Prioritization of zoonotic diseases of public health significance in Nigeria using the one-health approach

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A B S T R A C T

Nigeria, with a population of over 190 million people, is rated among the 10 countries with the highest burden of infectious and zoonotic diseases globally. In Nigeria, there exist a sub-optimal surveillance system to monitor and track priority zoonoses. We therefore conducted a prioritization of zoonotic diseases for the first time in Nigeria to guide prevention and control efforts. Towards this, a two-day in-country consultative meeting involving experts from the human, animal, and environmental health backgrounds prioritized zoonotic diseases using a modified semi-quantitative One Health Zoonotic Disease Prioritization tool in July 2017. Overall, 36 of 52 previously selected zoonoses were identified for prioritization. Five selection criteria were used to arrive at the relative importance of prioritized diseases based on their weighted score. Overall, this zoonotic disease prioritization process marks the first major step of bringing together experts from the human-animal-environment health spectrum in Nigeria. Importantly, the country ranked rabies, avian influenza, Ebola Virus Disease, swine influenza and anthrax as the first five priority zoonoses in Nigeria. Finally, this One Health approach to prioritizing important zoonoses is a step that will help to guide future tracking and monitoring of diseases of grave public health importance in Nigeria.

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1. Introduction

Pathogenic agents transmissible in nature between vertebrate animals and humans pose significant public health and socio-economic threats globally [1]. These zoonotic agents are implicated in more than half of all pathogens infectious to humans, two-thirds of emergent and re-emergent infections and three-quarters of new diseases that have affected humans in the past 10 years [2,3] with the burden and impact varying in time and geographical settings [4]. The geographical variations require that each country identify and prioritize zoonotic diseases (ZDs) of major public health importance affecting its population.

In developing countries like Nigeria, the burden of zoonotic diseases is often underestimated due to weak surveillance, poor awareness and paucity of data [4]. Additionally, because of the diverse nature of these countries given their different geographic and environmental settings, they harbor a wide range of zoonotic disease pathogens with varying epidemiology and severity [5]. These challenges present limitations to effective prevention and control of zoonoses. In most instances, only zoonotic diseases that cause pandemics and attract global concerns gain the attention of national policy makers and international partners in control and prevention compared to endemic zoonotic diseases that impact rural communities sometimes more significantly [6,7]. For example, the first avian influenza outbreak in Nigeria in 2006 attracted huge investment from both the national government and international agencies due to its pandemic nature; while rabies, a preventable and endemic disease, with high mortality rates in different parts of the country attracts little or no attention [8]. Prioritizing zoonotic diseases is critical across countries for optimizing resources, improving surveillance, enhancing data quality, information dissemination and risk communication and promoting multi-sectoral collaboration. [5,9–11].

Nigeria is the most populous country in Africa with an estimated population of 188 million [12] and has one of the highest populations of livestock (19.5 million cattle, 72.5 million goats, 41.3 million goats) in the continent [13]. Agriculture is the economic mainstay of Nigeria, employing about 70% of the labor force with livestock production accounting for 6–8% of the national Gross Domestic Product (GDP) and 20–25% of agricultural GDP [13]. Despite these valuable contributions, the livestock sub-sector is neglected and therefore prone to myriad of problems, one of which is weak veterinary care and support system, thus, creating huge opportunities for several livestock diseases, including those of zoonotic importance, to thrive and spread. This becomes more pronounced because livestock farming is mainly subsistence [14]. Most households have close contact with domestic animals and are unaware of the public health implications of zoonotic diseases [15,16]. The situation is further exacerbated by the intensification of livestock production, due to the huge demand for animal protein, which favors the circulation of pathogens at the human-animal-ecosystem interface [17,18]. Given the aforementioned and other intrinsic as well as extrinsic factors (e.g. war, drought and climate change) beyond the control of government, Nigeria becomes highly vulnerable to the effect of several zoonotic diseases and ranks very high in the health burden of neglected zoonotic diseases [19].

In 2012, the government of Nigeria rolled out the Agriculture Transformation Agenda (ATA) in a bid to revamp the agriculture sector, ensure food security, diversify the economy and enhance foreign exchange earnings [20]. The Livestock Transformation Agenda (LITA), a subset of ATA, focused on intensification of livestock production without a major emphasis on intensification of zoonotic disease surveillance and other animal disease control measures. Weak surveillance systems, lack of coordination among human and animal health sectors and inadequate resources for public health systems have remained prominent barriers to effective response to public health threats posed by zoonotic diseases in Nigeria [15,21]. Ultimately, there is a lack of empirical data on zoonotic diseases in the country that can be used for evidence-based policy formulation and effective implementation of public health control measures and activities. In keeping with the Global Health Security Agenda, LITA necessitates the development of parallel strategies to prioritize and control zoonotic diseases of major public health and strengthening of existing surveillance systems for prioritized zoonoses [15,22].

To address the challenges, a zoonotic disease prioritization workshop using a one health approach was jointly organized. One Health is an approach that recognizes the interconnectivity between the health of people, animals and their shared environment. It adopts a collaborative, multi-sectoral, and transdisciplinary approach across local, regional, national, and global levels to optimize health systems and outcomes. The one health zoonotic prioritization workshop was initiated by the Nigeria Centre for Disease Control (NCDC) and the Federal Ministry of Agriculture and Rural Development’s Department of Veterinary and Pest Control Services with support from the Africa Field Epidemiology Network (AFENET), Global Implementation Solution (GIS), US Centers for Disease Control and Prevention (CDC) and the Zoonotic Disease Unit (ZDU) of Kenya. The primary objectives of the prioritization process were to identify priority zoonotic diseases in Nigeria, strengthen the links between the human, animal and environmental health sectors to jointly address these diseases and increase the coordination, collaboration and networking on zoonoses prevention and control activities among stakeholders. This paper therefore describes the outcome and product of a semi-quantitative, multi-sectoral process that led to the prioritization of zoonotic diseases in Nigeria, ranking them in order of relative importance towards guiding prevention and control strategies in the country.

