities and research centres in the United States, the United Kingdom, Germany, France, Belgium and Canada. The findings may be consistent with the concept that it is not the absolute number of collaborators that makes an impact on the citation number or the influence of a publication but rather the quality of such collaboration with regard to the researchers involved, their institutes, and the ongoing contribution to the advances of research. The relatively small number of females in the authorship reflects the gender gap and the fact that women still compose a minority of the authors of original research and reviews in gastroenterology. The higher level of evidence demonstrated in most top-cited articles may have contributed to the higher number of citations received by these articles.

Acknowledgement: The author would like to thank Diana Sanad for her assistance and reviewing the manuscript.

Funding support: This work was funded by the College of Medicine, Research Center Deanship of Scientific Research, King Saud University, Riyadh, Saudi Arabia.

Ethical approval: Not applicable to this study.

Contributors SAA and SA shared equally the different roles and responsibilities to complete the submitted article including, the research idea, the search of databases, the evaluation of data collected, the statistical analysis, the interpretation of findings, the creation of tables and figures, writing the manuscript and the approved the final version of the manuscript.

Competing interests: Both authors (SAA and SA) declare that they have no competing interests and have completed the International Committee of Medical Journal Editors (ICMJE) form

Provenance and peer review: Not commissioned; externally peer reviewed

Data sharing statement: No further data available to share

REFERENCES

1. MacMaster FP, Swansburg R, Rittenbach K. Academic Productivity in Psychiatry: Benchmarks for the H-Index. Acad Psychiatry. 2017 Apr 18. [Epub ahead of print]

2. Susarla HK, Dhar V, Karimbux NY, Tinanoff N. Do Standard Bibliometric Measures Correlate with Academic Rank of Full-Time Pediatric Dentistry Faculty Members? J Dent Educ. 2017 Apr;81(4):427-432.

3. Milone MT, Bernstein J. On Track to Professorship? A Bibliometric Analysis of Early Scholarly Output. Am J Orthop (Belle Mead NJ). 2016 Mar-Apr;45(3):E119-23.

4. Azer SA, Holen A, Wilson I, Skokauskas N. Impact factor of medical education journals and recently developed indices: Can any of them support academic promotion criteria? J Postgrad Med. 2016 Jan-Mar;62(1):32-39. doi: 10.4103/0022-3859.173202.

5. Jones AW. Impact of JAT publications 1981-2003: the most prolific authors and the most highlycited articles. J Anal Toxicol. 2004 Oct;28(7):541-545.

6. Patsopoulos NA, Ioannidis JP, Analatos AA. Origin and funding of the most frequently cited papers in medicine: database analysis. BMJ 2006;332:1061–1064.

7. Garfield E. Fortnightly review: how can impact factors be improved? BMJ 1996;313:411–413.

8. Azer SA. Exploring the Top-Cited and Most Influential Articles in Medical Education. J Contin Educ Health Prof. 2016 Summer;36 Suppl 1:S32-41.

9. Wilks S. Morbid appearances in the in- testines of Miss Bankes. Med Times Gazette 1859;2:264-265.

10. Crohn BB, Ginzburg L, Oppenheimer GD. Regional ileitis: a pathologic and clinical entity. JAMA 1932;99:1323-1329.

11. Van Noorden R, Maher B, Nuzzo R. The top 100 papers. Nature. 2014;514(7524):550.

12. Kulkarni AV, Aziz B, Shams I, Busse JW. Comparisons of citations in Web of Science, Scopus, and Google Scholar for articles published in general medical journals. JAMA. 2009 Sep 9;302(10):1092-1096.

13. Powell AGMT, Bevan V, Brown C, Lewis WG. Altmetric Versus Bibliometric Perspective Regarding Publication Impact and Force. World J Surg. 2018 Mar 13.

14. Yi F, Ma J, Ni W, Chang R, Liu W, Han X, Pan D, Liu X, Qiu J. The top cited articles on glioma stem cells in Web of Science. Neural Regen Res. 2013 May 25;8(15):1431-8. doi: 10.3969/j.issn.1673-5374.2013.15.011.

15. Mu Y, Li N, Guan L, Wang C, Shang S, Wang Y. Therapies for children with cerebral palsy: A Web of Science-based literature analysis. Neural Regen Res. 2012 Nov 25;7(33):2632-9. doi: 10.3969/j.issn.1673-5374.2012.33.009.

16. Azer SA. Top-Cited Articles in Problem-Based Learning: A Bibliometric Analysis and Quality of Evidence Assessment. J Dent Educ. 2017 Apr;81(4):458-478.

17. Oxford Centre for Evidence-based Medicine – Levels of Evidence (March 2009). Available at: http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009 [Accessed 20 May 2017].

18. Azer SA. The top-cited articles in medical education: a bibliometric analysis. Acad Med 2015;90(8):1147-1161.

19. D'Antiga L, Betalli P, De Angelis P, et al. Interobserver agreement on endoscopic classification of oesophageal varices in children. J Pediatr Gastroenterol Nutr 2015;61(2):176-181.

20. Hugot JP, Chamaillard M, Zouali H, Lesage S, Cézard JP, Belaiche J, Almer S, Tysk C, O'Morain CA, Gassull M, Binder V, Finkel Y, Cortot A, Modigliani R, Laurent-Puig P, Gower-Rousseau C, Macry J, Colombel JF, Sahbatou M, Thomas G. Association of NOD2 leucine-rich repeat variants with susceptibility to Crohn's disease. Nature. 2001 May 31;411(6837):599-603.

21. Ogura Y, Bonen DK, Inohara N, Nicolae DL, Chen FF, Ramos R, Britton H, Moran T, Karaliuskas R, Duerr RH, Achkar JP, Brant SR, Bayless TM, Kirschner BS, Hanauer SB, Nuñez G, Cho JH. A frameshift mutation in NOD2 associated with susceptibility to Crohn's disease. Nature. 2001 May 31;411(6837):603-6.

22. Kühn R, Löhler J, Rennick D, Rajewsky K, Müller W.Interleukin-10-deficient mice develop chronic enterocolitis. Cell. 1993 Oct 22;75(2):263-74

23. Best WR, Becktel JM, Singleton JW, Kern F Jr. Development of a Crohn's disease activity index. National Cooperative Crohn's Disease Study. Gastroenterology. 1976 Mar;70(3):439-44.

24. Hanauer SB, Feagan BG, Lichtenstein GR, Mayer LF, Schreiber S, Colombel JF, Rachmilewitz D, Wolf DC, Olson A, Bao W, Rutgeerts P; ACCENT I Study Group. Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial. Lancet. 2002 May 4;359(9317):1541-1549.

25. Podolsky DK. Inflammatory bowel disease. N Engl J Med. 2002 Aug 8;347(6):417-429.

26. Targan SR, Hanauer SB, van Deventer SJ, Mayer L, Present DH, Braakman T, DeWoody KL, Schaible TF, Rutgeerts PJ. A short-term study of chimeric monoclonal antibody cA2 to tumor necrosis factor alpha for Crohn's disease. Crohn's Disease cA2 Study Group. N Engl J Med. 1997 Oct 9;337(15):1029-35.

27. Xavier RJ, Podolsky DK. Unravelling the pathogenesis of inflammatory bowel disease. Nature. 2007 Jul 26;448(7152):427-434.

28. Truelove SC and Witts LJ. Cortisone in ulcerative colitis; final report on a therapeutic trial. Br Med J. 1955 Oct 29;2(4947):1041-1048.

29. Duerr RH, Taylor KD, Brant SR, Rioux JD, Silverberg MS, Daly MJ, Steinhart AH, Abraham C, Regueiro M, Griffiths A, Dassopoulos T, Bitton A, Yang H, Targan S, Datta LW, Kistner EO, Schumm LP, Lee AT, Gregersen PK, Barmada MM, Rotter JI, Nicolae DL, Cho JH. A genome-wide association study identifies IL23R as an inflammatory bowel disease gene. Science. 2006 Dec 1;314(5804):1461-1463.

30. Rutgeerts P, Sandborn WJ, Feagan BG, Reinisch W, Olson A, Johanns J, Travers S, Rachmilewitz D, Hanauer SB, Lichtenstein GR, de Villiers WJ, Present D, Sands BE, Colombel JF. Infliximab for induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2005 Dec 8;353(23):2462-76.

31. Present DH, Rutgeerts P, Targan S, Hanauer SB, Mayer L, van Hogezand RA, Podolsky DK, Sands BE, Braakman T, DeWoody KL, Schaible TF, van Deventer SJ. Infliximab for the treatment of fistulas in patients with Crohn's disease. N Engl J Med. 1999 May 6;340(18):1398-405.

32. Frank DN, St Amand AL, Feldman RA, Boedeker EC, Harpaz N, Pace NR. Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. Proc Natl Acad Sci U S A. 2007 Aug 21;104(34):13780-13785

33. Jostins L, Ripke S, Weersma RK, Duerr RH, McGovern DP, Hui KY, Lee JC,

Schumm LP, Sharma Y, Anderson CA, Essers J, Mitrovic M, Ning K, Cleynen I, Theatre E, Spain SL, Raychaudhuri S, Goyette P, Wei Z, Abraham C, Achkar JP, Ahmad T, Amininejad L, Ananthakrishnan AN, Andersen V, Andrews JM, Baidoo L, Balschun T, Bampton PA, Bitton A, Boucher G, Brand S, Büning C, Cohain A, Cichon S, D'Amato M, De Jong D, Devaney KL, Dubinsky M, Edwards C, Ellinghaus D, Ferguson LR, Franchimont D, Fransen K, Gearry R, Georges M, Gieger C, Glas J, Haritunians T, Hart A, Hawkey C, Hedl M, Hu X, Karlsen TH, Kupcinskas L, Kugathasan S, Latiano A, Laukens D, Lawrance IC, Lees CW, Louis E, Mahy G, Mansfield J, Morgan AR, Mowat C, Newman W, Palmieri O, Ponsioen CY, Potocnik U, Prescott NJ, Regueiro M, Rotter JI, Russell RK, Sanderson JD, Sans M, Satsangi J, Schreiber S, Simms LA, Sventoraityte J, Targan SR, Taylor KD, Tremelling M, Verspaget HW, De Vos M, Wijmenga C, Wilson DC, Winkelmann J, Xavier RJ, Zeissig S, Zhang B, Zhang CK, Zhao H; International IBD Genetics Consortium (IIBDGC)., Silverberg MS, Annese V, Hakonarson H, Brant SR, Radford-Smith G, Mathew CG, Rioux JD, Schadt EE, Daly MJ, Franke A, Parkes M, Vermeire S, Barrett JC, Cho JH. Host-microbe interactions have shaped the genetic architecture of inflammatory bowel disease. Nature. 2012 Nov 1;491(7422):119-24.

34. Barrett JC, Hansoul S, Nicolae DL, Cho JH, Duerr RH, Rioux JD, Brant SR, Silverberg MS, Taylor KD, Barmada MM, Bitton A, Dassopoulos T, Datta LW, Green T, Griffiths AM, Kistner EO, Murtha MT, Regueiro MD, Rotter JI, Schumm LP, Steinhart AH, Targan SR, Xavier RJ; NIDDK IBD Genetics Consortium, Libioulle C, Sandor C, Lathrop M, Belaiche J, Dewit O, Gut I, Heath S, Laukens D, Mni M, Rutgeerts P, Van Gossum A, Zelenika D, Franchimont D, Hugot JP, de Vos M, Vermeire S, Louis E; Belgian-French IBD Consortium; Wellcome Trust Case Control Consortium, Cardon LR, Anderson CA, Drummond H, Nimmo E, Ahmad T, Prescott NJ, Onnie CM, Fisher SA, Marchini J, Ghori J, Bumpstead S, Gwilliam R, Tremelling M, Deloukas P, Mansfield J, Jewell D, Satsangi J, Mathew CG, Parkes M, Georges M, Daly MJ. Genome-wide association defines more than 30 distinct susceptibility loci for Crohn's disease. Nat Genet. 2008 Aug;40(8):955-962.

35. Loftus EV Jr. Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. Gastroenterology. 2004 May;126(6):1504-1517.

36. Fiocchi C. Inflammatory bowel disease: etiology and pathogenesis. Gastroenterology. 1998 Jul;115(1):182-205.

37. Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. Lancet. 1980 Mar 8;1(8167):514.

38. 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 Jan;142(1):46-54.

39. Riddell RH, Goldman H, Ransohoff DF, Appelman HD, Fenoglio CM, Haggitt RC, Ahren C, Correa P, Hamilton SR, Morson BC, et al. Dysplasia in inflammatory bowel disease: standardized classification with provisional clinical applications. Hum Pathol. 1983 Nov;14(11):931-968.

40. Okayasu I, Hatakeyama S, Yamada M, Ohkusa T, Inagaki Y, Nakaya R A novel method in the induction of reliable experimental acute and chronic ulcerative colitis in mice. Gastroenterology. 1990 Mar;98(3):694-702.

41. Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut. 2001 Apr;48(4):526-535.

42. Sokol H, Pigneur B, Watterlot L, Lakhdari O, Bermúdez-Humarán LG, Gratadoux JJ, Blugeon S, Bridonneau C, Furet JP, Corthier G, Grangette C, Vasquez N, Pochart P, Trugnan G, Thomas G, Blottière HM, Doré J, Marteau P, Seksik P, Langella P. Faecalibacterium prausnitzii is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. Proc Natl Acad Sci U S A. 2008 Oct 28;105(43):16731-16736.

43. Silverberg MS, Satsangi J, Ahmad T, Arnott ID, Bernstein CN, Brant SR, Caprilli R, Colombel JF, Gasche C, Geboes K, Jewell DP, Karban A, Loftus EV Jr, Peña AS, Riddell RH, Sachar DB, Schreiber S, Steinhart AH, Targan SR, Vermeire S, Warren BF. Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. Can J Gastroenterol. 2005 Sep;19 Suppl A:5A-36A

44. Sadlack B, Merz H, Schorle H, Schimpl A, Feller AC, Horak I. Ulcerative colitis-like disease in mice with a disrupted interleukin-2 gene. Cell. 1993 Oct 22;75(2):253-261.

45. Franke A, McGovern DP, Barrett JC, Wang K, Radford-Smith GL, Ahmad T, Lees CW, Balschun T, Lee J, Roberts R, Anderson CA, Bis JC, Bumpstead S, Ellinghaus D, Festen EM, Georges M, Green T, Haritunians T, Jostins L, Latiano A, Mathew CG, Montgomery GW, Prescott NJ, Raychaudhuri S, Rotter JI, Schumm P, Sharma Y, Simms LA, Taylor KD, Whiteman D, Wijmenga C, Baldassano RN, Barclay M, Bayless TM, Brand S, Büning C, Cohen A, Colombel JF, Cottone M, Stronati L, Denson T, De Vos M, D'Inca R, Dubinsky M, Edwards C, Florin T, Franchimont D, Gearry R, Glas J, Van Gossum A, Guthery SL, Halfvarson J, Verspaget HW, Hugot JP, Karban A, Laukens D, Lawrance I, Lemann M, Levine A, Libioulle C, Louis E, Mowat C, Newman W, Panés J, Phillips A, Proctor DD, Regueiro M, Russell R, Rutgeerts P, Sanderson J, Sans M, Seibold F, Steinhart AH, Stokkers PC, Torkvist L, Kullak-Ublick G, Wilson D, Walters T, Targan SR, Brant SR, Rioux JD, D'Amato M, Weersma RK, Kugathasan S, Griffiths AM, Mansfield JC, Vermeire S, Duerr RH, Silverberg MS, Satsangi J, Schreiber S, Cho JH, Annese V, Hakonarson H, Daly MJ, Parkes M. Genome-wide meta-analysis increases to 71 the number of confirmed

Crohn's disease susceptibility loci. Nat Genet. 2010 Dec;42(12):1118-1125.

46. Baert F, Noman M, Vermeire S, Van Assche G, D' Haens G, Carbonez A, Rutgeerts P. Influence of immunogenicity on the long-term efficacy of infliximab in Crohn's disease. N Engl J Med. 2003 Feb 13;348(7):601-608.

47. Colombel JF, Sandborn WJ, Reinisch W, Mantzaris GJ, Kornbluth A, Rachmilewitz D, Lichtiger S, D'Haens G, Diamond RH, Broussard DL, Tang KL, van der Woude CJ, Rutgeerts P; SONIC Study Group. Infliximab, azathioprine, or combination therapy for Crohn's disease. N Engl J Med. 2010 Apr 15;362(15):1383-1395.

48. Cooper HS, Murthy SN, Shah RS, Sedergran DJ. Clinicopathologic study of dextran sulfate sodium experimental murine colitis. Lab Invest. 1993 Aug;69(2):238-249.

49. Ekbom A, Helmick C, Zack M, Adami HO. Ulcerative colitis and colorectal cancer. A population-based study. N Engl J Med. 1990 Nov 1;323(18):1228-1233.

50. Schroeder KW, Tremaine WJ, Ilstrup DM. Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study. N Engl J Med. 1987 Dec 24;317(26):1625-1629.

