

Evolution of Interdisciplinary Landscapes of HIV/AIDS Studies from 1983 to 2017: Results from the Global Analysis for Policy in Research (GAP_{RESEARCH})

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Abstract

In recent years, there have been numerous calls by researchers to adopt multi-disciplinary and international perspectives to address the HIV pandemic. Meaningful and prudent public health policy should be based on sound empirical data and research. Henceforth, our study aims to contribute to the current literature by conducting a comprehensive global mapping and determine the landscapes of HIV/AIDS research covering the years between 1983 and 2017. Bibliometric and content analysis was used to describe trends in research productivity, usages, research collaborations, and clusters of research topics. Exploratory factor analysis, Jaccard's similarity index, and Ward dendrogram were applied to abstracts' contents to determine the development of interdisciplinary research landscapes. The United States of America continues to lead in research production and be main hub for author- and country-level collaborations. Research employing an epidemiological, social, and/or behavioral perspective for studying HIV/AIDS was found to dwarf in the presence of basic and biomedical HIV research. Interdisciplinary approaches to HIV research have been increasing with the creation of various research landscapes: strong constructs of studies examining health status, clinical responses, and HIV treatment, risk behaviors have been formed, while research topics relating to psycho-behavioral and cultural aspects as well as services have emerged along. To effectively prevent and control the disease, more researches are needed to provide culturally relevant and/or contextualized evidence of effective inter-

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ventions. It is also necessary to enhance the ability and partnership of local researchers as well as invest in research infrastructure at national and regional levels to implement high-quality studies since they are the “gate-keepers” who could respond to local changes in a timely manner. These types of research could be a helpful guide for international donors, governments, and academicians to set up research priorities in target groups and settings, and to develop future research agendas globally.

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Key words

Scientometrics. HIV. AIDS. Global. Interdisciplinary. Policy.

Introduction

Since first case identification in literature in 1981^{1,2}, HIV/AIDS has become a global pandemic, continuing to exert heavy health burden worldwide². According to UNAIDS, as at 2017, there were approximately 36.9 million people living with HIV globally, with an estimated total of 77.3 million HIV-infected people since the beginning of the epidemic³. AIDS-related mortality in the year 2017 only was estimated to be about 940 thousand people³. Initially an epidemic of developed regions, HIV/AIDS has since been found throughout the world, disproportionately affected less developed areas⁴. It is most concentrated in South and East Africa with rates of 6.8% of adults living with HIV/AIDS in 2017⁵.

Over the past three decades, research has shed light on the many challenges – at times seem insurmountable and intractable – in tackling this pandemic. The challenges include but not limited to geographical, cultural, and economic characteristics of affected regions, which could exert influences on how the epidemic presents itself, including its prevalence, severity, accessibility, and adherence to treatment and associated factors⁴. Moreover, the social impacts of HIV/AIDS have also been documented to be complex and diverse, including issues such as stigma, discrimination, and barriers to treatment due to poverty, all of which would potentially hinder the effectiveness of treatment and prevention efforts⁶. There have been numerous calls by HIV/AIDS and health researchers to adopt multi-disciplinary and international perspectives to address this disease which does not have and respect geographical boundaries⁶.

Ample financial investment has supported research aimed at understanding HIV/AIDS and discovering effective approaches to treatment and prevention – over

US\$108.8 billion has been spent on these efforts between 2000 and 2015⁷. Such investments have played a key role in facilitating the introduction and continuing success of antiretroviral therapy (ART) and, subsequently the prevention of transmission from mother to child², which have supported, among others, the significant reduction of annual AIDS-related fatality (from 1.5 million in 2000 to 940 thousand in 2017) and new HIV infections (2.8 million in 2000 to 1.8 million in 2017)³. These achievements in terms of HIV/AIDS response have led to the ambitious goal of eliminating HIV in 2030⁸. Nonetheless, a recent study conducted by the Global Burden of Disease on development assistance for health has cautioned of a slow-down in the growth rate of funding for HIV/AIDS, both from national governments and international funds since 2010⁹. This decrease in financial investment would likely to adversely hinder progress in reaching the 2030 elimination goal.

Meaningful and prudent public health policy should be based on sound empirical data and research^{10,11}. In the context of increasing constraint in financial assistance for HIV/AIDS response, understanding the development of HIV/AIDS research, identifying trends, and potential gaps may be of great help in assisting the translation into effective policies and practices. To the best of our knowledge, there are few studies that document the existence of research on HIV/AIDS across cultures and nationalities. One study published in 2006 documented a lack of publications from developing countries, along with limited international collaborations⁴. Henceforth, our study aims to contribute to current literature by conducting a comprehensive global mapping of HIV/AIDS research covering the years between 1983 and 2017. Using a scientometric approach, we strive to elucidate research trends and potential research gaps which could inform evidence-based strategies for policies and prac-

tice enhancements as well as for further research endeavors.

