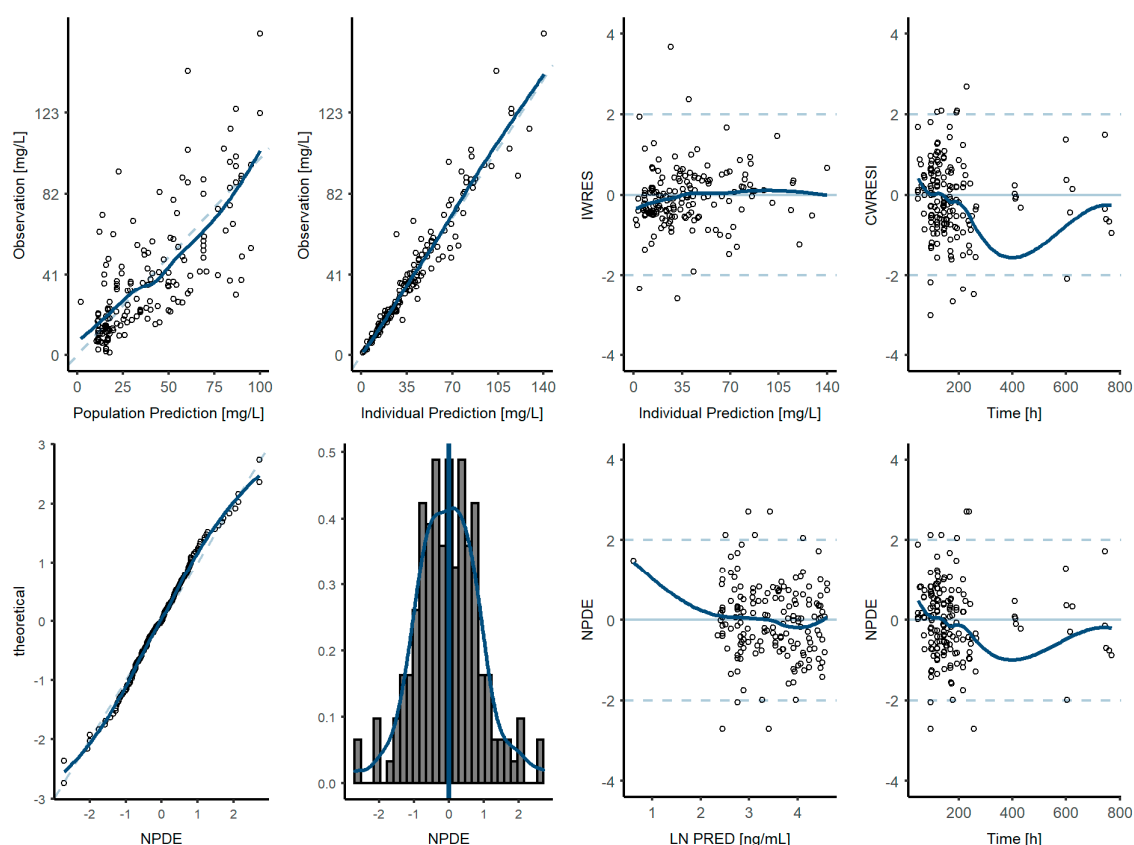


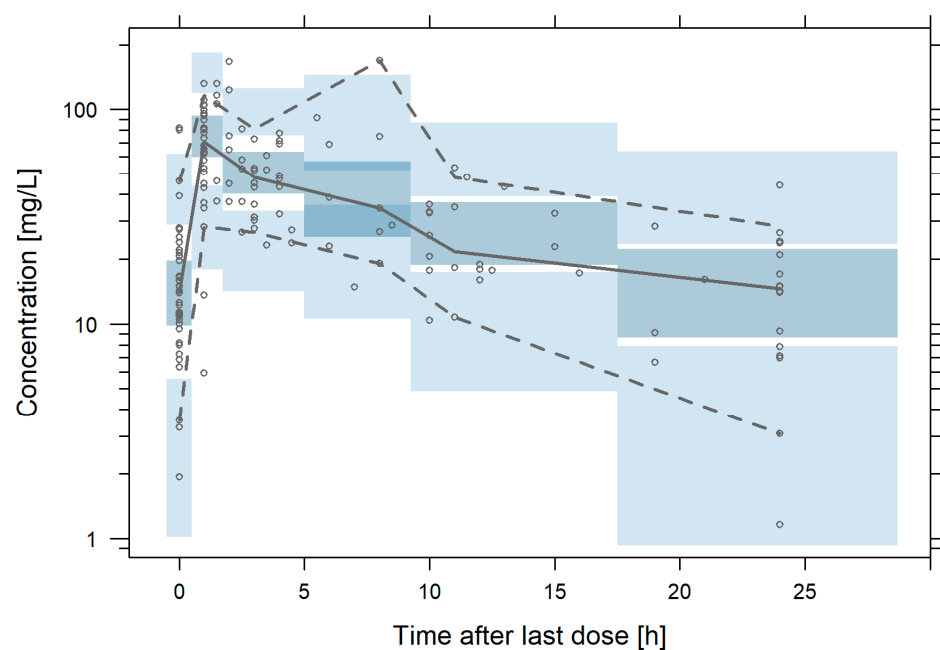
# Supplementary Materials: Population Pharmacokinetic/Pharmacodynamic Modelling of Daptomycin for Schedule Optimization in Patients with Renal Impairment

