



# The 100 most cited papers in nasopharyngeal carcinoma between 2000 and 2019: a bibliometric study

Cong-Yan Xing<sup>1#</sup>, Min-Qiang Lin<sup>1#</sup>, Wen-Ting Luo<sup>1</sup>, Long-Fei Chen<sup>1</sup>, San-Gang Wu<sup>2</sup>, Yi-Jia Cai<sup>3</sup>

<sup>1</sup>Department of Scientific Management, the First Affiliated Hospital of Xiamen University, School of Medicine, Xiamen University, Xiamen, China;

<sup>2</sup>Department of Radiation Oncology, Xiamen Cancer Center, Xiamen Key Laboratory of Radiation Oncology, the First Affiliated Hospital of Xiamen University, School of Medicine, Xiamen University, Xiamen, China; <sup>3</sup>Department of Scientific Management, the First Affiliated Hospital of Fujian Medical University, Fuzhou, China

**Contributions:** (I) Conception and design: SG Wu, YJ Cai; (II) Administrative support: SG Wu, YJ Cai; (III) Provision of study materials or patients: WT Luo, LF Chen; (IV) Collection and assembly of data: CY Xing, MQ Lin; (V) Data analysis and interpretation: CY Xing, MQ Lin; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

<sup>#</sup>These authors contributed equally to this work.

**Correspondence to:** San-Gang Wu. Department of Radiation Oncology, Xiamen Cancer Center, Xiamen Key Laboratory of Radiation Oncology, the First Affiliated Hospital of Xiamen University, School of Medicine, Xiamen University, Xiamen 361003, China. Email: wusg@xmu.edu.cn; Yi-Jia Cai. Department of Scientific Management, the First Affiliated Hospital of Fujian Medical University, Fuzhou 350005, China. Email: ejia\_cai@163.com.

**Background:** To identify the 100 most-cited papers that have contributed to the understanding and treatment of nasopharyngeal carcinoma (NPC).

**Methods:** We searched the NPC-related papers between 2000 and 2019 using the Web of Science database on October 12, 2022. Papers were identified in descending order according to the number of citations. The top 100 papers were analyzed.

**Results:** These 100 most cited papers on NPC have been cited for a total of 35,273 times, with a median number of citations of 281 times. There were 84 research papers and 16 review papers. The *Journal of Clinical Oncology* (n=17), *International Journal of Radiation Oncology Biology Physics* (n=13), and *Cancer Research* (n=9) published the most papers. *Cancer Epidemiology Biomarkers & Prevention*, *Lancet*, *Cancer Cell*, *Molecular Cancer*, and the *New England Journal of Medicine* had the largest average citations per paper. China contributed the most papers (n=71), followed by USA (n=13), Singapore (n=4) and, France (n=4). There were 55 clinical research papers and 29 laboratory research papers. Intensity-modulated radiation therapy technology (n=13), concurrent chemoradiotherapy (n=9), and neoadjuvant chemoradiotherapy (n=5) were the top three research topics. Epstein-Barr virus-related genes (n=9) and noncoding RNA (n=8) were the research domains in laboratory research papers. The top three contributors were Jun Ma (n=9), Anthony T C Chan (n=8), and Anne Wing-Mui Lee (n=6).

**Conclusions:** This study provides an overview of the major areas of interest in the field of NPC with bibliometric analyses. This analysis recognizes some important contributions in the field of NPC and stimulates future investigations in the scientific community.

