

# Antibiotic Resistance in Food Animals in Africa: A Systematic Review and Meta-Analysis

Luria Leslie Founou,<sup>1,2</sup> Daniel Gyamfi Amoako,<sup>1</sup>  
Raspail Carrel Founou,<sup>1,3</sup> and Sabiha Yusuf Essack<sup>1</sup>

**Objectives:** This study critically reviewed the published literature and performed a meta-analysis to determine the overall burden of antibiotic-resistant bacteria in food animals in Africa.

**Methods:** English and French published articles indexed in EBSCOhost, PubMed, Web of Science, and African Journals Online were retrieved, with searches being conducted up to August, 2015. Data were pooled and meta-analysis performed using a random-effects model, and the results are described as event rates.

**Results:** According to the predefined inclusion and exclusion criteria, 17 articles out of the 852 retrieved were eligible for the qualitative and quantitative analysis. The studies included were mainly conducted in Nigeria, with *Escherichia coli*, *Salmonella* spp., and *Campylobacter* spp. being the main bacteria. The pooled estimates showed high level of antibiotic resistance (ABR) (86%;  $p < 0.001$ ) and multidrug resistance (73%;  $p = 0.003$ ).

**Conclusion:** Our results suggest that ABR is substantively prevalent and poses a serious threat for food safety and security in Africa. These findings shed light on areas for future research concerning antibiotic-resistant and multidrug-resistant bacteria in food animals as etiological agents of infectious diseases in humans. They further yielded some interesting findings on the burden of ABR that could be useful in developing measures to contain this threat in the farm-to-plate continuum in Africa.

**Keywords:** antibiotic resistance, food-borne infection, zoonosis, food animals, One Health approach

## Background

ANTIBIOTIC RESISTANCE (ABR) is a worldwide public health concern, with serious health, economic, and societal repercussions.<sup>1</sup> Its emergence is attributed to the selective pressure exerted by antibiotic use in the community, hospitals, veterinary health, agriculture, aquaculture, and the environment. Additionally aggravating the situation is the fact that very few new antibiotics have recently been produced by pharmaceutical companies. It is widely acknowledged that food animals are key reservoirs of antibiotic-resistant bacteria and that antibiotic usage in this population favors the emergence, selection, and spread of resistance among animals and humans,<sup>2-4</sup> both through zoonoses (infectious diseases transmitted between animals and humans) and the food chain.<sup>4-6</sup>

Food animal production generally depends on the therapeutic and prophylactic use of antibiotics and can be enhanced by the use of antibiotics for growth promotion. Several antibiotic agents commonly used in food animals

are either identical or linked to those administered in humans.<sup>7</sup> This broad use of antibiotics in agriculture has increased the danger posed by the emergence and spread of ABR by selecting new antibiotic-resistant (commensal and/or pathogenic) bacteria and infections caused by these bacteria.<sup>4,6,8,9</sup> Accordingly, the presence of ABR in food animals threatens food safety and, by extension, global health. Given the sharing of bacteria between humans and animals, as well as the animal origin of 60%<sup>10,11</sup> of emerging human pathogens, the Food and Agriculture Organization of the United Nations (FAO), World Organization for Animal Health (OIE), and World Health Organization (WHO) fully endorse the One Health approach as articulated in the WHO Global Action Plan on Antimicrobial Resistance (AMR),<sup>12</sup> the OIE Strategy on AMR and Prudent Use of Antimicrobials,<sup>13</sup> and the FAO Action Plan on AMR.<sup>14</sup>

Notwithstanding the situation evidenced by this global health challenge, the dearth of information concerning ABR in food animals in Africa leads to an underestimation of the

<sup>1</sup>Antimicrobial Research Unit, College of Health Sciences, University of KwaZulu-Natal, Durban, South Africa.

Departments of <sup>2</sup>Food Safety and Environmental Microbiology and <sup>3</sup>Clinical Microbiology, Centre of Expertise and Biological Diagnostic of Cameroon, Yaoundé, Cameroon.

nature and extent of ABR, as well as the associated health and socioeconomic impacts on human, animal, and environmental health regionally and globally. This systematic review analyzed the published literature on the prevalence of ABR in food animals in Africa. By summarizing the available data, our objectives were to (1) describe the dissemination of antibiotic-resistant bacteria in food animals; (2) highlight the need to reduce, replace, and refine the use of antibiotics in agriculture; and (3) provide evidence to follow the One Health approach to contain the emergence and spread of ABR on this continent.

## Materials and Methods

The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA<sup>15</sup>) and Meta-analysis of Observational Studies in Epidemiology (MOOSE<sup>16</sup>) statements were followed. (Supplementary Table S1; Supplementary data are available online at <http://www.liebertpub.com/mdr>).

### Outcomes of interest

The primary outcome of interest was to identify the prevalence of antibiotic-resistant bacteria isolated from apparently healthy, sick, or dead food animals, products thereof, and exposed workers at farms, abattoirs/markets, or both. Resistance to beta-lactams, aminoglycosides, and fluoroquinolones, described by the WHO<sup>17</sup> and OIE<sup>18</sup> as critically important antibiotics in humans and animals, as well as tetracyclines listed as critically important veterinary antimicrobial agents in animals,<sup>18</sup> was used as the basis to ascertain multidrug resistance (MDR) in our study. The secondary outcome of interest was the prevalence of multidrug-resistant bacteria, which, for the purpose of this review, is regarded as resistance to three or more classes of antibiotics.

### Sources and literature search

A multifaceted search was conducted in four electronic databases, namely MEDLINE via PubMed, Web of Science, EBSCOhost, and African Journals Online, up to August, 2015, using a combination of boolean operators (AND/OR), Medical Subject Heading (MeSH), and predefined keywords, including “antimicrobial resist\*”, “antibiotic resist\*”, “drug\* resist\*”, “multi-drug resist\*”, “multiple-drug resist\*”, “multiple drug\* resist\*”, “food animal\*”, “farm animal\*”, “domestic animal\*”, “livestock animal\*”, “poultry”, “pig”, “cattle”, “sheep”, and “goat” and followed by refining terms: “Africa\*”, “East\* Africa\*”, “Western\* Africa\*”, “Southern\* Africa\*”, “Northern\* Africa\*”, “Central Africa\*”, and “Sub-saharan Africa\*”. The truncation mark (\*) specifies that diverse extensions were used during the search.

The reference lists of all included articles were further used to carry out a supplementary literature search. In addition, attempts were made to contact authors to obtain inaccessible abstracts and full texts of included studies. Articles in English and French were retrieved and assessed for potentially relevant studies pertaining to AMR in food producing animals in Africa. The authors independently screened and evaluated the full texts of the articles following the first duplicated and blinded screening on the basis of titles and abstracts for relevance to the study objectives.

Disagreements and inconsistencies among authors were resolved by consensus after discussion.

### Exclusion and inclusion criteria

The authors individually assessed articles using predesigned eligibility forms and according to predefined eligibility criteria (Table 1). Briefly, studies on parasites, viruses, and fungi, as well as those dealing with ABR in aquatic, companion and wildlife animals, and the environment, were excluded. Although studies dealing with ABR in humans were excluded, those reporting data of workers exposed to food animals and/or products thereof were included. Studies reporting data from outside Africa were further not selected nor was gray literature (foreign or domestic material usually inaccessible through relevant databases and indexes) and unpublished data.

The selection of French and English published articles was based on clearly defined populations involving living food animals at farms and/or processed/freshly slaughtered animals at abattoirs/markets. To be included, studies must have also performed antibiotic susceptibility testing with antibiotics belonging to beta-lactam/aminoglycoside, tetracycline, and fluoroquinolone classes of antibiotics through disk diffusion, agar dilution, broth microdilution, or E-test methods and results interpreted according to appropriate guidelines (Antibiogram Committee of the French Society of Microbiology [CA-SFM]; European Committee on Antimicrobial Susceptibility [EUCAST]; and Clinical Laboratory Standards Institute [CLSI] formerly known as National Committee on Clinical Laboratory Standards [NCCLS]).

TABLE 1. LIST OF INCLUSION AND EXCLUSION CRITERIA

#### Inclusion criteria

- Studies reporting prevalence and molecular epidemiology of bacterial resistance in livestock animals (including poultry) in Africa
- ABR in food animals and food products (meat, carcasses, egg, chicken, ready-to-eat meat/chicken, cheese, and sausage at supermarket)
- ABR in food animals and exposed workers (farmer and slaughterhouse workers)
- ABR in food animals, exposed workers, and food products
- Antimicrobial susceptibility testing by either disk diffusion or broth microdilution, agar dilution, E-test, or VITEK
- AST conducted using CLSI/EUCAST/SFM/other relevant committee guidelines
- Articles published in French and English.

