Original Article

Bibliometric analysis of the top 100 cited articles on HIV/AIDS

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Background: The human immunodeficiency virus (HIV) epidemic remains a significant global health issue with currently around 38 million people living with the illness. In 2019, 1.7 million new infections were recorded and 33 million people had died of related causes globally. This study aims to examine and analyse the scientific research progress on HIV/acquired immunodeficiency syndrome (AIDS) through a study of the 100 most cited articles during the years 2010 to 2020 by using bibliometric methods.

Methods: A comprehensive retrospective bibliometric analysis was performed on HIV/AIDS literature published from 2010 until August 19th, 2020 and retrieved from Web of Science (WoS). We used the entry terms of the Medical Subject Headings (MeSH) database to identify the top 100 cited articles.

Results: The top-cited articles received a number of citations ranging from 338 to 4,396 times, with a mean of 633.56 citations per article. Out of the 100, a total of 77 papers were citation classic, cited more than 400 times. The most published documents in the set were reported in 2011 (n=22). The articles were published in 32 journals, out of which, 8 had 3 or more cited publications. The University of California, San Francisco was the top-ranking institution with a total citation score of 9,482 while the authors Burton DR and Mascola JR were the most prolific with 9 published articles each. The United States Department of Health Human Services financially contributed to 82% of the publications.

Conclusions: This study analysis presents a recent prospect on the advancement of HIV/AIDS research worldwide that can be applied to enhance the understanding of HIV/AIDS research and support further work in this research field.

Keywords: HIV; bibliometric analysis; citations; bibliographic coupling; HistCite; VOSviewer

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Introduction

The human immunodeficiency virus (HIV) epidemic, has been one of the most challenging global health issues ever since the first case was reported over 4 decades ago (1). Although the introduction of antiretroviral treatment has significantly reduced the incidence and mortality associated with HIV, it still places a huge burden on households and communities at large.

In 2019, a total of 32.7 million people had died of HIV related illnesses counting from the beginning of the

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epidemic, 38 million were living with HIV, and 1.7 million newly infected people were diagnosed (2). As a disease that compromises the patient's immune system and weakens his defence against infections, it exposes the affected patient to a wide range of health risks. It is a sexually transmitted disease that affects young people and can potentially impair social capital, population structure, and economic growth by affecting the youth of working and reproductive ages (3). The fact is that to date, there is no effective cure that exists. However, scientific research on all aspects of the disease is on the increase with academic specialties emerging from these areas. With the emergence of these academic authorities in HIV, it is imperative to map and assess pathways of knowledge for ease of reference. Bibliometric methods have been identified as an effective tool for the assessment and evaluation of progress in scientific research products as well as to identify the most impactful articles by exploring the ground-breaking of significant contributions (4). Based on the use of bibliometric tools, large amounts of scientific literature have been produced in the world to give a better understanding and to shape future research directions (5-7). To date, according to the Google Scholar database, while some articles on scientific production on HIV/acquired immunodeficiency syndrome (AIDS) research have been published about individual countries (8) or regions (9-11), there is no recent study conducted to analyse and visualize the overall academic structure of global HIV/AIDS research using bibliometric analysis as a technique to develop an overview of large amounts of academic literature in this field. The objective of this study is to evaluate the research on HIV/AIDS by examining the 100 top-cited records indexed in Web of Science Core Collection, including Science Citation Index (SCI) and Science Citation Index Expanded (SCI-E) during the period beginning from 2010 until August 19th, 2020.

Methods

Search strategy

To identify the most frequently cited articles in the HIV/AIDS field, we used the Web of Science (WoS) Core Collection. To collect the bibliographic data, our search was limited to the articles indexed in Sciences Citation Index (SCI) and Sciences Citation Index-Expanded (SCI-E) as standard databases for WoS to screen the relevant articles. The search strategy was designed based on the list of Medical Subject Headings (MeSH) indexing of biomedical literature (https://meshb.nlm.nih.gov/search). The query used to retrieve was as follows: Title: "HIV" OR "HIV1" OR "HIV2" OR "HIV-1" OR "HIV-2" OR "human immunodeficiency virus" OR "Human Immuno-Deficiency Virus" OR "Acquired Immunodeficiency Syndrome" OR "Acquired Immuno-Deficiency Syndrome". All electronic searches on HIV/AIDS articles were performed by two independent reviewers (GG, THM) on a single day (August 19th, 2020) to avoid as much as possible, any potential changes that could occur in citation rate.

Inclusion and exclusion criteria

The 'document type' filter was applied, and only included original investigations for papers published as 'full research article'. Other types of documents were excluded. No language restriction was applied and we limited our search to articles published from 2010 to August 19th, 2020. This resulted in 69,310 HIV/AIDS-related articles; which were then sorted in descending order by the number of citations in WoS (from most cited to least cited). After ensuring the articles were all relevant to our search, we finally stored the top 100 most cited articles on HIV/AIDS in Excel and plain text file for further analysis.

Bibliometric analysis parameters

Bibliometric indicators such as article title, citation count, year of publication, corresponding author, country of origin, the institution of origin, and journal were extracted for each of the 100 records. The journal impact factors were defined based on the Journal Citation Reports (JCR) Science Edition 2020. The quality HIV/AIDS retrieved publications were assessed using Hirsh-index (h-index) (12).

Statistical analysis

The data was analyzed by using VOSviewer software (van Eck and Waltman 2010), which is freely available on http://www.VOSviewer.com (13); Bibliometrix (an R package) (14); as well as HistCite (15). Furthermore, Spearman correlations between the number of times an article has been cited and the number of years since its publication, as well as the number of authors, institutions, and countries involved, were calculated using the Statistical Package for Social Sciences (SPSS) version 25. Statistical significance was defined as a P value less than 0.05.

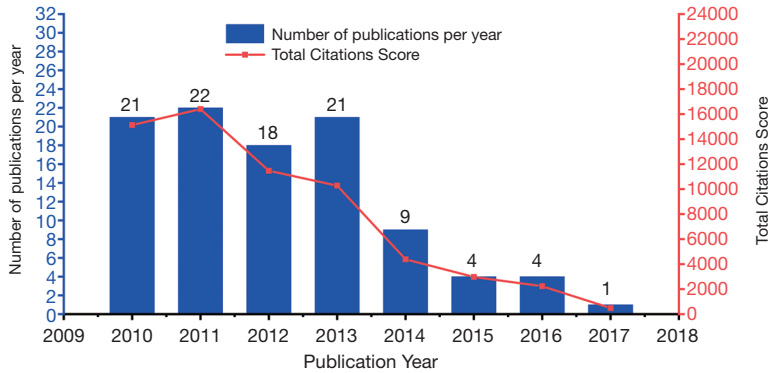

Figure 1 The trend of publication and citation analysis for the top 100 most-cited articles on HIV/AIDS. HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome.

