



Prevention of respiratory syncytial virus from 1991 to 2024: a systematic review and bibliometrics analysis

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Background: Respiratory syncytial virus (RSV) puts children and elderly individuals worldwide at risk for severe health issues and financial difficulties. Prevention is the main treatment for RSV infection, as there is currently no particular therapy. By using bibliometrics analysis, this study attempted to map the increasing tendency in the prevention of RSV infection from January 1991 to August 2024 and to examine the frontiers and hotspots of related research.

Methods: We extracted pertinent articles through the Web of Science Core Collection (WoSCC) on August 26, 2024, covering the period between January 1991 and August 2024. Then, an online bibliometric interface (<https://bibliometrics.com>), R software (version 4.3.2), CiteSpace V6.1R6 (64-bit) software, and the Online Analysis Platform of Literature Metrology were used to analyze the data.

Results: A total of 709 eligible data points pertaining to the prevention of RSV were included. The United States, England, and the Netherlands were the three major contributors to this field. The most productive journal was *Vaccine*. Centers for Disease Control and Prevention ranked first, with 22 publications in this field. The fusion (F) protein, nonstructural (NS) protein and glycoprotein (G) protein are the target proteins of RSV prevention drugs.

Conclusions: In the past 30 years, the research on RSV prevention has entered a stage of rapid development, and many vaccines and monoclonal antibodies have entered the clinical research stage, and some have been marketed.

Keywords: Respiratory syncytial virus (RSV); prevention; vaccine; monoclonal antibody

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Introduction

Respiratory syncytial virus (RSV) is a single-strand RNA virus that is transmitted mainly by coughing and sneezing and causes respiratory diseases such as pneumonia and bronchitis (1). It is associated with 64 million infections and is often regarded as a global health and financial burden (2). Twenty-seven thousand in-hospital fatalities, 140,000 hospitalizations, and more than 560,000 instances of RSV lower respiratory tract infections represent a significant amount of this burden, which primarily affects older persons over 65 years and children under 6 months of age (3-5). Because symptomatic infections persist throughout our lives, the burden of RSV infection persists, especially in low-income countries (6), and since few drugs are approved for the treatment of respiratory viruses (7), prevention is crucial.

Advances in the study of monoclonal antibodies and RSV vaccines have been achieved recently. To support researchers in their analysis of the significant amount of literature on this subject, in rapidly grasping the general course of this research, and in conducting research in this

area with little or no previous experience, it is essential to compile information from pertinent publications.

To our knowledge, the literature on RSV prevention has not been subjected to bibliometrics studies. In this work, we discuss this research field and present the literature on RSV prophylaxis in an attempt to direct future investigations. We present this article in accordance with the PRISMA reporting checklist (available at <https://tp.amegroups.com/article/view/10.21037/tp-24-271/rc>).

Methods

Data sources and search strategies

We decided to search pertinent papers in the Social Sciences Citation Index (SSCI) and the Web of Science Core Collection (WoSCC) Science Citation Index Expanded (SCI-Expanded) to guarantee the academic quality and integrity of the research materials. The search terms for this study were as follows: Title="Respiratory syncytial virus" or "RSV" AND Abstract="prevent" or "prevention" or "take precautions against" or "guard against" or "precaution" NOT Abstract="consensus" or "guideline" or "case report" or "meta" or "recommendation" or "review".

Bibliometrics and visualized analysis

All papers indexed from WoSCC were exported to TXT format for "Full-text Records and References". The title, author, research institute, abstract, journal, publication date, quantity of citations in the WoSCC database, and other details were included in the exported document records. In the CiteSpace program, the data were imported, and duplicates were checked. The deadline for submission was August 26, 2024. Two researchers (X.L. and X.Y.) independently examined every publication after the initial data search to make sure it was pertinent to the study's topic.

The time span (January 1991 to August 2024) and the number of years per slice (1), the trim (Pathfinder, Trim Slice Network), the selection criteria (g-index: k=25, top N=50, top N%=10%, maximum number of selections per slice =100), the link (intensity: cosine, range: within slice), and all other parameters stayed at their Standard set up in CiteSpace. For the node type parameter area, the following parameters are set: the country, institution and literature are selected for visual analysis, and a co-occurrence map is generated. The Bibliometrix package in R and

Highlight box

Key findings

- From 1991 to 2024, the United States, England, and the Netherlands were the main countries that contributed to research on respiratory syncytial virus (RSV) prevention. There was significant research collaboration among these countries, with the United States showing the strongest international research ties.

What is known and what is new?

- It is well-known that RSV poses significant health risks, particularly to children and the elderly, and that prevention is crucial due to the lack of specific therapies for RSV infection.
- An extensive bibliometrics examination of worldwide trends in RSV preventive research is provided by this study, highlighting the main contributors, and key research areas such as the fusion (F) protein, nonstructural protein, and glycoprotein protein as targets for RSV prevention.

What is the implication, and what should change now?

- There should be increased international collaboration, especially involving countries with fewer publications and citations, to enhance global understanding and prevention strategies for RSV.
- Future research should focus on developing effective and stable vaccines and monoclonal antibodies targeting the F protein in its pre-fusion state, addressing the gap in RSV prevention for children. At the same time, resource sharing should be studied to develop effective, safe and accessible RSV prevention products that can benefit low-income countries.