51. Rioux JD, Xavier RJ, Taylor KD, Silverberg MS, Goyette P, Huett A, Green T, Kuballa P, Barmada MM, Datta LW, Shugart YY, Griffiths AM, Targan SR, Ippoliti AF, Bernard EJ, Mei L, Nicolae DL, Regueiro M, Schumm LP, Steinhart AH, Rotter JI, Duerr RH, Cho JH, Daly MJ, Brant SR. Genome-wide association study identifies new susceptibility loci for Crohn disease and implicates autophagy in disease pathogenesis. Nat Genet. 2007 May;39(5):596-604.

52. Sands BE, Anderson FH, Bernstein CN, Chey WY, Feagan BG, Fedorak RN, Kamm MA, Korzenik JR, Lashner BA, Onken JE, Rachmilewitz D, Rutgeerts P, Wild G, Wolf DC, Marsters PA, Travers SB, Blank MA, van Deventer SJ. Infliximab maintenance therapy for fistulizing Crohn's disease. N Engl J Med. 2004 Feb 26;350(9):876-85.

53. Colombel JF, Sandborn WJ, Rutgeerts P, Enns R, Hanauer SB, Panaccione R, Schreiber S, Byczkowski D, Li J, Kent JD, Pollack PF. Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: the CHARM trial. Gastroenterology. 2007 Jan;132(1):52-65.

54. Hampe J, Franke A, Rosenstiel P, Till A, Teuber M, Huse K, Albrecht M, Mayr G, De La Vega FM, Briggs J, Günther S, Prescott NJ, Onnie CM, Häsler R, Sipos B, Fölsch UR, Lengauer T, Platzer M, Mathew CG, Krawczak M, Schreiber S. A genome-wide association scan of nonsynonymous SNPs identifies a susceptibility variant for Crohn disease in ATG16L1. Nat Genet. 2007 Feb;39(2):207-211.

55. Bouma G, Strober W. The immunological and genetic basis of inflammatory bowel disease. Nat Rev Immunol. 2003 Jul;3(7):521-533.

56. Lichtiger S, Present DH, Kornbluth A, Gelernt I, Bauer J, Galler G, Michelassi F, Hanauer S. Cyclosporine in severe ulcerative colitis refractory to steroid therapy. N Engl J Med. 1994 Jun 30;330(26):1841-1845.

57. Abraham C, Cho JH. Inflammatory bowel disease. N Engl J Med. 2009 Nov 19;361(21):2066-2078.

58. Summers RW, Switz DM, Sessions JT Jr, Becktel JM, Best WR, Kern F Jr, Singleton JW. National Cooperative Crohn's Disease Study: results of drug treatment. Gastroenterology. 1979 Oct;77(4 Pt 2):847-869

59. Satsangi J, Silverberg MS, Vermeire S, Colombel JF. The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications. Gut. 2006 Jun;55(6):749-53.

60. Elson CO, Sartor RB, Tennyson GS, Riddell RH. Experimental models of inflammatory bowel disease. Gastroenterology. 1995 Oct;109(4):1344-1367.

61. Greenstein AJ, Janowitz HD, Sachar DB. The extra-intestinal complications of Crohn's disease and ulcerative colitis: a study of 700 patients. Medicine (Baltimore). 1976 Sep;55(5):401-412.

62. Fujino S, Andoh A, Bamba S, Ogawa A, Hata K, Araki Y, Bamba T, Fujiyama Y. Increased expression of interleukin 17 in inflammatory bowel disease. Gut. 2003 Jan;52(1):65-70.

63. Sartor RB. Microbial influences in inflammatory bowel diseases. Gastroenterology. 2008 Feb;134(2):577-594.

64. Manichanh C, Rigottier-Gois L, Bonnaud E, Gloux K, Pelletier E, Frangeul L, Nalin R, Jarrin C, Chardon P, Marteau P, Roca J, Dore J. Reduced diversity of faecal microbiota in Crohn's disease revealed by a metagenomic approach. Gut. 2006 Feb;55(2):205-211.

65. Fuss IJ, Neurath M, Boirivant M, Klein JS, de la Motte C, Strong SA, Fiocchi C, Strober W. Disparate CD4+ lamina propria (LP) lymphokine secretion profiles in inflammatory bowel disease. Crohn's disease LP cells manifest increased secretion of IFN-gamma, whereas ulcerative colitis LP cells manifest increased secretion of IL-

5. J Immunol. 1996 Aug 1;157(3):1261-1270.

66. Rutgeerts P, Geboes K, Vantrappen G, Beyls J, Kerremans R, Hiele M. Predictability of the postoperative course of Crohn's disease. Gastroenterology. 1990 Oct;99(4):956-963.

67. Present DH, Korelitz BI, Wisch N, Glass JL, Sachar DB, Pasternack BS. Treatment of Crohn's disease with 6-mercaptopurine. A long-term, randomized, double-blind study. N Engl J Med. 1980 May 1;302(18):981-987.

68. Swidsinski A, Ladhoff A, Pernthaler A, Swidsinski S, Loening-Baucke V, Ortner M, Weber J, Hoffmann U, Schreiber S, Dietel M, Lochs H. Mucosal flora in inflammatory bowel disease. Gastroenterology. 2002 Jan;122(1):44-54.

69. van Dullemen HM, van Deventer SJ, Hommes DW, Bijl HA, Jansen J, Tytgat GN, Woody J. Treatment of Crohn's disease with anti-tumor necrosis factor chimeric monoclonal antibody (cA2). Gastroenterology. 1995 Jul;109(1):129-135.

70. Azer SA. Overview of molecular pathways in inflammatory bowel disease associated with colorectal cancer development. Eur J Gastroenterol Hepatol. 2013 Mar;25(3):271-281.

71. Azer SA, AlOlayan TI, AlGhamdi MA, AlSanea MA. Inflammatory bowel disease: An evaluation of health information on the internet. World J Gastroenterol. 2017 Mar 7;23(9):1676-1696.

72. Börner K, Maru JT, Goldstone RL. The simultaneous evolution of author and paper networks. Proc Natl Acad Sci U S A. 2004 Apr 6;101 Suppl 1:5266-73.

73 Sinatra R, Deville P, Szell M, Wang D, Barabasi AL. A century of physics. Nature Physics 2015; 11(10): 791-796.

74. Wren JD, Georgescu C, Giles CB, Hennessey J. Use it or lose it: citations predict the continued online availability of published bioinformatics resources. Nucleic Acids Res. 2017 Apr 20;45(7):3627-3633.

75. Shanahan DR. Auto-correlation of journal impact factor for consensus research reporting statements: a cohort study. PeerJ. 2016 Mar 31;4:e1887.

76. Royle P, Kandala NB, Barnard K, Waugh N. Bibliometrics of systematic reviews: analysis of citation rates and journal impact factors. Syst Rev. 2013 Sep 12;2:74.

77. Falagas ME, Kouranos VD, Michalopoulos A, Rodopoulou SP, Batsiou MA, Karageorgopoulos DE. Comparison of the distribution of citations received by articles published in high, moderate, and low impact factor journals in clinical medicine. Intern Med J. 2010 Aug;40(8):587-591.

78. García-Aroca MÁ, Pandiella-Dominique A, Navarro-Suay R, Alonso-Arroyo A, Granda-Orive JI, Anguita-Rodríguez F, López-García A. Analysis of Production, Impact, and Scientific Collaboration on Difficult Airway Through the Web of Science and Scopus (1981-2013). Anesth Analg. 2017 Jun;124(6):1886-1896.

79. Tanner-Smith EE, Polanin JR. Brief alcohol intervention trials conducted by higher prestige authors and published in higher impact factor journals are cited more frequently. J Clin Epidemiol. 2016 Feb 6.

80. Jagsi R, Guancial EA, Worobey CC, Henault LE, Chang Y, Starr R, Tarbell NJ, Hylek EM. The "gender gap" in authorship of academic medical literature--a 35-year perspective. N Engl J Med. 2006 Jul 20;355(3):281-287.

81. Long MT, Leszczynski A, Thompson KD, Wasan SK, Calderwood AH. Female authorship in major academic gastroenterology journals: a look over 20 years. Gastrointest Endosc. 2015;81(6):1440-1447.

82. Diamond SJ, Thomas CR Jr, Desai S, Holliday EB, Jagsi R, Schmitt C, Enestvedt BK. Gender Differences in Publication Productivity, Academic Rank, and Career Duration Among U.S. Academic Gastroenterology Faculty. Acad Med. 2016 Aug;91(8):1158-1163.

83. Nicholson JM, Ioannidis JP. Research grants: Conform and be funded. Nature. 2012 Dec 6;492(7427):34-36.

84. Lauer MS, Danthi NS, Kaltman J, Wu C. Predicting Productivity Returns on Investment: Thirty Years of Peer Review, Grant Funding, and Publication of Highly Cited Papers at the National Heart, Lung, and Blood Institute. Circ Res. 2015 Jul 17;117(3):239-243.

85. Cheng K, Dodson TB, Egbert MA, Susarla SM. Which Factors Affect Citation Rates in the Oral and Maxillofacial Surgery Literature? J Oral Maxillofac Surg. 2017 Apr 1. pii: S0278-2391(17)30361-0.

86. Connelly TM, Devane L, Kelly JC, Wrafter P, Messaris E. The 100 classic papers in ulcerative colitis: a bibliometric analysis. Expert Rev Gastroenterol Hepatol. 2016 Aug 22:1-9. [Epub ahead of print]

Glossary

Articles are scientific written composition representing a substantial advance in the understanding of a topic or problem. They raise questions, provide thoughtful, critical analysis and aim at establishing new directions.

Basic research is defined as fundamental research, which aims at improving scientific theories and our understanding of a phenomenon. Basic research may use animal models and include in vivo and in-vitro studies that target advances of fundamental knowledge.

Clinical research is defined as research applied to a clinical condition/disease with the aim to test an intervention or make a change to a phenomenon. Basic research usually fuels clinical research.

Reports are defined as brief articles with conclusions, results, and recommendations. They report on a substantial advance in an area/topic or a problem and aim at reporting findings and standardization of practice.

Review and meta-analysis are defined as an article reviewing the progress of knowledge in a particular topic, critically analysing the current status of knowledge and presenting an understanding of the subject by discussing related literature. A review should identify gaps in the literature and highlight future directions for further research. **A meta-analysis** is defined as a statistical analysis that combines the results from different scientific studies to provide conclusive evidence.

Figure Legend

Figure 1A: Number of citations of papers published before the year 2000 (mean±SD)

Figure 1B: Number of citations of papers published after the year 2000 (mean±SD)

Table 1 Top cited papers in inflammatory bowel disease identified by searching the Web of Science, summarized by year of publication and category

Article type	Year of publication: no of articles [References]							
	1950-1958	1959-1967	1968-1976	1977-1985	1986-1994	1995-2003	2004-2012	Total (%)
Article				1 [39]				1 [2%]
Review/ Meta-analysis			1 [61]			5 [25,36,41,55,60]	8 [27,34,35,45, 33,57,38,63]	14 [28%]
Report							2 [43,59]	2 [4%]
Research	1 [28]		1 [23]	3 [37,58,67]	8 [22,44,40,48,49, 56,50,66]	10 [20,21,26,24,31, 46,62,69,65,68]	10 [29,30,32,51, 52,42,54,47, 53,64]	33 [66%]
Total (%)	1 [2%	0 [0%]	2 [4%]	4 [8%]	8 [16%]	15 [30%]	20 [40%]	50 [100%]

Table 2 Top-cited papers in inflammatory bowel disease (IBD) identified by searching the Web of Science, summarized by category and topic

Topics on IBD	Category: no of articles [References]				
	Article	Review/ Meta-analysis	Report	Research	Total (%)
Epidemiology, prevalence		2 [35,38]			2 [4%]
CD genetic susceptibility and NOD2 mutation		2 [34,45]		4 [20,21,51,54]	6 [12%]
Animal models for IBD		1 [60]		4 [22,44,40,48]	5 [10%]
Pathogenesis of IBD		7 [25,27,36,55,33,57,63]		8 [29,32,42,62,65,68,66,64]	15 [30%]
Classification, index of disease activity	1 [39]		2 [43,59]	2 [23,37]	5 [10%]
Risk of developing colorectal cancer		1 [41]		1 [49]	2 [4%]
Extra-intestinal complications		1 [61]			1 [2%]
Infliximab in CD				6 [24,31,30,46,52,47]	6 [12%]
Corticosteroids in UC				1 [28]	1 [2%]
Drug treatment and cyclosporine in UC				2 [56,58]	2 [4%]
Adalimumab in CD				1 [53]	1 [2%]
5-aminosalicylic acid in				1 [50]	1 [2%]

UC					
6-mercaptopurine in CD				1 [67]	1 [2%]
Monoclonal antibodies, anti-tumor necrosis factor in CD				2 [26,69]	2 [4%]
Total (%)	1 [2%]	14 [28%]	2 [4%]	33 [66%]	50 [100%]

Table 3. The journals that published the top-cited inflammatory bowel disease (IBD) articles included in the study, the journal impact factor, and the number of papers published and reference number.

Journal*	2016-Journal Impact Factor (JIF)	Number of papers published [References]
New England Journal of Medicine	72.406	12 [25,26,31,30,46,49,56,52,47,50,67,57]
Gastroenterology	18.392	12 [23,36,35,40,58,60,53,69,38,68,63,66]
Nature	40.137	4 [20,21,27,33]
Nature Genetics	27.959	4 [34,51,45,54]
The Lancet	47.831	2 [24,37]
Proceedings of the National Academy of Sciences of the United States of America	9.661	2 [32,42]
Cell	30.410	2 [22,44]
Gut	16.658	4 [59,64,41,62]
British Medical Journal	20.785	1 [28]
Science	37.205	1 [29]
Human Pathology	3.014	1 [39]
Laboratory Investigation	4.857	1 [48]
Canadian Journal of Gastroenterology and Hepatology	2.147	1 [43]
Nature Reviews Immunology	39.932	1 [55]
Medicine (Baltimore)	1.804	1 [61]
Journal of Immunology	4.856	1 [65]

- Gastroenterology related journals (Gastroenterology, and Gut) only published 16 (32%) articles out of the top highly cited 50 articles

Table 4 Authors and co-authors of two or more articles of the top-cited articles in inflammatory bowel disease identified by searching the Web of Science

Author's name*	Number [References]		Author's Name*	Number [References]	
	First author	Coauthor		First author	Coauthor
Hugot, JP	1 [20]	2 [34,45]	Daly,MJ	-	5[29,34,51,45,33]
Podolsky, DK	1 [25]	3 [28,27,31]	Steinhart,AH	-	5[29,34,43,51,45]
Targan, SR	1 [26]	7 [29,31,34,43,51,45,33]	Griffiths,A	-	4[29,34,51,45]
Hanauer,SB	1 [24]	6 [21,26,31,30,56,53]	Dassopoulos,T	-	2[29,34]
Xavier,RJ	1 [27]	3 [34,51,33]	Bitton,A	-	3[29,34,33]
Duerr,RH	1 [29]	4 [21,34,45,33]	Datta,LW	-	3[29,34,51]
Present,DH	2 [31,67]	3 [26,30,56]	Kistner,EO	-	2[29,34]
Rutgeerts, P	1 [30]	9 [26,24,31,34,46,45,52,47,53]	Rotter,JI	-	5[29,34,51,45,33]
Fiocchi,C	1 [36]	1 [65]	Schumm,LP	-	5[29,34,51,45,52]
Barrett,JC	1 [34]	2 [45,33]	Lee,J	-	2[45,33]
Riddell,RH	1 [39]	2 [43,60]	Lees,CW	-	2[45,33]
Loftus,EV Jr	1 [35]	1 [43]	Sandborn,WJ	-	3[30,47,53]
Franke,A	1 [45]	2 [33,54]	Barmada,MM	-	3[29,34,51]
Silverberg,MS	1 [43]	5 [29,34,51,45,33]	Nicolae,DL	-	4[21,29,34,51]
Rioux,JD	1 [51]	4 [29,34,45,33]	Sands,BE	-	3[31,30,52]
Lichtiger,S	1 [56]	1 [47]	Belaiche,J	-	2[20,34]
Colombel,JF	2 [47,53]	5 [20,24,30,43,45]	Laukens,D	-	3[34,45,33]
Abraham,C	1 [57]	2 [29,33]	Lawrance,I	-	2[45,33]
Becktel,JM	-	2 [23,58]	Louis,E	-	3[34,33,45]

Singleton,JW	-	2 [23,58]	Vos,M	-	3[34,45,33]
Kern,F Jr	-	2 [23,58]	Vermeire,S	-	5[34,46,43,45,33]
Van Deventer,SJ	-	4 [26,31,52,69]	Satsangi,J	-	4[34,43,45,33]
Mayer,L	-	3 [26,24,31]	Bernstein,CN	-	2[43,52]
Braakman,T	-	2 [26,31]	Tremelling,M	-	2[34,33]
DeWoody,KL	-	2 [26,31]	Mansfield,J	-	3[34,45,33]
Schaible,TF	-	2 [26,31]	Jewell,D	-	2[34,43]
Feagan,BG	-	3 [24,30,52]	Mathew,CG	-	4[34,45,33,54]
Lichtenstein,GR	-	2 [24,30]	Parkes,M	-	3[34,45,33]
Schreiber,S	-	7 [24,43,45,33,54,53,68]	Georges,M	-	3[34,45,33]
Rachmilewitz,D	-	4 [24,30,52,47]	Karban,A	-	2[43,45]
Wolf,DC	-	2 [24,52]	Gossum,A	-	2[34,45]
Olson,A	-	2 [24,30]	Franchimont,D	-	3[34,45,33]
Taylor,KD	-	5 [29,34,51,45,33]	Newman,W	-	2[45,33]
Bayless,TM	-	2 [21,45]	Regueiro,M	-	5[29,34,51,45,33]
Cho, JH	-	7 [21,29,34,51,45,33,57]	Kornbluth,A	-	2[56,47]

*Author's name= family name, abbreviations of first or first and second names.