**Keywords:** Nasopharyngeal carcinoma (NPC); citation analysis; bibliometric analysis; Web of Science (WoS)

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## Introduction

Nasopharyngeal carcinoma (NPC) is defined as squamous cell carcinoma arising in the lining of the nasopharyngeal epithelium. It is notable for its wide geographic variation, with a high incidence of more than 30 per 100,000 people in southern China and Southeast Asia, and only an incidence of approximately one per 100,000 people globally (1,2). There are approximately 133,354 new NPC cases each year worldwide (1,2), with an estimated 64,165 new cases in China in 2022 (3). More than 90% of Chinese patients are type III NPC as defined by World Health Organization (WHO), an Epstein-Barr virus (EBV)-associated cancer (4). However, approximately 40% of western NPC are type I as defined by WHO, which is more closely associated with tobacco smoking, than that of type II or type III NPC (5,6). Radiotherapy is the key treatment plan for NPC, and the addition of neoadjuvant chemotherapy and concurrent chemotherapy improves survival rate (7). In recent decades, NPC-related mortality has gradually declined (8), reflecting the advancement on innovative techniques and treatments for managing NPC. However, there are a large number of literatures related to NPC, involving various researchers, countries, specialties, scientific journals, and countries. Clinicians and researchers are difficult to identify NPC-related literature with increased knowledge and improved clinical practice in this

field. Therefore, it is necessary to monitor global NPC research.

In recent years, several scientific papers have investigated NPC regarding screening, molecular classification, biological markers, intensity-modulated radiation therapy (IMRT) technology, targeted therapy, and immunotherapy (9-15). Citation analysis is a systematic approach to measure the influence of papers with high impacts in shaping the scientific discipline by identifying papers that have a significant impact in their field (16). Counting publications and citations are one of the methods to identify the most influential papers in a specific field. Bibliometric analysis describes the current trends and development of a specific field by extracting information and has been applied to identify the most impactful scientific papers in the field of hypertension (17), obstetrics and gynecology (18), breast cancer (19), and oral pathology & medicine (20). To the best of our knowledge, there are only two bibliometric studies analyzing NPC publications (21,22). However, one study covered papers published between 1970 and 2018 with 39% of papers published before 2000 (21). In addition, another bibliometric study investigated the 100 most cited papers in the head and neck oncology literature, but only 7 papers were related to NPC (22). Therefore, the above two bibliometric studies may not be very effective in reflecting the current trend of NPC research. Thus, this bibliometric analysis aimed to analyze the top 100 most cited papers on NPC published between 2000 and 2019 to better understand the development and trends of NPC research and to offer guidance for further studies.

### Highlight box

#### Key findings

- This study provides some insights into the progression of our understanding of nasopharyngeal carcinoma as well as treatment and related research.

#### What is known and what is new?

- The abundance of published literature on nasopharyngeal carcinoma benefits the development of the industry, but also creates challenges for researchers in their field to identify high-impact research.
- Through bibliometric methods, we assessed the current status of the top 100 most cited papers on nasopharyngeal carcinoma according to the institutions, authors, published journals, and research domains.

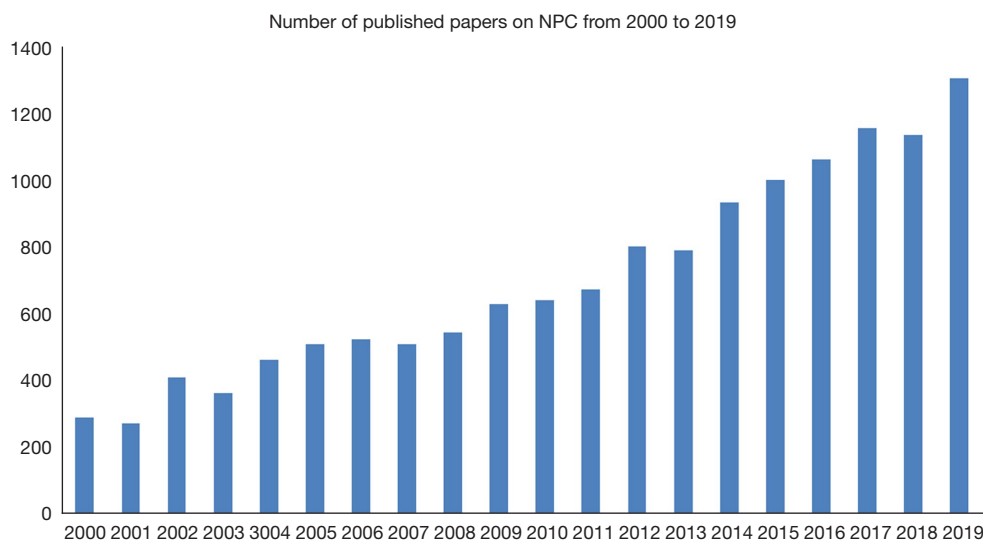
#### What is the implication, and what should change now?

