The global prevalence of Daptomycin, Tigecycline, Quinupristin/Dalfopristin, and Linezolid-resistant \textit{Staphylococcus aureus} and coagulase-negative staphylococci strains: a systematic review and meta-analysis

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\textbf{Abstract}

\textbf{Objective:} Methicillin-resistant \textit{Staphylococcus aureus} (MRSA) and methicillin-resistant coagulase-negative \textit{Staphylococcus} (MRCoNS) are among the main causes of nosocomial infections, which have caused major problems in recent years due to continuously increasing spread of various antibiotic resistance features. Apparently, vancomycin is still an effective antibiotic for treatment of infections caused by these bacteria but in recent years, additional resistance phenotypes have led to the accelerated introduction of newer agents such as linezolid, tigecycline, daptomycin, and quinupristin/dalfopristin (Q/D). Due to limited data availability on the global rate of resistance to these antibiotics, in the present study, the resistance rates of \textit{S. aureus}, Methicillin-resistant \textit{S. aureus} (MRSA), and CoNS to these antibiotics were collected.

\textbf{Method:} Several databases including web of science, EMBASE, and Medline (via PubMed), were searched (September 2018) to identify those studies that address MRSA, and CONS resistance to linezolid, tigecycline, daptomycin, and Q/D around the world.

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**Result:** Most studies that reported resistant staphylococci were from the United States, Canada, and the European continent, while African and Asian countries reported the least resistance to these antibiotics. Our results showed that linezolid had the best inhibitory effect on *S. aureus*. Although resistances to this antibiotic have been reported from different countries, however, due to the high volume of the samples and the low number of resistance, in terms of statistical analyzes, the resistance to this antibiotic is zero. Moreover, linezolid, daptomycin, and tigecycline effectively (99.9%) inhibit MRSA. Studies have shown that CoNS with 0.3% show the lowest resistance to linezolid and daptomycin, while analyzes introduced tigecycline with 1.6% resistance as the least effective antibiotic for these bacteria. Finally, MRSA and CoNS had a greater resistance to Q/D with 0.7 and 0.6%, respectively and due to its significant side effects and drug-drug interactions; it appears that its use is subject to limitations.

**Conclusion:** The present study shows that resistance to new agents is low in staphylococci and these antibiotics can still be used for treatment of staphylococcal infections in the world.

**Keywords:** Linezolid, Daptomycin, Tigecycline, Quinupristin/Dalfopristin, Synercid, Meta-analysis, *S. aureus*, MRSA, CoNS

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**Introduction**

Methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant coagulase-negative staphylococci (MRCoNS) represent main causes of hospital- and community-acquired infections; because of their increasing numbers and elevated mortality, morbidity, and medical expenses, they have become a global concern in recent years [1, 2]. Staphylococci contain virulence factors and toxins that cause various diseases including blood, skin and soft tissues infections, nosocomial infections connected with the presence of medical devices, and toxic shock syndrome [3]. The mecA gene, located in the SCCmec region, is responsible for the expression of methicillin resistance through PBP2a—an altered penicillin-binding protein that is characterized by its low affinity to penicillin and other beta-lactam drugs [4]. For both MRSA and MRCoNS, vancomycin is used as the first line drug for treatment. However, in recent years, decreased susceptibility and even resistance to vancomycin and other antibiotics, including aminoglycosides, tetracyclines, and lincosamides, have been reported in many parts of the world [5–7]. Therefore, for the treatment of severe infections caused by multi-drug resistant staphylococci, new antibiotics such as daptomycin, linezolid, tigecycline, and Quinupristin/Dalfopristin (Q/D) were introduced [8]. Daptomycin, a cyclic lipopeptide antibiotic, is the second most important anti-MRSA drug, which received FDA approval in 2003 and approval by the European Medicines Agency (EMA) in 2005. It is mostly used for the treatment of acute bacterial skin and soft tissues infections [9]. Daptomycin is still quite active against staphylococci and enterococci; however, resistance to this antibiotic has been reported over the past years due to mutation of various genes (*dltABCD* genes, *mprF* and *rpoB*), causing changes in membrane fluidity, cell wall thickness, and membrane charge [10, 11]. Tigecycline is an example of a new class of broad-spectrum antimicrobial agents known as glycylcyclines with activity against Gram-positive and Gram-negative organisms. This antibiotic was approved by FDA (2005–2009) for the treatment of skin infections, intra-abdominal infections and community-acquired bacterial pneumonia [12, 13]. Tigecycline provides an alternative treatment for complicated MRSA and vancomycin resistant enterococci (VRE) infections; due to mutations in *mepR* and *mepA* genes that result in overexpression of efflux pumps, resistant phenotypes have been reported in recent studies [13]. Linezolid is another new antibiotic that was approved in 2000 for the treatment of MRSA and MRCoNS infections and infections caused by VRE. Linezolid binds to the 50S ribosomal subunit of the 23S rRNA molecule and inhibits protein synthesis. *Cfr* gene encodes a methyltransferase that modifies the 23S rRNA site of the 50S ribosomal subunit and prevents linezolid from binding to it [14]. Q/D is composed of two streptogramins (70% dalfopristin (streptogramin A) and 30% quinupristin (streptogramin B)), which was approved in 1999 as a treatment option for VRE and MRSA infections. This drug consists of quinupristin that inhibits late-stage protein synthesis, while dalfopristin inhibits early-stage protein synthesis. It should be noted that, Synercid® (formerly RP59000; Rhone-Poulenc) is the first semisynthetic injectable streptogramin and it is used as a trade name for Q/D [15, 16]. The World Health Organization (WHO) has considered MRSA as important antibiotic-resistant bacteria and put them on their priority list. All organisms on that list require new treatment modalities and substantiate an urgent overall need for new antimicrobial drugs [17]. According to the authors’ knowledge, no comprehensive data are available on the resistance levels to daptomycin, Q/D, linezolid, and tigecycline among MRSA and MRCoNS strains. This study aims to investigate the prevalence of resistance to the mentioned antibiotics among staphylococcal strains isolated from clinical samples around the world.
Methods
We conducted a literature search through databases, including web of science, EMBASE, and Medline (via PubMed), using the versions of September 2018. The historic publication year was unrestricted and the search was limited to original articles. The following search keywords were obtained from the National Library of Medicine’s medical subject heading (MeSH) terms or titles or abstracts with the help of Boolean operators (and, or): “staph”, “staphylococcus”, “staphylococci”, “staphyloccocal”, “staphylococcaceae” and “Linezolid”, “Daptomycin”, “Tigecycline”, “Quinupristin/Dalfopristin”, and “Synercid”. Two independent reviewers screened the titles and abstracts of original articles and posters; if an article appeared relevant (Figs. 1 and 2), the full text was reviewed. We used the Clinical and Laboratory Standards Institute (CLSI) and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for daptomycin, linezolid, Q/D resistance and tigecycline resistance in Staphylococci, respectively (there is no standard for tigecycline in staphylococci in the CLSI). The resistance cut-off rates are defined in the following ranges ≤1 mg/L, ≥8 mg/L, ≥4 mg/L, and > 5 mg/L, respectively. We considered all articles that evaluated antibiotic resistance by different methods such as broth microdilution (BMD), agar dilution, disk diffusion (DD), E-test and Vitek or Vitek 2 or any other automated instruments. It should be noted that, the final version of the CLSI (2018) states that staphylococci with resistant results to linezolid by DD should be confirmed by using an MIC method, therefore, studies that only used the DD method for susceptibility to the linezolid were excluded. Moreover, case reports, basic research on the resistance mechanism of the mentioned antibiotics, and review articles were excluded from this study.