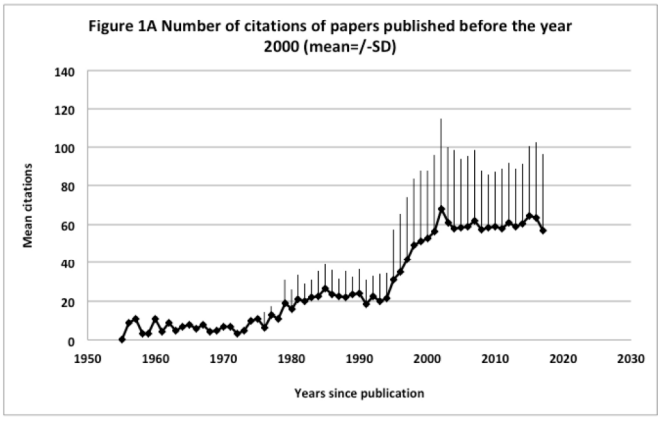
Table 5 Grading the top-cited articles in inflammatory bowel disease according to the Oxford Centre for Evidence-based Medicine – Levels of Evidence.

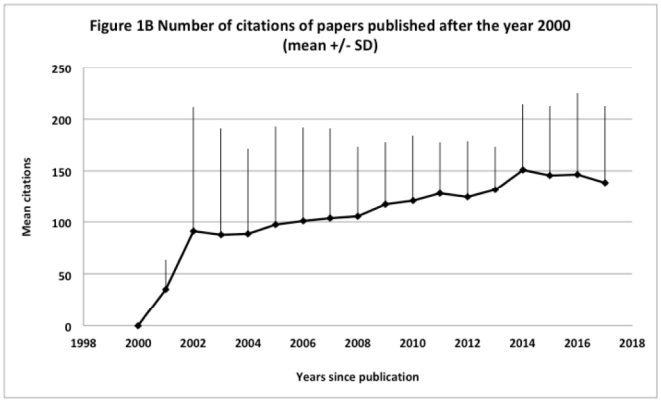
Level	Domain	Characteristics and description	Articles number [References]
1a	Therapeutic/ Prevention, Aetiology/Harm	Systematic reviews of RCTs (with consistent results from individual studies)	1 (33)
	Prognosis	Systematic reviews with homogeneity of inception cohort studies	
	Diagnosis	Systematic reviews with homogeneity of Level 1 diagnostic studies	
	Differential diagnosis/symptom prevalence study	Systematic reviews with homogeneity of prospective cohort studies.	
1b	Therapeutic/ Prevention, Aetiology/Harm	Individual RCT (with narrow confidence intervals)	12 [26,24,30,56,58,52,47,53,50,66,67, 59]
	Prognosis	Individual inception cohort study with >80% follow-up	
	Diagnosis	Validating cohort study with good reference standards	
	Differential diagnosis/symptom prevalence study	Prospective cohort study with good follow-up	
2a	Therapeutic/ Prevention, Aetiology/Harm	Systematic review of cohort studies (with consistent results from individual studies)	2 [34,63]

	Prognosis	Systematic review with homogeneity of either retrospective cohort studies or untreated control groups in RCT	
	Diagnosis	Systematic review with homogeneity of Level > 2 diagnostic studies	
	Differential diagnosis/symptom prevalence study	Systematic review with homogeneity of 2b and better studies	
2b	Therapeutic/ Prevention, Aetiology/Harm	Individual cohort study (including low quality RCT; e.g., <80% follow-up)	3 [31,46,49]
	Prognosis	Retrospective cohort study or follow-up untreated control patients in an RCT	
	Diagnosis	Exploratory cohort study with good reference standards	
	Differential diagnosis/symptom prevalence study	Retrospective cohort study or poor follow-up	
2c	Therapeutic/ Prevention, Aetiology/Harm	Outcome studies (analysis of large registries)	3 [38,60,61]
	Prognosis	Outcomes research	
	Diagnosis		
	Differential diagnosis/symptom	Ecological studies	

	prevalence study		
3a	Therapeutic/ Prevention, Aetiology/Harm	Systemic reviews of case-control studies (with consistent results from individual studies)	9 [25,27,36,35,41,43,55,45,57]
	Prognosis		
	Diagnosis	Systematic reviews with homogeneity of 3b and better studies	
	Differential diagnosis/symptom prevalence study	Systematic reviews with homogeneity of 3b and better studies	
3b	Therapeutic/ Prevention, Aetiology/Harm	Individual case-control study	15 [20,21,22,28,29,44,40,32,51,42,54,62,64,65,68]
	Prognosis		
	Diagnosis	Non consecutive study, or without consistently applied reference standards	
	Differential diagnosis/symptom prevalence study	Non consecutive cohort study or very limited population	
4	Therapeutic/ Prevention, Aetiology/Harm	Case series (and poor quality cohort and case-control studies)	5 [23,39,37,48,69]
	Prognosis	Case-series (and poor quality prognostic cohort studies)	
	Diagnosis	Case-control study, poor or non-	

		independent reference standard	
	Differential diagnosis/symptom prevalence study	Case-series or superseded reference standards	
5	Therapeutic/ Prevention, Aetiology/Harm	Expert opinion without explicit critical appraisal or based on physiology, or bench research.	0 [0]
	Prognosis	Expert opinion without explicit critical appraisal or based on physiology, or bench research.	
	Diagnosis	Expert opinion without explicit critical appraisal or based on physiology, or bench research.	
	Differential diagnosis/symptom prevalence study	Expert opinion without explicit critical appraisal or based on physiology, or bench research.	





209x296mm (300 x 300 DPI)

Appendix 1.

Top-cited articles on inflammatory bowel disease identified by searching the Web of Science database[a]

Rank	Authors, Year [Reference]	Article (*Journal*)	2016-JIF	Category	Number of citations, Web of Knowledge	Average citation per year[b]	Rank of the article in the journal publishing it[c]	Origin: First author's organization, location (country)
1	Hugot et al, 2001[20]	Association of NOD2 leucine-rich repeat variants with susceptibility to Crohn's disease. (*NATURE).*	40.137	Basic research	3,555	209.1	134	Fondation Jean Dausset CEPH (France)
2	Ogura et al, 2001[21]	A frameshift mutation in NOD2 associated with susceptibility to Crohn's disease. (*NATURE*).	40.137	Basic research	3,285	193.2	159	The University of Michigan Medical School, Michigan (United States).
3	Kuhn et al, 1993[22]	Interleukin-10-deficient mice develop chronic enterocolitis. (*CELL*)	30.410	Basic research	2,982	119.3	67	Institute for Genetics, University of Cologne, (Germany)
4	Best et al, 1976[23]	Development of a Crohns-disease activity index-National cooperative Chrons-disease study (*Gastroenterology*).	18.392	Clinical research	2,533	60.3	2	Hines Veterans Administration Cooperative Studies Support Center, University of Colorado Medical Center, Denver, Colorado, (United States).
5	Hanauer et al, 2002[24]	Maintenance infliximab for Crohn's disease: the ACCENT I randomized trial (*Lancet*)	47.831	Clinical research	2,442	152.6	46	University of Chicago Medical Center, Chicago, IL (United States).
6	Podolsky, 2002[25]	Inflammatory bowel disease. (*New England Journal of Medicine)*	72.406	Review	2,423	151.4	163	Massachusetts General Hospital and Harvard Medical School, Boston,

								Massachusetts (United States).
7	Targan et al, 1997[26]	A short-term study of chimeric monoclonal antibody cA2 to tumor necrosis factor alpha for Crohn's disease (*New England Journal of Medicine)*	72.406	Clinical research	2,364	112.6	169	Cedars-Sinai Medical Center, Los Angeles, California (United States)
8	Xavier and Podolsky, 2007[27]	Unravelling the pathogenesis of inflammatory bowel disease (*NATURE*)	40.137	Review	2,036	185.1	450	Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts (United States).
9	Truelove and Witts, 1955[28]	Cortisone in ulcerative colitis- Final report on a therapeutic trial (*British Medical Journal*).	20.785	Clinical research	1,871	29.7	20	Nuffield Department of Clinical Medicine, Oxford (United Kingdom)
10	Duerr et al, 2006[29]	A genome-wide association study identifies IL23R as an inflammatory bowel disease gene. **(***SCIENCE*).	37.205	Clinical research	1,862	155.2	530	Department of Medicine, School of Medicine, University of Pittsburgh, Pittsburgh, PA (United States).
12	Rutgeerts et al, 2005[30]	Infliximab for induction and maintenance therapy for ulcerative colitis (*New England Journal of Medicine*)	72.406	Clinical research	1,834	141.1	290	University Hospital Gasthuisberg, Leuven, (Belgium).
12	Present et al, 1999[31]	Infliximab for treatment of fistulas in patients with Crohn's disease (*New England Journal of Medicine*)	72.406	Clinical research	1,730	91.0	321	Mount Sinai Medical Center, New York, NY, (United States)

13	Frank et al, 2007[32]	Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. (*Proceedings of the National Academy of Sciences of the United States of America*)	9.661	Basic research	1,650	150.0	172	University of Colorado, Boulder, CO (United States)
14	Jostins et al, 2012[33]	Host-microbe interactions have shaped the genetic architecture of inflammatory bowel disease. (*Nature*)	40.137	Review Meta-analysis	1,643	273.8	683	Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, (*United Kingdom)*
15	Barrett et al, 2008[34]	Genome-wide association defines more than 30 distinct susceptibility loci for Crohn's disease. *(Nature Genetics*)	27.959	Review Meta-analysis	1,631	163.1	25	Wellcome Trust Centre for Human Genetics, University of Oxford, Roosevelt Drive, Oxford (United Kingdom)
16	Loftus, 2004[35]	Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences (*Gastroenterology*)	18.392	Review	1,566	111.9	10	Mayo Clinic, Rochester, Minnesota, (United States)
17	Fiocchi, 1998[36]	Inflammatory bowel disease: Etiology and pathogenesis (*Gastroenterology*)	18.392	Review	1,540	77.0	12	University Hospitals of Cleveland Case Western Reserve University School of Medicine, Ohio (United States)
18	Harvey and Bradshaw, 1980[37]	A simple index of Crohns-disease activity (*Lancet*)	47.831	Clinical research	1,466	38.6	166	Bristol Royal Infirmary and Frenchay Hospital, Bristol (United Kingdom)
19	Molodeck	Increasing incidence and prevalence	18.392	Review	1,438	239.7	19	University of Calgary,

	y et al, 2012[38]	of the inflammatory bowel diseases with time, based on systematic review. (*Gastroenterology*).						Calgary, Alberta, (Canada).
20	Riddell et al, 1983[39]	Dysplasia in inflammatory bowel disease- Standardized classification with provisional clinical applications (*Human Pathology)*	3.014	Article	1,398	39.9	2	National Foundation for Ileitis and Colitis, New York, (United States).
21	Okayasu et al, 1990[40]	A novel method in the induction of reliable experimental acute and chronic ulcerative-colitis in mice (*Gastroenterology)*	18.392	Basic research	1,396	49.9	24	School of Medicine, Tokyo Medical and Dental University, (Japan).
22	Eaden et al, 2001[41]	The risk of colorectal cancer in ulcerative colitis: a meta-analysis. (*Gut)*.	16.658	Review Meta-analysis	1,388	81.6	1	Leicester General Hospital, Gwendolen Road, Leicester (United Kingdom)
23	Sokol et al, 2008[42]	Faecalibacterium prausnitzii is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. *Proceedings of the National Academy of Sciences of the United States of America*)	9.661	Basic research	1,384	138.4	247	Institut National de la Recherche Agronomique U910, Domaine de Vilvert, Jouy-en-Josas, (France).
24	Siliverberg et al, 2005[43]	Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. *(Canadian Journal of Gastroenterology and Hepatology)*	2.147	Report	1,373	105.6	1	Mount Sinai Hospital IBD Centre, University of Tronto, Toronto, Ontario (Canada)

25	Sadlack et al, 1993[44]	Ulcerative colitis-like disease in mice with a disrupted interleukin-2 gene (*CELL*)	30.410	Basic research	1,358	54.32	387	Institute of Virology and Immunobiology, University of Würzburg, (Germany)
26	Franke et al, 2010[45]	Genome-wide meta-analysis increases to 71 the number of confirmed Crohn's disease susceptibility loci. *(Nature Genetics*)	27.959	Review Meta-analysis	1,321	165.1	63	Institute of Clinical Molecular Biology, Christian-Albrechts-University Kiel, Kiel, (Germany).
27	Baert et al, 2003[46]	Influence of immunogenicity on the long-term efficacy of infliximab in Crohn's disease. *(New England Journal of Medicine*)	72.406	Clinical research	1,297	86.5	562	University Hospital Gasthuisberg, Leuven, (Belgium).
28	Colombel et al, 2010[47]	Infliximab, azathioprine, or combination therapy for Crohn's disease (*New England Journal of Medicine*)	72.406	Clinical research	1,294	161.7	565	Hôpital Claude Huriez and Centre d'Investigation Clinique, Centre Hospitalier Universitaire de Lille, Université Lille Nord de France, Lille, (France).
29	Cooper et al, 1993[48]	Clinicopathologic study of dextran sulfate sodium experimental murine colitis. *(Laboratory Investigation*)	4.857	Basic research	1,219	48.8	4	Hahnemann University, Philadelphia, Pennsylvania. (United States)
30	Ekbom et al, 1990[49]	Ulcerative colitis and colorectal cancer. A population-based study. (*New England Journal of Medicine)*	72.406	Clinical research	1,168	41.7	684	University Hospital, Uppsala, (Sweden).

31	Schroeder et al, 1987[50]	Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study *(New England Journal of Medicine*)	72.406	Clinical research	1,156	37.3	695	Mayo Clinic, Rochester, MN (United States)
32	Rioux et al, 2007[51]	Genome-wide association study identifies new susceptibility loci for Crohn disease and implicates autophagy in disease pathogenesis. (*Nature Genetics*)	27.959	Basic research	1,152	104.7	89	Université de Montréal and the Montreal Heart Institute, Research Center, Montreal, Quebec (Canada).
33	Sands et al, 2004[52]	Infliximab maintenance therapy for fistulizing Crohn's disease. *(New England Journal of Medicine)*	72.406	Clinical research	1,146	81.8	706	Massachusetts General Hospital, and Harvard Medical School, Boston (United States)
34	Colombel et al, 2007[53]	Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: the CHARM trial. (*Gastroenterology*).	18.392	Clinical research	1,124	102.2	32	Hôpital Claude Huriez, Centre Hospitalier Universitaire de Lille, Rue Michel Polonovski, Lille, (France)
35	Hampe et al, 2007[54]	A genome-wide association scan of nonsynonymous SNPs identifies a susceptibility variant for Crohn disease in ATG16L1. *(Nature Genetics)*	27.959	Basic research	1,123	102.1	92	Institute for Clinical Molecular Biology, Christian-Albrechts University Kiel, University Hospital Schleswig-Holstein, (Germany).

36	Bouma and Strober, 2003[55]	The immunological and genetic basis of inflammatory bowel disease. *(Nature Reviews Immunology)*	39.932	Review	1,116	74.4	35	National Institutes of Health, and National Institutes of Allergy and Infectious Diseases, Bethesda, Maryland (United States)
37	Lichtiger et al, 1994[56]	Cyclosporine in severe ulcerative colitis refractory to steroid therapy. *(New England Journal of Medicine*)	72.406	Clinical research	1,104	46.0	755	Mount Sinai School of Medicine, New York (United States).
38	Abraham et al, 2009[57]	Inflammatory bowel disease. *(New England Journal of Medicine)*	72.406	Review	1,091	121.2	772	Yale University School of Medicine, New Haven, CT (United States)
39	Summers et al, 1979[58]	National Cooperative Crohn's Disease Study: results of drug treatment (*Gastroenterology*)	18.392	Clinical research	1,059	27.1	37	Division of gastroenterology, University of Iowa Medical Center, Iowa City, Virginia, (United States).
40	Satsangi, et al 2006[59]	The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications (*Gut*).	16.658	Report	1,054	87.8	7	Gstrointestinal Unit, Western General Hospital, University of Edinburg, (United Kingdom).
41	Elson, et al, 1995[60]	Experimental models of inflammatory bowel disease. (*Gastroenterology*).	18.392	Review	957	41.6	40	Department of Medicine, University of Alabama Hospital at Birmingham, AL, (United States).

