A bibliometric analysis of research on Ebola in Science Citation Index Expanded

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An unprecedented outbreak of the Ebola virus in 2014 claimed more than 1000 lives in West Africa and the World Health Organization declared a global public health emergency. This outbreak will undoubtedly promote additional research related to the Ebola virus and will create debate related to experimental drugs. This article identified the quantum of research in the field since 1991; the scientific disciplines that contributed to the field; the countries, organisations and authors that supported such research and the most cited articles. An increasing trend in annual production during 1991–2013 was observed. *Journal of Virology*, *Journal of Infectious Diseases*, and *Virology* were the three most productive journals in the field. Similarly, the field of virology dominated the 73 categories in which the Ebola research was classified. A total of 63 countries contributed to Ebola-related research, led by the USA. The most productive institutions were the United States Army Medical Research Institute of Infectious Diseases, the Centers for Disease Control and Prevention, and the National Institute of Allergy and Infectious Diseases. African countries were more likely to be involved in international collaboration than independent research. The most influential article exhibited a notable citation pattern and presented global trends in emerging infectious diseases.

Introduction

The worst Ebola outbreak in recorded history claimed more than 1000 victims[1] by 20 August 2014. It affected West Africa and Nigeria directly, but fears of its spreading affected the rest of the World. The World Health Organization called an international public health emergency and launched a USD 100 million response plan.[2]

The 2014 Ebola outbreak was first diagnosed in the remote southeastern area of Nzerekore in Guinea in February 2014, but subsequently spread to neighbouring Liberia, Sierra Leone and Nigeria.[3]

Ebola's origin is not known, but it is suspected that it is transmitted through forest bats. It can be transmitted between humans by touching sufferers or through body fluids.[4] The isolation of the aetiologic agent of Ebola haemorrhagic fever was reported for the first time during 1977.[5] According to the US Centers for Disease Control and Prevention,[4] since 1976 there have been 34 known outbreaks of Ebola. Before the latest outbreak, the deadliest episode was the first recorded outbreak in 1976 which killed 280 people in Central Africa.[4]

Apart from the mobilisation efforts to contain the virus and develop a relevant vaccine, the issue raised a number of ethical questions, as an experimental drug was used for two US health workers and not for African patients.[1]

The objective of this article is to report the results of an investigation aimed at mapping the research efforts related to Ebola virus internationally using scientometric techniques. These assessments are increasingly used as the basis for monitoring research performance of particular scientific disciplines and the support of appropriate policy actions. More specifically, the purpose of the study was to identify the state of Ebola virus research internationally and plot trends over time, to identify the institutions which undertake Ebola virus research and to pinpoint the scientific specialities which are emphasised in the field. The results of the investigation could possibly constitute benchmarks for monitoring the evolution of the research in this field and the impact of the outbreak on research efforts internationally.

Methodology

Following international best practice, we used evaluative scientometrics for the objectives of this investigation. Scientometrics is a tool by which the state of science and technology can be observed through the overall production of scientific literature at a given level of specialisation. Scientometric approaches have been used to map HIV/AIDS research[6,7], malaria research[8], and immunology[9].

Research articles indexed in the Science Citation Index Expanded (Sci-Expanded), a multidisciplinary database of the Thomson Reuters Web of Science, were identified for the objectives of this analysis (updated on 2014 August 05). The databases cover the most important international journals and the indices include the names and addresses of all co-authors, hence comprehensive coverage can be achieved. The keywords 'Ebola', 'Ebolas', and 'ebolavirus' were searched in the domain of topic (i.e. title, abstract, author keywords, and KeyWords Plus). KeyWords Plus provides search terms extracted from the titles of articles cited in Current Contents.[10] In order to ensure more exact information, another filter used was the 'front page'[11] approach. Only articles with the search keywords on their front page, including article title, abstract, and author keywords, were considered in this study and the time period examined was 1991–2013. The records were downloaded into a spreadsheet and were analysed using Microsoft Excel 2007. In the Sci-Expanded database, the corresponding author is designated as the 'reprint author'. In this study, the term 'corresponding author'[12] was used. The authors' corporate addresses determined the nationality of the article.