2. Methods

The Nigerian zoonotic disease prioritization process was carried out via a scoping literature and document review and subsequent organization of a two-day, in-country facilitated consultative workshop of 61 one-health stakeholders and experts in July 2017 (Fig. 1). The experts were drawn from key stakeholders’ agencies in public health, animal health and environmental health (Table 1) [4,15]. During the workshop, disease prioritization was conducted using the semi-quantitative One Health Zoonotic Disease Prioritization (OHZDP) tool developed by the USCDC [9,11], used by other countries [23,24,57] but modified in our context based on the Kenyan zoonotic disease prioritization process. [4,12]. In our prioritization process, we modified the OHZDP tool so that it could be administered to five groups consisting of 12–13 persons, rather than a maximum of 6–7 persons in the Kenyan prioritization. Though other disease prioritization approaches exist [25], we found the OHZDP process most suitable for Nigeria because of paucity of valid quantitative data for some zoonotic diseases and poor surveillance for most zoonotic diseases which made the application of other techniques impractical [4,9].

Prior to the workshop, key institutions and ministries involved in zoonotic disease prevention, surveillance, research and diagnostics in both human, animal and environmental health, across the six geopolitical zones of Nigeria were identified (Table 1). Subsequently, invitations were circulated to these institutions for selection of experts on zoonoses [4]. The selected experts indicated interest and willingness to participate in the prioritization process. Of the 61 participants that attended the workshop, 33 (54%) were animal health experts, 23 (38%) were human health experts, while 5 (8%) consisted of environmental health experts (Fig. 1). Participants were drawn from the academia 23 (37.7%), Government ministries 20 (32.8%), industry partners 12 (19.7%) and researchers from research institutes 6 (9.8%). During the workshop, participants were placed into five heterogenous groups of 12–13 participants per group ensuring even spread of all disciplines [6]. Participants from the same institution were put in different groups to minimize institutional and professional biases.

The prioritization process involved six steps (Fig. 2): i) selection of zoonotic diseases for prioritization; ii) selection of five measurable criteria for ranking these diseases; iii) ranking of the criteria using a
semi-quantitative analytic hierarchy process; iv) development of categorical questions for each criterion and scoring each criterion for each disease; v) aggregation of scores in order to assign weights to each disease using decision tree analysis; and vi) ranking the zoonotic disease based on the weighted criteria.

2.1. Literature review and selection of zoonotic diseases for prioritization

A literature review of existing published and unpublished works on zoonotic diseases in Nigeria and the West African region was carried out before the prioritization workshop to identify zoonoses of jurisdictional importance to the stakeholders and threat to the country. The literature review was conducted by three selected NFELTP [26] residents, with guidance from two One Health consultants from GIS and University of Ibadan, Nigeria. The review involved scoping literature searches in repositories of international human and animal health agencies like the World Organization for Animal Health (OIE) and World Health Organization, Google scholar, PubMed, BMJ, AJOL, PLoS, BioMed Central, CDC Publication and HINARI; and extensive review of available unpublished works on zoonoses from universities, research institutes and opinions from subject matter experts on zoonoses.

Publications from 2000 to 2017 were included in the review. The keywords’ combination used for the search were: “zoonotic”, “diseases”, “zoonosis”, “endemic”, morbidity, “mortality” “Nigeria” and “west Africa”. First, online literature was reviewed to identify zoonotic diseases that have occurred in Nigeria. Next, literature searches were conducted on zoonotic diseases that can cause epidemics in Nigeria and those that are threat to Nigeria especially those reported within the west Africa subregion [6,16,17,18,27–32,33–43]. After the listing of all identified zoonoses, searches were conducted on each of the listed zoonoses to obtain their epi-data. Upon assessment of publication abstract, articles on ZDs published in English and with relevant incidence/prevalence and/or socioeconomic burden data in humans and animals from Nigeria were included in listing the initial 52 zoonotic diseases [37,44–51].

The bibliographies of the articles that turned up in the initial search were also used to find other references relevant to zoonotic diseases in Nigeria. Articles without basic epi-data on animal and human cases and those reporting zoonotic events were excluded. Following the search, epi-data table was completed for each of the diseases covering incidence/prevalence [52–55] in humans and animals or both in Nigeria and neighboring West African countries (Table 2).

The database of 52 zoonotic diseases (Table 2) was presented to workshop participants in a plenary session for validation. The participants reviewed the list, and the number was pruned to 36 diseases known to have been reported in Nigeria and the West African region in the last 20 years and whose ecological and epidemiological conditions of occurrence exist in Nigeria.

2.2. Selection of measurable criteria for ranking the diseases

Each of the five (5) groups of participants was given a list of eight criteria (Table 3), adapted from published works on zoonotic disease prioritization [4,5,15], and tasked to select a set of five criteria as suggested by the OHZDP tool to justify prioritization. Giving participants a list of eight criteria to choose from was a modification of the OHZDP...
process aimed at fast-tracking the generation of suitable criteria from existing listings from other countries who have used the tool. Participants were also asked to suggest additional criteria where they deemed necessary. Each group selected a lead who moderated the discussions and a note taker who took minute of the discussions and conclusions by their group. The criteria selected by each group were subsequently discussed at a plenary session to produce a combined final list of five criteria including, epidemic potential, severity, economic impact, burden of zoonotic diseases and ability to prevent and control, that were used to evaluate the diseases (Table 4). To arrive at these criteria, three criteria chosen by all five groups were first selected; subsequently, two criteria, each cutting across three groups and two groups respectively were selected by majority vote after a debate for and against. Consequently, three criteria were unanimously discarded at plenary: i) transmission potential between humans and animals; ii) bioterrorism and iii) amenability to collaboration already established.

First, ‘transmission potential between humans and animals’ was deemed a general criterion that cuts across all zoonotic diseases and it was agreed that its variation across diseases may not be sufficient for ranking zoonotic diseases compared to other criteria. Secondly, most participants argued that ‘bioterrorism potential’ was not a major concern in Nigeria’s setting. It was agreed that this criterion was adequately captured in the “epidemic/pandemic potential” and “socio-economic burden of the disease” as these criteria were some of the considerations for using a disease pathogen for bioterrorism [56]. Finally, it was agreed at plenary that “amenability to collaborate/collaboration already established” was contained in “ability to prevent and control the zoonotic disease in the country” and thus, should not stand alone as a separate criterion.

