

Electronic supplementary material

Model-based estimation of iohexol plasma clearance for pragmatic renal function determination in the renal transplantation setting

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Development of HPLC-UV assay for iohexol quantification in plasma

Chemical and materials

Iohexol (Omnipaque 300) was purchased from GE Healthcare BV (Eindhoven, the Netherlands) and internal standard 1,3-dimethyluric acid from Sigma-Aldrich (Zwijndrecht, the Netherlands). Analytical grade phosphate buffered saline (PBS) was purchased from Braun (Oss, the Netherlands), perchloric acid (70%) from VWR (Amsterdam, the Netherlands) and acetonitrile and phosphoric acid (85%) from Merck (Darmstadt, Germany). Ultrapure water was produced onsite using a PURELAB® Flex purification system from ELGA LabWater (Lane End, UK).

Sample preparation

After collection, patient samples were transferred to the LUMC laboratory and stored at 4-8°C until analysis. All samples were analyzed within one week after collection. Iohexol high and low quality controls (QCs) and calibration standards were produced onsite by spiking blank serum with iohexol, which were homogenized on a tube roller bench for 15 min at 60 rpm and stored at -20°C. From each QC, calibration standard and patient sample, 200 µl was transferred to an Eppendorf tube and combined with 50 µl of a solution of 0.2 mg ml⁻¹ 1,3-dimethyluric acid in PBS and 250 µl 0.8 M perchloric acid. Subsequently, the mixture was vortex-mixed (VWR, Amsterdam, The Netherlands) for 5 s and centrifuged (ThermoFisher Scientific, Bleiswijk, The Netherlands) for 5 min at 13000 rpm, respectively. The supernatant was then transferred to an autosampler vial of which 20 µl was injected onto the HPLC-UV system.

HPLC-UV assay

Patient samples, QCs and calibration standards were analyzed on an HPLC-UV system, consisting of a UltiMate 3000 series UHPLC system connected to a UltiMate 3000 rapid separation (RS) diode array detector (DAD-3000RS), all from ThermoFisher Scientific. The HPLC system consisted of a WPS-3000RS autosampler and ISO-3100SD isocratic pump. Chromatographic separation was achieved using an Inertsil® ODS-2 (150 x 4.6 mm ID, particle size 5 µm) C18 column (Alltech, Ridderkerk, the Netherlands), protected by a SecurityGuard® C18 pre-column (4 x 3 mm ID) (Phenomenex, Utrecht, the Netherlands). Elution was performed with a mobile phase consisting of a mixture of 0.025% phosphoric acid and 4% acetonitrile in water. A constant flow rate of 1.2 ml min⁻¹ and pressure of 120 bar were applied at room temperature. The injection volume was set at 20 µl and the detection wavelength at 245 nm. The total run time was 12.0 min. Data were acquired and processed using ThermoFisher Scientific Chromeleon software v7.2.

Analytical validation

The assay was validated according to the European Medicines Agency guidelines on bioanalytical method validation, including selectivity, linearity, accuracy, precision, recovery, matrix effects, measurement error, cross validation and stability. The maximum tolerated validation limits were set as follows: linearity correlation coefficient >99%; accuracy 90-110%; within-run precision <10%CV; between-run precision <15%CV; LLQ imprecision <20%CV; ULQ imprecision <15%CV; stability content loss <10%; cross validation correlation coefficient ≥99% with slope 0.9-1.1 at ≤15%

divergence ($\leq 20\%$ for LLQ); and measurement error $< 15\%$. Linearity was first established over a concentration range of 25.9 to 129.5 $\mu\text{g ml}^{-1}$. In addition, the lower and upper limits of quantification were established at 10 $\mu\text{g ml}^{-1}$ and 500 $\mu\text{g ml}^{-1}$, respectively. Accuracy was evaluated on two separate days in sixfold (day 1) and eightfold (day 2) at QC low (25.9 $\mu\text{g ml}^{-1}$) and QC high (129.5 $\mu\text{g ml}^{-1}$), resulting in an average accuracy of 98% for QC low and 106% for QC high, showing adequate accuracy. The within-run precision was assessed in sixfold for both the QC low and QC high, resulting in a within-run precision of 3.0%CV for QC low and 2.7%CV for QC high. The between-run precision was evaluated in sevenfold for QC low and in eightfold for QC high, resulting in a between-run precision of 3.9%CV and 3.8%CV for QC low and QC high, respectively. The recovery was assessed in sixfold for the QC low and QC high, resulting in an average recovery of 101% (2.8%CV) for iohexol and 95% (1.3%CV) for 1,3-dimethyluric acid, showing adequate and reproducible recovery. Differences between matrix effects in plasma as compared to those in serum were found to be negligible. The measurement error was established at 11.8% and 9.8% for QC low and QC high, respectively. Any differences observed during cross validation did not exceed 10%, showing no clinically relevant divergence. The sample stability was determined in twofold at six time points at room temperature, in the refrigerator (4-8°C) and in the freezer (-20°C), with the maximum tolerable decrease in iohexol content set at $< 15\%$. The sample stability at room temperature, in the refrigerator and in the freezer were established up to 7 days, 14 days and 6 months, respectively. Calibration standards and QCs stored in the freezer were stable for a year and stock and working solutions for 14 days.

Cross-validation of LUMC (HPLC-UV) and ELCH (HPLC-MS/MS) bioanalytical assays for iohexol quantification in plasma

Cross-validation data

A total of 24 samples from NCT00734396 were re-analyzed at LUMC for the purpose of cross-validation. The iohexol concentrations in these samples as quantified at ELCH and re-quantified at LUMC are summarized in **Table S2.1**.

Passing-Bablok regression analysis

The Passing-Bablok regression fit is depicted in **Figure S2.1**, which showed a clear linear relationship between iohexol concentrations quantified at ELCH and LUMC, with a slope of 0.93 [95% CI: 0.89; 0.98] and intercept of 4.66 [0.19; 8.92].

Bland-Altman analysis

The Bland-Altman relative difference plot is depicted in **Figure S2.2**, which showed that the differences between iohexol concentrations quantified at ELCH and LUMC were evenly spread around the line of equality across the iohexol concentration range, with a mean bias of -1.24% [-4.81%; 2.34%] and 95% lower and upper limits of agreement of -17.8% [-24.0%; -11.6%] and 15.3% [9.15%; 21.5%], respectively. All but one (95.8%) of the iohexol concentrations re-quantified at LUMC fell within $\pm 15\%$ of the corresponding iohexol concentrations quantified at ELCH, and 21/24 (87.5%) within $\pm 10\%$.

Conclusion

The findings of the cross-validation indicated good agreement between both iohexol assays, and provided reassurance that iohexol measurements from both assays could be used interchangeably within this study.

Table S2.1. Iohexol concentrations as quantified at ELCH and re-quantified at LUMC for cross-validation, and their absolute and relative differences.

Sample	Iohexol concentration quantified at ELCH (mg/L)	Iohexol concentration quantified at LUMC (mg/L)
1	51.24	53.59
2	62.82	67.08
3	83.76	90.37
4	76.78	69.50
5	248.0	261.9
6	399.1	422.4
7	59.61	56.53
8	73.25	79.79
9	106.8	103.7
10	151.9	150.1
11	34.73	35.02
12	52.31	50.36
13	87.04	66.78
14	86.22	84.76
15	407.3	410.4
16	115.0	120.9
17	707.8	788.4 ^a
18	77.93	74.39
19	76.69	78.81
20	36.95	40.27
21	47.79	45.36
22	523.1	607.5 ^a
23	258.7	283.3
24	54.52	54.36

ELCH Evelina London Children’s Hospital; **LUMC** Leiden University Medical Center.

^a These samples initially exceeded the upper quantification limit for iohexol in plasma at LUMC (500 mg/L) and were, therefore, re-quantified after dilution.

Figure S2.1. Passing-Bablok regression fit of iohexol concentrations quantified at ELCH and re-quantified at LUMC. The solid black line represents the Passing-Bablok regression fit, whereas the solid grey line represents the line of equality.

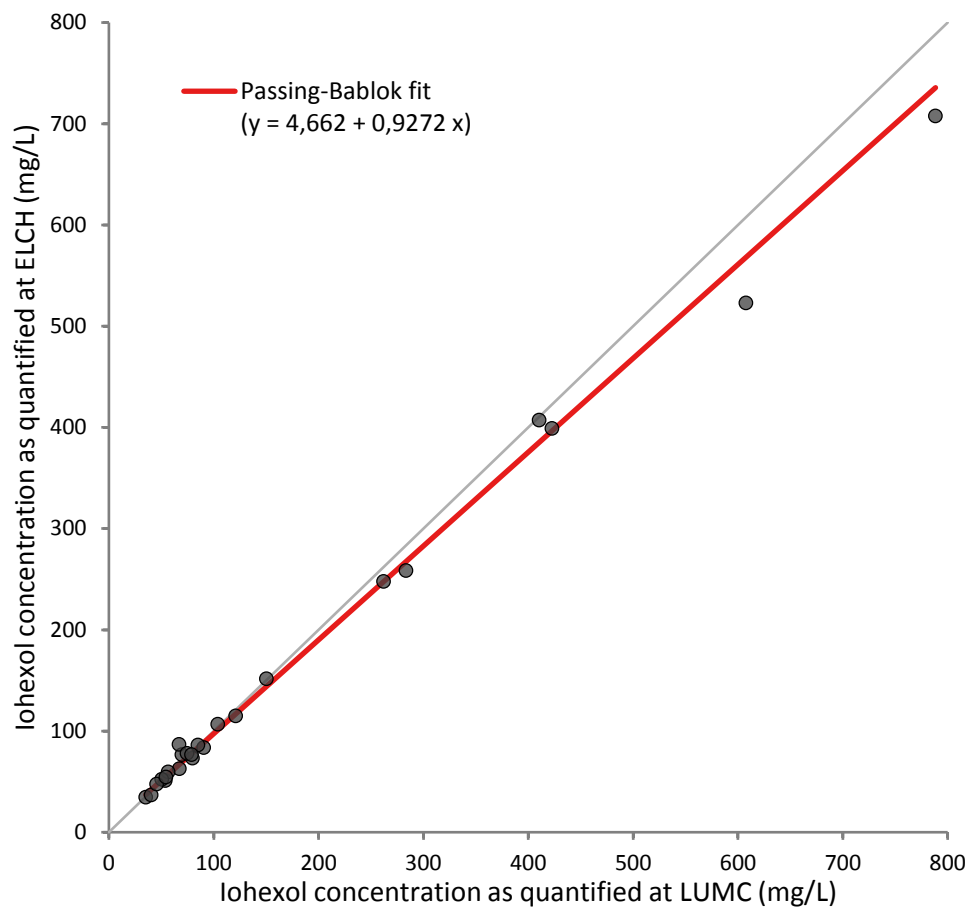
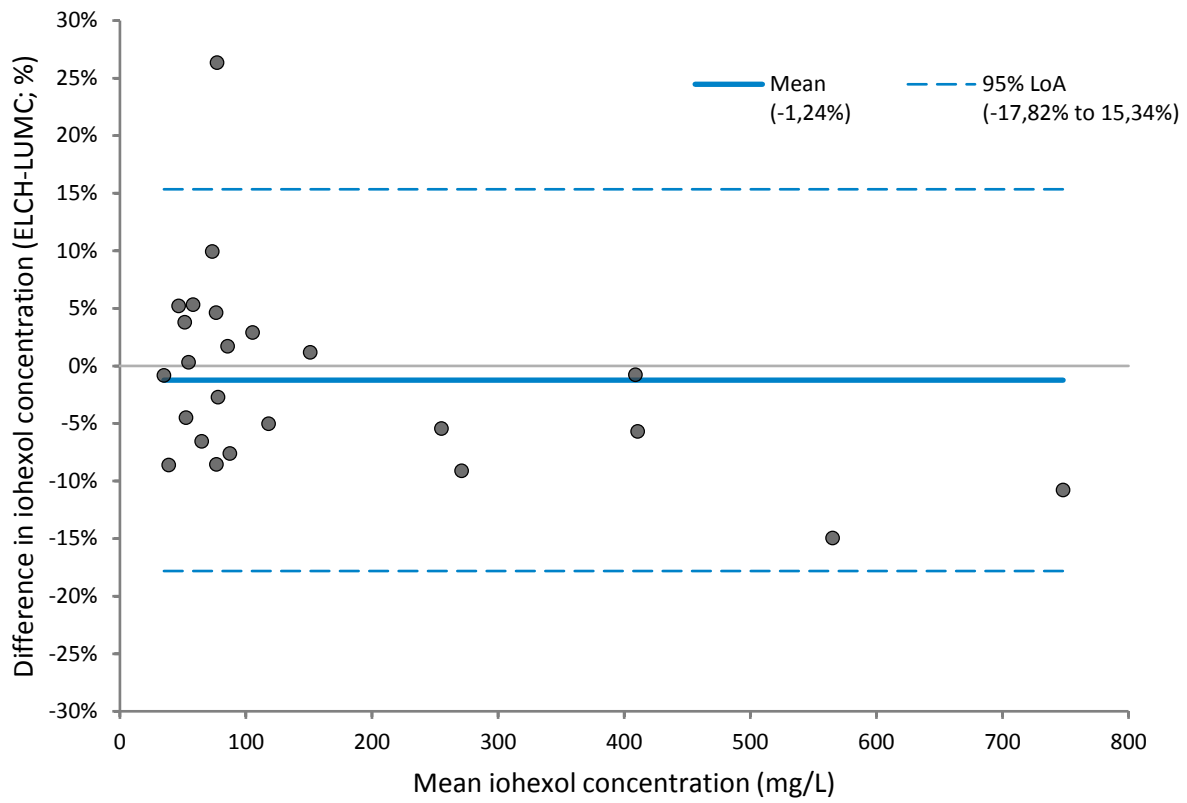


Figure S2.2. Bland-Altman relative difference plot of iohexol concentrations quantified at ELCH and re-quantified at LUMC. The solid blue line represents the mean bias, whereas the dashed blue lines represent the 95% limits of agreement (LoA) around the mean bias. The solid grey line represents the line of equality.



NONMEM code for the final model

\$SUBROUTINES ADVAN3 TRANS4

\$PK

; --- FAT FREE MASS CALCULATION -

IF (SEX.EQ.0) WHSMAX=42.92 ; MEN

IF (SEX.EQ.0) WHS50=30.93 ; MEN

IF (SEX.EQ.1) WHSMAX=37.99 ; WOMEN

IF (SEX.EQ.1) WHS50=35.98 ; WOMEN

HGT=HEIGHT/100

FFM=(WHSMAX*(HGT**2)*WEIGHT)/(WHS50*(HGT**2)+WEIGHT)

; --- ALLOMETRY SCALED TO 1.80M MAN OF 70 KG

ALLOCL=(FFM/57.18)**0.75

ALLOV=(FFM/57.18)

; --- PATIENT TYPE ON V1 AND CL

IF(TX.EQ.0) CLTX = 1

IF(TX.EQ.1) CLTX = (1 + THETA(7))

CLCOV=CLTX

IF(TX.EQ.0) V1TX = 1

IF(TX.EQ.1) V1TX = (1 + THETA(8))

V1COV=V1TX

; --- IOHEXOL PK

CL = THETA(1) * ALLOCL * CLCOV * EXP(ETA(1))

V1 = THETA(2) * ALLOV * V1COV * EXP(ETA(2))

Q = THETA(3) * ALLOCL * EXP(ETA(3))

V2 = THETA(4) * ALLOV * EXP(ETA(4))

S1 = V1

\$ERROR

IPRED = F

W = SQRT(THETA(5)**2*IPRED**2 + THETA(6)**2)

Y = IPRED + W*EPS(1)

IRES = DV-IPRED

IWRES = IRES/W

\$THETA

(0, 4.07) ; CL

(0, 8.36) ; V1

(0, 7.71) ; Q

(0, 6.88) ; V2

(0, 0.0523,1) ; Prop.RE (sd)

(0) FIX ; Add.RE (sd)

(-5, 0.483,5) ; CLCOV

(-5, 0.342,5) ; V1COV

\$OMEGA BLOCK(3)

0.0891 ; IIV CL

0.038 0.163 ; IIV V1

0.0642 -0.0706 0.381 ; IIV Q

\$OMEGA

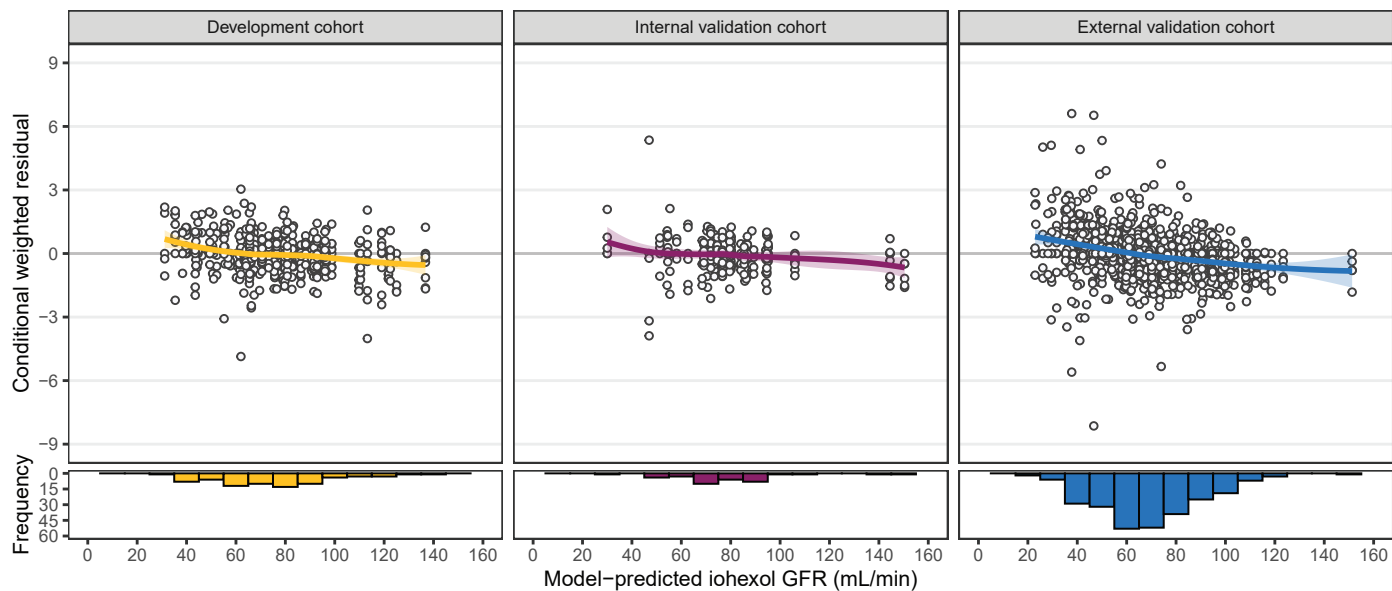
0.0554 ; IIV V2

\$SIGMA

1 FIX

Condition-weighted residuals versus model-predicted iohexol GFR

Figure S4.1 Conditional-weighted residuals versus the model-predicted iohexol glomerular filtration rate (GFR), for the development and validation cohorts. The solid gold, purple, and blue lines and gold-, purple- and blue-shaded areas represent the local weighted (loess) regression fits and their standard errors, respectively. The frequency histogram depicts the number of subjects within each iohexol GFR bin.



Model-predicted iohexol GFR versus slope-intercept GFR with Brøchner-Mortensen correction

Figure S5.1. Scatter plots of the model-predicted iohexol glomerular filtration rate (GFR) and the iohexol GFR as derived from the slope-intercept method with Brøchner-Mortensen correction. The solid red lines and red-shaded areas represent the local weighted (loess) regression fits and their standard errors, respectively.

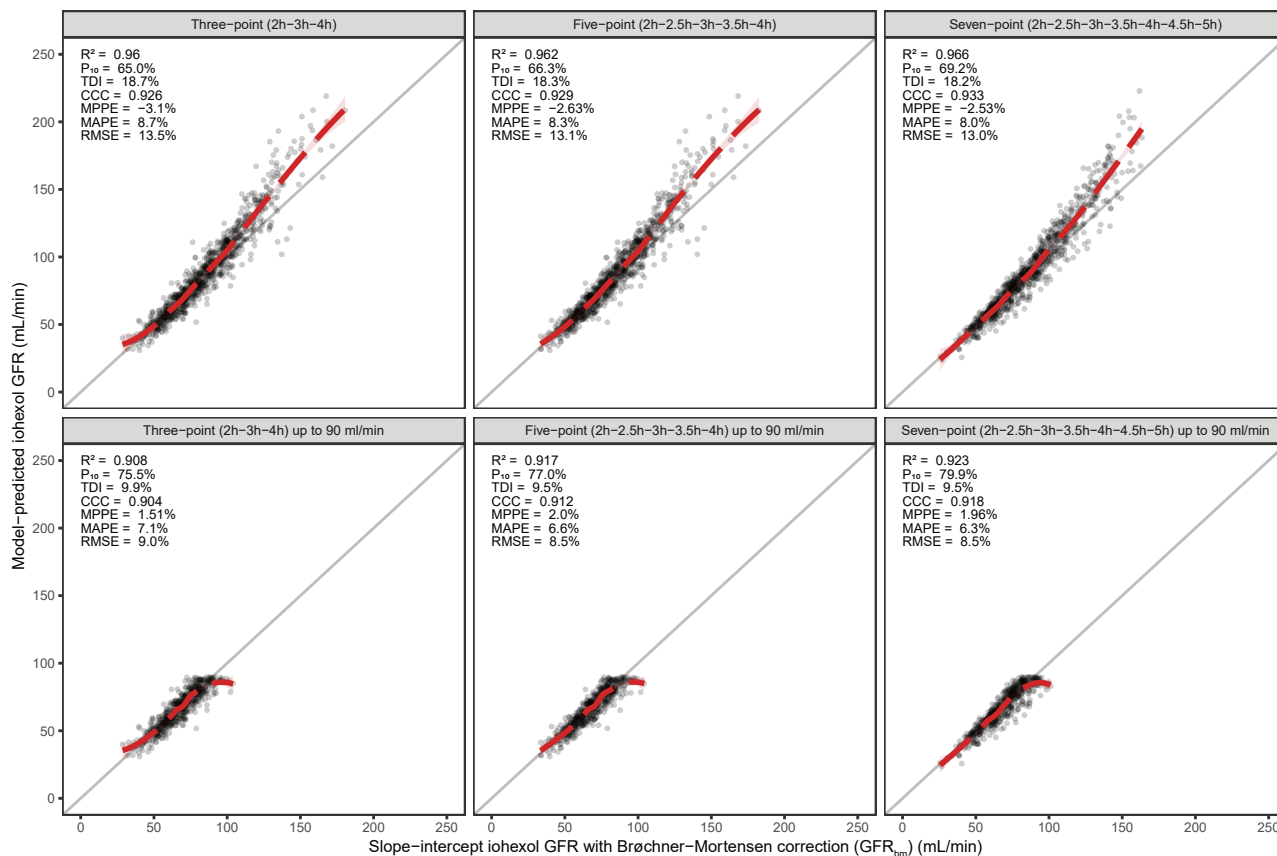


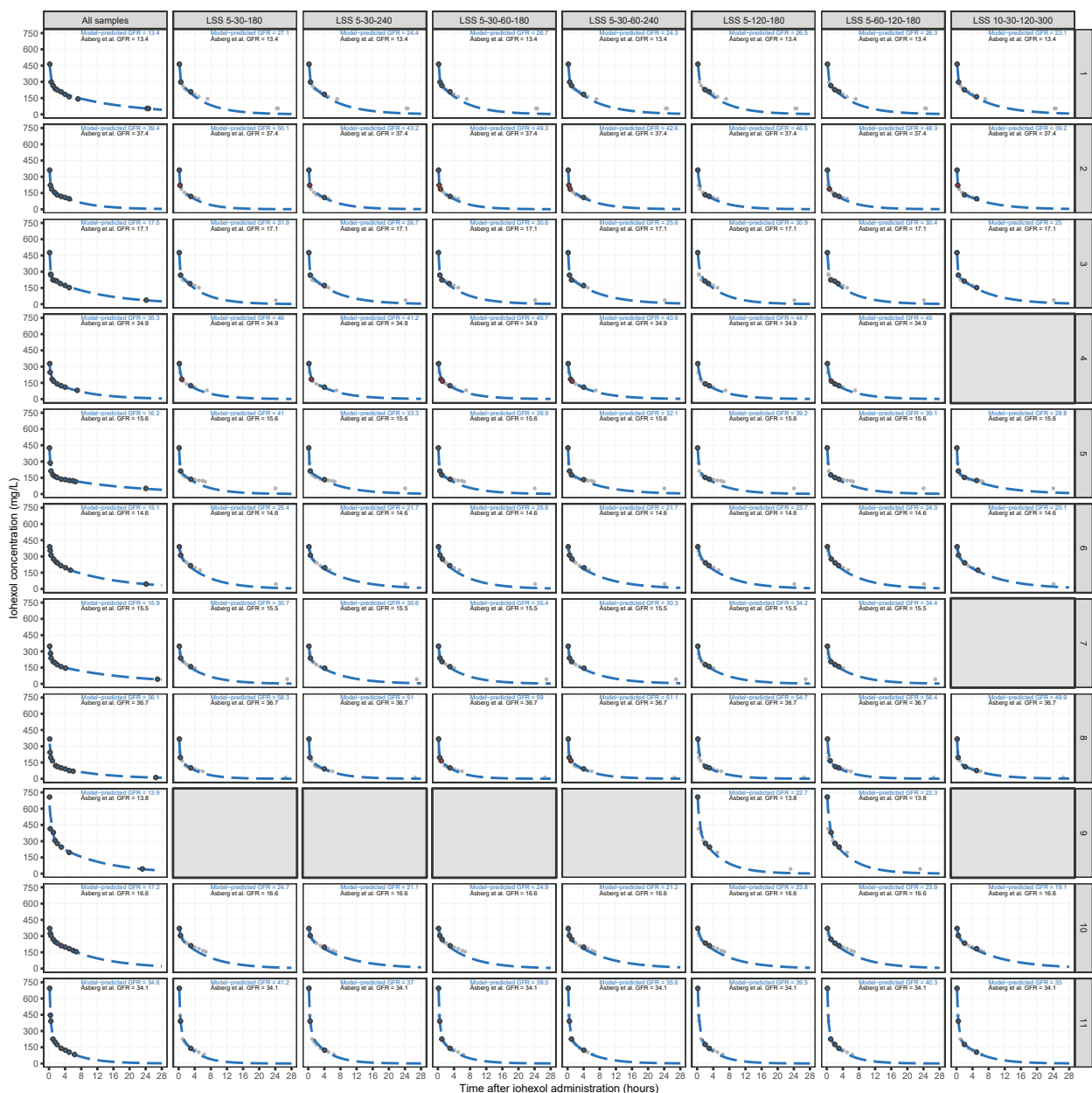
Table S5.1. Predictive performance of GFR_{bm} for model-predicted GFR.

