Molecular Epidemiology and Mechanisms of Antibiotic Resistance in Gram-positive Bacteria in Africa: A Systematic Review and Meta-Analysis from a One Health Perspective

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Running title: Resistance mechanisms of Gram-positive bacteria

HIGHLIGHTS

- Gram-positive bacteria (GPB) isolated from human, animal and environmental samples were of the same clones and/or shared common resistance genes and mobile genetic (MGEs).
- Multidrug resistant (MDR) clones such as *S. aureus* ST5 and *E. faecium* ST80 were isolated from human, animal and environmental sources.
- *mecA, erm*(B), *erm*(C) *tet*(M/K/L), and *vanA/B/C* were common in GPB, including VRSA.
- Mean drug resistance rates of isolates from humans, animals and the environment were respectively 62.0% (95% CI: 54.7 – 69.3%), 68.2% (95% CI: 58.0 -78.4%) and 84.6% (95% CI: 69.9 – 99.31%) (*P-value*<0.0001).
- SCC*mec,* IS*16,* and Tn*916* mobilized *mecA, erm*(B) and *tet*(M) respectively across various GPB species isolated from animals, humans, and the environment.
- A One Health approach to studying antibiotic resistance mechanisms and molecular epidemiology of GPB is warranted.

ABSTRACT

A systematic review and meta-analysis of antibiotic-resistant Gram-positive bacteria in Africa, showing the molecular epidemiology of resistant species from animal, human and environmental sources, is lacking. Thus, the current burden, type, and sources of Gram-positive bacterial resistance and their dissemination routes from farm to fork is absent. To fill this One Health information gap, we systematically searched PubMed, Web of Science and African Journals Online for English research articles reporting on the resistance mechanisms and clonality of resistant Gram-positive bacteria in Africa within 2007 to 2018. The review and all statistical analysis were undertaken with 130 included articles.

From our analyses, the same resistant Gram-positive bacterial clones, resistance genes, and mobile genetic elements (MGEs) are circulating in humans, animals and the environment. The resistance genes, *mecA*, *erm*(B), *erm*(C), *tet*(M), *tet*(K), *tet*(L), *vanB*, *vanA*, *vanC*, and *tet*(O), were found in isolates from

humans, animals and the environment. Commonest clones and mobile genetic elements identified from all three sample sources included *Staphylococcus aureus* ST5 (n=208 isolates), ST 8 (n=116 isolates), ST 80 (n=123 isolates) and ST 88 (n=105 isolates), and IS*16* (n=18 isolates), Tn*916* (n=60 isolates) and SCC*mec* (n=202 isolates). Resistance to penicillin (n=4 224 isolates, 76.2%), erythromycin (n=3 552 isolates, 62.6%), ampicillin (n=1 507 isolates, 54.0%), sulfamethoxazole/trimethoprim (n=2 261 isolates, 46.0%), tetracycline (n=3 054 isolates, 42.1%), vancomycin (n=1 281 isolates, 41.2%), streptomycin (n=1 198 isolates, 37.0%), rifampicin (n=2 645 isolates, 33.1%), ciprofloxacin (n=1 394 isolates, 30.5%), clindamycin (n=1 256 isolates, 29.9%) and gentamicin (n=1 502 isolates, 27.3%) (*p*-value <0.0001) were commonest.

Mean resistance rates of 14.2% to 98.5% were recorded in 20 countries within the study period, which were mediated by clonal, polyclonal and horizontal transmission of resistance genes. A One Health approach to research, surveillance, molecular epidemiology, and antibiotic stewardship to contain ABR should be prioritized.

Keywords: *Staphylococcus spp.*; *Enterococcus spp.*; *Streptococcus spp.*; MRSA; VRE

1. INTRODUCTION

Antibiotic resistance, a threat to public health

Limited research and surveillance data in Africa makes it impossible to track and monitor the true burden of antibiotic resistance (ABR) [1], particularly the distribution and dissemination of resistance genes between humans, animals and the environment. According to a recent WHO report, the potential for ABR to lead to higher mortalities and morbidities in low- and middle-income countries such as Africa may even be greater as a result of the higher burden of bacterial infections, limited diagnostic capacity and lower access to second-line antibiotics[1,2]. This makes it imperative to have a One Health analysis that describes the burden and epidemiology of resistance genes in bacteria isolated from humans, animals and the environment [3].

In a recent review, Gram-positive bacteria (GPB) were responsible for a high proportion of infections among children and showed a high level of resistance to WHO-recommended drugs in Africa [4]. In some African regions, as many as 80% of *Staphylococcus aureus* infections are methicillin-resistant *S. aureus* (MRSA), which show resistance to most standard licensed drugs including quinolones and peptides [25]. Although *Enterococcus spp.* are mostly not as virulent as *S. aureus*, their multidrug resistance (MDR) propensities restrict drug options for clinicians [7]. Patients infected with MRSA are estimated to be 64% more likely to demise than those infected with methicillin-susceptible *S. aureus* (MSSA) [6]. Reviews addressing GPB in Africa have reported on increasing rates of ABR from blood-stream infections, pneumonia, urinary tract infections and meningitis caused by *Streptococcus agalactiae*, *S. aureus*, *Streptococcus pneumoniae* and *Enterococcus faecium* in both children and adults. Sepsis due to *S. agalactiae* accounts for about 26% of all neonatal deaths and 10% maternal deaths in Sub-Saharan Africa [8] However, the potential dissemination of these resistant strains from farm (environment and animals) to fork (humans), are less described.

Sources and anthropogenic activities driving resistance

High-level ABR has been reported in humans, animals and the environment, with indiscriminate antibiotic use being fingered as a major contributor in Africa. Resistance genes have been detected in surface water fed with runoff effluents from farms utilizing antibiotics, hospitals, and sewage processing plants as well as in ground water [9–11]. Furthermore, genes mediating resistance to last-resort GPB antibiotics such as vancomycin have been recovered from raw milk and animal products, pigs, wild animals (buffalo, zebra and cattle), waste water, effluents and patients, implicating veterinary and agricultural use of antibiotics as potential sources of resistance genes in humans [12–14]. These reports suggest that a larger share of the antibiotics that end up polluting the environment and communities emanate from livestock production [15–17]. This interconnectivity between animals, humans and the environment, explains the need to adopt a One Health research policy.

Several studies have reported high rates of MDR among GPB isolates from humans, animals and the environment in Africa, mainly as a result of overuse, underuse and wrong choice of antibiotics [18–24]. Different factors have been implicated in the high rate of ABR to the limited drugs in Africa. These include: unrestricted access to antibiotics over-the-counter without prescription such as selling on the streets; inadequate hygienic practices; uncontrolled usage of antibiotics as growth promoters in food animals production; wrong diagnosis and prescription, off-label use and errors in dosage regimens; use of untreated poultry and cattle manure to fertilize agriculture lands; extensive use of broad-spectrum antibiotics in poultry production; and inefficient chlorination of hospital wastewater effluents before discharge into the environment [10,18,22,25–29]. Additionally, inadequate knowledge of animals' diseases, misdiagnosis and poor antibiotic handling practices in animal production add up to the overall burden of ABR in Africa [17].

Molecular ABR mechanisms

Selective pressures exerted by various antibiotics used in human and veterinary medicine, as well as in agriculture, have resulted in the emergence and dissemination of numerous mechanisms of resistance in GPB in Africa. Commonly reported mechanisms include *blaZ, erm*(B), *mecA, tet*(M), *vanB* and *vanC* [30–33]. These resistance genes have been found to be associated with mobile genetic elements (MGEs) such as transposons, conjugative plasmids, integrons, and insertion sequences, which are capable of mobilizing resistance genes across a wide spectrum of bacterial species [34,35]. SCC*mec, Tn916* and IS*16* are notable MGEs that carry major ABR determinants in Africa and are transmissible between clones of the same or different bacteria species by a conjugative mechanism. These MGEs have the potential to thus spread resistance genes from environmental and animal bacterial hosts to human pathogens in Africa; they have therefore been analysed herein [36–38].

Purpose of this review

Excellent reviews addressing antimicrobial resistance in some GPB and Gram-Negative ones in Africa have been published [4,39–44]. However, reviews discussing the molecular epidemiology and mechanisms of ABR in GPB such as *Staphylococcus spp., Streptococcus spp.* and *Enterococcus spp.* in Africa in the context of resistance rates, resistance mechanisms (and MGEs), clonality, and geographical distribution from a One Health perspective are non-existent, to the best of our knowledge. This review sought to fill this gap by analyzing the burden, types, and molecular epidemiology of resistant GPB from a One Health context.

1.1 Search strategy and inclusion criteria

English research articles published within the last ten years (01/01/2007 to 07/08/ 2018) and indexed in PubMed, Web of Science and African Journals Online were searched with the following keywords: "Enterococcus", and "Streptococcus", "Staphylococcus", in permutations and combinations with "resistance AND Africa". Studies which did not identify the underlying ABR mechanisms/genes as well as the clonality of antibiotic-resistant GPB were excluded. Thus, studies that only reported on antibiotic sensitivity testing (AST) results or undertook ABR surveillance studies without further molecular tests to characterize the ABR mechanisms and/or clonality of the isolates were excluded (Figure 1). In all, 248 studies were excluded because they only had MIC data (See Supplementary data 1). All searches were undertaken independently by both authors in triplicates to ensure replication of the results.

Data extracted from the articles included year of study, country, GPB species, clones, sample sources, sample size/number of isolates, number of resistant isolates, resistance genes and MGEs and antibiotics to which the strains were resistant (Tables 1-6; Supplementary data 2). The mean rate of ABR among GPB per country and in Africa was determined to identify countries with the highest or lowest levels of resistance in Africa (Table 5). As well, the antibiotics to which the isolates were most resistant were determined to evaluate their correlation with the detected/reported resistance mechanisms (Table 6).

The resistance mechanisms, as well as MGEs involved in the transmission of resistance genes per species or clone, were determined to assess the means of resistance transfer i.e., horizontal or vertical (through

clonal expansion), per specimen sources (animal, human, and environment) (Figures 2a & 2b). The distribution of clones, resistance genes, and MGEs were considered to identify countries with most resistant clones, resistance genes, and their associated MGEs (Figure 3a).

1.2 Statistical analysis.

The data was analyzed using Microsoft Excel® 2017 and Graph pad prism™ 6 (GraphPad Software, San Diego, CA, USA) (Supplementary data 2). Calculation for the statistical significance of the data was determined using the kolmogorov-smirnov test (with Dallal - wilkinson-Lilliefors p-value) and/or column statistics or one sample t-test, and the confidence intervals determined at 95%. The p-values were two tailed with a Gaussian approximation. A p-value of <0.05 was considered as statistically significant. Only studies that provided the required information were used in the analysis. In all, 130 articles were used for the data analysis (Fig. 1).

2. RESULTS AND DISCUSSION

Of the 1,486 articles returned from the systematic literature search from PubMed, Web of Science and African Journals Online, 130 studies representing 20 out of 54 African countries were included in this review and data analysis (Fig. 1). A total of 249 papers were excluded because they only had MIC data. Tunisia (n=33 studies) recorded the highest number of studies followed by South Africa (n=21 studies), Egypt (n=21 studies), Nigeria (n=13 studies) and Algeria (n=7 studies), Angola (n=6 studies), Uganda (n=5 studies), Democratic Republic of the Congo (n=3 studies), Ghana (n=3 studies), Kenya (n=3 studies), São Tomé and Príncipe (n=3 studies), Gabon (n=2 studies), Tanzania (n=2 studies), Cape Verde (n=1 study), Libya (n=1 study), Namibia (n=1 study), Senegal (n=1 study) and Sudan (n=1 study). Majority of the included studies were undertaken in Northern Africa (n=65 studies, 50%), Southern Africa (n=35 studies, 26.9%) and West Africa (n=18 studies, 13.9%). Different rates of resistance to antibiotics were reported in different countries in Africa (Tables 2-5; Supplementary data 1).

A meta-analysis of published literature confirmed the presence of a high mean rate of drug resistance in GPB isolated from humans (62.0%, 95% CI: 54.7 – 69.3%), animals (68.2%, 95% CI: 58.0 -78.4%) and the environment (84.6%, 95% CI: 69.9 – 99.3%) (*P-value*<0.0001) in Africa, albeit many studies that did not address the molecular mechanisms of resistance in GPB were excluded. Obviously, the mean rate of resistance would have been higher had all research articles using only phenotypic methods to describe ABR in GPB been included (Supplementary data 1). Interestingly, although a lesser number of GPB were isolated from environmental sources, they expressed higher ABR than those from humans and animals; hence, the higher mean resistance rate of 84.6%. This also underscores the fact that there is increasing ABR genes in the environment, obviously due to antibiotic pollution from human activity. Evidently, ABR is high among GPB in certain regions in Africa (Figures 3a & 3b) (Table 5) and underpins the need to up the ante against this menace through increased molecular surveillance research, education of clinical microbiologists on ABR, and antibiotic stewardship.

Studies describing detailed molecular mechanisms of GPB resistance and molecular epidemiology in Africa are few, making it difficult to paint a vivid comprehensive picture of ABR in Africa. However, this review shows that *S. aureus* ST5, *E. faecium* ST18, ST80 and ST910, *E. faecalis* and *S. agalactiae* harbouring *mec*A, *tet* and *erm* genes, were commonly found in humans, animals and the environment, particularly in Northern, Western, and Southern Africa. Thus, careful use of β-lactams, tetracyclines, and macrolides is warranted to prevent further selection and dissemination of these resistance genes and resistant clones. Furthermore, it will be prudent for countries within these regions to review their recommended antibiotic regimens, guidelines/protocols for infections caused by these species.

erm(B) and *tet*(M) were found in *S. aureus, Enterococcus spp. and Streptococcus spp.,* with *erm*(B), *tet*(M) and *vanA* genes being mobilized by Tn*916* and IS*16,* indicating horizontal transfer within same clones, different clones and species. The discovery of same clones and resistance genes in specimens from humans, animals and the environment suggest a possible transmission of these clones between humans, animals and the environment, corroborating the need for a One Health approach to infection

control and management of antibiotic-resistant infections. Further molecular epidemiological surveillance in the above-mentioned states is crucial to forestall further spread of these resistant pathogenic clones both within their borders and from their borders to other countries.

Resistance rates per countries and MDR GPB species

High mean resistance rates were reported in Sudan (98.5%), South Africa (82.7%) Nigeria (71.2%), Egypt (70.5%), Angola (66.2%), Tunisia (66.8%), Ghana (65.1%), Algeria (62.2%) etc. (Table 5). Cross-contamination of multi-drug resistant bacteria between patients and the environment accounted for the high rate of resistance in Algeria [45–49]. The high rate of ABR in Tunisia was attributed to cross contamination between hospital patients and hospital environment, immune deficiency [50], over-consumption of antibiotics, heavy consumption of sheep meat, which is a reservoir of MRSA, and high consumptions of antibiotics in animal feed [51,52]. In Egypt, inappropriate antibiotic prescription practices [29], inadequate hygienic handling and processing of food [12], and close contact with pet dogs accounted for the high resistance [53]. The high rate of drug resistance in Nigeria has been attributed to the exchange of resistance genes between farm animals or their products and man [54,55], existence of MRSA in clinical and community settings [56], uncontrolled usage of antibiotics [57] and the presence of efflux pumps in coagulase-negative staphylococcus strains [58]. Expansion of resistant clones [59], variability of hospital acquired MRSA clones [60], consumption of unpasteurized milk or inefficient thermal processing of milk [21], shedding of resistant clones from animals to the environment and heavy consumption of antibiotics to treat TB due to high HIV burden [61], were incriminated for the high-level resistance in South Africa.

Staphylococcus spp. (*S. aureus, S. haemolyticus* and *S. saprophyticus*); *Streptococcus spp.* (*S. pyogenes* and *S. agalactiae*), and *Enterococcus spp.* (*E. faecium, E. faecalis, E. hirae, E. durans,* and *E. gallinarum*) were the antibiotic-resistant GPB widely distributed in Northern, Southern, Western and Central Africa. The high number of *tet*(M/L/K), *erm*(A/B/C), *aph(3')-lll* and *vanA/B/C* in *Staphylococcus spp*., *Enterococcus spp*., and *Streptococcus spp*. reported in Tunisia, South Africa, Nigeria, Algeria and Egypt accounted for the high rate of resistance to tetracycline, erythromycin, kanamycin and vancomycin

(Figure 3a). Such resistant GPB are known to compromise the safety of invasive medical procedures such as organ transplants, orthopedic surgery, and cancer treatment. In addition, infections such as sepsis, endocarditis, deep wound infections, pneumonia, meningitis and urinary tract infections caused by these resistant pathogens are becoming increasingly fatal due to limited treatment options [62,63]. The abuse of antibiotics as growth promoters, prophylaxis, and metaphylaxis in food animals in these countries have been implicated in the selection of resistant bacteria that can pass on to humans through food consumption, direct contact with animals and the environment, as well as trade of animals and food products between countries [64].

Approximately 26, 385 GPB were isolated from humans (n=83 studies), animals (n=32 studies) and the environment (n=14 studies) (Tables 1-4), with mean rates of ABR varying from 14.2% to 98.5% across the 20 included countries (Tables 2-5). The antibiotics to which the isolates were most resistant to were penicillin (n=4 224 isolates, 76.2%), erythromycin (n=3 552 isolates, 62.6%), ampicillin (n=1 507 isolates, 53.9%), sulfamethoxazole/trimethoprim (n=2 261 isolates, 46.0%), tetracycline (n=3 054 isolates, 42.1%), vancomycin (n=1 281 isolates, 41.2%), streptomycin (n=1 198 isolates, 37.0%), rifampicin (n=2 645 isolates, 33.1%), ciprofloxacin (n=1 394 isolates, 30.5%), clindamycin (n=1 256 isolates, 29.9), and gentamicin (n=1 502 isolates, 27.3%) (p-value <0.0001) (Tables 2-4 & 6). Countries with high number of studies such as Tunisia, South Africa, Egypt and Nigeria recorded high number of ABR (Table 5) and high number of *mec*A, *erm*(B), *tet*(M), *drf*G and *vanB* resistance genes (Figure 3a). Vancomycin resistance was reported in seven studies each for animals and the environment, and 12 studies in Humans. Vancomycin-resistant *Enterococcus spp.* (n=102 isolates) and vancomycin-resistant *Staphylococcus spp.* (n=258 isolates) were reported in humans, animals and the environment (Tables 2-4; Figures 2). Vancomycin-resistant *Staphylococcus aureus* (VRSA) was reported in animals (n=238 isolates), the environment (n=15 isolates) and humans (n=5 isolates). A similar situation occurred with vancomycin-resistant *E. faecium*, which was isolated from the environment (n=306 isolates), animals (n= 671 isolates) and humans (n=26 isolates) (Supplementary data 1).