Meta-analysis
Quality assessment
All reviewed studies were subjected to a quality assessment (designed by the Joanna Briggs Institute) and only
high-quality investigations were evaluated in our final analysis [18–116].

Data analysis
The analysis was performed by STATA (version 14.0) software. The data were pooled using a fixed effects model (FEM) [117] and a random effects model (REM) [118]. Statistical heterogeneity was assessed by statistical methods [119] and was evaluated using the Q-test and the I2 statistical methods [118]. P-value < 0.1 was regarded as statistically significant [120].

Results
This study identified 1813, 2222, 512, and 636 articles for daptomycin, linezolid, Q/D (Synercid), and tigecycline, respectively, in the first step. Then, upon secondary screening, a large number of articles were excluded on the basis of title and abstract evaluation because of the lack of relevance to the study principles, and the reasons for the deletion of these articles are presented in Figs. 1 and 2. Therefore, 477, 768, 124, and 214 articles for the mentioned antibiotics were reviewed with full text, and a number of papers were excluded from the study for the reasons listed in Figs. 1 and 2. Finally, 37, 51, 17, and 22 eligible studies for daptomycin, linezolid, Q/D, and tigecycline were chosen for final analysis, respectively. Resistance percentage in S. aureus, MRSA and CONS to the mentioned antibiotics is shown in Table 1. The characteristics of the included articles are summarized in Tables 2, 3, 4 and 5. All pertinent studies were included from around the world (25 different countries) (Tables 2, 3, 4 and 5). The USA was the most frequently represented country for all antibiotics followed by Canada and European countries (Italy and Spain). From the African continent, only one study from Nigeria, where tigecycline resistance in one isolate was reported (Fig. 3). Linezolid-resistant staphylococci from 15 countries were included in the present study, which was more widely distributed among antibiotics (Fig. 4). Strains were isolated from various clinical samples including blood, wound, skin, urine, respiratory tract, sputum, catheter, bone,
Table 1 Resistance percentages in S. aureus, MRSA and CoNS to different antibiotics

| S. aureus | Linezolid | Daptomycin | Tigecycline | Q/D |
|----------|-----------|------------|-------------|-----|
| Resistance rate (%) | 0.0% [CI% (0.0–0.0)] | 0.1 [CI% (0.1–0.1)] | 0.1 [CI% (0.0–0.1)] | 0.1 [CI% (0.1–0.2)] |
| p-value | 0.04 | 0.02 | 0.09 | 0.88 |
| MRSA | Resistance rate (%) | 0.1 [CI% (0–0.1)] | 0.1 [CI% (0.1–0.1)] | 0.1 [CI% (0–0.1)] | 0.7 [CI% (0.3–1)] |
| p-value | 0.33 | 0.00 | 0.00 | 0.00 |
| CoNS | Resistance rate (%) | 0.3 [CI% (0.2–0.4)] | 0.3 [CI% (0.2–0.4)] | 1.6 [CI% (1.2–1.9)] | 0.6 [CI% (0.3–0.9)] |
| p-value | 0.04 | 0.37 | 0.00 | 0.00 |

MRSA; Methicillin-resistant Staphylococcus aureus, CoNS; Coagulase-negative staphylococci, Q/D; Quinupristin / Dalfopristin

etc. A majority of studies used BMD, E-test, agar dilution, disk diffusion, and Vitek or vitek 2. Our results showed that linezolid had the best inhibitory effect on S. aureus. Although resistance to the linezolid has been reported from different countries, due to the high volume of the samples and the low number of resistance, in terms of statistical analyzes, the resistance to this antibiotic is zero. Moreover, linezolid and tigecycline effectively (99.9%) inhibit MRSA (Table 1). Studies have shown that CoNS with 0.3% show the lowest resistance to linezolid and daptomycin, while analyzes introduced tigecycline with 1.6% resistance as the least effective antibiotic for these bacteria. Finally, MRSA and CoNS had a greater resistance to Q/D with 0.7 and 0.6%, respectively.

**Discussion**

MRSA is a frequent cause of skin and soft tissue infection, pneumonia, endocarditis, bone and joint infection in individuals with some risk factors such as indwelling devices, surgical interventions, long-term antibiotic use, intensive care admission, and dialysis [121, 122]. In recent years, this bacterium has had very high health costs for patients due to increased length of hospital stay and longer duration of antibiotic treatment [123]. Moreover, CoNS are opportunistic pathogens that lead to 30% of hospital-induced infections and 10% of uncomplicated urinary tract infections in young women and native valve endocarditis, especially in immunocompromised patients [124, 125]. Currently, the treatment of MRSA and CoNS is difficult due to the high antibiotic resistance to beta-lactams and other antibiotic classes, and newer agents such as linezolid, daptomycin, Q/D, and tigecycline can be used as alternative if available and deemed cost-effective. Accordingly, this study collected data from resistance to these antibiotics all over the world to determine the extent of their clinical application. The analysis of the results showed that linezolid had the highest inhibitory effect on S. aureus; due to the high volume of the samples in the studies and a small number of bacteria that have been reported as resistant (mostly in the United States), in terms of statistical analyzes, the percentage of resistance to this antibiotic is zero (Table 1). It should be noted that the studies (20 studies) that used the DD method as an antibiotic susceptibility test for linezolid were removed from this study and not entered into statistical analyses. Furthermore, the most linezolid-resistance S. aureus isolates isolated from pneumonia and blood infections were the highest in number. In addition to the good effect of linezolid on S. aureus, this drug also had the efficient activity against MRSA, while the resistance of CoNS was higher to this antibiotic. One of the reasons for the increased resistance in CoNS is the ability of these bacteria to develop resistance quite easily following linezolid exposure, even though this has not been proven in vitro, to the best of our knowledge. Furthermore, more Linezolid-resistant CoNS (LRCoNS) were associated with outbreaks; 50% of those studies that analysed LRCoNS involved clonal LRCoNS across one or more patients and facilities. The studies that used MLST for typing of resistant-linezolid CoNS, ST5, ST22 and for S. aureus ST228, ST8 and ST5 were reported to be more sequence types related to linezolid resistance [25, 67].

