Supplement Material

Cefepime precision dosing tool: From Standard to Precise Dose Using Nonparametric Population Pharmacokinetics

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Methods

Optimal initial dosing simulations

Matlab software vR2018b (The MathWorks Inc., Natick, MA, USA) was used then to calculate the OID of cefepime based on the final nonparametric model developed earlier [1,2]. Taking the support points generated by the nonparametric population PK model along with the associated probability and the influence of individual covariates, the *a priori* probability to reach a target PK/PD parameter can be calculated.

C_{min} was used as criteria to compute OID, after correction for cefepime protein binding (20%) [3]. For example, for a MIC cut-off of 8 mg/L, *f*C_{min}:MIC of 1 and 4 were translated to C_{min} target of 10 and 40 mg/L, respectively.

For a given dose ($dose_j$) of cefepime, the *a priori* probability (target attainment rate, TAR) that C_{min} is equal to or greater than a target value X is :

$$TAR(dose_j) = \sum_{i=0}^{n} prob_i \ (C_{min,i} \geq X))$$

where $prob_i$ are the probabilities related to each of the support points of the nonparametric model, and $C_{min,i}$ calculated for one possible set of PK parameters associated with $prob_i$.

The OID was computed as follows:

$$OID = min\left[arg\left\{TAR_{dose\ j} \geq 0.9\right\}\right]$$

In other words, the optimal dose was the minimal dose associated with 90% *a priori* probability of $C_{min} \geq X$. The algorithm was used to identify the optimal dose associated with maximum probability to achieve a target interval (i.e. $X \leq C_{min} \leq Y$). We used this approach to derive the OID targeting fC_{min}:MIC 1 to 4, assuming a MIC of 8 mg/L (equivalent to $10 \leq C_{min} \leq 40$ mg/L). OID were computed for adults and children separately, as those two populations presented different PK parameter values in the final model. An optimal dose was calculated for a pair of body weight and CrCl. In adults, we considered weight ranging from 30 to 250 kg, and CrCl ranging from 20 to 200 ml/min, with increments of 10 kg and 10 mL/min, respectively. In children, weight and CrCl ranges were 5-40 kg (5 kg increment) and 20-120 mL/min (10 mL/min increment), respectively.

Various candidate dosing regimens of cefepime were tested. In adults, 9 extended-infusion regimens were examined, with increasing magnitude, as follows: 0.5 g q 24 hr, 1g q 24 hr, 2 g q 24 hr, 0.5 g q 12 hr, 1 g q 12 hr, 2 g q 12 hr, 0.5 g q 8 hr, 1 g q 8 hr, and 2 g q 8 h. The infusion time was 4 hr for all these extended regimens. We also tested 4 continuous infusion regimens of 2, 4, 6 and 8g/24h. In children, three extended regimens (50 mg/kg q 24, 12 and 8 h as a 4-hr infusion) and four continuous infusion regimens (50, 100, 150 and 200 mg/kg/24h) were tested. Since increases in doses will eventually hit the PK/PD target of interest, we chose the lowest dose achieving that target as the optimal dose. When no extended regimen was optimal, the lowest continuous infusion regimen was selected.

To assess the adequacy of dosage regimens generated by this approach, the OID was simulated for each patient in the validation dataset using their individual PK parameters predicted by the PK model and the target attainment assessed. Results were compared to those obtained by simulating the administration of the dose recommended in the drug label.

