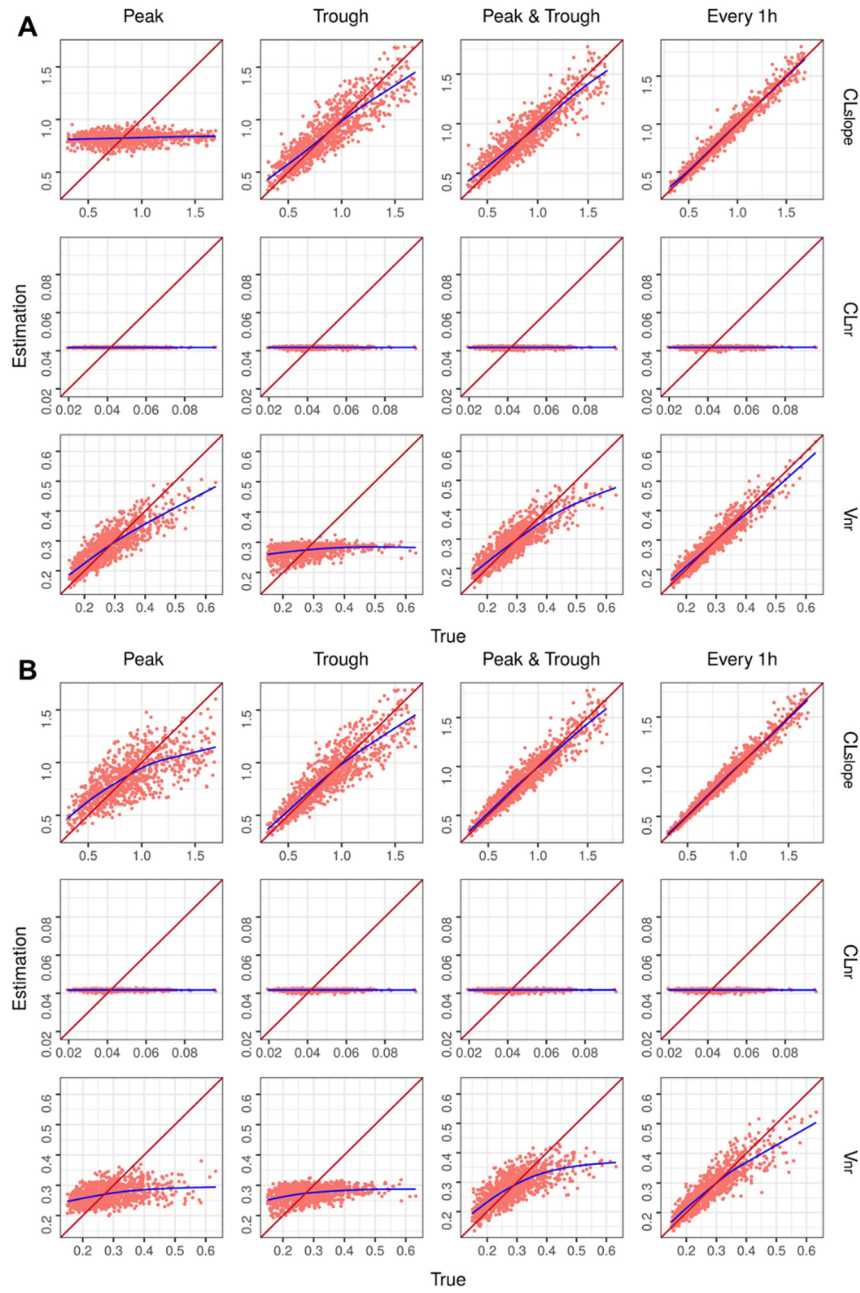


**Table S1.** Internal validation data estimation of amikacin pharmacokinetic parameters

Sampling time	Peak		Trough		Peak and trough		Every 1 h	
	MPE	RMSE	MPE	RMSE	MPE	RMSE	MPE	RMSE
<b>Single dose</b>								
CL <sub>slope</sub>	8.32	0.30	2.97	0.14	2.94	0.12	1.37	0.06
CL <sub>nr</sub> (mL/min/kg)	3.00	0.01	3.02	0.01	3.02	0.01	2.90	0.01
V <sub>nr</sub> (L/kg)	1.70	0.04	2.77	0.08	1.99	0.04	1.14	0.03
<b>Steady-state</b>								
CL <sub>slope</sub>	3.80	0.21	1.37	0.13	1.44	0.09	0.95	0.05
CL <sub>nr</sub> (mL/min/kg)	3.06	0.01	3.07	0.01	3.09	0.01	3.05	0.01
V <sub>nr</sub> (L/kg)	1.00	0.08	1.98	0.08	1.59	0.06	0.91	0.04

**Abbreviations:** MPE, mean percent error; RMSE, root mean squared error; CL<sub>slope</sub>, rate of change in drug clearance with respect to creatinine clearance; CL<sub>nr</sub>, clearance independent of renal function; V<sub>nr</sub>, distribution volume independent of renal function.



**Figure S1.** Graphs representing the estimated amikacin parameters versus true values under each internal validation scenario. The identity line is shown in red, and a trend line in blue has been drawn for each model: (A) single dose and (B) steady state.

**Abbreviations:**  $CL_{slope}$ , rate of change in drug clearance with respect to creatinine clearance;  $CL_{nr}$ , clearance independent of renal function;  $V_{nr}$ , distribution volume independent of renal function.

**Table S2.** Internal validation data estimation of vancomycin pharmacokinetic parameters

Sampling time	Peak		Trough		Peak and trough		Every 1 h	
