

ORIGINAL RESEARCH

# Global trends and hotspots on recurrent respiratory papillomatosis: A 20-year bibliometric analysis

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## Abstract

**Objectives:** Recurrent respiratory papillomatosis (RRP) is the most common benign laryngeal tumor in children. It can cause serious psychological and mental burden on patients since RRP requires repeated surgical treatment. This study aims to delineate the global trends and identify hotspots related to RRP over the past two decades.

**Methods:** We systematically gathered research findings on RRP from 2004 to 2023, utilizing the Web of Science as our data source. Subsequently, we performed a comprehensive bibliometric analysis of the literature using Vosviewer, CiteSpace, and Bibliometrics online analysis platform.

**Results:** A total of 839 publications were finally identified on RRP from 2004 to 2023. The United States has the largest number of publications (392), accounting for 46.7%. The Capital Medical University is the most productive organization (24), followed by the Centers for Disease Control and Prevention (18). The most productive journal was the *Laryngoscope*, with 86 publications. Comparatively, *Vaccine* is the most cited journal (2297). Craig S. Derkay ranked highest among all authors in publication (16). Burst detection shows onset, adjuvant therapy, management, juvenile-onset RRP, systemic bevacizumab, avastin, human papillomavirus vaccine are recent keywords of great interest to researchers.

**Conclusion:** Research on RRP has progressed significantly over the past two decades, especially in terms of therapeutic strategies. We strongly believe that this article will provide new research directions for other researchers and may contribute to future breakthroughs in the field.

## KEYWORDS

bibliometric analysis, recurrent respiratory papillomatosis

## 1 | INTRODUCTION

Recurrent respiratory papillomatosis (RRP) is a proliferative respiratory tract condition caused by infection with human papillomavirus

Chao Wang, Yufei Pan, and Huili Huang contributed equally to this study.

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(HPV) types 6 and 11.<sup>1</sup> The membranous part of the vocal folds is the most common site for the onset of RRP. Symptoms often manifest as hoarseness and breathing difficulties.<sup>2</sup> While surgical intervention enables most patients to manage these symptoms, the disease progression in juveniles is disproportionately influenced by repeated surgeries, pulmonary complications, and psychological distress. Over the past two decades, the treatment approaches for this disease have undergone significant changes as research has deepened. Nonetheless, as of the current date, bibliometric analysis has not yet been employed in the study of RRP.

The strength of bibliometric analysis lies in its objective quantification of research impact, offering evidence-based evaluations of scientific productivity and quality.<sup>3</sup> Furthermore, it efficiently tracks the dissemination trends and impact of research topics and outcomes over time, forecasting research trends and hotspots.<sup>4</sup> Hotspots and frontiers refer to unresolved issues in specific fields that attract global scholarly attention.

In this study, we aim to comprehensively assess the global academic status and hotspots related to RRP and to forecast future trends in this area.

## 2 | MATERIALS AND METHODS

### 2.1 | Data sources and search strategies

A systematic search for literature on RRP spanning from 2004 to 2023 was conducted using the Science Citation Index Expanded (SCI-EXPANDED) database via the Web of Science (WoS) Core Collection. For the precaution of bias in database updates, all searches were completed on January 14, 2024. The search strategy

was TS = (“Recurrent Respiratory Papillomatosis”). The scope was restricted to English-language original research articles and reviews.

