Title: Population pharmacokinetics and target attainment of pretomanid in rifampicin-resistant Tuberculosis patients

Running title: Pretomanid PK and PTA in RR-TB patients

*Bern-Thomas Nyang'wa [1,2], Ilaria Motta[3], Ronelle Moodliar[4], Varvara Solodovnikova[5], Shakira Rajaram[6], Mohammed Rasool [6], Catherine Berry[7], Zhonghui Huang[8], Geraint Davies[9], David Moore[10], *Frank Kloprogge[2]

[1] Médecins sans Frontières, Public Health Department, Amsterdam, The Netherlands

[2] Institute for Global Health, University College London, London, United Kingdom

[3] University College London, MRC-CTU, London, United Kingdom

[4] THINK (TB & HIV Investigative Network) Durban, South Africa.

[5] Republican Scientific and Practical Centre of Pulmonology and Tuberculosis, Minsk, Belarus.

[6] Clinical HIV Research Unit (CHRU), Wits Health Consortium (WHC), Department of Internal Medicine, School of Clinical medicine, Faculty of Health Sciences, University of Witwatersrand, Johannesburg, South Africa.

[7] Médecins sans Frontières, Manson Unit, Public Health Department, London, United Kingdom

[8] UCL-GOSH Institute of Child Health, University College London, London, United Kingdom

[9] University of Liverpool, Department of Clinical Infection, Microbiology and Immunology, Liverpool, United Kingdom

[10] London School of Hygiene and Tropical Medicine, Clinical Research Department, London, United Kingdom

