Knowledge mapping of Nigeria’s scientific contribution to antimicrobial resistance research: A visualized investigation using VOS viewer and cite space

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ABSTRACT
Aim: To identify the contribution and impact of Nigerian authors, institutions, and journal sources, assess the knowledge base, detect the trends regarding antimicrobial resistance research through bibliometric analysis. Methods: Data from a query of antimicrobial resistance (AMR) articles in the dimensions database (PubMed included) were subjected to bibliometric analysis (1972–2022). Bibliometric indicators, topic networks were established, and topic trends were analysed by frequency, relevance scores, and trends over time. Results and conclusion: A total of 0.2% of the papers on AMR published worldwide were written by authors or institutions from Nigeria. In 2021, publications grew by 13.6%. The vast majority of publications (57.18%) were in the field of medical and health sciences, with 2428 papers. The top journal for AMR papers with at least one Nigerian institution affiliation was African Journal of Clinical and Experimental Microbiology, which published 1.8% of these papers. Antimicrobial stewardship, clinical and laboratory practices on AMR, public health implications, traditional and molecular methods, and phytomedicine and drug discovery were prominent areas of focus for Nigerian researchers. This study provided a comprehensive overview of the AMR research output, highlighting the need of increased research capacity to address the burden of AMR in Nigeria. Because Nigeria is overly reliant on conventional methods of discovery and development, innovation is essential for the future of antibiotics.

Introduction
Microbes can become resistant to antimicrobials through mutation or adaptation, which renders treatments ineffective. This phenomenon is known as antimicrobial resistance (AMR) [1]. The World Health Organization (WHO) estimates that AMR kills over 700,000 people across the globe yearly, an estimate that may well soar to 10 million by the year 2050 [2]. According to a needs assessment on antimicrobial use and resistance in Nigeria published in 2017 by the federal ministries of health, agriculture, and the environment, certain antimicrobial agents have increased resistance rates of 70% to 100% in certain states [3]. In a country where infectious diseases are a major cause of morbidity and mortality, Nigeria considers AMR a priority on the national public health agenda[3]. The Nigerian response to antimicrobial resistance led by the Nigeria Centre...
for Disease Control (NCDC) began in 2016 following a situational analysis that investigated common antimicrobial-resistant pathogens recovered from hospitals, animal sources, agricultural and environmental sources[4]. Overall, the National Action Plan (NAP) strives to address five key pillars in accordance with the WHO Global Action Plan on AMR [5]. The fundamentals entail boosting knowledge and awareness of AMR among health personnel and the general public; developing a one health surveillance system; strengthening prevention efforts, control, and biosecurity; promoting rational use of antimicrobials and access to quality medications; and conducting research into antimicrobial alternatives, new diagnostics, and drug discovery[4]. The problem of AMR in Nigeria is multisectoral. The ease with which antibiotics are available and can be purchased without the need for a prescription thrives in an environment where the antibiotic market is poorly regulated. The problem of improper disposal of expired antibiotics and leftover medicines by the general public, which mostly end up in conventional waste bins and dumps due to lack of awareness on the part of the users and weak enforcement on the part from regulatory authorities[6]. The problem of indiscriminate use impacts human health and animal welfare alike [7]. In the human health sector, many incidences of fever are addressed empirically with antibiotics[8]. Although a few antimicrobials are prescribed by a doctor, patients and their families frequently press healthcare professionals for antimicrobials and, in most cases, self-medicate with antimicrobials even for mild viral infections[9]. Even with the Nigerian veterinary council’s warnings against excessive use of antimicrobials in the animal health sector, several farmers habitually add antimicrobials into animal feed or water to promote growth and, in the case of poultry farming, to boost egg size to ensure better profit. Several farmers in the country use antimicrobials in post-harvest storage to preserve the yield[10]. As a result, human and animal waste, particles from crop sprays, discharge from health facilities, pharmaceutical companies, and farmlands carrying antimicrobial-resistant pathogenic microbes and antimicrobial residues find their way into the ecosystem[11]. It thus results in successions of negative impact on food production, bodies of water, as well as fish farms[11]. Despite increased awareness of antimicrobial resistance, the general situation is deteriorating, and the scientific community and Institutions have endured in research and publications to fashion newer antimicrobial peptides (AMPs), antibiotic combinations, and monitoring systems to effectively control AMR[12]. The amount of reliance on data increases with the growth of scientific publications and information technologies in healthcare. These big data raise various issues to be resolved by innovative big data analytics, like Knowledge mapping via bibliometrics.

