AFRICAN'S GROWING CONTRIBUTION TO ANTIRETROVIRAL DRUG RESISTANCE RESEARCH: BIBLIOMETRIC ANALYSIS OF 2004 TO 2024

Authors:
Azi, S.O.[1,2], Oshim, I.O.[1,3]*

Author Affiliations:
[1]Department of Medical Laboratory Science, Faculty of Health Sciences and Technology, David Umahi Federal University of Health Science, Uburu, Ebonyi State, Nigeria
[2]International Institute of Infectious Disease, Biosafety and Biosecurity, Uburu, Ebonyi State, Nigeria
[3]International Institute for Oncology and Cancer, Uburu, Ebonyi State, Nigeria

***Corresponding Author**
Ifeanyi Onyema Oshim
Department of Medical Laboratory Science,
Faculty of Health Sciences and Technology,
David Umahi Federal University of Health Sciences,
Uburu, Ebonyi State, Nigeria
oshimio@dufuhs.edu.ng

xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

ABSTRACT

Background: The threat of antiretroviral drug resistance developing and spreading is of greater public health importance as antiretroviral therapy is scaled up. Therefore, this study was designed to assess the growing contribution to Africa's antiretroviral drug resistance Research.

Materials and Methods: This investigation presents a bibliometric analysis of all research articles on antiretroviral drug resistance published from May, 2004 to May 2024, indexed in the PubMed database.

Result: The overall number of articles published was 1,601 papers, which has an average annual productivity of 123.15. South Africa accounted for the highest productive outputs with the total number of publications of 216, followed by the Switzerland (n = 56), Uganda (n = 52), Kenya (n = 18), Zimbabwe (n = 18), Netherlands (n = 15), Cameroon (n = 12), Botswana (n = 10), Malawi (n = 10), Zambia (n = 6), Ethiopia 6 (n = 6), and Nigeria (n = 5). Since 2015, publications on ARV Drug Resistance Research have fluctuated, with the highest number in 2020. Following that trend, the number of productive outputs dramatically reduced from 2021 to

2024. The University of Cape Town, South Africa, emerged as the leading institution in ARV Drug Resistance Research. In Nigeria, ARV Drug Resistance Research is the least prolific.
Conclusion: The overall trend in this field is characterized as decreasing yet evolving. This suggests that while fewer studies are being published overall, the focus of the research is shifting, likely toward these previously understudied areas rather than repeating established research.

Keywords: Antiretroviral drug, AIDS, Africa, Drug resistance

INTRODUCTION

The genetic diversity of Human Immunodeficiency virus (HIV) poses a significant challenge to the global management of HIV infection [1-7]. Even with the increasing availability of antiretroviral (ARV) medications, treatment failure is still a frequent issue among patients [8-10]. Besides, other factors such as; absence of plasma viral load and CD4 T lymphocyte count monitoring, drugs interactions, treatment disruptions due to stock shortages, and the use of substandard antiretroviral treatment regimens play role in the development of drug resistance in Africa [11-15].

Though, the emergence of drug-resistant variants of HIV-1 has been linked to mutations in the HIV-1 pol genes, which encode the key targets for major antiretroviral (ARV) medications [16, 17]. Evidences indicate that the effectiveness of ARV therapy is also affected by both the viral subtype and pre-existing mutations [18, 19]. Additionally, it has been suggested that the pathways leading to drug resistance might be influenced by pre-existing polymorphisms across different HIV-1 subtypes [20-22].

It had been reported that older age, ART regimen, lower CD4 count, higher viral load (VL) and inadequate adherence were predictors of virologic failure (VF), which is defined as 2 consecutive VL > 1000 copies/mL after at least 6 months of ART and intensive adherence counselling could lead to the accumulation of HIV drug-resistance-associated mutations [23-26]. Previous studies showed that ARVs status, CD4 <100 cells/mm^3, Viral subtype G is more likely to have Drug Resistance Mutation (DRM) than subtype Circulating Recombinant Form 2 (CRF02)_AG, frequent use of Non-nucleoside Reverse Transcriptase inhibitors (NNRTI), and ART duration are predisposing factors to Human Immunodeficiency Virus Drug Resistance (HIVDR) [27, 28].

The threat of HIV drug resistance developing and spreading is a greater public health concern as ART is scaled up [29-32]. World Health Organization (WHO) supports monitoring HIVDR, whether acquired or transmitted, to increase the efficacy of treatment programs for individuals living with HIV [33, 34]. Numerous studies suggest implementing specific measures in areas where the prevalence of NNRTI pre-treatment resistance is greater than or

equivalent to 10% [35]. These measures include initiating antiretroviral therapy (ART) with dolutegravir or selecting antiretroviral drugs based on a genotypic resistance test [12, 24, 36-42]. It is speculated that one in ten individuals starting antiretroviral therapy (ART) had a virus with one or more resistance mutations, with females two times more likely to be affected than males [1, 43, 44]. However, there is relatively limited information available from developing nations where non-B subtypes are more prevalent. In Africa, where the epidemic is primarily caused by non-B subtypes, studies on HIV drug resistance and polymorphisms have mostly investigated in resistance to non-nucleoside reverse transcriptase inhibitors (NNRTIs) and nucleoside reverse transcriptase inhibitors (NRTIs), while the resistance to protease inhibitors (PIs) has not been thoroughly examined [10, 45-48].

Bibliometric studies are valuable tools for assessing a specific discipline over a designated period, both socially and scientifically. It acts as an indicator of research activities in a particular field [49]. These studies analyze advancements and highlight research deficiencies. The performance evaluation of a chosen area of study is frequently conducted through bibliometrics and social network analysis (SNA). While bibliometric data provides fundamental metrics, social network analysis sheds light on the impact of social connections and interactions. This research aimed to examine the trends and contributions of Africa in the field of ARV Drug resistance mutation research. The results of this research are intended to assess progress, pinpoint gaps in Antiretroviral Drugs Resistance Mutation within Africa, and guide future research efforts and funding opportunities.

METHOD

We examined bibliometric data on Antiretroviral (ARV) drugs resistance mutations in Africa research published in PUBMED from May 13, 2004, to May 14, 2024.

The search was conducted on January 18, 2025. Utilizing advanced search features in PUBMED, we employed “MESH” terms for “HIV Antiretroviral drugs Resistance mutations” and “ AIDS Antiretroviral drugs Resistance mutations” and incorporated the following keywords: “HIV Antiretroviral drugs Resistance mutations” [Title/Abstract] OR “AIDS Antiretroviral drugs Resistance mutations” [Title/Abstract] OR “Acquired Immunodeficiency Syndrome Antiretroviral drugs Resistance mutations” [Title/Abstract] OR “Human Immunodeficiency Virus Antiretroviral drugs Resistance mutations” [Title/Abstract] OR “polymorphism of non-subtype B HIV strain” [Title/Abstract]AND “Africa” [Title/Abstract] OR “Sub-Sharan Africa” [Title/Abstract] We retrieved all relevant data according to the pre-established search criteria without restrictions on the type of articles. The collected data were used to calculate bibliometric measures. Since PUBMED does not maintain citation records, we obtained citation details for authors and articles through Google Scholar. We also re-conducted searches in PUBMED using the previously mentioned search terms along with “Retraction” and “Expression of

Concern." Furthermore, we searched the Retraction database with the location specified as Africa.

Screening protocol and criteria

Only articles specifically addressing Antiretroviral drugs Resistance mutations and polymorphism of non-sub type B HIV strains in Africa were considered for inclusion. Articles that mentioned Antiretroviral drugs in that manner but didn't focus on it were excluded, as were those that did not pertain to neither Africa nor Sub-Sharan Africa. There were no limitations regarding the type of article accepted. Duplicate articles were also eliminated. Two separate review teams among the authors independently conducted the article selection. Any disagreements were resolved through consensus between both groups.

Visualization of social network analysis

We employed VOS viewer (Center for Science and Technology Studies, Leiden University, The Netherlands) version 1.6.18 to create a visual representation of "ARV Drug resistance mutation", "Polymorphism non-subtype B HIV strains", "Africa" terminology and collaboration based on the data obtained from PUBMED.

Impact factor

The impact factor (IF) serves as an indicator of a journal's influence and was first established by the Institute for Scientific Information in Philadelphia, PA, USA, as a bibliometric measure. It is refreshed yearly in the Journal Citation Report (JCR) published by Clarivate Analytics, and the figure is frequently seen as a sign of prestige. We referenced the JCR data from 2024.

Authors/Institution participations index

We assessed the total scientific publications from 2004 to 2024 related to "ARV Drug resistance mutation", "Polymorphism non-subtype B HIV strains", "Africa". This reflects the count of documents authored by an individual or institution on the subject of Antiretroviral drugs Resistance mutations and polymorphism of non-sub type B HIV strains in Africa compared to the overall publications in that field.

Keyword analysis

We utilized keyword evaluation to confirm the trends of discussion and research regarding the "ARV Drug resistance mutation", "Polymorphism non-subtype B HIV strains", "Africa"

Co-authorship analysis

Co-authorship signifies the collaboration among authors who contribute to a specific area of research. The collaboration between authors can be observed through the co-authorship of publications (26). The co-authorship network diagram created by VOS viewer illustrates the collaborative social network within research domains.

Bibliometric mapping

Bibliometric mapping consists of two components: co-authorship mapping and co-occurrence mapping. Co-authorship highlights the collaborative efforts of authors within institutions contributing to the field of research, while co-occurrence

emphasizes the relationships among keywords.

The visualization of co-authorship network analysis employs the following interpretative keys: The size of the nodes or bubbles (circles) in the network signifies the frequency or quantity of documents associated with an author or institution. Furthermore, the lines or arcs connecting nodes represent the existence and strength of the co-authorship relationship. Lastly, the color of the node is determined by the VOS viewer clustering algorithm, which assigns colors based on the calculated similarity measure among them. As a result, it can be concluded that nodes sharing the same color are interconnected. Moreover, the proximity of two (2) nodes indicates the closeness of their relationship.

RESULTS

Publications output

We gathered a total of 1,601 papers publications, after excluding 65 publications that were either irrelevant to Africa (only mentioning Antiretroviral drugs briefly) or not directly focused on neither Antiretroviral drug resistance in Africa nor mutation in Africa. Among these, 54.3 % (N = 576) consisted of original articles, 22.4% (N = 238) were Clinical Trials, 22.1 % (N= 235) were narrative reviews, 14.7 % (N= 164) were Randomized Controlled Trial, 10.2% (N = 163) were Book and Document, 7.9 % (N = 84) were Comparative study, 5.6 % (N = 59) were Observation study, 4.3% (N= 46) were systematic reviews, and 2.5 % (N = 27) were Medical. Analysis Additional types of publications identified included Newspaper (0.4%), Expression of interest (0.3%), conference/Retracted paper (0.1%) (table 1).

