

## The need for Africa to develop capacity for vaccinology as a means of curbing antimicrobial resistance

Akegbe, Hope; Onyeaka, Helen; Michael Mazi, Ifeanyi; Alex Olowolafe, Opeyemi; Dolapo Omotosho, Adeola; Olatunji Oladunjoye, Iyiola; Amuda Tajudeen, Yusuf; Seun Ofeh, Augustine

DOI:

[10.1016/j.jvacx.2023.100320](https://doi.org/10.1016/j.jvacx.2023.100320)

License:

Creative Commons: Attribution-NonCommercial-NoDerivs (CC BY-NC-ND)

*Document Version*

Publisher's PDF, also known as Version of record

*Citation for published version (Harvard):*

Akegbe, H, Onyeaka, H, Michael Mazi, I, Alex Olowolafe, O, Dolapo Omotosho, A, Olatunji Oladunjoye, I, Amuda Tajudeen, Y & Seun Ofeh, A 2023, 'The need for Africa to develop capacity for vaccinology as a means of curbing antimicrobial resistance', *Vaccine: X*, vol. 14, 100320. <https://doi.org/10.1016/j.jvacx.2023.100320>

[Link to publication on Research at Birmingham portal](#)

### General rights

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

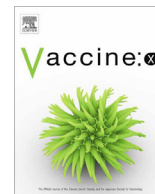
Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

### Take down policy

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact [UBIRA@lists.bham.ac.uk](mailto:UBIRA@lists.bham.ac.uk) providing details and we will remove access to the work immediately and investigate.



# The need for Africa to develop capacity for vaccinology as a means of curbing antimicrobial resistance



Hope Akegbe<sup>a</sup>, Helen Onyeaka<sup>b,\*</sup>, Ifeanyi Michael Mazi<sup>a</sup>, Opeyemi Alex Olowolafe<sup>a</sup>, Adeola Dolapo Omotosho<sup>c</sup>, Iyiola Olatunji Oladunjoye<sup>d</sup>, Yusuf Amuda Tajudeen<sup>d</sup>, Augustine Seun Ofeh<sup>e</sup>

<sup>a</sup> Department of Microbiology, Faculty of Life Sciences, University of Benin, Benin City, Nigeria

<sup>b</sup> School of Chemical Engineering, University of Birmingham, Edgbaston, Birmingham B15 2TT, UK

<sup>c</sup> Department of Cell Biology, Faculty of Life Sciences, University of Lagos, Nigeria

<sup>d</sup> Department of Microbiology, Faculty of Life Sciences, University of Ilorin, Ilorin, Nigeria

<sup>e</sup> Department of Microbiology, Faculty of Science, Delta State University, Abraka, Nigeria

## ARTICLE INFO

### Article history:

Received 9 November 2022

Received in revised form 8 March 2023

Accepted 26 May 2023

Available online 27 May 2023

## ABSTRACT

The high prevalence of infectious diseases in Africa, combined with weak healthcare systems, poor antimicrobial stewardship, and an unchecked drug supply chain, is steadily reversing the trend in the fight against infectious diseases in this part of the world, posing severe threats to antimicrobial resistance (AMR). AMR continuously evolves and threatens to undermine antimicrobial efficacy and undo advances against infectious diseases. This brewing pandemic is now recognized as a significant worldwide health danger, implicated in several cases of morbidity, mortality, and increasing healthcare costs. Vaccine technology has been proven to be the principal remedy to this imminent danger since it prevents microbial infections. However, since Africa cannot produce its vaccines, it relies on external sources and, as a result, it is significantly affected by vaccine nationalism, hoarding, and instabilities in global supply chains. This has further adversely impacted the ability of African governments to regulate rollouts, protect their citizens, and ultimately rejoin the global economy. This dependency is a severe challenge to Africa's health resilience, as it is unsustainable. Given the inevitability of potential global pandemics and the alarming incidences of multi-drug resistance infections reported daily, Africa must develop the capability to produce its vaccines.

The review utilized a systematic search of academic databases and grey literature, as well as a manual search of relevant reports and articles. In this review, we outline the public health threats and concerns that AMR poses to Africans, and the hurdles and advances achieved in vaccine development over the years. We also highlight possible strategies, particularly collaborative efforts, that will accelerate vaccine production and ease the strain of infectious diseases and antimicrobial resistance in Africa. Key findings indicate that Africa has significant gaps in its vaccine manufacturing and distribution capacity, with only a few countries having the ability to produce vaccines. Additionally, existing vaccine production facilities are often outdated and require significant investment to meet international standards. The review also highlights successful initiatives in Africa, such as the mRNA vaccine hub and the African Vaccine Manufacturing Initiative, which have demonstrated the potential for building local vaccine manufacturing capacity. The study concludes that Africa needs to prioritize investment in vaccine research and development, regulatory capacity, and infrastructure to build a sustainable vaccine manufacturing ecosystem.

Overall, this review emphasizes the urgent need for Africa to develop its vaccine manufacturing capacity to improve vaccine access and strengthen its ability to respond to future pandemics. The findings underscore the importance of collaboration between African governments, international organizations, and the private sector to build a resilient vaccine ecosystem in Africa.

© 2023 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

\* Corresponding author.

## Contents

Introduction . . . . .	2
Impact of infectious disease and antimicrobial resistance on Africa . . . . .	3
High mortality . . . . .	3
Loss of capital and human resources . . . . .	3
Increasing the virulence of existing diseases . . . . .	3
Vaccine- an efficient combatant against antimicrobial resistance . . . . .	3
Limiting the use of antimicrobial agents . . . . .	3
Lowering the emergence of resistant serotypes . . . . .	3
Providing immunity by a method of action that is less prone to cause resistance . . . . .	3
Providing immunity by a method of action that is less prone to cause resistance . . . . .	4
Directly targeting antimicrobial-resistant microbes or resistance-mediating factors . . . . .	4
Africa's current source of vaccines . . . . .	4
Impediments to successfully developing vaccine capacity . . . . .	4
High Start-Up and operation cost . . . . .	4
Human resources . . . . .	4
Source of raw materials . . . . .	4
Time factor . . . . .	5
Limited Partnership opportunities . . . . .	5
Recommendations for improving vaccine technology in Africa . . . . .	5
Fostering strong multilateral cooperation and collaboration between global scientists . . . . .	5
Building strong pharmacovigilance capacity in Africa . . . . .	5
Boosting research and development of vaccine development in Africa . . . . .	5
Strong African government commitment . . . . .	6
Decisively addressing the issue of vaccine hesitancy in Africa . . . . .	6
Careful application of technological innovation and advancement . . . . .	6
Understudying case studies of the successful vaccine development in other countries . . . . .	6
The benefit of successfully developing vaccine-manufacturing capabilities in Africa . . . . .	6
Security of quality vaccine supply . . . . .	6
Addressing the Africa-specific disease burden and efficiently dealing with pandemic diseases and outbreaks . . . . .	7
Socioeconomic, industry, and life science development/ Partnership opportunities . . . . .	7
Conclusion . . . . .	7
Authors' Contributions . . . . .	7
Consent of publication . . . . .	7
Funding . . . . .	7
Declaration of Competing Interest . . . . .	7
Acknowledgment . . . . .	7
References . . . . .	7