Knowledge mapping is an assessment tool that blends concepts and techniques from mathematics, visuals, and other disciplines with bibliometric methods[13]. Cite space, and visualization of similarities (VOS) are the most popular bibliometric analysis tool for knowledge mapping via bibliometrics[14]. Knowledge mapping has been applied in many research fields[13, 15, 16]. To date, a knowledge mapping analysis of AMR research contributions and inclinations in Nigeria has remained hidden. This study aims to identify the contribution and impact of Nigerian authors, institutions, and journal sources, assess the knowledge base, detect the trends regarding antimicrobial resistance research through bibliometric analysis. Understanding Nigeria’s contribution to AMR research requires quantifying and mapping AMR-related publications. This study examines the research conducted by institutions in Nigeria using the Dimensions database as a foundation. This descriptive study focuses on bibliometric elements like international collaboration, subject area classification, active authors and institutions, journals and highly cited papers. In this study, we generated visualized knowledge maps of AMR research in Nigeria and analysed scientific hotspots, emerging/future trends, prolific authors and key research institutions of momentous research activities in AMR, which we hope will provide clarity about the nation’s priority for AMR research; and serve as reference for future collaborative networks.

Methods

Data acquisition and query criteria
Bibliographic data on antimicrobial resistance publications authored by a Nigerian researcher were retrieved from the Dimensions™ database on August 20th, 2022. The database is one of the most comprehensive for bibliometric and patometric analysis. It contains millions of publications cited over 1.6 billion times linked with patents, clinical trials, policy documents, datasets and grants [15, 17]. This database is completely inclusive of
PubMed, making it highly reliable. We used the search criteria: ‘antibiotics OR antifungal OR antibacterial OR antimicrobial resistance AND Nigeria’ to spotlight research articles published between 1972 and 2022. The search was not limited by language, and it included all accessible data sets. Both title and abstracts were search to ensure subject-specific outcome for the benefit of accuracy. Publications indexed in the database that featured a minimum of one author connected to a Nigerian institution, including a university or organization, qualified for inclusion.

**Data processing and parsing**
The dplyr and ggplot2 packages of R-studio v.4.1.2 (2022-02-16) was used to examine, parse and visualize bibliographic data. Imported raw files were cured of false positives and duplicates. Top 100 documents were arbitrarily selected per year and checked for presence of false positive results. A key term was ascribed to noun-phrases with similar meanings (e.g., “Antimicrobial sensitivity test”, and “AST” were merged to “antimicrobial susceptibility test”). Multiple or similar keyword occurrences in a publication were consolidated as a single count.

**Network mapping**
Network mapping was rendered with visualization of similarities (VOS) viewer software (Leiden University, Netherlands)[18]. This method adopts diverse clusters and color spectrum; the bubble size symbolizes the total frequency, the colours indicate the cluster type, and the lines of conjunct (straight or curved) illustrates connectedness [19]. Indices like, scientific production, mean citations, authors productivity, affiliation and countries, preferred journals and keywords, were used to assess the present and likely future trends of AMR research in Nigeria [20, 21]. The terms used in keyword clustering analysis were extracted from title and abstract fields of included bibliographic documents. Copyright statements and structured abstract labels were ignored in the analysis. Full counting method with minimum occurrence threshold of 20 (T≥20) was used. The top 60% of calculated relevance scores were used in the analysis.

**Citation burst and centrality index**
In order to determine the burstness and centrality index of the bibliographic components, cite space (Version 6.1.R3 Basic) was used[22]. The following limits were set: time span (1972 to 2022), years per slice (one), pruning (pathfinder and Pruning Sliced Networks), selection criteria (g-index), link strength (cosine) and scope (within slices) and other default settings.

Furthermore, the top cited articles were also extracted and sorted by field citation ratio. The field citation ratio (FCR) and relative citation ratio (RCR) are citation-based measures of an articles’ scholarly impact[23]. FCR was determined by dividing the number of citations received by an article by average number of citations received by articles published within the same year and fields of research (FOR) class. While the RCR is measured as the number of citations received by a paper adjusted to the citation count garnered by National Institute of Health (NIH) funded publications in the same research field and year[23].

