

Figure 12. Time Concentration Profile

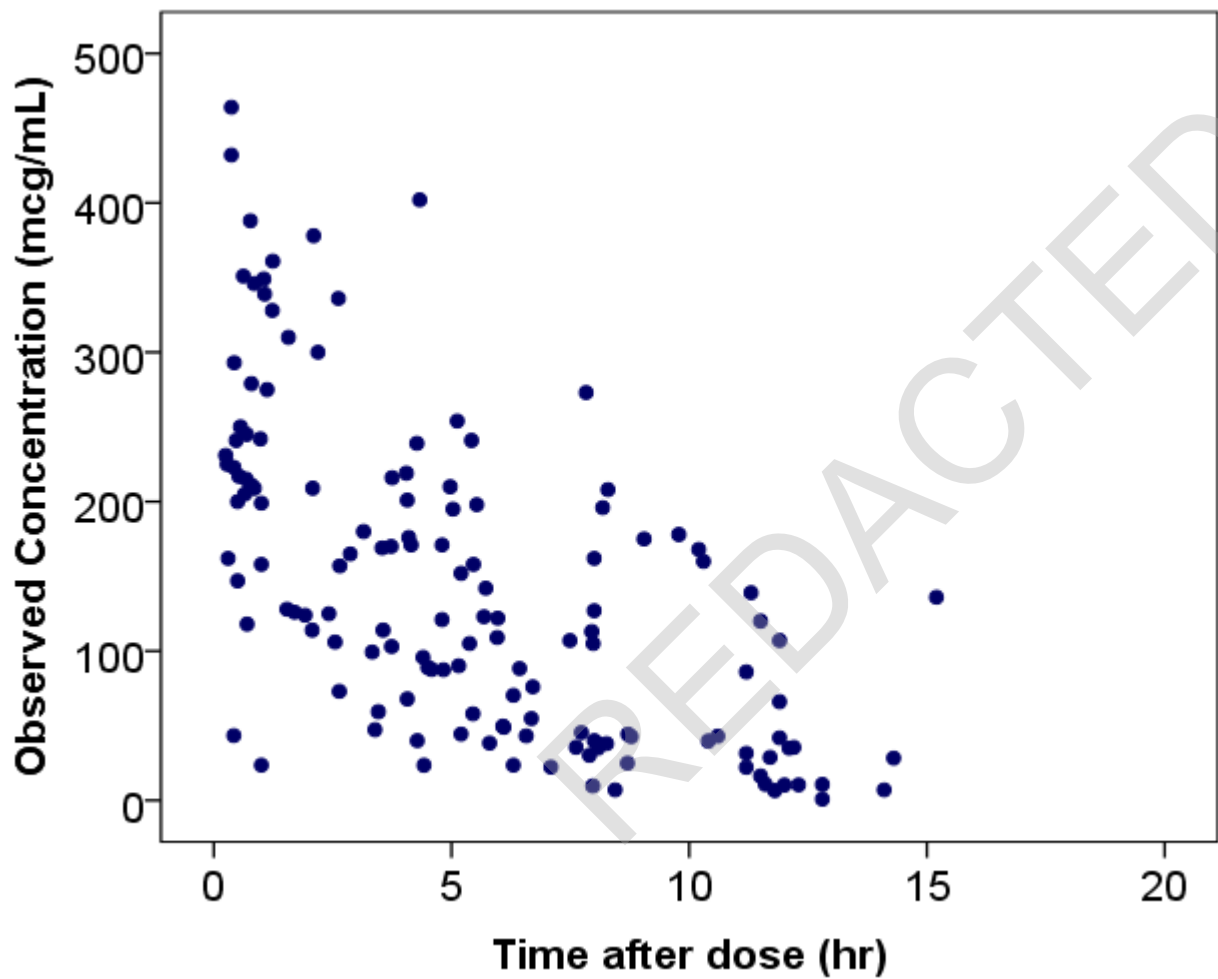


Figure 13. Time Concentration Profile - Semi-Log Scale

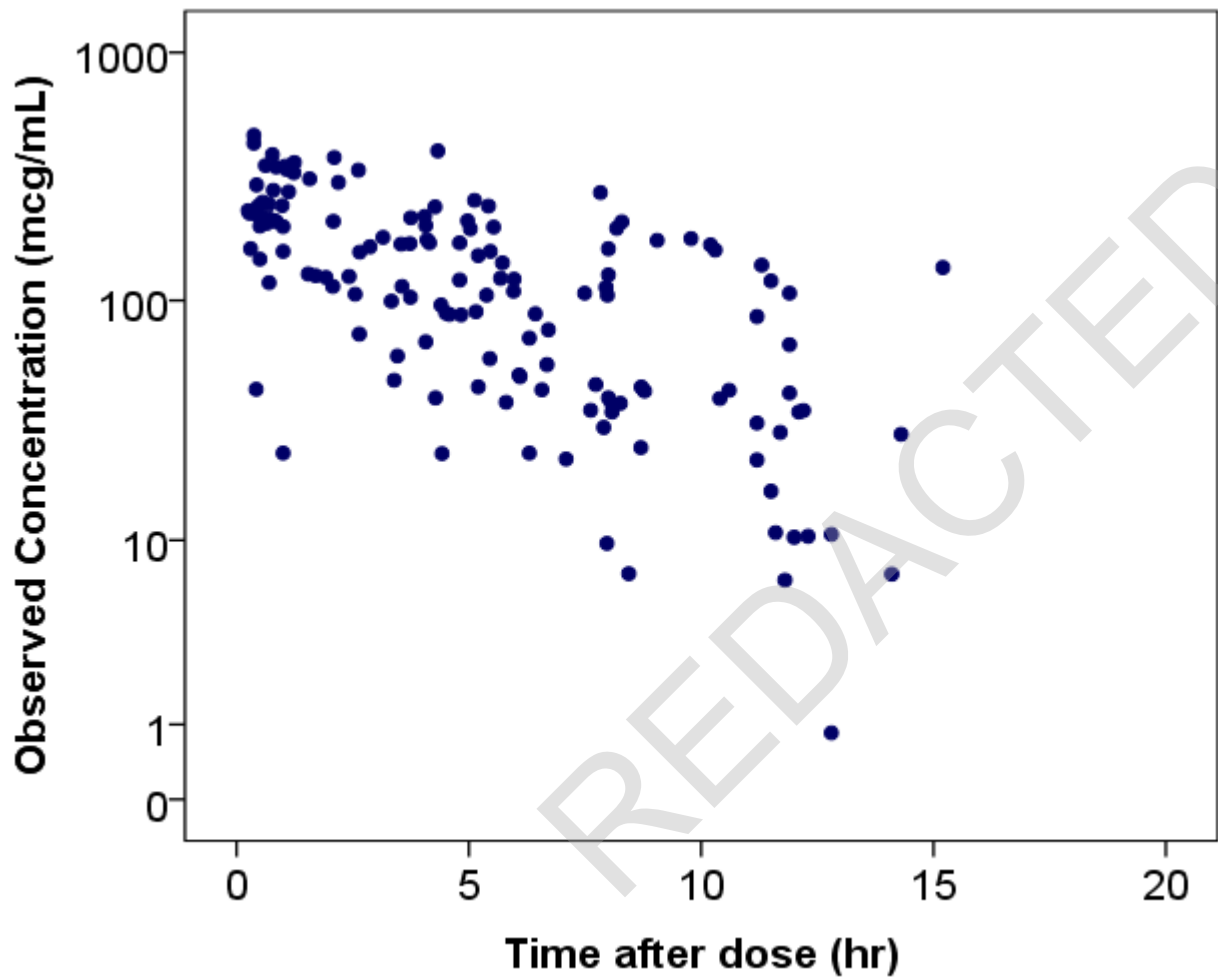


Figure 14. Time Concentration Profile - Semi-Log Scale Group 1

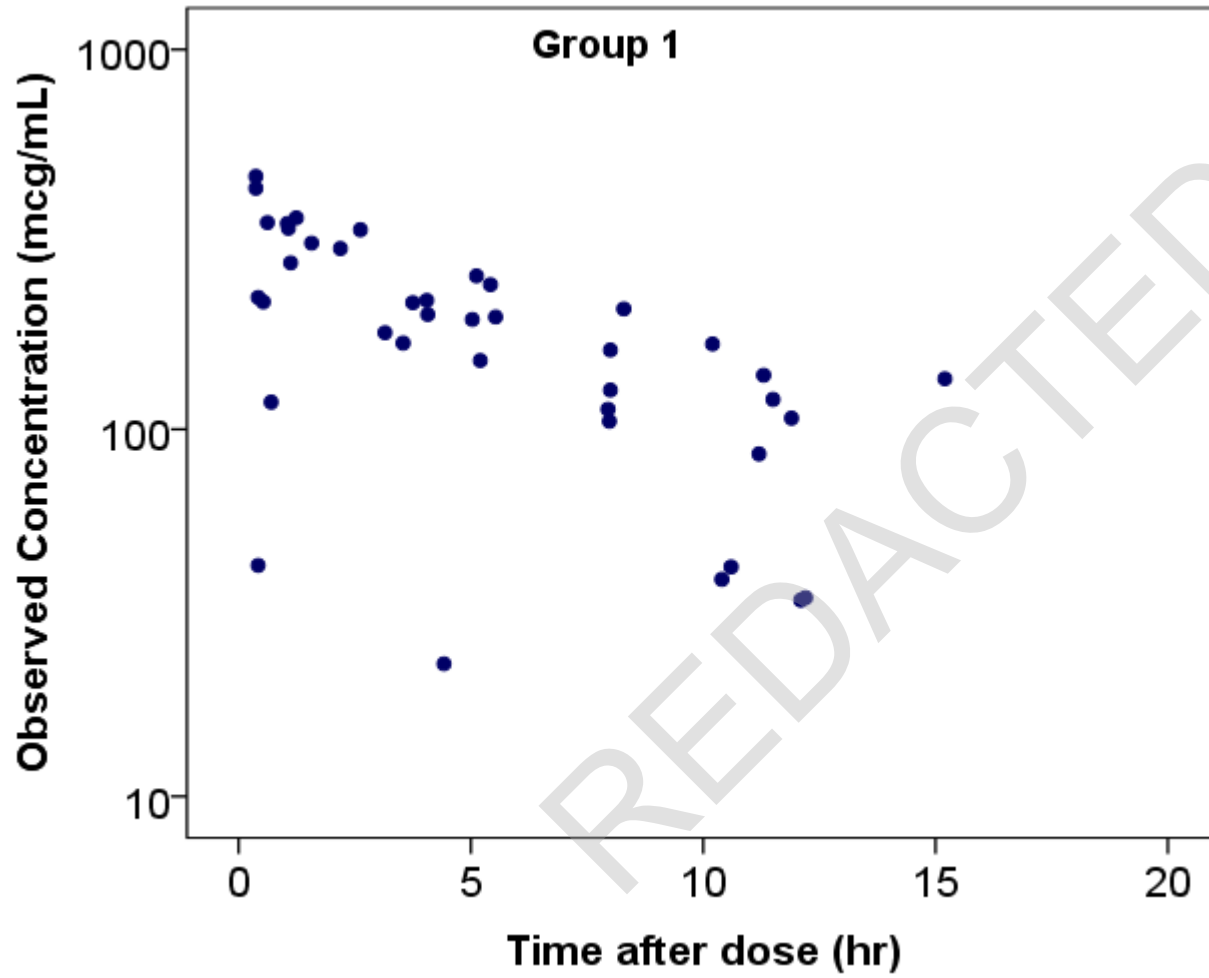


Figure 15. Time Concentration Profile - Semi-Log Scale Group 2

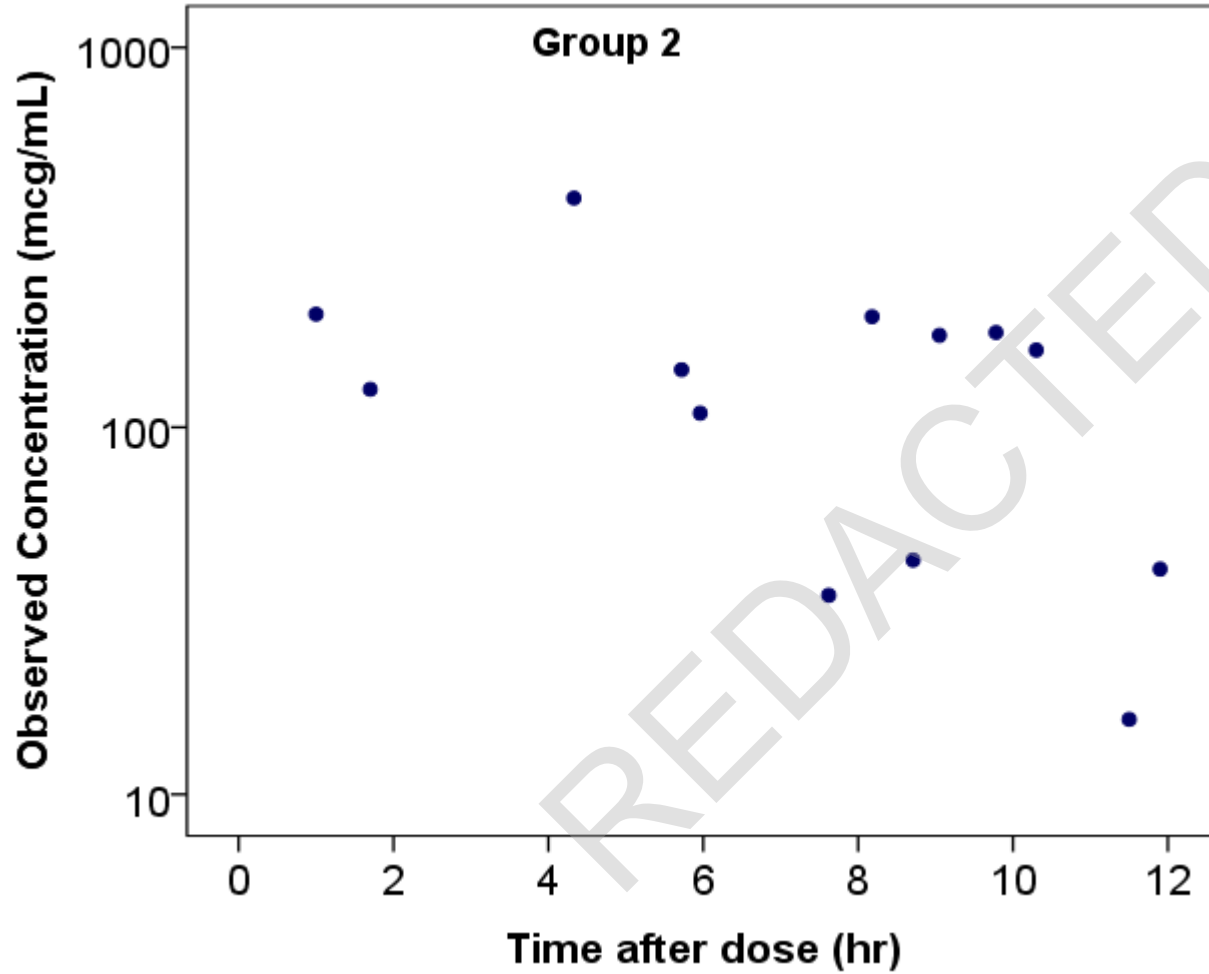


Figure 16. Time Concentration Profile - Semi-Log Scale Group 3

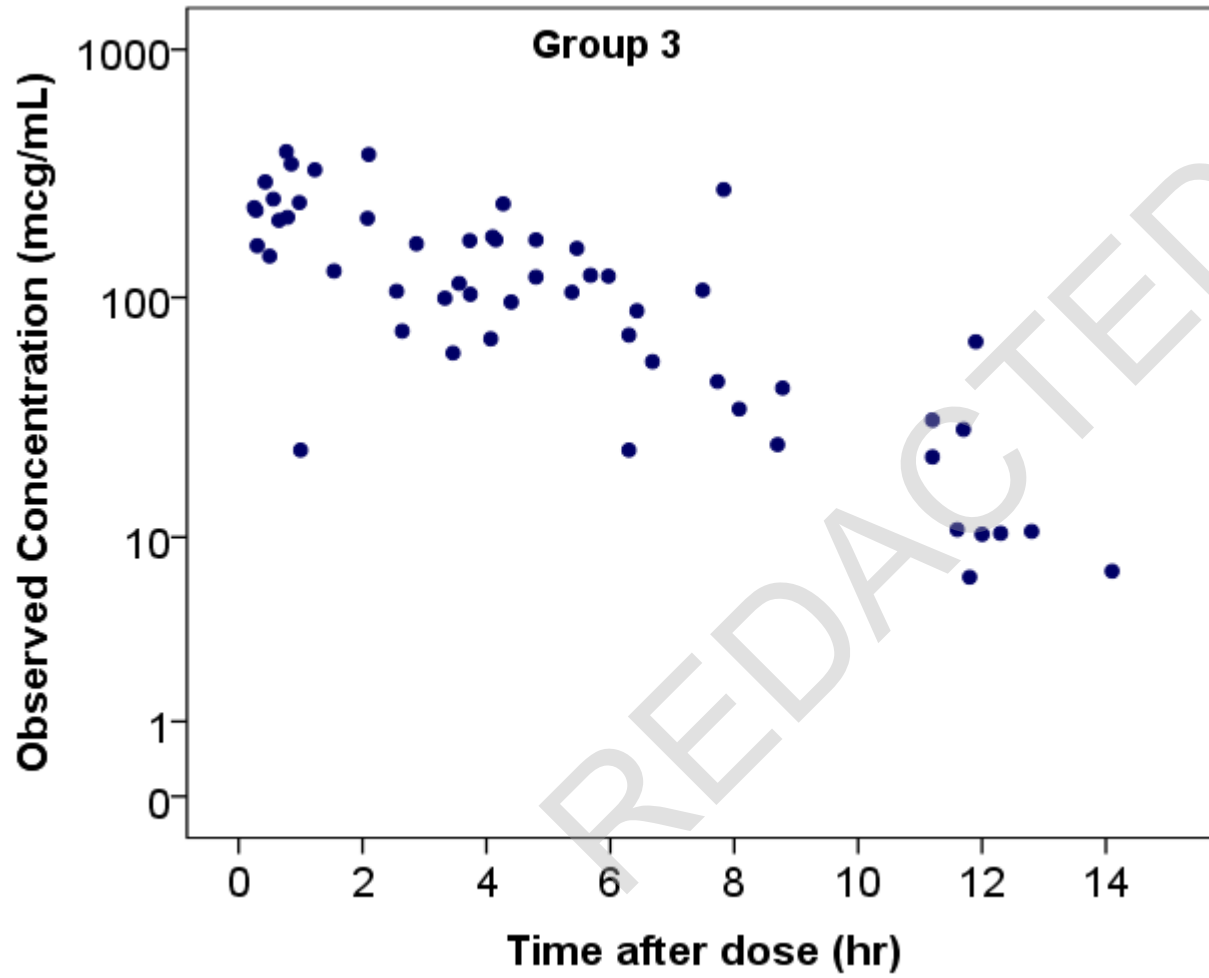


Figure 17. Time Concentration Profile - Semi-Log Scale Group 4

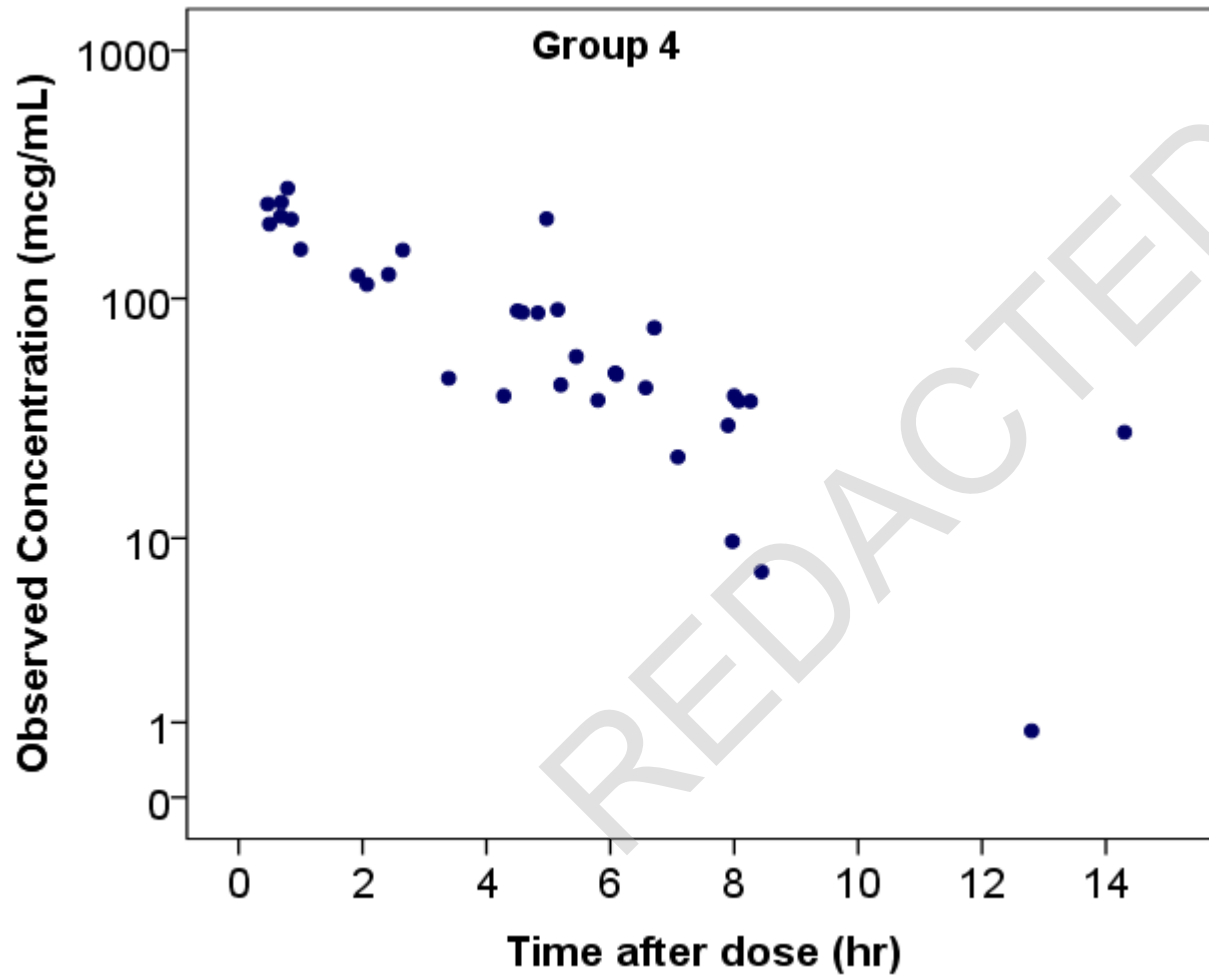


Figure 18. Observed vs. Population Predicted Concentration - Base Model

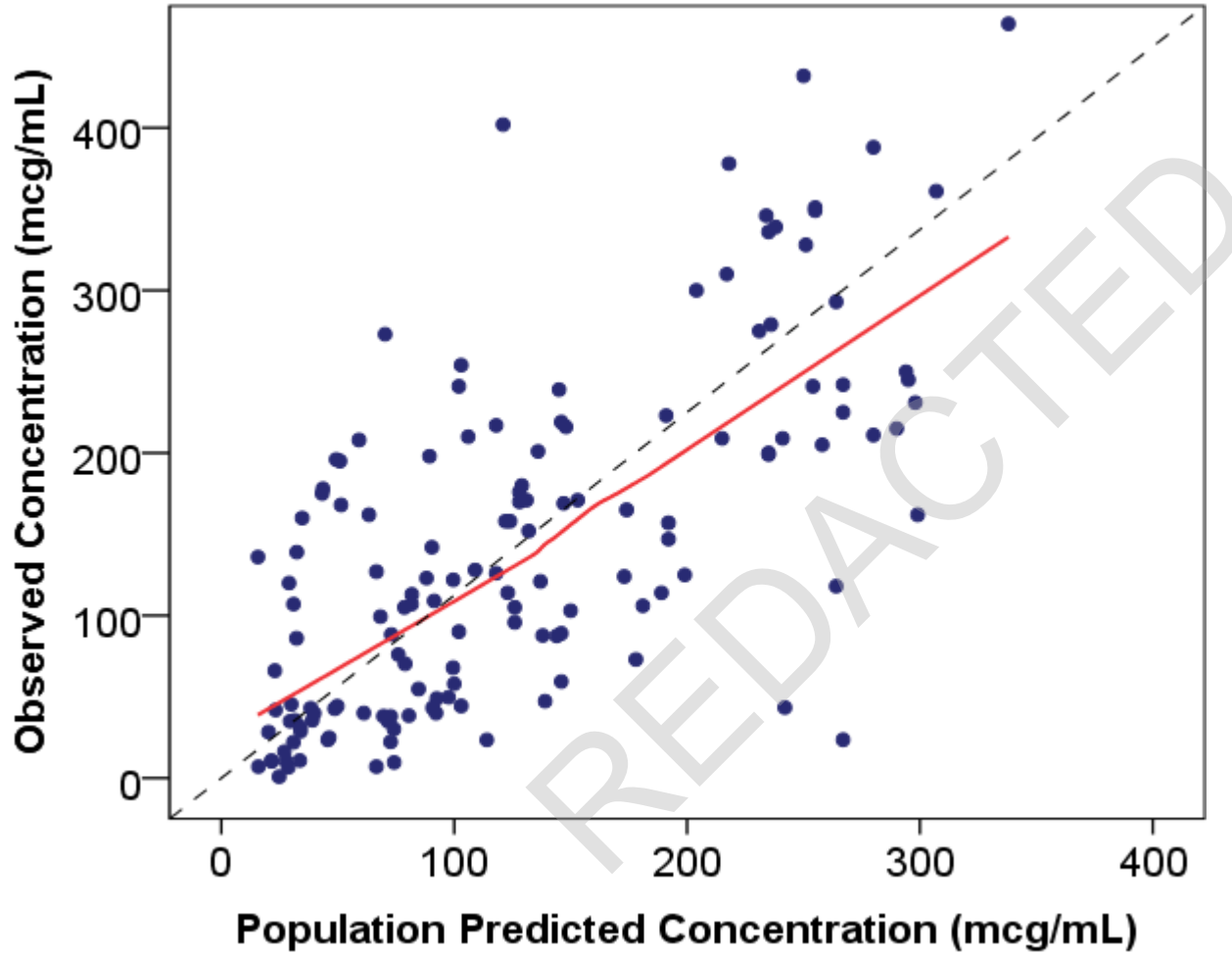


Figure 19. Observed vs. Post-Hoc Predicted Concentration - Base Model

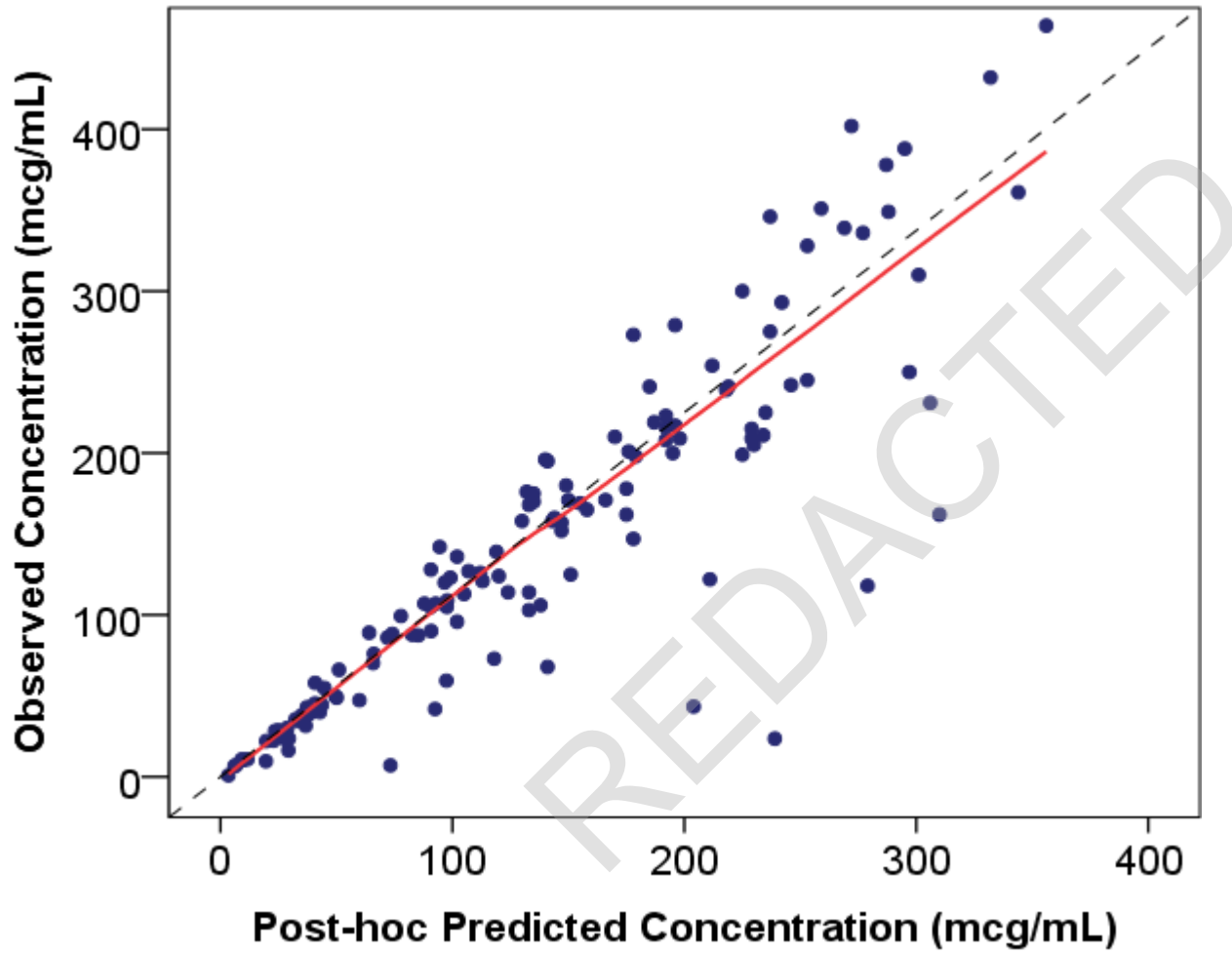


Figure 20. Conditional Weighted Residual vs Time After First Dose - Base Model

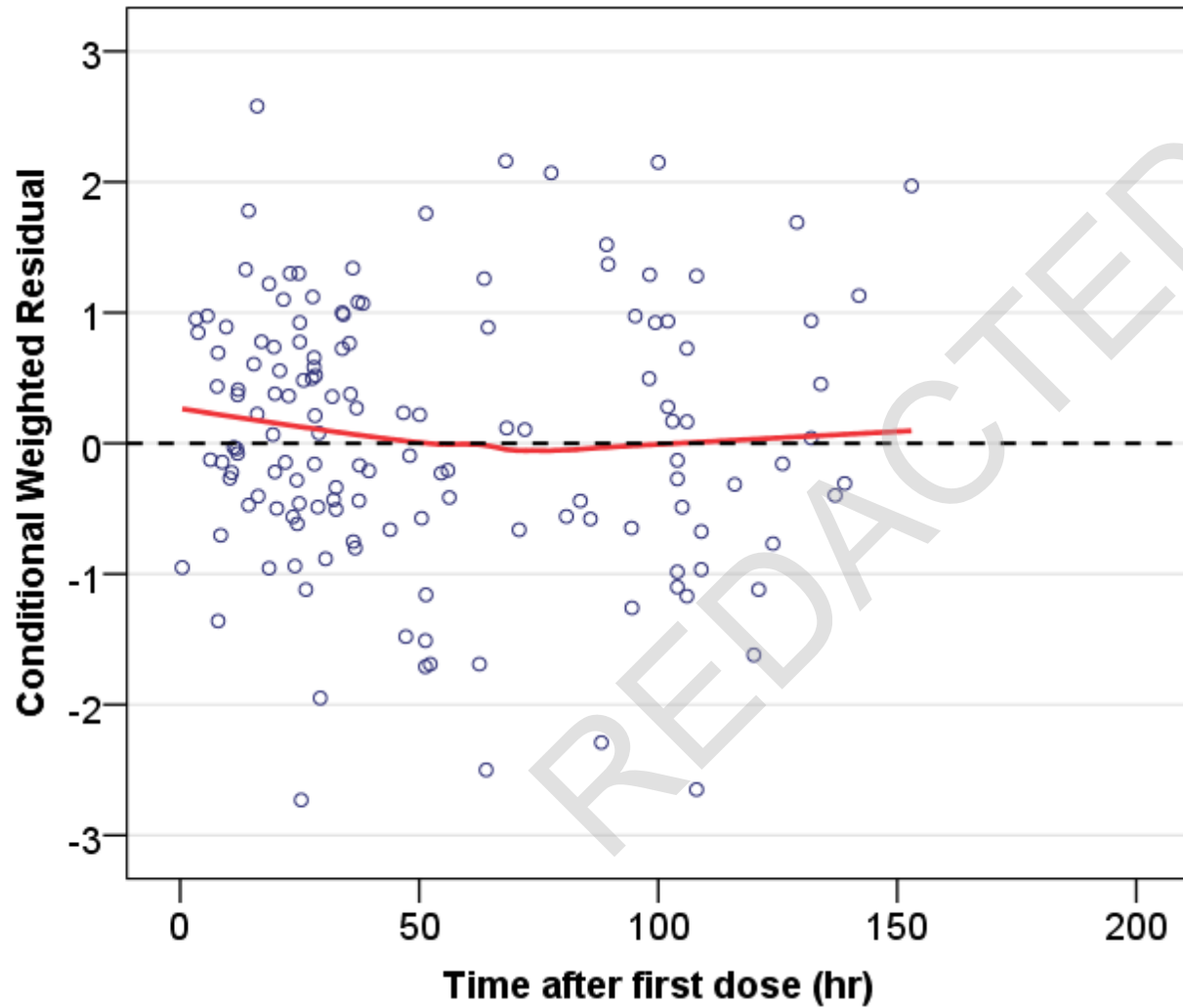


Figure 21. Conditional Weighted Residual vs Population Predicted Concentration - Base Model