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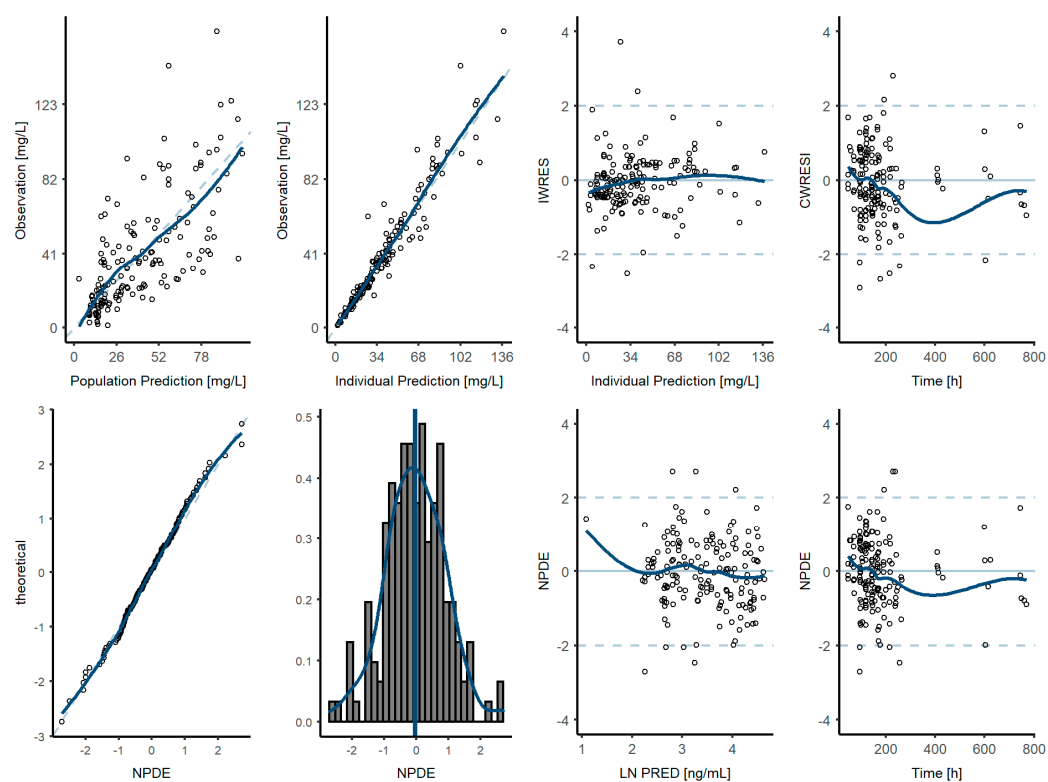


**Figure S1.** Goodness-of-fit plots of the base population pharmacokinetic model of daptomycin. NPDE: normalized prediction distribution error; LN: log-transformed observations.