To investigate the citations received by the various articles, we estimated the number of times a paper was cited from Web of Science Core Collection. Total citations for a paper from its publication date to the end of a year, were recorded as $TC_{year.}$[13] Affiliations in England, Scotland, Northern Ireland, and Wales were reclassified as being from

the United Kingdom (UK). Affiliations in Hong Kong before 1997 and Macao before 1999 were included with China, while affiliations in USSR were amended to Russia.

Results and Discussion

Document type and language of publication

During the period under examination, 1623 documents from 12 document types were indexed. Of these documents, 70% were research articles, 10% reviews, 7.8% news items, 4.7% meeting abstracts, 4.5% editorial material, 3.9% proceedings papers, 1.6% letters, 0.62% corrections, 0.49% notes, 0.43% reprints, 0.12% book chapters and 0.062% biographical-items. The percentage of articles related to Ebola was lower than general medically-related fields, such as asthma in children[14] and Japanese lung cancer research[15], but was much higher than special infection research of severe acute respiratory syndrome[16] and *Helicobacter pylori*[17]. It was also noticeable that the document type, 'news items', took the third position. A high percentage of news items could also be found in severe acute respiratory syndrome (SARS) research[16], which was studied after its outbreak in 2003[18].

The 1133 articles were analysed more thoroughly and revealed that the majority (96%) were in English. The second most popular language was Russian with 2.2%, followed by French (11 articles), German (three articles) and Spanish (one article).

Figure 1 shows the number of relevant articles and citations per article for the period 1991–2013. The number of publications exhibited an increasing trend, albeit starting from a small base. During the recent years, there were approximately 100 articles produced per year. It is interesting to note that HIV/AIDS (another African disease) attracted more than 7000 articles per year.[7] It should however be emphasised that HIV/AIDS affects millions of people[7], while Ebola affected a few thousand patients for first time in the recorded history.

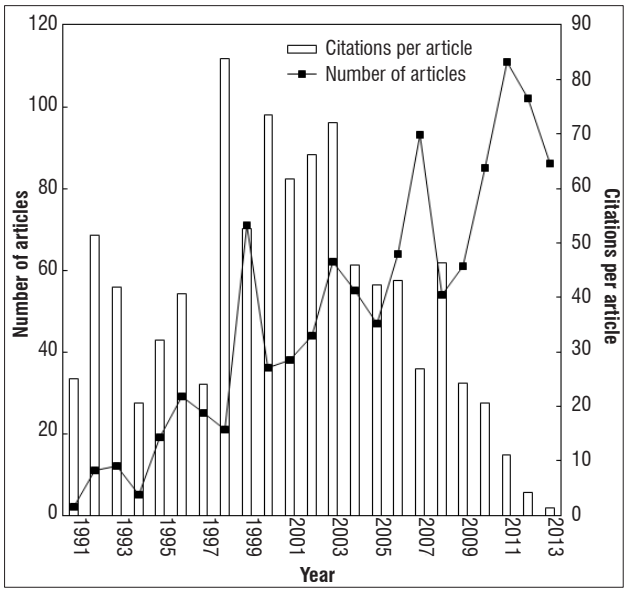


Figure 1: Ebola related research publications and citations per article 1991–2013.

Web of Science categories and journals

Distribution of Web of Science categories and journals have been studied in research topics.[19] In 2013, the Journal Citation Reports (JCR) indexed 8474 journals with citation references across 175 scientific disciplines in the science edition. The articles on Ebola were published in journals listed in 73 Web of Science categories in the science edition. During the period of the study, five categories published more than 100 articles, with the category virology contributing the most with 426 articles (38% of 1132 articles), followed by immunology (226 articles; 20%), microbiology (218; 19%), infectious diseases (203; 18%), and biochemistry and molecular biology (107; 9.5%). In 1999, 2007, and 2011, there were citation peaks in the categories immunology, microbiology and infectious diseases (Figure 2).

