

Erratum to: Likelihood based approaches to handling data below the quantification limit using NONMEM VI

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The following list of corrections applies to the article, “Likelihood based approaches to handling data below the quantification limit using NONMEM VI” by Jae Eun Ahn, Mats O. Karlsson, Adrian Dunne, Thomas M. Ludden. The article appeared in the *Journal of Pharmacokinetics and Pharmacodynamics*, Volume 35, Number 4, August 2008, pp. 401–421.

Page 402:

- Method 7 (M7): Replace all BQL observations with 0 and apply extended least squares estimation.

Page 419, Appendix Part I.b, M3 Code:

$DUM = (LOQ - IPRED)/(SIG*IPRED)$

The online version of the original article can be found under doi:[10.1007/s10928-008-9094-4](https://doi.org/10.1007/s10928-008-9094-4).

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Page 419, Appendix Part I.b, M4 Code:
 $DUM = (LOQ - IPRED)/(SIG*IPRED)$
 $DUM0 = (0 - IPRED)/(SIG*IPRED)$

Page 419, Appendix Part I.b, \$ERROR:
 Adding “CALLFL=0” or “(ONLY OBSERVATIONS)” is necessary to prevent division by zero for dosing records.

In Part I, the negatively biased estimates for RUV with all data, M1, and M2 were due to the fact that an incorrect true value (0.025) was used in calculating estimation error. The value should have been 0.0225. The corrected values for RUV assessment are provided in Table 4-7c.

Estimation in Part I.b was redone with the correct code above but using a different Fortran compiler, g77. Simulated data are the same. The new results are provided in Tables 8c–10c. M2 tended to be less stable than M3 or M4 at high LOQ values (Table 8c) but still gave less biased estimates than M1. M1 was also fitted to the untransformed data but its estimates were still severely biased as in Part I.a and the results are not presented. M3 and M4 gave very similar and the least biased estimates (Table 9c). Overall precision seems comparable (Table 10c).

Table 4-7c Part I.a: Corrections to Mean Estimation Error (MEE, %) and Root Mean Squared Estimation Error (RMSE, %) of RUV

Tables	LOQ	0	0.2			0.25			0.3			0.4		
			M1	M2	M3	M1	M2	M3	M1	M2	M3	M1	M2	M3
	Methods	<i>All data</i>												
4	MEE	6.43	-1.83	3.69	4.29	-3.67	3.86	3.25	-4.15	4.59	2.78	-3.68	5.43	3.39
5	RMSE	7.36	4.30	5.76	5.73	5.34	5.71	5.07	5.87	6.59	5.14	5.93	7.60	6.01
6	MEE	6.21	-0.191	5.52	4.49	-2.00	5.96	3.25	-0.716	7.67	5.05	2.39	8.68	4.22
7	RMSE	7.99	5.59	8.37	7.24	6.24	9.11	5.07	6.32	10.9	8.33	8.31	12.4	8.89

Corrected values in bold

Table 8c Part I.b: The Proportion of BQL Data and the Success Rate (%) (Extensive Design: 24 samples/individual; untransformed data)

LOQ	BQL Proportion (%)	<i>All data</i>	Success Rate (%)		
			M2 (YLO)	M3 (F_FLAG)	M4 (F_FLAG)
0	0.00	86			
0.2	12.9		88	87	88
0.25	21.6		82	85	91
0.3	29.9		81	87	85
0.4	42.9		61	80	78

Table 9c Part I.b: Mean Estimation Error (%) of Parameter Estimates (Extensive Design, Untransformed Data, Successful Termination Only)