Subsequently, each group conducted criteria ranking using the
Table 2
Epidemiological Data for Zoonotic Diseases in Nigeria from Literature search.

| S/N | Disease/Condition | Prevalence in Nigeria | Prevalence/incidence in other African Countries | Estimated impact or burden, Socio-economic and non-monetary losses |
|-----|-------------------|------------------------|-----------------------------------------------|------------------------------------------------------------------|
|     |                   | Humans | Animals | Humans | Animals | CFR in humans | Production losses in animals |
| 1   | Candidiasis       | 7% (82%) | 6.30%   | 56.3% in Nigeria | 51.2% in Cameroon | 30–50% | €10,530 and €51,033, depending on the certainty of infection and the duration of follow-up |
| 1   |                   |        |         |        |         |              |                                  |
| 2   | Staphylococcus    | 21–30% | 18–34%  | 21.3–30% in Nigeria, Cameroon | 81.8% in Cameroon | 20–40% | $35,300 per patient for community acquired infections |
| 2   | infection         |        |         |        |         |              |                                  |
| 3   | Staphylococcus    | 0.7–1.1% | Nil    | Incidence rate ~ 4 per 1000 |        | 0.0–11.7% | $39–64.2 m (2005) |
| 3   | infection         |        |         |        |         |              |                                  |
| 4   | Candidiasis       | 4.50%  | 18%     | 25% in Northeast Nigeria | 90.3% in Nigeria | 3–15% | $778 m (1999–2012) approx. $56 m per year |
| 4   |                   |        |         |        |         |              |                                  |
| 5   | Rabies            | 8.0–18.5% | 0.09% in goats and cattle – 12.7% in cheetah | 2.9% in Nigeria | 2.3–4% in dogs in Nigeria | 28–40% | $1.7 to 7 cases per million persons from 2000 to 2007 in the US |
| 5   |                   |        |         |        |         |              |                                  |
| 6   | Psittacosis       | 15.80% | 1% in cattle to 43% in goats | 67.9% in Tanzania | 1.7 to 7 cases per million persons from 2000 to 2007 in the US | 0.3–2.2% | $11.2 m from 2002 to 2011 |
| 6   |                   |        |         |        |         |              |                                  |
| 7   | West Nile fever   | 4.50%  | 18%     | 25% in Northeast Nigeria | 90.3% in Nigeria | 3–15% | $778 m (1999–2012) approx. $56 m per year |
| 7   |                   |        |         |        |         |              |                                  |
| 8   | Glanders          | 8.0–18.5% | 0.09% in goats and cattle – 12.7% in cheetah | 2.9% in Nigeria | 2.3–4% in dogs in Nigeria | 28–40% | $1.7 to 7 cases per million persons from 2000 to 2007 in the US |
| 8   |                   |        |         |        |         |              |                                  |
| 9   | Trichinosis       | 2.2% in the US | 3.8% in Ethiopia | 3.8% in Ethiopia | 3.8% in Ethiopia | 3–15% | $778 m (1999–2012) approx. $56 m per year |
| 9   |                   |        |         |        |         |              |                                  |
| 10  | Streptococcal     | 51–60% | 12% | 53.7% in under fives | 30.7% in Nigeria | 29–45% | $24 to $539 million per year. |
| 10  | infection         |        |         |        |         |              |                                  |
| 11  | Tuberculosis      | 2.4–3% | 8.50%   | 17.5% in Ethiopia | 8% in Zaire (DRC) | 9.7–17% | $5B (2012) Globally, $1.8 (2008–2012) in Benue state, Nigeria |
| 11  |                   |        |         |        |         |              |                                  |
| 12  | Brucellosis       | 5.2–7.8% | 5.3–8.6% in Chad and 41% in Togo | 5.8–5.9% in Kenya | 4.9–5.6% in Cameroon | 0.8–2% | $575,605 (2016) in Nigeria |
| 12  |                   |        |         |        |         |              |                                  |
| 13  | Ebola             | 2% | *Not documented in published literatures | 0.074% in Liberia | 0.03% in Sierra Leone | 31.8% in Gabon | 25–90% | $219 (2014–2017) in Sierra Leon $1.4b in Nigeria (2014) |
| 13  |                   |        |         |        |         |              |                                  |
| 14  | Avian Influenza   | 18.90% | 18.1–27.3% in Senegal and 35.3–93.4% in Cameroon | 17.5–40% in Senegal | 29% in Cameroon | 16–88% in Egypt | $700 m (2006) in Nigeria |
| 14  |                   |        |         |        |         |              |                                  |
| 15  | Cryptosporidiosis | 21–30.5% | 16.6–28.1% in Chad and 14.1–25.4% in Cameroon | 3.5–22.3% in Chad and 1.5–14.4% in Cameroon | 18.9–50.6% in Ghana | 7.8–10.3% | $46 m hospitalization cost in USA $1.58 m Euros in Netherlands |
| 15  |                   |        |         |        |         |              |                                  |
| 16  | Leishmaniasis     | 6.80%  | 3.03–4.40% in Ghana | 12.2–32.3% in Ghana | 2.7% in Mali | 8.8–17.7% | $81.2 m in Afghanistan |

