gentamicin showed no synergy, but linezolid prevented selection of resistant mutants. An *in vitro* study of linezolid and vancomycin against five MRSA isolates found the combination was antagonistic against three strains and indifferent against the remaining two (Singh *et al.,* 2009). Dailey *et al.* (2003) demonstrated neither synergy nor antagonism with the combination of linezolid and rifampicin for rabbit endocarditis due to MSSA. In contrast, linezolid was shown to be synergistic with rifampicin (although not vancomycin) against one MRSA strain in a time-kill curve assay, and synergistic with both drugs against a glycopeptide-intermediate strain (Cabellos *et al.,* 2014). Kelesidis *et al.* (2010) reported synergy between linezolid and rifampicin against MRSA using a checkerboard assay; time-kill assay showed synergy at 0.5× MIC, but indifference at the MIC. Linezolid plus daptomycin was antagonistic (time-kill) or indifferent (checkerboard) in the same study; however, the triple combination of linezolid, daptomycin, and rifampicin was synergistic with the fastest kill-time of any combination used. An *in vitro* model of MRSA biofilm found combining linezolid with daptomycin enhanced the activity compared with either agent alone, although only three strains were used (Parra-Ruiz *et al.,* 2012). Luther and LaPlante (2015) similarly used an *in vitro* biodynamic model of MRSA biofilm, and documented antagonism between linezolid and daptomycin (and with vancomycin) against their two strains. Varying results suggest that the effects may be strain-dependent.

Linezolid was synergistic with oritavancin against 10 strains of MRSA (5 heterogeneous vancomycin-intermediate *Staphylococcus aureus* [hVISA], 5 VISA) (Lin *et al.,* 2014). The combination of fosfomycin and linezolid tested against 104 MRSA strains using a checkerboard assay found synergy against 98%, indifference in 2%, and no antagonism (Xu-Hong *et al.,* 2014), supporting an earlier study showing synergy between the two agents against hVISA using time-kill curves (Pachón-Ibáñez *et al.,* 2011), which also fund the combination effective in a mouse peritonitis model. Tang *et al.* (2012) reported enhanced activity of linezolid and fosfomycin against biofilm-embedded MRSA *in vitro* compared with linezolid alone. An *in vitro* dynamic model suggested synergy between linezolid and doxycycline against MRSA, as well as suppression of selection of doxycycline-resistant mutants (Smirnova *et al.,* 2011), a result that differed from an earlier checkerboard study that found predominant indifference with this combination (Sahuquillo Arce *et al.,* 2006). Linezolid was tested in combination with a new des-F(6)-quinolone (DX-619) but did not show any synergy against *S. aureus,* including glycopeptide-resistant strains (Credito *et al.,* 2007).

In vitro and *in vivo* synergy of linezolid in combination with the carbapenems imipenem or ertapenem has been demonstrated against MRSA (Jacqueline *et al.,* 2005, 2006). Despite the bacteriostatic action of linezolid against staphylococci, and no activity of the carbapenems against MRSA, bactericidal activity was demonstrated with the combination of the carbapenem plus linezolid in a rabbit endocarditis model (Jacqueline *et al.,* 2005, 2006). Conversely, the combination of linezolid and meropenem against MSSA was unfavorable, with the linezolid fully antagonizing the bactericidal action of the meropenem (Wicha *et al.,* 2015).

Thirty-seven isolates of CoNS of various species were subjected to synergy testing by Etest of several antibiotic combinations, including linezolid with rifampicin, clindamycin, fusidic acid, ciprofloxacin, and trimethoprim–sulfamethoxazole. The predominant finding was indifference, with a few cases of synergy (fusidic acid 3%, clindamycin 5%) and antagonism (rifampicin 1%, clindamycin 8%, trimethoprim–sulfamethoxazole 11%) (Hellmark *et al.,* 2010).

Linezolid was either additive or synergistic in combination with fosfomycin against VRE (*E. faecium*) (Descourouez *et al.,* 2013). Tang *et al.* (2013b) had similar positive findings with this combination in broth for both VR *E. faecium* and *E. faecalis,* but no enhancement of activity was seen in a biofilm model. In an *in vitro* pharmacodynamic infection model with simulated endocardial vegetations, the addition of gentamicin to linezolid improved activity somewhat against VRE (*E. faecium*) at 72 hours but did not alter activity against biofilm-forming *E. faecalis*. The addition of rifampicin to linezolid did not significantly change activity against *E. faecalis* and was antagonistic against VRE (Luther *et al.,* 2014). A single study looked at the combination of linezolid and minocycline against 30 enterococcal strains (22 *E. faecium*; 20 VRE) and found synergy against 27%; the remainder showed indifference. Selection of mutants resistant to either agent was reduced (Wu *et al.,* 2013a).

Against *H. pylori,* linezolid, in combination with amoxicillin, clarithromycin, or metronidazole, showed either partial synergy or indifference for the majority of strains (Hirschl *et al.,* 2000).

In a mouse model of *N. brasiliensis* infection the combination of linezolid and amoxicillin–clavulanic acid was synergistic in the majority of mice tested (Gomez-Flores *et al.,* 2004). An *in vitro* study of drug combinations against nine clinical *Nocardia* isolates (various species) demonstrated antagonism between linezolid and amikacin (eight cases), imipenem (two cases), and piperacillin–tazobactam (one case); the remainder showed indifference (Tripodi *et al.,* 2011).

The addition of linezolid did not affect the activity of moxifloxacin against *M. tuberculosis* when tested in one mouse model of infection (Fattorini *et al.,* 2003), but in another was seen to increase the activity of various multidrug regimens over 2 months of therapy, most significantly the combination of levofloxacin, amikacin, paraaminosalicylic acid, pyrazinamide, and clofazimine (Zhao *et al.,* 2014). *In vitro*, linezolid demonstrated synergy with clarithromycin against *M. tuberculosis* (85% of 40 isolates tested), ethambutol (63%), clofazimine (30%), amikacin (45%), and moxifloxacin. Little synergy was seen with levofloxacin (2.5%; 43% antagonism). The effect was seen with MDR and XDR strains, to a lesser extent than with more susceptible isolates (Zou *et al.,* 2015). Synergy between linezolid and clarithromycin had been previously demonstrated by Bolhuis *et al.* (2014). In a human macrophage model, linezolid appeared to be antagonistic in combinations also containing levofloxacin (Rey-Jurado *et al.,* 2013a),