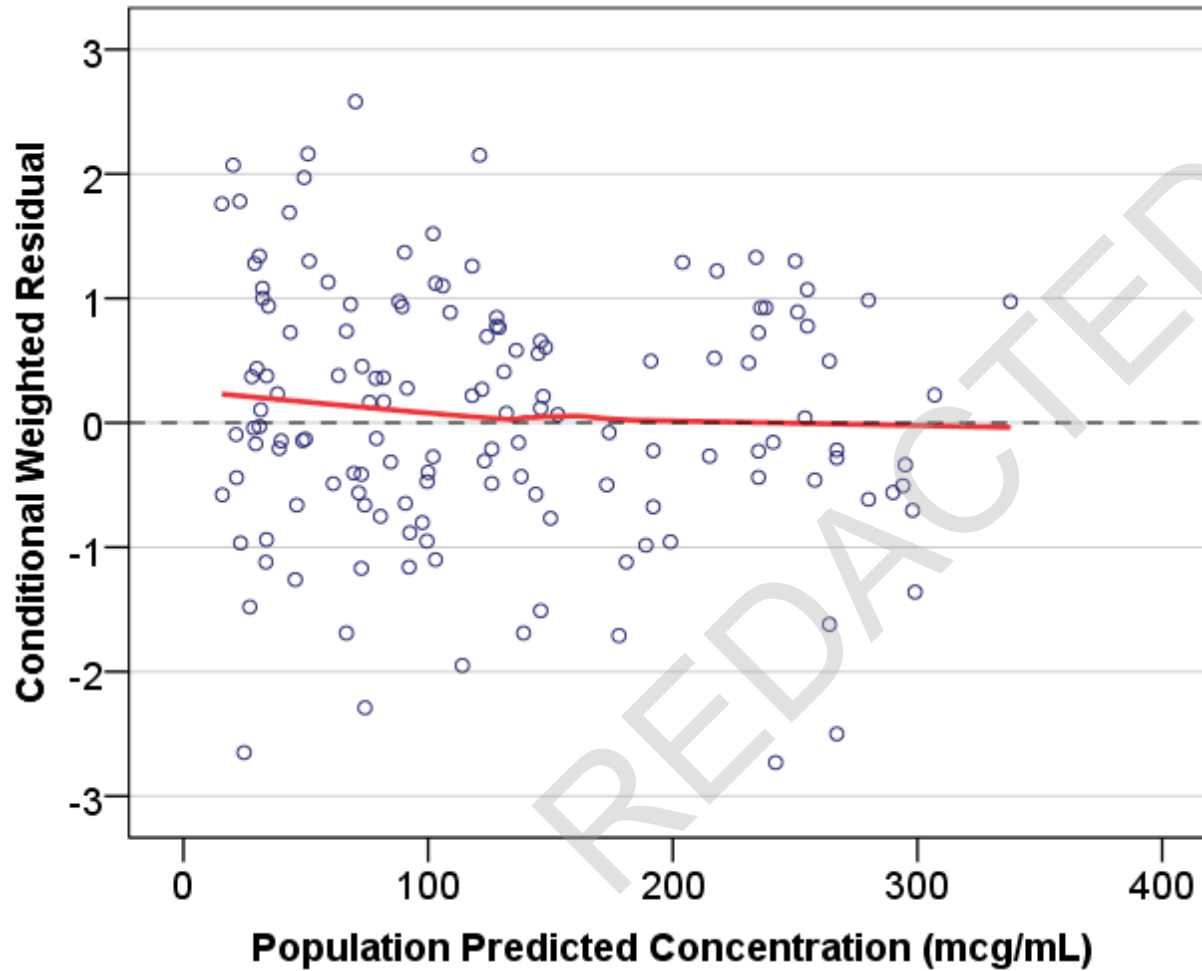


Figure 22. Ln(DV/IPRED) vs Time After Dose - Base Model

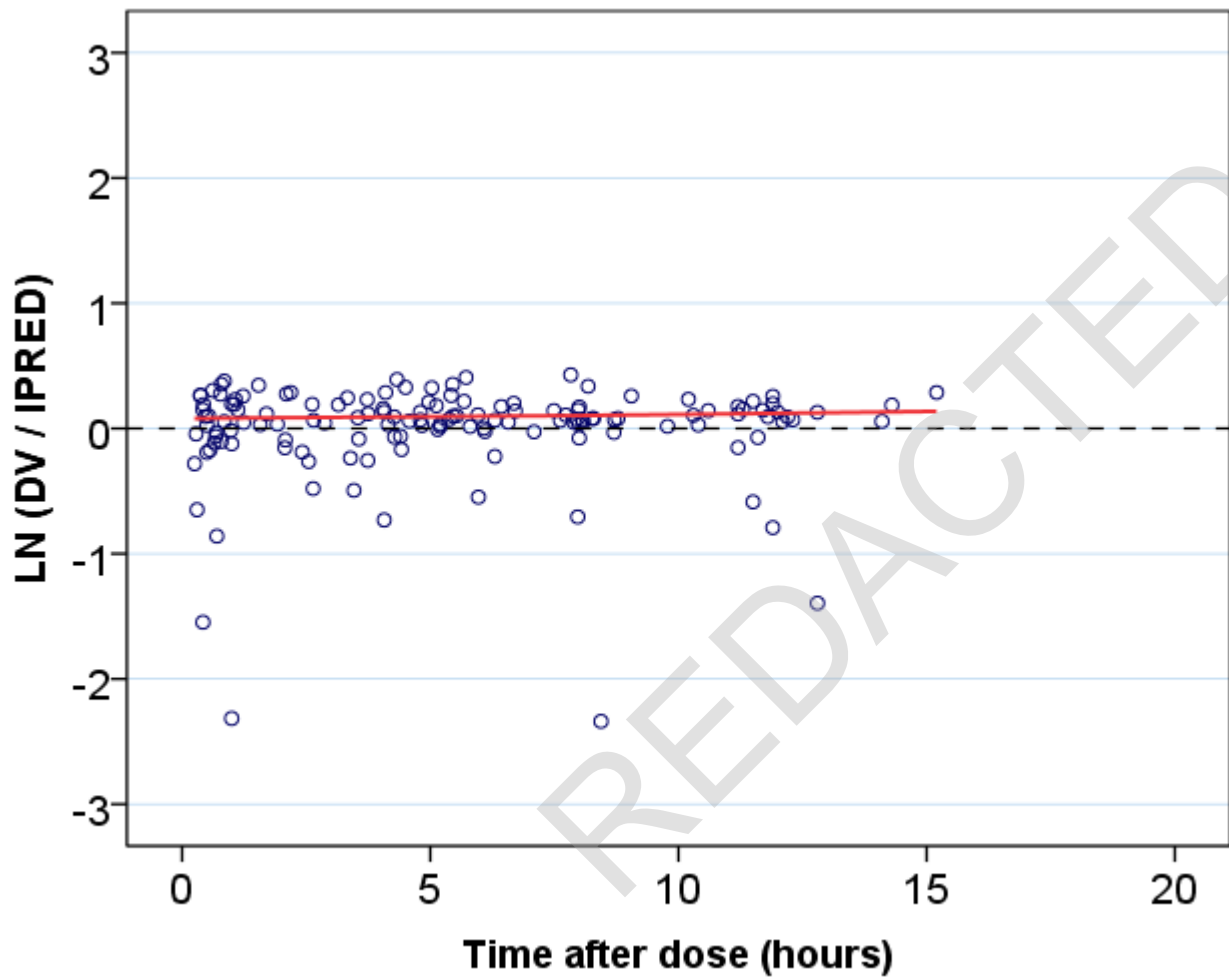


Figure 23. Ln(DV/IPRED) vs Post-hoc Predicted Concentration - Base Model

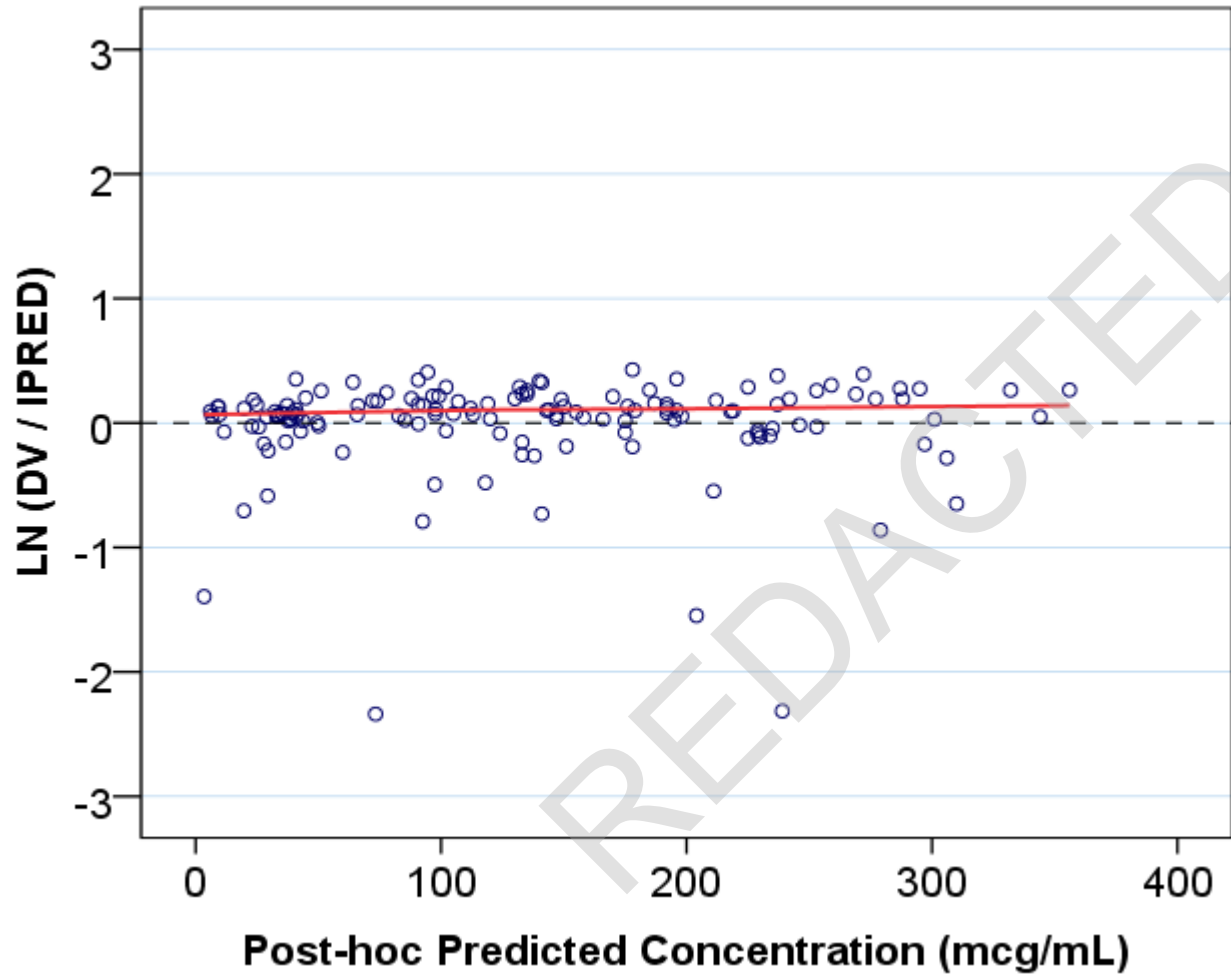


Figure 24. Ln(DV/PRED) vs Time After Dose - Base Model

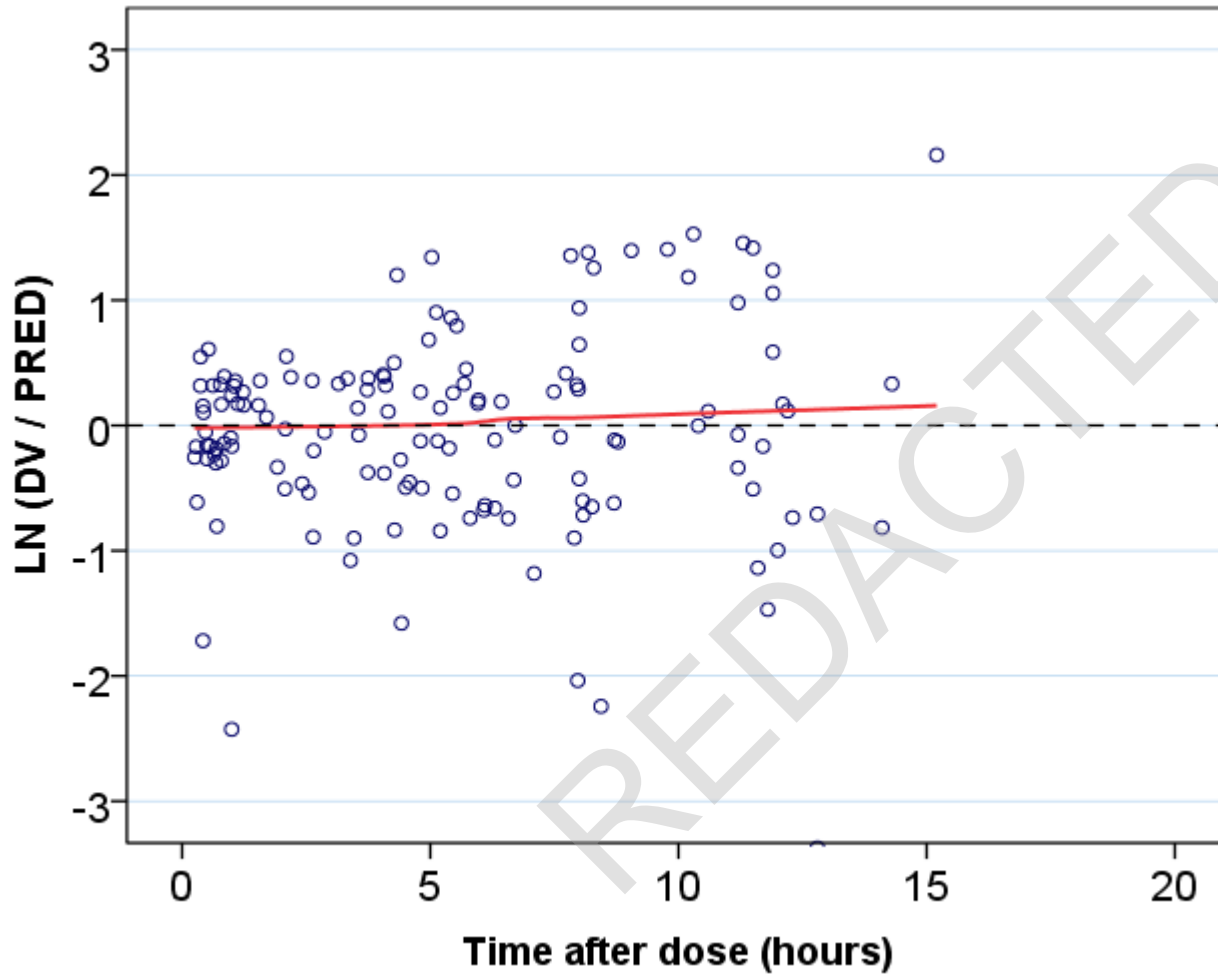


Figure 25. Observed vs Population Predicted Concentrations - Final Model

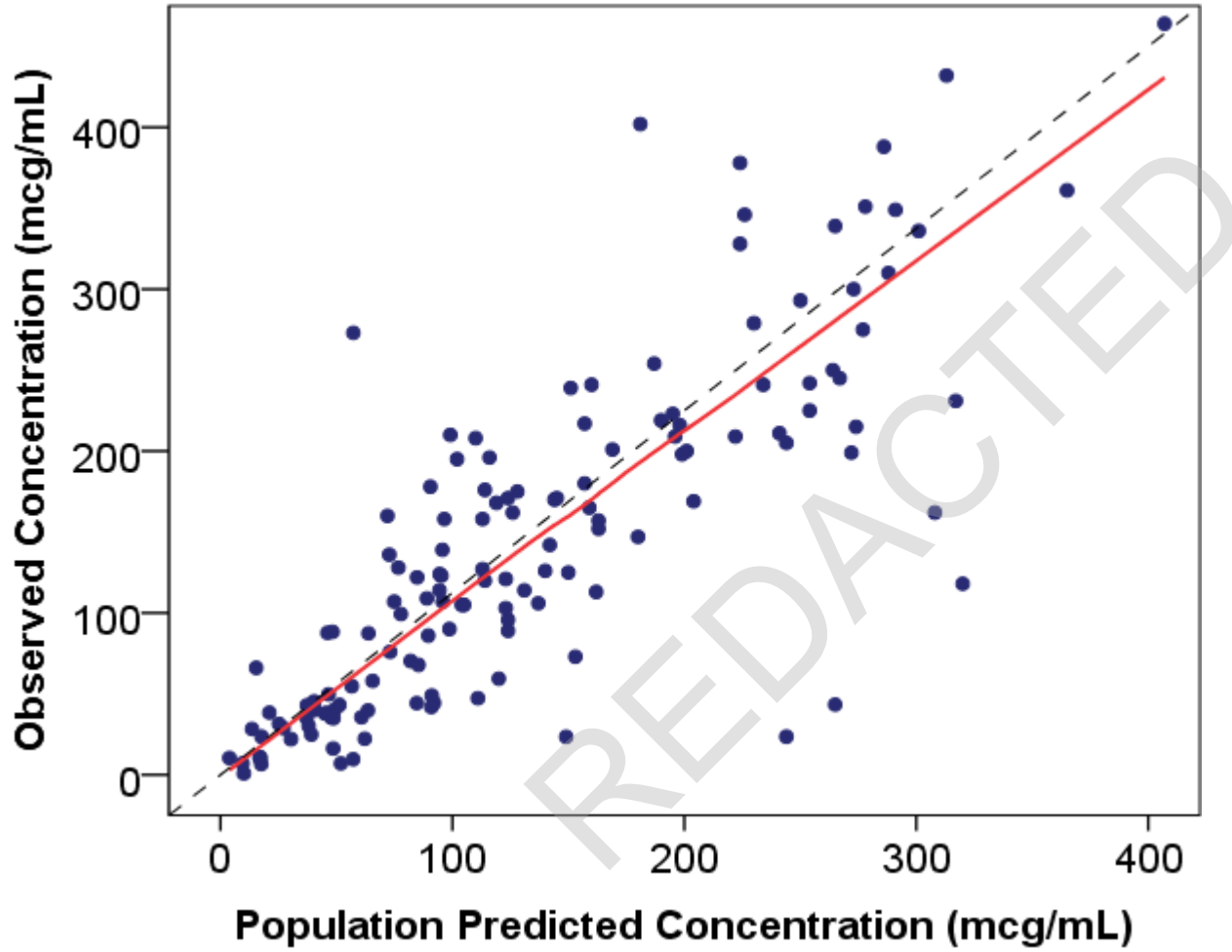


Figure 26. Observed vs Post-hoc Predicted Concentrations - Final Model

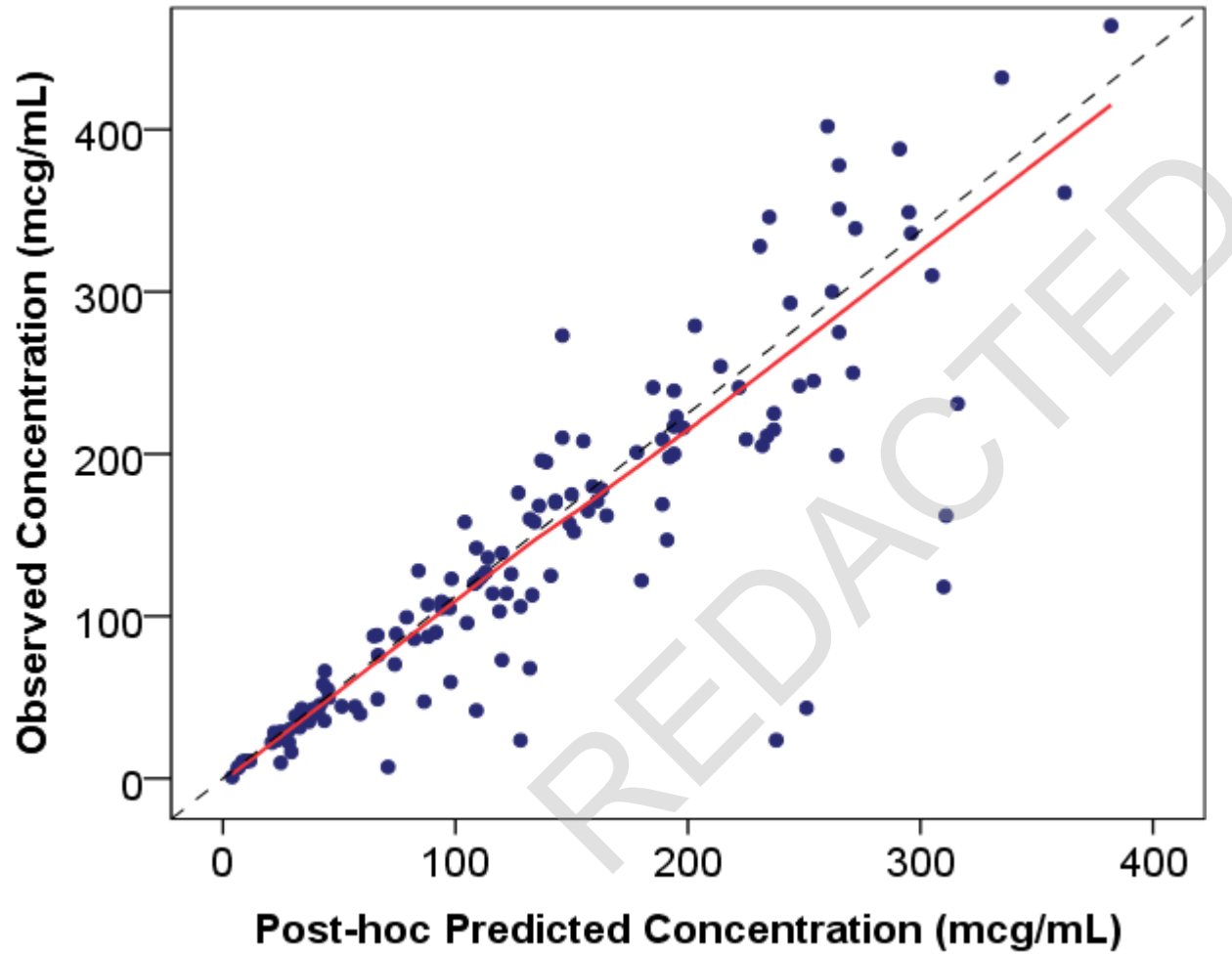


Figure 27. Conditional Weighted Residual vs Time After First Dose - Final Model

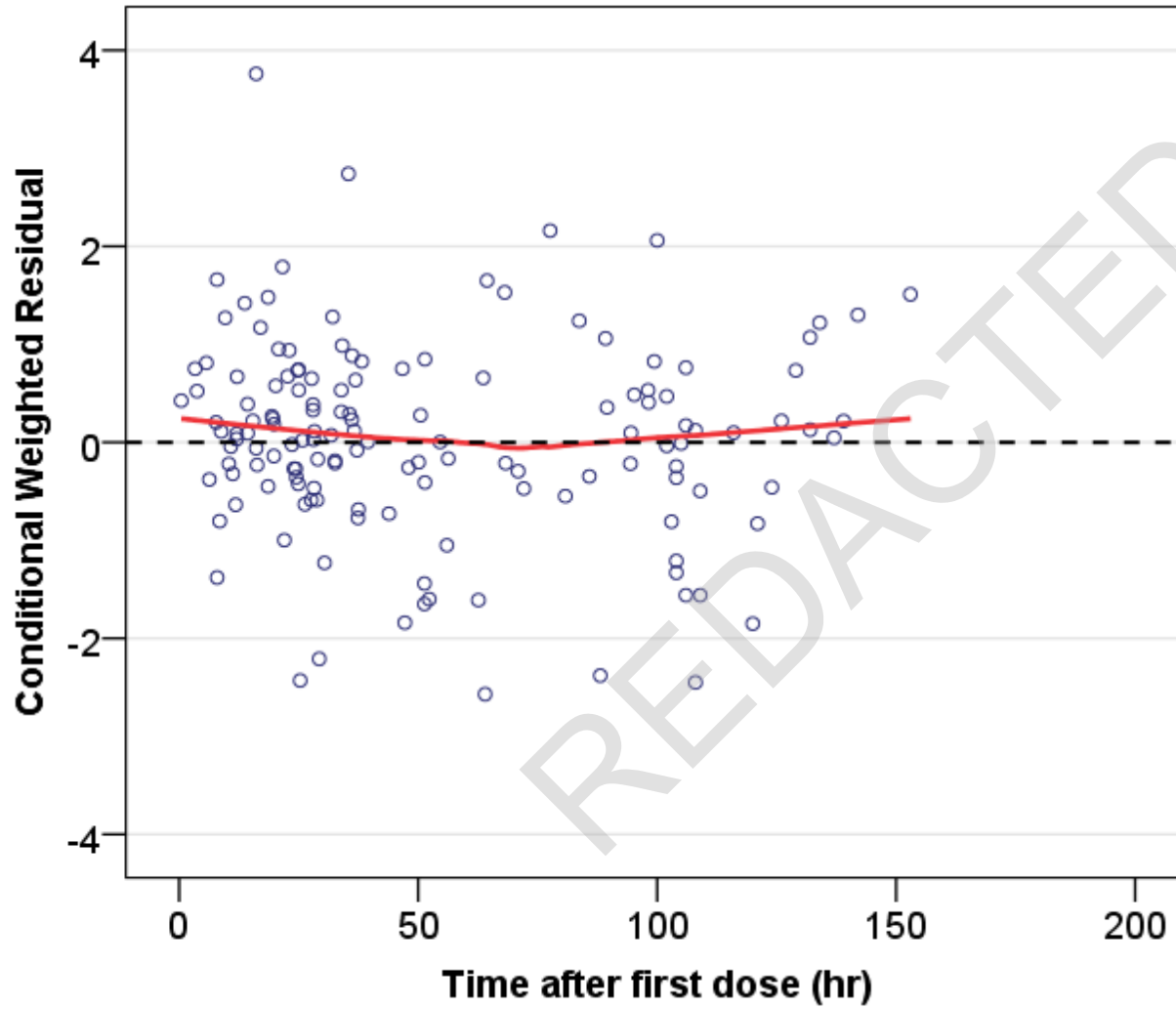


Figure 28. Conditional Weighted Residual vs Population Predicted Concentration - Final Model