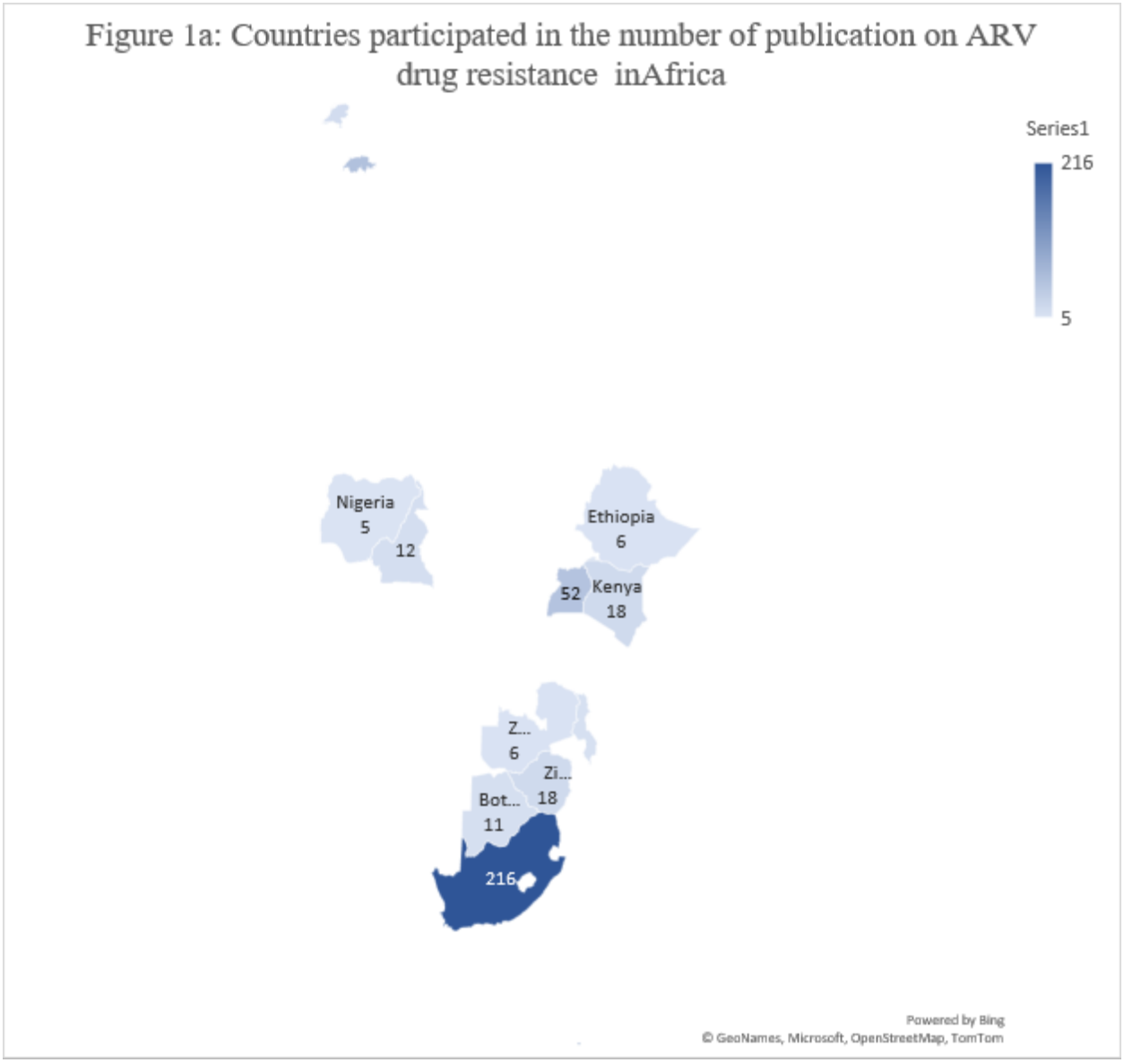
Table 1: Demonstration of Research out within study period with respect to article types

Type of Articles	Frequency (%)
Original articles	576 (54.3)
Clinical Trial	238 (22.4)
Narrow Review	235(22.1)
Randomized Controlled Trial	164(14.7)
Book and Document	163(10.2)
Comparative study	84(7.9)
Observation study	59(5.6)
Systematic Review	46(4.3)
Medical Analysis	27(2.5)
Newspaper	4(0.4)
Expression of Interest	3(0.3)
Clinical Conference	1(0.1)
Retracted paper	1(0.1)

Analysis of Africa with the highest publications

The current prevalence rate of publications on ARV Drug resistance in Africa and stratification based on countries showed the highest productive outputs in South Africa 216 (48.6%), Switzerland 56 (12.6%), Uganda 52 (11.7%), Kenya 18 (4.0 %), Zimbabwe 18 (4.0 %), Netherlands 15 (3.4%), Cameroon 12 (2.7%), Botswana 10 (2.5%), Malawi 10 (2.3%), Zambia 6 (1.4 %), Ethiopia 6 (1.4%), Nigeria 5 (1.1%) (Figure 1a and Figure 1b)

Figure 1a: Countries participated in the number of publication on ARV drug resistance inAfrica



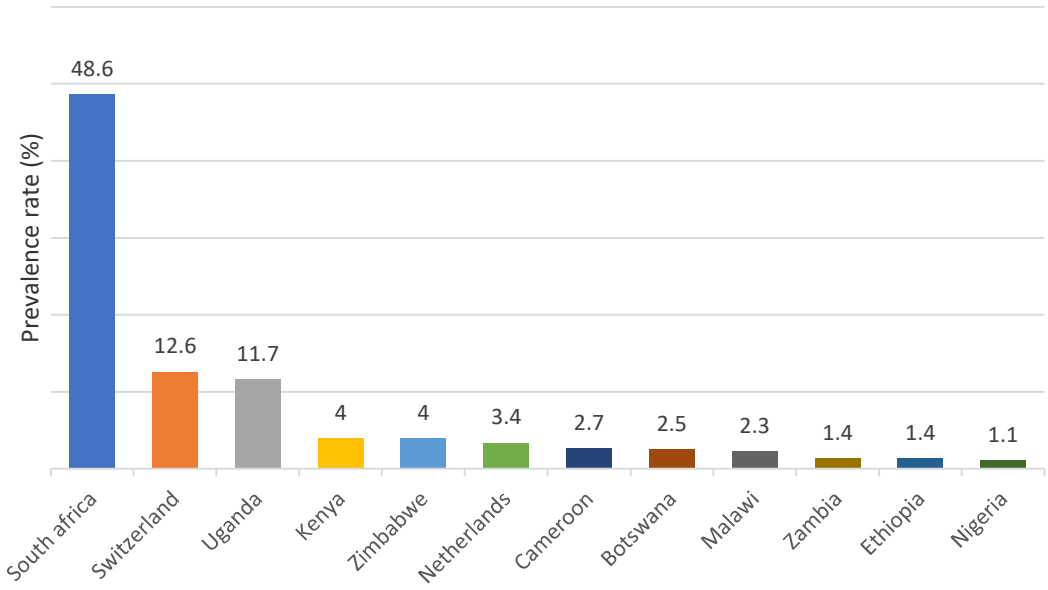
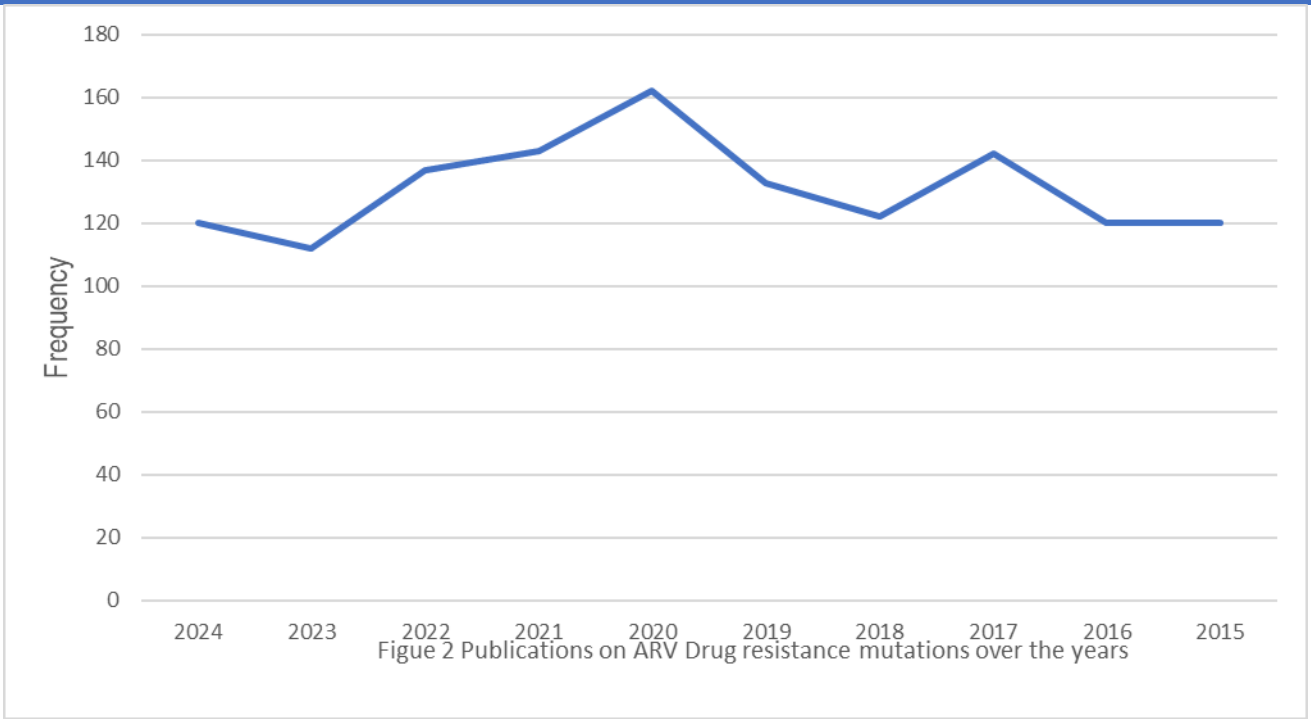


Figure 1b:Prevalence rate of countries participated in publications on ARV Drug resistance

It is speculated that there was a scarcity of publications on ARV Drug resistance in Africa from 2004 to 2014 until when 120 publications were released in 2015. Following that trend, the output of ARV Drug resistance in Africa -related literature experienced a slow increase until 2020, when there was a dramatic rise of over 40 times. Since then, the pace of research has been maintained to the initial publication, with a steady output of at least 120 publications annually after 2023 (figure 2)



Figue 2 Publications on ARV Drug resistance mutations over the years

Evaluation of the distribution of articles based on author count

Our findings indicated a wide range in the number of authors per publication, from single-author to those with more than 4 authors. Additionally, the results revealed that over 90% (n = 1726) of the published papers were produced through collaboration more than 4 authors (Table 2).

