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

John Osei Sekyere\textsuperscript{a,c#} and Eric Mensah\textsuperscript{b}

Department of Pharmaceutics, Faculty of Pharmacy and Pharmaceutical Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.\textsuperscript{a}

Kumasi Center for Collaborative Research in Tropical Medicine, School of Medical Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.\textsuperscript{b}

Department of Medical Microbiology, School of Medicine, Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa.\textsuperscript{c}

#Address correspondence to John Osei Sekyere, jod14139@yahoo.com

Running title: Resistance mechanisms of Gram-positive bacteria
HIGHLIGHTS

- There is substantial resistance to antibiotics among Gram-positive bacteria (GPB) in Africa.
- Multidrug-resistant (MDR) *S. aureus, E. faecium, E. faecalis, S. pyogenes,* and *S. haemolyticus* of the same clones were common in humans, animals and the environment.
- MDR clones such as *S. aureus ST5* and *E. faecium ST80* were found in humans, animals and the environment.
- *mecA, ermB, ermC, tetM/K/L,* and *vanA/B/C* were common in GPB, including in VRSA.
- Meta-analysis confirmed a high mean rate of drug resistance in GPB from humans (35.68%), animals (69.63%) and the environment (88.33%) (*p*-value= 0.0301) in Africa.
- *SCCmec, IS16,* and *Tn916* mobilized *mecA, ermB* and *tetM* respectively across various GPB species in animals, humans, and the environment.
- A One Health approach to studying resistance mechanisms and molecular epidemiology of antibiotic-resistant GPB is warranted.

ABSTRACT

The emergence and dissemination of antibiotic resistance (ABR) in bacteria are being driven by antibiotics use in humans, animals and the environment, threatening global health and strengthening calls for a One Health approach to contain ABR.

A systematic search in PubMed for English research articles reporting on ABR in Gram-positive bacteria in Africa within the last ten years from 2007 to 2017 was undertaken. This finally yielded 76 articles that were included in this review and all statistical analysis.
The same ABR Gram-positive bacterial clones, resistance genes, and mobile genetic elements (MGEs) were found in humans, animals and the environment. IS16 and Tn916 were highly associated with *erm* (B) and *tet*(M) in *E. faecium* (ST18, ST80 and ST910), *S. agalactiae* (ST612, ST616 and ST617), *E. faecalis* and *S. pyogenes* (emm18, emm42, emm76 and emm118) whilst *SCCmec* was associated with *mecA* in *S. aureus* (ST5, ST80, ST8, and ST88) and *S. haemolyticus*. The resistance genes, *mecA, erm*(B), *erm*(C), *tet*(M), *tet*(K), *tet*(L), *van*(B), *van*(A), *van*(C), and *tet*(O), were found in isolates from humans, animals and the environment. An ABR rate of 39.55% in Gram-positive bacteria is estimated in Africa. Meta-analysis reveal that isolates were most resistant to erythromycin (≥ 2 482) (37.37%), rifampicin (≥ 2 323) (33.42%), tetracycline (≥ 2 181) (40.72%), penicillin (≥ 2 127) (73.47%), sulfamethoxazole/trimethoprim (≥1 377) (45.97%), ciprofloxacin (≥846) (35.37%), gentamicin (≥805) (23.87%), vancomycin (≥712) (42.24%), ampicillin (≥691) (48.25%), streptomycin (≥551) (32.03%) and chloramphenicol (≥376) (11.50%) (p-value <0.0001).

There is substantial resistance to antibiotics among Gram-positive bacteria in clinical and environmental settings in Africa, mediated by clonal and polyclonal expansion as well as horizontal transmission of resistance genes. A One Health approach to research, surveillance, and molecular epidemiology, as well as antibiotic stewardship to contain ABR in humans, animals and the environment should be prioritised.

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

Antibiotic resistance, a threat to public health

The emergence of multiple antibiotic resistance (ABR) determinants in clinically important Gram-positive bacteria (GPB) such as *Staphylococcus* spp., *Streptococcus* spp., and *Enterococcus* spp. is a major threat to the successful treatment of infectious diseases worldwide as they result in high morbidity and mortality rates, and limited therapeutic options. A recent report projects that the current rate of 700,000 deaths/annum caused by drug-resistant pathogens could increase to 10 million by 2050 if unchecked. In the European Union (EU), methicillin-resistant *Staphylococcus aureus* (MRSA) alone affects approximately 150,000 patients annually within the health-care sector, resulting in an expenditure of €380 million. Additionally, there were 80,461 invasive MRSA infections and 11,285 MRSA-attributable mortality cases with an estimated annual cost of $1.4 billion to $13.8 billion in the United States of America. In USA, staphylococci and enterococci together comprise 42% of all pathogens involved in device-associated and procedure-associated infections. As well, 29–63% of hospital-recorded mortalities have been attributed to *S. aureus*-mediated bacteremia.

A significant increase in vancomycin-resistant *Enterococci* (VRE) has been reported in many countries recently. For instance, vancomycin-resistant *E. faecium* increased from <5% in 2001 to 14.5% in 2013 in Germany. Moreover, of the 9.6% *Enterococcus* spp. isolated from all nosocomial infections in Europe, 10.2% were VRE. The rate of nosocomial infections due to VRE is much higher in intensive care units with a significant mortality compared to vancomycin susceptible Enterococcus. According to studies in USA, a hospital cost of between $9,949 and $77,558, and $12,766 was attributed to treating VRE blood stream infections and surgical site...
infections respectively \(^{12,13}\). Puchter et al., (2018) reported a median cost of €13,147 for treating a single case of nosocomial infections due to VRE \(^{14}\).

*Streptococcus pyogenes*-associated infections and sequelae pose a devastating burden on public health and national economies \(^{11}\). There are approximately 517,000 deaths annually due to severe *Streptococcus pyogenes* infections such as rheumatic heart disease, post-streptococcal glomerulonephritis and acute rheumatic fever globally. A prevalence of 18.1 million cases of severe Streptococcus-mediated diseases has been estimated, with 1.7 million new cases reported annually \(^{15}\). *S. agalactiae* is capable of causing life-threatening diseases in pregnant women, newborns and patients with underlying conditions such as diabetes and liver disease \(^{16,17}\). Sepsis due to *S. agalactiae* accounts for about 26% of all neonatal deaths and 10% maternal deaths in Sub-Saharan Africa \(^{18}\). *Bacillus spp.*, such as *Bacillus cereus*, is among the important aetiologies of foodborne diseases that threaten food security, and is capable of causing serious sequelae such as neurological disorders, multi-organ damage and abortion \(^{19}\).

Limited data in Africa makes it impossible to track and monitor the true burden of ABR. 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 \(^{20}\).

In a recent review, GPB were responsible for a high proportion of infections among children and showed a high level of resistance to WHO-recommended drugs in Africa \(^{21}\). In some African regions, as many as 80% of *S. aureus* infections are 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. Patients infected with MRSA are estimated to be 64% more likely to
demise than those infected with MSSA.

**Sources and anthropogenic activities driving resistance**

ABR has been reported in humans, animals and the environment at alarming proportions
worldwide, with indiscriminate antibiotic use being fingered as a major contributor.

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 groundwater. Furthermore,
genres 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. Current reports reveal that global agricultural antibiotics
consumption exceeds that of humans. An estimated 63,151 tonnes of antibiotics were consumed
globally in livestock production in 2010, and a significant amount of this was used for
veterinary purposes. These reports suggest that a larger share of the antibiotics that end up
polluting the environment and communities emanate from livestock production. This
interconnectivity between animals, humans and the environment, explains the need to adopt a One
Health research policy.

Several studies have reported high rate 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
41–47. 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 \(^{28,41,45,48-52}\). 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 \(^{40}\).

**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. These mechanisms include drug target-site modification(s), enzymatic hydrolysis/inactivation of antibiotics, reduced cell wall/membrane permeability and active efflux \(^{53-56}\). Resistance is often acquired through 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. These include between commensals and medically important Gram-positive pathogens \(^{57,58}\). Tn916 and IS16 are notable MGEs that carry major ABR determinants and are transmissible between clones of the same or different bacteria species by a conjugative mechanism. Some MGEs are excised from donor cells and transferred during cell-to-cell contact prior to being inserted into recipient cells by a site-specific recombinase. The capability of these MGEs to pick up extra clinically relevant resistance genes contributes to the emergence of multidrug resistance \(^{59-61}\).

**Purpose of this review**

Excellent reviews addressing antimicrobial resistance in some GPB in Africa have been published \(^{21,62-67}\). 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 are non-existent, to the best of our knowledge. This review sought to identify species, clones and MGEs responsible for the spread of resistance genes in GPB in Africa from a One Health perspective. It is our aim that the geographical distribution of resistant strains and GPB resistance mechanisms in Africa presented herein will inform the choice of anti-infective agents or treatment guidelines, infection control strategies and ABR study designs.