### 2.2 | Data collection and statistical analysis

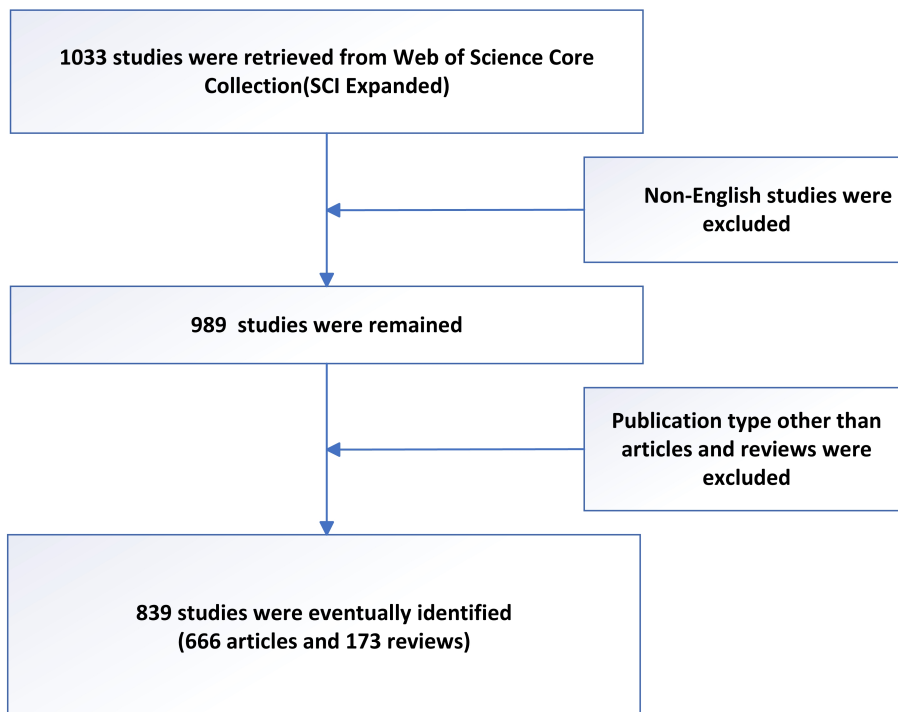
Two authors (W.C. and H.H.L.) independently collected all data, with an agreement rate of 0.99, which implies a high level of agreement.<sup>5</sup> After converting WoS data to txt format, Vosviewer version 1.6.20 (Leiden University, Leiden, The Netherlands) and CiteSpace version 6.2.R7 (Drexel University, Philadelphia, PA, USA) were used to screen and compute the data, as well as the Online Analysis Platform of Literature Metrology.<sup>6-8</sup>

All literature characteristics were selected to analyze, respectively. VOSviewer was applied to analyze and visualize bibliometric data, such as countries, institutions, journals, and authors. Furthermore, we created network visualization plots and density visualization. Concurrently, CiteSpace's burst-time analysis, a technique for detecting the time point when a certain research direction becomes a hotspot, was employed. This enabled us to generate a plot of authorship-keyword bursts from bibliographic records, facilitating the exploration of historical trends and potential future research directions.

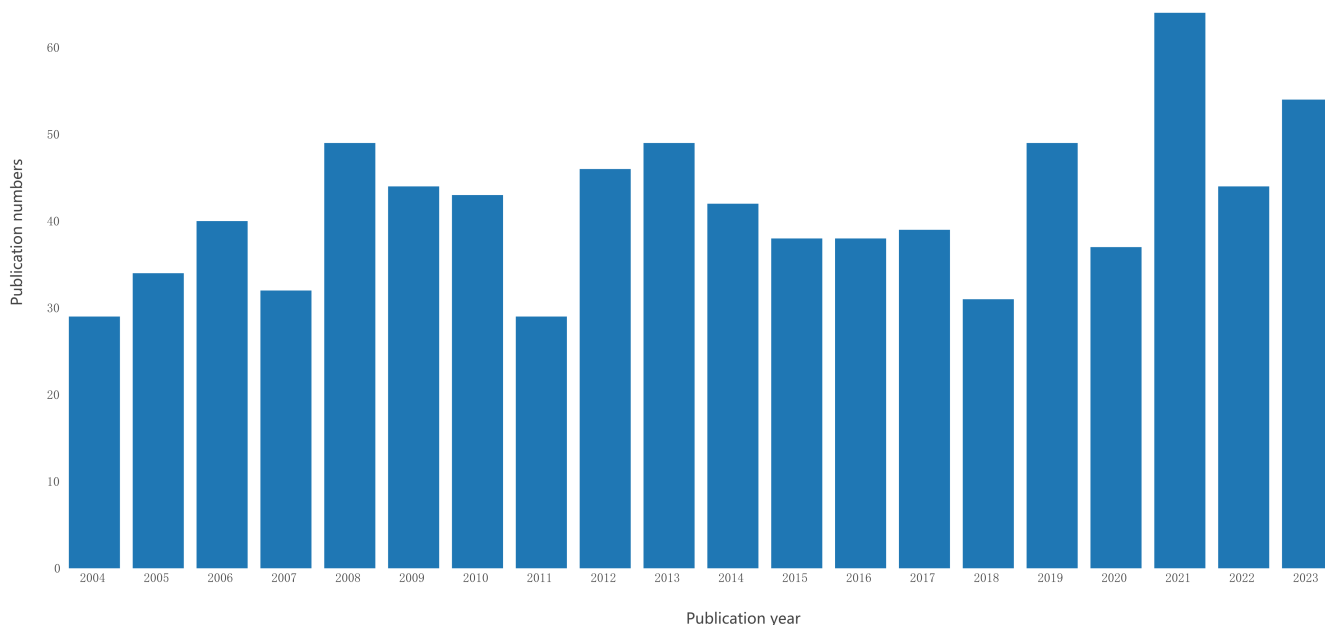
## 3 | RESULTS

### 3.1 | Performance of countries/regions

As shown in the flowchart (Figure 1), the initial search retrieved a total of 1033 publications. After limiting the



