The 100 most-cited articles in the field of colorectal diseases from 1955 to 2018: A bibliometric analysis

Mengqi LuoLuo [Equal first author, 1], **Chunmei Zhang** [Equal first author, 1], **Yutang Ren** [2], **Wei Peng** [1], **Chunyu Zhong** [1], **Yan Peng** [1], **Xiaowei Tang** [Corresp. 1]

[1] the Affiliated Hospital of Southwest Medical University, Luzhou, China

[2] Beijing Tsinghua Changgung Hospital, Beijing, China

Corresponding Author: Xiaowei Tang
Email address: solitude5834@hotmail.com

Abstract

Background: The number of times that an article was cited reflected its impact. In this study, we aimed to recognize and analyze the characteristics of the most frequently cited articles in the field of colorectal diseases.

Methods: We identified the 100 highest cited articles using the terms ‘colorectal’ or ‘colon’ or ‘rectal’ or ‘IBD’ or ‘ulcerative colitis’ or ‘Crohn disease’ or ‘colonoscopy’ in Web of Science. Articles were analyzed to evaluate the characteristics including number of citations, country of origin, institutions of origin based on the first author affiliation, study type and others.

Results: Of the top cited publications, the number of citations ranged from 1479 to 8834 with a mean of 2304.85 citations per article. The journal with the greatest number of most-cited articles was New England Journal of Medicine (n=23), followed by Science (n=13) and Nature (n=12). These papers were published in 14 different countries, of which more than half were from the United States (n=64). The most popular field was colorectal cancer (n=51), followed by colonic tumor (n=21). Most of the papers were basic science studies (n=44) and randomized controlled trials (n=29).

Conclusion: Our study could provide a historical perspective on the scientific progress in the field of colorectal diseases, which would lay a firm foundation for future research.

The 100 most-cited articles in the field of colorectal diseases from 1955 to 2018: A bibliometric analysis

Short title: The 100 most-cited articles in colorectal diseases

Mengqi Luo,[1]* M.D., Chunmei Zhang,[1]* M.D., Yutang Ren,[2] M.D., Wei Peng, M.D.[1], Chunyu Zhong, M.D.[1], Yan Peng,[1] M.D., Xiaowei Tang,[1] M.D., Ph.D.

[1]Department of Gastroenterology, the Affiliated Hospital of Southwest Medical University, Luzhou, China

[2]Departmemt of Gastroenterology, Beijing Tsinghua Changgung Hospital, School of Clinical Medicine, Tsinghua University, Beijing, China

*These authors contributed equally to this work.

Corresponding author: Xiaowei Tang, Department of Gastroenterology, Affiliated Hospital of Southwest Medical University, Street Taiping No.25, Region Jiangyang, Luzhou, 646099, Sichuan Province, China. Tel.: +8608303165200, Fax: +86083061641541, E-mail: solitude5834@hotmail.com.

Abstract

Background: The number of times that an article was cited reflected its impact. In this study, we aimed to recognize and analyze the characteristics of the most frequently cited articles in the field of colorectal diseases.

Methods: We identified the 100 highest cited articles using the terms 'colorectal' or 'colon' or 'rectal' or 'IBD' or 'ulcerative colitis' or 'Crohn disease' or 'colonoscopy' in Web of Science. Articles were analyzed to evaluate the characteristics including number of citations, country of origin, institutions of origin based on the first author affiliation, study type and others.

Results: Of the top cited publications, the number of citations ranged from 1479 to 8834 with a mean of 2304.85 citations per article. The journal with the greatest number of most-cited articles was New England Journal of Medicine (n=23), followed by Science (n=13) and Nature (n=12). These papers were published in 14 different countries, of which more than half were from the United States (n=64). The most popular field was colorectal cancer (n=51), followed by colonic tumor (n=21). Most of the papers were basic science studies (n=44) and randomized controlled trials (n=29).

Conclusion: Our study could provide a historical perspective on the scientific progress in the field of colorectal diseases, which would lay a firm foundation for future research.

Keywords

Colorectal disease; citation classics; most-cited article; potential articles; bibliometric analysis

Introduction

As the Internet is becoming more accessible, the speed of updating knowledge and publicating studies in each field are getting more rapid. Researchers would get overwhelmed as a result. It is necessary to identify the most influential study in each field using a simple way. The bibliometric citation analysis [1], by means of mathematical and statistical methods, can filter out a large number of relevant articles with high impact quickly.

At present, citation analysis has been widely used in various specialties, including urology [2], anesthesiology [3], general surgery [4], aortic aneurysms [5], myeloid neoplasms [6], regenerative endodontics[7], and others. As yet, there is a lack of a comprehensive list of the citation classics with emphasis on the specialty of colorectal diseases. Therefore, the purpose of our study was to identify and evaluate the characteristics of highly-cited publications of colorectal diseases, and try to gain insights into this area.

Material and methods

Data sources and searches

The ISI Web of science (including Science Citation Index) database was searched using the keyword ‘colorectal’ or ‘colon’ or ‘rectal’ or ‘IBD’ or ‘ulcerative colitis’ or ‘Crohn disease’ or ‘colonoscopy’ for manuscripts relating to colorectal diseases published from 1955 (the earliest year for which data were available) up to [8]. The search was performed on 1 specific day, December 30th, 2018 to avoid possible changes in citation rate. Sorted by the category “Times

Cited", a list of the top cited articles in the area of colorectal disease was given. The full article were obtained by PubMed, ScienceDirect and Embase.

Study selection and data extraction

The articles were selected by reading the abstract to estimate whether they are related to colorectal diseases by two researchers (W. Peng and Y. Peng). Then, the 100 most cited articles were included and analyzed. Data were extracted from each of the top cited articles by researchers (M. Luo, C. Zhong) using a predesigned Microsoft Excel template and was checked by another researcher (C. Zhang). All the data were analyzed by two investigators (Y. Ren and X. Tang) regarding to authorship (only considering the first, and second authors), institution, journal name, publication date, country of origin, number of citations, average citations per year, topic, study type (eg, meta-analysis or systematic review, randomized controlled trial, prospective study, retrospective study, review, guideline, comment, or case report) and level of evidence. There are multiple methods of grading level of evidence [9]. In our analysis, the level of evidence was determined using the Australian National Health and Medical Research Council evidence hierarchy [10].

Statistical analysis

Tables and charts were created using Microsoft Word and Microsoft Excel, respectively. Data visualization was conducted using the VOSviewer (Leiden University, Leiden, The Netherlands) technique to create scientific landscapes and networks based on keyword frequency in titles and

abstracts. In order to depict the frequency of the research topics, a word cloud was created using a free-software Wordle (http://www.wordle.net/), which generates "word clouds" from the text that the user provides and places more emphasis on words that appear with greater frequency in the source text. The research topic of the top cited article was identified by subject category on Web of science.

Results

The top 100 citation classics in the field of colorectal disease between 1955 and 2018 were identified and shown in Table 1, and the number of citations ranged from 1479 to 8834 with a mean of 2304.85 citations per article.

Year, Country and Number of citations

The number of articles, citations per year and country distribution were shown in Figure 1-3. The top 100 cited articles covered a wide range of countries, and the majority of them were from the United States (US) (n=64), with the remaining from France (n=10), England (n=10), Netherlands (n=3), Canada (n=3), Japan (n=3), Belgium (n=2), Australia (n=2), Denmark (n=2), China（n=1），Germany (n=1), Finland (n=1), Italy (n=1) and Spain (n=1) respectively. US had the highest number of citations (n=141121) and Spain had the lowest (n=1639).

During the year from 1955 to 1985, there were only four articles (3.8%) included. However, a total of 104 articles (96.2%) were published from 1986 to 2014, followed by year with citations: 2004 (n=12), 1993 (n=7), 1999 (n=6), 2006 (n=6), 2007 (n=6), 2008 (n=6), 1990 (n=5), 2001

(n=5) and 2005 (n=5).