Results

Publication year

The publication years for the 100 most-cited articles on HIV/AIDS between 2010 and 2020 ranged from 2010 to Aug. 2017. The highest number of the article published and the number of citations in a single year were 22 and 16,400 respectively and were both recorded in 2011 (*Figure 1*).

Description of main characteristics of the articles

The total number of citations for the top 100 articles was 63,356. The average number of citations per article was 633, with a range of 338 to 4,396. Of the 100 top-cited articles, 77 had 400 or more citations in WoS qualifying to the definition of citation classic (16); 50 were cited more than 500 times, and only 9 were cited over 1,000 times.

The number of articles annual citations representing the number of times the article was cited per year ranged from 43.25 to 628. The top-cited article was published in the New England Journal of Medicine in August 2011 (17) as presented in *Table 1*.

Contributing authors

Overall, the 100 publications involved a total of 2,101 authors. *Table 2* shows a list of the most frequently appearing authors who contributed with more than six articles each. The top productive authors are Burton DR, affiliated to Scripps Research Institute, and Mascola JR, from the National Institute of Allergy and Infectious Diseases (NIAID), who each had 9 publications.

Journal of publication and impact factors

The top 100 cited articles were published in 32 different journals. Eight journals, all of which were in the top quartiles, had three or more cited publications. Close to half of all the articles (48%) were published in only the top 3 journals, which include: *Nature* (n=17), *New England Journal of Medicine* (n=16), and *Science* (n=15) articles (*Table 3*).

Institutions & institutions with subdivision

In *Table 4*, the top institutions and institutions with subdivisions involved in HIV/AIDS publications in the recent 10 years are shown. The University of California San Francisco took the lead institutions with 19,482 citations, followed by NIAID with 18,469 citations, among other reported ones.

Funding agencies

The analysis of the main funding agencies revealed that the United States Department of Health Human Services (USA, 82%), the National Institutes of Health NIH (USA, 80%) and NIH National Institute of Allergy Infectious Diseases (USA, 63%) accounted for the highest amount of financial support towards HIV research (*Figure 2*).

Keyword analysis

A keyword analysis was performed to help understand the main searches in the HIV/AIDS field. “Infection” (n=21) was a frequently used keyword plus. Other common ones

Table 1 The top 100 cited articles on HIV/AIDS

R	Authors, year	Document title	TC
1	Cohen MS, *et al*. 2011	Prevention of HIV-1 Infection with Early Antiretroviral Therapy. New England Journal of Medicine. 2011 AUG 11; 365 (6): 493-505	4,396
2	Grant RM, *et al*. 2010	Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men. New England Journal of Medicine. 2010 DEC 30; 363 (27): 2587-2599	2,743
3	Baeten JM, *et al*. 2012	Antiretroviral Prophylaxis for HIV Prevention in Heterosexual Men and Women. New England Journal of Medicine. 2012 AUG 2; 367 (5): 399-410	1,666
4	Karim QA, *et al*. 2010	Effectiveness and Safety of Tenofovir Gel, an Antiretroviral Microbicide, for the Prevention of HIV Infection in Women. SCIENCE. 2010 SEP 3; 329 (5996): 1168-1174	1,540
5	Lundgren D, *et al*. 2015	Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection. New England Journal of Medicine. 2015 AUG 27; 373 (9): 795-807	1,317
6	Heaton RK, *et al*. 2010	HIV-associated neurocognitive disorders persist in the era of potent antiretroviral therapy CHARTER Study. Neurology. 2010 DEC 7; 75 (23): 2087-2096	1,259
7	Haynes BF, *et al*. 2012	Immune-Correlates Analysis of an HIV-1 Vaccine Efficacy Trial. New England Journal of Medicine. 2012 APR 5; 366 (14): 1275-1286	1,183
8	Thigpen MC, *et al*. 2012	Antiretroviral Preexposure Prophylaxis for Heterosexual HIV Transmission in Botswana. 2012 AUG 2; 367 (5): 423-434	1,133
9	Wu XL, *et al*. 2010	Rational Design of Envelope Identifies Broadly Neutralizing Human Monoclonal Antibodies to HIV-1. SCIENCE. 2010 AUG 13; 329 (5993): 856-861	1,089
10	Walker LM, 2011	Broad neutralization coverage of HIV by multiple highly potent antibodies. Nature. 2011 SEP 22; 477 (7365): 466-470	964
11	Laguette N, *et al*.2011	SAMHD1 is the dendritic- and myeloid-cell-specific HIV-1 restriction factor counteracted by Vpx. Nature. 2011 JUN 30; 474 (7353): 654-657	929
12	Van Damme L, *et al*. 2012	Preexposure Prophylaxis for HIV Infection among African Women. New England Journal of Medicine. 2012 AUG 2; 367 (5): 411-422	908
13	Beyrer C, *et al*. 2012	Global epidemiology of HIV infection in men who have sex with men. Lancet. 2012 JUL 28; 380 (9839): 367-377	838
14	Heaton RK, *et al*. 2011	HIV-associated neurocognitive disorders before and during the era of combination antiretroviral therapy: differences in rates, nature, and predictors. Journal of Neurovirology. 2011 FEB; 17 (1): 3-16	821
15	Hrecka K, *et al*. 2011	Vpx relieves inhibition of HIV-1 infection of macrophages mediated by the SAMHD1 protein. NATURE. 2011 JUN 30; 474 (7353): 658-661	764
16	Zhou TQ, *et al*. 2010	Structural Basis for Broad and Potent Neutralization of HIV-1 by Antibody VRC01. Science. 2010 AUG 13; 329 (5993): 811-817	755
17	Tebas P, *et al*. 2014	Gene Editing of CCR5 in Autologous CD4 T Cells of Persons Infected with HIV. New England Journal of Medicine. 2014 MAR 6; 370 (10): 901-910	753
18	McCormack S, *et al*. 2016	Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. LANCET. 2016 JAN 2; 387 (10013): 53-60	753
19	Prejean J, *et al*. 2011	Estimated HIV Incidence in the United States, 2006-2009. PLOS ONE. 2011 AUG 3; 6 (8): Art. No. e17502	722
20	Choopanya K, *et al*. 2013	Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet. 2013 JUN 15; 381 (9883): 2083-2090	719

Table 1 (*continued*)