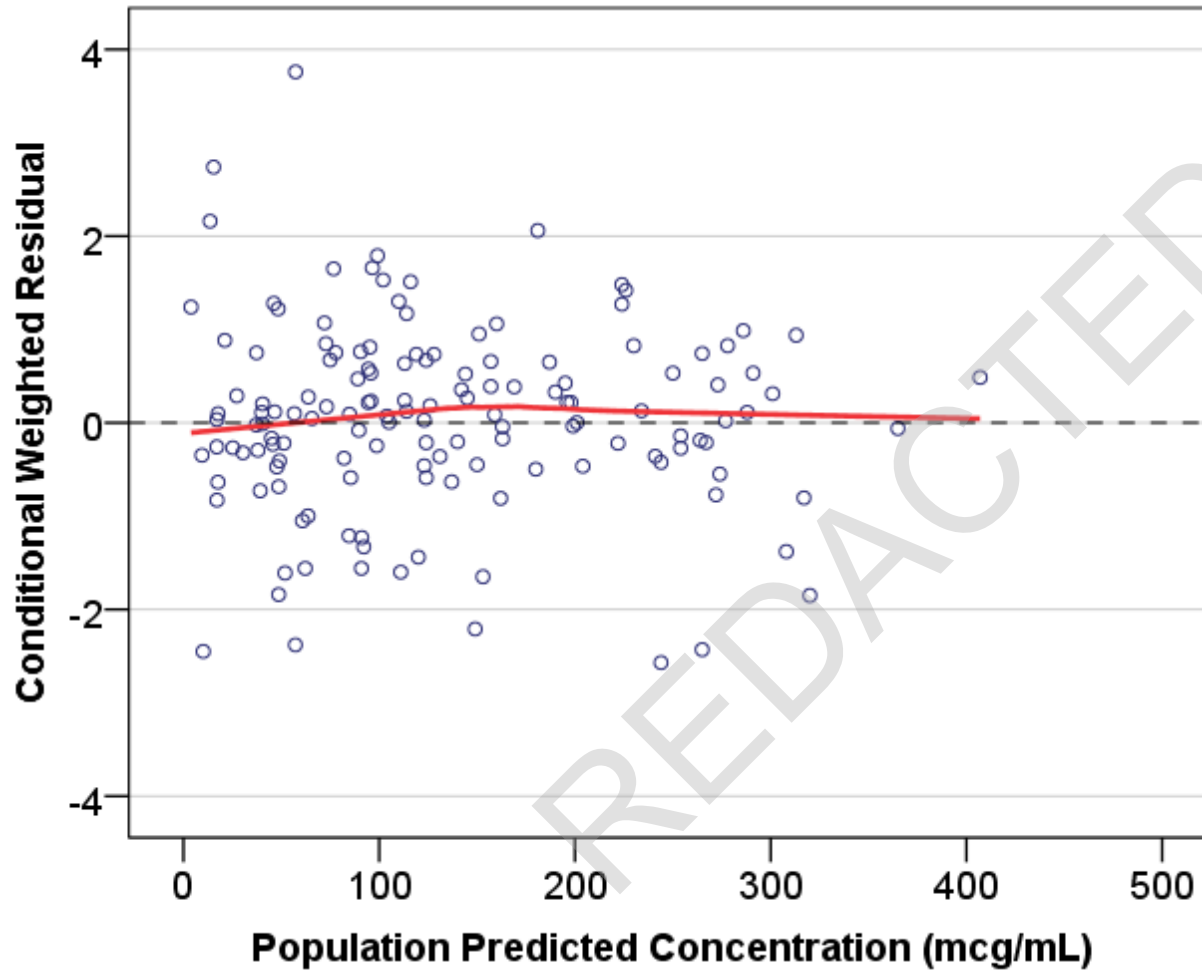


Figure 29. LN (DV/IPRED) vs Time After Dose - Final Model

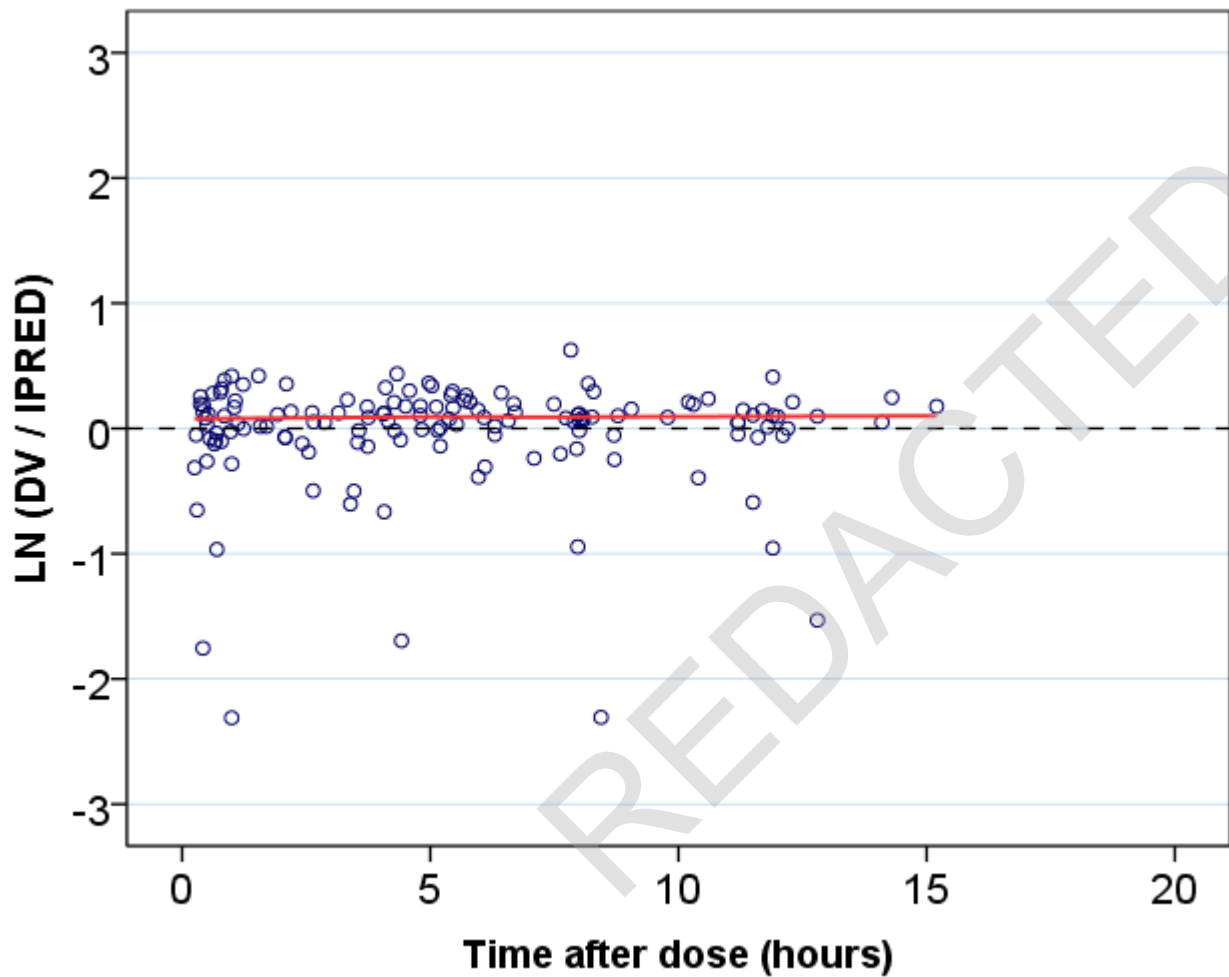


Figure 30. Ln(DV/IPRED) vs Post-hoc Individual Predicted Concentration - Final Model

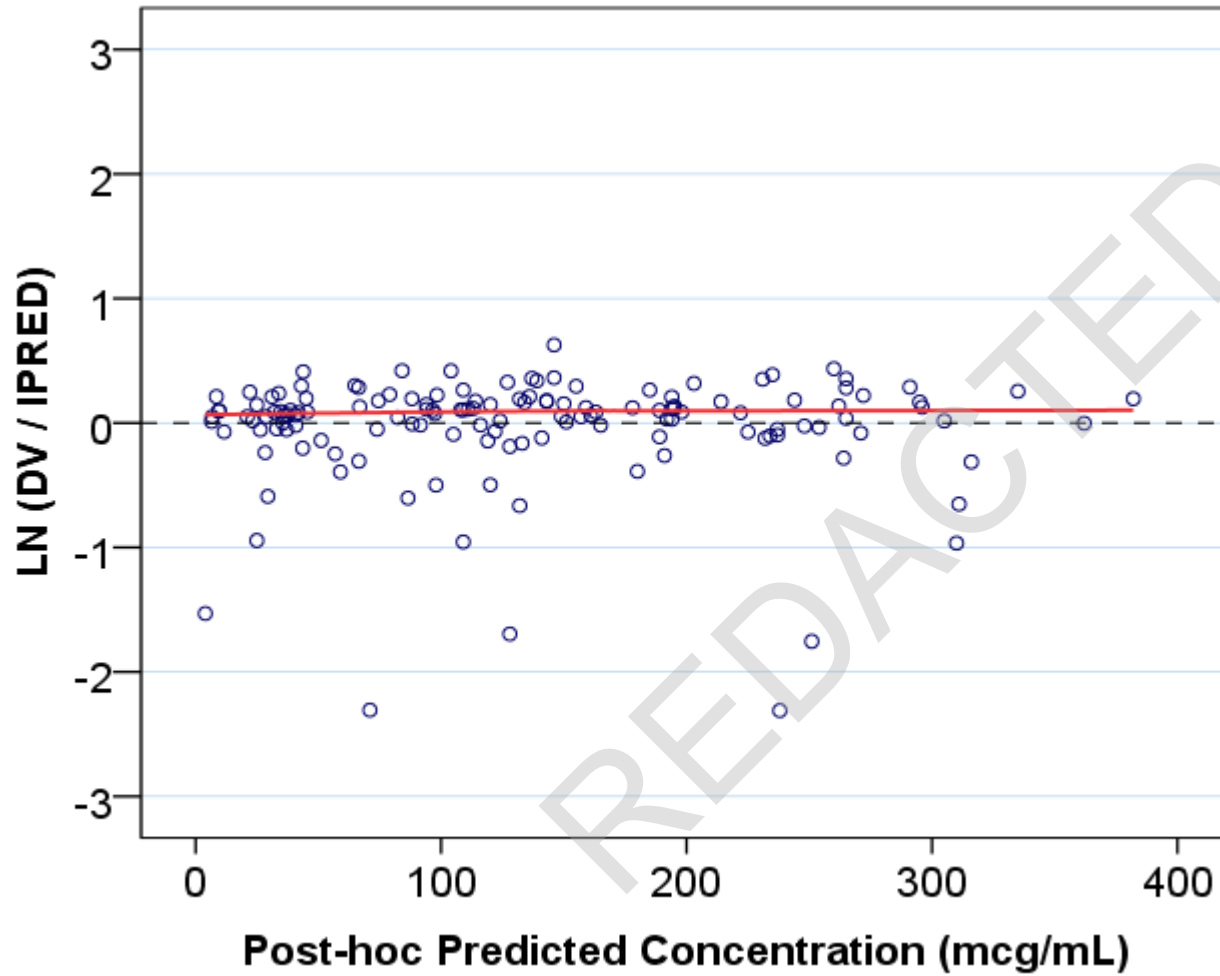


Figure 31. Ln(DV/PRED) vs Time After Dose - Final Model

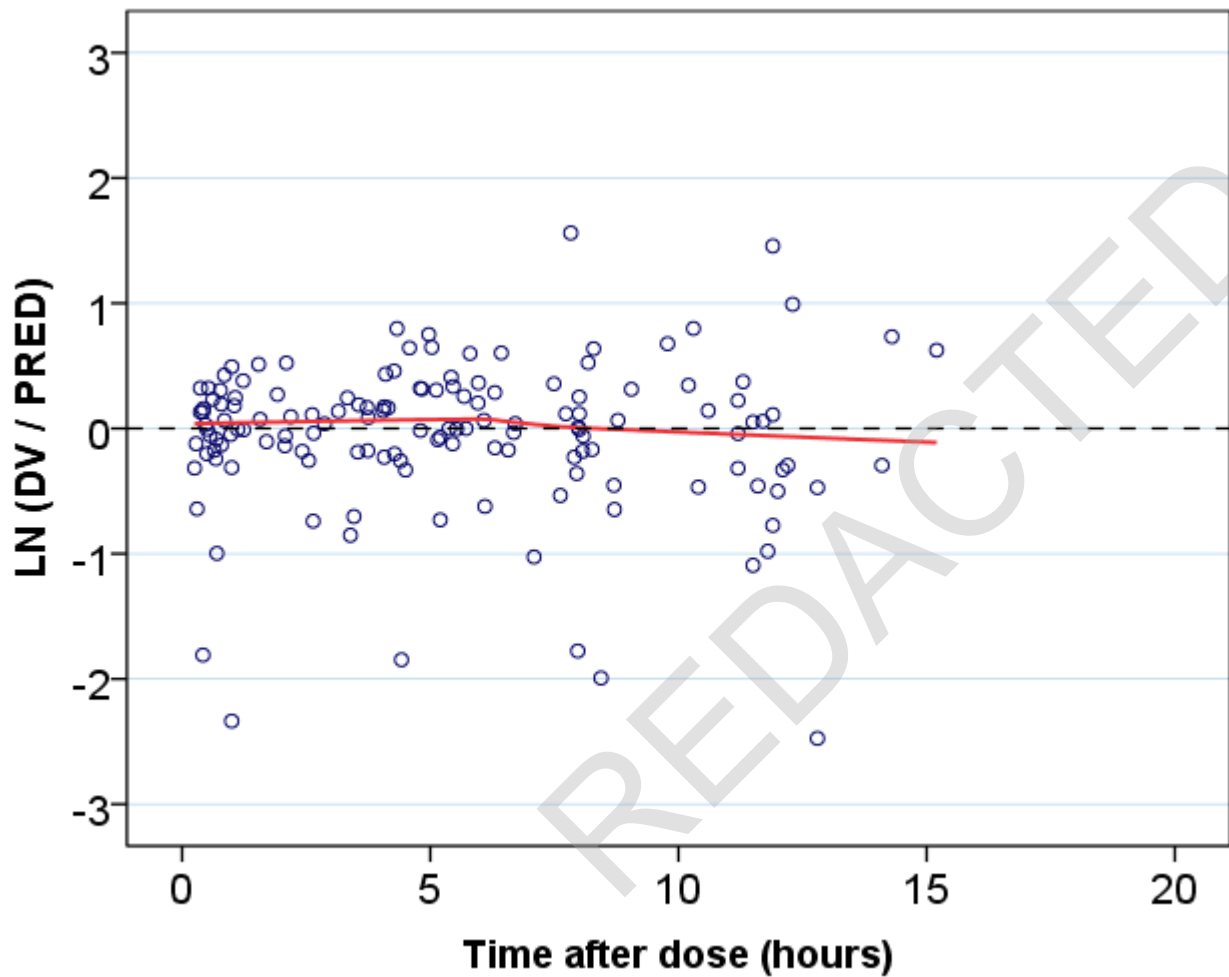
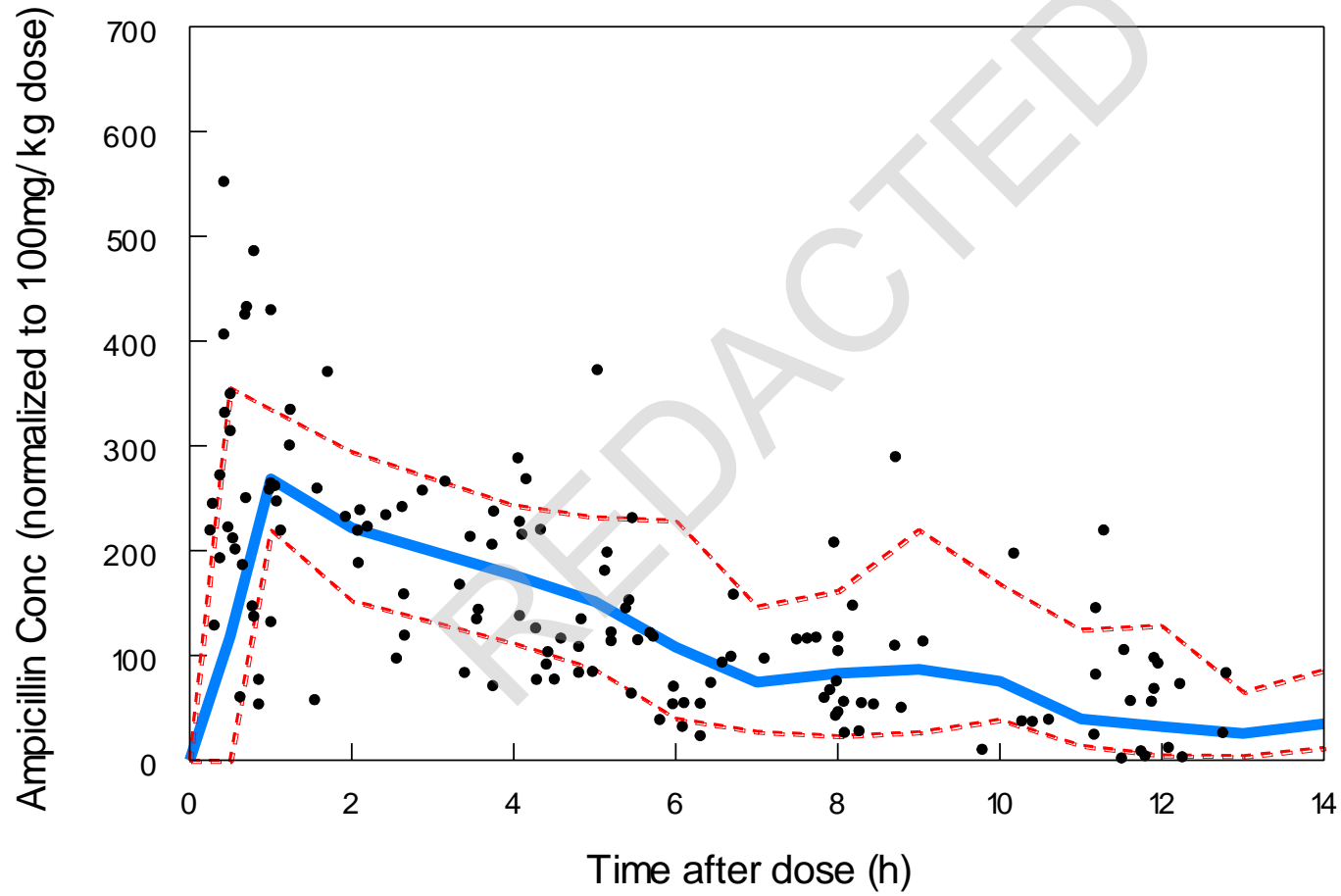


Figure 32. Visual Predictive Check - Final Model

Median with 90%CI



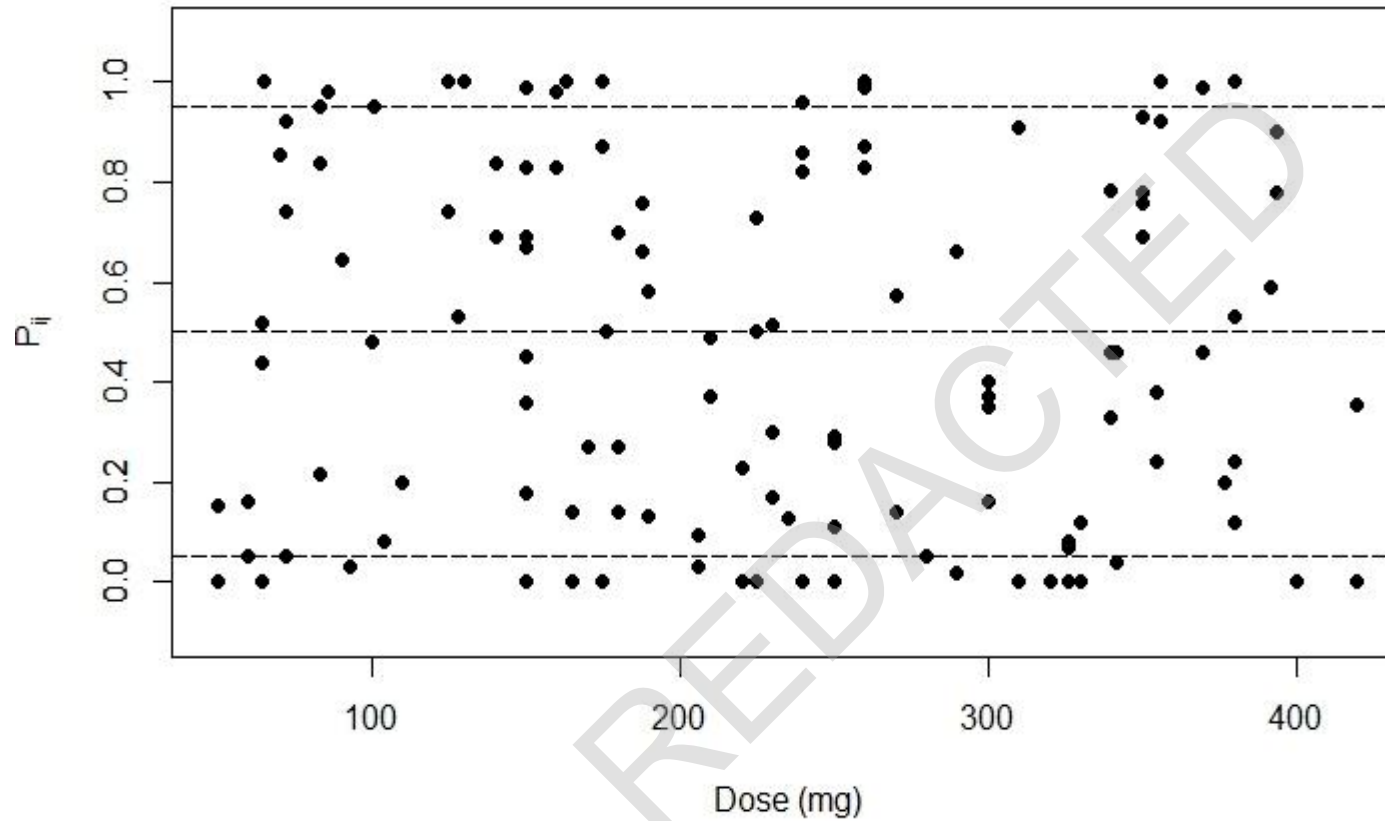


Figure 33. Standardized Visual Predictive Check (SVPC) Plot by Dose - Final Model

Circles represent calculated P_{ij} for each observation versus dose; dashed line, model-predicted 5th, 50th, and 95th percentiles of model-predicted P_{ij} .