GFR _{bm} model	R ²	MPE [95%CI] (%)	MAPE [95%CI] (%)	RMSE [95%CI] (%)	CCC [95%CI]	TDI [95%CI] (%)	P ₅ (%)	P ₁₀ (%)	P ₁₅ (%)	P ₂₀ (%)
3-point	0.960	-3.10 [-3.77; -2.43]	8.72 [8.28; 9.16]	13.5 [13.4; 13.5]	0.93 [0.92; 0.93]	18.7 [17.3; 20.1]	36.4	65.0	84.0	93.0
3-point (≤90 ml/min)	0.908	1.51 [0.77; 2.24]	7.08 [6.60; 7.56]	8.95 [8.93; 8.98]	0.90 [0.89; 0.92]	9.95 [9.23; 10.7]	45.2	75.5	91.0	96.4
5-point	0.962	-2.63 [-3.27; -1.99]	8.33 [7.91; 8.74]	13.1 [13.1; 13.1]	0.93 [0.92; 0.94]	18.3 [16.9; 19.8]	38.7	66.3	86.2	93.9
5-point (≤90 ml/min)	0.917	2.00 [1.34; 2.67]	6.63 [6.21; 7.06]	8.54 [8.52; 8.56]	0.91 [0.90; 0.92]	9.53 [8.88; 10.3]	47.3	77.0	92.9	97.6
7-point	0.966	-2.53 [-3.16; -1.90]	8.02 [7.60; 8.43]	13.0 [12.9; 13.0]	0.93 [0.93; 0.94]	18.2 [16.8; 19.7]	42.5	69.2	85.2	93.7
7-point (≤90 ml/min)	0.923	1.96 [1.31; 2.61]	6.29 [5.86; 6.73]	8.48 [8.46; 8.50]	0.92 [0.90; 0.93]	9.47 [8.82; 10.1]	52.5	79.9	91.7	97.3

GFR_{bm} slope-intercept method with Brøchner-Mortensen correction; **R²** Pearson's correlation coefficient; **MPE** mean prediction error; **MAPE** mean absolute prediction error; **RMSE** root mean squared prediction error; **CCC** concordance correlation coefficient; **TDI** total deviation index; **P₅-P₂₀** percentage of GFR_{bm} GFR predictions within 5-20% of model-based GFR predictions; **95%CI** 95% confidence interval.

Model and limited sampling schedule performance in patients with impaired renal function

Figure S6.1 Individual plots of observed and model-predicted iohexol curves in patients with impaired renal function. The dashed blue lines depict the individual predicted iohexol curve. Observed iohexol concentrations utilized for the individual GFR prediction within an acceptable range of the limited sampling schedule times are shaded blue, whereas those with substantially deviating sampling times are shaded red. Observed iohexol concentrations not utilized for the individual GFR prediction are shaded grey. Individual plots with one or more missing samples for that particular limited sampling schedule are greyed out.



Numerical predictive performance of all evaluated limited sampling schedules

Table S7.1. Numerical predictive performance of all evaluated limited sampling schedules, sorted according to the number of sampling instances in the limited sampling schedule and the total deviation index (TDI).

N	LSS	R ²	MPE [95%CI] (%)	MAPE [95%CI] (%)	RMSE [95%CI] (%)	CCC	TDI [95%CI] (%)	P ₅ (%)	P ₁₀ (%)	P ₁₅ (%)	P ₂₀ (%)
One	T210	0.957	-3.81 [-4.45; -3.17]	8.37 [7.93; 8.81]	11.06 [11.04; 11.07]	0.95 [0.95; 0.96]	16.07 [15.14; 17.08]	40.0	67.7	85.2	93.6
	T240	0.956	-3.54 [-4.16; -2.92]	7.89 [7.45; 8.33]	11.07 [11.05; 11.09]	0.95 [0.95; 0.96]	16.09 [15.02; 17.11]	42.0	72.5	86.9	93.7
	T180	0.954	-4.10 [-4.81; -3.40]	9.16 [8.67; 9.66]	11.39 [11.37; 11.41]	0.95 [0.94; 0.96]	16.55 [15.51; 17.64]	35.2	64.9	82.6	91.2
	T150	0.945	-3.25 [-4.03; -2.48]	9.98 [9.47; 10.49]	12.21 [12.19; 12.22]	0.94 [0.94; 0.95]	17.74 [16.57; 19.11]	31.6	58.6	78.8	89.9
	T120	0.934	-2.59 [-3.44; -1.75]	10.79 [10.25; 11.32]	13.28 [13.26; 13.30]	0.93 [0.92; 0.94]	19.29 [18.20; 20.39]	29.3	55.6	74.3	86.1
	T90	0.910	-2.19 [-3.18; -1.19]	12.18 [11.52; 12.84]	15.61 [15.59; 15.63]	0.91 [0.90; 0.92]	22.68 [21.36; 24.11]	26.8	51.5	69.9	81.3
	T60	0.873	-3.03 [-4.21; -1.85]	14.16 [13.34; 14.97]	18.18 [18.15; 18.21]	0.87 [0.85; 0.88]	26.42 [24.88; 27.91]	24.7	46.5	64.4	77.1
	T45	0.833	-4.20 [-5.52; -2.87]	15.92 [14.99; 16.84]	20.47 [20.44; 20.50]	0.82 [0.80; 0.84]	29.75 [27.95; 31.39]	21.3	42.4	58.7	73.0
	T30	0.782	-4.05 [-5.51; -2.58]	17.88 [16.89; 18.87]	23.16 [23.13; 23.19]	0.75 [0.72; 0.77]	33.65 [31.56; 35.73]	18.8	36.3	53.4	66.1
	T15	0.697	-3.63 [-5.30; -1.96]	20.79 [19.70; 21.87]	26.77 [26.73; 26.80]	0.64 [0.60; 0.67]	38.89 [36.44; 41.23]	15.9	29.9	44.3	58.5
	T5	0.634	-3.55 [-5.36; -1.75]	22.74 [21.59; 23.89]	28.92 [28.88; 28.96]	0.56 [0.53; 0.60]	42.02 [39.59; 44.49]	13.1	25.6	40.7	53.4
Two	T45T240	0.991	-2.09 [-2.43; -1.75]	4.35 [4.11; 4.60]	5.42 [5.42; 5.43]	0.99 [0.99; 0.99]	7.88 [7.34; 8.41]	66.7	92.2	97.8	99.4
	T30T240	0.990	-2.65 [-3.00; -2.29]	4.62 [4.35; 4.89]	5.77 [5.77; 5.78]	0.99 [0.99; 0.99]	8.39 [7.91; 8.86]	66.1	89.4	96.3	99.1
	T60T240	0.986	-1.20 [-1.59; -0.81]	4.81 [4.56; 5.07]	6.39 [6.38; 6.40]	0.99 [0.98; 0.99]	9.29 [8.36; 10.42]	64.1	89.4	97.4	99.1
	T45T210	0.985	-1.83 [-2.26; -1.41]	5.49 [5.21; 5.77]	6.48 [6.47; 6.49]	0.98 [0.98; 0.99]	9.41 [8.90; 9.93]	56.1	86.6	95.9	99.0
	T30T210	0.986	-2.29 [-2.72; -1.87]	5.63 [5.35; 5.92]	6.48 [6.47; 6.49]	0.98 [0.98; 0.99]	9.42 [9.00; 9.85]	55.3	84.3	95.3	98.6
	T15T240	0.986	-2.88 [-3.29; -2.47]	5.17 [4.86; 5.49]	6.76 [6.75; 6.77]	0.98 [0.98; 0.99]	9.83 [9.08; 10.69]	62.8	86.5	94.6	97.5
	T60T210	0.980	-0.86 [-1.33; -0.39]	5.96 [5.66; 6.25]	7.36 [7.35; 7.37]	0.98 [0.98; 0.98]	10.69 [10.02; 11.57]	50.8	83.2	94.4	98.7
	T15T210	0.981	-2.32 [-2.79; -1.84]	6.11 [5.79; 6.42]	7.40 [7.39; 7.41]	0.98 [0.98; 0.98]	10.75 [10.11; 11.54]	51.7	81.5	93.4	97.6
	T5T240	0.982	-2.99 [-3.46; -2.52]	5.82 [5.47; 6.18]	7.49 [7.48; 7.50]	0.98 [0.98; 0.98]	10.89 [10.18; 11.65]	56.6	83.4	92.5	96.9
	T30T180	0.980	-2.10 [-2.63; -1.56]	6.78 [6.43; 7.13]	7.55 [7.54; 7.56]	0.98 [0.98; 0.98]	10.97 [10.48; 11.47]	45.6	78.1	92.1	96.6
	T45T180	0.978	-1.84 [-2.38; -1.30]	6.84 [6.49; 7.19]	7.83 [7.82; 7.84]	0.98 [0.97; 0.98]	11.38 [10.86; 11.95]	44.7	78.5	91.9	96.5

T15T180	0.976	-1.75 [-2.31; -1.19]	7.25 [6.90; 7.61]	8.17 [8.16; 8.19]	0.98 [0.97; 0.98]	11.88 [11.34; 12.40]	41.7	72.6	90.8	96.7
T5T210	0.976	-2.69 [-3.22; -2.16]	6.81 [6.44; 7.17]	8.25 [8.24; 8.27]	0.98 [0.97; 0.98]	12.00 [11.39; 12.58]	46.8	78.1	90.5	95.9
T90T240	0.977	-3.57 [-4.07; -3.07]	6.51 [6.14; 6.88]	8.42 [8.41; 8.43]	0.97 [0.97; 0.98]	12.24 [11.33; 13.15]	50.3	80.7	90.5	95.9
T60T180	0.971	-0.86 [-1.44; -0.27]	7.39 [7.02; 7.75]	8.84 [8.83; 8.86]	0.97 [0.97; 0.97]	12.85 [12.13; 13.58]	41.5	73.2	89.1	96.1
T5T180	0.969	-2.40 [-3.02; -1.77]	7.92 [7.51; 8.33]	9.29 [9.28; 9.30]	0.97 [0.96; 0.97]	13.50 [12.76; 14.25]	39.5	71.4	88.0	94.2
T30T150	0.968	-1.28 [-1.93; -0.63]	8.31 [7.91; 8.71]	9.36 [9.34; 9.37]	0.97 [0.96; 0.97]	13.59 [13.03; 14.17]	36.8	66.1	87.6	94.8
T120T240	0.970	-3.60 [-4.14; -3.06]	6.99 [6.59; 7.38]	9.36 [9.35; 9.37]	0.97 [0.96; 0.97]	13.60 [12.55; 14.76]	47.9	77.7	89.6	95.5
T90T210	0.968	-2.57 [-3.17; -1.96]	7.59 [7.19; 8.00]	9.46 [9.45; 9.48]	0.97 [0.96; 0.97]	13.75 [12.89; 14.64]	42.9	73.4	88.1	94.6
T45T150	0.965	-1.38 [-2.04; -0.72]	8.31 [7.89; 8.73]	9.77 [9.76; 9.78]	0.96 [0.96; 0.97]	14.20 [13.47; 15.01]	38.1	67.8	86.1	94.0
T15T150	0.964	-0.35 [-1.01; 0.31]	8.57 [8.18; 8.96]	9.93 [9.91; 9.94]	0.96 [0.96; 0.97]	14.42 [13.78; 15.05]	34.9	63.4	85.4	95.1
T120T210	0.965	-4.37 [-4.99; -3.76]	8.07 [7.63; 8.51]	10.21 [10.20; 10.22]	0.96 [0.96; 0.97]	14.84 [13.80; 15.92]	41.5	70.7	85.1	93.3
T180T240	0.961	-3.03 [-3.62; -2.45]	7.33 [6.92; 7.75]	10.35 [10.34; 10.37]	0.96 [0.95; 0.96]	15.04 [13.92; 16.33]	44.8	75.4	88.4	94.9
T150T240	0.961	-3.16 [-3.75; -2.58]	7.18 [6.76; 7.61]	10.45 [10.44; 10.47]	0.96 [0.95; 0.96]	15.19 [13.63; 17.06]	47.3	77.0	89.0	94.6
T180T210	0.961	-3.62 [-4.24; -3.00]	8.00 [7.57; 8.43]	10.57 [10.55; 10.58]	0.96 [0.95; 0.96]	15.35 [14.34; 16.33]	41.2	70.3	87.4	94.1
T210T240	0.959	-3.04 [-3.63; -2.45]	7.44 [7.02; 7.85]	10.65 [10.64; 10.67]	0.96 [0.95; 0.96]	15.48 [14.41; 16.66]	45.1	75.5	87.9	94.7
T5T150	0.958	-0.64 [-1.34; 0.06]	9.05 [8.63; 9.46]	10.69 [10.68; 10.70]	0.96 [0.95; 0.96]	15.53 [14.79; 16.19]	31.9	61.2	83.1	93.9
T150T210	0.960	-3.91 [-4.54; -3.29]	8.01 [7.56; 8.46]	10.69 [10.67; 10.70]	0.96 [0.95; 0.96]	15.53 [14.18; 17.07]	42.0	71.4	86.6	93.5
T60T150	0.957	-0.73 [-1.42; -0.03]	8.75 [8.31; 9.19]	10.80 [10.79; 10.82]	0.96 [0.95; 0.96]	15.69 [14.75; 16.80]	36.4	65.3	83.7	92.1
T90T180	0.956	-0.22 [-0.92; 0.47]	8.76 [8.33; 9.19]	10.97 [10.96; 10.99]	0.96 [0.95; 0.96]	15.94 [15.04; 16.88]	36.5	64.6	81.5	92.6
T150T180	0.956	-4.48 [-5.17; -3.78]	9.03 [8.53; 9.54]	11.23 [11.22; 11.25]	0.95 [0.95; 0.96]	16.32 [15.08; 17.53]	36.8	66.5	82.7	91.3
T120T180	0.958	-5.46 [-6.17; -4.74]	9.41 [8.87; 9.94]	11.27 [11.26; 11.29]	0.95 [0.95; 0.96]	16.38 [15.31; 17.53]	37.6	64.9	80.4	89.2
T30T120	0.948	-0.62 [-1.41; 0.16]	9.66 [9.15; 10.16]	11.90 [11.88; 11.91]	0.94 [0.94; 0.95]	17.29 [16.35; 18.12]	34.5	62.1	78.1	88.5
T45T120	0.946	-1.19 [-1.98; -0.40]	9.72 [9.20; 10.24]	12.03 [12.02; 12.05]	0.94 [0.94; 0.95]	17.48 [16.56; 18.39]	34.5	61.4	79.2	88.4
T15T120	0.947	0.89 [0.14; 1.64]	9.65 [9.19; 10.11]	12.21 [12.20; 12.23]	0.94 [0.93; 0.95]	17.75 [16.86; 18.66]	32.8	59.2	77.3	89.9
T90T150	0.945	0.20 [-0.57; 0.97]	9.61 [9.13; 10.09]	12.25 [12.24; 12.27]	0.94 [0.94; 0.95]	17.80 [16.67; 18.90]	34.5	60.3	78.4	89.4
T120T150	0.944	-2.98 [-3.77; -2.19]	10.14 [9.63; 10.66]	12.33 [12.31; 12.35]	0.94 [0.93; 0.95]	17.91 [16.94; 18.90]	32.3	59.6	77.7	88.5
T5T120	0.944	1.08 [0.33; 1.83]	9.71 [9.26; 10.17]	12.50 [12.48; 12.51]	0.94 [0.93; 0.95]	18.16 [17.24; 19.13]	32.5	57.1	77.4	90.3
T60T120	0.939	-0.84 [-1.67; -0.02]	10.14 [9.61; 10.68]	12.78 [12.76; 12.80]	0.94 [0.93; 0.95]	18.57 [17.46; 19.47]	33.2	59.6	77.4	88.1
T90T120	0.928	-0.92 [-1.78; -0.05]	10.71 [10.16; 11.26]	13.92 [13.90; 13.94]	0.93 [0.92; 0.94]	20.23 [18.98; 21.53]	31.2	57.3	73.7	86.1
T5T90	0.931	1.86 [1.01; 2.71]	10.80 [10.27; 11.34]	13.96 [13.94; 13.98]	0.92 [0.91; 0.93]	20.29 [19.20; 21.39]	29.2	54.4	72.7	86.1

	T15T90	0.929	2.09 [1.22; 2.97]	11.08 [10.53; 11.63]	14.25 [14.23; 14.27]	0.92 [0.91; 0.93]	20.71 [19.53; 21.75]	29.9	53.4	71.8	85.9
	T30T90	0.921	-0.57 [-1.53; 0.39]	11.56 [10.93; 12.20]	14.55 [14.53; 14.57]	0.91 [0.90; 0.92]	21.15 [20.01; 22.35]	29.6	53.6	71.9	83.9
	T45T90	0.919	-1.87 [-2.84; -0.90]	11.56 [10.89; 12.22]	14.62 [14.60; 14.64]	0.92 [0.91; 0.93]	21.25 [19.93; 22.49]	32.4	55.3	71.8	84.1
	T60T90	0.911	-2.00 [-3.00; -1.01]	11.95 [11.28; 12.63]	15.35 [15.32; 15.37]	0.91 [0.90; 0.92]	22.30 [20.96; 23.64]	30.2	52.7	71.4	82.9
	T5T60	0.908	0.78 [-0.21; 1.77]	12.47 [11.85; 13.10]	15.78 [15.76; 15.80]	0.90 [0.89; 0.91]	22.93 [21.79; 24.11]	26.5	49.3	67.1	79.9
	T15T60	0.904	0.83 [-0.18; 1.84]	12.61 [11.97; 13.24]	16.11 [16.08; 16.13]	0.90 [0.88; 0.91]	23.40 [22.15; 24.77]	26.0	48.0	66.8	80.5
	T30T60	0.887	-0.03 [-1.11; 1.06]	13.37 [12.67; 14.08]	17.28 [17.26; 17.31]	0.88 [0.87; 0.89]	25.11 [23.86; 26.56]	25.6	47.8	64.8	77.5
	T5T45	0.879	-1.05 [-2.17; 0.08]	14.01 [13.29; 14.73]	17.76 [17.73; 17.78]	0.87 [0.85; 0.88]	25.80 [24.52; 27.33]	22.2	44.2	61.9	77.4
	T45T60	0.878	-2.82 [-3.97; -1.66]	13.95 [13.17; 14.74]	17.80 [17.77; 17.82]	0.88 [0.86; 0.89]	25.86 [24.29; 27.27]	24.7	46.6	64.7	77.9
	T15T45	0.870	-1.36 [-2.53; -0.19]	14.48 [13.73; 15.23]	18.32 [18.30; 18.35]	0.86 [0.84; 0.87]	26.62 [25.10; 28.10]	22.4	42.3	60.2	76.6
	T30T45	0.841	-2.82 [-4.12; -1.53]	15.58 [14.70; 16.46]	20.06 [20.03; 20.08]	0.83 [0.81; 0.85]	29.14 [27.27; 30.86]	20.0	40.9	59.3	73.4
	T5T30	0.835	-2.42 [-3.68; -1.16]	15.72 [14.91; 16.53]	20.42 [20.39; 20.45]	0.82 [0.80; 0.84]	29.67 [27.86; 31.63]	20.9	39.4	57.1	72.1
	T15T30	0.821	-3.08 [-4.41; -1.75]	16.50 [15.63; 17.37]	21.16 [21.13; 21.19]	0.80 [0.78; 0.82]	30.74 [29.01; 32.62]	20.5	39.1	54.0	68.0
	T5T15	0.742	-4.71 [-6.27; -3.14]	19.50 [18.47; 20.53]	24.87 [24.84; 24.91]	0.71 [0.69; 0.74]	36.14 [34.03; 38.35]	16.6	32.5	48.7	60.7
Three	T5T45T240	0.995	-0.33 [-0.58; -0.07]	3.14 [2.98; 3.31]	3.76 [3.75; 3.76]	0.99 [0.99; 1.00]	5.46 [5.17; 5.73]	79.0	97.2	99.8	100.0
	T5T30T240	0.994	-1.04 [-1.30; -0.78]	3.25 [3.08; 3.43]	4.10 [4.10; 4.11]	0.99 [0.99; 0.99]	5.96 [5.60; 6.34]	78.5	97.2	99.8	100.0
	T15T45T240	0.993	-0.50 [-0.79; -0.21]	3.54 [3.34; 3.73]	4.32 [4.32; 4.33]	0.99 [0.99; 0.99]	6.28 [5.95; 6.65]	75.8	95.4	99.1	100.0
	T30T45T240	0.992	-1.31 [-1.63; -0.99]	3.94 [3.71; 4.16]	4.78 [4.77; 4.78]	0.99 [0.99; 0.99]	6.94 [6.57; 7.34]	72.0	93.1	98.2	99.7
	T15T60T240	0.992	0.59 [0.28; 0.91]	3.88 [3.67; 4.09]	4.83 [4.82; 4.84]	0.99 [0.99; 0.99]	7.02 [6.67; 7.41]	72.5	93.7	98.9	99.8
	T5T60T240	0.992	0.33 [0.02; 0.64]	3.78 [3.58; 3.98]	4.86 [4.85; 4.87]	0.99 [0.99; 0.99]	7.06 [6.62; 7.56]	72.6	94.4	99.0	99.9
	T30T60T240	0.991	-0.28 [-0.63; 0.06]	4.16 [3.93; 4.38]	5.10 [5.09; 5.11]	0.99 [0.99; 0.99]	7.41 [7.07; 7.78]	69.9	92.9	97.6	99.8
	T5T30T210	0.991	-0.72 [-1.06; -0.38]	4.27 [4.05; 4.48]	5.10 [5.10; 5.11]	0.99 [0.99; 0.99]	7.42 [7.05; 7.75]	65.8	92.9	98.7	99.9
	T45T210T240	0.991	-1.76 [-2.08; -1.44]	4.10 [3.88; 4.33]	5.10 [5.10; 5.11]	0.99 [0.99; 0.99]	7.42 [6.91; 7.95]	70.0	93.1	98.2	99.6
	T15T30T240	0.991	-1.52 [-1.84; -1.20]	4.02 [3.80; 4.24]	5.15 [5.14; 5.15]	0.99 [0.99; 0.99]	7.48 [6.94; 8.10]	70.3	93.1	98.5	99.5
	T30T210T240	0.992	-2.24 [-2.57; -1.91]	4.19 [3.94; 4.43]	5.16 [5.15; 5.17]	0.99 [0.99; 0.99]	7.50 [7.08; 7.88]	70.9	91.1	97.0	99.6
	T30T180T240	0.992	-2.37 [-2.72; -2.02]	4.28 [4.02; 4.55]	5.20 [5.20; 5.21]	0.99 [0.99; 0.99]	7.56 [7.16; 7.96]	70.2	90.1	96.7	99.1
	T45T60T240	0.991	-1.48 [-1.83; -1.14]	4.18 [3.93; 4.42]	5.27 [5.26; 5.28]	0.99 [0.99; 0.99]	7.66 [7.15; 8.21]	69.2	93.1	97.6	99.2
	T30T150T240	0.991	-2.54 [-2.90; -2.18]	4.36 [4.08; 4.64]	5.34 [5.33; 5.35]	0.99 [0.99; 0.99]	7.76 [7.32; 8.18]	70.9	90.5	95.7	98.8
	T5T45T210	0.990	0.03 [-0.32; 0.38]	4.40 [4.18; 4.63]	5.36 [5.35; 5.37]	0.99 [0.99; 0.99]	7.78 [7.43; 8.15]	64.4	92.4	98.9	99.8
	T45T150T240	0.991	-2.19 [-2.53; -1.84]	4.29 [4.03; 4.54]	5.40 [5.40; 5.41]	0.99 [0.99; 0.99]	7.85 [7.33; 8.42]	69.4	91.6	97.3	99.1