**FIGURE 1** Flow chart of the inclusion process.



**FIGURE 2** Growth trends of publications on RRP from 2004 to 2023.

**TABLE 1** Top 10 productive countries and regions.

Rank	Country	Articles	Citations	Total link strength
1	USA	392	12,773	176
2	China	59	488	49
3	The United Kingdom	55	3254	83
4	Germany	49	966	110
5	Canada	40	1135	86
6	Italy	40	1819	79
7	Brazil	37	626	30
8	Netherlands	33	1994	89
9	France	29	656	81
10	Japan	27	222	32

language to English and further excluding literature that does not belong to articles and reviews, a total of 839 articles were finally identified. Publications related to Recurrent Respiratory Papillomatosis (RRP) have fluctuated annually from 2004 to 2023 (Figure 2).

Over the past two decades, at least 49 countries or regions have published studies on RRP. The top 10 national publications are presented in Table 1. The United States (392, 46.7%) was the largest publication contributor, followed by China (59, 7.0%), The United Kingdom (55, 6.6%), Germany (49, 5.8%), and Canada (40, 4.8%). Figure 3 demonstrates the cooperation among the countries/regions. The cooperation between the United States and The United Kingdom was the closest, followed by the cooperation between the United States and Canada. Furthermore, Figure 3 also indicates that there is a lack of academic exchange between countries with abundant publications and countries with a limited number of publications.

### 3.2 | Performance of organization

According to our research, a total of 176 organizations had conducted studies on RRP, and we presented the top 10 most prolific institutions in Table 2. The most productive organization was the Capital Medical University (24), followed by the Centers for Disease Control and Prevention (18), the Eastern Virginia Medical School (18), and the Johns Hopkins University (18). Among the top 10 institutions, 7 of 10 were from the United States, corresponding to the data in Table 1. In addition, the density visualization of institutions, which depicts the extent of co-authorship contributions on RRP research, was created by VosViewer (Figure 4).

### 3.3 | Performance of journals

A total of 175 journals published articles on RRP. We have compiled a list of the top 10 journals in Table 3. *Laryngoscope* is leading the list,



**FIGURE 3** The density visualization depicts the extent of co-authorship contributions by various institutions on RRP research. It employs a color gradient, transitioning from blue through green and yellow to red, to represent a progressive increment in the volume of publications.

Rank	Organization	Country	Documents	Citations
1	Capital Medical University	China	24	86
2	Centers for Disease Control and Prevention	United States	18	997
3	Eastern Virginia Medical School	United States	18	882
4	Johns Hopkins University	United States	18	409
5	Harvard University	United States	17	1299
6	University of Groningen	Holland	14	512
7	University of Sao Paulo	Brazil	14	184
8	University of Washington	United States	14	215
9	Massachusetts General Hospital	United States	13	259
10	National Cancer Institute	United States	13	1155

**TABLE 2** Top 10 productive organizations.

having contributed 86 publications. This is closely followed by the *International Journal of Pediatric Otolaryngology*, which has 52 publications. In addition, we have included the top 10 most cited journals in the field of RRP research in Table 4. Furthermore, we conducted a citation analysis and visualized the network using Vosviewer (Figure 5). Vaccine emerged as the most frequently cited journal with a total of 2297 citations, followed by *Laryngoscope*, which has 1603 citations.