Methods

Search strategy

We choose the web of science (WOS) as the online database to design a cross-sectional study for HIV/AIDS bibliography analyzing. WOS was chosen because it covers (i) more research fields compared with PubMed, and (ii) research dated from 1900 to the present¹². A combination of the keywords, namely: HIV and AIDS was employed to build our search query. We only included English-language research articles and research reviews published between 1983 and 2017. Although HIV was observed in 1981, we chose the year of 1983 due to the lag time in publications.

Data extraction

All articles found through the search process were sorted by the citation frequency before data downloading process. In addition to article-specific data, we also downloaded the automatically-generated citation reports provided by the WOS. Downloaded data were converted to XLSM form (Microsoft Excel) for data checking error. Two researchers then engaged in a standardization process to reconcile author names (different typing of an author name, for instance, "De Clercq E" or "Declercq E") as well as institution names (for example, Katholieke Universiteit Leuven and Catholic University of Leuven are one university in Belgium). After that, we filtered these obtained data by dropping-out the papers which are: (1) not original articles and reviews, (2) not HIV/AIDS-related, and (3) not in English. Due to the huge number of records related to this topic, four researchers were involved and worked collaboratively on data filtering. Then, two research teams worked independently to make sure that the results matched. One research team excluded 120,187 papers based on the document type that has been shown by the WOS, the title and keywords of the papers. The other team applied the same process to verify the results. Any conflict was solved by discussion (Fig. 1).

Data extracted from each publication included: name(s) of the author(s); the title of the paper, the name of the journal, keywords, institutional affiliation(s), frequency of citation, subject category, and abstract.

Data analysis

Data were analyzed through a sequence of methods. First, descriptive statistics including the basic characteristics of the article (authors, year of publication, and research category), keywords (most common and cooccurrence), most prolific authors (having from 500 papers), countries with substantial numbers of publications (over 1000 papers), high impact journals, as well as influencing papers (being cited exceeding 1500 times) were conducted. After downloading and extracting the data, we applied Macro; a programming code run on Excel environment to calculate a country citation, and intra and inter-country collaboration. Connections among countries were presented by network graph which was created using the specific threshold of 230 papers for each collaboration – chosen after a number of trials to best reflecting the collaboration while maintaining the visual ease (Fig. 2). The author keyword cooccurrence network and countries network were also created. We utilized the free version of VOS-viewer software (version 1.6.8, Center for Science and Technology, Leiden University, the Netherlands), to create the networks of cooccurrence and countries.

We applied exploratory factor analysis to identify research domains emerging from all contents of the abstracts; loadings of 0.4. Jaccard's similarity index was utilized to identify research topics or terms most frequently cooccurring with each other. It was defined as the size of the intersection divided by the size of the union of two sets of cooccurring terms. Proximity values of all included keywords were computed by employing multidimensional scaling and presented graphically. In the map, each topic category was presented by a point, and the likelihood of these items appearing together was represented by the distance between each pair of items. Different colors represent membership of specific items to different partitions which were created by applying hierarchical clustering. Stata software was used for statistical analyses.

Ethics

Not applicable.

Results

Publication volumes and trend

Figure 1 illustrates the process of selecting papers. After excluding non-research article and review, our

