Supplementary data

Table S1. Summary of demographic characteristics of the patient population from the PreDiCT-TB and CPTR database.

Study	Demographic characteristics						
	N (F/M)[a]	**Age (yrs)**	**Weight (kg)**	**Height (cm)**	**BMI (kg/m^2)**	**HIV (N/P/U)[b]**	**Study locations**
Benator_2002 (CDC22/TB-1001)[1]	1073 (264/809)	43 (18-88)	62 (34-129)	170 (132-203)	21 (13-57)	1002/71/0	North-America
Burman_2006 (CDC27/TB-1006)[2]	332 (112/220)	32 (18-81)	55 (34-141)	166 (131-193)	20 (14-48)	290/42/0	North-America/ Uganda/ South-Africa
Dorman_2009 (CDC28/TB-1009)[3]	435 (123/312)	31 (17-79)	56 (35-105)	168 (130-195)	20 (13-44)	413/22/0	North-America/ Uganda/ South-Africa/Brazil/ Spain
Johnson_2006[4]	51 (7/44)	35 (18-58)	56 (41-76)	169 (149-184)	20 (17-25)	51/0/0	Brazil
Johnson_2009[5]	393 (154/239)	28 (18-59)	54 (32-98)	165 (142-199)	20 (12-38)	393/0/0	Brazil/Uganda/ Philippines
Rustomjee_2008[6]	119 (48/71)	34 (18-65)	52 (32-79)	163 (136-185)	20 (15-33)	96/23/0	South-Africa
Sokolova_2009[7]	60 (27/33)	30 (18-55)	62 (45-91)	-	-	60/0/0	Russia
Thwaites_2011[8]	61 (25/36)	35 (15-70)	49 (21-68)	-	-	53/3/5	Vietnam
Total	2524 (760/1764)	36 (15-88)	58 (21-141)	168 (130-203)[3]	20 (12-57)[c]	2358/161/5	

Continuous variables are presented as median and range; categorical variables are presented as absolute number.
N=size of the population; **BMI**=body mass index.
[a]**F**= female, **M**= male; [b]**N**= HIV negative, **P**=HIV positive, **U**= HIV status unknown; [c]Calculated from 2054 patients.

Table S2. Median height values stratified by sex and WHO weight band that were imputed to patients with missing value.

	Height (cm)	
Weight band	**Female**	**Male**
<40 kg	151.0	158.0
40-54 kg	157.5	166.0
>54-70 kg	160.0	172.0
>70 kg	164.0	178.0

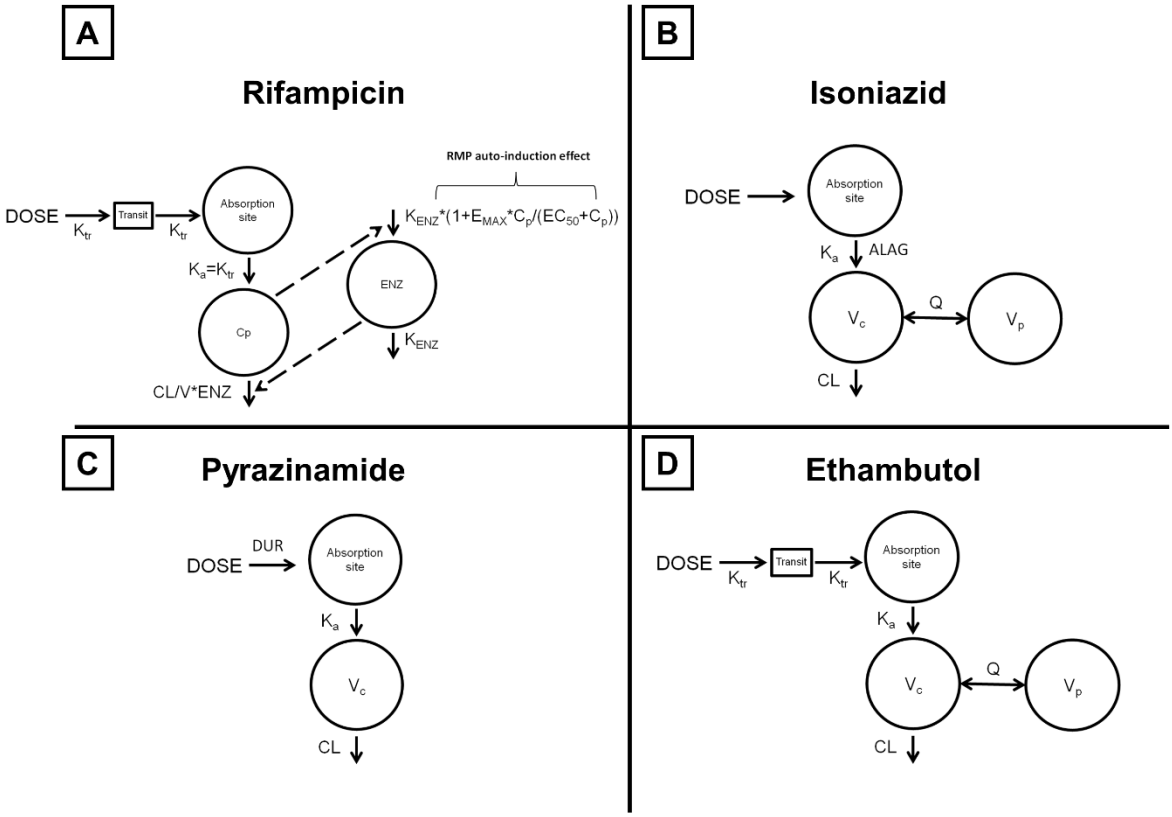

Figure S1. A schematic representation of the selected PK models used for simulations. **A)** Rifampicin PK model included one-compartment disposition and a transit absorption compartment model [9]. The drug is absorbed into the central compartment via the rate constant Ktr. Auto-induction was characterized by an enzyme turnover mechanism which assumed RIF concentration (Cp) increasing enzyme production rate (KENZ) and subsequently the enzyme pool (ENZ) in a nonlinear manner, which leads to increased RIF clearance (CL). Normal fat mass (NFM) was included as covariate for CL and volume of distribution (V). **B)** Isoniazid PK model included a two-compartment disposition with absorption lag time (ALAG) and first-order elimination [10]. Body weight was a covariate on drug disposition (Vc, Vp) and elimination (CL, Q) whereas sex was found to influence central volume of distribution. **C)** Population PK of pyrazinamide was best described with one-compartment model with first-order absorption (Ka), first-order elimination and duration of zero-order release (Dur) of the drug from formulation into the absorption site [11]. Sex and body weight were included as covariate on Vc and CL. **D)** Ethambutol PK was described with a two-compartment model with one transit compartment prior to absorption and first order [12]. Body weight was found to influence distribution and elimination process. Allometric scaling was used to describe the effect of size on the disposition of rifampicin, isoniazid and ethambutol. A proportional relationship was used to describe weight effect on CL of pyrazinamide [11].

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