Table 1 Supplemental Digital Content. Summary of previously published single dose oral omeprazole studies in healthy subjects.

Study reference	N	Omeprazole oral dose (mg)	Assay used	Subject Demographics			PK sampling time points post-dose (h)	CYP2C19 Genotype Data
				Median Age (yr)	Median Weight (kg)	Sex (M=male, F=female)		
Allegrini et al. [9]	50	20 mg	HPLC + UV	Unknown	Unknown	Unknown	0.5, 1, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, 5.0, 6.0, 8.0, 10, 12	No
Baldwin et al. [10]	18	40 mg	HPLC + UV	32	70.8	33.3% M 66.7% F	0, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10	Yes
Cho et al. [3]	13	40 mg	HPLC + UV	20	61	76.9% M 23.1% F	0, 0.33, 0.66, 1, 1.5, 2, 3, 4, 5, 6, 8, 12, 24	Yes

Hussein et al. [11]	36	20 mg	HPLC + UV	Unknown	Unknown	100% M	0.25, 0.50, 0.75, 1.0, 1.25, 1.50, 1.75, 2.0, 2.25, 3, 4, 5, 6, 8, 10, 12	No
Johnson et al. [12]	15	40 mg	HPLC + MS/MS	41	81.9	46.7% M 53.3% F	0, 0.5, 1, 1.5, 2, 2.5, 3, 4, 6, 8, 10	Yes
Rhim et al. [13]	12	20 mg	HPLC + UV	Unknown	Unknown	100% M	0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 8, 9	No
Yin et al. [8]	26	40 mg	HPLC + UV	22	60.7	100% M	0, 0.33, 0.67, 1, 1.5, 2, 2.5, 3, 4, 6, 8, 10, 12	Yes

Abbreviations: HPLC=high performance liquid chromatography; h=hour; kg=kilogram; MS=mass spectrometry; PK=pharmacokinetic, UV=ultraviolet; yr-year.

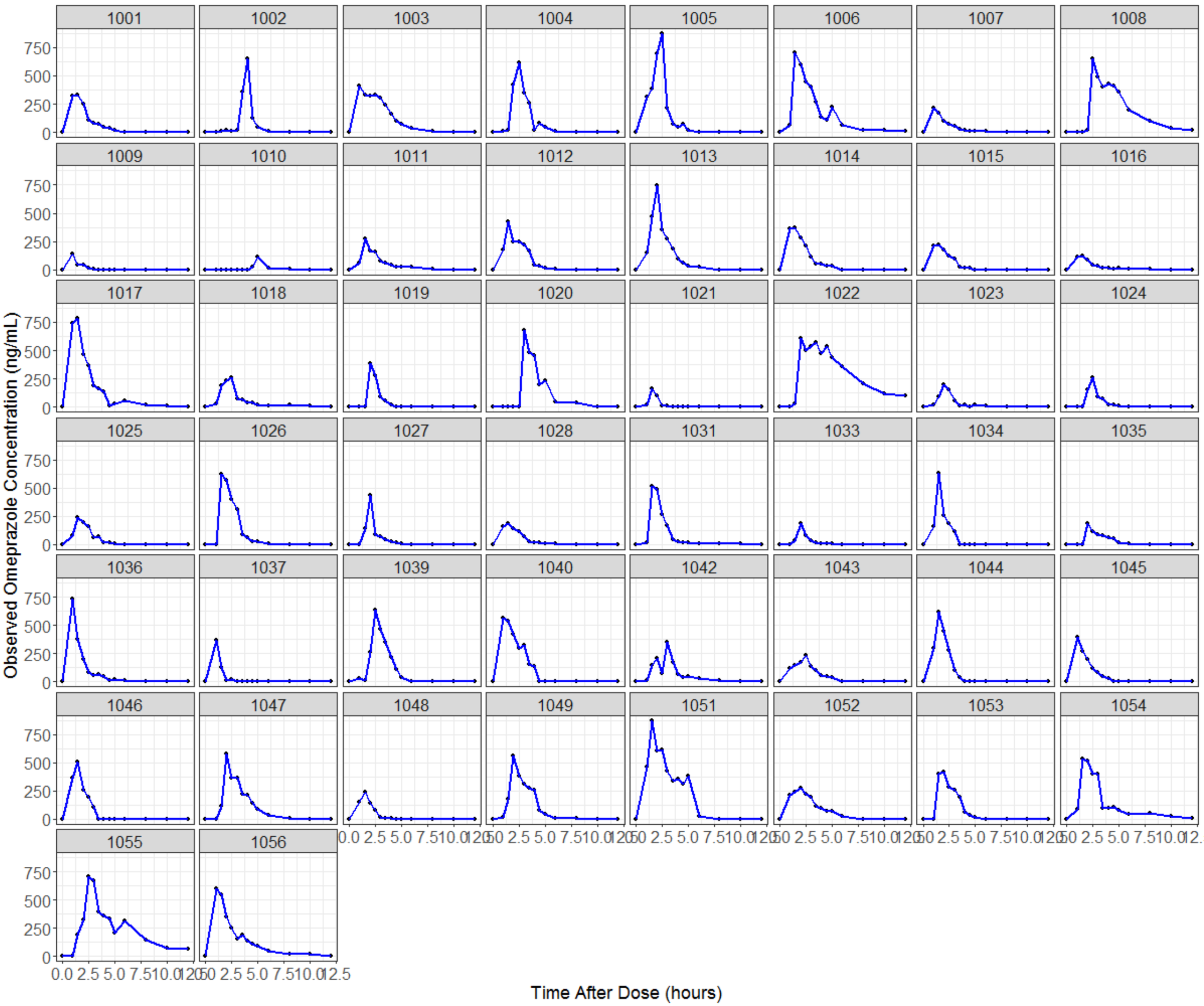
Table 2 Supplemental Digital Content. Pharmacokinetic parameter estimates by non-compartmental analysis and population pharmacokinetic final model