### 1.1 Search strategy and inclusion criteria

Research articles published within the last ten years (2007 to January 2018) in English and indexed in PubMed 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 results or undertook ABR surveillance studies without further molecular tests to characterize the ABR mechanisms and/or clonality of the isolates were excluded. 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 such as integrons, plasmids, transposons and insertion sequences, and antibiotics to which the strains were resistant (Tables 1-5). 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. As well, the antibiotics to which the isolates were most resistant were determined to evaluate their correlation with the detected/reported resistance mechanisms.
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). The distribution of clones, resistance genes, and MGEs were considered to identify countries with most resistant clones, resistance genes, and their associated MGEs.

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). 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, 76 articles were used for the data analysis.

2. RESULTS AND DISCUSSION

Antibiotic usage in humans, food, wild and domestic animals, as well as in agriculture, is selecting for ABR genes and resistant bacteria in hospitals, farms, and the environment. The constant interactions between man, animals, food and the environment enhances the easy transmission of resistance genes and resistant bacteria between humans, animals and the environment. Thus, ABR is not limited to clinical settings, farms, the environment or to individual countries as increased globalization, trade and international travel put all humans and animals at risk of contracting difficult-to-treat antibiotic-resistant infections. This limitless capability for resistance genes and resistant bacteria to spread across a broad-spectrum of hosts or
niches makes the menace even more worrying, underscoring the need for a One Health approach to contain the situation by looking at resistance from all spheres: humans, animals and the environment.

A meta-analysis of published literature confirmed the presence of a high mean rate of drug resistance in GPB from humans (35.68%), animals (69.63%) and the environment (88.33%) ($p$-value= 0.0301) 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. 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 88.33%. 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 (Figure 3) 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*, *S. pneumoniae* and *S. agalactiae* harbouring mecA, 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
218 prudent for countries within these regions to review their recommended antibiotic regimens, 
219 guidelines/protocols for infections caused by these species.
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Erm(B), tet(M) and vanA genes were mobilized by Tn916 and IS16. Moreover, erm(B) and 
tet(M) were found in S. aureus, Enterococcus spp. and Streptococcus spp., 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.

2.1 Resistance rates per countries and MDR GPB species

230 Of the 1,466 articles returned from the systematic literature search (Fig. 1), 76 studies 
231 representing 20 out of 54 African countries were included in this review and data analysis.
232 Tunisia (n= 19) recorded the highest number of studies followed by South Africa (n=1, 4), Egypt 
233 (n=9), Nigeria (n=7) and Algeria (n=4) (p-value 0.0054). Majority of the included studies were 
234 undertaken in Northern Africa (n=32, 43.83%), Southern Africa (n=16, 21.92%) and Western 
235 Africa (n=10, 12.99%). Different rates of resistance to antibiotics were reported in different 
236 countries in Africa (Tables 2-4). High mean resistance rates were reported in Nigeria, Tunisia, 
237 Algeria, and South Africa. Cross-contamination of multi-drug resistant bacteria between patients 
238 and the environment accounted for the high rate of resistance in Algeria 79,101,108–110. The high 
239 rate of ABR in Tunisia was attributed to cross contamination between hospital patients and 
240 hospital environment, immune deficiency 111, over-consumption of antibiotics, heavy
consumption of sheep meat, which is a reservoir of MRSA, and high consumptions of antibiotics in animal feed. In Egypt, inappropriate antibiotic prescription practices, inadequate hygienic handling and processing of food, and close contact with pet dogs accounted for the high resistance.

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, existence of MRSA in clinical and community settings, uncontrolled usage of antibiotics and the presence of efflux pumps in coagulase-negative staphylococcus strains. Expansion of resistant clones, variability of hospital acquired MRSA clones, consumption of unpasteurized milk or inefficient thermal processing of milk, shedding of resistant clones from animals to the environment and heavy consumption of antibiotics to treat TB due to high HIV burden, 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, 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 van(A/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 (43.76%, 95% CI=34.37-52.36)(p-value=0.0001), erythromycin (42.05%, 95% CI=33.16-50.94)(p-value = .0001), kanamycin (34.99%, 95% CI=18.34-51.65%) and vancomycin (42.24%, 95% CI=19.71-64.76) (p-value = .0001). 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. 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.

Approximately 26,108 GPB were isolated from humans (n=47 studies, 64.38%), animals (n=16 studies, 21.92%) and the environment (n=10 studies, 13.70%), of which 10,326 were resistant, equivalent to 39.55% overall resistance rate in Africa (Tables 1-4). Countries such as Algeria, Egypt, Ghana, Nigeria, Uganda, Tunisia recorded at least 51% mean rates of ABR (Tables 2-4). Nigeria recorded the highest mean rates of resistant isolates (n=74.62%) followed by Egypt (n=71.79%), Ghana (n=70.41%), Tunisia (n=66.55%), Algeria (n=57.40%), Angola (n=56.77%), Uganda (n=51.43%), Democratic Republic of Congo (49.45%), Kenya (n=37.3%), Tanzania (n=35.75%), São Tomé & Príncipe (n=34.85%), and South Africa (n=31.50%). Resistant isolates were reported in Angola (17.29%), Gabon (49.06%), Libya (33.69%), Morocco (83.33%), Mozambique (19.15%), Namibia (29.31%), and Senegal (100%) in single studies (Table 1-3).

The antibiotics to which the isolates were most resistant to were erythromycin (≥ 2 482) (37.37%), rifampicin (≥ 2 323) (33.42%), tetracycline (≥ 2 181) (40.72%), penicillin (≥ 2 127) (73.47%), sulfamethoxazole/trimethoprim (≥ 1 377) (45.97%), ciprofloxacin (≥ 846) (35.37%), gentamicin (≥ 805) (23.87%), vancomycin (≥ 712) (42.24%), ampicillin (≥ 691) (48.25%), streptomycin (≥ 551) (32.03%) and chloramphenicol (≥ 376) (11.50%) (p-value <0.0001) (Tables 2-4). Countries with high number of studies such as Tunisia, South Africa, Egypt and Nigeria recorded high number of ABR. These countries recorded high number of mecA, erm(B), tet(M), drfG and vanB resistance.
genes. Vancomycin resistance was reported in six studies in both animals and the environment, and five studies in Humans. Vancomycin-resistant *Enterococcus* spp. (≥594 isolates) and vancomycin-resistant *Staphylococcus* spp. (≥118 isolates) were reported in humans, animals and the environment. Vancomycin-resistant *Staphylococcus aureus* (VRSA) was reported in animals (≥47 isolates), the environment (≥15 isolates) and humans (≥2 isolates); whilst vancomycin-resistant *E. faecium* was reported in the environment (n≥238 isolates), animals (≥330 isolates) and humans (≥20 isolates).

*S. aureus* (≥ 24 321 isolates in 47 studies) accounted for approximately 92.55% of all GPB involved in hospital- and community-acquired infections, followed by *E. faecium* (≥1 121 isolates in 18 studies, 4.27%), *S. agalactiae* (≥750 in 6 studies, 2.85%) *E. faecalis* (≥284 isolates in 13 studies, 1.08%). Antibiotic-resistant *S. aureus* (ST5), *E. faecium* (ST18, ST80 and ST910) and *E. faecalis* harbouring mecA, *erm*(B), *erm*(C), *tet*(M), *tet*(K), *tet*(L) and *van*(B) were isolated from humans, animals and the environment, albeit in higher proportion in humans and animals than the environment (Tables 1-2). For instance, Farhat et al. (2014) 79, van Rensburg et al. (2012) 80 and De Boeck et al. (2015) 81 in Algeria, South Africa and Democratic Republic of Congo respectively, reported on resistant *S. aureus* ST5 in humans whilst Fall et al. (2012) 82 reported on the same clone (*S. aureus* ST5) in pigs from Senegal. Further, Mariem et al. (2013) 47 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 83.
and recent evidence suggest that it has spread from hospitals into communities, resulting in community-acquired MRSA.  

Similarly, Lochan et al. (2016) in South Africa, Dziri et al. (2016) and Elhani et al. (2014) 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) and Dziri et al. (2016). 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, animals and the environment, underpinning the broad host range and transmissibility of these strains between animals, humans and the environment. Although mecA was the predominant resistance gene, higher resistance was recorded to erythromycin probably due to lesser use of penicillin(s) in antibiotic susceptibility testing or lesser inclusion of erm primers in PCR analysis to detect resistance genes. MRSA strains were the most commonly isolated strains (≥ 2,350). This is consistent with the global report of increasing prevalence of MRSA. MRSA harbours the mecA gene, which is carried by the SCCmec MGE, and mediates resistance to multiple antibiotics. 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.
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 52.13% (95% CI=21.75 - 82.51) (p-value = 0.0006) to vancomycin. Multidrug resistance in VREs increases VRE-associated mortality rates, which is likely to increase to 75% compared with 45% from susceptible strains. As well, evolution of macrolide resistance (45.96%, 95% CI=0.04 – 91.88) (p-value = 0.049) in drug-resistant streptococci is limiting treatment options and resulting in high mortalities.

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 in such infections whilst awaiting susceptibility results. The empirical therapy can be changed or maintained based on the susceptibility report.