#### Exclusion criteria

- Data emanating from outside Africa
- Antimicrobial resistance in parasite, viruses, and fungi
- Antimicrobial resistance in humans (not exposed to food animals), companion and aquatic animals, and wildlife
- Antimicrobial resistance in food products and animal feed
- Reports published in languages other than French and English
- Nonpublished articles, letters to editor, books, abstracts, posters, review

ABR, antibiotic resistance; AST, antimicrobial susceptibility testing; EUCAST, European Committee on Antimicrobial Susceptibility; CLSI, Clinical Laboratory Standards Institute; SFM, French Society of Microbiology.

Multisite and intercontinental studies involving ABR in food animals in African countries were also considered.

#### Framework for literature screening and data extraction

EndNote (version X7; Thomson Reuters) was used for literature management, and relevant data from included articles were extracted as outlined in Table 2. The data were abstracted and analyzed using a framework onto an Excel<sup>®</sup> (Microsoft<sup>®</sup> Office Excel 2013) spreadsheet, including for each study, first author details, country of study, year of publication, aims, study population (*e.g.*, pigs, poultry, cattle, sheep, goat, and human), type of sample (*e.g.*, nasal swabs, rectal swabs, fecal samples, and meat products), sample size, clinical status (*e.g.*, apparently healthy, sick, and dead), study site (*viz.* slaughterhouse, farm, and market), type of study (*e.g.*, single, multisite, and international study), bacteria of interest (*e.g.*, *Staphylococcus aureus*, *Salmonella* spp.,

1 indicating moderate quality, and 0 low quality. Summing up the scores of each item provided the overall score of the study, with the highest being 16. A total score  $\geq 12$  was regarded as high quality (low risk of bias), between 6 and 12 as moderate quality (medium risk of bias), and  $< 6$  as low quality (high risk of bias). Only high-quality studies were included in the study. The quality assessment was undertaken individually by the authors.

#### Statistical analysis

Microsoft Excel (2013 for Windows) was used to analyze the data following an initial extraction. Meta-analyses were performed for outcomes of which there were four or more studies that could be combined. Analyses were conducted across animal populations for the two selected end points (resistance and MDR). The rates of antibiotic-resistant and multidrug-resistant bacteria among included studies were calculated as follows:

$$\text{Bacterial ABR rate (\%)} = \frac{\text{Number of strains confirmed resistant}}{\text{Number of strains isolated and screened for resistance}}$$

$$\text{Bacterial MDR rate (\%)} = \frac{\text{Number of strains confirmed multi-drug resistant}}{\text{Number of strains confirmed resistant}}$$

*Campylobacter* spp., *Escherichia coli*, and *Enterococcus* spp.), antibiotics tested, antimicrobial susceptibility testing (AST) methods (disk diffusion, micro-broth dilution, agar dilution, E-test, and automated methods), guidelines of interpretation of AST (*e.g.*, CA-SFM, EUCAST, CLSI, and NCCLS), and ABR/MDR prevalence and results.

#### Quality assessment

Various types of observational studies addressing prevalence were considered in this systematic review. There are numerous reporting measures assessing the study quality in systematic reviews and meta-analyses, but these are generally limited to specific type of studies such as randomized-controlled trials, with no standard method for conducting quality assessment of prevalence data studies. We could therefore not use preexisting scales to assess study quality. The modified critical appraisal tool (high-quality item rating scale) developed by Munn *et al.* was used to assess the quality of all included studies<sup>19</sup>: (1) Was the basic data, including study period, sample type, bacteria of interest, and study site, provided? (2) Were the study participants recruited in an appropriate way? (3) Was the sample size representative of the target population? (4) Were the study subjects and setting described in detail? (5) Was the data analysis conducted with sufficient coverage of the identified bacteria? (6) Were all important confounding factors/subgroups/differences identified and accounted for? (7) Were objectives and standard criteria used to measure the condition? (8) Was the condition measured reliably?

Each item was answered with a yes, no, or unclear and scored on a three-point scale, with 2 indicating high quality,

Meta-analyses of rates were undertaken to determine the overall prevalence of antibiotic-resistant and multidrug-resistant bacteria among food animals and exposed workers. Subgroup analyses were conducted for population-, sample-, setting-, organism-, and country-defined subgroups.

Forest plots of pooled event rates for the primary and secondary outcomes, with 95% confidence intervals (CIs), were generated using the Comprehensive Meta-Analysis Software (Biostat, Inc., New Jersey) version 3 for Windows. Studies were weighted in favor of those with more precise results (narrower CIs), and results are presented as event rates. Data were pooled and meta-analyses performed using the random-effects model to provide a more conservative estimate of resistance, allowing for any heterogeneity between studies. This method was used to assess the extent of bacterial resistance of the entire relevant population, not only the population in the included studies. The  $I^2$  statistic with cutoff values of 25% (low), 50% (moderate), and 75% (high) was used to assess heterogeneity between studies, and the chi-square test with  $p$ -value  $< 0.05$  was used to define a significant degree of heterogeneity within studies. Publication bias was assessed and visualized by a funnel plot and Egger's tests for small study effects.

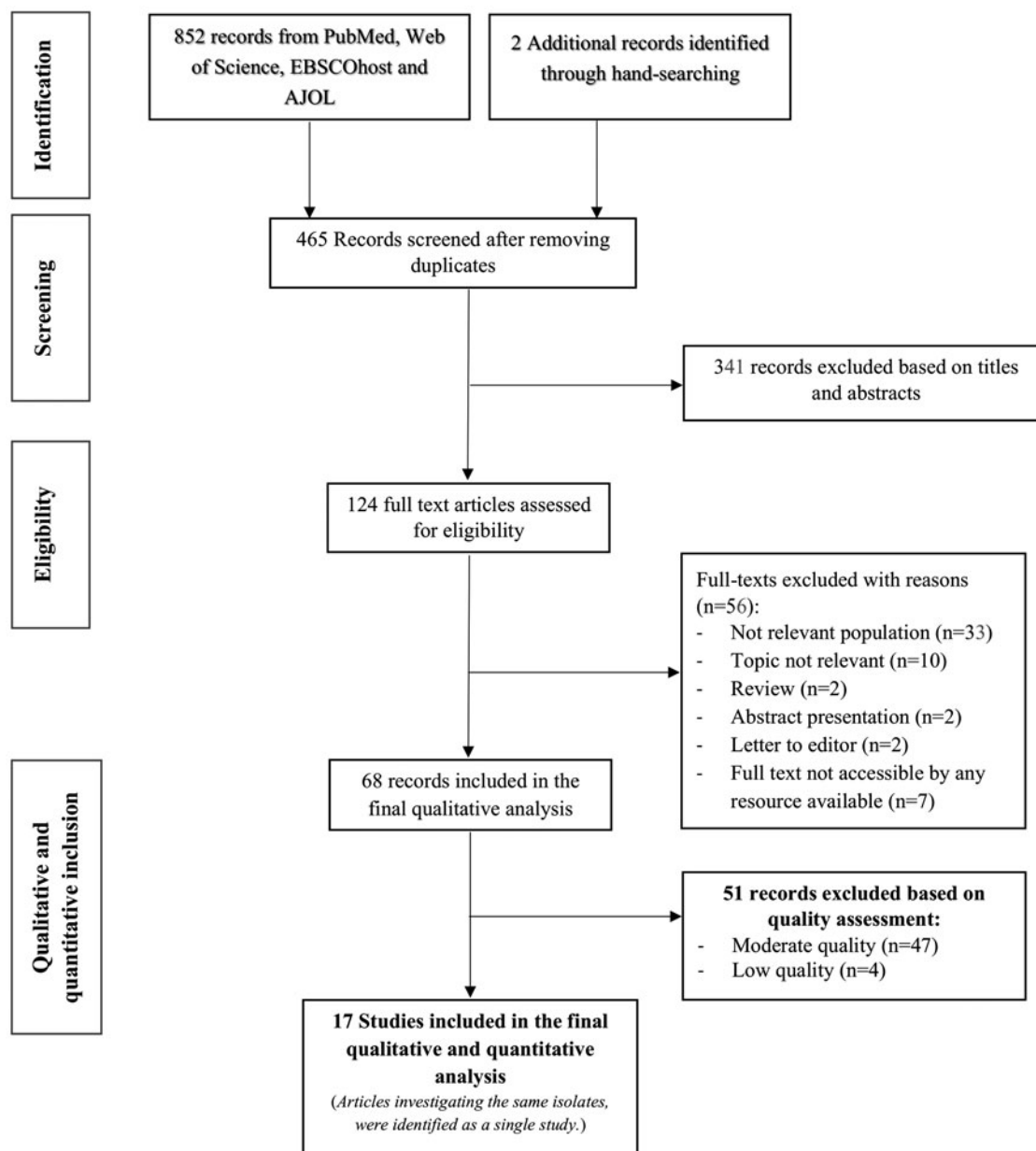
#### Results

Figure 1 outlines the workflow of the study selection process with reason of exclusion. The systematic search from the four electronic databases identified 852 articles. After duplicates were removed, 463 articles were screened for potential inclusion based on their titles and abstracts, with 124 full-text articles being entirely assessed. Two