Table 2: Distribution of articles based on Author number

Number of Authors	Number of Publications
1 author	26(1.3%)
2 authors	72(3.7%)
3 authors	105(5.4%)
> 4 authors	1726(89.6%)

Evaluation of the institutions with the highest productivity in ARV Drug resistance mutation in Africa research

The institutions in Africa with the highest productivity in ARV Drug resistance mutation in Africa. The University of cape town, cape town emerged as the leading institution (n = 42), followed closely by the University of the Witwatersrand, Johannesburg (n =36), Joint clinical research Centre, Kampala, (n = 22), University of Zurich, Zurich (n =17), among others. The top six institutions alone accounted for over 5% of the total published literature. It is significant that both the University of cape town, cape town and its associated university (University of the Witwatersrand, Johannesburg) are among the most productive institutions. Likewise, the Joint clinical research Centre, Kampala also feature on the list of top institutions.

Among the leading 20 institutions, there are 9 institutions found in South Africa, 5 institutions found in Switzerland, 3 institutions found in Uganda, 1 institution located in Cameroon, and other countries (Table 3)

Table 3: Top 20 most productive institutions in ARV Drug resistance mutation in Africa research

Participating institutions	Countries	No.of documents (%)
University of cape town, cape town	South Africa	42 (15.6)
University of the witwatersrand, johannesburg	South Africa	36 (13.3)
Joint clinical research centre, kampala,	Uganda	22 (8.2)
University of zurich, zurich	Switzerland	17 (6.3)
University of basel, basel	Switzerland	15 (5.6)
University of yaoundé i, yaoundé	Cameroon	14 (5.2)
University of kwazulu-natal, durban	South Africa	13 (4.8)
Africa health research institute, durban	South Africa	12 (4.4)
Mrc/uvri uganda research unit on aids, entebbe	Uganda	11 (4.1)
Right to care, johannesburg	South Africa	10 (3.7)
Hiv department, world health organization, geneva	Switzerland	9 (3.3)
stichting hiv monitoring, amsterdam	Netherlands	9 (3.3)
University of kwazulu-natal, durban	South Africa	8 (2.9)
Ndlovu research consortium, elandsdoorn	South Africa	8 (2.9)
University of bern, bern	Switzerland	8 (2.9)
Uganda virus research institute,entebbe	Uganda	8 (2.9)
Josha research, bloemfontein	South Africa	8 (2.9)
National health laboratory service, johannesburg	South Africa	7 (2.6)
Swiss tropical and public health institute, basel	Switzerland	7 (2.6)
Africa health research institute, kwazulu-natal	South Africa	6 (2.2)

Analysis of publications from sources with the most output

Table 4 illustrates the journals that have published the highest volume of research related to ARV Drug resistance mutation research in Africa. The top sources include PLoS ONE, AIDS Research Human and Retroviruses, Aids, Journal of Acquired Immune Deficiency Syndromes, Journal of Antimicrobial Chemotherapy, Lancet Infectious Disease, Clinical Infectious Disease, Antiviral Therapy, Journal of International AIDS Society, AIDS Reviews, HIV Medicine, Viruses, Pediatric Infectious Disease Journal, Current Opinion Virology, PLoS Med, Antimicrobial Resistance Infectious Control, Medicine (Baltimore), South African Medical Journal Pan African Medical Journal, Of these sources, five journals have an impact factor (JCR 2024). Three of them, Lancet Infectious Disease, Clinical Infectious Disease, Current Opinion Virology have an impact factor exceeding 5. Ten of the journals are based in United State of America while Five and four of the journals were published in United Kingdom and Africa respectively.

Table 4: Analysis of sources with the highest number of publications in Africa

Article Source	No of Document	Impact factor	Country of Origin	Abbreviation
PLoS One	160	2.9(2023)	USA	PLoS One,
AIDS Research Human and Retroviruses	136	N/A	USA	AIDS Res Hum Retroviruses
Aids	110	4.6 (2021)	USA	Aids
Journal of Acquired Immune Deficiency Syndromes	96	3.863(2018)	USA	Acq.Imm.Def.Syn
Journal of Antimicrobial Chemotherapy	91	5.2 (2023)	UK	J Antimicrob Chemother
Lancet Infectious Disease	80	36.4 (2024)	UK	Lancet Infect Dis
Clinical Infectious Disease	71	8.2(2024)	USA	Clin Infect Dis
Antiviral Therapy	50	1.3(2025)	USA	Antivir Ther
BMC Infectious Disease	50	N/A	UK	BMC Infect Dis
Journal of International AIDS Society	48	5.3(2020)	USA	J Int AIDS Soc
AIDS Reviews	46	0.5(2024)	Spain	AIDS Rev
HIV Medicine	32	3.0(2022)	UK	HIV Med
Viruses	30	4.0(2023)	Switzerland	Viruses
Pediatric Infectious Disease Journal	30	3.4(2023)	USA	Pediatr Infect Dis J
Current Opinion Virology	22	5.7(2024)	Netherlands	Curr Opin Virol
PLoS Med	20	10.5(2023)	USA	PLoS Med
Antimicrobial Resistance Infectious Control	18	4.6 (2023)	UK	AntimicrobResist Infect Control

Medicine (Baltimore)	17	4.2(2024)	USA	Medicine (Baltimore)
South African Medical Journal	16	3.0(2023)	South Africa	S Afr Med J
Pan African Medical Journal	15	0.9(2023)	Nigeria	Pan Afr Med J

Analysis of co-authorship among involved institutions

The collaborative network among institutions conducting ARV Drug resistance mutation research in Africa is depicted in Fig 3a and Fig 3b. The mapping criterion was established at a minimum of 5 collaborative efforts. Out of the 6139 institutions that met the criteria, only 66 (%) were interconnected through collaborations. The institutions with the highest collaboration totals include the Joint Clinical Research Centre, Kampala, (18 link strength), HIV Department, World Health Organization, Geneva (8 link strength), Africa health research institute, Durban (8 link strength), Institute of Medical Virology, University of Zurich, Zurich, Switzerland (15 link strength), Division of Clinical Pharmacology, University of Cape Town, South Africa (11 link strength), Center for the aids programme of Research in South Africa (13 link strength), Department of Molecular Medicine And Haematology, Johannesburg (14 link strength), University of Witwaterand Right to care, Johannesburg, South Africa (10 link strength), Desmond tutu, HIV centre, University of cape town, South Africa (15 link strength), and University of Basel, Basel, Switzerland (10 link strength) Among the notable collaborations of the Joint Clinical Research Centre, Kampala are: Division of Clinical Pharmacology, University of Cape Town, South Africa, Division of infection and immunity, University College, London, United Kingdom, Department of Molecular Medicine And Haematology, Johannesburg, National Health Laboratory Service, Johannesburg, South Africa, Stitching HIV monitoring, Amsterdam, the Netherland, Josha Research, Bloemfontein. Nonetheless, the strongest overall collaboration, with a link strength of 9, occurred between the Division of Infection and Immunity, University College, London, United Kingdom, and the Joint Clinical Research Centre, Kampala (Fig 3a and Fig 3b)

The leading first authors in ARV Drug resistance mutation in Africa research include Fokam J, Kityo C, Wallis CL, Kaleebu P, Moyo S, Ndembi N, Sigaloff KCE, Van zyl G, Manasa J, Hunt G, Aghokeng AF, and Steegen K. Out of the 20 authors listed, 11 are based in Nigeria while the remaining 9 are affiliated with institutions in the USA, Indonesia, United Kingdom, and France respectively (Table 5 and Table 6).

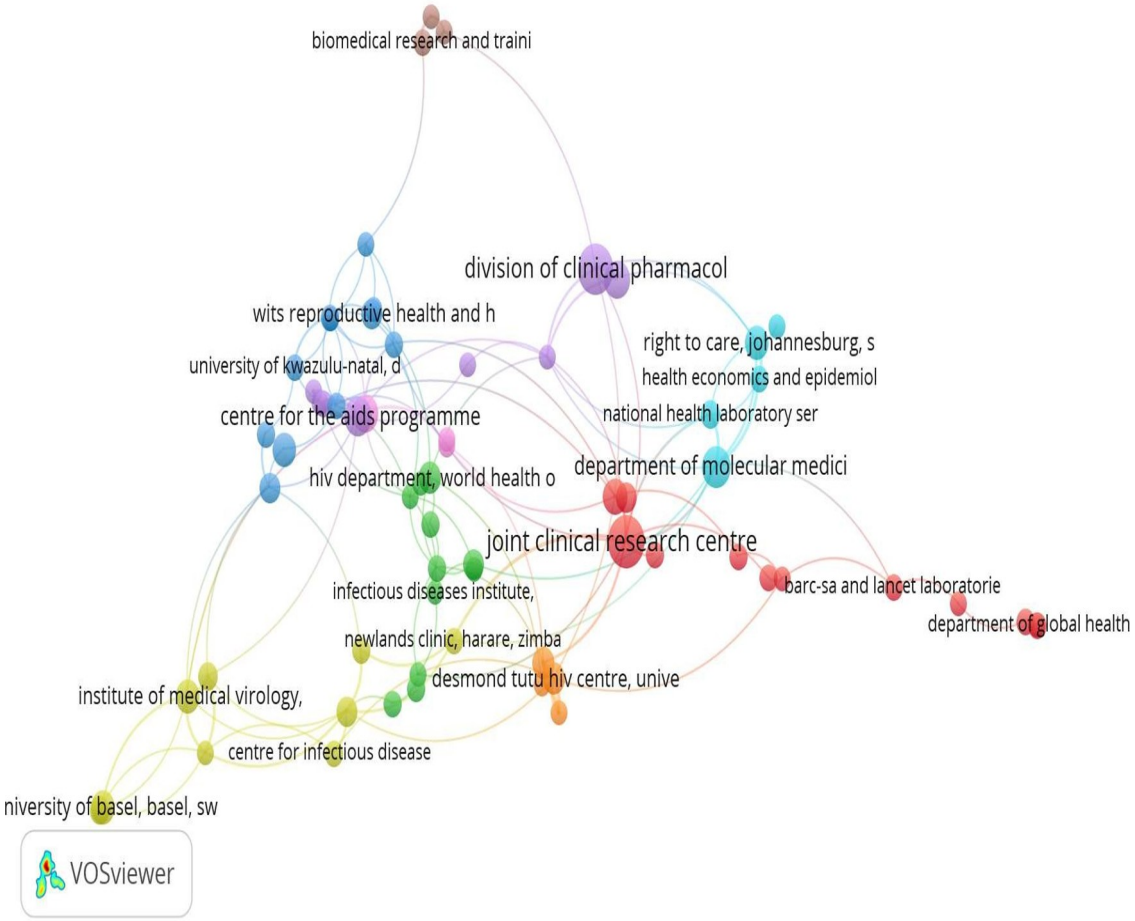


Fig.3a: Collaborative network among institutions publishing Drug resistance mutation related research in Africa