### 2.2 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 source. Among environmental isolates, 94.30% (95% CI=83.49–105.1)(p-value = 0.0001) were resistant to penicillin, 81.99% (95% CI=40.57–123.4)(p-value 0.0082) were resistant to sulfamethoxazole/trimethoprim, 75.53% (95% CI=1.92–149.1)(p-value = 0.0480) were resistant to ampicillin, 68.30% (95% CI=23.12–104.5) (p-value = 0.0063) were resistant to ciprofloxacin, 62.78% (95% CI=–56.96–105.5)(p-value = 0.153) were resistant to clindamycin, 60.93% (95% CI=39.70–82.17)(p-value = 0.0002) were resistant to erythromycin, and 59.37% (95% CI=15.10–103.6)(p-value = 0.0183) were resistant to vancomycin.
Among animal isolates, 58.80% (95% CI=17.87–100)(p-value = 0.0148) were resistant to penicillin, 49.24% (95% CI=13.76–84.71)(p-value = 0.016) were resistant to clindamycin, 46.22% (95% CI=26.77–65.67)(p-value = 0.0017) were resistant to ciprofloxacin, 44.91% (95% CI=17.31–60.82)(p-value = 0.046) were resistant to ampicillin, 39.24% (95% CI=14.53–63.96)(p-value = 0.0081) were resistant to trimethoprim/sulfamethoxazole, 36.35% (95% CI=20–52.67)(p-value = 0.0005) were resistant to erythromycin, and 25.84% (95% CI=13.94–64.99)(p-value = 0.15) were vancomycin resistant.

The rates of resistance were much lower in humans for most of the antibiotics used. Among the various species, *Enterococcus spp.* and *Staphylococcus spp.* recorded high rates of resistance for most antibiotics. *Streptococcus spp.* reported low rates of resistance except for tetracycline that recorded a high rate of 57.60% (95% CI=25.18–90.03) (p-value = 0.065). Resistance to vancomycin was not reported in any *Streptococcus spp.* isolates.

*Enterococcus spp.*, mainly *E. faecium* and *E. faecalis*, recorded a resistance rate of 99.38% (95% CI=91.43–107.3)(p-value = 0.004) to clindamycin, 82.26% (95% CI=43.37–121.1)(p-value = 0.0042) to trimethoprim/sulfamethoxazole, 61.39% (95% CI=44.22–78.55)(p-value = 0.0001) to erythromycin, 55.59% (95% CI=22.98–88.20)(p-value = 0.0035) to vancomycin, 54.39% (95% CI=29.17–70.52)(p-value = 0.047) to ciprofloxacin, 50.75% (95% CI=30.96–70.54)(p-value = 0.0002) to tetracycline, 47.09% (95% CI=23.65–70.52)(p-value = 0.0017) to ampicillin, 42.52% (95% CI=14.47–70.57)(p-value = 0.0089) to kanamycin, 30.93% (95% CI=10.91–50.95)(p-value = 0.007) to streptomycin and 30.07% (95% CI=18.20–41.96)(p-value = 0.0001) to gentamicin.

*S. aureus* showed high resistance (71.33%) to penicillin (95% CI=50.43–92.22)(p-value = 0.0001), 55.36% to ampicillin (95% CI=15.77–94.22)(p-value = 0.0156), 47.34% to streptomycin (95%
CI=60.24–154.9)(p-value = 0.20), 37.63% to tetracycline (95% CI=26.14–49.11)(p-value = 0.0001), 31.38% to trimethoprim/sulfamethoxazole (95% CI=18.01–44.76)(p-value = 0.0001), 30.37% to ciprofloxacin (95% CI=18.38–42.37)(p-value = 0.0001), 37.63% to tetracycline (95% CI=26.14–49.11)(p-value = 0.20), 37.63% to tetracycline (95% CI=26.14–49.11)(p-value = 0.0001), 30.37% to ciprofloxacin (95% CI=18.38–42.37)(p-value = 0.0001), 29.71% to rifampicin (95% CI=8.78–50.63)(p-value = 0.010), 27.74% to erythromycin (95% CI=17.67–37.80)(p-value = 0.0001), 25.37% to clindamycin (95% CI=12.33–38.41)(p-value = 0.128), 22.57% to gentamicin (95% CI=5.97–51.11)(p-value = 0.0003) and 18.97% to vancomycin (95% CI=5.34–43.27)(p-value = 0.096).

2.3 Resistance mechanisms, clones, and MGEs

Few studies identified the clones and MGEs in the resistant isolates. Of the 76 included studies, 32 identified the clones whilst 22 described the MGEs, which was used in the statistical analysis. The most dominant gene detected in Africa, which was widespread and responsible for resistance in GPB, was mecA (≥2 603), followed by erm(B) (≥984), tet(M) (≥620), dfrG (≥400), vanB (≥380) blaZ (≥362), aph(3’)-IIIa (≥139) and mefA/E (≥47) (p-value = 0.0011) (Fig. 2a). Isolates from humans had the highest mecA (≥2 079), ermB (≥721) and tet(M) (≥461) (p-value = 0.048) resistance genes. This was followed by animals (mecA ≥ 208), erm(B) (≥362) and tet(M) (≥78) (p-value = 0.343). (Tables 1-4). The 21 studies that described the MGEs included 15 SCCmec(≥ 2 138), two IS16 (≥18) and two Tn916(≥ 99)(Table 1).

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), van(B), van(A), van(C) and tet(O) were reported in isolates from humans, animals and the environment (Table 1).
IS16 and Tn916 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 (emm18, emm42, emm76 and emm118) isolated from humans, animals and the environment (Tables 2-4).

TetM was associated with Tn916 transposon in tetracycline-resistant S. agalactiae and S. pyogenes in humans in Tunisia. Fischer et al. (2013) also reported the association between Tn916 and tetM in tetracycline resistance S. agalactiae in camel in Kenya. Similarly, IS16 element was found in vancomycin-resistant E. faecium (ST80, ST180 and ST910) in humans and the environment in Tunisia. Investigations into the association between MGEs and resistance genes were limited by few studies (n=22) 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) respectively, were widely distributed in Northern Africa (Tunisia, Algeria, Egypt, Morocco, and Libya) and Southern Africa (South Africa and Namibia). All the three different MGEs (Tn916, SCCmec and IS16) were reported in Tunisia, with two being reported in Kenya (SCCmec and Tn916). IS16 was only reported in an E. faecium infection in Tunisia (Figure 3) whilst mecA was mostly associated with SCCmec. erm (B) and tet (M) were highly associated with Tn916 and IS16.

In Africa, different studies have reported SCCmec-borne mecA in S. aureus in humans, animals and the environment besides the discovery of IS16 and Tn916 in the environment of erm(B) and tetM 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.
species in humans, animals and the environment (Tables 1-4) 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 \(^{60,104,105}\), 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 \(^{69,71,72,106}\).

### 2.6 Molecular epidemiology of antibiotic-resistant GPB

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

*Staphylococcus* spp., including *mecA*-harbouring methicillin resistant clones, have been described in humans, animals and the environment in Northern, Western, Central, Eastern and Southern Africa with varying but substantial frequencies and resistance rates. Common STs, resistance genes and MGEs were identified in humans, animals and the environment.

**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 \(^{79}\). 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 tobramycin (n=6), gentamicin (n=1), trimethoprim/sulfamethoxazole (n=2), tetracycline (n=3) and erythromycin (n=1). MRSA ST80 is
a well-known and frequent etiological agent of infections in North Africa and Middle-East countries\textsuperscript{119,120}. Typing of 64 MRSA isolated from human pus (n=47), venous catheters (n=7), tracheal aspirates (n=4), punction fluids (n=3), blood (n=2) and urine (n=1) in 64 Algerian patients revealed that 50 were hospital acquired (HA-MRSA) and 14 community acquired (CA-MRSA), which were all resistant to cefoxitin and oxacillin \textsuperscript{101}. MecA, mobilized by $SCCmec$, was the only detected mechanism of resistance.

\textit{Egypt}

MRSA have been respectively isolated in five animal-based and two human-based studies in Egypt between 2011 to 2017. Hashem et.al (2013) isolated 94 \textit{S. aureus} strains from blood and wounds in which 45 were MRSA while 25 were fluoroquinolone-resistant \textsuperscript{52}. Mutations such as C\textsuperscript{2402}T, T\textsuperscript{2409}C, T\textsuperscript{1497}C, and A\textsuperscript{1578}G in gyrase enzymes, which leads to fluoroquinolones’ target-site alterations, were implicated in resistance to fluoroquinolones (ciprofloxacin, levofloxacin, ofloxacin). The high rate of fluoroquinolone resistance (55.56\%) among MRSA infections is rather concerning as patients unable to tolerate vancomycin are treated with other antibiotics such as fluoroquinolones. Vancomycin is often reserved as a last-resort therapy for MRSA infections due to their high resistance to several antibiotics.

