SUPPLEMENTAL MATERIAL

Population pharmacokinetics and outcomes of critically ill pediatric patients treated with intravenous colistin at higher than recommended doses

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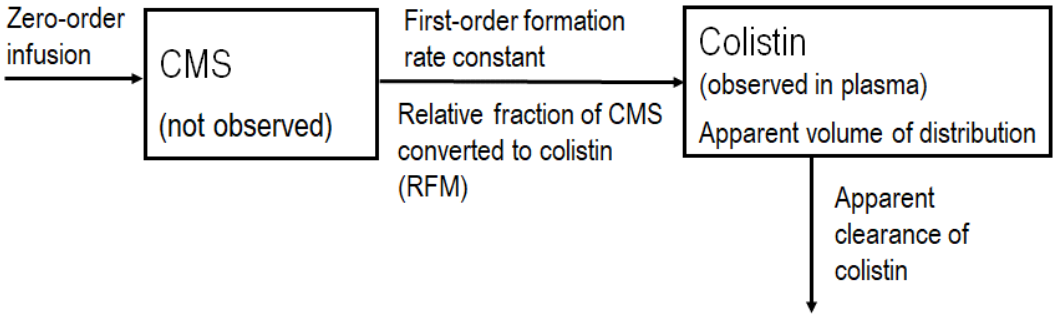

FIG S1A. Diagram of the structural pharmacokinetic model.

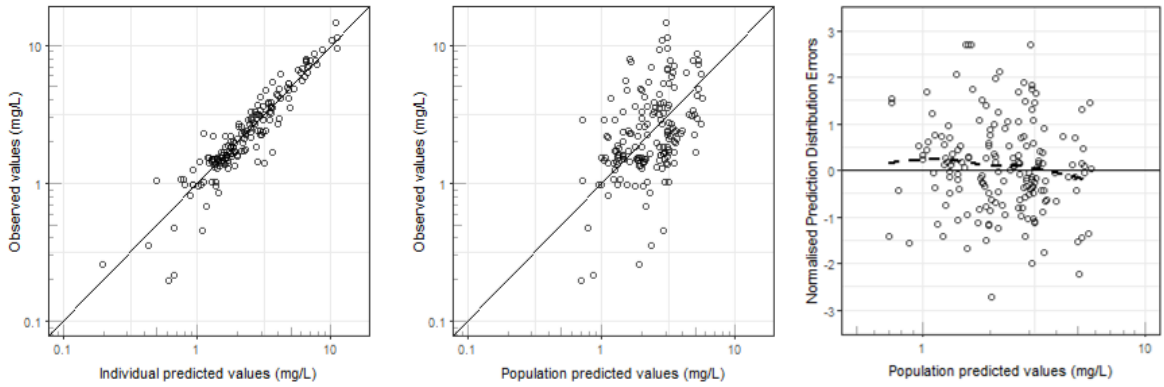

FIG S1B. Observed *versus* individual and population fitted concentrations, and normalized prediction distribution errors (including Loess smoother), for the final population pharmacokinetic model including covariate effects.