	MPE	RMSE	MPE	RMSE	MPE	RMSE	MPE	RMSE
<b>Single dose</b>								
CL <sub>slope</sub>	4.21	0.25	3.34	0.16	3.57	0.16	2.96	0.12
CL <sub>nr</sub> (mL/min/kg)	1.07	0.01	1.09	0.01	1.10	0.01	1.11	0.01
V <sub>nr</sub> (L/kg)	0.69	0.04	1.93	0.04	0.51	0.04	0.14	0.03
k <sub>12</sub> (1/h)	4.28	0.19	6.08	0.22	4.01	0.19	4.42	0.19
k <sub>21</sub> (1/h)	3.37	0.11	2.28	0.12	2.93	0.11	1.45	0.09
<b>Steady-state</b>								
CL <sub>slope</sub>	0.47	0.15	1.78	0.11	0.53	0.08	0.68	0.04
CL <sub>nr</sub> (mL/min/kg)	1.11	0.01	1.16	0.01	1.10	0.01	1.21	0.01
V <sub>nr</sub> (L/kg)	1.58	0.04	1.51	0.04	1.08	0.04	0.42	0.04
k <sub>12</sub> (1/h)	5.43	0.22	5.58	0.22	4.56	0.20	4.53	0.20
k <sub>21</sub> (1/h)	3.05	0.12	2.91	0.12	3.17	0.12	2.64	0.10

**Abbreviations:** MPE, mean percent error; RMSE, root mean squared error; CL<sub>slope</sub>, rate of change in drug clearance with respect to creatinine clearance; CL<sub>nr</sub>, clearance independent of renal function; V<sub>nr</sub>, distribution volume independent of renal function; k<sub>12</sub>, first-order transfer rate constant from the central compartment to peripheral compartment; k<sub>21</sub>, first-order transfer rate constant from the peripheral compartment to central compartment.

