

Table S1. Summary of previously published VPA population pharmacokinetic model.

PMID	Year	Patient	Sample size	Model	Covariates	Country
25751467	2015	Children	80	-	UGT1A6	India
26088889	2015	Adult	102	-	UGT2B7	China
26484865	2015	Adult	77	OCM	SCN1A, sex, age, seizure type	Japan
27795544	2016	Children	102	-	UGT2B7, UGT1A4	China
28273397	2017	Adult	279	-	CYP2C9, CYP2A6	China
28280887	2017	Children	96	OCM	Body weight	Belgium
28187395	2017	Adult	20	TCM	Previous VPA therapy, decontamination	Poland
28483293	2017	Adult	206	OCM	Total daily dose, body weight	Thailand
29564480	2018	Children	98	OCM	Body weight, age, sex, height, body surface area, alanine transaminase, aspartate transaminase, liver and renal function	France
29724294	2018	Adult	187	-	ABCC2	China
29666902	2018	Children	290	OCM	CYP2C19, UGT1A8, UGT2B7, total daily dose, body surface area	China
29981400	2018	Children	264	OCM	Body weight, co-administration, total daily dose, LEPR	China
29340733	2018	Children	182	OCM	UGT1A4, UGT2B7, UGT2B7	China
30693367	2019	Adult	354	-	SCN1A, SCN2A	China

OCM: one compartment model; TCM: two compartment model; -: only the association between covariates and concentration was analyzed.

Table S2. Modeling process

Scenario	-2LL	nPar m	nOb s	nSu b	EpsShrinka ge
Base model	851.8131	5	98	60	0.47618
cstep001 V-GNDR	838.989	6	98	60	0.39418
cstep002 CI-GNDR	848.243	6	98	60	0.43147
cstep003 CI-AGE	850.8981	6	98	60	0.47448
cstep004 V-AGE	850.2853	6	98	60	0.47261
cstep005 V-WT	849.7784	6	98	60	0.46711
cstep006 V-BMI	851.667	6	98	60	0.47837
cstep007 CI-COM	851.6003	6	98	60	0.47391
cstep008 CI-CYP2C19	833.552	6	98	60	0.47078
cstep009 V-height	844.3429	6	98	60	0.43293
cstep010 CI-ALB	842.5	6	98	60	0.46684
cstep011 CI-GLB	851.5863	6	98	60	0.47616
cstep012 CI-AST	851.3616	6	98	60	0.47535
cstep013 CI-ALT	850.6396	6	98	60	0.4753
cstep014 CI-SCR	851.1399	6	98	60	0.47792
cstep015 CI-TP	847.8778	6	98	60	0.47032
cstep016 V-GNDR CI-CYP2C19	824.3447	7	98	60	0.40966
cstep017 CI-GNDR CI-CYP2C19	831.0932	7	98	60	0.42736
cstep018 CI-AGE CI-CYP2C19	832.978	7	98	60	0.46916
cstep019 V-AGE CI-CYP2C19	831.511	7	98	60	0.46229
cstep020 V-WT CI-CYP2C19	832.1008	7	98	60	0.46545
cstep021 V-BMI CI-CYP2C19	833.4959	7	98	60	0.47259
cstep022 CI-COM CI-CYP2C19	831.0177	7	98	60	0.45996
cstep023 CI-CYP2C19 V-height	826.972	7	98	60	0.42991
cstep024 CI-CYP2C19 CI-ALB	828.7074	7	98	60	0.4663
cstep025 CI-CYP2C19 CI-GLB	833.4742	7	98	60	0.47036
cstep026 CI-CYP2C19 CI-AST	833.385	7	98	60	0.46905
cstep027 CI-CYP2C19 CI-ALT	832.9627	7	98	60	0.46948
cstep028 CI-CYP2C19 CI-SCR	833.5325	7	98	60	0.47089
cstep029 CI-CYP2C19 CI-TP	831.5171	7	98	60	0.46769
cstep030 V-GNDR CI-GNDR CI-CYP2C19	822.6046	8	98	60	0.4031
cstep031 V-GNDR CI-AGE CI-CYP2C19	823.6057	8	98	60	0.40766
cstep032 V-GNDR V-AGE CI-CYP2C19	823.363	8	98	60	0.41498
cstep033 V-GNDR V-WT CI-CYP2C19	823.9692	8	98	60	0.40439
cstep034 V-GNDR V-BMI CI-CYP2C19	824.3426	8	98	60	0.4099
cstep035 V-GNDR CI-COM CI-CYP2C19	821.5007	8	98	60	0.39909
cstep036 V-GNDR CI-CYP2C19 V-height	821.9963	8	98	60	0.39516
cstep037 V-GNDR CI-CYP2C19 CI-ALB	817.623	8	98	60	0.39054
cstep038 V-GNDR CI-CYP2C19 CI-GLB	824.1918	8	98	60	0.40961
cstep039 V-GNDR CI-CYP2C19 CI-AST	824.2853	8	98	60	0.40893
cstep040 V-GNDR CI-CYP2C19 CI-ALT	823.9395	8	98	60	0.40936

cstep041 V-GNDR CI-CYP2C19 CI-SCR	824.2773	8	98	60	0.41049
cstep042 V-GNDR CI-CYP2C19 CI-TP	821.6247	8	98	60	0.3984
cstep043 V-GNDR CI-GNDR CI-CYP2C19 CI-ALB	815.7674	9	98	60	0.38476
cstep044 V-GNDR CI-AGE CI-CYP2C19 CI-ALB	817.5039	9	98	60	0.38923
cstep045 V-GNDR V-AGE CI-CYP2C19 CI-ALB	817.1127	9	98	60	0.39385
cstep046 V-GNDR V-WT CI-CYP2C19 CI-ALB	817.099	9	98	60	0.38569
cstep047 V-GNDR V-BMI CI-CYP2C19 CI-ALB	817.6289	9	98	60	0.39009
cstep048 V-GNDR CI-COM CI-CYP2C19 CI-ALB	815.442	9	98	60	0.38187
cstep049 V-GNDR CI-CYP2C19 V-height CI-ALB	815.2095	9	98	60	0.37967
cstep050 V-GNDR CI-CYP2C19 CI-ALB CI-GLB	817.5908	9	98	60	0.38971
cstep051 V-GNDR CI-CYP2C19 CI-ALB CI-AST	817.6014	9	98	60	0.38973
cstep052 V-GNDR CI-CYP2C19 CI-ALB CI-ALT	817.5496	9	98	60	0.39026
cstep053 V-GNDR CI-CYP2C19 CI-ALB CI-SCR	817.5351	9	98	60	0.38885
cstep054 V-GNDR CI-CYP2C19 CI-ALB CI-TP	817.4676	9	98	60	0.39051
cstep055 V-GNDR CI-ALB	827.0672	7	98	60	0.3758