Tigecycline had the best effect (equal to linezolid) on MRSA, and very low resistance in S. aureus was observed; however, CoNS with 1.6% showed the highest percentage of resistance to this antibiotic (Table 1). Since very few studies have reported the resistance of CoNS to tigecycline (Fig. 3), the high percentage of resistance noted by tigecycline cannot be deemed. The geographic diversity of the countries that reported the tigecycline resistance was higher than those with linezolid, thus showing more use of this antibiotic in different parts of the world. Recent MRSA infection treatment guidelines have not incorporated tigecycline. The reason is the FDA’s September 2010 safety statement, which describes increased overall mortality among severely infected patients.
| First name | Time of study | Published time | Country | Total staphylococcus | S. aureus | MRSA | CoNS | S. aureus Tigecycline-Resistant | MRSA Tigecycline-Resistant | CoNS Tigecycline-Resistant | Susceptibility testing method | Isolation source                        |
|------------|---------------|----------------|---------|----------------------|-----------|------|-----|-------------------------------|-----------------------------|-----------------------------|--------------------------------|----------------------------------|
| Morrissey  | 2011–2012     | 2011–2012      | Germany | 81                   | 43        | 43   | 38  | 1                             | 1                           | 6                           | BMD                            | Bacteraemia and Skin infection   |
| Ayepola    | 2015          | 2015           | Nigeria | 209                  | 209       | 6    | 1   | 1                             | 1                           |                             | Automated VITEK-2 system         | Clinical specimens               |
| Garza-González E | 2009–2013 | 2009–2013      | Honduras | 61                   | 61        | 21   | 1   | 1                             | 1                           |                             | BMD                            | Urine, Blood, Respiratory tract, Skin, Wound, Body fluid |
| Garza-González E | 2009–2013 | 2009–2013      | El Salvador | 34                   | 34        | 19   | 2   | 2                             | 2                           |                             | BMD                            | Urine, Blood, Respiratory tract, Skin, Wound, Body fluid |
| Xi         | 2014–2016     | 2014–2016      | China   | 15                   | 13        | 11   | 2   | 1                             | 1                           |                             | DD                             | Clinical specimens               |
| Wang       | 2006–2010     | 2010–2010      | Taiwan  | 670                  | 670       | 670  | 3   | 3                             | 3                           |                             | Automated VITEK-2 system         | Blood infection                   |
| Adam       | 2007–2011     | 2010–2011      | Canada  | 4177                 | 4177      | 1266 | 6   | 3                             |                             |                             | BMD                            | Blood, Respiratory tract, Urine, Wound |
| Cassetari  | 2010–2011     | 2010–2011      | Italy   | 280                  | 201       | 102  | 79  | 1                             |                             |                             | BMD                            | Skin and soft tissue infections, Hospital-acquired pneumonia |
| Bongiorno  | 2012          | 2012           | Italy   | 50                   | 50        | 50   | 2   | 2                             |                             |                             | BMD                            | Lower respiratory tract infections, Skin and soft-tissue, Blood |
| Zhanel     | 2007–2011     | 2007–2011      | Canada  | 6623                 | 5443      | 2500 | 1180| 8                             | 4                           |                             | BMD                            | Wound, Urinary tract, Blood          |
| Flamm      | 2010          | 2010           | USA     | 4049                 | 3105      | 1578 | 944 | 2                             | 1                           |                             | BMD                            | Blood, Pneumonia, Skin            |
| Flamm      | 2013          | 2013           | USA     | 3433                 | 3035      | 1454 | 398 | 1                             |                             |                             | BMD                            | Blood, Skin, Soft tissue          |
| Yousefi    | 2014–2015     | 2014–2015      | Iran    | 54                   | 54        | 54   | 2   | 2                             |                             |                             | BMD                            | UTI                             |
| Hodile     | 2010–2014     | 2010–2014      | France  | 440                  | 440       | 325  | 5   | 2                             |                             |                             | BMD                            | Bronchopulmonary infections        |
| Chen       | 2009–2010     | 2009–2010      | Taiwan  | 1725                 | 1725      | 1725 | 1   | 1                             |                             |                             | BMD                            | Blood, Pus                       |
| Zhanel     | 2007–2009     | 2007–2009      | Canada  | 3910                 | 3589      | 889  | 321 | 5                             | 1                           |                             | BMD                            | Wound, Urinary tract, Blood, Respiratory tract |
| Vega       | 2004–2015     | 2004–2015      | Latin America | 4563        | 4563      | 2202 | 4   | 2                             |                             |                             | BMD                            | Clinical specimens               |
| Sader      | 2006–2012     | 2006–2012      | USA     | 28,278               | 28,278    | 14,756 | 2 | 2                           |                             |                             | BMD                            | Blood, Wound, Skin, Pneumonia       |
| Putnam     | 2004–2008     | 2004–2008      | USA     | 18,917               | 18,917    | 10,242 | 3 | 3                           |                             |                             | BMD                            | Skin, Intra-abdominal, Bacteraemia |
| Karlowys   | 2011–2015     | 2011–2015      | Canada  | 3760                 | 3408      | 728  | 18  | 14                           |                             |                             | BMD                            | Urine, Blood, Respiratory tract, Skin, Wound, Body fluid |
| Morrissey  | 2011          | 2011           | Italy   | 82                   | 41        | 41   | 41  | 1                             |                             |                             | BMD                            | Bacteraemia, Skin infection       |
| First name            | Time of study | Country | Total *S. aureus* | *S. aureus* Tigecycline-Resistant | Total MRSA | MRSA Tigecycline-Resistant | Total CoNS | CoNS Tigecycline-Resistant | Susceptibility testing method | Isolation source                  |
|----------------------|---------------|---------|------------------|-------------------------------|------------|--------------------------|------------|----------------------------|-------------------------------|--------------------------------|
| Brzychczywolch [26]  | 2009          | Poland  | 100              | 100                           |            |                          |            |                            | Disk diffusion                | Blood, Pneumonia               |
| Jan [56]             | 2006–2009     | France  | 216              | 26                            | 6          | 190                      |            |                            | Agar dilution                 | Implantable cardioverter defibrillator infection |
| Sader [101]          | 2000–2004     | USA     | 12,335           | 8765                          | 3050       | 3570                     | 5          |                            | Broth microdilution            | Blood                           |