*** Corresponding authors**

Bern-Thomas Nyang'wa; bern.nyangwa@london.msf.org

ORCID: 0000-0001-9915-5878

Frank Kloprogge: f.kloprogge@ucl.ac.uk

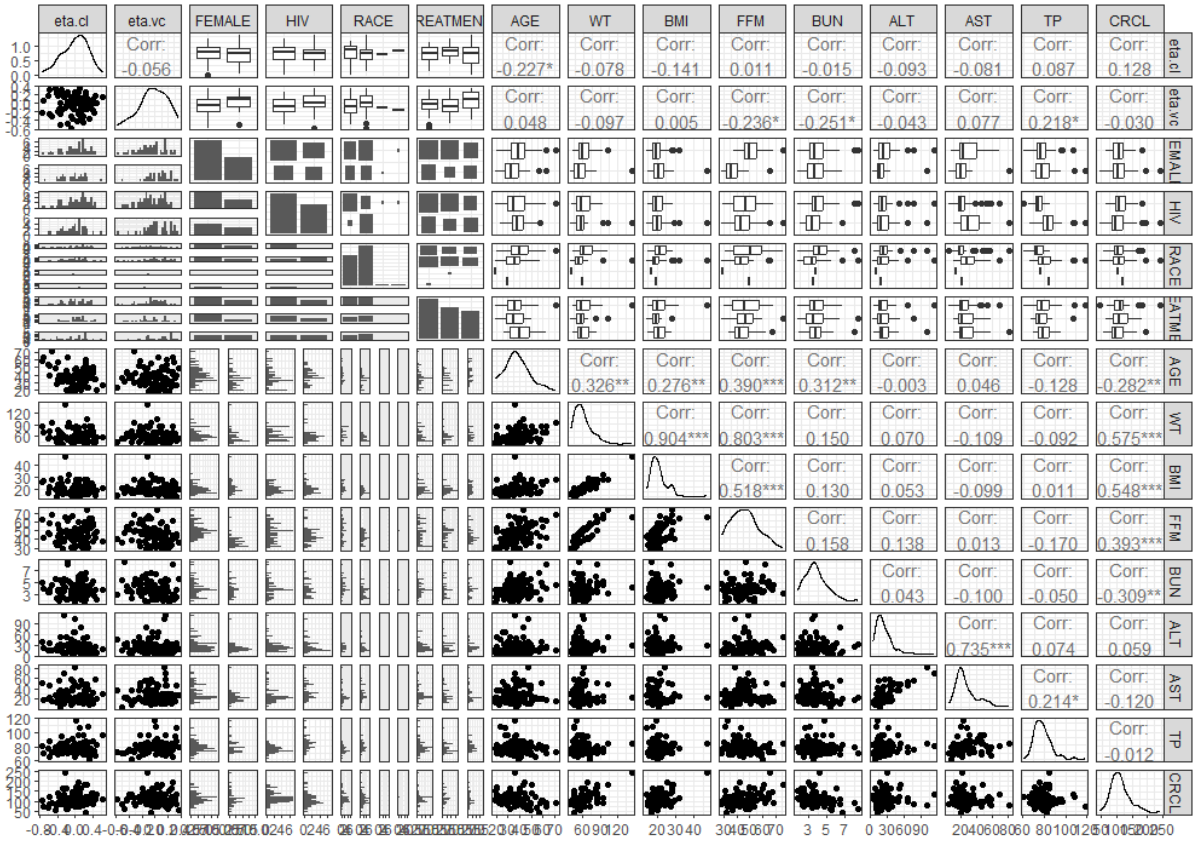
ORCID: 0000-0001-7213-4559

Supplementary appendix

Appendix 1: R code for the pretomanid model

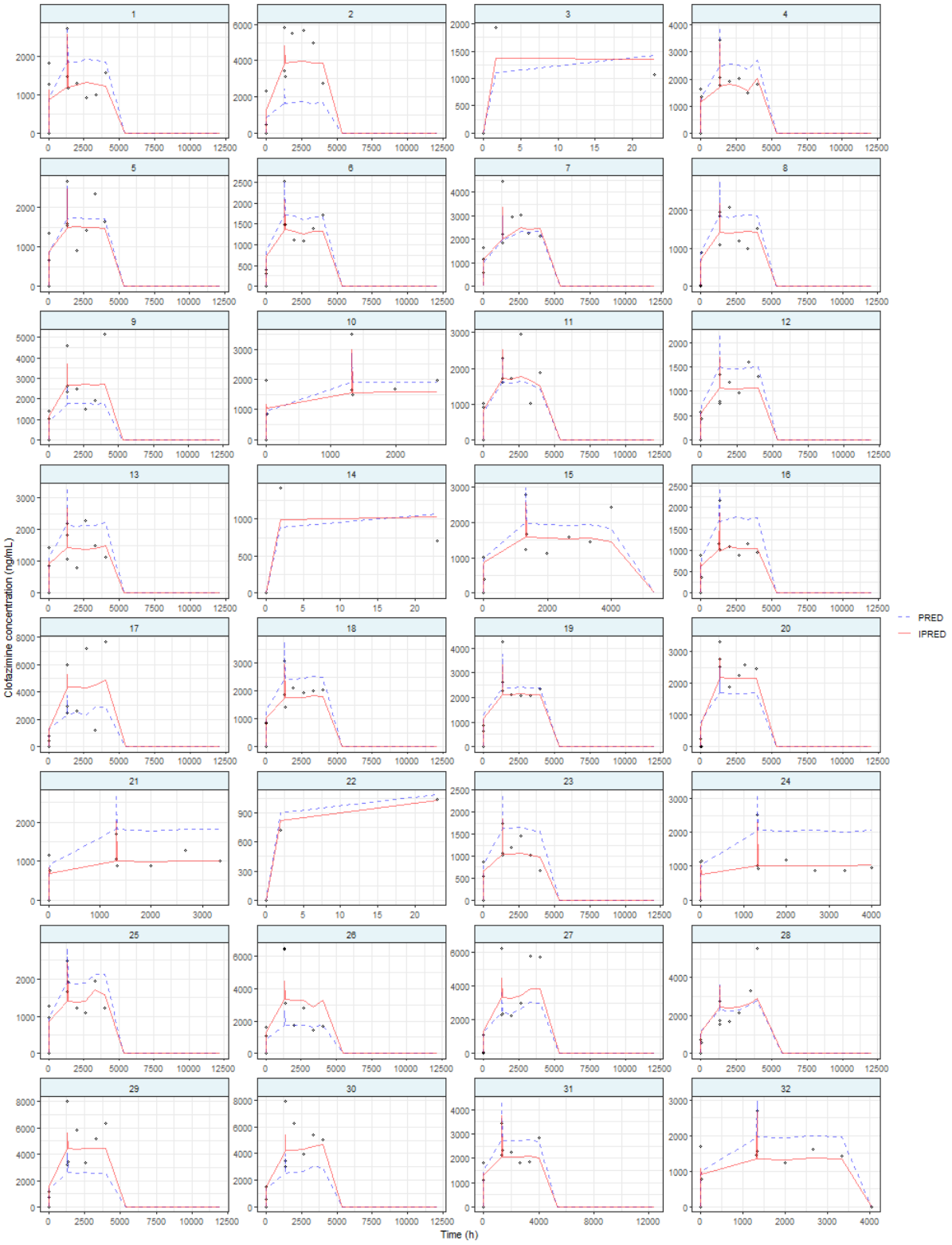
```
# Pretomanid population pharmacokinetic model code (nlmixr2)
ini({
        lka <- -1.15259732127294
label("Absorption rate")
lcl <- 1.13008124732802
label("Clearance")
lvc <- 4.62170931536226
label("Central volume of distribution")
prop.err <- c(0, 0.321731821549103)
add.err <- c(0, 367.831309683669)
covffmPow1 <- fix(0.75)
covffmPow2 <- fix(1)
eta.cl ~ 0.102674627530168
eta.vc ~ 0.10705836808838
 })

model({
ka <- exp(lka)
cl <- exp(lcl + eta.cl + logFFM * covffmPow1)
vc <- exp(lvc + eta.vc + logFFM * covffmPow2)
linCmt() ~ prop(prop.err) + add(add.err)
 })
```