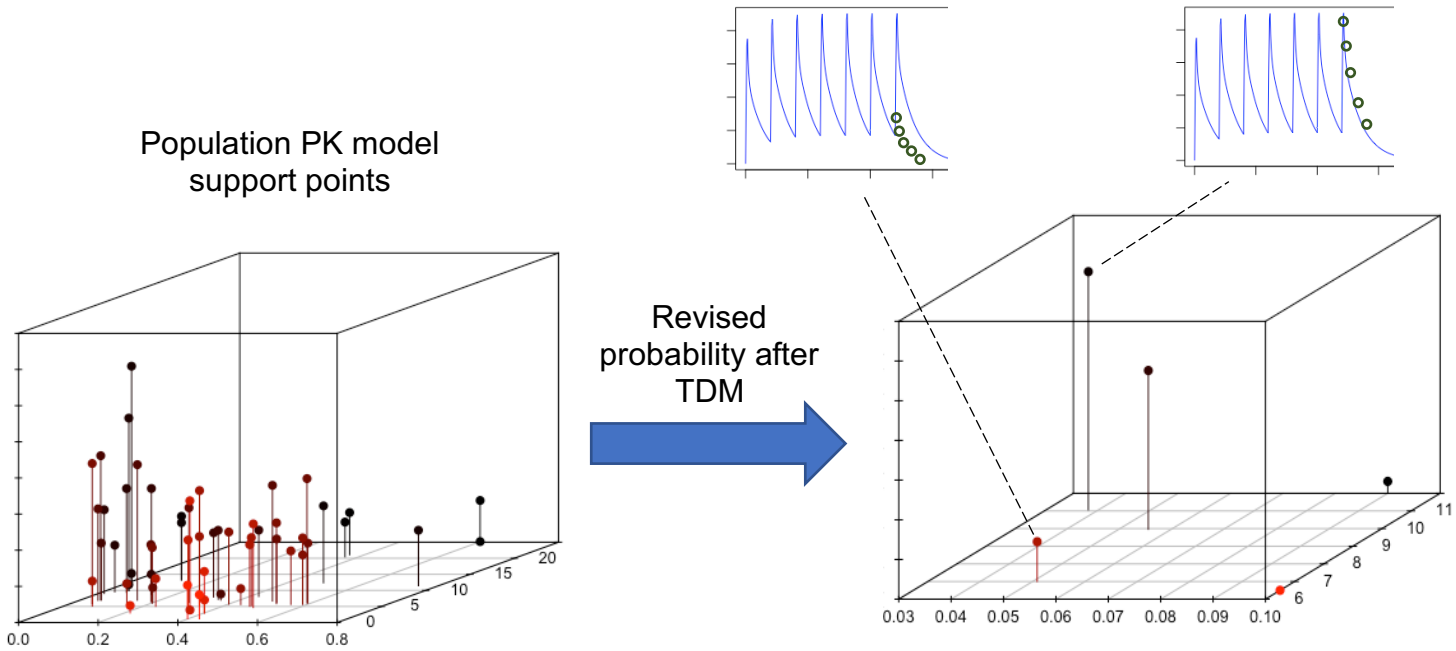
References

[1] D'Argenio DZ, Rodman JH. Targeting the systemic exposure of teniposide in the population and the individual using a stochastic therapeutic objective. Journal of pharmacokinetics and biopharmaceutics. 1993 Apr 1;21(2):223-51.

[2] Boidin C, Bourguignon L, Cohen S, Roger C, Lefrant JY, Roberts JA, Allaouchiche B, Lepape A, Friggeri A, Goutelle S. Amikacin initial dose in critically ill patients: a nonparametric approach to optimize a priori pharmacokinetic/pharmacodynamic target attainments in individual patients. Antimicrobial agents and chemotherapy. 2019 Nov 1;63(11):e00993-19.

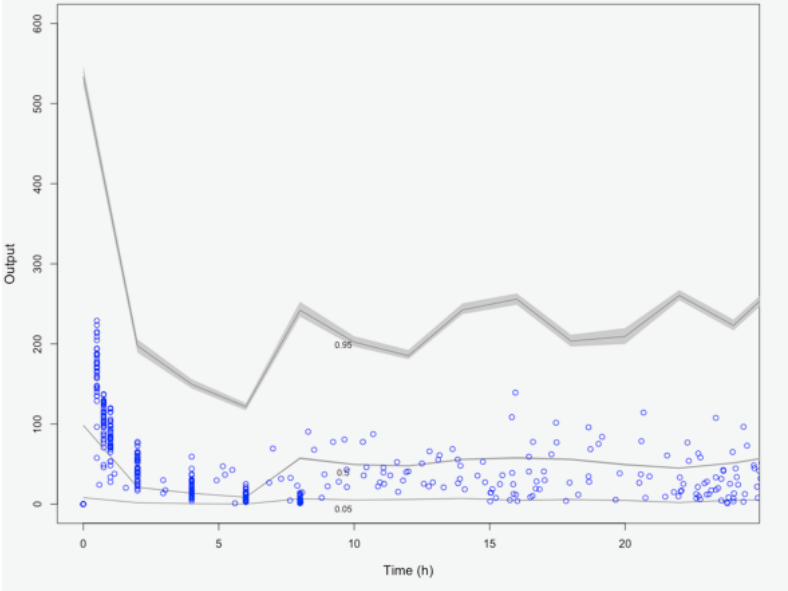
[3] Bristol-Myers Squibb. Maxipime (cefepime) package insert. 2007. Bristol-Myers Squibb, NewYork, NY.

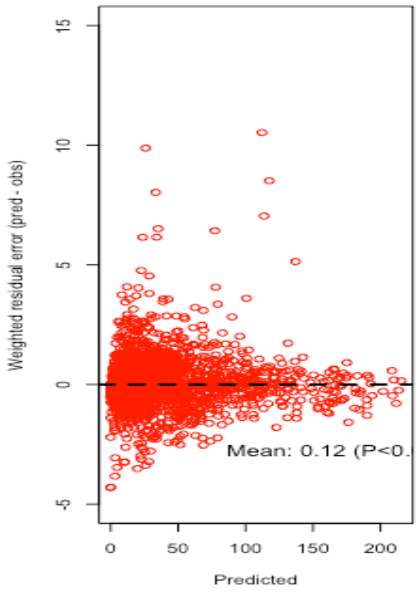
Figure S1. How BestDose uses the PK model to generate the drug exposure after revising the probability of support points