42	Greenstein et al, 1976[61]	The extra-intestinal complications of Crohn's disease and ulcerative colitis: a study of 700 patients. *Medicine (Baltimore)*.	1.804	Review	945	22.5	10	Department of Surgery, Mount Sinai School of Medicine and the City University of New York, New York, (United States.)
43	Fujino et al, 2003[62]	Increased expression of interleukin 17 in inflammatory bowel disease. (*Gut*).	16.658	Basic research	931	62.1	12	Shiga University of Medical Science, Seta-Tukinowa, Otsu, (Japan).
44	Sartor, 2008[63]	Microbial influences in inflammatory bowel diseases. (*Gastroenterology*).	18.392	Review	925	92.5	44	Department of Medicine, Center for Gastrointestinal Biology and Disease, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, (United States).
45	Manichanh et al, 2006[64]	Reduced diversity of faecal microbiota in Crohn's disease revealed by a metagenomic approach. (*Gut)*.	16.658	Basic research	913	76.1	13	Unité d'Ecologie et de Physiologie du système Digestif, INRA-UEPSD, 78350 Jouy-en-Josas, (France)
46	Fuss et al, 1996[65]	Disparate CD4+ lamina propria (LP) lymphokine secretion profiles in inflammatory bowel disease. Crohn's disease LP cells manifest increased secretion of IFN-gamma, whereas ulcerative colitis LP cells manifest increased secretion of IL-5. *(Journal of Immunology*)	4.856	Basic research	893	40.6	68	National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, (United States)
47	Rutgeerts	Predictability of the postoperative	18.392	Clinical	884	31.6	50	Department of Medicine,

	et al, 1990[66]	course of Crohn's disease. (*Gastroenterology*).		research				University Hospital Gasthuisberg, University of Leuven, (Belgium).
48	Present et al, 1980[67]	Treatment of Crohn's disease with 6-mercaptopurine. A long-term, randomized, double-blind study. *(New England Journal of Medicine)*	72.406	Clinical research	874	23.0	1150	Lenox Hill Hospital and the Mount Sinai School of Medicine of City University of New York (United States)
49	Swidsinski et al, 2002[68]	Mucosal flora in inflammatory bowel disease. (*Gastroenterology*).	18.392	Basic research	873	54.6	52	Charité Humboldt Universität, Berlin, (Germany).
50	Vandullemen et al, 1995[69]	Treatment of Crohn's disease with anti-tumor necrosis factor chimeric monoclonal antibody (cA2). **(***Gastroenterology*).	18.392	Clinical research	871	37.9	53	Academic Medical Center, Amsterdam, (The Netherlands).

[a] The search was conducted in April, 2018 by searching the Web of Knowledge.
[b] The average citation per year = total number of citation / number of years since publication.
[c] This ranking was identified by searching each journal for a top-cited article and identifying its ranking based on the number of citations received in comparison to the number of citations received by other articles published in that journal.

BMJ Open

What can we learn from top-cited articles in inflammatory bowel disease? A bibliometric analysis and assessment of the level of evidence

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-021233.R2
Article Type:	Research
Date Submitted by the Author:	31-May-2018
Complete List of Authors:	Azer, Samy; King Saud University, Medical Education; Australian Professional Teaching, Azer, Sarah; St Vincent Hospital
Primary Subject Heading:	Gastroenterology and hepatology
Secondary Subject Heading:	Gastroenterology and hepatology, Medical education and training, Medical publishing and peer review
Keywords:	Inflammatory bowel disease (IBD), Ulcerative colitis (UC), Crohn's disease (CD), Bibliometric analysis, Top-cited articles, Quality of evidence

Amended version

What can we learn from top-cited articles in inflammatory bowel disease? A bibliometric analysis and assessment of the level of evidence

Samy A. Azer[1] and Sarah Azer[2]

Dr Azer is a Consultant Gastroenterologist and Professor of Medical Education and the chair of Curriculum Development and Research Unit, College of Medicine, King Saud University, Riyadh, Saudi Arabia[1]

Registrar, St Vincent Hospital, University of Melbourne, Victoria, Australia[2]

Correspondence and requests for reprints should be addressed to:
Professor Samy Azer
Curriculum Development and Research Unit,
College of Medicine, King Saud University
P O Box 2925, Riyadh 11461
Saudi Arabia
Telephone: (966) 11-4699178
Fax: (966) 11-4699174

Email:azer2000@optusnet.com.au

SHORT TITLE: Top-cited Inflammatory Bowel Disease

ABSTRACT

Background and Objectives: Despite increasing number of publications in inflammatory bowel disease (IBD) no bibliometric analysis has been conducted to evaluate the significance of highly-cited articles. Our objectives were to identify the top-cited articles in IBD, assessing their characteristics, and determining the quality of evidence provided by these articles.

Design and outcome measures: IBD and related terms were used in searching the Web of Science to identify English language articles. The 50 top-cited articles were analyzed by year, journal impact factor (JIF), authorship, females in authorship, institute, country, and grants received. The level of evidence was determined using the Oxford Centre for Evidence-Based Medicine guidelines.

Results: The number of citations varied from 871 to 3555 with a total of 74638, and a median 1339.50, (IQR= 587). No correlations were found between the number of citations and number of years since publication (r=0.042, p=0.771), JIF (r= 0.186, p=0.196), number of authors (r= 0.061, p=0.674), females in authorship (r=0.064, p=0.661), number of institutes (r= 0.076, p=0.602), number of countries (r= 0.101, p=0.483), or number of grants (r= - 0.015, p=0.915). The first authors were from the United States (n= 24), United Kingdom (n= 6), Germany (n=5), France (n=5), Belgium (n=3), and Canada (n=3). The levels of evidence were 12 articles at level 1b, 9 articles at level 3a, and 15 articles at level 3b and fewer were at other levels.

Conclusions: Research papers represented 66% of articles. The majority of items have reasonably high levels of evidence; which may have contributed to the higher number of citations. The study also shows a gender gap in authorship in this area.

Key words

Inflammatory bowel disease (IBD), Ulcerative colitis (UC), Crohn's disease (CD), Top-cited articles, Bibliometric analysis, Quality of evidence, Number of authors, Female authors, Grants/funds, Institutes, Countries.

Strengths and limitations of the study

- More than one method was used in searching the Web of Science to maximize the yield of the search.
- The articles represent a historic perspective on key discoveries in the area of inflammatory bowel disease.
- A number of characteristics including journal impact factor, number of authors, number of females in authorship, number of institutes, number of countries involved, and grants received have been studied against citations received.
- The level of evidence for each article has been evaluated.
- The search was limited to articles in the English language, raising the possibility of failing to include top-cited articles in other languages.

INTRODUCTION

The number of citations received by an article has been used for several years by universities and grant funding bodies in assessing the quality of research produced by researchers, ranking research performance and in making decisions regarding professional promotion and grant applications [1-4]. Thomson Reuters gather the names of these authors in the Highly Cited Researchers database where they are acknowledged for the quality of their work and the size of their research input in a particular area [5]. Although the number of citations cannot explain why researchers cited a particular paper nor reflect the quality of the research and the outcomes identified in a manuscript, the number of citations and the reputation of contribution to research in a particular field cannot be ignored. This is particularly important when there is a pattern of consistency and progressive input into a discipline over years (a life experience), and a demonstration from publication records and citation history of collaboration with other researchers from other institutes at local and international levels. Hence the credits given to an author or a group of authors and the impact of the work in a particular area can be proportionally related to the citation records [6]. The greater the citation history over years, the more influential they are in their specialty [7]. In this study, we hypothesized that examining the most cited in IBD may provide more insight into the significance of these articles and the level of evidence they present [8]. Considering the fact that there are over 91,000 articles on IBD in the literature as per our preliminary search of Web of Science, it is important to consider the characteristics of highly cited articles.

Inflammatory bowel disease comprises ulcerative colitis (UC) and Crohn's disease (CD); both pursue a relapsing and remitting course over years. While the two diseases share several similarities, they have a number of differences with regard to structures involved, pathogenesis, clinical presentation, and management approaches. UC was first reported briefly in mid 1800 [9], while CD was reported in *the Journal of the American Medical Association (JAMA)* later by Crohn, Ginzburg and Oppenheimer in 1932 [10]; describing it as a chronic inflammatory bowel disease of the ileum. Later, it was discovered that CD can involve any part of the gastrointestinal tract from the lips to the anal margin but the ileocolonic disease represents the common presentation. Since then both diseases have been extensively researched in their different aspects.

We assumed that these articles may be a cornerstone in IBD, and may enable researchers in understanding a range of aspects related to IBD. Therefore, the bibliometric analysis of these articles including journal impact factor, authorship, females in authorship, institute, country and grants received may explain key features of a successful or influential article in IBD. The aims of the present research were (1) identify the top-cited articles in IBD, and analyze their characteristics and (2) assess the quality of evidence provided by articles.

METHODS

Study Design

The Web of Science database was searched for the identification of the top-cited articles and tracking the citation records of each publication. Although Scopus and

Google Scholar also provide citation records, it was decided to limit the search to Web of Science database. Compared to other databases, the Web of Science is regularly updated and the 2015 Journal Citation Reports (JCRs) included more than 6,500 journals across 150 disciplines. Although Google Scholar database is freely available, it was not used because it is difficult to search, and it cites textbooks, monographs, conference proceedings, as well as non-peer reviewed publications [11]. It is also not possible to track the yearly records of citations attracted by each article since publication. Scopus database was not used because it is not extensive in its coverage and its records only go back to 1996 [12]. Furthermore, several other researchers have used Web of Science to identify top-cited articles [13,14,15]

To achieve the aims of this study we planned to identify the highly cited articles in IBD and assess if there were any correlation between the number of citations and any of the parameters characterizing these highly cited articles. We also aim to grade each article against the level of evidence hierarchy as per the Oxford Centre for Evidence-Based Medicine (OCEBM-2011 Levels of Evidence and the accompanying Table of Evidence Glossary) [16,17].

Searching the Web of Science database

On 15 and 16 April 2018,the authors searched the Web of Science database to retrieve top-cited articles in inflammatory bowel disease. The search words used were the following: “Inflammatory bowel disease”, “Ulcerative colitis”, “Crohn’s disease”, ‘IBD”, “Experimental colitis”, “Animal models for Colitis”, “Animal models for inflammatory bowel disease”, “Pathology IBD”, “Pathology UC”, Pathology CD”,

"Pathogenesis IBD", "Pathogenesis UC", "Pathogenesis CD", "Treatment IBD", "Treatment UC", "Treatment CD", "Investigation IBD" and "Regional ileitis". To increase the yield of the search, we used the full terms- inflammatory bowel disease, ulcerative colitis, and Crohn's disease for the abbreviations IBD, UC, and CD, respectively. These search words were identified from the terminology used in gastroenterology journals and the proceedings of major conferences on inflammatory bowel disease and gastroenterology such as the British Society of Gastroenterology (BSG), the American Gastroenterological Association (AGA), American College of Gastroenterology (ACG), Canadian Association of Gastroenterology (CAG), Scottish Society of Gastroenterology (SSG), and Gastroenterological Society of Australia (GESA). For each search word, the results were arranged using a link on the Web of Science system, "sort-by" – "Time Cited- highest to lowest". The results showed the articles organized in a descending order with the articles most frequently cited at the top. A copy of the results was printed out for further analysis. The findings from each search word were then arranged on one Excel sheet (Microsoft Excel 2010, Microsoft Corp, Redmond, WA) in descending order based on the number of citations. Duplicate articles and articles not in the English language were excluded. In addition to the absolute number of citations, we calculated the average citations per year for each article. The average number of citations per year is the ratio calculated from the number of citations obtained by an article divided by the number of years since publication [18].

Using the above mentioned search words, we conducted another search of major gastroenterology journals and the 2016-JCR under the category "Gastroenterology

and Hepatology". This category comprises 76 journals at the time of conducting the search; of these seven journals were in languages other than English and were not searched. Gastroenterology journals publishing articles not in the English language were excluded because neither the author nor the assistant researchers are competent in the Spanish, Italian or German languages. Since the language recommended by the journal publishing this work is English and its readers are most likely interested in research publications in the English language, we decided not to search these journals.

Interestingly, after identifying the list of top-cited articles in IBD, and again checking these seven non-English journals, none had a paper with a citation higher than the paper ranked number 50 on the list.

These key words were also used in searching the websites of major general medicine, surgery and research journals including the *New England Journal of Medicine, Lancet, the British Medical Journal, the Journal of the American Medical Association, Annals of Internal Medicine, Archives of Medicine, PLOS Medicine, Annals of Surgery, Archives of Surgery, British Journal of Surgery, American Journal of Surgical Pathology, Nature, Science, Nature Reviews Cancer, Nature Genetics, Nature Medicine, Cell, Nature Reviews Microbiology, Immunity, Nature Reviews Immunology, Nature Reviews Molecular Cell Biology, and Journal of Immunology.*

A list identifying the 50 top-cited articles was reviewed again and checked regarding authorship, year of publication, title of the article, journal publishing the work, the Journal Impact Factor (JIF) at the time of the search, the number of citations and the institution of the first author (Appendix 1).

Inclusion And Exclusion Criteria

The inclusion criteria were: papers focusing on IBD (ulcerative colitis or Crohn's disease) written in the English language. The exclusion criteria were: (i) articles on inflammatory bowel disease in languages other than English, (ii) articles that focused on other diseases and inflammatory bowel disease was not the main focus, and (iii) studies that focus on other types of colitis and not inflammatory bowel disease.

Assessing Articles

The full text of the identified 50-top cited articles was obtained and a copy was given to each researcher. The following information was collected for each article: (i) the authors' names, the number of authors, their affiliations, and the number of females contributing to authorship, (ii) the number of institutes involved in the publication, (iii) the city and country of the origin of the publication, (iv) the total number of citations obtained up to the day of searching the database, and the number of yearly citations since publication, (v) the year of publication and the calculated number of years since publication, and (vi) the number of funds/grants stated in the publication and the Web of Science.

We have not used the classification provided by the Web of Science regarding study type because we noted that the Web of Science groups publications as original research, articles, practical guides and reviews and identifies them as articles or reviews. For consistency and the purpose of this study, the top-cited articles were grouped into four types - article, review paper/meta-analysis, report, and research. A definition of each type is given in the glossary (Appendix 2). Two researchers

independently allocated each of the top-cited articles under its type as per the definition given. Any differences between the researchers were discussed in a meeting until a decision was reached.

The topics covered by the top-cited articles were identified by each researcher independently and were discussed in a meeting to harmonize the grouping into a logical, simple and practical way. Articles that covered more than one topic were classified on the basis of the aim of the study and the main outcomes. For other evaluations of an article including the number of authors, the number of females represented in authorship, the number of institutes, and countries contributing to the work, and the number of grants/funds received we checked the original article for such details. Institute was defined as the university where an author belonged. If an author belonged to two universities, this was considered to be two different institutes. Regarding the identification of females in the authorship we noted that several journals use abbreviations of the first and second name rather than the full name. In order to identify the females in these articles we tried to search the Google database to find the university, personal website of the author, their LinkedIn or ResearchGate accounts. We also tried to identify them by searching the Google Scholar database and identify their account, where we can find other publications under their name and the full first name. In two papers, despite our efforts, we failed to identify the gender of five authors and we contacted the corresponding authors. We received a response from one correspondence, making us unable to identify the gender of three authors in the second paper.

Evaluating the Journals

The publishing journals of the top 50 articles in IBD were identified and evaluated in regard to the following: (i) the 2016-Journal Impact Factor (JIF) of each journal, and (ii) the ranking order of each article in comparison to other articles published in that journal. This was based on the number of citations obtained in comparison to the citation numbers received by other articles published in the journal. For example, an article ranked number one, in its publishing journal, means that the article received the highest number of citations in comparison to all other articles published in that journal. This evaluation aimed at assessing the position order of articles identified among the 50 top-cited articles in IBD in regard to their ranking among other articles published in the journal. Such assessment highlights the significance of the inflammatory bowel disease articles among other topics published in gastroenterological journals as well as general medicine journals such as *The New England Journal of Medicine, The Lancet, the British Medical Journal, Medicine,* and top research journals such as *Nature, Nature Genetics, Science, Cell,* and top journals in immunology *such as Nature Reviews Immunology* (Appendix 1).