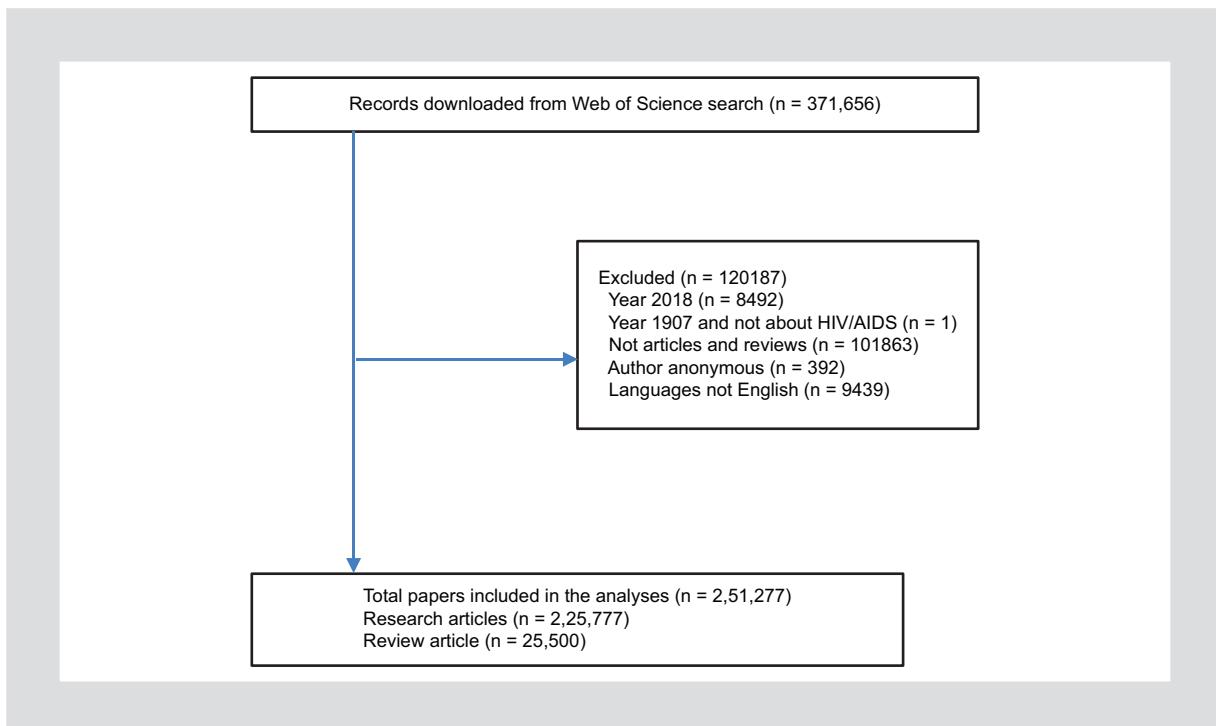


Figure 1. Selection of papers.

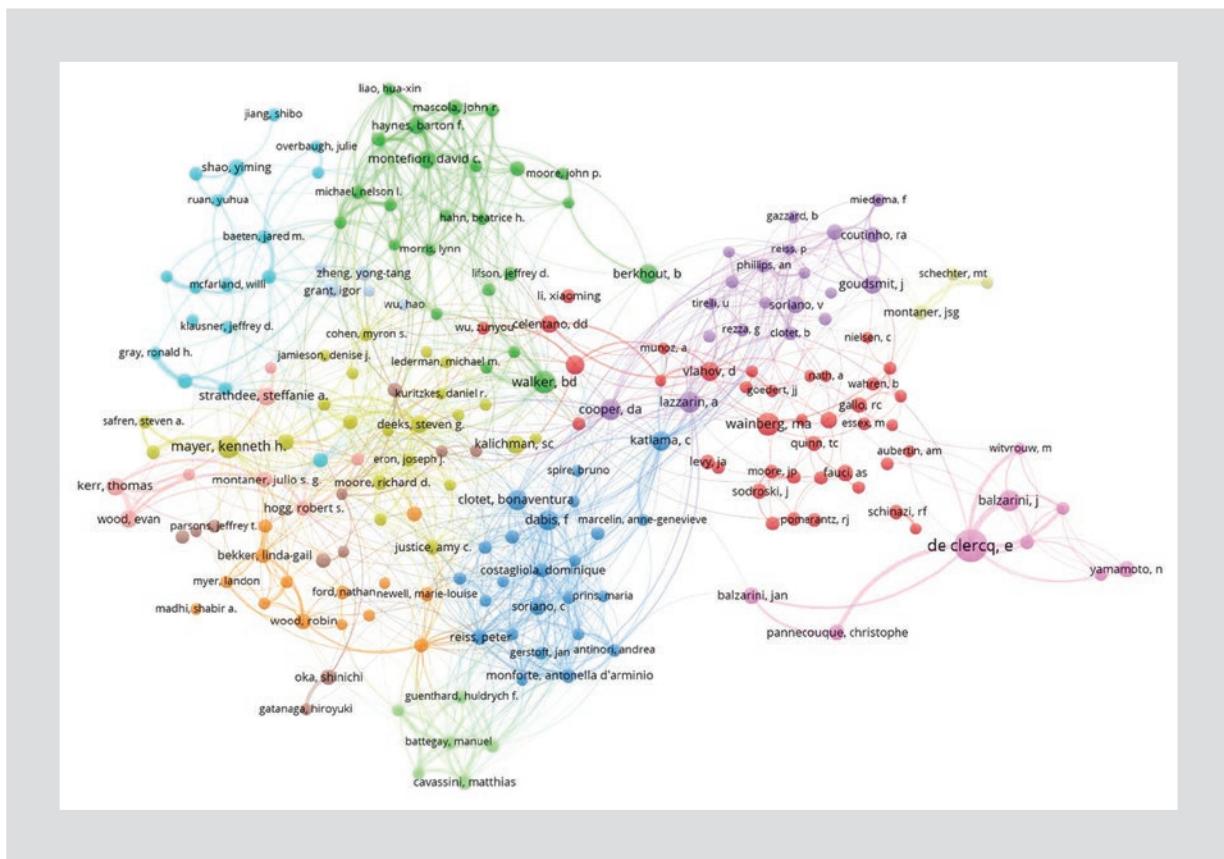


Figure 2. Most productive authors.

analysis covered a total of 251,277 research papers (of which 225,777 were articles and 25,500 were reviews).