- This analysis recognizes some important contributions in the field of nasopharyngeal carcinoma and stimulates future investigations in the scientific community.
- Report here about implications and actions needed.

## Methods

### *Data sources and search strategy*

Literature search on the Web of Science (WoS) database was performed. The introduction of IMRT to the clinical practice of head and neck cancer was published in 1999 (23), and the first paper regarding IMRT on NPC was published in 2000 (24). Therefore, this study included the papers published from January 2000 to December 2019. The literature search of this study was conducted on October 12, 2022, to avoid the potential impact of paper citation counting. The keywords searched were as follows: ALL = (nasopharyngeal carcinoma) OR ALL = (nasopharyngeal neoplasm) OR ALL = (nasopharyngeal cancer) OR ALL = (nasopharyngeal tumor). Only papers with peer-reviewed articles and reviews were included. The retrieved papers



**Figure 1** The number of published papers from 2000 to 2019. NPC, nasopharyngeal carcinoma.

were sorted in descending order of citation counts. The 100 most cited papers were included in the analyses. Two researchers (Min-Qing Lin and Yi-Jia Cai) reviewed and screened the research types and research domains of the papers. Ethics approval was not required because no human subjects were included in this study.

### Data collection

After filtering the papers, the following contents in each paper were extracted carefully. The title of the papers, year of publication, citation count, source journal, corresponding author, the institution of the corresponding author, and the country. Secondly, the papers were further classified as clinical research papers, laboratory research papers, or reviews.

### Statistical analysis

Descriptive statistics were applied with the citation counts or percentages of the parameters. Data were analyzed using IBM SPSS 22.0 package (IBM Corp., Armonk, NY, USA) and Microsoft EXCEL 2007 were used for statistical analyses.

## Results

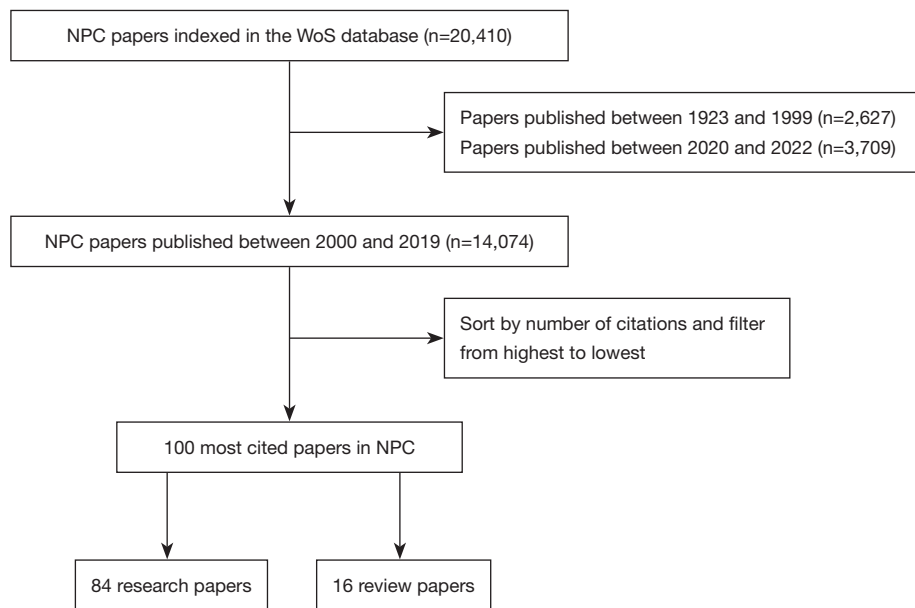
### Time distribution, article type, and citations