Authors and Journals

As shown in Table 2, a total of 14 authors published two or more articles. Among these, Fearon, E R authored the most papers (n=5). Twenty-five journals made contributions to the top-cited articles. The journals with the highest impact factor (IF) included New England Journal of Medicine (NEJM) (IF=79.258), Science (IF=41.058), Nature (IF=51.941), Gastroenterology (IF=20.773), Cell (IF=35.612), Lancet (IF=53.254) and Journal of Clinical Oncology (IF=26.303). Among them, 23 articles were published in New England Journal of Medicine (NEJM) (n=59614 citations), 13 in Science (New York, N. Y.) (n=28513 citations), 12 in Nature (n=31584 citations), 10 in Gastroenterology (n=17821), 9 in Cell (n=27831 citations), 7 in Lancet (n=14159), 6 in Journal of Clinical Oncology (n=12067 citations). In addition, 8 journals published only one article (Table 3).

Institutions

With regard to institutions, the Johns Hopkins University School of Medicine devoted the largest number of articles (n=8). Yale University School of Medicine and University of California contributed 3 papers, respectively. Moreover, there were 13 institutions with 2 literatures and more than half of the organizations (n=64) held only one article (Table 4).

Top used keywords related to colorectal disease

There were 53 keywords that were used at least 5 times. Mostly used keywords were cancer (n=52), gene (n=25), mutation (n=21), tumor (n=20), data (n=19), cell (n=17), colon (n=14), colon cancer (n=14), crohn (n=14), role (n=14), combination (n=13), inflammatory bowel disease (n=13), metastatic colorectal cancer (n=13), overall survival (n=13), progression (n=13), week (n=13), fluorouracil (n=12), primary end point (n=12), ulcerative colitis (n=12), chromosome (n=11) respectively. The top-cited keywords among these are demonstrated in Figure 4.

Fields, Types, Level of evidence and topics of Study

In terms of the study fields, 76 articles focused on tumor. Among them, 51 papers (57%) involved colorectal tumor, 21 (20%) were only colonic tumor and 4 (6%) were only rectal tumor. The remaining 22 papers concentrated on colorectal inflammation, of which 8 (10%) papers were Crohn's disease, 4 (5%) were ulcerative colitis and 10 (2%) were inflammatory bowel disease. As for types of studies, there were basic science study (n=44), randomized controlled trials (RCTs) (n=29), reviews (n=14), prospective studies (n=5), guideline and consensus (n=3), retrospective study (n=1), case report (n=1), comment (n=1) and meta-analysis (n=1) (Table 5). As shown in Table 6, the types of clinical study and level of evidence in the top-cited articles were summarized.

The majority of the citation classics were gastroenterology & hepatology (n=86), oncology (n=68), biochemistry & molecular biology (n=52), genetics & heredity (38), cell biology (n=28), geriatrics & gerontology (n=28), pharmacology & pharmacy (n=28), immunology (n=21),

mathematics (n=18), surgery (n=13), demography (n=12), hematology (n=7), science & technology - other topics (n=7), general & internal medicine (n=6), health care sciences & services (n=5), microbiology (n=5), pathology (n=5) and others (n=13). (Figure 5).

Discussion

During recent years, the world incidence of colorectal diseases, especially colorectal cancer and inflammatory bowel disease, is accelerating [11, 12]. A great number of recourses and funds have been devoted to the researches of colorectal diseases, including the pathogenesis, epidemiology, genetics, immunology and other aspects. Citations of one article in a certain field represents it's influence and credibility, and it can also show the author's academic achievement level. At present, the citation classics had been widely used in urology [2], anesthesiology [3], general surgery [4], and other disciplines. As for the area of digestive system disease, analysis of citation classics in gastroenterology and hepatology [13], gastric cancer [14], acute pancreatitis [15], ulcerative colitis [16] had been discussed. However, there is no study that reported citation classics in the field of colorectal diseases. So we aimed to analyzed the characteristics of the 100 top-cited articles in colorectal diseases.

In this study, we found that the number of cited times in colorectal disease literature was higher compared with some other digestive diseases, such as gastric cancer (n=299-2893) and acute pancreatitis (n=163-1281) [14, 15], which confirmed that colorectal diseases was a hot topic. But in terms of origin of country and published journal, citation characteristics of colorectal diseases and other gastrointestinal diseases were similar. For example, the top cited articles were mostly

distributed in the US, and the inflammatory research was mainly published in Gastroenterology, while cancer studies were generally published in NEJM [14-16].

In our study, these articles were distributed in various countries, with US occupying the first. Not only did the US have citation classic every year, but also it ranked the first in the number of articles almost every year since 1986. The reason is probably due to the strong comprehensive national strength, the advanced science and the technology. More importantly, for a long time, the education and healthcare cost take a large proportion of American fiscal expenditure, and a mass of extraordinary scholars are cultivated and a variety of powerful academic institutions are established in the US, making prominent contributions in medical profession.

Colorectal cancer was the third most commonly diagnosed cancer in males and the second in females in the developed countries based on the global cancer statistics in 2018 [11]. In our study we discovered that the research on colorectal cancer accounted for a large proportion in colorectal diseases, which mainly concentrated on drugs and surgery. Combined biological agents and chemotherapy was one of the hot topics in these 100 citation classics [17, 18], such as bevacizumab, cetuximab, LV5FU2-oxaliplatin combination, flurouracil-based combination chemotherapy, irinotecan combined with flurouracil and calcium folinate. Two articles indicated that laparoscopic surgery was better than open surgery in postoperative morbidity, hospitalization time, tumor recurrence and cancer-related survival [19, 20]. One study demonstrated that preoperative chemoradiotherapy for colorectal cancer had a good effect on local control, but it had no effect on the overall survival rate [21]. In addition, a number of citation classics highly emphasized the importance of early diagnosis or screening of colorectal

cancer and precancerous lesions using different modalities. The screening methods, including fecal occult-blood testing with rehydration of the samples [22], sigmoidoscopy [23], CT virtual colonoscopy with the use of a three-dimensional approach [24], stool DNA test [25], double contrast barium enema and so on [25], were mentioned in the 100 classic articles. The occurrence of the colorectal cancer would be largely prevented by endoscopic resection if the precancerous lesions, such as the adenomatous polyp, were detected in screening [26].

The researches related to genes in the filed of colorectal cancer were also of great concern, including oncogene activation (K-ras and EGFR) [27, 28], tumor-suppressor gene inactivation (APC and P53) [29, 30], mismatch repair gene mutations (hMSH2, PMS1 and PMS2) [31, 32] and excessive gene expression (cox-2 and CD33) [33, 34]. From the etiological point of view, patients with familial adenomatous polyposis had a nearly 100 percent risk of colorectal cancer [35]. There were various stages of hyperplasia, adenoma and canceration in morphology as well as corresponding chromosome changes (5q, 17p, and 18q) [36]. These studies above indicated that the development of colorectal cancer was a multi-step, multi-stage, multi-gene mutations disease, which is a widespread consensus among gastroenterologists now.

The 100 top-cited articles were mainly published in 19 journals, which published the highest level of papers in these fields at the fastest speed and had the strictest standards. Most of the articles were published in NEJM. The reasons may be as follows. Firstly NEJM, a medical journal published by the American Massachusetts Medical Society, has continually published medical papers for the longest time in the world. Secondly, it is one of the most authoritative medical journals with high impact factor (79.258 in 2017). The NEJM has become the preferred

choice of publications by excellent scholars all over the world. Science and Nature also published a number of top-cited articles, both of which enjoy high reputation in the world. These three kinds of magazines mentioned above covered more than half of the articles in the classic citations of colorectal disease. The NEJM was the main source of a majority of clinical research, while Science and Nature were the main sources of the great mass of basic research.