### 3.4 | Performance of author

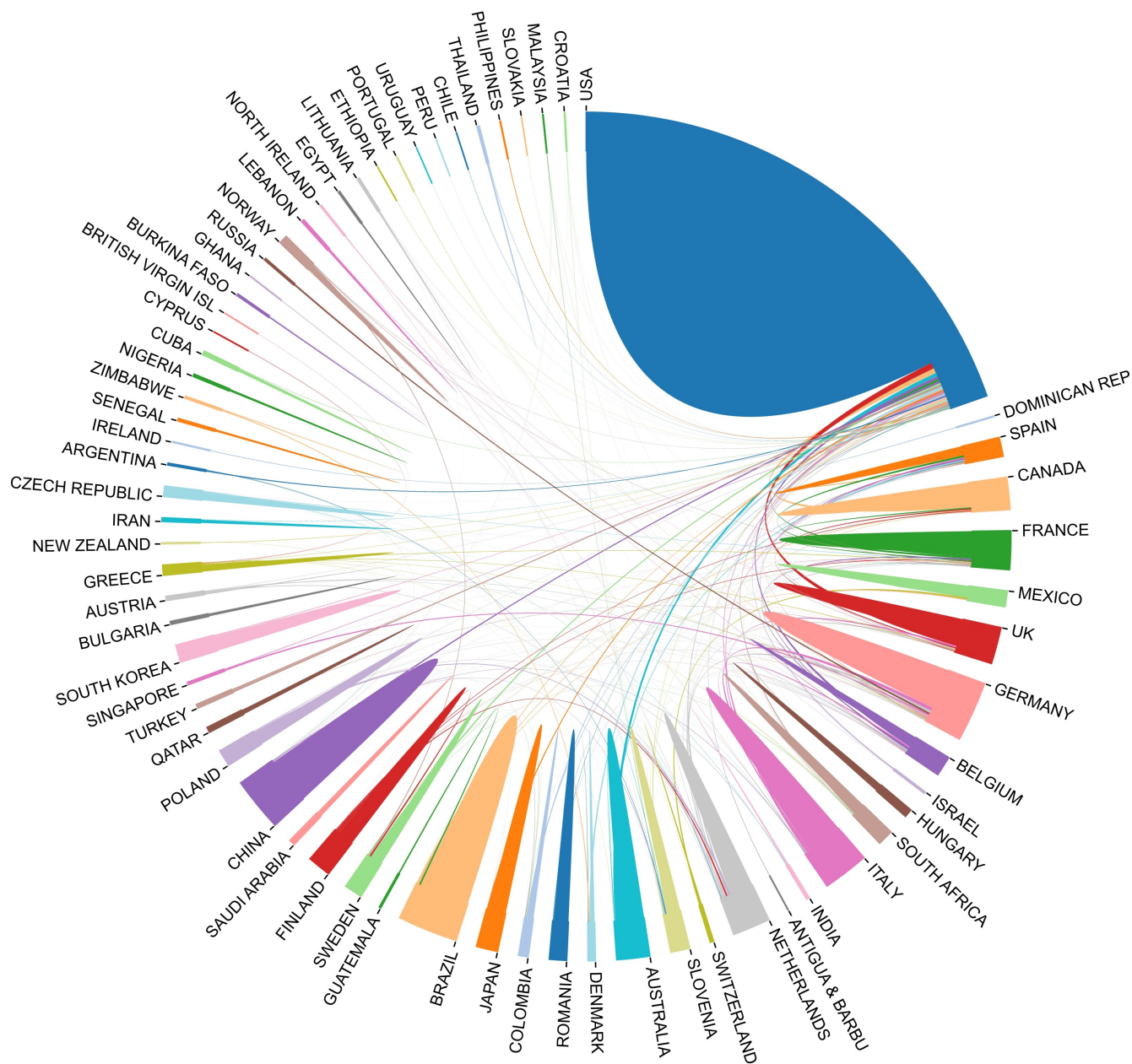
Based on our study, 839 articles were published by 112 authors, with at least 3 articles (Figure 6). Table 5 shows the top 10 most prolific

authors who published articles or reviews in the RRP field. Among all the authors, Craig S. Derkay ranked highest with 16 publications among all author, closely followed by Lauri E. Markowitz and Xiao Yang, each with 15 publications.

### 3.5 | Burst detection with keywords

The term “burst words” refers to keywords whose frequency of citations suddenly increases within a short period, providing insight into areas of research that are on the verge of breakthroughs.<sup>9</sup> In Figure 7, the green line sliced by year represents the timeline, while the red grid represents the beginning and ending year and the time interval of citation bursts. Management itself ranked first, with the strongest burst





**FIGURE 4** The cooperation between countries on RRP. The thickness of the line between the two countries indicates their cooperative relationship strength.

**TABLE 3** Top 10 journals of publication in RRP research.

Rank	Journal title	Country	Articles	Impact factor (2022)	h Index
1	<i>Laryngoscope</i>	United States	86	2.6	134
2	<i>International Journal of Pediatric Otorhinolaryngology</i>	Netherlands	52	1.5	69
3	<i>Annals of Otolaryngology and Laryngology</i>	United States	45	1.4	81
4	<i>Otolaryngology—Head and Neck Surgery</i>	United States	30	3.4	109
5	<i>European Archives of Oto-rhino-laryngology</i>	Germany	29	2.6	61
6	<i>Journal of Voice</i>	United States	18	2.2	77
7	<i>Vaccine</i>	The United Kingdom	17	5.5	164
8	<i>Head and Neck</i>	United States	16	2.9	113
9	<i>JAMA Otolaryngology—Head &amp; Neck Surgery</i>	United States	15	2.66	115
10	<i>Journal of Laryngology and Otology</i>	The United Kingdom	14	1.7	58

