



Statistical Methodologies for Pragmatic AUC Estimation in Longitudinal Data

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AUC Calculation: Ideal vs. Reality

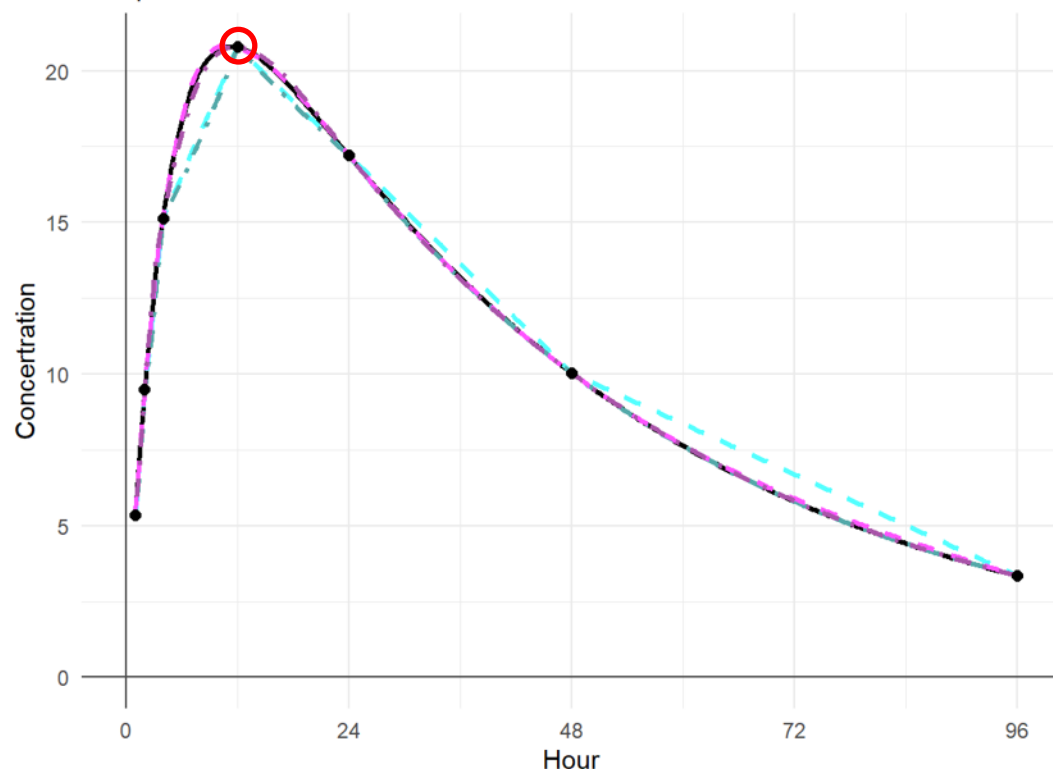
- // AUC (Area Under the Curve) is a critical metric for summarizing longitudinal data in
 - // Pharmacokinetics
 - // Radiopharmaceuticals
- // In this simulation study
 - // Robustness of 7 interpolation methods for AUC calculation are compared
 - // Based bias and RMSE under 8 scenarios



