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## Original article

# Trends in monkeypox research: A sixty year bibliometric analysis

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## Abstract

**Aim:** The purpose of the study was to identify common descriptors and publication hotspots that may form reference themes for future monkey pox research. **Method:** Bibliometric analysis of monkeypox related studies between 1962 and 2022 was carried out to ascertain and describe this body of literature. **Results and conclusion:** A total of 1,134 documents were analysed for bibliometric indicators. The studies had 3,478 authors, an average of 5.72 co-authors per publication and a 3.73 author collaboration index. Annual scientific production peaked in 2004 (5.5%) and 2020 (5.3%). Monkeypox research accumulated 128 grants, 68 policy documents, 9 clinical trials, and 50 patents. The United States placed first in terms of the number of documents and citations, followed by Germany with 73, United Kingdom with 53, Russia and the Democratic Republic of the Congo (DRC) with 34 documents each. The DRC and Nigeria had the most documents among African countries. Text mining showed researchers have put their efforts into studies related to infectious disease ‘epidemiology’: the ‘emergence’, ‘Case diagnosis and ‘surveillance’ of ‘outbreaks’. The top keywords were ‘monkeypox’ (570 times), ‘monkeypox virus’ (411 times), ‘poxviridae infections’ (332 times), ‘small pox’ (266 times), ‘orthopox virus’ (248 times), ‘vaccinia virus’ (203 times), and ‘disease outbreaks’ (179 times). The most cited treatment related noun phrases were ‘tecovirimat’ (brand name Tembexa), ‘Cidofovir’/ ‘CMX001’ (Brincidofovir), ‘ACAM2000’ (imvanex vaccine) and ‘Vaccinia’ Immune Globulin (‘VIG’). This result will serve as a foundation for future research, guiding decision-making in monkeypox research and therapy.

## Introduction

The monkey pox virus (MPXV) is an oval shaped double stranded DNA virus (poxvirus) that causes monkeypox (smallpox-like) disease in humans and animals including rodents [1,2]. It is about 140 to 260nm in size with a dumbbell shaped core. Monkey pox virus belongs to the Orthopoxvirus genus, Chordopoxvirinae subfamily and Poxviridae family [3,4]. The DNA virus was first discovered in monkeys in 1958 at the Staten Serum Institute in Copenhagen, Denmark [2,5].

Since the zoonotic disease was first diagnosed in the Democratic Republic of the Congo (DRC) in 1970, it has remained endemic and has spread to Central and West African countries such as Sierra Leone, Liberia and Nigeria [6]. The DRC documented over 18,000 suspected or confirmed cases between 2010 and 2019 and more than 6,000 unconfirmed cases by 2020 [7,8]. According to the World Health Organization (WHO), Nigeria has reported more than 700 suspected and reported cases since 2017

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[9]. The Central and West African genetic clades are responsible for monkeypox (MPX) disease with the former clade being more virulent [10]. The West African clades have a case fatality rate (CFR) of less than 1% to ~ 3.6% compared to ~ 10.6% of the Congo basin clade [1,2,10,11]. The MPXV genome is more than six times larger and harder to analyse and as such contains many mysteries that may be responsible for the remarkable difference between the two clades [1]. Recently, the numbers of MPX cases are increasing around the world, especially in North America and Western Europe [12]. Preliminary polymerase chain reaction (PCR) analysis shows that most cases reported in non-endemic countries are genetically linked to West African strains [9,13,14]. Between May 13, 2022 and June 14, 2022, over 1600 laboratory-confirmed cases of MPX and 1500 suspected cases were reported in 39 WHO member States across four non-endemic regions [15,16]. Out of these countries, seven countries (where the virus has been detected for years) reported 72 deaths [16]. Although there are reports of positive cases among some travellers from Nigeria, the vast majority of cases had travelled to non-endemic areas (Europe and North America) [16]. The recent concurrent and multicountry incidence of MPX cases in endemic and non-endemic regions suggests that this strain may have thrived in the environment unnoticed for some time [17].