Abbreviations: DD; disk diffusion, BMD; broth microdilution
| First name | Time of study | Published time | Country | Total staphylococcus | S. aureus | MRSA | CoNS | S. aureus Q/D-Resistant | MRSA Q/D-Resistant | CoNS Q/D-Resistant | Susceptibility testing method | Isolation source |
|------------|---------------|----------------|---------|----------------------|-----------|------|------|------------------------|------------------|------------------|-------------------------------|----------------|
| Petrelli [79] | 2003–2004    | 2007           | Italy   | 37                   | 37        | 16   | 1    | DD                     |                  |                  | Blood infection              | Blood infection |
| McDonald [72] | 1998–2000    | 2004           | Taiwan  | 554                  | 400       | 240  | 154  | 1                      |                  |                  | Blood, Urine, Wound, Respiratory tract | Blood, Urine, Wound, Respiratory tract |
| Luh [69]    | 1996–1999    | 2000           | Taiwan  | 554                  | 149       | 80   | 405  | 1                      | 1                | 32               | Blood, Respiratory tract, Cerebrospinal fluid, Bile, Wound, Rectal swab | Blood, Respiratory tract, Cerebrospinal fluid, Bile, Wound, Rectal swab |
| Picazo [85] | 2010         | 2011           | Spain   | 702                  | 503       | 187  | 199  | 1                      |                  |                  | Medical canters              | Medical canters |
| Sader [103] | 2002–2004    | 2006           | Germany | 1232                 | 715       | 517  | 1    | 1                      |                  |                  | Skin infection, Blood            | Skin infection, Blood |
| Sader [103] | 2002–2004    | 2006           | Italy   | 685                  | 386       | 299  | 1    | 1                      |                  |                  | Skin infection, Blood            | Skin infection, Blood |
| Sader [103] | 2002–2004    | 2006           | UK      | 593                  | 531       | 62   | 1    | 1                      |                  |                  | Skin infection, Blood            | Skin infection, Blood |
| Draghi [36] | 2004         | 2005           | USA     | 3368                 | 2872      | 1556 | 496  | 2                      |                  |                  | Skin infection, Blood            | Skin infection, Blood |
| Ballow [21] | 2002         | 2002           | North America | 11,671         | 7038      | 2721 | 4633 | 10                     | 10                | 20               | BMD                          | Medical canters |
| Decousser [34] | 2000        | 2003           | France  | 364                  | 242       | 87   | 122  | 1                      |                  |                  | E-test                      | Blood |
| Hsuhe [52]  | 1991–2003    | 2005           | Taiwan  | 100                  | 100       | 100  | 1    | 1                      |                  |                  | Agar dilution                | Clinical specimens |
| Limoncu [68] | 2003         | 2003           | Turkey  | 149                  | 149       | 52   | 30   | 5                      |                  |                  | BMD                          | Clinical specimens |
| Jones [59]  | 1996–1997    | 2001           | USA     | 1778                 | 1290      | 623  | 488  | 7                      | 6                 | 1                | DD                          | Wound, Abdominal cavity, Respiratory tract, Urinary tract, Blood |
| Anastasiou [19] | 2001–2003   | 2008           | North America | 360            | 360       | 360  | 6    | 6                      |                  |                  | BMD                          | Hospital |
| Picazo [82] | 2008         | 2009           | Spain   | 703                  | 520       | 201  | 183  | 5                      | 5                 |                  | BMD                          | Blood |
| Jones [63]  | 2007         | 2008           | USA     | 4338                 | 3318      | 1930 | 1020 | 2                      | 2                 |                  | BMD                          | Medical canters |
| Pfaller [80] | 2002–2005   | 2010           | USA     | 13,053               | 10,917    | 4947 | 2136 | 1                      |                  |                  | BMD                          | Medical canters |
| John [58]   | 2002         | 2002           | Canada  | 658                  | 658       | 15   | 1    | 1                      |                  |                  | Agar dilution                | Patient in hospitals |
| Sader [103] | 2002–2004    | 2006           | France  | 1479                 | 1100      | 379  | 16   | 7                      |                  |                  | BMD                          | Skin infection, Blood |
| Sader [103] | 2002–2004    | 2006           | Greece  | 185                  | 128       | 57   | 2    | 2                      |                  |                  | BMD                          | Skin infection, Blood |
who are treated with tigecycline; besides, cause of the excess deaths in these trials usually remains uncertain. However, it is likely that most cases of death among such patients were associated with the infection progression. Moreover, this antibiotic is not authorized for pneumonia or diabetic foot infections. Although tigecycline is recommended for treating skin and soft tissue infections, previous studies have shown no significant difference between this antibiotic and other new drugs, and tigecycline is referred to as the second or third line of treatment for infections caused by MRSA [129]. Therefore, although the present study showed that S. aureus resistance to tigecycline is low, the use of this drug still has limitations in treating staphylococcal infections. Daptomycin is another new drug used to treat infections caused by Gram-positive bacteria including MRSA and VRE. It kills microorganisms by rapid membrane depolimerisation, loss of membrane potential and disruption of DNA, as well as RNA and protein-synthesis [128]. The daptomycin resistance among staphylococcal strains has been reported from around the world, although there has been no resistance report from the African continent. The United States had the highest rate of resistance (42.5% of studies); India, Taiwan, and Saudi Arabia reported resistance to this antibiotic from the Asian continent, and most of the bacteria were isolated from wounds and blood infections. In the United States and Europe, daptomycin is used for treating skin and soft tissue infections, bacteraemia, and endocarditis caused by S. aureus [129]. Previous studies have reported that it is not very practical to use daptomycin for the treatment of pneumonia, because it is deactivated by pulmonary surfactants. Therefore, vancomycin and linezolid are recommended to treat pneumonia caused by MRSA [130]. Our results have shown that daptomycin has the best performance with linezolid regarding CoNS, indicating that this antibiotic can be used for a therapeutic approach to infections caused by these bacteria. Furthermore, the present study showed that resistance to daptomycin has been very low (0.1–0.3%); considering that this antibiotic shortens the duration of the treatment of soft-tissue infections due to MRSA compared to vancomycin [131], it can be used to a greater degree for treating the mentioned infections. However, spontaneous resistance to daptomycin seems to occur rarely [132], and vancomycin can also decrease the function of this drug [130, 133]. Therefore, it is possible to isolate daptomycin-resistant strains from the areas where this antibiotic is not even used, and physicians usually use alternative agents (linezolid and vancomycin) instead of daptomycin, which can be considered as a factor. Daptomycin can be one of the choices for treating staphylococci-induced infections if there is a strong possibility based on local microbiological data or recent treatment history of vancomycin in an infected patient with MIC of > 1 μg/mL.