T45T180T240	0.990	-1.94 [-2.28; -1.59]	4.30 [4.05; 4.56]	5.40 [5.39; 5.41]	0.99 [0.99; 0.99]	7.85 [7.28; 8.43]	67.2	92.1	97.4	99.2
T30T90T240	0.991	-2.79 [-3.15; -2.43]	4.44 [4.15; 4.73]	5.41 [5.40; 5.41]	0.99 [0.99; 0.99]	7.86 [7.40; 8.29]	70.6	89.1	95.1	98.8
T30T120T240	0.991	-2.72 [-3.09; -2.35]	4.51 [4.22; 4.80]	5.46 [5.45; 5.46]	0.99 [0.99; 0.99]	7.93 [7.45; 8.39]	71.0	89.3	95.1	98.5
T45T120T240	0.990	-2.33 [-2.69; -1.98]	4.36 [4.09; 4.63]	5.46 [5.46; 5.47]	0.99 [0.99; 0.99]	7.94 [7.40; 8.46]	68.4	91.4	96.9	98.8
T45T90T240	0.990	-2.49 [-2.84; -2.13]	4.47 [4.19; 4.74]	5.58 [5.58; 5.59]	0.99 [0.99; 0.99]	8.11 [7.56; 8.70]	67.5	90.3	96.7	98.8
T15T45T210	0.988	0.06 [-0.32; 0.44]	4.72 [4.47; 4.96]	5.71 [5.71; 5.72]	0.99 [0.99; 0.99]	8.30 [7.91; 8.70]	62.5	90.1	97.9	99.3
T5T15T240	0.989	-2.14 [-2.49; -1.79]	4.41 [4.15; 4.66]	5.89 [5.88; 5.90]	0.99 [0.99; 0.99]	8.56 [7.79; 9.58]	68.5	90.4	96.8	99.2
T15T210T240	0.989	-2.33 [-2.72; -1.95]	4.63 [4.34; 4.93]	5.95 [5.94; 5.96]	0.99 [0.99; 0.99]	8.64 [8.11; 9.18]	66.2	88.7	95.7	98.1
T15T30T210	0.987	-1.03 [-1.42; -0.64]	5.02 [4.77; 5.26]	5.95 [5.94; 5.96]	0.99 [0.99; 0.99]	8.65 [8.23; 9.06]	60.1	88.1	97.1	99.6
T15T90T240	0.988	-1.97 [-2.39; -1.55]	4.90 [4.58; 5.21]	5.96 [5.95; 5.97]	0.99 [0.99; 0.99]	8.66 [8.16; 9.13]	67.3	86.8	94.8	97.5
T30T45T210	0.987	-0.85 [-1.26; -0.43]	5.12 [4.85; 5.39]	5.98 [5.98; 5.99]	0.99 [0.99; 0.99]	8.70 [8.25; 9.11]	58.7	87.8	96.5	98.9
T15T180T240	0.988	-2.42 [-2.82; -2.02]	4.81 [4.51; 5.12]	6.04 [6.03; 6.05]	0.99 [0.99; 0.99]	8.78 [8.20; 9.33]	66.3	88.3	95.4	97.7
T30T180T210	0.987	-2.14 [-2.55; -1.73]	5.40 [5.12; 5.67]	6.09 [6.08; 6.10]	0.99 [0.98; 0.99]	8.85 [8.44; 9.23]	57.6	85.2	95.9	98.9
T60T210T240	0.987	-1.00 [-1.37; -0.63]	4.54 [4.30; 4.79]	6.14 [6.14; 6.15]	0.99 [0.98; 0.99]	8.93 [7.96; 10.17]	65.2	91.6	97.6	99.1
T15T150T240	0.988	-2.58 [-2.99; -2.17]	4.80 [4.48; 5.13]	6.20 [6.20; 6.21]	0.99 [0.98; 0.99]	9.02 [8.42; 9.63]	68.3	86.5	95.2	97.5
T60T180T240	0.987	-1.39 [-1.77; -1.01]	4.68 [4.42; 4.94]	6.22 [6.21; 6.22]	0.99 [0.98; 0.99]	9.03 [8.04; 10.26]	65.4	90.7	97.3	98.9
T45T180T210	0.986	-1.75 [-2.17; -1.33]	5.39 [5.12; 5.66]	6.28 [6.27; 6.29]	0.99 [0.98; 0.99]	9.13 [8.64; 9.57]	56.1	86.7	96.3	99.0
T15T60T210	0.986	1.25 [0.85; 1.66]	5.13 [4.87; 5.39]	6.28 [6.27; 6.29]	0.99 [0.98; 0.99]	9.13 [8.65; 9.58]	59.1	87.9	97.1	99.1
T60T120T240	0.987	-1.82 [-2.21; -1.44]	4.79 [4.52; 5.06]	6.29 [6.28; 6.29]	0.99 [0.98; 0.99]	9.13 [8.23; 10.49]	64.3	89.7	96.6	98.5
T5T60T210	0.986	0.73 [0.33; 1.13]	5.02 [4.76; 5.27]	6.34 [6.33; 6.35]	0.99 [0.98; 0.99]	9.21 [8.70; 9.75]	59.5	88.1	97.0	99.6
T60T90T240	0.986	-1.89 [-2.28; -1.50]	4.80 [4.52; 5.07]	6.37 [6.36; 6.38]	0.99 [0.98; 0.99]	9.26 [8.33; 10.48]	65.6	88.5	96.4	98.8
T5T15T210	0.986	-1.88 [-2.29; -1.48]	5.24 [4.97; 5.51]	6.39 [6.38; 6.39]	0.99 [0.98; 0.99]	9.28 [8.79; 9.76]	57.1	86.8	96.5	99.0
T30T60T210	0.985	0.24 [-0.20; 0.67]	5.37 [5.09; 5.65]	6.39 [6.38; 6.40]	0.99 [0.98; 0.99]	9.29 [8.82; 9.74]	57.4	86.1	95.8	98.8
T15T120T240	0.987	-2.88 [-3.31; -2.44]	5.08 [4.73; 5.42]	6.40 [6.39; 6.41]	0.99 [0.98; 0.99]	9.30 [8.75; 9.85]	67.5	85.6	93.6	96.6
T30T150T210	0.986	-2.57 [-3.01; -2.13]	5.60 [5.29; 5.91]	6.41 [6.40; 6.42]	0.98 [0.98; 0.99]	9.31 [8.85; 9.76]	58.5	83.9	93.9	98.0
T60T150T240	0.986	-1.73 [-2.11; -1.35]	4.69 [4.42; 4.95]	6.42 [6.42; 6.43]	0.99 [0.98; 0.99]	9.34 [8.02; 11.08]	66.1	90.5	96.5	98.7
T45T60T210	0.985	-1.11 [-1.54; -0.68]	5.42 [5.14; 5.70]	6.48 [6.47; 6.49]	0.98 [0.98; 0.99]	9.42 [8.90; 9.95]	55.9	86.8	96.0	98.8
T5T30T180	0.984	-0.72 [-1.15; -0.28]	5.43 [5.15; 5.71]	6.52 [6.51; 6.53]	0.98 [0.98; 0.99]	9.48 [8.97; 9.98]	54.4	85.0	96.4	98.9
T5T90T240	0.984	-0.61 [-1.03; -0.19]	4.92 [4.63; 5.22]	6.55 [6.54; 6.56]	0.98 [0.98; 0.99]	9.52 [8.83; 10.25]	63.5	88.1	95.0	98.6
T45T150T210	0.985	-2.17 [-2.60; -1.74]	5.54 [5.25; 5.84]	6.57 [6.56; 6.58]	0.98 [0.98; 0.99]	9.55 [9.03; 10.15]	56.3	85.8	94.9	98.5

T30T120T210	0.986	-2.93 [-3.38; -2.48]	5.72 [5.39; 6.05]	6.59 [6.58; 6.60]	0.98 [0.98; 0.99]	9.58 [9.09; 10.04]	58.3	83.6	92.8	97.0
T45T120T210	0.985	-2.56 [-3.00; -2.12]	5.61 [5.30; 5.92]	6.66 [6.65; 6.67]	0.98 [0.98; 0.99]	9.68 [9.17; 10.25]	56.1	86.4	94.3	97.7
T30T90T210	0.985	-2.81 [-3.27; -2.34]	5.82 [5.48; 6.15]	6.78 [6.77; 6.79]	0.98 [0.98; 0.99]	9.86 [9.34; 10.35]	56.3	82.6	92.6	97.2
T45T90T210	0.985	-2.80 [-3.25; -2.35]	5.73 [5.41; 6.05]	6.81 [6.80; 6.82]	0.98 [0.98; 0.98]	9.89 [9.34; 10.48]	55.3	84.7	94.2	97.3
T15T180T210	0.983	-2.06 [-2.52; -1.61]	5.83 [5.53; 6.14]	6.98 [6.97; 6.99]	0.98 [0.98; 0.98]	10.14 [9.51; 10.79]	52.7	82.8	93.7	98.1
T15T30T180	0.982	-0.79 [-1.27; -0.31]	6.04 [5.73; 6.35]	7.06 [7.05; 7.07]	0.98 [0.98; 0.98]	10.25 [9.73; 10.75]	50.4	81.6	94.1	98.4
T5T210T240	0.983	-2.36 [-2.80; -1.91]	5.38 [5.05; 5.71]	7.05 [7.04; 7.06]	0.98 [0.98; 0.98]	10.25 [9.56; 10.92]	61.5	85.9	93.6	97.6
T15T45T180	0.982	0.29 [-0.19; 0.77]	5.95 [5.65; 6.25]	7.08 [7.07; 7.09]	0.98 [0.98; 0.98]	10.29 [9.82; 10.76]	51.8	83.0	94.7	98.3
T5T45T180	0.981	0.08 [-0.39; 0.55]	5.83 [5.53; 6.12]	7.12 [7.11; 7.13]	0.98 [0.98; 0.98]	10.35 [9.81; 10.91]	50.9	85.0	95.2	98.2
T5T180T240	0.982	-2.26 [-2.72; -1.80]	5.55 [5.21; 5.88]	7.21 [7.20; 7.22]	0.98 [0.98; 0.98]	10.47 [9.69; 11.28]	58.9	85.7	94.1	97.4
T15T150T210	0.982	-2.51 [-2.99; -2.03]	6.03 [5.69; 6.37]	7.29 [7.28; 7.30]	0.98 [0.98; 0.98]	10.59 [10.00; 11.25]	54.7	80.9	92.9	96.8
T60T120T210	0.981	-1.86 [-2.33; -1.39]	5.88 [5.56; 6.19]	7.35 [7.34; 7.36]	0.98 [0.98; 0.98]	10.68 [9.82; 11.80]	53.2	83.2	93.8	97.8
T60T180T210	0.980	-0.94 [-1.41; -0.48]	5.88 [5.59; 6.17]	7.38 [7.37; 7.39]	0.98 [0.98; 0.98]	10.73 [9.81; 11.88]	52.0	82.8	94.8	99.0
T30T150T180	0.981	-2.24 [-2.77; -1.71]	6.70 [6.34; 7.06]	7.41 [7.40; 7.42]	0.98 [0.98; 0.98]	10.76 [10.25; 11.23]	47.1	77.9	91.8	96.6
T30T45T180	0.980	-0.69 [-1.22; -0.17]	6.49 [6.15; 6.83]	7.41 [7.40; 7.42]	0.98 [0.98; 0.98]	10.77 [10.28; 11.23]	48.2	80.1	93.7	97.3
T60T150T210	0.980	-1.51 [-1.98; -1.04]	5.89 [5.58; 6.19]	7.42 [7.41; 7.43]	0.98 [0.98; 0.98]	10.78 [9.76; 12.24]	52.0	83.5	94.7	98.3
T15T120T210	0.981	-3.00 [-3.51; -2.49]	6.30 [5.93; 6.68]	7.52 [7.51; 7.53]	0.98 [0.98; 0.98]	10.92 [10.37; 11.47]	56.1	79.2	91.1	95.2
T60T90T210	0.980	-1.81 [-2.30; -1.33]	6.04 [5.72; 6.36]	7.55 [7.53; 7.56]	0.98 [0.98; 0.98]	10.96 [10.19; 11.83]	52.0	81.6	93.1	97.8
T5T120T240	0.980	-2.36 [-2.86; -1.87]	5.68 [5.31; 6.05]	7.64 [7.63; 7.65]	0.98 [0.98; 0.98]	11.10 [10.30; 12.00]	61.9	83.8	91.4	96.1
T5T15T180	0.979	-1.96 [-2.47; -1.46]	6.43 [6.10; 6.76]	7.67 [7.66; 7.68]	0.98 [0.98; 0.98]	11.15 [10.55; 11.74]	49.2	79.7	91.9	97.2
T5T150T240	0.979	-2.22 [-2.69; -1.74]	5.60 [5.24; 5.95]	7.67 [7.66; 7.68]	0.98 [0.98; 0.98]	11.15 [10.26; 12.17]	60.5	84.7	92.8	96.5
T15T90T210	0.978	0.29 [-0.22; 0.81]	6.21 [5.86; 6.55]	7.71 [7.70; 7.72]	0.98 [0.98; 0.98]	11.21 [10.57; 11.79]	53.8	78.9	91.1	97.5
T45T150T180	0.979	-1.96 [-2.49; -1.43]	6.74 [6.40; 7.09]	7.74 [7.73; 7.75]	0.98 [0.98; 0.98]	11.25 [10.73; 11.76]	45.0	77.9	92.1	96.7
T15T60T180	0.979	1.50 [0.99; 2.00]	6.43 [6.11; 6.75]	7.79 [7.78; 7.80]	0.98 [0.97; 0.98]	11.33 [10.81; 11.83]	48.3	79.7	92.3	97.9
T5T180T210	0.978	-2.09 [-2.61; -1.58]	6.46 [6.11; 6.80]	7.87 [7.86; 7.89]	0.98 [0.97; 0.98]	11.44 [10.81; 12.05]	48.8	79.7	91.9	96.9
T30T60T180	0.978	0.59 [0.04; 1.13]	6.77 [6.42; 7.11]	7.90 [7.89; 7.91]	0.98 [0.97; 0.98]	11.48 [10.98; 11.98]	45.0	77.7	91.6	97.5
T30T120T180	0.979	-3.03 [-3.60; -2.47]	7.07 [6.66; 7.47]	7.91 [7.90; 7.92]	0.98 [0.97; 0.98]	11.50 [10.92; 12.05]	48.0	75.1	89.3	94.8
T45T120T180	0.978	-2.74 [-3.29; -2.18]	7.02 [6.64; 7.41]	8.06 [8.05; 8.07]	0.98 [0.97; 0.98]	11.72 [11.13; 12.30]	45.4	77.3	90.3	95.5
T45T60T180	0.976	-1.06 [-1.62; -0.51]	6.94 [6.58; 7.30]	8.08 [8.07; 8.09]	0.98 [0.97; 0.98]	11.74 [11.21; 12.31]	44.7	76.9	91.0	96.7
T5T90T210	0.976	0.21 [-0.30; 0.73]	6.14 [5.78; 6.49]	8.08 [8.07; 8.09]	0.98 [0.97; 0.98]	11.74 [11.02; 12.47]	54.5	81.8	91.3	97.3

T5T30T150	0.976	-0.11 [-0.65; 0.43]	6.74 [6.40; 7.07]	8.13 [8.12; 8.14]	0.98 [0.97; 0.98]	11.82 [11.18; 12.46]	45.5	77.3	92.5	97.6
T15T150T180	0.976	-1.90 [-2.47; -1.33]	7.11 [6.73; 7.49]	8.18 [8.17; 8.19]	0.98 [0.97; 0.98]	11.89 [11.31; 12.49]	45.1	73.1	89.8	96.4
T5T60T180	0.976	0.89 [0.36; 1.42]	6.53 [6.19; 6.87]	8.22 [8.21; 8.24]	0.98 [0.97; 0.98]	11.95 [11.32; 12.62]	47.6	79.4	92.3	97.3
T45T90T180	0.976	-2.74 [-3.31; -2.16]	7.24 [6.83; 7.64]	8.32 [8.31; 8.33]	0.97 [0.97; 0.98]	12.09 [11.51; 12.68]	46.0	76.8	88.6	95.2
T30T90T180	0.974	-1.61 [-2.22; -1.00]	7.30 [6.88; 7.71]	8.35 [8.34; 8.37]	0.97 [0.97; 0.98]	12.14 [11.55; 12.76]	47.0	74.8	88.0	94.6
T90T150T240	0.975	-1.53 [-2.03; -1.03]	6.01 [5.67; 6.36]	8.36 [8.34; 8.37]	0.97 [0.97; 0.98]	12.14 [11.25; 13.20]	53.6	83.7	92.5	96.7
T5T150T210	0.975	-2.12 [-2.66; -1.58]	6.74 [6.36; 7.11]	8.38 [8.37; 8.39]	0.97 [0.97; 0.98]	12.17 [11.49; 12.95]	51.3	78.5	89.7	96.1
T90T120T240	0.975	-2.26 [-2.77; -1.75]	6.30 [5.95; 6.66]	8.42 [8.41; 8.43]	0.97 [0.97; 0.98]	12.24 [11.29; 13.19]	51.6	81.0	91.2	96.5
T90T210T240	0.975	-2.09 [-2.61; -1.58]	6.28 [5.92; 6.64]	8.46 [8.45; 8.47]	0.97 [0.97; 0.98]	12.29 [11.40; 13.34]	52.2	81.2	90.8	96.4
T5T120T210	0.974	-2.23 [-2.80; -1.67]	6.85 [6.45; 7.25]	8.60 [8.58; 8.61]	0.97 [0.97; 0.98]	12.49 [11.77; 13.22]	51.0	78.7	88.9	94.8
T90T180T240	0.973	-1.34 [-1.85; -0.82]	6.23 [5.88; 6.58]	8.62 [8.61; 8.63]	0.97 [0.97; 0.98]	12.52 [11.52; 13.59]	51.9	81.4	91.6	96.6
T5T15T150	0.972	-1.25 [-1.82; -0.67]	7.32 [6.95; 7.68]	8.75 [8.74; 8.77]	0.97 [0.97; 0.97]	12.72 [12.04; 13.38]	42.9	74.5	89.3	96.0
T60T150T180	0.971	-1.16 [-1.75; -0.58]	7.31 [6.94; 7.68]	8.89 [8.88; 8.90]	0.97 [0.97; 0.97]	12.91 [12.04; 14.10]	42.5	73.8	89.1	96.0
T5T150T180	0.971	-1.86 [-2.47; -1.25]	7.55 [7.14; 7.95]	8.93 [8.91; 8.94]	0.97 [0.97; 0.97]	12.97 [12.31; 13.60]	43.2	73.6	88.0	94.4
T15T30T150	0.971	0.01 [-0.59; 0.60]	7.49 [7.12; 7.86]	8.95 [8.94; 8.96]	0.97 [0.97; 0.97]	13.01 [12.33; 13.66]	41.1	71.2	89.3	96.6
T60T120T180	0.971	-1.94 [-2.54; -1.34]	7.51 [7.11; 7.91]	9.01 [8.99; 9.02]	0.97 [0.97; 0.97]	13.09 [12.22; 14.20]	43.1	73.1	88.0	95.2
T15T120T180	0.971	-2.78 [-3.41; -2.14]	7.75 [7.31; 8.20]	9.01 [9.00; 9.03]	0.97 [0.97; 0.97]	13.10 [12.46; 13.75]	46.2	69.6	86.5	93.1
T5T45T150	0.970	0.59 [0.00; 1.17]	7.24 [6.87; 7.62]	9.12 [9.10; 9.13]	0.97 [0.97; 0.97]	13.25 [12.57; 14.01]	44.2	74.3	89.7	96.0
T120T150T240	0.971	-3.03 [-3.57; -2.49]	6.74 [6.36; 7.13]	9.16 [9.14; 9.17]	0.97 [0.96; 0.97]	13.31 [12.18; 14.46]	49.2	78.8	90.7	95.4
T15T45T150	0.970	0.95 [0.36; 1.54]	7.46 [7.09; 7.83]	9.19 [9.17; 9.20]	0.97 [0.96; 0.97]	13.35 [12.67; 14.03]	42.2	73.0	89.4	95.9
T60T90T180	0.969	-1.62 [-2.24; -1.01]	7.66 [7.27; 8.06]	9.28 [9.27; 9.29]	0.97 [0.96; 0.97]	13.48 [12.73; 14.30]	41.3	73.1	86.5	94.6
T120T210T240	0.969	-3.24 [-3.78; -2.69]	6.76 [6.36; 7.16]	9.38 [9.36; 9.39]	0.97 [0.96; 0.97]	13.62 [12.51; 14.85]	50.9	78.5	89.5	95.4
T15T90T180	0.971	2.24 [1.66; 2.82]	7.56 [7.19; 7.94]	9.38 [9.37; 9.39]	0.97 [0.96; 0.97]	13.63 [12.98; 14.29]	43.0	71.1	86.7	96.3
T120T180T240	0.969	-3.05 [-3.60; -2.50]	6.92 [6.52; 7.31]	9.41 [9.40; 9.43]	0.97 [0.96; 0.97]	13.68 [12.54; 14.95]	49.7	78.3	89.9	95.4
T5T120T180	0.967	-1.79 [-2.44; -1.14]	7.72 [7.27; 8.16]	9.51 [9.49; 9.52]	0.97 [0.96; 0.97]	13.81 [13.07; 14.60]	44.8	71.9	87.4	93.8
T90T150T210	0.967	-1.44 [-2.03; -0.85]	7.21 [6.82; 7.60]	9.51 [9.49; 9.52]	0.97 [0.96; 0.97]	13.81 [12.90; 14.79]	45.4	75.2	88.3	94.7
T30T45T150	0.967	-0.05 [-0.69; 0.59]	8.06 [7.66; 8.46]	9.53 [9.51; 9.54]	0.97 [0.96; 0.97]	13.84 [13.14; 14.54]	38.7	68.5	87.5	94.9
T30T120T150	0.966	-1.36 [-2.03; -0.69]	8.29 [7.86; 8.72]	9.54 [9.52; 9.55]	0.97 [0.96; 0.97]	13.86 [13.18; 14.56]	39.7	66.3	86.7	93.4
T90T120T210	0.967	-2.29 [-2.88; -1.69]	7.38 [6.98; 7.78]	9.56 [9.54; 9.57]	0.97 [0.96; 0.97]	13.89 [12.94; 14.88]	46.2	74.2	87.2	94.0
T5T90T180	0.966	0.82 [0.19; 1.45]	7.55 [7.13; 7.97]	9.67 [9.66; 9.68]	0.96 [0.96; 0.97]	14.05 [13.28; 14.85]	44.6	73.4	86.6	93.6

T90T180T210	0.965	-1.13 [-1.74; -0.53]	7.39 [7.00; 7.79]	9.77 [9.76; 9.78]	0.96 [0.96; 0.97]	14.20 [13.22; 15.25]	44.4	73.8	87.7	94.6
T45T120T150	0.964	-1.54 [-2.21; -0.87]	8.42 [8.00; 8.85]	9.86 [9.85; 9.87]	0.96 [0.96; 0.97]	14.33 [13.65; 15.05]	36.5	68.8	85.4	93.7
T15T60T150	0.966	1.95 [1.33; 2.56]	7.83 [7.43; 8.23]	9.90 [9.88; 9.91]	0.96 [0.96; 0.97]	14.38 [13.73; 15.12]	42.2	69.2	86.8	94.1
T180T210T240	0.964	-2.82 [-3.39; -2.25]	7.09 [6.70; 7.49]	9.95 [9.93; 9.96]	0.96 [0.96; 0.97]	14.46 [13.46; 15.49]	47.6	76.6	89.8	95.3
T45T60T150	0.963	-0.68 [-1.35; -0.01]	8.30 [7.87; 8.73]	9.96 [9.95; 9.98]	0.96 [0.96; 0.97]	14.48 [13.72; 15.25]	38.6	68.9	85.5	93.2
T30T60T150	0.964	0.94 [0.28; 1.59]	8.22 [7.80; 8.64]	10.02 [10.01; 10.03]	0.96 [0.96; 0.97]	14.56 [13.89; 15.27]	38.8	66.9	85.3	93.6
T5T60T150	0.964	1.53 [0.91; 2.15]	7.78 [7.38; 8.18]	10.12 [10.11; 10.14]	0.96 [0.96; 0.97]	14.71 [13.86; 15.62]	41.5	69.9	86.8	94.3
T120T150T210	0.965	-3.88 [-4.49; -3.27]	7.87 [7.43; 8.30]	10.12 [10.11; 10.14]	0.96 [0.96; 0.97]	14.71 [13.66; 15.88]	43.0	72.1	86.3	93.7
T120T180T210	0.964	-4.07 [-4.69; -3.45]	7.96 [7.51; 8.41]	10.27 [10.26; 10.29]	0.96 [0.96; 0.96]	14.93 [13.92; 15.99]	42.9	71.2	85.9	93.1
T150T210T240	0.961	-2.94 [-3.52; -2.37]	6.95 [6.53; 7.37]	10.36 [10.35; 10.38]	0.96 [0.95; 0.96]	15.05 [13.34; 16.66]	49.8	78.4	89.4	94.7
T150T180T240	0.961	-3.11 [-3.69; -2.53]	7.10 [6.68; 7.53]	10.39 [10.38; 10.40]	0.96 [0.95; 0.96]	15.10 [13.47; 16.86]	48.3	77.3	89.4	94.7
T30T90T150	0.961	0.33 [-0.38; 1.04]	8.78 [8.32; 9.24]	10.40 [10.38; 10.41]	0.96 [0.95; 0.96]	15.11 [14.40; 15.81]	37.2	65.2	83.5	92.2
T5T30T120	0.960	0.42 [-0.23; 1.08]	8.08 [7.66; 8.51]	10.40 [10.39; 10.42]	0.96 [0.95; 0.96]	15.12 [14.28; 15.87]	42.1	67.7	84.4	93.0
T45T90T150	0.960	-1.56 [-2.26; -0.86]	8.68 [8.22; 9.14]	10.45 [10.43; 10.46]	0.96 [0.95; 0.96]	15.18 [14.44; 15.90]	38.7	67.5	82.8	92.2
T15T120T150	0.961	0.68 [0.00; 1.37]	8.66 [8.23; 9.09]	10.48 [10.47; 10.50]	0.96 [0.95; 0.96]	15.23 [14.42; 16.01]	36.5	65.2	83.2	92.8
T150T180T210	0.961	-3.89 [-4.51; -3.27]	7.86 [7.41; 8.31]	10.57 [10.55; 10.58]	0.96 [0.95; 0.96]	15.36 [13.92; 16.89]	41.9	71.6	86.8	93.7
T5T120T150	0.958	0.14 [-0.55; 0.83]	8.51 [8.06; 8.95]	10.72 [10.70; 10.73]	0.96 [0.95; 0.96]	15.57 [14.72; 16.56]	38.3	66.5	84.0	94.0
T5T15T120	0.957	-0.59 [-1.27; 0.10]	8.39 [7.94; 8.84]	10.77 [10.76; 10.79]	0.96 [0.95; 0.96]	15.65 [14.80; 16.54]	40.5	68.1	83.4	92.1
T60T120T150	0.957	-0.88 [-1.59; -0.18]	8.83 [8.39; 9.28]	10.78 [10.77; 10.80]	0.96 [0.95; 0.96]	15.67 [14.69; 16.62]	36.0	65.0	83.9	91.9
T15T90T150	0.962	2.89 [2.23; 3.54]	8.48 [8.05; 8.91]	10.80 [10.78; 10.81]	0.96 [0.95; 0.96]	15.69 [14.86; 16.57]	40.0	65.8	83.2	92.4
T60T90T150	0.954	-1.13 [-1.86; -0.41]	9.02 [8.56; 9.48]	11.11 [11.09; 11.12]	0.95 [0.95; 0.96]	16.14 [15.19; 17.27]	35.7	65.0	82.7	90.9
T120T150T180	0.958	-4.69 [-5.40; -3.98]	9.14 [8.62; 9.66]	11.11 [11.10; 11.13]	0.95 [0.95; 0.96]	16.15 [15.01; 17.34]	37.8	66.2	81.4	90.1
T90T120T180	0.954	-1.91 [-2.63; -1.20]	8.92 [8.45; 9.38]	11.12 [11.11; 11.14]	0.95 [0.95; 0.96]	16.16 [15.12; 17.33]	38.6	65.8	80.0	91.0
T90T150T180	0.954	-0.66 [-1.36; 0.04]	8.61 [8.16; 9.06]	11.14 [11.13; 11.16]	0.95 [0.95; 0.96]	16.19 [15.17; 17.34]	39.2	66.2	81.9	91.9
T5T90T150	0.956	1.90 [1.21; 2.59]	8.53 [8.07; 9.00]	11.22 [11.20; 11.23]	0.95 [0.95; 0.96]	16.30 [15.37; 17.27]	40.5	68.1	82.5	92.4
T5T45T120	0.954	1.07 [0.38; 1.76]	8.59 [8.15; 9.03]	11.24 [11.22; 11.25]	0.95 [0.95; 0.96]	16.33 [15.42; 17.27]	38.8	65.9	84.3	92.5
T15T30T120	0.953	0.68 [-0.03; 1.39]	8.84 [8.39; 9.29]	11.33 [11.31; 11.34]	0.95 [0.94; 0.96]	16.46 [15.53; 17.47]	37.3	64.7	80.7	91.2
T15T45T120	0.953	1.37 [0.67; 2.06]	8.74 [8.29; 9.19]	11.43 [11.42; 11.45]	0.95 [0.94; 0.96]	16.62 [15.61; 17.54]	37.9	65.0	82.6	92.2
T15T60T120	0.951	2.21 [1.49; 2.94]	9.17 [8.70; 9.63]	11.93 [11.92; 11.95]	0.95 [0.94; 0.95]	17.34 [16.32; 18.25]	36.1	62.8	80.6	91.1
T30T45T120	0.947	0.14 [-0.65; 0.92]	9.53 [9.01; 10.04]	12.03 [12.01; 12.05]	0.94 [0.94; 0.95]	17.48 [16.58; 18.39]	36.4	62.7	79.4	89.3