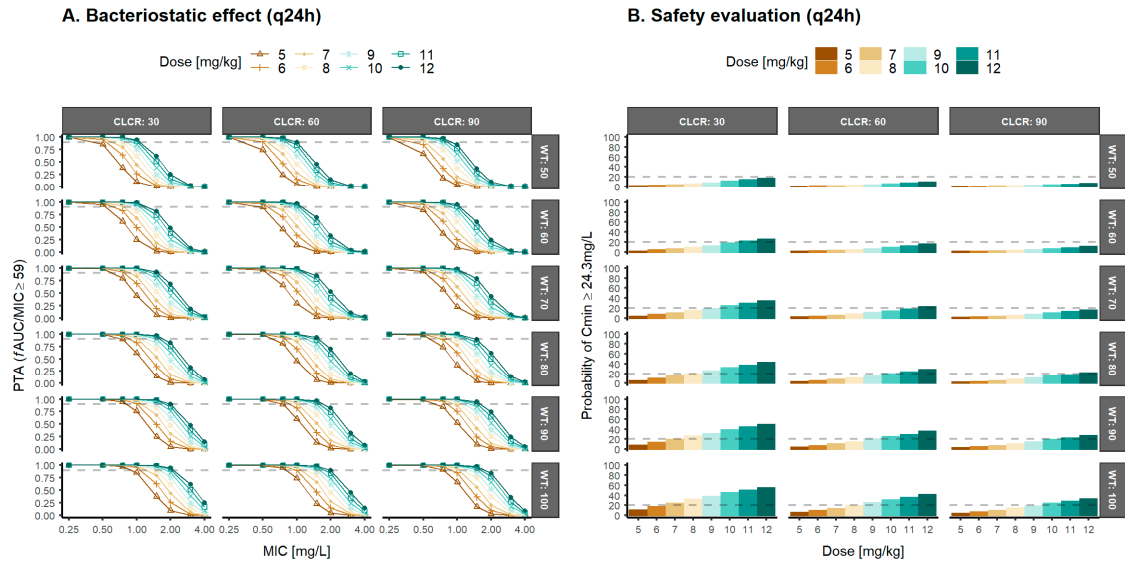
## Base population PK model



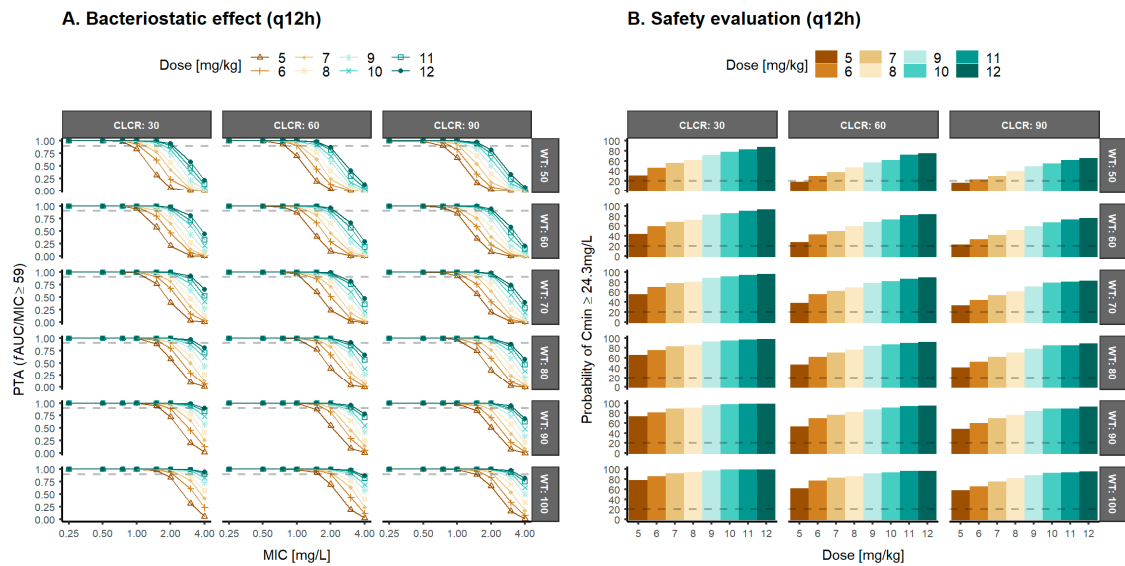
**Figure S2.** Visual Predictive check of the base population pharmacokinetic model of daptomycin. Grey lines represent the 2.5<sup>th</sup>, 50<sup>th</sup> and 97.5<sup>th</sup> experimental percentiles. Blue shaded areas represent the 95% prediction interval of the 2.5<sup>th</sup>, 50<sup>th</sup> and 97.5<sup>th</sup> percentiles. Empty grey dots represent the experimental daptomycin observations.