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R	Authors, year	Document title	TC
21	Pereyra FP, *et al*. 2010	The Major Genetic Determinants of HIV-1 Control Affect HLA Class I Peptide Presentation. SCIENCE. 2010 DEC 10; 330 (6010): 1551-1557	714
22	ScheidJF, *et al*. 2011	Sequence and Structural Convergence of Broad and Potent HIV Antibodies That Mimic CD4 Binding. SCIENCE. 2011 SEP 16; 333 (6049): 1633-1637	710
23	Archin NM, *et al*. 2012	Administration of vorinostat disrupts HIV-1 latency in patients on antiretroviral therapy. NATURE. 2012 JUL 26; 487 (7408): 482-485	689
24	Ho YC, *et al*. 2010	Replication-Competent Noninduced Proviruses in the Latent Reservoir Increase Barrier to HIV-1 Cure. CELL. 2013 OCT 24; 155 (3): 540-551	665
25	Jewkes RK, *et al*. 2010	Intimate partner violence, relationship power inequity, and incidence of HIV infection in young women in South Africa: a cohort study. Lancet. 2010 JUL 3; 376 (9734): 41-48	663
26	Freiberg MS, *et al*. 2013	HIV Infection and the Risk of Acute Myocardial Infarction. JamaInternalMedicine. 2013 APR 22; 173 (8): 614-622	662
27	Donnell D, *et al*. 2010	Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. Lancet. 2010 JUN 12; 375 (9731): 2092-2098	654
28	Sandler NG, *et al*. 2011	Plasma Levels of Soluble CD14 Independently Predict Mortality in HIV Infection. Journal of Infectious Diseases. 2011 MAR 15; 203 (6): 780-790	654
29	Samji H, *et al*. 2013	Closing the Gap: Increases in Life Expectancy among Treated HIV-Positive Individuals in the United States and Canada. PLOS ONE. 2013 DEC 18; 8 (12): Art. No. e81355	654
30	Molina JM, *et al*. 2015	On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection. New England Journal of Medicine. 2015 DEC 3; 373 (23): 2237-2246	643
31	Marrazzo JM, *et al*. 2015	Tenofovir-Based Preexposure Prophylaxis for HIV Infection among African Women. New England Journal of Medicine. 2015 FEB 5; 372 (6): 509-518	641
32	Baral S, *et al*. 2012	Burden of HIV among female sex workers in low-income and middle-income countries: a systematic review and meta-analysis. Lancet Infectious Diseases. 2012 JUL; 12 (7): 538-549	620
33	Liao HX, *et al*. 2013	Co-evolution of a broadly neutralizing HIV-1 antibody and founder virus. Nature. 2013 APR 25; 496 (7446): 469-476	599
34	Guaraldi G, *et al*. 2011	Premature Age-Related Comorbidities Among HIV-Infected Persons Compared With the General Population. ClinicalInfectiousDiseases. 2011 DEC 1; 53 (11): 1120-1126	598
35	Saez-Cirion A, *et al*. 2013	Post-Treatment HIV-1 Controllers with a Long-Term Virological Remission after the Interruption of Early Initiated Antiretroviral Therapy ANRS VISCONTI Study. PLOS PATHOGENS. 2013 MAR; 9 (3): Art. No. e1003211	594
36	Wu XL, *et al*. 2011	Focused Evolution of HIV-1 Neutralizing Antibodies Revealed by Structures and Deep Sequencing. Science. 2011 SEP 16; 333 (6049): 1593-1602	580
37	McLellan JS, *et al*. 2011	Structure of HIV-1 gp120 V1/V2 domain with broadly neutralizing antibody PG9. Nature. 2011 DEC 15; 480 (7377): 336-343	576
38	Julien JP, *et al*. 2013	Crystal Structure of a Soluble Cleaved HIV-1 Envelope Trimer. Science. 2013 DEC 20; 342 (6165): 1477-1483	564
39	Grant RM, *et al*. 2014	Uptake of pre-exposure prophylaxis, sexual practices, and HIV incidence in men and transgender women who have sex with men: a cohort study. Lancet Infectious Diseases. 2014 SEP; 14 (9): 820-829	561

Table 1 (*continued*)

Table 1 (*continued*)

R	Authors, year	Document title	TC
40	Montaner JSG, *et al*. 2010	Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study. Lancet. 2010 AUG 14; 376 (9740): 532-539	550
41	Doitsh G, *et al*. 2014	Cell death by pyro ptosis drives CD4 T-cell depletion in HIV-1 infection. Nature. 2014 JAN 23; 505 (7484): 509-+	537
42	Cohen MS, *et al*. 2016	Antiretroviral Therapy for the Prevention of HIV-1 Transmission. New England Journal of Medicine. 2016 SEP 1; 375 (9): 830-839	522
43	Murray CJL, *et al*. 2014	Global, regional, and national incidence and mortality for HIV, tuberculosis, and malaria during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014 SEP 13; 384 (9947): 1005-1070	518
44	Tanser F, *et al*. 2013	High Coverage of ART Associated with Decline in Risk of HIV Acquisition in Rural KwaZulu-Natal, South Africa. SCIENCE. 2013 FEB 22; 339 (6122): 966-971	514
45	Huang JH, *et al*. 2012	Broad and potent neutralization of HIV-1 by a gp41-specific human antibody. Nature. 2012 NOV 15; 491 (7424): 406-412	512
46	Das M, *et al*. 2010	Decreases in Community Viral Load Are Accompanied by Reductions in New HIV Infections in San Francisco. PLOS ONE. 2010 JUN 10; 5 (6): Art. No. e11068	511
47	Neuhaus J, *et al*. 2010	Markers of Inflammation, Coagulation, and Renal Function Are Elevated in Adults with HIV Infection. Journal of InfectiousDiseases. 2010 JUN 15; 201 (12): 1788-1795	510
48	Rodger AJ, *et al*. 2016	Sexual Activity Without Condoms and Risk of HIV Transmission in Serodifferent Couples When the HIV-Positive Partner Is Using Suppressive Antiretroviral Therapy. JAMA-Journal of the American Medical Association. 2016 JUL 12; 316 (2): 171-181	506
49	Hemelaar J, *et al*. 2011	Global trends in molecular epidemiology of HIV-1 during 2000-2007. AIDS. 2011 MAR 13; 25 (5): 679-689	504
50	Shan L, *et al*. 2012	Stimulation of HIV-1-Specific Cytolytic T Lymphocytes Facilitates Elimination of Latent Viral Reservoir after Virus Reactivation. IMMUNITY. 2012 MAR 23; 36 (3): 491-501	504
51	Lahouassa H, *et al*. 2012	SAMHD1 restricts the replication of human immunodeficiency virus type 1 by depleting the intracellular pool of deoxynucleoside triphosphates. NATURE IMMUNOLOGY. 2012 MAR; 13 (3): 223-228	497
52	Mathers BM, *et al*. 2010	HIV prevention, treatment, and care services for people who inject drugs: a systematic review of global, regional, and national coverage. Lancet. 2010 MAR 20; 375 (9719): 1014-1028	494
53	Pejchal R, *et al*. 2011	A Potent and Broad Neutralizing Antibody Recognizes and Penetrates the HIV Glycan Shield. Science. 2011 NOV 25; 334 (6059): 1097-1103	492
54	Goldstone DC, *et al*. 2011	HIV-1 restriction factor SAMHD1 is a deoxynucleoside triphosphate triphosphohydrolase. Nature. 2011 DEC 15; 480 (7377): 379-82	492
55	Rajasingham R, *et al*. 2017	Global burden of disease of HIV-associated cryptococcal meningitis: an updated analysis. Lancet InfectiousDiseases. 2017 AUG; 17 (8): 873-881	485
56	Gao DX, *et al*. 2013	Cyclic GMP-AMP Synthase Is an Innate Immune Sensor of HIV and Other Retroviruses. SCIENCE. 2013 AUG 23; 341 (6148): 903-906	484
57	Holt N, *et al*. 2010	Human hematopoietic stem/progenitor cells modified by zinc-finger nucleases targeted to CCR5 control HIV-1 in vivo. Nature Biotechnology. 2010 AUG; 28 (8): 839-47	477