We acknowledged that there were some limitations in this study. First, articles in this field might not be sought out fully owing to the differences in the keywords and the insensitivity of the database search. We had exerted our best efforts to input multiple combinations of key words about colorectal diseases in Web of Science to find out as many relevant articles as possible. Second, we merely screened the articles published in English, so papers with significance of milepost in other languages might be missed. Third, the composition of the ranking list and the comparative 'order and degree' of publications are dynamic and constantly changing. So the citation classics obtained at different times is various, but the general trend will not change.

In conclusion, our study reviewed 100 citation classics in the last 60 years in the field of colorectal disease, which reflected the research progress and hot topics, laying a solid footstone for future study.

233

234 **Reference**

235 1. Joyce CW, Kelly JC, Sugrue C. 2014. A bibliometric analysis of the 100 most influential
236 papers in burns. Burns 40: 30-37 DOI: 10.1016/j.burns.2013.10.025.
237 2. Heldwein FL, Rhoden EL, Morgentaler A. 2010. Classics of urology: a half century history of
238 the most frequently cited articles (1955-2009). Urology 75: 1261-1268 DOI:
239 org/10.1016/j.urology.2009.09.043.
240 3. Tripathi RS, Blum JM, Papadimos TJ, et al. 2011. A bibliometric search of citation classics in
241 anesthesiology. BMC Anesthesiol 11: 24 DOI: org/10.1186/1471-2253-11-24
242 4. Paladugu R, Schein M, Gardezi S, et al. 2002. One hundred citation classics in general
243 surgical journals. World J Surg 26: 1099-1105 DOI: org/10.1007/s00268-002-6376-7.
244 5. Zhou KZ, Maingard J, Phan K, et al. 2018. The 100 most cited articles in the endovascular
245 treatment of thoracic and abdominal aortic aneurysms. J Vasc Surg 68: 1566-1581 DOI:
246 org/10.1016/j.jvs.2018.08.151.
247 6. Iqbal U, Rehan A, Akmal M, et al. 2019. Top 100 Most Influential Articles in the Field of
248 Myeloid Neoplasms: A Bibliometric Study. Acta Haematol 141: 68-78 DOI:
249 org/10.1159/000493251.
250 7. Adnan S, Ullah R. 2018. Top-cited Articles in Regenerative Endodontics: A Bibliometric
251 Analysis. J Endod 44: 1650-1664 DOI: org/10.1016/j.joen.2018.07.015
252 8. Web of Science. 2018. Scientific Citation Index Expanded; available from
253 https://clarivate.com/ (accessed 30 December 2018).

9. Fargen KM, Mocco J, Spiotta AM, et al. 2017. A pilot study of neurointerventional research level of evidence and collaboration. J Neurointerv Surg 9: 694-697 DOI: org/10.1136/neurintsurg-2016-012504

10. Merlin T, Weston A, Tooher R. 2009. Extending an evidence hierarchy to include topics other than treatment: revising the Australian 'levels of evidence'. BMC Med Res Methodol 9: 34 DOI: org/10.1186/1471-2288-9-34

11. Bray F, Ferlay J, Soerjomataram I, et al. 2018. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 68:394-424 DOI: org/10.3322/caac.21492

12. Ng SC, Shi HY, Hamidi N, et al. 2018. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. Lancet 390(10114): 2769-2778 DOI: org/10.1016/S0140-6736(17)32448-0

13. Azer SA, Azer S. 2016. Bibliometric analysis of the top-cited gastroenterology and hepatology articles. BMJ Open 6:e009889 DOI: org/10.1136/bmjopen-2015-009889

14. Powell AG, Hughes DL, Wheat JR, et al. 2016. The 100 most influential manuscripts in gastric cancer: A bibliometric analysis. Int J Surg 28:83-90 DOI: org/10.1016/j.ijsu.2016.02.028

15. Cao F, Li J, Li A, et al. 2012. Citation classics in acute pancreatitis. Pancreatology 12: 325-330 DOI: org/10.1016/j.pan.2012.05.001.

16. Connelly TM, Devane L, Kelly JC, et al. 2016. The 100 classic papers in ulcerative colitis: a bibliometric analysis. Expert Rev Gastroenterol Hepatol 22: 1-9 DOI: org/10.1080/17474124.2016.1216786

17. Hurwitz H, Fehrenbacher L, Novotny W, et al. 2004. Bevacizumab plus irinotecan, fluorouracil, and leucovorin for metastatic colorectal cancer. N Engl J Med 350: 2335-2342 DOI: org/10.1056/NEJMoa032691.

18. Cunningham D, Humblet Y, Siena S, et al. 2004. Cetuximab monotherapy and cetuximab plus irinotecan in irinotecan-refractory metastatic colorectal cancer. N Engl J Med 351: 337-345 DOI: org/10.1056/NEJMoa033025

19. Clinical Outcomes of Surgical Therapy Study Group, Nelson H, Sargent DJ, et al. 2004. A comparison of laparoscopically assisted and open colectomy for colon cancer. N Engl J Med 350: 2050-2059 DOI: 10.1056/NEJMoa032651.

20. Guillou PJ, Quirke P, Thorpe H, et al. 2005. Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. Lancet 365: 1718-1726 DOI: org/10.1016/S0140-6736(05)66545-2.

21. Sauer R, Becker H, Hohenberger W, et al. 2004. Preoperative versus postoperative chemoradiotherapy for rectal cancer. N Engl J Med 351: 1731-1740 DOI: org/10.1056/NEJMoa040694

22. Mandel JS, Bond JH, Church TR, et al.1993. Reducing mortality from colorectal cancer by screening for fecal occult blood. Minnesota Colon Cancer Control Study. N Engl J Med 328: 1365-1371 DOI: org/10.1056/NEJM199305133281901.

23. Selby JV, Friedman GD, Quesenberry CP Jr, et al. 1992. A case-control study of screening sigmoidoscopy and mortality from colorectal cancer. N Engl J Med 326: 653-657 DOI:

org/10.1056/NEJM199203053261001.

24. Pickhardt PJ, Choi JR, Hwang I, et al. 2003. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. N Engl J Med 349: 2191-2200 DOI: org/10.1056/NEJMoa031618.

25. Winawer S, Fletcher R, Rex D, et al. 2003. Colorectal cancer screening and surveillance: clinical guidelines and rationale-Update based on new evidence. Gastroenterology 124: 544-560 DOI: org/10.1053/gast.2003.50044

26. Levin B, Lieberman DA, McFarland B, et al. 2008. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. Gastroenterology 134: 1570-1595 DOI: org/10.1053/j.gastro.2008.02.002

27. Vogelstein B, Fearon ER, Hamilton SR, et al. 1988. Genetic alterations during colorectal-tumor development. N Engl J Med 319: 525-532 DOI: org/10.1056/NEJM198809013190901

28. Cunningham D, Humblet Y, Siena S, et al. 2004. Cetuximab monotherapy and cetuximab plus irinotecan in irinotecan-refractory metastatic colorectal cancer. N Engl J Med 351: 337-345 DOI: org/10.1056/NEJMoa033025

29. Powell SM, Zilz N, Beazer-Barclay Y, et al. 1992. APC mutations occur early during colorectal tumorigenesis. Nature 359: 235-237 DOI: org/10.1038/359235a0

30. Baker SJ, Markowitz S, Fearon ER, et al. 1990. Suppression of human colorectal carcinoma cell growth by wild-type p53. Science 249: 912-915 DOI: org/10.1126/science.2144057