TABLE 2. CHARACTERISTICS OF ELIGIBLE STUDIES

Country	Study population (N)	Clinical status	Type of sample (N)	Study site (N)	Bacteria (N)	R	MDR	Detection of genes		
								ABR	Virulence	References
Studies conducted only in food animals										
Algeria	Poultry (300)	NR	Dropping (100), ceca (100), neck skins (100)	Farm (6), Abattoir (4)	<i>Campylobacter</i> spp. (263)	+	+	N/A	N/A	33
Cameroon	Poultry (150)	NR	Carcasses (150)	Abattoir (8)	<i>Salmonella</i> spp. (103)	+	+	N/A	N/A	34
Kenya	Cattle (80) Pig (105) Poultry (50)	NR	Carcasses (90), feces (95), cloacal swab (48), pharyngeal swab (12)	Abattoir (2)	<i>Escherichia coli</i> (235)	+	+	+	N/A	35,36 <sup>a</sup>
Nigeria	Poultry (100)	Healthy	Fecal samples (200)	Abattoir (NR)	<i>E. coli</i> (162)	+	+	+	N/A	37
Nigeria	Poultry (400)	Healthy and sick	Cloacal swabs (201), tracheal swabs (196), internal organs (903)	Farm (100)	<i>E. coli</i> (805) <i>Staphylococcus aureus</i> (660)	+	NR	+	N/A	38
Nigeria	Poultry (525)	NR	Internal organs (235), feces (140), cloacal swabs (150)	Abattoir (3)	<i>Salmonella</i> spp. (41)	+	+	N/A	N/A	39
Nigeria	Pig (306)	NR	Fecal samples (306)	Farm (31)	<i>Salmonella</i> spp. (229)	+	+	+	N/A	40
South Africa	Pig (400)	NR	Fecal samples (400)	Farm (2)	<i>Enterococcus</i> spp. (320)	+	+	N/A	+	41
Tunisia	Poultry (136)	Healthy	Fecal samples (136)	Farm (36)	<i>E. coli</i> (67)	+	+	+	N/A	42
Uganda	Pig (465)	Sick and healthy	Fecal samples (465)	Farm (93)	<i>Salmonella</i> spp. (53)	+	+	N/A	N/A	43
Zambia	Cattle (376)	NR	Fecal samples (376)	Farm (104)	<i>E. coli</i> (371)	+	+	N/A	N/A	44
Zimbabwe	Poultry (14,165)	NR	Cloacal swabs (2, 833)	Farm (NR)	<i>Salmonella</i> spp. (206)	+	+	N/A	N/A	45
Studies conducted in food animals, food products, and exposed workers										
Ethiopia	Cow (195) Food products (195)	NR	Fecal (195) Milk samples (195)	Farm (23)	<i>Salmonella</i> spp. (24)	+	+	N/A	N/A	46
Ghana	Human (22) Goat (51) Sheep (44) Pig (12) Poultry (103) Human (395)	NR	Human stool (22) Animal feces (210) Human stool (58)	Farm (NR)	<i>E. coli</i> (178)	+	+	N/A	N/A	47
Studies conducted in food animals and food products										
Nigeria	Cattle (407) Sheep (168) Goat (281) Pig (409) Meat (868) Cattle (800)	NR	Fecal samples (1, 265) Pork (200) Mutton (450) Beef (448) Goat-meat (175) Carcasses (800) Meats (250) Carcasses (250)	Farm (NR) Abattoir (NR) Meat market (NR)	<i>E. coli</i> (154)	+	+	N/A	+	48
Senegal	Poultry (250)	NR	Carcasses (250)	Abattoir (4) Abattoir (80)	<i>E. coli</i> (227) <i>Campylobacter</i> spp. (205)	+	+	N/A	N/A	49
						+	NR	+	N/A	50–52 <sup>a</sup>

<sup>a</sup>Articles that investigated the same population and isolates, despite answering different research questions, were identified as a single study. N, sample size; NR, not reported; N/A, not applicable; +, positive result; R, resistance; MDR, multidrug resistance.



**FIG. 1.** Study flowchart demonstrating the identification and inclusion process for the qualitative and quantitative synthesis.

articles were added following hand searching and according to the predefined inclusion and exclusion criteria, yielding a final number of 68 studies being eligible for the quality assessment. Of these 68 studies, 17 were rated as good quality (low risk of bias), 47 were of moderate quality (medium risk of bias), and 4 were of poor quality (high risk of bias). Only good quality studies were finally included in the qualitative and quantitative synthesis.

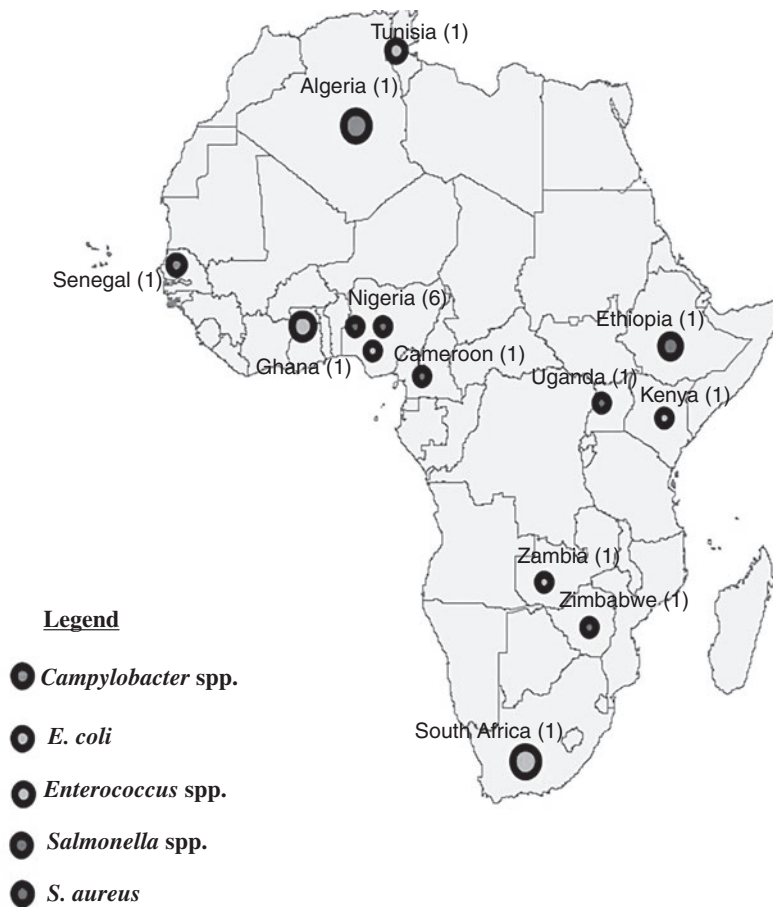
#### Description and characteristics of included studies

Most of the data analyzed were obtained from single center studies conducted mainly in Nigeria ( $n=6$ ) (Table 2; Fig. 2). The majority of studies ( $n=12$ ) reported ABR only in food animals while two studies investigated ABR concomitantly in food animals, food products, and exposed workers.<sup>20,21</sup> Similarly, three studies reported ABR conjointly in food animals

and food products.<sup>22–25</sup> *E. coli* ( $n=8$ ), *Salmonella* spp. ( $n=6$ ), and *Campylobacter* spp. ( $n=2$ ) were the main antibiotic-resistant bacteria investigated and reported (Table 2; Fig. 2).