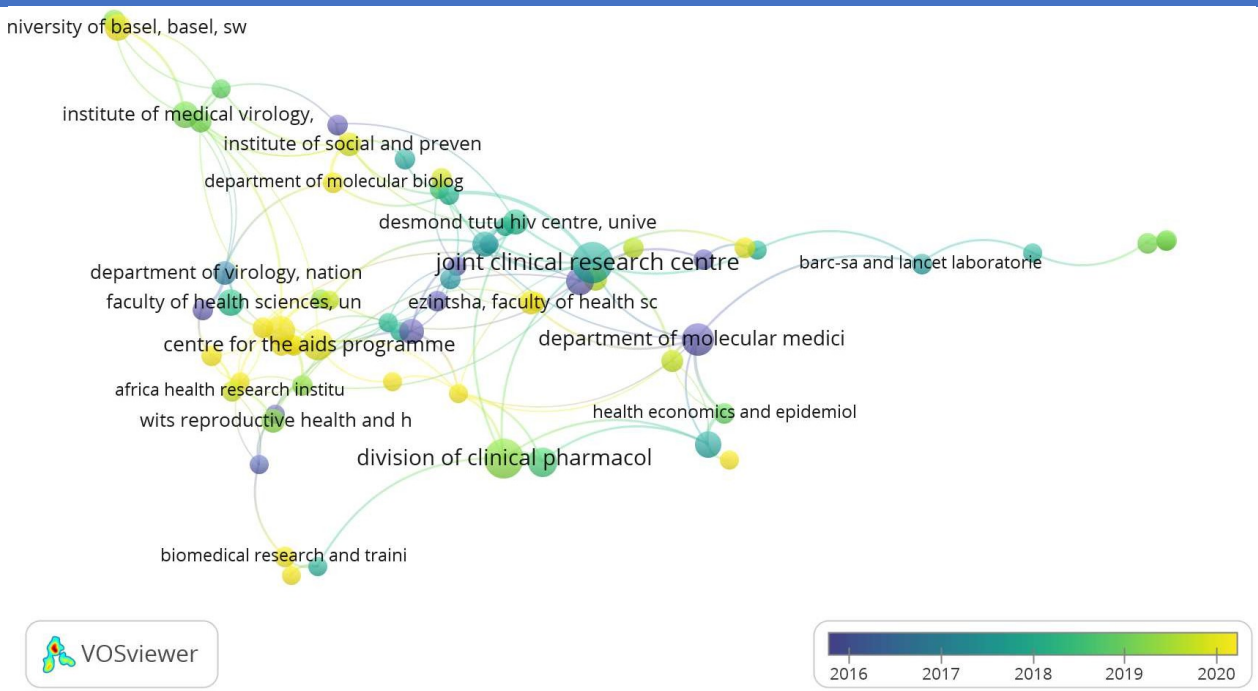


Fig. 3b: Overlay visualization of collaborative network among institutions publishing Drug resistance mutation related research in Africa

Table 5: Top 20 most productive Principal author (First author) in ARV Drug resistance mutation in Africa research

Author	h-index	Country	Affiliation	Documents (%)
Fokam, J	N/A	Cameroon	University of Buea,Buea, Cameroon	45(8.0)
kityo, C	N/A	Uganda	Joint Clinical Research Center	40 (7.1)
Hamers, RL	44	Indonesia	Oxford University Clinical Research	39 (6.9)
Wallis, CL	28	South African	Lancet Laboratories, Johannesburg	39 (6.9)
Jordan, MR (6.2)	N/A	USA	Tufts University and Tufts Medical Center	35
Kaleebu, P	47	Uganda	Uganda Virus Research Institute	32 (5.7)
Eshleman,SH	52	USA	Johns Hopkin University School of Medicine	32 (5.7)
Moyo,S	41	South African	Botswana-Harvard AIDS Institute partnership	30 (5.3)
Gupta, RK	63	United Kingdom	University of Cambrigde	27 (4.8)
Ndembi,N	37	Nigeria	Institute of Human Virology,Abuja	26 (4.6)
Sigaloff,KC	15	Netherlands	Amsterdam UMC	25 (4.4)
Van zyl, G	25	South Africa	University of Cape town and National Health Laboratory	24 (4.2)
Lockman,S	182	USA	Harvard University, Cambridge	23 (4.0)
Charpentier, C	47	France	University of Paris	23 (4.0)
Manasa,J	19	Zimbabwe	University of Zimbabwe	21(3.7)
Hunt,G	30	Switzerland	National Institute for Communicable Diseases	20 (3.5)
Aghokeng,AF	NA	Cameroon	Virology Laboratory CREMER-IMPM	20 (3.5)
Abrams, EJ	NA	USA	Columbia University Medical Center	20 (3.5)
Steegen,K	18	South Africa	National Health Laboratory Service	20 (3.5)
Meintjes,G	90	South Africa	University of Cape town	20 (3.5)

Table 6: Mapping the most influential Authors through co-Authorship collaboration Networks

Author		Number of documents	Total Link strength	Affiliation
Kityo, C	40	151		Joint Clinical Research Center
Fokam, J	45	133		University of Buea,Buea, Cameroon
Wallis, CL	39	117		Lancet Laboratories, Johannesburg
Moyo, S	30	108		Botswana-Harvard AIDS Institute
Chimukangara,B	18	66		National Institutes of Health (NIH)
Hunt, G	35	85		National Institute for Communicable Diseases
Charpentier,C	23	35		University of Paris
Meintjes, G	20	27		University of Cape town

Overall analysis of co-authorship among authors

Figure 4a and 4b illustrates the network and overlay visualization of co-authors comprised of individuals who have published at least 10 (ten) research articles related to ARV Drug resistance mutation and polymorphism non-subtype B strains in Africa research. The network consists of 145 nodes, 988 co-authorship links, a total link strength of 2902, and is divided into 8 clusters.

Each node symbolizes an author, with the size of the node indicating the author's activity or number of publications, while the connections between authors represent their collaborative relationships. Notably, 160 (19.80%) of the 10140 authors who satisfied the minimum requirements (at least 10 publications) were found to have no collaborative connections. Regarding total link strength, Kityo, Cissy (151; blue cluster), Fokam Joseph (133; Brown cluster), Wallis, Carole l (117; purple cluister), Moyo, Sikhulile (108; orange cluster), Chimukangara, Benjamin (66; yellow cluster), Hunt, Gillian (85; red cluster), Charpentier, Charlotte (35; green cluster), and Meintjes, Graeme (27; turquoise), were the leading authors in the network of ARV Drug resistance mutation in Africa research.

Analysis of the authors with the greatest impact based on collaborative co-authorship relationships (including both principal and co-author roles), the most productive authors were Fokam, Joseph (n= 45), Kityo, Cissy (n= 40), Wallis, Carole l (n= 39), Hunt, Gillian (n= 35), Moyo, Sikhulile (n= 30), Charpentier, Charlotte (n = 23), Meintjes, Graeme (n= 20), Chimukangara, Benjamin (n= 18), listed in that order. Kityo, Cissy and Fokam, Joseph appeared to be the most collaborative authors and achieved the highest total link strength, with affiliations to the Tufts University and Tufts Medical Center, USA; Uganda Virus Research Institute; Institute of Human Virology, Nigeria and Virology Laboratory CREMER-IMPM, Cameroon respectively (Table 7).

Interestingly, Kityo, Cissy (from Joint Clinical Research Center, Uganda) held the

2nd position for the most productive author based on principal author analysis (n = 40) and ranked as the 1st most collaborative author (n = 151), while Fokam, joseph secured the 2nd highest total link strength. Likewise, Wallis, Carole l and Moyo, Sikhulile maintained both lists as the 3rd and 4th most published principal author as well as the most collaborative author, total link strength (Tables 5 and 6).