317 31. Fishel R, Lescoe MK, Rao MR, et al. 1993. The human mutator gene homolog MSH2 and its
318 association with hereditary nonpolyposis colon cancer. Cell 75: 1027-1038 DOI:
319 org/10.1016/0092-8674(93)90546-3
320 32. Nicolaides NC, Papadopoulos N, Liu B, et al. 1994. Mutations of two PMS homologues in
321 hereditary nonpolyposis colon cancer. Nature 371:75-80 DOI: 10.1038/371075a0.
322 33. Eberhart CE, Coffey RJ, Radhika A, et al. 1994. Up-regulation of cyclooxygenase 2 gene
323 expression in human colorectal adenomas and adenocarcinomas. Gastroenterology 107: 1183-
324 1188 DOI: org/10.1016/0016-5085(94)90246-1
325 34. O'Brien CA, Pollett A, Gallinger S, et al. 2007. A human colon cancer cell capable of
326 initiating tumour growth in immunodeficient mice. Nature 445: 106-110 DOI:
327 10.1038/nature05372.
328 35. Steinbach G, Lynch PM, Phillips RK, et al. 2000. The effect of celecoxib, a cyclooxygenase-
329 2 inhibitor, in familial adenomatous polyposis. N Engl J Med 29;342:1946-1952 DOI:
330 10.1056/NEJM200006293422603.
331 36. Thibodeau SN, Bren G, Schaid D. 1993. Microsatellite instability in cancer of the
332 proximal colon. Science 260: 816-819 DOI: org/10.1126/science.8484122.
333
334
335
336
337

Figure legend

Figure 1 Distribution of top-cited articles from 1955 to 2014

Figure 2 Total citations of the articles in the top 100 list every year

Figure 3 The countries of origin of the top-cited 100 articles.

Figure 4 Network visualization map of relationships between the most commonly used keywords in the abstract and title.

Figure 5 Word cloud for the frequency of research topics.

Table 1(on next page)

Table1

The top-cited 100 citation classics in colorectal disease

PeerJ Preprints | https://doi.org/10.7287/peerj.preprints.27602v1 | CC BY 4.0 Open Access | rec: 19 Mar 2019, publ: 19 Mar 2019

1 Table 1 The top-cited 100 citation classics in colorectal disease

Rank	Title	No. of citations	Average citations per year
1	Fearon ER1, Vogelstein B. A genetic model for colorectal tumorigenesis. Cell 1990; 61:759-67.	8834	304.62
2	Hurwitz H1, Fehrenbacher L, Novotny W, et al. Bevacizumab plus irinotecan, fluorouracil, and leucovorin for metastatic colorectal cancer. N Engl J Med 2004;350:2335-42.	7384	492.27
3	Vogelstein B1, Fearon ER, Hamilton SR, et al. Genetic alterations during colorectal-tumor development. N Engl J Med 1988;319:525-32.	5387	173.77
4	Gibson GR1, Roberfroid MB. Dietary modulation of the human colonic microbiota: introducing the concept of prebiotics. J Nutr 1995;125:1401-12.	3808	158.67
5	Kinzler KW1, Vogelstein B. Lessons from hereditary colorectal cancer. Cell 1996;87:159-70.	3801	165.26
6	Hugot JP1, Chamaillard M, Zouali H, et al.Association of NOD2 leucine-rich repeat variants with susceptibility to Crohn's disease. Nature 2001;411:599-603.	3787	210.39
7	Cunningham D1, Humblet Y, Siena S, et al. Cetuximab monotherapy and cetuximab plus irinotecan in irinotecan-refractory metastatic colorectal cancer. N Engl J Med 2004;351:337-45.	3694	246.27
8	Ogura Y1, Bonen DK, Inohara N, et al. A frameshift mutation in NOD2 associated with susceptibility to Crohn's disease. Nature 2001;411:603-6.	3471	192.83
9	Sauer R1, Becker H, Hohenberger W, et al. Preoperative versus postoperative chemoradiotherapy for rectal cancer. N Engl J Med 2004;351:1731-40.	3454	230.27
10	Andersen CL1, Jensen JL, Ørntoft TF. Normalization of real-time quantitative reverse transcription-PCR data: A model-based variance estimation approach to identify genes suited for normalization, applied to bladder and colon cancer	3347	223.13

	data sets. Cancer Res 2004;64:5245-50.		
11	Sjöblom T1, Jones S, Wood LD, et al. The consensus coding sequences of human breast and colorectal cancers. Science 2006;314:268-74.	3202	246.31
12	Muzny DM, Bainbridge MN, Chang K, et al. Comprehensive molecular characterization of human colon and rectal cancer. Nature 2012;487:330-7.	3115	445.00
13	Boland CR, Thibodeau SN, Hamilton SR, et al. A National Cancer Institute Workshop on Microsatellite Instability for Cancer Detection and Familial Predisposition: Development of International Criteria for the Determination of Microsatellite Instability in Colorectal Cancer. Cancer Res 1998;58:5248-57.	3052	145.33
14	Winawer SJ1, Zauber AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy. N Engl J Med 1993;329:1977-81.	3050	117.31
15	Tetsu O1, McCormick F. Beta-catenin regulates expression of cyclin D1 in colon carcinoma cells. Nature 1999;398:422-6.	2916	145.80
16	Groux H1, O'Garra A, Bigler M, et al. A CD4(+) T-cell subset inhibits antigen-specific T-cell responses and prevents colitis. Nature 1997;389:737-42.	2877	130.77
17	Longstreth GF1, Thompson WG, Chey WD, et al. Functional bowel disorders. Gastroenterology 2006;130:1480-91.	2788	214.46
18	Galon J1, Costes A, Sanchez-Cabo F, et al. Type, density, and location of immune cells within human colorectal tumors predict clinical outcome. Science 2006;313:1960-4.	2780	213.85
19	Chen X1, Ba Y, Ma L, et al. Characterization of microRNAs in serum: a novel class of biomarkers for diagnosis of cancer and other diseases. Cell Res 2008;18:997-1006.	2777	252.45
20	O'Brien CA1, Pollett A, Gallinger S, et al. A human colon cancer cell capable of initiating tumour growth in immunodeficient mice. Nature 2007;445:106-10.	2763	230.25
21	Ricci-Vitiani L1, Lombardi DG, Pilozzi E, et al. Identification and expansion	2747	228.92

	of human colon-cancer-initiating cells. Nature 2007;445:111-5.		
22	Hanauer SB1, Feagan BG, Lichtenstein GR, et al. Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial. Lancet 2002;359:1541-9.	2699	158.76
23	de Gramont A1, Figer A, Seymour M, et al. Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced colorectal cancer. J Clin Oncol 2000;18:2938-47.	2682	141.16
24	Korinek V1, Barker N, Morin PJ, et al. Constitutive transcriptional activation by a beta-catenin-Tcf complex in APC(-/-) colon carcinoma. Science 1997;275:1784-7.	2664	121.09
25	Thibodeau SN1, Bren G, Schaid D. Microsatellite instability in cancer of the proximal colon. Science 1993;260:816-9.	2645	101.73
26	Podolsky DK1. Inflammatory bowel disease. N Engl J Med 2002;347:417-29.	2596	152.71
27	Kapiteijn E1, Marijnen CA, Nagtegaal ID, et al. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer. N Engl J Med 2001;345:638-46.	2587	143.72
28	Rakoff-Nahoum S1, Paglino J, Eslami-Varzaneh F, et al. Recognition of commensal microflora by toll-like receptors is required for intestinal homeostasis. Cell 2004;118:229-41.	2549	169.93
29	Alon U1, Barkai N, Notterman DA, et al. Broad patterns of gene expression revealed by clustering analysis of tumor and normal colon tissues probed by oligonucleotide arrays. Proc Natl Acad Sci U S A 1999;96:6745-50.	2530	126.50
30	Aaltonen LA1, Peltomäki P, Leach FS, et al. Clues to the pathogenesis of familial colorectal cancer. Science 1993;260:812-6.	2506	96.38
31	Targan SR1, Hanauer SB, van Deventer SJ, et al. A short-term study of chimeric monoclonal antibody cA2 to tumor necrosis factor alpha for Crohn's disease. N Engl J Med 1997;337:1029-35.	2479	112.68
32	Mandel JS1, Bond JH, Church TR, et al. Reducing mortality from colorectal cancer by screening for fecal occult blood. N Engl J Med 1993;328:1365-71.	2421	93.12