#### Assessment of ABR of bacterial species

All articles (100%) included antibiotic susceptibility testing of the identified bacterial species. Overall, *E. coli* isolates were screened with 16 different antibiotics across all respective studies using disk diffusion (75%; 6/8) and broth microdilution (25%; 2/8). Similarly, 19 antibiotics were tested against *Salmonella* spp. isolates with disk diffusion (50%; 3/6) and broth microdilution (33.3%; 2/6) being the main AST methods (Table 3). The use of standardized guidelines was reported in all 17 studies. Susceptibility testing was performed most frequently to ampicillin (75%) followed by tetracycline, gentamicin, trimethoprim–sulfamethoxazole, streptomycin,



**FIG. 2.** Graphical representation of antibiotic-resistant bacteria reported in food animals in Africa. Each bacterium is annotated with a shaded circle. The number of studies carried out in each country is also indicated. Map was created using ArcGIS® and ArcMap™ software version 10.3 (Esri, CA).

ciprofloxacin, nalidixic acid, chloramphenicol, and cefuroxime in *E. coli* (Table 3). Regarding *Salmonella* spp. the order was as follows: streptomycin, gentamicin, ciprofloxacin, tetracycline, chloramphenicol, ampicillin, nalidixic acid, sulfonamides, and trimethoprim-sulfamethoxazole. The overall estimated effects for *Campylobacter* spp., *S. aureus*, and *Enterococcus* spp. were not calculated due to insufficient reports.

#### Primary analyses

Figures 3A and 4A represent forest plots of untransformed event rate estimates of ABR and MDR in selected studies. Pooled estimates generated 86% (95% CI, 76.3–92.20%,  $p=0.000$ ) of ABR and 73% (95% CI; 58.3–83.9%,  $p=0.003$ ) of MDR. Subgroup analyses were performed per population, bacterium, setting, sample, and country to allow more specific results.

#### Subgroup analyses

**Population.** Figures 3B and 4B show forest plots of ABR and MDR per population with 95% CIs. The prevalence of ABR was very high in pigs with a prevalence of 93.6% (95% CIs; 77.7–98.4%;  $p<0.001$ ). The prevalence of ABR was 78.2% (95% CIs; 44.1–94.3%;  $p=0.098$ ) in cattle and 73.1% (95% CIs; 48.8–88.6%;  $p=0.062$ ) in poultry. Despite the highest level of ABR being in pigs (93.6%; 95% CIs; 77.7–98.4%;  $p<0.001$ ), MDR was assessed to be largely lower in this population (51.1% [95% CIs; 23.3–78.3%;  $p=0.942$ ]) although it was not statistically significant. Conversely,

overall prevalence of MDR was elevated in cattle and poultry, with 74.3% (95% CIs; 43.4–91.6%;  $p=0.117$ ) and 84.3% (95% CIs; 56.0–95.8%;  $p=0.022$ ) prevalence, respectively. Pooled estimates for goats and sheep were not calculated due to insufficient data (only two reports). The  $I^2$  values of the logit event estimates in cattle, poultry, and pigs were 95.53%, 95.57%, and 96.84%, respectively ( $p=0.000$ ).

**Bacterial species.** *E. coli* was the principal bacterium of interest (8 out of 17 studies) and was most frequently investigated individually with no other bacterial species in different populations. Significant levels of ABR (86.50% [95% CIs; 73.20–93.8%;  $p=0.000$ ]) and MDR (77.50% [95% CIs; 58.90–89.2%;  $p=0.006$ ]) were identified in *E. coli*. Similarly, rate of ABR was high in *Salmonella* spp. (80.9% [95% CIs; 54–93.8%;  $p=0.028$ ]), whereas MDR was estimated at 34.6% (95% CIs; 19.80–53.20%;  $p=0.102$ ) (Figs. 3C and 4C).

**Setting.** Pooled estimates were conducted for isolates collected from farms and abattoirs. Overall prevalence of ABR was higher in farms (88.6%, [95% CIs; 74.4–95.4%;  $p=0.000$ ]) than abattoirs (79.3%, [95% CIs; 52.4–93.0%;  $p=0.032$ ]). Similarly, MDR prevalence was higher in farms (86.6% [95% CIs; 69.1–94.9%;  $p=0.001$ ]) than in abattoirs (52.4% [95% CIs; 23.2–79.9%;  $p=0.886$ ]) (Supplementary Figs. S1A and S2A; Supplementary Data are available online at [www.liebertpub.com/mdr](http://www.liebertpub.com/mdr)).

**Sample.** Supplementary Figures 1B and 2B depict forest plot of ABR and MDR analyzed per sample. Fecal samples were the main isolation site with elevated rates of ABR (96.1%; 95% CIs, 89.2–98.6%,  $p=0.000$ ) and MDR (69.5%; 95% CIs, 49.6–84%,  $p=0.054$ ). Pooled estimates for carcasses were not calculated due to insufficient reports.

**Country.** Subgroup analyses per country provided a 95.9% (95% CIs; 78.1–99.3%;  $p=0.001$ ) prevalence of ABR in Nigeria (Supplementary Fig. S1C), while the level of MDR was 61.9% (95% CIs; 35.4–82.80%;  $p=0.552$ ) (Supplementary Fig. S2C). Prevalence in other countries could not be ascertained as only, respectively, one report was available for these countries.

## Discussion

ABR is one of the greatest public health challenges facing the world. The situation has become particularly worrying as a result of the escalating global emergence of multidrug resistant bacteria in the food chain.<sup>6,26</sup> This systematic review and meta-analysis was undertaken to analyze the published literature reporting prevalence of ABR in food animals in Africa. Out of the 852 records found through database searching, 20 records describing 17 different studies were included in the qualitative and quantitative analysis. The study proved that antibiotic-resistant foodborne pathogens are underinvestigated on this continent with reports from only 12 of the 54 African countries. The overall prevalence of ABR and MDR was 86% and 73%, respectively. These results could be attributed to agricultural practices being overreliant on antibiotic use in Africa.<sup>4,5,27</sup> This is consistent with a recent modeling study, which suggested that a shift on agricultural practices from small to industrial scale in developing countries will lead to up to a third of the global increase in antibiotic consumption in food animals by 2030.<sup>28</sup>

At the animal species level, pigs and poultry were the leading population colonized or infected by antibiotic-resistant bacteria and multidrug-resistant bacteria in our study. The high prevalence of multidrug-resistant bacteria observed among poultry isolates reflects the relatively large consumption of various antibiotics for their breeding, whereas the high rate of single resistance in pigs suggests that few classes of antibiotics are used to treat or prevent infections. Our findings are in accordance with that reported elsewhere in other developing countries such as Thailand and Vietnam.<sup>29–31</sup> In Denmark, the first country to have implemented a surveillance program of ABR, as well as in the rest of the European Union, the prevalence of antibiotic-resistant and multidrug-resistant bacteria in food animals was relatively lower (range: 4–65%) than in our study.<sup>20–23,26</sup> Differences in the level of resistance could be associated with long-term surveillance programs, infection prevention and control and biosecurity measures, antibiotic use monitoring, and a ban on antimicrobials as growth promoters for many years in food animals in these high-income European countries. It is probable that such measures and policies would also be appropriate to contain the emergence and spread of ABR in food animals in Africa.

A sound analysis and interpretation of our findings raised some fundamental questions: (1) As antibiotic-resistant and multidrug-resistant bacteria have been isolated from healthy and sick animals across the continent, what are the genetic

elements (resistance and virulence genes) and clonal relatedness of these bacteria within and between both populations, as well as within and between countries? (2) Are healthy animals becoming clinically ill following the asymptomatic carriage of antibiotic-resistant bacteria? (3) What are the global health, societal, and economic implications if these animal-originating strains succeed in spreading and undergoing host-adaptive micro-evolutionary changes that could lead to the emergence of new and more resistant/virulent strains in the human population? There were unfortunately limited data to answer these questions, thereby highlighting areas for future research.

Subgroup analysis per bacteria displayed high prevalence of ABR and MDR in *Salmonella* spp. A meta-analytical study carried out in Ethiopia revealed a diverse prevalence of *Salmonella* spp., these being 7.07% in cattle, 8.41% in sheep, 9.01% in goats, and 43.81% in pigs with AST data not reported.<sup>24</sup> Our results are also higher than that described in the Netherlands where 12% and 43% of ESBL-producing and fluoroquinolone-resistant *Salmonella* spp. were observed in poultry, respectively.<sup>25</sup> This finding could be correlated to poor farming/slaughterhouse practices and suboptimal hygiene measures.