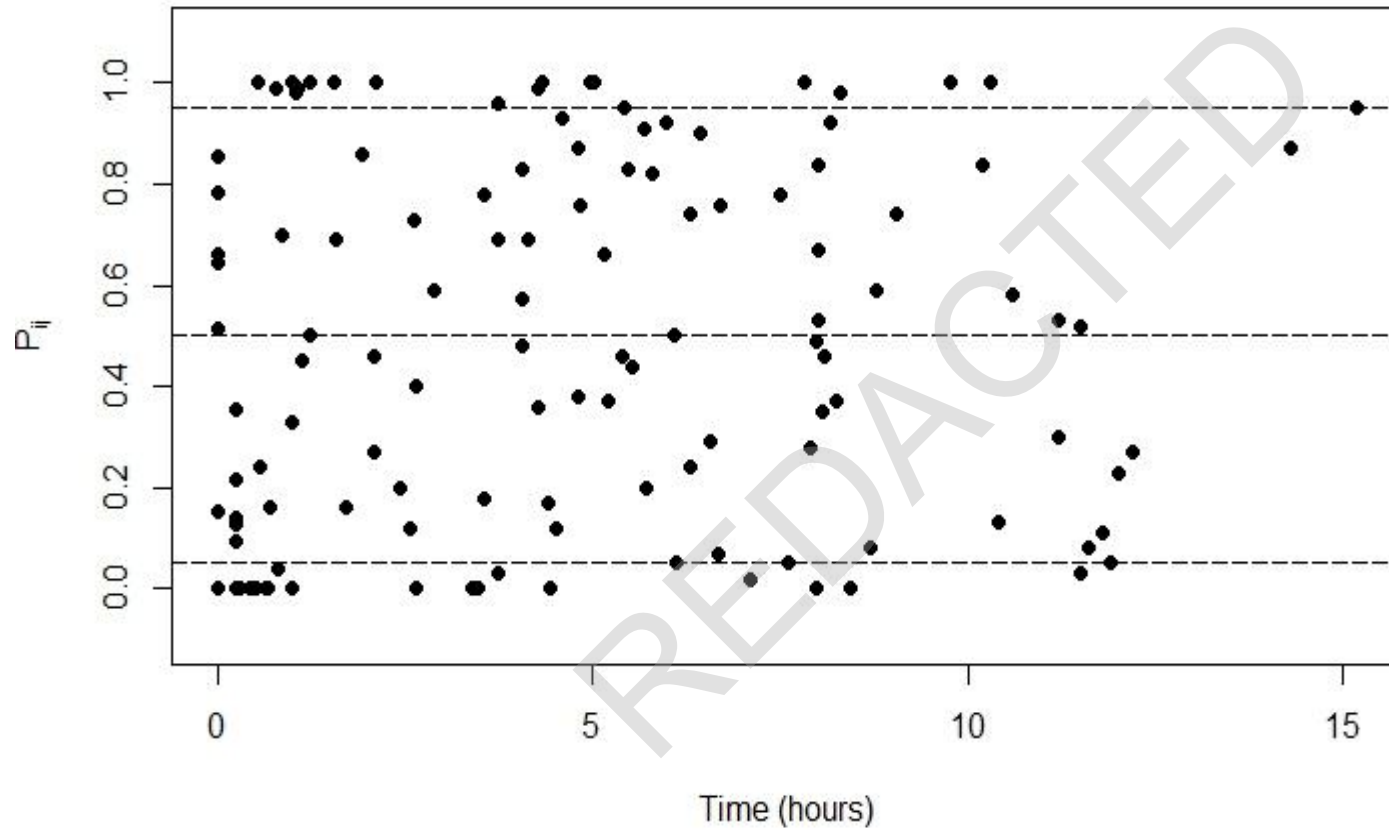
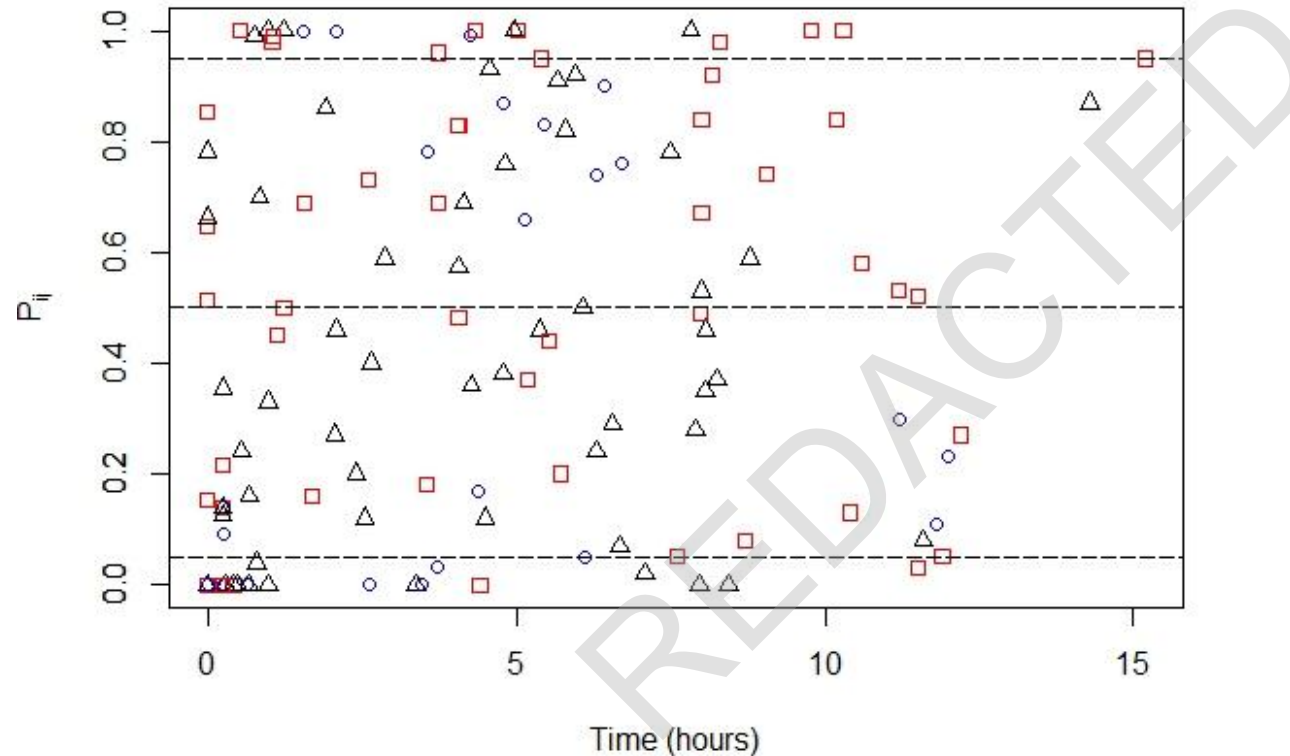


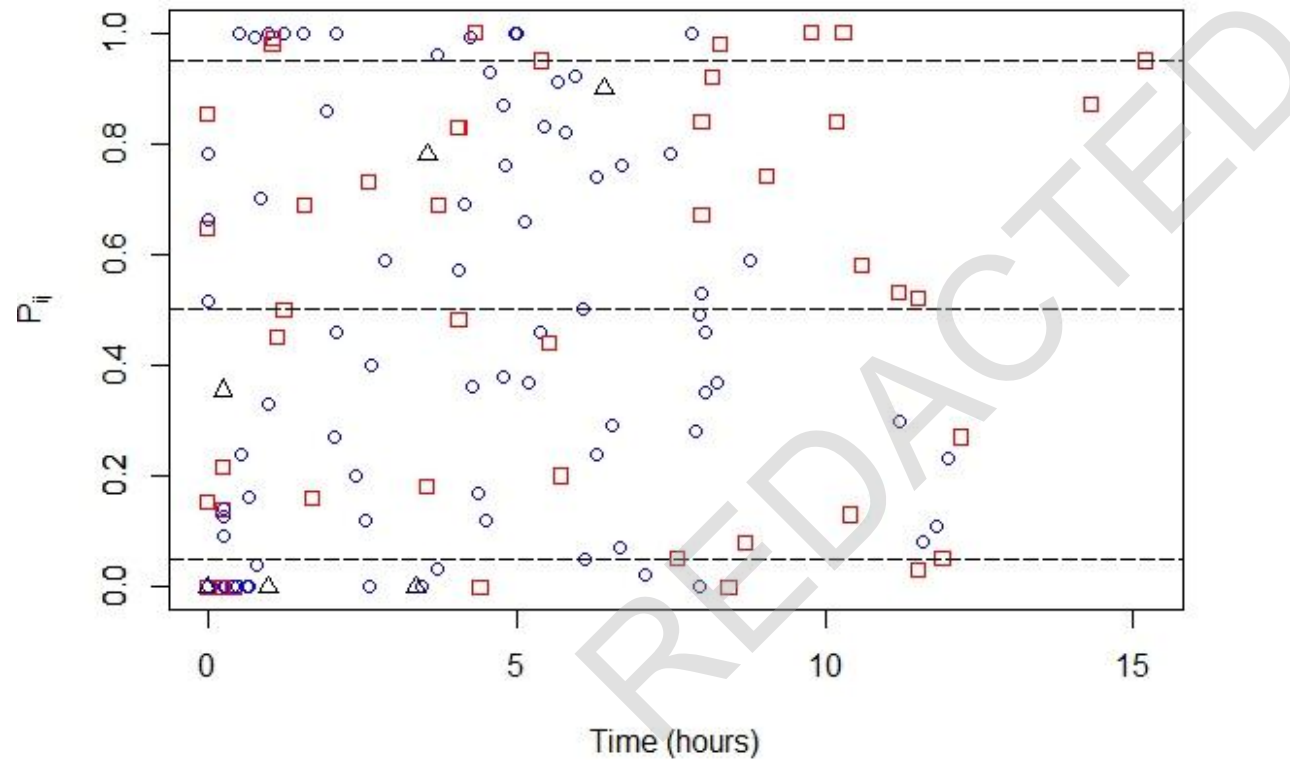
Figure 34. Standardized Visual Predictive Check (SVPC) Plot by Time - Final Model

Circles represent calculated P_{ij} for each observation versus time; dashed line, model-predicted 5th, 50th, and 95th percentiles of model-predicted P_{ij}.

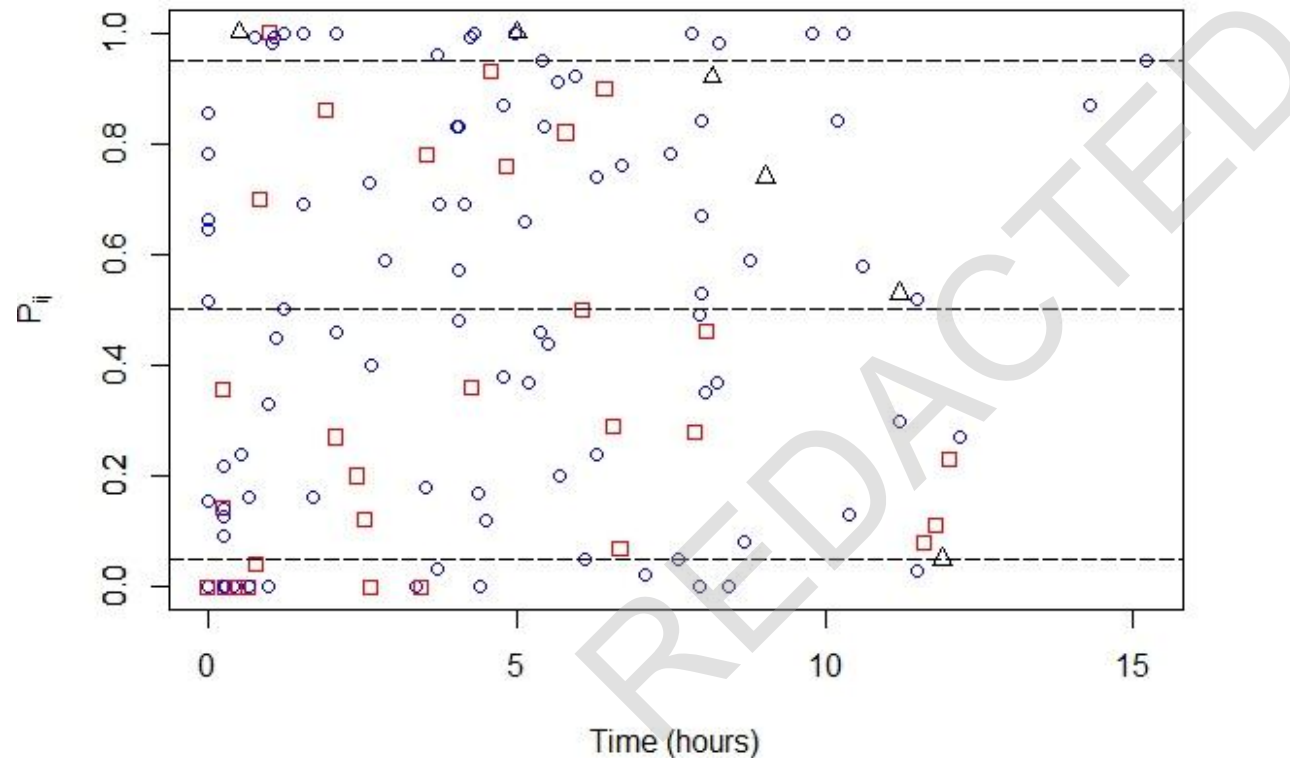
REDACTED

Figure 35. Standardized Visual Predictive Check (SVPC) Plot by Post-menstrual Age - Final Model

Symbols represent calculated P_{ij} for each observation, with red square for subjects with post-menstrual age < 35 weeks, blue circle for post-menstrual age 35 to 38 weeks, and black triangle for post-menstrual age > 35 weeks; dashed line, 5th, 50th, and 95th percentiles of the calculated P_{ij} values for all the observations at each time point.

Figure 36. Standardized Visual Predictive Check (SVPC) Plot by Weight - Final Model

Symbols represent calculated P_{ij} for each observation, with red square for subjects with weight < 2 kg, blue circle for weight 2 to 4 kg, and black triangle for weight > 4 kg; dashed line, 5th, 50th, and 95th percentiles of the calculated P_{ij} values for all the observations at each time point.

Figure 37. Standardized Visual Predictive Check (SVPC) Plot by Serum Creatinine - Final Model

Symbols represent calculated P_{ij} for each observation, with red square for subjects with serum creatinine < 0.5 mg/dL, blue circle for serum creatinine 0.5 to 1.0 mg/dL, and black triangle for serum creatinine > 1.0 mg/dL; dashed line, 5th, 50th, and 95th percentiles of the calculated P_{ij} values for all the observations at each time point.