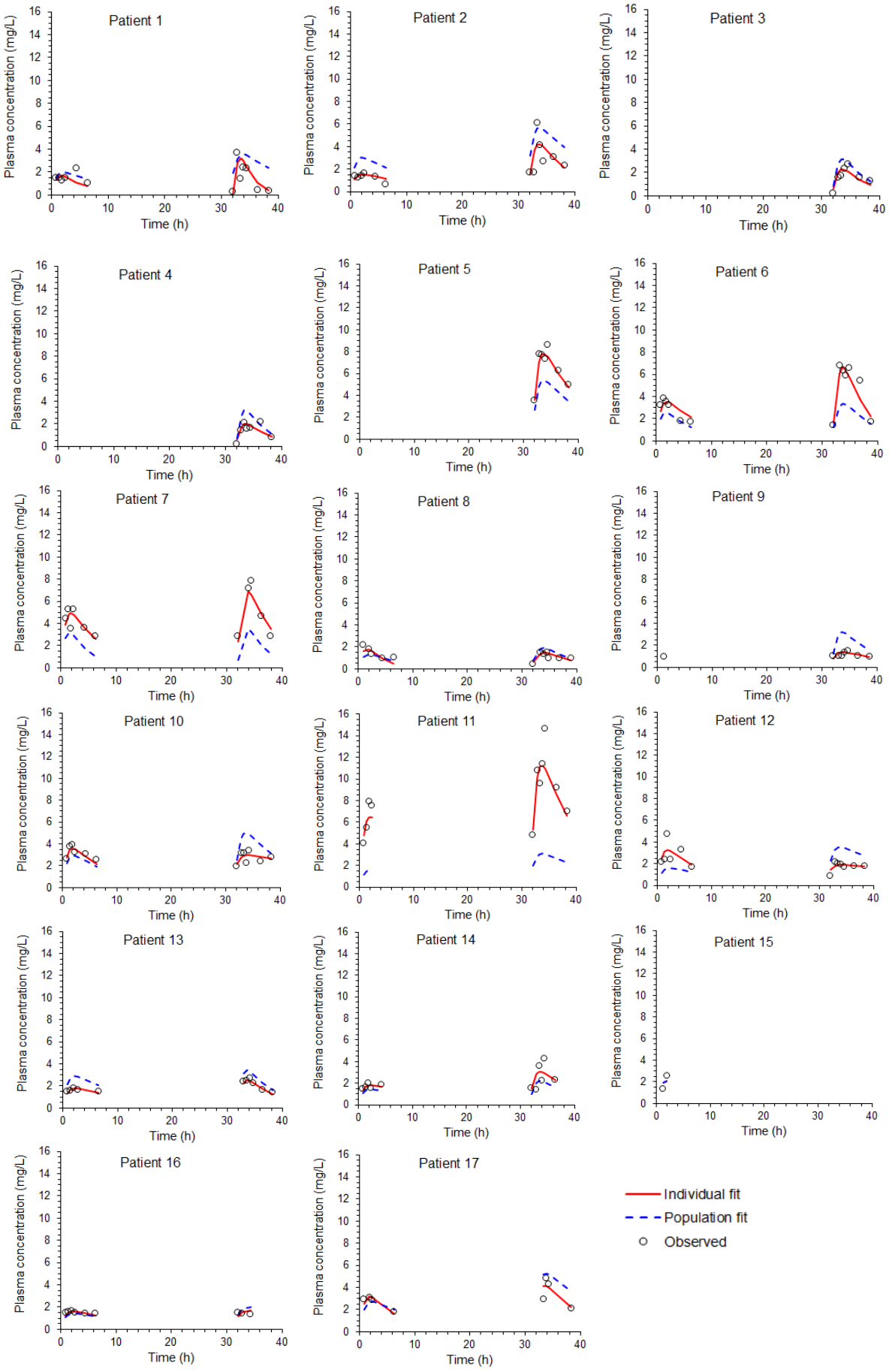

FIG S1C. Fits of the final population pharmacokinetic model including covariate effects.