Although transmission is through respiratory droplets, bodily fluids, lesions and fomites the most recent cases have occurred through sexual networks [18]. Monkey pox virus cases classically have a median recovery time of 2 to 4 weeks [19]. The disease is usually characterized by a rash that appears on the face and spreads to other parts of the body, eventually crusting and falling off [19]. The recent COVID-19 pandemic made people aware of the virulence potential of viruses and the trail of excruciating memories they conjure up [20].

Since its discovery, researchers have studied MPXV and hundreds of articles have been published. A researcher's workflow usually involves meticulously identifying search trends and hot spots from disparate data pools [21]. A study is needed that sorts and summarizes information from databases to aid future research.

Quantitative and qualitative measurement of scientific research is carried out using bibliometric tools [22]. Combined with spatio-temporal visualization techniques, this tool is useful for identifying infectious disease outbreaks [23]. These methods were employed in this study to establish connections within the MPX research domains. This work provides important references and guidance for scientists.

## Method

Bibliometric analysis of monkeypox related studies between 1962 and 2022 was carried out to ascertain and describe this body of literature. Published papers, chapters, Books and preprints were searched using a topic search (title/abstract) on Dimensions™ database (on 2022-05-31)[24]. Only documents in English language with a focus on MPX were included in the analysis. The search terms used were “monkey pox” OR “monkey pox Virus”. These search terms were used in the title/abstract fields. Retrieved articles were exported in CSV file format (CSV for VOS viewer and CSV for Bibliometrix package) and duplicates were removed. Descriptive analyses were conducted to evaluate the characteristics and types of articles retrieved using Bibliometrix™ and Biblio™ packages in R-Studio™ version 4.1.2 (2022-02-16). Spatiotemporal and text mining analysis were carried out with Visualization of Similarities (VOS) software - VOS viewer™ (V.1.6.18), a tool for building and visualising bibliometric connections [25].

## Results

A total of 1,134 documents were published in 386 sources (Journals (n=994), Chapters (n=91), Books (n=3), preprint (n=43), proceeding (n=3)) within the survey period of 1962 to 2022. The studies involved 3,478 authors, with 0.326 documents per author (3.07 authors per article), 5.72 co-authors per article and an author collaboration index of 3.73. Single-authored documents were 178; Authors of multi-author articles were 3,342. An average citation per documents of 23.34 was obtained from the study breakdown. At the time of this study, monkeypox research has accumulated 128 grants, 68 policy documents, 9 clinical trials, and 50 patents. Annual Scientific output fluctuated during the survey period peaking in 2004 (5.5% [62/1134]) and 2020 (5.3% [60/1134]) in respect of number of documents and 2005 (56.3) in terms of mean total citations per articles (**Figure 1a**). Though

we documented 1134 publications on MPXV, only 52 (4.5%) had citations above 100 citations, 142 (12.5%) had more than 50 and 546 (48.1%) had over 10 citations, whereas 588 (51.9%) documents had less than 10 citations (Supplementary data).

**Figure 1b** shows the top 10 countries that produced MPX literature. All countries in the chart produced over 10 documents within our sample frame. Only one country produced close to 500 documents. The United States of America (USA) ranked first with 497 documents and 15,982 citations, followed by Germany with 73, United Kingdom with 53, Russia and the DRC with 34 documents each. The African countries with the most documents were Democratic Republic of the Congo and Nigeria with 34 and 26 respectively. Of the top 30 organizations, Center for Disease Control and Prevention (CDC) produced 110 documents and 3,535 citations, followed by the US Army Medical Research Institute for Infectious Diseases with 54 papers and 2,917 citations. The University of Kinshasa, DRC is the only African institution in the top 5, ranking 5th with 28 papers and 612 citations (**Figure 1c**).

**Figure 1d** shows the top 20 sources of MPXV literature. *Virology*, *Journal of Virology* and *PLOS-ONE* emerged as the top sources with 37 publications, 1,532 citations, 36 publications with 739 citations, and 36 publications with 1,434 citations respectively.

**Figure 1e** showed the top 10 authors. Inger Damon (88, 7.8%) of the CDC and Emory University in Atlanta ranked first, followed by Reynolds, MG (52, 4.6%) and Kareem, KL (47, 4.1%) from the CDC.