Supplementary table 1 presents the exponential growth of HIV/AIDS research. WOS shows a growth trend over the study period, especially over 14,000 papers were published annually in the past 5 years. The number of publications has increased gradually since 1991 and 56% of papers were published in 2008-2017, accounting for over 60% citations. There were 8594 journals publishing papers on HIV/AIDS. Of those 2347 (23.7%) journals published one paper, 1091 (12.7%) journals published two, 720 (8.38%) journals published three, and 4436 (55.22%) journals published at least four papers during the whole study period. Two journals that published the highest number of papers were AIDS ($n = 7759$; 3.1%) and Journal of Virology ($n = 7513$; 3%), followed by PLOS ONE ($n = 6738$; 2.7%), AIDS Research and Human Retroviruses ($n = 4,786$; 1.9%), and Journal of AIDS ($n = 3853$; 1.5%). Most of the papers were assorted into one ($n = 138,348$; 55%) or two ($n = 69,000$; 27.4%) subject categories of the journals. The two major subject categories were infectious diseases ($n = 52,680$; 20.9%) and immunology ($n = 46,095$; 18.3%).

Table 1 shows the detailed list of the most productive journals (published over 1000 papers) along with the rate of citations per paper. AIDS published the most papers, yet Journal of Virology ranked first in the number of citations with 390,626 citations for 7515 papers. The highest number of citations per paper belonged to retrovirology with 62.1 citations per paper. Among 32 journal, 15 journals are about HIV, AIDS, immunology, sexually transmitted diseases (STDs), and infectious diseases; four are about virology; one about HIV treatment; one about HIV prevention; and ten journals addressing multi-categories.

Most productive authors and established research areas

Figure 2 shows the most productive authors (those with at least 300 papers published during our study period) and their networks. The United States housed some of the most prolific ones with 14 top contributors. However, Erik De Clercq from the Rega Institute for Medical Research, Katholieke Universiteit Leuven (KU University), Belgium led in both the number of published papers (933 publications) and the number of citations (52,888). Jun Wang from Anhui Medical University, The Third People's Hospital of Hangzhou, Hangzhou Clinical

Institute (the People's Republic of China) was the most productive Asian author with 328 papers.

Figure 3 illustrates the global network between countries with 230 and above papers in coauthorship. The size of nodes reflects the proportional contribution of each country to the total number of papers while the thickness of lines represents the percentage of the number of collaborations.

Table 2 presents the top 40 of 153 research areas related to HIV/AIDS studies, accounting for over 90% of total paper-classifications. Infectious diseases (20.9%), immunology (18.3%), and virology (14%) were three main subject categories. Most of the papers were assorted into one ($n = 138,348$; 55%) or two ($n = 69,000$; 27.4%) subject categories of the journals. While analyzing the number of categories that a paper listed, we found a significant trend of multidisciplinary research, increasing from 20-30% in 1990s to 40-50% in the recent decade.

Supplementary figure 1 presents the groups of research areas in coincidence analysis. Using principal components analysis, the research areas have been structured into five multidisciplinary categories, including: (1) clinical medicine, (2) biomedical technology, (3) mathematics and informatics, (4) management sciences, and (5) social sciences. The coincidence of major individual research areas is also illustrated in figure 4. Noticeably, there have been some interesting connections between research areas, for example, (i) psychology and respiratory systems, and (ii) social sciences, education, nursing, and science, and technology.