The high prevalence of ABR and MDR in *E. coli* reported in our study is of further great concern as the involved antibiotic resistance genes (ARGs) may be carried on mobile genetic elements. ABR and MDR in *E. coli* could be responsible for serious infections in humans on this continent and serve as reservoirs of ARGs that could potentially be disseminated to other commensal and pathogenic bacteria such as *Salmonella* spp. which, in turn, may spread through the food chain.<sup>2,4,6</sup> This therefore confirms that monitoring ABR in indicator bacteria such as *E. coli* in food animals and products thereof is imperative to understand the evolution and transmission dynamics of antibiotic-resistant bacteria and ARGs in the food chain.<sup>23,26,32</sup> Despite the fact that we did not ascertain the nature and extent of antibiotic use in food animals, the high prevalence of ABR and MDR observed among *E. coli* and *Salmonella* spp. isolates is indicative of widespread use of antibiotics in farming practices both for prevention and treatment of infectious diseases in food animals in Africa.

Antibiotic-resistant and multidrug-resistant bacteria were highly prevalent in food animals at farms and abattoirs. Multidrug-resistant bacteria detected in food animals at farms (86.6%; 95% CIs, 69.1–94.9%,  $p=0.001$ ) were directly representative of the antimicrobial use in these settings, whereas those detected at abattoirs (52.4%; 95% CIs, 23.2–79.9%,  $p=0.886$ ) reflected bacteria surviving the processing stage and, therefore, able to reach the consumer. This is a grave public health threat, as given the globalization of trade in food animals and food products, as well as international travels, there are no geographic borders to contain the global dissemination of antibiotic-resistant and multidrug-resistant bacteria emerging in Africa.

A 95.9% and 61.9% prevalence of ABR and MDR were, respectively, described in Nigeria. However, we were not able to compare these data with other African countries due to insufficient reports. These findings should in no way implicate Nigeria as a country with a high prevalence of ABR, but rather that ABR in the food chain has been recognized as serious public health concern in this country. Our results suggest that more high-quality studies are needed on this continent, that a minimum package of criteria for monitoring systems needs to

TABLE 3. SUMMARY OF ANTIBIOTIC RESISTANCE PROFILES ACROSS INCLUDED STUDIES

Study	Guidelines	Bacterial species	AST methods	No. of strains	Resistant isolates (%)	MDR isolates (%)	Antibiotic resistance profiles of bacterial species isolated (%)																						
							Beta-lactam/beta-lactams inhibitors				Aminoglycosides				Macrolides Fluoroquinolones Tetracyclines Phenicols Furazolidone Sulfonamides														
							Ampicillin	Amoxicillin	Amoxicillin – clavulanate	Cefuroxime	Cefoxitin	Ceftazoxime	Ceftriaxone	Gentamicin	Streptomycin	Kanamycin	Amikacin	Neomycin	Erythromycin	Nalidixic acid	Ciprofloxacin	Enrofloxacin	Tetracycline	Chloramphenicol	Nitrofurantoin	Sulfonamides	Trimethoprim – sulfamethoxazole		
33	CA-SFM	<i>Campylobacter jejuni</i> and <i>coli</i>	Disk diffusion	263	100	100	75.3	46.8	0	0	0	0	0	0	0	0	0	0	21.7	100	83.7	83.7	0	0	0	0	0	0	
50–52 <sup>a</sup>	CLSI	<i>Campylobacter jejuni</i> and <i>coli</i>	E-test method	205	34	N/A																							
41	CLSI	<i>Enterococcus</i> spp.	Disk diffusion	320	100	93.8	39.1								100	77.3	92	98.7	69										
44	EUCAST	<i>E. coli</i>	Disk diffusion	371	16.4	NR	6.5		2																				4
47	NCCLS	<i>E. coli</i>	Disk diffusion	187	NR	91.6	90.35	49.5	0	84.5	56																		62
35,36 <sup>b</sup>	CLSI	<i>E. coli</i>	Disk diffusion	235	65.5	37.9	40.6		1	36	11.6																		22
37	EUCAST	<i>E. coli</i>	Disk diffusion	162	100	NR	100								NR	NR	NR												NR
48	CLSI	<i>E. coli</i>	Broth microdilution	154	96.2	69.5	82.5								50.3		24												42.9
49	NCCLS	<i>E. coli</i>	Disk diffusion	116	100	100	72.9	65.7							11.4														44.3
42	EUCAST	<i>E. coli</i>	Disk diffusion	67	100	100			6		6																		73.1
38	NCCLS	<i>E. coli</i> <i>S. aureus</i>	Broth microdilution	805 660	11 8.8	100 100	13.5 24.3	13.5							13.5														14 24

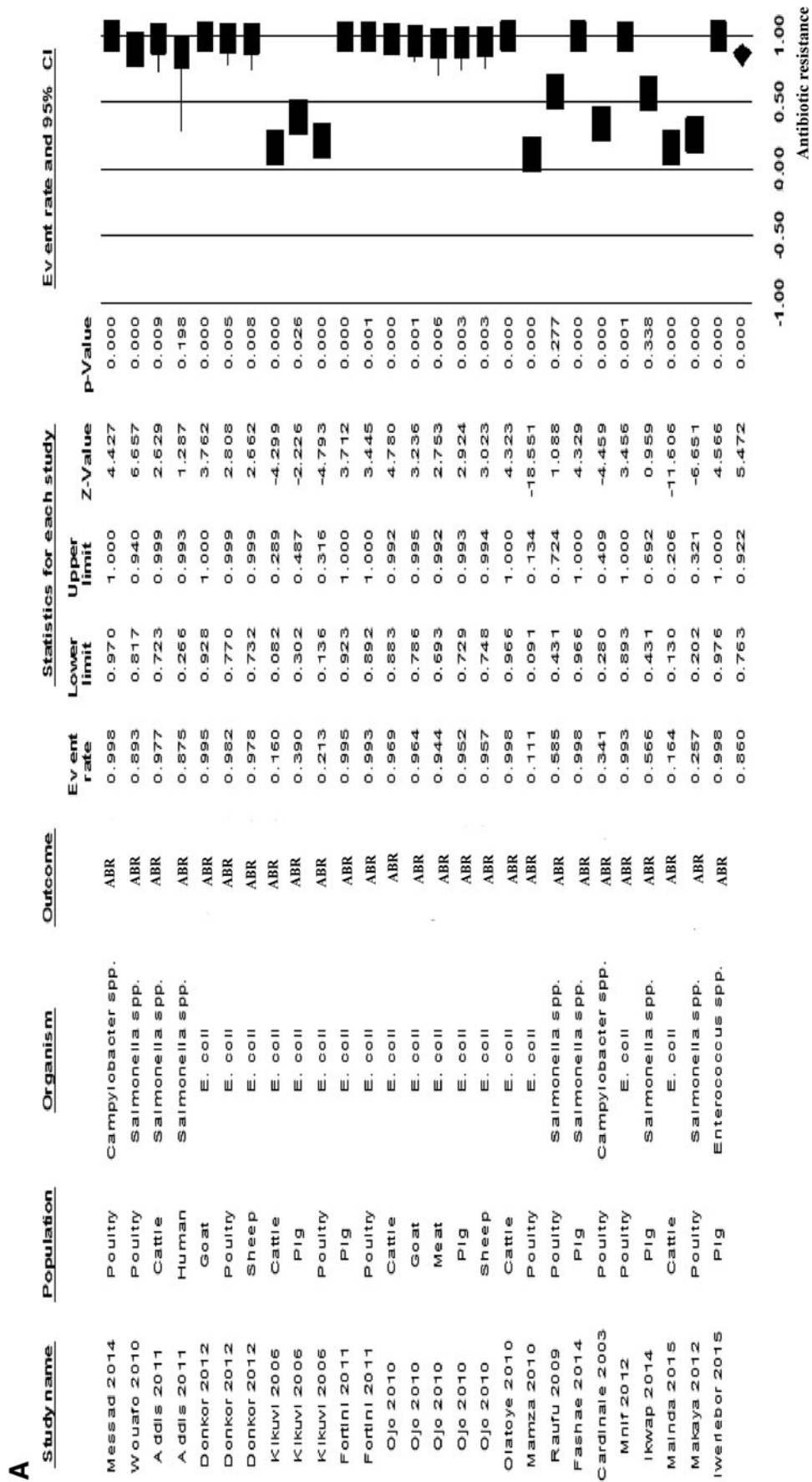
(continued)



TABLE 3. (CONTINUED)