**Figure 2a** depicts the global collaborative network for MPXV literature. There are 506 entries for global collaborations, with a maximum of 113 collaborations per country. The strongest connections are between the USA (113 links), Germany (61 links), and the DRC (47 links).

The result of author's collaboration links is presented in **figure (2b)**. The size of the bubbles depicts the number of documents, and the line between two authors represents the collaboration between them. The colours represent the collaboration clusters. In the cooperation network, sixteen clusters can be distinguished. The most prolific contributions in the network are that of Damon Inger K, McCollum Andrea, Marrennikova SS and Meyer Hermann. Other researchers are linked to one of these core researchers. In the Figure

2c authors in the yellow density cloud are authors that have recently published articles.

Coauthorship network analysis by organization (**Figure 3**) reveals that they share direct or indirect links to the most productive institutions in MPX research. However, the strongest co authorship links by organization occurred between the CDC, the University of Kinshasa and the National Institute of Biomedical Research. This was followed by moderate links between the CDC and the National institute of allergy and infectious diseases. There was little or no direct links between United State Army Medical Research Institute and the CDC.

The most prominent authors of monkeypox-related studies in Africa are listed in **table (1)**. Malekani Jean (n=16) of the University of Kinshasa, DRC led the pack, followed by Ihekweazu Chikwe (n=14) of the World Health Organization. Kabamba Joelle placed third with 13 articles. The co-occurrence network reveals that all of the prominent authors are linked to each other, either directly or indirectly. Yinka-Ogunleye Adesola and Ihekweazu Chikwe are the authors with the most recent publications (**Figure 4**).

Author keyword co-occurrence analysis was conducted to identify research direction of MPX research globally. The authors' keyword analysis of MPXV literature using VOS viewer software is shown in Figure 5a. With a minimum occurrence requirement of 10, only 520 terms out of 17,542 met this criterion. The relevant scores were calculated. Based on these scores, 60% (312) of the most relevant scores were selected [25]. The top keywords were monkeypox (570 times), monkeypox virus (411 times), poxviridae infections (332 times), small pox (266 times), orthopox virus (248 times), vaccinia virus (203 times), and disease outbreaks (179 times).

Co-occurring terms and phrases are those that occur in the same publication at the same time [25]. Strong co-occurrence relationships between keywords can identify research hotspots more precisely than a single term [25]. In our spatiotemporal visualization, highly related noun phrases share the same color space, indicating a potential connection. In the figure, color shifts across the red Gray and blue (RBG) spectrum is consistent with cluster formation. Keywords depicted in red are roughly connected to Epidemiology and public health research themes. The red cluster demonstrates that researchers have

put their efforts into studies related to infectious disease 'epidemiology': the 'emergence', 'Case diagnosis' and 'surveillance' of 'outbreaks' of infectious diseases like the human monkeypox 'COVID', 'SARS', 'Ebola' and 'HIV' among others, since the outbreak puts public 'health', policies under discussion.

The blue cluster houses noun phrases related to research themes of molecular biology and clinical diagnosis. This cluster shows scientific endeavors to improve on the molecular aspect of infectious diseases to foster better 'differentiation' of etiological agents. The overall theme of this cluster can be expressed as follows; Cytoplasmic inclusions (A-type and B-type) are found in the 'cytoplasm' of 'host cells' 'infected' with pox viruses of the 'orthopoxvirus' genus. These inclusions constitute viral factories where 'DNA' is harvested for analysis. Electron microscopic, serological (Enzyme-Linked Immunosorbent Assay, 'ELISA') and 'PCR' (recently 'real time PCR'), DNA 'microarray' test are methods used by scientists and researchers in the laboratory detection of pox viruses.