33	Douillard JY1, Cunningham D, Roth AD, et al. Irinotecan combined with fluorouracil compared with fluorouracil alone as first-line treatment for metastatic colorectal cancer: a multicentre randomised trial. Lancet 2000;355:1041-7.	2412	126.95
34	Fishel R1, Lescoe MK, Rao MR, et al. The human mutator gene homolog MSH2 and its association with hereditary nonpolyposis colon cancer. Cell 1993;75:1027-38.	2408	92.62
35	Karapetis CS1, Khambata-Ford S, Jonker DJ ,et al. K-ras mutations and benefit from cetuximab in advanced colorectal cancer. N Engl J Med 2008;359:1757-65.	2390	217.27
36	Saltz LB1, Cox JV, Blanke C, et al. Irinotecan plus fluorouracil and leucovorin for metastatic colorectal cancer. N Engl J Med 2000;343:905-14.	2344	123.37
37	Van Cutsem E1, Köhne CH, Hitre E, et al. Cetuximab and Chemotherapy as Initial Treatment for Metastatic Colorectal Cancer. N Engl J Med 2009;360:1408-17.	2293	229.30
38	Xavier RJ1, Podolsky DK. Unravelling the pathogenesis of inflammatory bowel disease. Nature 2007 ;448:427-34.	2261	188.42
39	Groden J1, Thliveris A, Samowitz W, et al. Identification and characterization of the familial adenomatous polyposis coli gene. Cell 1991;66:589-600.	2244	80.14
40	Ionov Y1, Peinado MA, Malkhosyan S, et al. Ubiquitous somatic mutations in simple repeated sequences reveal a new mechanism for colonic carcinogenesis. Nature 1993;363:558-61.	2231	85.81
41	Fong Y1, Fortner J, Sun RL, et al. Clinical score for predicting recurrence after hepatic resection for metastatic colorectal cancer - Analysis of 1001 consecutive cases. Ann Surg 1999;230:309-18.	2216	110.80
42	Amado RG1, Wolf M, Peeters M, et al. Wild-type KRAS is required for panitumumab efficacy in patients with metastatic colorectal cancer. J Clin Oncol 2008;26:1626-34.	2188	198.91
43	Oshima M1, Dinchuk JE, Kargman SL, et al. Suppression of intestinal	2153	93.61

	polyposis in Apc(Delta 716) knockout mice by inhibition of cyclooxygenase 2 (COX-2). Cell 1996;87:803-9.		
44	Eberhart CE1, Coffey RJ, Radhika A, et al. Up-regulation of cyclooxygenase 2 gene expression in human colorectal adenomas and adenocarcinomas. Gastroenterology 1994;107:1183-8.	2122	84.88
45	GOLD P, FREEDMAN SO. DEMONSTRATION OF TUMOR-SPECIFIC ANTIGENS IN HUMAN COLONIC CARCINOMATA BY IMMUNOLOGICAL TOLERANCE AND ABSORPTION TECHNIQUES. J Exp Med 1965;121:439-62.	2120	39.26
46	André T1, Boni C, Mounedji-Boudiaf L, et al. Oxaliplatin, fluorouracil, and leucovorin as adjuvant treatment for colon cancer. N Engl J Med 2004;350:2343-51.	2102	140.13
47	Wood LD1, Parsons DW, Jones S, et al. The genomic landscapes of human breast and colorectal cancers. Science 2007;318:1108-13.	2080	173.33
48	Leach FS1, Nicolaides NC, Papadopoulos N, et al. Mutations of a mutS homolog in hereditary nonpolyposis colorectal cancer. Cell 1993;75:1215-25.	2075	79.81
49	Tournigand C1, André T, Achille E, et al. FOLFIRI followed by FOLFOX6 or the reverse sequence in advanced colorectal cancer: a randomized GERCOR study. J Clin Oncol 2004;22:229-37.	2074	138.27
50	Tsujii M1, Kawano S, Tsuji S, et al. Cyclooxygenase regulates angiogenesis induced by colon cancer cells. Cell 1998;93:705-16.	2071	98.62
51	Rutgeerts P1, Sandborn WJ, Feagan BG, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. N Engl J Med 2005;353:2462-76.	2064	147.43
52	Markowitz S1, Wang J, Myeroff L, et al. Inactivation of the type II TGF-beta receptor in colon cancer cells with microsatellite instability. Science 1995;268:1336-8.	2051	85.46
53	Duerr RH1, Taylor KD, Brant SR, et al. A genome-wide association study identifies IL23R as an inflammatory bowel disease gene. Science 2006;314:1461-3.	1998	153.69

54	Hardcastle JD1, Chamberlain JO, Robinson MH, et al. Randomised controlled trial of faecal-occult-blood screening for colorectal cancer. Lancet 1996;348:1472-7.	1987	86.39
55	TRUELOVE SC, WITTS LJ. Cortisone in ulcerative colitis; final report on a therapeutic trial. Br Med J 1955;2:1041-8.	1978	30.91
56	Jostins L1, Ripke S, Weersma RK, et al. Host-microbe interactions have shaped the genetic architecture of inflammatory bowel disease. Nature 2012;491:119-24.	1911	273.00
57	Guillou PJ1, Quirke P, Thorpe H, et al. Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. Lancet 2005;365:1718-26.	1905	136.07
58	Frank DN1, St Amand AL, Feldman RA, et al. Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. Proc Natl Acad Sci U S A 2007;104:13780-5.	1899	158.25
59	Nelson H, Sargent DJ, Wieand HS, et al. A comparison of laparoscopically assisted and open colectomy for colon cancer. N Engl J Med 2004;350:2050-9.	1898	126.53
60	Saltz LB1, Clarke S, Díaz-Rubio E, et al. Bevacizumab in combination with oxaliplatin-based chemotherapy as first-line therapy in metastatic colorectal cancer: A randomized phase III study. J Clin Oncol 2008;26:2013-9.	1890	171.82
61	Steinbach G1, Lynch PM, Phillips RK, et al. The effect of celecoxib, a cyclooxygenase-2 inhibitor, in familial adenomatous polyposis. N Engl J Med 2000;342:1946-52.	1860	97.89
62	Round JL1, Mazmanian SK. The gut microbiota shapes intestinal immune responses during health and disease. Nat Rev Immunol 2009;9:313-23.	1845	184.50
63	Present DH1, Rutgeerts P, Targan S, et al. Infliximab for the treatment of fistulas in patients with Crohn's disease. N Engl J Med 1999;340:1398-405.	1843	92.15
64	Baker SJ1, Markowitz S, Fearon ER, et al. Suppression of human colorectal	1841	63.48

	carcinoma cell growth by wild-type p53. Science 1990;249:912-5.		
65	Moertel CG1, Fleming TR, Macdonald JS, et al. Levamisole and fluorouracil for adjuvant therapy of resected colon carcinoma. N Engl J Med 1990;322:352-8.	1831	63.14
66	Kronborg O1, Fenger C, Olsen J,et al.Randomised study of screening for colorectal cancer with faecal-occult-blood test. Lancet 1996;348:1467-71.	1827	79.43
67	Baker SJ1, Fearon ER, Nigro JM, et al. Chromosome 17 deletions and p53 gene mutations in colorectal carcinomas. Science 1989;244:217-21.	1819	60.63
68	Bresalier RS1, Sandler RS, Quan H, et al. Cardiovascular events associated with rofecoxib in a colorectal adenoma chemoprevention trial. N Engl J Med 2005;352:1092-102.	1810	129.29
69	Bronner CE1, Baker SM, Morrison PT, et al. Mutation in the DNA mismatch repair gene homologue hMLH1 is associated with hereditary non-polyposis colon cancer. Nature 1994;368:258-61.	1809	72.36
70	Muto T, Bussey HJ, Morson BC. The evolution of cancer of the colon and rectum. Cancer 1975;36:2251-70.	1781	40.48
71	Molodecky NA1, Soon IS, Rabi DM, et al. Increasing Incidence and Prevalence of the Inflammatory Bowel Diseases With Time, Based on Systematic Review. Gastroenterology 2012;142:46-54.	1746	249.43
72	Barrett JC1, Hansoul S, Nicolae DL, et al. Genome-wide association defines more than 30 distinct susceptibility loci for Crohn's disease. Nat Genet 2008;40:955-62.	1740	158.18
73	Toyota M1, Ahuja N, Ohe-Toyota M, et al. CpG island methylator phenotype in colorectal cancer. Proc Natl Acad Sci U S A 1999;96:8681-6.	1732	86.60
74a	Loftus EV Jr1. Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. Gastroenterology 2004;126:1504-17.	1712	114.13
74b	Umar A1, Boland CR, Terdiman JP, et al. Revised Bethesda Guidelines for	1712	114.13