Multidrug resistance to drugs such as gentamicin, ampicillin, amoxicillin, cefepime, tetracycline and chloramphenicol in MRSA is mediated by diverse resistance mechanisms including impermeability effects and efflux pumps. Unrestricted access to antibiotics and inappropriate prescriptions were responsible for the high rates of drug resistance in this study \textsuperscript{52}. In a similar study, MRSA was isolated from patients suffering from surgical wound infections, diabetic foot, abscess and burns. Although \textit{mecA} was the only mechanism of resistance, the isolates were
multiple-resistant to several antibiotics belonging to the β-lactams, aminoglycosides, fluoroquinolones, macrolides, lincosamides, tetracyclines and glycopeptides, indicating other mechanisms of resistance. It therefore implies that administration of such antibiotics will not relieve patients from *S. aureus* infections. The high rate of *S. aureus* isolation confirms it to be the most prevalent Gram-positive pathogen isolated from soft tissue and wound infections.

Al-Ashmawy *et. al.* detected a high rate of MRSA (53%) in milk and dairy products believed to originate from human contamination rather than contamination from animals. Besides being resistant to β-lactams and other antibiotics, thirty-six of the isolates were resistant to vancomycin known to be effective in treating MRSA infections, making milk and dairy products a significant source of multidrug-resistant and toxigenic *S. aureus* infections. The occurrence of MRSA in pets such as dogs admitted in a veterinary clinic may confirm a possible route in the community transmission of this pathogen, which is emerging as a veterinary pathogen of public health importance.

In 2017, Osman and colleagues detected *Staphylococcus spp.* in imported beef meat. Sixteen of these isolates were MDR and showed resistance to different groups of antibiotics due to resistance mechanisms such as *mecA*, and mutations in *gyrA* and *gyrB*. Indeed, MRSA has made methicillin and other β-lactams antibiotics clinically useless as a result of their high MDR. Imported meat acts as a transmission vector for MRSA and is worrisome as *Staphylococcus spp.* are among the most common foodborne pathogens causing food poisoning outbreaks worldwide. Of 133 *S. aureus* recovered from animal origin, more than 70% were MDR and 30 were MRSA, exhibiting high resistance to clindamycin, co-trimoxazole, tetracycline, oxacillin, cefoxitin, ceftriaxone and erythromycin; four of the isolates were resistant to vancomycin. The isolates showed the maximum sensitivity to imipenem, chloramphenicol and rifamycin, which is consistent with
similar reports in China and Pakistan\textsuperscript{123,124}, indicating their effectiveness in treating \textit{S. aureus} infections.

In 2016, MRSA was isolated from chicken products mainly due to poor hygienic handling processes, posing a risk to public health. The mean \textit{S. aureus} count in the chicken products were beyond the permissible limits of the Egyptian organization for Standardization and Quality Control (EOSQC 2005), coupled with resistance to different antibiotics classes; thus, retail chicken products could constitute a high health risk to human consumers\textsuperscript{51}.

\textit{Morocco}

In a study to assess \textit{S. aureus} carriage among end-stage renal diseases patients undergoing hemodialysis, 42.9\% were carriers, of which only one was MRSA. The methicillin-susceptible \textit{S. aureus} (MSSA) was resistant to many of the local antibiotics, thus limiting the successful treatment of MSSA infections. Moreover 81.8\% of the MSSA were penicillin-resistant. The male gender and age 30 or below were identified as risk factors of \textit{S. aureus} nasal carriage (\textit{P}-value < 0.001)\textsuperscript{50}. Periodic monitoring of patients with hemodialysis is crucial as they are at increased risk of \textit{S. aureus} infection due to periodic hospitalization, immunosuppression and high invasive vascular interventions.

\textit{Tunisia}

Resistant \textit{S. aureus} was isolated from the environment, animals and humans between 2011 to 2017. Ben Said, et al. recovered 12 MSSA from wastewater samples that were resistant to penicillin (n=12 isolates), erythromycin (n=7 isolates), tetracycline (n=1 isolate) and clindamycin (n=1 isolate) due to the presence of \textit{blaZ} (n=7), \textit{msr(A)} (n=7) and \textit{tetK}(n=1). These resistant strains were of ST3245(n=7) and ST15(n=1)\textsuperscript{41}, which have been also reported in animals and humans.
In an investigation to evaluate the prevalence of coagulase-negative Staphylococcus (CoNS) in the hospital environment, MDR *S. haemolyticus* and *S. saprophyticus* were the most dominant. Methicillin resistance was detected in *S. haemolyticus, S. epidermidis* and *S. saprophyticus*. These isolates were resistant to erythromycin, tetracycline, gentamicin, kanamycin, tobramycin and streptomycin due to the presence of *msrA* (32), *ermC* (8), *tetK* and *tetM, aac(6’)-Ie-aph(2’)-Ia (16), aph(3’)-IIIa(19), ant(4’)-Ia (n=14) and ant(6’)-Ia (3) 125. The high prevalence of MDR *Staphylococi* spp. isolates may result from transmission between the staff, patients and the environment. Strict infection controls are needed as infections caused by CoNS are common causes of death, particularly in low-birth-weight children, and are opportunistic infections in immunocompromised patients 126.

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 107.

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) 111. For the first time, clonal lineage ST398, which has been reported in pigs from several studies in USA, South America, Asia and Canada 127–130, 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 ST80 (n=41), ST1440 (n=1), ST1 (n=2), ST5 (n=5), ST22 (n=1), ST97 (n=2), ST239 (n=4), ST241 (n=3), ST247 (n=3), ST1819 (n=3), ST153 (n=2), ST256 (n=1)

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, 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 SCCmec-borne mecA (Table 2), which agrees with a report on S. haemolyticus’ MDR capacity, particularly in immunocompromised patients

**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. 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
Moreover, mecA was detected in only nine isolates, implying the presence of other β-lactam resistance mechanisms. The MRSA clones included ST88 (n=2), ST8 (n=1), ST789 (n=1), ST72 (n=1), ST2021 (n=1), ST250 (n=2), and ST239 (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, 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 (TMP/SMX). Mechanisms of resistance included mecA (≥54), blaZ (n=284), dfra (≥5) and dfg (≥152). *S. aureus*-resistant clones ST8, ST152, ST772, ST14, ST241, ST37, ST39, and ST88 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 cotrimoxazole or TMP/SMX because of low cost and easy obtainability through lenient medication regulations were implicated for the high resistance. 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. All the S. haemolyticus isolates detected were resistant to at least three antibiotics classes (Tables 2-4). 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%). 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 recommended. In a study to examine the genetic mechanism(s) of resistance in CoNS in faecal samples, all the 53 isolated CoNS were Penicillin V-resistant and between three to 19 exhibited multidrug resistance (Table 2); mecA (n=15), ermC, tetM (n=4) and tetK (n=6) were identified. 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 (10.52%) 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 cotrimoxazole and 16 were resistant to tetracycline. Five of the MRSA were of ST5, evincing the spread of this clone in animals, humans, and the environment; the importance of this clone as a cause of human infections is well-established.

Cape verde

[27]
In Cape Verde, a low prevalence of 5.6% (6/107) MRSA nasal carriage was documented in 2015. The predominant MRSA clones was ST5 (n=3), ST88 (n=2) and ST8 (n=1). These isolates showed significant level of resistance to ERY, SXT and PEN.602

Central Africa: Gabon, D.R. Congo

Gabon

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

D.R. Congo (DRC)

A total of 215 (79.34%) drug-resistant S. aureus isolates were collected between 2015 to 2017 from nasal swab and bloodstream infections in the D. R. Congo; 70 isolates were MRSA. Other major resistance genes mediating resistance to trimethoprim/sulfamethoxazole, aminoglycoside, macrolides, tetracycline, penicillin, and chloramphenicol were dfrG (≥120), tetK (≥98), and femA (≥98). MRSA showed high-level resistance to β-lactams, aminoglycoside, macrolides and tetracycline. The pathogen caused severe infections such as pneumonia, meningitis, complicated urinary tract infections, gynaecological infections and peritonitis. S. aureus ST8 (≥47) was the dominant clone, followed by ST152 (≥17), ST5 (≥2) and ST88 (≥2). In DRC, MRSA ST8 outnumbers the African MRSA clone ST88, which is dominant in Africa. The high-level oxacillin resistance in DRC was associated with a mutation in femA (Y195F) whilst high-level trimethoprim resistance was due to the detection of dfrG, which is consistent with trimethoprim resistance in Africa and Asia. In Africa, TMP/SMX 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. Hence, prophylactic use of TMP/SMX 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.

**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 ST22 (n=4), ST88 (n=1), ST789 (n=1), ST5 (n=1), ST8 (n=2), ST241 (n=12) and ST239 (n=2). Approximately 41% of the MRSA in the study were MDR (Table 2), showing resistance to clindamycin, erythromycin and TMP/SMX. 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-Saharan Africa.

**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 368.

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 369.

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

Angola

Conceição et al (2014) reported a nasal S. aureus carriage of 23.7% (n=128), out of which 58.1% (n=77) 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, FOX and PEN 370. 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 São Tomé & Príncipe, making them potential OS-MRSA reservoirs. OS-MRSA have been reported worldwide in humans, animals and food animals 371–374. The OS-MRSA isolates expressed MDR (Table 2) and belonged to ST88 (n=15) and ST8 (n=9). 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, TMP/SMX, 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, 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 hospitalisation 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. 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.