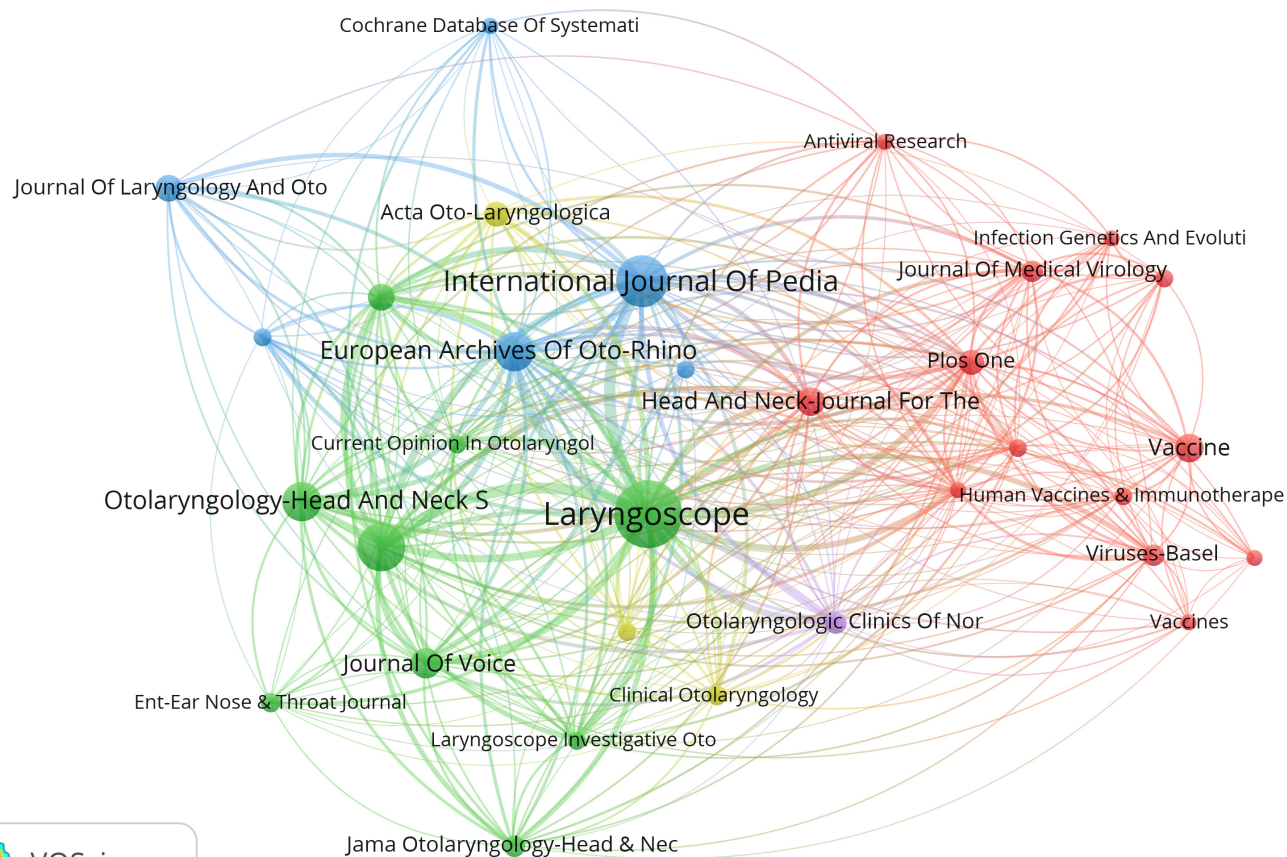
power in the past 20 years (7.9), followed by intralesional cidofovir (7.16), particle vaccine (6.86), and injections (6.64). RRP-related research has currently focused on the onset, adjuvant therapy, management, juvenile-onset RRP, systemic bevacizumab, HPV vaccine, avastin, suggesting that these topics are of great interest to researchers.