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| S/N | Disease/Condition | Prevalence in Nigeria | Prevalence/Incidence in other African Countries | Estimated impact or burden, Socio-economic and non-monetary losses | Production losses in animals |
|-----|-------------------|-----------------------|-----------------------------------------------|---------------------------------------------------------------|----------------------------|
|     |                   | Humans | Animals | Humans | Animals | CFR in humans | Intervention costs |                     |                        |
| 1   | Echinococcosis    | 1.1–2.6% | 7.5–38.3% in Cameroon | 5.9–11.7% in Algeria | 12,491,280 (2000–2011) human deaths in Brazil | $28.5 (2006) human deaths in India | $2.3 billion in Developing countries |                     |                        |
| 17  |                   | 5.10% | 12.45% | 5–10% in Argentina | 9.3–56% in Ethiopia | 0.3–25% in Haiti | 0.5% in Tanzania | 8.1–66.6%                | 1.2–5.0%          |
| 18  | Plague            | 7.80% | 0.10% | 50–80% in London | 17.9 in Peru | 0.5% in Tanzania | 52 (1994) deaths in India | 60 million deaths in China | 14th century |
| 19  | Tularemia         | *Not documented in published literatures | 2.22–7.46% in Turkey | 1.3–16% in the US | 3–35% | $12.6 (1993) billion following bioterrorist attack in the US | $159,659.6 (2008) in Iran |                     |                        |
| 20  | Cat Scratch Fever | *Not documented in published literatures | 10–45.5% | 26–28% in the US | 13–60% in Kenya | 2–40% in Italy | $3.5 m (2000) in the US | 500 hospitalized humans in the US |                     |
| 21  | Rabies            | 505 cases (1912–1978), 6 of 149 (4%) (2004–2013) | 1.3% in Malawi | 1.4 per 1000 in Chad | 100% | $46 per DALYs averted |                     |                        |                        |
| 22  | Lassa fever       | 623 (3.4 cases/million) | 5.80% | 26% in Ivory Coast | 19.4% in Mali | 37.9% - 50.0% | Affects 100,000 to 500,000 persons/year in West Africa | > 50% CFR |                     |
| 23  | Yellow fever      | 20% | 0% in Africa in 2015 | 661–884 lab confirmed cases in Angola in 2015 | 0.8% | 0.8% in Sierra Leone | 31% | 200,000 cases per year in South America and Africa | 52% CFR in Western Nigeria |
| 24  | Western equine encephalitis | No lit available | No lit available | No lit available | No lit available |                     | Economic loss of over N40,000 per cattle ($103 @ N390/1$) |                     |                        |
| 25  | Streptotrichosis  | No Lit available | 3.11% | 5.3% in India | 13.55% in Bangladesh | N/A | Economic loss of over N40,000 per cattle ($103 @ N390/1$) |                     |                        |
| 26  | Clostridial disease | 14-43% among HIV | 26.60% | 6.7% in India | 22.5–36% in India | 4.7–13.8% | $1,223,376 attributable cost in outbreak setting in the Netherlands | $3.2 billion Annual management cost in US |                     |
| 27  | Shigelllosis      | 20.70% | 10.60% | 2.3%, 13.3%, 6.9% in Ethiopia | 15.6–58.4% in Egypt | 9.80% | 163.2 million episode in developing countries with 1.1 million death annually | 4218 cases in Sierra Leone |                     |
Table 2 (continued)

| S/ N | Disease/Condition             | Prevalence in Nigeria | Prevalence/Incidence in other African Countries | Estimated impact or burden, Socio-economic and non-monetary losses |
|------|--------------------------------|-----------------------|-------------------------------------------------|------------------------------------------------------------------|
|      |                                | Humans | Animals | Humans | Animals | CFR in humans | Production losses in animals |
|      |                                |        |         |        |         |              | Intervention costs |
| 28   | Toxoplasmosis                  | 24%    | 13.9%, 29.1% | 75.7%, 94.4% in Ethiopia | 55.18–58.18% in Ethiopia | 70.0% in Kenya | 70.0% in Kenya | Indeterminate | 26 cases of cerebral toxoplasmosis in Dakar, Cameroon | 2.6% ocular toxoplasmosis in Ghana | 29% Maternal-fetal transmission rate |
| 29   | Rat bite fever                 | No lit available | No lit available | No lit available | No lit available | 10%          | No lit available | No lit available | No lit available | 40 cases of conjunctivitis of 90 poultry workers |
| 30   | Newcastle disease              | No available lit. 17% | No available lit. 25–35.7% | No available lit. 28.3–34.5% in Cameroon | 93.8–54.4% in Senegal | 30%          | No available | No available | 200,000 cases estimated per year |
| 31   | Hantavirus                     | No available lit. | No available lit. | 1.2–4.4% in Guinea | 0.24% in Sierra Leone | 0.16% in Guinea | 0.16% in Guinea | 57.50% | No treatment available |
| 32   | African trypanosomiasis        | No data | Cattle (Jos) 46.8% | No data | No data | 40.90% | 4.30% | No data | costs Africa US$5 billion a year and Africa spends every year at least $30 million to control cattle trypanosomiasis Direct losses due to trypanosomiasis are estimated to between US$ 1–1.2 billion each year. |
| 33   | Aspergillosis                  | 36.94% | 47.87% in apparently healthy birds | No data | No data | 58% | No data | No data |
| 34   | Anthrax                        | No data | No data | No data | No data | 90% South of Tanzania | 87% hyena Tanzania | 50% | No data |
| 35   | Leptospirosis                  | 13.5% Enugu 27.2% horses 3.5% abattoir cattle Kaduna | Uganda 35% | No data | No data | 1–5% | No data | No data |
| 36   | Visceral larval migrans        | No data | 33.8% dogs in Nigeria | No data | No data | Most cases of visceral larva migrants are subclinical, Fatalities are rare but have occurred in cases with severe pneumonia, cardiac involvement or neurological disease51 | Puppies can die occasionally from the effects of larval migration (especially pneumonia) and rarely from intestinal complications. In dogs, maternal transmission is very efficient |
| 37   | Cutaneous larval migrans       | No data | No data | No data | No data | No data | No data | No data |
| 38   | Dermatophytosis                | 9% primary school children 39.6% domesticated animals 17.6% Horses Kaduna state | 23.4% children in Ethiopia | No data | No data | No data | No data | No data |
| 39   | Pasteurellosis                 | No data | No data | No data | No data | Sheep 37.1%, goats 21.9% | 86% in Ethiopia | 2.85% camels in Cairo | No data | No data |
| 40   | Diphyllobothriosis             | No data | 32.1% Ekiti | No data | No data | 7.1% dogs in Ghana | No data | No data | No data |
| 41   | Cetosporichis                  | No data | No data | No data | No data | No data | No data | No data |
| 42   | Salmonellosis                  | 5.70% | 43.6% (95%CI [39.7–48.3%]) | 8.7%, 5.68% and 1.08% in children, adults, and carriers respectively (Ethiopia) | 84.0% in Ghana | 1.03%/10 years | No data | No data | Salmonella-contaminated meats and poultry, was estimated to cost Americans around one billion dollars in 1987 |
| 43   | Escherichia coli O157          | 5.00% | Cattle 49.4% | 7.5% South Africa | 44.50–50% in pigs (S/ Africa) | 3 to 5% | No data | No data | The annual cost of illness due to O157 STEC was $405 million (in 2003 dollars) |
|      |                                |        |         |        |         |              | Intervention costs | No data | No data |

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2.4. Ranking the zoonotic disease based on aggregation of scores of the weighted criteria

The final step of the prioritization (Table 5) was to multiply categorical question scores for each pathogen by the weight given to the specific criteria. This was done using decision tree analysis in the OHZDP tool based on Microsoft® Excel. For each disease, the weighted scores for each criterion were summed up to obtain a total weighted score by group. Subsequently, an average weighted score (from all five groups) was obtained and normalized in relation to the maximum score, yielding a normalized final score within a range of 1 to 0 that was used to rank the diseases. Afterwards, the final ranked disease list was reviewed during a plenary session and adopted as the prioritized zoonotic diseases for the country.

