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| **Supplementary Table 3** Correlation between antibiotic use and antibiotic resistance in time series analysis |
| **Antibiotic use** | **Resistance** | **Bacteria** | **AUD** | **DOT** |
|  |  |  | **ρ** | **P** | **ρ** | **P** |
| Piperacillin/tazobactam | Piperacillin/tazobactam | *Escherichia coli* | -0.276 | 0.472 | -0.183 | 0.637 |
|  |  | *Klebsiella pneumoniae* | 0.326 | 0.391 | 0.3 | 0.433 |
|  |  | *Serratia marcescens* | -0.759 | **0.018\*** | -0.743 | **0.022\*** |
|  |  | *Enterobacter cloacae* | 0.1 | 0.797 | 0.017 | 0.966 |
|  |  | *Pseudomonas aeruginosa* | 0.711 | **0.032\*** | 0.767 | **0.016\*** |
| Third-generation cephalosporins | Cefotaxime | *Escherichia coli* | -0.567 | 0.112 | -0.517 | 0.154 |
|  |  | *Klebsiella pneumoniae* | -0.517 | 0.154 | -0.367 | 0.332 |
|  |  | *Proteus mirabilis* | 0.008 | 0.983 | 0.335 | 0.379 |
|  |  | *Serratia marcescens* | – | – | – | – |
|  |  | *Enterobacter cloacae* | -0.467 | 0.205 | -0.417 | 0.265 |
|  | Ceftriaxone | *Escherichia coli* | -0.257 | 0.623 | -0.2 | 0.704 |
|  |  | *Klebsiella pneumoniae* | -0.1 | 0.873 | -0.2 | 0.747 |
|  |  | *Proteus mirabilis* | 0.1 | 0.873 | 0.2 | 0.747 |
|  |  | *Serratia marcescens* | 0.3 | 0.624 | 0.1 | 0.873 |
|  |  | *Enterobacter cloacae* | -0.2 | 0.747 | -0.1 | 0.873 |
|  | Ceftazidime | *Escherichia coli* | -0.6 | 0.088 | -0.55 | 0.125 |
|  |  | *Klebsiella pneumoniae* | -0.867 | **0.003\*\*** | -0.75 | **0.02\*** |
|  |  | *Proteus mirabilis* | -0.548 | 0.127 | -0.274 | 0.476 |
|  |  | *Serratia marcescens* | 0.259 | 0.5 | 0.552 | 0.123 |
|  |  | *Enterobacter cloacae* | -0.083 | 0.831 | -0.067 | 0.865 |
|  |  | *Pseudomonas aeruginosa* | -0.35 | 0.356 | -0.233 | 0.546 |
|  |  | *Acinetobacter baumannii* | 0.617 | 0.077 | 0.417 | 0.265 |
| Fourth-generation cephalosporins | Cefepime | *Escherichia coli* | 0 | 1 | 0 | 1 |
|  |  | *Klebsiella pneumoniae* | 0.617 | 0.077 | 0.617 | 0.077 |
|  |  | *Proteus mirabilis* | 0.226 | 0.559 | 0.226 | 0.559 |
|  |  | *Serratia marcescens* | -0.137 | 0.725 | -0.137 | 0.725 |
|  |  | *Enterobacter cloacae* | -0.65 | 0.058 | -0.65 | 0.058 |
|  |  | *Pseudomonas aeruginosa* | -0.267 | 0.488 | -0.267 | 0.488 |
|  |  | *Acinetobacter baumannii* | -0.25 | 0.517 | -0.25 | 0.517 |
| Carbapenems | Meropenem | *Escherichia coli* | 0.22 | 0.569 | -0.203 | 0.6 |
|  |  | *Klebsiella pneumoniae* | 0.244 | 0.527 | -0.252 | 0.512 |
|  |  | *Enterobacter cloacae* | 0.712 | **0.031\*** | 0.644 | 0.061 |
|  |  | *Pseudomonas aeruginosa* | 0.767 | **0.016\*** | 0.383 | 0.309 |
|  |  | *Acinetobacter baumannii* | -0.257 | 0.504 | 0.337 | 0.376 |
|  | Imipenem/cilastatin | *Escherichia coli* | 0.102 | 0.795 | -0.39 | 0.3 |
|  |  | *Klebsiella pneumoniae* | 0.244 | 0.527 | -0.252 | 0.512 |
|  |  | *Proteus mirabilis* | – | – | – | – |
|  |  | *Serratia marcescens* | – | – | – | – |
|  |  | *Enterobacter cloacae* | -0.017 | 0.966 | -0.367 | 0.332 |
|  |  | *Pseudomonas aeruginosa* | 0.267 | 0.488 | -0.183 | 0.637 |
|  |  | *Acinetobacter baumannii* | 0 | 1 | 0.791 | 0.111 |
| Aminoglycosides | Gentamicin | *Escherichia coli* | 0.033 | 0.932 | -0.117 | 0.765 |
|  |  | *Klebsiella pneumoniae* | -0.317 | 0.406 | -0.567 | 0.112 |
|  |  | *Proteus mirabilis* | -0.277 | 0.47 | -0.235 | 0.542 |
|  |  | *Serratia marcescens* | 0.621 | 0.074 | 0.518 | 0.154 |
|  |  | *Enterobacter cloacae* | 0.329 | 0.388 | 0.511 | 0.16 |
|  |  | *Pseudomonas aeruginosa* | 0.283 | 0.46 | 0.05 | 0.898 |
|  |  | *Acinetobacter baumannii* | 0.067 | 0.865 | 0.05 | 0.898 |
|  | Amikacin | *Escherichia coli* | -0.583 | 0.099 | -0.65 | 0.058 |
|  |  | *Klebsiella pneumoniae* | -0.347 | 0.36 | -0.584 | 0.099 |
|  |  | *Proteus mirabilis* | 0 | 1 | -0.137 | 0.725 |
|  |  | *Serratia marcescens* | 0.274 | 0.476 | 0.137 | 0.725 |
|  |  | *Enterobacter cloacae* | -0.274 | 0.476 | -0.411 | 0.272 |
|  |  | *Pseudomonas aeruginosa* | 0.05 | 0.898 | -0.15 | 0.7 |
|  |  | *Acinetobacter baumannii* | 0.383 | 0.308 | 0.456 | 0.217 |
| Quinolones | Levofloxacin | *Escherichia coli* | 0.661 | 0.053 | 0.7 | **0.036\*** |
|  |  | *Klebsiella pneumoniae* | 0.427 | 0.252 | 0.417 | 0.265 |
|  |  | *Proteus mirabilis* | -0.197 | 0.612 | 0.035 | 0.929 |
|  |  | *Serratia marcescens* | 0.07 | 0.858 | -0.078 | 0.841 |
|  |  | *Enterobacter cloacae* | 0.301 | 0.431 | -0.083 | 0.831 |
|  |  | *Pseudomonas aeruginosa* | 0.1 | 0.797 | 0.067 | 0.865 |
| 　 | 　 | *Acinetobacter baumannii* | 0.149 | 0.703 | 0.078 | 0.841 |
| Antibiotic use was evaluated as both AUD (DDDs/100 patient-days) and DOT (DOTs/100 patient-days).Abbreviations: AUD, antibiotic use density; DDDs, defined daily doses; DOT, days of therapy.ρ indicates Spearman’s correlation coefficient.P values marked in bold are < 0.05.\* and \*\* indicate statistically significant correlations (P < 0.05 and P < 0.01, respectively). |