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Supplementary files

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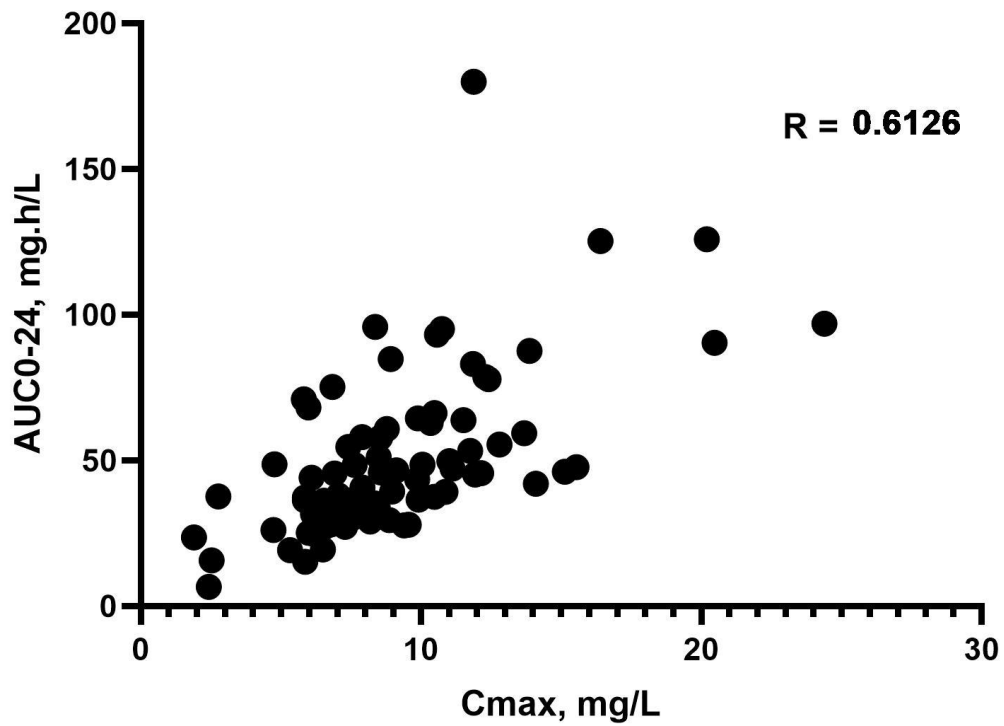
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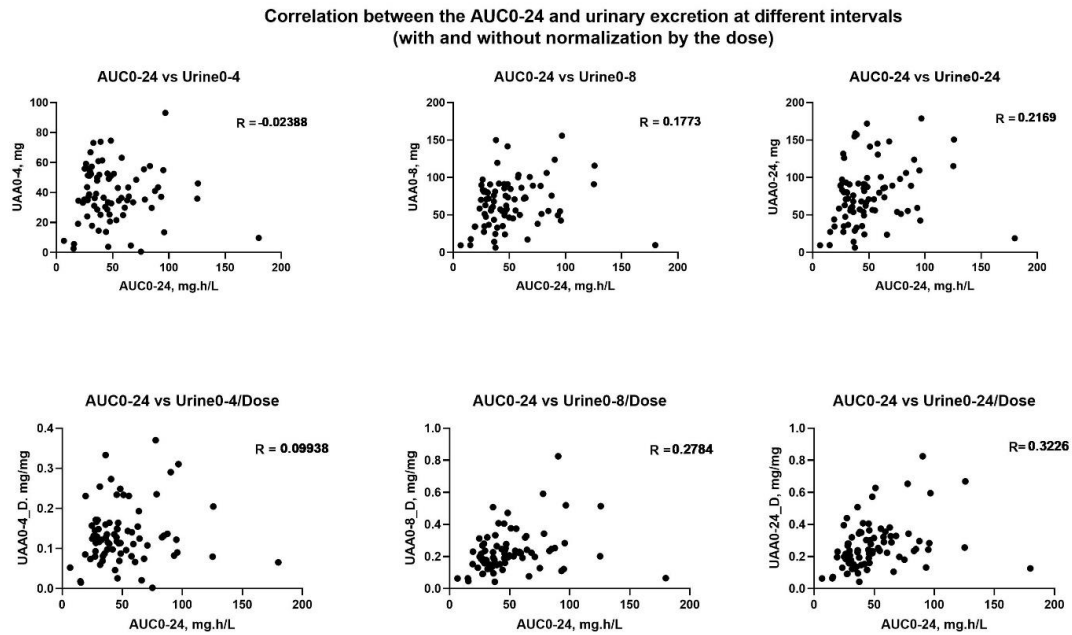
2

Correlation between Cmax and AUC0-24



Supplementary Figure 1 legend: Correlation of serum peak concentration (Cmax) and serum total area under the concentration time curve (AUC0-24). N= 82 with calculable AUC0-24.