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, ermB and tetM, 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. Evidently, raw and pasteurized milk can harbour MDR *S. aureus*, exposing consumers to colonization and/or infections. Again, *Staphylococcus spp.*, including *S. aureus, S. haemolyticus, S. xylosus* and *S. capitis* were isolated from healthy pigs and cattle, of which between 75 to 100% were resistant to penicillin G, tetracycline, sulfamethoxazole and nalidixic acids, due to their use as growth promoters; *MecA* and *mphC* were identified. Additionally, 12% of the isolates were resistant to vancomycin and erythromycin, evincing the important role of animals in the dissemination of resistance determinants and the importance of commensals to public health.

Van Rensburg et al. detected 43.4% (1432/3298) and 3.1% (328/10448) rifampicin resistance rate among MRSA and MSSA respectively. Similar studies in South Africa have also reported of high rifampicin resistance in MRSA, obviously due to frequent use of rifampicin among tuberculosis patients, who are highly prevalent in South Africa. MRSA ST5 and ST612 were detected while *H481Y/N* and *I527M* mutations in *rpoB* were associated with high-level rifampicin resistance, similar to reports in Italy. Additionally, novel *H481N, I527M, K579R* mutations were also detected.

Three studies reported a prevalence of 29.1%, 45.44% and 100% MRSA recovered from humans, expressing resistance to macrolides, tetracycline, aminoglycoside, cotrimoxazole and rifampicin. MRSA ST612, ST239, ST36 and ST5 were the dominant strains similar to other...
findings in Australia and Europe\textsuperscript{164}. The study showed that \textit{S. aureus} bacteremia is common and account for high mortality in South Africa. For instance, in a study by Perovic et al.,\textsuperscript{162} 202 patients died from \textit{S. aureus} bacteremia infections, with HIV patients being more likely to acquire HA-MRSA. The isolates were however susceptible to glycopeptides, fluoroquinolones, linezoid, tigecycline, fosfomycin and fusidic acid, confirming their clinical usefulness in treating MRSA infections. In a recent study, a high prevalence and genetic diversity of multi-drug efflux (MDE) resistance genes were found in clinical \textit{S. aureus} isolates, including 81 MRSA and 16 MSSA \textsuperscript{165}. \textit{NorA}, \textit{norB}, \textit{mepA}, \textit{tet38}, \textit{sepA}, \textit{mdeA}, \textit{imrs} and \textit{sdrM} were present in at least 86\% of the isolates, predicting resistance to broad-spectrum biocides and fluoroquinolones, which is disturbing. Efforts to develop efflux pump inhibitors can mitigate such resistance mechanisms.

\textbf{Sao Tome & Principe}

MRSA prevalence of 26.9\% \textsuperscript{166} and 25.5\% \textsuperscript{141} was reported in nasal swabs in 2014 and 2015, respectively, in Sao Tome & Principe. Additionally, a high prevalence of oxacillin-susceptible \textit{mecA}-positive \textit{S. aureus} was reported in the same study in Sao Tome & Principe and Angola\textsuperscript{151}. The most dominant MRSA clone was ST8 (n=25), followed by ST5 (n=13) and ST80 (n=13). 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.

\textbf{Streptococcus spp. (\textit{S. pyogenes}, \textit{S. pneumoniae} and \textit{S. agalactiae})}

Drug resistant \textit{Streptococcus spp.} including \textit{S. agalactiae} and \textit{S. pyogenes} have been identified in Northern, Eastern and Southern Africa. \textit{S. pyogenes} were reported in only humans whilst \textit{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)- and erythromycin-resistant (43.18%, 19/44) S. agalactiae from vaginal swabs; tetM; and ermB respectively mediated this resistance. A high diversity of resistant clones viz., ST1, ST19, ST10, ST158, ST166, ST233, ST460, ST521 and ST677 were detected, which have been reported worldwide for causing life-threatening invasive diseases such as meningitis and sepsis.

**Egypt**

Similarly, Shabayek et al. (2014) detected 98% and between 14-17% S. agalactiae resistance to tetracycline and macrolides respectively. TetM was detected in all the 98 tetracycline-resistant isolates whilst ermB and ermA mediated erythromycin resistance. Efflux pump genes such as tetK (n=12), tetL (n=1) and mefA/E (n=1) were also found, which reflects the increasing reports of S. agalactiae resistance to tetracycline and macrolides. 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.

**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), 40% (90/226) and 19.1% (43/226) were resistant to tetracycline, erythromycin and rifampicin respectively. Additionally, seven isolates were resistant to aminoglycoside (gentamycin and streptomycin) and chloramphenicol. TetM (n=205), 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 Tn916 (p-value = 0.0002). Other resistance genes including ermB (n=79) and tetO (n=50) were detected. All isolates were however susceptible to β-lactams and quinupristin-dalfopristin. Between 2005 and 2007, 160 erythromycin-resistant S. agalactiae were isolated from humans, with a high resistance rate of 84.3% (135/160) to the constitutive macrolides-lincosamides, streptogramines B (MLSB).

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 tetM, associated with Tn916, being responsible for tetracycline resistance. 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.

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 Tn916-borne tetM. ST616 (n=22) was the major resistant clone, followed by ST612 and ST617. 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) 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 ermB and mefA genes. 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)

Enterococcus spp., predominately MDR and vancomycin-resistant (VR) E. faecium and E. faecalis, were isolated from humans, animals and the environment in Northern, Western, Eastern and Southern Africa. From the meta-analysis, Enterococcus isolates recorded the highest rate of resistance followed by S. aureus. Common resistance genes, clones and MGEs were found in humans, animals and the environment.
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), tetracycline (82.4, 103/125), levofloxacin (71.2%, 89/125) and gentamicin (54.4, 68/125). Only 3.2% (4/125) 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%). ErmB (≥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, which is also prevalent in Asian (Japan, Taiwan, China and Korea) and European (Italy and Germany) countries. 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.

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 \textsuperscript{42,45,71,181–183}. 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 \textit{E. faecium}, followed by \textit{E. faecalis}. TetM, tetL, ermB, \textit{ant (6)-la}, \textit{vanA} and \textit{aph(3')-llla} were the major resistance mechanisms, with \textit{IS16} being the main MGE disseminating the resistance genes. \textit{E. faecium ST80}, \textit{ST910} and \textit{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**

\textit{Enterococcus} \textit{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 \textsuperscript{184}. 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 \textit{E. faecium} from vegetables, soil, farms, animal and manure \textsuperscript{48}. Approximately 95% (35/37) and 8% (5/63) of the aminoglycoside- and ampicillin-resistant clones were recognized as high-level aminoglycosides- and ampicillin-resistant \textit{E. faecium} respectively. Modifying enzymes’ genes
such as aac(6')-Ie-aph(2")-Ia, aph(2')-Ic.aph(3')-Illa, 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. TetW and sulI 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. ErmB (≥300), vanC 2/3(162), vanB (≥138), vanC (≥120), strA (≥120) were the major resistance genes. The vancomycin-resistant isolates were from patients with haematological malignancies, bacteremia, pigs, wastewater and underground water. 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.

3. CONCLUSION AND STUDY LIMITATIONS

The high rate of ABR among GPB to important antibiotics in Africa is 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 77 articles. Among these, only few studies reported on MGEs and resistant clones.

**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. 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), perfoxacin (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.

Role of Funding Source: Not applicable.

Contributors: JOS conceived, designed and supervised the study, analysed and vetted the results, wrote the paper, edited and formatted it for publication. EM co-conceived and co-designed the study, gathered and analysed the data and drafted the paper. Both authors approved the final version for submission.

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Table 1. Frequency distribution of species, clones, resistance genes and MGEs isolated from animals, humans and environmental specimens.