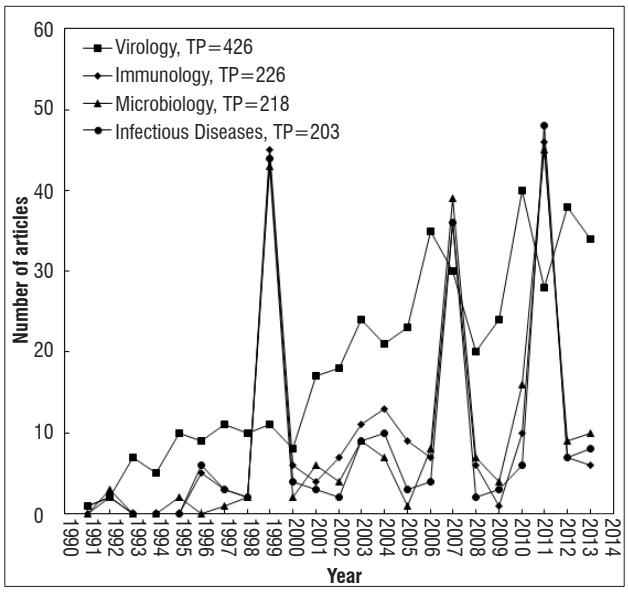


Figure 2: The number of articles in the five most productive Web of Science categories from 1991 to 2013.

The citation peak in 1999 could be because of the article 'Clinical virology of Ebola hemorrhagic fever (EHF): Virus, virus antigen, and IgG and IgM antibody findings among EHF patients in Kikwit, Democratic Republic of the Congo, 1995'[20] with TC_{2013}=119 in immunology and infectious diseases. The citation peak in 2007 could be attributed to the article 'The Ebola virus VP35 protein is a suppressor of RNA silencing'[21] with TC_{2013}=141 the category of microbiology.

The Ebola set of articles was further analysed according to the journals in which they were published. In total, 1133 articles were published in a range of 282 journals. According to Bradford's Law of Scattering[22], the journals were sorted in descending order in terms of number of articles, and then divided into three 'zones'. Zone 1 represented the most productive one-third of the total articles, with three (1.1%) of 282 journals. Zone 2 represented the next most productive one-third of total articles, with 28 (9.9%) of 282 journals (9.9%), and Zone 3 represented the least productive one-third of total articles with 251 (89%) of 282 journals. The three most productive core journals were *Journal of Virology,* which published the most proteome articles (172; 15% of 1133 articles), followed by *Journal of Infectious Diseases* (126; 11%), and *Virology* (71; 6.3%). In addition, regarding journal impact factor (IF), *Nature* gained first place with the highest IF_{2013} (42.351) with seven articles, followed by *Cell* (IF_{2013}=33.116) with two articles, *Science* (IF_{2013}=31.477) with eight articles, *Nature Medicine* (IF_{2013}=28.054) with 7 articles, and one article each for *Nature Immunology* (IF_{2013}=24.973) and *Nature Reviews Microbiology* (IF_{2013}=23.317).

Publications of country and institution

Excluding 11 articles without affiliation information of authors in Web of Science, there were 1122 articles with author information. Of these 1122 articles, 705 (63%) were single country articles and 417 (37%) were internationally collaborative articles. The top 10 countries, taking 93%, are listed in Table 1 under six indicators: total number of articles, single country articles, internationally collaborative articles, first author articles, corresponding author articles, and single author articles.[23] Of the articles ranked in the list of top 10 publications, 2 were from American countries, 5 were from European countries, 2 were Asian and 1 was from an African country, Gabon. Except for Italy, the Group of Eight (G8) (France, Germany, Italy, Japan, the UK, the USA, Canada, and Russia) were ranked in the top 7. This is no coincidence, as the earliest Ebola research took place in these industrialised countries

(e.g. 'A case of Ebola virus-infection'[24] and 'Ebola virus: Comparison, at ultrastructural level, of the behaviour of the Sudan and Zaire strains in monkeys').[25]