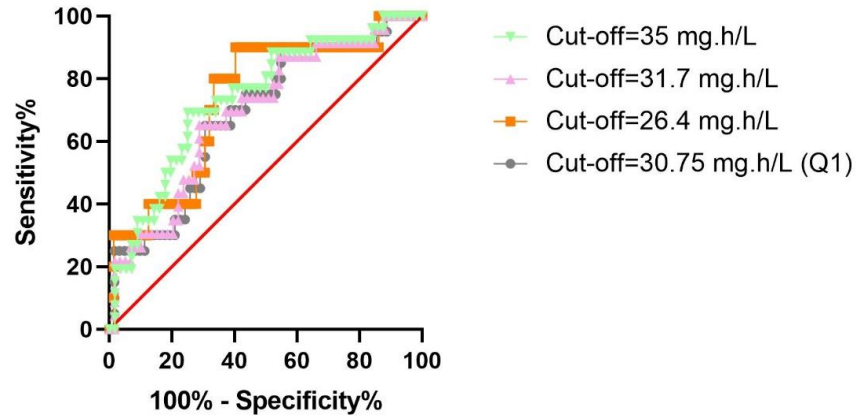
3



Supplementary Figure 2 legend: Correlation of rifampin serum area under the concentration time curve over the 24 hour dosing interval (AUC0-24) and urinary excretion of rifampin at different time intervals (0-4 hours, 0-8 hours and 0-24 hours) following dose. Urinary excretion is both unadjusted for dose (top panels) and adjusted (bottom panels).

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ROC curves with different thresholds for AUC0-24 vs Urine0-24/Dose



cut-off=26.4 mg.h/L

Area under the ROC curve	
Area	0.7333
Std. Error	0.08360
95% confidence interval	0.5695 to 0.8972
P value	0.0173

cut-off=31.7 mg.h/L

Area under the ROC curve	
Area	0.6927
Std. Error	0.06395
95% confidence interval	0.5674 to 0.8180
P value	0.0070