Assessing Level of Evidence

Two researchers independently used the Oxford Centre for Evidence-Based Medicine (OCEBM-2011 Levels of Evidence and the accompanying Table of Evidence Glossary) [16,17] to rank each article regarding level of evidence. In 1998 this hierarchical of evidence was first produced to make the process of finding relevant evidence feasible. Since then the levels have been reviewed and amended, and the

version used in this research is the currently available version. This evaluation aimed at identifying the level of evidence of each article and assessing whether the highly cited articles have received higher scores in regard to level of evidence as per the Oxford hierarchy. The assessment required extensive review of each article since quality descriptors exist for different types of studies and level of evidence vary depending on therapeutic, prevention, prognostic, diagnostic, or prevalence design [13,14].

Statistical Analysis

Pearson's correlation coefficient (r) was calculated to determine if the high citation numbers obtained was related to the age of the article. Other correlations were between the number of citations and the number of authors, the percentage of females in authorship, the number of institutes, the number of countries involved, the number of grants received, and the Journal Impact Factor (JIF) of the journals in which articles were published. Because of the assumption that researchers usually cite recently published articles, it was decided to compare the mean yearly citations received of articles published before the year 2000 and compare them with those published after the year 2000. All analyses were conducted using SPSS Software (IBM SPSS Statistics Premium version 22.0 for Mac OS-SPSS Inc., Chicago, IL, USA) and the results were reported at total, mean, median, IQR, and percentage. The inter-rater agreement between evaluators was calculated using the Fleiss kappa scale [19].

Patient and Public involvement

This study did not involve patients or the public.

RESULTS

Top-Cited Papers Identified

The 50 top-cited articles in IBD identified by searching the Web of Science [20-69] have been summarized in Appendix 1. The articles are listed in an order from 1 to 50 with the highest absolute citation number is ranked 1 and the article with the lowest citation ranked 50 as per the day of the search.

Table 1 summarizes the year of publication and article type. The articles were published over 57 years (from 1955 to 2012). During the period from 1955 to 1976, only 3 articles (6%) were published. However, the number increased significantly from 1977 to 1994 making a total of 12 (24%) articles. The number of publications increased significantly to 35 (70%) during the years from1995 to 2012. No correlation was found between the number of citations of these papers and the number of years since published (Pearson correlation (r) = 0.042, p = 0.771). To assess if there were differences between old articles (published before the year 2000) and those published after the year 2000, it was decided to study the mean number of citations received by top-cited articles in each year after their publications. The year 2000 was taken as a midpoint for comparison because the majority of articles identified were published in the period after the year 1986, and hence the year 2000 could represent such point. As shown from Figures 1A and 1B, the mean numbers of citations were higher for articles published after the year 2000 compared to those published before

the year 2000. Approximately one fourth of the top-cited papers were reviews/meta-analysis (n= 14, 28%), two-thirds were research papers (n= 33, 66%), and the remaining were an article (n= 1, 2%) and two reports (n=2, 4%).

Table 2 summarizes the distribution of IBD topics covered in the top-cited articles. These can be summarized as follows: epidemiology and prevalence (n=2, 4%), Crohn's disease genetic susceptibility and NOD2 mutation (n=6, 12%), Animal models (n= 5, 10%), Pathogenesis of IBD (n= 15, 30%), classification and index of disease activity (n= 5, 10%), risk of developing colorectal cancer (n= 2, 4%), extra-intestinal complications (n= 1, 2%), Infliximab in Crohn's disease (n= 6, 12%), corticosteroids in ulcerative colitis (n=1, 2%), drug treatment and cyclosporine in ulcerative colitis (n= 2, 4%), adalimumab in Crohn's disease (n=1, 2%), 5-aminosalicylic acid in ulcerative colitis (n=1, 2%), 6-mercaptopurine in Crohn's disease (n=1, 2%), and monoclonal antibiotics, and anti-tumour necrosis factor in Crohn's disease (n=2, 4%). As shown in Appendix 1, 14 (28%) were basic research and 19 (38%) were clinical research. The level of evidence is discussed later in the results.

The articles were published in the following journals: *New England Journal of Medicine* (n= 12, 24%), *Gastroenterology* (n= 12, 24%), *Nature* (n=4, 8%), *Nature Genetics* (n=4, 8%), *The Lancet* (n= 2, 4%), *Proceedings of the National Academic of Sciences of the United States of America* (n=2, 4%), *Cell* (n= 2, 4%), and *Gut* (n= 4, 8%). See Table 3 for more details about the journals publishing these articles.

Looking at the ranking of the top-cited articles in IBD in the journals they were published in could provide a better picture about the influence of these articles. This influence would be clearly demonstrated when the journal has a relatively higher Journal Impact Factor. The ranking is based on the number of citations received by an article compared to the number of citations received by other articles that were published in that journal. The article by Best et al (1976) [23] is ranked number 4 in the list, and also ranked number 2 among all articles published in *Gastroenterology* (2016-JIF = 18.392). The article by Eaden et al [41] is ranked number 22 in the list and also ranked number 1 among all articles published in *Gut* (2016-JIF= 16.658). The ranking of other articles in List and their rankings in the journals in which they were published are shown in Appendix 1.

The first authors of the top-cited articles were from the United States (n= 24, 48%), the United Kingdom (n=6, 12%), Germany (n= 5, 10%), France (n= 5, 10%), Belgium (n= 3, 6%), Canada (n= 3, 6%), Japan (n=2, 4%), Sweden (n=1, 2%), and the Netherlands (n=1, 2%).

Table 4 summarises the 70 authors who have published two papers or more in the top-cited IBD. Of these 18 authors were the first author and coauthors of more than two papers in total, all the remaining, 52 were coauthors of more than two papers. Top authors were Rutgeers, P (n=10 papers), Targan, SR (n=8 papers), Schreiber, S (n=7 papers), Cho, JH (n=7 papers), Colombel, JF (n=7 papers), Hanauer, SB (n=7 papers), Silverberg, MS (n=6 papers), and each of the following authors have 5 papers: Podolsky, DK, Rioux, JD, Daly MJ, Steinhart, AH, Rotter, JI, Schumm, LP, Taylor, KD, Vermeire, S, Duerr, RH, and Regueiro, M.

The leadership of universities and institutes that have contributed to the creation of these publications were Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, the United States, Mount Sinai School of Medicine, New York, the United States, Mayo Clinic, Rochester, Minnesota, the United States, Cedars-Sinai Medical Center, Los Angeles, California, the United States, University of Chicago Medical Center, Chicago, Illinois, the United States, University of Pittsburgh, Pittsburgh, Pennsylvania, the United States, University Hospital of Cleveland Case Western Reserve University School of Medicine, Ohio, the United States, Wellcome Trust Centre for Human Genetics, University of Oxford, Roosevelt Drive, Oxford, the United Kingdom, Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Cambridge, the United Kingdom, and Institute of Virology and Immunobiology, University of Würzburg, Germany. See Appendix 1 for more detail.

Characteristics of the Top-Cited Articles

These articles were created by 667 authors, median 7.0, minimum 1, maximum 106, IQR 9.5; the females in authorship were 111, median 1.0, minimum 0, maximum 20, IQR 2. It is worth mentioning here that it was difficult to identify the gender of some authors in two papers because the full first and middle names were not shown and it was difficult to find more information or clues to make a decision. We contacted the corresponding authors of these two articles; we received information for one article but we had no response from the corresponding author of the second article. Thus the gender of three authors could not be identified. The number of institutes involved were 436, median 3.0, minimum 1, maximum 88, IQR 9; the countries involved were 141, median 1.0, minimum 1, maximum 16, IQR 2.75; and the number of grants/funds

were 328, median 1.0, minimum 0, maximum 94, IQR 2.75. No correlations were found between the number of citations and the Journal Impact Factor (JIF) (Pearson correlation (r) = 0.186; p=0.196), the number of authors (r =0.061; p= 0.674), number of females in authorship (r =0.064; p= 0.661), the number of institutes involved (r =0.076; p= 0.602), the number of countries involved (r =0.101; p= 0.483), and the number of grants received (r= - 0.015; p=0.915).

Level of Evidence

Table 5 summarizes the grading of articles according to the Oxford Center for evidence-based medicine. The table shows that most articles were graded at levels 1b and 3a and 3b evidence (12 papers had level 1b evidence, 9 papers at level 3a, and 15 papers had level 3b evidence). Five articles had a level of evidence of 4 and no article at level 5. The remaining articles were at levels 1a, 2a, 2b and 2c. The overall agreement between the evaluators was acceptable; Fleiss kappa= 0.8252; 95% CI 0.79-0.85.

DISCUSSION

This study aimed at identifying the characteristics of the top 50 most frequently cited papers in IBD and assessing the quality of evidence provided. The papers covered a number of key topics related to IBD including: epidemiology and prevalence, pathogenesis and genetic susceptibility, animal models, clinical classification and indices of disease activity, risks of developing colorectal cancer, extra-intestinal complications, and use of infliximab, adalimumab, monoclonal antibodies and anti-tumour necrosis factor, and 6- mercaptopurine in CD, and use of 5-aminosalicylic

acid, corticosteroids, and cyclosporine in treating UC. While these topics cover key issues related to IBD, topics related to molecular biology, surgical management, patient education, nutritional aspects, radiological and other investigations were not represented in the top-cited articles list [70,71].

The assessment of the characteristics of the top 50 highly cited articles identified in this study reveals the following:

First, the lack of correlations between the number of citations and the number of years since publication may indicate that the high-citations is not caused by ageing of these articles. In fact, only 15 articles (30%) were published in the period from 1955 to 1994 (39 years), while the majority, 35 (70%) were published in the last 17 years. No papers were published after 2012. This article also shows that the mean number of citations of articles published before the year 2000 were much lower than those of articles after the year 2000. This may be related to the tendency of researchers to cite recently published research and new findings [72] and papers that they have read [18]. Also the number of citations and the papers' age might be attributed to the changes in citation behaviour over time. For example, in the 50s and 60s, the authors used to cite fewer papers compared to what was practiced over the last 20 years [73]. The higher citations have been found to be the strongest predictor of current online availability after a long time since publication. Therefore, the higher citation could be a protective mechanism for continued availability of a publication despite aging and hence continuing citation [74].

Second, the lack of a correlation between the number of citations and the Journal Impact Factor (JIF). The JIF has been widely used in ranking and evaluating journals. It stands as a proxy for the relative importance of a journal with its field [75]. Although the top-cited articles identified were published in journals with high impact factors, the impact factors of some journals were not necessarily the highest in their fields. For example, *Laboratory Investigation, Canadian Journal of Gastroenterology and Hepatology, Medicine (Baltimore), and Journal of Immunology* had JIFs in the range of 1.804 to 4.857. With this information in mind one may postulate that the high JIF is not necessarily related to the higher citation numbers received. Two recent works showed that the JIF is not an accurate indicator of citations an average article receives, articles published in low impact factor journals can still be highly cited and vice versa [76,77].

Third, the study showed negative correlation between the number of citations and the number of authors, the number of female authors, or the number of institutes. The number of authors and females in authorship varied from one to 106 and from zero to 20, respectively. Also the number of institutes involved varied from one to 88. The question that can be raised in this regards; are we expecting an increase in number of citations as the number of authors or the number institutes involved increased? The work of Garcia-Aroca et al [78] shows that collaboration between authors increases their impact and increases citation rates. However, they showed that publishing in English in certain journals and collaborating with certain authors and institutes increase the visibility of the manuscripts published on the subject. Hence it is the quality of collaboration rather than the absolute number of these parameters.

Recently Tanner-Smith and Polanin showed that studies conducted by more established authors (have higher h-indices) and reported in more prestigious journal outlets are more likely to be cited by other scholars, even after controlling for various proxies of study quality [79].

Although the proportion of women in authorship of original research in the United States in general has significantly increased in the last four decades, women still compose a minority of the authors of original research [80]. In the field of gastroenterology, the percentage of the United States female physician authors of original research in the field has relatively increased over time, yet the senior author position remains lower than expected [81,82].

Fourth, the study showed no correlation between the number of citations and the number of funds/grants received. This finding is not surprising. Recently it was shown that too many of the United States authors of most influential papers in science do not receive NH funding [83]. Another group of researchers found no association between grant percentile ranking and grant outcome as assessed by number of top-10% articles per dollar million spent [84].

The United States, the United Kingdom, Germany, France, Belgium, and Canada contributed to the majority of these articles. The leadership of universities from these countries in gastrointestinal research particularly IBD is no surprise, top universities identified from this study were Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, the United States, Mount Sinai School of Medicine, New York, the United States, Mayo Clinic, Rochester, Minnesota, the United States,

Cedars-Sinai Medical Center, Los Angeles, California, the United States, University of Chicago Medical Center, Chicago, Illinois, the United States. Other institutes and research centres that had lead these studies are shown in Appendix 1.

All articles were published in the English language. The most productive journals were the *New England Journal of Medicine*, and *Gastroenterology* with a total of 24 articles. Others were *Nature, Nature Genetics, the Lancet, and Proceedings of the National Academy of Sciences of the United States of America, Cell, Gut, British Medical Journal, Science*, and *Nature Reviews Immunology* making a total of 20 articles. While these journals have a relatively high JIF, other journals published one article each and had a relatively low JIF compared to journals included in their categories. For example*, Human Pathology* listed number 22 under the category of Pathology, and *Canadian Journal of Gastroenterology and Hepatology*, listed number 74 under the category Gastroenterology and Hepatology. The high level of evidence as outlined in the top-cited articles could be an important contributing factor to the higher number of citations received by these articles [85].

After the submission of our study we came across the study by Connelly et al [86] on top 100 articles on IBD. While they indicated that their findings covered the period between 1955-2012 which is consistent with our findings, our study has examined a range of parameters including correlation of citation numbers with JIF, number of years since publication, number of authors, females in authorship, institutes, and number of countries and grants, which were not addressed by Connelly's work. Also we have examined the level of evidence of highly cited articles.

CONCLUSIONS

Our list of top-cited articles in IBD highlights key contributions that based the foundation of research and examination of different aspects of the disease over 57 years. This scholarly contribution came from universities and research centres in the United States, the United Kingdom, Germany, France, Belgium and Canada. The findings may be consistent with the concept that it is not the absolute number of collaborators that makes an impact on the citation number or the influence of a publication but rather the quality of such collaboration with regard to the researchers involved, their institutes, and the ongoing contribution to the advances of research. The relatively small number of females in the authorship reflects the gender gap and the fact that women still compose a minority of the authors of original research and reviews in gastroenterology. The higher level of evidence demonstrated in most top-cited articles may have contributed to the higher number of citations received by these articles.

Acknowledgement: The author would like to thank Diana Sanad for her assistance and reviewing the manuscript.

Funding support: This work was funded by the College of Medicine, Research Center Deanship of Scientific Research, King Saud University, Riyadh, Saudi Arabia.

Ethical approval: Not applicable to this study.

Contributorship Statement: SAA and SA shared equally the different roles and responsibilities to complete the submitted article including, the research idea, the search of databases, the evaluation of data collected, the statistical analysis, the interpretation of findings, the creation of tables and figures, writing the manuscript and the approved the final version of the manuscript.

Competing interests: There are no competing interests for any author

Provenance and peer review: Not commissioned; externally peer reviewed

Data sharing: No further data available to share

REFERENCES

1. MacMaster FP, Swansburg R, Rittenbach K. Academic Productivity in Psychiatry: Benchmarks for the H-Index. Acad Psychiatry. 2017 Apr 18. [Epub ahead of print]

2. Susarla HK, Dhar V, Karimbux NY, Tinanoff N. Do Standard Bibliometric Measures Correlate with Academic Rank of Full-Time Pediatric Dentistry Faculty Members? J Dent Educ. 2017 Apr;81(4):427-432.

3. Milone MT, Bernstein J. On Track to Professorship? A Bibliometric Analysis of Early Scholarly Output. Am J Orthop (Belle Mead NJ). 2016 Mar-Apr;45(3):E119-23.

4. Azer SA, Holen A, Wilson I, Skokauskas N. Impact factor of medical education journals and recently developed indices: Can any of them support academic promotion criteria? J Postgrad Med. 2016 Jan-Mar;62(1):32-39. doi: 10.4103/0022-3859.173202.

5. Jones AW. Impact of JAT publications 1981-2003: the most prolific authors and the most highlycited articles. J Anal Toxicol. 2004 Oct;28(7):541-545.

6. Patsopoulos NA, Ioannidis JP, Analatos AA. Origin and funding of the most frequently cited papers in medicine: database analysis. BMJ 2006;332:1061–1064.

7. Garfield E. Fortnightly review: how can impact factors be improved? BMJ 1996;313:411–413.

8. Azer SA. Exploring the Top-Cited and Most Influential Articles in Medical Education. J Contin Educ Health Prof. 2016 Summer;36 Suppl 1:S32-41.

9. Wilks S. Morbid appearances in the in- testines of Miss Bankes. Med Times Gazette 1859;2:264-265.

10. Crohn BB, Ginzburg L, Oppenheimer GD. Regional ileitis: a pathologic and clinical entity. JAMA 1932;99:1323-1329.

11. Van Noorden R, Maher B, Nuzzo R. The top 100 papers. Nature. 2014;514(7524):550.

12. Kulkarni AV, Aziz B, Shams I, Busse JW. Comparisons of citations in Web of Science, Scopus, and Google Scholar for articles published in general medical journals. JAMA. 2009 Sep 9;302(10):1092-1096.