Q/D comprises quinupristin and dalfopristin in a 30:70 ratio, which prevents protein synthesis in bacteria [134]. Studies have shown that Q/D with 0.7% has the highest resistance rate amongst MRSA strains (Table 1). Resistance reports were gathered from the continents of America, Asia, and Europe, although more studies have been carried out in European countries. This antibiotic is used for the treatment of VRE bloodstream infection and complicated skin and soft tissues infections caused by MRSA and Staphylococcus pyogenes. However, the results of this study showed that Q/D had a weaker inhibitory effect than linezolid and daptomycin on S. aureus, MRSA, and CoNS (Table 1); on the other hand, it has significant side effects (myalgia, arthralgia, increased alkaline phosphatase, and nausea), high drug interactions, and treatment costs [135], which led to the limited use of this antibiotic. Therefore, it is better to use other new alternative antibiotics instead of Q/D for treating of staphylococcal infections. The present study showed that although linezolid, Q/D, daptomycin, and

### Table 3

Characteristics of the articles that were included in the meta-analysis and reported resistance to Q/D (Continued)

| First name | Time of study | Published time | Country | Total staphylococcus | S. aureus | MRSA CoNS | S. aureus Q/D-Resistant | MRSA Q/D-Resistant | CoNS Q/D-Resistant | Susceptibility testing method | Isolation source |
|-----------|---------------|----------------|---------|---------------------|-----------|-----------|-------------------------|-------------------|----------------|-----------------------------|----------------|
| Sader [103] | 2002–2004 | 2006 | Turkey | 462 | 291 | 171 | 2 | BMD | Skin infection, Blood |
| Khan [66] | 2012–2013 | 2014 | Saudi Arabia | 190 | 190 | 4 | Microscan Walk Away system (40si, siemens) | Blood |

Abbreviations: DD; disk diffusion, BMD; broth microdilution
Table 4 Characteristics of the articles that were included in the meta-analysis and reported resistance to daptomycin

| First name   | Time of study | Published time | Country | Total staphylococcus | S. aureus | MRSA | CoNS | S. aureus Daptomycin-Resistant | MRSA Daptomycin-Resistant | CoNS Daptomycin-Resistant | Susceptibility testing method | Isolation source                              |
|--------------|---------------|----------------|---------|----------------------|-----------|------|------|-------------------------------|--------------------------|---------------------------|---------------------------------|--------------------------------|
| Morrissey    | 2011          | 2012           | Italy   | 82                   | 41        | 41   | 41   | 3                             | 3                        | 1                         | BMD                             | Bacteraemia                     |
| Mendes       | 2007–2009     | 2010           | USA     | 4077                 | 4077      | 4077 | 6    | 6                             | 6                        | 1                         | BMD                             | Bacteraemia, Pneumonia           |
| Biedenbach   | 2003–2004     | 2007           | Australia | 1559                | 1257      | 480  | 302  | 1                             | 1                        | BMD                      |                                 | Skin, Blood, Respiratory tract infection |
| Picazo       | 2001–2010     | 2011           | Spain   | 1130                 | 1130      | 1130 | 1    | 1                             | 1                        | BMD                      |                                 | Medical centers                |
| Picazo       | 2001–2006     | 2010           | Spain   | 1186                 | 755       | 755  | 431  | 1                             | 1                        | BMD                      |                                 | Blood                           |
| Vamsimohan   | 2011          | 2014           | India   | 50                   | 50        | 50   | 2    | 2                             | 2                        | E-test                   |                                 | Wound, Pus swab                |
| Pfüller      | 2002–2005     | 2010           | USA     | 13,053               | 10,497    | 2136 | 5    | 2                             | 4                        | BMD                      |                                 | Medical centers                |
| Jevitt       | 1996–2001     | 2003           | USA     | 119                  | 88        | 47   | 31   | 3                             | 3                        | 2                        | BMD                             | Medical centers                |
| Rouse        | 1985–2005     | 2007           | USA     | 184                  | 68        | 68   | 116  | 2                             | 2                        | BMD                      |                                 | Endocarditis, Joint infection   |
| Rolston      | 2011          | 2013           | USA     | 165                  | 106       | 72   | 59   | 1                             | 1                        | 3                        | E-test                          | Surgical wounds, Pleural, Ascitic fluid |
| Cuny         | 2011–2013     | 2015           | Germany | 1952                 | 1952      | 1952 | 7    | 7                             | 7                        | BMD                      |                                 | Blood                           |
| Sader        | 2007–2008     | 2009           | USA     | 9230                 | 8077      | 4514 | 1153 | 8                             | 8                        | 6                        | BMD                             | Blood, Skin, Pneumonia           |
| Kao          | 2006–2008     | 2011           | Taiwan  | 470                  | 470       | 470  | 2    | 2                             | 2                        | BMD                      |                                 | Blood                           |
| Jain         | 2011–2012     | 2013           | India   | 73                   | 68        | 31   | 5    | 3                             | 3                        | E-test                   |                                 | Soft tissue, Blood, Intra-abdominal infection |
| Jones        | 2007          | 2008           | USA     | 4338                 | 3318      | 1930 | 1020 | 4                             | 3                        | 4                        | BMD                             | Medical centers                |
| Jones        | 2006          | 2007           | USA     | 3721                 | 2913      | 1648 | 808  | 3                             | 3                        | BMD                      |                                 | Pneumonia, Wound, Urinary tract |
| Sader        | 2005–2010     | 2011           | USA     | 22,858               | 22,858    | 12,858 | 13     | 12                         | BMD                      |                                 |                                 | Blood                           |
| Flamm        | 2010          | 2012           | USA     | 4049                 | 3105      | 1578 | 944  | 5                             | 5                        | BMD                      |                                 | Blood, Pneumonia, Skin           |
| Farrell      | 2008          | 2009           | USA     | 4012                 | 3156      | 1752 | 856  | 3                             | 3                        | 6                        | BMD                             | Pneumonia, Wound, Urinary tract |
| Flamm        | 2013          | 2015           | USA     | 3433                 | 3035      | 1454 | 398  | 1                             | 1                        | BMD                      |                                 | Blood, Skin, Soft tissue       |
| Karlowsky    | 2011–2015     | 2017           | Canada  | 3760                 | 3408      | 728  | 1    | 1                             | 1                        | BMD                      |                                 | Urine, Blood, Respiratory tract, Skin, Wound, Body fluid |
| Sader        | 2009–2013     | 2015           | USA     | 4426                 | 4426      | 2013 | 7    | 7                             | 7                        | BMD                      |                                 | Blood                           |
| Chen         | 2006–2010     | 2014           | Taiwan  | 1725                 | 1725      | 1725 | 2    | 2                             | 2                        | BMD                      |                                 | Blood                           |
| Mendes       | 2007–2009     | 2012           | USA     | 9282                 | 8042      | 4278 | 1240 | 8                             | 3                        | BMD                      |                                 | Bacteraemia, Respiratory tract   |
| Richter      | 2009          | 2011           | USA     | 4210                 | 4210      | 2247 | 10   | 9                             | 9                        | BMD                      |                                 | Wound Blood, Lower respiratory tract, and Joint fluid |
| Biswas       | 2010          | 2012           | India   | 115                  | 80        | 80   | 35   | 5                             | 5                        | E-test                   |                                 | Abscesses, Wound, Skin          |
Table 4  Characteristics of the articles that were included in the meta-analysis and reported resistance to daptomycin (Continued)