Table 1: Ebola virus research: Country of publication

Country	TP	TPR (%)	IPR (%)	CPR (%)	FPR (%)	RPR (%)	SPR (%)
USA	772	1 (68)	1 (67)	1 (71)	1 (57)	1 (57)	1 (53)
Germany	154	2 (14)	3 (4.9)	2 (29)	2 (6.9)	2 (6.8)	4 (3.9)
Canada	112	3 (9.9)	4 (3.4)	3 (21)	5 (4.2)	5 (4.1)	N/A
France	104	4 (9.2)	5 (3.0)	5 (20)	3 (4.8)	3 (4.9)	4 (3.9)
Japan	96	5 (8.5)	9 (1.1)	3 (21)	4 (4.7)	4 (4.6)	8 (2.0)
UK	60	6 (5.3)	6 (2.3)	6 (11)	7 (2.3)	7 (2.2)	2 (7.8)
Russia	53	7 (4.7)	2 (5.8)	18 (2.9)	6 (3.8)	6 (3.8)	N/A
Gabon	42	8 (3.7)	15 (0.42)	7 (9.4)	7 (2.3)	7 (2.2)	N/A
Belgium	40	9 (3.5)	10 (1.0)	8 (7.9)	9 (1.8)	9 (1.8)	4 (3.9)
Spain	29	10 (2.6)	7 (1.8)	14 (3.8)	10 (1.5)	10 (1.6)	8 (2.0)

TP, total articles; TPR (%), rank and the percentage of total articles; IPR (%), rank and the percentage of independent articles; CPR (%), rank and the percentage of internationally collaborative articles; FPR (%), rank and the percentage of first author articles; RPR (%), rank and the percentage of the corresponding authored articles; SPR (%), rank and the percentage of single author articles; N/A, not available.

The USA dominated the table producing 68% of the articles during the period. It ranked top in all six indicators and was followed distantly by other countries. The USA had the most-frequent partners, accounting for 71% of all the internationally collaborative articles. Gabon was ranked in 8th position but had no single author articles. A number of African countries appeared to produce Ebola related publications including Uganda (25 articles), Congo (21), Zaire (18), South Africa (18), Central African Republic (7), Cote Ivoire (7), Cameroon (6), Zambia (6), Kenya (4), Ghana (3), Sierra Leone (2), Tanzania (2), Zimbabwe (2), and 1 article each from Angola, Burkina Faso, Egypt, Guinea, Rwanda, Senegal and Sudan.

The contribution of different institutions was estimated by their affiliation to at least 1 author of the Ebola articles. Of the 1122 Ebola articles analysed, 327 (29% of 1122 articles) were single institution publications and 795 (71%) were inter-institutionally collaborative publications. The top 10 institutions were ranked according to their number of articles. This included the number of single institution articles and inter-institutionally collaborative articles; first author articles; and single author articles (Table 2). Out of the top 11 most productive institutions, seven were affiliated to the USA, two were from Canada, and one each from Germany and Japan, respectively. The United States Army Medical Research Institute of Infectious Diseases in the USA was the most productive institution, followed by Centers for Disease Control and Prevention and National Institute of Allergy and Infectious Diseases (NIAID) in the USA. Centers for Disease Control and Prevention and National Institute of Allergy published the most single author articles. The top 10 productive institutions in Africa were Centre International de Recherches Médicales de Franceville in Gabon (32 articles), Uganda Virus Research Institute in Uganda (13), Ministry of Health in Uganda (8), Ministry of Health in the Democratic Republic of Congo (6), National Institute for Virology in South Africa (6), National Institute for Communicable Diseases in South Africa (6), University of Zambia in Zambia (6), Institut de Recherche pour le Développement in Gabon (5), Kikwit General Hospital in Congo (5), and Institut Pasteur in Central African Republic (5).

Table 2: Prolific institutions in Ebola research

Institution	TP	CPR (%)	FPR (%)	SPR (%)
United States Army Medical Research Institute of Infectious Diseases, USA	181	1 (11)	1 (7.4)	6 (2.0)
Centers for Disease Control and Prevention, USA	126	3 (6.3)	3 (5.0)	1 (7.8)
National Institute of Allergy and Infectious Diseases (NIAID), USA	106	5 (3.6)	2 (5.2)	3 (3.9)
University of Marburg, Germany	85	4 (4.2)	5 (2.4)	N/A
University of Manitoba, Canada	73	N/A	55 (0.27)	N/A
Public Health Agency of Canada, Canada	72	18 (0.60)	6 (2.1)	N/A
University of Tokyo, Japan	68	44 (0.30)	7 (2.0)	N/A
University of Wisconsin, USA	56	N/A	9 (1.8)	N/A
University of Pennsylvania, USA	51	2 (7.2)	4 (3.3)	6 (2.0)
Harvard University, USA	33	44 (0.30)	19 (0.71)	6 (2.0)
Scripps Research Institute, USA	33	7 (1.8)	9 (1.8)	6 (2.0)

TP, total articles; CPR (%), rank and the percentage of inter-institutionally collaborative articles; FPR (%), rank and the percentage of first author articles; SPR (%), rank and the percentage of single author articles; N/A not available.