Antibiotic-resistant *S. aureus* ST5, *E. faecium* (ST18, ST80 and ST910) and *E. faecalis* harbouring *mec*A, *erm*(B), *erm*(C), *tet*(M), *tet*(K), *tet*(L) and *vanB* were isolated from humans, animals and the environment, albeit in higher proportion in humans and animals than the environment (Tables 2-4). For instance, Farhat et al. (2014) [46], van Rensburg *et al.* (2012) [59] and De Boeck et al. (2015) [65] in Algeria, South Africa and Democratic Republic of Congo respectively, reported on resistant *S. aureus* ST5 in humans whilst Fall et al. (2012) [66] reported on the same clone (S. *aureus* ST5) in pigs from Senegal. Further, Mariem et al. (2013) [24] isolated the same clone (*S. aureus* ST5) from the environment in Tunisia, suggesting that this clone is widely distributed in Africa in humans, animals and environment. It is currently not clear whether this clone first emerged from humans, animals or the environment, but its presence in all three spheres shows the possibility of resistant species and clones being disseminated between animals, humans and the environment. Notably, *S. aureus* ST5 is among the frequently reported clones in Asia [67] and recent evidence suggest that it has spread from hospitals into communities, resulting in community-acquired MRSA [68].

Similarly, Lochan et al. (2016) [30] in South Africa, Dziri et al. (2016) [20] and Elhani et al. (2014) [69] in Tunisia isolated resistant *E. faecium* ST80 from humans. For the first time, E. faecium ST80 was isolated from environmental samples in a hospital in Tunisia by Elhani et al. (2013) [69] and Dziri et al. (2016) [70]. Transmission of this resistant clone to animals is possible, although not yet reported. This implies that these resistant species and clones are circulating between humans and the environment, underpinning the broad host range and transmissibility of these strains between humans and the environment.

mecA was the predominant resistance gene, which corresponded with the higher penicillin resistance recorded (Figure 2aii). MRSA strains were the most commonly isolated strains (≥ 2,350) [71–74]. This is consistent with the global report of increasing prevalence of MRSA [75,76]. MRSA harbours the *mecA* gene, which is carried by the SCC*mec* MGE, and mediates resistance to multiple β-lactam antibiotics [77]. From this review, MRSA showed resistance to eleven different antibiotic classes: aminoglycosides (gentamicin, tobramycin), β-lactams (penicillin, ampicillin, oxacillin, cefoxitin), fluoroquinolones (ciprofloxacin,

levofloxacin, ofloxacin), glycopeptides (vancomycin), lincosamide (clindamycin), macrolides (erythromycin), phenicols (chloramphenicol), rifamycins (rifampicin), streptogramins (pristinamycin), sulfonamides (trimethoprim/sulfamethoxazole), and tetracyclines (tetracycline). MRSA is thus a worrying public health threat as some strains have evolved resistance to almost all licensed drugs (26). Vancomycin-resistant Enterococci (VREs) (≥ 594), which were reported in Northern and South Africa, also pose a serious threat to public health as they are resistant to vancomycin, a glycopeptide that is reserved for fatal or life-threatening Gram-positive infections, and other important antibiotics such as ampicillin, erythromycin, fluoroquinolones (ciprofloxacin, levofloxacin), gentamicin, rifampicin, streptomycin, trimethoprim/sulfamethoxazole and tetracycline. In this study, enterococcus isolates had a resistance rate of 60.1% (95%, CI=32.2 -87.9) (p-value = 0.0005) to vancomycin (Table 6). Multidrug resistance in VREs increases VRE-associated mortality rates, which is likely to increase to 75% compared with 45% from susceptible strains [13,80]. As well, evolution of macrolide resistance (42.0%, 95% CI: 12.02 – 72.1) (p-value = 0.0129) in drug-resistant streptococci is limiting treatment options and resulting in high mortalities [81–83]. In this study, MRSA, VRE and drug-resistant streptococci remain major public health threats, calling for measures to contain ABR. Novel antibiotics such as linezolid, synercid, and daptomycin should be used empirically whilst awaiting susceptibility results. The empirical therapy can be changed or maintained based on the susceptibility report [84].

Resistance rates of species per animals, humans and the environment

The rates of ABR in isolates recovered from the environment was highest, followed by isolates from animal sources. Among environmental isolates, 91.2% (95%, CI=78.8–103.6) were resistant to penicillin, 82% (95%, CI=40.6–123.4) were resistant to sulfamethoxazole/trimethoprim, 68.5% (95%, CI=24.1–100) were resistant to ampicillin, 60.8% (95%, CI=25.0–96.6) were resistant to vancomycin, 56.9% (95%, CI=-40.7–73.2) were resistant to erythromycin, 54.5% (95%, CI=29.49–79.5) were resistant to ciprofloxacin, and 51.3% (95%, CI=21.3–100) were resistant to clindamycin (Table 6). Among animal isolates, 71.8% (95%, CI=54.9–88.73) were resistant to penicillin, 58.9% (95%, CI=36.1–81.7) were resistant to clindamycin, 58.5% (95%, CI=37.6 –79.4) were resistant to ampicillin, 49.6% (95%,

CI=30.1–69.1) were resistant to trimethoprim/sulfamethoxazole, 42.3% (95% CI=17.7–67.0) were resistant to vancomycin, 47.6% (95% CI=34.0–61.2) were resistant to erythromycin, and 38.8% (95% CI=21.3–56.3)(p-value = 0.15) were ciprofloxacin resistant (Table 6; Supplementary file 1).

The rates of resistance were much lower in humans for most of the antibiotics used (Tables 2-4). Among the various species, *Enterococcus spp*. and *Staphylococcus spp.* recorded high rates of resistance for most antibiotics (Figure 3b). *Streptococcus spp*. reported low rates of resistance except for tetracycline to which it recorded a high rate of 55.13% (95%, CI=20.63.18–89.64) (p-value = 0.006). Resistance to vancomycin was not reported in any *Streptococcus spp.* Isolate (Table 6).

Enterococcus spp., mainly *E. faecium* and *E. faecalis*, recorded a resistance rate of 98.5% (95%, CI=94.5–102.6)(p-value = 0.0001) to clindamycin, 81.6% (95%, CI=52.1–110)(p-value = 0.0008) to trimethoprim/sulfamethoxazole, 64.0% (95%, CI=50.0–78.1)(p-value=0.0001) to erythromycin, 60.1% (95%, CI=32.2–87.9)(p-value = 0.0005) to vancomycin, 57.3% (95%, CI=24 -90.7)(p-value=0.0057) to penicillin, 51.7% (95%, CI=35.8–67.6)(p-value=0.0001) to tetracycline, 49.9% (95% CI=31.3–68.5)(p-value = 0.0001) to ciprofloxacin, 48.9% (95% CI=20.6–77.2)(p-value=0.004) to kanamycin, 47.1% (95% CI=26.7–67.7)(p-value=0.0006) to ampicillin, 40.8% (95% CI=24.3–57.4)(p-value=0.0001) to streptomycin and 34.0% (95% CI=19.7–48.4)(p-value=0.0002) to gentamicin (Table 6).

S. aureus showed high resistance (79.6%) to penicillin (95% CI=69.7–89.5)(p-value = 0.0001), 67.8% to erythromycin (95% CI=11.5–147.0)(p-value = 0.0917), 55.5% to ampicillin (95% CI=44.50–88.5)(p-value = 0.0001), 39.3% to trimethoprim/sulfamethoxazole (95% CI=39.3–47.8)(p-value = 0.0001), 36.9% to tetracycline (95% CI=29.3–44.5(p-value = 0.0001), 35.8 to streptomycin (95% CI=14.7–57.0)(p-value = 0.004), 33.6% to rifampicin (95% CI=20.1–47.03)(p-value = 0.0001), 24.0% to clindamycin (95% CI=14.9–33.1)(p-value = 0.0001), 23.9% to ciprofloxacin (95% CI=17.6-30.2)(p-value= 0.0001), 22.7% to vancomycin (95% CI=4.3–41.2)(p-value = 0.0212) and 22.2% to vancomycin (95% CI=15.7–28.3)(p-value = 0.0001) (Table 6).

Resistance mechanisms, clones, and MGEs

Few studies identified the clones and MGEs in the resistant isolates. Of the 130 included studies, 32 identified the clones whilst 22 described the MGEs, which were used in the statistical analysis. The most dominant gene detected in Africa, which was widespread and responsible for resistance in GPB, was *mecA* (n=3 547), followed by *erm*(B) (n=1 268), *vanC*1/2/3 (n=971), *tet*(M) (n=720), *blaZ* (≥565), *dfrG* (n=422), *vanB* (≥451), *aph(3')-IIIa* (≥170) and *aac(6')-aph(2')*(≥ 268) (p-value = 0.0011) (Fig. 2a).

Figure 2b represents MGEs per clone. *S. aureus* clones ST5, ST8, ST 80 and ST88 were highly associated with *mecA*. Resistant *S. aureus, E. faecium* and *E. faecalis* clones such as *S. aureus* ST5, and *E. faecium* clones ST18, ST80, and ST16 were widely distributed in humans, animals and the environment. Similarly, *mecA, erm*(B), *erm*(C), *tet*(M), *tet*(K), *tet*(L), *vanB*, *vanA*, *vanC* and *tet*(O) were reported in isolates from humans, animals and the environment (Table 1).

IS*16* and Tn*916* were found with the resistance genes *erm*(B) and *tet*(M) in *E. faecium* (ST18, ST80 and ST910), *S. agalactiae* (ST612, ST616 and ST617), *E. faecalis* and *S. pyogenes (emm*18*, emm*42*, emm*76 and *emm*118) isolated from humans, animals and the environment (Tables 2-4; Figure 2b). *tet*(M) was associated with Tn*916* transposon in tetracycline-resistant *S. agalactiae* [85] and *S. pyogenes* [81] in humans in Tunisia. Fischer et al. (2013) also reported the association between Tn*916* and *tet*(M) in tetracycline-resistant *S. agalactiae* in camel in Kenya [86]. Similarly, IS*16* was found in vancomycin-resistant *E. faecium* (ST80, ST180 and ST910) in humans and the environment in Tunisia [69,70]. Investigations into the association between MGEs and resistance genes were limited by few studies (n=22 studies) on MGEs.

From Tables 2-4, majority of the resistance genes namely, *mecA*, *erm*(B), *tet* (M), *vanA* etc. were responsible for drug resistance to antibiotics such as aminoglycosides (gentamicin, streptomycin, kanamycin), β-lactams (penicillins, cephalosporins), fluoroquinolones (ciprofloxacin), macrolide (erythromycin), sulfamethoxazole/trimethoprim, tetracycline and glycopeptides (vancomycin). These resistance genes were widely distributed in Northern Africa (Tunisia, Algeria, Egypt, Morocco, and

Libya) and Southern Africa (South Africa and Namibia). All the three different MGEs (Tn*916*, SCC*mec* and IS*16*) were reported in Tunisia, with two being reported in Kenya (SCC*mec* and Tn*916*). IS*16* was only reported in an *E. faecium* infection in Tunisia (Figure 3) whilst *mecA* was mostly associated with SCC*mec*. *erm*(B) and *tet*(M) were highly associated with Tn*916* and IS*16*.

In Africa, different studies have reported SCC*mec*-borne *mecA* in *S. aureus* in humans, animals and the environment [23,47,60,66,87] besides the discovery of IS*16* and Tn*916* in the environment of *erm*(B) and *tet*(M) genes in Enterococcus and Streptococcus. These reports show that MGEs are mediating the dissemination of these (and possibly other) resistance genes across different GPB clones and species. MGEs-mediated mobilization of various resistance genes in different GPB clones and species in humans, animals and the environment (Tables 1-4; Figure 2b) calls for prompt measures to contain ABR as the situation may worsen if additional resistance genes are acquired by the MGEs. Resistance genes on MGEs can be horizontally transferred to susceptible cells or vertically transferred to daughter clones [37,88,89], which can easily spread these resistance genes to susceptible pathogens. The higher number of resistant Gram-positive cocci and mean resistance rate in Tunisia may be due to the presence of these three MGEs in this region [69,70,81,90]

Molecular epidemiology of antibiotic-resistant GPB

Staphylococcus spp. (S. aureus, S. haemolyticus and S. saprophyticus)

North Africa: Algeria, Egypt, Morocco, Tunisia, Libya

Algeria.

S. aureus was recovered from two different studies in Algeria. In assessing the nasal carriage of *S. aureus* in patients with medical conditions including pneumonia, urinary tract infections, osteoarthritis, heart diseases, diabetes and chronic kidney disease, Djoudi *et al.* (2014) isolated MRSA [46]. They also found nasal carriage of *S. aureus* to be significantly associated with cancer and previous hospitalization of patients with kidney failure due to immunological suppression and hemodialysis. The nine MRSA isolates, i.e. ST80 (n=4), ST5 (n=2), ST22 (n=2) and ST535 (n=1), harboured *mecA* and were resistant to

363 tobramycin (n=6), gentamicin (n=1), trimethoprim/sulfamethoxazole (n=2), tetracycline (n=3) and
364 erythromycin (n=1). MRSA ST80 is a well-known and frequent etiological agent of infections in North
365 Africa and Middle-East countries[91,92]. Typing of 64 MRSA isolated from human pus (n=47), venous
366 catheters (n=7), tracheal aspirates (n=4), punction fluids (n=3), blood (n=2) and urine (n=1) in 64
367 Algerian patients revealed that 50 were hospital acquired (HA-MRSA) and 14 community acquired (CA-
368 MRSA), which were all resistant to cefoxitin and oxacillin [47]. *mecA*, mobilized by SCC*mec,* was the only
369 detected mechanism of resistance.

370 ***Egypt***

371 MRSA have been respectively isolated in five animal-based and two human-based studies in Egypt
372 between 2011 to 2017. Hashem et.al (2013) isolated 94 *S. aureus* strains from blood and wounds in which
373 45 were MRSA while 25 were fluoroquinolone-resistant [29]. Mutations such as C**2402**T, T**2409**C,
374 T**2460**G, T**1497**C, and A**1578**G in gyrase enzymes, which leads to fluoroquinolones' target-site
375 alterations, were implicated in resistance to fluoroquinolones (ciprofloxacin, levofloxacin, ofloxacin). The
376 high rate of fluoroquinolone resistance (55.56%) among MRSA infections is rather concerning as patients
377 unable to tolerate vancomycin are treated with other antibiotics such as fluoroquinolones. Vancomycin is
378 often reserved as a last-resort therapy for MRSA infections due to their high resistance to several
379 antibiotics.

380 Multidrug resistance to drugs such as gentamicin, ampicillin, amoxicillin, cefepime, tetracycline and
381 chloramphenicol in MRSA is mediated by diverse resistance mechanisms including impermeability
382 effects and efflux pumps. Unrestricted access to antibiotics and inappropriate prescriptions were
383 responsible for the high rates of drug resistance in this study [29]. In a similar study, MRSA was isolated
384 from patients suffering from surgical wound infections, diabetic foot, abscess and burns. Although *mecA*
385 was the only mechanism of resistance, the isolates were multiple-resistant to several antibiotics belonging
386 to the β-lactams, aminoglycosides, fluoroquinolones, macrolides, lincosamides, tetracyclines and

387 glycopeptides, indicating other mechanisms of resistance [93]. It therefore implies that administration of
388 such antibiotics will not relieve patients from *S. aureus* infections. The high rate of *S. aureus* isolation
389 confirms it to be the most prevalent Gram-positive pathogen isolated from soft tissue and wound
390 infections.

391 Al-Ashmawy *et. al*. detected a high rate of MRSA (53%) in milk and dairy products believed to originate
392 from human contamination rather than contamination from animals. Besides being resistant to β-lactams
393 and other antibiotics, thirty-six of the isolates were resistant to vancomycin known to be effective in
394 treating MRSA infections [12], making milk and dairy products a significant source of multidrug-resistant
395 and toxigenic *S. aureus* infections. The occurrence of MRSA in pets such as dogs admitted in a veterinary
396 clinic [53] may confirm a possible route in the community transmission of this pathogen, which is emerging
397 as a veterinary pathogen of public health importance.
398 In 2017, Osman and colleagues detected *Staphylococcus spp.* in imported beef meat. Sixteen of these
399 isolates were MDR and showed resistance to different groups of antibiotics due to resistance mechanisms
400 such as *mecA*, and mutations in *gyrA* and *gyrB.* Indeed, MRSA has made methicillin and other β-lactams
401 antibiotics clinically useless as a result of their high MDR [94]. Imported meat acts as a transmission vector
402 for MRSA and is worrisome as *Staphylococcus spp.* are among the most common foodborne pathogens
403 causing food poisoning outbreaks worldwide. Of 133 *S. aureus* recovered from animal origin, more than
404 70% were MDR and 30 were MRSA, exhibiting high resistance to clindamycin, co-trimoxazole,
405 tetracycline, oxacillin, cefoxitin, ceftriaxone and erythromycin; four of the isolates were resistant to
406 vancomycin [23]. The isolates showed the maximum sensitivity to imipenem, chloramphenicol and
407 rifamycin, which is consistent with similar reports in China and Pakistan [95,96], indicating their
408 effectiveness in treating *S. aureus* infections.
409 MRSA was isolated from chicken products mainly due to poor hygienic handling processes, posing a risk
410 to public health in 2016. The mean *S. aureus* count in the chicken products were beyond the permissible
411 limits of the Egyptian organization for Standardization and Quality Control (EOSQC 2005), coupled with

412 resistance to different antibiotics classes; thus, retail chicken products could constitute a high health risk
413 to human consumers [28]

414 ***Morocco***

415 In a study to assess *S. aureus* carriage among end-stage renal diseases patients undergoing hemodialysis,
416 42.9% *were* carriers, of which only one was MRSA. The methicillin-susceptible *S. aureus* (MSSA) was
417 resistant to many of the local antibiotics, thus limiting the successful treatment of MSSA infections.
418 Moreover 81.8% of the MSSA were penicillin-resistant. The male gender and age 30 or below were
419 identified as risk factors of *S. aureus* nasal carriage (*P-value* < 0.001) [27]. Periodic monitoring of patients
420 with hemodialysis is crucial as they are at increased risk of *S. aureus* infection due to periodic
421 hospitalization, immunosuppression and high invasive vascular interventions.