Supplementary figure 2 is a pictorial representation of the keyword cooccurrence which illustrates the probability of appearance on WOS search results of a particular word. As it can be seen from the figure, "HIV," "HIV/AIDS," "AIDS," and "HIV-1" were four common nomenclatures, followed by "ART" and "epidemiology." The thickness of a line indicates the strength in relation of one given keyword with another, for instance, the strong association of "HIV" to "ART," "AIDS" or "HAART." "HIV-1" was a particularly prominent keyword, reflecting the general concerns regarding HIV-1 resistance with drug or inflammation in HIV infection. From supplementary figure 2, we could also identify the main groups including (1) location: India, Vietnam, Brazil, Africa, South Africa, Africa, and China; (2) Subject study: women, children, adolescents, men who have sex with men (MSM) and pregnancy; (3) certain opportunistic infections: hepatitis C, hepatitis B, tuberculosis; (4) risk factors: pregnancy, MSM, sex work, and injection drug use, sexually transmitted in-

Table 1. The most productive journals

No	Journal	Number	Percent	Number of citations	Citation per paper
1	AIDS	7757	3.08	269858	34.8
2	Journal of virology	7515	2.99	390626	52.0
3	PLOS ONE	6738	2.68	294855	43.8
4	AIDS research and human retroviruses	4785	1.90	163262	34.1
5	Journal of AIDS	3853	1.53	136865	35.5
6	AIDS care-psychological and socio-medical aspects of AIDS/HIV	3280	1.30	97500	29.7
7	Clinical infectious diseases	2792	1.11	106476	38.1
8	AIDS and behavior	2705	1.08	117307	43.4
9	International journal of STD and AIDS	2609	1.04	58011	22.2
10	Virology	2543	1.01	128462	50.5
11	Journal of infectious diseases	2518	1.00	86069	34.2
12	Journal of biological chemistry	2162	0.86	106029	49.0
13	Proceedings of the national academy of sciences of the united states of America	2084	0.83	81196	39.0
14	Journal of immunology	1911	0.76	97568	51.1
15	Antimicrobial agents and chemotherapy	1855	0.74	64762	34.9
16	AIDS patient care and STDs	1597	0.64	57233	35.8
17	Sexually transmitted diseases	1486	0.59	44511	30.0
18	Journal of clinical microbiology	1469	0.58	39998	27.2
19	Journal of acquired immune deficiency syndromes and human retrovirology	1413	0.56	41365	29.3
20	Vaccine	1300	0.52	59152	45.5
21	Sexually transmitted infections	1292	0.51	34421	26.6
22	BMC infectious diseases	1273	0.51	46327	36.4
23	International journal of tuberculosis and lung disease	1235	0.49	36493	29.5
24	Antiviral therapy	1215	0.48	41477	34.1
25	BMC public health	1205	0.48	47690	39.6
26	Journal of medical virology	1157	0.46	37371	32.3
27	AIDS education and prevention	1123	0.45	37827	33.7
28	HIV medicine	1105	0.44	40621	36.8
29	Journal of medicinal chemistry	1088	0.43	49101	45.1
30	Journal of antimicrobial chemotherapy	1031	0.41	33555	32.5
31	Bioorganic and medicinal chemistry letters	1027	0.41	21927	21.4
32	Retrovirology	1012	0.40	62804	62.1