AUC Calculation: Ideal vs. Reality

Oral, peak at 12h, analytical curve vs. interpolants

Samples at t = 1, 2, 4, 12, 24, 48, 96

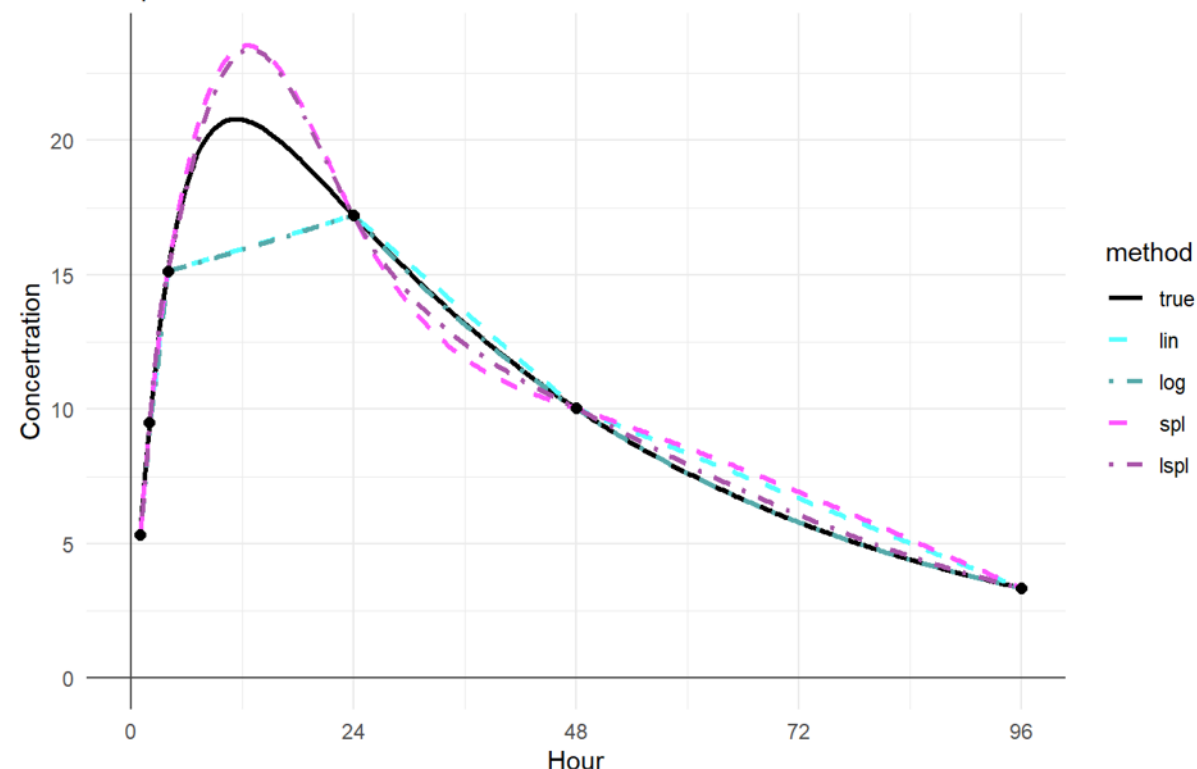


Existing methodological comparisons:

- focus on samples with all key time points
- even if they claimed to be “poorly” sampled

Oral, peak at 12h, analytical curve vs. interpolants

Samples at t = 1, 2, 4, 24, 48, 96



Realistic lab conditions:

- key time points may be missing



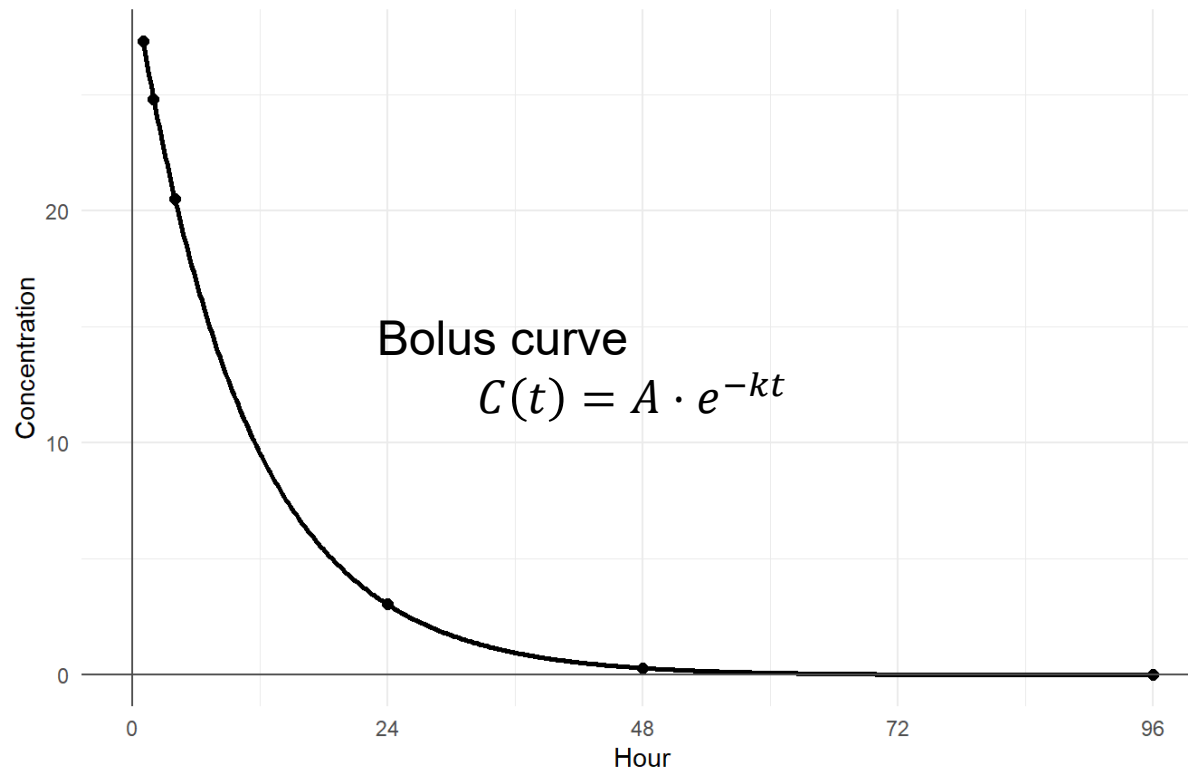
Which AUC calculation methods have more robust performances?