422 ***Tunisia***

423 Resistant *S. aureus* was isolated from the environment, animals and humans between 2011 to 2017. Ben
424 Said, et al. recovered 12 MSSA from wastewater samples that were resistant to penicillin (n=12 isolates),
425 erythromycin (n=7 isolates), tetracycline (n=1 isolate) and clindamycin (n=1 isolate) due to the presence
426 of *blaZ* (n=7), *msr*(A) (n= 7) and *tet*(K)(n=1). These resistant strains were of ST3245(n=7) and
427 ST15(n=1) [18], which have been also reported in animals and humans. In an investigation to evaluate the
428 prevalence of coagulase-negative Staphylococcus (CoNS) in the hospital environment, MDR *S.*
429 *haemolyticus* and *S. saprophyticus* were the most dominant. Methicillin resistance was detected in *S.*
430 *haemolyticus*, *S. epidermidis and S. saprophyticus*. These isolates were resistant to erythromycin,
431 tetracycline, gentamicin, kanamycin, tobramycin and streptomycin due to the presence of *msrA* (32),
432 *erm*(C) (8), *tet*(K) and *tet*(M), *aac(6´)-Ie-aph(2´´)-Ia (16),), aph(3`)-IIIa(19), ant(4´)-Ia (n=14)* and
433 *ant(6´)-Ia (3)* [97]. The high prevalence of MDR *Staphyloccoci spp.* isolates may result from transmission
434 between the staff, patients and the environment. Strict infection controls are needed as infections caused
435 by CoNS are common cause of death, particularly in low-birth-weight children, and are opportunistic
436 infections in immunocompromised patients [98].

Moreover, nasal swab from sheep detected five MRSA (*mecA*=5), which were all of ST153 and carried *blaZ*, *ant(6)-Ia*, *aph(30)-IIIa*, *erm*(C), *tet*(K), and *fusB* genes that respectively encoded resistance to penicillin, streptomycin, kanamycin, erythromycin, tetracycline and fusidic acid. This study shows that the nares of healthy sheep could act as reservoirs of MRSA [99].

Between 2011 to 2012, 99 MRSA strains were detected from nasal swabs, blood, catheter, wounds, pleural puncture and abscess, among which 39 were tetracycline resistant. These isolates were resistant to aminoglycosides, fluoroquinolones, macrolides and lincosamide, with mechanisms of resistance including *mecA* (n=24), *tet*(K) (n=6), *tet*(L) (n=1) and/or *tet*(M) (n=18), *erm*(A)(n=14), *aph(2')-acc(6')* (n=13). Identified drug-resistant strains included ST247 (n=12), ST239 (n=6), ST728 (n=2), ST241 (n=1), ST398 (n=1), ST5 (n=1) and ST641 (n=1) [50]. For the first time, clonal lineage ST398, which has been reported in pigs from several studies in USA, South America, Asia and Canada [100–103], was found in human MRSA isolates in Africa in a nasal swab of a 74-year old patient.

Additionally, 69 MRSA strains were isolated from hospital-acquired and community-acquired infections. Although *mecA* (n=59) was the only mechanism of resistance identified, the isolates were resistant to aminoglycosides, tetracycline, fluoroquinolones, macrolides and rifampicin. The resistant clones were ST1 (n=2), ST5 (n=5), ST22 (n=1), ST80 (n=41), ST97 (n=2), ST153 (n=2), ST239 (n=4), ST241 (n=3), ST247 (n=3), ST256 (n=1), ST1819 (n=3) and ST1440 (n=1) [24].

Mezghani Maalej and colleagues (2012) isolated five pristinamycin-resistant *S. aureus* strains from patients with skin infections. These isolates were MDR (Table 2), being the first detection of resistance to streptogramins due to *vat*(B) and *vga*(B) resistance genes [104], which emerged due to selective pressure from the use of pristinamycin. Thirty-six methicillin-resistant *S. haemolyticus* (MRSHae) were isolated from neutropenic patients (suffering from febrile neutropenia) with hematological cancer between 2002 and 2004. These MDR isolates carried SCC*mec*-borne *mecA* (Table 2) [105], which agrees with a report on *S. haemolyticus'* MDR capacity, particularly in immunocompromised patients [106,107]

Libya

Due to the high risk of MRSA colonization developing into infections in children, nasal samples were collected from children inpatients, their mothers, healthcare workers and outpatients' workers, which yielded a MRSA nasal carriage rate of 8.3%, 11% ,12.3% and 2.2% respectively in Libya [108]. Thus, nasal carriage of MRSA is common in inpatients children, their mothers and health workers in Libya and could be a source of MRSA infections.

West Africa: Ghana, Nigeria, Senegal

Ghana

Among 308 staphylococcus isolates collected across Northern, Central and Southern Ghana in 2013, low prevalence of antibiotic resistance was reported except for penicillin (97%), tetracycline (42%) and erythromycin (6%) [109]. Moreover, *mecA* was detected in only nine isolates, implying the presence of other β-lactam resistance mechanisms. The MRSA clones included ST8 (n=1), ST72 (n=1), ST88 (n=2), ST239 (n=1), ST250 (n=2), ST789 (n=1), and ST2021 (n=1). In a similar study that characterized 30 MRSA isolates resistant to tetracycline, fluoroquinolones and macrolides, *tet*(M) (n=13), *tet*(K) (n=10), *aphA3* (n=7), *aacA–aphD* (n=5) *and erm*(C) (n=4) were detected. Similar and different resistant clones, viz. ST88 (n=8), ST8 (n=5), and ST247 (n=4) were detected [110], indicating high MRSA clonal diversity in Ghana. These studies show a high rate of resistance to non-β lactams that further complicate MRSA treatment. Furthermore, the isolation of USA300 and other epidemic multidrug-resistant MRSA clones calls for MRSA surveillance and adequate control measures.

Nigeria

Five different studies reported drug-resistant *S. aureus* from several human anatomical sites such as throat swabs, soft skin and tissue infection, urinary tract and respiratory infections, wound, vagina, otitis, conjunctivitis, septicemia and bronchitis. Of a total ≥602 isolates, ≥433 were resistant to several antibiotic classes (Table 1). Of note, 429 of the ≥433 drug-resistant isolates were all resistant to cotrimoxazole or trimethoprim/sulfamethoxazole (SXT). Mechanisms of resistance included *mecA* (≥54), *blaZ* (n=284),

dfrA (≥5) and *dfrG* (≥152). *S. aureus*-resistant clones ST8, ST14, ST37, ST39, ST88, ST152, ST241, and ST772 were present. Colonized persons, including immune-compromised individuals, facilitated the spread of *S. aureus* and MRSA ST8 identified as ubiquitous in various geographic areas of Nigeria. High utilization of co-trimoxazole or SXT because of low cost and easy obtainability through lenient medication regulations were implicated for the high resistance [56]. Besides *S. aureus, S. haemolyticus* was the major species isolated, and is considered as the second most detected and clinically important *Staphylococci spp*., particularly in immunocompromised patients [111]. All the *S. haemolyticus* isolates detected were resistant to at least three antibiotics classes (Tables 2-4) [112].

Moreover, O. Ayepola *et al.* (2015) reported a higher rate of 20.8% *S. aureus* from UTIs than the reported ranges in Africa (6.3-13.9%), and far exceed the rate reported from Europe and Brazil (1.1%) [113]. None of the isolates exhibited resistance to vancomycin, linezolid, daptomycin and mupirocin; indicating their usefulness in treating *S. aureus* infections. Co-trimoxazole, which was previously clinically valuable in treating MRSA infections, demonstrated the highest level of resistance, hence it's not recommendable [56,57,90,112]. In a study to examine the genetic mechanism(s) of resistance in CoNS in faecal samples, all the 53 islolated CoNS were Penicillin V-resistant and between three to 19 exhibited multidrug resistance (Table 2); *mecA* (n=15), *erm*(C), *tet*(M) (n=4) and *tet*(K) (n=6) were identified [112]. CoNS isolates from faeces carrying tetracycline, macrolides and aminoglycosides resistance genes may transfer them inter- and intra-species, disseminating MDR in Staphylococcus.

Senegal

A low prevalence of MRSA (10.5%) was reported in Senegalese pigs compared to those reported in developed countries. This might be due to a lesser veterinary antibiotic use as growth promoters and/or for therapy. However, all the isolates were resistant to penicillin, 27 were resistant to co-trimoxazole and 16 were resistant to tetracycline [66]. Five of the MRSA were of ST5 [66], evincing the spread of this clone in

509 animals, humans [46,59], and the environment [24] ; the importance of this clone as a cause of human infections
510 is well-established [68].

511 ***Cape verde***

512 In Cape Verde, a low prevalence of 5.6% (6/107) MRSA nasal carriage was documented in 2015. The
513 predominant MRSA clones was ST5 (n=3), ST8 (n=1) and ST88 (n=2). These isolates showed significant
514 level of resistance to erythromycin (ERY), sulphamethoxazole-trimethoprim (SXT) and penicillin G
515 (PEN) [114] .

516 **Central Africa: Gabon, D.R. Congo**

517 ***Gabon***

518 In Gabon, *S. aureus* isolated from colonized persons, blood, as well as soft and skin tissue infections
519 resulted in 49% (104/212) resistance to trimethoprim: *dfrA* (n=1), *dfrG* (n=100), *dfrK+G* (n=1), *dfrB*
520 (n=2), and *mecA* (n=1) were detected in the isolates [55]. Thus, *dfrG* is obviously the most abundant and
521 common trimethoprim resistance mechanism in Africa, refuting *dfrB* mutation as the main mechanism of
522 resistance to trimethoprim [115–117].

523 ***D.R. Congo (DRC)***

524 A total of 215 (79.3%) drug-resistant *S. aureus* isolates were collected between 2015 to 2017 from nasal
525 swab and bloodstream infections in the D. R. Congo; 70 isolates were MRSA. Other major resistance
526 genes mediating resistance to trimethoprim/sulfamethoxazole, aminoglycoside, macrolides, tetracycline,
527 penicillin, and chloramphenicol were *dfrG* (≥120), *tet*(K) (≥98), and *femA* (≥98). MRSA showed high-
528 level resistance to β-lactams, aminoglycoside, macrolides and tetracycline. The pathogen caused severe
529 infections such as pneumonia, meningitis, complicated urinary tract infections, gynaecological infections
530 and peritonitis. *S. aureus* ST8 (≥47) was the dominant clone, followed by ST152 (≥17), ST5 (≥2) and
531 ST88 (≥2). In DRC, MRSA ST8 outnumbers the African MRSA clone ST88, which is dominant in
532 Africa. The high-level oxacillin resistance in DRC was associated with a mutation in *femA* (Y**195**F) whist

high-level trimethoprim resistance was due to the detection of *dfrG*, which is consistent with trimethoprim resistance in Africa and Asia. In Africa, SXT or cotrimoxazole is frequently administered as prophylactic to immuno-suppressed patients such as HIV/AIDS patients to prevent opportunistic infections such as *Pneumocystis carinii* pneumonia, toxoplasmosis and bacterial pneumonia [118] Hence, prophylactic use of SXT in HIV patients may impact resistance. Additionally, there was high-level MDR among MRSA, which is a great concern as microbiological laboratories/facilities and second-line antibiotics are rare in DRC. Moreover, the detection of nasal carriage among healthcare workers' demands strict infection controls and surveillance [65,119,120].

East Africa: Kenya, Tanzania

Kenya

In contrast to earlier studies done in Kenya, Omuse and colleagues (2016) detected a wide genetic diversity of MRSA and well-established epidemic MRSA clones among clinical isolates. MRSA clonal complexes 5, 22 and 30, implicated in several outbreaks were described. These clones included ST5 (n=1 isolates), ST8 (n=2 isolates), ST22 (n=4 isolates), ST88 (n=1 isolates), ST241 (n=12 isolates), ST239 (n=2 isolates) and ST789 (n=1 isolates). Approximately 41% of the MRSA in the study were MDR (Table 2), showing resistance to clindamycin, erythromycin and SXT [87]. Detection of these clones in referral hospitals in Kenya calls for implementation of strict infection control measures to reduce the high morbidities and mortalities associated with HA-MRSA infections.

Tanzania

In a study to investigate the molecular epidemiology of trimethoprim resistance in MSSA causing skin and soft tissues infections, *dfrG* was detected in all 32-trimethoprim resistant isolates. Other reported trimethoprim resistance mechanisms such as *dfrA*, *dfrB* and *dfrK* were missing, confirming *dfrG* as the main trimethoprim resistance mechanism in Sub-Sahara Africa [55].

Uganda

A MRSA carriage of 56.1% (23/41) was detected in milk from pastoral communities in Uganda, exactly 70% of which were tetracycline-resistant. MRSA clones ST97 and ST1 were identified. Furthermore, over 90% of the isolates carried genes encoding enterotoxin that causes food-borne diseases. The weak veterinary delivery system and the high dependency on animals and animal products for food in Uganda was implicated for the high prevalence of MRSA [121].

S. aureus isolates, including 24 MRSA and 40 MSSA, were isolated from patients with surgical site infections (SSI). The MRSA isolates were MDR (including resistance to oxacillin, gentamicin, ciprofloxacin and chloramphenicol) compared to the MSSA. Inducible clindamycin resistance was found in 17.2% of the isolates, mostly in MRSA. In a multivariate analysis, inducible clindamycin resistance and cancer were identified as independent predictors of MRSA-SSI [122].

Southern Africa: Angola, Malawi, Mozambique, Namibia, South Africa

Angola

Conceica˜o et al (2014) reported a nasal *S. aureus* carriage of 23.7% (n=128 isolates), out of which 58.1% (n=77 isolates) were MRSA. Fifty-seven of the MRSA clones were of ST5, followed by ST88 (n=9), ST8 (n=5) and ST72 (n=3). This study represents the first description of the spread of MRSA ST5 in Africa. All the 77 MRSA strains were resistant to SXT, cefoxitin (FOX) and PEN [123] . In a study to identify oxacillin-susceptible *mecA*-positive *S. aureus* (OS-MRSA) for the first time in Africa, a prevalence of 17.7% was detected among healthy healthcare workers in Angola and Sa˜o Tome´ & Principe, making them potential OS-MRSA reservoirs [124]. OS-MRSA have been reported worldwide in humans, animals and food animals [125–128]. The OS-MRSA isolates expressed MDR (Table 2) and belonged to ST88 (n=15 isolates) and ST8 (n=9 isolates). In sub-Saharan Africa, the identification of clinically important *S. aureus* is heavily based on phenotypic agar-screening and oxacillin disc-diffusion methods.

Mozambique

The prevalence of HA-MRSA and CA-MRSA in Mozambique was found to be 15.1% and 1%, respectively. MRSA showed high-level resistance to penicillin, cefoxitin, gentamicin, ciprofloxacin, erythromycin, SXT, chloramphenicol and tetracycline, compared to MSSA. Additionally, inducible macrolide–lincosamide–streptogramin B (MLSB) resistance was 41.7% and 10.7% in hospital-acquired *S. aureus* (HA-SA) and community-acquired *S. aureus* (CA-SA) isolates respectively [129], further limiting therapeutic options for *S. aureus* infections. This study, which is the first to detect the emergence of HA-MRSA within post-operative abdominal wounds and burn wounds in Mozambique, reported that patients with infected burn wounds had a significantly longer hospitalization than patients with post-operated abdominal wounds. Efforts to prevent the transmission of MDR HA-SA, such as education on proper hand-washing techniques, are urgently needed.

Namibia

The dominant resistance gene mediating trimethoprim resistance in MRSA and MSSA in Namibia was *dfrG*. This is similar to reports in other Africa countries [55]. Moreover, *dfrG* was frequently detected in *S. aureus* from SSTIs in travelers returning from other African countries, suggesting that *dfrG* can be transmitted into populations with low antifolate resistance such as North America and Europe [130,131].

South Africa

Thirty MDR *S. aureus* were recovered between April 2015 to April 2016 from ten beaches in the Eastern Cape Province, South Africa (Table 2). Notably, the isolates harbored *mecA, femA, rpoB*, *blaZ, erm*(B) and *tet*(M) [11], making marine environments and public beaches potential depositaries of MDR *S. aureus* that can be transmitted to animals and humans. Further, the 50% resistance to vancomycin recorded is concerning to global health due to its role as a last-resort antibiotic for treating MRSA infections.

S. aureus was detected in raw and pasteurized milk at an isolation rate of 75% and 29% respectively, due to inefficient thermal processing and post-process contamination. A high proportion (60%-100%) of these isolates showed resistance to aminoglycosides, β-lactams, vancomycin, tetracycline and erythromycin, albeit only 19 *mecA* genes were present [21]. Evidently, raw and pasteurized milk can harbour MDR *S. aureus*, exposing consumers to colonization and/or infections. Again, *Staphylococcus spp*., including *S.*

606 *aureus, S. haemolyticus*, *S. xylosus* and *S. capitis* were isolated from healthy pigs and cattle, of which
607 between 75 to 100% were resistant to penicillin G, tetracycline, sulfamethoxazole and nalidixic acids, due
608 to their use as growth promoters; *mecA* and *mphC* were identified. Additionally, 12% of the isolates were
609 resistant to vancomycin and erythromycin, evincing the important role of animals in the dissemination of
610 resistance determinants and the importance of commensals to public health [61].
611 Van Rensburg et al. [59] detected 43.4% (1432/3298 isolates) and 3.1% (328/10448 isolates) rifampicin
612 resistance rate among MRSA and MSSA respectively. Similar studies in South Africa have also reported
613 of high rifampicin resistance in MRSA [132,133], obviously due to frequent use of rifampicin among
614 tuberculosis patients, who are highly prevalent in South Africa. MRSA ST5 and ST612 were detected
615 while H**481**Y/N and I**527**M mutations in *rpoB* were associated with high-level rifampicin resistance,
616 similar to reports in Italy [134]. Additionally, novel H**481**N, I**527**M, K**579**R mutations were also detected.