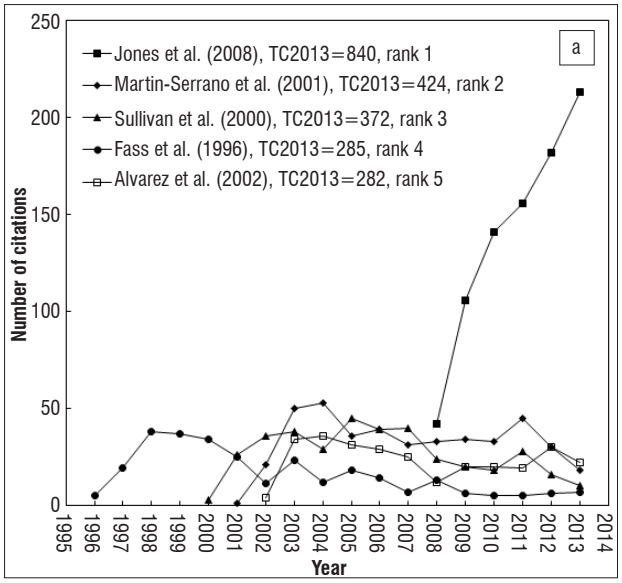
Highly cited articles

The total number of times an article was cited from Web of Science Core Collection since its publication to the end of 2013 (TC_{2013}) was estimated.[13] TC_{2013}, an accumulative number, could reach a large value as long as the time span is long enough. The citation lives of the top 10 articles ($TC_{2013}>250$) are shown in Figure 3. The only 1 article that kept a sharply increasing citation trend after its publication was 'Global trends in emerging infectious diseases'[26] published in by 7 authors from Wildlife Trust in China, Zoological Society of London in the UK, Columbia University in the USA, and University of Georgia in the USA. In this article, 335 emerging infectious diseases (EID) events were analysed and the authors demonstrated non-random global patterns between 1940 and 2004. A conclusion was that EID events are dominated by zoonoses (60.3% of EIDs), with the majority of these (71.8%) originating in wildlife (for example, severe acute respiratory virus, Ebola virus), and increasing significantly over time. Global trends in emerging infectious diseases'[26] not only discussed Ebola but also other emerging infectious diseases. Table 3 presents the top 21 articles cited more than 200 times ($TC_{2013}>200$). Out of these 21 articles, eight (38% of 21 articles) were published in the 1990s and 13 (62%) in the 2000s. The first article, which was cited more than 200 times, was published in 1996. The latest one was published in 2008. The journals in which these articles were published were *Proceedings of the National Academy of Sciences of the United States of America* ($IF_{2013}=9.809$) with six articles, followed by *Nature* (four articles; $IF_{2013}=42.351$), *Nature Medicine* (two articles; $IF_{2013}=28.054$), *Journal of Virology* (two articles; $IF_{2013}=4.648$), and one for each of *Bulletin of the World Health Organization* ($IF_{2013}=5.112$), *Journal of Clinical Microbiology* ($IF_{2013}=4.232$), *Journal of Experimental Medicine* ($IF_{2013}=13.912$), *Molecular Cell* ($IF_{2013}=14.464$), *Molecular Membrane Biology* ($IF_{2013}=1.729$), *Nature Structural Biology* ($IF_{2013}=11.579$), and *Science* ($IF_{2013}=31.477$), respectively. *Nature Structural Biology* was not listed in Sci-Expanded after 2003. In 1998 and 1999, Weissenhorn from European Molecular Biology Laboratory in France published 2 highly cited papers as first author: 'Crystal structure of the Ebola virus membrane fusion subunit, GP2, from the envelope glycoprotein ectodomain'[27] with $TC_{2013}=254$ and 'Structural basis for membrane fusion by enveloped viruses'[28] with $TC_{2013}=256$. In 2000 and 2003, both Sullivan from National Institutes of Health in the USA and Basler from Mount Sinai School of Medicine in the USA also published 2 highly cited papers as first authors.