	hereditary nonpolyposis colorectal cancer (Lynch syndrome) and microsatellite instability. J Natl Cancer Inst 2004;96:261-8.		
74c	Fearon ER, Cho KR, Nigro JM, et al. Identification of a chromosome 18q gene that is altered in colorectal cancers. Science 1990;247:49-56.	1712	59.03
75	Heald RJ, Husband EM, Ryall RD. The mesorectum in rectal cancer surgery--the clue to pelvic recurrence? Br J Surg 1982;69:613-6.	1702	46.00
76	Greten FR1, Eckmann L, Greten TF, et al. IKK beta links inflammation and tumorigenesis in a mouse model of colitis-associated cancer. Cell 2004;118:285-96.	1696	113.07
77	Bos JL, Fearon ER, Hamilton SR, et al. Prevalence of ras gene mutations in human colorectal cancers. Nature 1987;327:293-7.	1696	53.00
78a	Guarner F1, Malagelada JR. Gut flora in health and disease. Lancet 2003;361:512-9.	1690	105.63
78b	Papadopoulos N1, Nicolaides NC, Wei YF, et al. Mutation of a mutL homolog in hereditary colon cancer. Science 1994;263:1625-9.	1690	67.60
79	Goldberg RM1, Sargent DJ, Morton RF, et al. A Randomized controlled trial of fluorouracil plus leucovorin, irinotecan, and oxaliplatin combinations in patients with previously untreated metastatic colorectal cancer. J Clin Oncol 2004;22:23-30.	1656	110.40
80	Lacy AM1, García-Valdecasas JC, Delgado S, et al. Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomised trial. Lancet 2002;359:2224-9.	1639	96.41
81	Fiocchi C1. Inflammatory bowel disease: Etiology and pathogenesis. Gastroenterology 1998;115:182-205.	1631	77.67
82	Hidalgo IJ1, Raub TJ, Borchardt RT. Characterization of the human colon carcinoma cell line (Caco-2) as a model system for intestinal epithelial permeability. Gastroenterology 1989;96:736-49.	1619	53.97
83	Sokol H1, Pigneur B, Watterlot L, et al. Faecalibacterium prausnitzii is an	1602	145.64

	anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. Proc Natl Acad Sci U S A 2008;105:16731-6.		
84	Vasen HF1, Watson P, Mecklin JP, et al. New clinical criteria for hereditary nonpolyposis colorectal cancer (HNPCC, Lynch Syndrome) proposed by the International Collaborative Group on HNPCC. Gastroenterology 1999;116:1453-6.	1598	79.90
85	Winawer S, Fletcher R, Rex D, et al. Colorectal cancer screening and surveillance: Clinical guidelines and rationale - Update based on new evidence. Gastroenterology 2003;124:544-60.	1595	99.69
86	Siegel R, Desantis C, Jemal A. Colorectal cancer statistics, 2014. CA Cancer J Clin 2014;64:104-17.	1591	318.20
87	Bosset JF1, Collette L, Calais G, et al. Chemotherapy with preoperative radiotherapy in rectal cancer. N Engl J Med 2006;355:1114-23.	1588	122.15
88	Giantonio BJ1, Catalano PJ, Meropol NJ, et al. Bevacizumab in combination with oxaliplatin, fluorouracil, and leucovorin (FOLFOX4) for previously treated metastatic colorectal cancer: Results from the Eastern Cooperative Oncology Group Study E3200. J Clin Oncol 2007;25:1539-44.	1577	131.42
89	Silverberg MS1, Satsangi J, Ahmad T, et al. 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;19 Suppl A:5A-36A.	1575	112.50
90	Lennard-Jones JE1. Classification of inflammatory bowel disease. Scand J Gastroenterol Suppl 1989;170:2-6.	1558	51.93
91	Eaden JA1, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut 2001;48:526-35.	1550	86.11
92	Vasen HF, Mecklin JP, Khan PM, Lynch HT. The International Collaborative Group on Hereditary Non-Polyposis Colorectal Cancer (ICG-HNPCC). Dis Colon Rectum 1991;34:424-5.	1530	54.64
93	Nishisho I1, Nakamura Y, Miyoshi Y, et al. Mutations of chromosome 5q21	1525	54.46

	genes in FAP and colorectal cancer patients. Science 1991;253:665-9.		
94	Thun MJ1, Namboodiri MM, Heath CW Jr. Aspirin use and reduced risk of fatal colon cancer. N Engl J Med 1991;325:1593-6.	1524	54.43
95	Solomon SD1, McMurray JJ, Pfeffer MA, Wittes J, et al. Cardiovascular risk associated with celecoxib in a clinical trial for colorectal adenoma prevention. N Engl J Med 2005;352:1071-80.	1512	108.00
96	Okayasu I1, Hatakeyama S, Yamada M, et al. A novel method in the induction of reliable experimental acute and chronic ulcerative colitis in mice. Gastroenterology 1990;98:694-702.	1507	51.97
97	Herman JG1, Umar A, Polyak K, et al. Incidence and functional consequences of hMLH1 promoter hypermethylation in colorectal carcinoma. Proc Natl Acad Sci U S A 1998;95(12:6870-5.	1505	71.67
98a	Colombel JF1, Sandborn WJ, Reinisch W, et al. Infliximab, Azathioprine, or Combination Therapy for Crohn's Disease. N Engl J Med 2010;362:1383-95.	1503	167.00
98b	Winawer SJ1, Fletcher RH, Miller L, et al. Colorectal cancer screening: Clinical guidelines and rationale. Gastroenterology 1997;112:594-642.	1503	68.32
99	Topping DL1, Clifton PM. Short-chain fatty acids and human colonic function: Roles of resistant starch and nonstarch polysaccharides. Physiol Rev 2001;81:1031-64.	1486	82.56
100	Lièvre A1, Bachet JB, Le Corre D, et al. KRAS mutation status is predictive of response to cetuximab therapy in colorectal cancer. Cancer Res 2006;66:3992-5.	1479	113.77

PeerJ Preprints | https://doi.org/10.7287/peerj.preprints.27602v1 | CC BY 4.0 Open Access | rec: 19 Mar 2019, publ: 19 Mar 2019

Table 2(on next page)

Table 2

Authors with two or more citation classics

PeerJ Preprints | https://doi.org/10.7287/peerj.preprints.27602v1 | CC BY 4.0 Open Access | rec: 19 Mar 2019, publ: 19 Mar 2019

1 Table 2 Authors with two or more citation classics

Author	Articles	First author	Second author
Fearon, ER	5	2	3
Vogelstein, B	3	1	2
Cunningham, D	2	1	1
Boland, CR	2	1	1
Thibodeau, SN	2	1	1
Winawer, SJ	2	2	0
Hanauer, SB	2	1	1
Andre, T	2	1	1
Nicolaides, NC	2	0	2
Rutgeerts, P	2	1	1
Markowitz, S	2	1	1
Baker, SJ	2	2	0
Umar, A	2	1	1
Vasen, HFA	2	2	0

2

Table 3(on next page)

Table 3

Authors with two or more citation classics Journals in which the top 100 citation classics were published

1 Table 3 Journals in which the top 100 citation classics were published

Journal title	Number of manuscripts in the 100 citation classics	Number of citations	Average number of citations	Impact factor [a]
The New England Journal of Medicine	23	59614	2591.91	79.258
Science	13	28513	2193.31	41.058
Nature	12	31584	2632.00	51.941
Gastroenterology	10	17821	1782.10	20.773
Cell	9	27831	3092.33	35.612
Lancet	7	14159	2022.71	53.25
Journal of Clinical Oncology	6	12067	2011.17	26.303
Proceedings of the National Academy of Sciences of the United States of America	5	9268	1853.60	9.504
Cancer Research	3	7878	2626.00	10.199
Others	16	30969	1935.56	-

2 a: Journal impact factor was based on Thomson Reuters Web of Knowledge Journal Citation
3 Reports Ranking (2017).