cut-off=35 mg.h/L

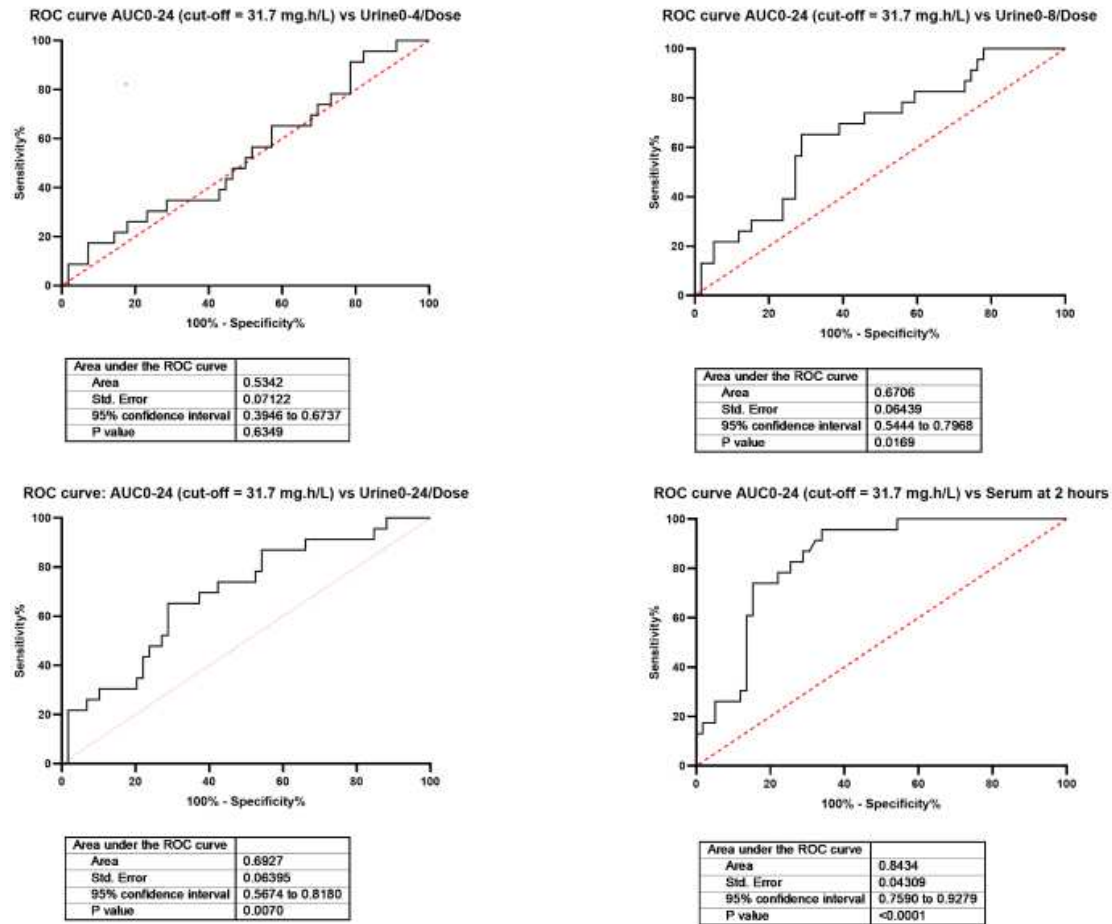
Area under the ROC curve	
Area	0.7356
Std. Error	0.05902
95% confidence interval	0.6199 to 0.8513
P value	0.0006

cut-off=30.75 mg.h/L (Q1)

Area under the ROC curve	
Area	0.6847
Std. Error	0.06738
95% confidence interval	0.5526 to 0.8167
P value	0.0134

Supplemental Figure 3 legend: ROC= Receiver Operator Characteristic curves for rifampin urinary dose excretion over 24 hours predicting different serum area under the concentration time curve (AUC0-24) threshold values: cut-off 26.4 mg*h/L derived from weekly rifampin AUC to achieve <5% treatment failure among population of children from India [supplemental citation 1]; cut-off 31.7 mg*h/L derived from weekly rifampin AUC to achieve <5% treatment modeled among a multinational population of children [supplemental citation 2 and manuscript citation 22]; 35 mg*h/L derived from AUC0-24 predictive of treatment failure in an adult cohort from South Africa [supplemental citation 3]; cut-off 30.75 mg*h/L as first quartile (Q1) of median drug AUC0-24 in Tanzanian cohort of this study.

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Supplementary Figure 4 legend: ROC= Receiver Operator Characteristic curves for rifampin urinary dose excretion over 0-4 hours, 0-8 hours, and 0-24 hours, and serum 2hr value (C2hr) to predict calculated serum area under the concentration time curve (AUC0-24) threshold value previously associated with tuberculosis treatment outcome in pediatric cohorts. C2hr has been commonly used estimate of peak concentration when applying therapeutic drug monitoring for rifampin in clinical settings.

References for Supplementary Files (Supplementary Figure 3)

1. Guiastrenec B, Ramachandran G, Karlsson MO, Kumar AKH, Bhavani PK, Gangadevi NP, Swaminathan S, Gupta A, Dooley KE, Savic RM. Suboptimal Antituberculosis Drug Concentrations and Outcomes in Small and HIV-Coinfected Children in India: Recommendations for Dose Modifications. *Clin Pharmacol Ther* 2018;104(4):733-741.
2. Radtke K, Dooley K, Dodd P et al. Alternative dosing guidelines to improve outcomes in childhood tuberculosis: a mathematical modelling study. *Lancet Child Adolescent Health* 2019; 3(9):636-645.
(reference #22 in manuscript)
3. Pasipanodya JG, McIlleron H, Burger A, Wash PA, Smith P, Gumbo T. Serum drug concentrations predictive of pulmonary tuberculosis outcomes. *J Infect Dis* 2013; 208(9):1464-73.