## Introduction

In the past, humanity was constantly plagued by infectious diseases, and their life expectancy was regulated by the activity of ubiquitous and active microscopic organisms. Treatment with antimicrobials alleviated the condition and gave hope to a somewhat dystopian future [1]. However, these antimicrobials had a significant limitation: a phenomenon known as antimicrobial resistance (AMR) [2]. AMR was initially described in Japan in 1956 when strains of *Shigella flexneri* resistant to streptomycin, tetracycline, chloramphenicol, and sulfonamides were isolated [1]. AMR has risen to epidemic proportions, with myriad pathogenic bacteria discovered to be antibiotic resistant. In a few scenarios, some bacterial species have acquired resistance to a plethora of extant antibiotics, and the diseases they cause are likely to become incurable if the situation persists. As a result, AMR is undoubtedly the most concerning emerging public health threat. AMR has now become a global epidemic, claiming over 700,000 lives per year globally, and is estimated to cost around 10 million lives and US \$100 trillion annually by 2050 [1,3]. AMR poses a significant problem to the health sector, as it hampers the effective treatment of a wide range of infectious diseases previously treatable with regular medications [4]. The World Health Organization suggested antibiotic resistance measures, which include infection prevention and control, strengthening healthcare systems, increasing antimicrobial stewardship, and developing novel medications

and vaccines [4]. Several authors have emphasized the potential usefulness of vaccines in preventing and combating infectious diseases as it reduces the consumption of antibiotics which is the major predisposing factor to antimicrobial resistance [4,5]. This was later seen in the case of the Pneumococcal Conjugate Vaccine (PCV), which resulted in the reduction of resistant *Streptococcus pneumoniae* in the vaccinated population, a phenomenon that conferred herd immunity on the general population [6]. In addition, vaccines can be used indefinitely with pathogens acquiring little or no resistance. As a result, they can be used to manage illnesses for a long time without becoming outdated [7]. This happens because vaccinations function prophylactically to prevent infections. In contrast, antimicrobials work therapeutically on an ongoing infection where microbes are actively growing and evolving, creating a selective pressure that induces the microbes to evolve to resistant versions [7]. Africa's success in terms of novel vaccine launches, eradication of vaccine-preventable diseases (VPDs), and decreased morbidity and death due to infectious diseases are not as impressive as other continents. According to the World Health Organization, a country is deemed self-sufficient when domestic output covers 90% of household consumption or the export/import rate exceeds one [8]. This is not the case in Africa, where inequitable resource distribution means that a significant proportion of neonates and children are at risk of potentially lethal vaccine-preventable infections. Africa has the highest infectious disease mortality rate but cannot make necessary vaccines to reduce mor-

tality, improve longevity, and promote economic growth [9]. Though the Global Alliance for Vaccine and Immunization (GAVI) has significantly aided in introducing new vaccines in Africa, its long-term viability is questionable, and new vaccines are scarce [9]. The population of developing countries is expected to reach 2.9 billion by 2100, with the Democratic Republic of the Congo, Ethiopia, Uganda, and the United Republic of Tanzania, leading the way [10]. In addition to this, the ongoing COVID-19 pandemic revealed Africa's weakness, as the continent relied utterly on Europe and America for its vaccine. The goal of this review is to identify the risks that antimicrobial resistance poses to Africans, highlight the gaps and opportunities for expediting vaccine development and reaffirm the urgent need for African countries to collaborate and improve self-sufficiency in vaccine production to reduce infectious disease transmission, health costs, and, as a result, morbidity, and mortality from infectious diseases.

#### *Impact of infectious disease and antimicrobial resistance on Africa*

The risk of AMR is increasing at an alarming rate, and the situation may exacerbate in underdeveloped nations due to widespread antimicrobial misuse [11]. In 2014, the World Health Organization (WHO) reported Africa and South East Asia as zones with no existing AMR surveillance and monitoring systems [12]. The paucity of quality data, particularly in Africa, is a major challenge that often leads to insufficient treatment regimens and do not completely eliminate pathogens implicated in infections [11]. From the few data sources available, it has been discovered that AMR has a lot of adverse effects on Africa.

#### *High mortality*

According to WHO, AMR will be implicated in over 4 million deaths in Africa by 2050, a figure behind only Asia [13]. Most of the countries in Africa are low and middle-income countries which increases the potential for AMR to cause increased morbidity and mortality. In 2019, antibiotic-resistant bacteria accounted for over 1.2 million deaths [13], and a recent survey indicates that about 24 deaths per 100,000 in Sub-Saharan Africa result from AMR [14]. This is due to the high prevalence of bacterial illness in developing countries, delayed reporting and treatment of infections, lack of access to standard diagnostic tools, and access to second-line or alternative antibiotics [15].

#### *Loss of capital and human resources*

It is estimated that emerging economies in Africa could lose up to 5 percent of the Gross Domestic Product (GDP) due to AMR. This could lead to a financial difficulty that is much worse than the 2008 world economic meltdown. Besides losing valuable human resources, AMR costs countries money on healthcare. Due to antibiotic resistance, hospitalized patients might need to stay longer in the hospital before recovery, which will cost more money [16].

#### *Increasing the virulence of existing diseases*

Killer infections, such as tuberculosis (TB), have developed resistance to life-saving antibiotics. On the other hand, malaria is implicated in the death of 3,000 African children every day and is resistant to several drugs it was once susceptible to. Since AMR makes even minor infections more difficult to treat, nations with weaker healthcare systems bear the brunt of the consequences of this global crisis. This results in higher healthcare expenses, longer hospitalization, and higher mortality [17,18].