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<tr>
<th>BACTERIAL SPECIES, RESISTANCE GENES AND MGEs</th>
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<th>HUMANS</th>
<th>ANIMALS</th>
<th>ENVIRONMENT</th>
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1 Mobile genetic elements
### Table 2. Geographical distribution, species, clones, and resistance mechanisms of antibiotic-resistant Gram-positive bacteria isolated from humans in Africa from 2007-2017

<table>
<thead>
<tr>
<th>Country (n)</th>
<th>Year</th>
<th>Organism/Species (n)</th>
<th>Specimen Sources (n)</th>
<th>Sample size (Resistant isolates)</th>
<th>Resistance rate (%)</th>
<th>Clones (n)</th>
<th>Resistance genes/mechanisms (n)</th>
<th>Antibiotics to which strains were resistant</th>
<th>MGEs 2 (n)</th>
<th>Reference</th>
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<td><strong>Algeria</strong> (4)</td>
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<td>S. agalactiae (44)</td>
<td>Vaginal swab (44)</td>
<td>(44)</td>
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<td>Nasal swab (159)</td>
<td>159 (9)</td>
<td>5.66</td>
<td>ST80 (4), ST5 (2), ST22 (2), ST535 (1)</td>
<td>mecA (9)</td>
<td>GEN5(3), TET (3), TOB6(6), SXT7 (2)</td>
<td>SCC mec (9)</td>
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<td>2012</td>
<td><strong>E. faecium</strong> (80), <strong>E. faecalis</strong> (39)</td>
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<td>erm(B) (92), vanC1(4)</td>
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<td>S. aureus (64)</td>
<td>Pus (47), venous catheters (7) tracheal aspirates (4),</td>
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2 Mobile genetic elements: plasmids, transposons, integrons
3 Tetracycline
4 Erythromycin
5 Gentamicin
6 Tobramycin
7 Sulphamethoxazole-trimethoprim
8 Ampicillin
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<th>Country/Region</th>
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<th>Staphylococcus Aureus (Nasal swabs/Blood)</th>
<th>Number</th>
<th>Penetration (%)</th>
<th>ST Types</th>
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<td>Angola (3) and Sao Tome principe</td>
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<td><em>S. aureus</em> (164) Nasal swab (164)</td>
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<td>17.68</td>
<td>ST88(15), ST8(9)</td>
<td>MecA (NS)</td>
<td>FOX (29), SXT (26), TET (18), ERY (16), CIP (9) and CLI (8)</td>
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<td><em>S. aureus</em> (203) Nasal (203)</td>
<td>203 (128)</td>
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<td>ST8(16), ST5(83), ST88(19), ST72(5), ST789(1), ST5/2629(2), ST30(2), ST22(1)</td>
<td>MecA (127)</td>
<td>SXT (136), FOX (128), TET (39), PEN (200), RIF (156), CLI (4), ERY (14), CIP (20), GEN (43), CHL (18)</td>
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<td>Cape verde</td>
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<td><em>S. aureus</em> Nasal swab (113)</td>
<td>113 (16)</td>
<td>14.16</td>
<td>ST88(2), ST8(1), ST5(3)</td>
<td>MecA (6)</td>
<td>FOX (5), TET (5), PEN (109), CIP (2), CLI (3), SXT (12), ERY (16), (FUS (5), MUP (6)</td>
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<td>Democratic Republic of Congo (3)</td>
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<td><em>S. aureus</em> blood(108)</td>
<td>108 (27)</td>
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<td>ST5(11), ST8(30), ST88(1), ST152(17)</td>
<td>dfrG(24), aac(6')-aph(2&quot;)(25), tetK(23), ermA(20)</td>
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<td><em>S. aureus</em> (100) Nasal swab (100)</td>
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<td>ST8 (9)</td>
<td>dfrG(72), tet(K)(44), FemA(98), mecA (33)</td>
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<td><em>S. aureus</em> (63) Nasal swabs (63)</td>
<td>63 (10)</td>
<td>15.87</td>
<td>ST8 (8), ST5 (1), ST88 (1)</td>
<td>MecA (10)</td>
<td>TET(21), ERY(12), CLI(8), PG(60), CHL(9), KAN(12), GEN(12), TOB(12), SXT(6)</td>
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<td>Egypt</td>
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<td><em>E. faecium</em> (26), <em>E. faecalis</em> (47)</td>
<td>Urine (100)</td>
<td>100</td>
<td>VanA (2)</td>
<td>PEN(17), AMP(38), CIP(22), GEN(41), STR(73), CHL(12), TET(50), VAN(2)</td>
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<td>Vaginal swab (100)</td>
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<td>ermB (9), ermA (1), mefA/E (1), tetM (99), tetL (12), tetK (1), tetO (1)</td>
<td>ERY(17), CLI(14), AZI(16), TET(98) and CHL(1)</td>
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<td>Diabetic foot ulcers (39), surgical site infection (48) and abscess infections (25), burn discharges (15).</td>
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<td>mecA (29)</td>
<td>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)</td>
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<td>gyrA (C2402T, T2409C, T2460G) (60), gyrB (T1497C, A1578G) (5)</td>
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<td><em>S. aureus</em> (212)</td>
<td>Skin and soft tissue (100) and bloodstream (12)</td>
<td>212 (104)</td>
<td>dfrA (1), dfrG (100), dfrK+G (1), dfrB (2)</td>
<td>TMP(104), SXT(100), SMZ(6)</td>
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<td>tet(M) (13), tet(K) (10), aphA3 (7), aacA–aphD (5) and erm(C) (4).</td>
<td>TET(20), NOR(12), MXF(11), ERY(11), CLI(9), KAN(9), GEN(9) and CPT (6)</td>
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<td>PEN(208), TET(129), and ERY(18)</td>
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<td>Blood (93)</td>
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<td>MecA (32)</td>
<td>CLI(10), ERY(9) and SXT(9), MXF(1), RIF(3), TET(6), LUX(5)</td>
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<td>ST8 (5), ST152 (1), ST772 (1), ST14(1)</td>
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<td>PEN(53), OXA(15), GEN(3), ERY(5), TET(7), SXT(19), CHL(4), AMC (31), CIP(1)</td>
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<td>FOX(29), PEN(114), TET(30), CIP(28), RIF(6), GEN(20), CLIN(20), SXT(58), ERY(25), CH2</td>
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<td>S. aureus(27)</td>
<td>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)</td>
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<td>100</td>
<td>MechA(27) and blaZ(27), aac(6')–aph(2&quot;) (25), ermC (13)</td>
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<td>2016</td>
<td><em>E. faecium</em> (120) <em>E. faecalis</em> (40)</td>
<td>Blood (4)</td>
<td>4</td>
<td>ST80 (1), ST203 (1), ST18 (1), ST817 (1) van A (3) and van B (1) VAN (4) ND</td>
</tr>
<tr>
<td>2015</td>
<td><em>S. agalactiae</em> (128)</td>
<td>Vaginal and rectal swabs (128)</td>
<td>128 (121)</td>
<td>ND ermB, linB (28), mefA (48) ERY (27), CLI (32), TET (111), CIP (24) ND</td>
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<tr>
<td>2015</td>
<td><em>S. aureus</em> (2709)</td>
<td>Blood (2709)</td>
<td>2709 (1231)</td>
<td>ND mecA (1160) TET (NS), RIF (NS), MUP (NS), CIP (NS) and SXT (NS) MET (1231) SCC mec (1160)</td>
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<tr>
<td>2012</td>
<td><em>S. aureus</em> (13746)</td>
<td>Human (13746)</td>
<td>13746 (3298)</td>
<td>24 ST5 (1), ST612 (44), RpoB (H481Y, H481N, I527M) (NS) RIF (1760) ND</td>
</tr>
<tr>
<td>2014</td>
<td><em>S. aureus</em> (87)</td>
<td>Skin and soft tissue (39) and bloodstream (2)</td>
<td>87 (32)</td>
<td>ND dfrG (32) SMZ (5), TMP (32) ND</td>
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</tbody>
</table>

**Tanzania (1)** 2014

<table>
<thead>
<tr>
<th>Year</th>
<th>Species</th>
<th>Source/Location Description</th>
<th>Isolate Count</th>
<th>Antimicrobial Resistance Profile</th>
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<tbody>
<tr>
<td>2014</td>
<td><em>S. aureus</em> (87)</td>
<td>Skin and soft tissue (39) and bloodstream (2)</td>
<td>87 (32)</td>
<td>36.78 ND dfrG (32) SMZ (5), TMP (32) ND</td>
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<td>Year</td>
<td>Pathogen</td>
<td>Source(s)</td>
<td>ISOLATES</td>
<td>Antimicrobial Resistance Patterns</td>
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<tr>
<td>2015</td>
<td>S. aureus</td>
<td>Human</td>
<td>100</td>
<td>MecA (24), tet(K) (6), tet(L) (1) and/or tet(M)(18), erm (A), aph(2')-acc(6') (13)</td>
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<tr>
<td>2014</td>
<td>E. faecium, E. gallinarum</td>
<td>Blood (8), pus (3), urine (2), and rectal swabs (3)</td>
<td>100</td>
<td>VanA (13), vanC1 (3), erm(B) (16), tet(M)(15), tet(1), aac(6')-aph(2')(13) aph(3')-Illa (16), ant(6)(3)</td>
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<tr>
<td>2013</td>
<td>S. aureus</td>
<td>Human</td>
<td>100</td>
<td>MecA (59), Kan (62), Amk (62)</td>
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<tr>
<td>2012</td>
<td>S. agalactiae</td>
<td>Female genital (120), gastric fluid (106)</td>
<td>97.34</td>
<td>erm(B) (79), mef(A) (2), tet(M) (205), tet(L)(10), tet(O) (5), tet(T)(1)</td>
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</table>

