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Bibliometric Analysis and Key Messages of Monkeypox Research (2003–2022)

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Abstract: Objective: At the global level, a multi-country outbreak of monkeypox has attracted global attention. The purpose of this study is to explore the growing contribution of global research on monkeypox. Methods: Publications related to monkeypox were retrieved from PubMed and Web of Science. Bibliometric analyses were conducted by VOSviewer and CiteSpace software to generate network maps, evaluate hot topics in the field, and identify cooperation patterns between different authors and countries. Results: A total of 1822 publications were retrieved to reflect the global overall monkeypox research output, including clinical trials, systematic reviews, case reports, and laboratory studies. The most productive country and institution were respectively the United States and Centers for Disease Control and Prevention—USA (CDC). The top three authors with the highest number of publications were all from the CDC. Research hotspots included some monkeypox-related diseases, such as smallpox and vaccinia, and the prevention and treatment of monkeypox diseases, such as antiviral drugs and smallpox vaccines. Research fronts included real-time PCR, immune evasion, animal models, and monkeypox outbreak countries (Democratic Republic of Congo and others). Conclusions: Research on monkeypox is mainly carried out from the aspects of its source, transmission route, virus prevalence, and prevention and control measures. Controlling monkeypox is a global responsibility, and the future research into monkeypox control methods is suggested to focus on more than vaccines.

Keywords: monkeypox; infectious disease; outbreaks; bibliometric analysis

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1. Introduction

Monkeypox is a zoonotic infectious disease caused by the monkeypox virus (MPXV) with smallpox-like clinical manifestations. Monkeypox first appeared in the Democratic Republic of Congo in 1970 [1,2]. On 7 May 2022, the UK Health Safety Authority (UKHSA) notified the World Health Organization (WHO) of the first case of monkeypox in this outbreak. Now, an emerging outbreak of monkeypox infection is quickly spreading worldwide, and cases of human monkeypox have been reported from 110 countries. On 23 July 2022, the WHO declared the monkeypox outbreak a "public health emergency of international concern" (PHEIC), and there were more than 82,000 cases of monkeypox globally according to WHO reports. At present, a multi-country monkeypox outbreak has attracted global attention [3–5]. Monkeypox has a heavy disease burden and may become a major public health disaster, posing a huge challenge to global public health [6]. As a potential global threat, it can cause numerous deaths and great economic and social upheaval [7].

Specific treatment modalities for monkeypox patients depend on supportive symptoms. There is currently no dedicated monkeypox vaccine, and various compounds that may be effective against monkeypox virus infection are being developed and tested. Raising community awareness and educating health workers can prevent and control monkeypox infection in humans, prevent infection, and stop transmission. As an emerging global threat, the monkeypox outbreak has contributed to an explosion of publications. Monkeypox-related publications continue to emerge, and scientific research will continue to grow with the collaborative efforts of researchers and clinicians worldwide.

A bibliometrics analysis of publications allows us to apply statistics to describe our present relationships between monkeypox published works [8,9]. It can also analyze the quality of research in the field, explore key topics, and predict future directions [10]. However, few studies of bibliometric analysis on monkeypox has been performed. Therefore, our purpose is to describe the scientific outputs of monkeypox to identify research hotspots and future trends to guide future research.

2. Methods

2.1. Search Strategies

Articles related to monkeypox from the Web of Science and PubMed were selected as the databases of this study, and selected data is as of 30 November 2022. The search terms used were the following: ("monkeypox" OR "monkey pox"). Only experiments, trials, and reviews written in English language studies were included. Figure 1 showed the schematic flow of the study sample. A total of 1822 documents were retrieved for data analysis.