#### *Vaccine- an efficient combatant against antimicrobial resistance*

The advancement of AMR poses a significant risk to modern medicine, and new approaches to tackling drug-resistant bacteria, such as the development of novel treatments, are desperately required [19]. Currently, it is difficult to find new, beneficial bioactive compounds with an optimum alignment of antimicrobial properties, drug metabolism, pharmacokinetic characteristics, and safety [20]. Furthermore, the numerous uncertainties involved in developing new drugs and the high cost of large clinical trials make introducing new therapies to the market nearly impossible [21]. Vaccines might thus become an essential and successful weapon in the fight against antibiotic resistance [19]. Vaccines can affect microorganisms and curb antimicrobial resistance in numerous ways:

#### *Limiting the use of antimicrobial agents*

To prevent potential severe health consequences, including mortality, physicians in various developing nations frequently prescribe antibiotics to patients without an adequate initial diagnosis of the causative agent [20]. Also, studies indicate that several cases of febrile illness that mimic some of the symptoms of bacterial diseases such as typhoid fever are caused by viruses, making antibiotic administration inappropriate [22]. Generally, the use and misuse of antimicrobial agents put microorganisms under selective pressure, encouraging resistance formation and diffusion. However, whereas antibiotic resistance is a common side effect of antibiotic therapy, vaccine resistance is uncommon [23]. This is because vaccines protect the host when it makes contact with the infectious agent before they can cause disease, mutate, or transmit their genetic material to other microbes [7]. Since vaccines prevent pathogenesis, they can help to avoid the improper use of antibiotics in viral infections and the antibiotic therapy required to treat ensuing secondary infections [24]. Therefore, the World Health Organization recommends prioritizing vaccination where antibiotic resistance is prevalent [22].

#### *Lowering the emergence of resistant serotypes*

Vaccination has a significant impact not just on vulnerable strains but also on resistant serotypes [23]. The introduction of the Pneumococcal Conjugate Vaccine (PCV) in South Africa was able to lower the number of instances of Invasive Pneumococcal Disease (IPD) among 2-year-olds with *Streptococcus pneumoniae* strains that were resistant to penicillin, ceftriaxone, and a combination of several drugs [25]. In the United States, the introduction of the PCV resulted in a decrease in penicillin-non-susceptible Invasive Pneumococcal Disease (IPD) by 64% in children under the age of five and 45% in people over the age of 65 by 2008 [26]. Research has shown that introducing a 50 percent effective influenza vaccination with 30 percent coverage to individuals over 65 in South Africa or children aged 2 to 5 years in Senegal would prevent 390 prescriptions per 100,000 population every year [27]. The researchers also believed that if administered to children aged 5 years, the same vaccination might avert at least 24,000 antibiotic prescriptions for severe acute respiratory infections each year [27]. Also, routine immunization of infants at age 9 months with Typhoid Conjugate Vaccine (TCV) with booster doses at age 15 months is estimated to prevent 46–74% of all typhoid fever cases in 73 Gavi-eligible countries [28]. It was predicted that vaccination would reduce the relative incidence of antimicrobial-resistant typhoid fever by 16% [30]. Over a 10-year period, vaccine introduction in conjunction with sensitization and awareness was estimated to prevent 425 million cases and 506 000 deaths from

fluoroquinolone typhoid fever, as well as 212 million cases and 342 000 deaths from multidrug-resistant typhoid [29].

*Providing immunity by a method of action that is less prone to cause resistance*

There is currently no evidence that vaccines negatively impact the microbiome; however, broad-spectrum antimicrobials may disrupt the host microbiome, potentially causing bacterial species to develop resistance [30]. Antibiotics have an immediate and long-term impact on the gut microbiota. They do this by reducing diversity, altering function, increasing host's susceptibility to infection, and increasing selection for resistant organisms. Following gut dysbiosis, many bacteria in the gut create an ideal environment for horizontal transfer of resistance genes between bacteria. Adults' and children's gut microbiota have been identified as an important repository of antibiotic resistance genes [31–33]. Most vaccines also often elicit immunological reactions to target sites, implying that microbes must undergo several modifications to avoid vaccination-induced immunity. While antimicrobial resistance is a natural phenomenon with some pathogens, vaccinations will not accelerate the process. Most vaccines continue to provide protection even after extended durations of usage [7].

*Directly targeting antimicrobial-resistant microbes or resistance-mediating factors*

Antibiotic resistance is a significant issue in Gram-positive organisms, including *Staphylococcus aureus*, *Clostridium difficile* and Enterococci [34]. Also, *Candida* species are usually implicated in mucosal and disseminated infections in patients with compromised immune systems, which antimicrobial therapy exacerbates [35]. Vaccines against these infections are now achievable and likely to succeed, thanks to advancements in vaccine technology and a better knowledge of immunologic responses. Many of these pathogens contain polysaccharides on their surfaces that vaccines are most likely to target. This is the technique behind the highly effective vaccines against *Haemophilus influenza* type b, meningococci, and pneumococci [25]. Vaccines against virulence determinants may also be viable strategies for combating most of these pathogens [25]. Toxins and adhesins, for example, are generally conserved among pathogenic individuals of a species such as *Escherichia coli* but are not seen in commensal members [36]. These virulence factors might be promising antigens for multicomponent vaccines targeting several diseases since they selectively eliminate pathogens while leaving commensal species [37]. Similar methods might be used to eliminate other pathogens, such as *Clostridium difficile*, which includes both pathogenic and commensal members [37].

*Africa's current source of vaccines*

Africa, a continent of about 1,407,204,731 people, according to the United Nations estimate on July 31, 2022, is relatively poor in terms of good healthcare practices, including vaccine production, procurement, and even immunization [38]. There are fewer than ten vaccine manufacturers in Africa, and they are concentrated in five countries: Egypt, Morocco, Senegal, South Africa, and Tunisia. There is very little upstream production, with most local businesses involved in packaging and labelling, as well as fill and finish steps on occasion [38]. It took the pandemic to show that nearly all Africa's vaccines are imported. As of 2021, the African leaders meeting in Addis Ababa reiterated a goal of ensuring that about 70% of their population are vaccinated against the SARS coronavirus [38]. Notwithstanding, the World Health Organization (WHO) estimated that this would necessitate a six - fold increase in

weekly vaccines, bringing the total to 36 million people, a situation which was discovered to be impracticable in most of the countries represented. Only Mauritius and Seychelles have met the 70% target as COVAX which disburses vaccines to low- and middle-income countries is running low on funds [38]. Currently, UNICEF, supported by Gavi, supplies about 1.5 billion doses to 99% of the continent's vaccine consumption, except for a few counties that are self-sufficient in vaccine procurement [38]. The African Union, ECOWAS, among others, could play a pivotal role in the vaccine story in Africa, serving as a middleman between the vaccine manufacturers and the government of each country, seeking funds for this purpose over time, and upscaling vaccine production capability in Africa [38].