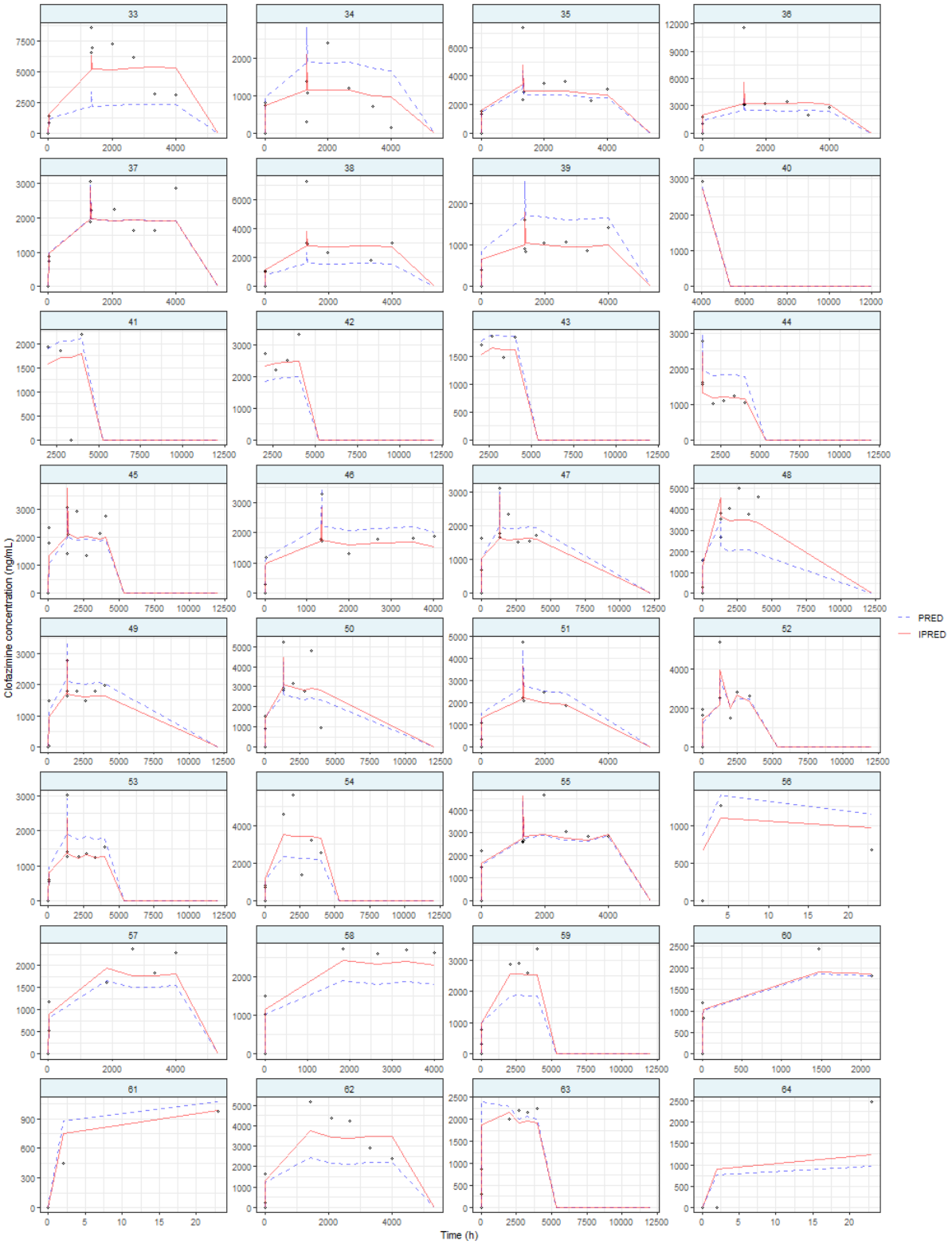
Appendix 2: Continuous covariate and parameter correlation matrix.