617 Three studies reported a prevalence of 29.1% [135], 45.44% [60] and 100% [136] MRSA recovered from humans,
618 expressing resistance to macrolides, tetracycline, aminoglycoside, cotrimoxazole and rifampicin. MRSA
619 ST612, ST239, ST36 and ST5 were the dominant strains similar to other findings in Australia and
620 Europe[137]. The study showed that *S. aureus* bacteremia is common and account for high mortality in
621 South Africa. For instance, in a study by Perovic et al., [135] 202 patients died from *S. aureus* bacteremia
622 infections, with HIV patients being more likely to acquire HA-MRSA. The isolates were however
623 susceptible to glycopeptides, fluoroquinolones, linezoid, tigecycline, fosfomycin and fusidic acid,
624 confirming their clinical usefulness in treating MRSA infections. In a recent study, a high prevalence and
625 genetic diversity of multi-drug efflux (MDE) resistance genes were found in clinical *S. aureus* isolates,
626 including 81 MRSA and 16 MSSA [138]. *nor*A*, norB, mepA, tet*(38)*, sepA, mdeA, imrs* and *sdrM* were
627 present in at least 86% of the isolates, predicting resistance to broad-spectrum biocides and
628 fluoroquinolones, which is disturbing. Efforts to develop efflux pump inhibitors can mitigate such
629 resistance mechanisms.

630 ***Sao Tome & Principe***

MRSA prevalence of 26.9% [139] and 25.5% [114] was reported in nasal swabs in 2014 and 2015, respectively, in Sao Tome & Principe. Additionally, a high prevalence of oxacillin-susceptible *mecA*-positive *S. aureus* was reported in the same study in Sao Tome & Principe and Angola [124]. The most dominant MRSA clone was ST8 (n=25 isolates), followed by ST5 (n=13 isolates) and ST80 (n=13 isolates). High genetic variability was found in the MSSA strains. Both MRSA and MSSA showed different levels of resistance to SXT, ERY, CIP and TET; however, all the MRSA isolates were resistant to cefoxitin.

Streptococcus spp. (S. pyogenes, S. pneumoniae and S. agalactiae)

Drug resistant *Streptococcus spp*. including *S. agalactiae* and *S. pyogenes* have been identified in Northern, Eastern and Southern Africa. *S. pyogenes* were reported in only humans whilst *S. agalactiae* was reported in both animals (camels) and humans with a high rate of resistance to tetracycline and erythromycin.

North Africa: Algeria, Egypt, Morocco, Tunisia, Libya

Algeria

A sole study has so far detected 44 tetracycline (100%, 44/44 isolates)- and erythromycin-resistant (43.18%, 19/44 isolates) *S. agalactiae* from vaginal swabs; *tet*(M); and *erm*(B) respectively mediated this resistance. A high diversity of resistant clones viz., ST1, ST19, ST10, ST158, ST166, ST233, ST460, ST521 and ST677 were detected [45], which have been reported worldwide for causing life-threatening invasive diseases such a meningitis and sepsis [140,141].

Egypt

Similarly, Shabayek et al. (2014) detected 98% and between 14-17% *S. agalactiae* resistance to tetracycline and macrolides respectively. *tet*(M) was detected in all the 98 tetracycline-resistant isolates whilst *erm*(B) and *erm*(A) mediated erythromycin resistance. Efflux pump genes such as *tet*(K) (n=12 isolates), *tet*(L) (n=1 isolates) and *mefA/E* (n=1 isolates) were also found [32], which reflects the increasing reports of *S. agalactiae* resistance to tetracycline and macrolides [142]. This study also showed that

vancomycin and fluoroquinolones are effective replacement for erythromycin and clindamycin, and for patients allergic to penicillin. Although penicillin is the antibiotic of choice for treating *S. agalactiae* infections, reports of penicillin resistance in USA and China calls for increased surveillance in Africa [142].

Tunisia

S. agalactiae

From January 2007 to December 2009, 226 *S. agalactiae* were isolated from female genitals and gastric fluid of infected newborns. Of these, 97.35% (220/226 isolates), 40% (90/226 isolates) and 19.1% (43/226 isolates) were resistant to tetracycline, erythromycin and rifampicin respectively. Additionally, seven isolates were resistant to aminoglycoside (gentamycin and streptomycin) and chloramphenicol. *tet*(M) (n=205 isolates), encoding a ribosomal protection protein, which protect the ribosome from the action of tetracycline, was the main tetracycline resistance mechanism, and was significantly associated with Tn*916* (p-value = 0.0002). Other resistance genes including *erm*(B) (n=79 isolates) and *tet*(O) (n=50 isolates) were detected. All isolates were however susceptible to β-lactams and quinupristin-dalfopristin [85]. Between 2005 and 2007, 160 erythromycin-resistant *S. agalactiae* were isolated from humans, with a high resistance rate of 84.3% (135/160 isolates) to the constitutive macrolides-lincosamides, streptogramines B (MLSB) [143].

S. pyogenes

Hraoui *et al.,* (2011) reported a low macrolide resistance rate (5%, 5/103) and a high tetracycline resistance rate (70%, 72/103) among human isolates, with *tet*(M), associated with Tn*916*, being responsible for tetracycline resistance [144]. Increase tetracycline use in food animals was implicated in this instance, leading to selection and dissemination of resistance genes from animals to human. Macrolide resistance was only detected in seven isolates, which is corroborated by the findings of Ksia et al. (2010), who detected low-level macrolides resistance among Children [145].

East Africa: Kenya, Tanzania

Kenya

S. agalactiae

In the horn of Africa, camel plays a significant role in the survival of humans by providing milk, meat and transportation. In 2013, Fischer et al. detected 36% (37/92) tetracycline resistance in *S. agalactiae* isolates from camels' wound infections and mastitis that was mainly mediated by a Tn*916*-borne *tet*(M). ST616 (n=22) was the major resistant clone, followed by ST612 and ST617 [146]. Shifting from tetracycline to other antibiotics is evidently necessary for effective treatment outcomes in camel infections in Kenya.

Southern Africa: Angola, Malawi, Mozambique, Namibia, South Africa

South Africa

S. agalactiae

A *S. agalactiae* colonization rate of 30.9% was detected from vaginal and rectal swabs of pregnant women. Similar to other reports in Africa, a high rate of tetracycline (94.5%, 120/128 isolates) and macrolide (21.1%, 27/128) resistance was documented. All the isolates were however sensitive to penicillin, ampicillin, vancomycin and gentamicin. Macrolide and clindamycin resistance were associated with *erm*(B) and *mefA* genes [147]. The study highlights the need for research on treatment options for patients allergic to penicillin due to high-level resistance in alternative drugs such as macrolides and lincosamides.

Enterococcus spp. (E. faecium, E. faecalis, E. hirae, E. durans, E. gallinarum)

North Africa: Algeria, Egypt, Morocco, Tunisia, Libya

Algeria

The first study to molecularly characterize *Enterococcus spp.* from urinary tract and wound infections in Algeria revealed a high rate of resistance to erythromycin (86.4%, 108/125 isolates), tetracycline (82.4, 103/125 isolates), levofloxacin (71.2%, 89/125 isolates) and gentamicin (54.4, 68/125 isolates). Only

3.2% (4/125 isolates) were VRE, confirming glycopeptides as ideal antibiotics for treating Enterococcus infections. A mortality rate of 10% was reported due to infections caused by Enterococcus. *E. faecium, E. faecalis* and *E. gallinarum* were the main Enterococcus isolated. Majority of these isolates were from females (53%). *erm*(B) (≥92) and *vanC1*(≥4) were the main mechanisms of resistance. A high genetic diversity among strains was seen in *E. faecium* and *E. faecalis*, with *E. faecium* ST78 being the dominant resistant strain [148], which is also prevalent in Asian (Japan, Taiwan, China and Korea) and European (Italy and Germany) countries [149–151]. A novel ST317 (n=33) clone was predominant among the *E. faecalis* isolates. Rational use of antibiotics, as well as close monitoring of the epidemiology of the strains are crucial.

Egypt

In a similar study to characterize *E. faecium* and *E. faecalis* from patients, 82% of the isolates were MDR, showing high-level resistance to aminoglycosides, β-lactams and tetracycline. *VanA* was detected in two *E. faecium* isolates, all of which were resistant to all antibiotics tested. Bioinformatic (sequence) analysis revealed that *vanA* was transmitted horizontally to *S. aureus*, showing the importance of horizontal gene transfer in ABR and subsequent management of enterococci infections such as bacteremia, endocarditis and urinary tract infections [152].

Tunisia

Antimicrobial-resistant Enterococcus was found in faeces of pet and camel, irrigation water from farm environments, food vegetables, hospital environments, animal meat and patients in Tunisia [19,22,31,51,52,69]. High-level resistance to vancomycin, macrolides, aminoglycosides, β-lactams and tetracycline was detected in the environment, animals and humans with majority of the isolates being *E. faecium*, followed by *E. faecalis*. *tet*(M), *tet*(L), *erm*(B), *ant (6)-la, vanA* and *aph(3')-llla* were the major resistance mechanisms, with IS*16* being the main MGE disseminating the resistance genes. *E. faecium* ST80, ST910 and ST16 were the dominant resistant clones in Tunisia. The studies show that meat, animals, pets,

hospital environment and wastewater used for farm irrigation play a crucial role in the spread of antibiotic resistant Enterococcus.

West Africa: Cape Verde, Ghana, Nigeria, Senegal

Nigeria

Enterococcus spp. isolated from poultry and cattle as well as their manure demonstrated high-level resistance to tetracycline, erythromycin, gentamicin, ampicillin and streptomycin. Sixty isolates were MDR, showing resistance to three or more antimicrobials [153]. The rate of MDR is a reflection of the substantial use of broad-spectrum antibiotics in Nigeria, raising major public health concerns as practices such as the use of untreated poultry and cattle manure for fertilizing agricultural soils, particularly vegetables, are a common practice in Africa. This could transfer MDR Enterococci to humans, and cause serious nosocomial infections including endocarditis, bacteremia and urinary tract infections that can result in high morbidities and mortalities.

Ngbede et al. (2017) recently characterized 63 ampicillin- and 37 gentamicin-resistant *E. faecium* from vegetables, soil, farms, animal and manure [25]. Approximately 95% (35/37 isolates) and 8% (5/63 isolates) of the aminoglycoside- and ampicillin-resistant clones were recognized as high-level aminoglycosides- and ampicillin-resistant *E. faecium* respectively. Modifying enzymes' genes such as *aac(6')-Ie-aph(2")-Ia), aph(2')-1c,aph(3')-llla,,* and *ant(4')-la* accounted for the aminoglycoside resistance.

East Africa: Kenya and Tanzania

Tanzania

In a study to determine if cattle co-grazing with wild life influence ABR, ABR in wild animals such as buffalo, zebra and wildebeest was higher than in cattle, although wildlife is periodically treated with antibiotics. Ten VRE and ampicillin-resistant Enterococcus were found in the wild animals but not cattle. Additionally, Enterococcus isolates from wildlife were highly resistant to tetracycline, rifampicin, macrolides, aminoglycosides and cotrimoxazole [14]. *tet*(W) and s*ul1* were the resistance genes identified in the isolates. The practice of co-grazing possibly resulted in transmission of ABR genes from livestock

to wildlife. The high presence of ABR bacteria in wildlife was likely due to contact with more environmental surfaces that have been contaminated with human, birds or animal excreta. Result from this study demonstrates the presence of ABR Enterococci in wild animals without antibiotic pressure.

Southern Africa: Angola, Malawi, Mozambique, Namibia, South Africa

South Africa

Multiple antibiotic-resistant Enterococci were isolated from borehole water, waste water, pigs and humans in South Africa. Notably, a very high-level vancomycin, aminoglycoside, β-lactam, macrolides and fluoroquinolones resistance was detected among the Enterococci isolates compared to other countries. *erm*(B) (≥300 isolates), *vanC* 2/3(162 isolates), *vanB* (≥138 isolates), *vanC* (≥120 isolates), *strA* (≥120 isolates) were the major resistance genes. The vancomycin-resistant isolates were from patients with haematological malignancies, bacteremia, pigs, wastewater and underground water [9,10,26,30]. Inefficient chlorination to kill bacteria accounted for the high resistance rates in the final effluents' discharge into the environment. Hospital wastewater is therefore a major source of MDR Enterococcus. Sub-therapeutic antibiotic usage in animal feed also accounted for the emergence of ABR in pigs whilst the construction of boreholes near pit toilets resulted in high enterococcal isolation and resistance rates in South Africa.

Experimental procedures used in included studies

The studies included in this review basically used the following experimental procedures. Transport media such as stuart agar, cary-blair medium, and gel transport swabs with charcoal were used to transport the samples to the laboratory [53,65]. Cotton swabs were used to swab sample specimens, tissues, surfaces, fluids, etc. and cultured on nutrient agar, blood agar, tryptone soya agar, mannitol salt-phenol red agar, brain-heart infusion broth, Slanetz-Bartley mannitol salt agar, and Edwards agar media prior to identifying the 24-hour colonies using Gram-staining and different biochemical tests such as catalase and coagulase tests, latex coagulase test and DNase agar test. Subsequently, antimicrobial susceptibility testing (AST) using disc diffusion (Kirby-Bauer method or E-test) on Mueller Hinton agar plates and a 0.5 McFarland bacterial inoculum was performed. Antibiotics such as ampicillin (AMP), amoxicillin

(AMX), amikacin (AMK), ampicillin-Sulbactam (SAM), amoxicillin-clavulanic acid (AMC), azithromycin (AZI), apramycin (APR), chloramphenicol (CHL), cefoxitin (FOX), ceftazidime (CFZ), clarithromycin (CLR), ciprofloxacin (CIP), cefuroxime (CXM), clindamycin (CLI), cephalexin(LEX), cefoperazone (CFP), cefepime (FEP), cefotaxime (CTX), ceftaroline (CPT), cephalothin (CET), cloxacillin (CLX), doxycycline (DOX), erythromycin (ERY), fusidic acid (FUS), fosfomycin (Fof), gatifloxacin (GAT), gentamicin (GEN), imipenem (IPM), kanamycin (KAN), levofloxacin (LVX), linezolid (LZD), lincomycin (LIN), meropenem (MER), mupirocin (MUP), minocycline (MIC), moxifloxacin (MXF), methicillin (MET), metronidazole (MTZ), nitrofurantoin (NIT), norfloxacin (Nor), nalidixic acid (NAL), netilmicin (NEL), oxacillin (OXA), ofloxacin (OFX), perfloxacin (PF), penicillin (PEN), pristinamycin (PRI), rifampicin (RIF), streptomycin (STR), streptogramin B (SB), sulfamethoxazole (SMZ), tetracycline (TET), teicoplanin (TEC), telithromycin (TEL), tobramycin (TOB), trimethoprim-sulfamethoxazole (SXT), and vancomycin (VAN) were mostly used for the AST. Polymerase chain reaction (PCR) was used to detect the antimicrobial resistance genes and clones (i.e. molecular typing) of the isolates.

3. CONCLUSION AND STUDY LIMITATIONS

We report of high rate of ABR among GPB in several African countries, mediated largely by *S. aureus* ST5, ST8, and ST80*, Enterococcus faecium* and *Enterococcus faecalis* strains, *SCCmec,* Tn*916* and IS*16* MGEs are a major threat to clinical medicine, the economy and socio-economic development. This calls for national as well as international rules and regulations to contain resistance. Heavy consumption of antibiotics in animal feed, exchange of resistance genes between animals and food animal products to man, uncontrolled and inappropriate antibiotics prescription practices, inadequate hygienic handling and processing of food, close contact with pet dogs, shedding of resistant clones from animals to humans and the environment, as well as high consumption of antibiotics in humans, particularly in HIV patients, account for the high rate of ABR in Africa.

Effective surveillance and monitoring of antimicrobial drug usage and licensing, banning or restricting the prescription of reserved, expired and substandard drugs, periodic monitoring of pharmacies and veterinary shops, and antibiotic stewardship are recommended measures to contain ABR. Improving animal health through hygienic practices on farms, avoiding prophylactic or growth-promoting antibiotic usage in veterinary medicine, integrative efforts between human and veterinary medicine as well as environmental health are urgently needed to contain ABR. Implementation of these policies will decrease the high rate of ABR in Africa, reduce longer hospital stays and the resort to expensive but toxic antibiotic alternatives, with a concomitant reduction in morbidity and mortality rates. Few studies reporting on the molecular determinants of ABR in GPB in Africa limited the study to 130 articles. Among these, only few studies reported on MGEs and resistant clones.

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Table 1. Frequency distribution of Gram-positive bacterial species, resistance genes and MGEs isolated from animals, humans and environmental specimens.