Parameter Estimates	**Non-compartmental analysis (n=170)**	**Population pharmacokinetic model (n=71)**	
		Final Model	**Bootstrap**
CL/F (L/h)	23.7 (4.0-131.4)	19.3 (5.3-75.7)	17.8 (13.7-24)
V (L)	35.6 (10.8-246.8)	23.7 (16.7-31.4)	26.7 (22.3-32.3)
Half-life (h)	0.95 (0.4-3.1)	0.9 (0.2-2.6)	1.1 (0.8, 1.3)
AUC_{inf} (h*ng/mL)	980.2 (165.5-9320.7)	2077.4 (544.4-7537.0)	2247.2 (1666.7-2919.7)
T_{max} (h)	1.8 (0.8-5.0)	2.2 (0.8-10.7)	1.8 (0.8, 2.3)

Data are median (2.5th and 97.5th percentiles) values. Population PK parameter estimates from the final model and bootstrap are median typical values.

Abbreviations: CL/F= apparent oral clearance; V=volume of distribution; AUC_{inf}, area under the concentration time curve from time 0 to infinity; T_{max}=time to maximum concentration.

Figure 1. Individual plasma concentration time profiles from each previously published study.


1001
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1003
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1019
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1023
1024
1025
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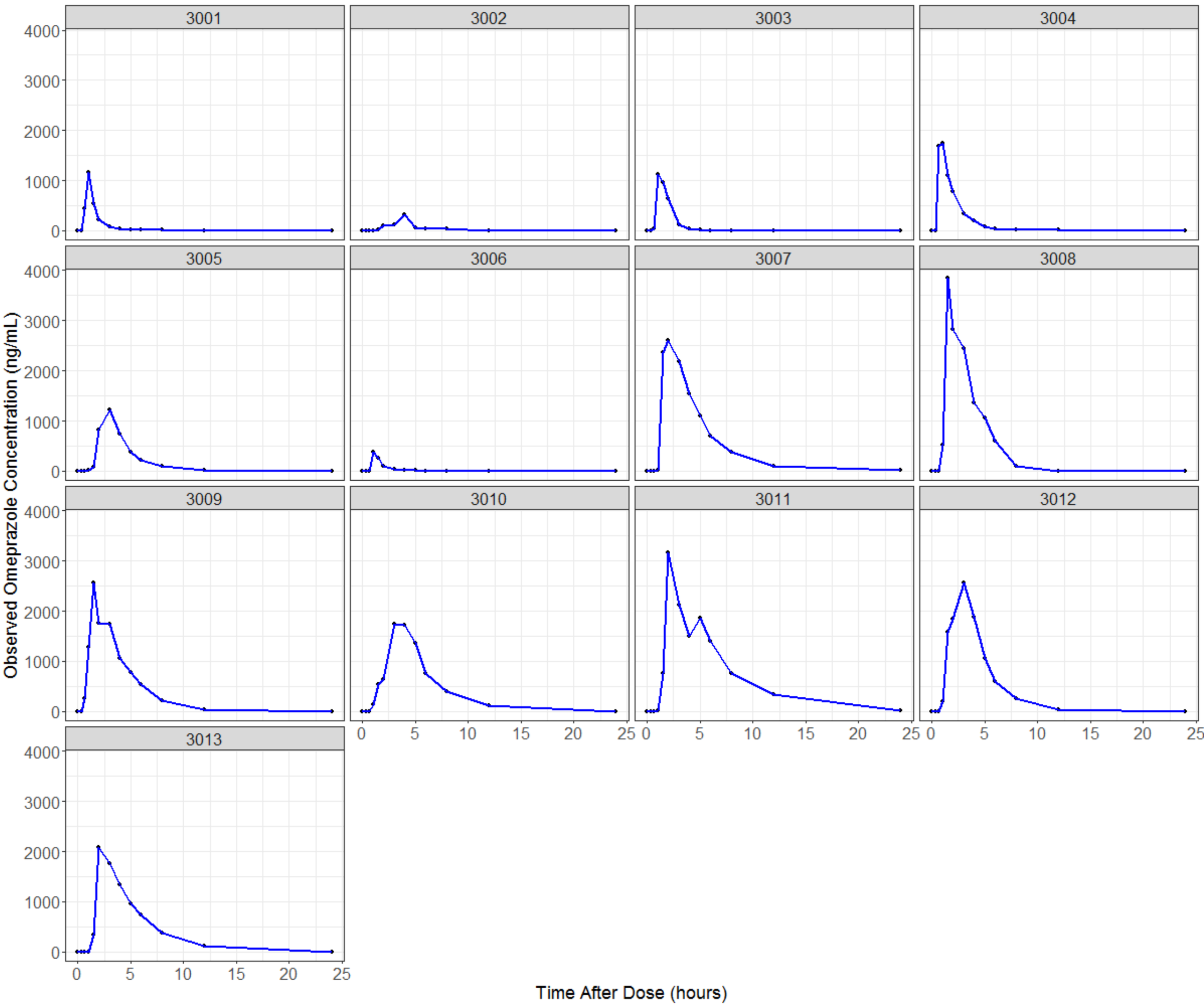
1027
1028
1031
1033
1034
1035
1036
1037
1039
1040
1042
1043
1044
1045
1046
1047
1048
1049
1051
1052
1053
1054
1055
1056
0
250
500
750
0.0 2.5 5.0 7.5 10.0 12.5
Observed Omeprazole Concentration (ng/mL)
Time After Dose (hours)