## 4 | DISCUSSION

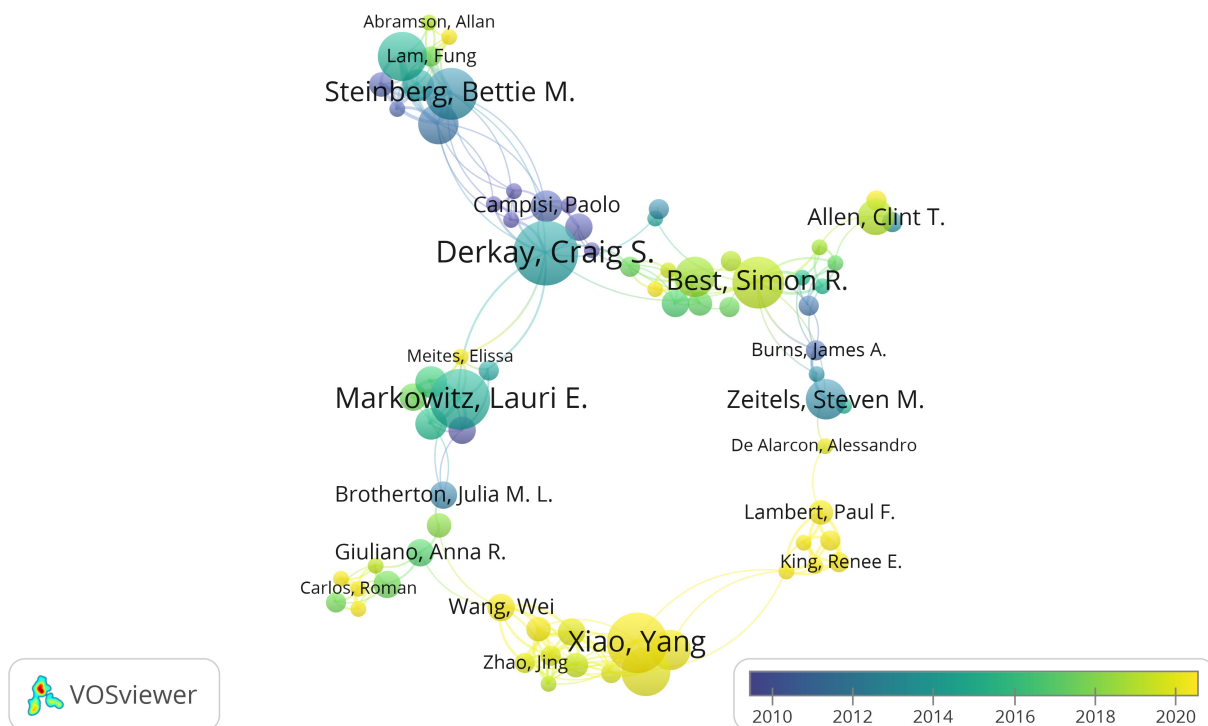
RRP remains a key area of interest, characterized by well-established etiological factors, as well as unresolved questions regarding the disease's pathogenesis. The analysis results of this article indicate that research on RRP has made significant progress, with an increasing

**TABLE 4** Top 10 journals of citation in RRP research.

Rank	Journal Title	Country	Citations	Impact factor (2022)	h Index
1	Vaccine	The United Kingdom	2297	5.5	164
2	Laryngoscope	United States	1603	2.6	134
3	Annals of Otolaryngology Rhinology and Laryngology	United States	974	1.4	81
4	International Journal of Pediatric Otorhinolaryngology	Netherlands	829	1.5	69
5	European Archives of Oto-rhino-laryngology	Germany	596	2.6	61
6	Apmis	Denmark	591	2.8	82
7	Reviews in Medical Virology	The United Kingdom	520	11.1	84
8	Otolaryngology—Head and Neck Surgery	United States	457	3.4	109
9	New England Journal of Medicine	United States	395	158.5	933
10	Plos One	United States	379	3.7	268



**FIGURE 5** The network visualization of the citation network for journals cited at least three times on RRP employs color coding to represent clustering, illustrating inter-journal relationships and thematic groupings.



**FIGURE 6** The network visualization of authors that contributed at least three articles on RRP, using dot size for publication count and color shifts, from blue through green to yellow to indicate publication timing.