The pharmaceutical microbiology and immunology cluster (gray) shows that recent studies imply concerns about the contagion, (Monkeypox virus) because of its prior neglect. The discontinuation of small pox vaccination in the late 1970s left us vulnerable to orthopoxviruses. 'Invitro' 'mouse' model 'experiments' have shown that the orthopoxviruses including 'vaccinia virus'

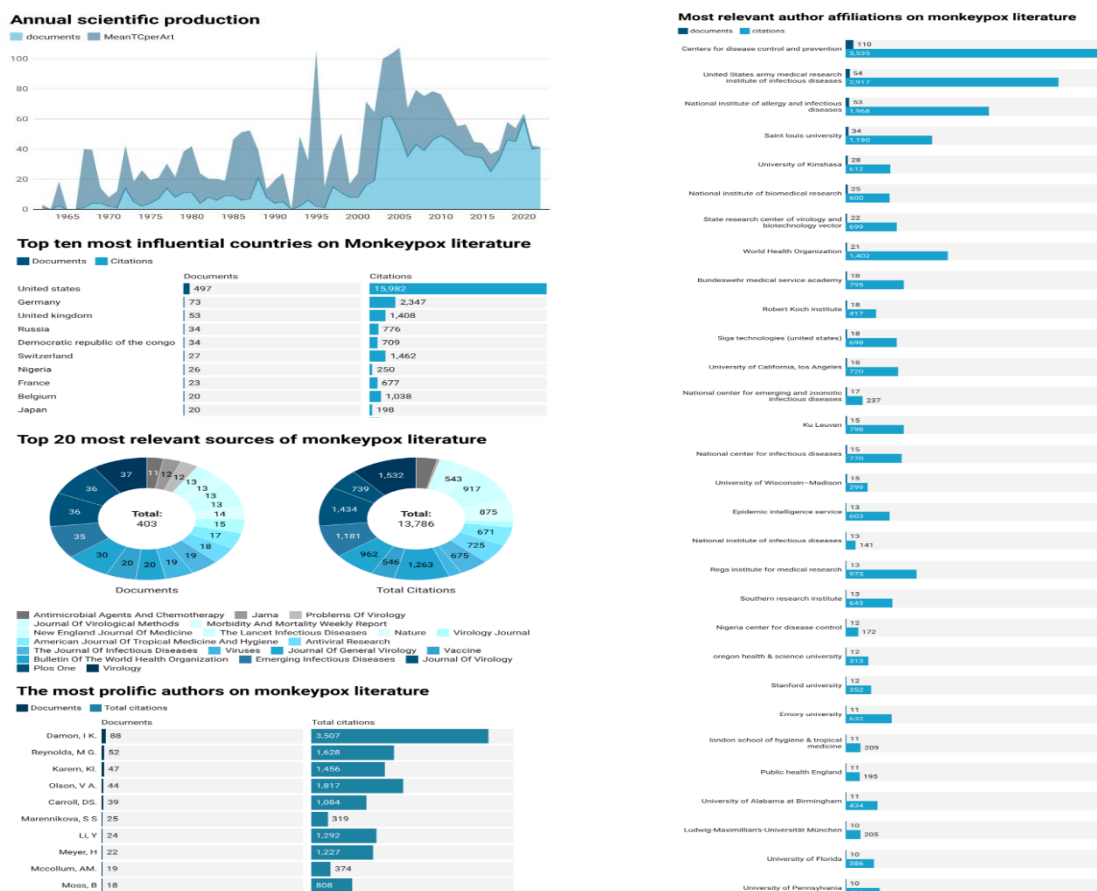
and the monkey pox viruses evades the 'host immune' response by inhibiting the cellular interferon ('IFN') antiviral immune response. This similarity prompted researchers to the immunologic mechanism of cross protection by immunization against small pox with 'vaccinia virus' ('VACV') where 'neutralizing antibodies' play a crucial role. Given that there are no specific drug or vaccines for its treatment, recent research has discussed the repurposing of antiviral drugs and vaccines used for treatment of other pox viruses like 'tecovirimat' (brand name Tembexa), 'Cidofovir'/'CMX001' (Brincidofovir), 'ACAM2000' (Imvanex vaccine) and 'Vaccinia' Immune Globulin (VIG) in treatment and vaccination against monkeypox [26–29].