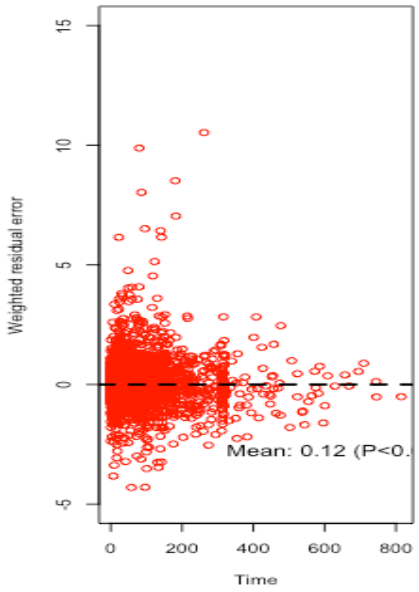


PK, pharmacokinetic; TDM, therapeutic drug monitoring

Figure S2: Visual predicted checks and weighted residual error plots







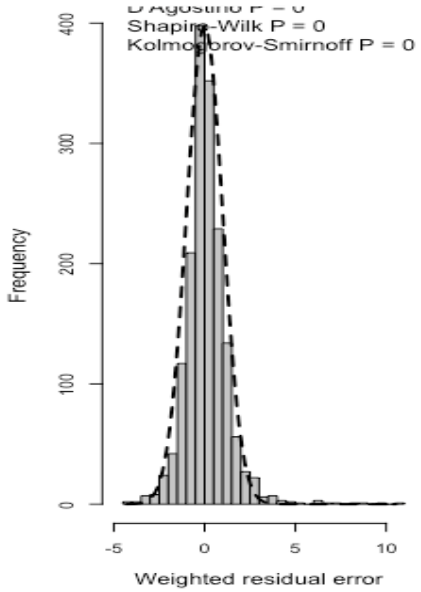
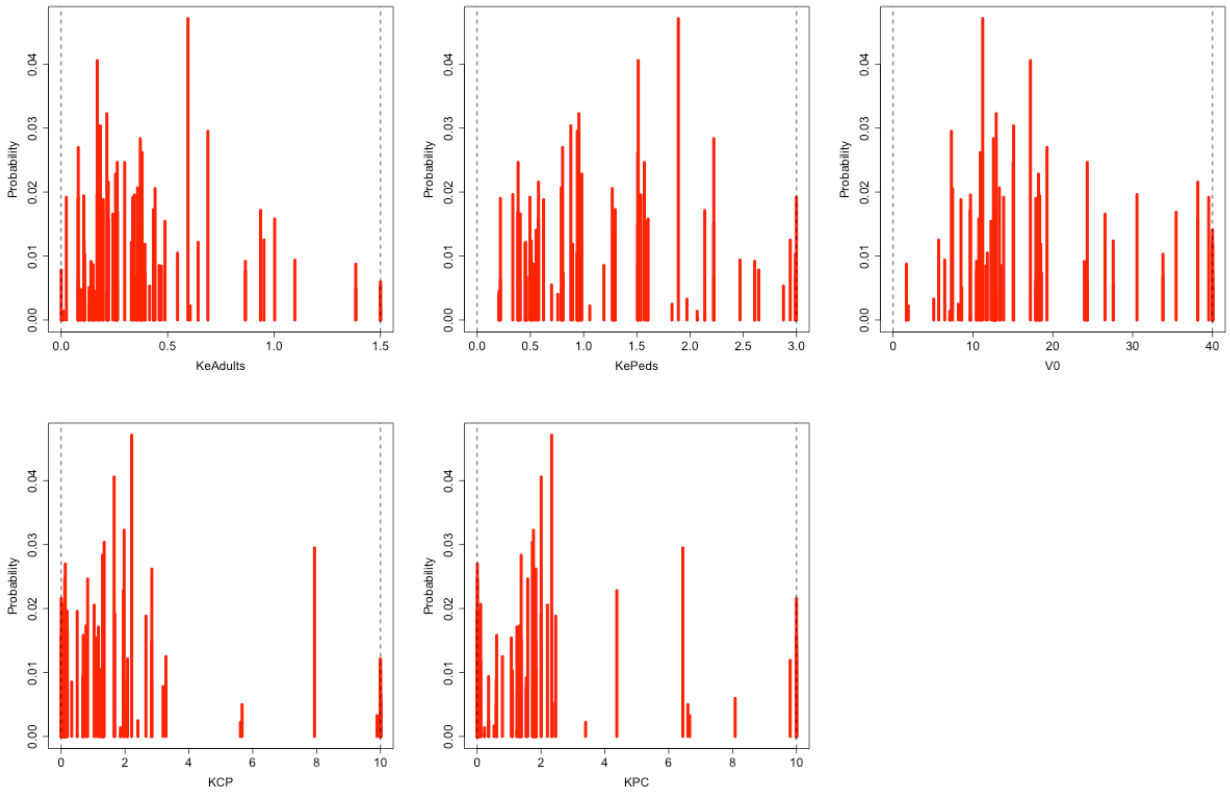


Figure S3. Support points generated by cefepime population pharmacokinetic model



k_{cp}, rate of transfer from the central to the peripheral compartment; k_e, elimination rate constant; k_{pc}; rate of transfer from the peripheral to the central compartment; V0, central volume of distribution.