## Impediments to successfully developing vaccine capacity

There are significant barriers to developing vaccine production capacity in Africa. Some of them are highlighted below:

### *High Start-Up and operation cost*

To establish commercial vaccine production facilities in Africa, considerable investment, in massive amounts, is required. Additionally, it requires significant fixed and ongoing maintenance costs [39]. Facilities can cost 50–500 million dollars (USD) per vaccine and up to 700 million dollars (USD) for multiple vaccines (combination vaccines) due to the high intricacies of architecture, automation, separation, utilities, and contaminants monitoring [39]. Spaces that are not in conformance with good manufacturing practices may cost up to 350 USD/ft<sup>2</sup>, though the clean and containment facilities may be more complex and costly [40]. The cost of procuring the necessary raw materials, skilled employees with superior technical know-how, and running vaccine manufacturing facilities is relatively high. Many of these costs are spent even if no product is produced. Most operating expenses are attributed to fixed costs resulting from facility design [39].

### *Human resources*

Workers' degree of technical competence is a significant problem for designing vaccines and maintaining production plants. Understanding biological and chemical processes throughout the vaccine's extensive production cycle duration requires scientific expertise [40]. The scientific network (technical institutions, universities, research centers, and others) located near vaccine production plants is crucial. It is essential not just for the scientific and technical knowledge and abilities within the institution but also the links and interconnections with science and technology in the surrounding environment [40]. A sufficient degree of skill sets for facility maintenance, the stability of power supply, the availability of vital spare parts, and cold chain management are vital, particularly in the setting of African nations' tropical environments. Setting up a new vaccine production plant necessitates the use of specialized knowledge [39]. Hiring foreign expertise to work in critical facility jobs is frequently required. Local skilled employees will need extensive training, which may entail sending them abroad for months at a time. Companies worldwide frequently underestimate the time and expense of recruiting and training local and ex-pat workers [39]. Strategies to acquire, train, and maintain highly qualified local employees are critical to ensuring the future success and sustainability of developing countries' vaccine manufacturing capability [40].



### Source of raw materials

Acquiring raw materials is usually a time-consuming and labor-intensive procedure. Every raw material must be obtained from a GMP-certified supplier. For example, raw animal materials (e.g., calf serum, lactalbumin) must be made in bovine spongiform encephalitis-free nations such as Australia and New Zealand. Raw materials (such as yeast extract, and natural or recombinant enzymes) are primarily required in vaccine production to add intrinsic biological diversity to production or analytical procedures [39]. These raw materials are unique, and their supply may be limited and subject to shortages [40].

### Time factor

Building a fully integrated commercial vaccine manufacturing plant takes several years. Unless a separate functional business operates during this time, there is generally no or very minimal income until product registration and commercialization are finished [41]. In addition, various extra expenditures in millions of dollars (USD) and several other elements contribute to a 5–10 year or even more extended timeframe. Other significant components that require time to align include selecting an appropriate market niche and purchaser; identifying a suitable technology transfer partner; employing qualified personnel, consultants, and specialized organizations; constructing GMP-compliant facilities; and managing all parts of the project [41].

### Limited Partnership opportunities

Vaccine manufacturing is a complex and challenging process, and many corporations are often hesitant to devote resources, transmit information, or offer products to a new and unproven company that may be a potential rival [42]. The key factors are the significance of technology transfer and the receiving sites for technology transfer, which are facilities in these nations that manufacture vaccines locally and have appropriate equipment and staff. In manufacturing, national regulatory agencies (NRAs) play a crucial role in ensuring product safety, effectiveness, and quality in low and middle-income countries. According to WHO, only 30% of its member countries' National Regulatory Authorities (NRAs) can appropriately control therapeutic goods in their respective countries [42]. Expansion of vaccine manufacturing in these nations without proper regulatory capability might result in poor product quality and unpleasant impacts, substantially undermining public faith. All of these variables may be a barrier to company-to-company vaccine production collaborations.

### Recommendations for improving vaccine technology in Africa

Looking at the current COVID-19 pandemic, low-income countries have suffered negligence as countries worldwide took steps to vaccinate their citizens against the virus. The global vaccine inequity has resulted in a dire situation in which the world's poorest countries were estimated to have received only about 0.2 percent of the 700 million COVID-19 vaccine doses by the first quarter of 2021, while the world's wealthiest economies secured over 87 percent of total global vaccine stocks [43]. Point of fact, it must be noted that increasing Africa's vaccine development capability from less than 1% to 60% by 2040 is a project that goes beyond a quick-fix strategy [44]. African leaders' resolve to increase vaccine production in Africa on April 13, 2021, will necessitate short- and long-term actions [44]. Combining the options suggested here might help Africa better prepare to address the scourge of vaccine-preventable diseases in the continent and prepare for the

next pandemic by developing enough vaccines for its people and achieving vaccine self-sufficiency.

### Fostering strong multilateral cooperation and collaboration between global scientists

With over 1 billion people living in Sub-Saharan Africa, where most of the countries are known to be low- and middle-income nations (LMICs), it is evident that foreign supply of vaccines from rich countries alone will not be enough to address the demands of African's vaccine needs [45]. For example, in the present global COVID-19 pandemic, it is projected that between 4 and 5 billion doses of COVID-19 vaccinations (at two doses per vaccine) will be needed to at least minimize the scourge of hospitalization and death because of the virus, and subsequently curtail the virus transmission in and out of low- and middle-income countries worldwide [45]. Therefore, successfully vaccinating Africa's many billions of people against vaccine-preventable and infectious illnesses would necessitate high levels of international cooperation, culminating in an innovative and equitable transfer of vaccine development technology to local vaccine manufacturers in Africa. In addition, local vaccine producers must be sufficiently supported and funded to establish a low-cost manufacturing capacity and enhance local supply channels beyond the global setting [45]. Although the African Union's Africa Vaccine Acquisition Task Team has made significant progress in securing COVID-19 vaccines for Africa through pivotal multilateral deals during the COVID-19 pandemic [43], future efforts should be focused on acquiring vaccine development technological know-how from foreign partners so that vaccine manufacturers on the continent can begin to scale up production in earnest.