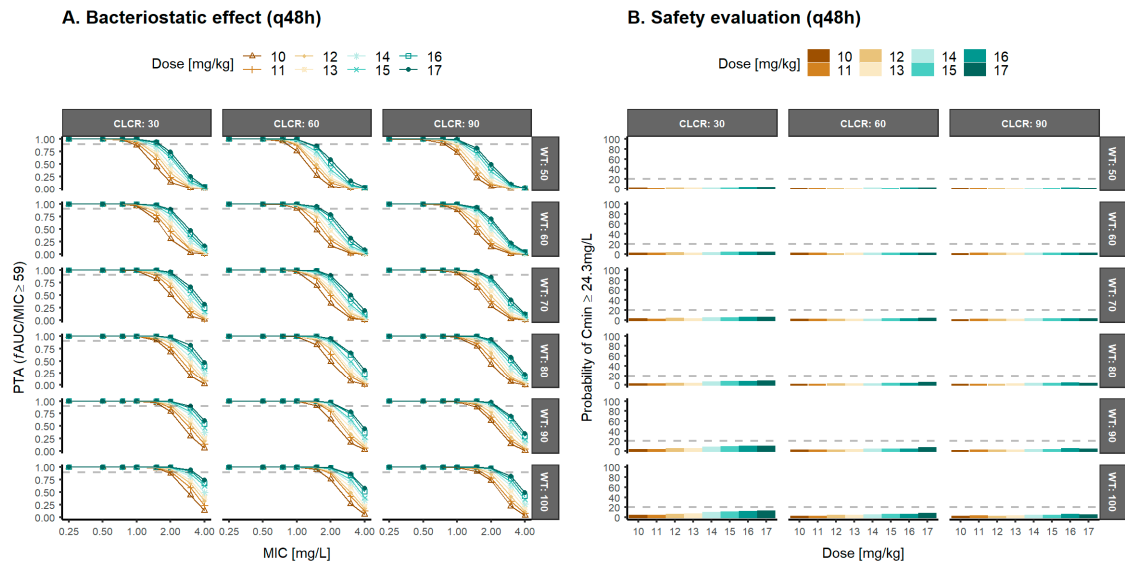
**Figure S3.** Goodness-of-fit plots of the final population pharmacokinetic model of daptomycin. NPDE: normalized prediction distribution error; LN: log-transformed observations.



**Figure S4.** Probability of target attainment (PTA) after once daily (q24h) dose levels (5-12 mg/kg) of daptomycin in patients with different creatinine clearance ( $CL_{CR}$ ) and body weight (WT) for an (A)  $fAUC/MIC$  greater or equal to 59 (bacteriostatic effect), and (B) Predicted probability of achieving through concentrations of total daptomycin greater or equal to 24.3 mg/L MIC: minimum inhibitory concentration;  $fAUC/MIC$ : unbound drug area under the concentration-time curve/minimum inhibitory concentration ratio.