Table 3: Top 21 most cited articles (TC_{2013}>200)

Rank	TC_{2013}	Reference
1	840	Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, Daszak P. Global trends in emerging infectious diseases. Nature. 2008;451(7181):990–993.
2	424	Martin-Serrano J, Zang T, Bieniasz PD, HIV-I and Ebola virus encode small peptide motifs that recruit Tsg101 to sites of particle assembly to facilitate egress. Nat Med. 2001;7(12):1313–1319.
3	372	Sullivan NJ, Sanchez A, Rollin PE, Yang Z, Nabel GJ. Development of a preventive vaccine for Ebola virus infection in primates. Nature. 2000; 408(6812):605–609.
4	285	Fass D, Harrison, SC, Kim PS. Retrovirus envelope domain at 1.7 angstrom resolution. Nat Struct Biol. 1996;3(5):465–469.
5	282	Alvarez CP, Lasala F, Carrillo J, Muniz O, Corbi AL, Delgado R. C-type lectins DC-SIGN and L-SIGN mediate cellular entry by Ebola virus in cis and in trans. J Virol. 2002;76(13):6841–6844.
6	275	Simonsen L, Kane A, Lloyd J, Zaffran M, Kane M. Unsafe injections in the developing world and transmission of bloodborne pathogens: A review. B World Health Organ. 1999;77(10):789–800.
7	262	Chandran K, Sullivan NJ, Felbor U, Whelan SP, Cunningham JM. Endosomal proteolysis of the Ebola virus glycoprotein is necessary for infection. Science, 2005;308(5728):1643–1645.
8	261	Takada A, Robison C, Goto H, Sanchez A, Murti KG, Whitt MA. Kawaoka YA system for functional analysis of Ebola virus glycoprotein. P Nat Acad Sci USA. 1997;94(26):14764–14769.
9	256	Weissenhorn W, Dessen A, Calder LJ, Harrison SC, Skehel JJ, Wiley DC. Structural basis for membrane fusion by enveloped viruses. Mol Memb Biol. 1999;16(1):3–9.
10	254	Weissenhorn W, Carfi A, Lee KH, Skehel JJ, Wiley DC. Crystal structure of the Ebola virus membrane fusion subunit, GP2, from the envelope glycoprotein ectodomain. Mol Cell. 1998;2(5):605–616.
11	248	Bavari S, Bosio CM, Wiegand E, Ruthel G, Will AB, Geisbert TW, et al. Lipid raft microdomains: A gateway for compartmentalized trafficking of Ebola and Marburg viruses. J Exp Med. 2002;195(5):593–602.
12	244	Sanchez A, Trappier SG, Mahy BWJ, Peters CJ, Nichol ST. The virion glycoproteins of Ebola viruses are encoded in two reading frames and are expressed through transcriptional editing. P Nat Acad Sci USA. 1996;93(8):3602–3607.
13	241	Sullivan NJ, Geisbert W, Geisbert JB, Xu L, Yang ZY, Roederer, et al. Accelerated vaccination for Ebola virus haemorrhagic fever in non-human primates. Nature. 2003;424(6949):681–684.
14	240	Basler CF, Wang XY, Muhlberger E, Volchkov V, Paragas J, Klenk HD. The Ebola virus VP35 protein functions as a type IIFN antagonist. P Nat Acad Sci USA. 2000;97(22):12289–12294.
15	233	Harty RN, Brown ME, Wang G, Huibregtse J, Hayes FP. A PPxY motif within the VP40 protein of Ebola virus interacts physically and functionally with a ubiquitin ligase: Implications for filovirus budding. P Nat Acad Sci USA. 2000;97(25):13871–13876.
16	219	Baize S, Leroy EM, Georges-Courbot MC, Capron M, Lansoud-Soukate J, Debre P. Defective humoral responses and extensive intravascular apoptosis are associated with fatal outcome in Ebola virus-infected patients. Nat Med. 1999;5(4):423–426.
17	214	Strack B, Calistri A, Accola MA, Palu G, Gottlinger HG. A role for ubiquitin ligase recruitment in retrovirus release. P Nat Acad Sci USA. 2000;97(24):13063–13068.
18	212	Drosten C, Gottig S, Schilling S, Asper M, Panning M, Schmitz H, et al. Rapid detection and quantification of RNA of Ebola and Marburg viruses, Lassa virus, Crimean-Congo hemorrhagic fever virus, Rift Valley fever virus, Dengue virus, and Yellow fever virus by real-time reverse transcription-PCR. J Clin Microbiol. 2002;40(7):2323–2330.
18	212	Volchkov VE, Feldmann H, Volchkova VA, Klenk HD. Processing of the Ebola virus glycoprotein by the proprotein convertase furin. P Nat Acad Sci USA. 1998;95(10):5762–5767.
20	210	Walsh PD, Abernethy KA, Bermejo M, Beyersk R, De Wachter P, Akou ME, et al. Catastrophic ape decline in western equatorial Africa. Nature. 2003;422(6932):611–614.
21	209	Basler CF, Mikulasova A, Martinez-Sobrido L, Paragas J, Muhlberger E, Bray M, et al. The Ebola virus VP35 protein inhibits activation of interferon regulatory factor 3. J Virol. 2003;77(14):7945–7956.