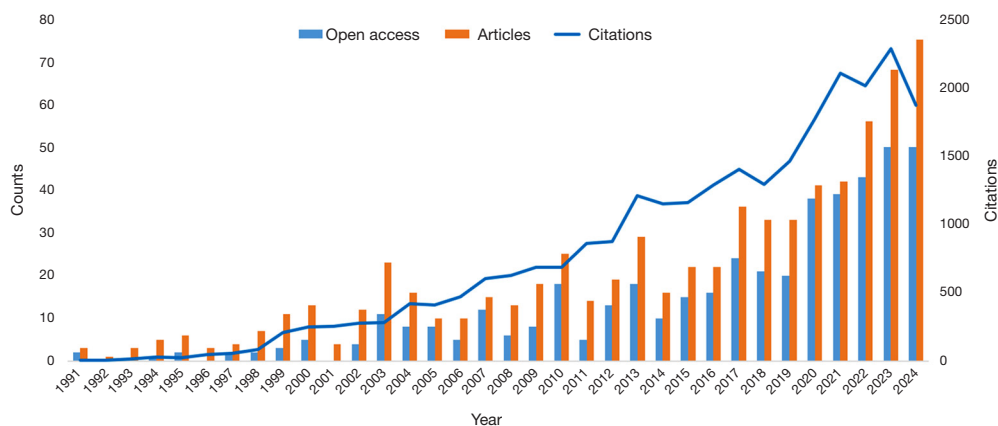


Figure 1 The overall quantity of publications, the quantity of open-access papers and citation rate about the avoidance of respiratory syncytial virus annually.

the web interface “biblioshiny” of bibliometrix (<https://bibliometrics.com>) are utilized to utilize the stored data and facilitate the examination of cooperative networks across various nations.

The mathematical statistics-based literature and information mining method known as “bibliometrics analysis” offers a model for the quantitative evaluation of research publications (8,9). Research hotspots were identified with the “bibliometrix” R package and “biblioshiny”, and future trends were further predicted (10). CiteSpace was also utilized as a visualization tool to analyze nations, journals, institutions, keywords, literature, and their interactions to fully grasp how the research area has developed (11).

Results

Overview of the annual growth trend

In total, 797 publications on RSV prevention were published in the WoSCC between January 1991 and August 26, 2024; 88 of them were eliminated from review and had no duplicates, leaving 709 articles included in this study. A steady growth trend was shown (Figure 1). Prior to 1998, very few papers were produced annually; however, in 1999, the number of publications increased to ten for the first time. The bulk of those publications were available online. Furthermore, throughout the previous three decades, the annual number of citations had generally increased.

The most contributing countries

The papers related to prevention of RSV originated from 90 countries. The top 10 contributing countries were displayed in Figure 2A. The top 10 countries were split up in the United States, England, the Netherlands, China, Canada, France, Spain, Australia, Italy and Germany. The most fertile country, the United States, has 349 publications, and England (77 publications) and the Netherlands (65 publications) placed second and third, in that order. We constructed a cooperation network based on the linkages between publications in each nation in Figure 2B after filtering and visualizing 10 countries based on the quantity of publications greater than or equal to 26. The map indicated a great deal of academic impact in this field by highlighting the United States, England, the Netherlands, China, Canada, and so on. According to the outcomes of the cooperation network, there were 667 connections between the 90 countries that have formed partnerships. The United States clearly had a strong cooperative relationship with various countries. A country’s reputation is affected not only by the number of papers it produces but also by citation rate of its publications. It is worth noting that although Canada did not have the highest number of articles, its average citation rate is indeed the highest, which shows that the quality of their articles is recognized (Figure 2C).