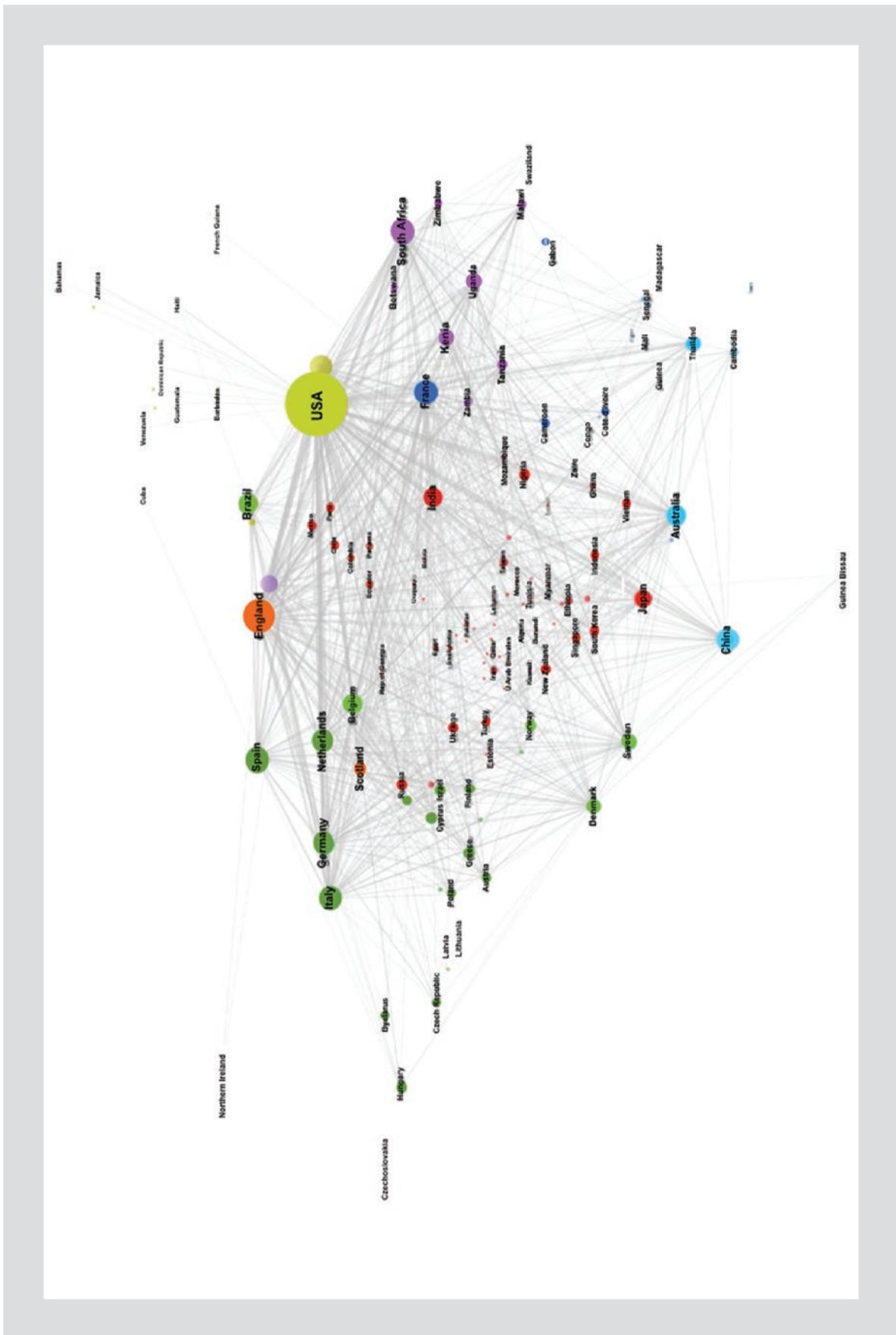


Figure 3. The global networking of 142 countries with a minimum number of 30 papers.

Table 2. Research areas

Rank	Research areas	Frequency	% of total papers
1	Infectious diseases	52,420	20.9
2	Immunology	45,928	18.3
3	Virology	35,299	14
4	Public, environmental, and occupation	28,357	11.3
5	Biochemistry and molecular biology	21,805	8.7
6	Pharmacology and pharmacy	21,744	8.7
7	Microbiology	15,774	6.3
8	General and internal medicine	14,603	5.8
9	Chemistry	11,738	4.7
10	Science and technology - other top	11,568	4.6
11	Psychology	9,815	3.9
12	Biomedical social sciences	8,490	3.4
13	Research and experimental medicine	8,146	3.2
14	Health-care sciences and services	7,707	3.1
15	Respiratory system	6,699	2.7
16	Cell biology	6,535	2.6
17	Neurosciences and neurology	6,153	2.4
18	Biotechnology and applied microbiology	5,412	2.2
19	Pediatrics	4,653	1.9
20	Hematology	4,526	1.8
21	Substance abuse	4,042	1.6
22	Oncology	3,841	1.5
23	Psychiatry	3,687	1.5
24	Biophysics	3,660	1.5
25	Pathology	3,379	1.3
26	Tropical medicine	3,324	1.3
27	Obstetrics and gynecology	3,103	1.2
28	Gastroenterology and hepatology	3,000	1.2
29	Genetics and heredity	2,946	1.2
30	Nursing	2,476	1
31	Dermatology	2,364	0.9
32	Social sciences - other topics	2,343	0.9
33	Mathematical and computational bio	2,220	0.9
34	Mathematics	2,168	0.9
35	Education and educational research	2,164	0.9
36	Parasitology	2,092	0.8
37	Surgery	2,080	0.8
38	Life sciences and biomedicine - Ot	1,776	0.7
39	Urology and nephrology	1,573	0.6
40	Family studies	1,525	0.6