	T5T60T120	0.949	2.01 [1.29; 2.74]	9.13 [8.67; 9.60]	12.11 [12.09; 12.12]	0.94 [0.94; 0.95]	17.59 [16.64; 18.57]	37.2	63.4	80.3	90.8
	T45T60T120	0.945	-0.57 [-1.37; 0.23]	9.82 [9.30; 10.34]	12.20 [12.18; 12.21]	0.94 [0.94; 0.95]	17.72 [16.84; 18.63]	34.7	60.1	79.2	88.2
	T45T90T120	0.944	-0.82 [-1.62; -0.01]	9.78 [9.25; 10.31]	12.25 [12.24; 12.27]	0.94 [0.93; 0.95]	17.81 [16.85; 18.74]	35.3	61.4	78.8	88.6
	T30T60T120	0.946	0.97 [0.18; 1.76]	9.75 [9.24; 10.26]	12.29 [12.27; 12.30]	0.94 [0.93; 0.95]	17.85 [16.87; 18.77]	34.0	62.1	78.0	88.5
	T90T120T150	0.943	-0.24 [-1.02; 0.55]	9.78 [9.28; 10.27]	12.42 [12.40; 12.43]	0.94 [0.93; 0.95]	18.04 [16.91; 19.18]	34.9	60.5	78.2	88.3
	T30T90T120	0.945	0.72 [-0.08; 1.53]	9.86 [9.34; 10.39]	12.43 [12.41; 12.45]	0.94 [0.93; 0.95]	18.06 [17.22; 18.98]	35.4	61.3	77.1	87.5
	T15T90T120	0.948	2.65 [1.90; 3.39]	9.57 [9.10; 10.05]	12.45 [12.44; 12.47]	0.94 [0.93; 0.95]	18.10 [17.15; 19.08]	34.5	61.0	77.1	89.3
	T5T30T90	0.941	0.27 [-0.54; 1.09]	9.96 [9.43; 10.49]	12.63 [12.62; 12.65]	0.94 [0.93; 0.95]	18.36 [17.31; 19.38]	32.5	60.5	77.5	88.6
	T5T15T90	0.939	-0.50 [-1.33; 0.33]	10.04 [9.49; 10.58]	12.74 [12.72; 12.76]	0.94 [0.93; 0.94]	18.51 [17.42; 19.51]	33.8	60.3	76.4	89.2
	T5T90T120	0.945	2.63 [1.88; 3.37]	9.50 [9.02; 9.98]	12.74 [12.72; 12.76]	0.94 [0.93; 0.94]	18.52 [17.55; 19.64]	35.2	60.8	78.0	89.2
	T60T90T120	0.937	-0.76 [-1.59; 0.07]	10.15 [9.60; 10.69]	12.96 [12.94; 12.98]	0.94 [0.93; 0.94]	18.84 [17.77; 19.96]	33.7	59.6	77.5	87.3
	T5T45T90	0.936	0.74 [-0.10; 1.58]	10.18 [9.63; 10.73]	13.25 [13.23; 13.27]	0.93 [0.92; 0.94]	19.25 [18.11; 20.36]	35.3	58.5	77.6	87.3
	T5T60T90	0.936	1.68 [0.85; 2.51]	10.39 [9.86; 10.92]	13.45 [13.43; 13.47]	0.93 [0.92; 0.94]	19.54 [18.34; 20.66]	33.2	56.6	75.4	87.3
	T15T45T90	0.934	1.03 [0.18; 1.88]	10.45 [9.90; 11.01]	13.55 [13.53; 13.57]	0.93 [0.92; 0.94]	19.69 [18.58; 20.89]	33.8	57.2	75.9	86.4
	T15T30T90	0.933	0.58 [-0.29; 1.45]	10.72 [10.16; 11.29]	13.57 [13.55; 13.59]	0.93 [0.92; 0.94]	19.72 [18.63; 20.81]	31.5	55.8	74.6	86.8
	T15T60T90	0.934	1.74 [0.89; 2.59]	10.63 [10.09; 11.18]	13.69 [13.67; 13.71]	0.93 [0.92; 0.93]	19.90 [18.78; 21.08]	32.5	56.8	74.2	87.6
	T30T45T90	0.922	-0.36 [-1.31; 0.59]	11.31 [10.68; 11.95]	14.48 [14.46; 14.50]	0.92 [0.91; 0.93]	21.04 [19.88; 22.24]	31.8	55.2	72.5	83.5
	T30T60T90	0.922	0.32 [-0.63; 1.26]	11.42 [10.80; 12.04]	14.56 [14.54; 14.58]	0.92 [0.91; 0.92]	21.15 [19.91; 22.29]	30.4	54.8	71.1	83.5
	T45T60T90	0.918	-1.56 [-2.53; -0.59]	11.61 [10.95; 12.27]	14.68 [14.66; 14.70]	0.92 [0.91; 0.93]	21.33 [20.03; 22.63]	31.5	54.0	73.2	83.5
	T5T45T60	0.914	0.31 [-0.66; 1.28]	12.17 [11.56; 12.78]	15.19 [15.17; 15.22]	0.91 [0.90; 0.92]	22.08 [20.92; 23.12]	25.0	52.1	68.6	82.5
	T5T15T60	0.912	-0.73 [-1.72; 0.26]	12.37 [11.75; 13.00]	15.26 [15.24; 15.28]	0.91 [0.90; 0.92]	22.17 [21.06; 23.32]	25.0	48.9	69.0	81.6
	T5T30T60	0.912	-0.26 [-1.25; 0.72]	12.33 [11.71; 12.95]	15.30 [15.28; 15.32]	0.91 [0.90; 0.92]	22.23 [21.15; 23.29]	25.7	49.7	68.1	81.4
	T15T45T60	0.910	0.56 [-0.43; 1.55]	12.37 [11.75; 12.99]	15.58 [15.56; 15.60]	0.90 [0.89; 0.91]	22.64 [21.47; 23.86]	25.0	50.7	68.6	81.5
	T15T30T60	0.905	0.03 [-0.99; 1.04]	12.64 [11.99; 13.28]	15.88 [15.86; 15.91]	0.90 [0.89; 0.91]	23.08 [21.87; 24.39]	24.6	48.4	67.4	81.4
	T30T45T60	0.890	-0.46 [-1.54; 0.62]	13.24 [12.54; 13.95]	17.01 [16.99; 17.04]	0.88 [0.87; 0.90]	24.72 [23.25; 26.15]	23.5	48.5	65.5	79.1
	T5T30T45	0.882	-1.19 [-2.30; -0.07]	13.85 [13.14; 14.56]	17.55 [17.52; 17.57]	0.87 [0.86; 0.89]	25.50 [24.06; 26.98]	22.2	44.7	63.0	76.8
	T5T15T45	0.880	-1.63 [-2.76; -0.49]	14.01 [13.28; 14.74]	17.65 [17.63; 17.67]	0.87 [0.86; 0.89]	25.65 [24.23; 27.06]	22.0	43.8	62.4	77.4
	T15T30T45	0.874	-1.39 [-2.54; -0.23]	14.36 [13.62; 15.10]	18.05 [18.03; 18.08]	0.86 [0.85; 0.88]	26.23 [24.86; 27.60]	22.0	42.2	59.5	77.0
	T5T15T30	0.835	-2.37 [-3.63; -1.11]	15.71 [14.90; 16.52]	20.41 [20.39; 20.44]	0.82 [0.80; 0.84]	29.66 [27.68; 31.43]	21.2	39.5	56.6	72.0
Four	T5T30T45T240	0.996	-0.44 [-0.65; -0.22]	2.64 [2.50; 2.79]	3.15 [3.15; 3.16]	1.00 [1.00; 1.00]	4.58 [4.32; 4.84]	87.7	98.9	99.9	100.0

T5T30T60T240	0.996	-0.28 [-0.50; -0.06]	2.70 [2.55; 2.84]	3.37 [3.36; 3.37]	1.00 [1.00; 1.00]	4.89 [4.60; 5.19]	87.5	98.6	99.8	100.0
T5T30T210T240	0.996	-0.65 [-0.87; -0.43]	2.67 [2.52; 2.82]	3.38 [3.38; 3.39]	1.00 [1.00; 1.00]	4.91 [4.60; 5.22]	86.7	98.8	99.9	100.0
T5T15T45T240	0.996	-0.60 [-0.83; -0.37]	2.83 [2.67; 2.98]	3.44 [3.44; 3.45]	1.00 [1.00; 1.00]	5.00 [4.71; 5.29]	84.3	97.5	99.9	100.0
T5T45T210T240	0.996	0.04 [-0.19; 0.27]	2.80 [2.64; 2.95]	3.47 [3.47; 3.48]	1.00 [1.00; 1.00]	5.05 [4.76; 5.35]	84.7	97.7	100.0	100.0
T5T45T60T240	0.996	0.01 [-0.23; 0.25]	2.87 [2.71; 3.03]	3.52 [3.52; 3.53]	1.00 [0.99; 1.00]	5.12 [4.84; 5.39]	82.6	97.8	99.6	100.0
T5T30T180T240	0.996	-0.67 [-0.91; -0.44]	2.87 [2.71; 3.03]	3.58 [3.58; 3.59]	1.00 [0.99; 1.00]	5.20 [4.89; 5.52]	82.9	98.4	99.7	100.0
T5T45T120T240	0.995	-0.28 [-0.52; -0.04]	2.83 [2.66; 3.00]	3.66 [3.65; 3.66]	1.00 [0.99; 1.00]	5.32 [4.94; 5.73]	84.5	97.8	99.2	100.0
T5T30T150T240	0.995	-0.67 [-0.91; -0.43]	2.90 [2.73; 3.06]	3.68 [3.68; 3.69]	1.00 [0.99; 1.00]	5.35 [5.02; 5.66]	84.8	97.7	99.5	99.9
T5T45T180T240	0.995	-0.06 [-0.30; 0.19]	2.95 [2.79; 3.12]	3.70 [3.69; 3.70]	1.00 [0.99; 1.00]	5.37 [5.02; 5.77]	81.8	97.5	99.7	100.0
T5T30T120T240	0.995	-0.54 [-0.79; -0.30]	2.87 [2.70; 3.04]	3.73 [3.73; 3.74]	0.99 [0.99; 1.00]	5.42 [5.08; 5.82]	85.8	97.4	99.2	99.8
T5T45T150T240	0.995	-0.13 [-0.37; 0.11]	2.86 [2.70; 3.02]	3.73 [3.72; 3.74]	0.99 [0.99; 1.00]	5.42 [5.00; 5.88]	83.2	97.8	99.4	100.0
T5T45T90T240	0.995	-0.31 [-0.55; -0.06]	2.91 [2.74; 3.08]	3.75 [3.74; 3.76]	0.99 [0.99; 1.00]	5.45 [5.09; 5.80]	83.3	97.3	99.2	100.0
T5T30T90T240	0.995	-0.43 [-0.67; -0.19]	2.86 [2.70; 3.02]	3.77 [3.76; 3.77]	0.99 [0.99; 1.00]	5.48 [5.09; 5.89]	86.0	97.7	99.4	100.0
T5T15T60T240	0.995	-0.36 [-0.61; -0.11]	3.04 [2.87; 3.21]	3.85 [3.84; 3.85]	0.99 [0.99; 1.00]	5.59 [5.28; 5.90]	82.8	97.0	99.6	100.0
T15T45T210T240	0.994	-0.12 [-0.39; 0.15]	3.19 [3.01; 3.37]	3.95 [3.95; 3.96]	0.99 [0.99; 0.99]	5.74 [5.39; 6.07]	80.6	96.4	99.3	99.9
T5T15T30T240	0.995	-1.07 [-1.32; -0.82]	3.17 [3.00; 3.34]	4.01 [4.00; 4.01]	0.99 [0.99; 0.99]	5.82 [5.43; 6.26]	79.6	97.2	99.7	100.0
T15T30T45T240	0.994	-0.58 [-0.85; -0.30]	3.39 [3.21; 3.57]	4.09 [4.09; 4.10]	0.99 [0.99; 0.99]	5.95 [5.61; 6.28]	78.3	96.2	99.5	100.0
T15T45T60T240	0.994	0.14 [-0.14; 0.42]	3.31 [3.12; 3.50]	4.10 [4.09; 4.11]	0.99 [0.99; 0.99]	5.96 [5.65; 6.27]	79.0	95.8	98.8	99.9
T15T45T180T240	0.994	-0.35 [-0.64; -0.06]	3.37 [3.17; 3.57]	4.22 [4.22; 4.23]	0.99 [0.99; 0.99]	6.14 [5.76; 6.50]	78.1	95.2	98.8	99.6
T15T45T150T240	0.993	-0.57 [-0.88; -0.26]	3.36 [3.13; 3.59]	4.27 [4.27; 4.28]	0.99 [0.99; 0.99]	6.21 [5.81; 6.63]	79.8	95.0	98.0	99.3
T15T45T90T240	0.993	-0.81 [-1.12; -0.50]	3.45 [3.22; 3.69]	4.35 [4.34; 4.36]	0.99 [0.99; 0.99]	6.32 [5.93; 6.75]	80.3	94.0	98.0	99.2
T15T30T60T240	0.993	-0.14 [-0.44; 0.15]	3.49 [3.29; 3.69]	4.36 [4.35; 4.37]	0.99 [0.99; 0.99]	6.33 [6.00; 6.66]	77.5	95.9	98.9	99.8
T15T45T120T240	0.993	-0.89 [-1.21; -0.57]	3.42 [3.17; 3.66]	4.38 [4.37; 4.39]	0.99 [0.99; 0.99]	6.36 [5.94; 6.79]	80.6	94.6	97.6	99.0
T30T45T210T240	0.993	-1.07 [-1.37; -0.76]	3.62 [3.41; 3.84]	4.39 [4.38; 4.40]	0.99 [0.99; 0.99]	6.38 [6.03; 6.72]	75.8	94.1	98.2	99.9
T15T30T180T240	0.993	-1.28 [-1.59; -0.98]	3.65 [3.43; 3.88]	4.54 [4.53; 4.54]	0.99 [0.99; 0.99]	6.59 [6.20; 6.99]	75.1	94.2	98.3	99.5
T15T30T210T240	0.993	-1.09 [-1.38; -0.80]	3.50 [3.30; 3.70]	4.54 [4.53; 4.54]	0.99 [0.99; 0.99]	6.59 [6.12; 7.14]	76.2	95.0	99.0	99.9
T15T60T210T240	0.993	0.85 [0.55; 1.16]	3.56 [3.35; 3.78]	4.62 [4.61; 4.63]	0.99 [0.99; 0.99]	6.71 [6.35; 7.10]	76.3	94.4	98.7	99.7
T5T60T210T240	0.992	0.64 [0.35; 0.92]	3.43 [3.24; 3.63]	4.64 [4.63; 4.65]	0.99 [0.99; 0.99]	6.74 [6.26; 7.31]	78.3	95.2	98.9	99.9
T5T60T150T240	0.992	0.23 [-0.05; 0.51]	3.31 [3.11; 3.50]	4.64 [4.63; 4.65]	0.99 [0.99; 0.99]	6.74 [6.14; 7.46]	79.1	96.3	98.7	99.6
T5T30T45T210	0.992	-0.16 [-0.47; 0.15]	3.86 [3.66; 4.06]	4.65 [4.64; 4.65]	0.99 [0.99; 0.99]	6.75 [6.44; 7.07]	70.6	95.1	99.1	99.9

T15T60T180T240	0.992	0.44 [0.13; 0.76]	3.62 [3.40; 3.84]	4.66 [4.65; 4.66]	0.99 [0.99; 0.99]	6.77 [6.36; 7.19]	76.6	94.8	98.6	99.4
T5T60T120T240	0.992	0.15 [-0.14; 0.43]	3.37 [3.18; 3.57]	4.66 [4.65; 4.66]	0.99 [0.99; 0.99]	6.77 [6.14; 7.37]	78.0	95.7	98.7	99.8
T5T60T180T240	0.992	0.51 [0.22; 0.80]	3.49 [3.30; 3.68]	4.68 [4.67; 4.68]	0.99 [0.99; 0.99]	6.79 [6.25; 7.40]	75.4	96.0	99.1	99.7
T30T45T180T240	0.993	-1.34 [-1.67; -1.01]	3.83 [3.58; 4.07]	4.68 [4.68; 4.69]	0.99 [0.99; 0.99]	6.81 [6.43; 7.19]	72.9	93.1	97.9	99.3
T5T30T60T210	0.992	-0.09 [-0.41; 0.22]	3.86 [3.66; 4.07]	4.69 [4.69; 4.70]	0.99 [0.99; 0.99]	6.82 [6.41; 7.18]	71.5	94.1	99.1	99.8
T15T30T150T240	0.992	-1.42 [-1.75; -1.10]	3.71 [3.46; 3.95]	4.73 [4.72; 4.73]	0.99 [0.99; 0.99]	6.87 [6.44; 7.40]	75.9	93.6	97.7	99.1
T5T30T180T210	0.992	-0.40 [-0.71; -0.08]	3.89 [3.68; 4.09]	4.73 [4.73; 4.74]	0.99 [0.99; 0.99]	6.88 [6.51; 7.27]	70.7	94.8	98.6	99.9
T30T60T210T240	0.992	-0.22 [-0.55; 0.12]	3.84 [3.60; 4.07]	4.75 [4.74; 4.75]	0.99 [0.99; 0.99]	6.90 [6.52; 7.26]	74.5	92.9	97.8	99.7
T15T30T90T240	0.992	-1.18 [-1.51; -0.84]	3.78 [3.53; 4.03]	4.76 [4.75; 4.77]	0.99 [0.99; 0.99]	6.92 [6.47; 7.34]	76.3	92.9	97.5	99.1
T15T60T150T240	0.992	-0.21 [-0.53; 0.11]	3.53 [3.29; 3.77]	4.77 [4.76; 4.78]	0.99 [0.99; 0.99]	6.93 [6.49; 7.39]	79.4	94.4	97.7	99.1
T30T45T150T240	0.992	-1.71 [-2.04; -1.37]	3.86 [3.61; 4.12]	4.79 [4.78; 4.80]	0.99 [0.99; 0.99]	6.96 [6.56; 7.35]	75.6	92.7	97.1	99.3
T30T60T180T240	0.992	-0.56 [-0.90; -0.23]	3.86 [3.62; 4.10]	4.79 [4.79; 4.80]	0.99 [0.99; 0.99]	6.97 [6.59; 7.35]	74.7	93.3	98.0	99.3
T30T45T60T240	0.992	-0.43 [-0.76; -0.09]	3.88 [3.65; 4.11]	4.82 [4.81; 4.83]	0.99 [0.99; 0.99]	7.00 [6.61; 7.40]	73.3	93.1	97.6	99.6
T5T15T90T240	0.992	-0.98 [-1.30; -0.65]	3.72 [3.49; 3.95]	4.83 [4.82; 4.83]	0.99 [0.99; 0.99]	7.01 [6.54; 7.46]	77.4	93.3	97.6	99.3
T30T60T150T240	0.992	-1.16 [-1.50; -0.82]	3.83 [3.58; 4.09]	4.83 [4.82; 4.84]	0.99 [0.99; 0.99]	7.02 [6.57; 7.46]	76.2	93.2	97.0	99.1
T30T45T120T240	0.992	-1.90 [-2.24; -1.56]	3.90 [3.63; 4.16]	4.84 [4.83; 4.85]	0.99 [0.99; 0.99]	7.03 [6.58; 7.47]	77.0	92.5	96.5	98.8
T15T60T120T240	0.991	-0.39 [-0.73; -0.04]	3.69 [3.43; 3.94]	4.89 [4.89; 4.90]	0.99 [0.99; 0.99]	7.11 [6.67; 7.57]	78.1	93.5	97.3	98.8
T5T60T90T240	0.991	0.24 [-0.06; 0.54]	3.53 [3.33; 3.74]	4.89 [4.89; 4.90]	0.99 [0.99; 0.99]	7.11 [6.50; 7.68]	76.3	94.8	98.4	99.9
T15T30T120T240	0.992	-1.58 [-1.92; -1.24]	3.80 [3.54; 4.07]	4.91 [4.90; 4.91]	0.99 [0.99; 0.99]	7.13 [6.63; 7.62]	76.9	92.8	97.0	98.7
T30T180T210T240	0.992	-2.17 [-2.49; -1.84]	3.99 [3.74; 4.24]	4.91 [4.91; 4.92]	0.99 [0.99; 0.99]	7.14 [6.74; 7.53]	73.5	91.1	97.0	99.4
T5T15T45T210	0.991	-0.38 [-0.71; -0.06]	4.03 [3.81; 4.24]	4.92 [4.91; 4.93]	0.99 [0.99; 0.99]	7.15 [6.80; 7.50]	69.5	94.1	99.0	99.8
T15T60T90T240	0.991	-0.13 [-0.46; 0.20]	3.76 [3.53; 4.00]	4.94 [4.93; 4.94]	0.99 [0.99; 0.99]	7.17 [6.75; 7.59]	76.4	92.7	98.0	99.1
T45T60T210T240	0.992	-1.15 [-1.48; -0.83]	3.90 [3.68; 4.13]	4.94 [4.94; 4.95]	0.99 [0.99; 0.99]	7.18 [6.72; 7.68]	72.8	93.7	98.3	99.5
T30T60T120T240	0.992	-1.36 [-1.72; -1.01]	4.00 [3.74; 4.27]	4.95 [4.94; 4.95]	0.99 [0.99; 0.99]	7.19 [6.76; 7.61]	75.7	92.6	96.6	98.7
T5T30T150T210	0.991	-0.35 [-0.68; -0.02]	4.03 [3.81; 4.24]	4.95 [4.94; 4.96]	0.99 [0.99; 0.99]	7.19 [6.74; 7.62]	70.4	93.7	98.6	99.9
T30T150T210T240	0.992	-2.33 [-2.67; -2.00]	3.97 [3.70; 4.24]	4.97 [4.97; 4.98]	0.99 [0.99; 0.99]	7.22 [6.82; 7.63]	74.9	91.4	96.1	98.9
T30T60T90T240	0.991	-1.47 [-1.81; -1.12]	3.98 [3.72; 4.23]	5.00 [5.00; 5.01]	0.99 [0.99; 0.99]	7.27 [6.80; 7.73]	73.9	92.0	96.7	99.4
T5T15T30T210	0.991	-0.84 [-1.17; -0.51]	4.14 [3.93; 4.35]	5.03 [5.02; 5.03]	0.99 [0.99; 0.99]	7.31 [6.96; 7.68]	69.1	93.5	98.8	99.9
T5T30T90T210	0.991	-0.33 [-0.66; 0.00]	3.95 [3.72; 4.17]	5.05 [5.04; 5.05]	0.99 [0.99; 0.99]	7.33 [6.89; 7.79]	72.2	93.1	98.0	99.7
T30T45T90T240	0.992	-2.05 [-2.41; -1.69]	4.07 [3.79; 4.36]	5.06 [5.06; 5.07]	0.99 [0.99; 0.99]	7.36 [6.90; 7.81]	74.0	91.1	95.9	98.8