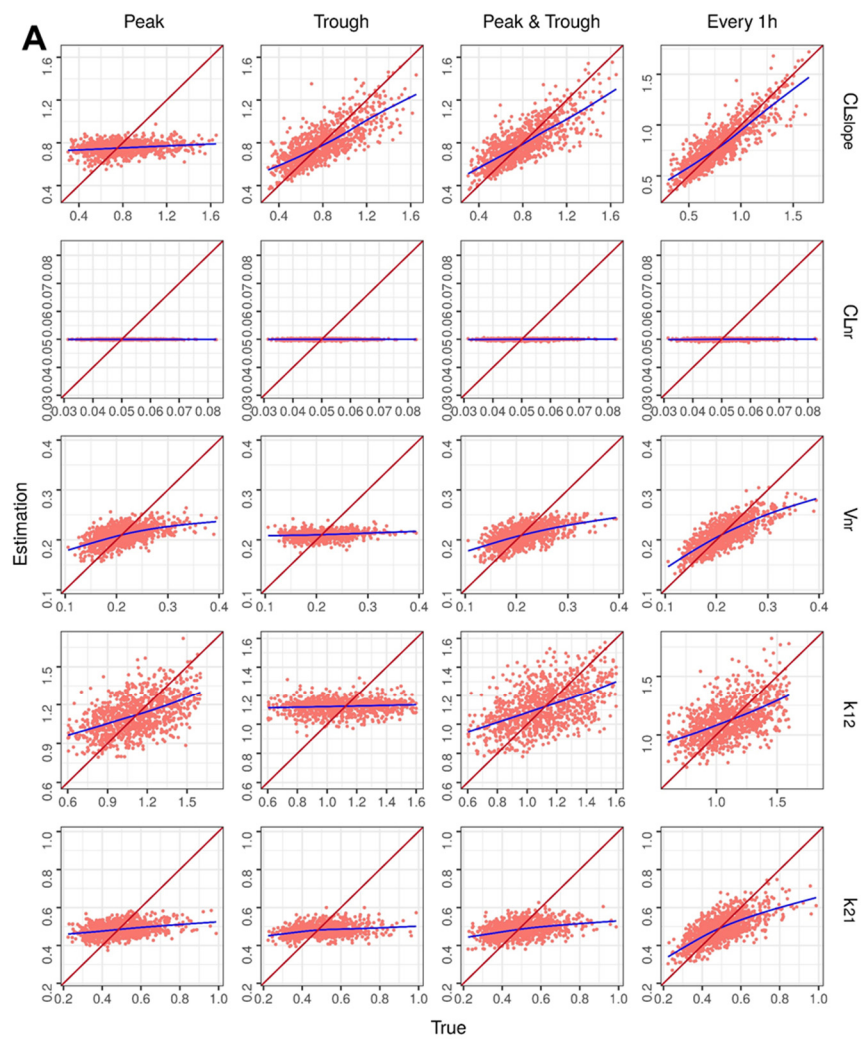
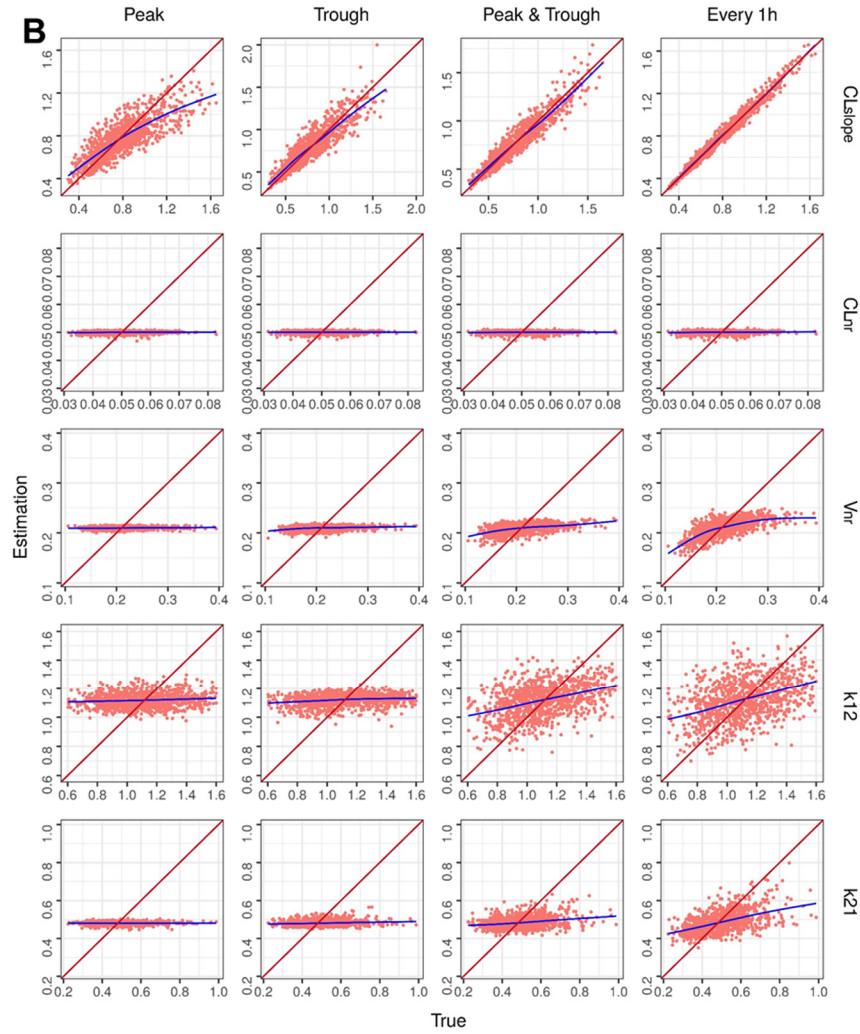