**Figure 5b** show that the MPX disease and monkeypox virus share a meaningful comparison with other large outbreaks of infectious diseases of public health concern like Severe Acute Respiratory Syndrome (SARS), Human Immunodeficiency Virus (HIV), cowpox, small pox, Ebola virus disease, white pox, rabbit pox, avian influenza and camelpox. The virus is also associated with hosts like the Gambian rat, African rodent, bird, sheep and human (children). The figure also links monkeypox to endemic niche (DRC, Cameroon, Nigeria, and Central African Republic) and non-endemic niche (North America, Indonesia etc.). Annual word growth in monkey pox related research is shown in **figure (5c)**.

**Table 1.** Top ten most prolific authors of monkey pox related research in Africa.

ID	Author	n	Affiliation	Country
1	Malekani, Jean	16	University of Kinshasa	DRC
2	Ihekweazu, Chikwe	14	World Health Organization	Nigeria
3	Kabamba, Joelle	13	U.S. Centers for Disease Control and Prevention, Kinshasa	DRC
4	Okitolonda, Emile	12	Kinshasa School of Public Health, Kinshasa	DRC
5	Karhemere, Stomy	10	National Institute for Biomedical Research	DRC
6	Yinka-Ogunleye, Adesola	9	Us Centers for Disease Control and Prevention	Nigeria
7	Muyembe, Jean-Jacques	8	National Institute for Biomedical Research	DRC
8	Likafi, Toutou	7	School Of Public Health	DRC
9	Asogun, Danny	3	Irrua Specialist Teaching Hospital	Nigeria
10	Ndakala, Nestor	3	Field Epidemiology and Laboratory Training Program, Kinshasa	DRC
Key: n = number of documents				

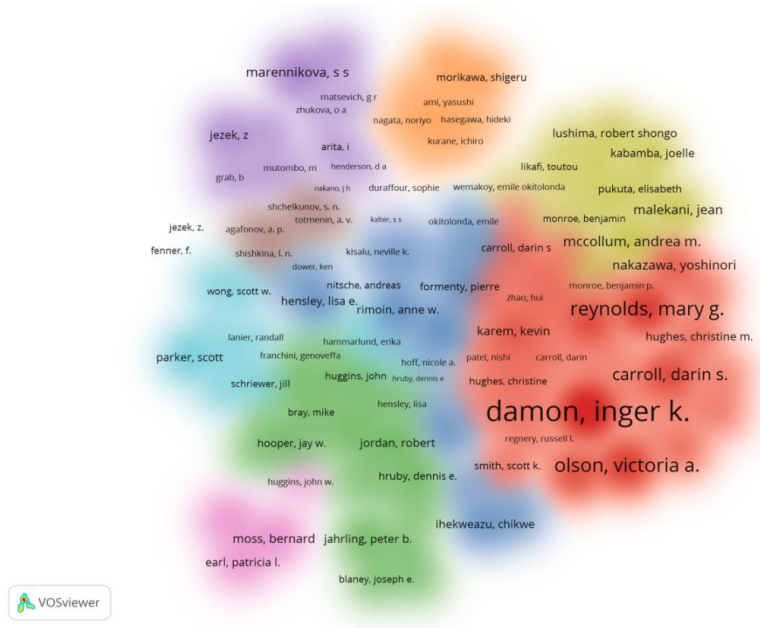
**Figure 1.** (a) Annual scientific production (b) Top 10 most influential countries (c) Top 20 most relevant source (d) most relevant author affiliation (e) Most prolific authors in monkey pox research



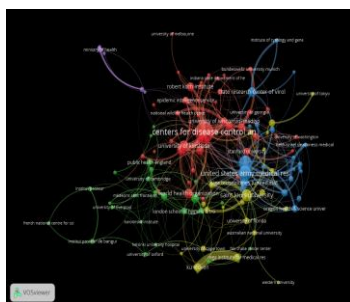
**Figure 1 (a) Annual scientific production (b) Top 10 most influential countries (c) Top 20**