**Results**
**Nigeria’s annual contribution in AMR Research**
Nigerian authors and institutions have played a key role in production of a total of 4,246 papers on antimicrobial resistance. As noted in figure (1), AMR-related research in Nigeria have shown an annual upward tendency that peaked in 2021(13.6%). Based on our research, there are 2,176,583 publications on AMR globally and Nigeria have contributed at least 0.2% of that number. Table S1 shows the distribution of scientific output by field of research; medical and health sciences (n = 2428, 57.18%), biological sciences (n = 806, 18.98%), agricultural and veterinary sciences (n = 409, 9.63%).

**Influential contributor analyses**
**1. Authors and journals contributing to AMR research**
A total of 14391 Nigerian authors were involved in AMR research. OKEKE IN published the most papers indexed in Dimension database (n = 31), followed by LAMIKANRA A (n = 28), and OLAYINKA BO (n = 27) (Figure 2a). By analysing the distribution of journals accepting Nigeria’s contribution in this field, we could accurately identify the main part of the academic research, and papers published in such journals. Figure 2b shows the top journals that published Nigeria’s contributions in AMR research. The number of publications in these journals was about 21.83% of the total number of contributions in this field. The number of articles published in african journal of clinical and experimental microbiology was the largest, with 75 articles, accounting for 1.8% of the total. Followed by PLoS One and african journal of medicine and medical sciences, with 50 articles each (1.2%). In terms of mean citation, American Journal of Tropical Medicine and Hygiene had the highest (33.3%). The top cited author by centrality is BAUER AW (1985) with centrality of 0.13 followed by Okeke IN (2000), with centrality of 0.07 (Figure 3a).
2. Contributions and cooperation network among institutions/organizations

The top ranked institutions/organizations in AMR research collaboration by centrality are University of Ibadan, with centrality of 0.33. The second one was Ahmadu Bello University, with centrality of 0.14. The third was University of Lagos, with centrality of 0.13. The 4th was International Institute of Tropical Agriculture, with centrality of 0.13. The 5th was Obafemi Awolowo University, with centrality of 0.10 (Figure 3b).

A co-authorship network map constructed based on authors (n = 1000) who had published at least five papers on AMR is shown in Figure (4). In the figure, authors that share the same colour space represent the same cluster. There were active collaborations in AMR research in Nigeria, especially among authors in the same cluster, such as OKEKE IN AND LAMIKANRA A (green), SOWUNMI A and ODUOLA AMJ (coffee brown), ILLIYASU G and HABIB AG (lime green), OLAYINKA BO AND ONAOLAPO JA (yellow) etc.

Authors with citation bursts are defined as those that are cited frequently over a while. Through detecting bursts, Table 1 lists the top authors of publications on AMR with the strongest citation bursts. COKER A., led the list with the maximum burst duration of 15 years and strength of 4.54, followed by OGUNSOLA F with a 14-year citation burst with 4.45 burst strength. NGWAI Y had a minimum burst duration of 1 year and the highest strength of 8.7. Recently published authors of AMR research with the strongest burst were NGWAI Y (8.7), OLAYINKA B (8.53) and OKEKE IN (7.27). This shows that their work may have formed a hot and leading topic. The table also show a list of the top cited authors of publications in AMR with the strongest citation bursts. AKO-NAI AK on the top of the list with the maximum burst duration of 18 years and strength of 6.5, followed by TENOVER FC A with an 8-year citation burst with 5.86 burst strength. OKEKE IN had the strongest burst 11.6 among cited authors.

Figure 5, depicts the cooperation network among Nigerian institutions/organizations on AMR research, where the nodes represent the institutions/organizations, and the sizes denote number of publications. The lines between two institutions/organizations denote that they cooperate. The density of the links of an institutions/organization indicates the cooperation degree. The denser of the lines, the more collaboration for one institutions/organization with other institutions/organization. From the figure, University of Ibadan (n =366, links = 1586), University of Lagos (n =218, links = 1079), University of Nigeria (n =172, links = 430), Ahmadu Bello University (n =152, links = 647), Obafemi Awolowo University (n =141, links = 566) and Nigerian Institute of Medical Research (n =132, links = 883) have more lines. Therefore, they have more cooperation with other institutions/organizations.