Bacteria species, ARGs and MGEs		**Human (n)[1]**	**Animal(n)[2]**	**Environment(n)[3]**
Species	*E. faecalis*	225	129	66

[1] Total number of species or ARGs or MGEs in human isolates
[2] Total number of species or ARGs or MGEs in animal isolates
[3] Total number of species or ARGs or MGEs in environmental isolates

	E. faecium	299	577	523
	S. agalactiae	658	92	0
	S. aureus	25559	1609	65
	S. haemolyticus	96	43	38
	S. pyogenes	296	0	0
ARGs	*mecA*	3057	462	28
	erm(B)	551	520	197
	erm(C)	102	23	8
	tet(M)	524	115	81
	tet(K)	179	80	22
	tet(L)	25	57	37
	vanB	4	387	60
	vanA	23	0	23
	*vanC*1/2/3	8	862	101
	dfrA/G	422	0	0
	aph(3')-*llla*	50	5	115
	aac(6')-*aph*(2')	178	17	73
	ant(6)-*la*	5	24	38
	blaZ	403	127	35
MGEs	IS*16*	3	0	5
	SCC*mec*	2471	27	8
	Tn*916*	62	37	0

1526 **Table 2. Geographical distribution, species, clones, and resistance mechanisms of antibiotic-resistant Gram-positive bacteria isolated from**

1527 **humans in Africa from 2007-2018**

Country (n)[4]	Year	Organism/ Species (n)[5]	Specimen Sources (n)[6]	Sample size (Resistant isolates)	Resistance rate (%)	Clones (n)[7]	Resistance genes/ mechanisms (n)[8]	Antibiotics to which strains were resistant(n)[9]	MGEs (n)[10]	Reference
Algeria (6)	2015	*S. agalactiae* (44)	Vaginal swab (44)	(44)	100	ST1(9), ST19(14), ST10(4), ST158, ST166, ST233, ST460, ST521, ST677	*tet*(M)(44), *erm*(B) (19), *mefA/E* (1), *erm*(A) (1)	TET (44) ERY (13)	ND	45
	2014	*S. aureus* (159)	Nasal swab (159)	159 (9)	5.66	ST80 (4), ST5 (2), ST22 (2), ST535 (1)	*mecA* (9)	GEN ((3), TET (3), TOB(6) SXT(2)	*SCCmec* (9)	46
	2013	*S. aureus*(85),*E .faecalis*(7),*CONs*(31)	Human(123)	123(NS)	NS	NS	*mecA*(73),*aphA*(70), *aacA-aphD*	Methicillin(73)	*ND*	154
	2012	*E. faecium* (80), *E. faecalis* (39) *E. gallinarum* (4), *E. raffinosus* (1), and *E. durans*(1).	Urinary (85), cutaneous (24), blood (14), pus (2)	125 (108)	87	ST 317 (33), ST51(20), ST52(11), ST175 (8), ST78(25), ST578(4), ST81(2), ST16(2)	*erm*(B) (92), *vanC1*(4)	AMP (38), GEN (68), TET (103), ERY (106), CAM (18), LVX ((89), NIT (24), VAN (4).	ND	148
	2012	*S. aureus* (64)	Pus (47), venous catheters (7	(64)	100	ND	*mecA* (64)	MET (64), OXA (64), FOX (64)	*SCCmec*	47

[4] Total number of studies per country
[5] Total number of isolates
[6] Total number of specimen source
[7] Total number of resistant clones
[8] Total number of resistant genes
[9] Total number of antibiotics to which strains were resistant to.
[10] Total number of MGEs

			tracheal aspirates (4), punction fluids (3), blood (2), urine (1)						*(46)*	
	2010	*S. aureus*(221)	Skin and soft tissue(158),bone and joint (infection(25),bacteraemia(20),pneumonia(12),eye infection(7),meningitis(3),UTI(2)	221(41)	18.55	ST80(13),ST241(9)	*mecA*(97)	KAN(29),TET(25),ERY(25),FUS(41)	*SCCmec(97)*	
Angola (4) and Sao Tome principe (1)	2015	*S. aureus* (164)	Nasal swab (164)	164 (29)	17.68	ST88(15), ST8(9)	*mecA* (NS)	FOX (29), SXT (26), TET (18), ERY (16), CIP (9) and CLI (8)	*SCCmec (NS)*	49
	2015	*S. aureus* (203)	Nasal (203)	203(128)	63.05	ST8(16), ST5(83), (ST88(19), ST72(5), ST789(1), ST5/2629(2), ST30(2), ST22(1)	*mecA* (127)	SXT (136), FOX (128), TET (39), PEN (200), RIF (156), CLI (4), ERY (14), CIP (20), GEN (43), CHL (18)	*SCCmec (128)*	114
	2015	*S. aureus*(70)	Nasal swab(70)	70(61)	87.14	ST5(13),ST88(6),ST601(1)	*mecA*(20)	PEN(67),FOX(20),RIF(61),SXT(15),CHL(6),GEN(3),TET(7),FUS(1),CIP(1)	*ND*	155
	2014	*S. aureus*	Nasal swab (128)	128(124)	96.88	ST8(57), ST88(9), ST8(5), ST72(3), ST789(1)	*mecA* (77)	PEN (124), FOX (77), SXT (80), GEN (24), RIF (97), CHL (11), CIP (10), TET (16), ERY (8)	*SCCmec (128)*	123
Cape verde (1)	2015	*S. aureus*	Nasal swab (113)	113(16)	14.16	ST88(2), ST8(1), ST5(3)	*mecA* (6)	FOX (5), TET (5), PEN (109), CIP (2), CLI (3), SXT (12), ERY (16), (FUS (5), MUP (6)	*SCCmec (6)*	
Democratic Republic of Congo (3)	2017	*S. aureus* (108)	blood(108)	108(27)	25	ST5(11),ST8(30),ST88(1), ST152(17)	*dfrG*(24),*aac(6')-aph(2'')(25)*,*tet*(K)(23),*erm*(C)(*20*)	TET(61),LIN(20),CIP(20),PEN(87),CHL(5),SXT(4),	ND	120

	2016	*S. aureus* (100)	Nasal swab (100)	100 (97)	97	ST8 (9)	*dfrG*,(72),*tet*(K) (44), *fem*A (98), *mecA* (33)	TMP(72), PEN (97), TET(45),GEN(25),OXA(24),ERY (20),LUV(16),RIF(7),CHL(7),CLI(4)	ND	119
	2015	*S. aureus* (63)	Nasal swabs (63)	63(10)	15.87	ST8 (8), ST5 (1), ST88 (1)	*mecA* (10)	TET(21),ERY(12),CLI(8),PG(60) ,CHL(9),KAN(12),GEN(12),TOB(12), SXT(6)	*SCCm ec (10)*	65
Egypt (10)	2017	*S. aureus* (20),*S. haemolyticus* (9), *S. schleifer*(3),*S . warnei* (2), *S. lugdunensis* (4)	Urine(NS), Blood(NS)	58(38)	65.52	ND	*mecA* (19)	FOX(25),CIP(21),CLI(21), SXT(21),ERY(38),GEN(32),RIF(14),TET(27)	*SCCm ec*	156
	2016	*E. faecalis* (57)	Urine(57)	57(52)	91.23	ND	*acc(6)Ia-aph(2)Ia*(21), *erm*(B)(51),*mef(A/E)* (1)	AMX(14),VAN(2),FoF(36),GEN(20),AMK(52)	*ND*	157
	2016	*Staphylococcus spp*	Urine(3),blood(10), pus(7),sputum(4),b ronchoalveolar lavage(2)	81(26)	32.1	ND	*fusB*(8),*fusC*(9)	GEN(14),RIF(5),AMP(17)	*ND*	158
	2016	*S. aureus*(60)	Human(60)	60(NS)	NS	ST22(1),ST239(1)	*mec*A(14), *erm*(C)(14*)*	CLI(NS),CIP(NS),GEN(NS),SXT (NS),VAN(NS),OXA(NS),ERY(N S).	*ND*	159
	2016	*S. aureus(64)*	Sputum(18),pus(35),urine(10),CSF(1)	64(45)	69.23	ND	*mecA*(NS)	CRO(45),ERY(38),OXA(38),SXT (31),GEN(22),CIP(19),CLI(17),V AN(3)	*ND*	160
	2015 H	*E. faecium* (26), *E. faecalis* (47)	Urine (100)	(73)	100	ND	*vanA* (2)	PEN(17), AMP(38), CIP(22), GEN(41), STR(73), CHL(12), TET(50), VAN(2)	ND	80

	2014	*S. agalactiae* (100)	Vaginal swab (100)	100 (98)	98	ND	*erm*(B) (9), *erm*(A) (1) ,*mef*A/E(1),*tet*(M) (99) ,*tet*(L)(12), *tet*(K)(1) , *tet*(O) (1)	ERY(17), CLI(14), AZI(16), TET(98) and CHL(1)	ND	32
	2014	*S. aureus* (127)	Diabetic foot ulcers (39), surgical site infection (48) and abscess infections (25), burn discharges (15).	127 (111)	87.40	ND	*mecA* (29)	AMP(111), AMX(104), OXA(31), LEX(83), CXM(67), CFP(43), FEP(56), CTX(32), SAM(37), AMC(41), AMK(3) CIP(32), NOR(37), OFX(31), LVX(11), GAT(5), ERY(59), Cli(34), TET(66), VAN(2), CHL(44), RIF(35)	ND	93
	2013	*S. aureus* (94)	Blood and wound	94 (45)	47.87	ND	*gyrA* (C**2402**T, T**2409**C, T**2460**G) (60), *gyrB*(T1497C, A**1578**G) (5)	CIP(26), LUX(26), AMC(26), FEP(24), GEN(11), TET(17),CHL(5)	ND	29]
	2008	*S. aureus* (60)	Sputum(13),throat swabs(11), nasal swabs(31), blood(9)	60(31)	51.67	ND	mecA(18)	MET(31)	ND	161
Gabon (2)	2016	*S. aureus* (103)	Throat swab(79),skin lesions(24)	103(61)	59.22	ND	*mec*A(3),*bla*Z(90),*mrs*(A)(8),*aph*A3(1),*dfr*A(2),*tet*(K)(56),*tet*(M)(6),*qac*C(4)	PEN(90),OXA(1), CXM(1),ERY(8),TET(61),SXT(51),CIP(3)	ND	162
	2014	*S. aureus* (212)	Skin and soft tissue (100) and bloodstream (12)	212 (104)	49.06	ND	*dfr*A (1), *dfr*G (100), *dfr*K+G (1), *dfr*B (2) *mec*A(1)	TMP;(104), SXT(100), SMZ(6)	ND	55
Ghana (3)	2015	*S. aureus* (30)	Skin and Soft Tissue Infections (16) , bacteraemia (5), nasal swab (9)	(30)	100	ST88 (8),ST8 (5), ST247 (4)	*tet*(M) (13) , *tet*(K) (10), *aph*A3 (7), *aacA–aph*D (5), *erm*(C) (4).	TET(20), NOR(12), MXF(11), ERY(11), CLI(9), KAN(9),GEN(9) and CPT (6)	ND	110
	2014	*S. aureus* (308)	Blood (112), SST1(173), others (23)	308 (208)	67.53	ST88 (2), ST8 (1), ST789 (1), ST72 (1), ST2021 (1), ST250 (2), ST239 (1)	*mecA* (9)	PEN(208), TET(129), and ERY(18)	ND	109

	2013	*S. aureus* (105)	Nasal swab(105)	105(29)	27.62	ST88(4),ST8(1),ST172(1)	*mecA*(6)	PEN(98),FUS(13),TET(29),FOX(6),SXT(3),ERY(5),CLI(3),NOR(2),GEN(2),RIF(1),MUP(1)	SCCmec(6)	163
Kenya (2)	2016	*S. aureus* (93)	Blood(93)	93 (32)	34.41	ST22(4),ST88(1),ST789(1),ST5(1),ST8(2),ST241(12),ST239(2)	*mecA* (32)	CLI(10), ERY(9) and SXT(9),MXF(1) ,RIF(3), TET(6),LUX(5)	SCCmec (32)	87
	2013	*S. aureus* (82)	Boil(39),abscess(14),cellulitis(18),ulcer(11),	82(69)	84.12	ND	*mecA* (52)	ERY(56),CLI(31),CIP(55),OXA(69),FOX(69),SXT(51),GEN(69)	SCCmec	164
Libya (1)	2014	*S. aureus* (208)	Nasal swab (44)	208(70)	33.69	ND	*mecA* (35)	CIP(22), GEN(24), FUS(49)	ND	165
Morocco (2)	2013	*S. aureus* (30)	Nasal swab (30)	30 (25)	83.33	ND	*mecA* (1)	PEN(25), GEN(1), TOB(1), KAN(1), PF(1), TET(1), ERY(1), SXT(1)	ND	27
	2012	*S. aureus* (79)	Human(79)	79(43)	54.43	ND	*mecA* (28)	PEN(74),KAN(29),TOB(27),GEN(27),ERY(21),FUS(25),PF(30),TET(43),MIC(34),RIF(25),SXT(19)	ND	166
Mozambique (1)	2013	*S. aureus* (24)	Wound (24)	24 (9)	19.15	ND	*mecA* (9)	FOX(9), OXA(8)	ND	129
Namibia (1)	2014	*S. aureus* (116)	skin and soft tissue (31), urinary tract(19), respiratory tract (37), ear (7), eye (4) and bloodstream (3)	116 (34)	29.31	ND	*dfrA* (14), *dfrG* (20) *mecA* (11)	SXT(20), TMP(34) SMZ(20)	ND	55
Nigeria (9)	2015	*S. aureus* (38)	throat (40), nasal (23), wound (10)	38 (32)	84.21	ST8 (5), ST152 (1), ST772 (1), ST14(1)	*mecA (16)*	TET(32),LUX(7), GEN(5), ERY(5), PEN, SXT(29)	ND	167
	2015	*S. aureus*	Skin and nasal		72.76	ND	*mecA (7), blaZ*	PEN(284), SXT(233),	SCCm	58

		(290)	swab (120), wounds, blood	290 (211)			*(284))*	TET(51),OXA(7),GEN(11),TOB(11),LUX(23),MXF(21),TGC(51),	ec (7)	
	2014	*S. epidermidis* (20), *S. haemolyticus* (10), *S. saprophyticus* (5), *S. capitis*, (5), *S. lugdunensis* (2), *S. warneri* (4), *S. xylosus* (n4),*S. cohnii* (3).	Stool (53)	(53)	100	ND	*mecA* (15), *aac(6')–aph(2")* (3),*erm(C)*(4), *msr*A(1), *tetK (6)* ,*tet*(M)(4)	PEN(53), OXA(15), GEN(3), ERY(5), TET(7), SXT(19), CHL(4),AMC (31),CIP(1)	SCCmec(15)	[58]
	2014	*S. aureus* (183)	Skin and soft tissue (32), urinary tract (9), ear (7), unknown site (4), oropharynx (3), eye (3) and bloodstream (1)	183 (154)	84.15	ND	*dfrA* (2), *dfrG* (152), *mecA*(16)	(TMP)(154), SXT(83),SMZ(85)	ND	[55]
	2013	*S. aureus* (61)	Human(61)	61(27)	44.26	ST39(1),ST5(2),ST241(1),ST250(1),ST88(2)	*mecA*(7)	PEN(45),TET(26),CLI(2),GEN(10),LVX(6), SXT(27)	SCCmec(2)	[168]

	2012	*S. aureus* (51) *S. haemolyticus* (21),*S. sciuri* (9), *S. saprophyticus* (5), *S. warneri* (3),*S. epidermidis* (1) and *S. hominis* (1),	wounds, (11) skin and soft tissues (12), osteomyelitis (5), burns (1), urinary tract infection (6), septicaemia (17), urinary tract infection (10), otitis media (2), bronchitis (2)	91 (36)	39.56	ST241 (1), ST8 (1),ST152 (1),ST37 (37),ST39,ST88	*mec*A (15), *dfr*A (3)	SXT(13), PEN(15),OXA(15), GEN(6), CIP(7), MXF(1),ERY(5),CLI(4),TET(13), SXT(13), RIF(2)	*SCCmec* (15)	112
	2011	*S. aureus*	Human(68)	68(49)	72	ND	*mecA*(11),*erm*(A)(6),*msr*A(2),*aacA-aph*D(10),*tet*(M)(11), *tet*(K)(27)	PEN(60),OXA(11),GEN(10),TET(38),CIP(20),MXF(7),SXT(49),ERY(8),CLI(6)	*SCCmec(11)*	169
	2009	*S. aureus* (96)	Human(96)	96(12)	12.5	ST241(12)	*mecA*(12)	PEN(12),OXA(12), FOX(12),GEN(12),ERY(12),CLI(9),SXT(12),CIP(12)	*ND*	170
	2009	*S. aureus* (346)	Human(346)	346(206)	59.54	ST5 (72), ST7 (44), ST121 (38),ST250(28), ST88 (33), ST30(26), ST8(18), ST1(20), ST15(8), ST80 (8), ST241 (7), ST25 (5), ST72 (3)	*mecA*(70)	PEN(316),SXT(206),TET(182),CIP(58),ER7(26),GEN(42)	*SCCmec(70)*	171

Sa˜o Tome´ Pri´ncipe (3)	2015	*S. aureus* (114)	Nasal swab (114)	114(29)	25.5	ST5(2),ST88(11), ST8(13),ST1(2),ST 105(1)	*mecA*(29)	FOX(29),PEN(114),TET(30),CIP (28),RIF(6),GEN(20) ,CLIN(20),SXT(58),ERY(25),CH	SCCm ec (29)	114
Sao Tome principe and Angola	2015	*S. aureus* (164)	Nasal swab (164)	164 (29)	17.68	ST88(15),ST8(9)	*mecA* (NS)	FOX(29), SXT(26), TET(18), ERY(16), CIP (9) and CLI(8)	*SCCm ec (NS)*	49
		S. aureus (52)	Nasal swab (52)	52(27)	51.92	ST8(3), ST88(2),ST5(1),S T105(1)	*mecA* (14)	SXT(27),ERY(11), CIP(11),TET(12),FOX(14),RIF(2)	SCCm ec	139
South Africa (11)	2017	*S. aureus* (1914)	Blood (1914)	1914(557)	29.10	ST239(8),ST612(8),ST4121(1),ST36(4),ST5(4),ST33(3)	*mecA*(483)	β-lactams(557),TET(NS),aminogly coside(NS),SXT(NS)	SCCm ec (482)	135
	2017	*S. aureus* (97)	Human	97(96)	99	ND	*norA*(96), *norB* (96), *mepA*(95),*tet*(38)(96),*sepA*(94), *mdeA*(93), *imrs*(86), *sdrM*(83),*norC*(77),*q acA/B*(34),*smr*(42)	NS	ND	138
	2017	*E. faecalis (1)*	Urine (1)	1	100	ST6(1)	*aph(3')-lll(1), ant(6)-la* (1), *aac(6')-aph(2")* (1), *isa*(A)(1),*mph*d(1), *tet*(M)(1)	GEN(1),STR(1),ERY(1),CLI(1),T ET(1),CLI(1),TET(1),CIP(1)	ND	172
	2017	*E.faecium (1)*	Urine (1)	1	100	ST18(1)	*aph(3')-lll*(1), *ant(6)-la* (1),*tet*(M)(1),*erm*(B)(1),*msr*(C)(1), *tet(L)*	GEN(1),STR(1),ERY(1),CLI(1),T ET(1),CLI(1),TET(1),CIP(1)	ND	173