A total of 14,074 papers regarding NPC were published

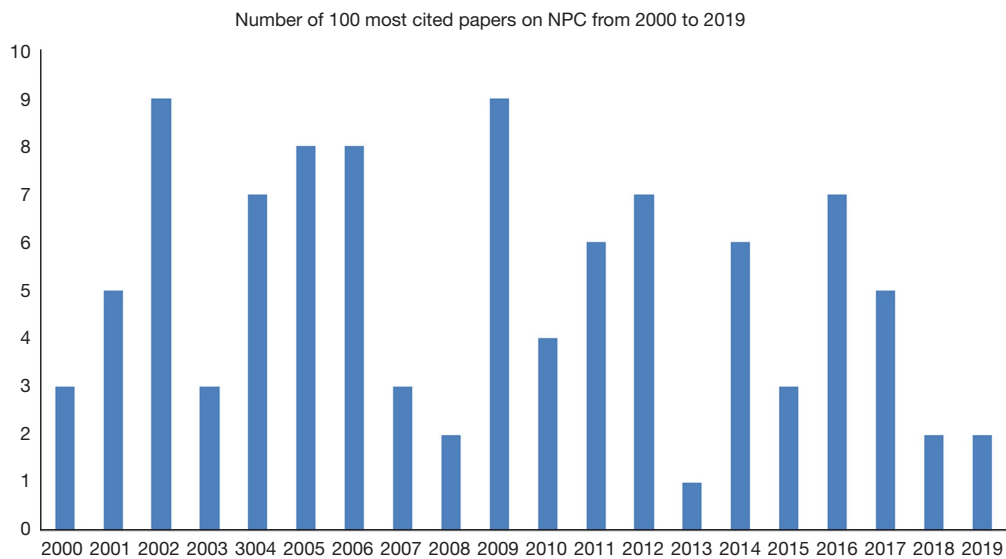
between 2000 and 2019. *Figure 1* shows the number of published papers over the period. There were 290 papers published in the year 2000 and 1,312 papers published in the year 2019. *Figure 2* shows the flowchart of paper selection. The table (<https://cdn.amegroups.com/static/public/tcr-22-2621-1.xls>) lists the 100 most cited papers and *Figure 3* shows the time distribution of the papers. There were 57 (57%) papers published between 2000 and 2009 and 43 (43%) papers published between 2010 and 2019. All the top 100 papers had been cited 35,273 times, with a median citation number of 281 times (range, 190–1,121 times). There were 55 clinical research papers, 29 laboratory research papers, and 16 review papers. Of the 10 most cited papers (*Table 1*), the review paper regarding “Nasopharyngeal carcinoma” by Wei *et al.* (25) was the most cited paper (1,121 times), and the updated reviews by Chen *et al.* (26) and Chua *et al.* (27) came in the third and fifth citations, respectively. In addition, two papers reviewed on the epidemiology of NPC (28,29), one paper investigated the role of EBV DNA in NPC (30), and the other papers investigated the treatment of NPC (31–34).

### Journals

The top 100 papers were mainly published in 34 journals (*Figure 4*). The top three journals were the *Journal of Clinical Oncology* (n=17), *International Journal of Radiation Oncology Biology Physics* (n=13), and *Cancer Research* (n=9). The *Cancer Epidemiology Biomarkers & Prevention* (977.0 citations per



**Figure 2** Flow diagram of the study cohort. NPC, nasopharyngeal carcinoma; WoS, Web of Science.



**Figure 3** The publication time distribution of the 100 most cited papers. NPC, nasopharyngeal carcinoma.

paper), *Lancet* (814.5 citations per paper), *Cancer Cell* (470.0 citations per paper), *Molecular Cancer* (445.0 citations per paper), and *New England Journal of Medicine (NEJM)* (420.8 citations per paper) had the highest number of average citations per paper.