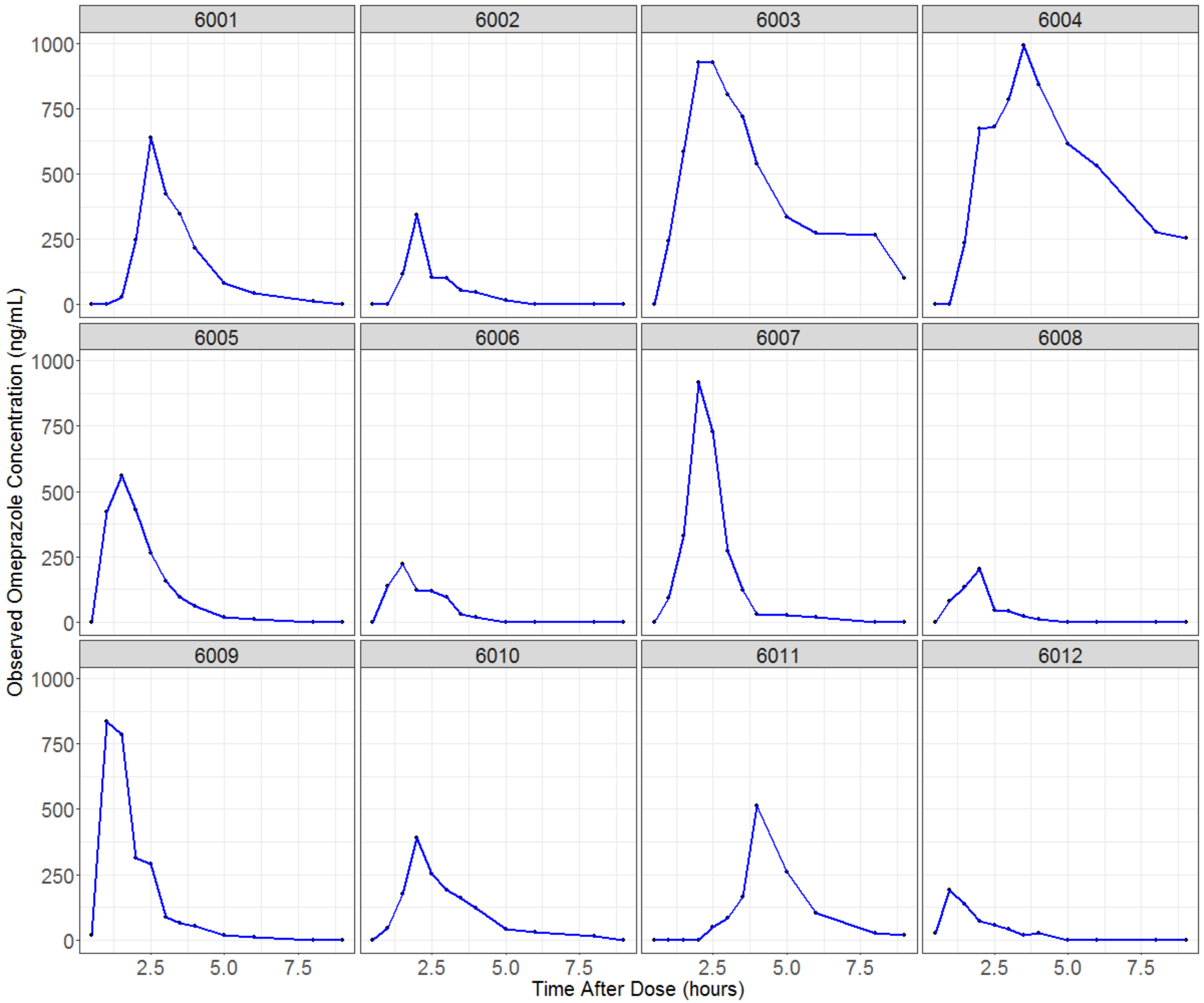
2001 2002 2003 2004 2005
2006 2007 2008 2009 2010
2011 2012 2013 2014 2015
2016 2017 2018
Observed Omeprazole Concentration (ng/mL)
0 1000 2000 3000 4000 5000
0.0 2.5 5.0 7.5 10.0
Time After Dose (hours)


3001
3002
3003
3004
3005
3006
3007
3008
3009
3010
3011
3012
3013
Observed Omeprazole Concentration (ng/mL)
Time After Dose (hours)
0
1000
2000
3000
4000
0
5
10
15
20
25

Observed Omeprazole Concentration (ng/mL)

Time After Dose (hours)

5001
5002
5003
5004
5005
5006
5007
5008
5009
5010
5011
5012
5013
5014
5015
1500
1000
500
0
0.0
2.5
5.0
7.5
10.0
Observed Omeprazole Concentration (ng/mL)
Time After Dose (hours)


6001
6002
6003
6004
6005
6006
6007
6008
6009
6010
6011
6012
1000
750
500
250
0
2.5
5.0
7.5
Observed Omeprazole Concentration (ng/mL)
Time After Dose (hours)

7011 7012 7013 7014 7015 7021
7022 7023 7024 7025 7031 7032
7033 7034 7035 7041 7042 7043
7044 7051 7052 7053 7054 7061
7063 7064