2.5. Sensitivity analysis

To assess the strength of the prioritization outcome and sensitivity of the process, the variability in weighting of the selection criteria, consensus building in groups and scoring of disease data by expert opinion were evaluated [4,20] using the sensitivity analysis. First, the five criteria were given equal weights of 1 to obtain normalized scores for each of the preselected zoonotic disease [4]. Next, normalized scores for each zoonotic disease were obtained by systematically removing for each zoonotic disease [4]. Next, normalized scores for each of the five criteria from the process. Finally, each of the five groups considered significant at p-values < 0.05 [4,20]. This study did not require ethical approval because the activity was not a human subject research but an expert elicitation process for assembling information on zoonotic disease prioritization using data that was publicly available. The process entailed experts’ opinions and perceptions based on their knowledge of the field. No personal data was collected from the experts that participated in producing the final prioritization outcome.

Analytical Hierarchy process (AHP) in the OHZDP tool [20] to assign weights to the five criteria based on their relative importance as perceived by each group [57,58]. The most important criterion was assigned the highest weight, and the least important criterion the lowest weight. The group results were then combined at plenary to produce the overall rank and weights for each criterion (Table 4) [4]. A final consistency ratio of less than 0.1 was acceptable in the analytic hierarchy process.

2.3. Development of questions for each criterion

Participants in each of the five groups developed a set of categorical questions that adequately addressed each criterion to be applied to each of the pathogens/diseases (Table 4). The outcome was 19 categorical questions that addressed all the five criteria. In the five groups, each disease/pathogen received a score for each question. A slight modification of the standard OHZDP tool method allowed us to develop multiple questions for some criteria (Table 4). The questions had binomial (yes/no) or ordered multinomial response levels with a maximum of 5 categories (e.g. scoring 0–4) for each question [15]. For criteria with multiple questions, scores were summed up to obtain the total score [4]. To score the pathogens using the criteria questions, participants scored the pathogens against each of the categorical questions.

C. Ihekweazu et al.  One Health 13 (2021) 100257

Table 2 (continued)

| S./N. | Disease/Condition                | Prevalence in Nigeria | Prevalence/Incidence in other African Countries | Estimated impact or burden, Socio-economic and non-monetary losses | Production losses in animals | Intervention costs |
|-------|----------------------------------|-----------------------|------------------------------------------------|---------------------------------------------------------------|-----------------------------|-------------------|
| 44    | Rift valley fever                | Humans 6.7–31.2%      | Animals 3.3–18.7%                              | 29.3% in Tanzania                                             | 7.67% in Burkina Faso       | 1.4%–30%          | $50 m (2007), $540 m (2007–2008) combined for East Africa livestock trade losses. |
| 45    | Swine influenza                  | Humans are not susceptible | 9% of serum samples and 48% of tissue samples | Humans are not susceptible | Humans are not susceptible | Humans are not susceptible | $80 billion and $1.15 billion, of which control cost constitute 42%–59%. (Singapore) |
| 46    | Dengue                           | 30.8% (among febrile children) | 17.2% (among healthy children) | 17.8% in Somalia | Largely unknown due to sparse data | 2.5% (treated) | $0.85 billion and $1.15 billion, of which control cost constitute 42%–59%. (Singapore) |
| 47    | Fascioliasis                     | Cattle (27.68%)       | 7.3% in the Nile delta, Egypt                  | 37% in Sudan, 45% in Cameroon                                 | Rarely kills in humans      | The cost due to condemnation of goat-livers has been estimated to be US $115 per thousand livers (4.0 million annually (England)) |
| 48    | Cysticercosis/ Taeniasis         | 8.60%                 | 45.3% in Tanzania                              | 24.6 and 32.2% for Ag-ELISA and Ab-ELISA, respectively (Cameroon) | The total intervention cost in agriculture amounted approximately 35,000 Euro per DALY occurred (controlling the Q fever epidemic in 2007–2011 in the Netherlands) |
| 49    | Abattoir fever                   | 44% (Sokoto)          | Total prevalence rate herd prevalence rates (14.5%) and (57.1%) | 16% in Egypt | 13% of cattle, 23% of goats, 33% of sheep, 0% of buffalo (Cairo, Egypt) | Vary between 5 and 50% | The cost due to condemnation of goat-livers has been estimated to be US $115 per thousand livers (4.0 million annually (England)) |
| 50    | Listeriosis                      | (22.3%) of HIV/AIDS patients | 91.8% (poultry) | 20% | £ 10.9 million annually |
| 51    | Campylobacteriosis               | 8.30%                 | 15.4% in Ethiopia                              | 43.6% domestic fowls, goats (33.3%) and sheep (23%) | < 0.01% to 8.8% | £ 10.9 million annually |
| 52    | Giardiasis                       | 33.20%                | 27.68%                                          | 5.8% in Ghana |                                      |                   |
Table 3
List of sample criteria given to each group for zoonotic disease prioritization.

| Criteria | Summary |
|----------|---------|
| (i) Transmission potential between humans and animals | Horizontal transmission of disease from humans to animals or vice versa. |
| (ii) Burden of disease in humans | Disease causes high prevalence or incidence rate/year in human. |
| (iii) Epidemic/pandemic potential in humans | Capacity of the infectious agent to spread across state, national, or political borders. |
| (iv) Bioterrorism potential | Capacity of the infectious agent to be used as a weapon against human populations. |
| (v) Amenable to collaboration/collaboration already established | Capacity of public health organizations (including the Government) to work together to diminish burden of disease. |
| (vi) Socio-economic burden of disease | Social as well as financial costs that are associated with the disease. |
| (vii) Severity of illness in humans | Morbidity and/or mortality associated with the disease. |
| (viii) Ability to prevent and control the zoonotic disease in the country | Capacity of the country to prevent, contain, and control the disease. |