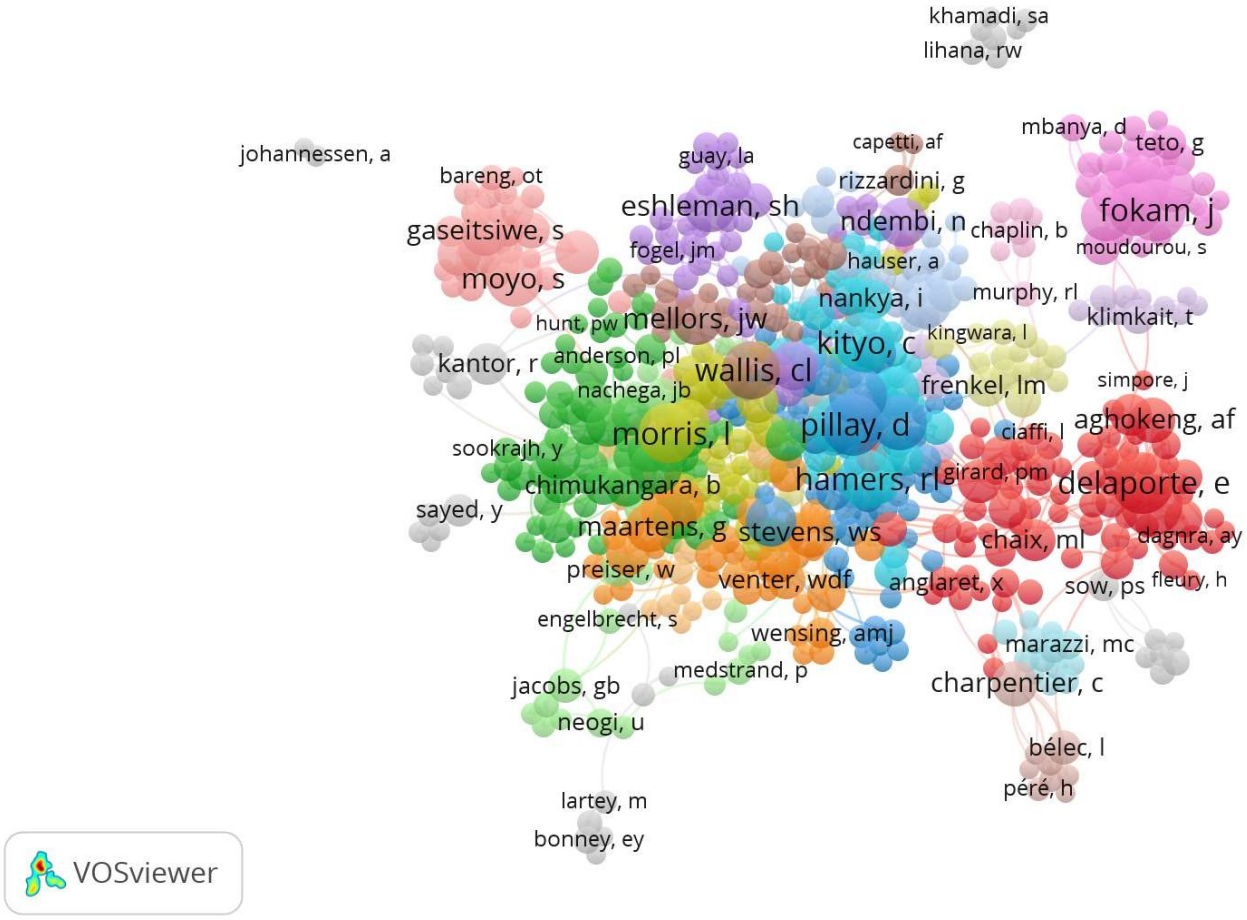


Fig. 4a: Co-authorship network among authors publishing Drug resistance mutation related articles in Africa

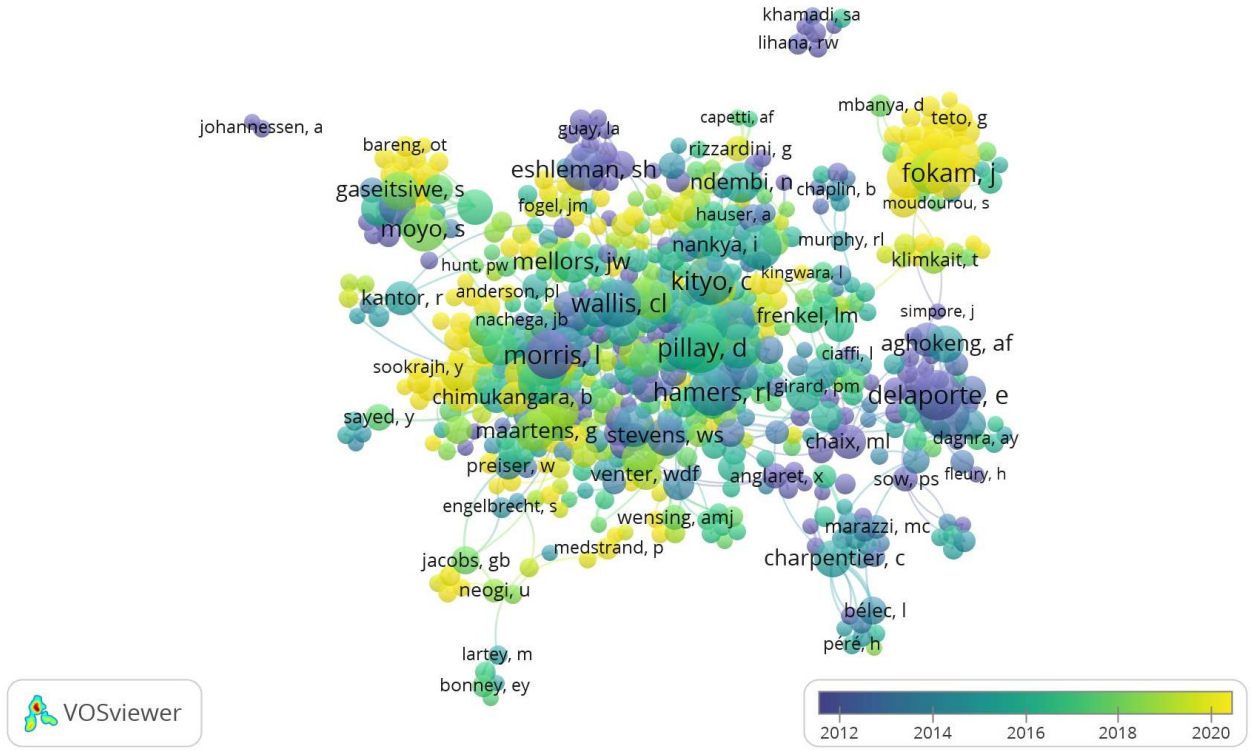


Fig. 4b: Overlay visualization of Co-authorship among authors publishing article per year related to drug resistance mutation research in Africa.

Analysis of keywords and hotspots

The hotspot analysis of author keywords used in ARV Drug resistance mutation related research conducted in Africa is displayed in Figure 5a and Figure 5b. The map contains keywords that appeared more than 5 times. For this, precisely 501 keywords were eligible. The keywords were categorized into 6 clusters by the network visualization. female (n=1224), human (n= 1849), Antiretroviral agent (n=383), CD4 Lymphocyte count (n= 267), risk factors (n=93), Medical Adherences (n=104), acquired immunodeficiency syndrome (n= 58), HIV (n=349) and PMTCT (n=6) were all represented by Cluster 1 (red). The two most prevalent keywords in cluster 1 were Female (n=1224), and human (n= 1849) respectively. Nevertheless, while Antiretroviral agent, CD4 lymphocyte counts, Risk factors and medical adherence were less common although there was a higher total link strength of Antiretroviral agent (4126), CD4 Lymphocyte count (3534), risk factors (1059), Medical Adherences (1276), acquired immunodeficiency syndrome (534), and HIV (3636) respectively.

Antiviral Drug resistance (n=1030), HIV-1 (1017), Mutation (n=446), Genotype (n=

327), Phylogeny (n=145), Missense mutation (n=101), DNA sequency analysis (n=125), genetic polymorphism (n= 53), Amino acid sequence (n=28), Molecular sequence data (n=128), HIV reverse transcriptase (n= 121), HIV protease inhibitor (107) were the main topics of Cluster 2 (green). Cluster 3 (blue) represented keywords related to molecular detection of antiretroviral drug resistance. The most common keywords in cluster 3 were Adolescent (n= 435), child (n=301), genotyping technique (61), HIV integrase (n= 48), Dolutegravir (n=28), Acquired drug resistance (n=5).

Cluster 4 (yellow) stood for mother-to-child transmission on antiretroviral drugs and drug resistance mutations -related terms. In cluster 4, the most common keywords were newborn infant (n= 84), nevirapine (n= 142), pregnancy (n= 184), pregnancy complications (n= 92), vertical infectious disease transmission (n=153), HIV 1-drug resistance (n=14), pretreatment drug resistance (n=9), High through put nucleotide sequence (n= 21), Drug Resistance mutations (n=11). In contrast, conduct in category 4 exhibited the strongest correlation (when combined with other terms).

Cluster 5 (purple) depicted keywords related to viral load and prevalence of young adult. In cluster 5, the most often occurring keywords were viral load (n=625) and young adult (n=368). Overall, the most used keywords were those that dealt with human, female related to hiv-1 and mutation (Fig. 5a).

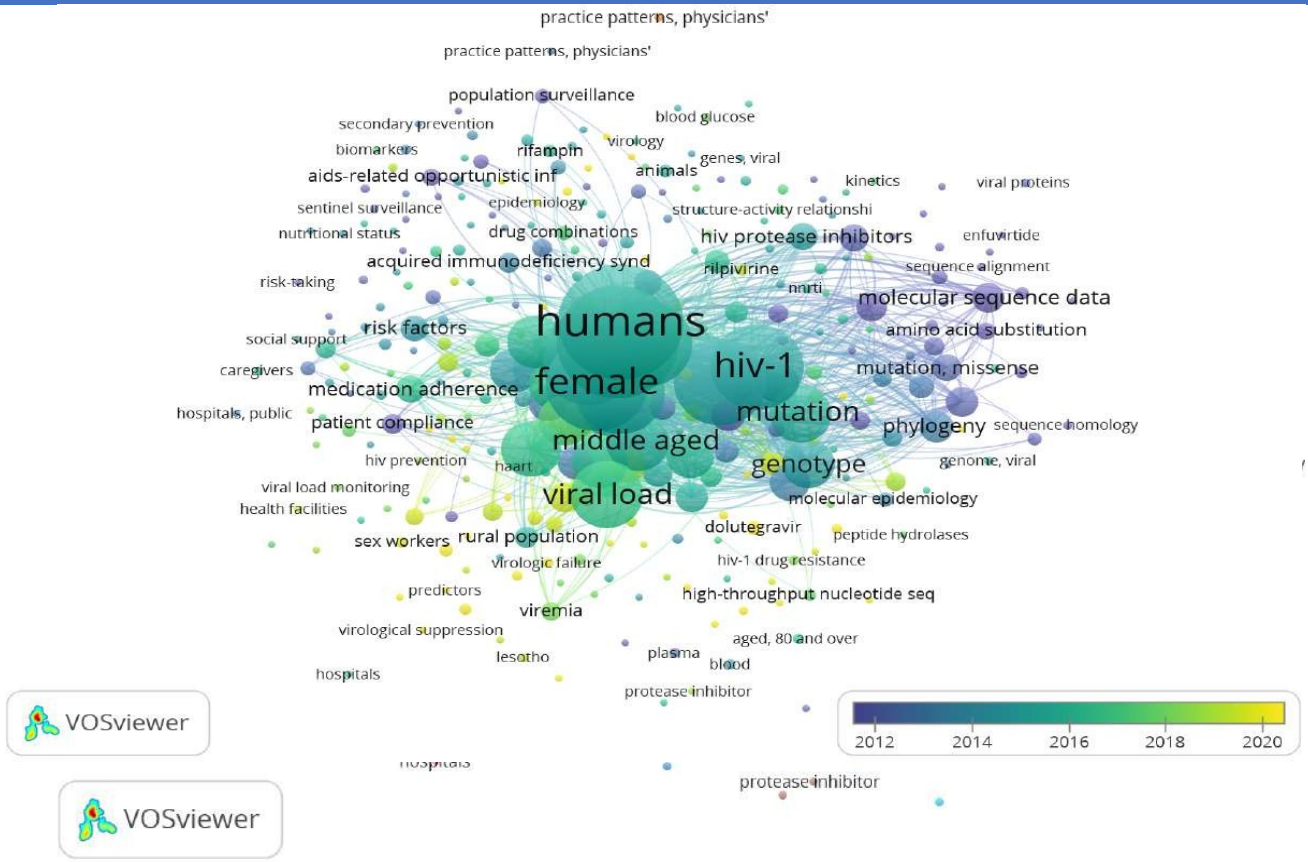


Fig. 5a: Network visualization of Keyword hotspots

Under overlay visualization, VOSviewer highlighted keywords included in the map with multiple colors based on the average year of keywords' appearance (Fig. 5b). Green keywords were more prominent than purple and yellow ones. In more recent years, keywords from yellow cluster emerged, indicating that Adherence, HIV integrase inhibitors, pyridines, antiretroviral therapy, HIV drug resistance, and 3-ring heterocyclic compound are now being discussed in ARV Drug resistance mutation related research in Africa (2012 to 2020) (Fig. 5b).