T5T30T120T210	0.991	-0.27 [-0.61; 0.06]	4.00 [3.77; 4.22]	5.07 [5.06; 5.08]	0.99 [0.99; 0.99]	7.37 [6.92; 7.85]	72.0	93.2	98.3	99.7
T45T150T210T240	0.992	-2.00 [-2.32; -1.68]	3.95 [3.71; 4.19]	5.09 [5.08; 5.10]	0.99 [0.99; 0.99]	7.39 [6.89; 7.94]	72.5	92.4	97.8	99.1
T30T120T210T240	0.992	-2.44 [-2.79; -2.10]	4.05 [3.77; 4.34]	5.10 [5.09; 5.11]	0.99 [0.99; 0.99]	7.41 [6.98; 7.82]	75.5	89.8	95.7	98.6
T30T90T210T240	0.991	-2.07 [-2.44; -1.71]	4.11 [3.82; 4.40]	5.14 [5.14; 5.15]	0.99 [0.99; 0.99]	7.47 [7.04; 7.92]	75.9	89.1	95.2	98.4
T45T60T180T240	0.991	-1.37 [-1.71; -1.02]	4.08 [3.83; 4.32]	5.16 [5.15; 5.16]	0.99 [0.99; 0.99]	7.49 [7.01; 8.02]	70.8	93.1	97.8	99.2
T5T15T210T240	0.991	-1.71 [-2.02; -1.40]	3.75 [3.52; 3.98]	5.16 [5.16; 5.17]	0.99 [0.99; 0.99]	7.50 [6.85; 8.18]	74.0	92.9	97.9	99.4
T5T45T180T210	0.990	0.29 [-0.05; 0.62]	4.17 [3.95; 4.39]	5.16 [5.15; 5.17]	0.99 [0.99; 0.99]	7.50 [7.11; 7.92]	67.9	93.1	98.6	99.9
T45T180T210T240	0.991	-1.75 [-2.08; -1.43]	4.06 [3.82; 4.29]	5.16 [5.15; 5.17]	0.99 [0.99; 0.99]	7.50 [6.98; 8.07]	71.1	93.2	98.0	99.3
T45T60T150T240	0.991	-1.73 [-2.07; -1.39]	4.00 [3.75; 4.26]	5.17 [5.16; 5.18]	0.99 [0.99; 0.99]	7.52 [7.00; 8.06]	71.6	93.4	97.2	99.0
T30T150T180T240	0.992	-2.41 [-2.76; -2.05]	4.26 [3.98; 4.54]	5.19 [5.18; 5.20]	0.99 [0.99; 0.99]	7.54 [7.12; 7.98]	71.9	90.9	95.5	98.7
T5T15T60T210	0.990	-0.16 [-0.50; 0.19]	4.21 [3.99; 4.44]	5.19 [5.19; 5.20]	0.99 [0.99; 0.99]	7.55 [7.17; 7.92]	67.7	92.1	98.4	99.8
T45T120T210T240	0.991	-2.12 [-2.45; -1.79]	3.96 [3.70; 4.21]	5.21 [5.21; 5.22]	0.99 [0.99; 0.99]	7.58 [6.97; 8.28]	74.0	92.2	97.3	98.7
T30T120T180T240	0.991	-2.41 [-2.77; -2.04]	4.31 [4.02; 4.60]	5.23 [5.22; 5.24]	0.99 [0.99; 0.99]	7.60 [7.14; 8.04]	71.6	90.2	95.2	98.1
T5T45T150T210	0.990	0.18 [-0.16; 0.52]	4.19 [3.97; 4.41]	5.23 [5.23; 5.24]	0.99 [0.99; 0.99]	7.60 [7.16; 8.03]	67.3	93.3	98.8	99.8
T30T90T180T240	0.991	-1.74 [-2.11; -1.37]	4.13 [3.85; 4.42]	5.23 [5.23; 5.24]	0.99 [0.99; 0.99]	7.61 [7.13; 8.12]	72.8	89.8	95.7	98.6
T5T15T150T240	0.991	-1.65 [-1.99; -1.31]	3.90 [3.64; 4.16]	5.25 [5.24; 5.25]	0.99 [0.99; 0.99]	7.62 [7.09; 8.21]	75.5	92.2	97.1	98.8
T5T45T60T210	0.990	0.29 [-0.05; 0.64]	4.25 [4.03; 4.48]	5.25 [5.25; 5.26]	0.99 [0.99; 0.99]	7.63 [7.23; 8.05]	67.1	92.4	98.6	99.8
T5T45T120T210	0.990	0.01 [-0.33; 0.35]	4.10 [3.87; 4.33]	5.25 [5.24; 5.26]	0.99 [0.99; 0.99]	7.63 [7.16; 8.10]	68.9	92.9	98.2	99.6
T5T15T120T240	0.991	-1.58 [-1.93; -1.23]	3.91 [3.64; 4.18]	5.27 [5.26; 5.27]	0.99 [0.99; 0.99]	7.65 [7.11; 8.21]	77.0	91.7	96.6	98.6
T45T90T210T240	0.991	-2.14 [-2.48; -1.80]	4.11 [3.85; 4.38]	5.27 [5.26; 5.28]	0.99 [0.99; 0.99]	7.66 [7.15; 8.18]	71.0	91.5	97.0	98.9
T5T15T180T240	0.991	-1.75 [-2.08; -1.42]	4.01 [3.77; 4.26]	5.28 [5.27; 5.29]	0.99 [0.99; 0.99]	7.67 [7.14; 8.24]	72.3	92.4	97.5	99.1
T30T90T150T240	0.991	-1.77 [-2.14; -1.39]	4.20 [3.91; 4.48]	5.28 [5.28; 5.29]	0.99 [0.99; 0.99]	7.68 [7.18; 8.15]	73.6	90.6	95.5	98.6
T45T150T180T240	0.991	-2.02 [-2.36; -1.68]	4.22 [3.97; 4.47]	5.31 [5.30; 5.32]	0.99 [0.99; 0.99]	7.71 [7.20; 8.26]	69.3	92.8	97.1	99.0
T45T60T90T240	0.991	-2.14 [-2.49; -1.80]	4.17 [3.91; 4.43]	5.33 [5.32; 5.34]	0.99 [0.99; 0.99]	7.75 [7.22; 8.33]	70.9	91.5	96.8	99.1
T5T45T90T210	0.990	-0.07 [-0.43; 0.28]	4.19 [3.95; 4.43]	5.34 [5.33; 5.35]	0.99 [0.99; 0.99]	7.76 [7.28; 8.24]	69.3	92.0	98.0	99.4
T30T120T150T240	0.991	-2.48 [-2.85; -2.11]	4.39 [4.10; 4.68]	5.40 [5.39; 5.40]	0.99 [0.99; 0.99]	7.84 [7.37; 8.32]	72.4	89.5	95.2	98.6
T45T90T150T240	0.990	-1.94 [-2.29; -1.58]	4.22 [3.95; 4.49]	5.43 [5.42; 5.44]	0.99 [0.99; 0.99]	7.89 [7.28; 8.44]	71.8	90.7	96.5	98.8
T45T90T180T240	0.990	-1.95 [-2.30; -1.59]	4.25 [3.99; 4.52]	5.43 [5.42; 5.44]	0.99 [0.99; 0.99]	7.89 [7.32; 8.44]	70.5	92.1	96.8	98.9
T30T90T120T240	0.990	-2.29 [-2.67; -1.91]	4.49 [4.19; 4.79]	5.46 [5.45; 5.47]	0.99 [0.99; 0.99]	7.93 [7.49; 8.41]	71.2	88.9	94.9	98.3
T45T120T180T240	0.990	-2.13 [-2.48; -1.78]	4.27 [4.01; 4.54]	5.47 [5.46; 5.47]	0.99 [0.99; 0.99]	7.94 [7.35; 8.58]	70.2	92.3	96.5	98.9

T45T60T120T240	0.990	-1.99 [-2.34; -1.64]	4.10 [3.84; 4.37]	5.48 [5.47; 5.49]	0.99 [0.99; 0.99]	7.96 [7.08; 9.03]	70.7	92.5	96.9	98.5
T15T45T180T210	0.989	0.24 [-0.12; 0.61]	4.49 [4.25; 4.73]	5.50 [5.49; 5.51]	0.99 [0.99; 0.99]	7.99 [7.60; 8.38]	65.3	90.9	98.2	99.5
T15T30T45T210	0.989	-0.11 [-0.48; 0.26]	4.58 [4.34; 4.82]	5.53 [5.52; 5.53]	0.99 [0.99; 0.99]	8.03 [7.62; 8.41]	63.6	91.3	98.0	99.6
T45T120T150T240	0.990	-2.23 [-2.58; -1.88]	4.30 [4.04; 4.56]	5.54 [5.53; 5.55]	0.99 [0.99; 0.99]	8.05 [7.42; 8.75]	69.8	91.3	97.1	99.1
T45T90T120T240	0.990	-2.26 [-2.62; -1.91]	4.33 [4.05; 4.60]	5.58 [5.57; 5.59]	0.99 [0.99; 0.99]	8.11 [7.46; 8.83]	69.1	90.8	96.6	98.7
T15T30T180T210	0.989	-0.71 [-1.08; -0.34]	4.63 [4.39; 4.87]	5.61 [5.60; 5.61]	0.99 [0.99; 0.99]	8.14 [7.70; 8.62]	64.5	89.8	97.6	99.9
T15T45T60T210	0.989	0.67 [0.30; 1.05]	4.55 [4.30; 4.79]	5.64 [5.63; 5.64]	0.99 [0.99; 0.99]	8.19 [7.72; 8.61]	64.3	90.3	97.8	99.3
T15T30T60T210	0.988	0.38 [-0.01; 0.76]	4.68 [4.42; 4.94]	5.74 [5.74; 5.75]	0.99 [0.99; 0.99]	8.35 [7.85; 8.82]	65.8	89.0	97.0	99.0
T30T45T180T210	0.988	-0.84 [-1.24; -0.44]	4.98 [4.72; 5.25]	5.76 [5.75; 5.76]	0.99 [0.99; 0.99]	8.37 [8.00; 8.73]	60.0	88.8	96.7	98.9
T15T180T210T240	0.989	-2.21 [-2.59; -1.83]	4.47 [4.18; 4.76]	5.78 [5.77; 5.78]	0.99 [0.99; 0.99]	8.39 [7.86; 8.99]	69.0	89.5	96.2	97.8
T15T90T150T240	0.988	-0.68 [-1.08; -0.28]	4.37 [4.06; 4.67]	5.82 [5.81; 5.83]	0.99 [0.99; 0.99]	8.45 [7.90; 9.02]	72.7	89.1	95.9	98.1
T15T45T150T210	0.988	-0.10 [-0.49; 0.29]	4.64 [4.38; 4.90]	5.81 [5.81; 5.82]	0.99 [0.99; 0.99]	8.45 [7.96; 8.94]	63.8	90.8	96.5	98.8
T15T90T210T240	0.987	-0.79 [-1.22; -0.36]	4.64 [4.31; 4.96]	5.94 [5.94; 5.95]	0.99 [0.99; 0.99]	8.64 [8.13; 9.14]	70.1	86.4	94.8	97.9
T5T60T120T210	0.987	0.51 [0.13; 0.88]	4.57 [4.32; 4.82]	5.96 [5.95; 5.96]	0.99 [0.99; 0.99]	8.65 [8.11; 9.26]	65.1	90.0	96.9	99.8
T60T120T210T240	0.988	-1.59 [-1.95; -1.23]	4.34 [4.08; 4.60]	5.96 [5.95; 5.97]	0.99 [0.99; 0.99]	8.66 [7.70; 9.98]	68.6	92.2	97.4	98.5
T15T150T210T240	0.988	-2.35 [-2.74; -1.96]	4.45 [4.13; 4.77]	5.96 [5.96; 5.97]	0.99 [0.99; 0.99]	8.67 [8.08; 9.25]	70.3	88.0	95.6	97.5
T15T45T90T210	0.987	-0.37 [-0.76; 0.03]	4.64 [4.36; 4.91]	5.99 [5.98; 5.99]	0.99 [0.99; 0.99]	8.70 [8.12; 9.19]	66.4	89.3	96.4	98.7
T15T45T120T210	0.987	-0.54 [-0.95; -0.12]	4.73 [4.43; 5.02]	6.01 [6.00; 6.02]	0.99 [0.98; 0.99]	8.74 [8.19; 9.25]	65.4	88.7	95.8	98.2
T5T15T90T210	0.987	-0.69 [-1.09; -0.29]	4.73 [4.46; 5.01]	6.05 [6.04; 6.05]	0.99 [0.98; 0.99]	8.79 [8.26; 9.34]	65.6	88.7	95.9	98.9
T30T45T150T210	0.987	-1.32 [-1.74; -0.90]	5.13 [4.85; 5.42]	6.06 [6.05; 6.07]	0.99 [0.98; 0.99]	8.80 [8.37; 9.19]	61.8	87.1	95.3	98.6
T5T60T150T210	0.987	0.75 [0.37; 1.12]	4.65 [4.40; 4.89]	6.06 [6.05; 6.06]	0.99 [0.98; 0.99]	8.80 [8.15; 9.43]	63.4	89.8	97.2	99.6
T5T30T150T180	0.987	-0.28 [-0.69; 0.13]	5.00 [4.73; 5.27]	6.06 [6.05; 6.07]	0.99 [0.98; 0.99]	8.81 [8.31; 9.29]	59.4	87.8	96.6	99.0
T5T15T180T210	0.987	-1.49 [-1.87; -1.10]	4.83 [4.57; 5.09]	6.07 [6.06; 6.08]	0.99 [0.98; 0.99]	8.82 [8.22; 9.51]	62.5	88.3	96.8	99.3
T15T30T90T210	0.987	-0.80 [-1.21; -0.38]	4.82 [4.52; 5.11]	6.07 [6.06; 6.08]	0.99 [0.98; 0.99]	8.82 [8.31; 9.31]	65.2	88.4	95.5	98.4
T15T30T150T210	0.986	-0.88 [-1.29; -0.47]	4.94 [4.66; 5.21]	6.10 [6.10; 6.11]	0.99 [0.98; 0.99]	8.87 [8.35; 9.40]	64.4	87.1	95.6	99.1
T15T150T180T240	0.988	-2.38 [-2.79; -1.97]	4.71 [4.39; 5.04]	6.12 [6.12; 6.13]	0.99 [0.98; 0.99]	8.90 [8.33; 9.48]	69.0	86.6	94.9	97.6
T15T30T120T210	0.986	-1.17 [-1.59; -0.74]	4.95 [4.65; 5.25]	6.13 [6.12; 6.13]	0.99 [0.98; 0.99]	8.90 [8.36; 9.45]	65.0	87.3	95.0	98.0
T15T60T180T210	0.987	1.34 [0.95; 1.74]	4.90 [4.64; 5.17]	6.12 [6.12; 6.13]	0.99 [0.98; 0.99]	8.90 [8.44; 9.37]	62.1	88.1	96.9	99.3
T15T90T120T240	0.987	-1.55 [-1.98; -1.12]	4.80 [4.47; 5.12]	6.13 [6.12; 6.14]	0.99 [0.98; 0.99]	8.91 [8.38; 9.45]	69.3	86.7	94.4	97.2
T30T45T60T210	0.986	0.06 [-0.37; 0.48]	5.10 [4.82; 5.39]	6.13 [6.12; 6.14]	0.99 [0.98; 0.99]	8.91 [8.45; 9.36]	59.6	87.9	96.1	98.5

T30T150T180T210	0.987	-2.47 [-2.90; -2.05]	5.41 [5.11; 5.72]	6.15 [6.14; 6.15]	0.99 [0.98; 0.99]	8.93 [8.51; 9.33]	58.9	85.2	94.7	98.3
T60T120T180T240	0.987	-1.64 [-2.02; -1.26]	4.63 [4.37; 4.90]	6.15 [6.14; 6.16]	0.99 [0.98; 0.99]	8.93 [7.94; 10.21]	66.4	91.8	96.7	98.6
T30T45T120T210	0.987	-1.89 [-2.33; -1.45]	5.23 [4.91; 5.55]	6.15 [6.14; 6.16]	0.99 [0.98; 0.99]	8.94 [8.52; 9.41]	62.0	87.8	94.0	97.0
T60T120T150T240	0.987	-1.78 [-2.16; -1.40]	4.66 [4.39; 4.93]	6.17 [6.16; 6.18]	0.99 [0.98; 0.99]	8.96 [8.04; 10.32]	66.1	90.3	96.7	98.4
T60T150T210T240	0.987	-1.50 [-1.86; -1.13]	4.36 [4.10; 4.62]	6.18 [6.17; 6.19]	0.99 [0.98; 0.99]	8.98 [7.68; 10.87]	68.1	91.2	97.0	98.8
T5T15T150T210	0.986	-1.29 [-1.69; -0.89]	4.89 [4.61; 5.17]	6.22 [6.21; 6.23]	0.99 [0.98; 0.99]	9.03 [8.39; 9.76]	63.0	87.9	95.9	99.0
T15T90T180T240	0.986	-0.27 [-0.70; 0.16]	4.71 [4.40; 5.02]	6.22 [6.21; 6.23]	0.99 [0.98; 0.99]	9.04 [8.43; 9.58]	69.1	87.5	94.7	98.1
T60T180T210T240	0.987	-1.23 [-1.59; -0.87]	4.41 [4.16; 4.65]	6.22 [6.22; 6.23]	0.99 [0.98; 0.99]	9.04 [7.77; 11.00]	67.2	92.0	97.3	98.9
T15T120T210T240	0.987	-2.50 [-2.92; -2.08]	4.69 [4.34; 5.03]	6.24 [6.23; 6.25]	0.99 [0.98; 0.99]	9.07 [8.48; 9.59]	71.5	85.9	94.1	96.8
T60T90T150T240	0.986	-1.52 [-1.90; -1.14]	4.61 [4.34; 4.87]	6.24 [6.23; 6.25]	0.99 [0.98; 0.99]	9.07 [8.14; 10.30]	67.4	90.4	96.5	98.9
T30T120T180T210	0.987	-2.75 [-3.19; -2.32]	5.40 [5.07; 5.72]	6.25 [6.25; 6.26]	0.99 [0.98; 0.99]	9.09 [8.62; 9.56]	61.3	84.7	93.3	97.4
T30T60T180T210	0.986	0.19 [-0.24; 0.61]	5.23 [4.95; 5.51]	6.25 [6.24; 6.26]	0.99 [0.98; 0.99]	9.09 [8.67; 9.54]	59.6	86.3	95.9	98.7
T60T90T210T240	0.986	-1.53 [-1.92; -1.15]	4.59 [4.32; 4.86]	6.27 [6.26; 6.27]	0.99 [0.98; 0.99]	9.10 [8.15; 10.26]	66.1	89.2	96.4	98.8
T5T30T45T180	0.986	-0.22 [-0.64; 0.20]	5.13 [4.86; 5.40]	6.27 [6.26; 6.28]	0.99 [0.98; 0.99]	9.11 [8.59; 9.63]	58.4	87.7	96.3	98.7
T5T60T90T210	0.986	0.71 [0.32; 1.09]	4.70 [4.45; 4.96]	6.27 [6.26; 6.28]	0.99 [0.98; 0.99]	9.11 [8.46; 9.80]	64.2	88.3	97.1	99.6
T15T60T120T210	0.986	0.12 [-0.30; 0.54]	4.85 [4.55; 5.14]	6.28 [6.28; 6.29]	0.99 [0.98; 0.99]	9.13 [8.54; 9.65]	63.9	88.4	95.1	98.3
T30T45T90T210	0.986	-1.85 [-2.30; -1.41]	5.29 [4.97; 5.61]	6.29 [6.28; 6.30]	0.99 [0.98; 0.99]	9.14 [8.65; 9.63]	60.5	86.0	94.2	97.6
T5T15T120T210	0.986	-1.19 [-1.60; -0.77]	4.86 [4.57; 5.16]	6.30 [6.29; 6.31]	0.99 [0.98; 0.99]	9.15 [8.56; 9.74]	64.2	87.4	95.3	98.4
T5T30T60T180	0.985	-0.26 [-0.68; 0.16]	5.09 [4.82; 5.37]	6.31 [6.30; 6.32]	0.99 [0.98; 0.99]	9.17 [8.66; 9.66]	58.1	87.9	96.6	98.7
T60T90T120T240	0.986	-1.75 [-2.14; -1.36]	4.77 [4.49; 5.04]	6.33 [6.32; 6.34]	0.99 [0.98; 0.99]	9.19 [8.32; 10.32]	64.8	89.8	96.8	98.5
T60T90T180T240	0.986	-1.45 [-1.83; -1.07]	4.61 [4.34; 4.87]	6.32 [6.31; 6.33]	0.99 [0.98; 0.99]	9.19 [8.11; 10.50]	66.1	91.3	96.7	98.9
T15T60T150T210	0.986	0.63 [0.21; 1.04]	4.92 [4.63; 5.20]	6.33 [6.32; 6.34]	0.99 [0.98; 0.99]	9.20 [8.68; 9.70]	63.2	87.2	95.7	98.5
T15T120T150T240	0.987	-2.36 [-2.78; -1.93]	4.85 [4.52; 5.19]	6.34 [6.33; 6.35]	0.99 [0.98; 0.99]	9.21 [8.58; 9.91]	68.3	86.0	94.1	96.9
T45T150T180T210	0.986	-2.03 [-2.45; -1.61]	5.40 [5.11; 5.68]	6.35 [6.34; 6.36]	0.99 [0.98; 0.99]	9.23 [8.74; 9.76]	56.7	87.1	95.4	98.6
T5T30T120T180	0.985	-0.32 [-0.75; 0.10]	5.17 [4.88; 5.45]	6.37 [6.36; 6.38]	0.99 [0.98; 0.99]	9.25 [8.74; 9.79]	57.6	87.1	96.3	98.9
T5T60T180T210	0.986	1.04 [0.65; 1.43]	4.86 [4.60; 5.12]	6.37 [6.36; 6.37]	0.99 [0.98; 0.99]	9.25 [8.63; 9.86]	63.1	89.2	97.0	99.2
T60T150T180T240	0.986	-1.64 [-2.02; -1.26]	4.60 [4.34; 4.87]	6.36 [6.35; 6.37]	0.99 [0.98; 0.99]	9.25 [7.95; 11.44]	66.9	90.9	96.7	98.6
T45T60T180T210	0.985	-1.00 [-1.43; -0.57]	5.37 [5.10; 5.65]	6.38 [6.37; 6.39]	0.99 [0.98; 0.99]	9.27 [8.80; 9.77]	58.1	86.3	95.7	99.0
T30T60T150T210	0.985	-0.58 [-1.01; -0.14]	5.22 [4.93; 5.51]	6.39 [6.38; 6.40]	0.99 [0.98; 0.99]	9.28 [8.80; 9.76]	61.7	85.9	94.9	98.6
T45T120T180T210	0.986	-2.45 [-2.87; -2.02]	5.41 [5.11; 5.72]	6.39 [6.38; 6.40]	0.99 [0.98; 0.99]	9.29 [8.77; 9.85]	59.8	86.8	95.1	97.9

T5T90T210T240	0.985	0.14 [-0.27; 0.55]	4.64 [4.35; 4.93]	6.41 [6.40; 6.42]	0.99 [0.98; 0.99]	9.31 [8.64; 10.02]	67.6	87.5	95.3	98.7
T15T120T180T240	0.986	-2.20 [-2.64; -1.76]	4.90 [4.55; 5.24]	6.46 [6.45; 6.46]	0.98 [0.98; 0.99]	9.38 [8.68; 10.06]	68.7	86.1	93.6	96.4
T45T60T120T210	0.986	-1.93 [-2.37; -1.50]	5.34 [5.03; 5.64]	6.45 [6.44; 6.46]	0.98 [0.98; 0.99]	9.38 [8.87; 9.88]	58.2	86.4	94.6	97.7
T5T15T30T180	0.985	-0.99 [-1.42; -0.55]	5.35 [5.07; 5.63]	6.46 [6.45; 6.47]	0.98 [0.98; 0.99]	9.38 [8.91; 9.91]	56.2	86.6	95.9	98.9
T30T60T120T210	0.985	-1.14 [-1.59; -0.68]	5.32 [4.99; 5.64]	6.48 [6.47; 6.49]	0.98 [0.98; 0.99]	9.41 [8.84; 9.92]	61.1	85.5	93.7	97.4
T5T30T90T180	0.985	-0.42 [-0.85; 0.00]	5.12 [4.84; 5.41]	6.48 [6.47; 6.49]	0.98 [0.98; 0.99]	9.41 [8.82; 9.98]	60.0	86.9	96.0	98.5
T30T120T150T210	0.986	-2.71 [-3.16; -2.26]	5.64 [5.31; 5.97]	6.52 [6.51; 6.52]	0.98 [0.98; 0.99]	9.47 [9.02; 9.92]	59.7	83.7	92.8	97.3
T15T60T90T210	0.985	0.53 [0.11; 0.95]	5.06 [4.77; 5.34]	6.53 [6.52; 6.54]	0.98 [0.98; 0.99]	9.48 [8.95; 10.03]	62.1	86.6	95.8	98.7
T5T15T45T180	0.984	-0.51 [-0.95; -0.08]	5.35 [5.07; 5.64]	6.54 [6.53; 6.54]	0.98 [0.98; 0.99]	9.50 [8.99; 10.00]	55.9	87.3	95.7	98.6
T45T90T180T210	0.985	-2.26 [-2.70; -1.82]	5.46 [5.15; 5.77]	6.54 [6.53; 6.55]	0.98 [0.98; 0.99]	9.51 [8.99; 10.09]	59.1	86.4	94.0	98.0
T5T90T120T240	0.984	-0.57 [-1.01; -0.13]	4.82 [4.50; 5.15]	6.57 [6.56; 6.57]	0.98 [0.98; 0.99]	9.54 [8.75; 10.31]	67.1	87.5	94.7	97.5
T45T60T150T210	0.985	-1.54 [-1.97; -1.11]	5.35 [5.06; 5.64]	6.57 [6.56; 6.58]	0.98 [0.98; 0.99]	9.55 [8.88; 10.47]	57.6	87.1	95.4	98.4
T30T60T90T210	0.984	-1.17 [-1.63; -0.71]	5.44 [5.12; 5.76]	6.59 [6.58; 6.60]	0.98 [0.98; 0.99]	9.58 [9.09; 10.12]	61.0	84.9	94.1	97.7
T45T120T150T210	0.985	-2.47 [-2.90; -2.03]	5.53 [5.22; 5.84]	6.59 [6.58; 6.60]	0.98 [0.98; 0.99]	9.58 [9.04; 10.16]	57.1	86.4	94.3	97.7
T30T90T150T210	0.984	-1.74 [-2.20; -1.27]	5.53 [5.19; 5.86]	6.60 [6.59; 6.61]	0.98 [0.98; 0.99]	9.59 [9.09; 10.07]	60.5	84.3	93.2	97.1
T45T60T90T210	0.985	-2.23 [-2.67; -1.79]	5.52 [5.21; 5.83]	6.62 [6.61; 6.62]	0.98 [0.98; 0.99]	9.61 [9.10; 10.17]	56.4	85.4	94.9	97.8
T30T90T180T210	0.984	-1.86 [-2.33; -1.39]	5.60 [5.26; 5.95]	6.64 [6.64; 6.65]	0.98 [0.98; 0.99]	9.65 [9.19; 10.12]	60.9	82.6	92.2	97.2
T30T90T120T210	0.985	-2.32 [-2.79; -1.84]	5.70 [5.36; 6.05]	6.64 [6.63; 6.65]	0.98 [0.98; 0.99]	9.65 [9.18; 10.16]	59.9	83.5	92.4	96.7
T5T45T120T180	0.984	0.08 [-0.36; 0.52]	5.43 [5.14; 5.72]	6.71 [6.70; 6.72]	0.98 [0.98; 0.99]	9.75 [9.21; 10.24]	56.0	86.9	95.7	98.3
T45T90T120T210	0.985	-2.52 [-2.96; -2.07]	5.60 [5.28; 5.92]	6.71 [6.70; 6.72]	0.98 [0.98; 0.99]	9.76 [9.17; 10.30]	57.4	86.2	94.4	97.2
T5T90T150T240	0.983	0.17 [-0.26; 0.59]	4.65 [4.34; 4.95]	6.74 [6.73; 6.75]	0.98 [0.98; 0.99]	9.79 [8.94; 10.65]	68.1	88.6	95.2	97.8
T5T45T90T180	0.983	-0.22 [-0.67; 0.23]	5.43 [5.13; 5.73]	6.77 [6.76; 6.78]	0.98 [0.98; 0.99]	9.84 [9.30; 10.36]	57.2	86.3	95.0	98.0
T5T45T150T180	0.983	0.27 [-0.17; 0.72]	5.45 [5.16; 5.75]	6.79 [6.78; 6.80]	0.98 [0.98; 0.99]	9.87 [9.31; 10.46]	56.6	85.9	95.7	98.6
T15T30T45T180	0.983	0.10 [-0.36; 0.56]	5.69 [5.39; 5.98]	6.80 [6.79; 6.81]	0.98 [0.98; 0.98]	9.88 [9.39; 10.38]	55.7	84.2	94.6	98.6
T45T90T150T210	0.984	-2.07 [-2.53; -1.62]	5.56 [5.24; 5.89]	6.80 [6.79; 6.81]	0.98 [0.98; 0.98]	9.88 [9.30; 10.50]	58.3	85.4	94.0	97.2
T5T90T180T240	0.983	0.43 [0.01; 0.86]	4.82 [4.52; 5.12]	6.87 [6.86; 6.88]	0.98 [0.98; 0.98]	9.98 [9.16; 10.85]	64.5	87.9	95.3	98.3
T5T15T60T180	0.982	-0.38 [-0.83; 0.08]	5.57 [5.27; 5.87]	6.93 [6.92; 6.94]	0.98 [0.98; 0.98]	10.06 [9.56; 10.60]	55.0	85.5	94.8	98.1
T15T30T150T180	0.982	-0.43 [-0.90; 0.05]	5.80 [5.48; 6.11]	6.97 [6.96; 6.98]	0.98 [0.98; 0.98]	10.13 [9.61; 10.68]	54.5	82.6	94.2	98.1
T5T45T60T180	0.982	0.25 [-0.21; 0.71]	5.65 [5.35; 5.94]	6.98 [6.97; 6.99]	0.98 [0.98; 0.98]	10.15 [9.60; 10.67]	54.6	84.9	95.1	98.1
T15T45T150T180	0.982	0.50 [0.02; 0.97]	5.78 [5.47; 6.09]	7.03 [7.02; 7.04]	0.98 [0.98; 0.98]	10.21 [9.70; 10.76]	55.4	84.1	94.4	98.3