LOQ	0	0.2				0.25				0.3				0.4			
		M2	M3	M4	M4	M2	M3	M4	M4	M2	M3	M4	M4	M2	M3	M4	
Methods	<i>All data</i>																
Parameters																	
Beta	-0.637	-4.06	-0.558	-0.673	-5.59	-1.07	-0.868	-6.83	-0.909	-1.14	-10.4	-2.64	-2.84				
CL	0.115	-0.979	-0.00659	0.0452	-1.75	-0.0567	-0.103	-2.50	-0.121	-0.0593	-5.03	-0.677	-0.552				
VC	3.36	3.84	3.18	3.46	3.17	3.74	3.39	3.21	3.45	3.61	2.51	3.94	4.07				
VP	0.414	4.47	0.412	0.440	6.72	0.834	0.689	8.87	0.777	1.05	15.8	2.94	3.16				
Q	-0.262	1.04	-0.0878	-0.226	2.27	-0.225	-0.105	3.78	-0.158	-0.134	8.29	0.0728	0.0288				
dKA	4.84	7.40	4.55	5.37	5.08	6.71	5.46	4.46	5.35	6.25	1.56	7.42	7.70				
IIV (CL)	-2.10	-3.27	-1.83	-1.57	-4.99	-1.47	-0.834	-5.30	-1.04	-1.25	-1.75	0.556	0.560				
IIV (VC)	-25.0	-24.2	-25.8	-23.8	-26.8	-25.3	-25.3	-25.8	-24.9	-24.5	-25.2	-25.7	-26.1				
IIV (VP)	0.484	15.0	2.34	1.74	25.5	5.41	2.57	31.7	5.62	7.9	30.0	14.9	24.1				
IIV (Q)	-6.84	-13.5	-6.87	-5.97	-20.6	-6.67	-6.46	-22.4	-7.54	-7.00	-28.5	-7.68	-9.34				
IIV (dKA)	84.9	80.9	80.5	75.5	92.9	77.9	74.3	93.7	80.5	72.2	82.8	70.5	79.1				
RUV	0.179	1.26	0.276	0.275	1.64	0.0212	-0.0109	2.45	0.102	0.133	3.06	0.615	0.252				

Table 10c Part I.b: Root Mean Squared Estimation Error (%) of Parameter Estimates (Extensive Design, Untransformed Data, Successful Termination Only)

LOQ	0	0.2				0.25				0.3				0.4			
		All data	M2	M3	M4	M2	M3	M4	M2	M3	M4	M2	M3	M4	M2	M3	M4
Methods																	
Parameters																	
Beta	3.04	5.64	3.58	3.17	7.38	3.88	3.83	9.13	4.79	4.73	15.0	8.17	8.05				
CL	2.18	2.61	2.35	2.32	3.11	2.46	2.43	3.72	2.46	2.59	6.28	3.01	2.98				
VC	4.53	4.87	4.48	4.43	4.54	4.76	4.65	4.68	4.76	4.79	4.93	5.28	5.38				
VP	2.71	6.11	3.31	2.95	8.55	3.62	3.62	11.5	4.72	4.81	21.3	9.19	8.98				
Q	2.18	2.34	2.14	2.07	3.23	2.32	2.25	4.66	2.35	2.42	9.49	3.13	3.10				
dKA	11.8	13.1	12.2	11.1	12.6	12.4	12.4	12.0	12.9	12.9	14.7	14.3	14.7				
IIV (CL)	13.8	14.1	14.4	14.1	15.3	13.8	13.8	14.9	14.0	13.7	17.0	14.6	15.2				
IIV (VC)	29.1	28.8	30.1	28.2	30.4	29.2	29.5	29.9	29.0	29.3	29.3	29.8	29.8				
IIV (VP)	24.5	47.2	31.9	30.9	60.9	43.5	39.5	79.1	49.8	53.4	99.3	86.9	100				
IIV (Q)	16.7	21.4	17.8	17.1	26.7	18.6	18.0	30.0	19.6	19.9	37.5	25.2	25.4				
IIV (dKA)	146	144	147	143	149	139	143	150	144	141	157	132	135				
RUV	3.30	4.53	3.52	3.62	4.60	3.84	3.64	5.15	4.02	3.94	5.88	4.39	4.34				