Simulation Study Design: Types of Curves

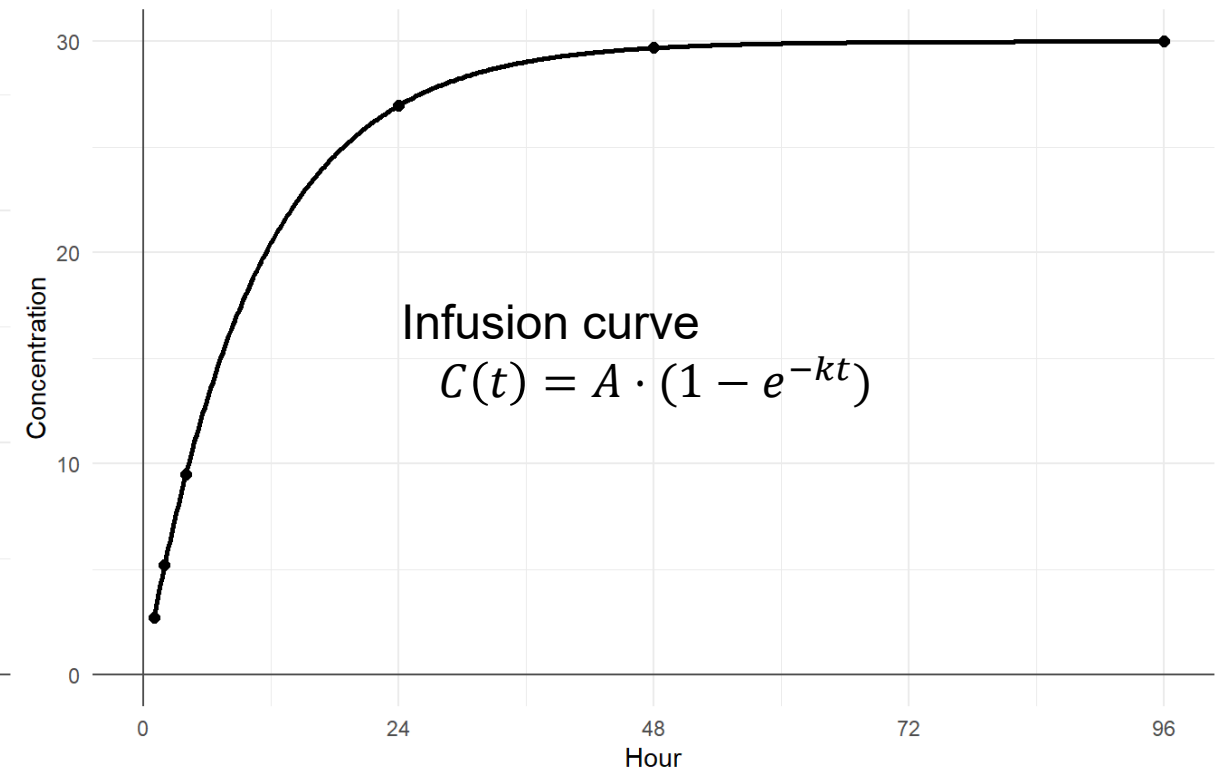
Bolus, analytical curve and sample points