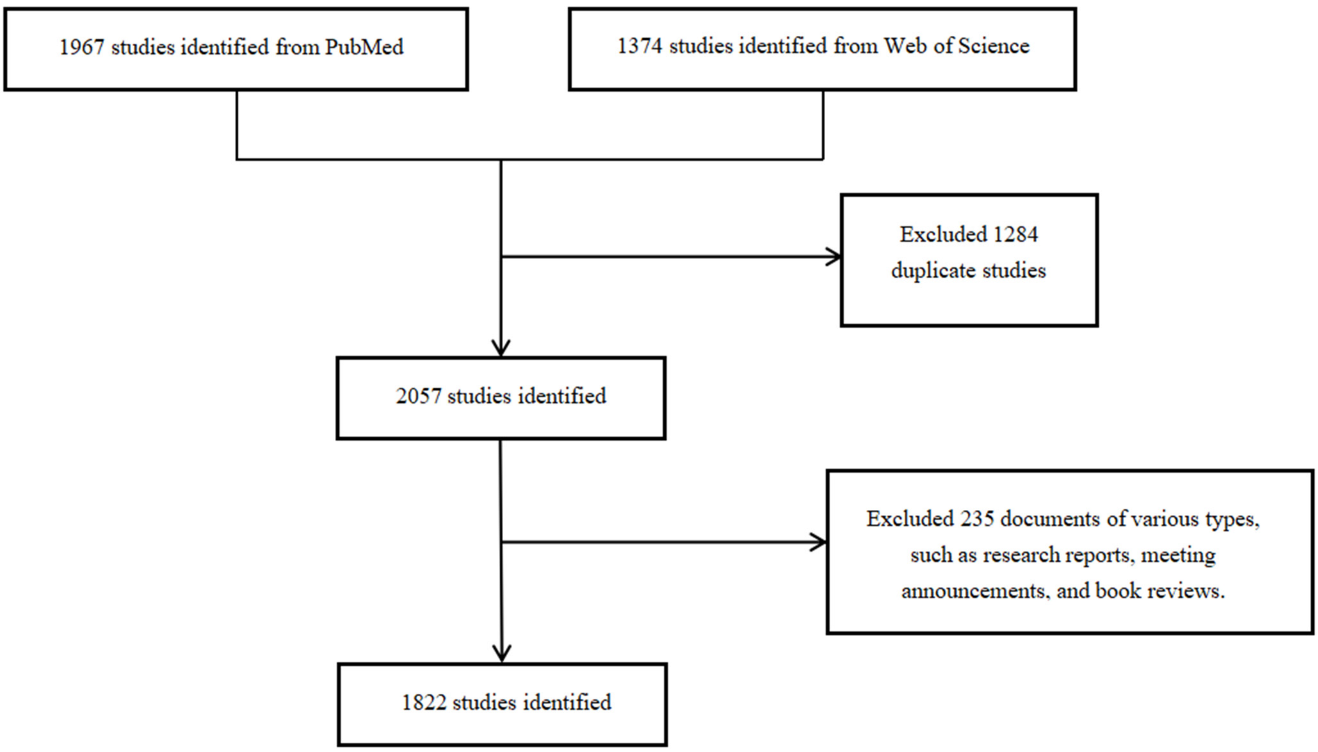

Figure 1. Publications screening flowchart.

2.2. Data Collection and Analysis

Two authors independently downloaded all records retrieved from Web of Science and PubMed databases, which include the following related information: countries/regions, journals, title, authors, affiliation, keywords, document type, abstract, and counts of citations. Any differences were resolved through consultations. Then, the data were exported to VOSviewer and CiteSpace for analysis of basic metrics.

VOSviewer was applied to create network visualization maps and analyze partnerships between high-frequency authors. The keywords were categorized with frequencies into several individual clusters and differentiated with different colors. Co-occurrence analysis identified partnerships and hot topics in this field. We selected different options as the unit of analysis. We used CiteSpace5.8.3R to analyze and plot collaborative relationships between countries/regions, the most cited literature, and its relationships, and to organize data on the basic characteristics of publications. Furthermore, CiteSpace can supplement the results section, especially the highlighted sections of references and keywords, which helped discover cutting-edge topics in the field of monkeypox research.

2.3. Materials and Methods

The parameters of VOSviewer were set as follows, and different node frequencies are set according to different node types (authors, keywords, etc.) to present suitable visualization maps. We set the following parameters of the CiteSpace software: time-slicing was performed from January 2003 to November 2022, per slice set to 1 year, a different node type was selected each time, used different options in term source according to different situations, selected criteria, and pruning options. Then we clicked the "compute node centrality" function in the node menu. The resulting visualization knowledge maps consisted of nodes and links. Each node in the map represented an essential factor to be analyzed, such as references, countries/regions, keywords. The connection lines between nodes were considered as the co-occurrence or co-citation relationship.

3. Results

3.1. Publication Output and Temporal Trend

A total of 1822 publications related to monkeypox were eventually included. The first monkeypox-related paper was published in 2003, and the annual publication continued to increase until 2010, but declined after that (Figure 2). As a result of a global outbreak of monkeypox in 2022, the annual publication production proliferated and increased to 1068, but due to deadlines, this figure would be lower than the number of publications in the full year. Among 1068 publications, reviews accounted for the highest proportion, with 503 articles, followed by clinical studies with a total of 256 articles, which included 169 case reports. In addition, there were a small number of experiments (six articles) in other categories, including five molecular cell experiments and one clinical experiment, the purposes of which included treatment (two articles), genetic research (two articles), and prevention (two articles), and one of the prevention articles was about vaccine development.