Research areas are still available for additional studies because keywords like virological failure, adolescent, HIV drug resistance, HIV integrase, high through put nucleotide sequencing, acquired drug resistance, drug resistance mutations, pretreatment drug resistance and dolutegravir did not provide any links.

Fig. 5b: Overlay visualization of Keyword hotspots

DISCUSSION

The trend of research output on ARV Drug resistance in Africa showed a very low output on ARV Drug resistance mutation in Africa from 2004 to 2014 until when a few publications were released in 2015. Following that trend, the output of ARV Drug resistance mutation in Africa -related literature experienced a slow increase until 2020, when there was a dramatic rise of over 40 times. Since then, there was a gradually decline in research output which continued to decrease until it maintained lag phase in 2024.

The prevalence rate of publications on ARV Drug resistance mutations in Africa based on countries indicated that South Africa recorded the highest productive outputs followed by Switzerland and Uganda while, Nigeria contributed to the lowest publications. Only the top five countries from the African regions—South Africa, Uganda, Kenya, and Zimbabwe—rank favorably on a global scale in terms of the number of publications concerning ARV Drug resistance mutation research, occupying the 1st, 2nd, 3rd, and 4th positions, respectively.

This study indicated that Nigeria nation is falling short compared to other countries and many African countries regarding the volume of publications on ARV Drug resistance mutation despite the high incidence rates of the disease in this country. For instance, a cross-sectional survey conducted in 2018 found that 19% of Nigerian adults with unsuppressed viral loads had evidence of drug-resistant mutations (DRMs) [50, 51]. The majority of DRMs observed conferred resistance to non-nucleoside reverse transcriptase inhibitors (NNRTIs) (17.6%) and nucleoside reverse transcriptase inhibitors (NRTIs) (11.2%) [50]. HIV drug resistance was associated with antiretroviral therapy (ART) experienced, longer duration on ART, and lower CD4 count [50]. However, a 2020 study published in the Journal of Acquired Immune Deficiency Syndromes reported a low prevalence of transmitted drug resistance among HIV-1-infected individuals in Switzerland [52, 53]. The study found that only 6.3% of participants had at least one drug-resistant mutation, with the majority being resistant to NRTIs (4.2%) [52, 53].

In addition, South Africa remains the most productive country in this research, together

with the highest prevalence rate of ARV Drug resistance mutation. Currently, a high prevalence of HIV-1 drug resistance mutations among individuals failing first-line ART in South Africa is reported [54]. The study found that 76.2% of participants had at least one drug resistance mutation, with the majority being resistant to NNRTIs (63.2%) and NRTIs (44.7%) [54].

Subsequently, Uganda ranked 3rd position in publication outputs and became 2nd position in the prevalence rate of ARV drug resistance mutation based on a study published in 2019 that reported a high prevalence of HIV drug resistance mutations among individuals failing first-line ART in Uganda [55]. The study found that 71.4% of participants had at least one drug-resistant mutation, with the majority being resistant to NNRTIs (57.1%) and NRTIs (40.0%) (55).

Kenya secured both 4th productive output country and the prevalence rate of ARV Drug resistance mutation according to a 2019 study published in the Journal of Acquired Immune Deficiency Syndromes reported a moderate prevalence of HIV-1 drug resistance mutations among individuals failing first-line ART in Kenya [56]. The study found that 44.1% of participants had at least one drug resistance mutation, with the majority being resistant to NNRTIs (34.6%) and NRTIs (23.1%) [57].

Unfortunately, the majority of the African countries that provided low publication outputs experienced a high prevalence rate of ARV Drug resistance mutation. Notably, a recent study found a high prevalence of HIV-1 drug resistance mutations among non-citizen adults living with HIV in Botswana [58, 59]. The study reported that 78.4% of participants had major HIV drug resistance mutations, with 83.3% of treatment-experienced individuals showing acquired drug resistance to any antiretroviral drug [60]. The most frequent drug resistance mutations were M184V (62.1%), V106M (41.4%), and K103N (34.4%) [60]. Furthermore, previous study reported a high prevalence of HIV-1 drug resistance mutations among individuals failing first-line antiretroviral therapy in Zambia [61]. The study found that 67.9% of participants had at least one drug-resistant mutation [62].

Limited institutions in the Africa have been previously integrated into ARV Drug resistance mutation research Centers such as University of Buea, Buea, Cameroon[35]; Joint Clinical Research Center, Uganda [18]; Lancet Laboratories, Johannesburg, South Africa [47]; Botswana-Harvard AIDS Institute partnership, South Africa[58]; Amsterdam UMC, Netherlands; University of Cape town and National Health Laboratory, South Africa; Institute of Human Virology, Abuja, Nigeria[50]; University of Zimbabwe, Zimbabwe; National Institute for Communicable Diseases, Switzerland[63]; Virology Laboratory CREMER-IMPM, Cameroon[64]; National Health Laboratory Service, South Africa ; University of Cape town, South Africa; discussed in various ARV Drug resistance mutation-related fields such as First line drugs [35-37], HIV drug resistance, integrase inhibitors [35], HIV Drug Resistance Mutations in Non-B Subtypes, Transmitted antiretroviral drug resistance[65], Protease inhibitor Resistance [37], HIV-1 drug resistance mutations in drug-naive patients[64].The research systems related to ARV drug resistance mutation in the

Africans are generally regarded as lacking productivity. South Africa stands out as the leading country in the number of publications related to ARV Drug resistance mutation research in Africa. One possible reason for this is the high prevalence of HIV/AIDS in the country, which has experienced numerous risk factors for HIV transmissions.

When compared to the global research output, the Nigeria has contributed less to the study of Drug resistance mutation. This discrepancy may stem from the generally struggling economies present in the low-income Economies countries, as indicated by the World Bank's online database [64]. Moreover, a high poverty-growth elasticity in most Africa, related to population size and gross domestic product (GDP) per capita, can result in insufficient funding for ARV Drug resistance mutation in Africa. Therefore, it is essential for governments in the African nations to prioritize ARV Drug resistance mutation research by providing increased manpower and resources to support it. Additionally, the developed world should be encouraged to establish more collaborative initiatives with Africa nations and to secure additional funding for research areas like virological failure, adolescent, HIV drug resistance, HIV integrase, high through put nucleotide sequencing, acquired drug resistance, drug resistance mutations, pretreatment drug resistance and dolutegravir are still available for further studies which did not provide any links.

Female, human, Antiretroviral agent, CD4 Lymphocyte count, risk factors, Medical Adherences, acquired immunodeficiency syndrome, HIV, Assessment of medical adherence, and PMTCT were all are the primary trending topics which reflected in the research emphasized in the most frequently cited publications for research in this field on a global scale and within the Africa [10, 35, 38-40].

Additionally, the main subjects of interest in the current study are Antiviral Drug resistance, Mutation, Genotype, Phylogeny, Missense mutation, DNA sequency analysis, genetic polymorphism, Amino acid sequence, Molecular sequence data, HIV reverse transcriptase, HIV protease inhibitor, genotyping technique, HIV integrase, virological failure, Tenofovir, Dolutegravir, Acquired drug resistance which provide significant and insightful perspectives on the publications and themes driving research advancements in this area over time[7, 9, 13, 31, 66-70].

The current study has some limitations that are typical of bibliometric analyses. Firstly, the criteria set by the PUBMED database dictate the outcome of the materials examined. Additionally, local journals that were not included in PUBMED during the study period could have been overlooked. It's possible that we missed ARV Drug resistance mutation research articles in Africa. if the authors did not use our specific search terms. Finally, since we were restricted to using PUBMED, a publicly accessible database, we may have overlooked articles that are indexed only in other databases. Nonetheless, we believe the findings accurately reflect the research trends in the area of study.

CONCLUSION

This research offers an original review of the existing studies related to drug resistance mutation in the Africa region and their connections to global findings. In conclusion, this study analyzed twenty years of drug resistance mutation publication outputs within the Africa. The results revealed that South Africa led in total publication numbers in the drug resistance mutation field as documented by PubMed during the analyzed timeframe, followed by the Uganda, Kenya, and Zimbabwe. Furthermore, the University of cape town, cape town emerged as the leading institution, followed closely by the University of the Witwatersrand, Johannesburg, Joint clinical research Centre, Kampala and University of Zurich, Zurich. Additionally, the developed world should be encouraged to establish more collaborative initiatives with Africa nations and to secure additional funding for research areas like virological failure, HIV drug resistance, HIV integrase, high through put nucleotide sequencing, acquired drug resistance, drug resistance mutations, pretreatment drug resistance and dolutegravir are still available for further studies which did not provide any links. Finally, the findings presented in this study through a novel approach depict a clear overview of the progress made in drug resistance mutation research and may assist relevant researchers and clinicians in guiding global drug resistance mutation in HIV/AIDS patients, particularly in African nations where the disease is prevalent.

Funding:

There was no specific funding for this Research

Availability of data and materials

The datasets produced and analyzed in this study are included within the article. The main data source, PUBMED, is publicly accessible.

Declarations

Ethics approval and consent to participate

This study utilized analyses based on secondary data, thereby not necessitating ethical clearance.

Consent for publication

Not applicable.