Study	Guidelines	Bacterial species	AST methods	No. of strains	Resistant isolates (%)	MDR isolates (%)	Antibiotic resistance profiles of bacterial species isolated (%)																						
							Beta-lactam/beta-lactams inhibitors				Aminoglycosides		Macrolides		Fluoroquinolones		Tetracyclines		Phenolics		Furazolidone		Sulfonamides						
							Ampicillin	Amoxicillin	Amoxicillin – clavulanate	Cefuroxime	Cefoxitin	Ceftazidime	Ceftaxime	Ceftriaxone	Gentamicin	Streptomycin	Kanamycin	Amikacin	Neomycin	Erythromycin	Nalidixic acid	Ciprofloxacin	Enrofloxacin	Tetracycline	Chloramphenicol	Nitrofurantoin	Sulfonamides	Trimethoprim – sulfamethoxazole	
40	EUCAST CLSI	<i>Salmonella enterica</i>	Broth microdilution	41	58	NR	0	0	0	0	0	0	0	0	4.8	0	4.6	0	0	4.6	56	56	0	0	2.4	0	0	0	0
39	CLSI	<i>Salmonella enterica</i>	Disk diffusion	224	NR	22.8	0	0	0	0.9	18.3	0	0	0	0	0	0	0	0	0	15.2	0.9	0	22.8	11.6	0	0	12.9	0
43	CLSI	<i>Salmonella</i> spp.	Broth microdilution	53	36	57.9	0	0	0	0	15	1.8	0	0	0	0	0	0	0	0	0	0	0	3.7	5.6	0	0	43.4	0
45	CLSI	<i>Salmonella</i> spp.	Disk diffusion	206	26	12.1	0	6.8	0	3.9	0	0	0	0	0	0	0	0	0	0	0	0	3.4	9.2	0	0	0	0	0
34	CA-SFM	<i>Salmonella enterica</i>	Disk diffusion and agar dilution	103	89.3	39.8	13.6	1	0	0	0	0	0	0	0	44.7	0	0	0	0	34	0	0	84.5	1	0	19.4	11.6	0
46	NCCLS	<i>Salmonella enterica</i>	Disk diffusion	24	100	83.3	100	0	0	0	15.5	55.6	31.1	0	0	0	0	0	0	0	0	0	0	36.6	7.8	35.6	0	0	0

<sup>a</sup>Articles that investigated the same population and isolates, despite answering different research question, were identified as a single study. CA-SFM, Antibiogram Committee of the French Society of Microbiology; NCCLS, National Committee on Clinical Laboratory Standards.



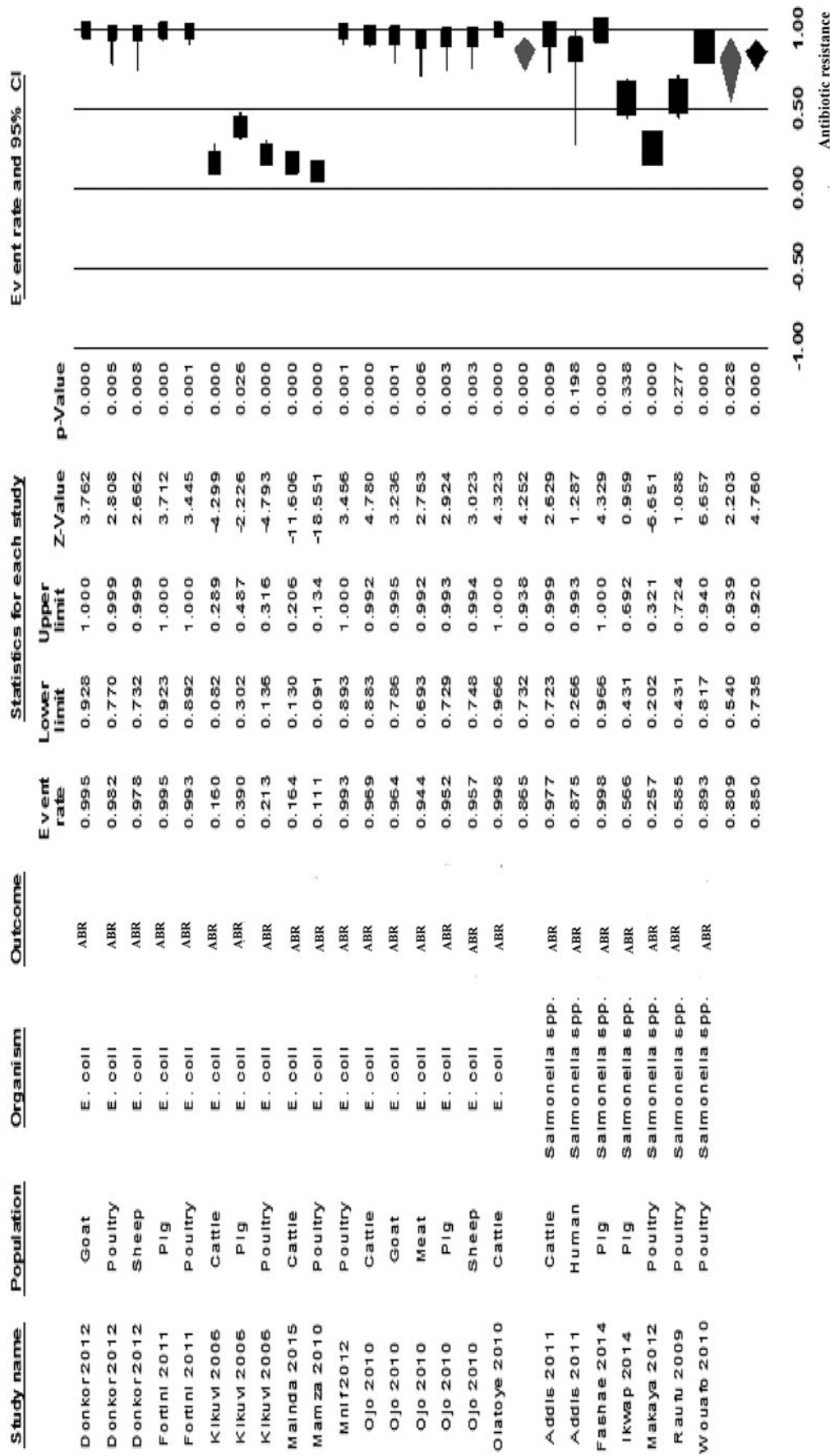
**FIG. 3.** Meta-analyses of overall rate and subgroup analyses of bacterial antibiotic resistance. Each box represents the value of each included study, while the diamond represents the overall and summary effect for each subgroup. The line in the middle is the line of null effect, the right-hand side of the line is in favor of resistance, whereas the left is in favor of susceptibility. (A) Pooled random-effects estimate of overall (95% CI) bacterial antibiotic resistance in selected studies. (B) Subgroup analysis per population. (C) Subgroup analysis per bacteria. CI, confidence interval.

**B**

Study name	Population	Organism	Outcome	Statistics for each study			p-Value
				Event rate	Lower limit	Upper limit	
Addis 2011	Cattle	Salmonella spp.	ABR	0.977	0.723	0.999	0.009
KIKUWI 2006	Cattle	E. coli	ABR	0.160	0.082	0.289	0.000
Malinda 2015	Cattle	E. coli	ABR	0.164	0.130	0.206	0.000
Ojo 2010	Cattle	E. coli	ABR	0.959	0.883	0.992	0.000
Olatoye 2010	Cattle	E. coli	ABR	0.958	0.966	1.000	0.000
Fashae 2014	Pig	Salmonella spp.	ABR	0.782	0.441	0.943	0.098
Fortini 2011	Pig	E. coli	ABR	0.995	0.966	1.000	0.000
Ikwap 2014	Pig	Salmonella spp.	ABR	0.566	0.431	0.692	0.338
Iweriebor 2015	Pig	Enterococcus spp.	ABR	0.998	0.976	1.000	0.000
KIKUWI 2006	Pig	E. coli	ABR	0.390	0.302	0.487	0.026
Ojo 2010	Pig	E. coli	ABR	0.952	0.729	0.993	0.003
Cardinale 2003	Poultry	Campylobacter spp.	ABR	0.936	0.777	0.984	0.000
Donkor 2012	Poultry	E. coli	ABR	0.341	0.260	0.409	0.000
Fortini 2011	Poultry	E. coli	ABR	0.982	0.770	0.999	0.005
KIKUWI 2006	Poultry	E. coli	ABR	0.993	0.892	1.000	0.001
Makya 2012	Poultry	Salmonella spp.	ABR	0.213	0.136	0.316	0.000
Mamza 2010	Poultry	E. coli	ABR	0.257	0.202	0.321	0.000
Messad 2014	Poultry	Campylobacter spp.	ABR	0.111	0.091	0.134	0.000
Mnif 2012	Poultry	E. coli	ABR	0.998	0.970	1.000	0.000
Raufu 2009	Poultry	Salmonella spp.	ABR	0.993	0.893	1.000	0.001
Wouab 2010	Poultry	Salmonella spp.	ABR	0.595	0.431	0.724	0.277
			ABR	0.893	0.617	0.940	0.000
			ABR	0.731	0.488	0.886	0.062
			ABR	0.832	0.610	0.940	0.007

FIG. 3. (Continued).