Table 1 (*continued*)

Table 1 (*continued*)

R	Authors, year	Document title	TC
58	Sanders RW, *et al*. 2013	A Next-Generation Cleaved, Soluble HIV-1 Env Trimer, BG505 SOSIP.664 gp140, Expresses Multiple Epitopes for Broadly Neutralizing but Not Non-Neutralizing Antibodies. PLOS Pathogens. 2013 SEP; 9 (9): Art. No. e1003618	458
59	Lyumkis D, *et al*. 2013	Cryo-EM Structure of a Fully Glycosylated Soluble Cleaved HIV-1 Envelope Trimer. Science. 2013 DEC 20; 342 (6165): 1484-1490	457
60	Kann L, *et al*. 2016	HIV-Related Risk Behaviors Among Male High School Students Who Had Sexual Contact with Males-17 Large Urban School Districts, United States, 2009-2013. Mmwr-Morbidity And Mortality Weekly Report. 2016 FEB 12; 65 (5): 106-109	455
61	Allers K, *et al*. 2011	Evidence for the cure of HIV infection by CCR5 Delta 32/Delta 32 stem cell transplantation. Blood. 2011 MAR 10; 117 (10): 2791-2799	440
62	Smith CJ, *et al*. 2014	Trends in underlying causes of death in people with HIV from 1999 to 2011 (D: A: D): Amulticohort collaboration. Lancet. 2014 JUL 19; 384 (9939): 241-248	440
63	Pancera M, *et al*. 2014	Structure and immune recognition of trimeric pre-fusion HIV-1 Env. Nature. 2014 OCT 23; 514 (7523): 455-461	440
64	Locci M, *et al*. 2013	Human Circulating PD-1(+) CXCR3 (-) CXCR5 (+) Memory Tfh Cells Are Highly Functional and Correlate with Broadly Neutralizing HIV Antibody Responses. Immunity. 2013 OCT 17; 39 (4): 758-769	438
65	Baggaley RF, *et al*. 2010	HIV transmission risk through anal intercourse: systematic review, meta-analysis and implications for HIV prevention. International Journal of EPIDEMIOLOGY. 2010 AUG; 39 (4): 1048-1063	434
66	Zhao GP, *et al*. 2013	Mature HIV-1 capsid structure by cryo-electron microscopy and all-atom molecular dynamics. Nature. 2013 MAY 30; 497 (7451): 643-646	427
67	Seaman MS, *et al*. 2010	Tiered Categorization of a Diverse Panel of HIV-1 EnvPseudoviruses for Assessment of Neutralizing Antibodies. Journal Of Virology. 2010 FEB; 84 (3): 1439-1452	425
68	Blanc FX, *et al*. 2011	Earlier versus Later Start of Antiretroviral Therapy in HIV-Infected Adults with Tuberculosis. New England Journal of Medicine. 2011 OCT 20; 365 (16): 1471-1481	423
69	Walmsley SL, *et al*. 2013	Dolutegravir plus Abacavir-Lamivudine for the Treatment of HIV-1 Infection. New England Journal of Medicine. 2013 NOV 7; 369 (19): 1807-1818	423
70	Worm SW, *et al*. 2010	Risk of Myocardial Infarction in Patients with HIV Infection Exposed to Specific Individual Antiretroviral Drugs from the 3 Major Drug Classes: The Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) Study. Journal of infectious diseases. 2010 FEB 1; 201 (3): 318-330	418
71	Doria-Rose NA, *et al*. 2014	Developmental pathway for potent V1V2-directed HIV-neutralizing antibodies. Nature. 2014 MAY 1; 509 (7498): 55-62	414
72	Kopp JB, *et al*. 2011	APOL1 Genetic Variants in Focal Segmental Glomerulosclerosis and HIV-Associated Nephropathy. Journal of The American Society of Nephrology. 2011 NOV; 22 (11): 2129-2137	413
73	Shiels MS, *et al*. 2011	Cancer Burden in the HIV-Infected Population in the United States. Journal of the national cancer Institute. 2011 MAY; 103 (9): 753-762	411
74	Buzon MJ, *et al*. 2010	HIV-1 replication and immune dynamics are affected by raltegravir intensification of HAART-suppressed subjects. Nature Medicine. 2010 APR; 16 (4): 460-465.	407
75	Sharp PM, 2011	Origins of HIV and the AIDS Pandemic. Cold Spring Harbor Perspectives In Medicine. 2011 SEP; 1 (1): Art. No. a006841	407

Table 1 (*continued*)

Table 1 (*continued*)