Figure S4. Observed versus population and individual predicted cefepime concentration in the validation dataset

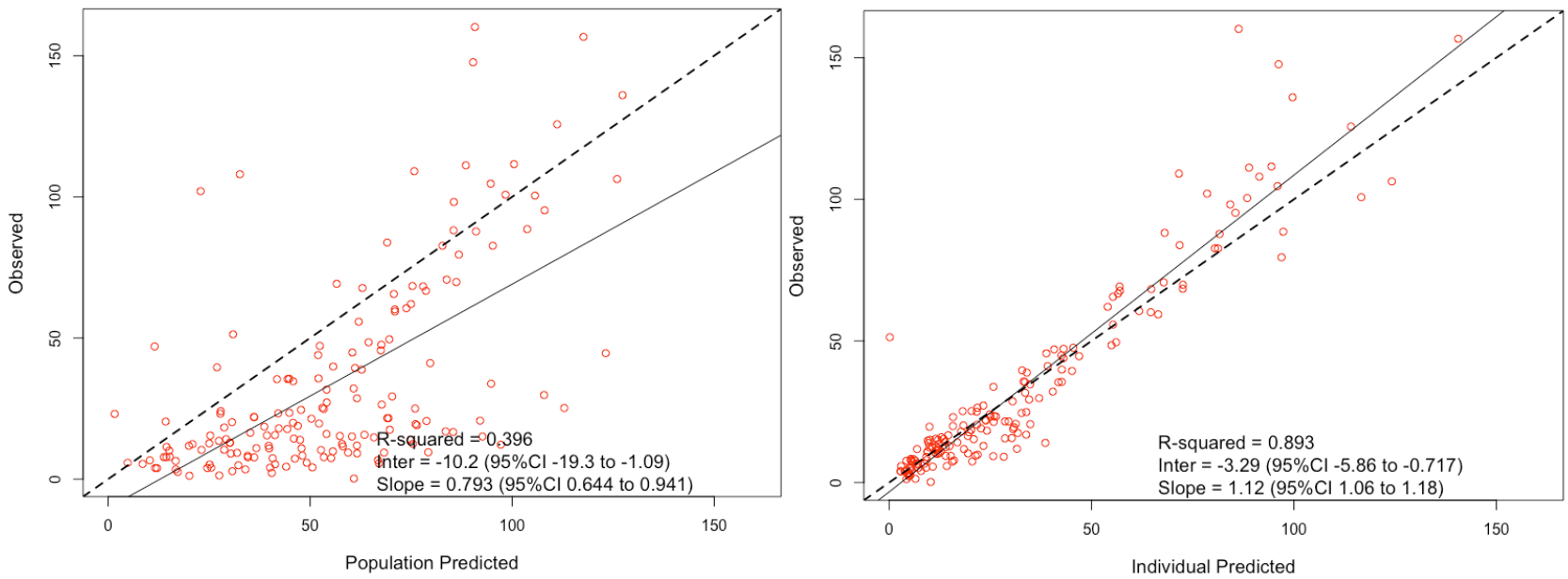


Table S1: Optimal initial dose in adult patients and associated probability to achieve fC_{min}:MIC 1 to 4 (MIC 8 mg/L)*