**C**



**FIG. 3.** (Continued).

**A**

Study name	Population	Organism	Outcome	Statistics for each study			Z-Value	p-Value	Event rate and 95% CI
				Event rate	Lower limit	Upper limit			
Messad 2014	Poultry	Campylobacter spp.	MDR	0.998	0.970	1.000	4.427	0.000	
Wouafo 2010	Poultry	Salmonella spp.	MDR	0.398	0.308	0.495	-2.056	0.040	
Adi's 2011	Cattle	Salmonella spp.	MDR	0.810	0.688	0.927	2.604	0.009	
Dankar 2012	Goat	E. coli	MDR	0.982	0.770	0.999	2.808	0.005	
Dankar 2012	Poultry	E. coli	MDR	0.995	0.928	1.000	3.762	0.000	
Dankar 2012	Sheep	E. coli	MDR	0.909	0.700	0.977	3.105	0.002	
Kikum 2006	Cattle	E. coli	MDR	0.688	0.352	0.750	0.724	0.469	
Kikum 2006	Pig	E. coli	MDR	0.669	0.503	0.786	1.994	0.046	
Kikum 2006	Poultry	E. coli	MDR	0.750	0.377	0.937	1.346	0.178	
Fortini 2011	Pig	E. coli	MDR	0.045	0.015	0.132	-5.152	0.000	
Fortini 2011	Poultry	E. coli	MDR	0.156	0.096	0.243	-5.999	0.000	
Ojo 2010	Cattle	E. coli	MDR	0.710	0.696	0.809	3.196	0.001	
Ojo 2010	Goat	E. coli	MDR	0.700	0.473	0.859	1.736	0.082	
Ojo 2010	Pig	E. coli	MDR	0.682	0.466	0.840	1.666	0.096	
Ojo 2010	Sheep	E. coli	MDR	0.706	0.468	0.872	1.645	0.100	
Olufemi 2010	Cattle	E. coli	MDR	0.998	0.996	1.000	4.323	0.000	
Mianza 2010	Poultry	E. coli	MDR	0.994	0.917	1.000	3.668	0.000	
Fashae 2014	Pig	Salmonella spp.	MDR	0.223	0.173	0.281	-7.870	0.000	
Mirif 2012	Poultry	E. coli	MDR	0.993	0.898	1.000	3.466	0.001	
Ikwap 2014	Pig	Salmonella spp.	MDR	0.367	0.216	0.549	-1.443	0.149	
Misinda 2015	Cattle	E. coli	MDR	0.262	0.167	0.386	-3.553	0.000	
Malsaya 2012	Poultry	Salmonella spp.	MDR	0.113	0.052	0.230	-4.748	0.000	
Iweriebor 2015	Pig	Enterococcus spp.	MDR	0.998	0.976	1.000	4.566	0.000	
				0.730	0.563	0.839	2.952	0.003	

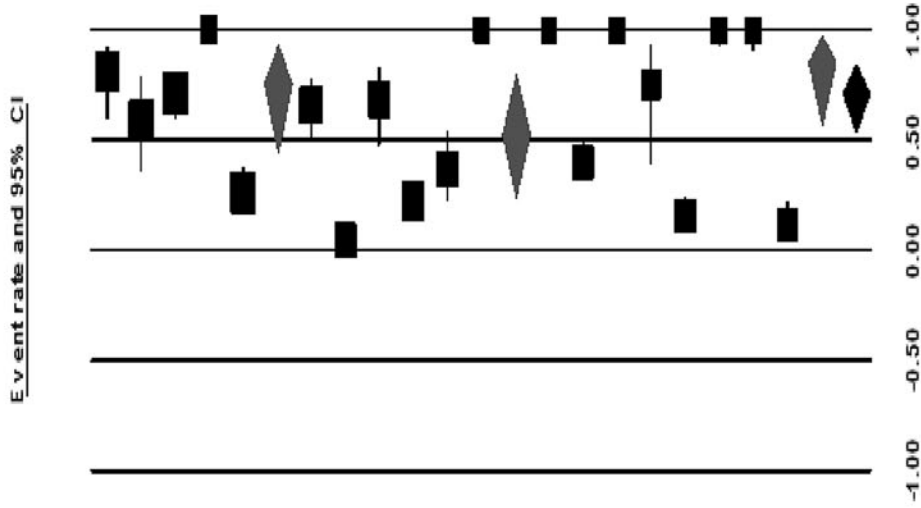
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**Multi-drug Resistance**

**FIG. 4.** Meta-analyses of overall rate and subgroup analyses of bacterial multidrug resistance. Each *box* represents the value of each included study, while the *diamond* represents the overall and summary effect for each subgroup. The *line* in the *middle* is the line of null effect, the *right-hand* side of the *line* is in favor of resistance, whereas the *left* is in favor of susceptibility. (A) Pooled random-effects estimate of overall (95% CI) bacterial multidrug resistance in selected studies. (B) Subgroup analysis per population. (C) Subgroup analysis per bacteria.