Journal analysis

Using Bradford’s Law, which described the distribution

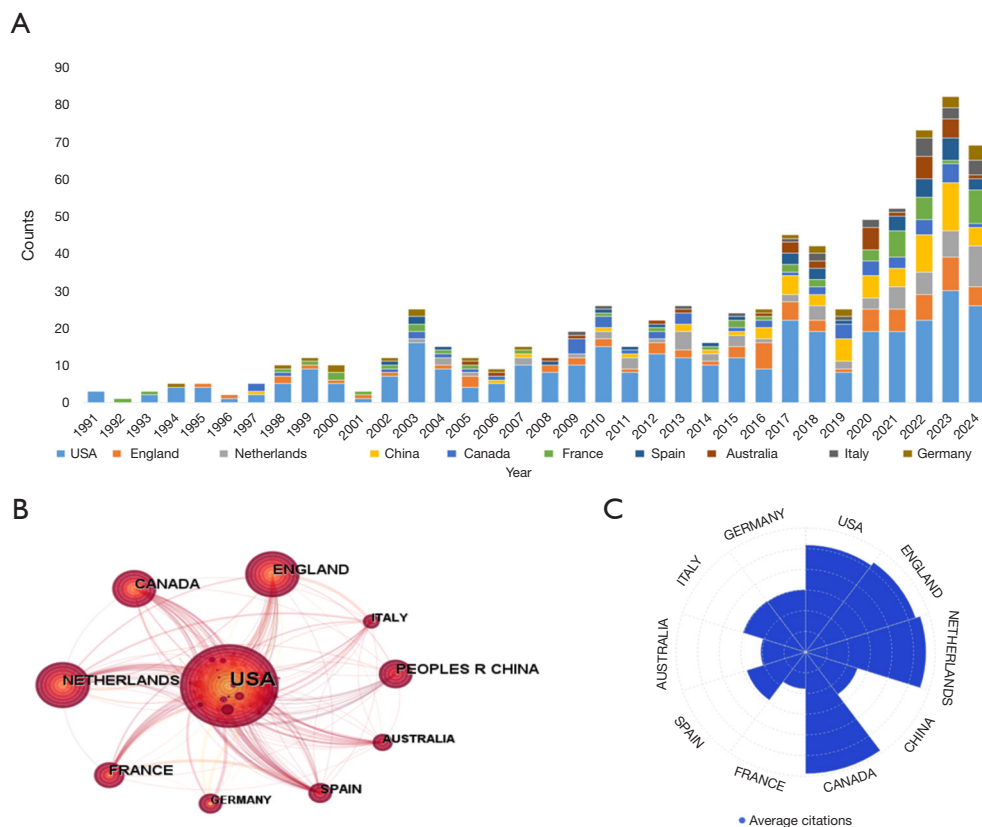


Figure 2 Spatial distribution of publications on the prevention of respiratory syncytial virus (January 1991 and August 2024). (A) The annual distribution of the prevention of respiratory syncytial virus research from top 10 influential countries between January 1991 and August 2024. (B) Cooperation network of the productive countries. The node size represented the number of publications, and the thickness of the links represented the close degree between countries. (C) Average citation rate per article in producing countries.

of scientific publications among different journals, we identified 12 core journals that were deemed to be the greatest choices for researchers (Figure 3 and Table 1). Remarkably, out of the twelve core publications, seven were located in the United States, two in the England and the Netherlands, and one in Switzerland. The highest number of publications was on *Vaccine* with 36, followed by the *Pediatric Infectious Disease Journal* [30] and the *Journal of Virology* [27]. In addition, *Pediatrics* had the highest citation rate [2,608] and the third highest impact factor [6.2].

Institutional analysis

The top 10 producing institutions in terms of RSV prevention can be found in Table 2. Most of them are from the United States. Centers for Disease Control and Prevention (22 publications), Baylor College of Medicine (18 publications), and Emory University (17 publications)

were the three universities that have produced the most pertinent research. Centers for Disease Control and Prevention not only had the highest publication but also had the highest citation rate. The highest output institution has been working hard for RSV prevention, and it deserves more attention. We then created a cooperation network on the basis of the relationships between each institution’s publications and the minimum number of publications equal to 12 choosing 10 institutions for visualization (Figure 4). The strong collaboration between several agencies indicated that they were collaborating on the prevention of RSV.

Analysis of keywords

Through the examination of keyword occurrence frequency, a researcher can uncover useful details about the goals, approaches, and viewpoints of a text (12-14).

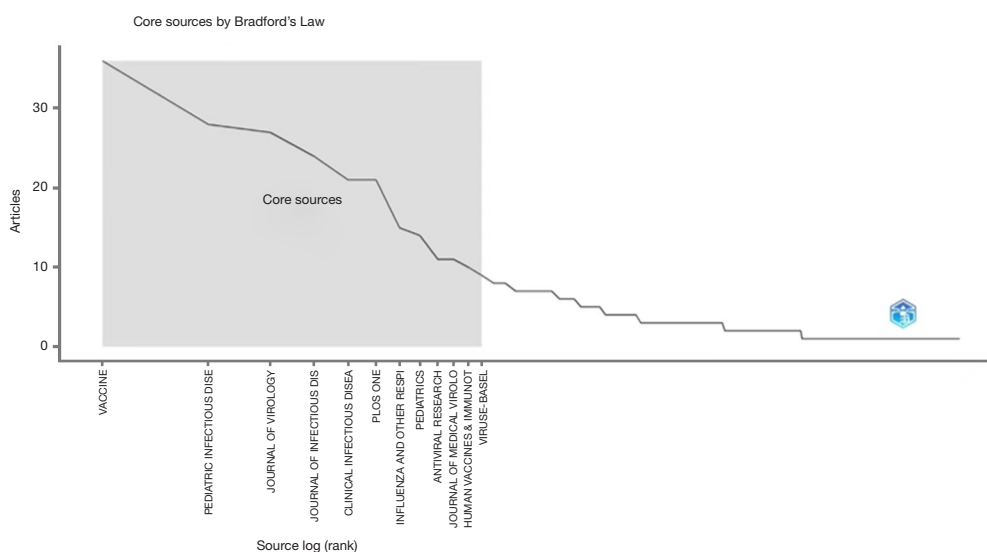


Figure 3 The plot of Bradford's Law identified twelve core journals on the prevention of respiratory syncytial virus (January 1991 and August 2024).

Table 1 The top 12 core journals that published articles in the prevention of respiratory syncytial virus

Rank	Journal title	Frequency	Total citations	Impact factor [2023]	Country
1	<i>Vaccine</i>	36	820	4.5	The Netherlands
2	<i>Pediatric Infectious Disease Journal</i>	30	1,097	2.9	The United States
3	<i>Journal of Virology</i>	27	1,212	4	The United States
4	<i>Journal of Infectious Diseases</i>	25	1,311	5	The United States
5	<i>Clinical Infectious Diseases</i>	21	1,234	8.2	England
6	<i>PLoS One</i>	21	624	2.9	The United States
7	<i>Influenza and Other Respiratory Viruses</i>	18	395	4.3	England
8	<i>Pediatrics</i>	15	2,608	6.2	The United States
9	<i>Antiviral Research</i>	12	283	4.5	The Netherlands
10	<i>Journal of Medical Virology</i>	12	138	6.8	The United States
11	<i>Human Vaccine & Immunotherapeutics</i>	11	53	4.1	The United States
12	<i>Viruses-Basel</i>	10	43	3.8	Switzerland

Analyses of keywords offer a useful way to identify fresh study opportunities on a certain subject (12,13,15). The cooperation network of terms was mapped by the researchers via CiteSpace to determine hotspots and comprehend the evolution of research interests. The co-occurrence network of keywords that appeared more than 36 times (*Figure 5A*) included infection, children, vaccines, monoclonal antibodies, etc. *Figure 5B* highlights the

trend topics for RSV prevention. In the first 20 years, the main concern was RSV infection in children, but in the last 10 years, researchers had focused more on vaccines, palivizumab and other preventive measures.