**Countries**

Of the 100 most cited papers, the corresponding authors were from 10 countries (*Figure 5*). China published the most papers (n=71), followed by USA (USA) (n=13), Singapore

**Table 1** The 10 most cited papers on nasopharyngeal carcinoma from 2000 to 2019

Rank	Title	Article type	Journal	Year	Total citations	Country
1	Nasopharyngeal carcinoma	Review	<i>Lancet</i>	2005	1,121	China
2	The enigmatic epidemiology of nasopharyngeal carcinoma	Review	<i>Cancer Epidemiology Biomarkers &amp; Prevention</i>	2006	977	USA
3	Nasopharyngeal carcinoma	Review	<i>Lancet</i>	2019	938	China
4	Intensity-modulated radiotherapy in the treatment of nasopharyngeal carcinoma: An update of the UCSF experience	Article	<i>International Journal of Radiation Oncology Biology Physics</i>	2002	904	USA
5	Nasopharyngeal carcinoma	Review	<i>Lancet</i>	2016	881	Singapore
6	Epidemiology of nasopharyngeal carcinoma	Article	<i>Seminars in Cancer Biology</i>	2002	727	USA
7	Phase III study of concurrent chemoradiotherapy versus radiotherapy alone for advanced nasopharyngeal carcinoma: Positive effect on overall and progression-free survival	Article	<i>Journal of Clinical Oncology</i>	2003	651	China
8	Quantification of plasma Epstein-Barr virus DNA in patients with advanced nasopharyngeal carcinoma	Article	<i>New England Journal of Medicine</i>	2004	635	China
9	Chemotherapy in locally advanced nasopharyngeal carcinoma: An individual patient data meta-analysis of eight randomized trials and 1753 patients	Article	<i>International Journal of Radiation Oncology Biology Physics</i>	2006	559	France
10	Treatment results for nasopharyngeal carcinoma in the modern era: The Hong Kong experience	Article	<i>International Journal of Radiation Oncology Biology Physics</i>	2005	549	China

DNA, deoxyribo nucleic acid; UCSF, University of California, San Francisco.

(n=4), France (n=4), England (n=2), and Canada (n=2). Of the 71 papers published from China, there were 38 papers (53.5%) published between 2000 and 2009, and 33 papers (46.5%) published between 2010 and 2019. *Figure 6* shows the trend of the paper published by China over the period.

### Research domains

Among them, 55 papers were clinical research papers (*Table 2*), IMRT technology (n=13), concurrent chemoradiotherapy (n=9), and neoadjuvant chemotherapy (n=5) were the top three research topics. The other topics of these highly cited papers were primarily exploring morbidity and mortality, screening, EBV-DNA, staging, neoadjuvant chemotherapy, adjuvant chemoradiotherapy, palliative chemotherapy, targeted therapy, survival outcomes, adverse effects of radiotherapy, and the patterns of failure after treatment. Immunotherapy in advanced NPC was also a research topic in recent years, there were

three papers published between 2017 and 2018 (9,10,35). In 29 papers regarding laboratory research, EBV-related genes (9 papers) and noncoding RNA (8 papers) were the research domains.

### Distribution of authors

The top three authors contributed a total of 23 papers (23%) relating to NPC. Dr. Jun Ma published the most papers in this field (9 papers), followed by Dr. Anthony T C Chan (8 papers), and Dr. Anne Wing-Mui Lee (6 papers). Dr. Ma, Dr. Chan, and Dr. Lee are from the Sun Yat-Sen University Cancer Center (SYSUCC), China, the Pamela Youde Nethersole Eastern Hospital, China, and the Chinese University of Hong Kong, China, respectively.