3. AMR research themes and trends in Nigeria

Keywords are the condensation and reaction to the main content of the article, which can reflect the hot topic and the development trend related to the research field. We ran keyword co-occurrence network analysis with VOS viewer and arrived with a graph with 953 nodes and 6 Clusters (Figure 6a). The keywords “Escherichia coli” and “Staphylococcus aureus” displayed the highest frequency of 881 and 540, respectively. Followed by the keywords “ESBL” (470), “Salmonella” (468), “tetracycline” (465) and “plasmid” (412). Thematic research group of focus by Nigeria authors are; antimicrobial stewardship (25.50%), clinical and laboratory (25.39%), public health implication (23.92%), traditional and molecular methods (16.79%) and phytomedicine and drug discovery (8.39%). Additional insights on the contents of the clusters are described below;

a) Antimicrobial stewardship theme-based cluster (red, n= 243 items, 25.50%)


b) Clinical and laboratory theme-based cluster (green, n= 242 items, 25.39%)


c) Public health implication theme-based cluster
(blue, n= 228 items, 23.92%)

d) Traditional and molecular methods cluster
(yellow, n= 160 items, 16.79%)

e) Phytomedicine and drug discovery themed cluster (purple, n= 80 items, 8.39%)

Figure 6b shows a Network map of the topics trend based on the most frequently used keywords. The current and future trends are highlighted in yellow.

Top cited articles with high field citation ratio (FCR) and relative citation ratio (RCR)
This study also revealed the top cited AMR articles indexed in Dimension database and sorted by FCR (Table 2). The FCR of the top 20 articles ranged from 4.09 to 36.54. The RCR ranged from 1.01 to 9.42. Table S2 shows the Nigeria’s top scholarly contributions to AMR indexed in Scopus database.
Table 1. Top 25 authors and cited authors in AMR research with the strongest citation bursts (sorted by beginning year).

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<thead>
<tr>
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<th>Begin</th>
<th>End</th>
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Top Cited Authors

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<th>End</th>
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Table 2. Top 20 scholarly contributions to AMR authored by a Nigerian (Sorted by FCR).

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Figure 1. Nigeria’s annual contribution to AMR publication growth.
Figure 2. The top authors and journals of AMR research in Nigeria.

Figure 3. Centrality of top Universities (a) and Authors (b). Notes: each node in the network represents cited Author/University, the number of papers published by the author is represented by the size of the nodes, and the stroked rings represent the centrality index.

Figure 2: The co-authorship map of 1000 authors of authors in AMR research domain (T≥5). Notes: The size of node reflects the author’s co-occurrence frequencies, the link specify the co-occurrence association between authors, and the same colour of node represent the same cluster. In the figure there are 74 clusters, 7063 links and a total link strength of 10240.
Figure 5. Institutional collaboration network: A minimum threshold of 20 (T = 20) documents per institution was set for inclusion. Notes: The size of the connecting lines, circles and color vary based on total link strength and number of publications and cluster respectively. Normalization method used was Lin/log modularity and full counting method.

Figure 6a. Keyword co-occurrence network and clusters of AMR research (T≥40, contains 1481 items, 14 clusters and 449516 links; max lines = 200, total link strength = 5333437). Notes: The node and word size reflects the co-occurrence frequencies, the link indicate the co-occurrence relationship, and the same color of node signify the same cluster.
Figure 6b. Network map of the trend topics according to the keywords used. Indicator shows the current publications from purple to yellow. The size of the circles represents the frequency of appearance as the keywords. The distance between the two circles indicates their correlation.

Discussion
Antimicrobial resistance (AMR) is an unfortunate result of antibiotic misuse and this study confirms that institutions in Nigerian have contributed at least 0.2% of the global research output on AMR. A marked rise in scientific output started in 2016 and peaked in 2021. Although data for 2022 was incomplete at the time of this study, evidence of a continuing rise in research output was apparent. In general, the number of AMR documents in the database has gradually increased, implying a significant scientific research output. A similar upward trend has also been reported in earlier bibliometric studies[24–26]. This parallels the increased burden of AMR in Nigeria. Further, the marked rise in scientific output coincides with Nigeria’s response to a national rise in the burden of antimicrobial resistance that led to the development of the NAP (2017–2022) that sought to address crucial risk factors in harmony with the WHO Global Action Plan on AMR. Connecting the gap between research institutions, pharmaceutical industries and legislators is pertinent because the role of research institutions does not end with the production of scientific data. Research should translate to development of actionable and sustainable policies and practices. These findings also highlight the importance of strengthening research capacity across Nigerian institutions.