Samples at $t = 1, 2, 4, 24, 48, 96$



Infusion, analytical curve and sample points

Samples at $t = 1, 2, 4, 24, 48, 96$

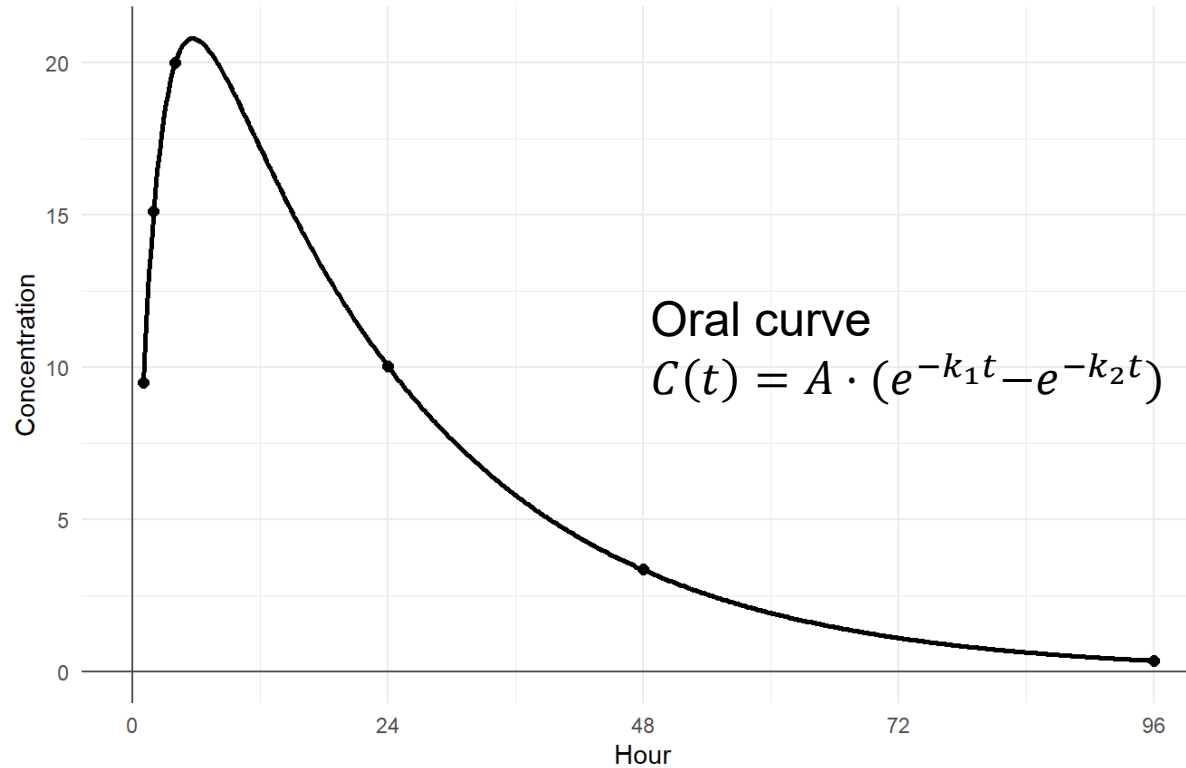




Simulation Study Design: Types of Curves

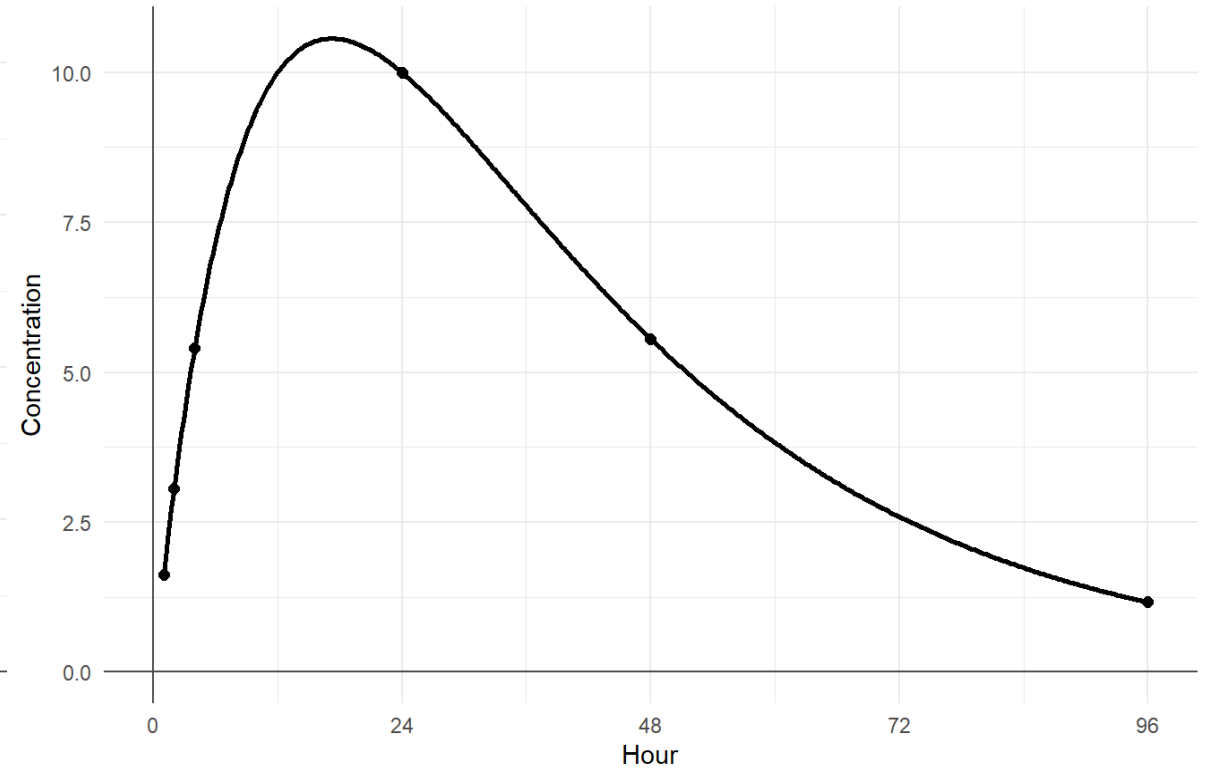
Oral, peak at 6h, analytical curve and sample points