Figure S2. *Cont.*



**Figure S2.** Graphs representing the estimated vancomycin parameters versus true values under each internal validation scenario.

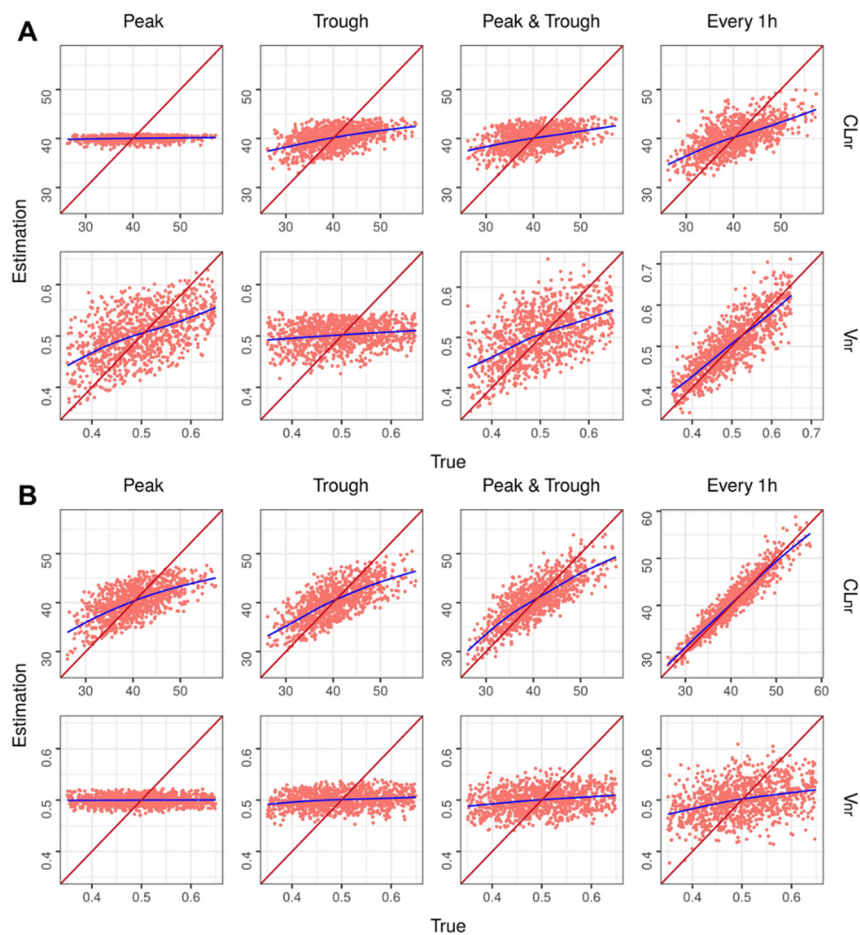
The identity line is shown in red, and a trend line in blue is drawn for each model: (A) single dose and (B) steady state.

