Supplement

The minimum inhibitory concentration (MIC) distributions for imipenem and meropenem were determined against 18,283 isolates of *Klebsiella* spp., *Enterobacter* spp. and *Escherichia coli* collected globally and against a subset of 464 isolates that carried genes encoding carbapenemases, including KPC (307 isolates), OXA-48-like enzymes (86 isolates), and metallo-β-lactamases (NDM-type, 29 isolates; VIM-type, 27 isolates; IMP-type, 15 isolates). The 464 isolates were genotypically carbapenemase-producing *Enterobacteriaceae* (CPE), but not all of them tested as resistant to carbapenems, presumably because some isolates produced low levels of carbapenemase.

Using the revised carbapenem breakpoints of ≤1 mg/L (susceptible), 2 mg/L (intermediate), and ≥4 mg/L (resistant), 17,367 isolates tested as susceptible to imipenem, including 22 CPE isolates (18 carrying OXA-48-like carbapenemases, 2 carrying KPC, and 1 each carrying IMP- and VIM-type metallo-β-lactamases). Four hundred-fourteen isolates tested with intermediate MIC values, including 28 CPE (15 OXA-48-like positive, 8 KPC-positive, 3 IMP-positive, 1 VIM-positive, and 1 NDM-positive isolates). A total of 502 isolates were resistant to imipenem, of which 414 were CPE (297 KPC-positive, 53 OXA-48-like positive, 28 NDM-positive, 25 VIM-positive, and 11 IMP-positive isolates) and 88 did not encode carbapenemases. Carbapenem-resistant isolates that did not encode carbapenemases were presumed to harbor changes in outer membrane permeability combined with high-level production of extended-spectrum or AmpC β-lactamases. Using the older breakpoints of ≤4 mg/L (susceptible), 8 mg/L (intermediate), and ≥16 mg/L (resistant), 17,882 isolates were susceptible to imipenem, including 110 CPE isolates (51 OXA-48-like positive, 44 KPC-positive, 7 IMP-positive, 6 VIM-positive, and 2 NDM-positive isolates). One hundred-fifteen isolates tested with intermediate MIC values, of which 101 isolates were CPE (73 KPC-positive, 13 OXA-48-like positive, 6 NDM-positive, 6 VIM-positive, and 3 IMP-positive isolates). A total of 286 isolates were resistant to imipenem, including 253 CPE (190 KPC-positive, 22 OXA-48-like positive, 21 NDM-positive, 15 VIM-positive, and 5 IMP-positive) and 33 additional isolates that were carbapenemase-negative.

When performing the same analysis using meropenem MIC values and revised breakpoints of ≤1 mg/L (susceptible), 2 mg/L (intermediate), and ≥4 mg/L (resistant), 17,741 isolates tested as susceptible, including 39 CPE isolates (27 OXA-48-like positive, 7 KPC-positive, 3 VIM-positive, and 2 IMP-positive isolates). Eighty-seven isolates tested with intermediate meropenem MIC values, including 35 CPE (16 KPC-positive, 15 OXA-48-like positive, 3 IMP-positive, and 1 VIM-positive isolates). Four hundred fifty-five isolates were resistant to meropenem, including 390 CPE (284 KPC-positive, 44 OXA-48-like positive, 29 NDM-positive, 23 VIM-positive, and 10 IMP-positive isolates) and 65 carbapenemase-negative isolates. Using the older breakpoints of ≤4 mg/L (susceptible), 8 mg/L (intermediate), and ≥16 mg/L (resistant), 17,912 isolates were meropenem-susceptible, including 124 CPE (57 KPC-positive, 52 OXA-48-like positive, 7 IMP-positive, 7 VIM-positive, and 1 NDM-positive isolates). Eighty-three isolates, including 70 CPE (56 KPC-positive, 6 VIM-positive, 3 NDM-positive, 3 IMP-positive, and 2 OXA-48-like positive isolates), tested with intermediate MIC values. A total of 288 isolates were resistant to meropenem, including 270 CPE (194 KPC-positive, 32 OXA-48-like positive, 25 NDM-positive, 14 VIM-positive, and 5 IMP-positive isolates) and 18 carbapenemase-negative isolates.