Figure 38. Clearance (L/hr/kg) by Study Group - Final Model

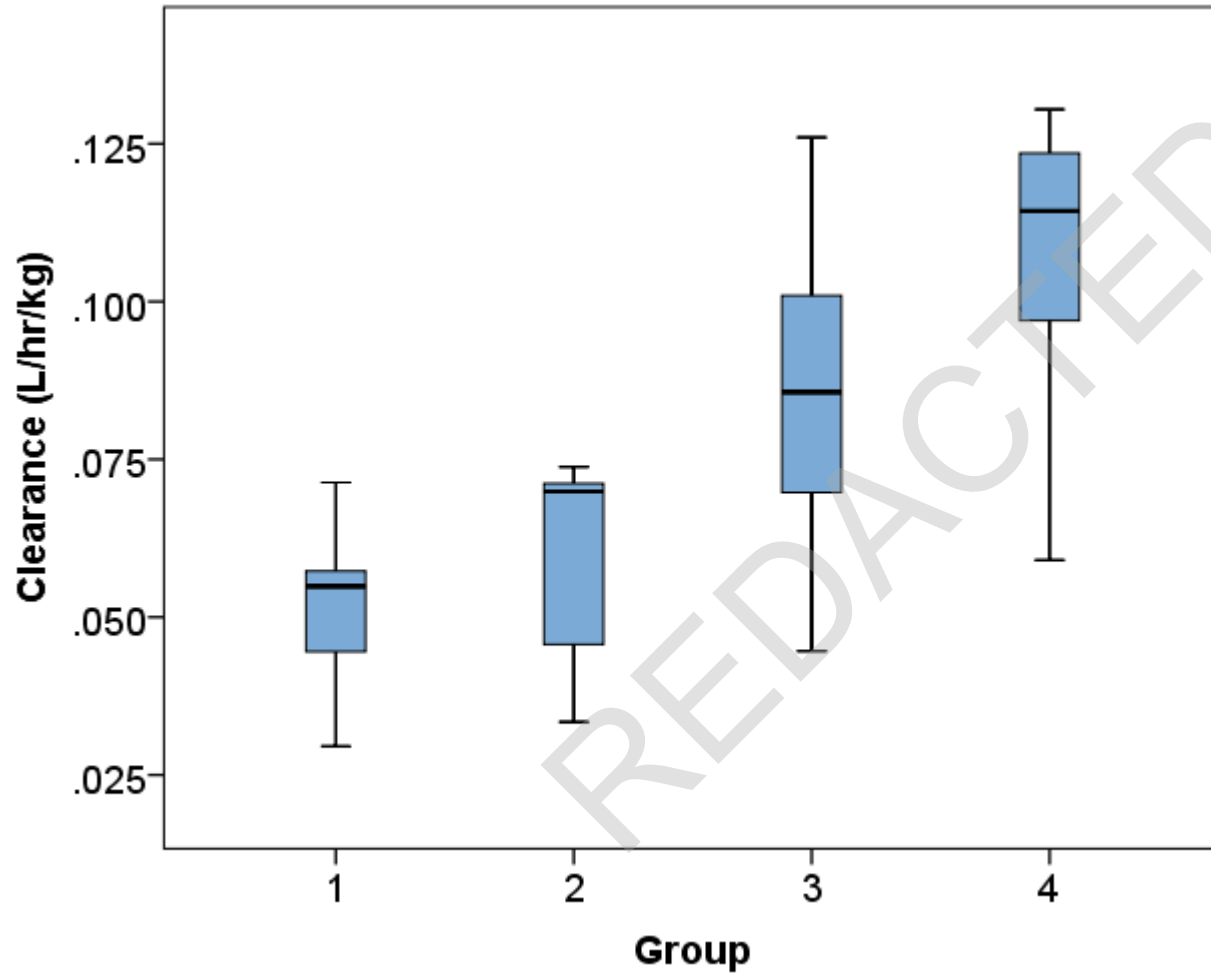


Figure 39. Clearance (L/hr/kg) vs Post-natal Age - Final Model

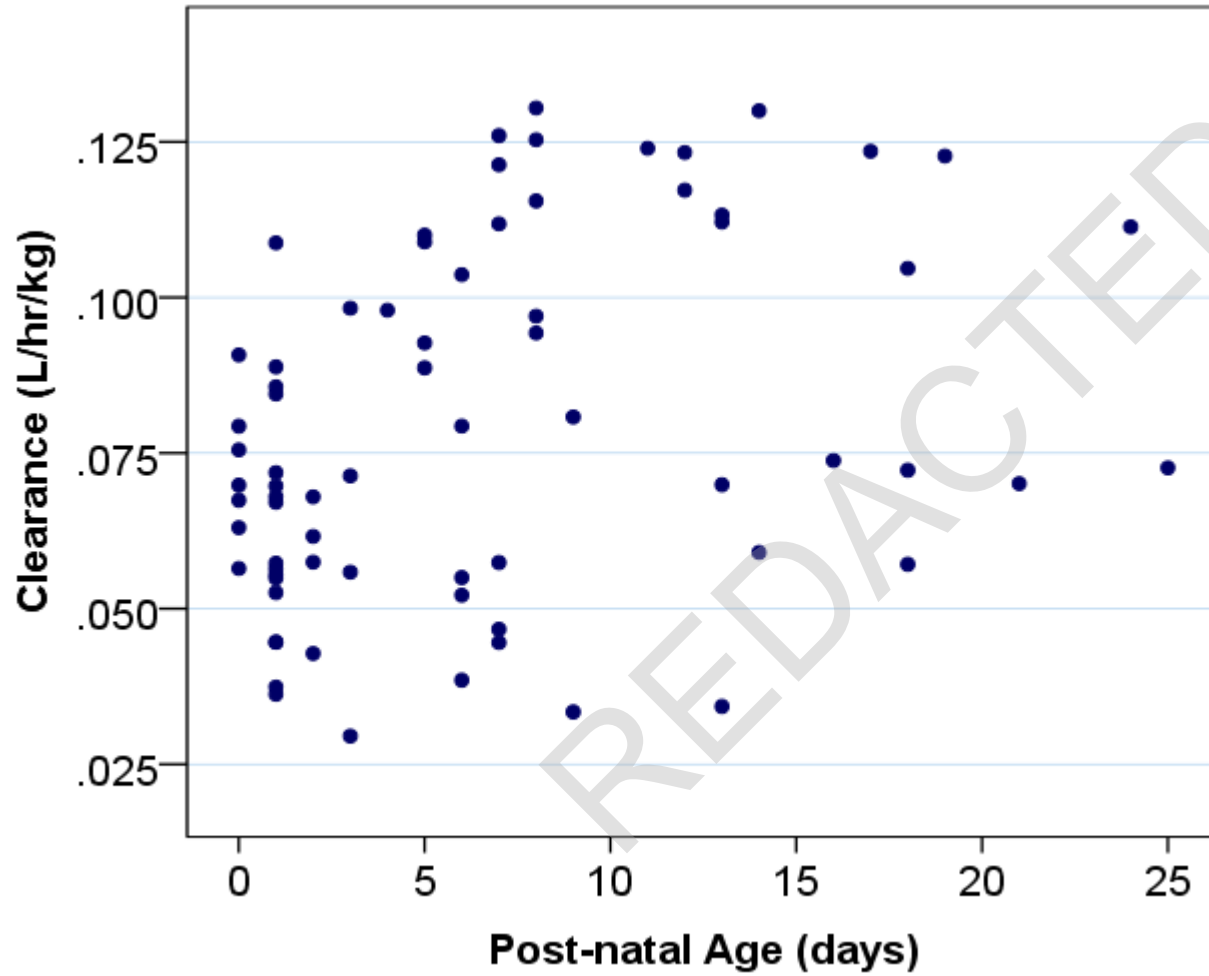


Figure 40. Clearance (L/hr/kg) vs Gestational Age - Final Model

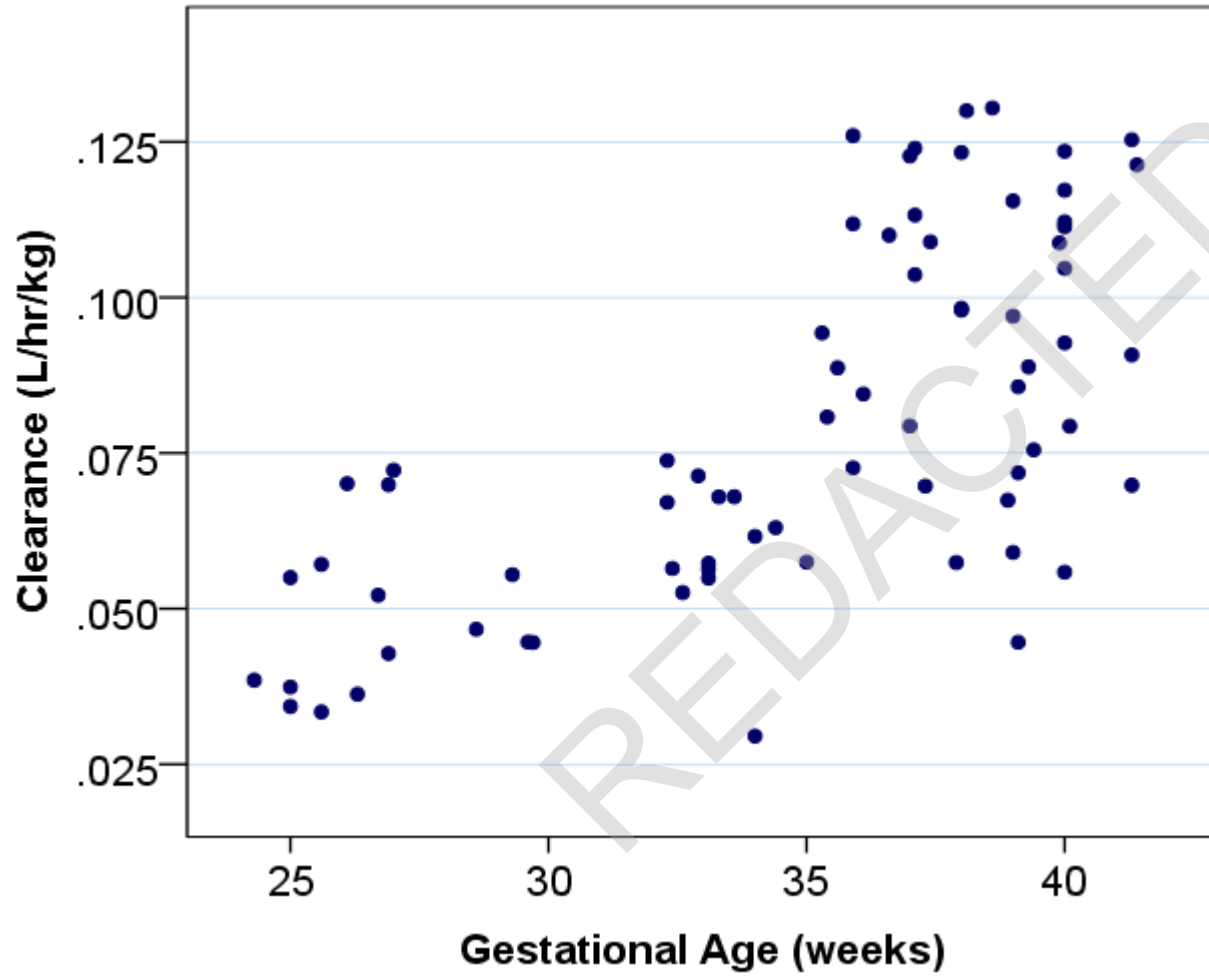


Figure 41. Clearance (L/hr/kg) vs Post-menstrual Age - Final Model

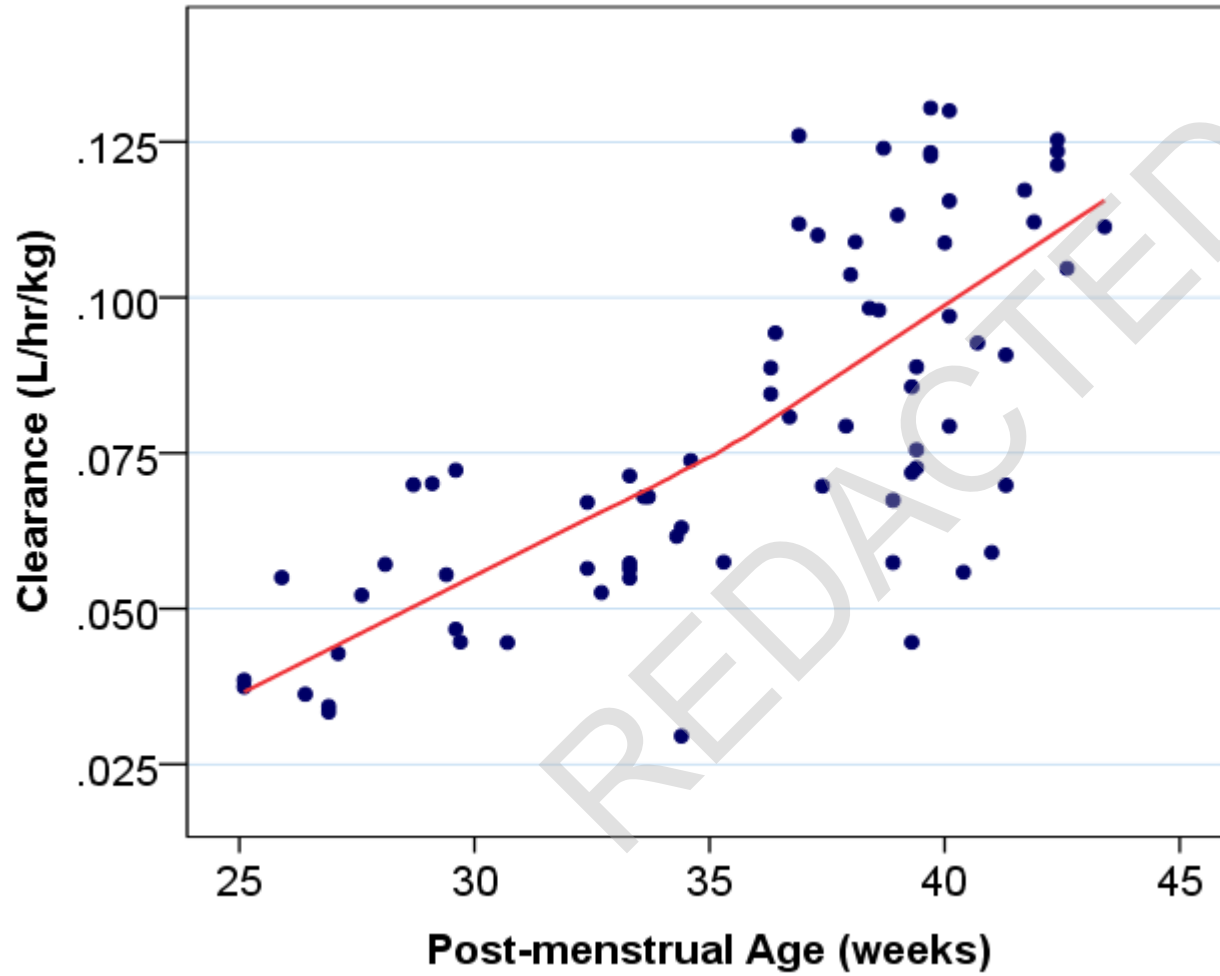


Figure 42. Clearance (L/hr/kg) vs Post-natal Age by Gestational Age Group - Final Model

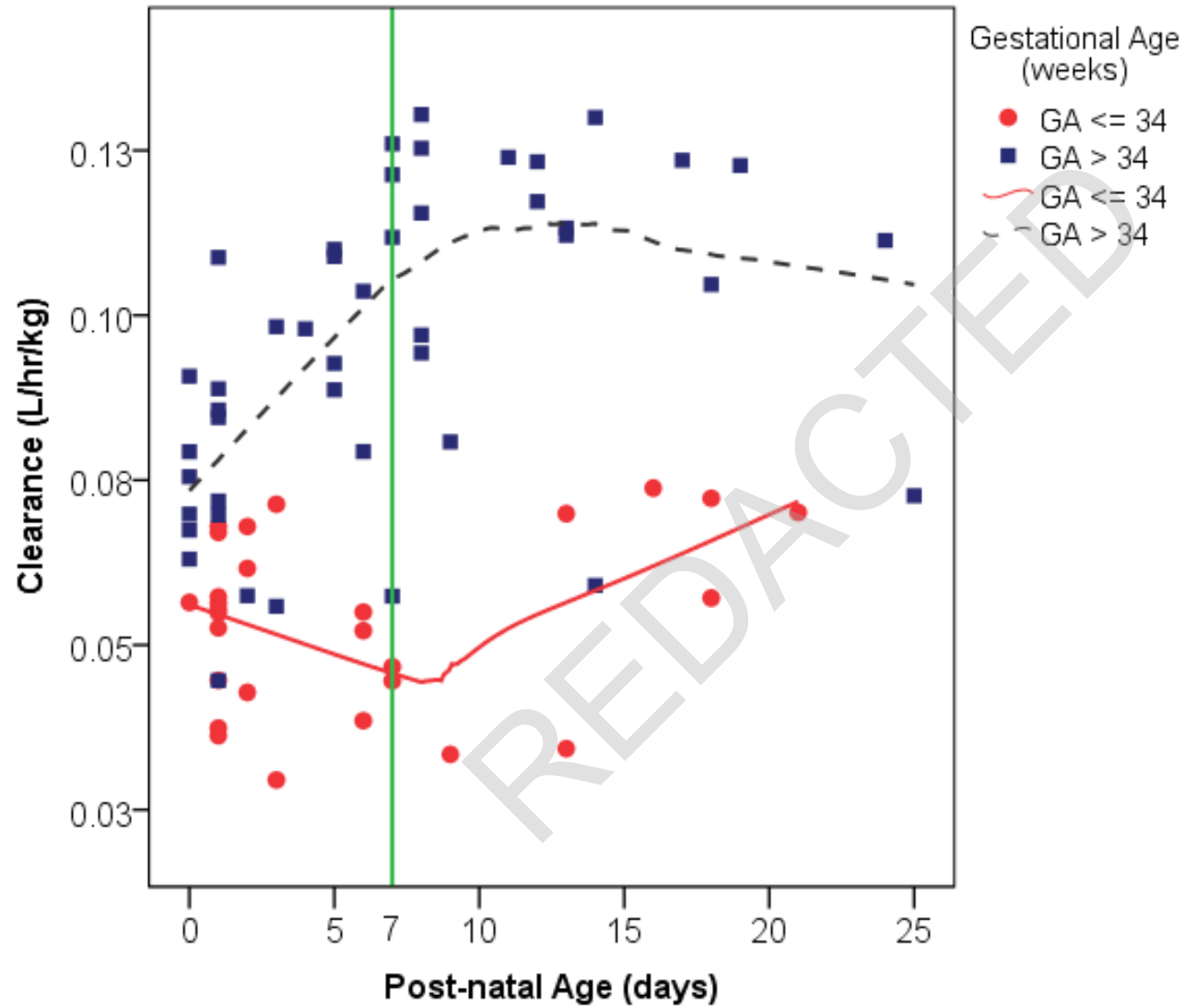


Figure 43. Clearance (L/hr/kg) vs Gestational Age by Post-natal Age Group - Final Model

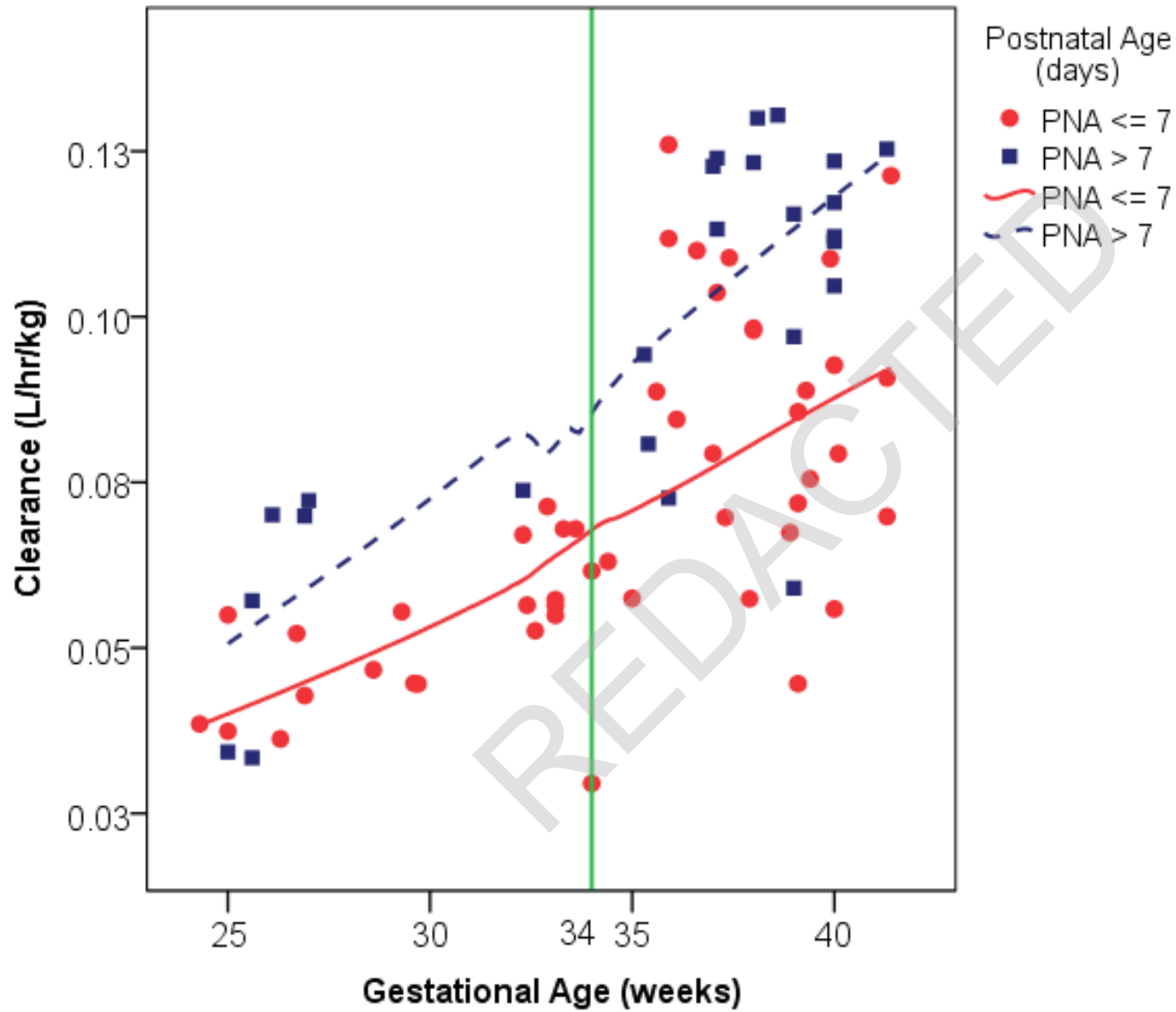


Figure 44. Clearance (L/hr/kg) vs Gestational Age and Post-natal Age - Final Model

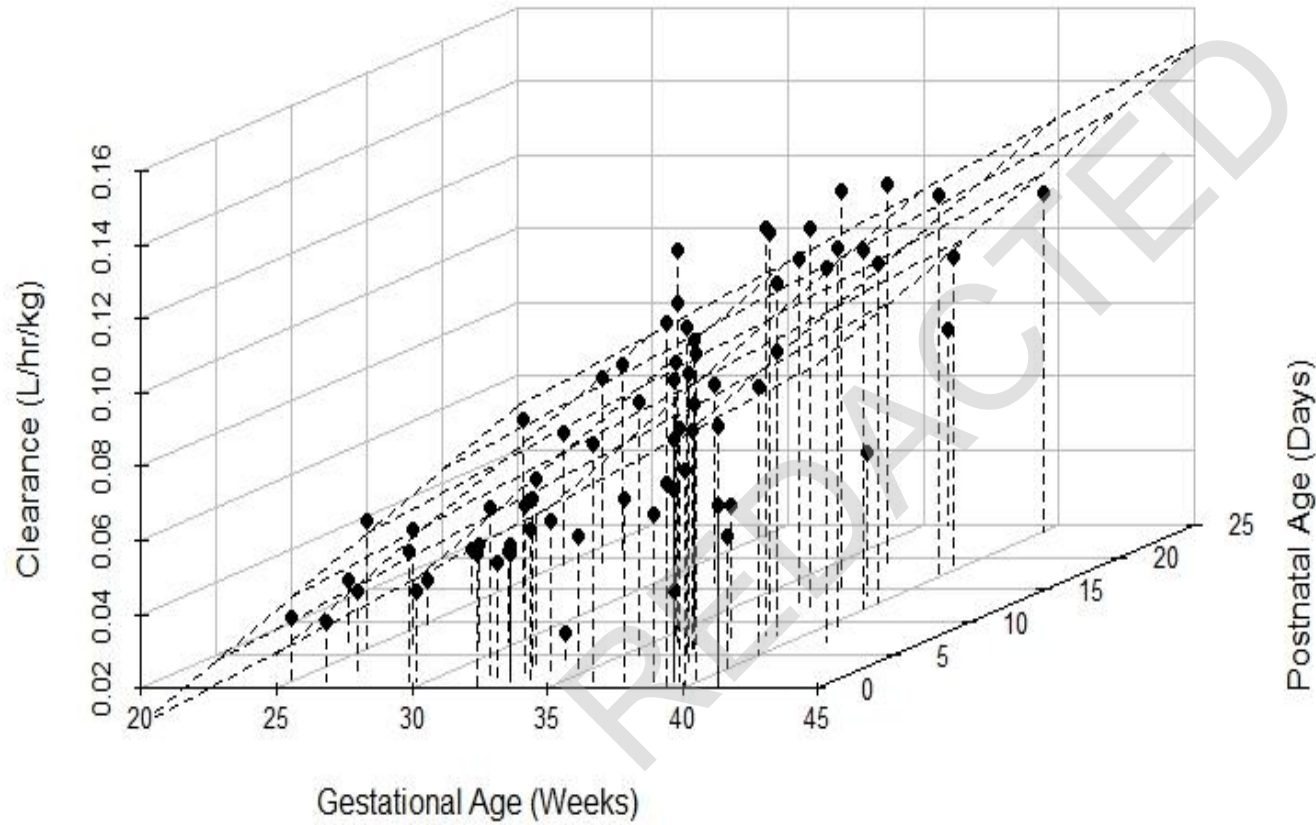


Figure 45. Clearance (L/hr/kg) vs Gestational Age and Post-menstrual Age - Final Model

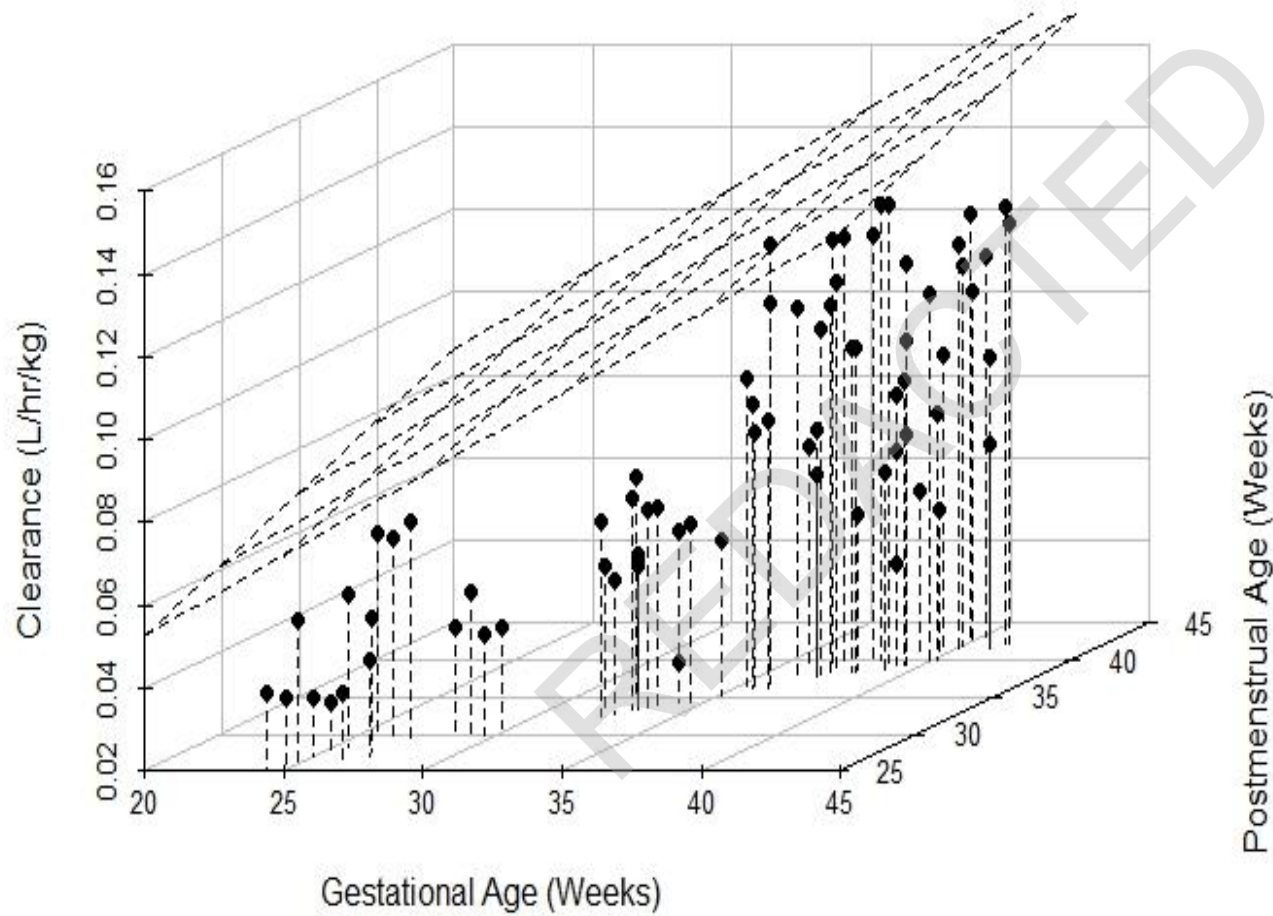


Figure 46. Clearance (L/hr/kg) vs Baseline Serum Creatinine - Final Model

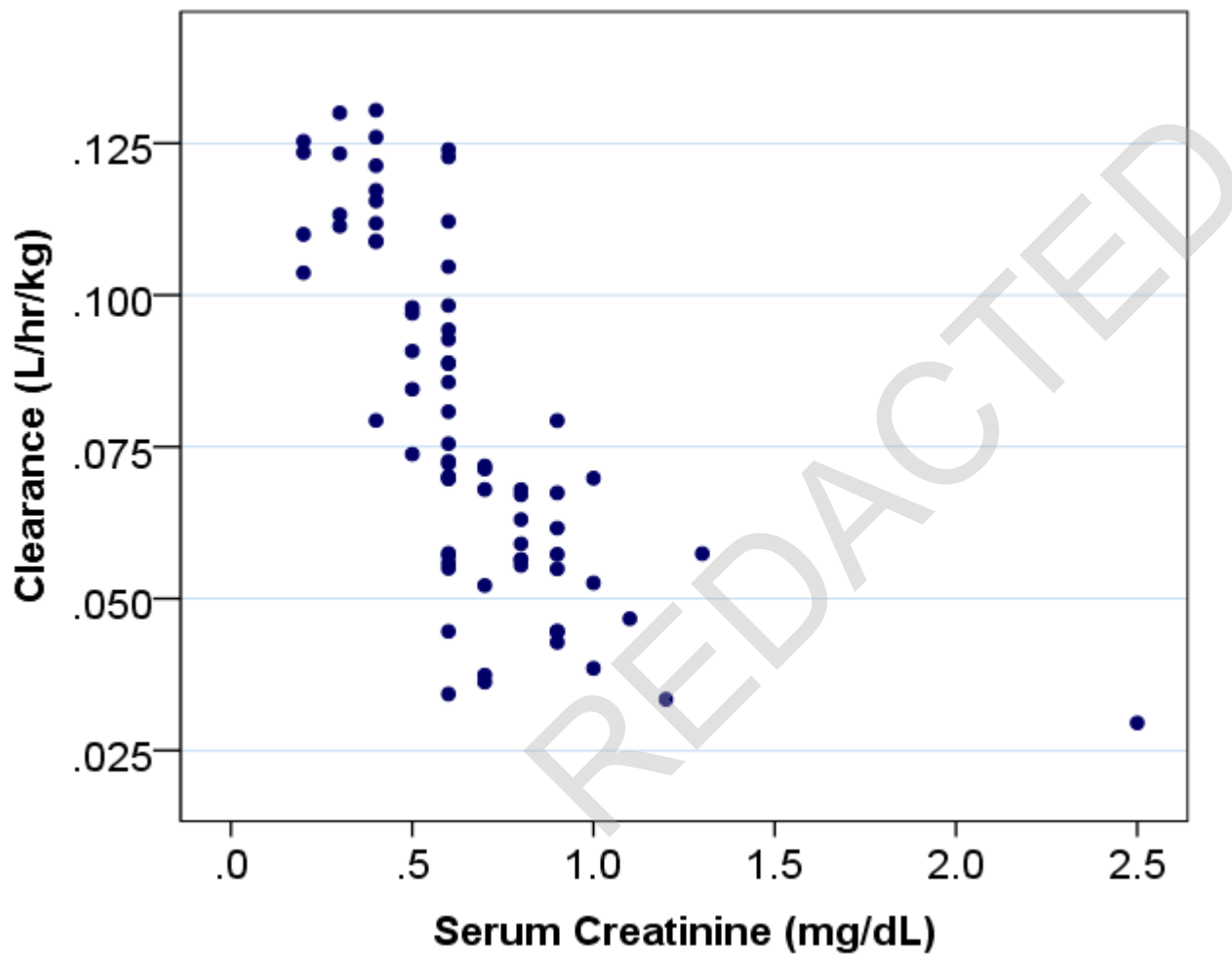
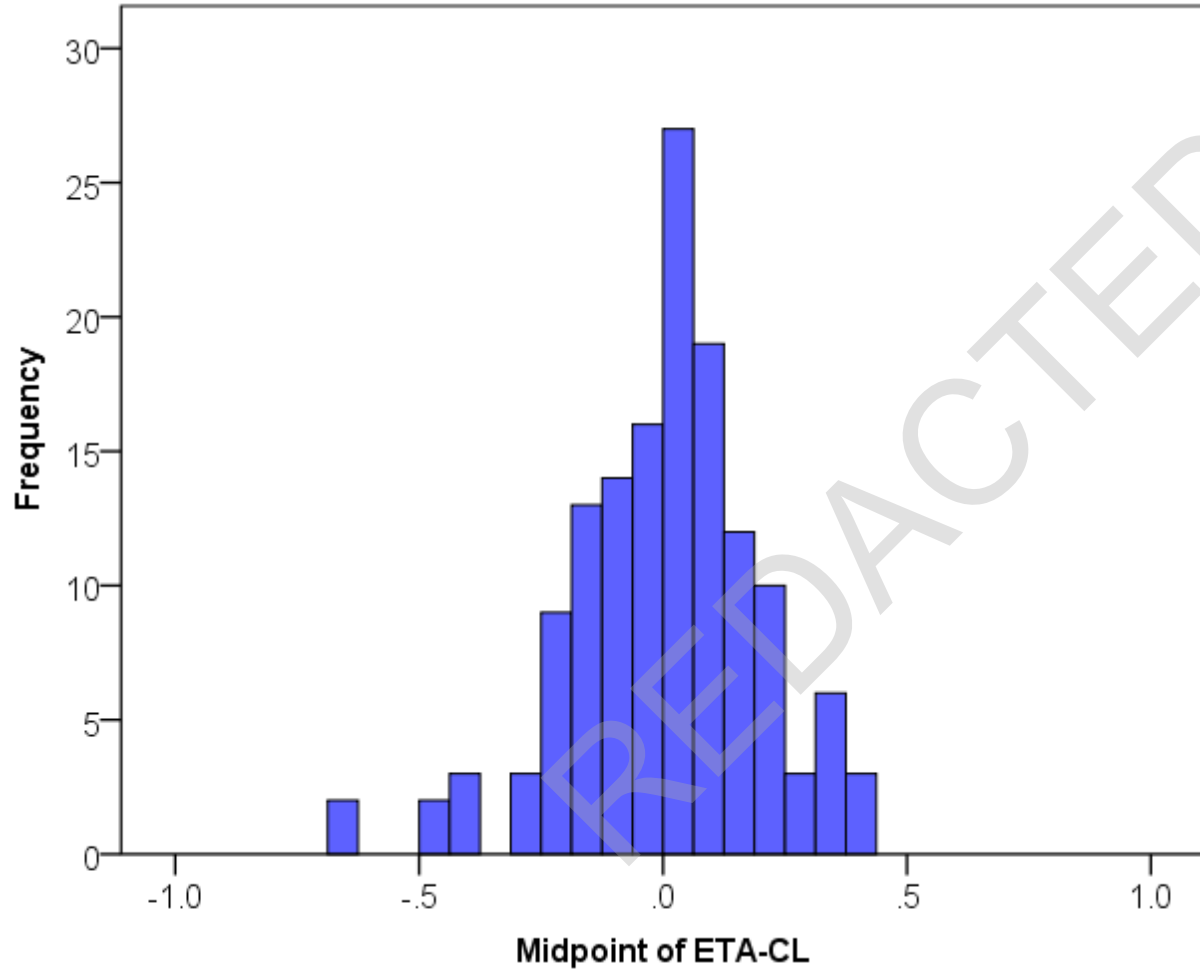