### Building strong pharmacovigilance capacity in Africa

In Africa's drive to launch and boost indigenous vaccine manufacturing, establishing the African Medicines Agency (AMA) in 2021 as a monitoring and regulatory entity is a step in the right direction. To ensure thorough quality inspections of locally made vaccines that meet international standards, the continent's vaccine regulatory structure must be harmonized and strengthened, allowing for faster vaccine production approval [45–47]. Such a strategy will also benefit Africa as it was for Cuba, Brazil, and India, where the expansion of vaccine manufacturing in the countries prompted regulatory agencies to develop their vaccine production approval and regulatory activities [46]. However, because many African nations have well-developed national regulatory authorities for monitoring their pharmaceutical industry, Africa's regulatory capacity for vaccines will remain underdeveloped until vaccine production plants are built on the continent [9].

### Boosting research and development of vaccine development in Africa

Africa has around ten vaccine manufacturing and packaging facilities [47]. Four of the ten companies have the capacity to both produce and package vaccines, two have plans to expand into full-fledged vaccine production companies, and two more have developed plans to be involved in vaccine filling, finishing, packaging, and labeling [47]. In addition, the Africa Centre for Disease Control announced plans to open five new vaccine manufacturing centers across the continent by 2040 to increase indigenous vaccine production by 60 percent [48]. The African Development Bank has also agreed to assist in financing vaccine manufacturing technological platforms with the potential of producing around 300 million vaccine doses per year [49]. The average financial investment for these undertaken is projected to be around US\$400 million [46–47]. With all these plans from African institutions and international

partners, it is necessary to encourage public–private solid partnerships to help lift the heavy burden of the long-term financial demand required to expand vaccine research and development in Africa.

### *Strong African government commitment*

The financing of the vaccine production effort is one critical area where the African government must be deeply committed. Around \$100 million is required to construct the proposed Africa Medicines Agency (AMA) [49]. By 2040, the average financial expenditure required to establish five vaccine production facilities in Africa is estimated to be over US\$400 million [49]. The strong political determination of African leaders to eradicate the group A meningitis epidemics in Africa played a crucial role in the successful development of a tailor-made vaccine against the disease in sub-Saharan Africa. The Meningitis Vaccine Project (MVP) also shows that funding for an exclusive vaccine made for Africa can be obtained with solid collaboration between local and international partners [9]. Furthermore, African governments and other stakeholders must be committed to buying the vaccines made in Africa and take steps to establish effective supply networks capable of delivering these vaccines to every part of Africa where they are needed to address Africa's public health problems [49].

### *Decisively addressing the issue of vaccine hesitancy in Africa*

Historically, Africans have been hesitant to adopt vaccination to combat vaccine-preventable illnesses [50]. This is mainly due to public mistrust of the government's responsiveness to disease outbreaks, a lack of community engagement in health-related decision-making, and an inability to dispel pre-mediated misconceptions about the adverse effects of a vaccine on an individual's health [43]. If vaccine development in Africa is to take root, African governments, the private sector, advocacy groups, and other relevant national and international players must develop a strategy that encourages the development of an enabling environment for vaccine marketing campaigns aimed at fostering high vaccine acceptability.

### *Careful application of technological innovation and advancement*

In terms of process stability and maintenance, life cycle, and lead-time, vaccine manufacturing technologies, particularly expression systems, play key factors in the cost of vaccine production [9]. Choosing which vaccine manufacturing technology to use significantly impacts the production output, especially in a context like Africa, where the rapid return on investments will encourage continued investments. Failure to manage risks factors related to process development, process maintenance, lead time, production facilities, equipment, life cycle management, and product portfolio management can result in undesired product failure and recalls, market suspensions, and sanctions if a manufacturer fails to meet supply agreements [9,40]. To lower the production costs of vaccine development and manufacturing in Africa, it will be good for indigenous African vaccine manufacturers to embrace and combine whole-genome sequencing (WGS) and epidemiological surveillance to understudy the evolutionary nature of infectious microorganisms and bolster infectious disease outbreak response in the continent [48]. Additionally, due to their simplicity, high output with low production cost, and the requirement for a relatively small manufacturing plant, technologies utilizing Generalized Modules of Membrane Antigens (GMMA) have been considered significantly profitable for Africa's vaccine manufacturing industry [48,51].

### *Understudying case studies of the successful vaccine development in other countries*

For Africa to attain vaccine self-sufficiency, it is worth noting that analyzing the successful building of a vaccine manufacturing industry by Brazil, Cuba, and India is a feat that will serve as a learning curve for Africa [9]. India is Africa's single biggest vaccine supplier, delivering about 70% of vaccines administered in Africa. To attain this vaccine self-sufficiency objective by 2040, policy-makers and key stakeholders in Africa's vaccine development must exhibit a high dedication and resilience by collaborating closely with external partners such as WHO and GAVI Foundation [47,49].

### *The benefit of successfully developing vaccine-manufacturing capabilities in Africa*

Africa presently imports nearly all its vaccines, making it susceptible during a pandemic when the whole world requires vaccines simultaneously. Therefore, the countries that manufacture them must prioritize protecting their people. To guarantee the continent's health security and avoid a repeat of the incidence that ensued during the COVID-19 pandemic, when India prohibited the export of vaccines manufactured by its local companies, consequently driving western countries to buy up the limited international global supply of vaccines, leaving Africa without enough vaccines to protect its citizens, Africa must resiliently develop vaccine-manufacturing capacity [52]. Tasamba reported a similar scenario in 2019 in which an estimated 19.8 million children globally did not obtain the measles vaccine through routine immunization coverage, with Africa constituting a significant proportion of those children [53]. In addition, Lassa fever, an acute viral hemorrhagic disease, is common in eight West African nations, and Sub-Saharan Africa accounted for 94 percent of malaria cases and fatalities in 2019 [54]. The surge in antimicrobial resistance-pathogen implicated infection in Africa could also be attributed to the paucity of vaccines [15]. The modality and mortality resulting due to these diseases could be prevented if Africa actively invest in vaccine production. Some advantages Africa can gain if it develops self-sufficiency in vaccine manufacturing are highlighted below.