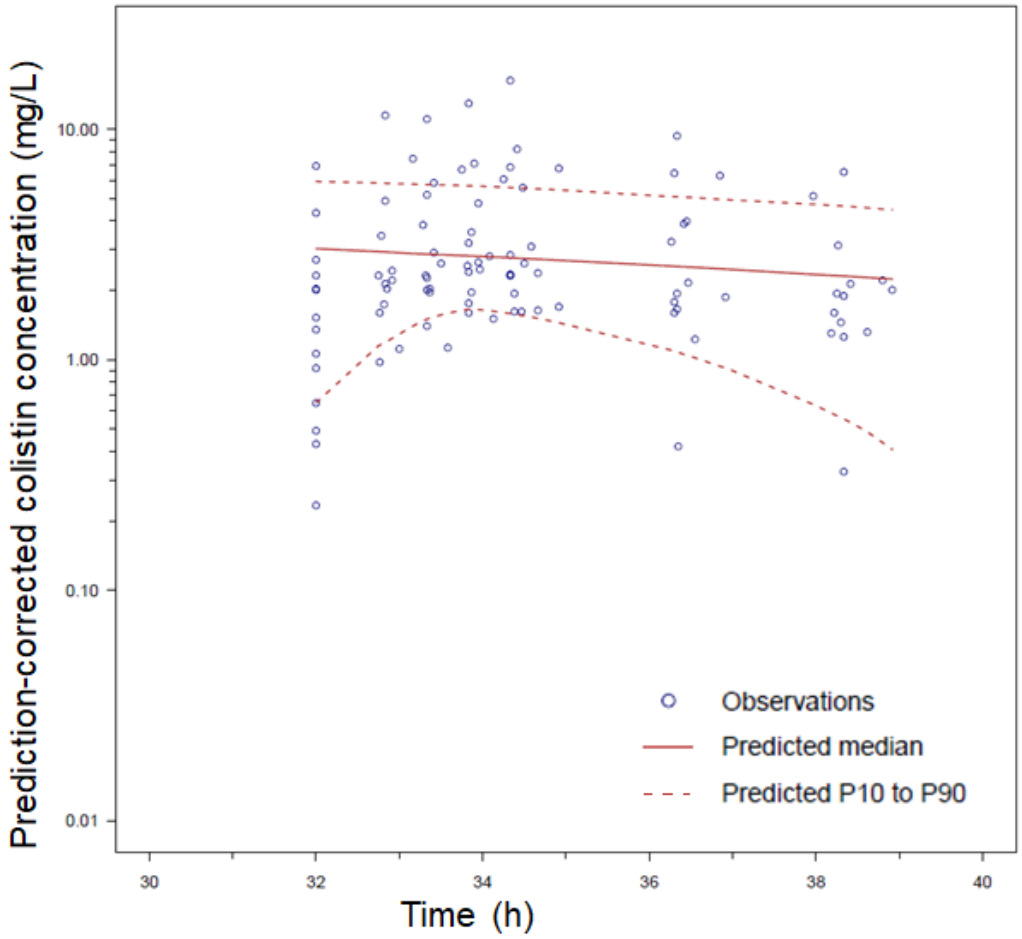

FIG S1D. Prediction-corrected visual predictive check (pcVPC) at steady state of the final population pharmacokinetic model including covariate effects. pcVPCs were evaluated stratified by dose and SIRS status and provided good predictive performance. Only for subjects who did not have SIRS the colistin concentrations following the first dose were slightly under predicted, however this does not affect the conclusions of the analysis which are based on the colistin concentrations at steady state. The normalized prediction distribution errors were normally distributed, indicating good predictive performance of the model overall.

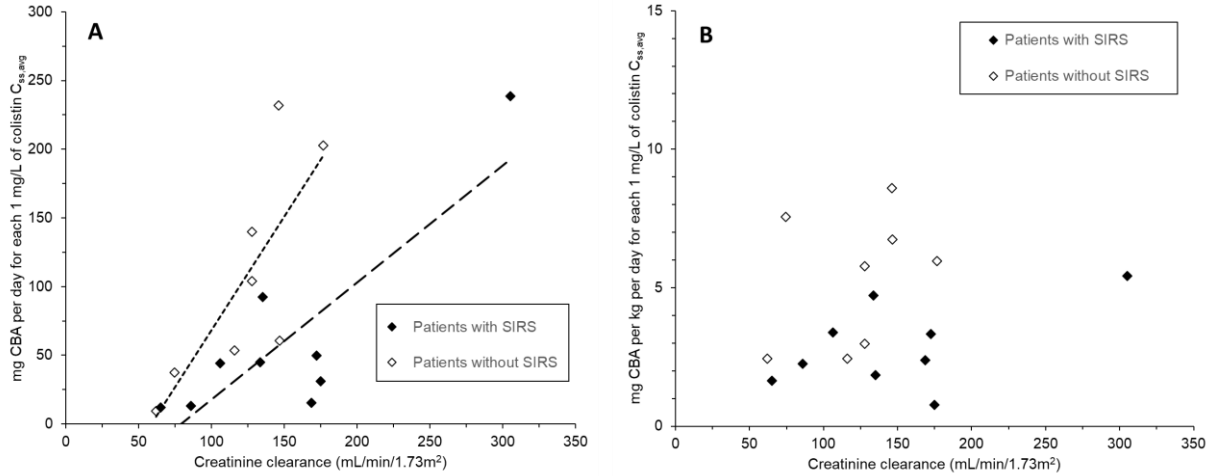

FIG S2. Relationships between the daily dose of colistin base activity (CBA), expressed as mg/d (Panel A) and as mg/kg/d (Panel B), needed for each 1 mg/L of the average steady-state plasma concentration of colistin ($C_{ss,avg}$) and creatinine clearance expressed as mL/min/1.73m^2. In panel A, data for patients with SIRS (filled symbols, long dashes; $R^2 = 0.70$) and without SIRS (empty symbols, short dashes; $R^2 = 0.61$) were regressed separately.