**Figure 2 (c). The density map of terms in MPX research**

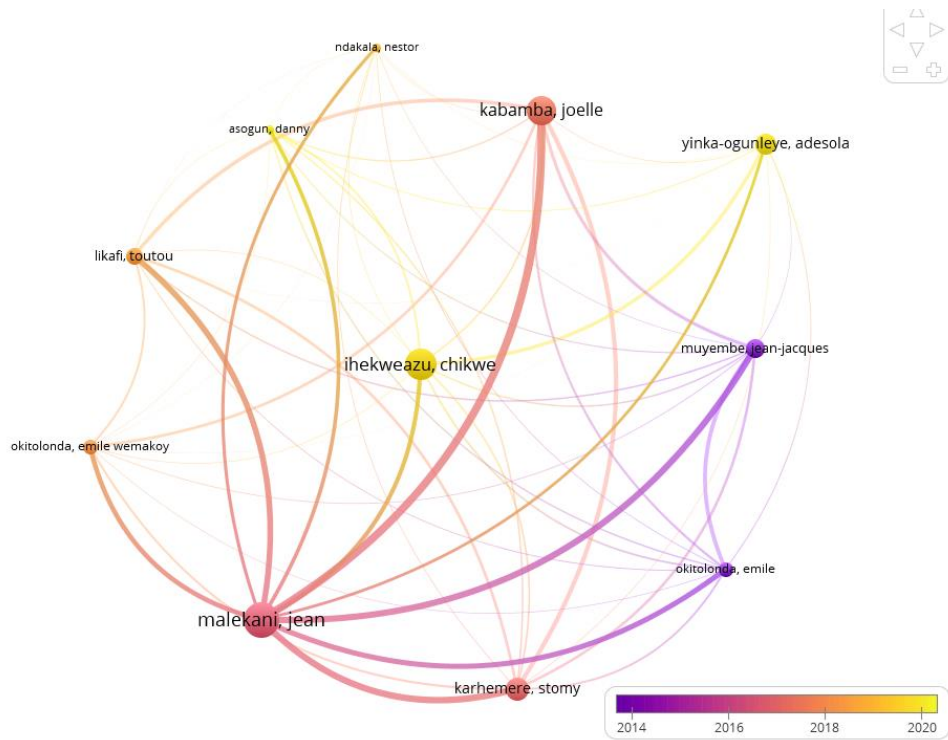


**Figure 3. Co-occurrence map of organizations in MPX research**

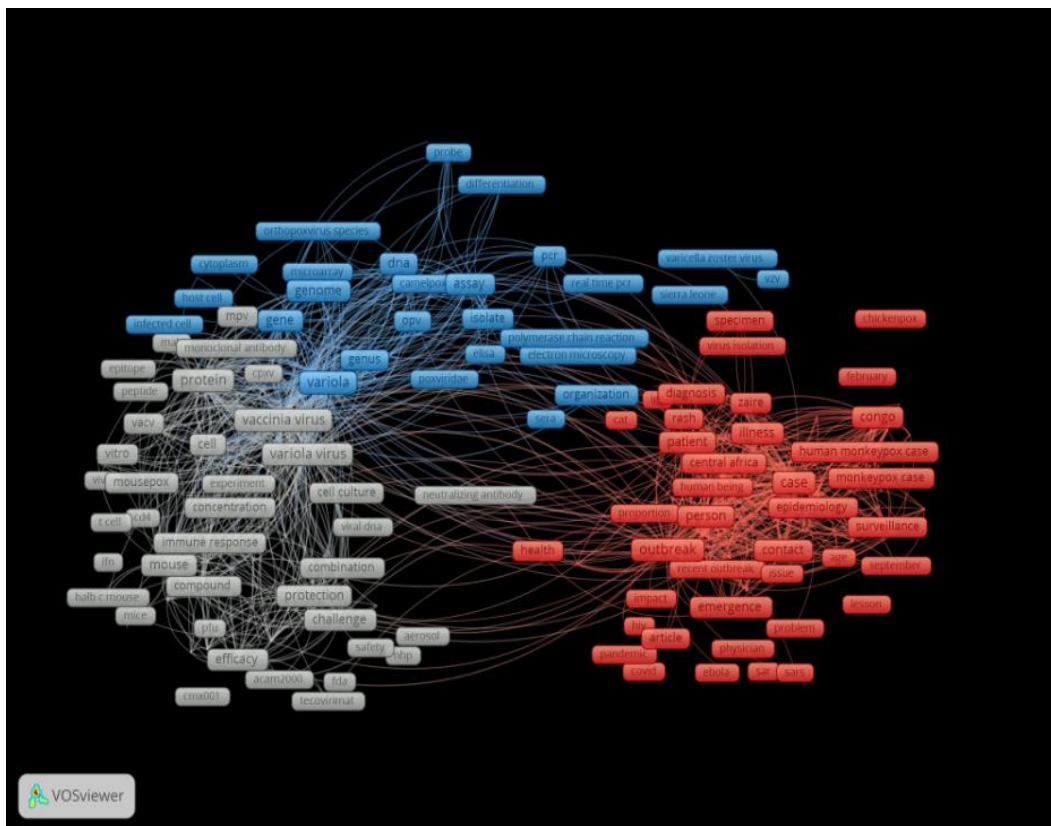




**Figure 4.** Co-occurrence networks of the top ten most prolific authors of monkey pox related research in Africa. Yellow color = Authors with recent publications (2019-2022)



**Figure 5a.** Co-occurrence network of author keywords







## Discussion

Monkey pox virus has been an area of modest concern since its discovery; several scientific documents have been published in the decades that followed. Prompt and effective control of the spread of the virus has become a significant challenge since the recent spread of the virus beyond Africa. This is partially due to the unclear knowledge map of its zoonosis and an insufficient knowledge of the present research trends that fosters superficial investigations and analysis of this virus. This may impede development of definitive prevention and control protocols. Bibliometric tools were used to analyze 1,134 MPX-related documents across six decades. The trends in the annual number of publications and mean total citation per MPX-related articles reverberates the measured interest and growth of this research domain [30,31]. The visual interpretation revealed dual citation and publication peaks in 2004 and 2020, consistent with the onset of outbreaks of MPXV. **Hurtado et al.** [32] reported that the amount of scientific output is consistent with degree and distribution of disease outbreak. As a result, the observed trend is indicative of the viral impact on health care. The second peak (2020 to 2022) fluctuated and then drifts uphill in 2022 which reflects the oscillating but progressive interest in MPX research. Based on this, we assert that a scientific productivity will improve as the trend continues.

The citation frequency of an article may not necessarily reflect its quality but the scope of its distribution and influence [33]. More than half (51.9%) of monkeypox related publications had less than 10 citations and only 4.5% were cited over a hundred times. This shows that only a slight percentage of monkeypox related studies are of high quality. Suggesting that more profound works need to be reached to improve the quality of MPX related research and comprehensive study of some specific areas may redirect the focus of future publications.