	Body weight															
	30		40		50		60		70		80		90		100	
CCR	Regimen	PTA	Regimen	PTA	Regimen	PTA	Regimen	PTA	Regimen	PTA	Regimen	PTA	Regimen	PTA	Regimen	PTA
20	0.5g q24h	0.621	0.5g q24h	0.623	0.5g q24h	0.628	0.5g q24h	0.655	1g q24h	0.636	1g q24h	0.609	0.5 g q12h	0.629	0.5 g q12h	0.654
30	1g q24h	0.604	1g q24h	0.689	0.5 g q12h	0.671	0.5 g q12h	0.749	0.5 g q12h	0.729	0.5 g q12h	0.658	0.5 g q12h	0.627	0.5 g q8h	0.696
40	0.5 g q12h	0.589	0.5 g q12h	0.691	0.5 g q12h	0.728	0.5 g q12h	0.701	0.5 g q12h	0.727	0.5 g q8h	0.741	0.5 g q8h	0.774	0.5 g q8h	0.774
50	0.5 g q12h	0.692	0.5 g q12h	0.690	0.5 g q12h	0.677	0.5 g q8h	0.754	0.5 g q8h	0.738	0.5 g q8h	0.728	0.5 g q8h	0.769	0.5 g q8h	0.826
60	0.5 g q8h	0.572	0.5 g q8h	0.695	0.5 g q8h	0.712	0.5 g q8h	0.701	0.5 g q8h	0.809	0.5 g q8h	0.814	1g q12h	0.755	2g/24h CI	0.772
70	0.5 g q8h	0.639	0.5 g q8h	0.688	0.5 g q8h	0.701	0.5 g q8h	0.785	0.5 g q8h	0.734	2g/24h CI	0.772	2g/24h CI	0.772	2g/24h CI	0.879
80	0.5 g q8h	0.642	0.5 g q8h	0.690	0.5 g q8h	0.739	2g/24h CI	0.692	2g/24h CI	0.741	2g/24h CI	0.813	2g/24h CI	0.863	2g/24h CI	0.860
90	0.5 g q8h	0.659	0.5 g q8h	0.651	2g/24h CI	0.695	2g/24h CI	0.722	2g/24h CI	0.843	2g/24h CI	0.851	2g/24h CI	0.848	2g/24h CI	0.839
100	0.5 g q8h	0.663	2g/24h CI	0.656	2g/24h CI	0.722	2g/24h CI	0.782	2g/24h CI	0.851	2g/24h CI	0.848	2g/24h CI	0.801	2g/24h CI	0.794
110	0.5 g q8h	0.603	2g/24h CI	0.688	2g/24h CI	0.722	2g/24h CI	0.848	2g/24h CI	0.848	2g/24h CI	0.776	2g/24h CI	0.794	2g/24h CI	0.728
120	2g/24h CI	0.620	2g/24h CI	0.718	2g/24h CI	0.833	2g/24h CI	0.835	2g/24h CI	0.776	2g/24h CI	0.794	2g/24h CI	0.728	4g/24h CI	0.722
130	2g/24h CI	0.637	2g/24h CI	0.718	2g/24h CI	0.821	2g/24h CI	0.813	2g/24h CI	0.769	2g/24h CI	0.728	4g/24h CI	0.718	4g/24h CI	0.722
140	2g/24h CI	0.669	2g/24h CI	0.829	2g/24h CI	0.817	2g/24h CI	0.776	2g/24h CI	0.782	4g/24h CI	0.718	4g/24h CI	0.722	4g/24h CI	0.848
150	2g/24h CI	0.699	2g/24h CI	0.801	2g/24h CI	0.813	2g/24h CI	0.769	2g/24h CI	0.716	4g/24h CI	0.718	4g/24h CI	0.829	4g/24h CI	0.821
160	2g/24h CI	0.699	2g/24h CI	0.804	2g/24h CI	0.776	2g/24h CI	0.759	4g/24h CI	0.699	4g/24h CI	0.762	4g/24h CI	0.833	4g/24h CI	0.804
170	2g/24h CI	0.770	2g/24h CI	0.783	2g/24h CI	0.769	2g/24h CI	0.716	4g/24h CI	0.718	4g/24h CI	0.813	4g/24h CI	0.821	4g/24h CI	0.813
180	2g/24h CI	0.790	2g/24h CI	0.783	2g/24h CI	0.757	4g/24h CI	0.699	4g/24h CI	0.789	4g/24h CI	0.821	4g/24h CI	0.817	4g/24h CI	0.813
190	2g/24h CI	0.782	2g/24h CI	0.776	2g/24h CI	0.734	4g/24h CI	0.699	4g/24h CI	0.813	4g/24h CI	0.804	4g/24h CI	0.783	4g/24h CI	0.776
200	2g/24h CI	0.765	2g/24h CI	0.769	4g/24h CI	0.691	4g/24h CI	0.739	4g/24h CI	0.801	4g/24h CI	0.817	4g/24h CI	0.776	4g/24h CI	0.769