| First name | Time of study | Published time | Country | Total staphylococcus | S. aureus | MRSA | CoNS | S. aureus Daptomycin-Resistant | MRSA Daptomycin-Resistant | CoNS Daptomycin-Resistant | Susceptibility testing method | Isolation source |
|------------|---------------|----------------|---------|----------------------|-----------|------|------|-----------------------------|---------------------------|-------------------------|----------------------------|-------------------|
| Morrissey  | 2011          | 2012           | Germany | 81                   | 43        | 43   | 38   | 3                           |                           |                         | BMD                        | Bacteraemia        |
| Hellmark   | 1993–2003     | 2009           | Sweden  | 33                   |           | 33   |      | 1                           |                           |                         | E-test                    | Infected Hip prostheses |
| Khan       | 2012–2013     | 2014           | Saudia Arabia | 190             | 190      |      |      | 3                           | Microscan Walk Away system(40s,siemens) |                       | Blood                      | Medical centers     |
| Picazo     | 2010          | 2011           | Spain   | 702                  | 503       | 187  | 199  | 1                           |                           |                         | BMD                        | Medical centers     |
| Isnard     | 2011–2014     | 2018           | France  | 200                  | 100       | 19   | 100  | 1                           | BMD                       | Prosthetic joint infections | Medical centers     |
| Sader      | 2003          | 2005           | Latin America | 787             | 536       | 143  | 251  | 1                           | BMD                       | Medical centers         | Blood                      | Medical centers     |
| Mathai     | 2006          | 2007           | India   | 1111                 | 741       | 335  | 370  | 1                           | BMD                       | Medical centers         | Blood                      | Blood              |
| Sader      | 2002–2006     | 2008           | USA     | 8027                 | 6497      | 3143 | 1530 | 1                           | BMD                       | Medical centers         | Blood                      | Medical centers     |
| Draghi     | 2004–2005     | 2008           | USA     | 2671                 | 2299      | 1082 | 372  | 4                           | BMD                       | Medical centers         | Blood                      | Medical centers     |
| Stuart     | 2011          |                | Canada  | 633                  |           | 633  |      | 7                           | Agar dilution method     | Clinical isolates        | Blood, Skin, Pneumonia  | Abscess, whitlows, diabetic foot infections, impetigo, Furunculosis, wounds infections, cellulite, etc. |
| Gales      | 2005–2008     | 2009           | Brazil  | 3030                 | 2218      | 687  | 812  | 2                           | BMD                       | Blood                    | Blood, Skin, Pneumonia  | Blood, Urine, wound/tissue, respiratory specimens |
| Gallon     | 2006–2007     | 2009           | France  | 498                  |           | 53   |      | 1                           | E-test                    |                          |                            |                               |
| Zhanel     | 2005–2006     | 2008           | Canada  | 1046                 |           | 162  |      | 2                           | BMD                       | Blood                    | Blood, Skin, Pneumonia  |                                |
| Sader      | 2005          | 2007           | Italy   | 422                  |           | 182  |      | 1                           | BMD                       | Blood                    | Blood, Skin, Pneumonia  |                                |