Among the top journals - *Virology*, *Journal of Virology* and *PLOS-ONE* were the most prolific and points to the authority and the receptiveness of this journal to publications on emerging viruses and related diseases. Additionally, core sources serve as leading lights for faster and effective research work [34,35].

The United States and Germany were the leading countries, which is not surprising given that Europe and the United States are at the forefront of

scientific research [36]. The DRC and Nigeria ranked among the top ten (10) of MPX-related research. This entails that African countries play a significant role in MPX disease research. This outcome is not surprising since the DRC is the African endemic region with the more virulent central African clade of the MPXV. Another reason that can be advanced to explain this outcome is the fact that there have been several outbreaks in African endemic areas during the sixty years of MPX [2] and the scientific community tends to drift towards a topic once there is a public concern of certain pathogen.

The sudden and concurrent spread of infectious disease is extensive and disastrous which made scientists grasp that reciprocal actions should be encouraged. Furthermore, intervening events like improved funding and national policies may have been helpful in research and development in these countries.

The United States, Germany, and the DRC are leading international collaboration efforts in MPX research in this study. This discovery could lead to more global political, academic, and research collaboration in the fight against infectious disease spread [37]. Monkeypox is endemic in low resource African countries and occasional spread to the Western hemisphere shouldn't be the only motive to direct research funds and collaboration to the African countries, in other words; The fact that funds and collaborations between high income countries and Low-and Middle-Income Countries (LMIC) with endemic enzootic MPX is peaking when the disease was imported to the USA and Europe would not be of great impact. Sustainable multidisciplinary collaboration is mandatory to control MPX.