T5T180T210T240	0.983	-2.06 [-2.51; -1.61]	5.27 [4.94; 5.60]	7.04 [7.03; 7.05]	0.98 [0.98; 0.98]	10.23 [9.46; 10.98]	63.2	87.0	94.5	97.6
T15T150T180T210	0.983	-2.40 [-2.87; -1.92]	5.85 [5.52; 6.19]	7.09 [7.08; 7.10]	0.98 [0.98; 0.98]	10.30 [9.71; 11.04]	55.4	82.1	93.2	97.2
T60T120T180T210	0.982	-1.68 [-2.14; -1.22]	5.70 [5.40; 6.01]	7.13 [7.12; 7.14]	0.98 [0.98; 0.98]	10.36 [9.48; 11.55]	54.6	84.6	94.2	98.1
T15T30T60T180	0.982	0.64 [0.16; 1.12]	5.90 [5.59; 6.21]	7.15 [7.14; 7.16]	0.98 [0.98; 0.98]	10.39 [9.89; 10.86]	53.0	81.7	93.7	98.1
T5T15T150T180	0.981	-1.29 [-1.77; -0.82]	5.86 [5.54; 6.17]	7.17 [7.16; 7.18]	0.98 [0.98; 0.98]	10.41 [9.78; 11.01]	54.1	82.2	93.2	97.7
T15T45T60T180	0.981	0.86 [0.38; 1.34]	5.93 [5.62; 6.24]	7.22 [7.21; 7.23]	0.98 [0.98; 0.98]	10.49 [9.97; 10.97]	52.9	83.3	93.8	98.1
T60T120T150T210	0.981	-1.82 [-2.28; -1.36]	5.84 [5.53; 6.15]	7.27 [7.26; 7.28]	0.98 [0.98; 0.98]	10.56 [9.69; 11.74]	51.6	82.8	94.3	97.9
T60T150T180T210	0.981	-1.37 [-1.82; -0.91]	5.78 [5.48; 6.08]	7.31 [7.30; 7.32]	0.98 [0.98; 0.98]	10.62 [9.59; 12.09]	52.3	84.2	94.9	98.4
T15T45T120T180	0.980	-0.06 [-0.55; 0.44]	5.94 [5.61; 6.28]	7.33 [7.32; 7.34]	0.98 [0.98; 0.98]	10.66 [10.05; 11.26]	53.0	83.1	93.4	97.4
T60T90T120T210	0.981	-1.86 [-2.33; -1.38]	5.88 [5.56; 6.21]	7.37 [7.36; 7.38]	0.98 [0.98; 0.98]	10.70 [9.90; 11.74]	52.7	83.5	93.4	97.4
T60T90T150T210	0.981	-1.58 [-2.05; -1.11]	5.84 [5.53; 6.16]	7.36 [7.35; 7.37]	0.98 [0.98; 0.98]	10.70 [9.87; 11.82]	52.7	83.5	93.5	97.8
T15T45T90T180	0.980	0.07 [-0.42; 0.56]	5.99 [5.67; 6.31]	7.42 [7.41; 7.43]	0.98 [0.98; 0.98]	10.78 [10.25; 11.36]	53.4	82.2	92.9	97.5
T30T45T150T180	0.980	-0.77 [-1.29; -0.25]	6.41 [6.07; 6.75]	7.44 [7.43; 7.45]	0.98 [0.98; 0.98]	10.80 [10.33; 11.35]	49.7	79.5	93.5	97.4
T5T120T150T240	0.980	-1.82 [-2.30; -1.35]	5.35 [4.99; 5.70]	7.45 [7.44; 7.46]	0.98 [0.98; 0.98]	10.83 [9.98; 11.78]	64.8	86.8	92.8	96.4
T15T30T120T180	0.980	-0.84 [-1.37; -0.32]	6.16 [5.80; 6.52]	7.46 [7.45; 7.47]	0.98 [0.98; 0.98]	10.84 [10.17; 11.50]	53.8	80.2	92.6	96.5
T15T90T150T210	0.980	0.09 [-0.41; 0.59]	5.86 [5.51; 6.20]	7.46 [7.45; 7.47]	0.98 [0.98; 0.98]	10.84 [10.27; 11.40]	57.7	81.3	92.4	97.0
T60T90T180T210	0.980	-1.51 [-1.98; -1.04]	5.85 [5.54; 6.16]	7.48 [7.47; 7.49]	0.98 [0.98; 0.98]	10.87 [9.96; 11.94]	54.3	81.9	93.3	98.1
T15T120T180T210	0.980	-2.63 [-3.15; -2.12]	6.18 [5.80; 6.56]	7.52 [7.51; 7.53]	0.98 [0.98; 0.98]	10.93 [10.36; 11.54]	57.2	79.1	90.9	96.1
T15T30T90T180	0.979	-0.49 [-1.02; 0.03]	6.18 [5.82; 6.54]	7.52 [7.51; 7.53]	0.98 [0.98; 0.98]	10.93 [10.36; 11.50]	53.8	81.1	92.0	96.6
T15T120T150T210	0.980	-2.41 [-2.92; -1.90]	6.11 [5.74; 6.48]	7.54 [7.53; 7.55]	0.98 [0.98; 0.98]	10.96 [10.29; 11.61]	58.0	80.0	91.2	95.9
T15T90T120T210	0.979	-0.66 [-1.18; -0.14]	5.94 [5.57; 6.31]	7.56 [7.55; 7.57]	0.98 [0.98; 0.98]	10.98 [10.35; 11.64]	59.3	80.3	91.0	96.2
T5T15T90T180	0.979	-0.80 [-1.30; -0.30]	5.96 [5.62; 6.30]	7.57 [7.56; 7.58]	0.98 [0.98; 0.98]	11.00 [10.30; 11.73]	55.1	82.3	92.7	96.7
T5T150T180T240	0.980	-2.05 [-2.53; -1.58]	5.53 [5.18; 5.88]	7.57 [7.56; 7.58]	0.98 [0.98; 0.98]	11.00 [10.08; 11.97]	61.6	85.4	92.7	96.8
T5T15T120T180	0.979	-1.11 [-1.61; -0.61]	6.07 [5.73; 6.42]	7.65 [7.64; 7.66]	0.98 [0.98; 0.98]	11.12 [10.42; 11.79]	53.6	81.3	92.4	96.8
T30T120T150T180	0.980	-2.78 [-3.34; -2.22]	6.91 [6.51; 7.31]	7.68 [7.67; 7.69]	0.98 [0.98; 0.98]	11.15 [10.61; 11.62]	49.3	77.0	89.2	95.5
T5T120T150T180	0.979	-2.00 [-2.47; -1.53]	5.32 [4.96; 5.67]	7.68 [7.67; 7.69]	0.98 [0.98; 0.98]	11.16 [10.25; 12.15]	64.8	85.5	93.2	96.4
T5T150T210T240	0.979	-2.00 [-2.47; -1.53]	5.32 [4.96; 5.67]	7.68 [7.67; 7.69]	0.98 [0.98; 0.98]	11.16 [10.20; 12.16]	64.8	85.5	93.2	96.4
T30T45T120T180	0.978	-1.65 [-2.21; -1.09]	6.60 [6.20; 7.00]	7.73 [7.72; 7.74]	0.98 [0.97; 0.98]	11.23 [10.65; 11.80]	50.9	79.0	91.0	95.4
T30T45T60T180	0.978	0.29 [-0.25; 0.82]	6.60 [6.26; 6.95]	7.76 [7.75; 7.77]	0.98 [0.97; 0.98]	11.27 [10.78; 11.80]	47.4	78.5	92.3	97.1
T5T120T210T240	0.978	-1.99 [-2.48; -1.50]	5.44 [5.06; 5.82]	7.81 [7.80; 7.82]	0.98 [0.97; 0.98]	11.34 [10.39; 12.34]	65.8	83.5	91.7	96.0

T15T90T180T210	0.978	0.76 [0.25; 1.27]	6.11 [5.77; 6.46]	7.83 [7.82; 7.84]	0.98 [0.97; 0.98]	11.38 [10.83; 11.97]	55.7	80.7	91.3	97.3
T45T60T150T180	0.978	-1.19 [-1.74; -0.65]	6.70 [6.35; 7.06]	7.84 [7.83; 7.85]	0.98 [0.97; 0.98]	11.40 [10.89; 11.94]	46.5	76.8	91.5	96.7
T5T120T180T240	0.978	-1.58 [-2.07; -1.09]	5.47 [5.11; 5.83]	7.85 [7.84; 7.87]	0.98 [0.97; 0.98]	11.41 [10.44; 12.38]	63.2	85.2	92.5	96.8
T15T60T150T180	0.978	1.52 [1.01; 2.03]	6.25 [5.91; 6.59]	7.89 [7.88; 7.90]	0.98 [0.97; 0.98]	11.47 [10.86; 12.07]	52.7	79.7	91.4	97.2
T45T120T150T180	0.978	-2.53 [-3.08; -1.98]	6.89 [6.51; 7.26]	7.91 [7.90; 7.92]	0.98 [0.97; 0.98]	11.49 [10.95; 12.02]	45.6	77.4	90.8	96.0
T30T45T90T180	0.977	-1.34 [-1.90; -0.78]	6.70 [6.32; 7.08]	7.91 [7.90; 7.92]	0.98 [0.97; 0.98]	11.49 [10.92; 12.03]	50.5	79.0	90.0	95.8
T5T60T120T180	0.977	0.64 [0.14; 1.14]	6.10 [5.77; 6.43]	7.91 [7.89; 7.92]	0.98 [0.97; 0.98]	11.49 [10.75; 12.22]	51.2	81.9	93.1	98.0
T5T30T60T150	0.977	0.11 [-0.41; 0.63]	6.42 [6.09; 6.75]	7.91 [7.90; 7.92]	0.98 [0.97; 0.98]	11.50 [10.86; 12.14]	48.7	79.8	93.1	97.3
T5T15T30T150	0.977	-0.52 [-1.05; 0.01]	6.54 [6.20; 6.87]	7.94 [7.93; 7.95]	0.98 [0.97; 0.98]	11.54 [10.89; 12.19]	47.6	79.1	92.4	97.2
T5T60T150T180	0.977	0.95 [0.44; 1.46]	6.12 [5.77; 6.46]	7.95 [7.94; 7.96]	0.98 [0.97; 0.98]	11.55 [10.85; 12.27]	53.5	80.5	91.9	97.3
T5T30T120T150	0.977	0.37 [-0.15; 0.88]	6.39 [6.06; 6.73]	7.96 [7.95; 7.97]	0.98 [0.97; 0.98]	11.56 [10.87; 12.30]	49.4	79.6	92.9	97.4
T5T60T90T180	0.977	0.78 [0.28; 1.28]	6.15 [5.82; 6.49]	7.97 [7.96; 7.98]	0.98 [0.97; 0.98]	11.58 [10.95; 12.26]	50.6	80.3	92.0	97.2
T5T30T45T150	0.977	0.23 [-0.30; 0.76]	6.55 [6.21; 6.88]	8.01 [8.00; 8.02]	0.98 [0.97; 0.98]	11.64 [11.00; 12.24]	47.9	77.5	93.2	97.7
T5T30T90T150	0.977	0.14 [-0.38; 0.67]	6.42 [6.09; 6.76]	8.01 [8.00; 8.03]	0.98 [0.97; 0.98]	11.64 [10.98; 12.32]	49.1	79.3	92.7	97.2
T15T60T90T180	0.977	1.21 [0.69; 1.73]	6.45 [6.11; 6.79]	8.06 [8.05; 8.07]	0.98 [0.97; 0.98]	11.72 [11.13; 12.27]	49.0	80.0	90.8	97.0
T15T60T120T180	0.977	0.73 [0.19; 1.27]	6.46 [6.09; 6.82]	8.08 [8.07; 8.09]	0.98 [0.97; 0.98]	11.74 [11.12; 12.41]	51.7	79.1	91.1	96.4
T90T150T180T240	0.976	-1.31 [-1.80; -0.83]	5.91 [5.57; 6.24]	8.08 [8.07; 8.09]	0.98 [0.97; 0.98]	11.74 [10.94; 12.54]	53.8	83.7	92.9	97.2
T45T90T150T180	0.977	-2.06 [-2.63; -1.50]	6.91 [6.52; 7.30]	8.09 [8.08; 8.10]	0.98 [0.97; 0.98]	11.76 [11.17; 12.30]	48.4	76.9	89.3	95.2
T30T60T150T180	0.976	0.15 [-0.41; 0.71]	6.74 [6.37; 7.11]	8.10 [8.09; 8.11]	0.98 [0.97; 0.98]	11.77 [11.19; 12.36]	46.4	76.7	90.0	96.6
T45T60T120T180	0.976	-2.02 [-2.58; -1.45]	6.97 [6.58; 7.35]	8.11 [8.10; 8.13]	0.98 [0.97; 0.98]	11.79 [11.17; 12.40]	47.4	77.4	90.2	95.6
T45T90T120T180	0.977	-2.77 [-3.34; -2.21]	7.02 [6.62; 7.42]	8.12 [8.11; 8.13]	0.98 [0.97; 0.98]	11.80 [11.20; 12.38]	47.5	77.5	89.2	95.0
T5T15T45T150	0.976	-0.20 [-0.74; 0.34]	6.53 [6.18; 6.88]	8.13 [8.12; 8.14]	0.98 [0.97; 0.98]	11.81 [11.13; 12.53]	48.8	78.1	91.8	97.0
T30T60T120T180	0.976	-0.73 [-1.31; -0.15]	6.93 [6.53; 7.33]	8.14 [8.13; 8.15]	0.98 [0.97; 0.98]	11.83 [11.23; 12.38]	46.2	77.2	90.2	95.2
T5T90T180T210	0.976	0.80 [0.29; 1.30]	5.94 [5.59; 6.29]	8.16 [8.14; 8.17]	0.98 [0.97; 0.98]	11.85 [11.05; 12.65]	56.7	82.0	91.3	96.9
T30T90T150T180	0.975	-1.12 [-1.72; -0.53]	7.01 [6.60; 7.43]	8.18 [8.17; 8.19]	0.97 [0.97; 0.98]	11.89 [11.27; 12.49]	49.7	75.5	88.6	94.9
T5T150T180T210	0.976	-2.01 [-2.54; -1.47]	6.56 [6.19; 6.93]	8.19 [8.18; 8.20]	0.98 [0.97; 0.98]	11.90 [11.17; 12.60]	50.8	78.9	90.0	96.3
T30T60T90T180	0.975	-0.44 [-1.01; 0.14]	6.89 [6.51; 7.27]	8.20 [8.19; 8.21]	0.97 [0.97; 0.98]	11.92 [11.36; 12.51]	47.9	76.3	89.4	96.1
T90T150T210T240	0.975	-1.40 [-1.88; -0.91]	5.79 [5.44; 6.13]	8.22 [8.21; 8.23]	0.97 [0.97; 0.98]	11.95 [10.90; 13.03]	56.8	84.3	92.9	97.1
T30T90T120T180	0.975	-1.97 [-2.56; -1.37]	7.17 [6.75; 7.59]	8.24 [8.23; 8.25]	0.97 [0.97; 0.98]	11.98 [11.39; 12.58]	48.3	75.5	88.5	94.3
T5T90T150T210	0.975	0.75 [0.24; 1.25]	5.96 [5.61; 6.31]	8.25 [8.24; 8.26]	0.97 [0.97; 0.98]	11.98 [11.13; 12.86]	56.6	82.3	90.9	96.9

T90T120T150T240	0.975	-1.63 [-2.13; -1.14]	5.96 [5.62; 6.30]	8.25 [8.24; 8.26]	0.97 [0.97; 0.98]	11.98 [11.00; 13.03]	54.0	84.1	92.5	96.8
T45T60T90T180	0.976	-2.07 [-2.65; -1.50]	7.05 [6.66; 7.44]	8.26 [8.25; 8.27]	0.97 [0.97; 0.98]	12.00 [11.41; 12.63]	46.4	76.4	89.2	95.6
T5T90T120T210	0.975	0.12 [-0.41; 0.66]	6.21 [5.84; 6.58]	8.26 [8.25; 8.27]	0.97 [0.97; 0.98]	12.00 [11.21; 12.84]	56.3	80.8	90.3	96.2
T90T120T210T240	0.975	-1.94 [-2.44; -1.45]	5.98 [5.63; 6.33]	8.26 [8.25; 8.27]	0.97 [0.97; 0.98]	12.01 [11.04; 12.93]	55.9	83.0	91.9	96.5
T5T15T60T150	0.975	-0.02 [-0.57; 0.52]	6.59 [6.24; 6.95]	8.30 [8.29; 8.31]	0.97 [0.97; 0.98]	12.06 [11.36; 12.79]	48.0	76.9	92.2	96.8
T90T120T180T240	0.974	-1.59 [-2.09; -1.08]	6.13 [5.78; 6.48]	8.41 [8.40; 8.42]	0.97 [0.97; 0.98]	12.22 [11.30; 13.17]	53.9	81.4	91.6	96.7
T90T180T210T240	0.974	-1.11 [-1.61; -0.61]	6.02 [5.68; 6.36]	8.44 [8.43; 8.46]	0.97 [0.97; 0.98]	12.27 [11.34; 13.24]	54.3	82.3	92.4	96.9
T5T15T120T150	0.973	-0.40 [-0.96; 0.15]	6.84 [6.48; 7.20]	8.53 [8.52; 8.54]	0.97 [0.97; 0.98]	12.40 [11.67; 13.17]	47.4	77.1	89.9	96.4
T5T15T90T150	0.972	-0.21 [-0.78; 0.35]	6.86 [6.49; 7.23]	8.73 [8.72; 8.74]	0.97 [0.97; 0.97]	12.69 [11.95; 13.45]	47.5	76.7	89.9	95.7
T5T45T90T150	0.972	0.45 [-0.11; 1.02]	6.86 [6.49; 7.22]	8.75 [8.74; 8.76]	0.97 [0.97; 0.97]	12.71 [11.95; 13.48]	46.7	75.9	90.9	96.3
T5T120T150T210	0.972	-1.74 [-2.30; -1.17]	6.71 [6.31; 7.10]	8.76 [8.75; 8.77]	0.97 [0.97; 0.97]	12.73 [11.90; 13.62]	53.2	79.1	89.1	94.7
T15T120T150T180	0.972	-2.13 [-2.75; -1.51]	7.46 [7.03; 7.89]	8.77 [8.75; 8.78]	0.97 [0.97; 0.97]	12.74 [12.11; 13.41]	47.6	72.0	87.6	93.6
T5T45T120T150	0.972	0.87 [0.31; 1.43]	6.87 [6.50; 7.23]	8.84 [8.83; 8.85]	0.97 [0.97; 0.97]	12.84 [12.09; 13.65]	49.0	76.6	91.1	96.3
T60T120T150T180	0.972	-1.74 [-2.33; -1.15]	7.36 [6.97; 7.75]	8.84 [8.83; 8.86]	0.97 [0.97; 0.97]	12.85 [12.03; 13.82]	44.5	74.0	88.0	95.0
T5T45T60T150	0.972	0.77 [0.20; 1.33]	6.93 [6.56; 7.30]	8.86 [8.84; 8.87]	0.97 [0.97; 0.97]	12.87 [12.08; 13.62]	46.2	76.0	90.5	96.3
T5T120T180T210	0.971	-1.78 [-2.35; -1.20]	6.74 [6.34; 7.14]	8.86 [8.84; 8.87]	0.97 [0.97; 0.97]	12.87 [12.08; 13.70]	53.5	77.5	88.2	94.3
T60T90T150T180	0.971	-1.38 [-1.97; -0.79]	7.30 [6.92; 7.68]	8.93 [8.92; 8.95]	0.97 [0.97; 0.97]	12.98 [12.19; 13.80]	44.7	74.0	88.2	95.5
T15T30T45T150	0.971	0.66 [0.08; 1.25]	7.34 [6.97; 7.71]	8.94 [8.93; 8.95]	0.97 [0.97; 0.97]	12.99 [12.30; 13.62]	43.6	72.8	91.0	96.3
T15T30T120T150	0.971	0.44 [-0.15; 1.03]	7.29 [6.90; 7.67]	9.00 [8.99; 9.01]	0.97 [0.97; 0.97]	13.08 [12.31; 13.91]	43.4	73.4	88.7	95.7
T60T90T120T180	0.971	-1.91 [-2.52; -1.31]	7.47 [7.06; 7.87]	9.00 [8.99; 9.01]	0.97 [0.97; 0.97]	13.08 [12.22; 14.00]	43.7	73.8	87.1	94.7
T120T150T210T240	0.971	-2.85 [-3.38; -2.32]	6.51 [6.13; 6.90]	9.08 [9.07; 9.09]	0.97 [0.97; 0.97]	13.19 [12.07; 14.39]	52.5	80.3	91.0	95.9
T15T30T90T150	0.970	0.42 [-0.19; 1.03]	7.36 [6.96; 7.76]	9.10 [9.08; 9.11]	0.97 [0.96; 0.97]	13.22 [12.48; 13.94]	45.7	73.3	89.1	94.8
T120T150T180T240	0.970	-2.79 [-3.34; -2.25]	6.71 [6.33; 7.10]	9.20 [9.19; 9.21]	0.97 [0.96; 0.97]	13.37 [12.20; 14.65]	50.3	79.9	90.6	95.4
T15T90T150T180	0.971	1.72 [1.14; 2.31]	7.21 [6.82; 7.60]	9.23 [9.22; 9.24]	0.97 [0.96; 0.97]	13.41 [12.70; 14.06]	47.2	72.0	87.2	95.3
T15T45T120T150	0.970	1.13 [0.54; 1.72]	7.31 [6.93; 7.70]	9.25 [9.24; 9.26]	0.97 [0.96; 0.97]	13.44 [12.68; 14.24]	44.4	75.0	89.2	95.2
T15T30T60T150	0.969	1.13 [0.53; 1.72]	7.44 [7.06; 7.82]	9.29 [9.28; 9.30]	0.97 [0.96; 0.97]	13.50 [12.75; 14.24]	43.7	71.7	88.8	95.3
T15T45T60T150	0.969	1.42 [0.83; 2.01]	7.37 [6.99; 7.76]	9.37 [9.36; 9.38]	0.97 [0.96; 0.97]	13.62 [12.83; 14.30]	43.5	72.5	89.0	95.3
T15T90T120T180	0.968	0.40 [-0.24; 1.04]	7.65 [7.23; 8.08]	9.40 [9.38; 9.41]	0.97 [0.96; 0.97]	13.65 [12.90; 14.34]	46.2	71.4	84.7	94.2
T90T120T150T210	0.967	-1.79 [-2.37; -1.20]	7.21 [6.81; 7.60]	9.41 [9.40; 9.42]	0.97 [0.96; 0.97]	13.68 [12.68; 14.77]	46.0	75.9	88.6	94.6
T15T45T90T150	0.968	0.77 [0.16; 1.37]	7.44 [7.04; 7.83]	9.45 [9.44; 9.46]	0.97 [0.96; 0.97]	13.73 [12.97; 14.46]	44.9	74.2	88.2	94.3