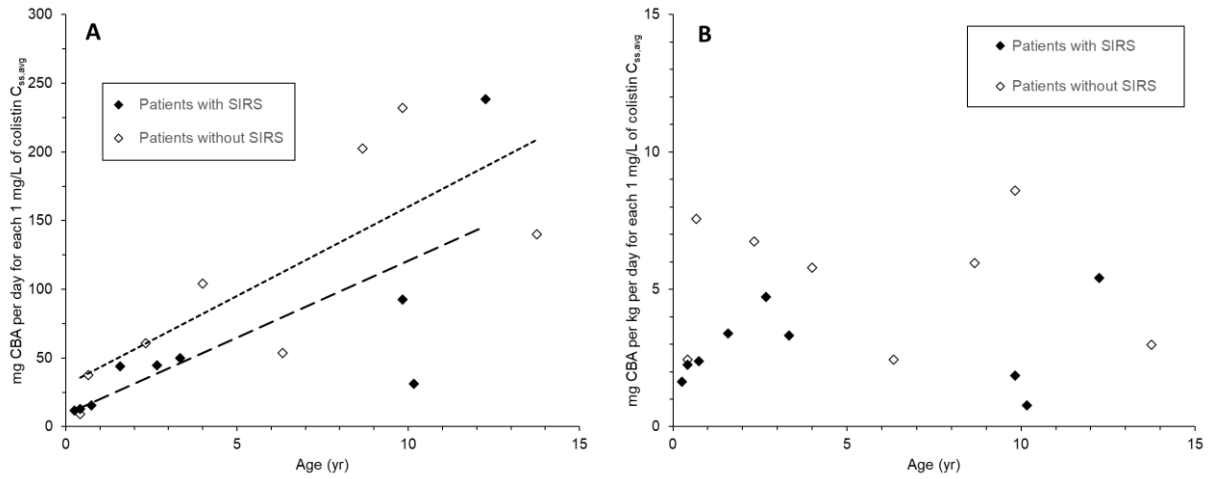

FIG S3. Relationships between the daily dose of colistin base activity (CBA), expressed as mg/d (Panel A) and as mg/kg/d (Panel B), needed for each 1 mg/L of the average steady-state plasma concentration of colistin ($C_{ss,avg}$) and age. In panel A, data for patients with SIRS (filled symbols, long dashes; $R^2 = 0.56$) and without SIRS (empty symbols, short dashes; $R^2 = 0.59$) were regressed separately.

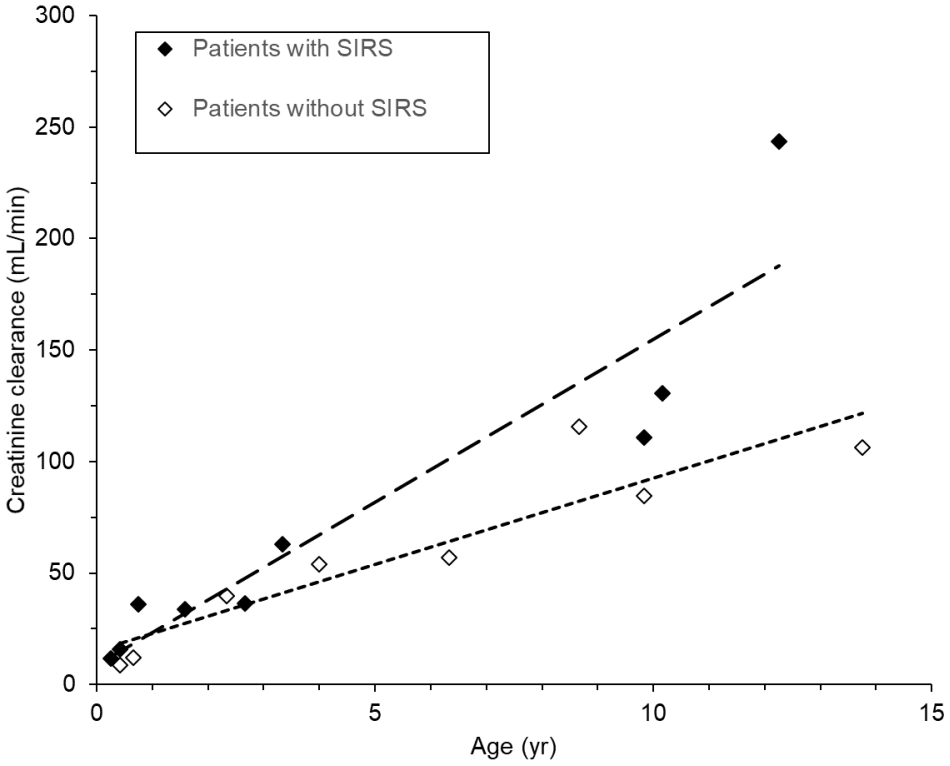

FIG S4. Relationships between creatinine clearance and age. Data for patients with SIRS (filled symbols, long dashes; $R^2 = 0.87$) and without SIRS (empty symbols, short dashes; $R^2 = 0.85$) were regressed separately.