Figure 47. Intersubject Variability of Clearance Distribution - Final Model



48. Intersubject Variability of Clearance vs Post-natal Age - Final Model

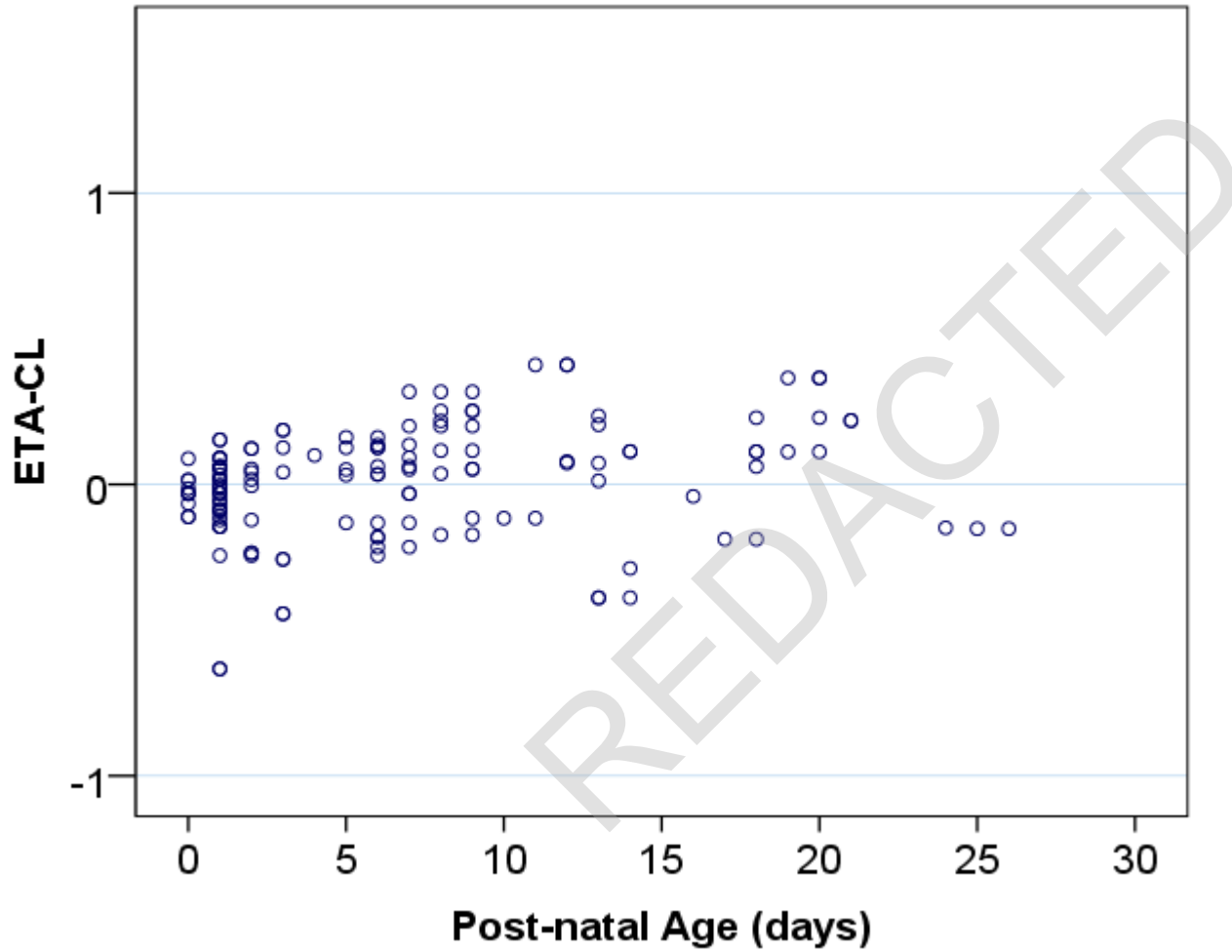


Figure 49. Intersubject Variability of Clearance vs Post-menstrual Age - Final Model

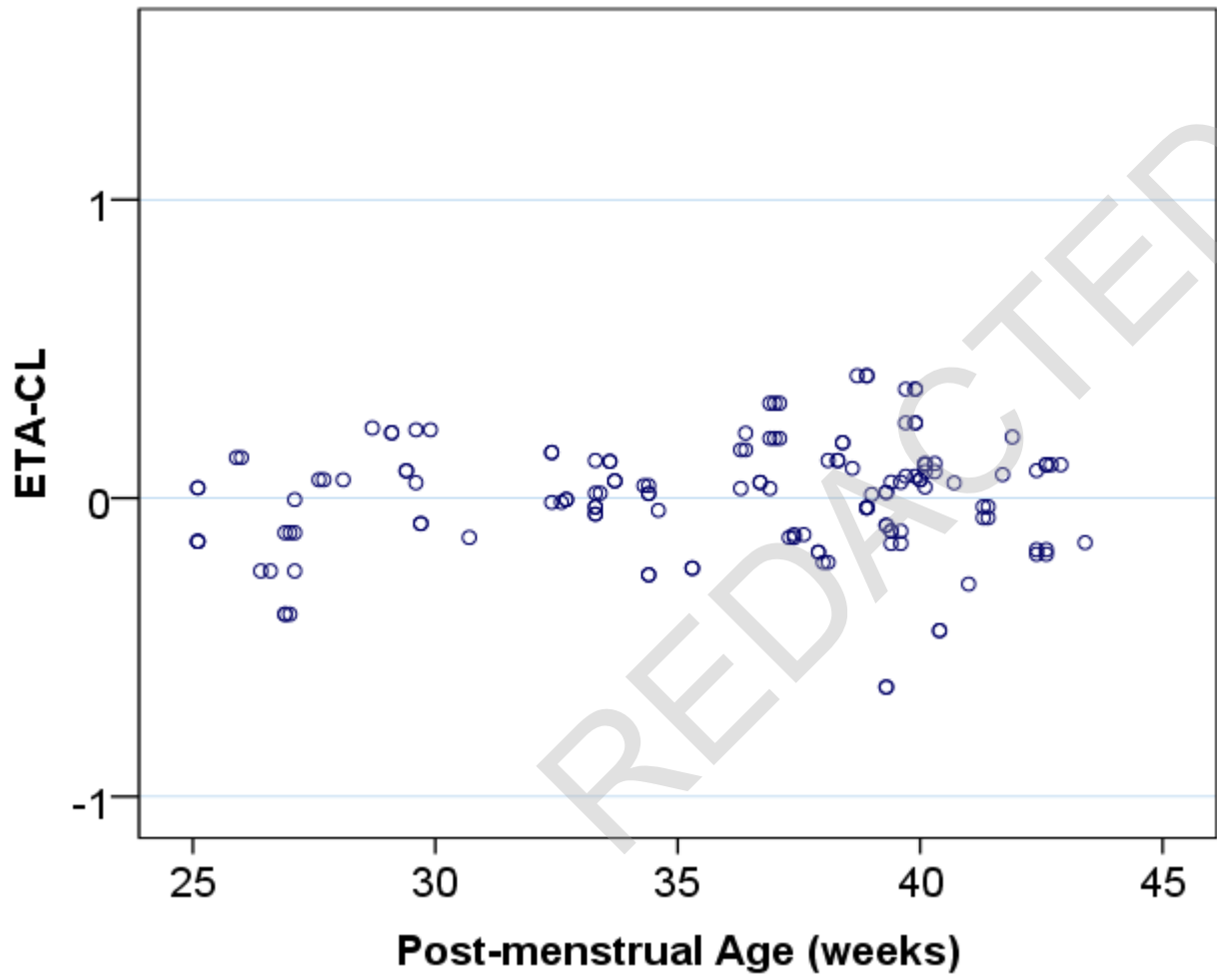


Figure 50. Intersubject Variability of Clearance vs Gestational Age - Final Model

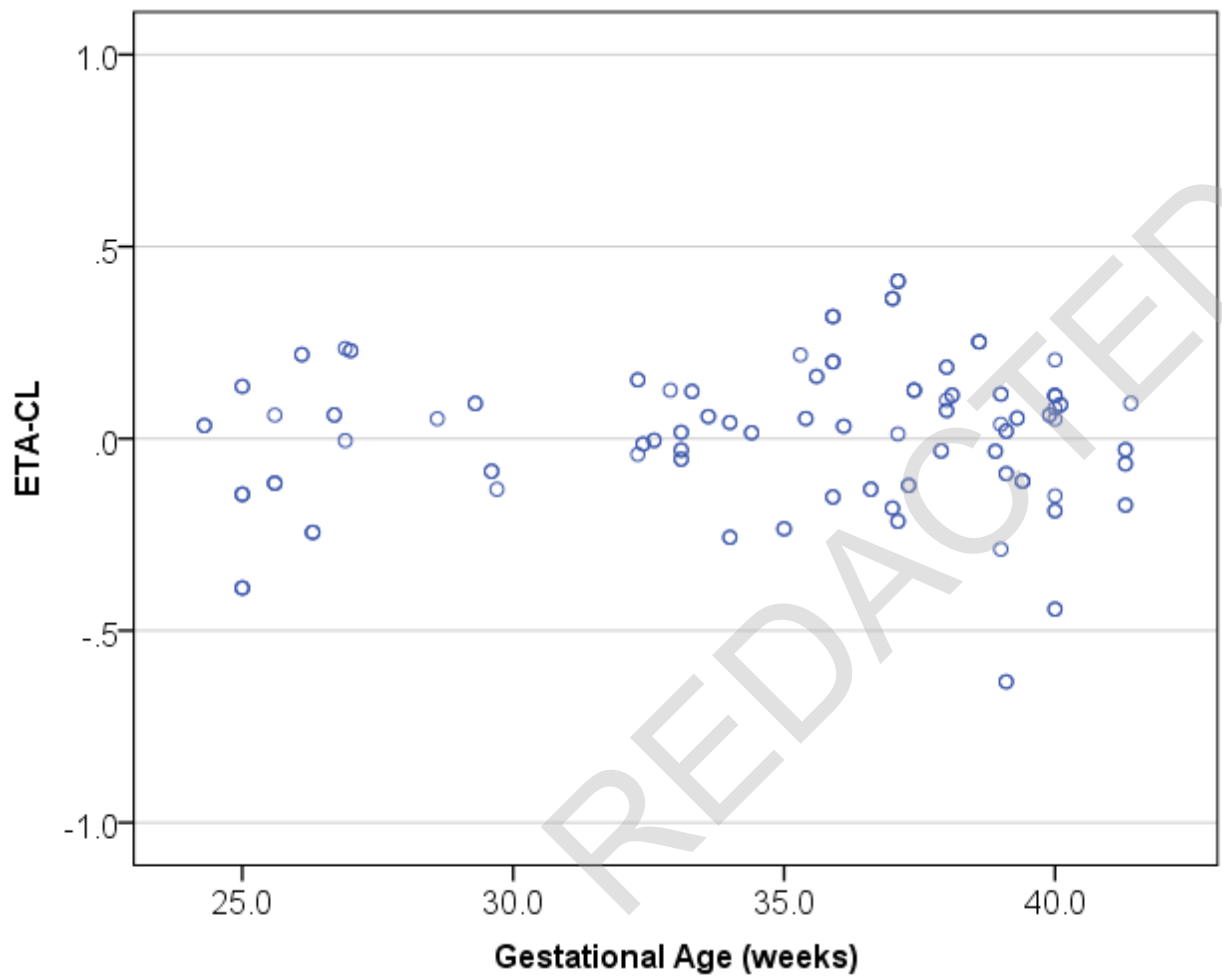


Figure 51. Intersubject Variability of Clearance vs Serum Creatinine - Final Model