3. Results

Thirty-six zoonotic diseases were shortlisted for prioritization (Table 6). Overall, bacterial zoonoses accounted for 15 (41.7%) of the zoonoses shortlisted for prioritization while viral, helminth and protozoan diseases constituted 10 (27.8%), seven (19.4%) and three (8.3%), respectively. Fungal zoonoses accounted for the least number of zoonoses shortlisted for prioritization, one (2.7%). Rabies, avian influenza, Ebola viral disease (EVD), swine influenza and anthrax emerged the first five priority diseases in the final prioritized list; while leptospirosis, toxoplasmosis and cryptococcosis ranked the least. Generally, zoonoses with scanty data for both animals and humans or those for which data were limited to animals alone or were unavailable such as dengue fever, campylobacteriosis, leishmaniasis and toxoplasmosis ranked the least. Generally, there are numerous indicators associated with socio-economic burden of disease. This is because they are known to have wildlife reservoirs which perpetuate them in nature and make their control and possible elimination difficult. In addition, these diseases have no known treatments currently. Conversely, most bacterial and protozoan diseases with effective treatment /control in humans and animals ranked highest. Transboundary animal diseases such as avian influenza, swine influenza, anthrax and tuberculosis, whose outbreaks in livestock and poultry cause productivity and market losses resulting from high mortality and associated trade bans, ranked highest on the socio-economic
impact scale. On the other hand, lower scores were assigned to EVD, Lassa fever, dengue, yellow fever, trichinosis and echinococcosis because they have low prevalence in livestock and poultry and do not cause significant productivity and market losses.

Of the eight suggested selection criteria (Table 3), five were adopted for the prioritization process (Table 4). The weighting and ranking of the selection criteria by the five groups were later summarized (Table 7). Overall, the criteria assessing epidemic potential of a disease with a final weight of 0.23, ranked highest while socioeconomic impact of a disease, with a final weight of 0.17, ranked the least (Table 7). Although severity of disease was ranked first across four groups, it however ranked second overall with a final weight of 0.22, due to it being ranked fourth by one of the groups.

3.1. Sensitivity analysis

The overall consistency ratio between normalized scores and adjusted scores calculated by the OHZDP tool when comparing weighted

| Table 5 |
|---|
| Summary of steps involved in arriving at prioritized zoonotic diseases in Nigeria. |
| S/ N | Activities/calculations involved in arriving at each conclusion | Conclusions/step arrived at |
|---|---|---|
| 1 | Extensive literature review of existing published and unpublished works on zoonotic diseases in Nigeria and the West African region | Zoonotic diseases to be prioritized |
| 2 | Selection of ranking criteria by groups, discussions, consensus and adoption of five criteria at plenary for ranking. | Development of ranking criteria |
| 3 | Conduct of semi-quantitative analytic hierarchy process using a Microsoft Excel® program from the OHZDP tool to assign weights to the five criteria based on their relative importance as perceived by each of the groups. | Weighing criteria by pair-wise comparison through analytical hierarchical process |
| 4 | Development of categorical questions that adequately addressed each criterion to be applied to each of the pathogens/diseases with slight modification of the standard OHZDP tool methods allowing for development of multiple questions for some criteria. | Scoring each zoonotic disease based on the criteria |
| 5 | Multiplication of the categorical question scores for each pathogen by the weight given to that specific criteria using OHZDP decision tree analysis based on Microsoft® Excel. Summation of weighted scores for each criterion for each disease to obtain a total weighted score by group | Aggregation of scores |
| 6 | Average weighted score (from all five groups) was obtained and normalized in relation to the maximum score, yielding a normalized final score within a range of 1 to 0 that was used to rank the diseases. | Ranking of the zoonotic diseases |
| 7 | Final ranked disease list was reviewed during a plenary session and adopted for the country | Adoption of ranked zoonotic diseases list |

| Table 6 |
|---|
| Prioritized zoonotic disease list for Nigeria ranked by criteria and final normalized scores, 2017. |

| Disease | Severity | Epidemic Potential | Burden of Disease | Ability to Prevent and Control | Socio-economic Impact | Normalized Final Score |
|---|---|---|---|---|---|---|
| Rabies | 1 | 5 | 1 | 3 | 4 | 1.00 |
| Avian influenza | 2 | 2 | 3 | 7 | 1 | 0.88 |
| EVD | 1 | 1 | 6 | 9 | 9 | 0.71 |
| Swine influenza | 5 | 3 | 5 | 7 | 1 | 0.68 |
| Anthrax | 4 | 6 | 1 | 3 | 2 | 0.67 |
| Bovine tuberculosis | 5 | 7 | 1 | 3 | 1 | 0.67 |
| African trypanosomiasis | 5 | 9 | 3 | 1 | 4 | 0.65 |
| Lassa fever | 2 | 3 | 5 | 6 | 9 | 0.65 |
| Colibacillosis | 6 | 4 | 6 | 5 | 4 | 0.61 |
| Brucellosis | 4 | 10 | 6 | 4 | 4 | 0.57 |
| Cysticercosis/ Taeniasis | 5 | 11 | 2 | 1 | 5 | 0.55 |
| Staphylococcal disease of animal origins | 7 | 6 | 6 | 1 | 5 | 0.53 |
| Rift valley fever | 7 | 6 | 3 | 6 | 5 | 0.51 |
| Clostridia disease | 3 | 9 | 6 | 6 | 5 | 0.50 |
| Salmonellosis | 7 | 8 | 4 | 4 | 4 | 0.50 |
| Visceral larva migrans | 5 | 11 | 5 | 1 | 7 | 0.48 |
| Schistosomiasis | 6 | 8 | 4 | 2 | 9 | 0.48 |
| Cutaneous larva migrans | 6 | 11 | 4 | 1 | 8 | 0.46 |
| Yellow fever | 8 | 8 | 5 | 8 | 8 | 0.45 |
| Listeriosis | 4 | 11 | 7 | 3 | 5 | 0.45 |
| Dermatophytosis | 7 | 9 | 5 | 3 | 6 | 0.43 |
| West Nile fever | 6 | 7 | 5 | 7 | 6 | 0.42 |
| Dengue | 6 | 3 | 5 | 10 | 9 | 0.42 |
| Campylobacteriosis | 6 | 9 | 6 | 3 | 7 | 0.41 |
| Pasteurelliosis | 8 | 11 | 6 | 2 | 3 | 0.40 |
| Paratonia/Oriithosis | 6 | 11 | 6 | 3 | 6 | 0.39 |
| Streptococcal diseases of animal origin | 7 | 9 | 6 | 3 | 7 | 0.37 |
| Echinococcosis | 5 | 10 | 5 | 6 | 9 | 0.36 |
| Rotavirus infections | 5 | 10 | 5 | 7 | 6 | 0.36 |
| Yersiniosis | 7 | 11 | 6 | 3 | 8 | 0.31 |
| Q Fever | 7 | 11 | 7 | 3 | 7 | 0.30 |
| Trichinosis | 6 | 11 | 7 | 3 | 9 | 0.30 |
| Leishmaniasis | 7 | 10 | 7 | 8 | 7 | 0.29 |
| Leptospirosis | 7 | 10 | 7 | 5 | 7 | 0.28 |
| Cryptosporidiosis | 7 | 9 | 6 | 9 | 8 | 0.23 |
| Toxoplasmosis | 6 | 11 | 6 | 9 | 8 | 0.23 |
and unweighted criteria was 0.06. There was moderate correlation between normalized scores and adjusted scores, calculated by the OHZDP tool, seen when comparing weighted and unweighted criteria ($r = 0.59$, $p < 0.05$), there was strong positive correlation when excluding each criterion from the model ($r = 0.78–0.91$, $p < 0.05$), and when excluding each group from the model ($r = 0.53$, $p < 0.05$).