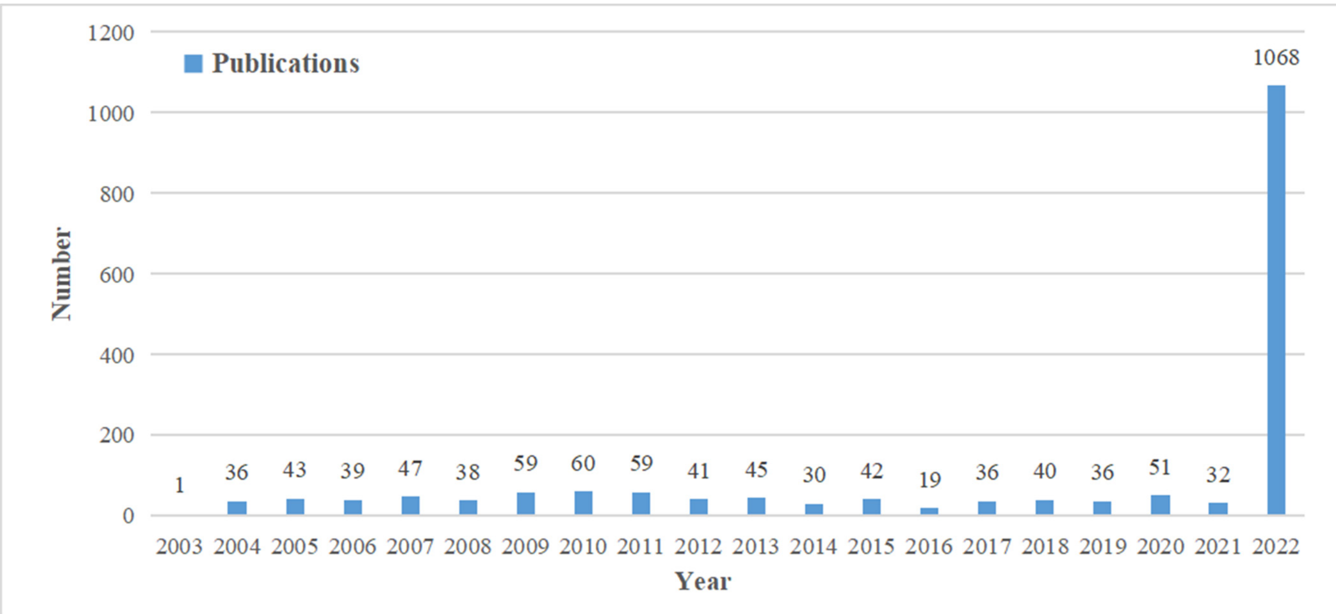

Figure 2. Distribution of annual publications of monkeypox research from 2003 to 2022.

3.2. Distribution by Country/Region

Among the top 11 countries/regions that contributed to publications, the United States possessed 615 (33.8%) articles, ranking first in the number of publications, followed by India (91), Germany (82), England (73), and Italy (62) (Figure 3). To investigate the international collaborations of countries/regions, we used CiteSpace to construct a network visualization knowledge map for publications on monkeypox. Figure 4 showed collaborations among countries/regions with more than 100 publications. The USA collaborated most closely with India, Germany, England, and Italy. France had relatively more publications, but weaker cooperative relationships.

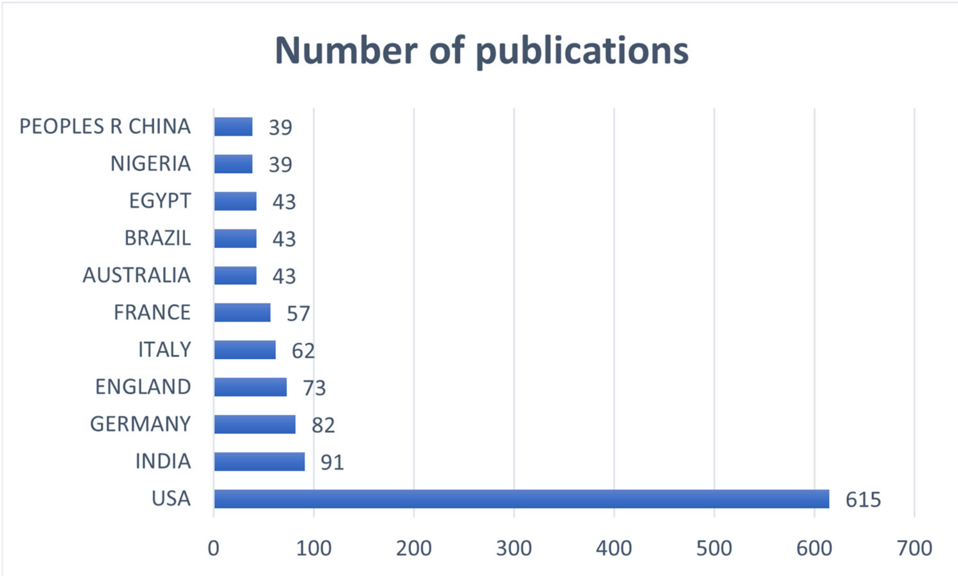

Figure 3. The number of publications of the top 10 most contributed countries.

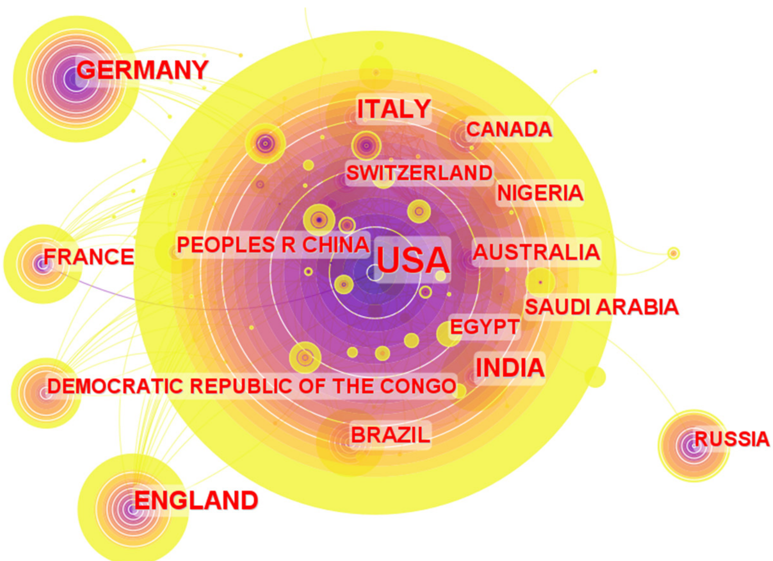

Figure 4. International collaboration of countries.

3.3. Distribution by Author

A total of 3873 authors contributed to the publications on monkeypox. The 10 most productive authors are shown in Table 1, who have contributed 411 (22.6%) of the all publications. Damon, IK ranked first (94 articles), then followed by Reynolds, MG (56 articles) and Carroll, DS (50 articles). The network visualization map of the social relationships of authors publishing more than four articles was showed in Figure 5. The authors were identified as cooperative relationships formed into clusters of authors with similar colors. It was found that 14 clusters were identified among 197 authors.