**Abbreviations:**  $CL_{slope}$ , rate of change in drug clearance with respect to creatinine clearance;  $CL_{nr}$ , clearance independent of renal function;  $V_{nr}$ , distribution volume independent of renal function;  $k_{12}$ , first-order transfer rate constant from the central compartment to peripheral compartment;  $k_{21}$ , first-order transfer rate constant from the peripheral compartment to central compartment.

**Table S3.** Internal validation data estimation of theophylline pharmacokinetic parameters

Sampling time	Peak		Trough		Peak and trough		Every 1 h	
	MPE	RMSE	MPE	RMSE	MPE	RMSE	MPE	RMSE
<b>Single dose</b>								
CL <sub>nr</sub> (mL/h/kg)	1.53	5.82	1.43	5.23	1.25	5.30	1.22	4.62
V <sub>nr</sub> (L/kg)	2.31	0.06	2.72	0.07	2.08	0.06	1.69	0.04
<b>Steady-state</b>								
CL <sub>nr</sub> (mL/h/kg)	1.08	4.55	1.11	4.20	1.20	3.55	0.71	1.80
V <sub>nr</sub> (L/kg)	2.45	0.07	2.47	0.07	2.33	0.07	2.15	0.07

**Abbreviations:** MPE, mean percent error; RMSE, root mean squared error; CL<sub>nr</sub>, clearance independent of renal function; V<sub>nr</sub>, distribution volume independent of renal function.