### Discussion

The abundance of published literature benefits the

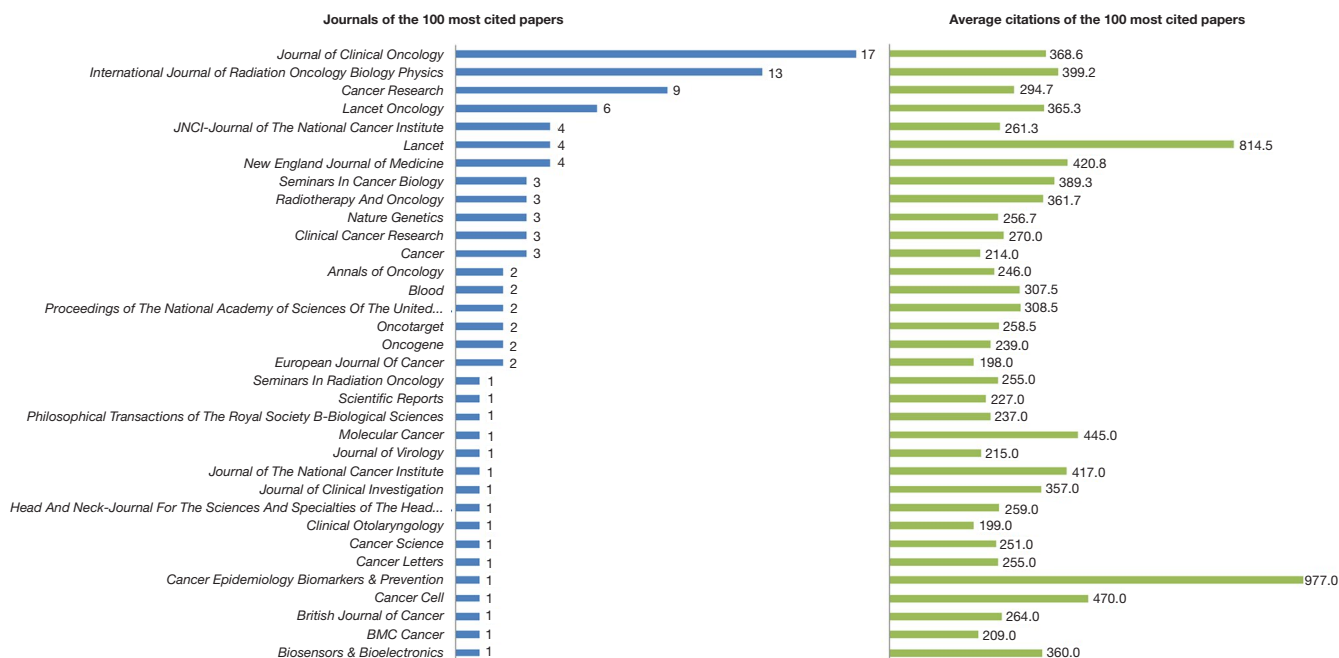


Figure 4 The distribution of the journals and average citations of the top 100 cited papers.

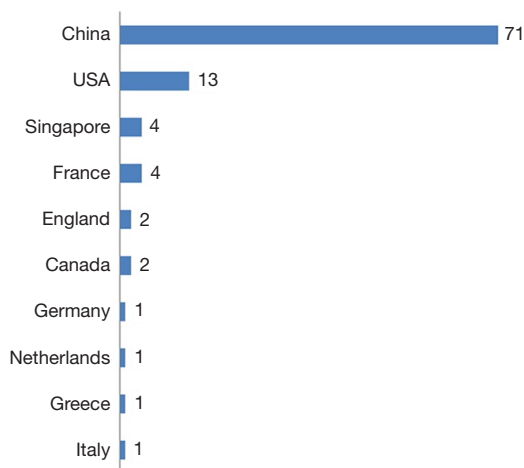
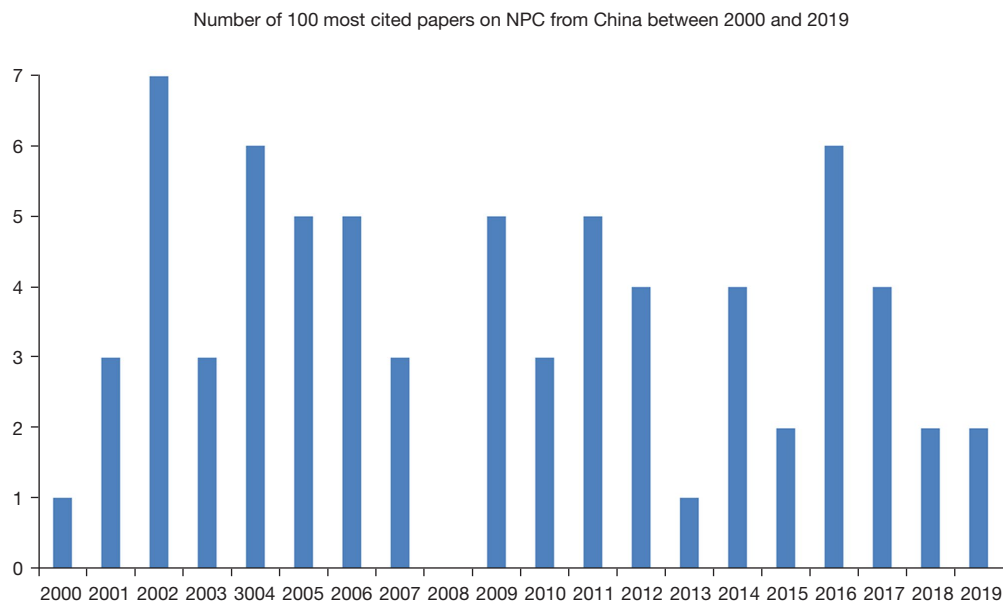