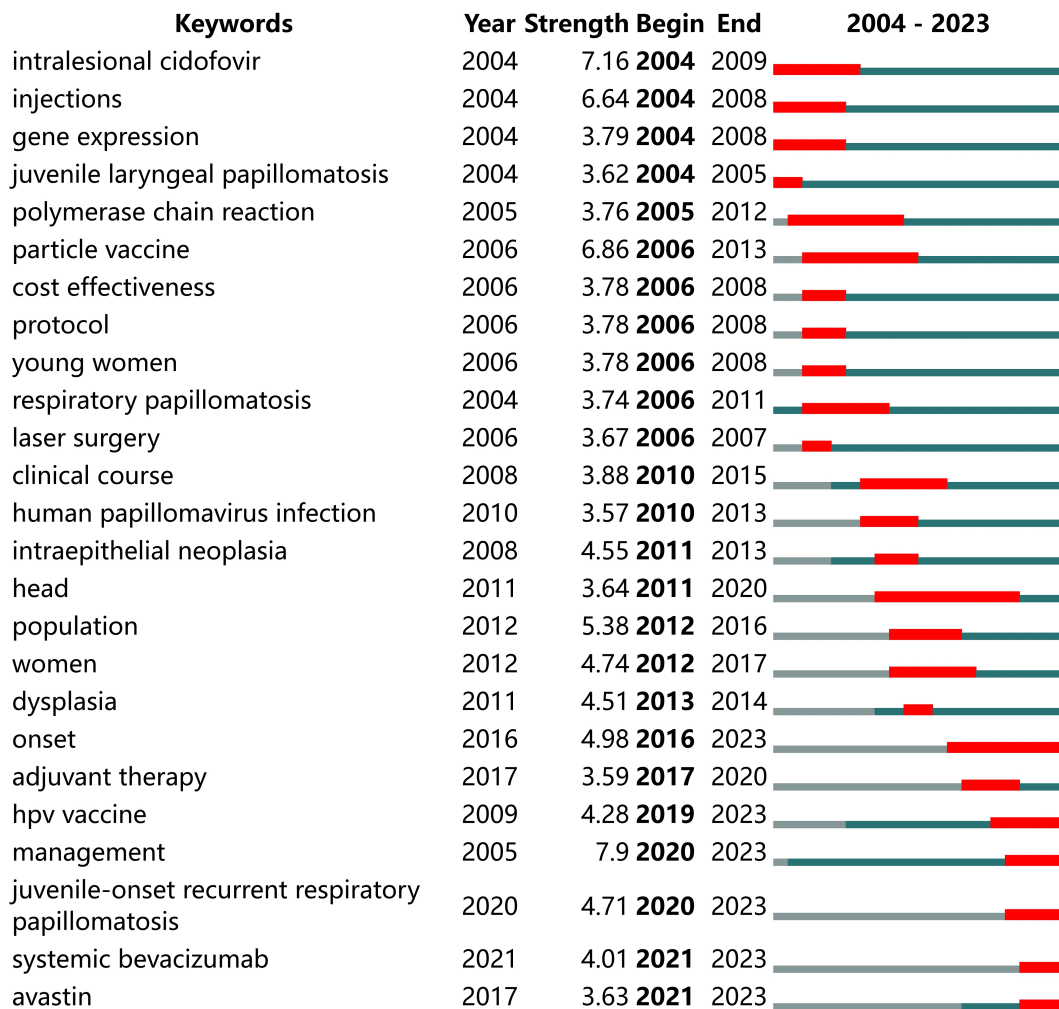
**TABLE 5** Top 10 authors of publication in RRP research.

Rank	Author	Documents	Citations
1	Craig S. Derkay	16	753
2	Lauri E. Markowitz	15	590
3	Xiao Yang	15	55
4	Frederik G. Dikkers	14	425
5	Simon R. Best	13	147
6	Bettie M. Steinberg	13	549
7	Vincent R. Bonagura	12	455
8	Wang Jun	12	50
9	Allan L. Abramson	10	384
10	Milan R. Amin	10	102

number of researchers entering this field. The United States holds a dominant position in the field of RRP research. Most contributing institutions and authors in this domain are from the United States, benefiting from advanced equipment, high-quality experimental settings, and superior clinical trial conditions. Despite this, international collaboration is not harmonious, and the effective sharing of research findings is limited, significantly hindering global understanding and research efficiency in RRP. Enhanced cooperation between countries could increase the number of research samples and prevent a substantial amount of redundant work. In addition, research on RRP has undergone significant changes over the past two decades, with a deepening of investigative efforts.