T120T180T210T240	0.968	-2.83 [-3.38; -2.29]	6.71 [6.32; 7.11]	9.46 [9.45; 9.48]	0.97 [0.96; 0.97]	13.75 [12.60; 14.99]	51.6	78.8	89.8	95.9
T90T120T180T210	0.967	-1.91 [-2.51; -1.32]	7.29 [6.88; 7.69]	9.50 [9.48; 9.51]	0.97 [0.96; 0.97]	13.80 [12.85; 14.74]	47.0	74.7	87.2	93.9
T30T45T120T150	0.966	-0.17 [-0.83; 0.49]	8.06 [7.62; 8.49]	9.58 [9.57; 9.59]	0.97 [0.96; 0.97]	13.92 [13.25; 14.63]	40.5	69.3	86.5	93.6
T90T150T180T210	0.966	-1.29 [-1.87; -0.70]	7.10 [6.71; 7.49]	9.59 [9.57; 9.60]	0.97 [0.96; 0.97]	13.93 [12.83; 15.11]	47.1	75.8	88.7	94.4
T5T90T120T180	0.966	0.67 [0.04; 1.29]	7.39 [6.96; 7.81]	9.65 [9.64; 9.66]	0.97 [0.96; 0.97]	14.02 [13.11; 14.86]	47.4	74.1	86.5	93.1
T5T90T150T180	0.966	1.21 [0.60; 1.83]	7.22 [6.79; 7.66]	9.72 [9.71; 9.74]	0.96 [0.96; 0.97]	14.13 [13.24; 15.01]	49.2	75.5	85.9	94.1
T15T60T120T150	0.967	2.12 [1.50; 2.73]	7.72 [7.31; 8.12]	9.90 [9.88; 9.91]	0.96 [0.96; 0.97]	14.38 [13.58; 15.19]	43.0	70.2	86.4	94.1
T30T45T60T150	0.965	0.81 [0.16; 1.46]	8.09 [7.67; 8.51]	9.93 [9.91; 9.94]	0.96 [0.96; 0.97]	14.42 [13.69; 15.18]	39.3	68.2	84.8	93.6
T5T60T120T150	0.966	1.76 [1.16; 2.36]	7.49 [7.09; 7.89]	9.94 [9.92; 9.95]	0.96 [0.96; 0.97]	14.44 [13.50; 15.32]	44.3	71.9	87.5	95.0
T5T60T90T150	0.965	1.39 [0.78; 2.00]	7.51 [7.11; 7.92]	9.98 [9.97; 10.00]	0.96 [0.96; 0.97]	14.51 [13.56; 15.43]	45.4	71.4	87.2	94.6
T45T60T120T150	0.963	-0.82 [-1.48; -0.15]	8.30 [7.87; 8.72]	10.01 [10.00; 10.03]	0.96 [0.96; 0.97]	14.55 [13.79; 15.42]	38.3	69.2	85.2	93.0
T30T60T120T150	0.964	0.73 [0.06; 1.41]	8.26 [7.81; 8.70]	10.02 [10.01; 10.04]	0.96 [0.96; 0.97]	14.56 [13.84; 15.26]	41.0	67.6	85.5	92.9
T120T150T180T210	0.965	-3.68 [-4.29; -3.07]	7.74 [7.30; 8.18]	10.04 [10.02; 10.05]	0.96 [0.96; 0.97]	14.58 [13.47; 15.74]	43.6	72.2	86.8	93.6
T15T60T90T150	0.965	1.94 [1.31; 2.58]	7.92 [7.50; 8.34]	10.12 [10.11; 10.13]	0.96 [0.96; 0.97]	14.71 [13.91; 15.46]	42.8	69.5	86.1	93.3
T45T90T120T150	0.962	-1.31 [-1.99; -0.62]	8.40 [7.95; 8.85]	10.13 [10.12; 10.15]	0.96 [0.96; 0.97]	14.72 [13.97; 15.45]	39.2	69.5	84.0	92.4
T5T30T90T120	0.963	0.70 [0.06; 1.34]	7.86 [7.44; 8.28]	10.16 [10.15; 10.18]	0.96 [0.96; 0.97]	14.77 [13.92; 15.63]	43.1	70.0	85.2	93.8
T30T90T120T150	0.962	0.28 [-0.41; 0.98]	8.54 [8.09; 8.99]	10.22 [10.21; 10.24]	0.96 [0.95; 0.96]	14.86 [14.13; 15.59]	39.2	66.2	84.3	91.8
T30T45T90T150	0.961	-0.07 [-0.76; 0.62]	8.45 [8.00; 8.89]	10.24 [10.22; 10.25]	0.96 [0.96; 0.96]	14.88 [14.13; 15.60]	39.7	67.0	83.7	92.5
T5T30T45T120	0.962	0.60 [-0.04; 1.25]	7.96 [7.55; 8.38]	10.25 [10.24; 10.27]	0.96 [0.96; 0.96]	14.90 [14.09; 15.75]	41.8	69.3	86.2	93.5
T5T30T60T120	0.962	0.48 [-0.17; 1.13]	8.00 [7.58; 8.42]	10.25 [10.24; 10.27]	0.96 [0.96; 0.96]	14.90 [14.05; 15.68]	41.2	69.5	84.5	94.0
T5T15T45T120	0.961	0.04 [-0.62; 0.70]	7.97 [7.53; 8.40]	10.26 [10.24; 10.27]	0.96 [0.96; 0.96]	14.90 [14.06; 15.72]	43.7	70.7	85.2	93.8
T5T15T30T120	0.961	-0.12 [-0.78; 0.54]	7.97 [7.54; 8.41]	10.29 [10.28; 10.31]	0.96 [0.96; 0.96]	14.96 [14.08; 15.75]	43.2	69.4	85.0	93.8
T30T60T90T150	0.962	0.69 [0.01; 1.37]	8.33 [7.89; 8.77]	10.30 [10.29; 10.31]	0.96 [0.95; 0.96]	14.97 [14.16; 15.71]	40.5	68.2	84.7	92.9
T5T15T60T120	0.960	0.17 [-0.50; 0.84]	8.06 [7.62; 8.50]	10.37 [10.36; 10.38]	0.96 [0.95; 0.96]	15.07 [14.16; 15.88]	41.3	69.7	85.5	93.5
T45T60T90T150	0.960	-1.11 [-1.81; -0.41]	8.59 [8.13; 9.04]	10.42 [10.40; 10.43]	0.96 [0.95; 0.96]	15.14 [14.35; 15.97]	38.5	67.5	83.7	91.9
T5T15T90T120	0.959	0.00 [-0.67; 0.67]	8.07 [7.62; 8.51]	10.53 [10.52; 10.55]	0.96 [0.95; 0.96]	15.30 [14.44; 16.20]	43.2	69.4	84.6	92.1
T150T180T210T240	0.959	-2.84 [-3.42; -2.27]	6.95 [6.53; 7.38]	10.57 [10.56; 10.59]	0.96 [0.95; 0.96]	15.37 [13.82; 17.28]	50.5	78.1	89.9	94.8
T60T90T120T150	0.955	-0.97 [-1.69; -0.25]	8.93 [8.47; 9.39]	10.97 [10.96; 10.99]	0.96 [0.95; 0.96]	15.95 [15.05; 16.96]	37.9	65.0	82.4	90.9
T15T90T120T150	0.961	2.75 [2.08; 3.43]	8.62 [8.17; 9.06]	10.98 [10.96; 11.00]	0.95 [0.95; 0.96]	15.96 [15.17; 16.72]	41.0	65.6	81.8	91.4
T5T45T90T120	0.956	1.09 [0.41; 1.78]	8.35 [7.90; 8.79]	11.03 [11.02; 11.05]	0.95 [0.95; 0.96]	16.03 [15.05; 17.01]	40.0	67.7	85.6	92.8

T90T120T150T180	0.954	-1.48 [-2.19; -0.77]	8.76 [8.30; 9.22]	11.07 [11.06; 11.09]	0.95 [0.95; 0.96]	16.09 [15.02; 17.18]	40.5	66.0	81.0	91.3
T5T45T60T120	0.956	1.16 [0.48; 1.84]	8.46 [8.02; 8.90]	11.11 [11.09; 11.12]	0.95 [0.95; 0.96]	16.14 [15.20; 17.06]	39.0	66.3	84.1	92.9
T15T30T45T120	0.955	1.14 [0.45; 1.83]	8.60 [8.15; 9.04]	11.19 [11.17; 11.20]	0.95 [0.95; 0.96]	16.26 [15.35; 17.18]	38.8	66.7	83.0	91.9
T5T90T120T150	0.955	1.87 [1.17; 2.56]	8.38 [7.91; 8.86]	11.39 [11.37; 11.41]	0.95 [0.94; 0.96]	16.55 [15.57; 17.54]	43.4	68.4	83.3	92.1
T15T45T60T120	0.954	1.83 [1.14; 2.53]	8.72 [8.27; 9.17]	11.43 [11.42; 11.45]	0.95 [0.94; 0.96]	16.61 [15.65; 17.63]	37.3	65.4	82.6	92.3
T15T30T60T120	0.953	1.39 [0.68; 2.10]	8.90 [8.45; 9.35]	11.45 [11.43; 11.46]	0.95 [0.94; 0.96]	16.63 [15.73; 17.62]	36.8	64.8	80.9	91.3
T15T30T90T120	0.953	1.04 [0.32; 1.76]	8.89 [8.42; 9.37]	11.45 [11.43; 11.46]	0.95 [0.94; 0.96]	16.63 [15.63; 17.57]	37.2	66.5	80.6	90.8
T15T45T90T120	0.953	1.51 [0.81; 2.21]	8.72 [8.26; 9.18]	11.50 [11.48; 11.52]	0.95 [0.94; 0.95]	16.71 [15.70; 17.61]	38.0	65.2	81.8	91.7
T15T60T90T120	0.951	2.39 [1.67; 3.12]	9.15 [8.68; 9.63]	12.00 [11.98; 12.02]	0.94 [0.94; 0.95]	17.44 [16.46; 18.43]	37.4	62.9	81.7	90.8
T5T60T90T120	0.949	2.05 [1.33; 2.76]	8.92 [8.45; 9.39]	12.07 [12.05; 12.08]	0.94 [0.94; 0.95]	17.54 [16.52; 18.58]	38.1	63.2	81.1	90.8
T30T45T60T120	0.947	0.90 [0.12; 1.69]	9.60 [9.09; 10.11]	12.17 [12.16; 12.19]	0.94 [0.94; 0.95]	17.69 [16.74; 18.68]	34.7	62.7	78.9	88.8
T30T45T90T120	0.946	0.46 [-0.33; 1.25]	9.51 [8.98; 10.04]	12.22 [12.21; 12.24]	0.94 [0.93; 0.95]	17.76 [16.86; 18.64]	36.7	63.5	79.6	88.2
T45T60T90T120	0.943	-0.47 [-1.28; 0.34]	9.84 [9.31; 10.37]	12.37 [12.35; 12.39]	0.94 [0.93; 0.95]	17.97 [17.05; 18.95]	35.2	60.0	79.2	88.3
T30T60T90T120	0.945	1.23 [0.44; 2.02]	9.70 [9.18; 10.22]	12.39 [12.37; 12.41]	0.94 [0.93; 0.95]	18.01 [17.12; 18.93]	36.3	62.3	77.6	88.0
T5T30T60T90	0.943	0.48 [-0.33; 1.28]	9.81 [9.29; 10.34]	12.42 [12.40; 12.43]	0.94 [0.93; 0.95]	18.04 [17.06; 19.02]	34.0	59.6	78.2	89.1
T5T15T60T90	0.943	-0.13 [-0.94; 0.69]	9.84 [9.29; 10.38]	12.45 [12.44; 12.47]	0.94 [0.93; 0.95]	18.09 [17.05; 19.20]	35.1	60.3	78.8	89.7
T5T15T45T90	0.942	-0.24 [-1.05; 0.57]	9.76 [9.22; 10.30]	12.46 [12.44; 12.48]	0.94 [0.93; 0.95]	18.11 [17.08; 19.13]	36.0	60.5	78.6	89.8
T5T15T30T90	0.942	-0.22 [-1.03; 0.60]	9.88 [9.35; 10.41]	12.47 [12.45; 12.49]	0.94 [0.93; 0.95]	18.12 [17.04; 19.18]	33.5	60.8	78.7	89.3
T5T30T45T90	0.942	0.39 [-0.42; 1.20]	9.84 [9.31; 10.38]	12.53 [12.51; 12.54]	0.94 [0.93; 0.95]	18.20 [17.23; 19.20]	34.1	60.5	78.6	88.5
T5T45T60T90	0.938	1.03 [0.20; 1.86]	10.11 [9.57; 10.66]	13.07 [13.05; 13.09]	0.93 [0.93; 0.94]	18.99 [17.95; 20.08]	35.0	58.2	76.7	87.3
T15T30T45T90	0.935	0.83 [-0.02; 1.68]	10.45 [9.90; 11.00]	13.40 [13.38; 13.41]	0.93 [0.92; 0.94]	19.46 [18.40; 20.58]	33.1	58.0	76.3	86.9
T15T45T60T90	0.935	1.37 [0.53; 2.21]	10.39 [9.85; 10.94]	13.45 [13.43; 13.47]	0.93 [0.92; 0.94]	19.54 [18.40; 20.66]	33.4	57.8	76.5	86.6
T15T30T60T90	0.934	1.10 [0.24; 1.95]	10.62 [10.07; 11.16]	13.50 [13.48; 13.52]	0.93 [0.92; 0.94]	19.61 [18.51; 20.88]	30.4	56.2	75.7	86.8
T30T45T60T90	0.922	0.26 [-0.67; 1.20]	11.31 [10.69; 11.94]	14.51 [14.49; 14.53]	0.92 [0.91; 0.93]	21.09 [19.90; 22.42]	31.8	54.3	72.3	82.7
T5T15T45T60	0.918	-0.38 [-1.34; 0.59]	12.06 [11.46; 12.67]	14.80 [14.78; 14.82]	0.91 [0.90; 0.92]	21.50 [20.39; 22.59]	24.6	51.7	70.0	83.2
T5T30T45T60	0.916	-0.01 [-0.98; 0.96]	12.10 [11.49; 12.72]	15.03 [15.01; 15.05]	0.91 [0.90; 0.92]	21.84 [20.73; 23.00]	25.2	51.6	68.8	82.9
T5T15T30T60	0.914	-0.63 [-1.61; 0.35]	12.30 [11.68; 12.92]	15.08 [15.06; 15.10]	0.91 [0.90; 0.92]	21.92 [20.84; 23.01]	25.6	50.2	68.5	82.4
T15T30T45T60	0.910	0.27 [-0.73; 1.27]	12.41 [11.77; 13.04]	15.55 [15.53; 15.57]	0.90 [0.89; 0.91]	22.60 [21.36; 23.82]	24.6	49.8	68.4	82.0
T5T15T30T45	0.885	-1.33 [-2.44; -0.22]	13.79 [13.08; 14.50]	17.34 [17.31; 17.36]	0.88 [0.86; 0.89]	25.19 [23.84; 26.58]	21.1	44.8	63.2	78.0

N number of sampling instances in the limited sampling schedule; **LSS** limited sampling schedule; **R²** Pearson's correlation coefficient; **MPE** mean prediction error; **MAPE** mean absolute prediction error; **RMSE** root mean squared prediction error; **CCC** concordance correlation coefficient; **TDI** total deviation index; **P₅-P₂₀** percentages of individual iohexol clearance predictions within 5%-20% of the reference individual iohexol clearance; **95%CI** 95% confidence interval.

Importance of covariate information for limited sampling schedule predictive performance

Table S8.1 Population pharmacokinetic parameter estimates from the final full covariate model (Model 1), and the reduced models without fat-free mass (Model 2), patient type (Model 3), or without both (Model 4) on the development cohort.

	Model 1	Model 2	Model 3	Model 4
	<i>Final model</i>	<i>No FFM</i>	<i>No patient type</i>	<i>Covariate-free</i>
	Estimate (RSE; η -shrinkage)	Estimate (RSE; η -shrinkage)	Estimate (RSE; η -shrinkage)	Estimate (RSE; η -shrinkage)
<i>Parameter</i>				
CL (L/h)	4.07 (5%)	3.76 (5%)	4.73 (4%)	4.19 (4%)
V _c (L)	8.36 (9%)	7.66 (8%)	9.32 (6%)	8.15 (5%)
Q (L/h)	7.71 (9%)	6.52 (9%)	7.89 (8%)	6.50 (8%)
V _p (L)	6.88 (5%)	6.05 (5%)	6.90 (5%)	6.07 (5%)
<i>Covariate relationships</i>				
Patient type on CL	0.483 (21%)	0.344 (28%)		
Patient type on V _c	0.342 (38%)	0.180 (65%)		
<i>Between-subject variability</i>				
CL (CV%)	29.8 (11%; 4%)	31.9% (9%; 3%)	34.5% (7%; 4%)	34.1% (8%; 3%)
V _c (CV%)	40.4 (8%; 5%)	40.9% (8%; 6%)	43.4% (9%; 5%)	42.2% (8%; 5%)
Q (CV%)	61.7 (12%; 27%)	68.0% (11%; 24%)	60.7% (14%; 28%)	67.7% (10%; 25%)
V _p (CV%)	23.5 (18%; 30%)	29.2% (26%; 26%)	23.2% (20%; 31%)	28.2% (23%; 27%)
<i>Random residual variability</i>				
Proportional error (CV%)	22.9 (14%; 30%)	22.9 (13%; 31%)	22.9 (13%; 31%)	23.0 (12%; 31%)
Additive error (CV%)	0 (FIX)	0 (FIX)	0 (FIX)	0 (FIX)

CL total body clearance; **FIX** fixed; **V_c** volume of distribution of the central compartment; **Q** intercompartmental clearance; **V_p** volume of distribution of the peripheral compartment; **RSE** relative standard error; **CV%** coefficient of variation; **95% CI** 95% confidence interval.

Table S8.2 Predictive performances of the best limited sampling schedules (LSSs) with the final covariate model (Model 1) and the models without fat-free mass (Model 2), patient type (Model 3), or both (Model 4) on the LSS dataset.

LSS	Model	R ²	MPE [95%CI] (%)	MAPE [95%CI] (%)	RMSE [95%CI] (%)	CCC [95%CI] (%)	TDI [95%CI] (%)	P ₅ (%)	P ₁₀ (%)	P ₁₅ (%)	P ₂₀ (%)
5-30-180	1	0.984	-0.72 [-1.15; -0.28]	5.43 [5.15; 5.71]	6.52 [6.51; 6.53]	0.98 [0.98; 0.99]	9.48 [8.97; 9.98]	54.4	85.0	96.4	98.9
	2	0.983	-2.53 [-3.00; -2.06]	6.03 [5.70; 6.35]	7.15 [7.14; 7.16]	0.98 [0.98; 0.98]	10.4 [9.82; 11.0]	53.0	80.6	93.1	98.2
	3	0.984	-0.55 [-1.00; -0.11]	5.52 [5.24; 5.81]	6.60 [6.59; 6.61]	0.98 [0.98; 0.99]	9.59 [9.11; 10.1]	54.9	84.6	96.3	98.9
	4	0.982	-2.44 [-2.92; -1.96]	6.17 [5.84; 6.49]	7.20 [7.19; 7.21]	0.98 [0.98; 0.98]	10.5 [9.93; 11.0]	52.3	80.1	92.4	97.9
5-30-150-180	1	0.987	-0.28 [-0.69; 0.13]	5.00 [4.73; 5.27]	6.06 [6.05; 6.07]	0.99 [0.98; 0.99]	8.81 [8.31; 9.29]	59.4	87.8	96.6	99.0
	2	0.985	-2.28 [-2.73; -1.83]	5.66 [5.35; 5.97]	6.73 [6.72; 6.73]	0.98 [0.98; 0.99]	9.77 [9.26; 10.3]	55.3	83.2	93.9	98.3
	3	0.986	-0.12 [-0.54; 0.30]	5.09 [4.81; 5.36]	6.16 [6.15; 6.17]	0.99 [0.98; 0.99]	8.95 [8.46; 9.45]	59.0	87.5	96.3	99.2
	4	0.984	-2.19 [-2.65; -1.73]	5.78 [5.46; 6.09]	6.75 [6.74; 6.76]	0.98 [0.98; 0.99]	9.81 [9.32; 10.3]	55.0	82.2	93.9	98.0
5-45-240	1	0.995	-0.33 [-0.58; -0.07]	3.14 [2.98; 3.31]	3.76 [3.75; 3.76]	0.99 [0.99; 1.00]	5.46 [5.17; 5.73]	79.0	97.2	99.8	100
	2	0.994	-1.40 [-1.69; -1.12]	3.67 [3.48; 3.86]	4.26 [4.26; 4.27]	0.99 [0.99; 0.99]	6.19 [5.88; 6.51]	73.5	95.4	99.2	100
	3	0.995	-0.29 [-0.55; -0.03]	3.18 [3.01; 3.35]	3.78 [3.77; 3.78]	0.99 [0.99; 1.00]	5.49 [5.19; 5.80]	80.0	96.7	99.8	100
	4	0.994	-1.30 [-1.59; -1.02]	3.67 [3.48; 3.87]	4.21 [4.20; 4.21]	0.99 [0.99; 0.99]	6.11 [5.81; 6.40]	73.4	95.2	99.3	99.9
5-30-45-240	1	0.996	-0.44 [-0.65; -0.22]	2.64 [2.50; 2.79]	3.15 [3.15; 3.16]	1.00 [1.00; 1.00]	4.58 [4.32; 4.84]	87.7	98.9	99.9	100
	2	0.995	-1.54 [-1.79; -1.30]	3.24 [3.07; 3.41]	3.79 [3.78; 3.79]	0.99 [0.99; 1.00]	5.50 [5.20; 5.79]	78.8	97.0	99.7	100
	3	0.996	-0.37 [-0.59; -0.15]	2.70 [2.56; 2.85]	3.20 [3.20; 3.21]	1.00 [1.00; 1.00]	4.65 [4.40; 4.88]	86.2	98.7	99.8	100
	4	0.995	-1.48 [-1.73; -1.23]	3.27 [3.09; 3.44]	3.78 [3.77; 3.78]	0.99 [0.99; 1.00]	5.49 [5.21; 5.78]	78.4	96.6	99.7	99.9

LSS limited sampling schedule; **R²** Pearson's correlation coefficient; **MPE** mean prediction error; **MAPE** mean absolute prediction error; **RMSE** root mean squared prediction error; **CCC** concordance correlation coefficient; **TDI** total deviation index; **P₅-P₂₀** percentage of GFR_{bm} GFR predictions within 5-20% of model-based GFR predictions; **95%CI** 95% confidence interval.

NONMEM code for Model 2

\$SUBROUTINES ADVAN3 TRANS4

\$PK

; --- PATTYPE ON V1 AND CL
IF(TX.EQ.0) CLTX = 1 ; Most common
IF(TX.EQ.1) CLTX = (1 + THETA(7))
CLCOV=CLTX
IF(TX.EQ.0) V1TX = 1 ; Most common
IF(TX.EQ.1) V1TX = (1 + THETA(8))
V1COV=V1TX

CL = THETA(1) * CLCOV * EXP(ETA(1))
V1 = THETA(2) * V1COV * EXP(ETA(2))
Q = THETA(3) * EXP(ETA(3))
V2 = THETA(4) * EXP(ETA(4))
S1 = V1

\$ERROR

IPRED = F
W = SQRT(THETA(5)**2*IPRED**2 + THETA(6)**2)
Y = IPRED + W*EPS(1)
IRES = DV-IPRED
IWRES = IRES/W

\$THETA

3.76 FIX ; CL
7.66 FIX ; V1
6.52 FIX ; Q
6.05 FIX ; V2
0.0525 FIX ; Prop.RE (sd)
0 FIX ; Add.RE (sd)
0.344 FIX ; CLCOV
0.18 FIX ; V1COV

\$OMEGA BLOCK(3)

0.102 ; IIV CL
0.0475 0.167 ; IIV V1
0.101 -0.0407 0.462 ; IIV Q
\$OMEGA
0.0855 FIX ; IIV V2

\$SIGMA

1 FIX ; Proportional error PK

\$EST METHOD=1 INTER MAXEVAL=0 NOABORT SIG=3 PRINT=1 POSTHOC

NONMEM code for Model 3

\$SUBROUTINES ADVAN3 TRANS4

\$PK

; --- ALLOMETRY SCALED TO 1.80M MAN OF 70 KG

ALLOCL=(FFM/57.18)**0.75

ALLOV=(FFM/57.18)

CL = THETA(1) * ALLOCL * EXP(ETA(1))

V1 = THETA(2) * ALLOV * EXP(ETA(2))

Q = THETA(3) * ALLOCL * EXP(ETA(3))

V2 = THETA(4) * ALLOV * EXP(ETA(4))

S1 = V1

\$ERROR

IPRED = F

W = SQRT(THETA(5)**2*IPRED**2 + THETA(6)**2)

Y = IPRED + W*EPS(1)

IRES = DV-IPRED

IWRES = IRES/W

\$THETA

(0, 4.73) FIX ; CL

(0, 9.32) FIX ; V1

(0, 7.89) FIX ; Q

(0, 6.9) FIX ; V2

(0, 0.0524,1) FIX ; Prop.RE (sd)

(0) FIX ; Add.RE (sd)

\$OMEGA BLOCK(3)

0.119 ; IIV CL

0.0657 0.188 ; IIV V1

0.0347 -0.0896 0.368 ; IIV Q

\$OMEGA

0.0537 FIX ; IIV V2

\$SIGMA

1 FIX ; Proportional error PK

\$EST METHOD=1 INTER MAXEVAL=0 NOABORT SIG=3 PRINT=1 POSTHOC

NONMEM code for Model 4

\$SUBROUTINES ADVAN3 TRANS4

\$PK

CL = THETA(1) * EXP(ETA(1))

V1 = THETA(2) * EXP(ETA(2))

Q = THETA(3) * EXP(ETA(3))

V2 = THETA(4) * EXP(ETA(4))

S1 = V1

\$ERROR

IPRED = F

W = SQRT(THETA(5)**2*IPRED**2 + THETA(6)**2)

Y = IPRED + W*EPS(1)

IRES = DV-IPRED

IWRES = IRES/W

\$THETA

(0, 4.19) FIX ; CL

(0, 8.15) FIX ; V1

(0, 6.5) FIX ; Q

(0, 6.07) FIX ; V2

(0, 0.0527,1) FIX ; Prop.RE (sd)

(0) FIX ; Add.RE (sd)

\$OMEGA BLOCK(3)

0.116 ; IIV CL

0.059 0.178 ; IIV V1

0.0766 -0.0583 0.459 ; IIV Q

\$OMEGA

0.0793 FIX ; IIV V2

\$SIGMA

1 FIX ; Proportional error PK

\$EST METHOD=1 INTER MAXEVAL=0 NOABORT SIG=3 PRINT=1 POSTHOC

pkiohexolzwardrenal

InsightRX model verification

Introduction

The InsightRX platform is a clinical decision support tool for selecting optimal drug regimens by optimizing on pharmacokinetic and pharmacodynamic characteristics of individual patients. Since it is essential that the core numeric functionality of the InsightRX platform is accurate and precise, many validation and verification tests are applied before any PK/PD modules are released on the InsightRX platform.

In this report, the simulation and individual estimation algorithms are documented:

- simulation: any model that is simulated within the platform should provide the exact same results as other (gold standard) methods.
- individual estimation: given a population PK model and some TDM data, the individual estimation algorithms in InsightRX should not differ relevantly from individual estimates obtained from commonly used gold standard softwares.

The tests included in this report are deployed in a continuous integration development workflow at InsightRX. This means that any potential disruptions of the numerical integrity of these models or the simulation or estimation algorithms will be caught and fixed before new versions are deployed to production environments.

Methods

Simulation

For simulation, the platform relies on the R software package `PKPDsim` (<http://github.com/InsightRX/PKPDsim>), which is developed internally by InsightRX and released under an open source license. The package allows the numeric integration of ordinary differential equations (ODE), and is specifically designed for use in pharmacometrics. Any PK/PD model that can be written in ODEs or analytical equations can be simulated with this package.

To ensure the numerical correctness of `PKPDsim`, predictions from the package are checked against a gold standard. As reference we use predictions from the same model implemented in NONMEM, which is considered a gold standard software in the field of pharmacometrics and used e.g. for most FDA new drug filings.

Estimation

For fitting of models to drug concentration data, the platform relies on the `PKPDmap` R package (proprietary). This package allows estimation of individual parameters based on prior distributions from a population PK model and observed concentration data, using maximum a posteriori (MAP) Bayesian fitting. In our verification tests, individual empirical Bayes estimates (EBEs) from `PKPDmap` are compared to EBEs calculated in NONMEM based on simulated data in a prespecified number of patient. By default, NONMEM employs the same MAP methodology as `PKPDmap` — based on the BFGS-algorithm for finding the maximum likelihood — so estimates are expected to be highly similar.

Comparison

Since exact numerical equivalence between test and reference results is not expected due to small differences in implementation of algorithms or internal rounding, we define equivalence thresholds, i.e. maximum allowed deviations from predicted concentrations or estimated parameters. The allowed deltas between test and reference values are shown in the diagram below.

Due to the difference in orders of magnitude of expected concentrations for the various drugs, the allowed deltas in simulated concentrations are defined for each drug/model separately. This is done by defining a relevant limit of quantification (rLOQ), a value close or equal to the bioanalytical LOQ, or if that is unknown the lowest value commonly observed for that drug. For data below this rLOQ the allowed difference with the reference value is measured in absolute terms and is defined as 15% of the rLOQ. For data above the rLOQ the allowed delta is defined relative to the reference value, and is allowed to differ <1%.

For parameter estimates, a distinction is made between primary and derived parameters. This is due to the fact that, especially with low amounts of data, the model is not always globally identifiable (the likelihood surface is very flat), and minute differences in the estimation algorithms can lead to noticeable differences in parameter estimates, and thus the set of reference parameter estimates is not necessarily the “optimal” solution. However, concentration predictions or other derived exposure estimates should still show near exact correspondence with the respective reference values. Therefore, to avoid false positive test results due to the issue of model identifiability, a derived parameter is defined, most commonly AUC for PK models, on which the test is run with a much lower allowed margin. The allowed deltas for model parameters and derived parameters are 10% and 1%, respectively.