Samples at $t = 1, 2, 4, 24, 48, 96$



Oral, peak at 18h, analytical curve and sample points

Samples at $t = 1, 2, 4, 24, 48, 96$

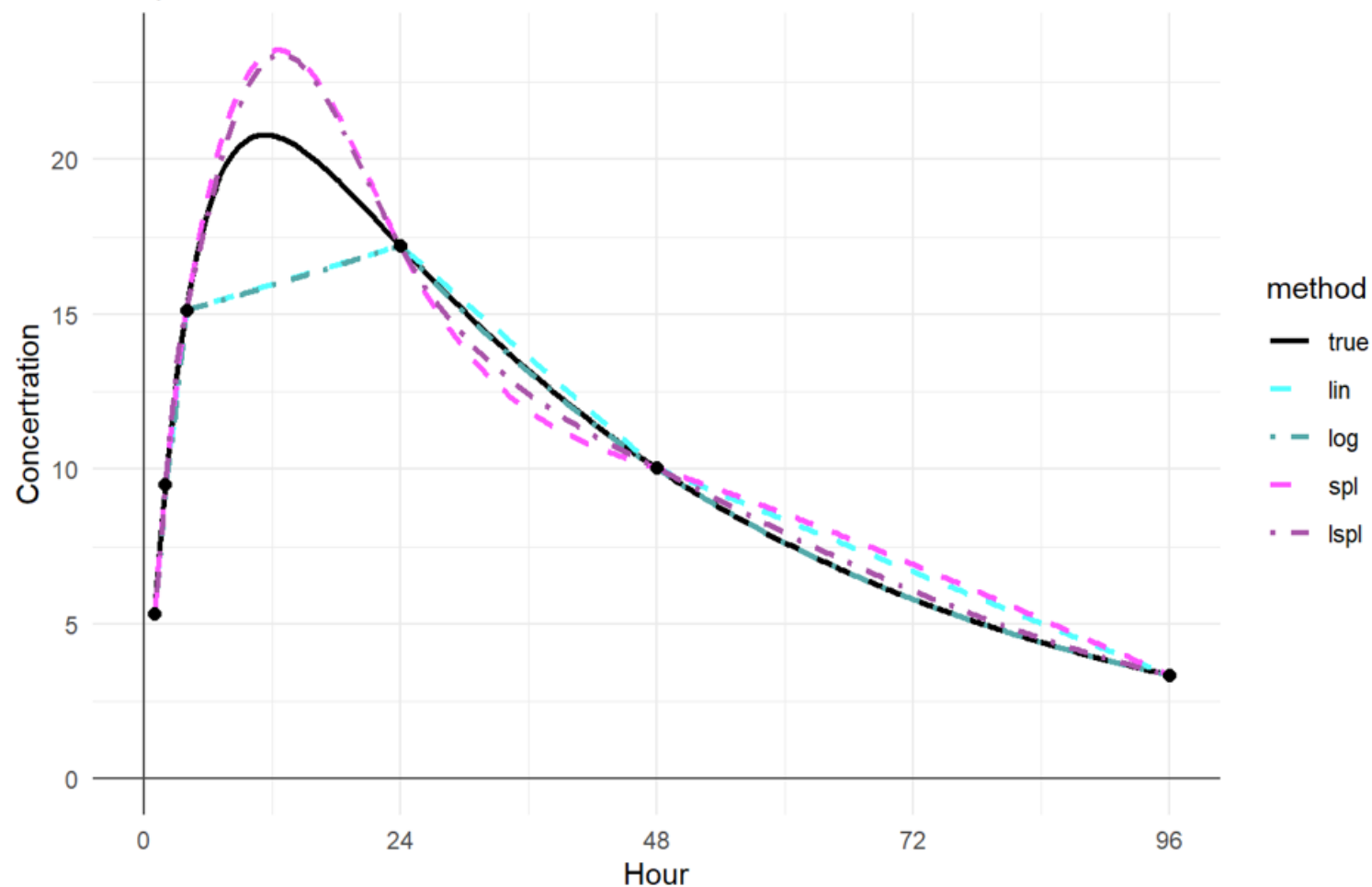




Simulation Study Design: Interpolation Methods

Oral, peak at 12h, analytical curve vs. interpolants

Samples at $t = 1, 2, 4, 24, 48, 96$



- lin: linear
- log
- lin-log: lin up, log down
- spl: natural cubic spline
- spl-log: spl up, log down
- lspl: spl applied to log-transferred endpoints
- lspl-log: lspl up, log down



Bias of AUC Calculation

GREEN represents no more than 1% more than minimum bias of the curve;
RED represents more than 10% more than minimum bias of the curve.

	lin	log	lin_log	spl	spl_log	lspl	lspl_log
Bolus	25.14%	0.69%	0.69%	3.28%	0.71%	5.92%	0.71%
Infusion	-1.53%	-2.91%	-1.58%	1.51%	0.55%	4.01%	2.03%
Oral, Peak 1.5h	23.61%	-0.36%	-0.35%	-25.69%	-0.30%	-3.14%	-0.30%
Oral, Peak 3h	9.92%	-0.66%	-0.63%	-7.35%	-0.50%	-1.90%	-0.51%
Oral, Peak 6h	4.74%	-4.25%	-4.16%	13.14%	-3.95%	6.79%	-3.89%
Oral, Peak 12h	-1.27%	-5.16%	-4.99%	6.03%	2.21%	6.08%	2.77%
Oral, Peak 18h	-2.50%	-9.47%	-8.48%	1.17%	-0.57%	4.45%	3.41%
Oral, Peak 24h	-1.47%	-6.88%	-5.33%	2.64%	-0.31%	5.76%	3.70%