Abbreviations: BMD; broth microdilution
| First name | Time of study | Published time | Country | Total staphylococcus | S. aureus | MRSA | CoNS | S. aureus Linezolid-Resistant | MRSA Linezolid-Resistant | CoNS Linezolid-Resistant | Susceptibility testing method | Isolation source |
|------------|---------------|----------------|---------|----------------------|-----------|-------|------|--------------------------------|------------------------|------------------------|-------------------------------|--------------------------|
| Mendes [75] | 2007–2009     | 2010           | USA     | 4077                 | 4077      | 4077  | 5    | 5                             | 5                      | 5                      | BMD                           | Bacteraemia, Pneumonia |
| Cassettari [28] | 2010–2011   | 2011           | Spain   | 299                  | 237       | 113   | 62   | 1                             | 1                      | 1                      | BMD                           | Skin and soft tissue infections, hospital-acquired pneumonia |
| Jain [55]    | 2011–2014     | 2015           | India   | 2008                 | 2008      | 384   | 3    | 3                             | 3                      | 1                      | E-test                         | Pneumonia |
| Duncan [37]  | 2013–2014     | 2016           | USA     | 1353                 | 1353      | 676   | 1    | 1                             | 1                      | 1                      | BMD                           | Bacteraemia, Pneumonia |
| Farrell [39] | 2008–2009     | 2011           | USA     | 4073                 | 3257      | 1673  | 816  | 5                             | 5                      | 12                     | BMD                           | Bacteraemia, Pneumonia, Wound infection, Pneumonia |
| Blażewicz [24] | 2014–2015   | 2016           | Poland  | 157                  | 157       | 11    | 3    | 3                             | 3                      | 3                      | BMD                           | Skin, Nasal swab |
| Picazo [85]  | 2010          | 2011           | Spain   | 702                  | 503       | 187   | 199  | 2                             | 2                      | 16                     | BMD                           | Medical centers |
| Sader [92]   | 2005–2009     | 2010           | Brazil  | 2637                 | 2637      | 846   | 2    | 2                             | 2                      | 20                     | BMD                           | Medical centers |
| Jevitt [57]  | 1996–2001     | 2003           | USA     | 119                  | 88        | 47    | 31   | 1                             | 1                      | 1                      | BMD                           | Medical centers |
| Curz [32]    | 2011–2013     | 2015           | Germany | 1952                 | 1952      | 1952  | 1    | 1                             | 1                      | 1                      | BMD                           | Blood |
| Sader [103]  | 2002–2004     | 2006           | Greece  | 185                  | 128       | 57    | 1    | 1                             | 1                      | 1                      | BMD                           | Skin infection, Blood |
| Campanile [27] | 2012–2015   | 2015           | Italy   | 1684                 | 1684      | 640   | 5    | 3                             | 3                      | 3                      | Automated VITEK-2 system, Broth microdilution | Lower respiratory tract, Skin and Soft tissue |
| Picazo [82]  | 2008          | 2009           | Spain   | 703                  | 520       | 201   | 183  | 6                             | 6                      | 3                      | BMD                           | Blood |
| Sader [100]  | 2007–2008     | 2009           | USA     | 9230                 | 8077      | 4514  | 1153 | 4                             | 4                      | 20                     | BMD                           | Blood, Skin, Pneumonia |
| Fuchs [44]   | 2000–2002     | 2002           | USA     | 108                  | 53        | 28    | 55   | 1                             | 1                      | 1                      | BMD                           | Medical centers |
| Sader [57]   | 2002–2006     | 2008           | USA     | 6497                 | 6497      | 3143  | 1530 | 6                             | 6                      | 6                      | BMD                           | Blood |
| Farrell [38] | 2008          | 2009           | USA     | 4012                 | 3156      | 1752  | 856  | 3                             | 3                      | 18                     | Broth microdilution, E-test | Pneumonia, Wound, Urinary tract, Pneumonia |
| Jones [61]   | 2007          | 2009           | Ireland | 141                  | 130       | 11    | 1    | 1                             | 1                      | 1                      | BMD                           | Blood |
| Jones [63]   | 2007          | 2008           | USA     | 4338                 | 3318      | 1930  | 1920 | 2                             | 2                      | 18                     | BMD                           | Medical centers |
| Jones [60]   | 2006          | 2007           | USA     | 3721                 | 2913      | 1648  | 808  | 1                             | 1                      | 13                     | BMD                           | Pneumonia, Wound, Urinary tract |
| Ross [90]    | 2002          | 2005           | USA     | 4557                 | 3687      | 1401  | 870  | 1                             | 1                      | 1                      | BMD                           | Medical centers |
| Mendes [73]  | 2002–2004     | 2008           | USA     | 1989                 | 1989      | 1989  | 1752 | 856  | 3                             | 3                      | 18                     | BMD                           | Medical centers |
| Flamm [40]   | 2010          | 2012           | USA     | 4049                 | 3105      | 1578  | 944  | 2                             | 2                      | 14                     | BMD                           | Blood, Pneumonia, Skin |
| Flamm [40]   | 2013          | 2015           | USA     | 3433                 | 3035      | 1454  | 398  | 2                             | 2                      | 3                      | BMD                           | Blood, skin, soft tissue |
| Putnam [86]  | 2004–2008     | 2010           | USA     | 18,917               | 18        | 917   | 242  | 3                             | 3                      | 3                      | BMD                           | Bacteraemia, Pneumonia |
| Pfäffler [81] | 2011–2015     | 2017           | USA     | 6741                 | 3031      | 1391  | 924  | 1                             | 1                      | 7                      | BMD                           | Medical centers |
Table 5 Characteristics of the articles that were included in the meta-analysis and reported resistance to linezolid (Continued)