	Body weight															
	110		120		130		140		150		160		170		180	
CCR	Regimen	PTA	Regimen	PTA	Regimen	PTA	Regimen	PTA	Regimen	PTA	Regimen	PTA	Regimen	PTA	Regimen	PTA
20	0.5 g q12h	0.712	0.5 g q12h	0.664	0.5 g q12h	0.674	0.5 g q12h	0.650	0.5 g q12h	0.645	0.5 g q12h	0.645	0.5 g q12h	0.686	0.5 g q8h	0.657
30	0.5 g q8h	0.772	0.5 g q8h	0.747	0.5 g q8h	0.757	0.5 g q8h	0.733	1g q12h	0.735	1g q12h	0.722	1g q12h	0.717	2g/24h CI	0.767
40	0.5 g q8h	0.749	1g q12h	0.732	0.5 g q8h	0.779	2g/24h CI	0.767	2g/24h CI	0.769	2g/24h CI	0.769	2g/24h CI	0.789	2g/24h CI	0.789
50	2g/24h CI	0.741	2g/24h CI	0.744	2g/24h CI	0.789	2g/24h CI	0.789	2g/24h CI	0.830	2g/24h CI	0.864	2g/24h CI	0.864	2g/24h CI	0.852
60	2g/24h CI	0.764	2g/24h CI	0.860	2g/24h CI	0.864	2g/24h CI	0.852	2g/24h CI	0.852	2g/24h CI	0.824	2g/24h CI	0.804	1g q8h	0.769
70	2g/24h CI	0.852	2g/24h CI	0.852	2g/24h CI	0.831	2g/24h CI	0.824	1g q8h	0.826	1g q8h	0.814	1g q8h	0.763	4g/24h CI	0.742
80	2g/24h CI	0.831	1g q8h	0.809	2g/24h CI	0.786	2g/24h CI	0.736	1g q8h	0.726	4g/24h CI	0.748	4g/24h CI	0.772	4g/24h CI	0.772
90	2g/24h CI	0.786	2g/24h CI	0.756	2g/24h CI	0.701	4g/24h CI	0.701	4g/24h CI	0.768	4g/24h CI	0.772	4g/24h CI	0.813	4g/24h CI	0.879
100	2g/24h CI	0.730	4g/24h CI	0.701	4g/24h CI	0.722	4g/24h CI	0.741	4g/24h CI	0.813	4g/24h CI	0.863	4g/24h CI	0.863	4g/24h CI	0.835
110	4g/24h CI	0.722	4g/24h CI	0.722	4g/24h CI	0.782	4g/24h CI	0.879	4g/24h CI	0.863	4g/24h CI	0.835	4g/24h CI	0.835	4g/24h CI	0.813
120	4g/24h CI	0.722	4g/24h CI	0.812	4g/24h CI	0.863	4g/24h CI	0.851	4g/24h CI	0.835	4g/24h CI	0.813	4g/24h CI	0.813	4g/24h CI	0.794
130	4g/24h CI	0.848	4g/24h CI	0.833	4g/24h CI	0.835	4g/24h CI	0.848	4g/24h CI	0.813	4g/24h CI	0.776	4g/24h CI	0.794	4g/24h CI	0.794
140	4g/24h CI	0.821	4g/24h CI	0.835	4g/24h CI	0.813	4g/24h CI	0.813	4g/24h CI	0.776	4g/24h CI	0.794	6g/24h CI	0.848	6g/24h CI	0.833
150	4g/24h CI	0.835	4g/24h CI	0.813	4g/24h CI	0.776	4g/24h CI	0.769	4g/24h CI	0.794	6g/24h CI	0.833	6g/24h CI	0.833	6g/24h CI	0.851
160	4g/24h CI	0.813	4g/24h CI	0.776	4g/24h CI	0.769	4g/24h CI	0.794	6g/24h CI	0.833	6g/24h CI	0.821	6g/24h CI	0.835	6g/24h CI	0.848
170	4g/24h CI	0.776	4g/24h CI	0.769	6g/24h CI	0.797	6g/24h CI	0.833	6g/24h CI	0.821	6g/24h CI	0.804	6g/24h CI	0.848	6g/24h CI	0.813
180	4g/24h CI	0.776	4g/24h CI	0.769	6g/24h CI	0.813	6g/24h CI	0.821	6g/24h CI	0.804	6g/24h CI	0.813	6g/24h CI	0.813	8g/24h CI	0.829
190	4g/24h CI	0.769	6g/24h CI	0.813	6g/24h CI	0.821	6g/24h CI	0.804	6g/24h CI	0.813	6g/24h CI	0.813	8g/24h CI	0.829	8g/24h CI	0.833
200	6g/24h CI	0.813	6g/24h CI	0.821	6g/24h CI	0.804	6g/24h CI	0.783	6g/24h CI	0.813	8g/24h CI	0.813	8g/24h CI	0.833	8g/24h CI	0.821