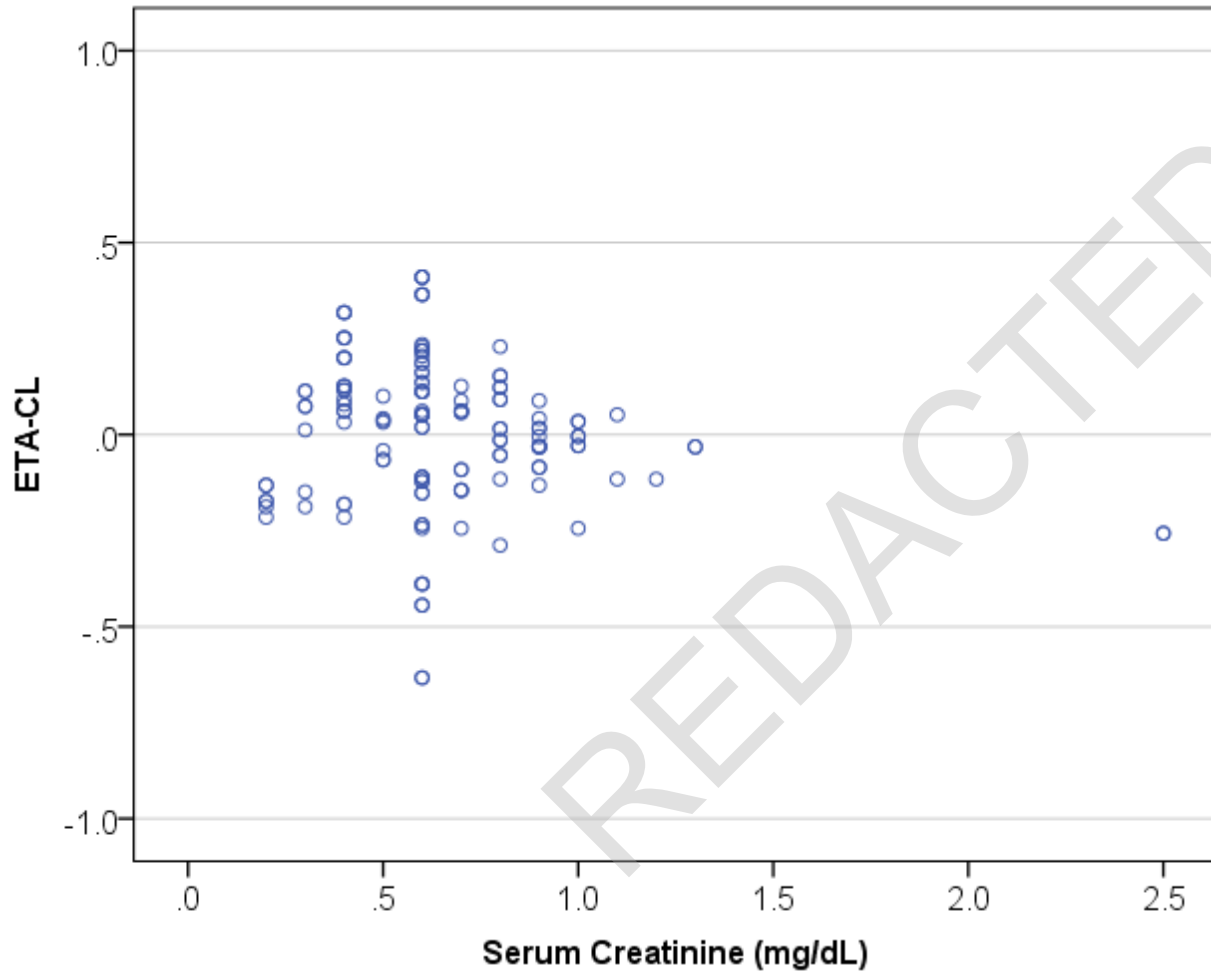


Figure 52. Intersubject Variability of Clearance vs Birthweight - Final Model

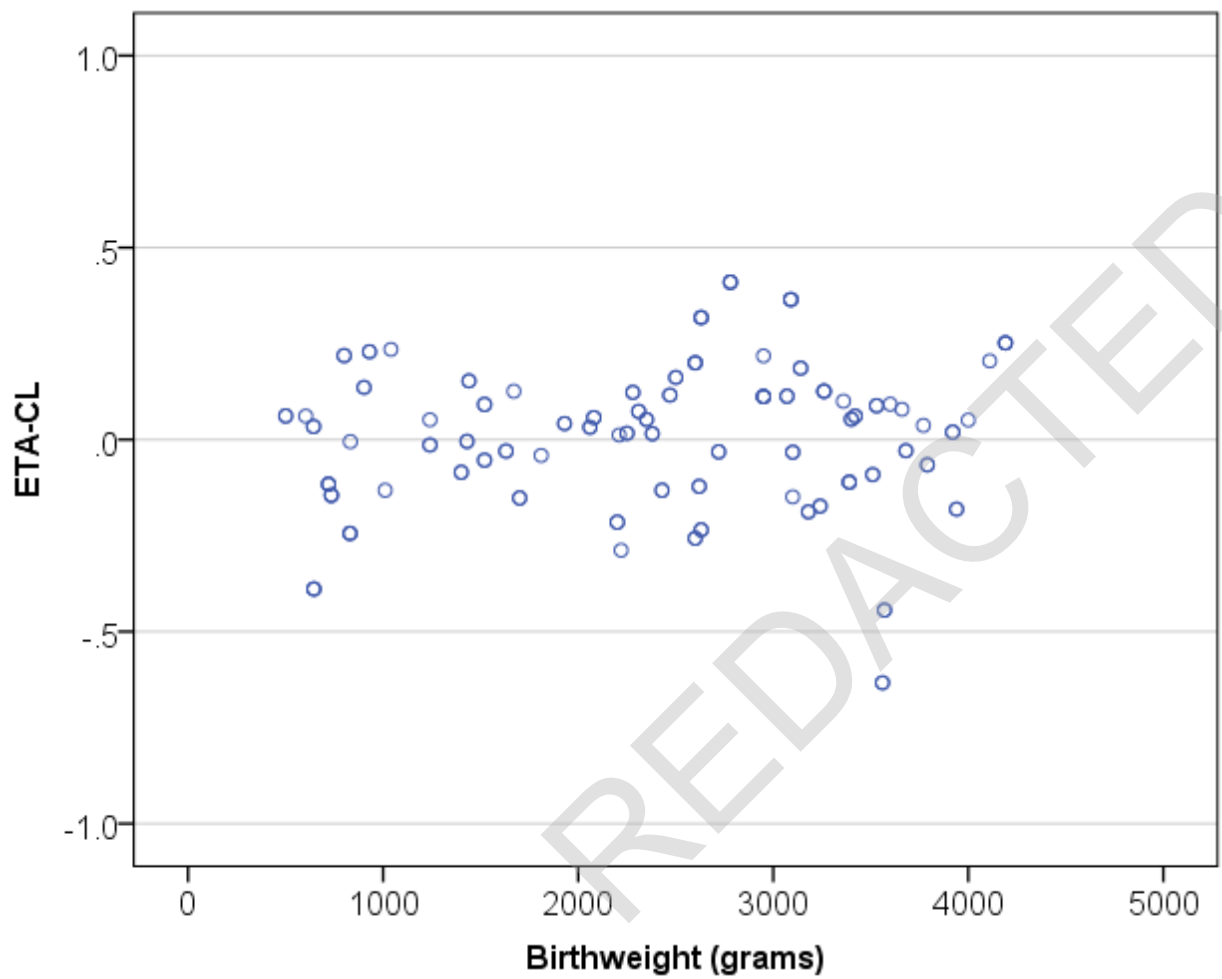


Figure 53. Intersubject Variability of Clearance vs Weight - Final Model

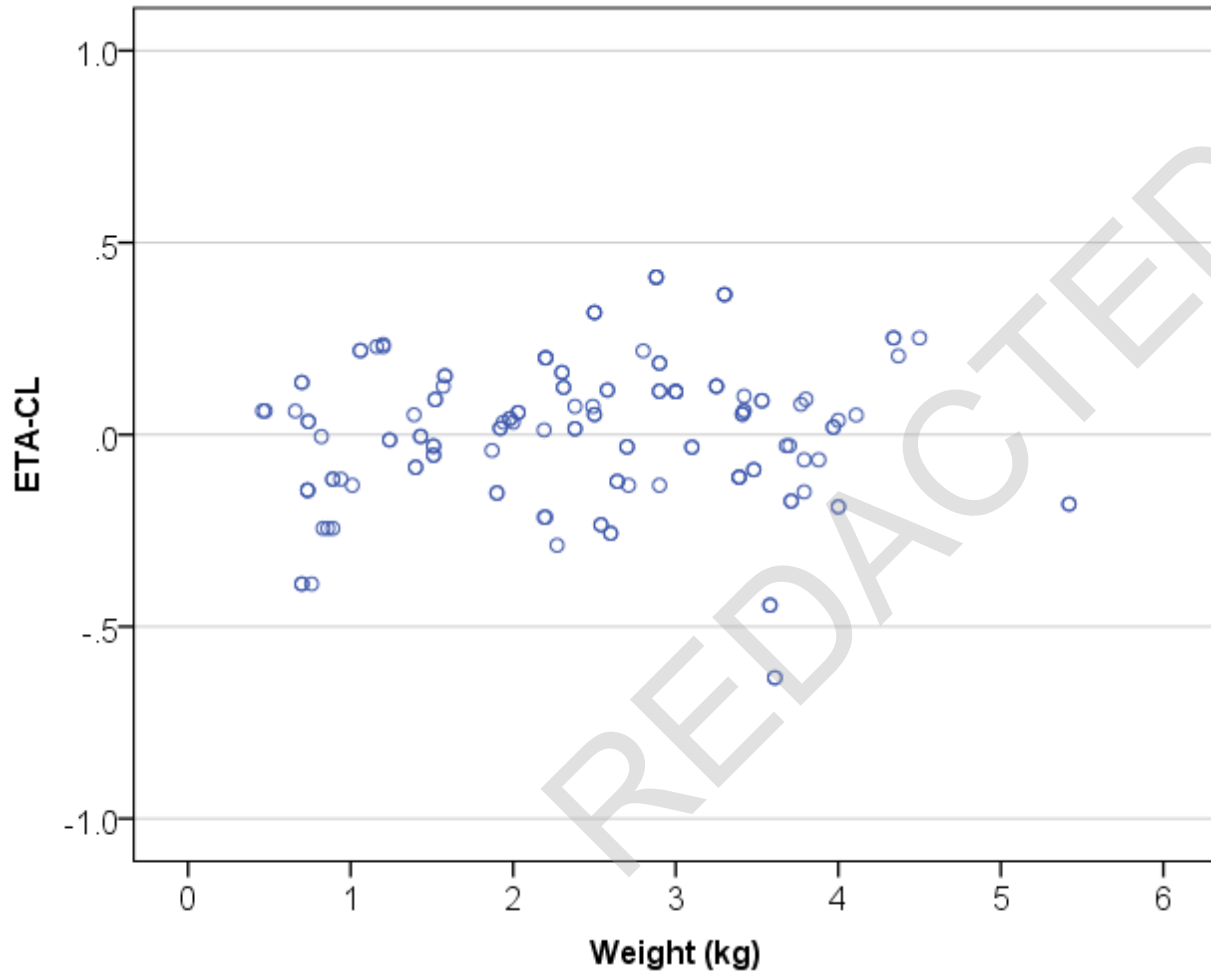


Figure 54. Intersubject Variability of Clearance by Gender - Final Model

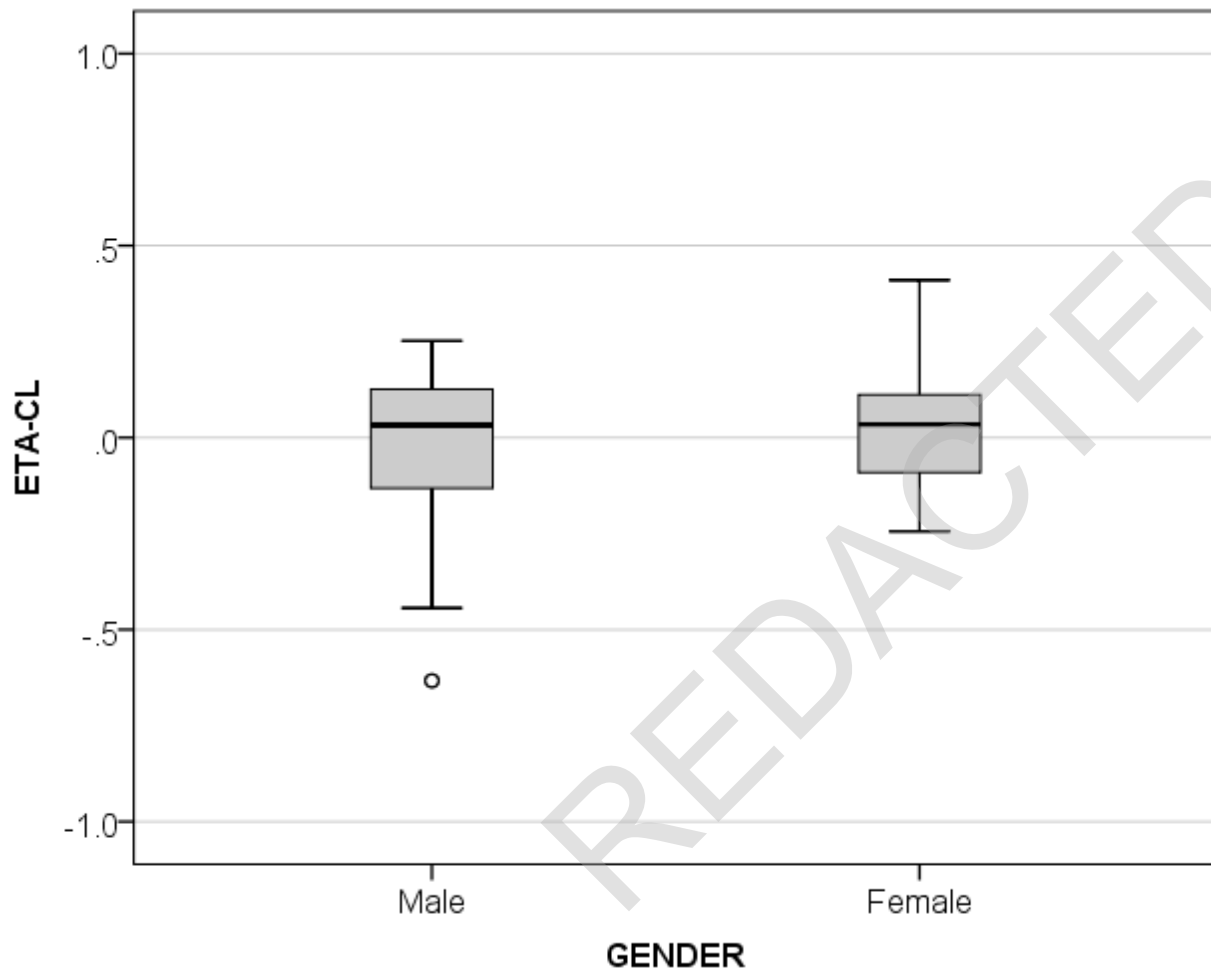


Figure 55. Intersubject Variability of Clearance by Race - Final Model

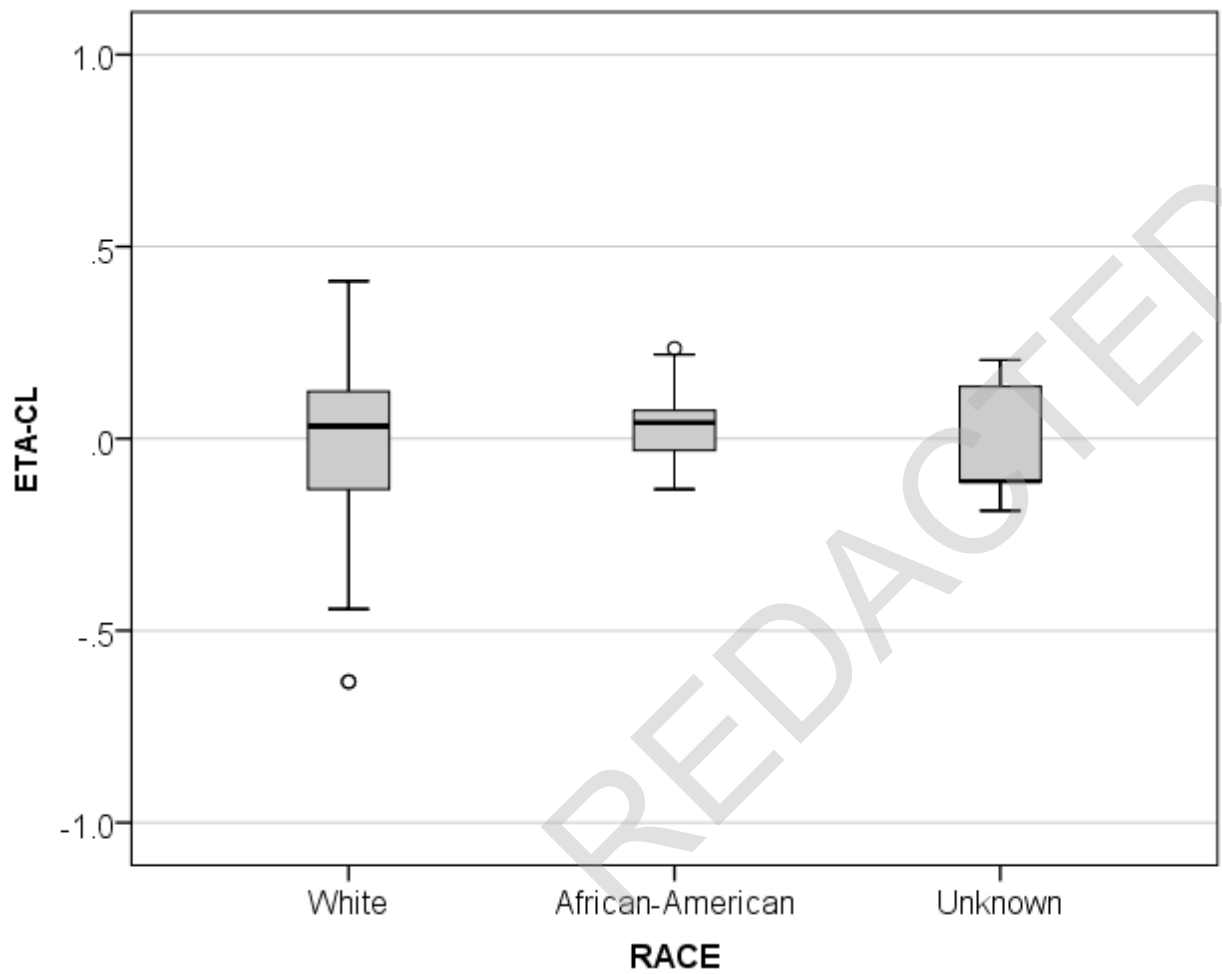


Figure 56. Intersubject Variability of Clearance by Ethnicity - Final Model

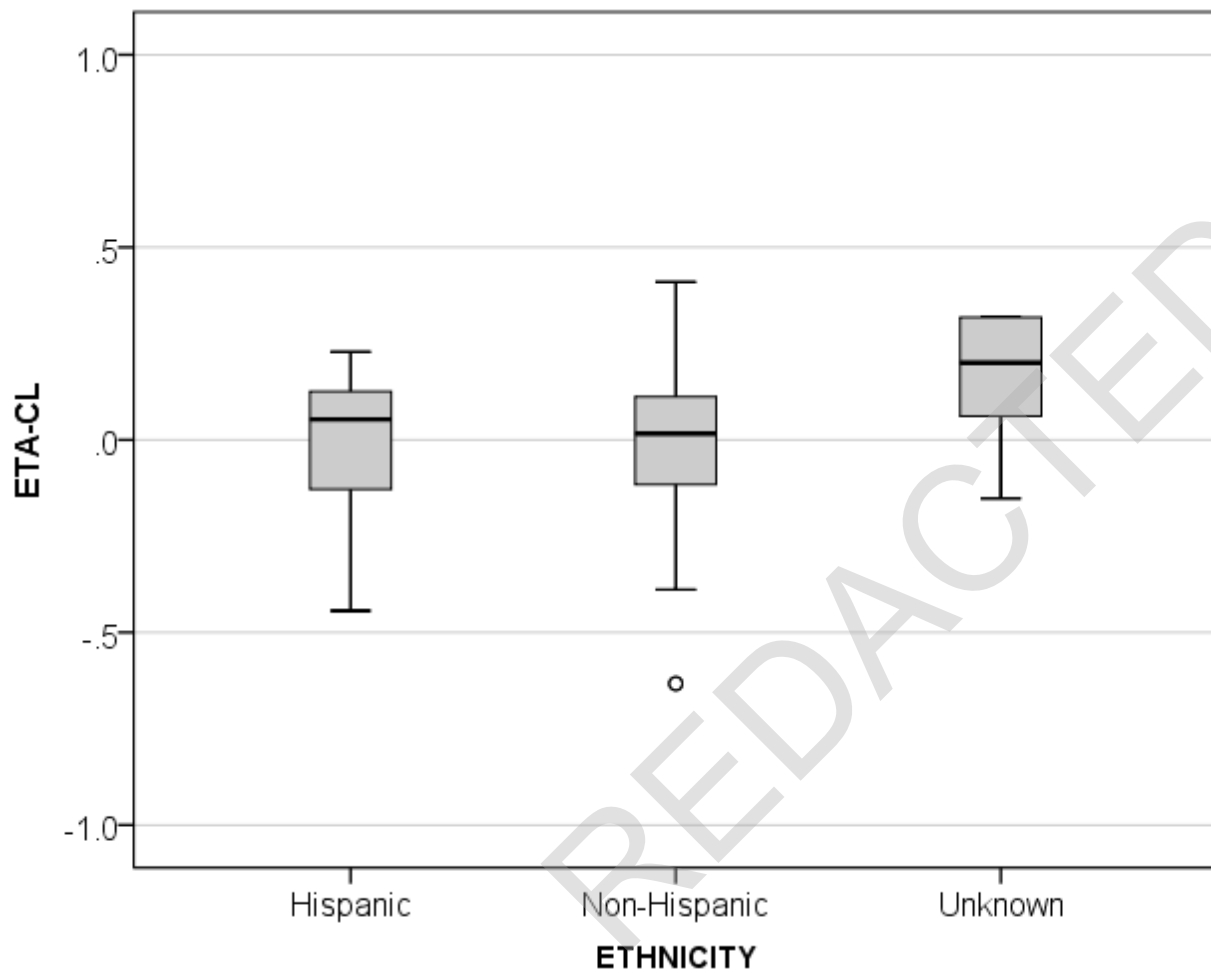


Figure 57. Volume (L/kg) by Group - Final Model

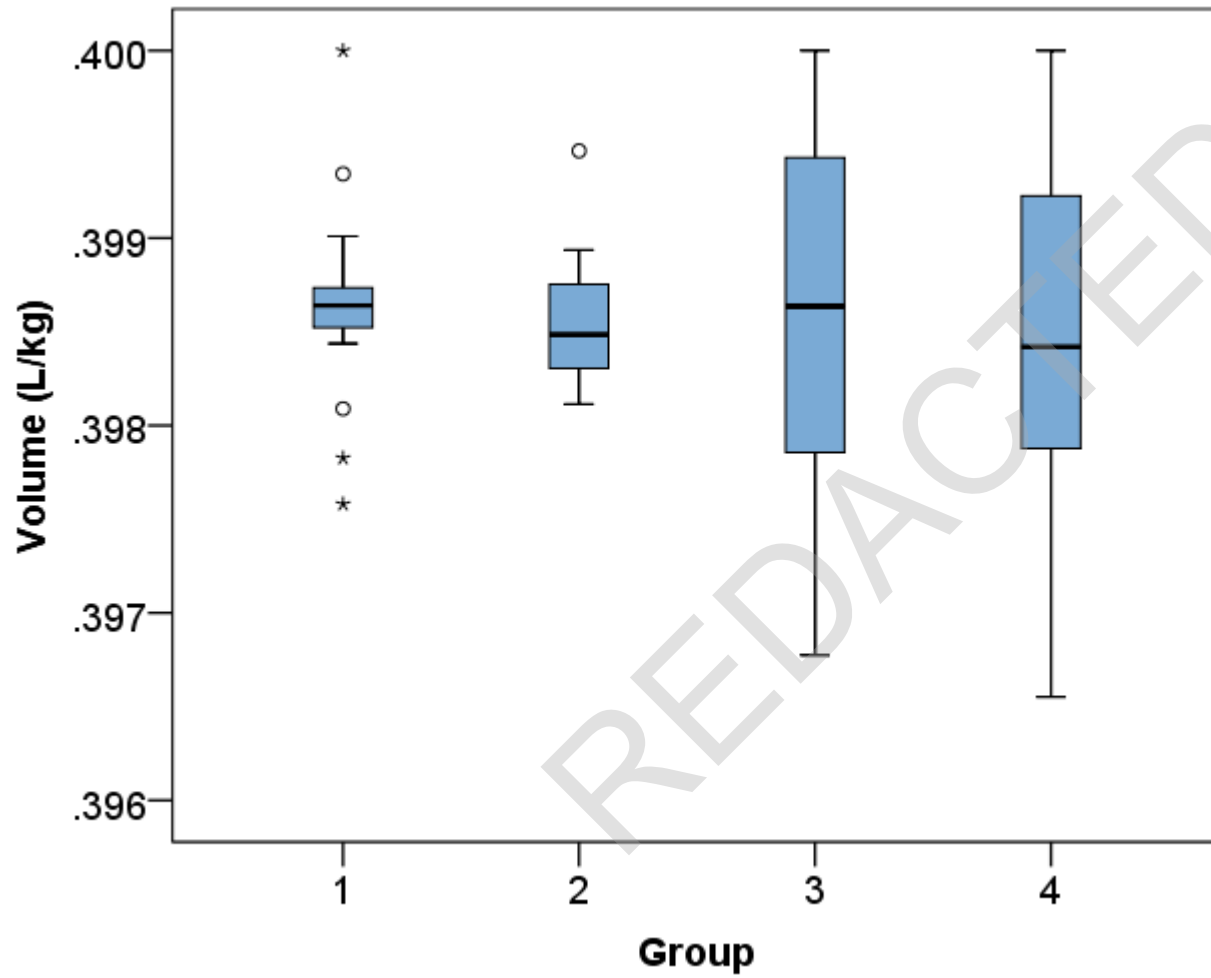


Figure 58. Volume (L/kg) vs Post-natal Age - Final Model

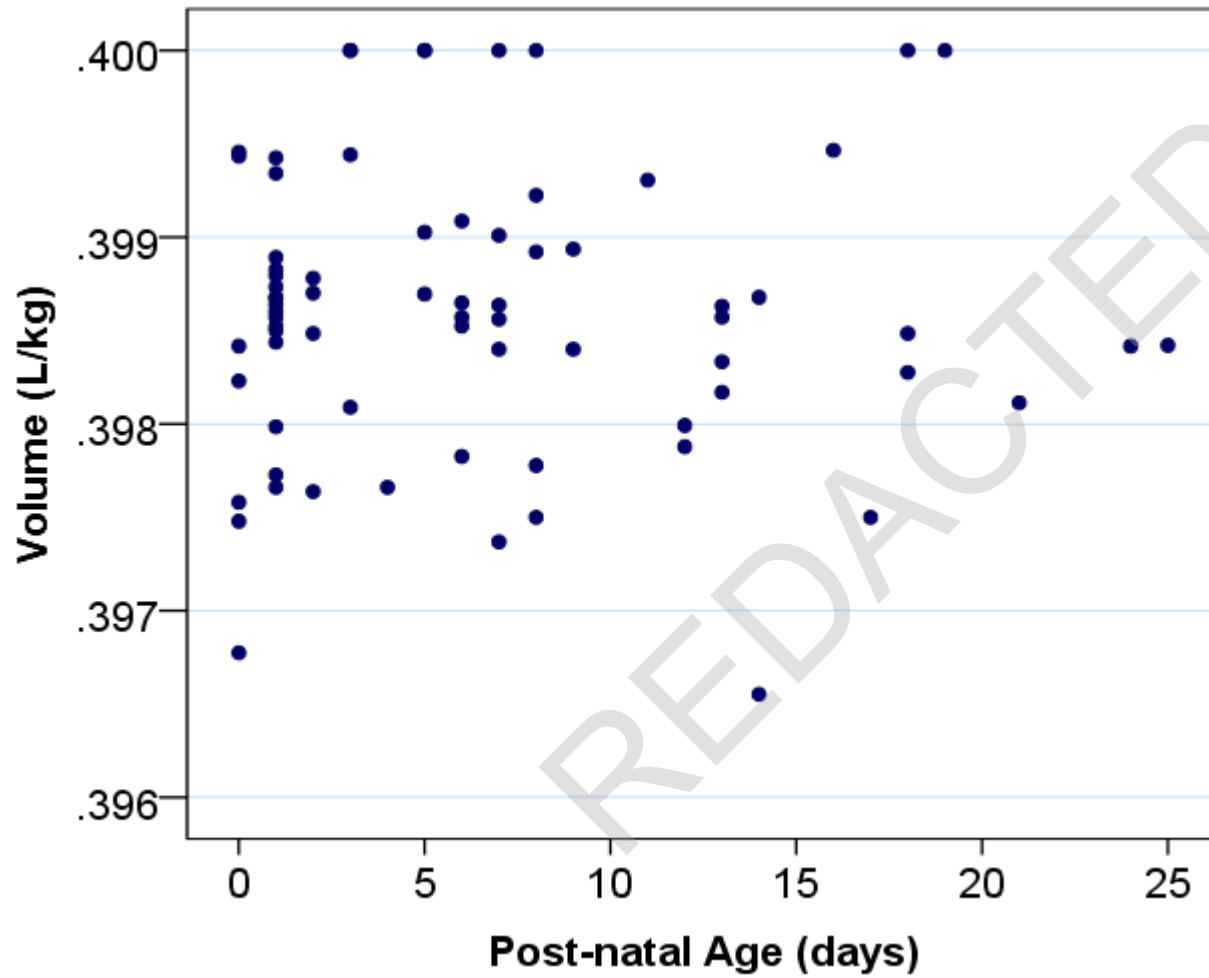


Figure 60. Volume (L/kg) vs Post-menstrual Age - Final Model

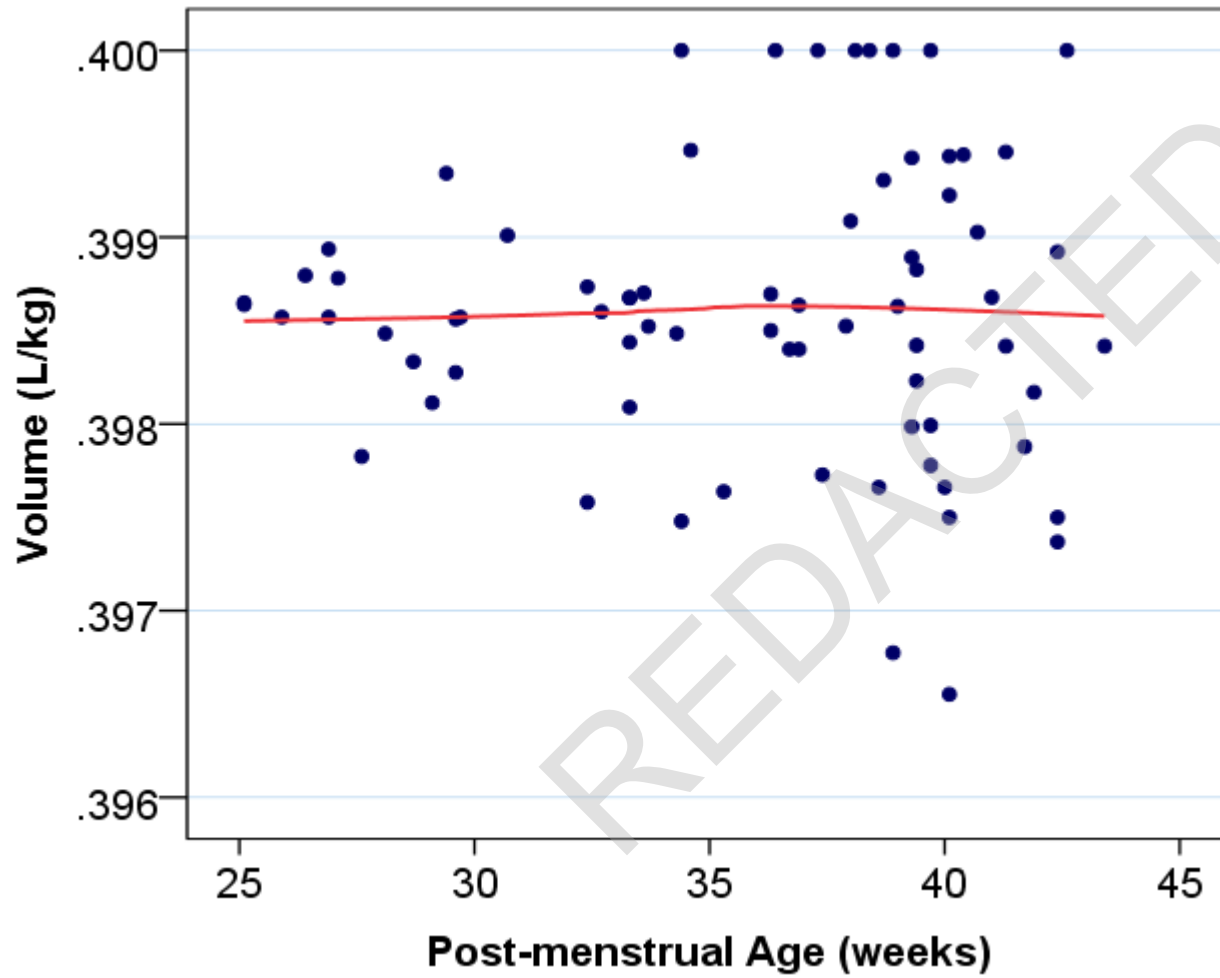


Figure 61. Volume (L/kg) vs Post-natal Age by Gestational Age Group - Final Model

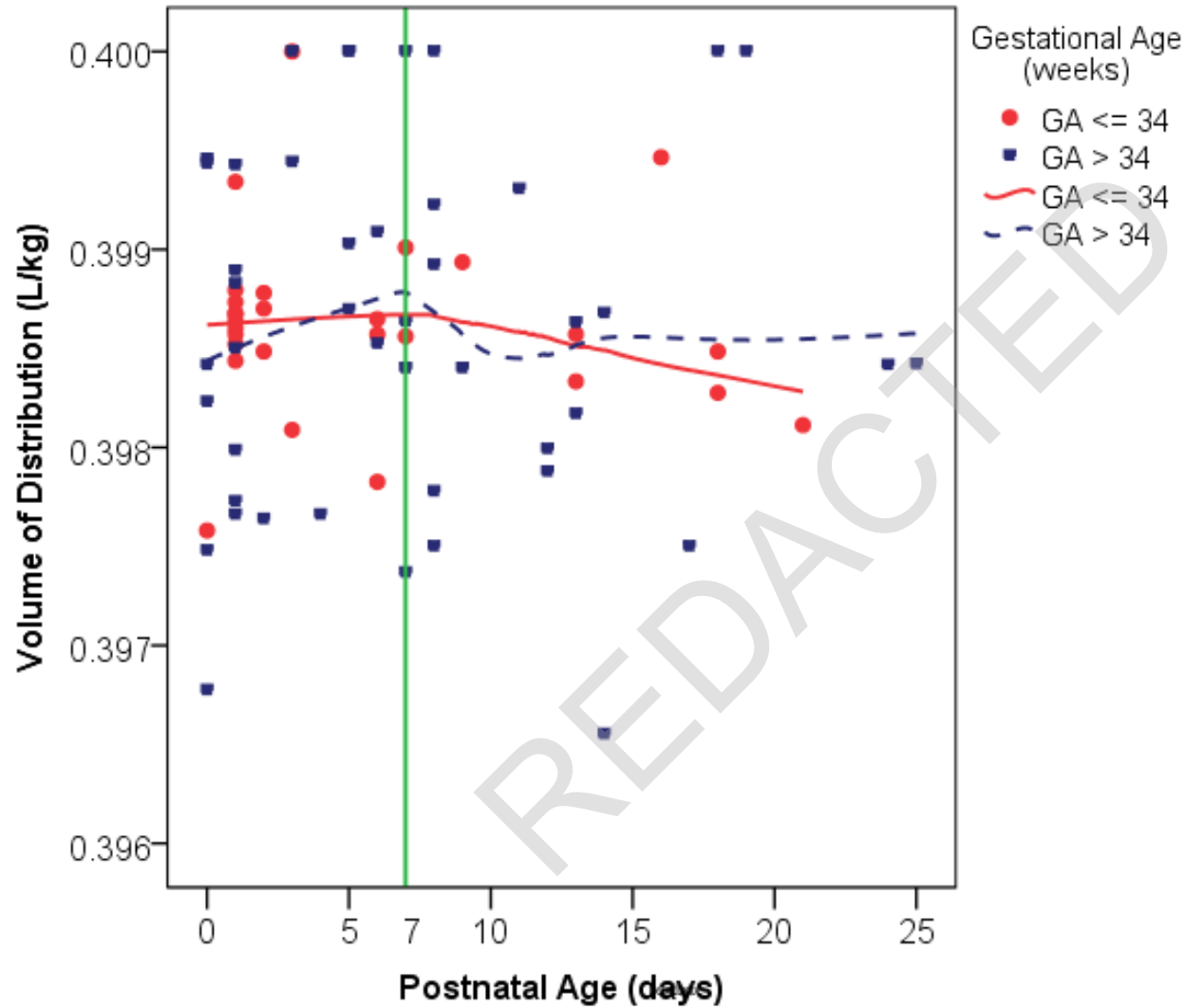


Figure 62. Volume (L/kg) vs Gestational Age by Post-natal Age Group - Final Model