| First name | Time of study | Published time | Country | Total staphylococcus | S. aureus | MRSA | CoNS | S. aureus Linezolid-Resistant | MRSA Linezolid-Resistant | CoNS Linezolid-Resistant | Susceptibility testing method | Isolation source |
|------------|--------------|----------------|---------|---------------------|-----------|------|------|-------------------------------|--------------------------|------------------------|-----------------------------|------------------|
| Flamm [42] | 2014         | 2016           | USA     | 3903                | 3106      | 797  | 2    | 2                             | 5                        | BMD                    | Blood, Pneumonia, Skin |
| Sahm [106] | 2011–2012    | 2015           | USA     | 4186                | 3743      | 443  | 5    | 2                             | BMD                      | Medical centers       |
| Tekin [108] | 2007–2011    | 2014           | Turkey  | 870                 | 90        | 771  | 1    | 1                             | 14                       | E-test                 | Blood                     |
| Rosenthal [89] | 2012     | 2014           | Haiti   | 16                  | 16        | 4    | 1    | E-test                        |                          | Different ward of hospital |
| Decousser [33] | 2004–2016  | 2018           | France  | 3437                | 3437      | 953  | 3    | BMD                           | All body sites         |
| Sader [96] | 2008–2014    | 2016           | USA     | 670                 | 670       | 339  | 2    | 1                             | BMD                      | Skin infection          |
| Hodeil [51] | 2010–2014    | 2016           | France  | 440                 | 440       | 325  | 2    | BMD                           | Bronchopulmonary infections |
| Sader [94] | 2009–2013    | 2015           | USA     | 4426                | 4426      | 2013 | 1    | BMD                           | Blood                   |
| Sader [95] | 2008–2011    | 2013           | USA     | 22620               | 19,350    | 9872 | 3270 | 14                            | BMD                      | Blood, Respiratory tract, Skin |
| Mendes [74] | 2007–2009    | 2012           | USA     | 9282                | 8042      | 4278 | 1240 | 4                             | 19                       | BMD                    | Bacteraemia, Respiratory tract |
| Richter [87] | 2009         | 2011           | USA     | 4210                | 4210      | 2247 | 1    | 1                             | BMD                      | Wound, Blood, Lower respiratory tract, Joint fluid |
| Gales [45] | 2005–2008    | 2009           | Brazil  | 3030                | 2218      | 687  | 812  | 1                             | 2                        | BMD                    | Blood, Skin, Pneumonia |
| Sader [98] | 2002–2006    | 2009           | USA     | 14009               | 14,009    | 58   | 5    | 2                             | BMD                      | Catheter related bloodstream infections (BSI) |
| Castanheira [29] | 2006     | 2008           | North America | 4873          | 4288      | 251  | 585  | 1                             | 14                       | BMD                    | Bloodstream infections, Skin and soft tissue infections, Pneumonia |
| Morrissey [76] | 2011        | 2012           | Italy   | 82                  | 41        | 41   | 1    | 2                             | BMD                      | Bacteraemia             |
| Morrissey [76] | 2011        | 2012           | Spain   | 79                  | 45        | 34   | 1    | Bacteraemia                   |                          |
| Cui [31] | 2009–2010    | 2013           | China   | 713                 | 713       | 4    | Agar dilution                          | Blood                   |
| Song [106] | 2013–2014    | 2017           | China   | 1104                | 1104      | 3    | Agar dilution                          | Blood                   |
| Pedroso [78] | 2008–2009   | 2018           | Brazil  | 58                  | 58        | 5    | 1                             | Automated VITEK-2 system | Blood                   |
| Li [67] | 2014         | 2016           | China   | 1798                | 1499      | 632  | 299  | 2                             | BMD                      | Pneumonia, Skin and soft tissue infection, Blood infection |
| Isnard [53] | 2011–2014    | 2018           | France  | 200                 | 100       | 19   | 100  | 2                             | BMD                      | Prosthetic joint infections |
| Gandra [47] | 2008–2014    | 2016           | India   | 5426                | 1089      | 608  | 4337 | 17                            | 21                       | BMD                    | Blood                     |
| Draghi [36] | 2004         | 2005           | USA     | 3368                | 2872      | 1556 | 496  | 1                             | BMD                      | Skin, Blood, Respiratory tract |
| Jones [61] | 2007         | 2009           | Italy   | 151                 | 98        | 53   | 2    | BMD                           | Blood                   |
Table 5 Characteristics of the articles that were included in the meta-analysis and reported resistance to linezolid (Continued)

| First name  | Time of study | Published time | Country | Total staphylococcus | S. aureus | MRSA | S. aureus Linezolid-Resistant | CoNS | Linezolid-Resistant | Susceptibility testing method | Isolation source                                      |
|------------|---------------|----------------|---------|----------------------|-----------|------|-----------------------------|------|---------------------|--------------------------------|------------------------------------------------------|
| Mutnick [77] | 2001–2002 | 2003 | USA | 5848 | 4677 | 1171 | 1 | BMD | Blood, Skin, Respiratory and Urinary tract |
| Jones [62] | 2008 | 2009 | Italy | 128 | 59 | 69 | 2 | BMD | Medical centers |
| Jones [62] | 2008 | 2009 | France | 140 | 100 | 40 | 1 | BMD | Medical centers |
| Martinez [70] | 2006 | 2013 | Mexico | 142 | 142 | 5 | BMD | Blood |
| Zhanel [116] | 2005–2006 | 2008 | Canada | 1046 | 162 | 2 | | Blood, urine, Wound/tissue, Respiratory specimens |

Abbreviations: BMD; broth microdilution
Tigecycline are prescribed by clinicians for about 15 to 20 years, there is still very low resistance to these antibiotics around the world. On the other hand, with the increasing resistance of staphylococci to vancomycin and the high side effects of other drugs such as cotrimoxazole, it seems that these antibiotics have to be used more often in the future. The results of a recent study on the global prevalence of vancomycin-nonsusceptible MRSA showed that the prevalence of vancomycin-intermediate S. aureus (VISA) was 3.01% in 68,792 MRSA strains. Furthermore, the pooled prevalence of heterogeneous vancomycin-intermediate S. aureus (hVISA) was 6.05% and is highly dangerous, because these bacteria lead to higher rates of vancomycin treatment failure. It should be noted that this study reported that the rate of vancomycin-nonsusceptible MRSA has been increasing in recent years, and this is a danger to the international community [136]. It should be noted that, still, some diseases caused by Staphylococcus genus, such as pneumonia, are treated easier with older drugs, and more studies are needed to evaluate the effect of the newer agents. The higher rates of resistance to the mentioned antibiotics in the United States and European countries compared to other parts of the world do not imply higher resistance to these antibiotics in this areas and are related to microbial susceptibility testing programs that are regularly carried out in these countries, while there are no such reports in the African and Asian countries (may because of non-availability and elevated prices in these regions). Therefore, by performing such programs in other countries, the exact resistance rates of the staphylococcal strains to the newer Gram-positive cocci antibiotics can be determined.
Conclusion

The present study shows that resistance to new agents is low in staphylococci and these antibiotics can still be used for treatment of staphylococcal infections in the world. It should be noted that the development of resistance to these antibiotics should be prevented by appropriate antibiotic resistance testing programs.

Abbreviations
MRCoNS: Methicillin-resistant coagulase-negative staphylococci; PBP2: Penicillin-Binding Protein 2; FDA: Food and Drug Administration; EMA: European Medicines Agency; VRE: Vancomycin resistant enterococci; MeSH: Medical subject heading; CLSI: Clinical and Laboratory Standards Institute; EUCAST: European Committee on Antimicrobial Susceptibility Testing; BMD: Broth microdilution; REM: Random effects model; FEM: Fixed effects model

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Authors’ contributions
Davood Darban-Sarokhali and Aref Shariati conceived and designed the study. Masoud Dadashi, Mehdi Mirzaei and Seyed Sajjad Khoramrooz contributed in comprehensive research. Zahra chegini designed the Figures. Aref Shariati, Masoud Dadashi and Davood Darban-Sarokhali wrote the paper. Alex van Belkum and Davood Darban-Sarokhali participated in manuscript editing. The author(s) read and approved the final manuscript.

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