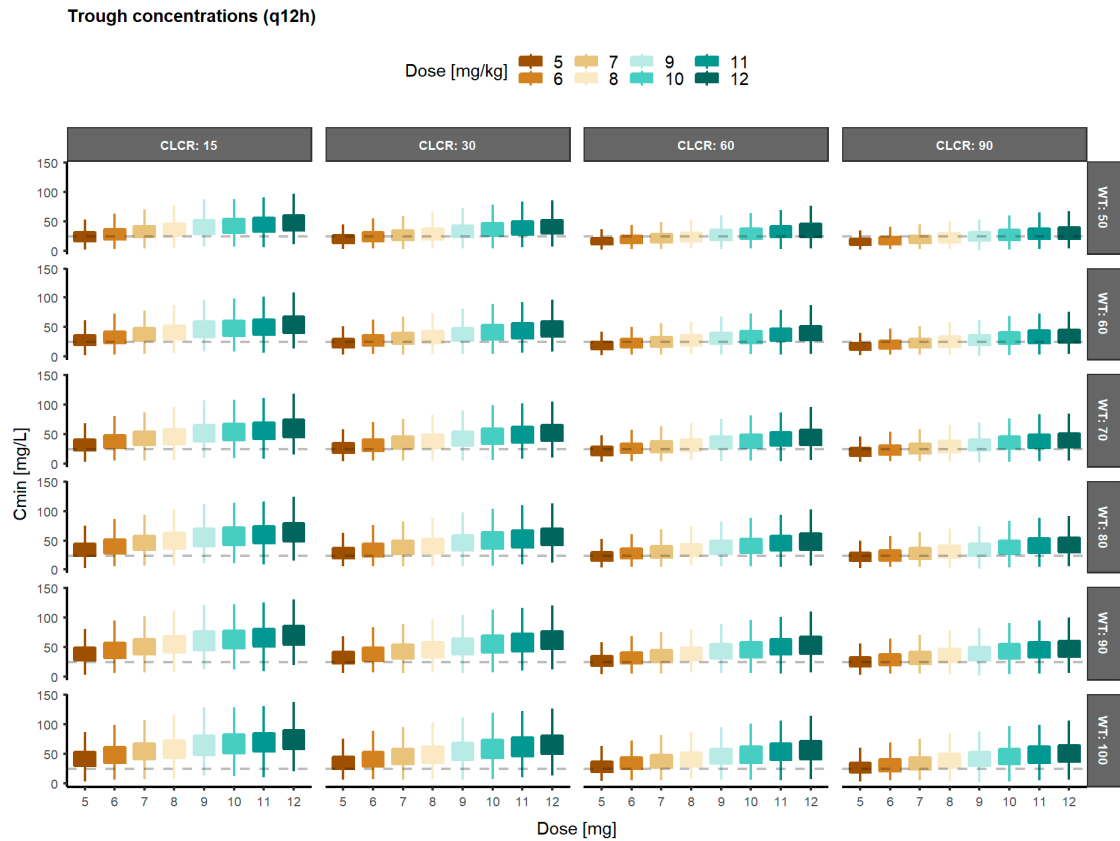
**Figure S5.** Probability of target attainment (PTA) after twice daily (q12h) dose levels (5-12 mg/kg) of daptomycin in patients with different creatinine clearance ( $CL_{CR}$ ) and body weight (WT) for an (A)  $fAUC/MIC$  greater or equal to 59 (bacteriostatic effect), and (B) Predicted probability of achieving through concentrations of total daptomycin greater or equal to 24.3 mg/L MIC: minimum inhibitory concentration;  $fAUC/MIC$ : unbound drug area under the concentration-time curve/minimum inhibitory concentration ratio.