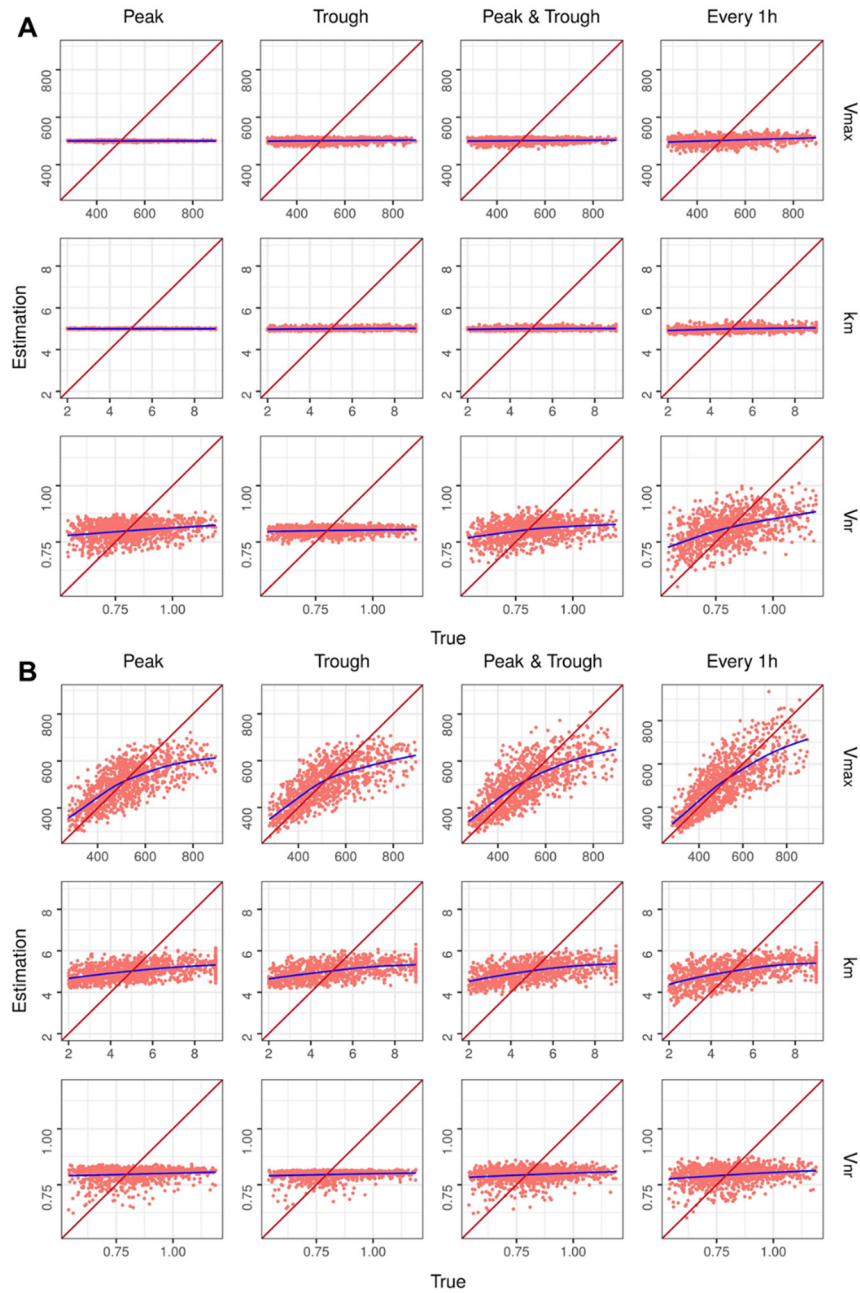
**Figure S3.** Graphs representing the estimated theophylline parameters versus true values under each internal validation scenario. The identity line is shown in red, and a trend line in blue is drawn for each model: **(A)** single dose and **(B)** steady state. **Abbreviations:** CL<sub>nr</sub>, clearance independent of renal function; V<sub>nr</sub>, distribution volume independent of renal function.

**Table S4.** Internal validation data estimation of phenytoin pharmacokinetic parameters

Sampling time	Peak		Trough		Peak and trough		Every 1 h	
	MPE	RMSE	MPE	RMSE	MPE	RMSE	MPE	RMSE
<b>Single dose</b>								
$V_{\max}$ (mg/kg/d)	3.31	135.33	3.34	134.71	3.42	134.69	3.55	132.14
$k_m$ (mcg/mL)	10.25	2.04	10.10	2.03	10.07	2.04	9.73	2.02
$V_{nr}$ (L/kg)	1.39	0.14	1.74	0.14	1.67	0.14	2.06	0.13
<b>Steady-state</b>								
$V_{\max}$ (mg/kg/d)	0.35	95.75	0.05	95.61	0.29	92.65	0.95	86.49
$k_m$ (mcg/mL)	9.17	1.89	9.18	1.88	8.63	1.85	7.62	1.82
$V_{nr}$ (L/kg)	1.20	0.15	1.06	0.14	0.91	0.14	0.68	0.14

**Abbreviations:** MPE, mean percent error; RMSE, root mean squared error;  $V_{\max}$ , maximum velocity;  $k_m$ , Michaelis constant;  $V_{nr}$ , distribution volume independent of renal function.





**Figure S4.** Graphs representing the estimated phenytoin parameters versus true values under each internal validation scenario.

The identity line is shown in red, and a trend line in blue is drawn for each model: **(A)** single dose and **(B)** steady state.

**Abbreviations:**  $V_{max}$ , maximum velocity;  $k_m$ , Michaelis constant;  $V_{nr}$ , distribution volume independent of renal function.