Clustered network in co-analysis

We conducted a cluster network analysis to examine the

Table 2 The top 10 most prolific institutions in the prevention of respiratory syncytial virus during January 1991 to May 2024

Rank	Institution	Articles	Total citations	Average citation per paper	Country
1	Centers for Disease Control and Prevention	22	4,781	104.68	The United States
2	Baylor College of Medicine	18	2,593	117.86	The United States
3	Emory University	17	2,810	133.81	The United States
4	Vanderbilt University	14	2,511	116.47	The United States
5	University of Colorado	13	2,892	103.29	The United States
6	National Institute of Allergy and Infectious Diseases (NIAID)	13	2,498	108.63	The United States
7	University Medical Center Utrecht	13	1,924	62.06	The Netherlands
8	Children's Hospital Colorado	13	2,156	154	The United States
9	University of Witwatersrand	12	874	54.63	South Africa
10	University of Edinburgh	12	513	34.56	England

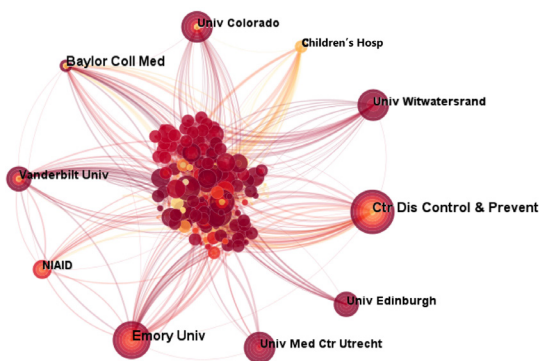


Figure 4 Diagram of the cooperation network between institutions. Each circle represents an institution. The link between the two circles denotes the collaboration of the two institutions on the same article, and the size of the circle is positively connected with the number of articles produced by the institution. Line thickness is positively correlated with the frequency of collaboration.

co-cited publications in further detail. On the basis of the logical conclusion of the homogeneity analysis—that two publications are more likely to be homogenous if they have a large number of references—we divided the 709 articles into many categories. After the “Show the Largest K Clusters” node (K=10) was selected, 10 noteworthy clusters were identified through the co-citation networks of 4,203 citations cited by 709 publications. Remarkable noun phrases that were taken from keywords are the cluster labels, including palivizumab and protein vaccines (Figure 6A). We further divided these drugs into

three categories according to the site of action, namely, the fusion (F) protein, nonstructural (NS) protein and glycoprotein (G) protein. Among them, palivizumab, nirsevimab, MEDI8897*, motavizumab, and antibodies against 5C4 and P27 interact with the F protein to play a role. The NS protein prevents the induction of β -IFN after virus infection or double-stranded RNA stimulation. Monoclonal antibody 131-2G against the G protein plays a role in the prevention of RSV infection.

To investigate the evolutionary tendency of the main subjects and their relationships, the chronology of the co-cited publications was also traced (Figure 6B). For the first 20 years, children’s RSV infections were the main concern; however, over the previous 10 years, researchers had focused their attention on vaccines, palivizumab, and other preventative measures. The bold period indicated that many conversations occurred at this time around the cluster. Citation tree rings of varying sizes indicate some of the significant research with many references on the timeline. In approximately 2012, research on RSV protein vaccines and monoclonal antibodies became a hot topic and has continued.

Discussion

Summary of results

In the WoSCC, we retrieved a total of 709 articles related to RSV prevention since 1991. Since the early 1990s, the number of articles on this had been increasing, probably