4

Table 4(on next page)

Table 4

Table 4 Institution with the highest number of papers in the top 100 citation classics

Institution	No. of articles
The Johns Hopkins University School of Medicine	8
Yale University School of Medicine	3
University of California	3
Gastroenterology and Nutrition Service, Memorial Sloan-Kettering Cancer Center	2
Hopital Saint-Antoine	2
Mayo Clinic	2
University Hospital Gasthuisberg	2
Vanderbilt University Medical Center	2
University Hospitals of Cleveland	2
Harvard University	2
University of Texas M.D. Anderson Cancer Center	2
Mount Sinai Hospital, University of Tronto	2
National Cancer Institute, National Institutes of Health	2
Queen's Medical Centre	2
American Cancer Society	2
Universite Paris-Descartes	2

Table 5(on next page)

Table 5

Field of study based on types of studies

Table 5 Field of study based on types of studies

Name of disease	Total	Clinical study				Basic science study	Review	Guideline and consensus	Meta-Analysis or Systematic review	Comment	Others
		RCTs	Prospective study	Retrospective study	Case report						
Tumor											
Only colonic cancer	21	4	1	—	—	16	—	—	—	—	—
Only rectal cancer	4	3	—	—	1	—	—	—	—	—	—
Colorectal cancer	51	17	3	1	—	18	6	3	1	—	2
Inflammation											
IBD	10	—	—	—	—	3	3	—	1	—	3
Only UC	4	1	1	—	—	2	—	—	—	—	—
Only CD	8	4	—	—	—	4	—	—	—	—	—
Microbiology	4	—	—	—	—	1	2	—	—	1	—
Functional bowel disorders	1	—	—	—	—	—	1	—	—	—	—
Others	1	—	—	—	—	—	1	—	—	—	—
Total	104	29	5	1	1	44	13	3	2	1	5

RCTs: Randomized controlled trials

Table 6(on next page)

Table 6

Levels of evidence and article type comprising the top 100 citation classics

1 Table 6 Levels of evidence and article type comprising the top 100 citation classics

Level of evidence	Article type	No. of articles
	Systematic review	1
I	Meta-analysis	1
	Guidelines	3
II	Randomized controlled trial	29
III	Prospective study	5
IV	Retrospective study	1
	Case Reports	1
V	Review	13
	Comment	1