An objective and detailed overview of a researcher's authority and scientific contribution is provided by a co authorship analysis of MPX-related studies [38,39]. The most prolific authors share a direct or indirect affiliation with the US-CDC, which gives an idea about the dominance of the United States and the CDC on MPX research. This knowledge may complement efforts to identify expert personnel and organizations in the research area ahead of future monkeypox outbreak.

Keyword co-occurrence analysis aids in the detection of research trends and directs scientists to areas of interest [31,40]. In this study, three

distinct research themes were identified within MPXV-related studies, which mostly involve features of epidemiology/public health, molecular biology/clinical diagnostics, and pharmaceutical microbiology/immunology research themes.

According to our findings, current research on the MPXV is mostly focused on detection, prevention, and therapy. Promoting appropriate public health measures may aid in the prevention of large-scale public transmission [41,42]. While the CDC recommends using smallpox vaccination and immune globulin as prophylaxis after exposure in high risk and highly immune impaired individuals, they do not prevent the disease. As a result, specialized antiviral medications or vaccines are required. Tecovirimat and brincidofovir are two antiviral drugs that have been adapted for the treatment of MPXV. For the time being, the most important thing is to keep MPXV from spreading [26].

All sequences from the multicountry epidemic are clustered within the West African clade, and Nigeria is thought to be its natural source, according to genome sequencing and evolutionary research [2]. The primary viral reservoir for human MPXV infection is uncertain; prior data suggests rodents are possible reservoirs. It infects a broad range of mammalian taxa. Only isolates from the *Funisciurus squirrel* and the mangabey monkey have been fully documented thus far. Contact with body fluids, skin lesions, respiratory droplets, and fomites all contribute to human transmission [18]. Further research into the reservoirs and spread of the human MPXV cannot be exaggerated, as it may become the focus of future research, facilitating the development of therapeutic medications and vaccinations.

This study found that author and organizational research collaborations need to be strengthened, particularly in Africa, where the majority of scientific production on MPXV was limited to a few contributors. The recent outbreak of MPXV has highlighted knowledge gaps in viral transmission dynamics as well as the virus's changing epidemiological character [42]. As a result, a more inclusive and harmonised approach is long overdue. Improved multidisciplinary and multi-sectoral collaboration should be encouraged.

Text mining revealed that some study domains remain unexplored. A global protocol to manage the MPXV spread, Single-cell sequencing

technology, the relationship between MPXV and immune metabolism, and the use of combination therapy are all areas of monkeypox research that are yet to be fully investigated.

### Conclusion

Since its inception, MPXV-related publications have been on the rise. In terms of scientific output, the US and the CDC are at the top. There are many co-authorship networks between the U S and the DRC. Despite budget constraints, African scientists are among the most competent experts in the field of MPXV research. Human MPXV infections have spread to many countries (endemic and non-endemic), and the number of positive cases is increasing globally, indicating that more research peaks are likely. According to our findings, current research on the MPXV is mostly focused on detection, prevention, and therapy.

This study has various limitations that should be mentioned. Because only data from Dimensions™ database was used in this analysis, relevant studies may have been overlooked. Only documents in English language with a focus on MPXV were included in the analysis. Citations counts are accumulated with increase in number of citable years and studies have shown that some documents require a least two citable years post publication to accumulate enough citations to be included in a citation analysis consequently, our results may have favoured earlier publications[43]. We used the Bibliometrix™, Biblio™ and VOS viewer™ tools. Other bibliometric tools, such as CitNetExplorer™, and Sci2tool™, and some others, should be employed to capture diverse points of view that may aid in the progression of monkeypox research theme. Quantitative methods were used in bibliometric analysis; as a result, the quality of individual articles was not assessed. This should be considered in future research.

### Competing interest

We declare that we have no conflict of interest.

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### Availability of data and materials

The raw datasets generated are accessible upon demand to the corresponding authors (suleykestler2@gmail.com, shuaibusuleiman60@yahoo.com)

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