Table 1. The top 10 authors of monkeypox research.

Number	Author	Documents	Total Link Strength	Country	Institution/Organization
1st	Damon, IK	94	481	USA	Centers for Disease Control and Prevention—USA
2nd	Reynolds, MG	56	333	USA	Centers for Disease Control and Prevention—USA
3rd	Carroll, DS	50	338	USA	Centers for Disease Control and Prevention—USA
4th	Karem, KL	50	297	USA	Centers for Disease Control and Prevention—USA
5th	Mccollum, A	32	212	USA	Centers for Disease Control and Prevention—USA
6th	Li, Y	30	209	USA	Centers for Disease Control and Prevention—USA
7th	Olson, VA	28	178	USA	Centers for Disease Control and Prevention—USA
8th	Jahrling, PB	25	61	USA	NIH National Institute of Allergy and Infectious Diseases
9th	Hruby, DE	23	64	USA	SIGA Technol Inc
10th	Nakazawa, YJ	23	171	USA	Centers for Disease Control and Prevention—USA

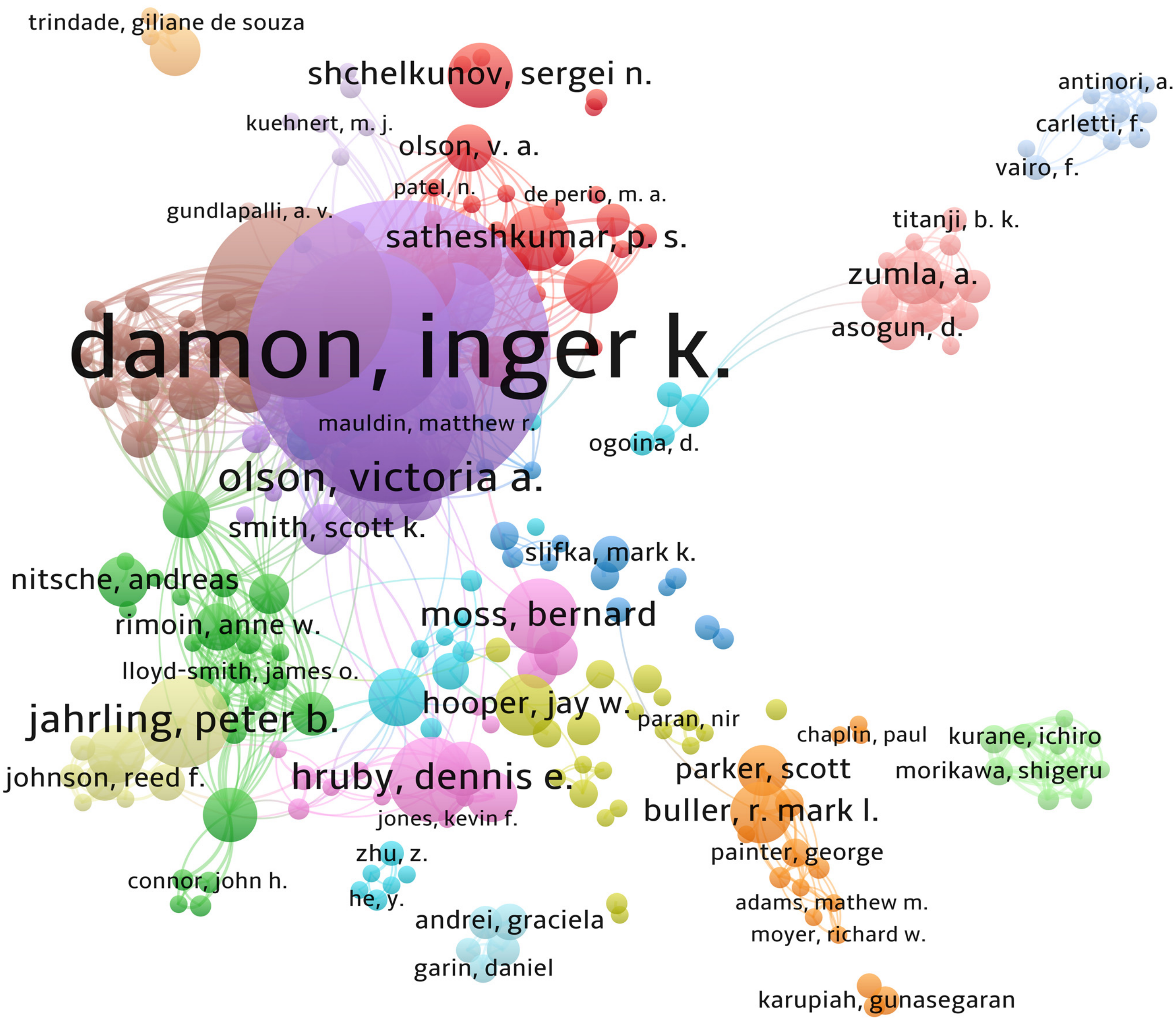

Figure 5. Author co-authorship analysis.

The coauthorship analysis is a direct relationship among authors, while the relationships among authors were measured by the cited author analysis based on the times cited in a third document. For clarity, only authors with more than 100 cocitations are shown (Figure 6). Node size was proportional to cocitation frequency. The top 10 authors are listed in Table 2. Buller, RML from Saint Louis University had the highest centrality of 0.26. The second was Abrahao, JS, from Universidade Federal de Minas Gerais.