2

Figure 1

Figure 1

Distribution of top-cited articles from 1955 to 2014

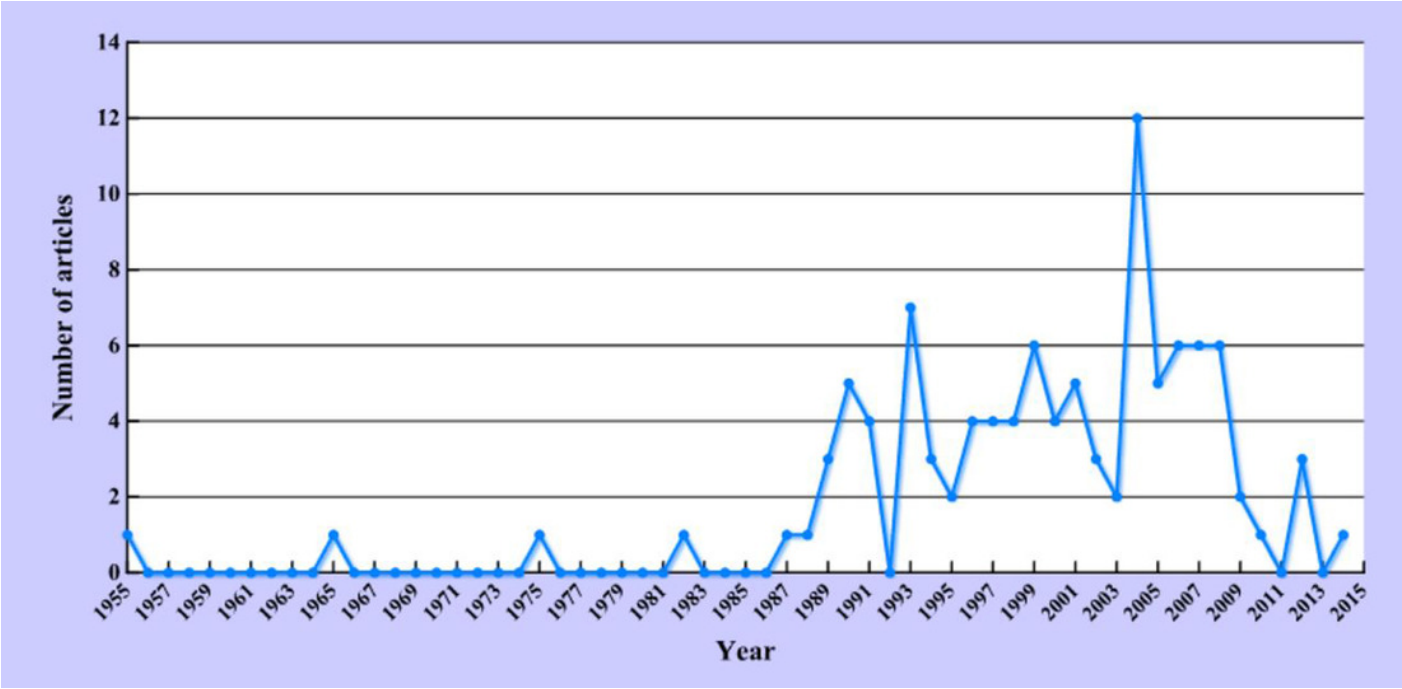

Figure 2

Figure 2

Total citations of the articles in the top 100 list every year

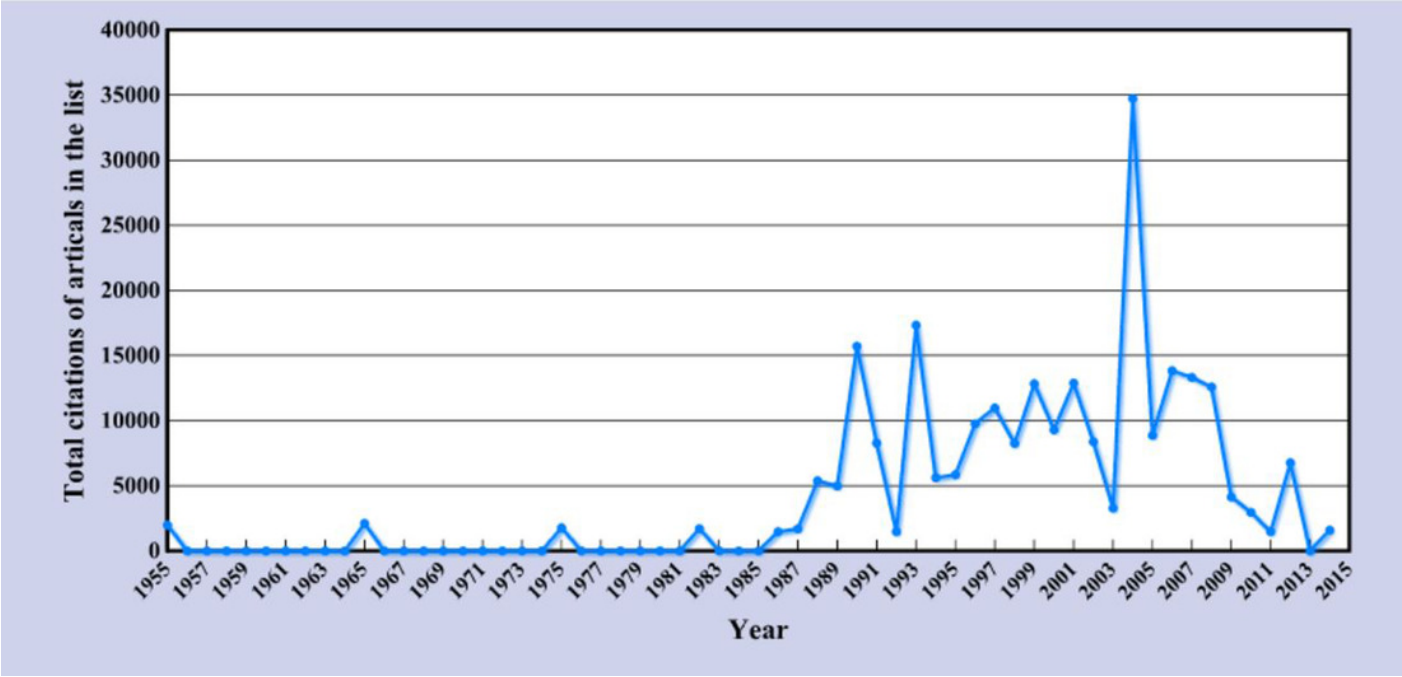

Figure 3

Figure 3

The countries of origin of the top-cited 100 articles.

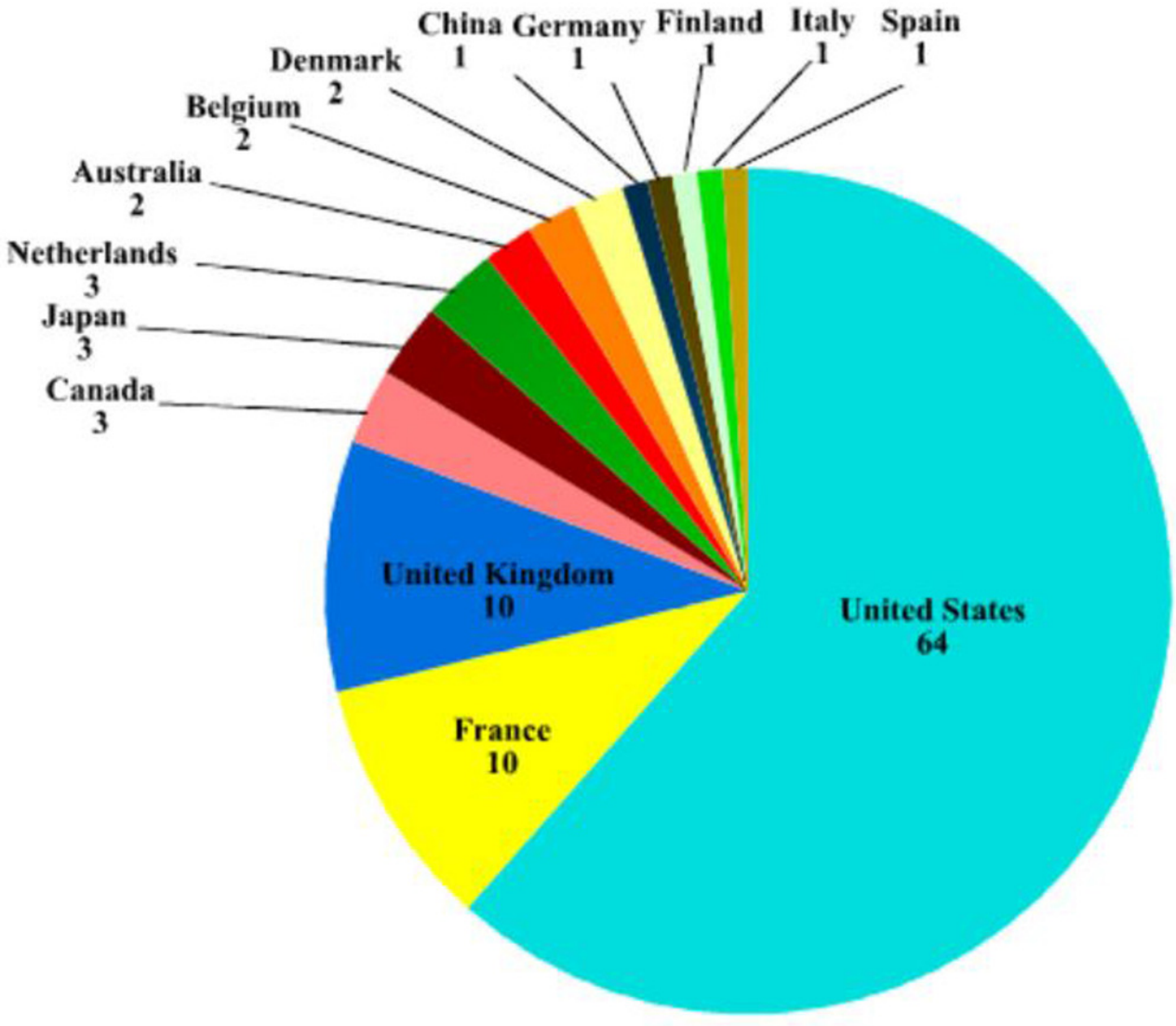

Figure 4

Figure 4

Network visualization map of relationships between the most commonly used keywords in the abstract and title.

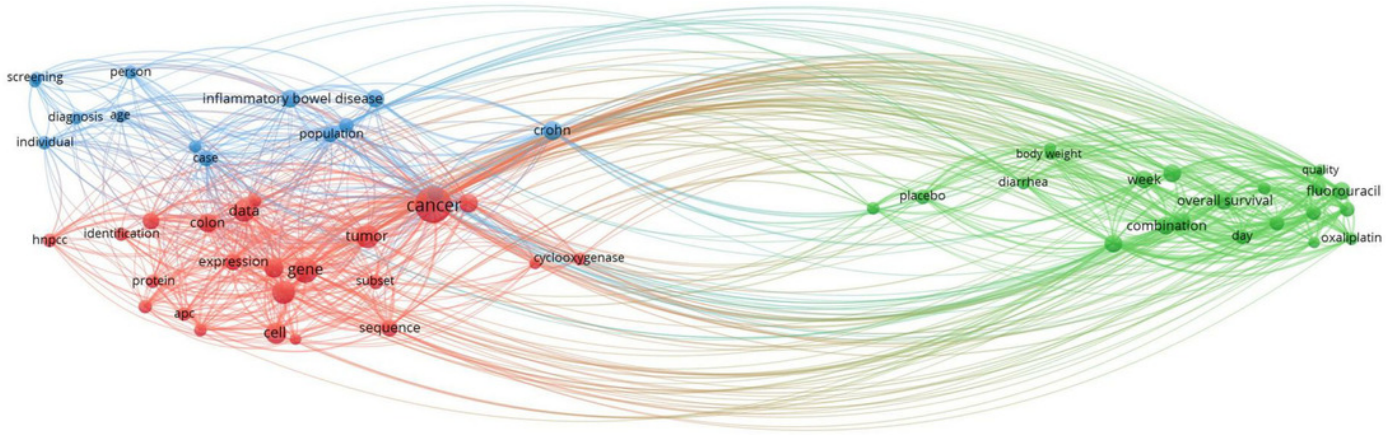

Figure 5

Figure 5

Word cloud for the frequency of research topics