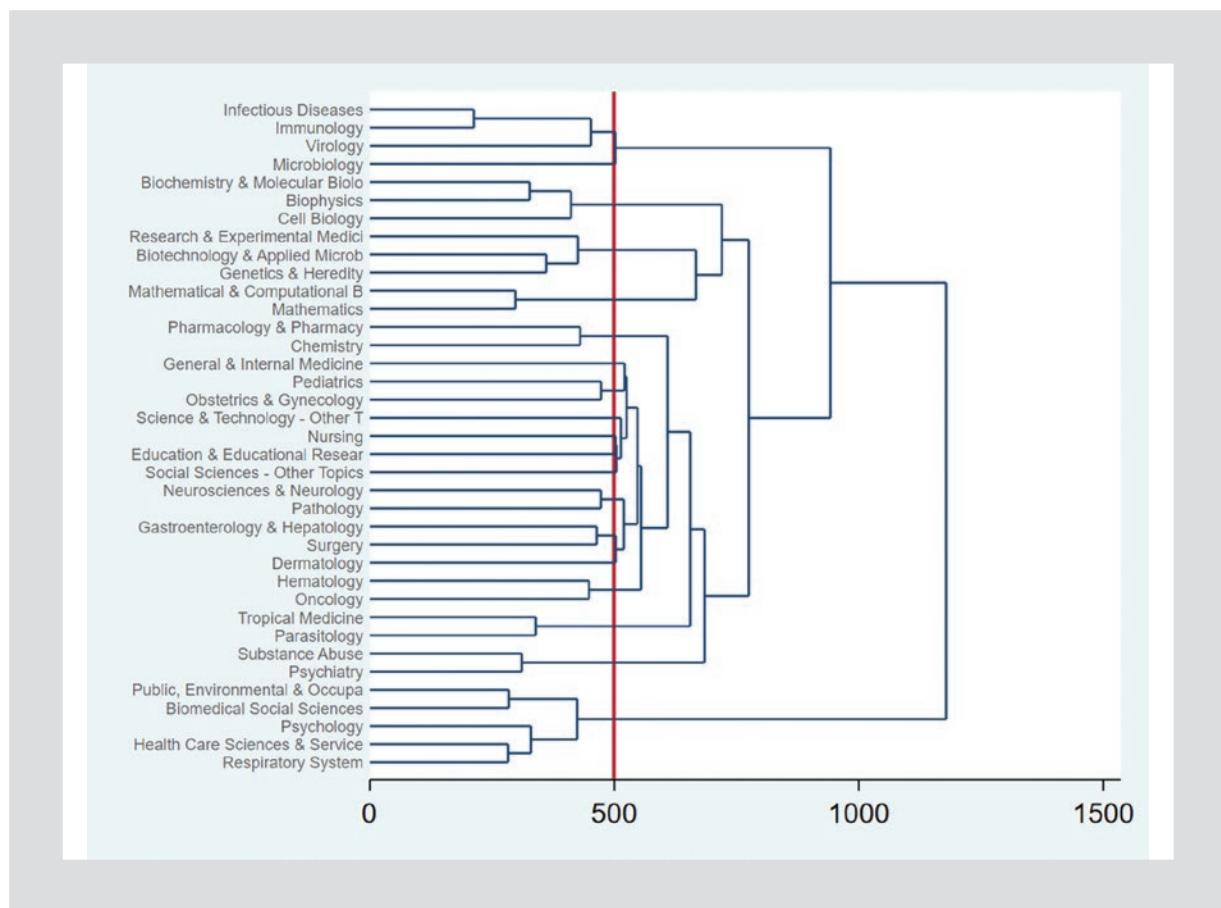


Figure 4. The association between research areas.

fection (STD); (5) prevention: condom use; and (6) HIV treatment: ART.

To further examine the development of research landscapes, supplementary figure 3 describes the creation of research landscapes by clustering research topics emerged from factor analysis of abstracts contents. We found a strong construct of studies examining health status, clinical responses and HIV treatment, risk behaviors, and especially in red cluster; it shows that research topics on psycho-behavioral, cultural, and services were emerged along.

The size of a node was scaled to the frequency of occurrences of a keyword; the thickness of a line was automatically drawn by the software based on the strength of two keywords.

Most cited papers

Table 3 lists the papers which were most cited. The total number of citations received by all papers included in this research received was about 7,948,979, in which 15,499 papers have more than 100 citations. This list also shows the comprehensive review of re-

search scope: HIV virus, cells and genes analysis (CD4) (paper number 2-5, 10, 13, 15-18, 21, 25, 28, 30, 31, 33-37, 40, 45-47, and 53 in Supplementary table 2); HIV infection (paper number 23, 24, 40, 50, and 52 in Supplementary table 2); HIV and other disease (paper 39, 44, 45, and 49 in Supplementary table 2); the application of other methods: polyoxometalates in medicine for anti-HIV activity (paper 20 in Supplementary table 2), ART (paper number 11 in Supplementary table 2); disability-adjusted life years for Global burden disease (paper number 12 in Supplementary table 2), and the global burden of disease (paper number 1, 7, 8, 27, 29, 38, 41, and 51 in Supplementary table 2).

Discussion

This study elucidates the expanding range of research landscapes in HIV/AIDS indicated by rapid growth in the quantity of publications and usages, as well as the evolution of interdisciplinary approaches. Scopes of study were characterized by research domains constructed using keywords, abstracts, and research fields. These findings help identify gaps in

knowledge production and translation, and more importantly the need for improving local research capacity.