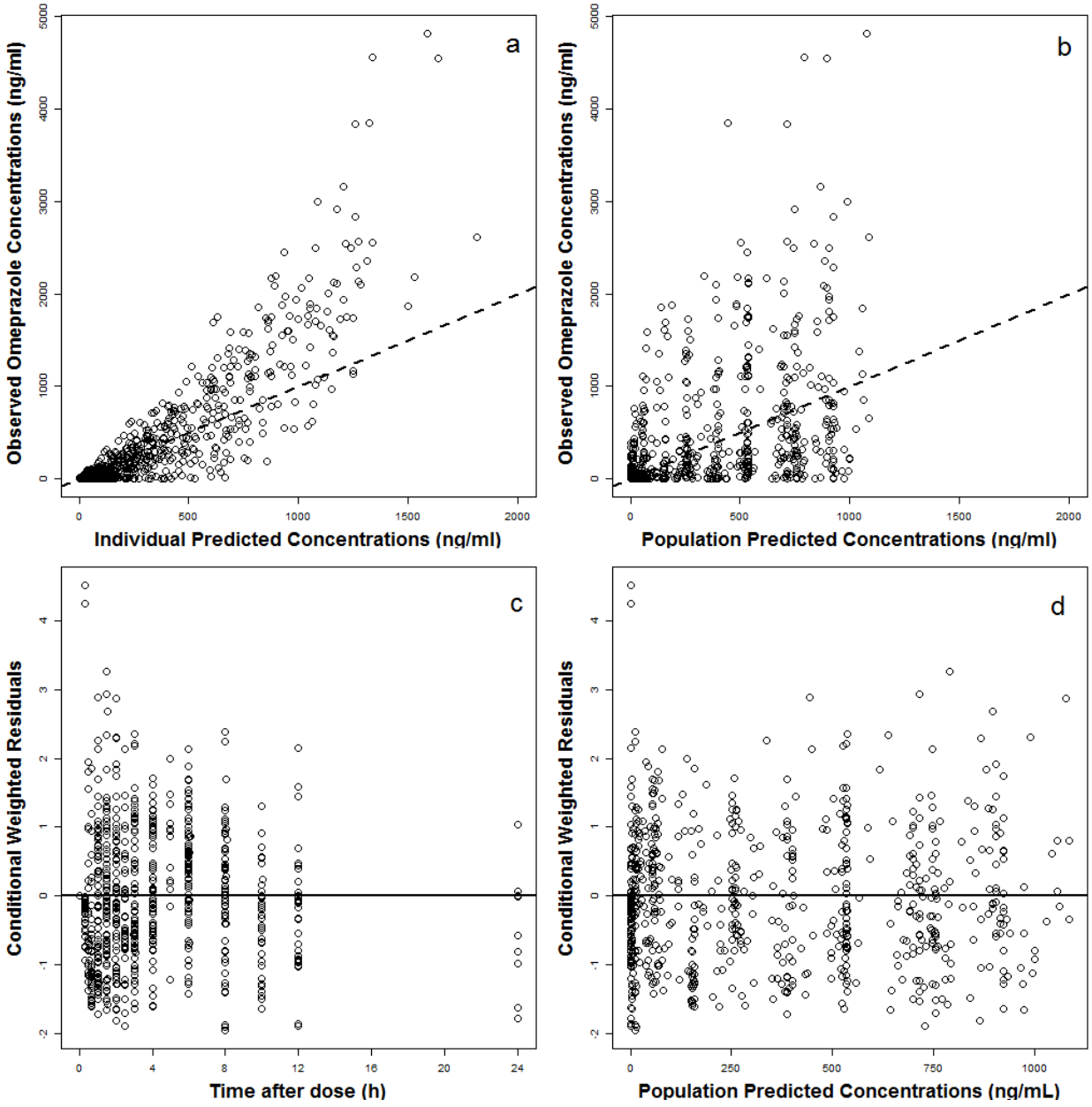
Observed Omeprazole Concentration (ng/mL)

0 1000 2000 3000

0.0 2.5 5.0 7.5 10.0 12.5

Time After Dose (hours)

Figure 2 Supplemental Digital Content. (See Figure Legend for additional details)



SUPPLEMENTAL DIGITAL CONTENT, FIGURE LEGENDS

Figure 1. Individual plasma concentration time profiles from each previously published study.

Figure 2. Goodness-of-fit plots for the final model of a. Observed versus individual predicted concentrations; b. observed versus population predicted concentrations; c. conditional weighted residuals (CWRES) versus time after dose; and d. CWRES versus population predicted concentrations. For panels a and b, the dashed line of identity is included as a reference. For panels c and d, a solid line at $y = 0$ is included as a reference.