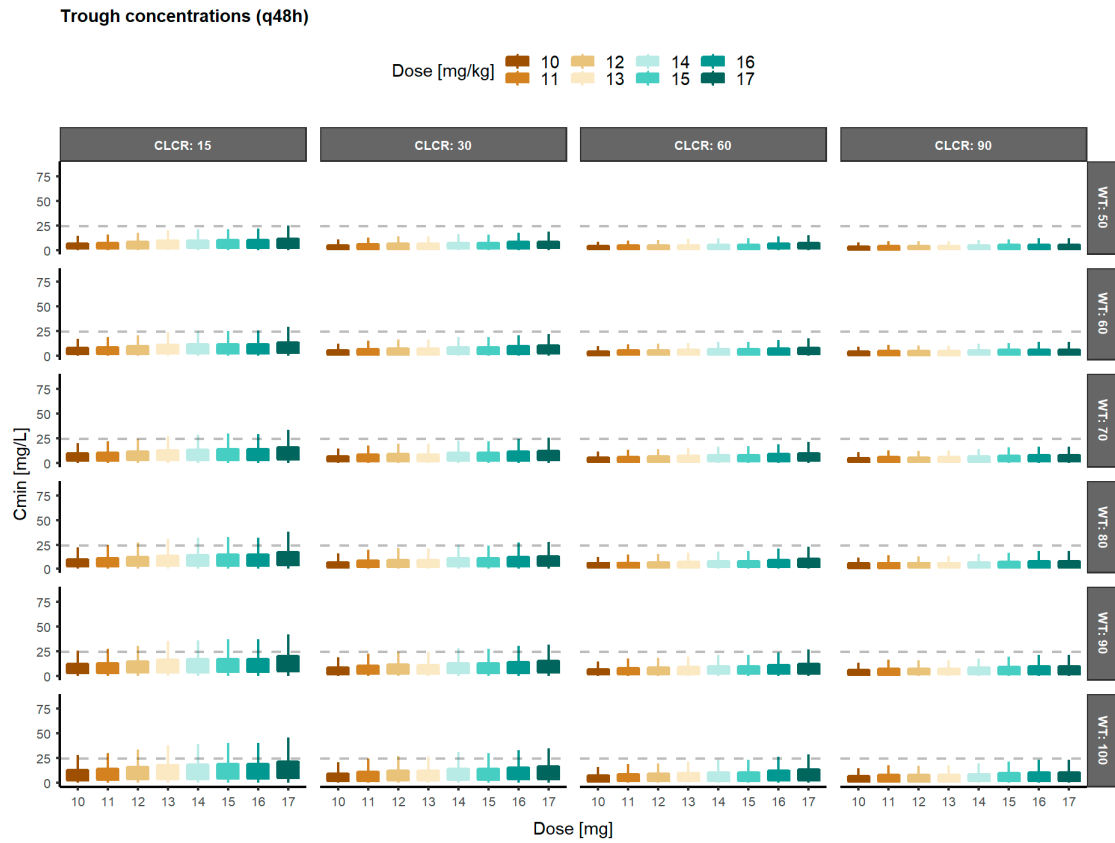
**Figure S6.** Probability of target attainment (PTA) after once every other day (q48h) dose levels (5-12 mg/kg) of daptomycin in patients with different creatinine clearance ( $CL_{CR}$ ) and body weight (WT) for an (A)  $fAUC/MIC$  greater or equal to 59 (bacteriostatic effect), and (B) Predicted probability of achieving through concentrations of total daptomycin greater or equal to 24.3 mg/L MIC: minimum inhibitory concentration;  $fAUC/MIC$ : unbound drug area under the concentration-time curve/minimum inhibitory concentration ratio.



**Figure S7.** Daptomycin trough concentrations ( $C_{min}$ ) after single dose levels (5-12 mg/kg) of daptomycin every 24 hours in patients with different creatinine clearance ( $CL_{CR}$ ) and body weight (WT). Grey dashed line represents the safety threshold of 24.3 mg/L of daptomycin. Boxplot represents the 25<sup>th</sup> and 75<sup>th</sup> percentiles (IQR) of the overall distribution and whiskers include the 1.5\*IQR.



**Figure S8.** Daptomycin trough concentrations (Cmin) after single dose levels (5-12 mg/kg) of daptomycin every 12 hours in patients with different creatinine clearance (CLCR) and body weight (WT). Grey dashed line represents the safety threshold of 24.3 mg/L of daptomycin. Boxplot represents the 25<sup>th</sup> and 75<sup>th</sup> percentiles (IQR) of the overall distribution and whiskers include the 1.5\*IQR.



**Figure S9.** Daptomycin trough concentrations (Cmin) after single dose levels (10-17 mg/kg) of daptomycin every 48 hours in patients with different creatinine clearance (CLCR) and body weight (WT). Grey dashed line represents the safety threshold of 24.3 mg/L of daptomycin. Boxplot represents the 25<sup>th</sup> and 75<sup>th</sup> percentiles (IQR) of the overall distribution and whiskers include the 1.5\*IQR.