	Body weight													
	190		200		210		220		230		240		250	
CCR	Regimen	PTA	Regimen	PTA	Regimen	PTA	Regimen	PTA	Regimen	PTA	Regimen	PTA	Regimen	PTA
20	0.5 g q12h	0.670	0.5 g q8h	0.719	0.5 g q8h	0.702	0.5 g q8h	0.695	0.5 g q8h	0.664	1g q12h	0.663	2g q24h	0.661
30	2g/24h CI	0.757	2g/24h CI	0.757	2g/24h CI	0.757	2g/24h CI	0.750	0.5 g q8h	0.724	0.5 g q8h	0.719	2g/24h CI	0.716
40	1g q8h	0.772	2g/24h CI	0.794	2g/24h CI	0.823	2g/24h CI	0.807	1g q8h	0.789	2g/24h CI	0.788	2g q12h	0.772
50	2g/24h CI	0.806	2g/24h CI	0.802	2g/24h CI	0.736	2g/24h CI	0.736	1g q8h	0.749	1g q8h	0.779	1g q8h	0.779
60	1g q8h	0.826	1g q8h	0.826	1g q8h	0.764	1g q8h	0.738	4g/24h CI	0.744	4g/24h CI	0.744	4g/24h CI	0.789
70	2g q12h	0.791	4g/24h CI	0.772	4g/24h CI	0.764	4g/24h CI	0.764	4g/24h CI	0.764	4g/24h CI	0.830	4g/24h CI	0.897
80	4g/24h CI	0.772	4g/24h CI	0.813	4g/24h CI	0.871	4g/24h CI	0.881	4g/24h CI	0.864	4g/24h CI	0.852	4g/24h CI	0.852
90	4g/24h CI	0.863	4g/24h CI	0.835	4g/24h CI	0.852	4g/24h CI	0.852	4g/24h CI	0.866	4g/24h CI	0.831	4g/24h CI	0.824
100	4g/24h CI	0.835	4g/24h CI	0.874	4g/24h CI	0.831	4g/24h CI	0.831	2g q8h	0.797	4g/24h CI	0.786	6g/24h CI	0.813
110	4g/24h CI	0.839	4g/24h CI	0.794	4g/24h CI	0.786	6g/24h CI	0.813	6g/24h CI	0.813	6g/24h CI	0.879	6g/24h CI	0.863
120	4g/24h CI	0.794	4g/24h CI	0.794	6g/24h CI	0.879	6g/24h CI	0.863	6g/24h CI	0.851	6g/24h CI	0.835	6g/24h CI	0.835
130	6g/24h CI	0.848	6g/24h CI	0.863	6g/24h CI	0.851	6g/24h CI	0.835	6g/24h CI	0.835	6g/24h CI	0.848	6g/24h CI	0.813
140	6g/24h CI	0.851	6g/24h CI	0.835	6g/24h CI	0.835	6g/24h CI	0.848	6g/24h CI	0.813	6g/24h CI	0.813	8g/24h CI	0.848
150	6g/24h CI	0.835	6g/24h CI	0.848	6g/24h CI	0.813	6g/24h CI	0.813	8g/24h CI	0.848	8g/24h CI	0.833	8g/24h CI	0.863
160	6g/24h CI	0.813	6g/24h CI	0.813	8g/24h CI	0.848	8g/24h CI	0.833	8g/24h CI	0.833	8g/24h CI	0.851	8g/24h CI	0.835
170	6g/24h CI	0.776	8g/24h CI	0.833	8g/24h CI	0.833	8g/24h CI	0.821	8g/24h CI	0.835	8g/24h CI	0.835	8g/24h CI	0.848
180	8g/24h CI	0.833	8g/24h CI	0.821	8g/24h CI	0.821	8g/24h CI	0.835	8g/24h CI	0.848	8g/24h CI	0.813	8g/24h CI	0.813
190	8g/24h CI	0.821	8g/24h CI	0.804	8g/24h CI	0.848	8g/24h CI	0.813	8g/24h CI	0.813	8g/24h CI	0.776	8g/24h CI	0.776
200	8g/24h CI	0.804	8g/24h CI	0.817	8g/24h CI	0.813	8g/24h CI	0.813	8g/24h CI	0.776	8g/24h CI	0.776	8g/24h CI	0.769

CCR, creatinine clearance in mL/min; CI, continuous infusion; PTA, probability of target attainment.

* All extended regimens are infused over 4 hours.

Table S2: Optimal initial dose in pediatric patients and associated probability to achieve *f*C_{min}:MIC 1 to 4 (MIC 8 mg/L)*

	Body weight							
	5		10		15		20	
CCR	Regimen	PTA	Regimen	PTA	Regimen	PTA	Regimen	PTA
20	50 mg/kg/24h CI	0.782	50 mg/kg/24h CI	0.672	50 mg/kg/24h CI	0.671	50 mg/kg/24h CI	0.622
30	50 mg/kg/24h CI	0.843	50 mg/kg/24h CI	0.843	50 mg/kg/24h CI	0.822	50 mg/kg/24h CI	0.817
40	100 mg/kg/24h CI	0.751	50 mg/kg/24h CI	0.805	50 mg/kg/24h CI	0.843	50 mg/kg/24h CI	0.843
50	100 mg/kg/24h CI	0.843	100 mg/kg/24h CI	0.787	100 mg/kg/24h CI	0.751	50 mg/kg/24h CI	0.765
60	100 mg/kg/24h CI	0.843	100 mg/kg/24h CI	0.843	100 mg/kg/24h CI	0.822	100 mg/kg/24h CI	0.787
70	150 mg/kg/24h CI	0.822	100 mg/kg/24h CI	0.843	100 mg/kg/24h CI	0.843	100 mg/kg/24h CI	0.843
80	150 mg/kg/24h CI	0.843	100 mg/kg/24h CI	0.805	100 mg/kg/24h CI	0.843	100 mg/kg/24h CI	0.843
90	150 mg/kg/24h CI	0.843	150 mg/kg/24h CI	0.843	100 mg/kg/24h CI	0.805	100 mg/kg/24h CI	0.838
100	200 mg/kg/24h CI	0.843	150 mg/kg/24h CI	0.843	150 mg/kg/24h CI	0.843	150 mg/kg/24h CI	0.822
110	200 mg/kg/24h CI	0.843	150 mg/kg/24h CI	0.843	150 mg/kg/24h CI	0.843	150 mg/kg/24h CI	0.843
120	200 mg/kg/24h CI	0.843	200 mg/kg/24h CI	0.843	150 mg/kg/24h CI	0.843	150 mg/kg/24h CI	0.843