	2016	*S. aureus* (27)	Blood (5), nasal (2), CVP(2), Endotracheal tube (2), pus (2), sputum (1), wound (20), Eye (1),humerus (1), bone (1), cheek (1), buttock (1), head (1)	(27)	100	ND	*mecA* (27) *and blaZ* (27),*aac (6')–aph (2'')* (25),*erm(*C) (13)	CIP(23), GEN(20), RIF(19), TET(18), ERY(17), CLI(3)	ND	174
	2016	*E. faecium* (120) *E. faecalis* (40)	Blood (4)	(4)	100	ST80 (1),ST203 (1),ST18 (1),ST817(1	*vanA* (3),*vanB* (1)	VAN (4)	ND	147
	2015	*S. agalactiae* (128)	vaginal and rectal swabs (128)	128 (121)	94.53	ND	*erm(*B), (28),*linB*(48) *mefA* (48)	ERY(27), CLI(32), CHL(32),TET(111),CIP(24)	ND	60
	2015	*S. aureus* (2709)	Blood (2709)	2709 (1231)	45.44	ND	*mecA* (1160)	TET(NS), RIF (NS),MUP(NS), CIP(NS) and SXT(NS) MET(1231)	SCCmec (1160)	59
	2012	*S. aureus* (13746)	Human (13746)	13746(3298)	24	ST5 (1), ST612 (44),	*RpoB* (H**481**Y, H**481**N, I**527**M) (NS)	RIF(1760)	ND	59
	2009	*S. aureus* (17)	Human(17)	17(13)	76.47	ND	*mupA*(3)	ERY(12),CIP(10),RIF(4),CHL(4)	ND	175
	2007	*S. aureus(3),S. .lugdunensis (2)*	Wound(4),blood(1)	5(5)	100	ND	*mecA*(5)	PEN(5), OXA(5),GEN(5),ERY(4),TET(5), SXT(5),RIF(5)	SCCmec(5)	176
Sudan(1)	2015	*S. aureus(200)*	Wound(49),ear swab(57),urine(47), nasal swab(47)	200(197)	98.5	ND	*mecA(*111)	PEN(197), AMP(197),GEN(122),KAN(136),IPM(89),AMO(87),CIP(123),CLI(113),SXT(105)	*ND*	177

Tanzania (1)	2014	*S. aureus* (87)	Skin and soft tissue (39) and bloodstream (2)	87 (32)	36.78	ND	*dfrG* (32)	SMZ(5), TMP (32)	ND	50
Tunisia (18)	2015	*S. aureus* (99)	Human (99)	(99)	100	ST247 (12), ST239 (6), ST728 (2), ST241 (1), ST398 (1), ST5 (1) and ST641 (1)	*mecA* (24), *tet*(K) (6), *tet*(L) (1), *tet*(M)(18), *erm*(A), *aph(2')-acc(6')* (13)	TET(24), GEN(18), ERY(15), FOF(1), CLI(14), OFX(16), TOB(20), FUS(5)	ND	69
	2014	*E. faeciun* (13),*E. gallinarum* (3)	blood (8), pus (3), urine (2) and rectal swabs (3).	(16)	100	ST18 (1)and ST80 (2)	*vanA* (13),*vanC1*(3), *erm*(B) (16), *tet*(M)(15),*tet*(L)(1), *aac(6')-aph(2")(13) aph(3')-IIIa* (16),*ant*(6)(3)	VAN(16),TEC(13), AMP(16),CIP(16), ERY, TET(16), KAN(13), STR(13), SXT(16), GEN(8),	*IS16 (3)*	178
	2013	*S. aureus* (69)	Human (69)	(69)	100	ST80 (41), ST1440 (1), ST1 (2), ST5 (5), ST22 (1), ST97 (2), ST239 (4), ST241 (3), ST247 (3), ST1819 (3),ST153 (2),ST256 (1)	*mecA* (59)	KAN(62), AMK(62(18), TETs(61), OFX(20) , CIP(31), ERY(38) , CLI(12), RIF(22)	*SCCmec* (59)	85
	2013	*S. aureus* (64)	Pus(53)pus, blood culture (6), articular Puncture (4), venous catheter r(1).	(64)	100	ST80(64)	*mecA*(64)	PEN(64),OXA(64),FOX(64),AMK (64),KAN(63),ERY(13),TET(3),LIN(3)	*SCCmec(64)*	179
	2012	*S. agalactiae* (226)	Female genital (120), gastric fluid (106)	226 (220)	97.34	ND	*erm*(B) (79), *mef*(A) (2), *tet*(M) (205), *tet*(L)(10), *tet*(O) (5), *tet*(T)(1)	CHL(7), RIF(43), ERY(90) and TET(220), STR(7),GEN(7)	*Tn916*	105

	2012	*S. haemolyticus* (46)	Blood (19), intravascular catheters (14), others (13)	46 (36)	78.26	ND	*mecA* (28)	PEN(36), OXA(36), GEN(34), kAN(34), and TOB(34), ERY(33), SXT(32), OFX(32), CIP(32), STR(25), fusidic acid(14), TET(11),RIF(9),LIN(6(,CHL(1),FOF(1)	*SCC mec* (28)	104
	2011	*S. aureus* (1463)	Skin (1463)	160 (5)	3.13	ND	*erm*(C)(3), *erm*(A) (1), *vat*(B) (5), *vga*(B) (5)	PEN(5),OXA(4), GEN(4), KAN(5), TOB(4(5) and RIF(5),LIN(5)	ND	144
	2011	*S. pyogenes* (103)	skin (43), respiratory tract (41), blood (12), fluids (4), endometrium (1), vagina (1), and urine (1).	103 (72)	70	*emm*18 (4), *emm*42 (9), *emm*76 (6), *emm*118(10)	*erm*(B) (5), *tet*(M) (63), tet(O)*(3)*	ERY(5), CLI (5), and TET(72),	*Tn916 (62)*	145
	2011	*S. epidermidis (34)*,*S. haemolyticus* (10),*S. hominis*(1)	Blood(45)	45(42)	93.33	ND	*mecA*(43),*mrs*A(13), *erm*(C)(7),*erm*(B)(2),*erm*(A)(6),*aac(6')-le-aph*(2'')(35),*ant(4')-la(18)*,*aph(3')-IIIa*(4),*tet*(K)(6),*tet*(M)(1)	PEN(45),OVA(43),GEN(35),KAN(42),TOB(40),ERY(25),CLI(11),TET(5),CHL(3),RIF(15),SXT(31), CIP(25),FUS(27),FOF(18)	*SCCmec(43)*	180
	2010	*S. pyogenes* (193)	throat (63), pus (89), punctures (30), blood (4), other sources (7)	193 (13)	6.74	ND	*ermB* (6), *mefA* (2)	ERY(7) and TET(6)	ND	143
	2010	*S. aureus* (55)	*Nasal swab(55)*	55(19)	35.55	ST80(1)	*mecA*(1), *ant(6)-la*(3),*tet*(K)(7),*aph(3')-IIIa*(4),*dfr*A(1),*tet(M)(1)*,*tet*(L)(1)	PEN(54),OXA(19),FOX(1),TET(11),STR(5),KAN(3)CIP(8)	SCCmec(1)	181
	2010	*S. agalactiae* (160)	Urinary tract (160)	(160)	100	ND	*erm*(B) (132), *erm*(TR) (13), *mef* (A) (3)	ERY(160), LIN(135) and SB (135)	ND	182

	2010	*S. aureus* (13)	Pus(32),blood(16), catheter(12)	72(42)	58.33	ND	*mecA*(13)	PEN(65),STR(11),GEN(4),KAN(11),OXA(13),TOB(4),LIN(3),TET(42)ERY(11),RIF(6),CHL(2),CIP(5),FUS(8),FOF(1)	ND	[183]
	2009	*S. epidermis* (77), *S. mitis* (50), *E. faecium* (45)	blood cultures (55), central venous catheters, (22),stool cultures (40), respiratory tract (2) and different sites (3), systematic nasopharyngeal specimens (42), upper respiratory tract(5)	172(95)	55.23	ND	*erm* (C) (18), *erm*(B) (6), *erm*(A)(11),*msr*A (5)	OXA(39), AMP(28),PEN(90),ERY(119),LIN(97), PRI (3),GEN(71),RIF(78), TEC(50),	ND	[82]
	2007	*E. faecalis*(34), *E. faecium*(12)	Blood(10), pus(26),catheter(7) ,plural aspirate(2)	46(46)	100	ND	*aac(6')-aph*(2")(46)	GEN(46),KAN(46),PEN(12),ERY(45),CHL(25),TET(32),STR(26)	ND	[184]
	2007	*E.faecium*(2)	Urine(2)	2	-	ND	*vanA*(2)	STR(2), ERY(2),CIP(2),VAN(2)	ND	[156]
	2007	*S.epidermidis* (346)	Human(346)	346(7)	2.02	ND	*erm*(A)(6),*erm*(C)(1),*vga(7)*	PRI(7),OXA(7),GEN(7),ERY(7),LIN(7),RIF(7),SXT(7)TEC(1)	ND	[185]
	2007	*S.epidermidis* (34)	Blood(55), urine(22)	(34)	100	ND	*icaA*(26), *erm*(C)(18),*erm*(A)(11),*mrs*A(5),*vga*(3),	ERY(34),OXA(28),GEN(34),LIN(33),OFX(33),RIF(28)	ND	[186]
Uganda (4)	2013	*S. aureus* (64)	Nasal swab (64)	64(24)	37.5	ND	*mec*A (24)	OXA(22), GEN(8), CIP(12), CHL(9)	*SCCmec (24)*	[187]
	2012	*S.epidermidis*(50)	Nasal swab(20),catheter(14),blood(9),wound (3)	50(26)	52	ND	*aph(')-IIa*(28),*blaZ*(2),*mecA* (3),*vanA*(3),*vanB*1(3),	ERY(20),GEN(26),PEN(32),TET(15),SXT(17),OXA(6)	IS256(33)	[188]
	2011	*S. aureus*(122)	pus	122(48)	39.34	ND	*mecA*(2)	AMP(48),CHL(42),CIP(1),ERY(5),TET(29),SXT(320	ND	[189]
	2009	*S. aureus* (54)	Human(54)	54(15)	27.78	ND	*mec*A(17)	CIP(12),GEN(10),SXT(15),CHL(15),ERY(15)	NG	[190]

1528

1529 **Table 3. Geographical distribution, species, clones, and resistance mechanisms of antibiotic-resistant Gram-positive bacteria isolated from**

1530 **animals in Africa from 2007-2018.**

Country (n)[11]	Year	Organism/ Species (n)[12]	Specimen Sources (n)[13]	Sample size (Resistant isolates)	Resistance rate (%)	Clones (n)[14]	Resistance genes/ mechanisms (n)[15]	Antibiotics to which strains were resistant (n)[16]	MGEs (n)[17]	Reference
Angola(1)	2015	*E. faecium* (3)	Pig faecies(1), Chicken faeces(2)	3	-	ST971, ST245(2)	*tet*(L)(1), *tet*(M)(2), *erm*(B)(2)	CIP(1),TET(3),ERY(2),STR(2),NIT(2),Q/D(2)	ND	[191]
Egypt (10)	2017	*S. aureus*(3),*S. hycus*(6), *S. intermedius*(3) ,*S. epidermis*(1) ,*S. hemolyticus*(1), *S. hominis*(1), *S.l ugdunensis*(3), *S. simulans*(1),*S. scuri*(4)	imported beef meat (23)	23(16)	69.57	ND	*mecA*(5), *gyrA*(12), *grlA*(10),*gyrB*(6),	AMP((6),CHL(1),CIP(8),CLI(15), ERY(6),GEN(14),MET(8),OXA(13) ,PEN(22), TET(6)	ND	[94]
	2017	*S. aureus* (84)	Milk(84)	84(80)	95.23	ND	*mecA*(42),*blaZ*(67)	AMX(54), SXT(66),GEN(20),CIP(12),CHL(58),PEN(70),RIF(32),AMK(14), VAN(64),STR(50),TET(44),ERY(40), AMP(80),OXA(42)	ND	[192]
	2016	*S. aureus* (73)	Animal(73)	73(NS)	NS	ST113(1), ST80(1)	*mecA*(14), *erm(*C)(14)	CLI(NS),CIP(NS),GEN(NS),SXT(NS),OXA(NS),ERY(NS)	ND	[159]

[11] Total number of studies per country
[12] Total number of bacteria isolated
[13] Total number of Specimen source
[14] Total number of resistant clones
[15] Total number of resistant genes
[16] Total number of isolates resistant to antibiotics
[17] Total number of mobile genetic elements: plasmids, transposons, integrons

	2016	*S. aureus* (30)	raw chicken breast fillet (40), sliced luncheon meat (20), and chicken nuggets (20),Human (18)	40 (21)	33.33	ND	*mecA* (10)	DOX(31), AMX(29), OFX(10), CFP(23), CLI(21), GEN(20), APR(16), ERY(21), SXT(23), LUX(18), NAL(20), OFX(10), CIP(16).	ND	28
	2016	*S. aureus* (70)	Bovine(70)	70(41)	58.57	ND	*mecA*(NS)	CRO(41),ERY(35),OXA(41),SXT(14),GEN(14),CIP(11),CLI(8),VAN(1)	ND	160
	2016	*S. aureus* (40)	Milk(30),meat(10)	40(22)	55	ND	*erm*(A)(18),*mrs*(A)(4),*mph*C(6),*erm(*B)(3)	ERY(22),CLI(4),TET(24),CIP(4),CHL(5),AMX(26),FOX(22),SXT(1),RIF(5),GEN(4),CRO(14)	ND	193
	2016	*S. aureus* (200)	Raw milk (40), Damietta Cheese (40), Kareish cheese (40), ice cream (40), and yogurt (40)	200 (106)	53	ND	*mecA*(106)	TET(270), NEL(78), AMX(230), CLX(314),STR(186),SXT(58), GEN(114), PEN(364), RIF(152), CHL(128), AMK(146), VAN(36)	ND	12
	2015	*S. aureus* (133)	cow milk samples (61), various origins (14), minced meat (6), sausage (4) and burger (7), pus (22), sputum (17), urine (1), cerebrospinal fluid (1)	133 (96)	72.18	ND	*mecA* (30)	CRO(96), TET(90), OXA(70), FOX(65), ERY(81),VAN(4),IPM(7),CRO(96),CHL(12),GEN(36),CLI(29), CIP(31),RIF (18)	SCCmec (25)	23
	2015	*S. aureus* (288)	Chicken(288)	288(256)	88.89	ND	*mecA*(76)	PEN(269),AMP(256),CLX(240),AMX(224),ERY(212), TET(197),STR(150),RIF(113),AMK(99),CH	ND	194

								L(91),GEN(70),CIP(39),NEL(48),SXT(39),VAN(17)		
	2011	*S. aureus* (4)	dogs swab (70), cats swab (48), human nasal and oral swabs (50).	(4)	100	ND	*mecA* (4)	OXA(4), FOX(4), AMP(3),FOX(4),RIF(3),GEN(2),CLI(2),RIF(2),CIP(2),TET(1)	ND	[53]
Kenya (1)	2013	*S. agalactiae* (92)	Camel(92)	92 (37)	36	ST617 (8), ST-612 (1),ST-616 (22)	*tet(*M) (37)	TET(37)	Tn916 (37)	[195]
Nigeria(3)	2017	*S. aureus* (30), *S. epidermidis*(16),*S. saprophyticus*(2), *S. sciuri*(1),*S. xylosus*(1)	Pork(26),beef(14),chicken(10)	50(48)	96	ND	*mecA*(49)	PEN(48),CLI(48),CHL(46),SXT(46),KAN(46),AMX(460	ND	[156]
	2016	*E. faecium (108), E. gallinarum, (30), E. faecalis (5), E. hirae. (5)* *E. mundtii (12)*	Cattle (130), chickens (130),manure (130)	167 (102)	61.0	ND	*tet(*K) (NS), *tet*(L) (NS), *tet(*M) (NS), *tet*(O) (NS) *and erm(*B) (NS)	TET (102), ERY (102), CHL (13), GEN(55), STR(47),AMP(75)	ND	[196]
	2014	*Coagulase negative staphylococcus*(16)	Groin swab of dogs(16)	(16)	100	ND	*mecA*(16),*blaZ*(1),*tetK*(12),*tet*(M)(8),*erm*(B)(3),*aacA-aph*D(11)	PEN(16),OXA(16),FOX(16),TET(13),ERY(9),CLI(9),GEN(5),KAN(12),TOB(1),SXT(10), CHL(7)	ND	[197]
South Africa (6)	2017	*E. faecium* (180),*E. durans*(80), *E. hirae*(29),*E. casseliflavus*(20)	Cattle (241)	100	100	ND	*vanB*(67),*vanC1*(85),*vanC2*/3(137),*erm*(B)(137)	ERY(338),CLI(330),VAN(341),PEN(310),CET(300),STR(320),CLX(100),AMK(252),CIP(41)	ND	[198]
	2017	*S. aureus* (104)	Chicken(104)	(104)	100	ND	*mecA*(45),*blaZ*(12), *tet(*K)(32)	AMP(46),GEN(29),ERY(64),FOX(71),KAN(52),STR(57),TET(82),VAN(43)		[156]
	2015	*S. aureus* (211)	Milk (211)	211 (124)	58.77	ND	*mecA* (19)	PEN (124), AMP(99), OXA (93), VAN(47), TEC(116), TET(56),ERY(56),STR(89),KAN(55),GEN(47),SXT (37)	ND	[21]

	2015	*E. faecalis* (40), *E. hirae* (100), *E. durans* (60), *E. faecium* (120)	Pigs (320)	(320)	100	ND	*vanB*,(320), *vanC*1 (320), *vanC*2/3 (320), *erm(*B)(300)	VAN(320), STR(320) and CLX(320),STR(320),CET(286),PEN(292),CIP(248),AMO(64), AMK(272),CLI(316),ERY (280),IPM (52),	ND	13
	2014	*Staphylococcus spp*(120)	Pigs(30),cattle(30),cows(30),goats(30)	120(53)	44.17	ND	*mecA*(12)	VAN(12),CRO(12),CFZ(37),CTX(19),SAM(13),PEN(53),MER(4)	ND	199
	2013	*S. xylosus* (18), *S. aureus* (28), *S. haemolyticus* (42), *S. capitis* (18), *and other Staphylococcus spp.* (14)	Animals (120)	(120)	100	ND	*mecA* (NS), *mphC(*NS)	PEN (90), MER(3), VAN(14), CTX(14), CFZ(48), OXA(46), MIC(19), TET(100), ERY(14), CLI(19), NAL(120), CIP(5), OFX(6), LUX(2)	*SCCmec (*NS)	61
Senegal (1)	2012	*S. aureus* (57)	Swabs from pigs (300) and farmers	57(35)	61.40	ST5 (5)	*mecA*(6)	PEN(57), SXT(35), TET(20)	*SCCmec (6)*	66
Tanzania (1)	2014	*E. faecium* (95) *E. faecalis*(9) *E. gallinarum* (7) *E. Hirae* (9)	Faecal samples of buffalo (35), wildebeest (40), zebra (40) and cattle (20)	120 (42)	35	ND	*tet*(W) (NS), *sulII* (NS)	VAN(10),AMP(10),TET(40),SXT(32),RIF(53),ERY(42),GEN(35),AMP(31)	*ND*	14
Tunisia (8)	2017	*E. faecium* (31),*E. faecalis* (14),*E. durans*(6),*E. casseliflavus* (2),*E .gallinarum* (2)	Faecal sample of cats(20), dogs(50)	58(31)	53.45	ND	*erm(*B)(22),*tet*(M)(5),*tet*(M), *tet*(L)(16),*tet*(L)(4),*ant(6')-Ia*(11),*aac(6')-Ie-aph(2")-Ia*(16),*aph(3')-IIIa*(11),*catA*(1)	AMP(1),ERY(26),CIP(30), PRI(9), STR(12), KAN(12),GEN(9),TET(21),CHL(7)	*ND*	22
	2017	*E. faecalis* (2), *E. faecium* (NS), *Enterococcus spp* (NS)	Urban wastewater (5)	5(2)	40	ST86(2)	*optr*A(2), *erm* (A),*erm*(B),*tet*(M)(1),*tet*(L)(1), aac(6')-aph(2"),	CHL(2),CIP(2),ERY(2),TET(1),GEN(1),STR (2)	*ND*	200