13. Powell AGMT, Bevan V, Brown C, Lewis WG. Altmetric Versus Bibliometric Perspective Regarding Publication Impact and Force. World J Surg. 2018 Mar 13.

14. Yi F, Ma J, Ni W, Chang R, Liu W, Han X, Pan D, Liu X, Qiu J. The top cited articles on glioma stem cells in Web of Science. Neural Regen Res. 2013 May 25;8(15):1431-8. doi: 10.3969/j.issn.1673-5374.2013.15.011.

15. Mu Y, Li N, Guan L, Wang C, Shang S, Wang Y. Therapies for children with cerebral palsy: A Web of Science-based literature analysis. Neural Regen Res. 2012 Nov 25;7(33):2632-9. doi: 10.3969/j.issn.1673-5374.2012.33.009.

16. Azer SA. Top-Cited Articles in Problem-Based Learning: A Bibliometric Analysis and Quality of Evidence Assessment. J Dent Educ. 2017 Apr;81(4):458-478.

17. Oxford Centre for Evidence-based Medicine – Levels of Evidence (March 2009). Available at: http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009 [Accessed 20 May 2017].

18. Azer SA. The top-cited articles in medical education: a bibliometric analysis. Acad Med 2015;90(8):1147-1161.

19. D'Antiga L, Betalli P, De Angelis P, et al. Interobserver agreement on endoscopic classification of oesophageal varices in children. J Pediatr Gastroenterol Nutr 2015;61(2):176-181.

20. Hugot JP, Chamaillard M, Zouali H, Lesage S, Cézard JP, Belaiche J, Almer S, Tysk C, O'Morain CA, Gassull M, Binder V, Finkel Y, Cortot A, Modigliani R, Laurent-Puig P, Gower-Rousseau C, Macry J, Colombel JF, Sahbatou M, Thomas G. Association of NOD2 leucine-rich repeat variants with susceptibility to Crohn's disease. Nature. 2001 May 31;411(6837):599-603.

21. Ogura Y, Bonen DK, Inohara N, Nicolae DL, Chen FF, Ramos R, Britton H, Moran T, Karaliuskas R, Duerr RH, Achkar JP, Brant SR, Bayless TM, Kirschner BS, Hanauer SB, Nuñez G, Cho JH. A frameshift mutation in NOD2 associated with susceptibility to Crohn's disease. Nature. 2001 May 31;411(6837):603-6.

22. Kühn R, Löhler J, Rennick D, Rajewsky K, Müller W.Interleukin-10-deficient mice develop chronic enterocolitis. Cell. 1993 Oct 22;75(2):263-74

23. Best WR, Becktel JM, Singleton JW, Kern F Jr. Development of a Crohn's disease activity index. National Cooperative Crohn's Disease Study. Gastroenterology. 1976 Mar;70(3):439-44.

24. Hanauer SB, Feagan BG, Lichtenstein GR, Mayer LF, Schreiber S, Colombel JF, Rachmilewitz D, Wolf DC, Olson A, Bao W, Rutgeerts P; ACCENT I Study Group. Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial. Lancet. 2002 May 4;359(9317):1541-1549.

25. Podolsky DK. Inflammatory bowel disease. N Engl J Med. 2002 Aug 8;347(6):417-429.

26. Targan SR, Hanauer SB, van Deventer SJ, Mayer L, Present DH, Braakman T, DeWoody KL, Schaible TF, Rutgeerts PJ. A short-term study of chimeric monoclonal antibody cA2 to tumor necrosis factor alpha for Crohn's disease. Crohn's Disease cA2 Study Group. N Engl J Med. 1997 Oct 9;337(15):1029-35.

27. Xavier RJ, Podolsky DK. Unravelling the pathogenesis of inflammatory bowel disease. Nature. 2007 Jul 26;448(7152):427-434.

28. Truelove SC and Witts LJ. Cortisone in ulcerative colitis; final report on a therapeutic trial. Br Med J. 1955 Oct 29;2(4947):1041-1048.

29. Duerr RH, Taylor KD, Brant SR, Rioux JD, Silverberg MS, Daly MJ, Steinhart AH, Abraham C, Regueiro M, Griffiths A, Dassopoulos T, Bitton A, Yang H, Targan S, Datta LW, Kistner EO, Schumm LP, Lee AT, Gregersen PK, Barmada MM, Rotter JI, Nicolae DL, Cho JH. A genome-wide association study identifies IL23R as an inflammatory bowel disease gene. Science. 2006 Dec 1;314(5804):1461-1463.

30. Rutgeerts P, Sandborn WJ, Feagan BG, Reinisch W, Olson A, Johanns J, Travers S, Rachmilewitz D, Hanauer SB, Lichtenstein GR, de Villiers WJ, Present D, Sands BE, Colombel JF. Infliximab for induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2005 Dec 8;353(23):2462-76.

31. Present DH, Rutgeerts P, Targan S, Hanauer SB, Mayer L, van Hogezand RA, Podolsky DK, Sands BE, Braakman T, DeWoody KL, Schaible TF, van Deventer SJ. Infliximab for the treatment of fistulas in patients with Crohn's disease. N Engl J Med. 1999 May 6;340(18):1398-405.

32. Frank DN, St Amand AL, Feldman RA, Boedeker EC, Harpaz N, Pace NR. Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. Proc Natl Acad Sci U S A. 2007 Aug 21;104(34):13780-13785

33. Jostins L, Ripke S, Weersma RK, Duerr RH, McGovern DP, Hui KY, Lee JC,

Schumm LP, Sharma Y, Anderson CA, Essers J, Mitrovic M, Ning K, Cleynen I, Theatre E, Spain SL, Raychaudhuri S, Goyette P, Wei Z, Abraham C, Achkar JP, Ahmad T, Amininejad L, Ananthakrishnan AN, Andersen V, Andrews JM, Baidoo L, Balschun T, Bampton PA, Bitton A, Boucher G, Brand S, Büning C, Cohain A, Cichon S, D'Amato M, De Jong D, Devaney KL, Dubinsky M, Edwards C, Ellinghaus D, Ferguson LR, Franchimont D, Fransen K, Gearry R, Georges M, Gieger C, Glas J, Haritunians T, Hart A, Hawkey C, Hedl M, Hu X, Karlsen TH, Kupcinskas L, Kugathasan S, Latiano A, Laukens D, Lawrance IC, Lees CW, Louis E, Mahy G, Mansfield J, Morgan AR, Mowat C, Newman W, Palmieri O, Ponsioen CY, Potocnik U, Prescott NJ, Regueiro M, Rotter JI, Russell RK, Sanderson JD, Sans M, Satsangi J, Schreiber S, Simms LA, Sventoraityte J, Targan SR, Taylor KD, Tremelling M, Verspaget HW, De Vos M, Wijmenga C, Wilson DC, Winkelmann J, Xavier RJ, Zeissig S, Zhang B, Zhang CK, Zhao H; International IBD Genetics Consortium (IIBDGC)., Silverberg MS, Annese V, Hakonarson H, Brant SR, Radford-Smith G, Mathew CG, Rioux JD, Schadt EE, Daly MJ, Franke A, Parkes M, Vermeire S, Barrett JC, Cho JH. Host-microbe interactions have shaped the genetic architecture of inflammatory bowel disease. Nature. 2012 Nov 1;491(7422):119-24.

34. Barrett JC, Hansoul S, Nicolae DL, Cho JH, Duerr RH, Rioux JD, Brant SR, Silverberg MS, Taylor KD, Barmada MM, Bitton A, Dassopoulos T, Datta LW, Green T, Griffiths AM, Kistner EO, Murtha MT, Regueiro MD, Rotter JI, Schumm LP, Steinhart AH, Targan SR, Xavier RJ; NIDDK IBD Genetics Consortium, Libioulle C, Sandor C, Lathrop M, Belaiche J, Dewit O, Gut I, Heath S, Laukens D, Mni M, Rutgeerts P, Van Gossum A, Zelenika D, Franchimont D, Hugot JP, de Vos M, Vermeire S, Louis E; Belgian-French IBD Consortium; Wellcome Trust Case Control Consortium, Cardon LR, Anderson CA, Drummond H, Nimmo E, Ahmad T, Prescott NJ, Onnie CM, Fisher SA, Marchini J, Ghori J, Bumpstead S, Gwilliam R, Tremelling M, Deloukas P, Mansfield J, Jewell D, Satsangi J, Mathew CG, Parkes M, Georges M, Daly MJ. Genome-wide association defines more than 30 distinct susceptibility loci for Crohn's disease. Nat Genet. 2008 Aug;40(8):955-962.

35. Loftus EV Jr. Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. Gastroenterology. 2004 May;126(6):1504-1517.

36. Fiocchi C. Inflammatory bowel disease: etiology and pathogenesis. Gastroenterology. 1998 Jul;115(1):182-205.

37. Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. Lancet. 1980 Mar 8;1(8167):514.

38. 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 Jan;142(1):46-54.

39. Riddell RH, Goldman H, Ransohoff DF, Appelman HD, Fenoglio CM, Haggitt RC, Ahren C, Correa P, Hamilton SR, Morson BC, et al. Dysplasia in inflammatory bowel disease: standardized classification with provisional clinical applications. Hum Pathol. 1983 Nov;14(11):931-968.

40. Okayasu I, Hatakeyama S, Yamada M, Ohkusa T, Inagaki Y, Nakaya R A novel method in the induction of reliable experimental acute and chronic ulcerative colitis in mice. Gastroenterology. 1990 Mar;98(3):694-702.

41. Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut. 2001 Apr;48(4):526-535.

42. Sokol H, Pigneur B, Watterlot L, Lakhdari O, Bermúdez-Humarán LG, Gratadoux JJ, Blugeon S, Bridonneau C, Furet JP, Corthier G, Grangette C, Vasquez N, Pochart P, Trugnan G, Thomas G, Blottière HM, Doré J, Marteau P, Seksik P, Langella P. Faecalibacterium prausnitzii is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. Proc Natl Acad Sci U S A. 2008 Oct 28;105(43):16731-16736.

43. Silverberg MS, Satsangi J, Ahmad T, Arnott ID, Bernstein CN, Brant SR, Caprilli R, Colombel JF, Gasche C, Geboes K, Jewell DP, Karban A, Loftus EV Jr, Peña AS, Riddell RH, Sachar DB, Schreiber S, Steinhart AH, Targan SR, Vermeire S, Warren BF. Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. Can J Gastroenterol. 2005 Sep;19 Suppl A:5A-36A

44. Sadlack B, Merz H, Schorle H, Schimpl A, Feller AC, Horak I. Ulcerative colitis-like disease in mice with a disrupted interleukin-2 gene. Cell. 1993 Oct 22;75(2):253-261.

45. Franke A, McGovern DP, Barrett JC, Wang K, Radford-Smith GL, Ahmad T, Lees CW, Balschun T, Lee J, Roberts R, Anderson CA, Bis JC, Bumpstead S, Ellinghaus D, Festen EM, Georges M, Green T, Haritunians T, Jostins L, Latiano A, Mathew CG, Montgomery GW, Prescott NJ, Raychaudhuri S, Rotter JI, Schumm P, Sharma Y, Simms LA, Taylor KD, Whiteman D, Wijmenga C, Baldassano RN, Barclay M, Bayless TM, Brand S, Büning C, Cohen A, Colombel JF, Cottone M, Stronati L, Denson T, De Vos M, D'Inca R, Dubinsky M, Edwards C, Florin T, Franchimont D, Gearry R, Glas J, Van Gossum A, Guthery SL, Halfvarson J, Verspaget HW, Hugot JP, Karban A, Laukens D, Lawrance I, Lemann M, Levine A, Libioulle C, Louis E, Mowat C, Newman W, Panés J, Phillips A, Proctor DD, Regueiro M, Russell R, Rutgeerts P, Sanderson J, Sans M, Seibold F, Steinhart AH, Stokkers PC, Torkvist L, Kullak-Ublick G, Wilson D, Walters T, Targan SR, Brant SR, Rioux JD, D'Amato M, Weersma RK, Kugathasan S, Griffiths AM, Mansfield JC, Vermeire S, Duerr RH, Silverberg MS, Satsangi J, Schreiber S, Cho JH, Annese V, Hakonarson H, Daly MJ, Parkes M. Genome-wide meta-analysis increases to 71 the number of confirmed

Crohn's disease susceptibility loci. Nat Genet. 2010 Dec;42(12):1118-1125.

46. Baert F, Noman M, Vermeire S, Van Assche G, D' Haens G, Carbonez A, Rutgeerts P. Influence of immunogenicity on the long-term efficacy of infliximab in Crohn's disease. N Engl J Med. 2003 Feb 13;348(7):601-608.

47. Colombel JF, Sandborn WJ, Reinisch W, Mantzaris GJ, Kornbluth A, Rachmilewitz D, Lichtiger S, D'Haens G, Diamond RH, Broussard DL, Tang KL, van der Woude CJ, Rutgeerts P; SONIC Study Group. Infliximab, azathioprine, or combination therapy for Crohn's disease. N Engl J Med. 2010 Apr 15;362(15):1383-1395.

48. Cooper HS, Murthy SN, Shah RS, Sedergran DJ. Clinicopathologic study of dextran sulfate sodium experimental murine colitis. Lab Invest. 1993 Aug;69(2):238-249.

49. Ekbom A, Helmick C, Zack M, Adami HO. Ulcerative colitis and colorectal cancer. A population-based study. N Engl J Med. 1990 Nov 1;323(18):1228-1233.

50. Schroeder KW, Tremaine WJ, Ilstrup DM. Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study. N Engl J Med. 1987 Dec 24;317(26):1625-1629.

51. Rioux JD, Xavier RJ, Taylor KD, Silverberg MS, Goyette P, Huett A, Green T, Kuballa P, Barmada MM, Datta LW, Shugart YY, Griffiths AM, Targan SR, Ippoliti AF, Bernard EJ, Mei L, Nicolae DL, Regueiro M, Schumm LP, Steinhart AH, Rotter JI, Duerr RH, Cho JH, Daly MJ, Brant SR. Genome-wide association study identifies new susceptibility loci for Crohn disease and implicates autophagy in disease pathogenesis. Nat Genet. 2007 May;39(5):596-604.

52. Sands BE, Anderson FH, Bernstein CN, Chey WY, Feagan BG, Fedorak RN, Kamm MA, Korzenik JR, Lashner BA, Onken JE, Rachmilewitz D, Rutgeerts P, Wild G, Wolf DC, Marsters PA, Travers SB, Blank MA, van Deventer SJ. Infliximab maintenance therapy for fistulizing Crohn's disease. N Engl J Med. 2004 Feb 26;350(9):876-85.

53. Colombel JF, Sandborn WJ, Rutgeerts P, Enns R, Hanauer SB, Panaccione R, Schreiber S, Byczkowski D, Li J, Kent JD, Pollack PF. Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: the CHARM trial. Gastroenterology. 2007 Jan;132(1):52-65.

54. Hampe J, Franke A, Rosenstiel P, Till A, Teuber M, Huse K, Albrecht M, Mayr G, De La Vega FM, Briggs J, Günther S, Prescott NJ, Onnie CM, Häsler R, Sipos B, Fölsch UR, Lengauer T, Platzer M, Mathew CG, Krawczak M, Schreiber S. A genome-wide association scan of nonsynonymous SNPs identifies a susceptibility variant for Crohn disease in ATG16L1. Nat Genet. 2007 Feb;39(2):207-211.

55. Bouma G, Strober W. The immunological and genetic basis of inflammatory bowel disease. Nat Rev Immunol. 2003 Jul;3(7):521-533.

56. Lichtiger S, Present DH, Kornbluth A, Gelernt I, Bauer J, Galler G, Michelassi F, Hanauer S. Cyclosporine in severe ulcerative colitis refractory to steroid therapy. N Engl J Med. 1994 Jun 30;330(26):1841-1845.

57. Abraham C, Cho JH. Inflammatory bowel disease. N Engl J Med. 2009 Nov 19;361(21):2066-2078.

58. Summers RW, Switz DM, Sessions JT Jr, Becktel JM, Best WR, Kern F Jr, Singleton JW. National Cooperative Crohn's Disease Study: results of drug treatment. Gastroenterology. 1979 Oct;77(4 Pt 2):847-869

59. Satsangi J, Silverberg MS, Vermeire S, Colombel JF. The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications. Gut. 2006 Jun;55(6):749-53.

60. Elson CO, Sartor RB, Tennyson GS, Riddell RH. Experimental models of inflammatory bowel disease. Gastroenterology. 1995 Oct;109(4):1344-1367.

61. Greenstein AJ, Janowitz HD, Sachar DB. The extra-intestinal complications of Crohn's disease and ulcerative colitis: a study of 700 patients. Medicine (Baltimore). 1976 Sep;55(5):401-412.