Figure 5 The country of the corresponding author in the top 100 cited papers.

development of the industry, but also creates challenges for researchers in their field to identify high-impact research. In the current study, the top 100 cited papers on NPC over the past 20 years were analyzed to investigate information about institutions, authors, published journals, and research domains in the field to gain insight into the future research directions for this fast-growing scientific field.

The literature on NPC has grown rapidly in the past 20 years. In our study, there were 256 papers published in the year 2000 and 1,311 papers published in the year 2019. Among the top 100 cited papers, China participated the most, followed by the USA and Singapore. It is noteworthy that most papers originated from China and Asia in our study (n=75), and only a few articles originated from North America and Europe (n=25). This may be due to a wide geographic variation in the incidence of NPC (1,2). In addition, there are growing economic resources to fund scientific research and a growing number of researchers in China over the past two decades (36). In our study, 5 of the 13 papers from the USA were clinical studies, and 4 of them explored the technique of IMRT on NPC. The USA was the first country to develop IMRT technology in 1995, which was subsequently promoted worldwide (37). Since 2001, the Cancer Hospital Chinese Academy of Medical Sciences and SYSUCC have taken the lead in carrying out IMRT technology for NPC, and then major radiation centers have successively started this technology in China. IMRT technology can not only improve the control rate of tumors but also play an important role in the protection of normal organs. This shows that the advancement of technology can bring better benefits to human health.

The journal impact factor (JIF) refers to the average



**Figure 6** The trends of the most cited papers published by China from 2000 to 2019. NPC, nasopharyngeal carcinoma.

**Table 2** The research domains of the 55 most cited clinical papers for nasopharyngeal carcinoma between 2000 and 2019

Research domains	Number of articles	Total number of citations	Average citations per year (per paper)	Publication year
Screening	2	575	287.5	2010–2017
Incidence and mortality	2	464	232	2006–2016
Staging	2	668	334	2009–2019
Imaging technology	1	324	324	2017
EBV-DNA	4	1,472	368	2002–2016
IMRT	13	4,683	360.231	2000–2015
Concurrent chemoradiotherapy	9	3,706	411.778	2002–2011
Neoadjuvant chemotherapy	5	1,864	372.8	2001–2019
Concurrent and adjuvant chemoradiotherapy	4	1,501	375.25	2004–2017
Prognostic analysis	2	867	433.5	2005–2016
Side effects of IMRT	3	1,428	476	2006–2012
Outcomes and patterns of failure	1	220	220	2011
Targeted therapy	2	484	242	2005–2012
Immunotherapy	4	441	110.25	2005–2012
Palliative chemotherapy	1	318	318	2016

EBV, Epstein-Barr virus; DNA, deoxyribo nucleic acid; IMRT, intensity-modulated radiation therapy.