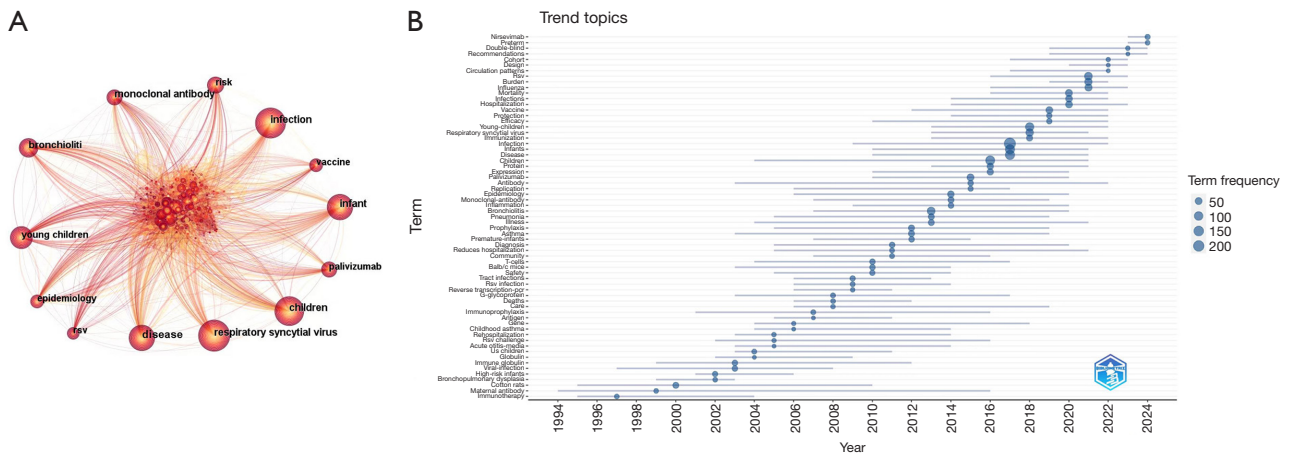


Figure 5 Analysis of keywords (A) and trend topic analysis (B).

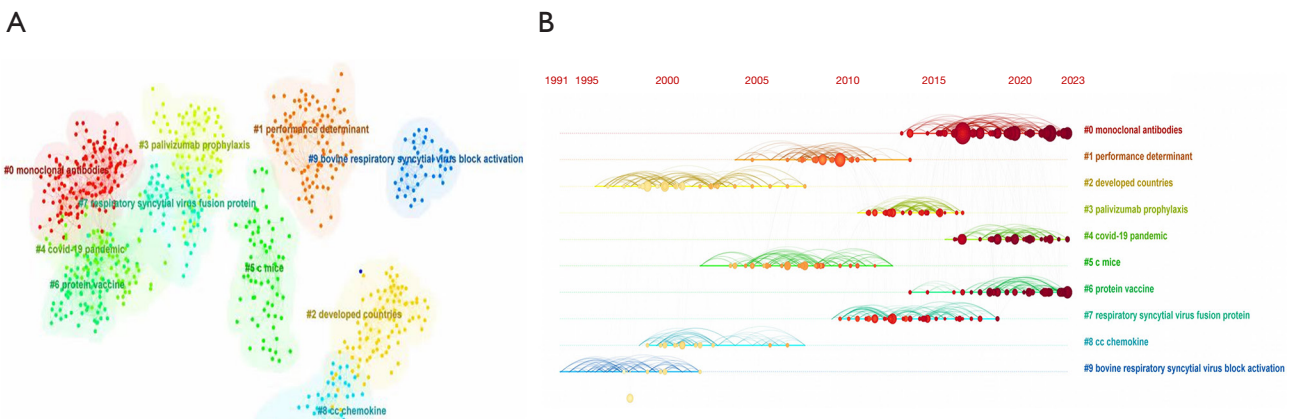


Figure 6 Cluster network analysis of reference co-citation. (A) A cluster network of co-citation status for references and cited articles via CiteSpace. Displays the top 10 largest clusters of the referenced article. (B) Timeline view of the top 10 clusters of the article is cited.

due to the increasing number of scientific journals that had been launched to provide a platform for publication. Research on a prophylactic antibody, licensed in 1999, and new insights into the immune response involving the pattern recognition receptors TLR4 and CD14, may contributed to the apparent increase in publications and citations after 2000 (16). In 2012, the F protein conformation was determined (17), and since then, the research on prophylactic drugs with pre-fusion F protein as the target protein had begun. The advantages of English and the fact that English is recognized as the “lingua franca of science” are consistent with the rich research found in our research in English-speaking countries such as the United States, England, and Canada. Cooperation between countries was also usually more common between these countries. The United States was the most productive

country, as evidenced by the dominance of other countries in terms of article volume, journals, and institutions, and the United States’ leading position may be related to the country’s major financial resources dedicated to research, which can support human resources and excellent scientific infrastructure. It is worth noting that the quantity of published articles in Canada and the average citation rate were among the highest, which showed that the quality of their articles was excellent and highly recognized by the scientific community.

To learn more about the field, we reviewed the contents of ten of the most referenced papers that were essential to the advancement of the field to gain a better understanding of the most often cited publications (Table 3). On the basis of the sites of action of prevention drugs in these 10 articles, we divided the research content into three categories,

Table 3 The top 10 most cited documents in the prevention of respiratory syncytial virus during January 1991 to May 2024

Rank	Title	First author	Year	Total citations	Source	DOI
1	Structure of RSV fusion glycoprotein trimer bound to a prefusion-specific neutralizing antibody	McLellan JS	2013	593	<i>Science</i>	10.1126/science.1234914
2	Single-Dose Nirsevimab for Prevention of RSV in Preterm Infants	Griffin MP	2020	303	<i>The New England Journal of Medicine</i>	10.1056/NEJMx200019
3	A highly stable prefusion RSV F vaccine derived from structural analysis of the fusion mechanism	Krarpup A	2015	232	<i>Nature Communications</i>	10.1038/ncomms9143
4	A highly potent extended half-life antibody as a potential RSV vaccine surrogate for all infants	Zhu Q	2017	178	<i>Science Translational Medicine</i>	10.1126/scitranslmed.aaj1928
5	Cost-effectiveness of respiratory syncytial virus prophylaxis among preterm infants	Joffe S	1999	149	<i>Pediatrics</i>	10.1542/peds.104.3.419
6	Nonstructural proteins NS1 and NS2 of bovine respiratory syncytial virus block activation of interferon regulatory factor 3	Bossert B	2003	136	<i>Journal of Virology</i>	10.1128/jvi.77.16.8661-8668.2003
7	Structural basis of respiratory syncytial virus neutralization by motavizumab	McLellan JS	2010	128	<i>Nature Structural & Molecular Biology</i>	10.1038/nsmb.1723
8	Characterization of a Prefusion-Specific Antibody That Recognizes a Quaternary, Cleavage-Dependent Epitope on the RSV Fusion Glycoprotein	Gilman MS	2015	102	<i>PLoS Pathogens</i>	10.1371/journal.ppat.1005035
9	Prevention of hospitalization due to respiratory syncytial virus: results from the Palivizumab Outcomes Registry	Frogel M	2008	89	<i>Journal of Perinatology</i>	10.1038/jp.2008.28
10	Prophylactic treatment with a G glycoprotein monoclonal antibody reduces pulmonary inflammation in respiratory syncytial virus (RSV)-challenged naive and formalin-inactivated RSV-immunized BALB/c mice	Radu GU	2010	62	<i>Journal of Virology</i>	10.1128/JVI.00451-10

