Supplemental Table T1: STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
Outcome data	15*	Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Supplemental Table T2: Pmetrics model file for the final covariate model

```
#Pri
Vc0,12,24
Kct,0.04,0.25
Ktc,0.2,1.33
Kon,0.22,0.75
Koff,9,24
Kcp,1.5,13.5
Kpc,0.2,12
CL,4,58
Vm0,4.5,12
#Cov
BMI
ALB
#Sec
Bmax=ALB*6.84*Vc*0.6
Vc=Vc0*(bmi/48.4)
Vm=Vm0*(bmi/48.4)
Ke=CL/Vc
#Diffeq
XP(1) = RATEIV(1) - (Kct+CL/Vc)*X(1) - (Kon/Vc)*(Bmax-X(2))*X(1) + Koff*X(2) +
Ktc*X(3) - Kcp*X(1)+ Kpc*X(4)
XP(2) = (Kon/Vc)*(Bmax-X(2))*X(1) - Koff*X(2)
XP(3) = Kct*X(1)-Ktc*X(3)
XP(4) = Kcp*X(1)-Kpc*X(4)
#Out
Y(1)=X(1)/Vc
Y(2)=(X(2)+X(1))/Vc
Y(3)=X(3)/Vm
#Err
G=2
0.05,0.02,0,0
0.2,0.1,0,0
0.1,0.05,0,0
```

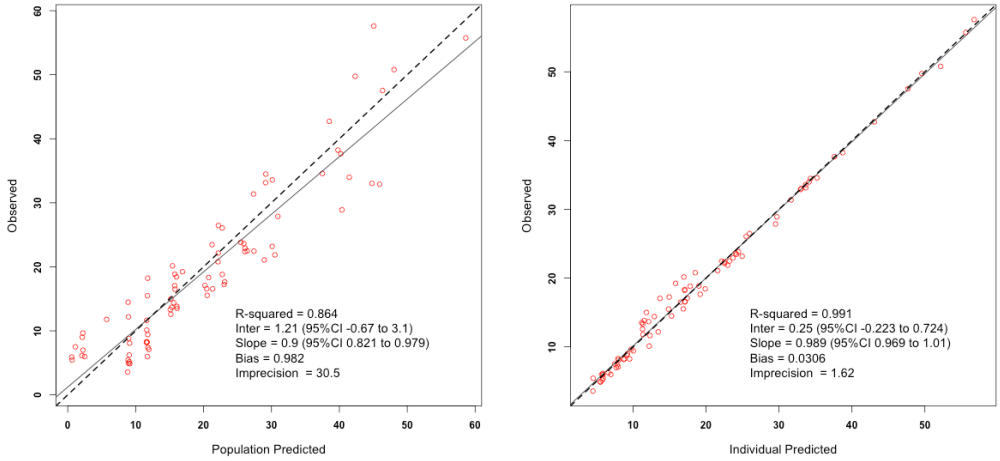
CL clearance ($L.h^{-1}$); Vc0, volume of the central compartment (L); Kct, first-order rate constant for distribution from central to tissue (microdialysis) compartment (h^{-1}); Ktc, first-order rate constant for distribution from tissue (microdialysis) to central compartment (h^{-1}); Kcp, first-order rate constant for distribution from central to peripheral compartment (h^{-1}); Kpc, first-order rate constant for distribution from peripheral to central compartment (h^{-1}); Kon, second-order association rate constant ($L.mg^{-1}.h^{-1}$); Koff, first-order dissociation rate constant (h^{-1}); alb, serum albumin concentration; BMI, body mass index; Vc, typical estimate of volume of the central compartment for a BMI of 48.4; Bmax, maximum binding amount of cefazolin (mg); Ke, first-order elimination rate constant (h^{-1}); XP(n), notation for dX(n)/dt where n is the compartment number; RATEIV(1), notation to indicate an infusion of drug (1); X(n),

amount of drug in compartment where n is the compartment number; Y(1), concentration of unbound drug in the central compartment; Y(2), concentration of total drug in the central compartment; Y(3), concentration of unbound drug in the peripheral compartment; Error, each observation is weighted by $1/(\text{Error})^2$ using a multiplicative error model (Error=SD*gamma), where SD is the standard deviation of each observation which is modelled by a polynomial equation with coefficients of the assay error specified in the bottom rows for unbound, total and microdialysis cefazolin concentrations, respectively, and G (gamma) is a value relating to extra process noise related to the observation, such as mis-specified dosing and observation times