Competing interests

The authors state that there are no competing interests.

REFERENCES

1. Fokam J, Elat JB, Billong SC, Kembou E, Nkwescheu AS, Obam NM, et al. Monitoring HIV Drug Resistance Early Warning Indicators in Cameroon: A Study Following the Revised World Health Organization Recommendations. PloS one. 2015;10(6):e0129210.

2. Murphy RA, Bedesi PH, Perumal N, Gosnell BI, Hatlen TJ, Brijkumar J. Dolutegravir Resistance in African Programmatic Settings Among Patients With Failure of Dolutegravir-based ART. Open forum infectious diseases. 2024;11(7):321.

3. Cox SN, Wu L, Wittenauer R, Clark S, Roberts DA, Nwogu IB, et al. Impact of HIV self-testing for oral pre-exposure prophylaxis scale-up on drug resistance and HIV outcomes in western Kenya: a modelling study. The lancet HIV. 2024;11(3):e167-e75.

4. Wenk BM, Mbunkah HA, Nsanwe NN, Mbu ET, Besong LM, Sama BA, et al. Prevalence of integrase strand transfer inhibitor resistance mutations in antiretroviral-naive HIV-1-infected individuals in Cameroon. The Journal of antimicrobial chemotherapy. 2021;76(1):124-9.

5. Kanise H, van Oosterhout JJ, Bisani P, Songo J, Matola BW, Chipungu C, et al. Virological Findings and Treatment Outcomes of Cases That Developed Dolutegravir Resistance in Malawi's National HIV Treatment Program. Viruses. 2023;16(1).

6. Seatla KK, Choga WT, Mogwele M, Diphoko T, Maruapula D, Mupfumi L, et al. Comparison of an in-house 'home-brew' and commercial ViroSeq integrase genotyping assays on HIV-1 subtype C samples. PloS one. 2019;14(11):e0224292.

7. Masresha SA, Alen GD, Kidie AA, Dessie AA, Dejene TM. First line antiretroviral treatment failure and its association with drug substitution and sex among children in Ethiopia: systematic review and meta-analysis. Scientific reports. 2022;12(1):18294.

8. Arimide DA, Szojka ZI, Zealiyas K, Gebreegziabxier A, Adugna F, Sasinovich S, et al. Pre-Treatment Integrase Inhibitor Resistance and Natural Polymorphisms among HIV-1 Subtype C Infected Patients in Ethiopia. Viruses. 2022;14(4).

9. Aghokeng AF, Ngo-Giang-Huong N, Huynh THK, Dagnra AY, D'Aquin Toni T, Maiga AI, et al. Prevalence of pretreatment HIV resistance to integrase inhibitors in West African and Southeast Asian countries. The Journal of antimicrobial chemotherapy. 2024;79(5):1164-8.

10. Huruy K, Maier M, Mulu A, Liebert UG. Limited increase in primary HIV-1C drug resistance mutations in treatment naïve individuals in Ethiopia. Journal of medical virology. 2015;87(6):978-84.

11. Fokam J, Chenwi CA, Tala V, Takou D, Santoro MM, Teto G, et al. Pre-Treatment HIV Drug Resistance and Genetic Diversity in Cameroon: Implications for First-Line Regimens. Viruses. 2023;15(7).

12. Adawaye C, Fokam J, Kamangu E, Alio HM, Chahad AM, Susin F, et al. Virological response, HIV-1 drug resistance mutations and genetic diversity among patients on first-line antiretroviral therapy in N'Djamena, Chad: findings from a cross-sectional study. BMC research notes. 2017;10(1):589.

13. Fofana DB, Diarra H, Guindo I, Savadogo MK, d'Almeida M, Diallo FI, et al. Prevalence of HIV-1 Natural Polymorphisms and Integrase-Resistance-

Associated Mutations in African Children. Viruses. 2023;15(2).

14. Vandormael A, Rego F, Danaviah S, Carlos Junior Alcantara L, Boulware DR, de Oliveira T. CD4+ T-cell Count may not be a Useful Strategy to Monitor Antiretroviral Therapy Response in HTLV-1/HIV Co-infected Patients. Current HIV research. 2017;15(3):225-31.

15. Levison JH, Orrell C, Gallien S, Kuritzkes DR, Fu N, Losina E, et al. Virologic failure of protease inhibitor-based second-line antiretroviral therapy without resistance in a large HIV treatment program in South Africa. PloS one. 2012;7(3):e32144.

16. Billong SC, Fokam J, Penda CI, Mvilongo EA, Fodjo R, Messeh A, et al. [National profile of early warning indicators of HIV pharmaco-resistance in Cameroon]. The Pan African medical journal. 2020;37:374.

17. Teto G, Tagny CT, Mbanya D, Fonsah JY, Fokam J, Nchindap E, et al. Gag P2/NC and pol genetic diversity, polymorphism, and drug resistance mutations in HIV-1 CRF02_AG- and non-CRF02_AG-infected patients in Yaoundé, Cameroon. Scientific reports. 2017;7(1):14136.

18. Kityo C, Thompson J, Nankya I, Hoppe A, Ndashimye E, Warambwa C, et al. HIV Drug Resistance Mutations in Non-B Subtypes After Prolonged Virological Failure on NNRTI-Based First-Line Regimens in Sub-Saharan Africa. Journal of acquired immune deficiency syndromes (1999). 2017;75(2):e45-e54.

19. Hamers RL, Siwale M, Wallis CL, Labib M, van Hasselt R, Stevens WS, et al. HIV-1 drug resistance mutations are present in six percent of persons initiating antiretroviral therapy in Lusaka, Zambia. Journal of acquired immune deficiency syndromes (1999). 2010;55(1):95-101.

20. Bellocchi MC, Forbici F, Palombi L, Gori C, Coelho E, Svicher V, et al. Subtype analysis and mutations to antiviral drugs in HIV-1-infected patients from Mozambique before initiation of antiretroviral therapy: results from the DREAM programme. Journal of medical virology. 2005;76(4):452-8.

21. Kantor R, Smeaton L, Vardhanabhuti S, Hudelson SE, Wallis CL, Tripathy S, et al. Pretreatment HIV Drug Resistance and HIV-1 Subtype C Are Independently Associated With Virologic Failure: Results From the Multinational PEARLS (ACTG A5175) Clinical Trial. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2015;60(10):1541-9.

22. Geretti AM, Abdullahi A, Mafotsing Fopoussi O, Bonnett L, Fokom Defo V, Moudourou S, et al. An apparent paradox: resistance mutations in HIV-1 DNA predict improved virological responses to antiretroviral therapy. The Journal of antimicrobial chemotherapy. 2019;74(10):3011-5.

23. Gupta-Wright A, Corbett EL, Wilson D, van Oosterhout JJ, Dheda K, Huerga H, et al. Risk score for predicting mortality including urine lipoarabinomannan detection in hospital inpatients with HIV-associated tuberculosis in sub-Saharan Africa: Derivation and external validation cohort study. PLoS medicine. 2019;16(4):e1002776.

24. Gupta-Wright A, Fielding K, van Oosterhout JJ, Alufandika M, Grint DJ, Chimbayo E, et al. Virological failure, HIV-1 drug resistance, and early mortality in adults admitted to hospital in Malawi: an observational cohort study. The lancet HIV. 2020;7(9):e620-e8.

25. Chaplin B, Imade G, Onwuamah C, Odaibo G, Audu R, Okpokwu J, et al. Distinct Pattern of Thymidine Analogue Mutations with K65R in Patients Failing Tenofovir-Based Antiretroviral Therapy. AIDS research and human retroviruses. 2018;34(2):228-33.

26. Bateman M, Wolf A, Chimukangara B, Brust JCM, Lessells R, Amico R, et al. Adherence Measured Using Electronic Dose Monitoring is Associated with Emergent Antiretroviral Resistance and Poor Outcomes in People with Human Immunodeficiency Virus/AIDS and Multidrug-Resistant Tuberculosis. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2022;75(9):1489-96.

27. Alakija Kazeem S, Fadeyi A, Ogunmodede JA, Desalu O. Factors influencing adherence to antiretroviral medication in Ilorin, Nigeria. Journal of the International Association of Physicians in AIDS Care (Chicago, Ill : 2002). 2010;9(3):191-5.

28. Derache A, Wallis CL, Vardhanabhuti S, Bartlett J, Kumarasamy N, Katzenstein D. Phenotype, Genotype, and Drug Resistance in Subtype C HIV-1 Infection. The Journal of infectious diseases. 2016;213(2):250-6.

29. Fokam J, Chenwi CA, Takou D, Santoro MM, Tala V, Teto G, et al. Laboratory Based Surveillance of HIV-1 Acquired Drug Resistance in Cameroon: Implications for Use of Tenofovir-Lamivudine-Dolutegravir (TLD) as Second- or Third-Line Regimens. Viruses. 2023;15(8).

30. Hurt CB, Eron JJ, Jr., Cohen MS. Pre-exposure prophylaxis and antiretroviral resistance: HIV prevention at a cost? Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2011;53(12):1265-70.

31. Obasa AE, Mikasi SG, Brado D, Cloete R, Singh K, Neogi U, et al. Drug Resistance Mutations Against Protease, Reverse Transcriptase and Integrase Inhibitors in People Living With HIV-1 Receiving Boosted Protease Inhibitors in South Africa. Frontiers in microbiology. 2020;11:438.

32. Obeng BM, Bonney EY, Asamoah-Akuoko L, Nii-Trebi NI, Mawuli G, Abana CZ, et al. Transmitted drug resistance

mutations and subtype diversity amongst HIV-1 sero-positive voluntary blood donors in Accra, Ghana. Virology journal. 2020;17(1):114.

33. Fokam J, Takou D, Teto G, Nforbih SE, Kome OP, Santoro MM, et al. Pre-treatment drug resistance and HIV-1 genetic diversity in the rural and urban settings of Northwest-Cameroon. PloS one. 2020;15(7):e0235958.

34. Fisher RG, Smith DM, Murrell B, Slabbert R, Kirby BM, Edson C, et al. Next generation sequencing improves detection of drug resistance mutations in infants after PMTCT failure. Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology. 2015;62:48-53.

35. Fokam J, Billong SC, Bissek AC, Kembou E, Milenge P, Abessouguie I, et al. Declining trends in early warning indicators for HIV drug resistance in Cameroon from 2008-2010: lessons and challenges for low-resource settings. BMC public health. 2013;13:308.