Figure 6. Cited author analysis.

Table 2. Cited authors.

Number	Count	Centrality	Year	Cited Authors	Country	Institution/Organization
1st	14	0.26	2004	Buller, RML	USA	Saint Louis University
2nd	24	0.22	2011	Abrahao, JS	Brazil	Universidade Federal de Minas Gerais
3rd	18	0.16	2017	Bera, BC	INDIA	ICAR—National Research Centre on Equine
4th	12	0.14	2008	Jordan, R	USA	Gilead Sciences
5th	12	0.13	2006	Fogg, C	USA	2013-2018 Freelance Sci Writer
6th	6	0.13	2008	Broyles, SS	USA	Purdue University
7th	9	0.12	2009	Berhanu, A	Ethiopia	CDC Ethiopia
8th	17	0.11	2005	Senkevich, TG	USA	National Institutes of Health (NIH)—USA
9th	11	0.11	2005	Wyatt, LS	USA	National Institutes of Health (NIH)—USA
10th	10	0.11	2004	Damaso, CR	Brazil	Universidade Federal do Rio de Janeiro

3.4. Distribution by Journal and Analysis of Co-Cited References

The top 10 most productive journals were listed in Table 3. Journal of Virology (482 publications) published the most articles, followed by Virology (442 publications) and Proceedings of the National Academy of Sciences of the United States of America (432 publications). These were the top three most influential journals on monkeypox.

Table 3. Top 10 productive journals on monkeypox research.

Number	Journal	Documents	Country	Journal Rank
1st	J VIROL	482	Netherlands	Q2
2nd	VIROLOGY	442	USA	Q3
3rd	P NATL ACAD SCI USA	432	USA	Q1
4th	EMERG INFECT DIS	425	USA	Q1
5th	J GEN VIROL	409	England	Q2
6th	NEW ENGL J MED	379	USA	Q1
7th	J INFECT DIS	374	UK	Q1
8th	CLIN INFECT DIS	311	UK	Q1
9th	NATURE	288	UK	Q1
10th	AM J TROP MED HYG	282	USA	Q2

We performed a temporal literature cocitation analysis (Figure 7). The node size reflected the number of referrals, and the connection reflected the relationship between referrals. The color depth of the nodes reflected the time when the articles were cited; the earlier the time is, the darker the color and the larger the node. Articles published between 2003 and 2022 were cited more frequently. Among them, the highest citation ranking was Reed KD (2004) [11], followed by Rimoin AW (2010) [12] and Parker S (2007) [13].

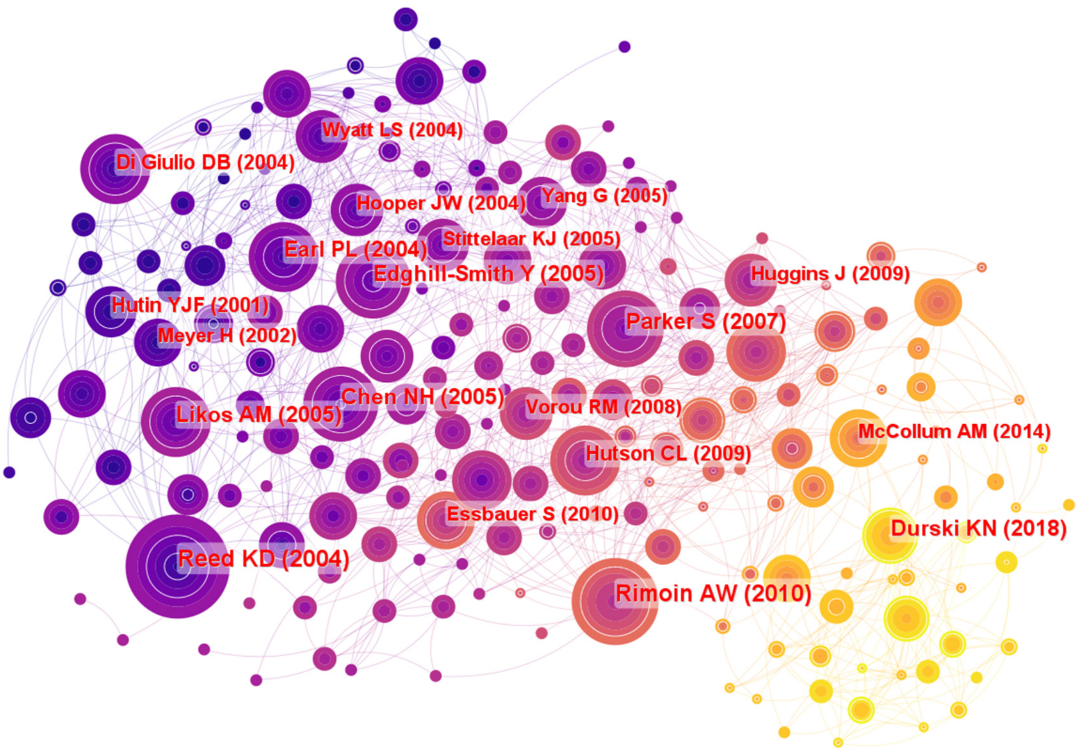

Figure 7. Reference co-citation analysis [11–13].