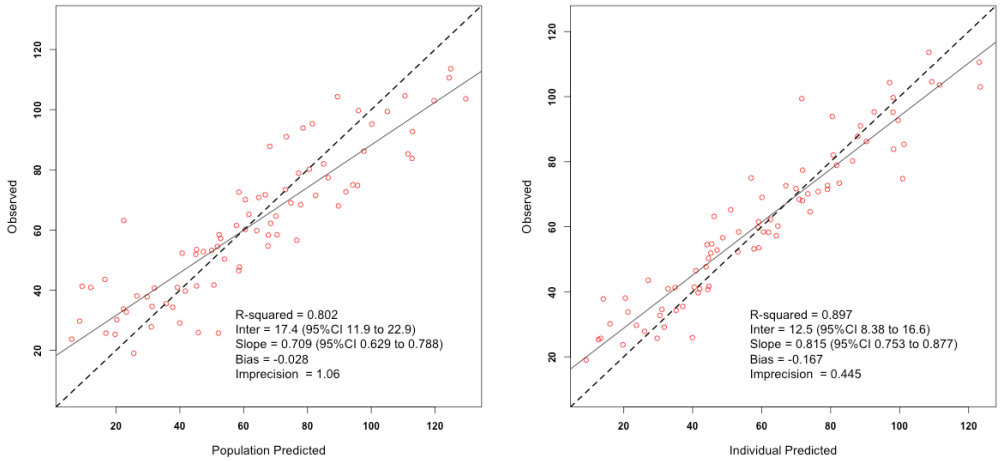
Supplemental Table T3: Individual estimates of the calculated maximum binding amount (B_{max}) for each patient, based on the final covariate model

Patient identification	Maximum binding amount (mg)
1	2850
2	1820
3	3221
4	2561
5	2081
6	2505
7	2773
8	2852
9	3785
10	2447
11	1953
12	2612
13	3743
14	2733