Keywords reflect the core themes and main content of articles, and we have identified emergent keywords in RRP research over this period. The traditional treatment for RRP involves surgical excision to remove the lesion, which alleviates the critical symptom of dyspnea and helps to restore the patient's voice. However, given the recurrent nature of RRP, simple surgical intervention is insufficient and fails to achieve a complete cure. Also, frequent repeated surgeries have caused great physical and psychological harm to the patients.<sup>10</sup> Scholars have turned their attention to adjuvant therapy. The keyword adjuvant therapy was also captured in our analysis (2017–2020). Local injection of cidofovir is the first burst keyword in this article (2004–2009). In 1993, cidofovir was proved to be one of the most effective inhibitors in the cotton-tailed rabbit papillomavirus model,<sup>11</sup> which has aroused widespread research interest. Cidofovir is an acyclic nucleoside phosphonate that functions by binding to the viral DNA chain, thereby inhibiting the viral DNA polymerization process and consequently suppressing viral replication.<sup>12</sup> Annie S. Lee and colleagues conducted a small sample prospective study and reported a patient remission rate of 76.9%. However, they also reported instances of ineffective treatment, raising questions about the drug's efficacy. In addition, some studies have shown potential carcinogenic effects of the drug, which is particularly concerning.<sup>13–16</sup> In summary, cidofovir, as an adjunct therapy, has always been controversial, with nearly all studies being small sample sizes or case studies. Therefore, cidofovir should still be considered as one of the key treatment methods to focus on in the future.

## Top 25 Keywords with the Strongest Citation Bursts



**FIGURE 7** Top 25 keywords with the strongest citation burst. The green line sliced by year represents the timeline, while the red grid represents the beginning and ending year and the time interval of citation bursts.

After cidofovir, bevacizumab (Avastin) is the second keyword regarding adjuvant therapy breakout (2021–2023), which is a humanized monoclonal antibody that blocks angiogenesis by inhibiting vascular endothelial growth factor (VEGF).<sup>17</sup> Rahbar et al.<sup>18</sup> demonstrated high endothelial expression of VEGF in the vasculature of RRP tissues, suggesting that VEGF may be involved in the pathogenesis of RRP and that the use of bevacizumab as a vascular endothelial growth factor inhibitor is a possible approach to treat RRP. The earliest clinical studies of bevacizumab were used as adjunctive therapy to KTP laser.<sup>19</sup> In 2014, bevacizumab was utilized for the first time as a systemic therapy. Most centers chose a dosage of 10 mg/kg. The outcomes of nearly all studies demonstrated the high efficacy of this therapy.<sup>20</sup> However, some adverse reactions of bevasumab have been reported, such as mucosal bleeding, proteinuria, hypertension, neutropenia, and so forth, there are still few related studies.<sup>21,22</sup>

Moreover, bevacizumab lacks the same authoritative guidelines as cidofovir. In the future, researchers should summarize and present authoritative working guidelines as soon as possible.

In this study, the HPV vaccine is another important burst keyword (2019–2023). The successful development of the HPV vaccine has become one of the most attention-grabbing vaccines in the world. Quadrivalent and nonavalent HPV vaccines provide a tool for preventing HPV 6 and 11 infections, which is precisely what researchers in various countries hope for to reduce the incidence of RRP. HPV vaccine is mainly divided into prophylactic and therapeutic types for RRP diseases. Preventive vaccines are represented by the L1 vaccine Gardasil® quadrivalent vaccine. L1 is the capping particles of the virus, which can be self-assembled into VLP particles, which can induce an immune response and produce antibodies in the patient's body.<sup>23</sup> These antibodies can be used to prevent the



virus from entering the basal cells in the epithelium, so as to achieve the purpose of preventing infection. While not designed for treating existing RRP, recent literature indicates the potential of the L1 vaccine as an adjunctive therapy.<sup>24</sup> In recent years, some studies have suggested that the L1 vaccine as an adjuvant therapy is effective for RRP treatment, although most of them are case reports or small sample size studies. A meta-analysis conducted by Anusha Ponduri et al.<sup>25</sup> in 2023 reviewed 13 studies involving 243 patients. Revealing that the vaccine extended the interval between surgeries and reduced the annual number of surgeries. These results show the feasibility of a preventive vaccine as an adjuvant treatment for RRP. However, the mechanism leading to this phenomenon needs to be further clarified. Therapeutic vaccines mainly include peptide vaccines and DNA vaccines. Compared with preventive vaccines, such vaccines generally contain an external antigen, such as the E6 and E7 proteins of the HPV virus, which kill the infected tumor tissue of the virus by inducing cytotoxic T cells.<sup>26</sup> Unfortunately, this kind of vaccine is not commercialized at present, probably because their intended market is confined to patients with the disease, a cohort markedly smaller than that for preventive vaccines. The development and clinical investigation of vaccines remains paramount in RRP research moving forward.

## 5 | CONCLUSIONS

Over the past two decades, research on RRP has advanced significantly, particularly in therapeutic strategies. Our bibliometric visualization analysis reveals the global trends and hotspot evolution of RRP research. We believe that this article will provide new research directions for other researchers and may contribute to future breakthroughs in this field.

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## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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