Figure 8 described the intensity and timing of citation bursts for the top 25 references with the strongest citation bursts to 2022. The red line indicated the period of the citation bursts. Among them, Rimion AW (2010) [12], Reed KD (2004) [11], and Durski KN (2018) [14] had the strongest citation burst intensity. According to the centralized time of the citation burst, the two upsurges of monkeypox research were 2004 to 2009 and 2010 to 2018. The most recent burst appeared between 2019 and 2022.

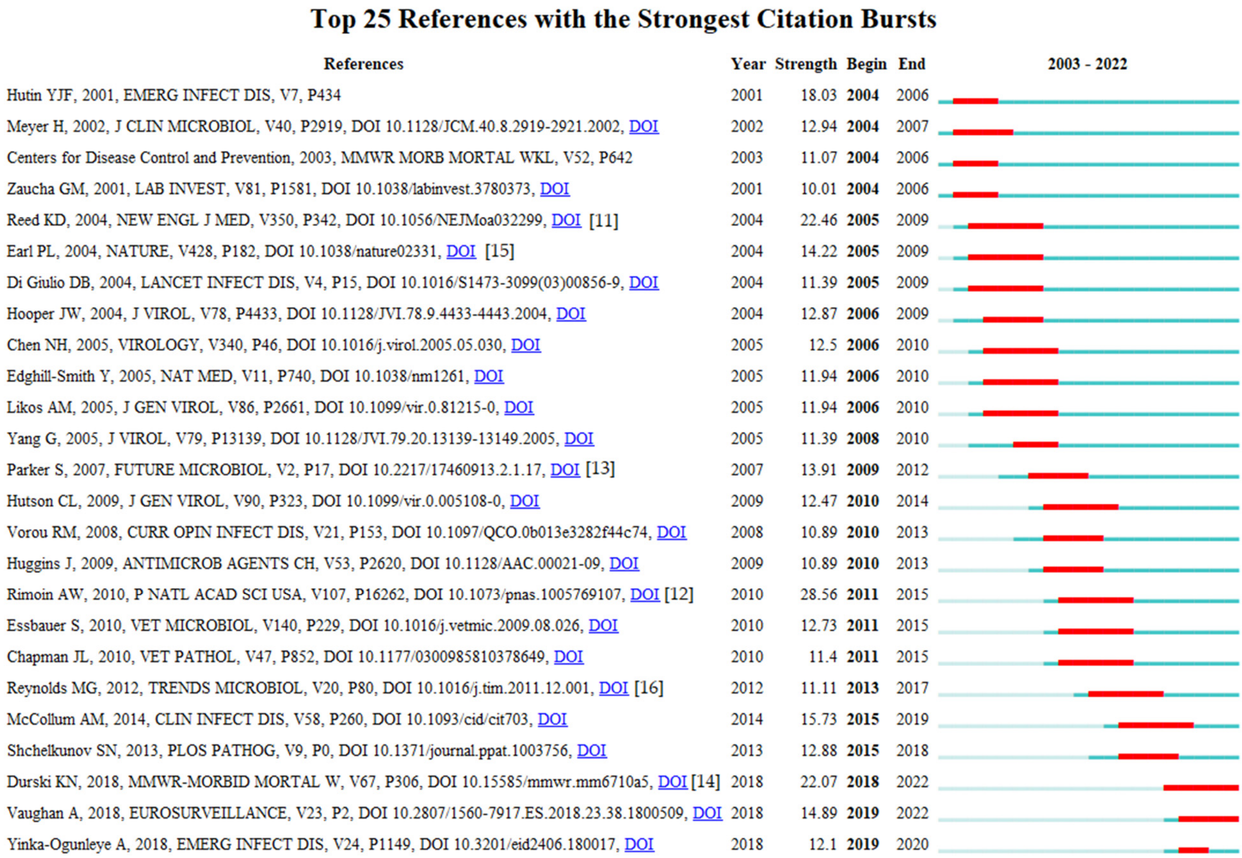

Figure 8. Top 25 references with the strongest citation bursts [11–16].

3.5. Analysis of Keywords Co-Occurrence Clusters

We used VOSviewer to software to plot the co-occurrence map of keywords, which contained 108 nodes (only nodes with more than three occurrences were filtered) (Figure 9). The size of the circles reflected the keyword occurrence frequency; the relatedness of the terms was presented by the proximity of two linked terms based on their number of co-occurrences. Figure 9 showed interrelated keyword clusters by different colors. "Monkeypox" was the most frequently used keyword, with 128 (total link strength 245) times, followed by "orthopoxvirus" (107, total link strength 230), "smallpox" (73, total link strength 193), "vaccinia virus" (69, total link strength 133), and "poxviruses" (56, total link strength 144) (Table 4), which presented the major topics in this field.

Among the top 20 keywords, some were related to monkeypox, e.g monkeypox and zoonosis, while others were associated with comparisons of similar diseases, such as smallpox, variola, vaccinia, and cowpox. Some were correlated with the treatment of monkeypox, e.g., antiviral, smallpox vaccine, vaccine, and cidofovir. Some were correlated to the research types on monkeypox, e.g., animal model and epidemiology.

3.6. Analysis of Burst Keywords

The top 10 keywords with the strongest bursts from 2003 to 2022 are shown in Figure 10. The top 10 keywords started to burst in 2004. The keyword with the longest bursts was real-time PCR. The keyword with the second longest bursts was immune evasion, which is the process by which viruses evade the immune effects of their hosts. The most recent burst was the Democratic Republic of Congo (2017–2019) and infectious disease (2019–2022).