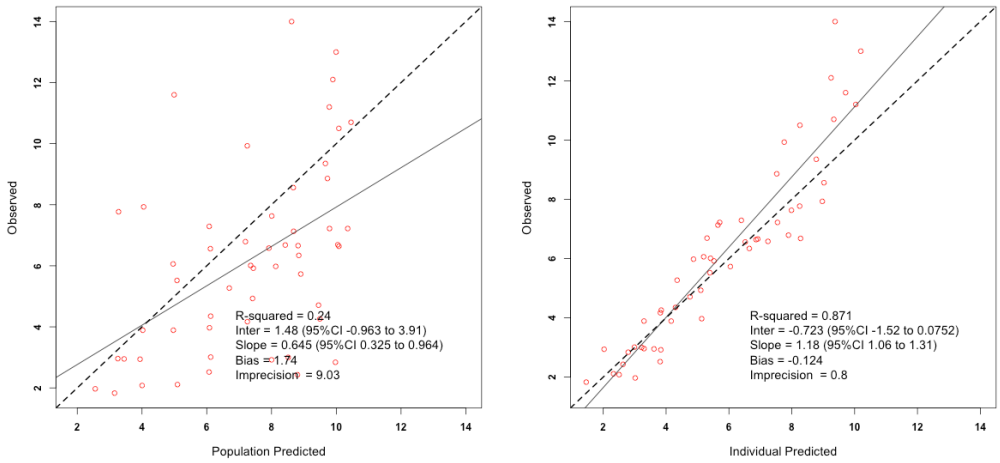
1A



1B

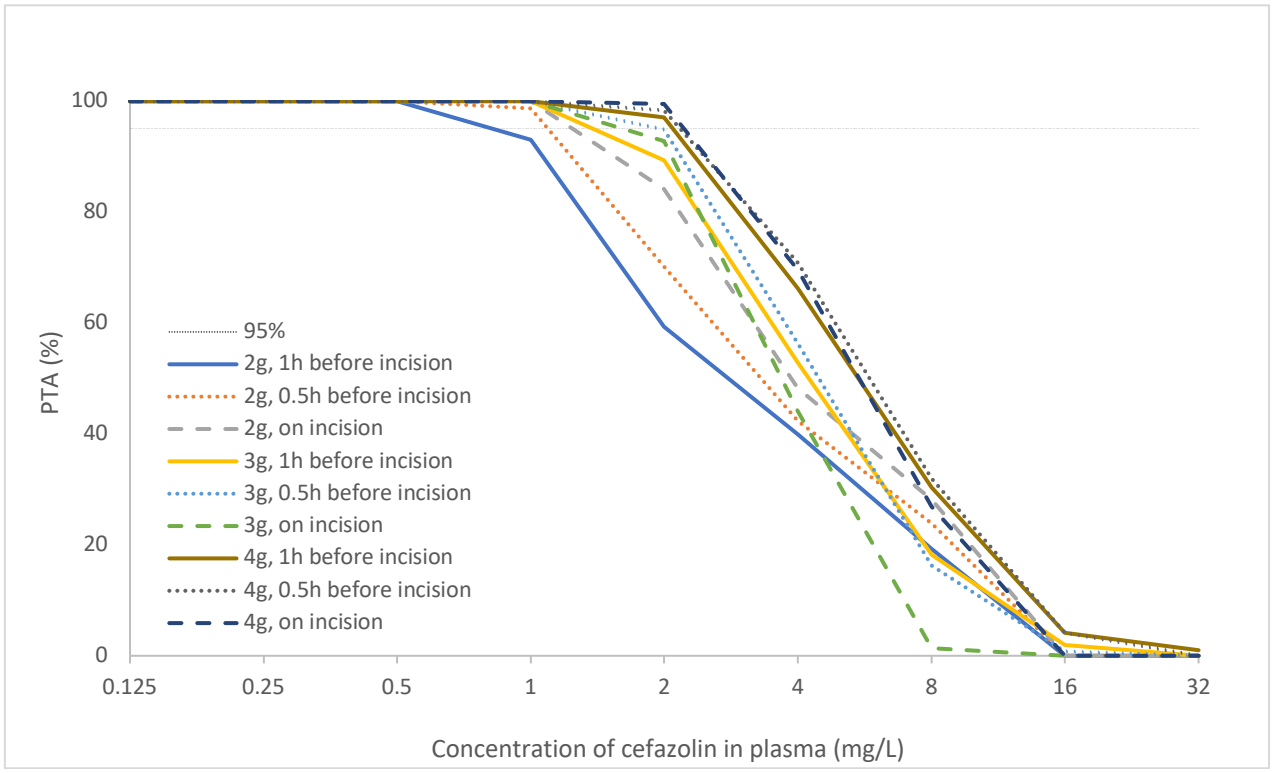


1C

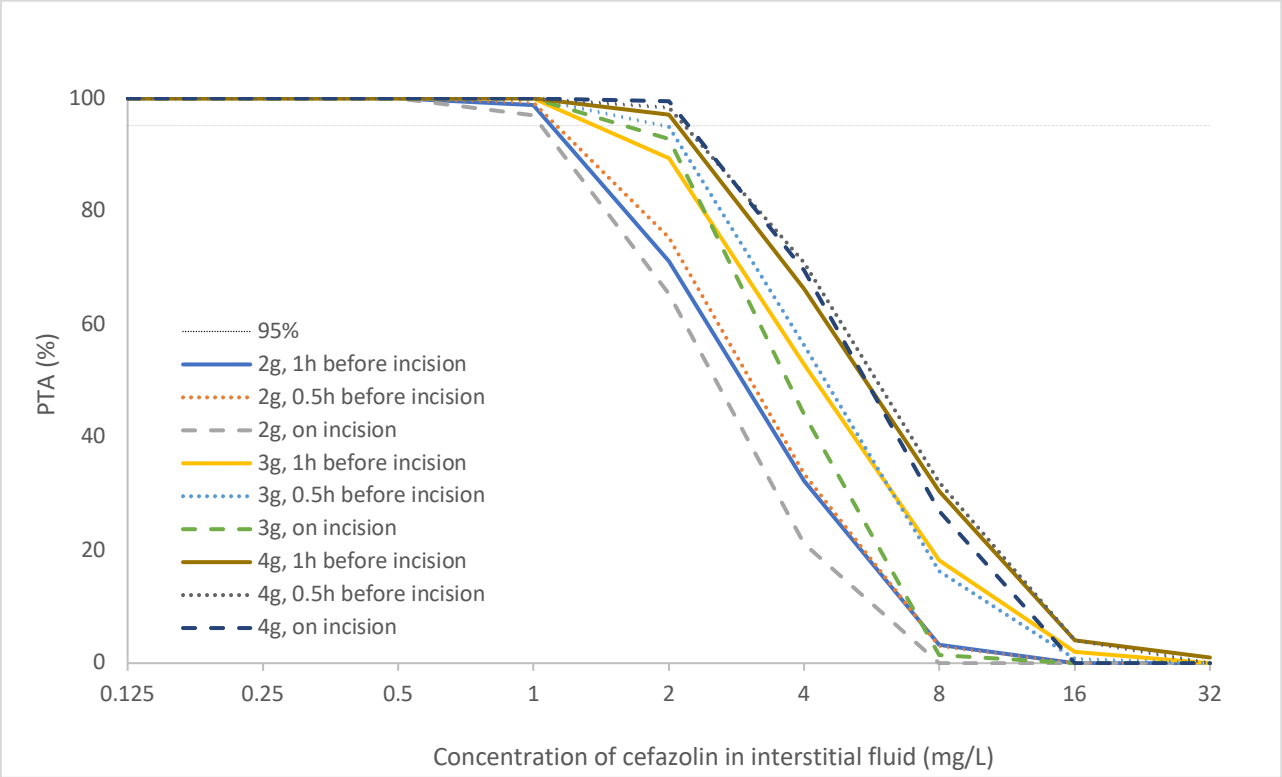


Supplemental Figure S1: Individual predicted concentration diagnostic plots for the final covariate model for unbound plasma cefazolin concentrations (A), total cefazolin in plasma concentrations (B), and unbound cefazolin in tissue concentrations (C). Data are presented in mg L^{-1}.

A.