TC_{2013}, total number of times the article was cited from Web of Science Core Collection since its publication to the end of 2013.



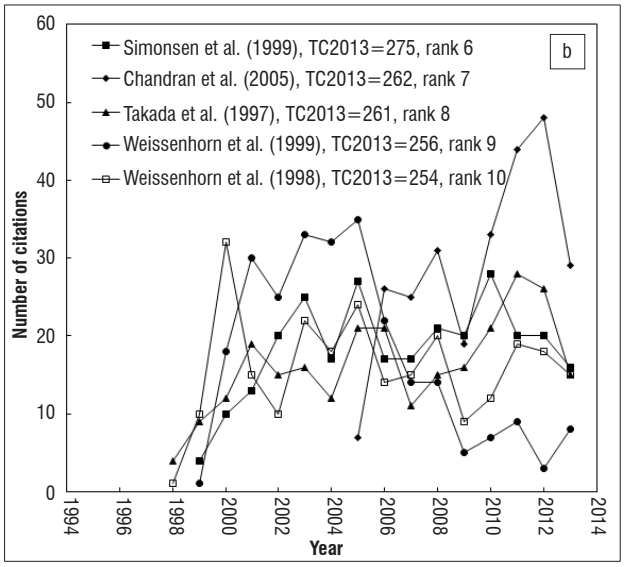


Figure 3: (a) The life of the top 5 most cited articles (TC_{2013}>280) and (b) the top 6–10 most cited articles (280 > TC_{2013} > 250).

Conclusions

This article provided for the first time an overview of research related to Ebola virus undertaken internationally and identified that there has been limited international research. The Ebola virus-related articles showed an increasing trend during 1991–2013. Virology was the most dominant discipline in the domain, and *Journal of Virology*, *Journal of Infectious Diseases*, and *Virology* were the most favoured journals. Industrialised countries contributed to more than 70% of the articles, while a number of African countries played an important role in international collaboration. The United States Army Medical Research Institute of Infectious Diseases, the Centers for Disease Control and Prevention, and the National Institute of Allergy and Infectious Diseases were the most prolific institutions researching the topic. The top 3 most cited articles in the field were published in *Nature*. The most cited article with a distinguished citation pattern included hundreds of emerging infectious diseases events and non-random global patterns from 1940–2004.

The Ebola crisis has raised a number of issues that are subject to further research. How can the authorities decide on the resources to be spent on various diseases and related prevention activities? A controversy about drug testing in Africa and who should benefit for limited experimental drugs are also complexities facing public health authorities internationally outside the critical issue of how to control the disease and prevent its spreading to other countries. Similarly, it will be interesting to identify how the outbreak will affect research activities in the field in the foreseeable future.

Authors' contributions

The authors made equal contributions to this article.

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