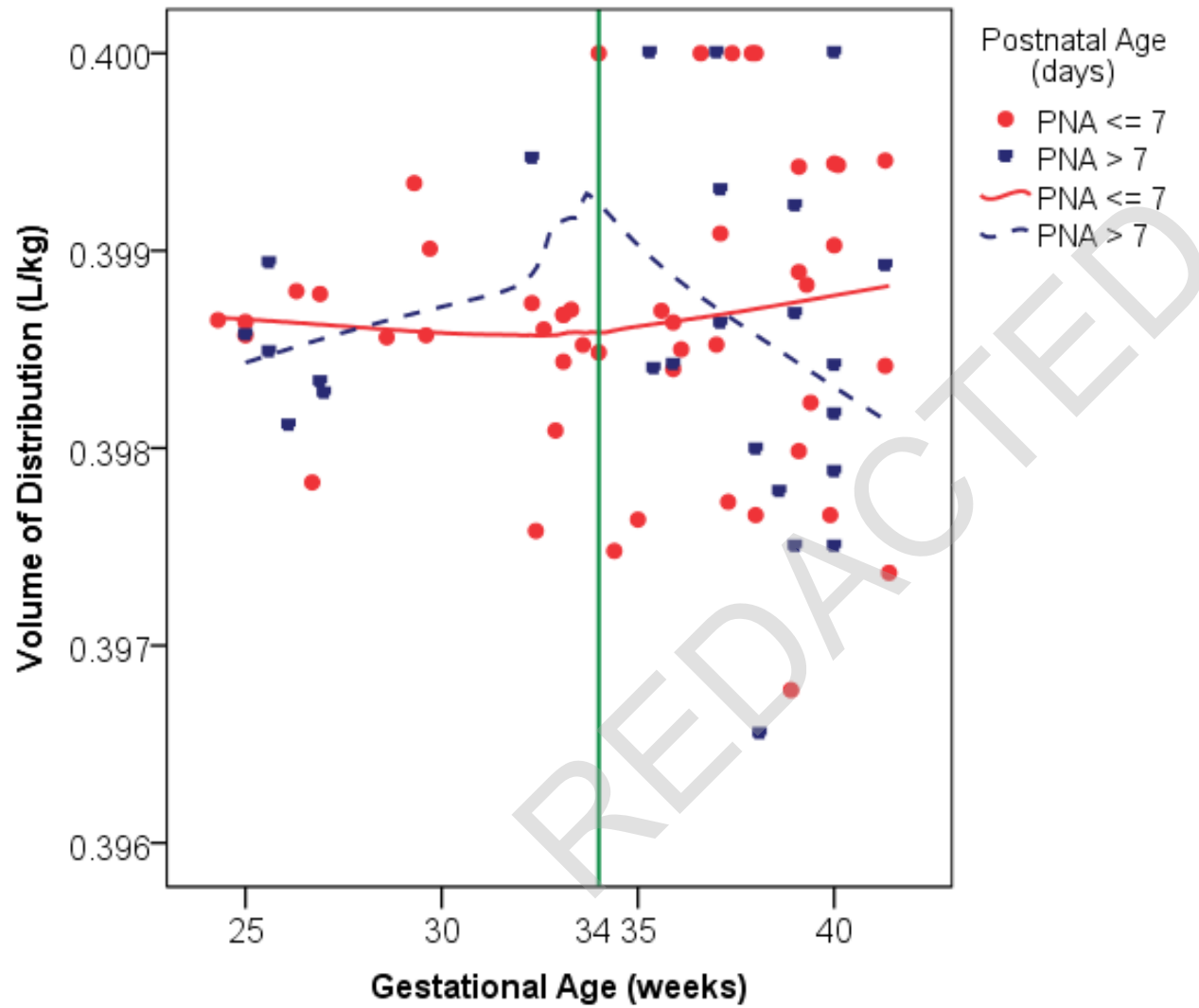


Figure 63. Volume (L/kg) vs Baseline Serum Creatinine - Final Model

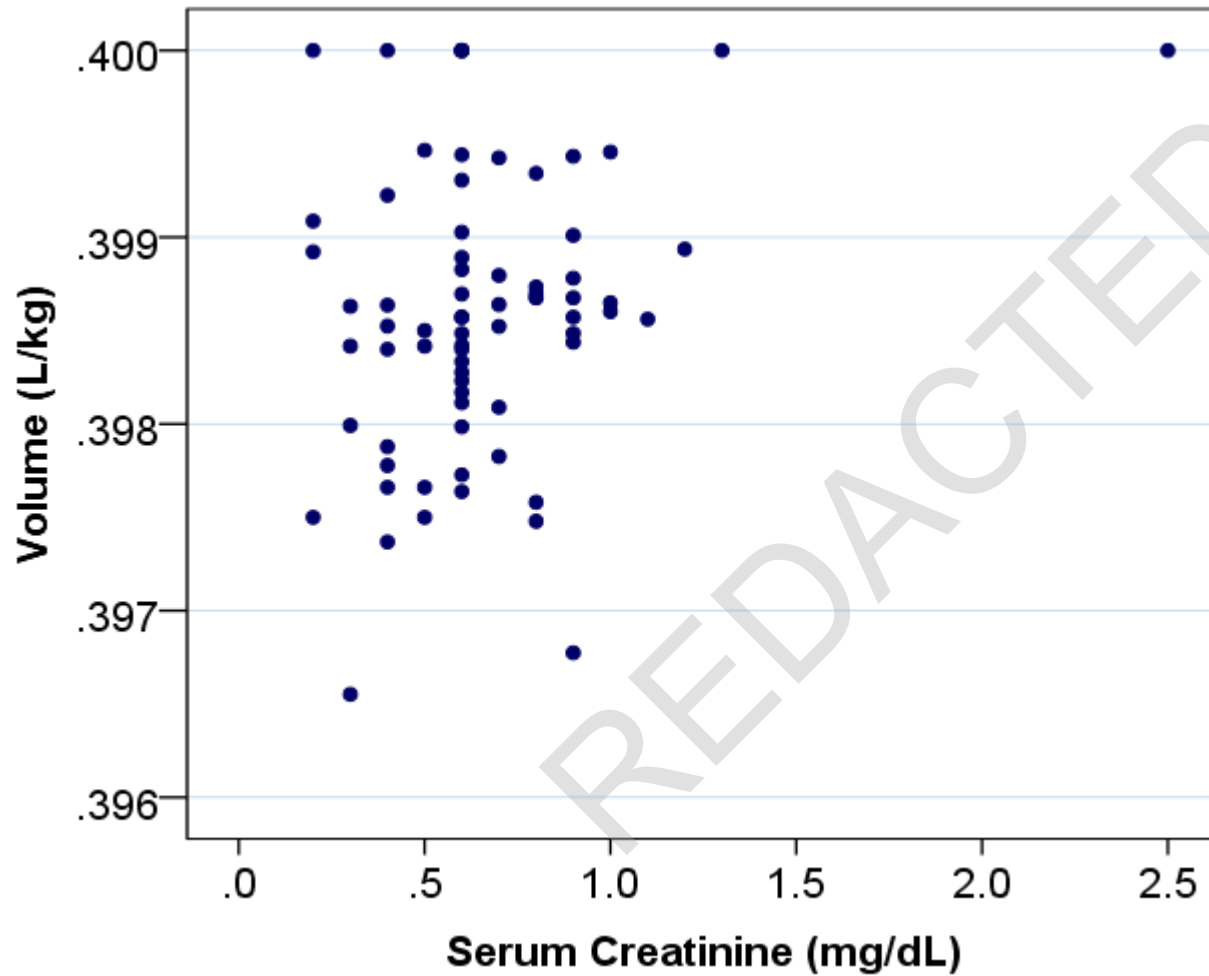


Figure 64. Half-life by Group - Final Model

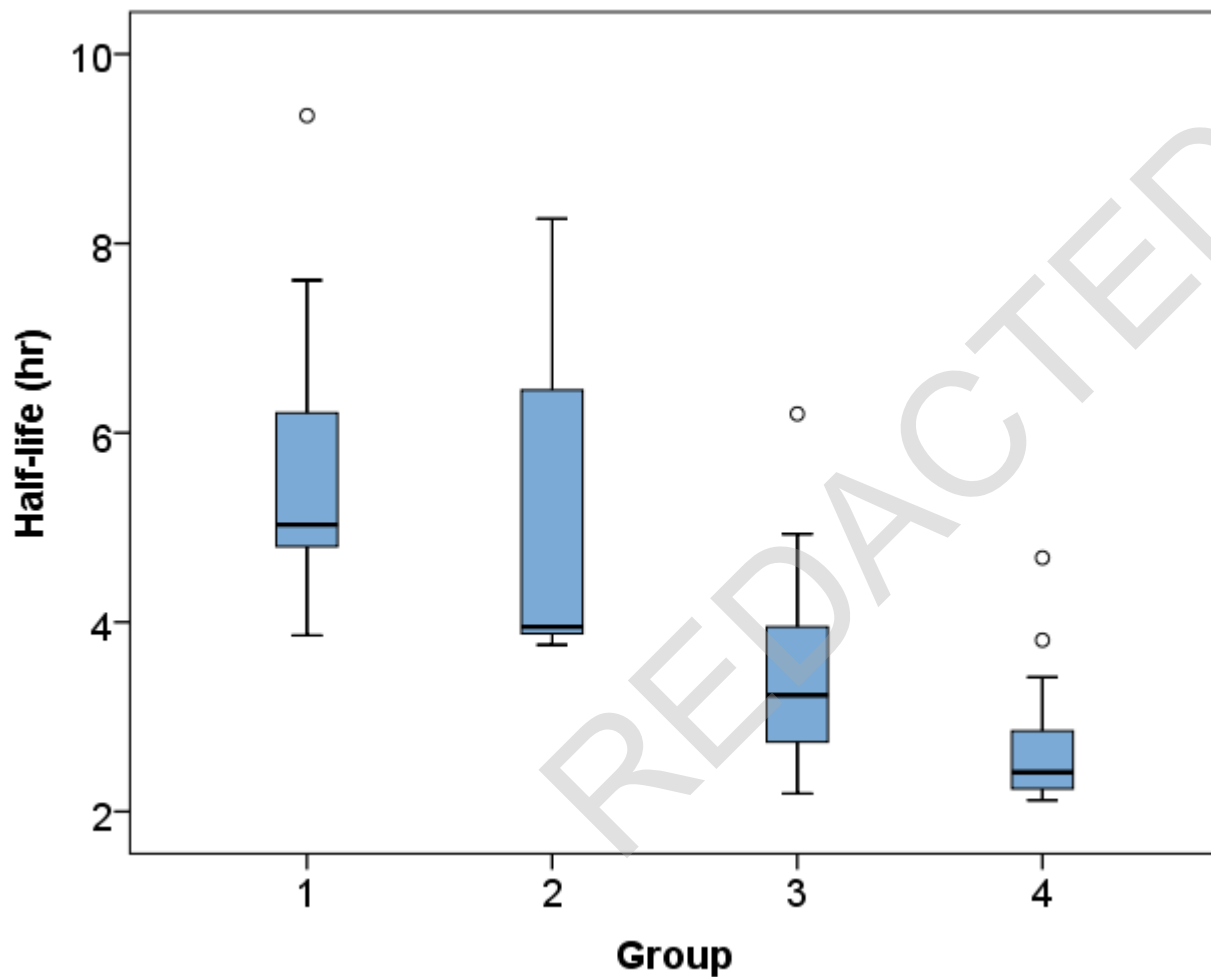


Figure 65. Half-life vs Post-natal Age - Final Model

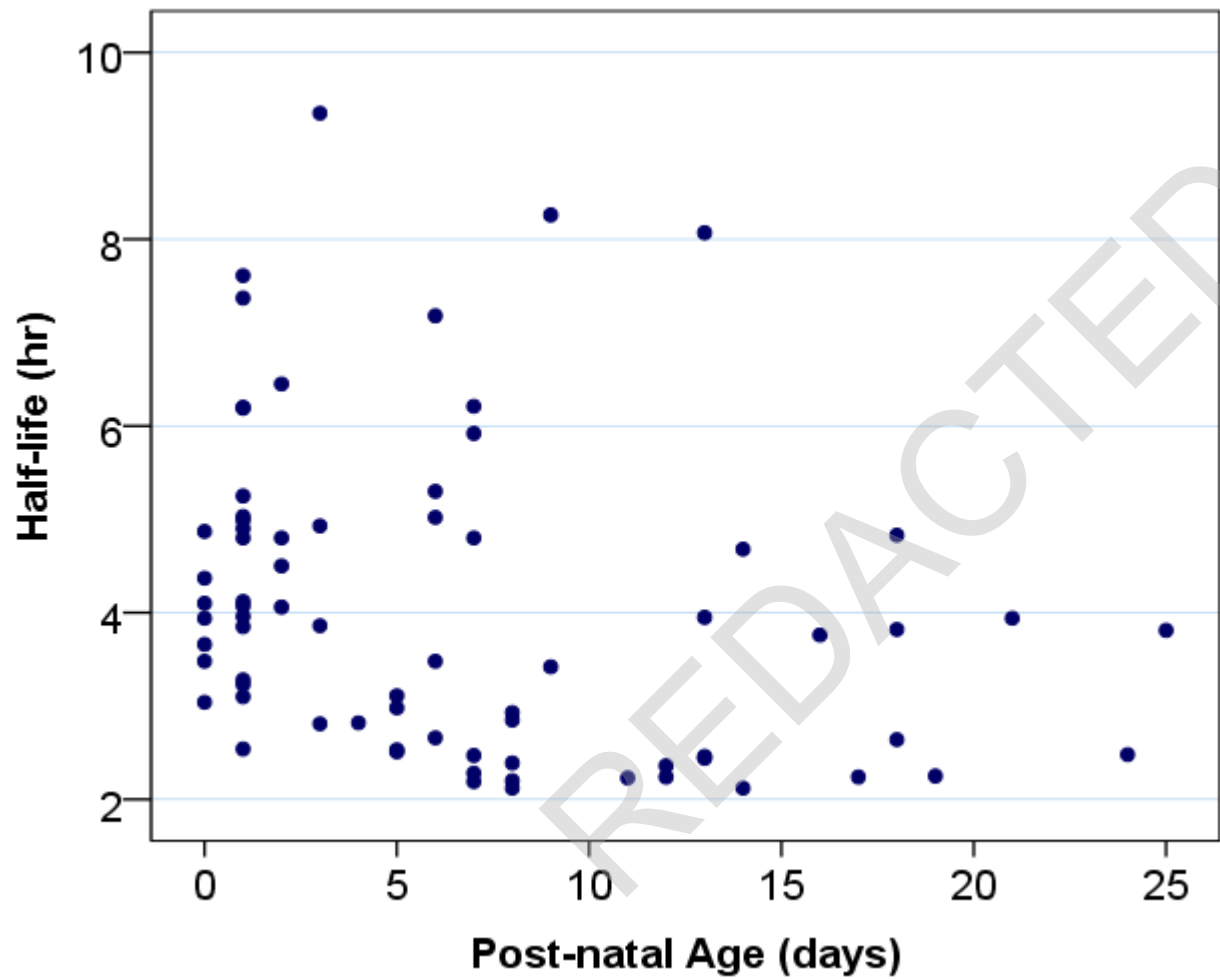


Figure 66. Half-life vs Gestational Age - Final Model

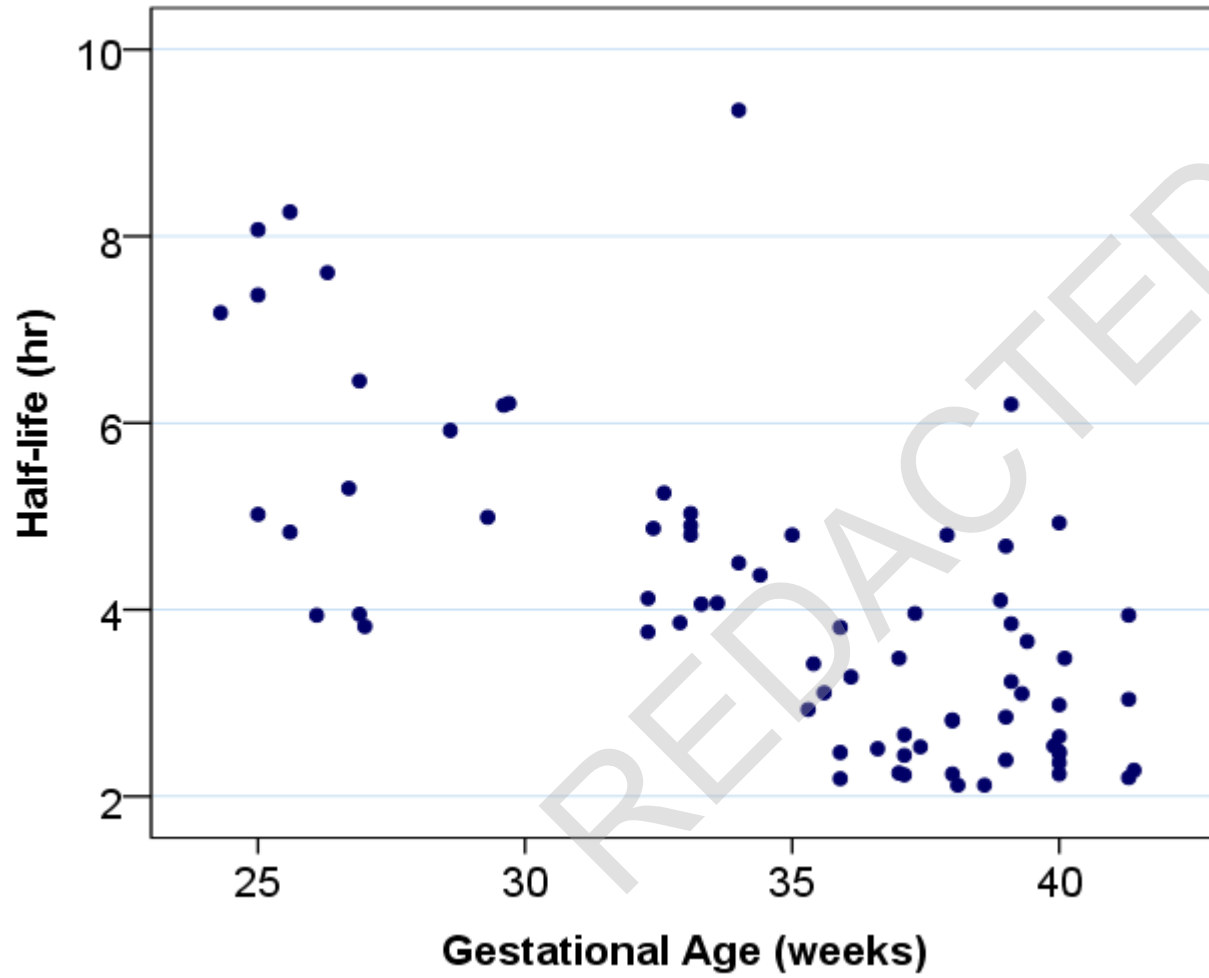


Figure 68. Half-life vs Post-menstrual Age - Final Model

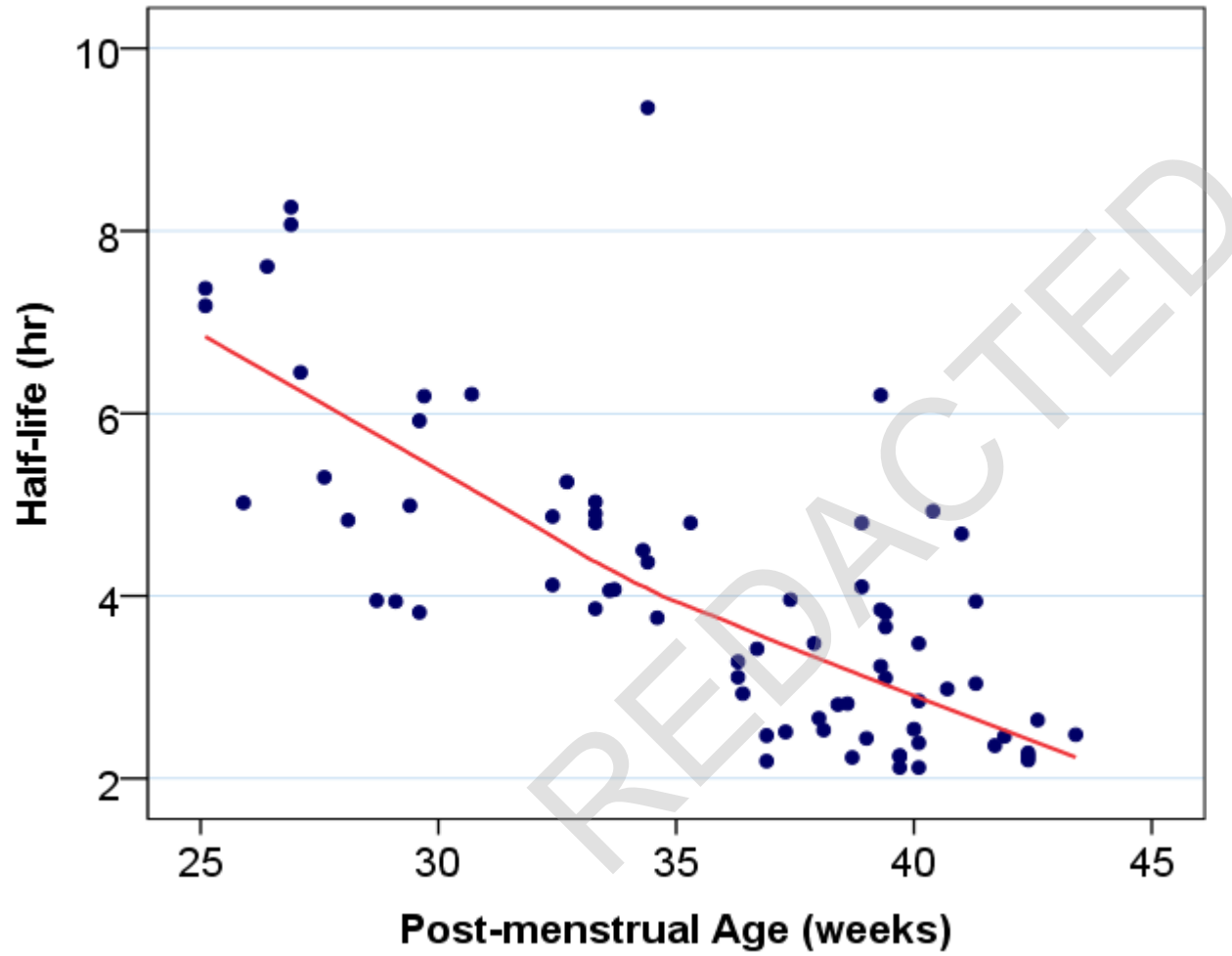


Figure 68. Half-life vs Serum Creatinine - Final Model

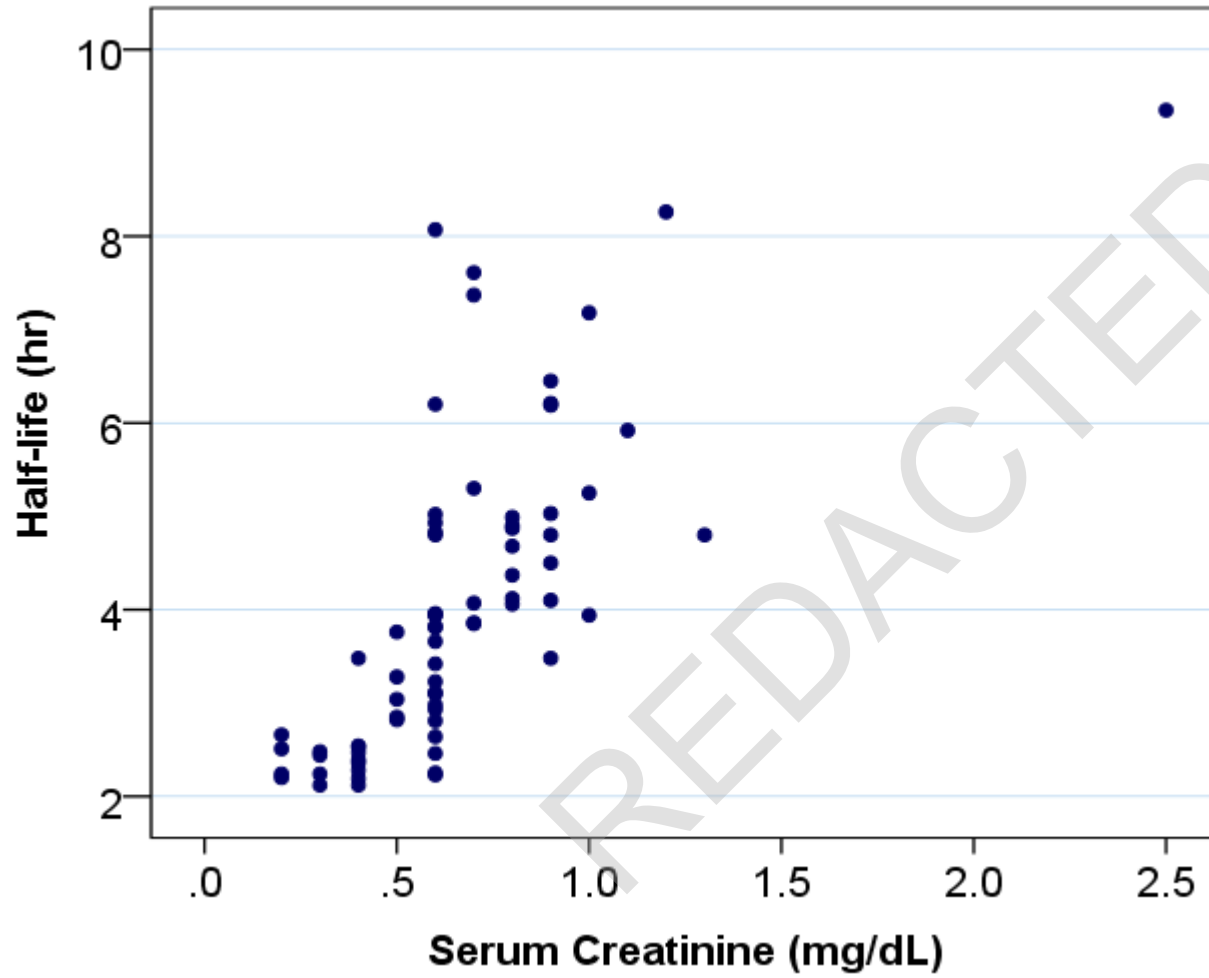


Figure 69. Trough Concentrations at Steady-State by Group - Final Model

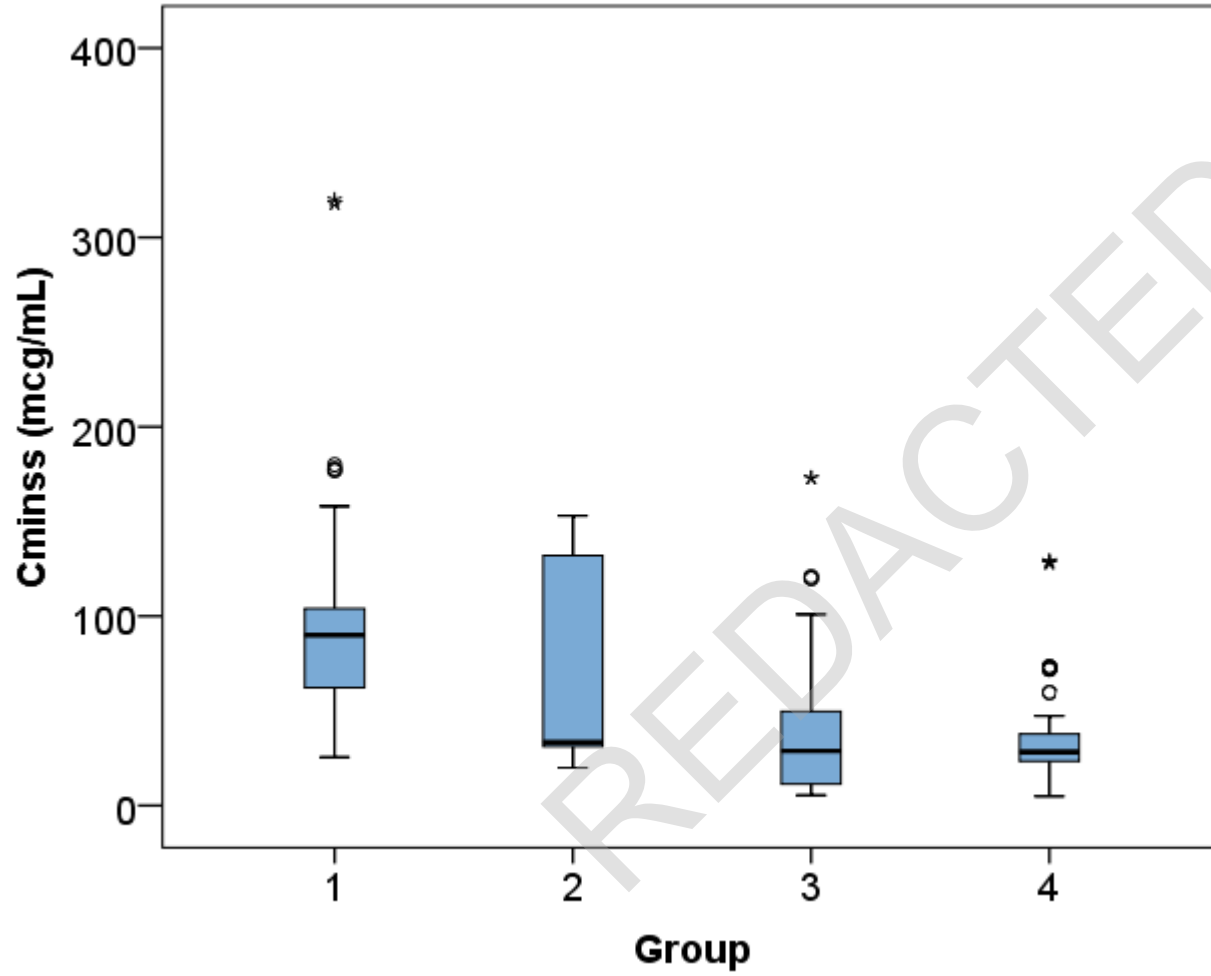


Figure 70. Distribution of Conditional Weighted Residual - Final Model