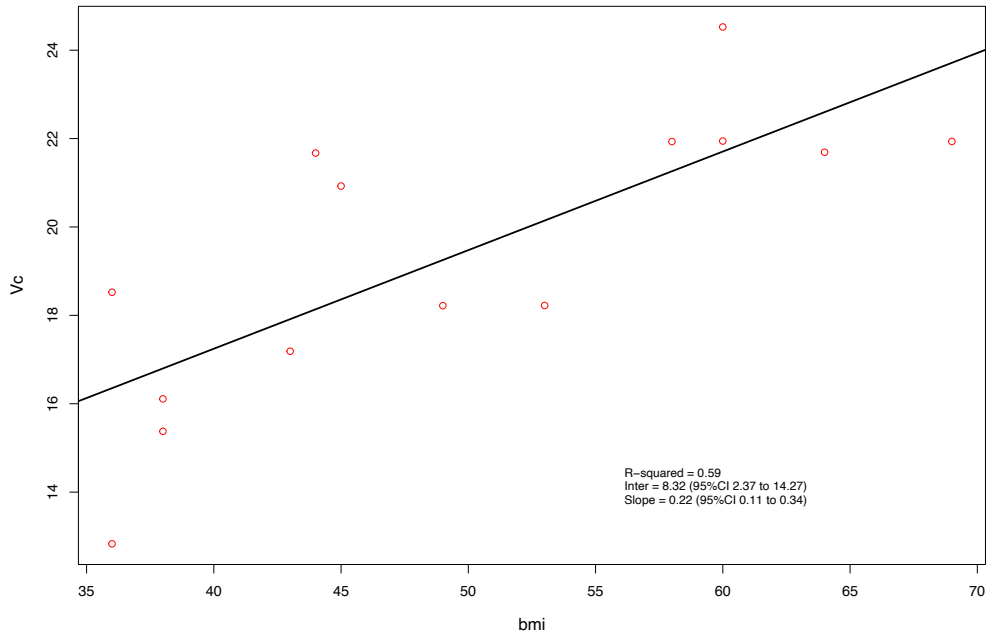

100
80
60
40
20
0
PTA (%)
95%
2g, 1h before incision
2g, 0.5h before incision
2g, on incision
3g, 1h before incision
3g, 0.5h before incision
3g, on incision
4g, 1h before incision
4g, 0.5h before incision
4g, on incision
0.125
0.25
0.5
1
2
4
8
16
32
Concentration of cefazolin in plasma (mg/L)

B.

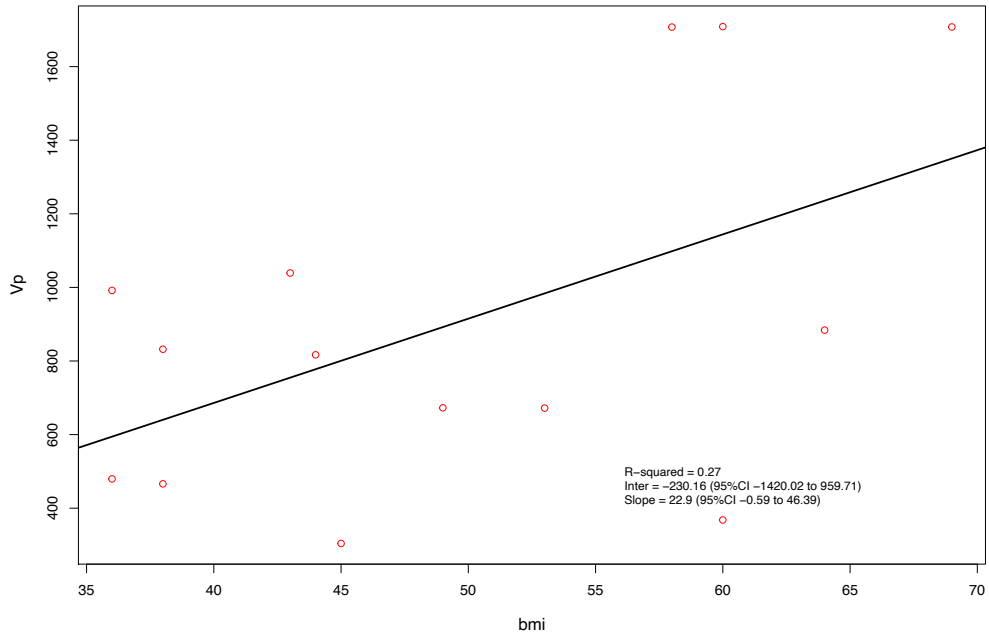


Supplemental Figure S2: Monte Carlo simulations (n = 5000) and probability of target attainment for achieving unbound cefazolin concentrations in plasma (A) and interstitial fluid (B) for pre-operative 2, 3 or 4 g dose regimens administered 0.5 h prior to incision as 3-min infusions and also including re-administration of a 1 g bolus dose 2 h after incision and a 2 g extended infusion at 0.5 h for 3 h, to a typically obese patient (body mass index of 50) undergoing bariatric surgery for up to 4 h duration, with surgery commencing on incision, after 0.5 h, and after 1 h. The horizontal broken line represents a PTA of 95%.