R	Authors, year	Document title	TC
76	BarouchDH, *et al*. 2013	Therapeutic efficacy of potent neutralizing HIV-1-specific monoclonal antibodies in SHIV-infected rhesus monkeys. Nature. 2013 NOV 14; 503 (7475): 224-228	404
77	Tan QX, *et al*. 2013	Structure of the CCR5 Chemokine Receptor-HIV Entry Inhibitor Maraviroc Complex. SCIENCE. 2013 SEP 20; 341 (6152): 1387-1390.	403
78	Simioni S, *et al*. 2010	Cognitive dysfunction in HIV patients despite long-standing suppression of viremia. AIDS. 2010 JUN 1; 24 (9): 1243-1250	397
79	Millett GA, *et al*. 2012	Comparisons of disparities and risks of HIV infection in black and other men who have sex with men in Canada, UK, and USA: a meta-analysis. Lancet. 2012 JUL 28; 380 (9839): 341-348	388
80	Thompson MA, *et al*. 2012	Guidelines for Improving Entry Into and Retention in Care and Antiretroviral Adherence for Persons With HIV: Evidence-Based Recommendations From an International Association of Physicians in AIDS Care Panel. Annals of Internal Medicine. 2012 JUN 5; 156 (11): 817-833	384
81	Gill J, *et al*. 2010	Causes of Death in HIV-1-Infected Patients Treated with Antiretroviral Therapy, 1996-2006: Collaborative Analysis of 13 HIV cohort studies. Clinical Infectious Diseases. 2010 MAY 15; 50 (10): 1387-1396	383
82	Jager S, *et al*. 2012	Global landscape of HIV-human protein complexes. Nature. 2012 JAN 19; 481 (7381): 365-370	383
83	Gonzalez JS, *et al*. 2011	Depression and HIV/AIDS Treatment Nonadherence: A Review and Meta-analysis. Jaids-Journal of Acquired Immune Deficiency Syndromes. 2011 OCT 1; 58 (2): 181-187	381
84	Havlir DV, *et al*. 2011	Timing of Antiretroviral Therapy for HIV-1 Infection and Tuberculosis. New England Journal of Medicine. 2011 OCT 20; 365 (16): 1482-1491	381
85	Perreau M, *et al*. 2013	Follicular helper T cells serve as the major CD4 T cell compartment for HIV-1 infection, replication, and production. Journal of Experimental Medicine. 2013 JAN 14; 210 (1): 143-156	380
86	Jardine J, *et al*. 2013	Rational HIV Immunogen Design to Target Specific Germline B Cell Receptors. SCIENCE. 2013 MAY 10; 340 (6133): 711-716	377
87	Maldarelli F, *et al*. 2014	Specific HIV integration sites are linked to clonal expansion and persistence of infected cells. Science. 2014 JUL 11; 345 (6193): 179-183	377
88	Caskey M, *et al*. 2015	Viraemia suppressed in HIV-1-infected humans by broadly neutralizing antibody 3BNC117. Nature. 2015 JUN 25; 522 (7557): 487-491	372
89	Baldauf HM, *et al*. 2012	SAMHD1 restricts HIV-1 infection in resting CD4(+) T cells. Nature Medicine. 2012 NOV; 18 (11): 1682-1687	367
90	Deeks SG. 2012	Towards an HIV cure: a global scientific strategy. Nature Reviews Immunology. 2012 AUG; 12 (8): 607-614	366
91	Persaud D, *et al*. 2013	Absence of Detectable HIV-1 Viremia after Treatment Cessation in an Infant. New England Journal of Medicine. 2013 NOV 7; 369 (19): 1828-1835	356
92	Eriksson S, *et al*. 2013	Comparative Analysis of Measures of Viral Reservoirs in HIV-1 Eradication Studies. PLOS PATHOGENS. 2013 FEB; 9 (2): Art. No. e1003174	354
93	Celum C, *et al*. 2010	Acyclovir and Transmission of HIV-1 from Persons Infected with HIV-1 and HSV-2. New England Journal of Medicine. 2010 FEB 4; 362 (5): 427-439	353
94	Fletcher CV, *et al*. 2014	Persistent HIV-1 replication is associated with lower antiretroviral drug concentrations in lymphatic tissues. Proceedings of the national academy of sciences of the United States of America. 2014 FEB 11; 111 (6): 2307-2312	352

Table 1 (*continued*)

Table 1 (*continued*)

R	Authors, year	Document title	TC
95	Sundquist WI, Krausslich HG 2012	HIV-1 Assembly, Budding, and Maturation. Cold spring harbor perspectives in medicine. 2012 JUL; 2 (7): Art. No. a006924	349
96	Bor J, *et al*. 2013	Increases in Adult Life Expectancy in Rural South Africa: Valuing the Scale-Up of HIV Treatment. Science. 2013 FEB 22; 339 (6122): 961-965	348
97	Jewkes R, Morrell R, 2010	Gender and sexuality: emerging perspectives from the heterosexual epidemic in South Africa and implications for HIV risk and prevention. Journal of the International AIDS Society. 2010 FEB 9; 13: Art. No. 6	346
98	Balazs AB, *et al*. 2012	Antibody-based protection against HIV infection by vectored immunoprophylaxis. Nature. 2012 JAN 5; 481 (7379): 81-84	343
99	Holodniy M, *et al*. 2011	Results of Antiretroviral Treatment Interruption and Intensification in Advanced Multi-Drug Resistant HIV Infection from the OPTIMA Trial. PLOS ONE. 2011 MAR 31; 6 (3): Art. No. e14764	342
100	Klein F, *et al*. 2012	HIV therapy by a combination of broadly neutralizing antibodies in humanized mice. Nature. 2012 DEC 6; 492 (7427): 118-122	338

HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome; TC, total citation; R, rank.

Table 2 Authors with six or more top-cited articles on HIV/AIDS research

Author	Affiliation	Publications	TC	Author ranking on list		
				First	Second	Other
Burton DR	Scripps Research Institute	9	5,124	0	0	9
Mascola JR	NIAID, Vaccine Research Center, NIH	9	5,390	0	0	9
Kwong PD	NIAID, Vaccine Research Center, NIH	8	4,965	0	0	8
Wilson IA	Scripps Research Institute	8	4,302	0	0	8
Julien JP	Scripps Research Institute	7	3,888	1	2	5
Ward AB	Scripps Research Institute	7	3,338	0	0	7
Haynes BF	Duke University	6	3,890	1	0	5
Louder MK	NIAID, Vaccine Research Center, NIH	6	3,630	0	0	6
Seaman MS	Harvard University, School of Medicine	6	3,338	1	0	5
Yang YP	NIAID, Vaccine Research Center, NIH	6	3,277	0	0	6
Zhou TQ	NIAID, Vaccine Research Center, NIH	6	4,039	1	2	3

HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome; NIH, National Institute of Health; TC, total citations.

included "transmission" (n=12), and "therapy" (n=11) (*Figure 3*). Keywords plus which are different from the keywords chosen by authors are extracted by Thomson Reuters, from the titles of the cited references without being in the title of the article itself. According to Garfield, they offer a greater picture in the exploration of the content of an article or a set of articles (18).

Bibliographic coupling analysis

Bibliographic coupling is a type of bibliometric network that analyses the number of articles that two articles share in their references; a bibliographic coupling strength increases as the number of references cited by both publications increases and that can be used as an indicator of how similar the articles are in their topic or field of research (19,20).