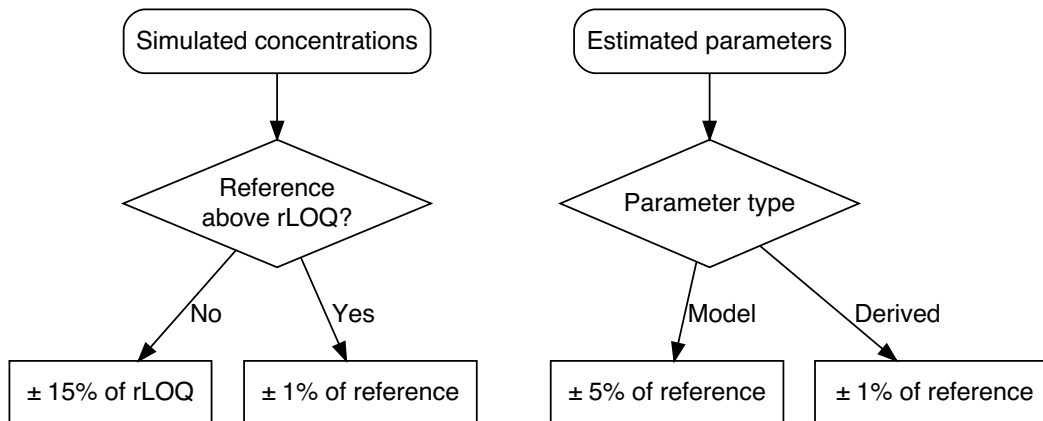


Figure 1: Limits for comparison with reference values

Simulated population

Below are distribution plots for the simulation population used in the simulation and estimation tests. For discrete covariates, the possible values of the covariate are sampled discretely, with equal probability for each possible value. For continuous covariates, a realistic range is defined for each covariate and values are sampled uniformly to ensure proper coverage of the population.

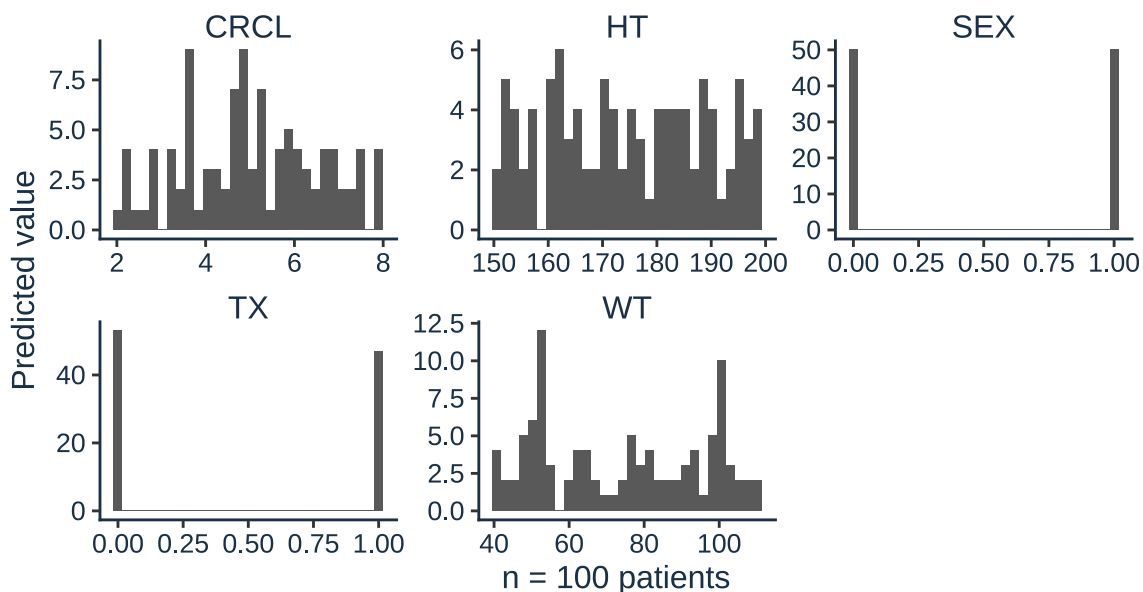


Figure 2: Simulated population characteristics

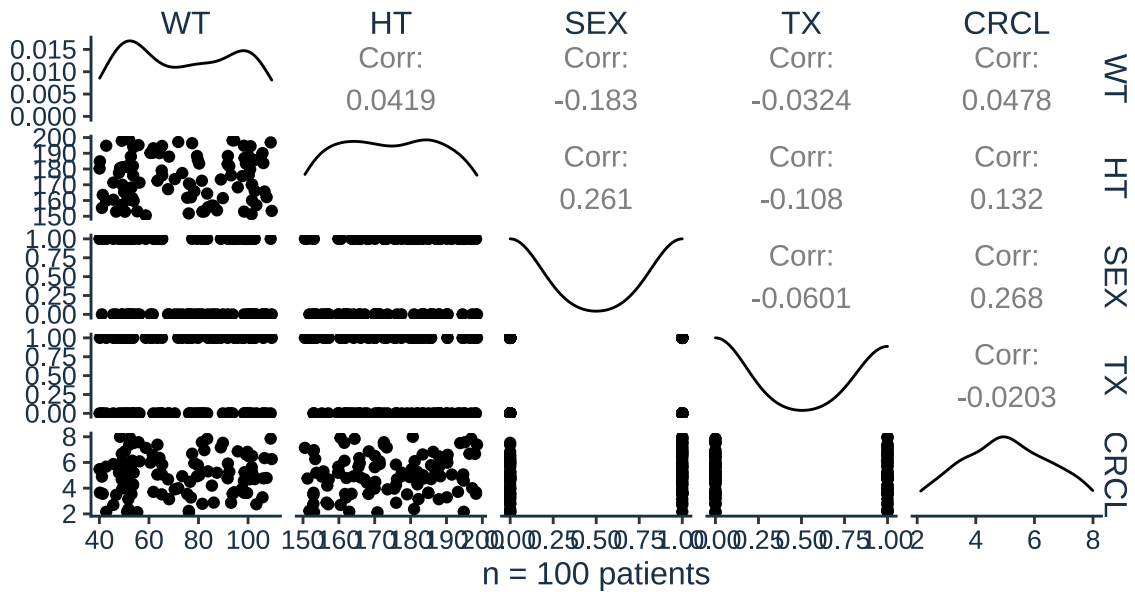


Figure 3: Simulated population characteristics

Verification results

Simulation results

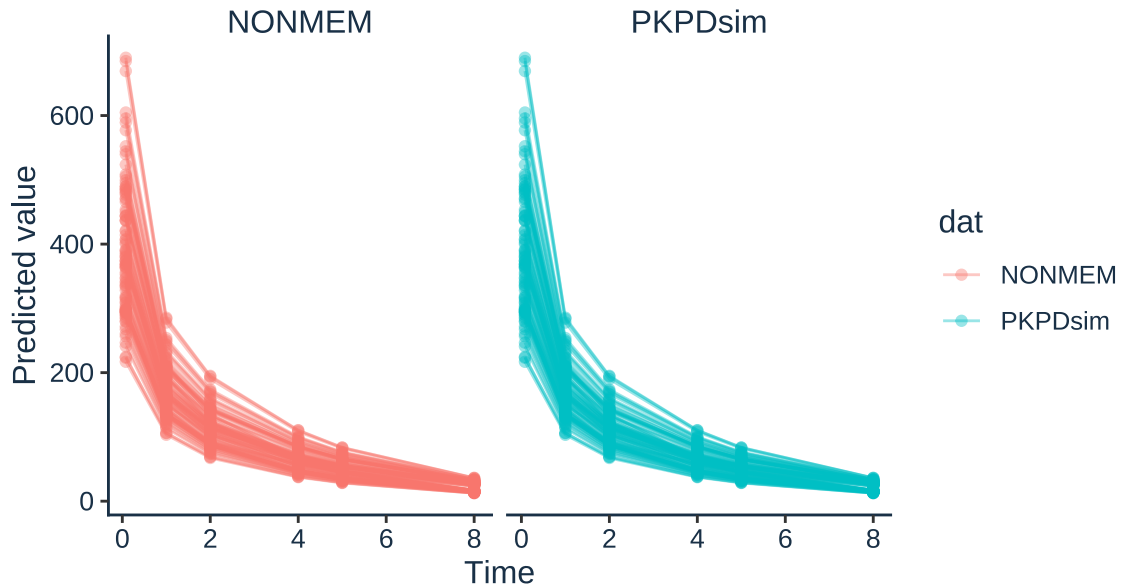


Figure 4: Predicted concentrations from PKPDsim and NONMEM

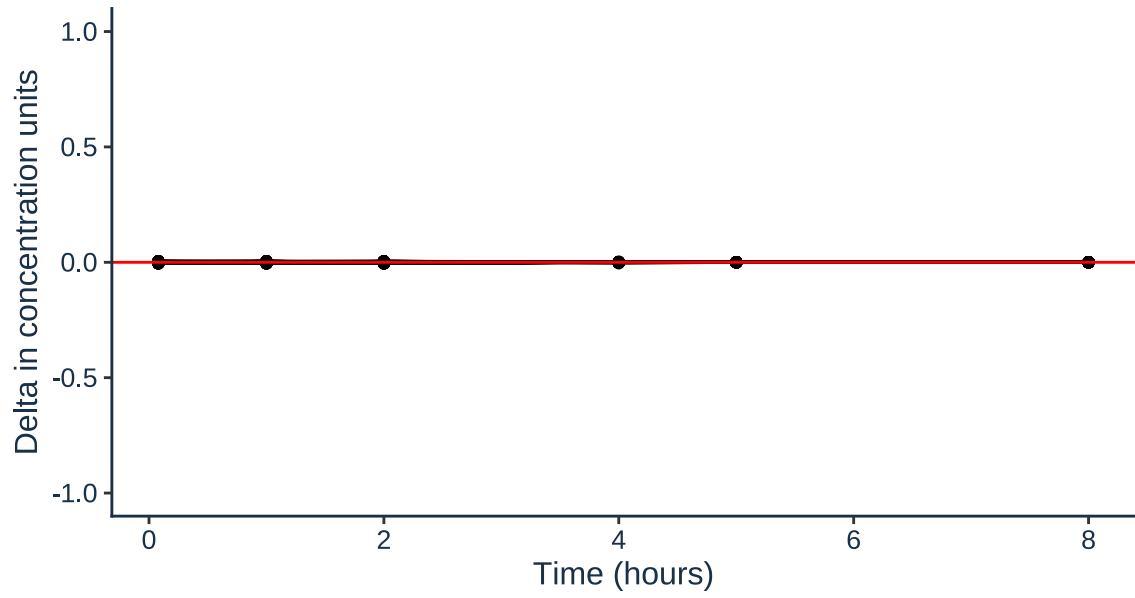


Figure 5: Differences between predicted concentrations PKPDsim and NONMEM.

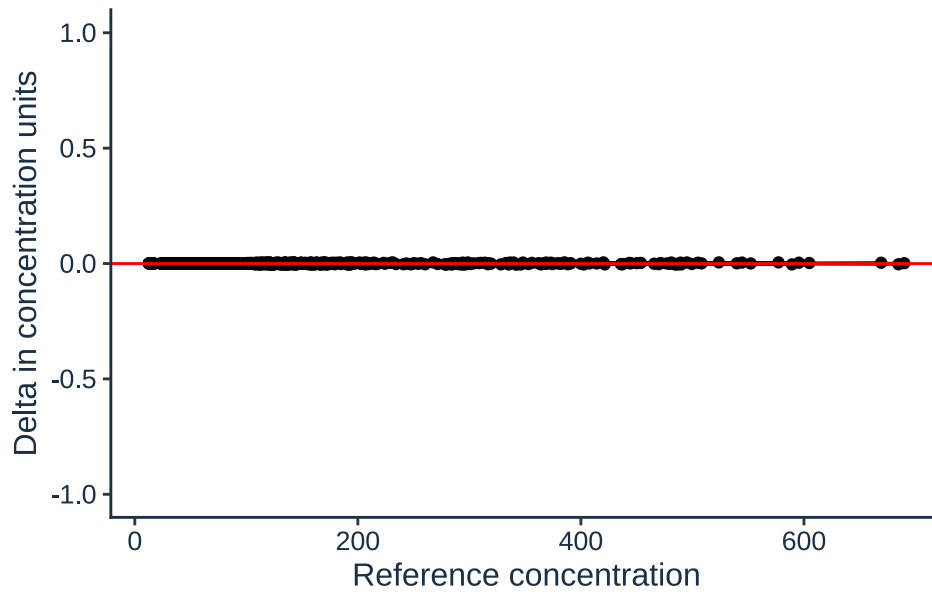


Figure 6: Differences between predicted concentrations PKPDsim and NONMEM.

Estimation results

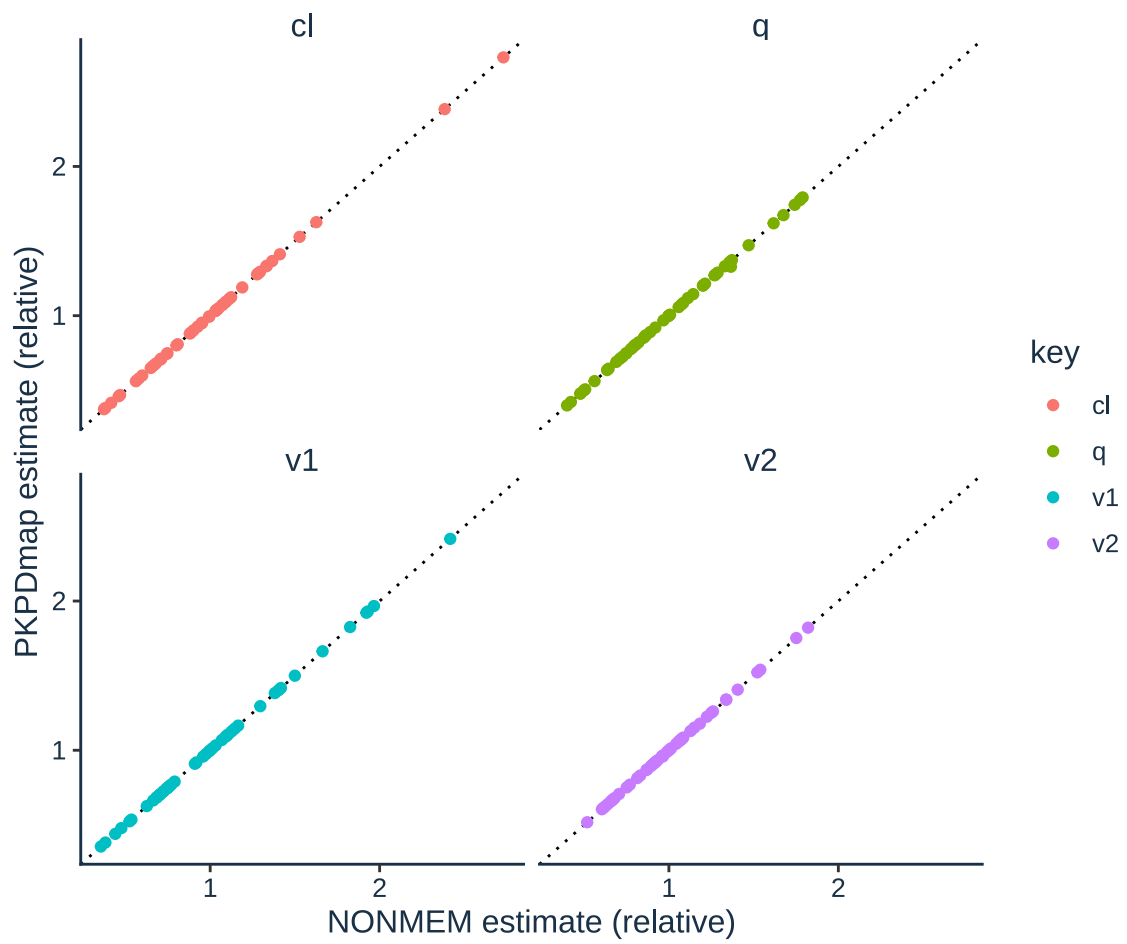


Figure 7: Correlation estimated parameters PKPDsim versus NONMEM

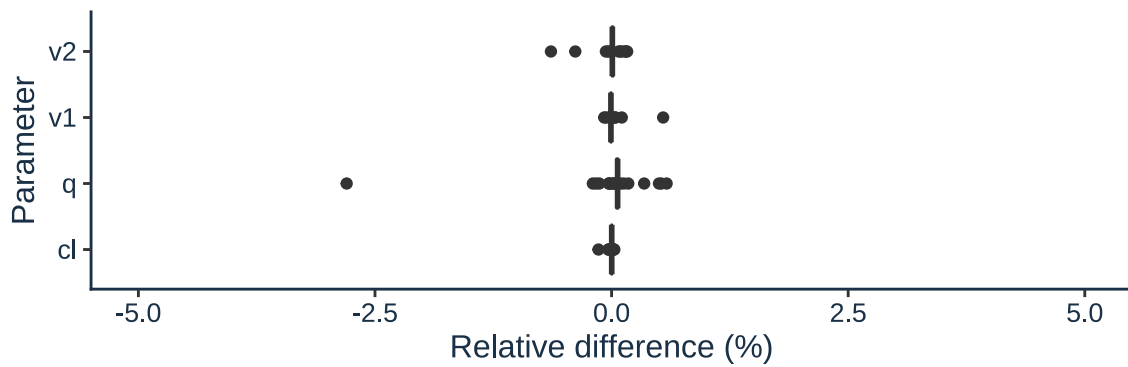


Figure 8: Difference in estimated parameters from PKPDsim and NONMEM

Numeric summary

Test	Result
data <= LOQ: absolute deltas < 15% of LOQ	passed
data > LOQ: relative deltas < 1%	passed
primary parameter estimates differ < 5%	passed

Additional information

Configuration

Setting	Value
rLOQ	1
Max absolute concentration delta < rLOQ	0.15
Max relative concentration delta >= rLOQ	0.01
Max delta model parameters	0.05
Max delta derived parameters	0.01

Libraries

Library	Version
PKPDsim	1.0.78
PKPDmap	0.33
pkiohexolzwartrenal	0.1.1

PKPDsim model code

ODE definition:

```
CLi = CL * pow(FFM/57.18, 0.75) * (1 + 0.483*(TX == 1)) ;
Vi = V * (FFM/57.18) * (1 + 0.342*(TX == 1)) ;
Qi = Q * pow(FFM/57.18, 0.75) ;
V2i = V2 * (FFM/57.18) ;
dAdt[0] = -(CLi/Vi)*A[0] - (Qi/Vi)*A[0] + (Qi/V2i)*A[1] ;
dAdt[1] = + (Qi/Vi)*A[0] - (Qi/V2i)*A[1] ;
dAdt[2] = A[0]/Vi;
;
```

PK event code:

```
if(SEX == 0) {;
  WHSMAX = 42.92;;
  WHS50 = 30.93;;
} else { WHSMAX = 37.99;;
  WHS50 = 35.98;;
};
FFM=(WHSMAX*(pow(HT/100.0, 2))*WT)/(WHS50*(pow(HT/100.0,2))+WT);
;
```

Required parameters: CL, V, Q, V2

Covariates: WT, HT, SEX, TX

Variables: CLi, Vi, Qi, V2i, FFM, WHSMAX, WHS50

Number of compartments: 3

Observation variable: NULL

Observation scaling: Vi

Lag time: none

IOV CV: {}

IOV bins: 1

Comments:

-

NONMEM model code

```
$PROBLEM
$INPUT
$DATA

$SUBROUTINES ADVAN3 TRANS4

$PK
; --- FAT FREE MASS CALCULATION -
IF (SEX.EQ.0) WHSMAX=42.92 ; MEN
IF (SEX.EQ.0) WHS50=30.93 ; MEN
IF (SEX.EQ.1) WHSMAX=37.99 ; WOMEN
IF (SEX.EQ.1) WHS50=35.98 ; WOMEN
HGT=HT/100
FFM=(WHSMAX*(HGT**2)*WT)/(WHS50*(HGT**2)+WT)

; --- ALLOMETRY SCALED TO 1.80M MAN OF 70 KG
ALLOCL=(FFM/57.18)**0.75
ALLOV=(FFM/57.18)

; --- PATIENT TYPE ON V1 AND CL
IF(TX.EQ.0) CLTX = 1 ; Most common
IF(TX.EQ.1) CLTX = (1 + THETA(7))
CLCOV=CLTX
IF(TX.EQ.0) V1TX = 1 ; Most common
IF(TX.EQ.1) V1TX = (1 + THETA(8))
V1COV=V1TX

; --- IOHEXOL PK
CL = THETA(1) * ALLOCL * CLCOV * EXP(ETA(1))
V1 = THETA(2) * ALLOV * V1COV * EXP(ETA(2))
Q = THETA(3) * ALLOCL * EXP(ETA(3))
V2 = THETA(4) * ALLOV * EXP(ETA(4))
S1 = V1

$ERROR
IPRED = F
W = SQRT(THETA(5)**2*IPRED**2 + THETA(6)**2)
Y = IPRED + W*EPS(1)
IRES = DV-IPRED
IWRES = IRES/W

$THETA
(0, 4.07) ; CL
(0, 8.36) ; V1
(0, 7.71) ; Q
(0, 6.88) ; V2
(0, 0.0523,1) ; Prop.RE (sd)
(0) FIX ; Add.RE (sd)
(-5, 0.483,5) ; CLCOV
(-5, 0.342,5) ; V1COV

$OMEGA BLOCK(3)
0.0891 ; IIV CL
```

0.038 0.163 ; IIV V1
0.0642 -0.0706 0.381 ; IIV Q

\$OMEGA
0.0554 ; IIV V2

\$SIGMA
1 FIX

test io

Date of birth 01/01/1960
 Age 60 years
 Sex Male

Iohexol (GFR)

First dose date 06/24/2020

Notes

Clinical info

Total body weight 80 kg 06/25/2020
 Height 180 cm 06/25/2020

Adjusted weight 77 kg
 Ideal weight 75 kg
 BSA 2 m²
 BMI 24.7 kg/m²
 Fat-free mass 61.7 kg

Treatment tags

Help

Info:

The calculated GFR for this subject is **84 ml/min** (95% CI: 73.4 - 94.6 ml/min).

The calculated GFR corrected for BSA is **72.8 ml/min/1.73m²** (95% CI: 63.6 - 82 ml/min/1.73m²).

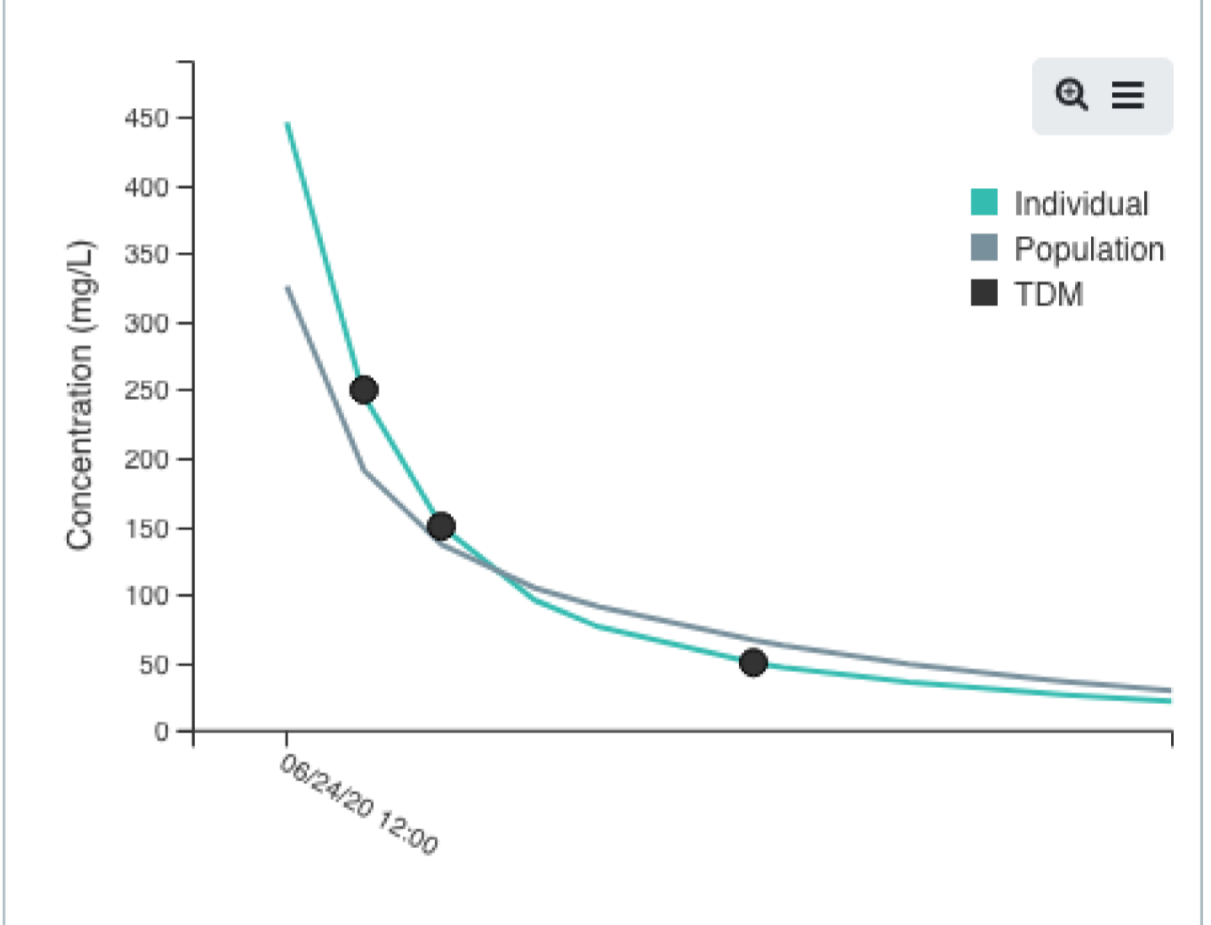
Dose information

Update

PK Fit info

Time	TDM	Prediction	Weight	Fit
06/24/2020 12:30	250	245.57 mg/L	100%	✓
06/24/2020 13:00	150	150.24 mg/L	100%	✓
06/24/2020 15:00	50	49.97 mg/L	100%	✓

Model fit: Good
 Model: Zwart TC et al. PAGE 2019
 Fitting method: MAP Bayesian
 Weighting scheme: Linear gradient



Drug monitoring Edit doses/markers

Dose	Start time	TDM	Since dose	Comments
3000 mg	06/24/2020 12:00			
	06/24/2020 12:30	TDM: 250 mg/L	0 h 30 m	
	06/24/2020 13:00	TDM: 150 mg/L	1 h 0 m	
	06/24/2020 15:00	TDM: 50 mg/L	3 h 0 m	