A

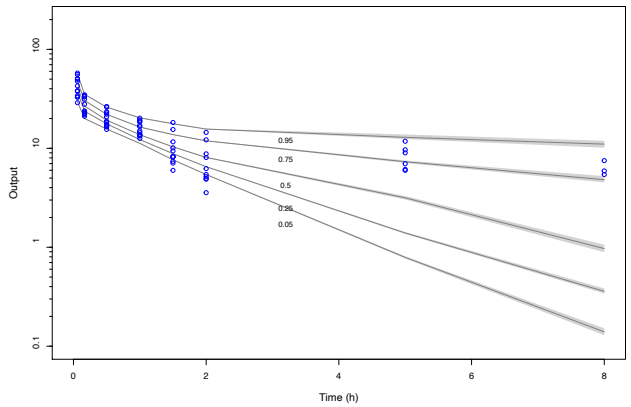


B

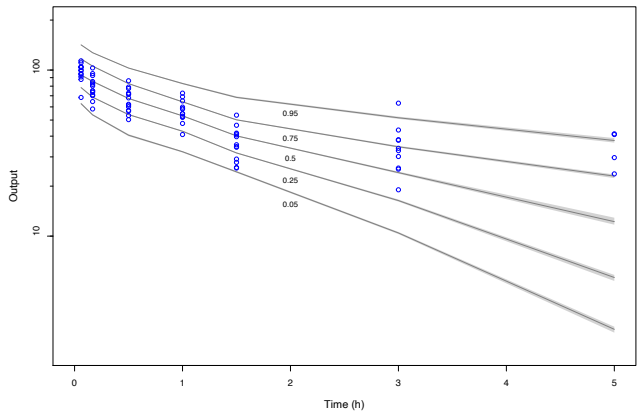


Supplemental Figure S3. Relationship between cefazolin concentration in (A) volume of central compartment and (B) volume of the peripheral compartment with body mass index (bmi), before the addition of BMI, as a covariate to the four-compartment model.