Table 3 Journals with three or more top-cited articles on HIV/AIDS research

Journal	Recs	TC	Impact factor [2020]	Quartile range
Nature	17	9,183	42.778	Q1
New England Journal of Medicine	16	17,841	74.699	Q1
Science	15	9,404	41.845	Q1
Lancet	10	6,017	60.392	Q1
PLoS One	4	2,229	2.74	Q2
Journal of Infectious Diseases	3	1,582	5.022	Q1
Lancet Infectious Diseases	3	1,666	24.446	Q1
PLOS Pathogens	3	1,406	6.218	Q1

HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome; TC, total citations; Q, journal quartile range.

Table 4 Top 10 institution and institution with subdivision on HIV/AIDS research

Institution, Country	TC	Institution with Subdivision, Country	TC
University of California, San Francisco, USA	19,482	University of California, San Francisco, USA	10,392
National Institute of Allergy and Infectious Diseases, USA	18,469	Harvard University, School of Public Health, USA	9,158
Harvard University, USA	17,791	Harvard Medical School, USA	6,963
University of Washington, USA	15,902	Johns Hopkins University, School of Medicine, USA	9,285
Johns Hopkins University, USA	14,922	National Institute of Allergy and Infectious Diseases, Vaccine Research Center, USA	5,993
Fred Hutchinson Cancer Research Center, USA	10,554	University of Amsterdam, Academic Medical Center, Netherlands	4,340
University of the Witwatersrand, South Africa	9,974	Scripps Research Institute, Department of Immunology & Microbial Science, USA	4,514
Chiang Mai University, Thailand	9,060	Scripps Research Institute, Skaggs Institute for Chemical Biology, USA	3,810
University of North Carolina, USA	8,918	University of California San Diego, USA	4,711
Fenway Community Health Center, USA	7,700	University of Washington, USA	8,673

HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome.

For the purpose of running a bibliographic coupling assessment between authors, countries, and organizations that had a contribution in 100 top-cited articles on HIV/AIDS, we used VOSviewer software to obtain a graphical visualization of networks. In *Figures 4-6*, the bibliographic coupling between authors, countries, and organizations respectively.

Authors

Out of 850 authors, those with a minimum of 2 documents were selected. That resulted in 88 authors included in this coupling (*Figure 4*). The total links strength (TLS) of bibliographic coupling links with other authors were calculated. The overall links between the authors were 1,462, and that made a TLS of 50,000. The top 5 authors accounting for the highest rates of TLS included: Julien JP (TLS =3,629), followed by Wilson IA (TLS =3,629), Burton DR (TLS =3,389), Ward AB (TLS =3,239), and Cupo A (TLS = 2,915).

Countries

Authors with a minimum of 2 documents were considered.

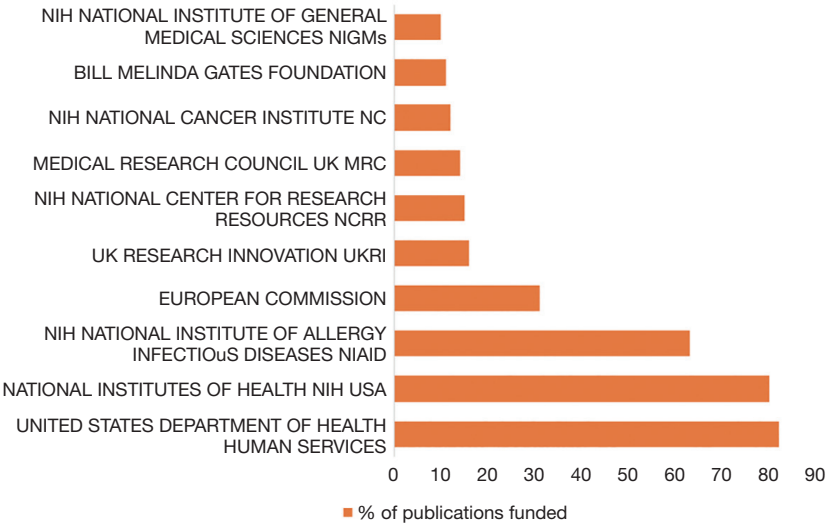

Figure 2 Top 10 agencies funding global HIV/AIDS research. HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome.

Figure 3 Word-clouds of keywords plus [2010–2020] in WoS for the top 100 most-cited articles on HIV/AIDS. HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome; WoS, Web of Science.

Figure 5 shows the bibliographic coupling between countries. A minimum of 4 documents per country was considered and 23 countries, subdivided into 3 clusters, met the thresholds. The 23 countries make up 253 Links, and the Total Link strength is equal to 31,169. In a similar way we did for authors, we also report the top 5 countries with the highest TLS. The first country was the USA (TLS =11,847), followed by South Africa (TLS =5,690), England (TLS =4,608), Netherlands (TLS =3,030), and France (TLS =2,929).

Organizations

Figure 6 shows institutions with a minimum of 7 documents. Out of 398 organizations 17 organizations met the threshold *Figure 4*. The total numbers of Links and TLS were 310 and 66,503, respectively. In terms of TLS, NIAID was in the lead

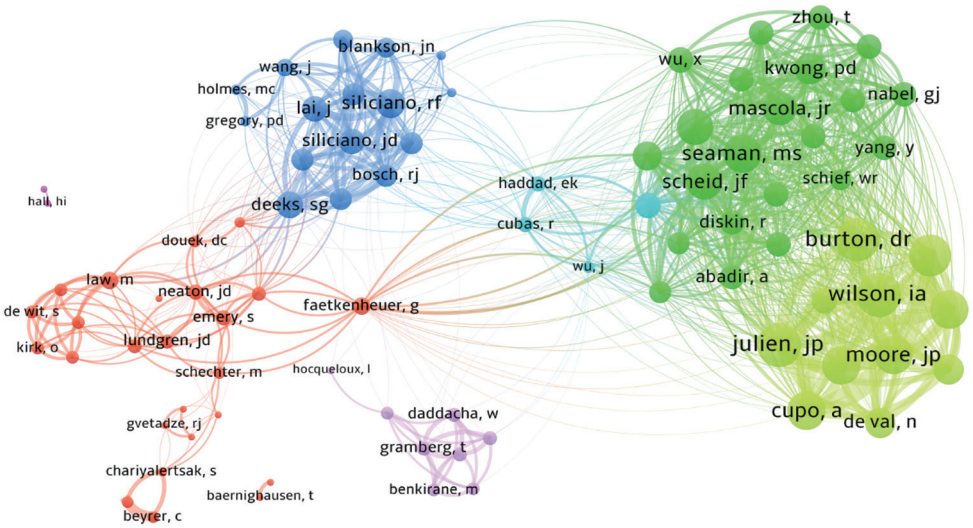

Figure 4 Bibliographic coupling of the authors that contributed to the 100 top-cited articles.