The majority of the documents (57.18%) were in the field of medical and health sciences. This result is comparable to [25,26], where the majority of research output was in a related field. There is a need for more research output in all subject areas, as well as more multidisciplinary research, to advance the science of AMR.

The centrality of an institution/organisation reflects its recognition in the field of AMR research[27]. By analysing both the centrality and number of articles, Nigeria’s AMR research strength was observed to be primarily focused at universities, research institutions and NGOs. The University of Ibadan was Nigeria’s leading research institution in terms of scientific outputs and centrality. International Institute of Tropical Agriculture was the leading nongovernmental organization (NGO) in terms of centrality and Nigerian institute of medical research lead in scholarly output among research institutes.

We found that OKEKE IN ranked first in publication frequency and second to BAUER AW (0.13) in terms of centrality (0.07), indicating that the author was part of an influential core author group in the field of AMR research in Nigeria. Majority of Nigerian authors had a centrality index of less than one. This result indicated that more
researchers should participate actively in studies on AMR burden and contribute important scientific input to this field.

African Journal of Clinical and Experimental Microbiology was ranked as the top journal, publishing AMR documents with a minimum of one Nigerian institutional affiliation. The same journal was also the most cited in terms of published documents. Although Nigerian journals were among the top publishers of AMR research featuring at least a Nigerian author, there is a need to invest in strengthening local journals in Nigeria in order to achieve comparable indexing status and scientific standards to those of the world’s top journals.

The frontier in a research area depicts the current growth path of a discipline in bibliometrics, and thus the references in the frontier article represent the field’s intellectual core[28]. We described Nigeria’s scholarly core in the field of AMR by mapping references. Themes on antimicrobial stewardship, clinical and laboratory practice, public health implication, traditional/molecular methods, and phytomedicine and drug discovery are major research trends of Nigeria’s scientific community. These thematic distributions align with the observations of [29]. It is pertinent to boost research in all thematic areas of AMR research in the country to significantly facilitate processes that will slow down the spread of AMR in the country. Research themes exploring the use of molecular and artificial intelligence (AI) systems for AMR detection, surveillance, and drug discovery must be enhanced to confront rising bacterial resistance by significantly reducing the time taken to find new antimicrobials, improving diagnostic and treatment precision, as well as lowering costs [30].

A hotspot is a scientific topic of discussion in a series of documents which are inextricably connected to a particular time period[31]. The keywords are generalizations of the literature’s topic[31]. A high-frequency keyword analysis can be used to identify hotspots in the field of AMR research. From our results “Escherichia coli” and “Staphylococcus aureus”, “ESBL”, “Salmonella”, “tetracycline” and “Plasmid” were the most frequently used keywords. Nigerian researchers could conduct advanced studies based on the frequently discussed topics in this field.

An FCR range of 4.09 to 36.54 reflect the moderate to high scientific influence of Nigerian researchers in AMR research field. The theme of the top-cited documents in both the dimension and Scopus databases discussed are similar. The articles were focused on key AMR issues and determinants of human and animal importance relevant to the Nigerian and African population. Including; infectious diseases, Clinical and community health. Specifically, they highlighted the prevalence and/or Emergence of colistin resistance Klebsiella pneumoniae, Community-associated methicillin-resistant Staphylococcus aureus, carbapenem resistance, Enterobacteriaceae, multidrug resistant non-o1/non-o139 Vibrio cholerae, trimethoprim resistance gene dfrG in Staphylococcus aureus, plasmid-mediated quinolone resistance and beta-lactamases in Escherichia coli, CTX-M-15 extended-spectrum Beta-lactamase from Klebsiella pneumoniae etc. The identification of top-cited articles is useful as it reflects the diverse scope and health research fields that are of high interest to the readership of AMR, in addition to helping researchers identify the authors and institutions that have highly contributed to such influential studies for future research collaborations.