Covariate vs parameter matrix on base model. WT: weight, BMI: body mass index, FFM: fat free mass, BUN: blood urea nitrogen, ALT: alanine transaminase, and AST: aspartate aminotransferase, TP: total protein, CRCL: estimated creatinine clearance, random.g: BPaLM, BPaLC or BPaL arm.

Appendix 3: Individual model fit plots.

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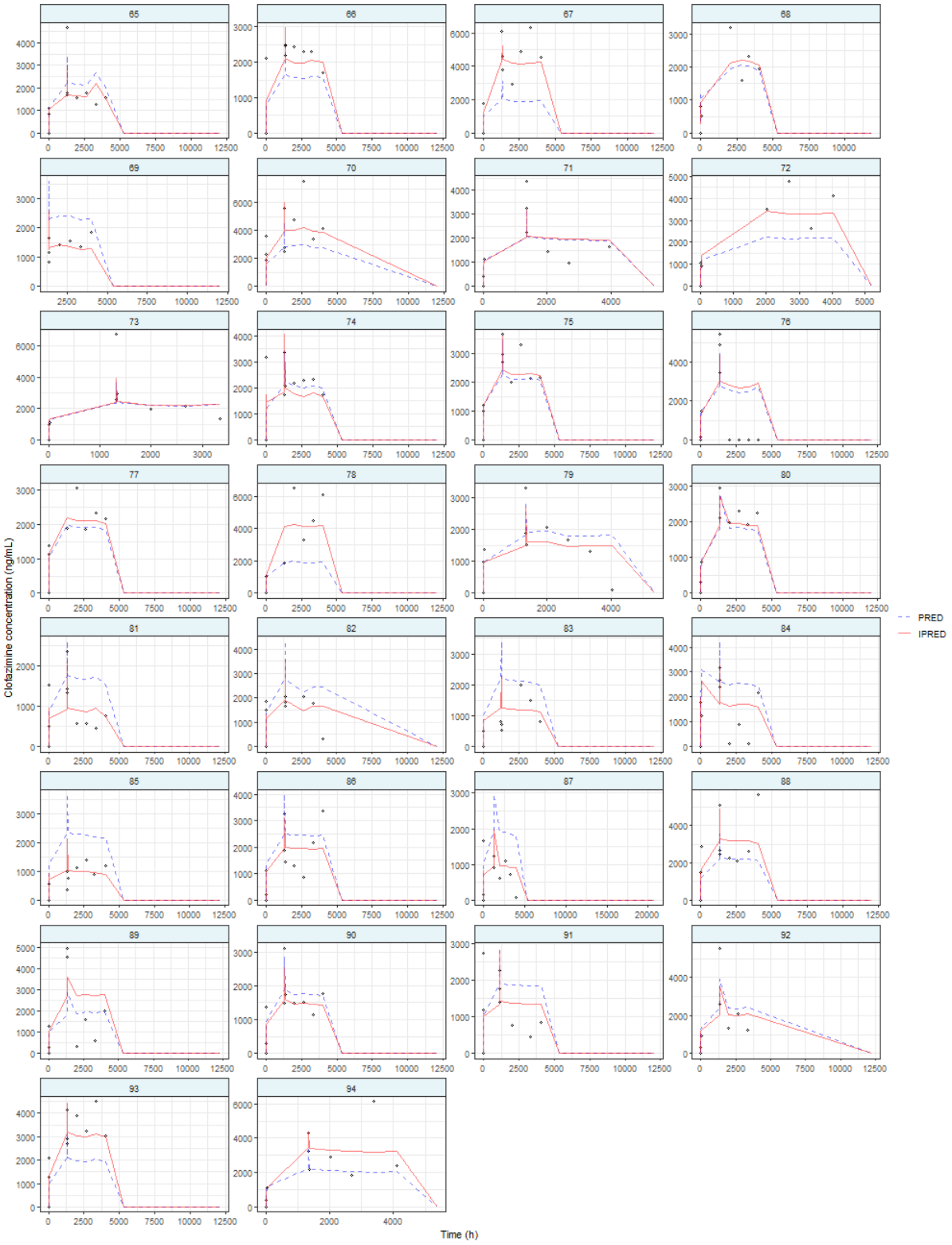
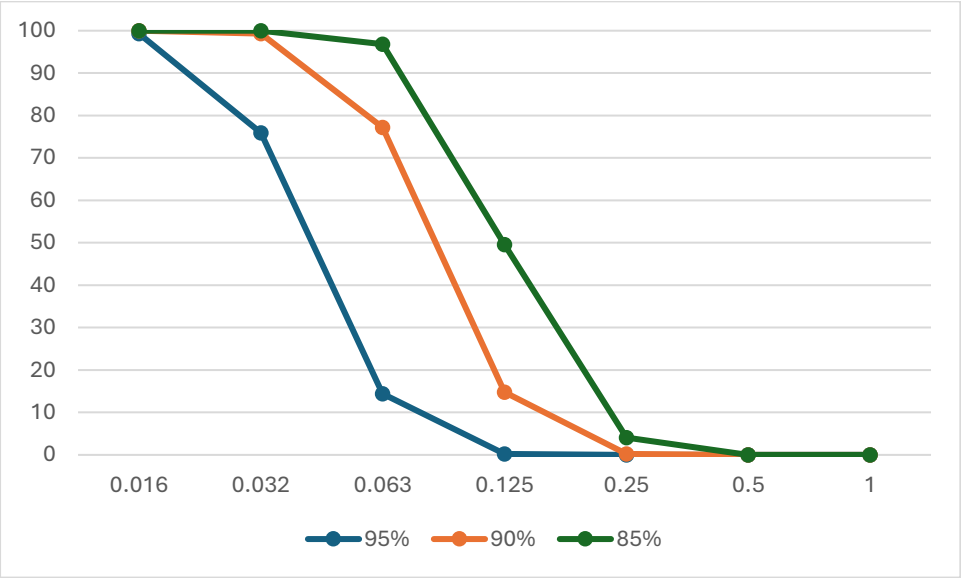
Clofazimine concentration (ng/mL)
Time (h)
PRED
IPRED



Individual linezolid plasma concentration - time profiles. Each panel represent a patient, with open circles representing observed plasma concentrations, the blue dashed line the population predictions by the developed model and the red solid lines the individual population predictions.

Appendix 4: PTA plots for a 200 mg pretomanid dose at escalating MIC's using varying plasma protein binding scenarios



Probability of attaining an $fAUC_{0\text{-}24}$/MIC of 167 for a 200mg dose, varying protein binding assumptions.

Appendix 5: Used r packages

```
library(rxode2)
library(nlmixr2)
library(reshape2)
library(ggplot2)
library(tidyverse)
library(PerformanceAnalytics)
library(psych)
library(dplyr)
library(GGally)
```