namely, F protein, NS protein, and G protein.

F protein

The F protein of RSV mediates the binding and fusion of the virus, and there are six different antigenic sites on pre-fusion F protein. At present, many RSV prevention drugs target F protein. After checking over ten papers, we discovered that eight of them had something to do with the F protein. Interestingly, the first of the ten articles was released in 1999. Palivizumab was approved by the

Food and Drug Administration (FDA) in 1998 and is the world's first approved drug for the prevention of RSV infection. Palivizumab is a recombinant humanized monoclonal immunoglobulin G1 that targets the virus's F protein by identifying an epitope within antigenic site II that is maintained on the F protein's pre-fusion and post-fusion conformations. Restraining from RSV replication is possible. In 1999, Joffe *et al.* reported that palivizumab was less expensive and more effective than RSV immune globulin (RSVIG) for RSV prophylaxis (18). A subsequent study by Frogel's team revealed that palivizumab reduced

hospitalizations in high-risk infants (19). With the advancement of technology, motavizumab has been used. Motavizumab is obtained by replacing each of the six complementarity-determining regions with the other 19 residues on the basis of palivizumab. In 2010, McLellan *et al.* reported that the structure of the 24-residue peptide complex corresponding to the glycoprotein epitope of motavizumab with RSV fusion F protein revealed the structural basis for this greater potency (20). Three years later, McLellan *et al.* proposed that D25 binds to the least conserved region of the F glycoprotein to neutralize RSV by immobilizing F in the pre-fusion conformation. Their results also revealed that the D25, AM22 and 5C4 antibodies recognize identical or highly related epitopes, naming them “antigenic sites Ø”. 5C4, which has a 50-fold greater potency than palivizumab (21). In 2015, Krarup *et al.* analyzed double mutants (N67I, S215P: SC-dm) and triple mutants (N67I, S215P, and E487Q: SC-tm) of the pre-fusion RSV F protein. They measured the thermal stability of the purified pre-fusion protein via differential scanning fluorescence and found that the protein contained the P27 region. Structural and biochemical analyses of pre-fusion variants have shown that P27 is functional (22). In the same year, Gilman’s team reported that a quaternary cleavage-dependent epitope, containing a section that experiences significant conformational changes in the pre-fusion to post-fusion F transition, is bound by the human antibody AM14. This is a new site that is different from the Ø site, which offers a fresh objective for the development of upcoming vaccinations (23). In 2017, Zhu *et al.* reported that MEDI8897* is a highly efficient human antibody against the pre-fusion conformation of the RSV fusion F protein optimized from the D25 antibody. Compared with those of palivizumab, the heavy and light chains of MEDI8897* have a wide range of interactions with RSV F proteins, with a 2-fold increase in potency against RSV laboratory strains *in vitro* and a nine-fold increase in activity *in vivo* (24). Nirsevimab is a recombinant human immunoglobulin G1 kappa monoclonal antibody that binds to a highly conserved zero-position epitope on the pre-fusion conformation of RSV fusion proteins and modifies the Fc region to prolong the half-life. It is also effective for RSV types A and B. In 2020, Griffin *et al.* reported that the incidence of hospitalizations for RSV-associated lower respiratory tract infections was 78.4% lower [95% confidence interval (CI): 51.9–90.3%] in the nirsevimab group than in the placebo group [0.8% (8 infants) vs. 4.1% (20 infants)] (25).

NS protein and G protein

The NS proteins NS1 and NS2 are multifunctional virulence factors specific to RSV and play a key role during RSV infection, including antagonizing interferon (IFN) signaling to modulate host response to RSV infection (26). As the first step in cell infection, anti-G antibodies effectively neutralize RSV in these cells. Therefore, conjugation of G proteins to vaccine-induced or passively administered antibodies has the potential to reduce disease by reducing virus-induced inflammation and viral replication (27). The properties of NS proteins and G proteins indicate that they have great potential in the design of RSV prevention. Each of the 10 articles discussed the roles of the NS protein and the G protein of RSV. In 2003, Bossert *et al.* reported that recombinant bovine respiratory syncytial virus infection devoid of the NS gene effectively induces the overexpression of IFN-stimulated genes, which is crucial for the development of live attenuated RSV vaccines (28). The central conserved region of the G protein contains four evolutionarily conserved cysteines in the cysteine lasso structure, which contains a CX3C chemokine motif, and the CX3C motif of the G protein is immunoactive. In 2010, after primary infection and FI-RSV immunization, Radu *et al.* assessed the impact of prophylactic administration of the mAb 131-2G on the pulmonary inflammatory response to RSV challenge in mice. They discovered that prophylactic anti-RSV G protein monoclonal antibody treatment decreased lung cell infiltration and RSV replication in mice (29).