### *Security of quality vaccine supply*

Though infectious disease is a global menace, the effect on the underprivileged in society has always been more severe due to the combined impacts of poverty, malnutrition, inadequate hygiene and sanitation, overcrowding, discrimination, and limited access to health care [54]. Since the beginning of the twentieth century, it has been a moral imperative and a human right for every individual to have access to reliable and safe vaccines [54]. Increased vaccine manufacturing in Africa would make it easier and less expensive to provide immunizations across the continent. Acquiring the knowledge and infrastructure required to produce vaccines independently and successfully would assure a steady supply of future pre-qualified vaccines and associated healthcare products. This would also assist in minimizing Africa's reliance on Europe and other foreign suppliers, bridging the gap between low- and high-income nations and, as a consequence, removing challenges caused by vaccine delays and uncertainty, as well as reinforcing the equitable distribution of vaccines throughout the public, particularly during pandemics. This will also position Africa to take a prominent role and seat at the global table and contribute to a more diverse global supply chain for vaccines.

## Addressing the Africa-specific disease burden and efficiently dealing with pandemic diseases and outbreaks

Vaccination coverage in low and middle-income countries, which predominantly constitute the African continent, is significantly low compared to high-income countries due to economic and political restrictions and limited access to non-governmental agencies such as Gavi [55]. Malaria, Ebola, HIV/AIDS, and many other re-emerging infectious diseases native to Africa would be readily tackled, lowering the strain on the health system and the cost of treating these diseases only with drugs if the continent could build capacity for vaccine production. It would primarily assist in easing the developing problem of antimicrobial resistance in Africa, as the medication requirement would be significantly reduced. Should Africa successfully create vaccine manufacturing self-sufficiency, the continent would not only be able to deal with future unplanned catastrophes and maintain current vaccines, but it would also be in a far better position to satisfy the need for future public-health solutions. Local expertise and capability would allow for more rapid development of vaccines against illnesses that are priorities for Africa but have a limited worldwide market, as well as aid in the provision of emergency vaccine supplies to Africans in the case of an outbreak or epidemic.

## Socioeconomic, industry, and life science development/ Partnership opportunities

The development and manufacture of vaccines in Africa will create long-term benefits in terms of health impact, socioeconomic and industrial development, development of biotechnology skills, and advancement of the life sciences in general. The need to create capacity for vaccine production in Africa will spur the nations of the continent to create enabling environment for scientists to conduct research and identify solutions to the challenges of vaccine delivery at the local level. This will further bolster collaboration with other continents and attract donor support. Partnership with other continents and access to the Gavi market could be possible if Africa focuses on manufacturing vaccines against neglected tropical diseases of interest to the continent [9].

## Conclusion

Vaccines are irrefutably essential for fighting antimicrobial resistance since they reduce antimicrobials' usage and avoid illnesses caused by resistant pathogens. Therefore, Africa must strengthen its resilience and focus on building the capacity to create its vaccines to combat antimicrobial resistance and sudden disease outbreaks and lessen reliance on Western nations. Furthermore, African policymakers must investigate how they can strengthen current vaccine manufacturing facilities in Africa by establishing a nexus that incorporates the capabilities of the various countries in the continent into a global industrial chain. Additionally, current vaccine manufacturing facilities should be expanded to cover upstream production.

## Authors' Contributions

HA developed the concept for this review. HA, IMM, OAO, and ADO wrote the first draft of the manuscript. HO, IOO, and YAT proofread and edited the language. HA and ASO revised the manuscript. HO supervised the project and critically revised the final manuscript. All authors contributed to the manuscript and approved the submitted version.

## Consent of publication

All authors consent to the publication of this article.

## Funding

The authors have not received any funding.

## Data availability

No data was used for the research described in the article.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgment

The authors appreciate the reviewers for their insightful comments in improving the quality of this manuscript.

## References

- [1] Tagliabue A, Rappuoli R. Changing priorities in vaccinology: antibiotic resistance moving to the top Available at: <https://www.frontiersin.org/articles/10.3389/fimmu.2018.01068/full>. Front Immunol 2018;9:1068.
- [2] Falkow S. *Infectious Multiple Drug Resistance*. London: Pion Limited (1975). 300 p. Available at: <https://www.cabdirect.org/cabdirect/abstract/19752262618>.
- [3] Tadesse BT, Ashley EA, Ongarelo S, Havumaki J, Wijegoonewardena M, González JJ, et al. Antimicrobial resistance in Africa: a systematic review. *BMC Infect Dis* 2017;17(1):1–17.
- [4] Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial resistance: a global, multifaceted phenomenon. *Pathogens Glob health* 2015;109(7):309–18.
- [5] Founou LL, Founou RC, Essack SY. Antibiotic resistance in the food chain: a developing country perspective. *Front Microbiol* 2016;7(1881):1–19.
- [6] Talbot, T. R., Poehling, K. A., Hartert, T. V., Arbogast, P. G., Halasa, N. B., Ed, M. and Griffin, M. R. (2004). Reduction in high rates of antibiotic-nonsusceptible invasive pneumococcal disease in Tennessee after introduction of the pneumococcal conjugate vaccine. *Clinical infectious diseases*, 39(5), 641 – 648.
- [7] Kennedy DA, Read AF. Why does drug resistance readily evolve but vaccine resistance does not? Available at: *Proc R Soc B Biol Sci* 2017;284(1851):20162562. <https://royalsocietypublishing.org/doi/full/10.1098/rspb.2016.2562?rss=1>.
- [8] World Health Organization. (1998). Regional self-sufficiency in vaccine and drug production. Available at: [https://apps.who.int/iris/bitstream/handle/10665/121695/em\\_rc45\\_tech\\_disc\\_1\\_en.pdf](https://apps.who.int/iris/bitstream/handle/10665/121695/em_rc45_tech_disc_1_en.pdf).
- [9] Makenga G, Bonoli S, Montomoli E, Carrier T, Auerbach J. Vaccine production in Africa: a feasible business model for capacity building and sustainable new vaccine introduction. *Front Public Health* 2019;7:56.
- [10] United Nation (2013). World population prospects: The 2012 revision. *UN Department of Economic and Social Affairs. Population and Development Review* 36:775–801. Available at: [https://population.un.org/wpp/publications/Files/WPP2012\\_Volume-II-Demographic-Profiles.pdf](https://population.un.org/wpp/publications/Files/WPP2012_Volume-II-Demographic-Profiles.pdf).
- [11] Byarugaba DK. A view on antimicrobial resistance in developing countries and responsible risk factors. *Int J Antimicrob Agents* 2014;24:105–10.
- [12] WHO. (2014). Resistance. Global report on surveillance.
- [13] <https://www.ox.ac.uk/news/2022-01-20-estimated-12-million-people-died-2019-antibiotic-resistant-bacterial-infections>.
- [14] <https://healthpolicy-watch.news/antimicrobial-resistance-to-bacterial-infections-killed-more-people-than-hiv-aids-in-2019-new-lancet-study-shows/#:~:text=Deaths%20from%20AMR%20were%20estimated,of%20antibiotic%20resistant%20pneumonia%20strains>.
- [15] WHO, 2022. <https://www.afro.who.int/ResistAMR>.
- [16] Akinde OS, Taiwo MO. Emerging antibiotic resistance in Africa, threat to healthcare delivery. *MedCrave Online Journal of Biology and Medicine* 2017;1(4):114–5.
- [17] O'Neill, J. (2016). Tackling drug-resistant infections globally: final report and recommendations. [http://amrreview.org/sites/default/files/160525\\_Final%20paper\\_with%20cover.pdf](http://amrreview.org/sites/default/files/160525_Final%20paper_with%20cover.pdf).
- [18] Koluman A, Dikici A. Antimicrobial resistance of emerging foodborne pathogens: status quo and global trends. *Crit Rev Microbiol* 2013;39:57–69.
- [19] Rosini R, Nicchi S, Pizza M, Rappuoli R. Vaccines against antimicrobial resistance Available at: *Front Immunol* 2020;11:1048. <https://www.frontiersin.org/articles/10.3389/fimmu.2020.01048/full>.