There was minimal variability in the scores and ranking between the weighted and unweighted criteria and all top 10 diseases were ranked. There was more variability of scores between the groups with statistically different scores for the diseases (Fig. 3A). However, in terms of ranking, for the top 10 diseases, each of the group scored 8. Rabies and avian influenza were consistently ranked first and second across the groups and across the criteria while tuberculosis, African trypanosomiasis and E. coli O157 were ranked 13, 11 and 3 by one group and 3, 4 and 21 by another group respectively. Comparing other criteria, least variability was observed when epidemic potential was excluded from the model (Fig. 3B).

### 4. Discussion

There have been various methods used for prioritizing zoonotic diseases in several developed (e.g. Canada, Japan, The Netherlands, Switzerland and USA) and few developing (Ethiopia, Kenya and Vietnam) countries of the world [11, 57–63]. To our knowledge, this is the first report that prioritized zoonotic diseases in the most populous African nation, Nigeria in the West African sub-region. Following a two-day meeting of a cross section of a multidisciplinary team of human, animals and environmental health experts selected from diverse backgrounds, a ranking process of prioritization of zoonotic diseases was done. The ranking process employed a structured technique by these team of experts to develop a systematic, interactive semi-quantitative consensus that had been previously used and validated [4, 5, 9, 15, 57]. The result of this prioritization process led to the ranking in order of importance: rabies, avian influenza, EVD, swine influenza and anthrax as the five most important zoonotic diseases in Nigeria, in accordance with the GHSA Action Package Prevent – 2 [22]. The findings of this prioritization process strongly favored coordinated, collaborative and multi-sectoral interventions towards the control and prevention of zoonotic diseases through a One Health approach in Nigeria as recommended by the joint external evaluation of the IHR core capacities of the Federal republic of Nigeria [64].

In general, our ranking process prioritized zoonotic diseases due to viruses over bacterial or parasitic pathogens with the topmost four being viral infections while none of the lowest seven was of viral origin. Indeed, rabies has been consistently recognized among the top three zoonotic diseases in similar prioritization surveys reported from Ethiopia, Kenya and Vietnam [4, 5, 11, 15]. There were important features common across the different processes. Diseases either “more prone to cause epidemics or more prevalent in certain regions” were ranked highly [65, 66]. In our prioritization, EVD ranked high given the recent outbreaks in West Africa. Similarly, avian influenza that has caused major outbreaks in poultry and affected humans in Nigeria and East Asia was ranked highly in this and the Vietnamese reports [5]. Conversely Rift Valley fever (RVF) and Streptococcus suis infection ranked high in Kenya and Vietnam, possibly due to their regional distribution and significance, respectively [4, 5]. In East Africa with large pastoral populations, brucellosis and echinococcosis were prioritized and ranked highly compared to their ranking in our case.

### Table 7

| Criteria                        | Group: weighted scores (ranks) | Final weight | Overall ranking |
|--------------------------------|--------------------------------|--------------|-----------------|
|                                 | Group 1 | Group 2 | Group 3 | Group 4 | Group 5 |              |        |
| Epidemic Potential              | 0.28 (2) | 0.31 (2) | 0.28 (2) | 0.46 (1) | 0.31 (2) | 0.23 | 1              |
| Severity                        | 0.42 (1) | 0.08 (4) | 0.37 (1) | 0.27 (2) | 0.42 (1) | 0.22 | 2              |
| Burden                          | 0.17 (3) | 0.41 (1) | 0.16 (3) | 0.05 (5) | 0.16 (3) | 0.2  | 3              |
| Ability to Prevent and Control  | 0.09 (4) | 0.16 (3) | 0.11 (4) | 0.07 (4) | 0.06 (4) | 0.18 | 4              |
| Socio-economic impact           | 0.04 (5) | 0.04 (5) | 0.08 (5) | 0.15 (3) | 0.04 (5) | 0.17 | 5              |

* Consistency ratio < 0.1 is significant.

Fig. 3. Comparison of normalized scores obtained from the weighted criteria (A) using equal weights; (B) excluding each of the five criteria.
Compared to the WHO global burden of zoonotic diseases list for Nigeria using DALYs and death rates, none of the viral diseases in our prioritized list was found in the WHO list rather, only parasitic diseases such as trypanosomiasis, Chagas disease, schistosomiasis, leishmaniasis, lymphatic filariasis and onchocerciasis were listed [67]. Additionally, only three of the WHO listed zoonotic diseases - trypanosomiasis, tae-niosis and leishmaniasis [1] featured in our prioritized zoonotic diseases list, ranking 3rd, 10th and 11th, respectively, in the burden of diseases ranking, and 7th, 11th and 33rd in the overall ranking. The variations between the global burden estimates and our prioritized list may have arisen from the different methods employed and the sources of data used in the two scenarios.

Of the bacterial infections, only anthrax was ranked among the top five in our prioritization list; even though potential risk for bioter-riskism was not a consideration and it is not a major human affliction in Nigeria. However, the socioeconomic importance of the disease, especially when large outbreaks occur in animals, and the associated severity and epidemic potential may have resulted in the high ranking. It is unclear the role played by higher proportion of veterinarians in the prioritization of anthrax in our work. Although Nigeria is among the top 30 countries with the highest burden of human tuberculosis (TB) globally [68], prevalence of zoonotic tuberculosis caused by M. bovis is not known despite bovine TB infection reported in about 5.7–11.7% of its cattle herds [40,46] consequently, bovine TB was not listed among the top five priority diseases. This is probably due to its low epidemic potential as well as perceived severity by the groups. Similarly, common cosmopolitan, mostly foodborne bacterial diseases (Campylobacteriosis, Clostridia disease, colibacillosis, Salmonellosis, Staphylococcal diseases, Streptococcal disease, listeriosis and leptospirosis) were not among the five prioritized zoonotic diseases, suggesting ubiquitous global health problems were rarely prioritized at developing country or regional level.