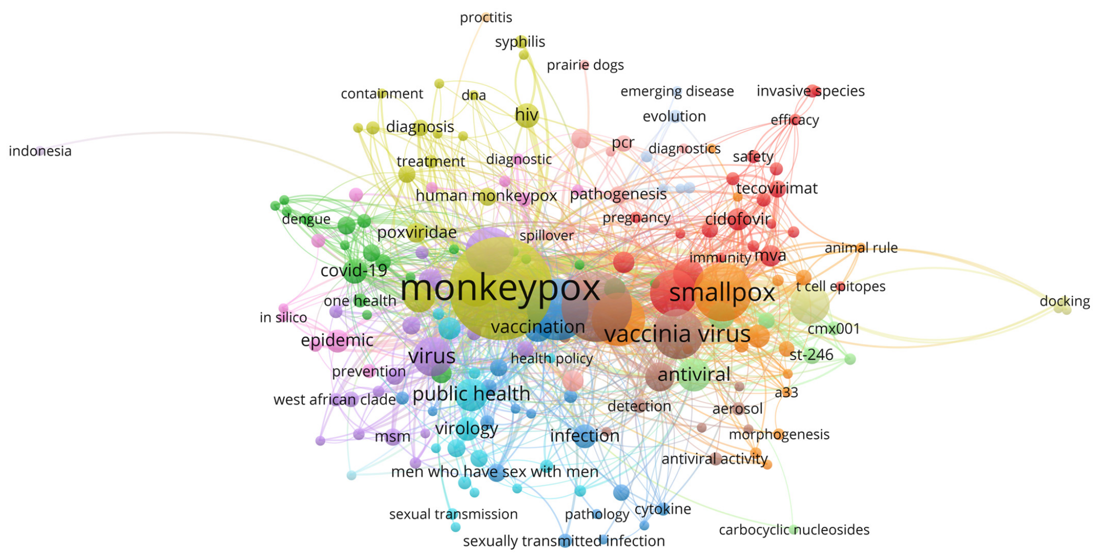

Figure 9. Keyword co-occurrence analysis.

Table 4. The top 20 keywords in terms of frequency for monkeypox research.

Number	Keyword	Occurrences	Total Link Strength
1st	monkeypox	128	245
2nd	orthopoxvirus	107	230
3rd	smallpox	73	193
4th	vaccinia virus	69	133
5th	poxvirus	56	114
6th	monkeypox virus	45	85
7th	variola	44	136
8th	zoonosis	42	91
9th	vaccinia	34	98
10th	antiviral	28	73
11th	smallpox vaccine	24	45
12th	vaccine	23	54
13th	cowpox virus	22	58
14th	animal model	20	60
15th	epidemiology	16	45
16th	virus	16	49
17th	cowpox	15	52
18th	bioterrorism	13	26
19th	cidofovir	13	38
20th	outbreak	13	31

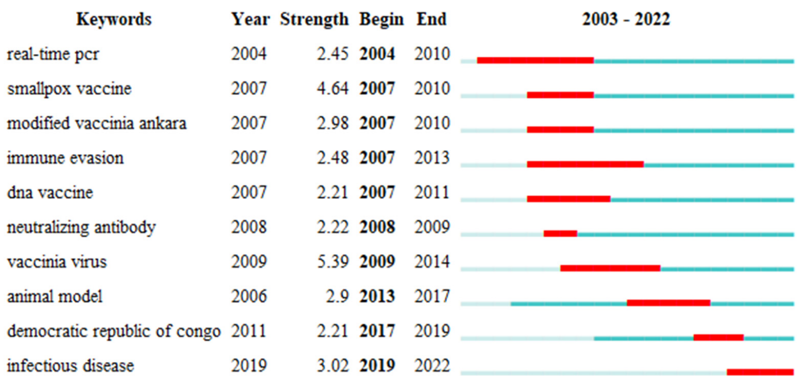

Figure 10. Top 10 keywords with the strongest citation bursts.

4. Discussion

The growing epidemic of monkeypox is likely to be a new potential threat to the world, and its epidemic problem will also increase as the number of cases soars. Our research focused on monkeypox through the bibliometric and visualization analysis method, and discussed the research status and characteristics of this field, including countries/regions, journals, authors, and keywords.

The annual publication output increased sharply in 2022, and it means that monkeypox is receiving increasing worldwide attention. The earliest development and research on monkeypox was initially conducted by American scholars who focused on monkeypox research earlier than researchers in other countries. The possible reason for its publication is that the monkeypox broke out in the American Midwest in June 2003 [17]. The United States ranked first in the number of publications on monkeypox worldwide. Authors affiliated with the Centers for Disease Control and Prevention—USA (CDC) are the most numerous, and the connection between them is also the strongest. As a result, the USA was the cardinal driving force and had the highest contribution to the retrieved documents in monkeypox research. In 2013, the CDC analyzed the factors that affect the possibility of monkeypox appearing and spreading in the post smallpox era through the ecological environment and the human-to-human transmission potential of monkeypox [16]. In the same year, it created a niche model based on reported human monkeypox cases in the Democratic Republic of the Congo, which mapped the risk of monkeypox transmission across time and space, providing a useful tool for identifying areas suitable for transmission [18]. In recent years, the CDC has paid more attention to the new situation, transmission risk, epidemiology, and intervention measures of monkeypox, and a CDC monkeypox call center was established to coordinate daily surveillance from 21 countries in the United State [14,19–21]. In addition, the CDC is very concerned about the role of the smallpox vaccine against monkeypox. One study has already investigated whether the second- and third-generation smallpox vaccine, after exposure to prairie dogs, has a protective effect on monkeypox disease in four exposure situations, and introduced the influence of postexposure vaccination and correlation with total and neutralizing antibody response survival, protein targets, take formation, weight loss, rash burden, and viral DNA [22].