	2015	*S. aureus* (43)	Chicken(19),Veal (9),sheep(14),horse(1)	43(13)	30.23	ST30(1), ST398(1)	*tet*(M)(2),*erm*(C)(4),*erm*(A)(2),*erm*(T)(1),*tet*(K)(6),*tet*(L)(3),*tet*(***M)(2),***aph(3')-IIIa*(4),*ant(4)-Ia*(1),*mrs*A(4)	PEN(41),OXA(2),FOX(2),KAN(4),TOB(1)	*SCCmec(2)*	201
	2015	*S. aureus* (17)	Goat, cats dogs(17)	17(7)	41.18	ST45(1),ST15(1),ST6(1),ST2121(1),ST188(1)	*blaZ*(7),*tet*(M)(1),*erm*(A)(1),*ant(6)-Ia*(1)	PEN(6),TET(1),ERY(1),STR(1),CIP(1)	*ND*	202
	2013	*E. faecalis* (49), *E. faecium* (30), *E. gallinarum* (12), *E. hirae*(12),*E. casseliflavus* (2),*E. durans* (2)	Meat (199)	(119)	78.5	ST260(1), ST454(1), ST452(1), ST22(1),ST300(1),ST455(1),ST453(1),ST456(1)	*tet*(M) (36), *tet*(L) (32), *erm*(B) (33), *aac(6')-aph(2")* (1),*ant*(6) (7)	TET(57), ERY(43), STR(17), CHLI(4),GEN (1)	*ND*	51
	2013	*E. mundtii*, (23) *E. casseliflavus* (20), *E. hirae* (19), *E. faecalis* (10), *E. faecium* (10), *E. durans* (7), *E. gallinarumd* (7), *E. dispar* (2)	Cattle (92)	92 (72)	78	ND	*erm*(B) (7), *tet*(M) (4),*tet*(L)(4)	ERY(10), TET(4) and SXT(72)	*ND*	52
	2012	*S. aureus* (73)	nasal swab from sheep (73)	73 (5)	6.85	ST153(5)	*mecA* (5),*blaZ* (28), *ant(6)-Ia* (5), *erm*(C) (5), *tet(*K) (30)	PEN(5), STR(5), KAN(5), ERY(5), TET (5), FUS(5)	ND	99
	2012	*S. aureus* (50)	Nasal swab of donkey(50)	50(30)	60	ST133(15),ST1738(4),ST1(2),ST6(4),ST2057(4),ST2110(1),ST2181(1), ST1660(1)	*ba*Z(12),*erm*(A)(8), *erm*(C)(2),*tet*(M)(1),*fus*C(1)	PEN(12),ERY(8),TET(1),Fusic acid(12),	*ND*	203

Uganda (1)	*2017*	*S. aureus* (41)	milk(30),sour milk sample(11)	41(30)	73.17	ST97(1),ST1(2)	*mecA*(23)	TET(30),RIF(1),SXT(2),ERY(1), GEN((1),CLI(1)	*ND*	[121]

1531

1532 **Table 4. Geographical distribution, species, clones, and resistance mechanisms of antibiotic-resistant Gram-positive bacteria isolated from**

1533 **the environment in Africa from 2007-2017.**

Country (n)[18]	Year	Organism/ Species (n)[19]	Specimen Sources (n)[20]	Sample size (Resistant isolates)	Resistance rate (%)	Clones (n)[21]	Resistance genes/ mechanisms (n)[22]	Antibiotics to which strains were resistant(n)[23]	MGEs (n)[24]	Reference
Angola	2015	*E. faecium*(5)	Chicken farm facility(4), water from hospital and community(1)	5(4)	80	ST245(1), ST650(2)	*tet*(M)(4),*erm*(B)(4),*tet*L (2)	TET(4),ERY(4),STR(4),NIT (2),Q/D	ND	[191]
Egypt	2016	*S. aureus*(23)	Food sample(23)	23(NS)	NS	ST689(1)	*mecA*(3), *van* A(1),*van*B(1)	VAN(NS), CIP(NS),GEN(NS),SXT(NS),OXA(NS),ERY(NS)	ND	[159]
Nigeria (1)	2017	*E. faecium (100)*	Vegetables soil, farm, Cloacal swabs (25), Manure (8), Rectal swabs(2)	(100)	100	ND	*aac(6')-Ie-aph(2")-Ia*(35),*aph(2')-Ic*(31),*aph(3')-IIIa*(32), *ant(4')-Ia(14)*	AMP (63), GEN(37)	ND	[25]
South Africa (4)	2017	*S. aureus*	Recreational waters and beach sand (30)	(30)	100	ND	*mecA*(5),*femA*(16). *rpoB*(11),*blaZ*(16),erm *B*(15),*tet*(M)(8)	AMP (29),PEN (29),RIF(24), CLI(24),OXA	ND	[204]

[18] Total number of studies per country
[19] Total number of isolates
[20] Total number of specimen source
[21] Total number of resistant clones
[22] Total number of resistant clones
[23] Total number of isolates resistant to antibiotics
[24] Total number of mobile genetic elements : plasmids,transposons, integrons

								(22),ERY(21),VAN(15), TET(13),SXT(13),CIP(10), GEN(1)		
	2016	*E. faecium* (30), *E. faecalis* (37) *E. mundtii*(36),*E. casseliflavus* (14), *E. gallinarum*(5), *E. hirae*(1), *E. sulfureus*(1)	Surface water(124)	124(86)	69.35	ND	*tet*(L)(17), *msrC*(9)	AMP(59),AMX(53),PEN(87),STR(8) ,VAN(86),CHL(23),CIP(47) , ERY(68),TET(59)	ND	205
	2015	*E. faecium* (30), *E. durans.* (15)	waste water (32) and effluent (32)	(45)	100	ND	*erm*(B) (40), *vanB*, (42), *vanC1* (42), *van C2/3*(42)	PEN(38), ERY(40), CTX(43), GEN(28),IPM(43), TET(45), KAN(43), CIP(43), VAN(42),CLI(45)	ND	10
	2013	*E. faecium* (179)	Borehole Water (179)	179 (172)	96.09	ND	*vanA* (17) *and vanB* (17)	AMP(158), VAN (166)and PEN(172),CHL(11),KAN(1 2),GEN(3),AMX (155), ERY(86)	ND	9
Tunisia (7)	2017	*S. aureus* (12)	Wastewater	12	100	ST3245(7), ST15(1)	*blaZ*(7),*msr*A(7),*tet*(K)(1)	PEN(12),ERY(7),TET(1),C LI(1)	ND	18
	2016	*E. faecium (86)*, *E. faecalis*(8), *E. casseliflavus* (6)	Hands (50), inanimate such as beds, treatment tables, toilets, faucets, wrists, sinks (250)	(100)	100	ST910 (13), ST80 (1)	*erm*(B) *(71)*, *tet*(M) (18), *aph(3')-IIIa* (27), *ant(6)-Ia (15)*,*cat*(A) (4), *vanC2*(6)	ERY(73), TET(20),STR(27) and KAN(28), VAN(14),CHL(10),SXT(100), CIP(48),PRI(18)	*IS16* (14)	20
	2016	*S. saprophyticus* (30), *S. haemolyticus* (38), *S. epidermidis* (NS), *S. cohnii* (NS), *S. warneri* (NS), *S. sciuri* (NS), *S. simulant*	Inanimate surfaces (83	83 (32)	38.55	ND	*mecA*(20), *msr*(A)(32), *erm*(C)(8), *tet*(K)and/or *tet*(M)(21), *aac*(6´)-Ie-*aph*(2´´)-Ia (16),(*aph*(3`)-IIIa(19), *ant*(4´)-Ia (n=14), *ant*(6´)-Ia (3)	ERY(32), TET(21), GEN(16), KAN(19), TOB(14), STR(3),	ND	97

		(NS)*s*, *S. pasteuri* (NS), *S. arlettae* (NS) and *S. xilosus*(NS)								
	2015	*E. faecium* (34), *E. hirae* (23), *E. faecalis (4)*, and *E. casseliflavus* (4)	Vegetable food (34), soil and irrigation water (27)	65 (40)	61.54	*ST2 (5), ST16 (2), , ST528 (2), ST56 (1), ST885 (1), ST886 (1)*	*erm*(B) (12), *tet(M)-tet(L)(10), aph(3')-III, (10) ant(6) (2),vanC2(4)*	CIP(42), ERY(12), TET(10), KAN(10), CHL(5), STR(2), and GEN(5), VAN(4)	ND	19
	2015	*E. faecium* (54), *E. faecalis*(17),*E. hirae* (8) *E. casseliflavus* (4), *E. durans* (2)	waste and surface water (114)	(85)	100	ST480 (1), ST531 (1),ST55 (1),ST532(1),ST202 (1),ST314(1), ST985(1),S T30 (1),ST986 (1),ST12 (1),ST296 (1),ST327(1)	*aph(3')-IIIa* (22), *ant(6)-Ia (4),erm*(B) (34), *tet*(M) (13), *tet(L)(8),aac(6')-Ie-aph*(2')(15)	GEN(22), KAN(22), STR(7), ERY(36), TET(13), SXT(79), CIP(6),	ND	31
	2015	*S. aureus* (12)	Hospital environment(12)	12(6)	50	ST247(2)	*bla*Z(12),*erm*(A),*tet*(M)(2),*aac(6')-aph(2')*(2),	STR(2),KAN(2),ERY(2),CL I(2),TET(2),FUS(2),TOB(2) ,GEN(2),AMK(2),OXA(6),P EN(12),FOX(2)	SCCm ec(2)	206
	2014	*E.faecium*(5),*E. casseliflavus*(7)	Hospital environment((be ds, treatment table, toilet, faucet, wrist and sink) (100)	(12)	100	ST80(1)	*van*A(5),*van*C2(7) ,*erm*B(12),*tet*M(5),*aph(3')-IIa*(5),*aac(6')-aph(2'')*(5)	VAN,(12),AMP(5),CIP(12), ERY(12),TET(8), STR(6),KAN(80,SXT(11),G EN(3),TEC(5)	*IS16(1)*	69

1534

1535 **Table 5. Mean antibiotic resistance rates per country in Africa**

Country	No. of studies N=130	Mean rate of ABR (%)	95% CI	P-value
Algeria	7	62.24	4.76 - 119.7	0.03
Angola	6	66.19	9.98 – 122.4	0.03
Cape Verde	1	14.16	-	-
Democratic Republic of the Congo	3	45.96	-	-
Egypt	21	70.49	59.30 – 81.68	0.0001
Gabon	2	54.14	-	-
Ghana	3	65.05	-	-
Kenya	3	51.51	-	-
Libya	1	33.69	-	-
Morocco	2	68.88	-	-
Mozambique	1	19.15	-	-
Namibia	1	29.31	-	-
Nigeria	13	71.23	54.81 – 87.65	0.0001
Sa˜o Tome´ Pri´ncipe	3	31.70	12.87 – 76.27	0.092
South Africa	21	82.72	70.73 – 94.69	0.0001
Sudan	1	98.5	-	-
Tanzania	2	35.89	24.58 – 47.00	0.016
Tunisia	33	66.82	54.73 – 78.91	0.0001
Uganda	5	45.96	24.25 – 67.66	0.0042
Senegal	1	61.40	-	-

Table 6: Antibiotic resistance rates of various Gram-positive bacterial species isolated from humans, animals and the environment in Africa between 2007 and 2018.

Species	Total isolates	Antibiotic resistance rate (%)											
		AMP[25]	CIP[26]	CLI[27]	ERY[28]	GEN[29]	KAN[30]	PEN[31]	RIF[32]	STR[33]	TET[34]	SXT[35]	VAN[36]
Human													
E. faecalis	179	30.4	26.3	-	91.35	77.2	100	26.0	-	56.5	76.0	19.30	52.6
E. faecium	205	56.1	19.0	-	88.0	61.4	90.6	21.5	-	70.3	75.5	100	51.3
S. agalactiae	658	-	18.8	19.5	50.6	3.1			19.0	3.1	68.8	-	-
S. aureus	24160	64.7	24.1	16.3	82.4	20.3	32.9	81.5	31.2	12.2	35.4	40.5	3.13
S. haemolyticus	91	-	62.6	24.4	63.7	75.9	73.9	78.3	31.2	12.2	35.4	69.2	-
S. pyogenes	148	-	-	4.9	5.8	-	-	-	-	-	36.5	-	-
Animal													
E. faecalis	129	24.2	64.6	98.8	43.5	19.5	20.7	16.6	44.17	16.7	32.7	52.5	50.1
E. faecium	577	31.4	43.7	97.8	57.5	23.0	20.7	53.7	44.2	37.9	43.9	52.5	66.7
S. aureus	1601	62.8	23.1	39.3	32.7	28.9	36.8	69.5	33.5	45.3	42.2	37.6	24.4
S. haemolyticus	43	-	-	-	-	-	-	59.6	-	-	-	83.3	-
Environment													
E. faecalis	66	47.6	47.6	-	45.7	20.5	23.1	70.2	-	17.0	23.6	96.5	29.8
E. faecium	523	59.2	69.2	100	64.6	26.1	39.7	83.6	-	29.1	49.3	94.9	62.7
S. aureus	77	96.7	25	35	48.2	10.0	16.67	98.9	80.0	16.7	25.8	43.0	50.0

[25] Ampicillin
[26] Ciprofloxacin
[27] Clindamycin
[28] Erythromycin
[29] Gentamicin
[30] kanamycin
[31] Penicillin
[32] Rifampicin
[33] Streptomycin
[34] Tetracycline
[35] Sulphamethoxazole-trimethoprim
[36] Vancomycin

Figure 1. PRISMA-adapted flow chart showing included and excluded articles. All search were conducted on PubMed, Web of Science and African Journals Online, and a final number of 130 articles were used for the quantitative analysis.

Figure 2. Frequency and distribution of resistance genes, antibiotics, and mobile genetic elements (MGEs) with recorded resistance in Gram-positive bacteria in Africa. 2ai) Shows the frequency of the various resistance genes found in the drug-resistant Gram-Positive bacterial strains. *mecA* and *erm*(B) were the most dominant resistance genes detected, followed by *tet*(M)*, dfrG, vanB, vanC1* etc. 2aii) Shows the antibiotics to which the isolates were most resistant: erythromycin (ERY) was the least effective drug, followed by rifampicin (RIF), tetracycline (TET), penicillin (PEN), sulphamethoxazole/trimethoprim (SXT), ciprofloxacin (CIP), gentamicin (GEN), vancomycin (VAN), ampicillin (AMP), clindamycin (CLI), streptomycin (STR), chloramphenicol (CHL), and kanamycin (KAN). 2b) Shows the MGEs per resistant Gram-positive bacterial clones in Africa. The figure represents resistant clones and the different MGEs they carry. Each colour represent a particular resistant clone. *S. agalactiae* (ST612, ST616, ST617) and *S. pyogenes* (*emm*18, *emm*42, *emm*76, *emm*118)*, E. faecium* (ST18, ST80, ST910) and *S. aureus* (ST5, ST22, ST35) were associated with Tn*916,* IS*16* and SCC*mec* respectively.

Figure 3. Frequency distribution of resistant Gram-positive bacterial species, clones and mobile genetic elements (MGEs) per country in Africa. 3a) Shows the distribution frequencies of the resistant species, clones and MGEs per country in Africa whilst 3b) shows the total frequency per clone in Africa. It is obvious that *S. aureus* ST5 is predominant in Tunisia, the DRC and Senegal whilst ST22 is highly prevalent in Algeria. SCC*mec* was the commonest MGE in most of the countries except in Tunisia where IS*16* and Tn*916* were higher in prevalence. *S. aureus* ST8 and ST80 were the most common clones reported, followed by *E. faecium* ST317.

Supplementary data 1. List of excluded articles on the basis of only phenotypic (antibiotic sensitivity) tests.

Supplementary data 2. Raw data and analysis of extracted information from included articles.