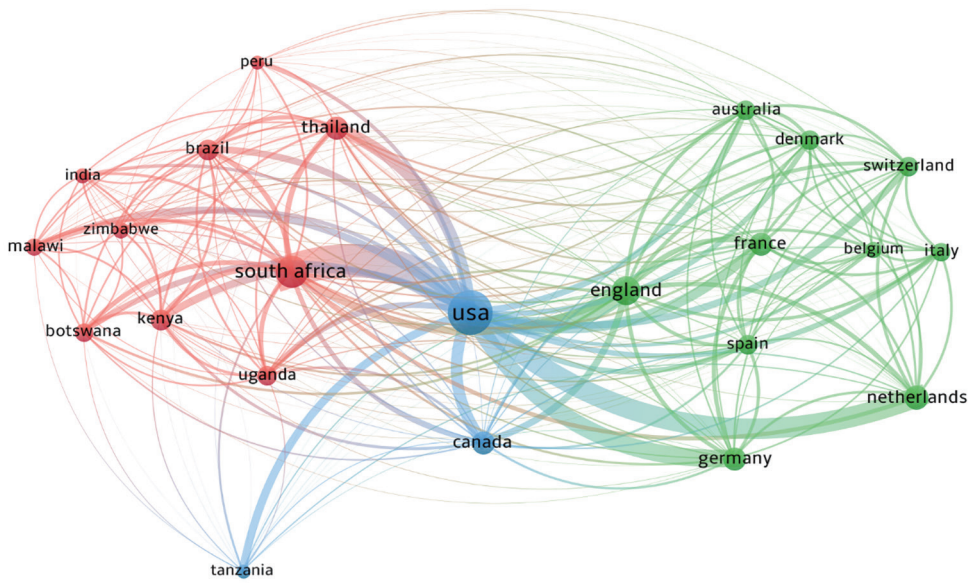

Figure 5 Bibliographic coupling of the countries that contributed to 100 top-cited articles on HIV/AIDS. Countries with a minimum of 4 documents (n=23) are shown. HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome.

with a 6,481, followed by Scripps Research Institute (TLS =5,462) and Harvard University (TLS =4,951).

Factors influencing citations analysis

Table 5 shows an analysis of factors that potentially determine the number of citations for the 100 top-cited articles on HIV/AIDS. We investigated potential relationships between citations and variables including the period of time since publication, the number of authors, the amount of organizations involved, the participating countries, and the journal impact factor. We found a positive correlation between the number of times articles were cited in WOS and the impact factor of the journal

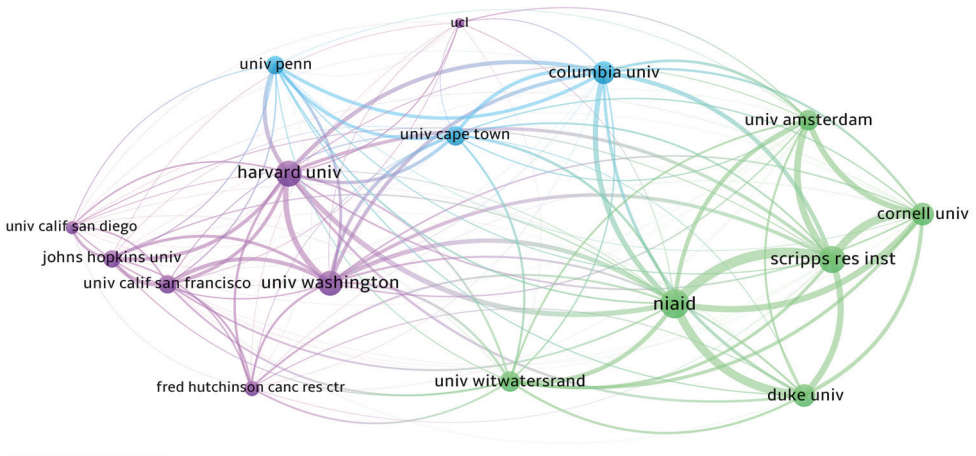

Figure 6 Bibliographic coupling of the organizations that had a contribution in 100 top-cited articles.

Table 5 Relationship between number of citations and number of years, authors, institution, and countries involved in HIV/AIDS research

Factors influencing citations	Journal impact factor	Journal quartile	Number of years since publication	Number of authors	Number of countries	Number of institutions
Spearman r	0.283	0.023	0.093	0.258	0.014	0.094
P value	0.004	0.823	0.358	0.010	0.893	0.351
P value summary	*	ns	ns	*	ns	ns

HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome; ns, not statistically significant; *, statistically significant.

in which it was published. (r=0.283, P=0.004). Similarly, a positive correlation was observed between the number of authors per publication and the number of citations (r=0.258, P=0.010). No significant correlations were found between the number of citations and years since publication (r=0.093 P=0.358), the number of countries per publications (r=0.014 P=0.893), or institutions involved (r=0.094 P=0.351).

Discussion

We used bibliometric methods to understand the state of main contributions towards HIV/AIDS research in the past decade. With this, we aimed to highlight and provide a historical perspective for future research directions. The analysis included the most cited articles among those published over the recent 10 years [2010–2020], however the results only cover the earlier eight years as the articles published after 2017 most probably have not yet had enough exposure in comparison to the older ones.

The citations for the top 100 were between 338 and 4,396, numbers close to those found in similar studies (21). A decrease in citation numbers was noted after 2013, suggesting that despite a non-significant association between the citation number and the time elapsed since publication, articles dating from earlier years were more cited than the recent ones. That may be wrongly perceived as a reduced interest in HIV research; however, a possible reason for that time factor is that older articles have had a long time to gain recognition and popularity among researchers in the field. Furthermore, studies have shown that it may take at least two to three years after publication for papers to accumulate enough citations for reliable bibliometric consideration (22,23).

Looking at the top 100 cited articles in the ten years prior to our study period, peaks in citation emerged in 2006, and 2008, which may lead to the assumption that influential publications precede or follow scientific breakthroughs in the field, since that period preceded the publication of a series of randomized controlled trials between 2005 and 2007 which shed the light on male circumcision as an effective intervention for HIV prevention. Following that, WHO and UNAIDS issued joint recommendations highlighting the potential efficacy of male circumcision for

HIV prevention (24,25).

The peak in publication numbers for our study period was observed in 2011 (22%) and for the whole period between 2010 and 2013. This period concurs with several shifts in HIV control. First, following the introduction of highly active antiretroviral therapy (HAART) in 1996 and the presentation of preliminary results at the 2006 International AIDS Conference showing a decrease in the number of HIV diagnoses as HAART use increased (26), Montaner *et al*. [2010] provided strong evidence of HAART use as a method of reducing the number of new infections (27).