The popularity of the references shows the focus of monkeypox research. At present, the main research hotspots are of the monkeypox source, transmission route, current situation, risk, diagnosis method, prevention and control measures, and impact on health practice [13,17,23,24]. The most cited article by Reed KD (2004) [11] summarized the preliminary epidemiological, clinical, and laboratory investigations of the Wisconsin outbreak, followed by Rimion AW (2010) [12], which analyzed the incidence and influencing factors of human monkeypox in monkeypox-endemic areas in the Congo Basin. Animal models of infection can be used to study the pathogenesis of monkeypox, evaluate the efficacy of drugs, and compare the pharmacokinetics and efficacy of potential smallpox therapeutic methods in animal models infected with monkeypox virus [25–27].

The analysis of keywords co-occurrence on monkeypox indicated three focus areas: monkeypox, the treatment of monkeypox, and the research types on monkeypox. From the analysis, we extracted terms such as monkeypox, smallpox, cowpox, and smallpox vaccines, and the connection between them was very close. The monkeypox virus and smallpox virus have great similarities. The nucleotide sequence in the central region of the monkeypox virus genome encodes essential enzymes and structural proteins, which is 96.3% identical to the nucleotide sequence of the smallpox virus. It is also clinically and immunologically very similar to the smallpox virus [28]. There are many studies on the connection between smallpox vaccines and the monkeypox virus. As early as 2004, studies pointed out that vaccination against smallpox affects the manifestation and severity of monkeypox, and it is feasible to treat monkeypox with a subunit vaccine method of smallpox-monkeypox immunization [15,29]. Studies have shown that the smallpox vaccine could achieve an 85% effectiveness rate in preventing monkeypox. On this premise, the use of the smallpox vaccine to treat monkeypox has become a research frontier. An antiviral drug developed for smallpox called tecovirimat was licensed for monkeypox in 2022 by the European Medicines Agency (EMA) based on data from animal and human studies, but it is not yet widely available [25,30].

However, due to the contraindications of live virus vaccines, a considerable number of people cannot be vaccinated [31]. We need more alternative therapeutic approaches to facilitate mass use and prevention. Smith, Scott K presented ST-246, a novel antiviral compound that inhibits the in vitro growth properties of six variola virus strains and seven monkeypox virus strains. In vitro phenotypic data showed that ST-246 inhibits smallpox and monkeypox viruses by reducing the production and release of enveloped orthopoxviruses, and supports the development of ST-246 as an antiviral therapeutic compound for the treatment of severe systemic orthopoxvirus infections [32]. Parker, S's research team discovered the efficacy of recombinant immunoglobulin (rVIG), which demonstrated efficacy against several orthopoxviruses, both in vitro and in vivo, in a prophylactic and therapeutic manner, and rVIG can reduce morbidity and adverse events, indicating that the immunoglobulins were well tolerated. His findings suggested that recombinant immunoglobulins may be candidates for further evaluation and possible licensing under FDA animal regulations [30].

The World Health Organization has also proposed the principles of clinical management, prevention, and treatment of monkeypox. It developed interim guidance on monkeypox vaccine and immunization, strongly encouraged countries to fully consider the context of the current monkeypox epidemic, and to establish their national immunization technical advisory groups (NITAGs) to review the evidence and develop policy recommendations for vaccine use that are appropriate to relevant national circumstances. In addition, the WHO, in collaboration with Uppsala Monitoring Centre (WHO Collaborating Centre), has developed a mobile application (VigiMobile App) to report adverse events following immunization with smallpox and monkeypox vaccines.

5. Limitation

Our study has some limitations. One limitation of our study was that we only focused on English journals, which could inevitably miss some important information in other languages. We obtained these points by analyzing the cooperation of countries/regions in this study. The cut-off date for the data inclusion may result in another limitation of our study; we undertook this study at the vortex of the epidemic before November 2022, which may miss the latest information for 2022. Moreover, inherent to any bibliometric approach, was that we did not check and record the full text of each article; although we checked random samples, we still cannot guarantee the accuracy of all articles.

6. Conclusions

With the global monkeypox virus epidemic, national or regional research teams gradually establish substantial collaborations, among which the USA is at the center of cooperation. The main research hotspots on monkeypox are related to source, transmission route, current situation, risk, diagnosis method, prevention and control measures, and impact on health practice. The use of vaccines to prevent and treat monkeypox is a hot issue today, and the use of animal models to carry out related research to discover prevention and treatment methods other than vaccines may be the frontier of future research. The outcomes of the current study will enable researchers, clinicians, and governments to provide help and information for future research, and understand further applications in the field of monkeypox.

Author Contributions: H.R. and J.L. conceived of the presented idea. H.R. and W.Y. developed the theory and performed the computations. W.Y. and X.Z. verified the analytical methods. W.Y., X.Z., M.D., Y.D. and L.L. collected and synthesized the data. J.L. and H.R. provided comments related to the presentation of the findings and critically reviewed the manuscript. All authors have read and agreed to the published version of the manuscript.

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