62. Fujino S, Andoh A, Bamba S, Ogawa A, Hata K, Araki Y, Bamba T, Fujiyama Y. Increased expression of interleukin 17 in inflammatory bowel disease. Gut. 2003 Jan;52(1):65-70.

63. Sartor RB. Microbial influences in inflammatory bowel diseases. Gastroenterology. 2008 Feb;134(2):577-594.

64. Manichanh C, Rigottier-Gois L, Bonnaud E, Gloux K, Pelletier E, Frangeul L, Nalin R, Jarrin C, Chardon P, Marteau P, Roca J, Dore J. Reduced diversity of faecal microbiota in Crohn's disease revealed by a metagenomic approach. Gut. 2006 Feb;55(2):205-211.

65. Fuss IJ, Neurath M, Boirivant M, Klein JS, de la Motte C, Strong SA, Fiocchi C, Strober W. Disparate CD4+ lamina propria (LP) lymphokine secretion profiles in inflammatory bowel disease. Crohn's disease LP cells manifest increased secretion of IFN-gamma, whereas ulcerative colitis LP cells manifest increased secretion of IL-

5. J Immunol. 1996 Aug 1;157(3):1261-1270.

66. Rutgeerts P, Geboes K, Vantrappen G, Beyls J, Kerremans R, Hiele M. Predictability of the postoperative course of Crohn's disease. Gastroenterology. 1990 Oct;99(4):956-963.

67. Present DH, Korelitz BI, Wisch N, Glass JL, Sachar DB, Pasternack BS. Treatment of Crohn's disease with 6-mercaptopurine. A long-term, randomized, double-blind study. N Engl J Med. 1980 May 1;302(18):981-987.

68. Swidsinski A, Ladhoff A, Pernthaler A, Swidsinski S, Loening-Baucke V, Ortner M, Weber J, Hoffmann U, Schreiber S, Dietel M, Lochs H. Mucosal flora in inflammatory bowel disease. Gastroenterology. 2002 Jan;122(1):44-54.

69. van Dullemen HM, van Deventer SJ, Hommes DW, Bijl HA, Jansen J, Tytgat GN, Woody J. Treatment of Crohn's disease with anti-tumor necrosis factor chimeric monoclonal antibody (cA2). Gastroenterology. 1995 Jul;109(1):129-135.

70. Azer SA. Overview of molecular pathways in inflammatory bowel disease associated with colorectal cancer development. Eur J Gastroenterol Hepatol. 2013 Mar;25(3):271-281.

71. Azer SA, AlOlayan TI, AlGhamdi MA, AlSanea MA. Inflammatory bowel disease: An evaluation of health information on the internet. World J Gastroenterol. 2017 Mar 7;23(9):1676-1696.

72. Börner K, Maru JT, Goldstone RL. The simultaneous evolution of author and paper networks. Proc Natl Acad Sci U S A. 2004 Apr 6;101 Suppl 1:5266-73.

73 Sinatra R, Deville P, Szell M, Wang D, Barabasi AL. A century of physics. Nature Physics 2015; 11(10): 791-796.

74. Wren JD, Georgescu C, Giles CB, Hennessey J. Use it or lose it: citations predict the continued online availability of published bioinformatics resources. Nucleic Acids Res. 2017 Apr 20;45(7):3627-3633.

75. Shanahan DR. Auto-correlation of journal impact factor for consensus research reporting statements: a cohort study. PeerJ. 2016 Mar 31;4:e1887.

76. Royle P, Kandala NB, Barnard K, Waugh N. Bibliometrics of systematic reviews: analysis of citation rates and journal impact factors. Syst Rev. 2013 Sep 12;2:74.

77. Falagas ME, Kouranos VD, Michalopoulos A, Rodopoulou SP, Batsiou MA, Karageorgopoulos DE. Comparison of the distribution of citations received by articles published in high, moderate, and low impact factor journals in clinical medicine. Intern Med J. 2010 Aug;40(8):587-591.

78. García-Aroca MÁ, Pandiella-Dominique A, Navarro-Suay R, Alonso-Arroyo A, Granda-Orive JI, Anguita-Rodríguez F, López-García A. Analysis of Production, Impact, and Scientific Collaboration on Difficult Airway Through the Web of Science and Scopus (1981-2013). Anesth Analg. 2017 Jun;124(6):1886-1896.

79. Tanner-Smith EE, Polanin JR. Brief alcohol intervention trials conducted by higher prestige authors and published in higher impact factor journals are cited more frequently. J Clin Epidemiol. 2016 Feb 6.

80. Jagsi R, Guancial EA, Worobey CC, Henault LE, Chang Y, Starr R, Tarbell NJ, Hylek EM. The "gender gap" in authorship of academic medical literature--a 35-year perspective. N Engl J Med. 2006 Jul 20;355(3):281-287.

81. Long MT, Leszczynski A, Thompson KD, Wasan SK, Calderwood AH. Female authorship in major academic gastroenterology journals: a look over 20 years. Gastrointest Endosc. 2015;81(6):1440-1447.

82. Diamond SJ, Thomas CR Jr, Desai S, Holliday EB, Jagsi R, Schmitt C, Enestvedt BK. Gender Differences in Publication Productivity, Academic Rank, and Career Duration Among U.S. Academic Gastroenterology Faculty. Acad Med. 2016 Aug;91(8):1158-1163.

83. Nicholson JM, Ioannidis JP. Research grants: Conform and be funded. Nature. 2012 Dec 6;492(7427):34-36.

84. Lauer MS, Danthi NS, Kaltman J, Wu C. Predicting Productivity Returns on Investment: Thirty Years of Peer Review, Grant Funding, and Publication of Highly Cited Papers at the National Heart, Lung, and Blood Institute. Circ Res. 2015 Jul 17;117(3):239-243.

85. Cheng K, Dodson TB, Egbert MA, Susarla SM. Which Factors Affect Citation Rates in the Oral and Maxillofacial Surgery Literature? J Oral Maxillofac Surg. 2017 Apr 1. pii: S0278-2391(17)30361-0.

86. Connelly TM, Devane L, Kelly JC, Wrafter P, Messaris E. The 100 classic papers in ulcerative colitis: a bibliometric analysis. Expert Rev Gastroenterol Hepatol. 2016 Aug 22:1-9. [Epub ahead of print]

Figure Legend

Figure 1A: Number of citations of papers published before the year 2000 (mean±SD)

Figure 1B: Number of citations of papers published after the year 2000 (mean±SD)

Table 1 Top cited papers in inflammatory bowel disease identified by searching the Web of Science, summarized by year of publication and category

Article type	Year of publication: no of articles [References]							
	1950-1958	1959-1967	1968-1976	1977-1985	1986-1994	1995-2003	2004-2012	Total (%)
Article				1 [39]				1 [2%]
Review/ Meta-analysis			1 [61]			5 [25,36,41,55,60]	8 [27,34,35,45, 33,57,38,63]	14 [28%]
Report							2 [43,59]	2 [4%]
Research	1 [28]		1 [23]	3 [37,58,67]	8 [22,44,40,48,49, 56,50,66]	10 [20,21,26,24,31, 46,62,69,65,68]	10 [29,30,32,51, 52,42,54,47, 53,64]	33 [66%]
Total (%)	1 [2%	0 [0%]	2 [4%]	4 [8%]	8 [16%]	15 [30%]	20 [40%]	50 [100%]

Table 2 Top-cited papers in inflammatory bowel disease (IBD) identified by searching the Web of Science, summarized by category and topic

Topics on IBD	Category: no of articles [References]				
	Article	Review/ Meta-analysis	Report	Research	Total (%)
Epidemiology, prevalence		2 [35,38]			2 [4%]
CD genetic susceptibility and NOD2 mutation		2 [34,45]		4 [20,21,51,54]	6 [12%]
Animal models for IBD		1 [60]		4 [22,44,40,48]	5 [10%]
Pathogenesis of IBD		7 [25,27,36,55,33,57,63]		8 [29,32,42,62,65,68,66,64]	15 [30%]
Classification, index of disease activity	1 [39]		2 [43,59]	2 [23,37]	5 [10%]
Risk of developing colorectal cancer		1 [41]		1 [49]	2 [4%]
Extra-intestinal complications		1 [61]			1 [2%]
Infliximab in CD				6 [24,31,30,46,52,47]	6 [12%]
Corticosteroids in UC				1 [28]	1 [2%]
Drug treatment and cyclosporine in UC				2 [56,58]	2 [4%]
Adalimumab in CD				1 [53]	1 [2%]
5-aminosalicylic acid in				1 [50]	1 [2%]

UC					
6-mercaptopurine in CD				1 [67]	1 [2%]
Monoclonal antibodies, anti-tumor necrosis factor in CD				2 [26,69]	2 [4%]
Total (%)	1 [2%]	14 [28%]	2 [4%]	33 [66%]	50 [100%]

Table 3. The journals that published the top-cited inflammatory bowel disease (IBD) articles included in the study, the journal impact factor, and the number of papers published and reference number.

Journal*	2016-Journal Impact Factor (JIF)	Number of papers published [References]
New England Journal of Medicine	72.406	12 [25,26,31,30,46,49,56,52,47,50,67,57]
Gastroenterology	18.392	12 [23,36,35,40,58,60,53,69,38,68,63,66]
Nature	40.137	4 [20,21,27,33]
Nature Genetics	27.959	4 [34,51,45,54]
The Lancet	47.831	2 [24,37]
Proceedings of the National Academy of Sciences of the United States of America	9.661	2 [32,42]
Cell	30.410	2 [22,44]
Gut	16.658	4 [59,64,41,62]
British Medical Journal	20.785	1 [28]
Science	37.205	1 [29]
Human Pathology	3.014	1 [39]
Laboratory Investigation	4.857	1 [48]
Canadian Journal of Gastroenterology and Hepatology	2.147	1 [43]
Nature Reviews Immunology	39.932	1 [55]
Medicine (Baltimore)	1.804	1 [61]
Journal of Immunology	4.856	1 [65]

- Gastroenterology related journals (Gastroenterology, and Gut) only published 16 (32%) articles out of the top highly cited 50 articles

Table 4 Authors and co-authors of two or more articles of the top-cited articles in inflammatory bowel disease identified by searching the Web of Science

Author's name*	Number [References]		Author's Name*	Number [References]	
	First author	Coauthor		First author	Coauthor
Hugot, JP	1 [20]	2 [34,45]	Daly,MJ	-	5[29,34,51,45,33]
Podolsky, DK	1 [25]	3 [28,27,31]	Steinhart,AH	-	5[29,34,43,51,45]
Targan, SR	1 [26]	7 [29,31,34,43,51,45,33]	Griffiths,A	-	4[29,34,51,45]
Hanauer,SB	1 [24]	6 [21,26,31,30,56,53]	Dassopoulos,T	-	2[29,34]
Xavier,RJ	1 [27]	3 [34,51,33]	Bitton,A	-	3[29,34,33]
Duerr,RH	1 [29]	4 [21,34,45,33]	Datta,LW	-	3[29,34,51]
Present,DH	2 [31,67]	3 [26,30,56]	Kistner,EO	-	2[29,34]
Rutgeerts, P	1 [30]	9 [26,24,31,34,46,45,52,47,53]	Rotter,JI	-	5[29,34,51,45,33]
Fiocchi,C	1 [36]	1 [65]	Schumm,LP	-	5[29,34,51,45,52]
Barrett,JC	1 [34]	2 [45,33]	Lee,J	-	2[45,33]
Riddell,RH	1 [39]	2 [43,60]	Lees,CW	-	2[45,33]
Loftus,EV Jr	1 [35]	1 [43]	Sandborn,WJ	-	3[30,47,53]
Franke,A	1 [45]	2 [33,54]	Barmada,MM	-	3[29,34,51]
Silverberg,MS	1 [43]	5 [29,34,51,45,33]	Nicolae,DL	-	4[21,29,34,51]
Rioux,JD	1 [51]	4 [29,34,45,33]	Sands,BE	-	3[31,30,52]
Lichtiger,S	1 [56]	1 [47]	Belaiche,J	-	2[20,34]
Colombel,JF	2 [47,53]	5 [20,24,30,43,45]	Laukens,D	-	3[34,45,33]
Abraham,C	1 [57]	2 [29,33]	Lawrance,I	-	2[45,33]
Becktel,JM	-	2 [23,58]	Louis,E	-	3[34,33,45]

Singleton,JW	-	2 [23,58]	Vos,M	-	3[34,45,33]
Kern,F Jr	-	2 [23,58]	Vermeire,S	-	5[34,46,43,45,33]
Van Deventer,SJ	-	4 [26,31,52,69]	Satsangi,J	-	4[34,43,45,33]
Mayer,L	-	3 [26,24,31]	Bernstein,CN	-	2[43,52]
Braakman,T	-	2 [26,31]	Tremelling,M	-	2[34,33]
DeWoody,KL	-	2 [26,31]	Mansfield,J	-	3[34,45,33]
Schaible,TF	-	2 [26,31]	Jewell,D	-	2[34,43]
Feagan,BG	-	3 [24,30,52]	Mathew,CG	-	4[34,45,33,54]
Lichtenstein,GR	-	2 [24,30]	Parkes,M	-	3[34,45,33]
Schreiber,S	-	7 [24,43,45,33,54,53,68]	Georges,M	-	3[34,45,33]
Rachmilewitz,D	-	4 [24,30,52,47]	Karban,A	-	2[43,45]
Wolf,DC	-	2 [24,52]	Gossum,A	-	2[34,45]
Olson,A	-	2 [24,30]	Franchimont,D	-	3[34,45,33]
Taylor,KD	-	5 [29,34,51,45,33]	Newman,W	-	2[45,33]
Bayless,TM	-	2 [21,45]	Regueiro,M	-	5[29,34,51,45,33]
Cho, JH	-	7 [21,29,34,51,45,33,57]	Kornbluth,A	-	2[56,47]

*Author's name= family name, abbreviations of first or first and second names.

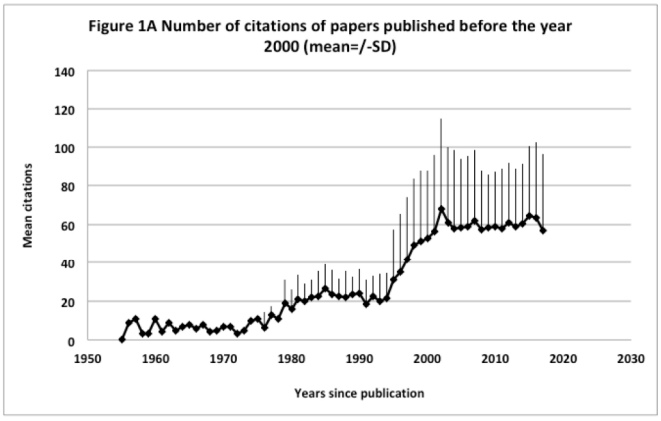
Table 5 Grading the top-cited articles in inflammatory bowel disease according to the Oxford Centre for Evidence-based Medicine – Levels of Evidence.