We are unlikely to witness a return to the heyday of antibiotic discovery, when numerous chemotypes were being regularly discovered and brought into clinical use in a short time frame. What does the antibiotic future hold? An assortment of approaches to infection treatment and prevention will have to be offered in the future. Anti-virulence strategies, small-molecule antibiotics, peptide-based antibiotics, bacteriophage monoclonal antibodies, probiotic strategies and vaccines are future trends in AMR and drug discovery.

Increasingly, the traditional Waksman platform returns recognized molecules, with recent breakthroughs in analytical chemistry, synthetic biology, genome mining, and genomics, the spectacular chemical diversity of nature can be taken advantage of by moving beyond the traditional Waksman platform. For instance, many environmental bacteria like actinomycetes harbour genetic programs to produce 20 to 40 natural products, while fungi can contain even more[32]. Avoiding actinomycetes bacteria is one strategy, for example. Some studies have identified 2 new antibiotics with new mechanisms of action, teixobactin, from the betaproteobacterium
Eleftheria terrae isolated from a soil specimen[33],
and darobactin, from the gamma proteobacterium
Photorhabdus khaini isolated from the gut of insect-
killing nematodes[34].

The Myers laboratory has developed
innovative modular pathways for the synthesis of
new therapeutic tetracycline, macrolide, and
lincosamide antibiotics, significantly expanding the
diversity of these compound classes well beyond
limits of natural biosynthesis[32]. Artificial
intelligence approaches could also mine chemical
libraries for therapeutic potential in order to develop
new synthetic scaffolds[30].

Despite the difficulties in bringing peptide-
based antibiotics to the clinic (most suffer from
haemolytic activity or nephrotoxicity), optimism
remains, and many AMPs are in various stages of
development, targeted toward a range of
pathogens[32].

Though naturally narrow in spectrum and
must be combined with antibiotics, Antivirulence
strategies aimed at abrogating pathogen virulence
are a future trend. Sibofimloc, which prevents
pathogenic E. coli from adhering to host epithelia is
entering phase 2 trials[35].

Adjuvants or antibiotic combinations, such
as β-lactamase inhibitors, can aid in the fight against
resistance. A combo of bedaquiline, pretomanid,
and linezolid, for instance, was recently approved to
treat extensively drug-resistant M. tuberculosis,
and more combinations are being studied[36].

In current history, the effectiveness and
narrow spectrum of phage have been acknowledged
as a valuable resource in the treatment of highly
drug-resistant infections. The concept of using
bacterial phages to treat drug-resistant infections is
becoming more appealing. Phage therapy is
increasingly being viewed as an alternative to
conventional antibiotics in medicine, spurring more
clinical trials, the majority of which are in phases
one and two[32].

There are currently only 3 approved
antimicrobial Monoclonal antibodies (mAbs), two
of which inhibit the virulence of Bacillus
anthracis (raxibacumab and obiltoxaximab), and
one of which inhibits the virulence of Clostridium
dificile (bezlotoxumab), reducing the incidence of
reoccurrence. Only bezlotoxumab withstood clinical
trials in its entirety[37], whereas the raxibacumab
and obiltoxaximab were approved under the animal
rule for bioterror organisms. But besides their
proven effectiveness, few are now in late-stage
clinical trials (phase 2, P. aeruginosa: panobacumab/Aerumab; phase 2, S.
aureus: omadenbamab/514G3 and; phase 3, S.
aureus: suvratuxumab and tosatoxumab[32].

Limitations

The data of this study were mainly derived
from the dimensions database on August 20th 2022,
and other literature databases like Web of Science,
Open Alex and Semantic scholar were not searched.
Therefore, we might not have been able to retrieve
all papers on this topic, and selection bias may have
been present.

Conclusion and recommendations

According to this research, Nigerian
institutions and organizations contributed meagerly
(0.2%) to AMR research output globally. There is a
pressing need to strengthen the country’s research
capacity and expedite the use of insights provided
by its scientists across all subject areas in order to
make a significant contribution to AMR response.
Although this response is not always tied to local
data but instead relies on adapting global policies
and those of global health organizations, developing
local data to better understand AMR trends is still an
excellent method for Nigeria to respond to health
emergencies. Nigeria’s potential to respond to health
issues needs to be strengthened, and investing in
research is one excellent way to do so.

Availability of data and materials

The raw datasets generated are accessible upon
demand to the corresponding authors
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Competing interest

We declare that we have no conflict of
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