- [20] Gupta SK, Nayak RP. Dry antibiotic pipeline: Regulatory bottlenecks and regulatory reforms Available at: J Pharmacol Pharmacother 2014;5(1):4–7. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3917165/>.
- [21] Richter MF, Drown BS, Riley AP, Garcia A, Shirai T, Svec RL, et al. Predictive compound accumulation rules yield a broad-spectrum antibiotic Available at: Nature 2017;545(7654):299–304. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5737020/>.
- [22] Andrews JR, Baker S, Marks F, Alsan M, Garrett D, Gellin BG, et al. Typhoid conjugate vaccines: a new tool in the fight against antimicrobial resistance Available at: Lancet Infect Dis 2019;19(1):26–30. <https://www.sciencedirect.com/science/article/pii/S1473309918303505>.
- [23] Buchy P, Ascioglu S, Buisson Y, Datta S, Nissen M, Tambyah PA, et al. Impact of vaccines on antimicrobial resistance Available at: Int J Infect Dis 2020;90:188–96. <https://www.sciencedirect.com/science/article/pii/S1201971219303972>.
- [24] Kwong JC, Maaten S, Upshur RE, Patrick DM, Marra F. The effect of universal influenza immunization on antibiotic prescriptions: an ecological study Available at: Clin Infect Dis 2009;49(5):750–6. <https://academic.oup.com/cid/article/49/5/750/308812>.
- [25] Rappuoli R, Bloom DE, Black S. Deploy vaccines to fight superbugs. Nature 2017;552(7684):165–7.
- [26] Hampton LM, Farley MM, Schaffner W, Thomas A, Reingold A, Harrison LH, et al. Prevention of antibiotic-nonsusceptible Streptococcus pneumoniae with conjugate vaccines Available at: J Infect Dis 2012;205(3):401–11. <https://academic.oup.com/jid/article/205/3/401/850073>.
- [27] Knight GM, Clarkson M, de Silva TI. Potential impact of influenza vaccine rollout on antibiotic use in Africa Available at: J Antimicrob Chemother 2018;73(8):2197–200. <https://academic.oup.com/jac/article/73/8/2197/4994361>.
- [28] <https://medicalxpress.com/news/2022-02-routine-immunization-typhoid-conjugate-vaccine.html>.
- [29] Birger R, Antillón M, Bilcke J, Dolecek C, Dougan G, Pollard AJ, et al. Estimating the effect of vaccination on antimicrobial-resistant typhoid fever in 73 countries supported by Gavi: a mathematical modelling study Available at: Lancet Infect Dis 2022;22(5):679–91. <https://www.sciencedirect.com/science/article/pii/S1473309921006277>.
- [30] Bloom DE, Black S, Salisbury D, Rappuoli R. Antimicrobial resistance and the role of vaccines Available at: Proc Natl Acad Sci 2018;115(51):12868–71. [https://scholar.google.com/scholar?output=instlink&q=info:4agDal8afn4j:scholar.google.com/&hl=en&as\\_sdt=0,5&scilfp=17657274467836461980&oi=ile](https://scholar.google.com/scholar?output=instlink&q=info:4agDal8afn4j:scholar.google.com/&hl=en&as_sdt=0,5&scilfp=17657274467836461980&oi=ile).
- [31] Francino, M. P. (2016). Antibiotics and the human gut microbiome: dysbioses and accumulation of resistances. *Frontiers in microbiology*, 6, 1543. Available at: [https://www.frontiersin.org/articles/10.3389/fmicb.2015.01543/full?source=post\\_page](https://www.frontiersin.org/articles/10.3389/fmicb.2015.01543/full?source=post_page).
- [32] Langdon A, Crook N, Dantas G. The effects of antibiotics on the microbiome throughout development and alternative approaches for therapeutic modulation Available at: Genome Med 2016;8(1):1–16. <https://genomemedicine.biomedcentral.com/articles/10.1186/s13073-016-0294-z>.
- [33] Lange K, Buerger M, Stallmach A, Bruns T. Effects of antibiotics on gut microbiota. Dig Dis 2016;34(3):260–8.
- [34] Spigaglia P. Recent advances in the understanding of antibiotic resistance in Clostridium difficile infection Available at: Therap Adv Infect Dis 2016;3(1):23–42. [https://scholar.google.com/scholar?output=instlink&q=info:ihwBoF4QDZY:scholar.google.com/&hl=en&as\\_sdt=0,5&scilfp=604650709976341295&oi=ile](https://scholar.google.com/scholar?output=instlink&q=info:ihwBoF4QDZY:scholar.google.com/&hl=en&as_sdt=0,5&scilfp=604650709976341295&oi=ile).
- [35] Lipsitch M, Siber GR. How can vaccines contribute to solving the antimicrobial resistance problem? Available at: MBio 2016;7(3):e00428–516. [https://scholar.google.com/scholar?output=instlink&q=info:lnUhuKdIQBQJ:scholar.google.com/&hl=en&as\\_sdt=0,5&scilfp=9990368624326526066&oi=ile](https://scholar.google.com/scholar?output=instlink&q=info:lnUhuKdIQBQJ:scholar.google.com/&hl=en&as_sdt=0,5&scilfp=9990368624326526066&oi=ile).