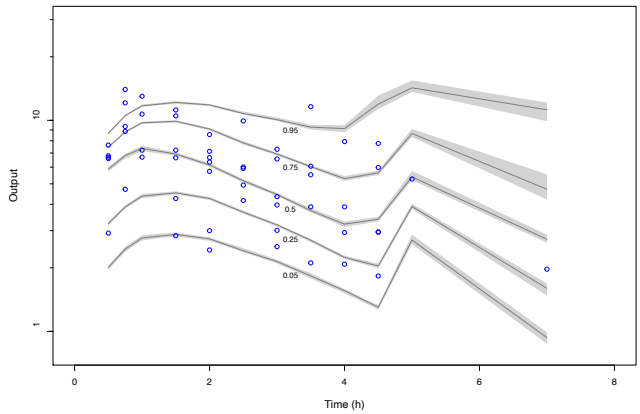
A



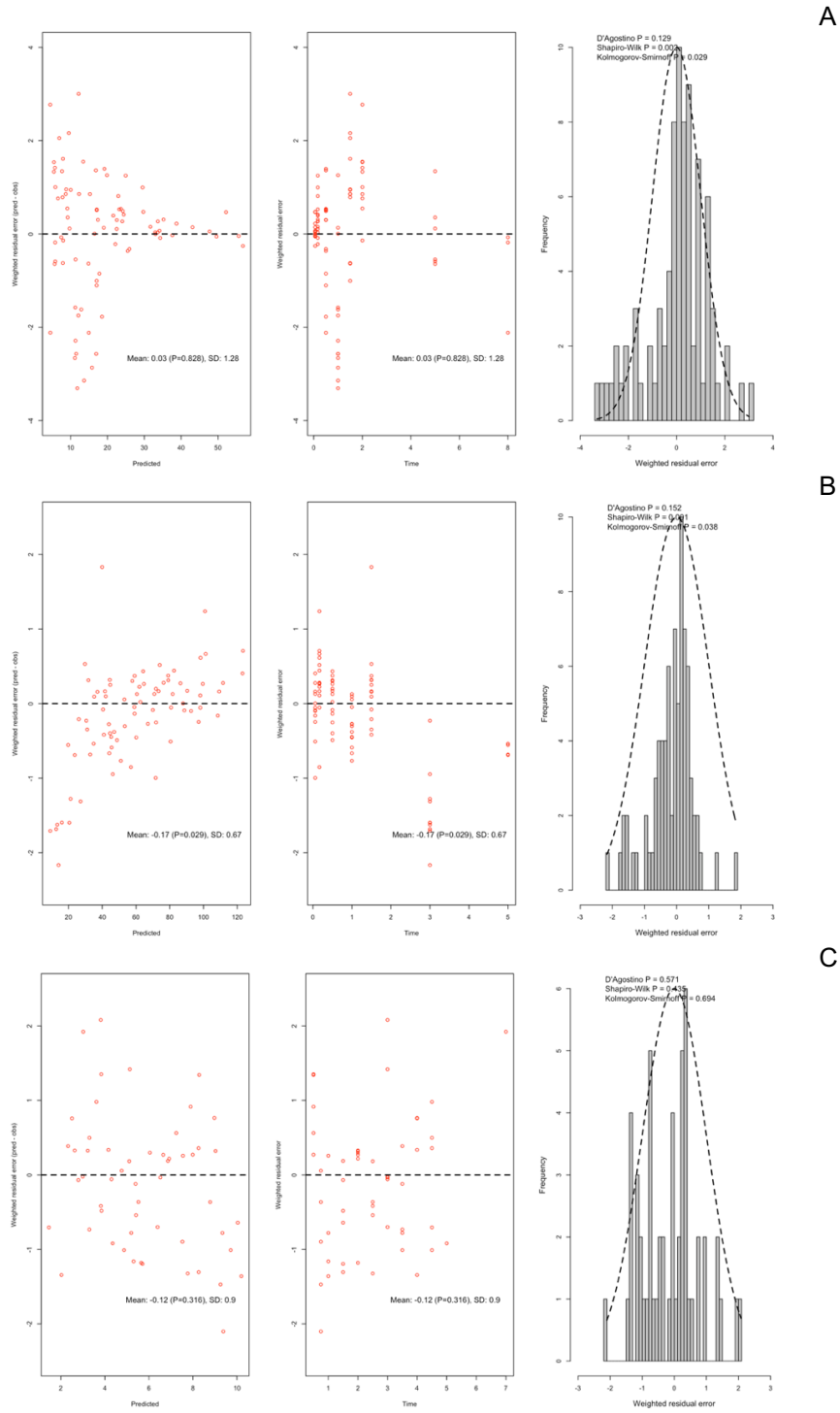
B



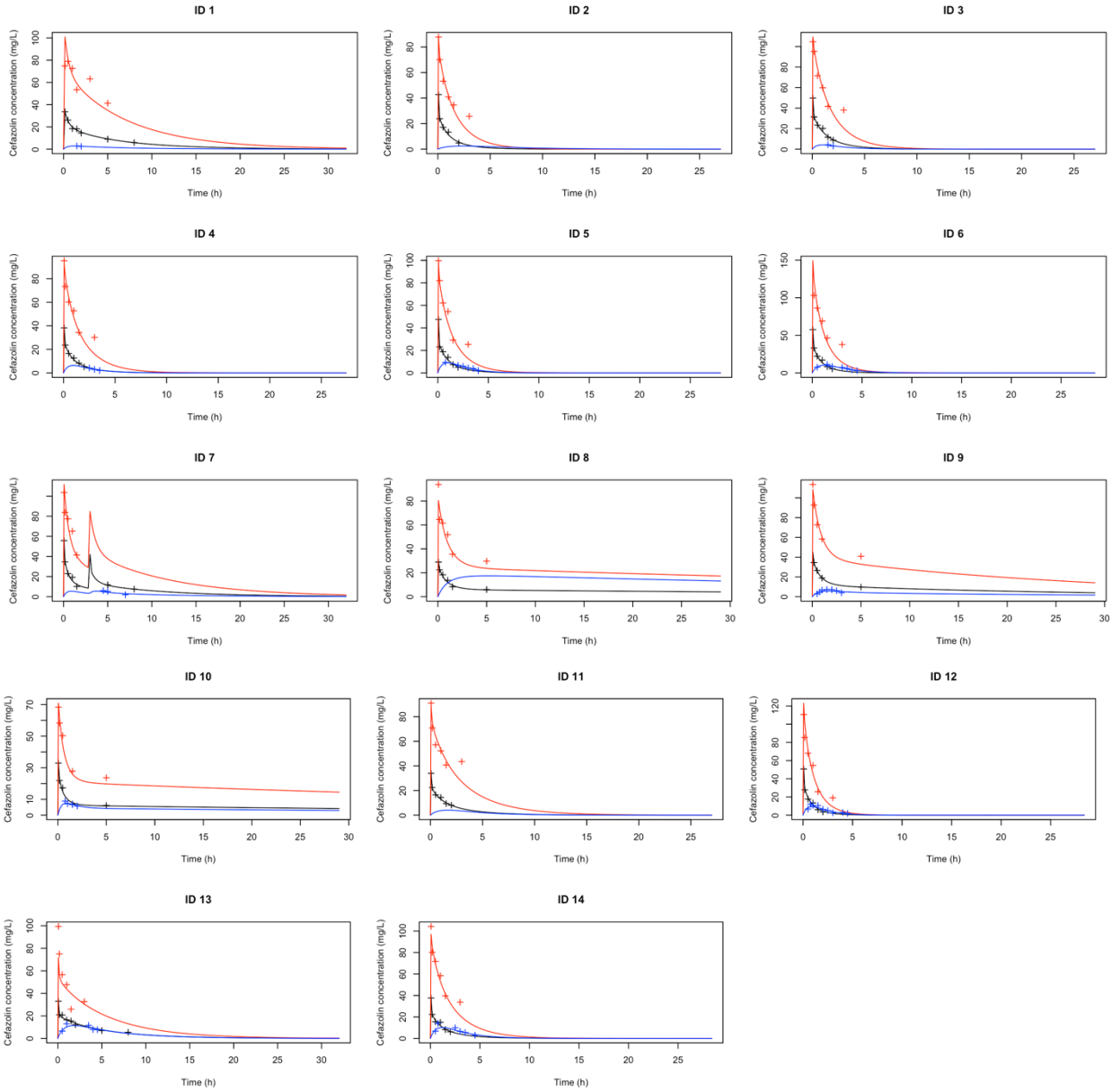
C



Supplemental Figure S4. Visual predictive checks of the final covariate model for (A) unbound, (B) total and (C) microdialysis cefazolin concentrations. The lines represent the percentiles of 1000 simulated cefazolin concentration-time profiles superimposed with observed cefazolin concentrations (circles). The distribution of the simulated unbound, total and microdialysis concentration profiles is similar to that of the observed unbound, total and microdialysis concentrations, with 89.3%, 99.0% and 96.3% of observed concentrations between 5th and 95th simulated percentiles, respectively, suggesting that the model describes the data adequately.



Supplemental Figure S5. Weighted residual error plots of the final covariate model for (A) unbound, (B) total and (C) microdialysis cefazolin concentrations. Bland-Altman plot of predicted – observed (pred-obs) versus mean (left), pred-obs versus time (centre), and frequency distribution (right).



Supplemental Figure S6: Individual patient observed cefazolin concentrations (+) and Bayesian posterior pharmacokinetic model results (line) for plasma total concentrations (red), unbound concentrations (black) and interstitial fluid (blue) over time while undergoing bariatric surgery. Patient ID7 received an additional 1 g dose of cefazolin 3 h after the initial dose.