Previously, Lakeh has reviewed about 200,000 papers extracted from the Scopus database and described the global trends and regional variation of studies of HIV/AIDS¹³. However, this study retrieved only papers which were published in 2012 or earlier. Another study by Fajardo-Ortiz et al. have developed the research fronts, but neither included a sufficient number of papers nor thoroughly determined the interconnections of research areas¹⁴. In the past 5 years, there have been multiple changes in drivers of HIV epidemics, impacts of ART, transitions, and decreasing international funding, etc., that might affect priority setting and research production, especially in resource-constraint settings^{15,16}.

Since the first papers on HIV/AIDS were published in 1983 (as recorded in the WoS), we have observed blooming literature on HIV and AIDS over the past three decades, as evidenced in the volume and range of research categories^{14,17-20}. This is a testimony to global and national efforts in responding to the HIV pandemic. We have also witnessed a rapid establishment of international collaborations in HIV/AIDS research with strongest leaderships by American and Europe¹⁹. These collaborations have played a very important role in supporting nations with the hardest hits of HIV pandemic, especially in Africa²⁰.

As for knowledge production, research employing an epidemiological, social, and/or behavioral perspective for studying HIV/AIDS dwarfs in the presence of basic and biomedical HIV research. The advancement made in basic and/or biomedical sciences HIV research is admirable, nonetheless, to effectively prevent and control the disease more research are needed to provide culturally relevant and/or contextualized data where HIV epidemics are concentrated; where the number of new infection in sub-groups of the population emerged; and where multiple transitions exist including changes in new transmission routes, health service delivery systems, and financial mechanisms. Cultural, political, and environmental contexts should be considered both in developing research agenda and in designing interventions. For example, to reap the full benefit of pre-exposure prophylaxis or PrEP (more than just a "magic pill") requires not only people's willingness to use it on a consistent and faithful manner but also needs a health-care system that can deliver it in a culturally competent manner. While many gay and bisexual men in Western countries welcome

PrEP, those who are racial/ethnic minorities and/or marginalized populations continue to have considerable distrust of the medical establishments (e.g. pharmaceutical companies) in general and this drug in particular (e.g., side effects).²¹⁻²⁴. In many countries, PrEP is not covered by general health insurance programs. The motivation for or against the use of PrEP needs to be systematically examined, and this is where social and behavioral sciences can contribute to the discourse of HIV prevention.

As for research capacity, it is necessary to enhance the ability and partnership of local researchers as well as invest in research infrastructure at national and regional levels to implement high-quality studies since they are the "gate-keepers" who could respond to local changes in a timely manner¹⁹. These types of research could be a helpful guide for international donors, governments, and academicians to set up research priorities in target groups and settings, and to develop future research agendas globally. In addition, it is crucial for the achievement of HIV/AIDS elimination target that more efforts be given to study the previously neglected populations such as MSM and transgender people, those of ethnic minorities, which have emerged as being particularly at higher risk of HIV^{25,26}.

This study, however, has some limitations. The use of electronic databases such as WOS Provides us a systematic collection of papers over years; however, the restriction on searchable peer-reviewed papers may impact the thoroughness of our results and analysis. In addition, since the included publications were in English only, non-English researches in Asian or Africa are not considered, which potentially contributed to the volume bias of English-speaking developed countries publications, compared to that of Asia or Africa regions. This study has also mainly focused on analyzing the text of the papers, without then having more complex analysis and calculations that can be found in the systematic reviews and meta-analyses of similar topic. However, it is worth noting that the study drew on the significantly large pool of publications on global level, which serve the purpose of the study of providing a comprehensive overview rather than deep-diving into any, particularly specific topics. Nonetheless, future researches may benefit from taking innovative methodological approaches when conducting review, for instance by combining bibliometric study with other research techniques that enable deeper analysis of papers' contents²⁷.

Conclusions

Global trend in HIV research has been increasing in both quantity and interdisciplinary approaches. Improving local research capacity to have better understandings of the contexts and target populations are important to accelerate knowledge production and translation to effectively control the epidemic.

Authors' contributions

BT, FW, KP, CL, GH, and GV conceived of the study, participated in its design and implementation, and wrote the manuscript. BT, GH, and GV analyzed the data. BT, GH, GV, and FW wrote the manuscript. CL, CH, and RH reviewed and edited the manuscript. All authors read and approved the final manuscript.

Supplementary data

Supplementary data are available at AIDS Reviews online (<http://www.aidsreviews.com/supplementary.php>). These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

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