36. Fokam J, Ngoufack Jagni Semengue E, Armenia D, Takou D, Dambaya B, Teto G, et al. High performance of integrase genotyping on diverse HIV-1 clades circulating in Cameroon: toward a successful transition to dolutegravir-based regimens in low and middle-income countries. Diagnostic microbiology and infectious disease. 2022;102(2):115574.

37. Fokam J, Takou D, Semengue ENJ, Teto G, Beloumou G, Dambaya B, et al. First case of Dolutegravir and Darunavir/r multi drug-resistant HIV-1 in Cameroon following exposure to Raltegravir: lessons and implications in the era of transition to Dolutegravir-based regimens. Antimicrobial resistance and infection control. 2020;9(1):143.

38. Boateng D, Kwapong GD, Agyei-Baffour P. Knowledge, perception about antiretroviral therapy (ART) and prevention of mother-to-child-transmission (PMTCT) and adherence to ART among HIV positive women in the Ashanti Region, Ghana: a cross-sectional study. BMC women's health. 2013;13:2.

39. Basson AE, Ntsala M, Martinson N, Tlale E, Corrigan GE, Shao X, et al. Development of phenotypic HIV-1 drug resistance after exposure to single-dose nevirapine. Journal of acquired immune deficiency syndromes (1999). 2008;49(5):538-43.

40. Etiebet MA, Shepherd J, Nowak RG, Charurat M, Chang H, Ajayi S, et al. Tenofovir-based regimens associated with less drug resistance in HIV-1-infected Nigerians failing first-line antiretroviral therapy. AIDS (London, England). 2013;27(4):553-61.

41. Hill A, McBride A, Sawyer AW, Clumeck N, Gupta RK. Resistance at virological failure using boosted protease inhibitors versus nonnucleoside reverse transcriptase inhibitors as first-line antiretroviral therapy--implications for sustained efficacy of ART in resource-

limited settings. The Journal of infectious diseases. 2013;207 Suppl 2:S78-84.

42. Aghokeng AF, Kouanfack C, Peeters M, Mpoudi-Ngole E, Delaporte E. Successful integrase inhibitor-based highly active antiretroviral therapy for a multidrug-class-resistant HIV type 1 group O-infected patient in Cameroon. AIDS research and human retroviruses. 2013;29(1):1-3.

43. Ajoge HO, Gordon ML, Ibrahim S, Shittu OS, Ndung'u T, Olonitola SO. Drug resistance pattern of HIV type 1 isolates sampled in 2007 from therapy-naive pregnant women in North-Central Nigeria. AIDS research and human retroviruses. 2012;28(1):115-8.

44. Inzaule SC, Jordan MR, Cournil A, Vitoria M, Ravasi G, Cham F, et al. Increasing levels of pretreatment HIV drug resistance and safety concerns for dolutegravir use in women of reproductive age. AIDS (London, England). 2019;33(11):1797-9.

45. Bansode V, Drebert ZJ, Travers SA, Banda E, Molesworth A, Crampin A, et al. Drug resistance mutations in drug-naive HIV type 1 subtype C-infected individuals from rural Malawi. AIDS research and human retroviruses. 2011;27(4):439-44.

46. de Felipe B, Pérez-Romero P, Abad-Fernández M, Fernandez-Cuenca F, Martinez-Fernandez FJ, Trastoy M, et al. Prevalence and resistance mutations of non-B HIV-1 subtypes among immigrants in Southern Spain along the decade 2000-2010. Virology journal. 2011;8:416.

47. Wallis CL, Mellors JW, Venter WD, Sanne I, Stevens W. Protease Inhibitor Resistance Is Uncommon in HIV-1 Subtype C Infected Patients on Failing Second-Line Lopinavir/r-Containing Antiretroviral Therapy in South Africa. AIDS research and treatment. 2011;2011:769627.

48. Boerma RS, Boender TS, Sigaloff KC, Rinke de Wit TF, van Hensbroek MB, Ndembi N, et al. High levels of pre-treatment HIV drug resistance and treatment failure in Nigerian children. Journal of the International AIDS Society. 2016;19(1):21140.

49. Doualla-Bell F, Gaseitsiwe S, Ndungú T, Modukanele M, Peter T, Novitsky V, et al. Mutations and polymorphisms associated with antiretroviral drugs in HIV-1C-infected African patients. Antiviral chemistry & chemotherapy. 2004;15(4):189-200.

50. Aliyu GG, Lawton JG, Mitchell AB, Abimiku AG, Jelpe T, Bassey O, et al. Prevalence of HIV drug resistance in Nigeria: results from a cross-sectional, population-based survey of Nigerian adults with unsuppressed viral load. AIDS (London, England). 2023;37(2):333-9.

51. Ndembi N, Murtala-Ibrahim F, Tola M, Jumare J, Aliyu A, Alabi P, et al. Predictors of first-line antiretroviral therapy failure among adults and adolescents living with HIV/AIDS in a large prevention and treatment program in Nigeria. AIDS research and therapy. 2020;17(1):64.

52. Abdissa A, Wiesner L, McIlleron H, Friis H, Andersen AB, Kaestel P. Evaluation of an immunoassay for determination of plasma efavirenz concentrations in resource-limited settings. Journal of the International AIDS Society. 2014;17(1):18979.

53. Amstutz A, Brown JA, Ringera I, Muhairwe J, Lejone TI, Klimkait T, et al. Engagement in Care, Viral Suppression, Drug Resistance, and Reasons for Nonengagement After Home-Based Same-Day Antiretroviral Therapy Initiation in Lesotho: A Two-Year Follow-up of the CASCADE Trial. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020;71(10):2608-14.

54. Chimukangara B, Kharsany ABM, Lessells RJ, Naidoo K, Rhee SY, Manasa J, et al. Moderate-to-High Levels of Pretreatment HIV Drug Resistance in KwaZulu-Natal Province, South Africa. AIDS research and human retroviruses. 2019;35(2):129-38.

55. Asio J, Watera C, Namuwenge N, Kirungi W, Musinguzi J, Mugagga K, et al. Population-based monitoring of HIV drug resistance early warning indicators in Uganda: A nationally representative survey following revised WHO recommendations. PloS one. 2020;15(4):e0230451.

56. Avihingsanon A, Hughes MD, Salata R, Godfrey C, McCarthy C, Mugyenyi P, et al. Third-line antiretroviral therapy, including raltegravir (RAL), darunavir (DRV/r) and/or etravirine (ETR), is well tolerated and achieves durable virologic suppression over 144 weeks in resource-limited settings: ACTG A5288 strategy trial. Journal of the International AIDS Society. 2022;25(6):e25905.

57. Abuogi L, Oyaro P, Wakjira G, Thomas KK, Scallon AJ, Mukui I, et al. HIV Drug Resistance Patterns and Characteristics Associated with Clinically Significant Drug Resistance among Children with Virologic Failure on Antiretroviral Treatment in Kenya: Findings from the Opt4Kids Randomized Controlled Trial. Viruses. 2023;15(10).

58. Bareng OT, Moyo S, Zahralban-Steele M, Maruapula D, Ditlhako T, Mokaleng B, et al. HIV-1 drug resistance mutations among individuals with low-level viraemia while taking combination ART in Botswana. The Journal of antimicrobial chemotherapy. 2022;77(5):1385-95.

59. Maruapula D, Ditshwanelo D, Pema MN, Bareng OT, Choga WT, Moraka NO, et al. Low prevalence of archived integrase strand transfer inhibitors resistance associated mutations in Botswana before the roll out of dolutegravir based first line antiretroviral therapy. Frontiers in microbiology. 2024;15:1482348.

60. Kotokwe K, Moyo S, Zahralban-Steele M, Holme MP, Melamu P, Koofhethile CK, et al. Prediction of Coreceptor Tropism in HIV-1 Subtype C in Botswana. Viruses. 2023;15(2).

61. Hamers RL, Kityo C, Sigaloff KC, de Wit TF. Pretreatment HIV-1 drug

resistance in Africa. The Lancet Infectious diseases. 2013;13(6):476.

62. Hamers RL, Sawyer AW, Tuohy M, Stevens WS, Rinke de Wit TF, Hill AM. Cost-effectiveness of laboratory monitoring for management of HIV treatment in sub-Saharan Africa: a model-based analysis. AIDS (London, England). 2012;26(13):1663-72.

63. Abana CZ, Sagoe KWC, Bonney EY, Maina EK, Aziati ID, Agbosu E, et al. Drug resistance mutations and viral load in human immunodeficiency virus type 2 and dual HIV-1/HIV-2 infected patients in Ghana. Medicine. 2019;98(6):e14313.

64. Aghokeng AF, Kouanfack C, Laurent C, Ebong E, Atem-Tambe A, Butel C, et al. Scale-up of antiretroviral treatment in sub-Saharan Africa is accompanied by increasing HIV-1 drug resistance mutations in drug-naive patients. AIDS (London, England). 2011;25(17):2183-8.

65. Aghokeng AF, Monleau M, Eymard-Duvernay S, Dagnra A, Kania D, Ngo-Giang-Huong N, et al. Extraordinary heterogeneity of virological outcomes in patients receiving highly antiretroviral therapy and monitored with the World Health Organization public health approach in sub-saharan Africa and southeast Asia. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2014;58(1):99-109.

66. Gupta R, Kemp S, Kamelian K, Cuadros D, Gupta R, Cheng M, et al. HIV transmission dynamics and population-wide drug resistance in rural South Africa. Research square. 2023.

67. Obasa AE, Ambikan AT, Gupta S, Neogi U, Jacobs GB. Increased acquired protease inhibitor drug resistance mutations in minor HIV-1 quasispecies from infected patients suspected of failing on national second-line therapy in South Africa. BMC infectious diseases. 2021;21(1):214.

68. Inzaule SC, Jordan MR, Bello G, Wadonda-Kabondo N, Mounerou S, Mbulli IA, et al. High levels of resistance to nucleoside/nucleotide reverse transcriptase inhibitors in newly diagnosed antiretroviral treatment-naive children in sub-Saharan Africa. AIDS (London, England). 2020;34(10):1567-70.

69. Fokam J, Inzaule S, Colizzi V, Perno CF, Kaseya J, Ndembi N. HIV drug resistance to integrase inhibitors in low- and middle-income countries. Nature medicine. 2024;30(3):618-9.

70. Kityo C, Mambule IK, Musaazi J, Sokhela S, Mugerwa H, Ategeka G, et al. Switch to long-acting cabotegravir and rilpivirine in virologically suppressed adults with HIV in Africa (CARES): week 48 results from a randomised, multicentre, open-label, non-inferiority trial. The Lancet Infectious diseases. 2024;24(10):1083-92.