**References:**

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- The copyright holder for this preprint (which was not this version posted July 10, 2018. ; https://doi.org/10.1101/366807doi: bioRxiv preprint
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<th>Year</th>
<th>Strain</th>
<th>Source</th>
<th>Isolates</th>
<th>MIC</th>
<th>Resistance</th>
<th>Antibiotics Sensitive</th>
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<tbody>
<tr>
<td>2012</td>
<td>S. haemolyticus (46)</td>
<td>Blood (19), intravascular catheters (14), others (13)</td>
<td>46 (36)</td>
<td>78.26</td>
<td>ND</td>
<td>mecA (28)</td>
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<tr>
<td>2012</td>
<td>S. aureus (1463)</td>
<td>Skin (1463)</td>
<td>160 (5)</td>
<td>3.13</td>
<td>ND</td>
<td>erm(C) (3), erm(A) (1), vat(B) (5), vga(B) (5)</td>
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<tr>
<td>2011</td>
<td>S. pyogenes (103)</td>
<td>Skin (43), respiratory tract (41), blood (12), fluids (4), endometrium (1), vagina (1), and urine (1).</td>
<td>103 (72)</td>
<td>70</td>
<td>emm18 (4), emm42 (9), emm76 (6), emm118 (10)</td>
<td>erm(B) (50), tet(M) (63), tet(O) (3)</td>
</tr>
<tr>
<td>2010</td>
<td>S. pyogenes (193)</td>
<td>Throat (63) (32.7%), pus (89), punctures (30), blood (4), other sources (7)</td>
<td>193 (13)</td>
<td>6.74</td>
<td>ND</td>
<td>ermB (6), mefA (2)</td>
</tr>
<tr>
<td>2010</td>
<td>S. agalactiae (160)</td>
<td>Urinary tract (160)</td>
<td>(160)</td>
<td>100</td>
<td>ND</td>
<td>erm(B) (132), erm(TR) (13), mef (A) (3)</td>
</tr>
<tr>
<td>2009</td>
<td>S. epidermis (77), S. mitis (50), E. faecium (45)</td>
<td>Blood cultures (55), central venous catheters, (29), stool cultures (40), respiratory tract (2) and different sites (3), systematic nasopharyngeal specimens (42), upper respiratory</td>
<td>172 (95)</td>
<td>55.23</td>
<td>ND</td>
<td>erm (C) (18), ermB (6), ermA (11), msrA (5)</td>
</tr>
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</table>

MIC: Minimum Inhibitory Concentration. ND: Not Determined.
tract(5) and other sources (3).

2008

<table>
<thead>
<tr>
<th>2013</th>
<th>S. aureus</th>
<th>Nasal swab</th>
<th>64(24)</th>
<th>37.5</th>
<th>ND</th>
<th>MecA (24)</th>
<th>OXA(22), GEN(8), CIP(12), CHL(9)</th>
<th>SCCmec (24)</th>
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[82]

<table>
<thead>
<tr>
<th>Country (n)</th>
<th>Year</th>
<th>Organism/Species (n)</th>
<th>Specimen Sources (n)</th>
<th>Sample size (Resistant isolates)</th>
<th>Resistant rate (%)</th>
<th>Clones (n)</th>
<th>Resistance genes/mechanisms (n)</th>
<th>Antibiotics to which strains were resistant</th>
<th>MGESs (n)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egypt (5)</td>
<td>2017</td>
<td>S. aureus(3), S.hycus(6), S.intermedns(3), S.epidermis(1), S.hemolytics(1), S.hominis(1), S.lugdunensis(3), S.simulans(1), S.scuri(4)</td>
<td>imported beef meat (23)</td>
<td>23(16)</td>
<td>69.57</td>
<td>ND</td>
<td>mecA(5)gyrA(12), grlA(10),gyrB(6),</td>
<td>AMP((6), CIP(8), CLI(15), ERY(6), GEN(14), MET(8), OXA(13), PEN(22), TET(6)</td>
<td>ND</td>
<td>122</td>
</tr>
<tr>
<td>2016</td>
<td>S. aureus (30)</td>
<td>raw chicken breast fillet (40), sliced luncheon meat (20), and chicken nuggets (20), Human (18)</td>
<td>40 (21)</td>
<td>33.33</td>
<td>ND</td>
<td>mecA (10)</td>
<td>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)</td>
<td>ND</td>
<td>51</td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td>S. aureus (200)</td>
<td>Raw milk (40), Damietta Cheese (40), Kareish cheese (40), ice cream (40), and yogurt (40)</td>
<td>200 (106)</td>
<td>53</td>
<td>ND</td>
<td>MecA(106)</td>
<td>TET(270), NEL(78), AMX(230), CLX(314), STR(186), SXT(58), GEN(114), PEN(364), RIF(152), CHL(128), AMK(146), VAN(36)</td>
<td>ND</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td>S. aureus (133)</td>
<td>cow milk samples (61), various origins (14), minced meat (6), sausage (4) and</td>
<td>133 (96)</td>
<td>72.18</td>
<td>ND</td>
<td>mecA (30)</td>
<td>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)</td>
<td>SCCmec (25)</td>
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9 Mobile genetic elements: plasmids, transposons; integrons
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<th>Country</th>
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<th>Isolate</th>
<th>Source</th>
<th>MDR Profile</th>
<th>Genotype</th>
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<tr>
<td>2011</td>
<td>S. aureus (4)</td>
<td>Dogs swab (70), cats swab (48), human nasal and oral swabs (50).</td>
<td>100</td>
<td>ND</td>
<td>mecA (4)</td>
<td>OXA(4), FOX(4), AMP(3), FOX(4), RIF(3), GEN(2), CLI(2), RIF(2), CIP(2), TET(1)</td>
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<tr>
<td>2011</td>
<td>S. agalactiae (92)</td>
<td>Camel (92)</td>
<td>92 (37)</td>
<td>ST617 (8), ST-612 (1), ST-616 (22)</td>
<td>TetM (37)</td>
<td>TET(37)</td>
<td>Tn916 (37)</td>
</tr>
<tr>
<td>2016</td>
<td>E. faecium (108), E. gallinarum, (30), E. faecalis (5), E. hirae. (5), E. mundii (12)</td>
<td>Cattle (130), chickens (130), manure (130)</td>
<td>167 (102)</td>
<td>61.0</td>
<td>ND</td>
<td>tetK (NS), tetL (NS), tetM (NS), telO (NS) and ermB (NS)</td>
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<td>2015</td>
<td>S. aureus (211)</td>
<td>Milk (211)</td>
<td>211 (124)</td>
<td>58.77</td>
<td>MecA (19)</td>
<td>PEN (124), AMP (99), OXA (93), VAN (47), TEC (116), TET (56), ERY (56), STR (89), KAN (55), GEN (47), SXT (37)</td>
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<tr>
<td>2015</td>
<td>E. faecalis (40), E. hirae (100), E. durans (60), E. faecium (120)</td>
<td>Pigs (320)</td>
<td>(320)</td>
<td>100</td>
<td>vanB, (320) vanC1 (320), vanC2/3 (320), ermB, (300)</td>
<td>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),</td>
<td>ND</td>
</tr>
<tr>
<td>2013</td>
<td>S. xylosus (18), S. aureus (28), S. haemolyticus (42), S. capitis (18), and other Staphylococcus spp. (14)</td>
<td>Animals (120)</td>
<td>(120)</td>
<td>100</td>
<td>mecA (NS), mphC (NS)</td>
<td>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)</td>
<td>SCCmec (NS)</td>
</tr>
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<td>Sample Type</td>
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<td>Antimicrobials</td>
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<td>----</td>
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<tr>
<td>Senegal</td>
<td>2012</td>
<td>S. aureus (57)</td>
<td>Swabs from pigs (300) and farmers</td>
<td>(57)</td>
<td>100</td>
<td>mecA (6)</td>
<td>PEN (57), SXT (35), TET (20)</td>
</tr>
<tr>
<td>Tanzania</td>
<td>2014</td>
<td>E. faecium (95) E. faecalis (9) E. gallinarum (7) E. Hirae (9)</td>
<td>Faecal samples of buffalo (35), wildebeest (40), zebra (40) and cattle (20)</td>
<td>120 (42)</td>
<td>35</td>
<td>ND</td>
<td>TetW (NS) and sulII (NS)</td>
</tr>
<tr>
<td>Tunisia</td>
<td>2017</td>
<td>E. faecium (31), E. faecalis (14), E. durans (6), E. casseliflavus (2), E. gallinarum (2)</td>
<td>Faecal sample of cats (20), dogs (50)</td>
<td>58 (31)</td>
<td>53.45</td>
<td>ND</td>
<td>ermB (22), tetM (5), tetL (16), tetL (4), ant (6) (7)</td>
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<tr>
<td></td>
<td>2013</td>
<td>E. faecalis (49), E. faecium (30), E. gallinarum (12), E. hirae (12), E. casseliflavus (2), E. durans (2)</td>
<td>Meat (199)</td>
<td>(119)</td>
<td>78.5</td>
<td>ST260 (1), ST454 (1), ST452 (1), ST22 (1), ST300 (1), ST455 (1), ST453 (1), ST456 (1)</td>
<td>tet(M) (36), tet(L) (32), erm(B) (33), aac(6)'-aph(2') (1), ant (6) (7)</td>
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<td>2013</td>
<td>E. mundtii (23), E. casseliflavus (20), E. hirae (19), E. faecalis (10), E. faecium (10), E. durans (7), E. gallinarum (7), E. dispar (2)</td>
<td>Cattle (92)</td>
<td>92 (72)</td>
<td>78</td>
<td>ND</td>
<td>erm(B) (7), tet(M) (4) and/or tet(L) (4)</td>
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<td></td>
<td>2012</td>
<td>S. aureus (73)</td>
<td>nasal swab from sheep (73)</td>
<td>73 (5)</td>
<td>6.85</td>
<td>MecA (5), blaZ (28), ant (6)'-la (5), , erm(C) (5), tet(K) (30)</td>
<td>PEN (5), STR (5), KAN (5), ERY (5), TET (5), FUS (5)</td>
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[85]