citation counts associated with a journal in each period. Several bibliometric studies showed that journals with high JIF, such as the *Lancet* and *NEJM*, were the leading journals for top-cited papers (38,39). In our study, The *Journal of Clinical Oncology* (5-year JIF =38.801) is the leading journal with the most papers (n=17) and has one paper in the top 10 cited papers. The *International Journal of Radiation Oncology Biology Physics* (5-year JIF =7.5) is the second highest number of papers (n=13) (5-year JIF =7.5) and has three papers in the top 10 cited papers. In our study, the *Lancet* and *NEJM* had the second and fifth average citations per paper, respectively. It should be noted that high JIF such as the *NEJM* (5 years JIF =125.115) (n=4) and *Lancet* (5 years JIF =130.838) (n=4) have fewer articles. Although high JIF journals accept a wider variety of medical papers, have wider audiences, and attract more submissions, authors may be more prefer to submit their studies to more specialized journals. As expected, these high JIF journals have higher citation counts in our study. Nevertheless, establishing the association between citation counts and clinical impact by determining whether high-cited papers are more often incorporated into clinical practice would be valuable for future research.

Several studies have shown that the USA produced the highest number of top-cited papers (19,40,41). In our study, Southern China including Guangdong Province and Hong Kong Special Administrative Region was the most productive region. Dr. Jun Ma, Anthony T C Chan, and Anne Wing-Mui Lee contributed 9, 8, and 6 top-cited papers, respectively. They are from the SYSUCC, the Chinese University of Hong Kong, and Pamela Youde Nethersole Eastern Hospital, respectively. The incidence of NPC has significant regional characteristics, with the highest incidence in Southern China. Therefore, there are sufficient clinical research cases of NPC in Southern China. These scholars from China not only participated in the formulation of staging for NPC but also made important contributions to the improvement of treatment strategies for NPC (4,42,43). These findings indicate that these institutes have advanced technology, management concepts, and enough clinical cases, and studying in the region or in-depth cooperation with researchers in the region can help expand the understanding of the field of NPC.

In addition to IMRT technology, chemotherapy including concurrent chemoradiotherapy (n=9) and neoadjuvant chemotherapy (n=5) of NPC were also the top research topics. Based on the above findings, the survival

benefit of concurrent chemoradiotherapy in NPC has been confirmed (32,43), and the addition of neoadjuvant chemotherapy could further improve the survival of NPC patients (42,44). These studies have important implications for improving the treatment strategies of NPC. Because the above studies were randomized controlled trials with large sample sizes, they provided reliable evidence to change the clinical practice for clinicians to treat NPC.

Radiotherapy is the main curative treatment for non-metastatic NPC. The combination of IMRT and chemotherapy is the main treatment for locally advanced NPC. However, approximately 15–30% of locally advanced patients will develop locoregional and/or distant recurrence (45,46). For patients with advanced NPC treated with first-line and second- or later-line therapies, the median progression-free time was only 7.6 and 5.4 months, respectively (47). The general immune landscape makes immunotherapy suitable for this patient subset (48). Therefore, many researchers have started to explore effective immunotherapy regimens for this patient subset. In our study, three papers regarding immunotherapy in advanced NPC were published in 2017 and 2018, respectively (9,10,35). They showed that pembrolizumab, camrelizumab, or nivolumab in advanced NPC had an antitumor effect and a manageable safety profile in advanced NPC (9,10,35). These results demonstrate that new papers with novel discoveries and advanced technologies are published continuously.

Several limitations should be acknowledged in this study. First, analyzing citation numbers in the scientific literature have inherently biased and cannot rank the impact of scientific literature on disciplines. Second, older papers have a longer time to accumulate citation counts, which may be accumulating enough citations for newer papers. Third, we only used the WoS database in this study, and the papers published from other sources were missed. Finally, the citation counts used in our analysis did not exclude the influence of self-citations.

## Conclusions

In conclusion, this study provides an overview of the major areas of interest in the field of NPC using bibliometric analyses. It provides some insights into the progression of our understanding of NPC as well as treatment and related research. This analysis recognizes some important contributions in the field of NPC and stimulates future



investigations in the scientific community.

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## Footnote

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <https://tcr.amegroups.com/article/view/10.21037/tcr-22-2621/coif>). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work and in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Ethics approval was not required because no human subjects were included in this study.

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