	Body weight							
	25		30		35		40	
CCR	Regimen	PTA	Regimen	PTA	Regimen	PTA	Regimen	PTA
20	50 mg/kg/24h CI	0.511	50 mg/kg q12h	0.486	50 mg/kg q12h	0.429	50 mg/kg/24h CI	0.400
30	50 mg/kg/24h CI	0.782	50 mg/kg/24h CI	0.751	50 mg/kg/24h CI	0.751	50 mg/kg/24h CI	0.703
40	50 mg/kg/24h CI	0.843	50 mg/kg/24h CI	0.843	50 mg/kg/24h CI	0.843	50 mg/kg/24h CI	0.822
50	50 mg/kg/24h CI	0.805	50 mg/kg/24h CI	0.838	50 mg/kg/24h CI	0.843	50 mg/kg/24h CI	0.843
60	100 mg/kg/24h CI	0.751	100 mg/kg/24h CI	0.751	50 mg/kg/24h CI	0.765	50 mg/kg/24h CI	0.765
70	100 mg/kg/24h CI	0.822	100 mg/kg/24h CI	0.819	100 mg/kg/24h CI	0.807	100 mg/kg/24h CI	0.770
80	100 mg/kg/24h CI	0.843	100 mg/kg/24h CI	0.843	100 mg/kg/24h CI	0.843	100 mg/kg/24h CI	0.822
90	100 mg/kg/24h CI	0.843	100 mg/kg/24h CI	0.843	100 mg/kg/24h CI	0.843	100 mg/kg/24h CI	0.843
100	100 mg/kg/24h CI	0.805	100 mg/kg/24h CI	0.838	100 mg/kg/24h CI	0.843	100 mg/kg/24h CI	0.843
110	150 mg/kg/24h CI	0.843	150 mg/kg/24h CI	0.822	100 mg/kg/24h CI	0.805	150 mg/kg/24h CI	0.788
120	150 mg/kg/24h CI	0.843	150 mg/kg/24h CI	0.843	150 mg/kg/24h CI	0.843	150 mg/kg/24h CI	0.822

CCR, creatinine clearance in mL/min; CI, continuous infusion; PTA, probability of target attainment.

* All extended regimens are infused over 4 hours.

Table S3: Target attainment (C_{min} 10-40 mg/L) of optimal initial dose and drug label dose simulations using the validation dataset[a]

ID	Cefepime label dose			C_{min} achieved, mg/L	Cefepime optimal initial dose			C_{min} achieved, mg/L
	Dose, mg	Frequency, hr	Infusion, hr		Dose, mg	Frequency, hr	Infusion, hr	
1	2000	8	0.5	14.31	4000	24	24	23.16
2	2000	8	0.5	11.77	2000	24	24	11.72
3	2000	8	0.5	1.23	4000	24	24	12.19
4	2000	8	0.5	11.72	2000	24	24	10.67
5	2000	8	0.5	10.01	4000	24	24	17.24
6	2000	8	0.5	20.55	2000	24	24	16.89
7	2000	8	0.5	11.16	2000	24	24	12.44
8	2000	8	0.5	12.66	2000	24	24	14.97
9	2000	8	0.5	2.21	4000	24	24	12.09
10	2000	8	0.5	24.56	2000	24	24	18.80
11	2000	8	0.5	8.28	2000	24	24	10.44
12	2000	8	0.5	35.71	2000	24	24	19.38
13	2000	8	0.5	14.15	2000	24	24	13.59
14	2000	8	0.5	50.66	500	8	4	16.75
15	2000	8	0.5	37.33	500	8	4	10.64
16	2000	8	0.5	6.49	2000	24	24	4.63
17	2000	8	0.5	37.95	2000	24	24	19.90
18	2000	8	0.5	10.75	2000	24	24	11.84
19	2000	8	0.5	24.41	4000	24	24	22.97
20	2000	8	0.5	12.31	2000	24	24	7.29
21	2000	8	0.5	3.09	2000	24	24	3.59
22	2000	8	0.5	0.13	4000	24	24	5.84
23	2000	8	0.5	41.23	2000	24	24	26.82
24	2000	12	0.5	32.37	500	8	4	13.09
25	2000	8	0.5	10.68	2000	24	24	8.67
26	2000	12	0.5	30.44	500	8	4	17.94
27	2000	8	0.5	12.29	4000	24	24	25.62
28	2000	8	0.5	8.55	4000	24	24	22.63
29	2000	8	0.5	10.96	4000	24	24	23.16
30	2000	8	0.5	64.29	2000	24	24	28.06
31	2000	12	0.5	564.86	500	12	4	147.17
32	2000	24	0.5	224.54	500	12	4	129.68
33	1000	24	0.5	30.25	500	24	4	15.21
34	2000	8	0.5	4.29	2000	24	24	1.65

[a)] These datasets are from Roberts, Sime, and Whited et al. which were used for model validation.