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<tr>
<th>Country (n)</th>
<th>Year</th>
<th>Organism/Species (n)</th>
<th>Specimen Sources (n)</th>
<th>Sample size (Resistant isolates)</th>
<th>Resistance rate (%)</th>
<th>Clones (n)</th>
<th>Resistance genes/mechanisms (n)</th>
<th>Antibiotics to which strains were resistant</th>
<th>MGEs&lt;sup&gt;10&lt;/sup&gt; (n)</th>
<th>Reference</th>
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<tr>
<td><strong>Nigeria (1)</strong></td>
<td>2017</td>
<td><em>E. faecium (100)</em></td>
<td>Vegetables, soil, farm, Cloacal swabs (25), Manure (8), Rectal swabs (2)</td>
<td>(100)</td>
<td>100</td>
<td>ND</td>
<td>aac(6’)-Ie-aph(2’)-la(35), aph(2’)-Ia(31), aph(3’)-Ila(32), ant(4’)-la(14)</td>
<td>AMP (63), GEN(37)</td>
<td>ND</td>
<td>48</td>
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<tr>
<td><strong>South Africa (3)</strong></td>
<td>2017</td>
<td><em>S. aureus</em></td>
<td>Recreational waters and beach sand (30)</td>
<td>(30)</td>
<td>100</td>
<td>ND</td>
<td>mecA(5), femA(16), rpoB(11), blaZ(16), ermB(15), tetM(8)</td>
<td>AMP (29), PEN (29), RIF(24), CLI(24), OXA (22), ERY(21), VAN(15), TET(13), SXT(13), CIP(10), GEN(1)</td>
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<td>195</td>
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<td><strong>E. faecium (30), E. durans. (15)</strong></td>
<td>2015</td>
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<td>waste water (32) and effluent (32)</td>
<td>(45)</td>
<td>100</td>
<td>ND</td>
<td>erm(B) (40), vanB, (42), vanC1 (42), vanC2/3(42)</td>
<td>PEN(38), ERY(40), CTX(43), GEN(28), IPM(43), TET(45), KAN(43), CIP(43), VAN(42), CLI(45)</td>
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<sup>10</sup> Mobile genetic elements: plasmids, transposons; integrons
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<th>Country</th>
<th>Species/Strain</th>
<th>Source</th>
<th>CIPs</th>
<th>Resistance Profile</th>
<th>mDNA Typing</th>
<th>IS16</th>
<th>Notes</th>
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</thead>
<tbody>
<tr>
<td>2013</td>
<td></td>
<td><em>E. faecium</em> (179)</td>
<td>Borehole Water (179)</td>
<td>179 (172)</td>
<td>96.09</td>
<td>ND</td>
<td>VanA (17) and vanB (17)</td>
<td>AMP(158), VAN (166)</td>
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<tr>
<td>2014</td>
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<td><em>S. aureus</em></td>
<td>Wastewater</td>
<td>12</td>
<td>100</td>
<td>ST3245(7), ST15(1)</td>
<td>blaZ(7), msrA(7), tetK(1), erm(8)</td>
<td>ND</td>
</tr>
<tr>
<td>2015</td>
<td></td>
<td><em>E. faecium</em> (86), <em>E. faecalis</em> (8), <em>E. casseliflavus</em> (6)</td>
<td>Hands (50), inanimate such as beds, treatment tables, toilets, faucets, wrists, sinks (250)</td>
<td>(100)</td>
<td>100</td>
<td>ST910 (13), ST80 (1)</td>
<td>erm(B) (71), tet(M) (18), aph(3')-llla (27), ant(6)-la (15), cat(A) (4), van(C2) (6)</td>
<td>ERY(73), TET(20), STR(27), and KAN(28), VAN(14), CHL(10), SXT(100), CIP(48), PRI(18)</td>
</tr>
<tr>
<td>2016</td>
<td></td>
<td><em>S. saprophyticus</em>, (30) <em>E. hirae</em> (23), <em>E. faecalis</em> (4), and <em>E. casseliflavus</em> (4)</td>
<td>Inanimate surfaces (83)</td>
<td>83 (32)</td>
<td>38.55</td>
<td>ND</td>
<td>MecA (20), msr(A) (32); erm(C) (8), tet(K) and/or tet(M) (21), aac(6')-le-aph(2')-la (16), (aph(3')-llla (19), ant(4')-la (n=14), ant(6'-la (3)</td>
<td>ERY(32), TET(21), GEN(16), KAN(19), TOB(14), STR(3), and GEN(5), VAN(4)</td>
</tr>
<tr>
<td>2016</td>
<td></td>
<td><em>E. faecium</em> (34), <em>E. hirae</em> (8), and <em>E. casseliflavus</em> (4)</td>
<td>Vegetable food (34), soil and irrigation water (27)</td>
<td>65 (40)</td>
<td>61.54</td>
<td>ST2 (5), ST16 (2), ST528 (2), ST56 (1), ST885 (1), ST886 (1)</td>
<td>erm(B) (12), tet(M), tet(L) (10), aph(3')-llla (10) ant(6) (2), vanC2 (4)</td>
<td>CIP(42), ERY(12), TET(10), KAN(10), CHL(5), STR(2), and GEN(5), VAN(4)</td>
</tr>
<tr>
<td>2016</td>
<td></td>
<td><em>E. faecium</em> (54), <em>E. faecalis</em> (17), <em>E. hirae</em> (8), <em>E. casseliflavus</em> (4), <em>E. durans</em> (2)</td>
<td>waste and surface water (114)</td>
<td>(85)</td>
<td>100</td>
<td>ST480 (1), ST531 (1), ST555 (1), ST532 (1), ST202 (1), ST314 (1), ST985 (1), ST30 (1), ST986 (1), ST12</td>
<td>aph(3')-llla (22), ant(6)-la (4), erm(B) (34), tet(M) (13), tet(L) (8), aac(6')-le-aph(2') (15)</td>
<td>GEN(22), KAN(22), STR(7), ERY(56), TET(13), SXT(79), CIP(6), and GEN(5), VAN(4)</td>
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Table 5. Distribution of resistance genes per clones in Africa.

<table>
<thead>
<tr>
<th>Clones</th>
<th>mecA</th>
<th>vanA</th>
<th>dfrG</th>
<th>tet(K)</th>
<th>tetM</th>
<th>Aph(3')-Ila</th>
<th>ermC</th>
<th>acc(6')-aph(2&quot;)</th>
<th>ermB</th>
<th>Van B</th>
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Figure 1. PRISMA-adapted flow chart showing included and excluded articles. All search was conducted on Pubmed and a final number of 77 manuscripts were used for the qualitative analysis.

Figure 2. Frequency and distribution of mobile genetic elements (MGEs), resistance genes and antibiotics 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 ermB were the most dominant resistance genes detected, followed by tetM, dfrG, vanB, vanC1 etc. 2a(ii) 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 (emm18, emm42, emm76, emm118), E. faecium (ST18, ST80, ST910) and S. aureus (ST5, ST22, ST35) were associated with Tn916, IS16 and SCCmec respectively.

Figure 3. Frequency 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. SCCmec was the commonest MGE in most of the countries except in Tunisia where IS16 and Tn916 were higher in prevalence. S. aureus ST8 and ST80 were the most common clones reported, followed by E. faecium ST317.

[90]
PRISMA 2009 Flow Diagram

Identification

Records identified through database searching (PubMed) (n = 1466)

Additional records identified through other sources (n = 20)

Records after duplicates removed (n = 1,127)

Screening

Records screened (n = 1,127)

Records (reviews, non-English papers) excluded (n = 854)

Eligibility

Full-text articles assessed for eligibility (n = 273)

Full-text articles excluded: (n = 196)

Included

Studies included in qualitative synthesis (n = 76)

Studies included in quantitative synthesis (meta-analysis) (n = 76)

For more information, visit www.prisma-statement.org.

Figure 2ai. Frequency and distribution of mobile genetic elements (MGEs), resistance genes and antibiotics with recorded resistance in Gram-positive bacteria in Africa.
Figure 2aii. Frequency and distribution of mobile genetic elements (MGEs), resistance genes and antibiotics with recorded resistance in Gram-positive bacteria in Africa.
Figure 2b. Frequency and distribution of mobile genetic elements (MGEs), resistance genes and antibiotics with recorded resistance in Gram-positive bacteria in Africa.
Figure 3a. Frequency 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