During the same time that treatment as a preventive measure for new infections was making a significant contribution to HIV control, patient disengagement remained a problem. Gardner *et al*. [2011] proposed a comprehensive model of ongoing patient care that included encouraging testing, treatment, and ensuring adherence with the goal of achieving undetectable viral load (28). This concept also known as "care cascade" is currently still at the heart of HIV control under the UNAIDS 90-90-90 strategy which aimed for 90 percent of people living with HIV to be diagnosed, 90 percent of those diagnosed to be on treatment, and 90 percent of those on treatment to have an undetectable viral load by 2020 (29). An undetectable viral load had previously been associated with a reduction in HIV transmission in the 2008 Swiss Statement (30), and despite initially facing controversy and being disputed as lacking tangible evidence, it was later supported by the famous HPTN 052 (17) and PARTNER (31) studies published in 2011 and 2015 respectively and showing evidence that ART significantly reduced risk of HIV transmission. According to our findings, Cohen *et al*. (17) publication of the HPTN 052 Study is the most cited in the last ten years. During the same time period, other studies focused on the potential benefits of early versus late ART start in different HIV patient groups (32,33). In 2015, the START study, led by Lundgren *et al*., concluded that starting ART in HIV-positive adults with a high CD4+ count provided significant benefits over starting such therapy in patients with a low cell count (34).

The complexity here is that, despite the fact that several publications have laid the groundwork for major shifts in HIV control and are expected to have greatly inspired and been cited by other researchers, the citations do not reflect such influence. As a result, it is prudent not to rely solely on the number of citations as a measure of a publication's influence and to interpret results with caution.

The most frequently covered topics in the top-cited articles in the last ten years have been those related to ART use in HIV-negative people, a concept known as pre-exposure prophylaxis (PrEP). This includes the CAPRISA004 trial, which used a vaginal gel containing Tenofovir (35) and the iPrEX study recommending the use of Truvada to reduce the risk of HIV among HIV-negative adults (36). The topics of vaccine and neutralizing antibodies also emerged as particularly frequent. Burton DR, Mascola JR, and Kwong PD were the most productive authors during our study period, with a common focus on HIV vaccine strategies research, particularly through antibody neutralisation; they worked together on several articles that are currently on the list of the most cited publications (37,38) and should be closely followed for HIV vaccine updates.

The most productive authors were affiliated to institutions based in USA with the Scripps Research Institute and NIAID at the top. The University of the Witwatersrand in South Africa and Chiang Mai University in Thailand were the only non-American institutions in the top ten with a significant contribution to HIV/AIDS research. This supports Falagas *et al*. recommendation's that developing countries with a high burden of infectious and tropical diseases increase and strengthen their research capacity and collaboration networks within and outside the region in order to achieve better knowledge dissemination through international level publications (39).

Nearly one-third of the top-cited articles came from the United States of America, which is a common finding in studies on infectious diseases such as malaria (40) and tuberculosis (21) but also in other medical fields such as breast cancer research (41) and surgery (42). Despite the fact that the Sub-Saharan Africa region has the highest HIV/AIDS burden (43), it is clear that, with the exception of South Africa, the remaining countries in the region had minimal involvement and only collaborated with institutions located in developed countries. That can be explained not only by a critical lack of adequate research capacity and infrastructure but also by the lack of funds which are often required to publish in high-end journals with high impact factor, given the fact that in 2019, the 15 countries with the lowest gross domestic product (GDP), a tool commonly used for comparison of national economies on the international market, were located in Sub-Saharan Africa (44).

It has been argued that an impact factor for a journal does not always accurately represent the quality of the articles it publishes. However, it is already a widely used technique for

determining a journal's impact (45). In this study, we found a positive relationship between the citation times and the impact factor of the journal of publication. Nonetheless, the association with journal quartile, an alternative journal impact metric was non-significant although 94 percent of the publications in the 100 most cited were published in Q1 journals, and the vast majority of the top articles were published in well-known non-topic-specific medical journals with high impact factors such as *The New England Journal of Medicine*, *Science*, *Nature*, and *Lancet*, among others. There were no African journals on the list, raising the question of whether the findings and recommendations made in these top-performing studies are easily accessible to professionals in the countries where that knowledge is most needed.

Julien JP had the highest bibliographic coupling strength among the authors in our analysis. Using the same method, the NIAID ranked first among institutions and was one of the top three funding agencies, alongside the US Department of Health and Human Services and the National Institutes of Health (NIH). According to the bibliographic coupling, two South African institutions, the University of Witwatersrand and the University of Cape Town, were among the top ten.

Limitations

There are some weaknesses to the study that should be acknowledged. The first is the fact that the publications in this study were retrieved from the Web of Science database, which is the world's largest database, however, other well-known databases, such as Scopus or PubMed, were not explored this time, despite the fact that they could have enriched our findings. Moreover, because this study only included articles published after 2010, it excludes several other seminal articles published prior to 2010 that were more frequently cited and paved the way for those included in this study. Besides, because the time span for this study's publications is recent, some relevant and prominent articles published more recently might have not made it to the top 100 most cited articles since they did not have enough time to accumulate the citations compared to older ones.

Finally, while the data analysis in this study aimed to be objective and comprehensive, the methods used were focused on the level of citations, which is not always a good indicator of quality; assessing scientific quality would necessitate taking into account more factors than the citation impact of publications. Citation frequency only reflects the overall attention paid to publications, which can be influenced and skewed by factors other than their quality. Self-citation, funder's influence, citation of articles involving prolific or famous researchers, citation of previously highly cited articles, and so on are all common factors. As a result, all of the findings presented should be interpreted in light of these limitations.

Conclusions

The current study investigated the most recent trends in HIV/AIDS research worldwide by examining contributions in the 100 most cited articles over the last ten years. In terms of the number of publications, the United States played a major role. Mascola JR, Burton DR, and Julien JP as well as other researchers from institutions such as Scripps Research Institute and NIAID, Vaccine Research Center are great scientists to keep an eye on for future developments in antiretroviral therapy and vaccine research. *Nature* was the most prolific journal publishing HIV/AIDS research in recent years. We also found that the majority of influential articles were available in free full texts format and were mostly experimental studies such as clinical and randomised controlled trials investigating the timing of antiretroviral therapy, pre-exposure prophylaxis, and lab experiments on broadly neutralising antibodies in search of a vaccine. A positive correlation was found between the number of citations and the journal impact factor of the journal as well as the number of authors per publication.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/aoi-20-17). The authors have no conflicts of

interest to declare.

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

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