This outcome conforms with the overarching goal of this work which aimed at identifying and prioritizing endemic zoonotic diseases which impact health and socio-economic well-being of Nigerians for collaborative intervention and management. Consequently, the prioritization process weighted diseases with prevention and control measures higher than those that lack any form of prevention, treatment or curative measures. Not surprisingly, higher weights were assigned to diseases with larger geographical occurrence nationally, as opposed to those that have occurred regionally or globally. The directionality of these choices stem from: the perceived ease and lower cost of addressing preventable zoonotic diseases compared to those lacking any form of prevention; perceived higher burden and risk of impact of endemic diseases compared to diseases that occur regionally and globally and increased risk of impact of diseases with wider geographic spread nationally compared with localized diseases of equal severity. The final list of prioritized zoonotic diseases provides the framework for the conceptualization, design and implementation of prevention and control programs for zoonoses. It also allows for allocation of resources to enhance the management, control and possible elimination of zoonotic diseases in Nigeria [40].

Although important concepts within or common to animal and human health such as antimicrobial resistance and non-communicable diseases such as snakebite were not included, we are aware that this list would not be static. It is anticipated that the list will be reviewed at regular intervals to accommodate other diseases and relevant concepts as new data emerge. For example, monkey pox was not considered in our prioritization process due to its absence in Nigeria since 1979 [69]. However, it occurred in Europe and Nigeria in 2019 with three confirmed cases reported in one of the southern states of Nigeria in September 2017 [70]. As at January 25, 2018, the outbreak had spread with 216 suspected cases reported across 24 states of Nigeria and 80 cases and 5 deaths confirmed in 14 states [71]. Similarly, a nationwide outbreak of yellow fever occurred, shortly after the prioritization process, from September 2017 to March 2018 across the 36 states of the Federation and the Federal Capital Territory [33,34]. A total of 1640 suspected, and 99 confirmed cases was recorded in 334 (43%) local government areas of Nigeria with a case fatality rate of 24.4% among confirmed cases. Yellow fever ranked 19th on the prioritized list but may have ranked higher if the outbreak was recorded prior to the prioritization. These incidences highlight the dynamic trend in the emergence and re-emergence of zoonotic diseases across the globe which necessitates periodic review of the prioritized list as deemed necessary.

The modified OHZDP tool used in this process facilitated a multi-stakeholder collaborative decision-making process that allowed groups of experts to provide input from a wide range of experience for ranking of criteria and consequently, ranking of the zoonotic diseases. The consultative nature of the process, we believe, would enhance ownership of the final list of prioritized diseases by different sectors in Nigeria for resource allocation, and convergence of human and animal health zoonotic disease management programs. Although various stakeholders in different regions have used the OHZDP semi-quantitative tool for prioritization [4,5,15,57], some applied varying degrees of modifications based on country-specific peculiarities, which may make it difficult to compare outputs across countries. In our case, we used a slightly modified version of the OHZDP tool which relied more on group consensus over individual opinion. The modified tool was similar to that used in Kenya [41] but differed slightly in application from those used in Ethiopia [15], Vietnam [5] and Japan [57]. Consequently, our prioritization outputs, like those obtained in Kenya, highlighted endemic diseases with high local public health importance such as rabies and not just diseases with high global attention such as the epidemic-prone diseases or those that impact negatively on trade.

The process employed has certain limitations. For instance, the zoonotic disease surveillance system in Nigeria is primarily passive with high rate of underreporting and limited diagnosis. This, coupled with manual, paper-based reporting at peripheral level provides a major challenge in using health system data to gauge true burden of zoonotic disease, majority of which are neglected in nature. This is why our review focused mainly on online data sources though it is a known fact that many diseases occur in Africa that are not detected by rigorous surveillance, or when detected are not published (on time, delayed or never) [72]. Furthermore, inappropriate group composition may lead to subjectively biased results especially if the groups disproportionately comprise of many participants from same background or even with few but highly influential participants from a given discipline. To avert this challenge, we ensured the use of multiple groups, and that participants within groups were balanced by cadre, professional background and geographical location. Similarly, to curb the disproportionate influence of anchors on the conclusions made, active contributions and participation through voting by raising of hands and name calling of seemingly silent participants for inputs was required for consensus building. Secondly, the measures of disease occurrence and burden (prevalence, mortality rate, case fatality rate, DALYs and zDALY [73] etc) required for decision tree analysis were not available for some diseases and where available, were limited to studies that may not be representative of the entire country. In such cases, experts provided estimates based on data from institutional research work, the West African region or from diseases closest in epidemiology to those being examined which may have introduced some error. Thirdly, overestimation of true burden of certain diseases based on their epidemiology in Nigeria could have resulted in the country ranking such diseases high. For example, in Nigeria, the population of dogs is not well known, and reporting of dog rabies is suboptimal making it difficult to ascertain the true burden of canine rabies. However, rabies ranked highest in the list due to its endemicity, perceived nationwide spread and the associated severity with a case fatality rate of 100% [49]. Conversely, the use of disease metrics such as case fatality rates and DALYs determined with data from the developed world could underestimate the public health burden of some of the endemic zoonotic diseases. Finally, using the modified OHZDP tool and semi-quantitative techniques limited the comparability of our output with outputs from other countries especially those that used the standard OHZDP tool version.
5. Conclusion

Using a systematic, semi-quantitative approach, a team of animal, human and environment health practitioners prioritized zoonotic diseases in Nigeria, ranking rabies, avian influenza, EVD, swine influenza and anthrax as the most important. It is recommended that coordinated collaborative multi-sectoral interventions towards the control and prevention of zoonotic diseases should be implemented through a One Health approach in the country. The data gained from this process will be used to optimize human and financial resources for the prevention, detection and control of zoonotic diseases in Nigeria. Following the prioritization, a multisectoral and multi-agency one-health technical working group coordinated by the Nigeria Centre for Disease Control has been established at the National level and have been actively meeting to move the Nigerian one health agenda forward.

Declaration of interests

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.

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