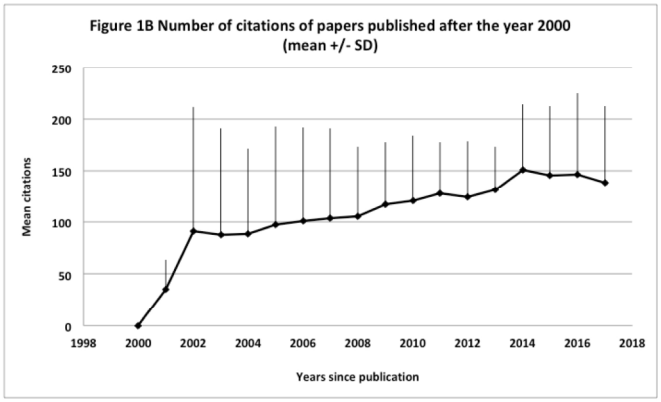
Level	Domain	Characteristics and description	Articles number [References]
1a	Therapeutic/ Prevention, Aetiology/Harm	Systematic reviews of RCTs (with consistent results from individual studies)	1 (33)
	Prognosis	Systematic reviews with homogeneity of inception cohort studies	
	Diagnosis	Systematic reviews with homogeneity of Level 1 diagnostic studies	
	Differential diagnosis/symptom prevalence study	Systematic reviews with homogeneity of prospective cohort studies.	
1b	Therapeutic/ Prevention, Aetiology/Harm	Individual RCT (with narrow confidence intervals)	12 [26,24,30,56,58,52,47,53,50,66,67, 59]
	Prognosis	Individual inception cohort study with >80% follow-up	
	Diagnosis	Validating cohort study with good reference standards	
	Differential diagnosis/symptom prevalence study	Prospective cohort study with good follow-up	
2a	Therapeutic/ Prevention, Aetiology/Harm	Systematic review of cohort studies (with consistent results from individual studies)	2 [34,63]

	Prognosis	Systematic review with homogeneity of either retrospective cohort studies or untreated control groups in RCT	
	Diagnosis	Systematic review with homogeneity of Level > 2 diagnostic studies	
	Differential diagnosis/symptom prevalence study	Systematic review with homogeneity of 2b and better studies	
2b	Therapeutic/ Prevention, Aetiology/Harm	Individual cohort study (including low quality RCT; e.g., <80% follow-up)	3 [31,46,49]
	Prognosis	Retrospective cohort study or follow-up untreated control patients in an RCT	
	Diagnosis	Exploratory cohort study with good reference standards	
	Differential diagnosis/symptom prevalence study	Retrospective cohort study or poor follow-up	
2c	Therapeutic/ Prevention, Aetiology/Harm	Outcome studies (analysis of large registries)	3 [38,60,61]
	Prognosis	Outcomes research	
	Diagnosis		
	Differential diagnosis/symptom	Ecological studies	

	prevalence study		
3a	Therapeutic/ Prevention, Aetiology/Harm	Systemic reviews of case-control studies (with consistent results from individual studies)	9 [25,27,36,35,41,43,55,45,57]
	Prognosis		
	Diagnosis	Systematic reviews with homogeneity of 3b and better studies	
	Differential diagnosis/symptom prevalence study	Systematic reviews with homogeneity of 3b and better studies	
3b	Therapeutic/ Prevention, Aetiology/Harm	Individual case-control study	15 [20,21,22,28,29,44,40,32,51,42,54,62,64,65,68]
	Prognosis		
	Diagnosis	Non consecutive study, or without consistently applied reference standards	
	Differential diagnosis/symptom prevalence study	Non consecutive cohort study or very limited population	
4	Therapeutic/ Prevention, Aetiology/Harm	Case series (and poor quality cohort and case-control studies)	5 [23,39,37,48,69]
	Prognosis	Case-series (and poor quality prognostic cohort studies)	
	Diagnosis	Case-control study, poor or non-	

		independent reference standard	
	Differential diagnosis/symptom prevalence study	Case-series or superseded reference standards	
5	Therapeutic/ Prevention, Aetiology/Harm	Expert opinion without explicit critical appraisal or based on physiology, or bench research.	0 [0]
	Prognosis	Expert opinion without explicit critical appraisal or based on physiology, or bench research.	
	Diagnosis	Expert opinion without explicit critical appraisal or based on physiology, or bench research.	
	Differential diagnosis/symptom prevalence study	Expert opinion without explicit critical appraisal or based on physiology, or bench research.	





209x296mm (300 x 300 DPI)

Appendix 1.
Top-cited articles on inflammatory bowel disease identified by searching the Web of Science database[a]

Rank	Authors, Year [Reference]	Article (*Journal*)	2016-JIF	Category	Number of citations, Web of Knowledge	Average citation per year[b]	Rank of the article in the journal publishing it[c]	Origin: First author's organization, location (country)
1	Hugot et al, 2001[20]	Association of NOD2 leucine-rich repeat variants with susceptibility to Crohn's disease. (*NATURE).*	40.137	Basic research	3,555	209.1	134	Fondation Jean Dausset CEPH (France)
2	Ogura et al, 2001[21]	A frameshift mutation in NOD2 associated with susceptibility to Crohn's disease. (*NATURE*).	40.137	Basic research	3,285	193.2	159	The University of Michigan Medical School, Michigan (United States).
3	Kuhn et al, 1993[22]	Interleukin-10-deficient mice develop chronic enterocolitis. (*CELL*)	30.410	Basic research	2,982	119.3	67	Institute for Genetics, University of Cologne, (Germany)
4	Best et al, 1976[23]	Development of a Crohns-disease activity index-National cooperative Chrons-disease study (*Gastroenterology*).	18.392	Clinical research	2,533	60.3	2	Hines Veterans Administration Cooperative Studies Support Center, University of Colorado Medical Center, Denver, Colorado, (United States).
5	Hanauer et al, 2002[24]	Maintenance infliximab for Crohn's disease: the ACCENT I randomized trial (*Lancet*)	47.831	Clinical research	2,442	152.6	46	University of Chicago Medical Center, Chicago, IL (United States).
6	Podolsky, 2002[25]	Inflammatory bowel disease. (*New England Journal of Medicine)*	72.406	Review	2,423	151.4	163	Massachusetts General Hospital and Harvard Medical School, Boston,

								Massachusetts (United States).
7	Targan et al, 1997[26]	A short-term study of chimeric monoclonal antibody cA2 to tumor necrosis factor alpha for Crohn's disease (*New England Journal of Medicine)*	72.406	Clinical research	2,364	112.6	169	Cedars-Sinai Medical Center, Los Angeles, California (United States)
8	Xavier and Podolsky, 2007[27]	Unravelling the pathogenesis of inflammatory bowel disease (*NATURE*)	40.137	Review	2,036	185.1	450	Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts (United States).
9	Truelove and Witts, 1955[28]	Cortisone in ulcerative colitis- Final report on a therapeutic trial (*British Medical Journal*).	20.785	Clinical research	1,871	29.7	20	Nuffield Department of Clinical Medicine, Oxford (United Kingdom)
10	Duerr et al, 2006[29]	A genome-wide association study identifies IL23R as an inflammatory bowel disease gene. **(***SCIENCE*).	37.205	Clinical research	1,862	155.2	530	Department of Medicine, School of Medicine, University of Pittsburgh, Pittsburgh, PA (United States).
12	Rutgeerts et al, 2005[30]	Infliximab for induction and maintenance therapy for ulcerative colitis (*New England Journal of Medicine*)	72.406	Clinical research	1,834	141.1	290	University Hospital Gasthuisberg, Leuven, (Belgium).
12	Present et al, 1999[31]	Infliximab for treatment of fistulas in patients with Crohn's disease (*New England Journal of Medicine*)	72.406	Clinical research	1,730	91.0	321	Mount Sinai Medical Center, New York, NY, (United States)

13	Frank et al, 2007[32]	Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. (*Proceedings of the National Academy of Sciences of the United States of America*)	9.661	Basic research	1,650	150.0	172	University of Colorado, Boulder, CO (United States)
14	Jostins et al, 2012[33]	Host-microbe interactions have shaped the genetic architecture of inflammatory bowel disease. (*Nature*)	40.137	Review Meta-analysis	1,643	273.8	683	Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, (*United Kingdom)*
15	Barrett et al, 2008[34]	Genome-wide association defines more than 30 distinct susceptibility loci for Crohn's disease. *(Nature Genetics*)	27.959	Review Meta-analysis	1,631	163.1	25	Wellcome Trust Centre for Human Genetics, University of Oxford, Roosevelt Drive, Oxford (United Kingdom)
16	Loftus, 2004[35]	Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences (*Gastroenterology*)	18.392	Review	1,566	111.9	10	Mayo Clinic, Rochester, Minnesota, (United States)
17	Fiocchi, 1998[36]	Inflammatory bowel disease: Etiology and pathogenesis (*Gastroenterology*)	18.392	Review	1,540	77.0	12	University Hospitals of Cleveland Case Western Reserve University School of Medicine, Ohio (United States)
18	Harvey and Bradshaw, 1980[37]	A simple index of Crohns-disease activity (*Lancet*)	47.831	Clinical research	1,466	38.6	166	Bristol Royal Infirmary and Frenchay Hospital, Bristol (United Kingdom)
19	Molodeck	Increasing incidence and prevalence	18.392	Review	1,438	239.7	19	University of Calgary,

	y et al, 2012[38]	of the inflammatory bowel diseases with time, based on systematic review. (*Gastroenterology*).						Calgary, Alberta, (Canada).
20	Riddell et al, 1983[39]	Dysplasia in inflammatory bowel disease- Standardized classification with provisional clinical applications (*Human Pathology)*	3.014	Article	1,398	39.9	2	National Foundation for Ileitis and Colitis, New York, (United States).
21	Okayasu et al, 1990[40]	A novel method in the induction of reliable experimental acute and chronic ulcerative-colitis in mice (*Gastroenterology)*	18.392	Basic research	1,396	49.9	24	School of Medicine, Tokyo Medical and Dental University, (Japan).
22	Eaden et al, 2001[41]	The risk of colorectal cancer in ulcerative colitis: a meta-analysis. (*Gut)*.	16.658	Review Meta-analysis	1,388	81.6	1	Leicester General Hospital, Gwendolen Road, Leicester (United Kingdom)
23	Sokol et al, 2008[42]	Faecalibacterium prausnitzii is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. *Proceedings of the National Academy of Sciences of the United States of America*)	9.661	Basic research	1,384	138.4	247	Institut National de la Recherche Agronomique U910, Domaine de Vilvert, Jouy-en-Josas, (France).
24	Siliverberg et al, 2005[43]	Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. *(Canadian Journal of Gastroenterology and Hepatology)*	2.147	Report	1,373	105.6	1	Mount Sinai Hospital IBD Centre, University of Tronto, Toronto, Ontario (Canada)

25	Sadlack et al, 1993[44]	Ulcerative colitis-like disease in mice with a disrupted interleukin-2 gene (*CELL*)	30.410	Basic research	1,358	54.32	387	Institute of Virology and Immunobiology, University of Würzburg, (Germany)
26	Franke et al, 2010[45]	Genome-wide meta-analysis increases to 71 the number of confirmed Crohn's disease susceptibility loci. *(Nature Genetics*)	27.959	Review Meta-analysis	1,321	165.1	63	Institute of Clinical Molecular Biology, Christian-Albrechts-University Kiel, Kiel, (Germany).
27	Baert et al, 2003[46]	Influence of immunogenicity on the long-term efficacy of infliximab in Crohn's disease. *(New England Journal of Medicine*)	72.406	Clinical research	1,297	86.5	562	University Hospital Gasthuisberg, Leuven, (Belgium).
28	Colombel et al, 2010[47]	Infliximab, azathioprine, or combination therapy for Crohn's disease (*New England Journal of Medicine*)	72.406	Clinical research	1,294	161.7	565	Hôpital Claude Huriez and Centre d'Investigation Clinique, Centre Hospitalier Universitaire de Lille, Université Lille Nord de France, Lille, (France).
29	Cooper et al, 1993[48]	Clinicopathologic study of dextran sulfate sodium experimental murine colitis. *(Laboratory Investigation*)	4.857	Basic research	1,219	48.8	4	Hahnemann University, Philadelphia, Pennsylvania. (United States)
30	Ekbom et al, 1990[49]	Ulcerative colitis and colorectal cancer. A population-based study. (*New England Journal of Medicine)*	72.406	Clinical research	1,168	41.7	684	University Hospital, Uppsala, (Sweden).

31	Schroeder et al, 1987[50]	Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study *(New England Journal of Medicine*)	72.406	Clinical research	1,156	37.3	695	Mayo Clinic, Rochester, MN (United States)
32	Rioux et al, 2007[51]	Genome-wide association study identifies new susceptibility loci for Crohn disease and implicates autophagy in disease pathogenesis. (*Nature Genetics*)	27.959	Basic research	1,152	104.7	89	Université de Montréal and the Montreal Heart Institute, Research Center, Montreal, Quebec (Canada).
33	Sands et al, 2004[52]	Infliximab maintenance therapy for fistulizing Crohn's disease. *(New England Journal of Medicine)*	72.406	Clinical research	1,146	81.8	706	Massachusetts General Hospital, and Harvard Medical School, Boston (United States)
34	Colombel et al, 2007[53]	Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: the CHARM trial. (*Gastroenterology*).	18.392	Clinical research	1,124	102.2	32	Hôpital Claude Huriez, Centre Hospitalier Universitaire de Lille, Rue Michel Polonovski, Lille, (France)
35	Hampe et al, 2007[54]	A genome-wide association scan of nonsynonymous SNPs identifies a susceptibility variant for Crohn disease in ATG16L1. *(Nature Genetics)*	27.959	Basic research	1,123	102.1	92	Institute for Clinical Molecular Biology, Christian-Albrechts University Kiel, University Hospital Schleswig-Holstein, (Germany).

36	Bouma and Strober, 2003[55]	The immunological and genetic basis of inflammatory bowel disease. *(Nature Reviews Immunology)*	39.932	Review	1,116	74.4	35	National Institutes of Health, and National Institutes of Allergy and Infectious Diseases, Bethesda, Maryland (United States)
37	Lichtiger et al, 1994[56]	Cyclosporine in severe ulcerative colitis refractory to steroid therapy. *(New England Journal of Medicine*)	72.406	Clinical research	1,104	46.0	755	Mount Sinai School of Medicine, New York (United States).
38	Abraham et al, 2009[57]	Inflammatory bowel disease. *(New England Journal of Medicine)*	72.406	Review	1,091	121.2	772	Yale University School of Medicine, New Haven, CT (United States)
39	Summers et al, 1979[58]	National Cooperative Crohn's Disease Study: results of drug treatment (*Gastroenterology*)	18.392	Clinical research	1,059	27.1	37	Division of gastroenterology, University of Iowa Medical Center, Iowa City, Virginia, (United States).
40	Satsangi, et al 2006[59]	The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications (*Gut*).	16.658	Report	1,054	87.8	7	Gstrointestinal Unit, Western General Hospital, University of Edinburg, (United Kingdom).
41	Elson, et al, 1995[60]	Experimental models of inflammatory bowel disease. (*Gastroenterology*).	18.392	Review	957	41.6	40	Department of Medicine, University of Alabama Hospital at Birmingham, AL, (United States).

42	Greenstein et al, 1976[61]	The extra-intestinal complications of Crohn's disease and ulcerative colitis: a study of 700 patients. *Medicine (Baltimore)*.	1.804	Review	945	22.5	10	Department of Surgery, Mount Sinai School of Medicine and the City University of New York, New York, (United States.)
43	Fujino et al, 2003[62]	Increased expression of interleukin 17 in inflammatory bowel disease. (*Gut*).	16.658	Basic research	931	62.1	12	Shiga University of Medical Science, Seta-Tukinowa, Otsu, (Japan).
44	Sartor, 2008[63]	Microbial influences in inflammatory bowel diseases. (*Gastroenterology*).	18.392	Review	925	92.5	44	Department of Medicine, Center for Gastrointestinal Biology and Disease, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, (United States).
45	Manichanh et al, 2006[64]	Reduced diversity of faecal microbiota in Crohn's disease revealed by a metagenomic approach. (*Gut)*.	16.658	Basic research	913	76.1	13	Unité d'Ecologie et de Physiologie du système Digestif, INRA-UEPSD, 78350 Jouy-en-Josas, (France)
46	Fuss et al, 1996[65]	Disparate CD4+ lamina propria (LP) lymphokine secretion profiles in inflammatory bowel disease. Crohn's disease LP cells manifest increased secretion of IFN-gamma, whereas ulcerative colitis LP cells manifest increased secretion of IL-5. *(Journal of Immunology*)	4.856	Basic research	893	40.6	68	National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, (United States)
47	Rutgeerts	Predictability of the postoperative	18.392	Clinical	884	31.6	50	Department of Medicine,

	et al, 1990[66]	course of Crohn's disease. (*Gastroenterology*).		research				University Hospital Gasthuisberg, University of Leuven, (Belgium).
48	Present et al, 1980[67]	Treatment of Crohn's disease with 6-mercaptopurine. A long-term, randomized, double-blind study. *(New England Journal of Medicine)*	72.406	Clinical research	874	23.0	1150	Lenox Hill Hospital and the Mount Sinai School of Medicine of City University of New York (United States)
49	Swidsinski et al, 2002[68]	Mucosal flora in inflammatory bowel disease. (*Gastroenterology*).	18.392	Basic research	873	54.6	52	Charité Humboldt Universität, Berlin, (Germany).
50	Vandullemen et al, 1995[69]	Treatment of Crohn's disease with anti-tumor necrosis factor chimeric monoclonal antibody (cA2). **(***Gastroenterology*).	18.392	Clinical research	871	37.9	53	Academic Medical Center, Amsterdam, (The Netherlands).

[a] The search was conducted in April, 2018 by searching the Web of Knowledge.
[b] The average citation per year = total number of citation / number of years since publication.
[c] This ranking was identified by searching each journal for a top-cited article and identifying its ranking based on the number of citations received in comparison to the number of citations received by other articles published in that journal.

Appendix 2

Glossary

Articles are scientific written composition representing a substantial advance in the understanding of a topic or problem. They raise questions, provide thoughtful, critical analysis and aim at establishing new directions.

Basic research is defined as fundamental research, which aims at improving scientific theories and our understanding of a phenomenon. Basic research may use animal models and include in vivo and in-vitro studies that target advances of fundamental knowledge.

Clinical research is defined as research applied to a clinical condition/disease with the aim to test an intervention or make a change to a phenomenon. Basic research usually fuels clinical research.

Reports are defined as brief articles with conclusions, results, and recommendations. They report on a substantial advance in an area/topic or a problem and aim at reporting findings and standardization of practice.

Review and meta-analysis are defined as an article reviewing the progress of knowledge in a particular topic, critically analysing the current status of knowledge and presenting an understanding of the subject by discussing related literature. A review should identify gaps in the literature and highlight future directions for further research. **A meta-analysis** is defined as a statistical analysis that combines the results from different scientific studies to provide conclusive evidence.