Maximum Abs	25.14%	9.47%	8.48%	25.69%	3.95%	6.79%	3.89%



RMSE of AUC Calculation

GREEN represents no more than 1% more than minimum RMSE of the curve;

RED represents more than 10% more than minimum RMSE of the curve.

	lin	log	lin_log	spl	spl_log	lspl	lspl_log
Bolus	26.70%	6.10%	6.10%	56.67%	6.11%	21.70%	6.11%
Infusion	5.49%	5.94%	5.50%	6.45%	5.58%	9.86%	7.54%
Oral, Peak 1.5h	25.00%	5.76%	5.76%	60.67%	5.75%	16.99%	5.75%
Oral, Peak 3h	11.49%	4.93%	4.93%	28.40%	4.97%	13.16%	4.98%
Oral, Peak 6h	7.37%	6.59%	6.54%	25.84%	6.42%	19.60%	6.39%
Oral, Peak 12h	5.47%	7.12%	7.03%	11.43%	8.62%	14.93%	13.59%
Oral, Peak 18h	5.78%	10.47%	9.67%	7.08%	6.03%	11.53%	11.97%
Oral, Peak 24h	5.95%	8.53%	7.52%	7.18%	5.87%	11.48%	10.60%
Maximum	26.70%	10.47%	9.67%	60.67%	8.62%	21.70%	13.59%



Practical Recommendations

- // Based on the results of our simulation study
 - // **spl-log** has the most robust performance based on bias and RMSE
- // Practically, **lin-log** is also a strong candidate as
 - // It is more widely understood and accepted
 - // It has the second most robust performance based on RMSE

Health for all, Hunger for none



Thank you!