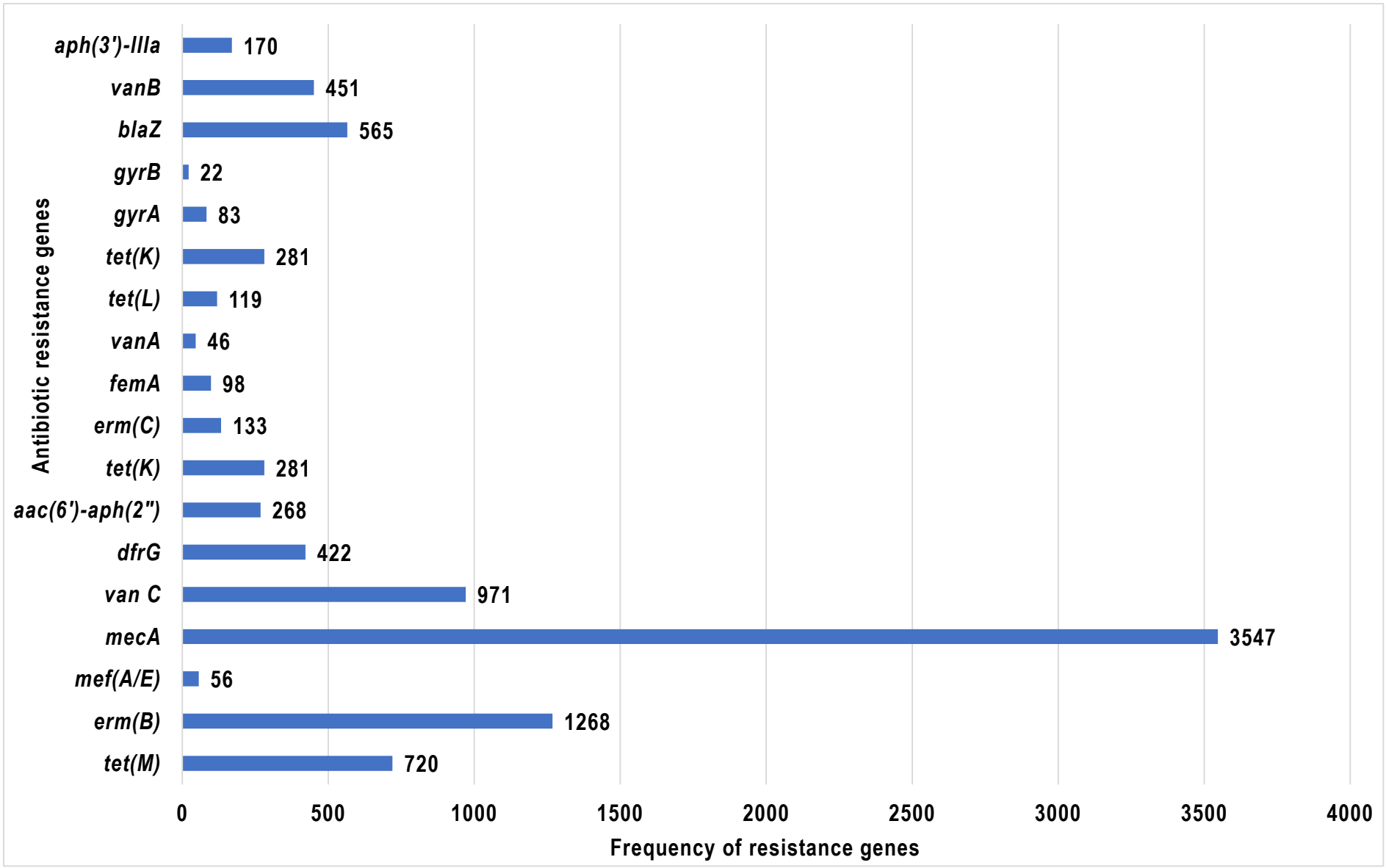

Figure 2ai. Frequency of resistance genes conferring resistance to antibiotics in Gram-positive bacteria in Africa.

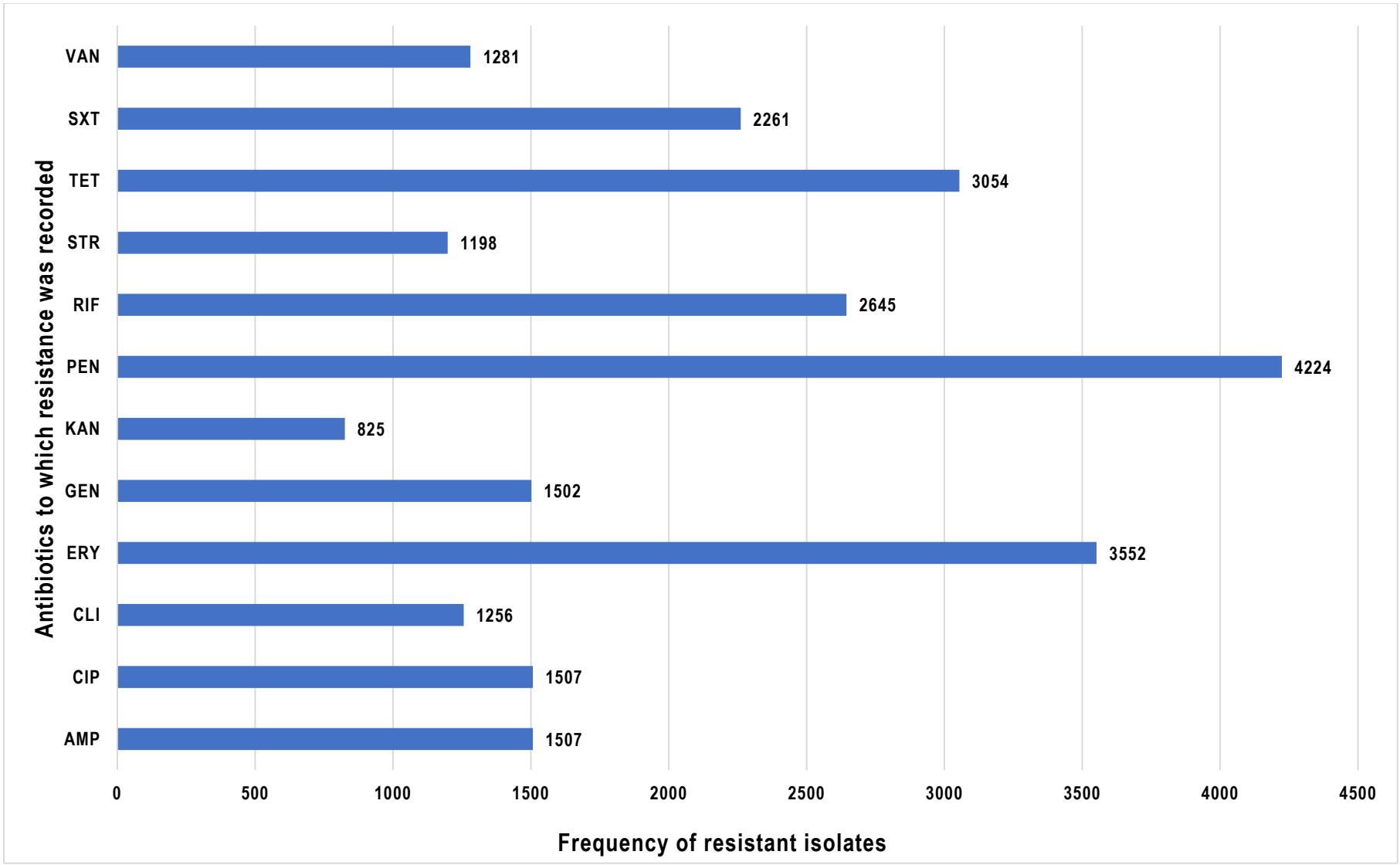

Figure 2aii. Frequency of antibiotics to which Gram-positive bacteria were resistant to in Africa.

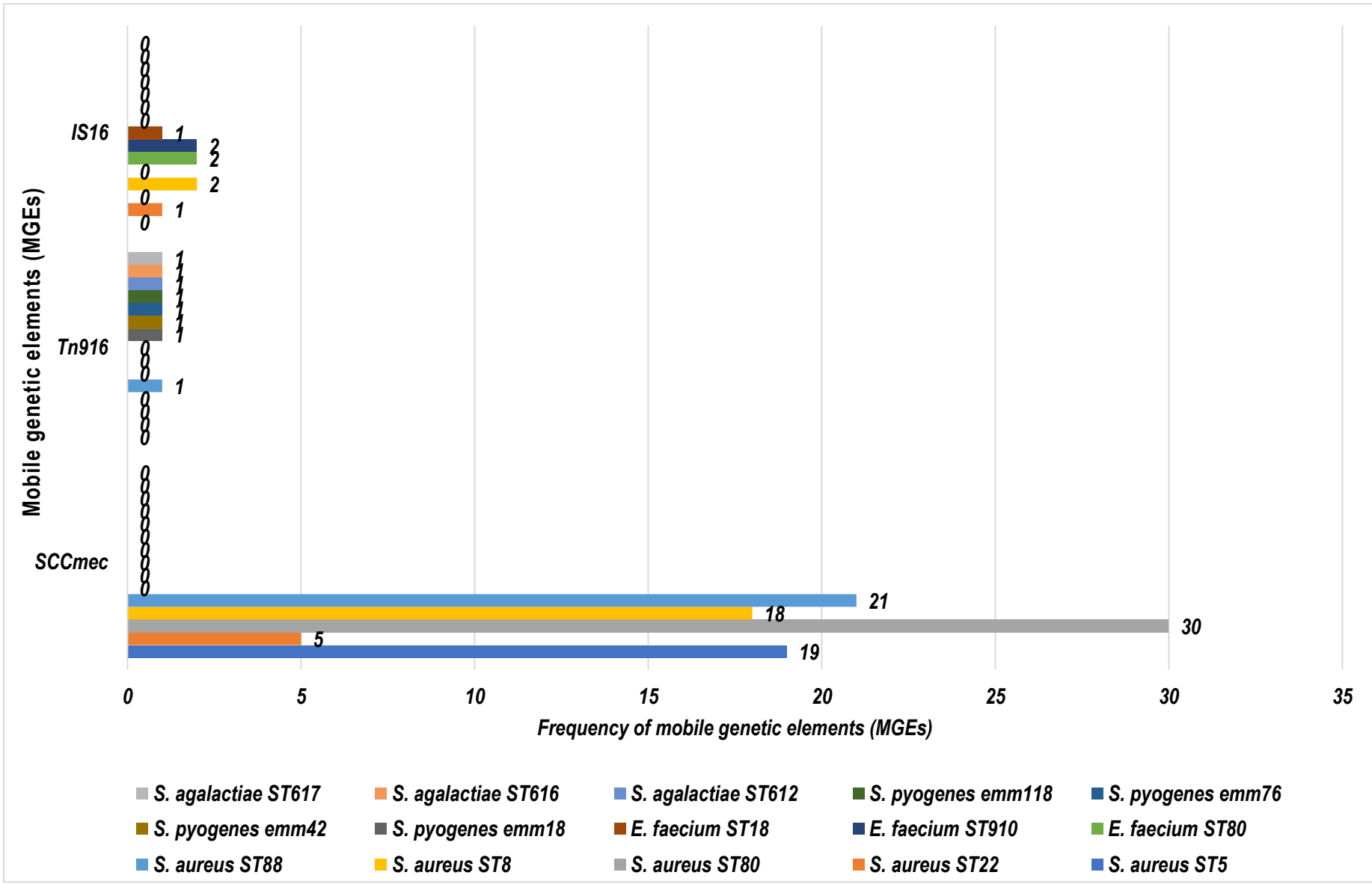

Figure 2b. Frequency and distribution of mobile genetic elements (MGEs) and resistant clones in Gram-positive bacteria in Africa.

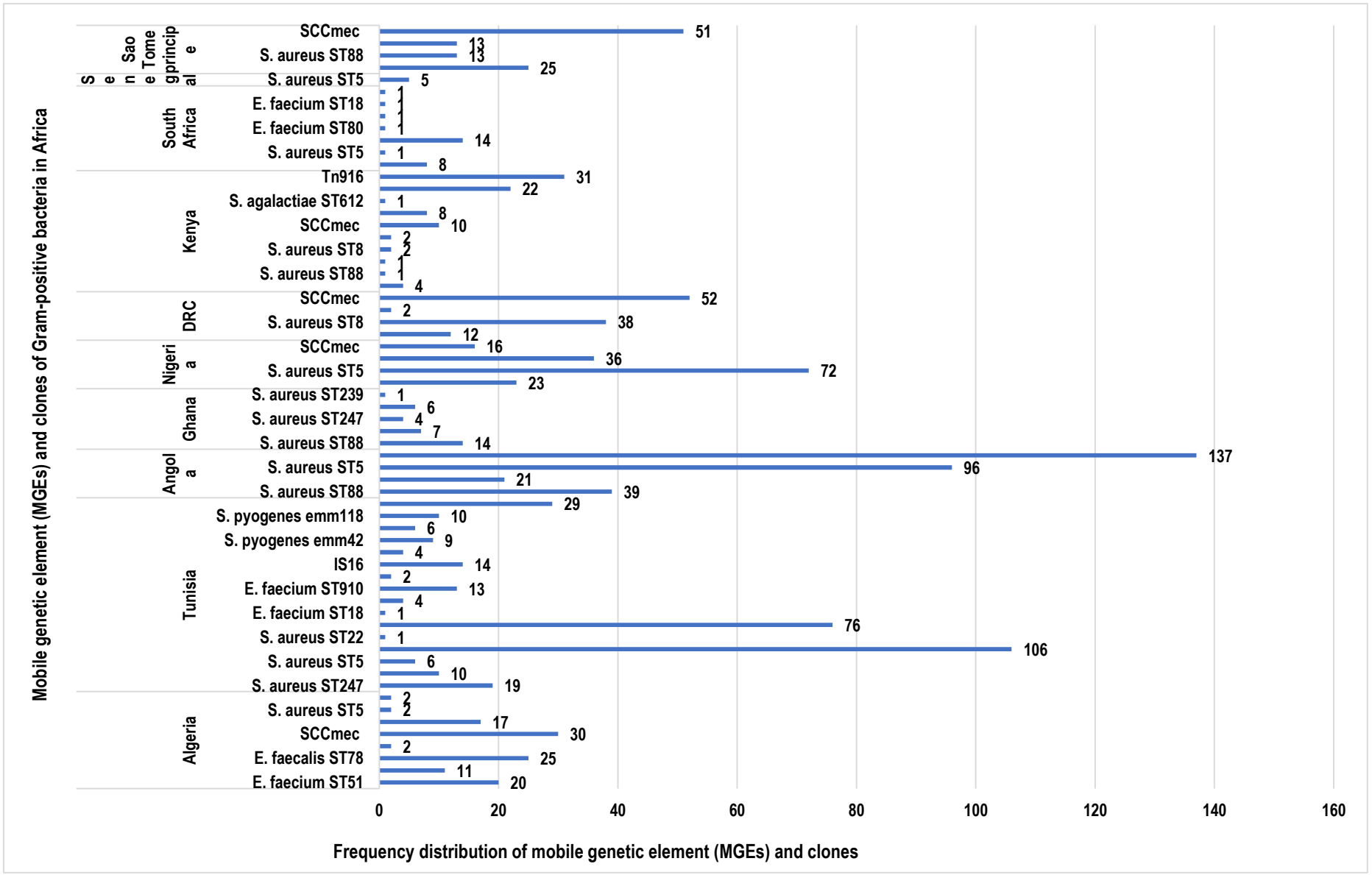

Figure 3a. Frequency distribution of resistant Gram-positive bacterial species, clones and mobile genetic elements (MGEs) per country in Africa.

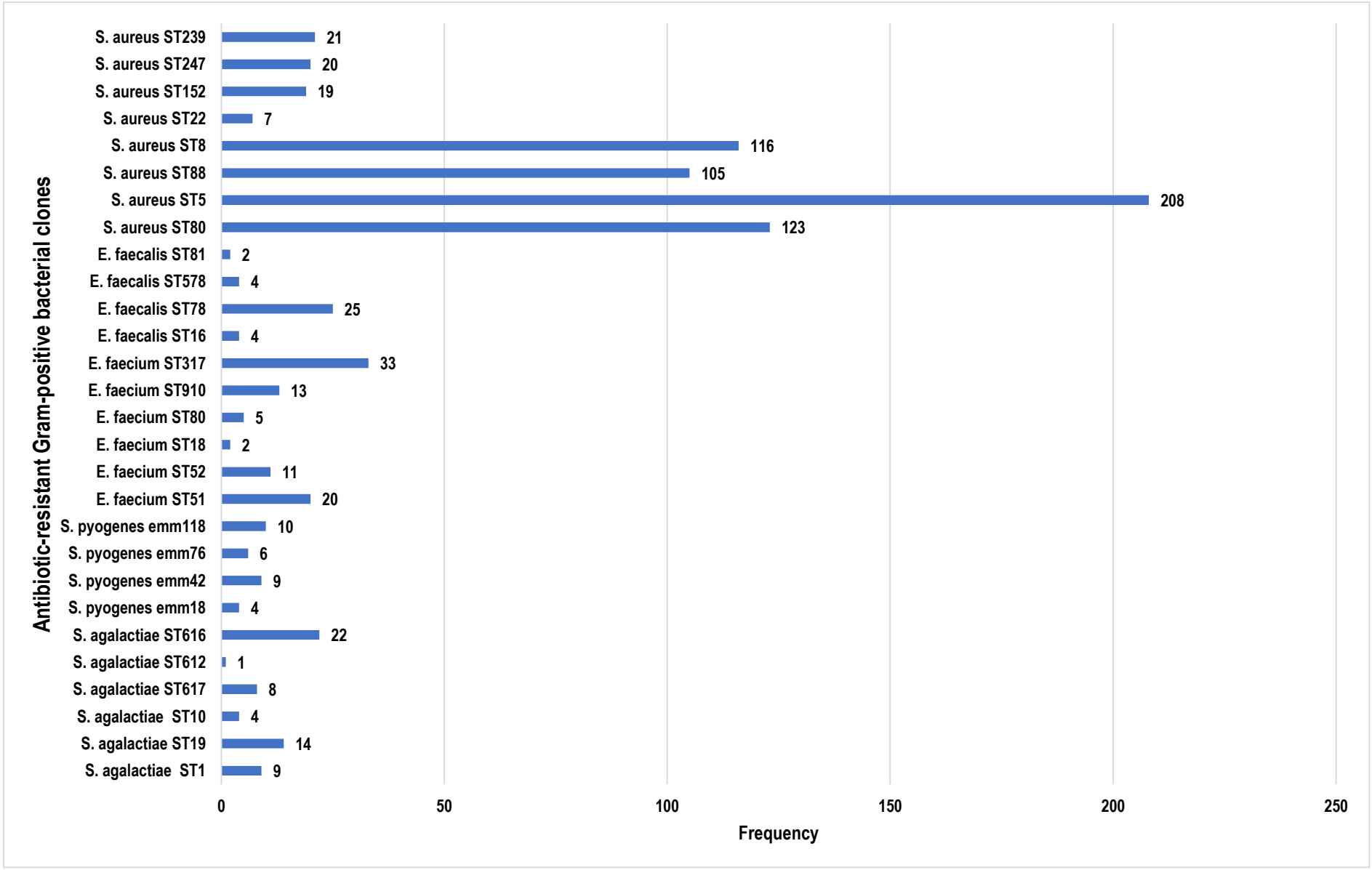

Figure 3b. Frequency of resistant Gram-positive bacterial species, clones and mobile genetic elements (MGEs) per country in Africa.