The development of RSV prevention drugs is fraught with twists and turns. Since the discovery of RSV in the 50s of the 20th century, mankind has been trying to develop a vaccine against RSV. In the 60s of the 20th century, infants and young children immunized with RSV’s formalin whole-virus inactivated vaccine (FI-RSV) developed symptoms of enhanced RSV disease after immunization, which led to a higher hospitalization rate and ultimately led to the death of two young children infected with RSV after FI-RSV immunization, which hindered the development of RSV vaccines (30). This was followed by a focus on the development of live attenuated vaccines, but study has found varying degrees of attenuation in children and adults, making this approach to vaccine development unreliable (31). With a better understanding of the structure and function of the F protein, the RSV vaccine field has undergone a major shift from empirical vaccine design to rational vaccine design over the past decade: support for the pre-fusion F protein as

an antigen. In this context, many vaccines and monoclonal antibodies with novel designs have entered clinical trials, some of which are already on the market. Nirsevimab was approved by the European Union in November 2022, by China in November 2023, and for the prevention of RSV infection in newborns and infants in January 2024 (32). In May 2023, the FDA approved the Arexvy vaccine, and in June it approved the Abrysvo vaccine for marketing (33,34). These two vaccines are used to prevent RSV infection in the elderly population aged 60 years and older. In the following August, the FDA has also approved the Abrysvo vaccine for pregnant women at 32–36 weeks to provide protection for newborns aged 0–6 months. The two pre-fusion F protein vaccines achieved a breakthrough of zero growth in RSV vaccines. With the application of the above-mentioned vaccines and monoclonal antibody, the health level of the elderly, maternal and newborns has been further guaranteed.

Despite promising progress in RSV vaccines and monoclonal antibodies, four issues remain noteworthy: first, accessibility, as the burden of RSV-associated respiratory infections is greater in low-income countries, access to vaccines and monoclonal antibodies is important. The use of delivery and storage methods that are achievable in low-income countries to preserve pharmacological properties is an issue that needs to be considered for future. Second, vaccines and monoclonal antibodies are available for the elderly, pregnant women and infants, but children still need protection. Third, RSV has evolved resistance to antibody binding and neutralization, so virus resistance monitoring is important. Fourth, the duration of protection against vaccines and monoclonal antibodies, which requires ongoing follow-up to determine their long-term efficacy.

It is important to consider the limitations of the current analysis. Given that the study documents were primarily based on the WoSCC, selection bias may exist. Whereas the WoSCC is undoubtedly a vast and trustworthy resource, additional websites such as Scopus and Google Scholar may offer a more in-depth comprehension and concepts. To gain more comprehensive and detailed knowledge about this research topic, we would like to use a multimethod approach in our next studies.

Conclusions

In the past 30 years, the research on RSV prevention has entered a stage of rapid development, and many vaccines and monoclonal antibodies have entered the clinical

research stage, and some have been marketed. Since the conformation of F protein was determined, it has been a hot protein in the development of respiratory syncytial virus prevention. But the current research and cooperation are mainly focused on developed countries such as the United States and England. In the future, research countries should study resource sharing and develop effective, safe and accessible RSV prevention products that can benefit the majority of low-income countries.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://tp.amegroups.com/article/view/10.21037/tp-24-271/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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References