- [36] Nesta, B., Spraggon, G., Alteri, C., Gomes Moriel, D., Rosini, R., Veggi, D., ... & Soriani, M. (2012). FdeC, a novel broadly conserved Escherichia coli adhesin eliciting protection against urinary tract infections. *MBio*, 3(2), e00010–12. Available at: [https://scholar.google.com/scholar?output=instlink&q=info:9KSigJhwFCWj:scholar.google.com/&hl=en&as\\_sdt=0,5&scilfp=16036207148195192486&oi=ile](https://scholar.google.com/scholar?output=instlink&q=info:9KSigJhwFCWj:scholar.google.com/&hl=en&as_sdt=0,5&scilfp=16036207148195192486&oi=ile).
- [37] Gerding DN, Meyer T, Lee C, Cohen SH, Murthy UK, Poirier A, et al. Administration of spores of nontoxigenic Clostridium difficile strain M3 for prevention of recurrent C difficile infection: a randomized clinical trial Available at: JAMA 2015;313(17):1719–27. <https://jamanetwork.com/journals/jama/articlepdf/2281703/joi150039.pdf>.
- [38] Overview of the health system in Egypt <https://dhsprogram.com/pubs/pdf/SPA5/02chapter02.pdf>.
- [39] Plotkin, S., Robinson, J., Cunningham, G., Iqbal, R., & Larsen, S. (2017). The complexity and cost of vaccine manufacturing—an overview. *Vaccine*, 35(33):4064–4071. Available at: <https://doi.org/10.1016/j.vaccine.2017.06.003>.
- [40] Hendriks J, Holleman M, Hamidi A, Beurret M, Boog C. Vaccinology capacity building in Europe for innovative platforms serving emerging markets Available at: Hum Vaccin Immunother 2013;9(4):932–6. <https://www.tandfonline.com/doi/pdf/10.4161/hv.23163>.
- [41] WHO/DHHS joint workshop on enhancing the global workforce for vaccine manufacturing (2012). [Accessed 2022 July 28]. Available at: [https://www.who.int/phi/WHO\\_IER\\_TTI\\_12.1\\_WEGWVM\\_Report\\_FINAL\\_May2012.pdf](https://www.who.int/phi/WHO_IER_TTI_12.1_WEGWVM_Report_FINAL_May2012.pdf).
- [42] Otu, A., Osifo-Dawodu, E., Atuhebwe, P., Agogo, E., & Ebenso, B. (2021). Beyond vaccine hesitancy: Time for Africa to expand vaccine manufacturing capacity amidst growing COVID-19 vaccine nationalism. *The Lancet Microbe*, 2(8), e347–e348. Available at: <https://doi.org/10.1016>.
- [43] Partnership for African Vaccine Manufacturing (PAVM). Concept note. December 7 2021 Available online: [https://africacdc.org/wp-content/uploads/2021/11/ENGLISH\\_PAVM\\_Public-Stakeholder-Engagement\\_Concept-note\\_Final-version.pdf](https://africacdc.org/wp-content/uploads/2021/11/ENGLISH_PAVM_Public-Stakeholder-Engagement_Concept-note_Final-version.pdf) (accessed on June 18, 2022).
- [44] Hotez PJ, Narayan KV. Restoring vaccine diplomacy. JAMA 2021;325(23):2337–8. <https://doi.org/10.1001/jama.2021.7439>.
- [45] Davies, M. (2022). Covid-19: WHO efforts to bring vaccine manufacturing to Africa are undermined by the drug industry, documents show. *bmj*, 376. <http://dx.doi.org/10.1136/bmj.o304>.
- [46] Irwin A. (2021). How COVID spurred Africa to plot a vaccines revolution. Available online: <https://www.nature.com/articles/d41586-021-01048-1> (accessed June 17, 2022).
- [47] Adepoju P. Genomic and epidemiologic surveillance could instruct future virus response. *Nature Africa* Available online 2021;2022. <https://doi.org/10.1038/d44148-021-00027-y> (accessed on June 18).
- [48] Adepoju P. Africa prepares for COVID-19 vaccines. *The Lancet Microbe* 2021;2(2):e59.
- [49] World Health Organization (WHO) (2015a). Vaccine hesitancy: A growing challenge for immunization programmes. Available online: <https://www.who.int/news/item/18-08-2015-vaccine-hesitancy-a-growing-challenge-for-immunization-programmes> (accessed June 18, 2022).
- [50] Gerke C, Colucci AM, Giannelli C, Sanzone S, Vitali CG, Sollai L, et al. Production of a Shigella sonnei vaccine based on generalized modules for membrane antigens (GMMA), 1790GAHB. *PLoS One* 2015;10:e0134478.
- [51] <https://healthpolicy-watch.news/vaccine-charity-or-building-africas-capacity/>.
- [52] <https://www.aa.com.tr/en/africa/reported-measles-cases-up-in-africa-says-global-report/2043257>.
- [53] [https://www.who.int/health-topics/lassa-fever#tab=tab\\_1](https://www.who.int/health-topics/lassa-fever#tab=tab_1).
- [54] Rodrigues CM, Plotkin SA. Impact of vaccines; health, economic and social perspectives Available at: Front Microbiol 2020;11:1526. <https://www.frontiersin.org/articles/10.3389/fmicb.2020.01526/full>.
- [55] Turner HC, Thwaites GE, Clapham HE. Vaccine-preventable diseases in lower-middle-income countries Available at: Lancet Infect Dis 2018;18(9):937–9. [https://ora.ox.ac.uk/objects/uid:776c4850-a109-4da8-a975-2f2d5b1cc37c/download\\_file?safe\\_filename=Turner%2Bet%2Bal.%2B2019.pdf&file\\_format=application%2Fpdf&type\\_of\\_work=Journal+article](https://ora.ox.ac.uk/objects/uid:776c4850-a109-4da8-a975-2f2d5b1cc37c/download_file?safe_filename=Turner%2Bet%2Bal.%2B2019.pdf&file_format=application%2Fpdf&type_of_work=Journal+article).