**B**

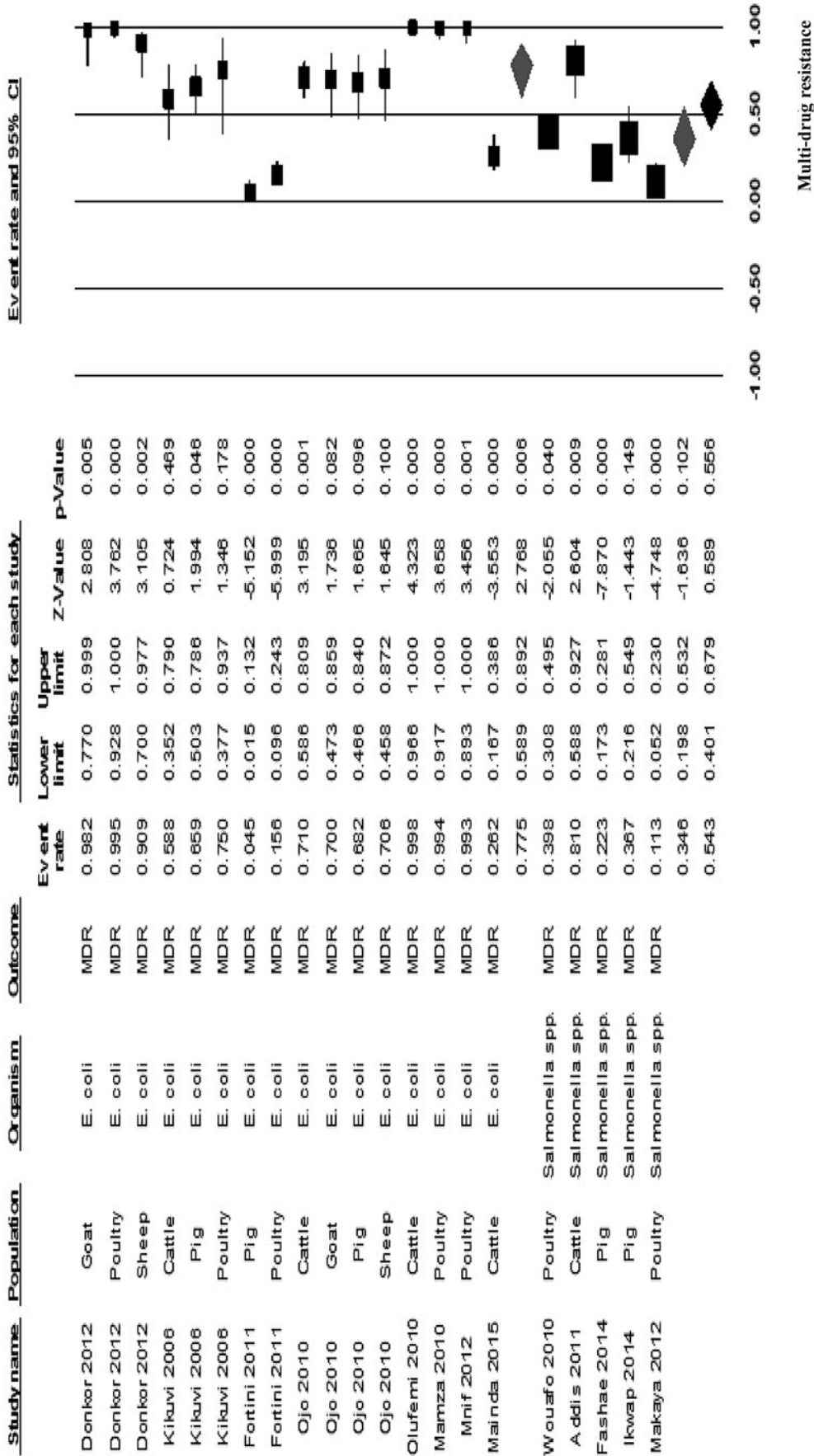
Study name	Population	Organism	Outcome	Statistics for each study		
				Event rate	Lower limit	Upper limit
Addis 2011	Cattle	Salmonella spp.	MDR	0.810	0.588	0.927
KIKUVI 2006	Cattle	E. coli	MDR	0.588	0.352	0.790
Ojo 2010	Cattle	E. coli	MDR	0.710	0.586	0.809
Olufermi 2010	Cattle	E. coli	MDR	0.998	0.966	1.000
Malinda 2015	Cattle	E. coli	MDR	0.262	0.167	0.386
KIKUVI 2006	Pig	E. coli	MDR	0.659	0.503	0.786
Fortini 2011	Pig	E. coli	MDR	0.045	0.015	0.132
Ojo 2010	Pig	E. coli	MDR	0.682	0.466	0.840
Fashae 2014	Pig	Salmonella spp.	MDR	0.223	0.173	0.281
Ikwap 2014	Pig	Salmonella spp.	MDR	0.367	0.216	0.549
IWERLEBOR 2015	Pig	Enterococcus spp.	MDR	0.998	0.976	1.000
Mes ad 2014	Poultry	Campylobacter spp.	MDR	0.511	0.233	0.783
Wouato 2010	Poultry	Salmonella spp.	MDR	0.998	0.970	1.000
Donkor 2012	Poultry	E. coli	MDR	0.398	0.308	0.495
KIKUVI 2006	Poultry	E. coli	MDR	0.995	0.928	1.000
Fortini 2011	Poultry	E. coli	MDR	0.750	0.377	0.937
Mamza 2010	Poultry	E. coli	MDR	0.156	0.096	0.243
Mnif 2012	Poultry	E. coli	MDR	0.994	0.917	1.000
Makaya 2012	Poultry	Salmonella spp.	MDR	0.993	0.893	1.000



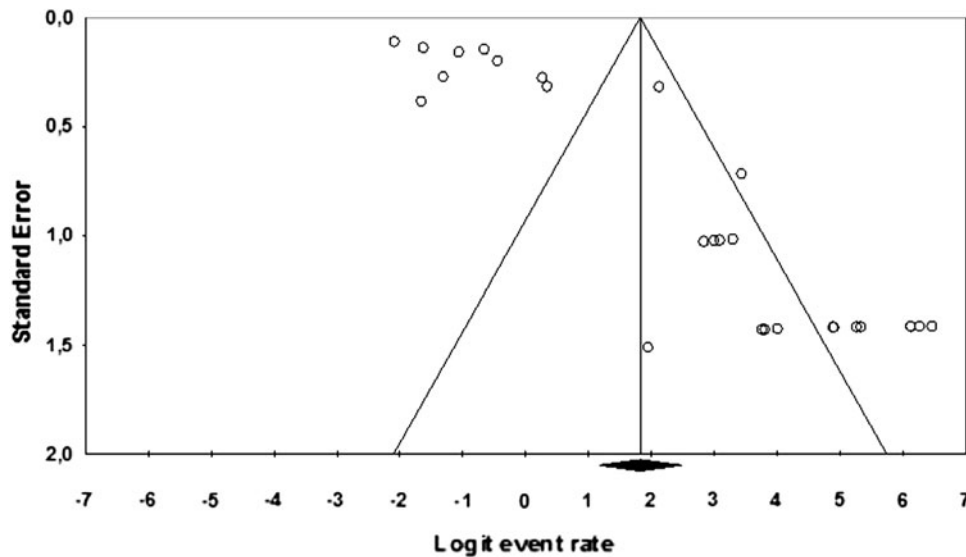
Multi-drug resistance

FIG. 4. (Continued).

**C**



**FIG. 4.** (Continued).



**FIG. 5.** Bias assessment (Funnel) plot with 95% confidence limits for studies included in the analysis.

be established and implemented, and collaboration of various sectors and disciplines has to be reinforced as advocated by the WHO's Advisory Group on Integrated Surveillance of Antimicrobial Resistance.<sup>32</sup>

Our study should be interpreted considering certain limitations. We were not able to provide information about antibiotic consumption in food animals in included African countries due to the scarcity of data in these nations. The resistance to specific antimicrobials, particularly those regarded as "critically important" in animal and human health, and correlation with resistance genes and virulence factors could not be ascertained in this study, reflecting the limited laboratory capacity in Africa. In addition, it is probable that there is publication bias due to the poor quality of studies and lack of reporting with only 17 published reports from 12 out of 54 countries meeting our strict inclusion criteria, with those not included failing to report on ABR (Fig. 5). A high level of heterogeneity associated with a number of factors, including origin of animals, farming and slaughterhouse practices, study design, and exposure to environmental aspects such as stress, was also observed. While the inclusion criteria and subgroup analyses used in this study helped in reducing heterogeneity, we could not confidently assume that studies were fully comparable. It is further important to note that effects of all presumptive factors, such as *Salmonella* and *Campylobacter* resistance epidemiology per serotype and species, could not be analyzed due to scarcity of data and limited number of studies in some subgroups.

## Conclusion

To the best of our knowledge, this is the first systematic review and meta-analysis of ABR in food animals in Africa. Given the findings of the review, it seems clear that ABR is substantively prevalent and poses a serious threat for food safety and security on this continent. We identified areas for future research concerning antibiotic-resistant and multidrug-resistant pathogens in food animals as etiological agents of infectious diseases in humans. Data generated in this study yielded some interesting findings on the burden of ABR that could be useful in developing measures to contain this threat from farm-to-plate in Africa. We therefore strongly recom-

mend that the One Health approach and recommendations advocated by the WHO, OIE, and FAO be followed to restrict the use of antibiotics and, thus, ABR in animal and human health. In addition, sound sampling and laboratory analysis schemes, cooperation and good communication between sectors (agriculture, veterinary, and public health sectors), qualitative and quantitative risk assessment for emerging and potential hazards, and sustainable political will and financial support across the food chain are required.

## Declarations

### Availability of data and materials

All data generated or analyzed during this study are included in this published article and its Supplementary Data.

### Ethics approval

This systematic review and meta-analysis was based on an appraisal of published reports and was therefore exempted from ethical approval. Moreover, it did not involve any direct research on human participants, and no informed consent was required.

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the study design, data collection and analysis, preparation of the article, nor decision to publish.

### Authors' Contributions

L.L.F. co-conceptualized the study, developed the protocol, searched the literature, screened title abstracts and full texts, extracted and summarized the data, performed quality assessment, statistical analysis, and interpreted the results, prepared tables and figures, and drafted the article. D.G.A. contributed to title and abstract screening and undertook critical review of the article. R.C.F. screened full texts, performed quality assessment, statistical analysis, interpreted the results, and prepared tables and figures. S.Y.E. co-conceptualized the study, developed the protocol, screened titles and abstracts, and undertook critical review of the article. All authors read and approved the final article.

### Disclosure Statement

Prof. S.Y.E. is a member of the Global Respiratory Infection Partnership and Global Analgesic Steering Committee sponsored by an unrestricted educational grant from Reckitt and Benckiser. All other authors declare there are no competing financial interests.

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Address correspondence to:  
 Luria Leslie Founou, PhD  
 Antimicrobial Research Unit  
 College of Health Sciences  
 University of KwaZulu-Natal  
 Durban 4000  
 South Africa

E-mail: luriafounou@gmail.com