- Kuppan JP, Mitrovich MD, Vahey MD. A morphological transformation in respiratory syncytial virus leads to enhanced complement deposition. *Elife* 2021;10:e70575.
- Nair H, Nokes DJ, Gessner BD, et al. Global burden of acute lower respiratory infections due to respiratory syncytial virus in young children: a systematic review and meta-analysis. *Lancet* 2010;375:1545-55.
- Shi T, Denouel A, Tietjen AK, et al. Global Disease Burden Estimates of Respiratory Syncytial Virus-Associated Acute Respiratory Infection in Older Adults in 2015: A Systematic Review and Meta-Analysis. *J Infect Dis* 2020;222:S577-83.
- Shi T, Vennard S, Mahdy S, et al. Risk Factors for Poor Outcome or Death in Young Children With Respiratory Syncytial Virus-Associated Acute Lower Respiratory Tract Infection: A Systematic Review and Meta-Analysis. *J Infect Dis* 2022;226:S10-6.
- Tin Tin Htar M, Yerramalla MS, Moïsi JC, et al. The burden of respiratory syncytial virus in adults: a systematic review and meta-analysis. *Epidemiol Infect* 2020;148:e48.
- Antillón M, Li X, Willem L, et al. The age profile of respiratory syncytial virus burden in preschool children of low- and middle-income countries: A semi-parametric, meta-regression approach. *PLoS Med* 2023;20:e1004250.
- Shang Z, Tan S, Ma D. Respiratory syncytial virus: from pathogenesis to potential therapeutic strategies. *Int J Biol Sci* 2021;17:4073-91.
- Chen C, Song M. Visualizing a field of research: A methodology of systematic scientometric reviews. *PLoS One* 2019;14:e0223994.
- Zheng Y, Mao S, Zhu J, et al. Current status of electrochemical detection of sunset yellow based on bibliometrics. *Food Chem Toxicol* 2022;164:113019.
- Wang S, Zhou H, Zheng L, et al. Global Trends in Research of Macrophages Associated With Acute Lung Injury Over Past 10 Years: A Bibliometric Analysis. *Front Immunol* 2021;12:669539.
- Zhu X, Hu J, Deng S, et al. Bibliometric and Visual Analysis of Research on the Links Between the Gut Microbiota and Depression From 1999 to 2019. *Front Psychiatry* 2020;11:587670.
- Afrane S, Ampah JD, Aboagye EM. Investigating evolutionary trends and characteristics of renewable energy research in Africa: a bibliometric analysis from 1999 to 2021. *Environ Sci Pollut Res Int* 2022;29:59328-62.
- Afrane S, Ampah JD, Mensah EA. Visualization and analysis of mapping knowledge domains for the global transition towards clean cooking: a bibliometric review of research output from 1990 to 2020. *Environ Sci Pollut Res Int* 2022;29:23041-68.
- Jin C, Ampah JD, Afrane S, et al. Low-carbon alcohol fuels for decarbonizing the road transportation industry: a bibliometric analysis 2000-2021. *Environ Sci Pollut Res Int* 2022;29:5577-604.
- Khan KI, Nasir A, Saleem S. Bibliometric Analysis of Post Covid-19 Management Strategies and Policies in Hospitality and Tourism. *Front Psychol* 2021;12:769760.
- Kurt-Jones EA, Popova L, Kwinn L, et al. Pattern recognition receptors TLR4 and CD14 mediate response to respiratory syncytial virus. *Nat Immunol* 2000;1:398-401.
- Magro M, Mas V, Chappell K, et al. Neutralizing antibodies against the preactive form of respiratory syncytial virus fusion protein offer unique possibilities for clinical intervention. *Proc Natl Acad Sci U S A* 2012;109:3089-94.
- Joffe S, Ray GT, Escobar GJ, et al. Cost-effectiveness of respiratory syncytial virus prophylaxis among preterm infants. *Pediatrics* 1999;104:419-27.
- Frogel M, Nerwen C, Cohen A, et al. Prevention of hospitalization due to respiratory syncytial virus: results from the Palivizumab Outcomes Registry. *J Perinatol* 2008;28:511-7.
- McLellan JS, Chen M, Kim A, et al. Structural basis of respiratory syncytial virus neutralization by motavizumab. *Nat Struct Mol Biol* 2010;17:248-50.
- McLellan JS, Chen M, Leung S, et al. Structure of RSV fusion glycoprotein trimer bound to a prefusion-specific neutralizing antibody. *Science* 2013;340:1113-7.
- Krarrup A, Truan D, Furmanova-Hollenstein P, et al. A highly stable prefusion RSV F vaccine derived from structural analysis of the fusion mechanism. *Nat Commun* 2015;6:8143.
- Gilman MS, Moin SM, Mas V, et al. Characterization of a Prefusion-Specific Antibody That Recognizes a Quaternary, Cleavage-Dependent Epitope on the RSV Fusion Glycoprotein. *PLoS Pathog* 2015;11:e1005035.
- Zhu Q, McLellan JS, Kallewaard NL, et al. A highly potent extended half-life antibody as a potential RSV vaccine surrogate for all infants. *Sci Transl Med*

- 2017;9:eaaj1928.
25. Griffin MP, Yuan Y, Takas T, et al. Single-Dose Nirsevimab for Prevention of RSV in Preterm Infants. *N Engl J Med* 2020;383:415-25.
 26. Merritt TN, Pei J, Leung DW. Pathogenicity and virulence of human respiratory syncytial virus: Multifunctional nonstructural proteins NS1 and NS2. *Virulence* 2023. [Epub ahead of print]. doi: 10.1080/21505594.2023.2283897.
 27. Anderson LJ, Jadhao SJ, Paden CR, et al. Functional Features of the Respiratory Syncytial Virus G Protein. *Viruses* 2021;13:1214.
 28. Bossert B, Marozin S, Conzelmann KK. Nonstructural proteins NS1 and NS2 of bovine respiratory syncytial virus block activation of interferon regulatory factor 3. *J Virol* 2003;77:8661-8.
 29. Radu GU, Caidi H, Miao C, et al. Prophylactic treatment with a G glycoprotein monoclonal antibody reduces pulmonary inflammation in respiratory syncytial virus (RSV)-challenged naive and formalin-inactivated RSV-immunized BALB/c mice. *J Virol* 2010;84:9632-6.
 30. Kapikian AZ, Mitchell RH, Chanock RM, et al. An epidemiologic study of altered clinical reactivity to respiratory syncytial (RS) virus infection in children previously vaccinated with an inactivated RS virus vaccine. *Am J Epidemiol* 1969;89:405-21.
 31. Karron RA, Buchholz UJ, Collins PL. Live-attenuated respiratory syncytial virus vaccines. *Curr Top Microbiol Immunol* 2013;372:259-84.
 32. Keam SJ. Nirsevimab: First Approval. *Drugs* 2023;83:181-7.
 33. Moghadas SM, Shoukat A, Bawden CE, et al. Cost-effectiveness of Prefusion F Protein-based Vaccines Against Respiratory Syncytial Virus Disease for Older Adults in the United States. *Clin Infect Dis* 2024;78:1328-35.
 34. Papi A, Ison MG, Langley JM, et al. Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults. *N Engl J Med* 2023;388:595-608.

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