Table S1: Genes and variants included in the panel. Inclusion is based on the panel developed by the U-PGx consortium.

Gene	Star-allele	RS-number	HGVS (GRCh37)
CYP2B6	*4	rs2279343	NC_000019.9:g.41515263A>G
	*18	rs28399499	NC_000019.9:g.41518221T>C
	*9	rs3745274	NC_000019.9:g.41512841G>T
	*16	rs2279343;	NC_000019.9:g.41515263A>G;
		rs28399499	NC_000019.9:g.41518221T>C
	*6	rs2279343;	NC_000019.9:g.41515263A>G;
		rs3745274	NC_000019.9:g.41512841G>T
CYP2C19	*17	rs12248560	NC_000010.10:g.96521657C>T
	*9	rs17884712	NC_000010.10:g.96535246G>A
	*4A/B	rs28399504	NC_000010.10:g.96522463A>G
	*8	rs41291556	NC_000010.10:g.96535173T>C
	*2	rs4244285	NC_000010.10:g.96541616G>A
	*3	rs4986893	NC_000010.10:g.96540410G>A
	*5	rs56337013	NC_000010.10:g.96612495C>T
	*10	rs6413438	NC_000010.10:g.96541615C>T
	*6	rs72552267	NC_000010.10:g.96535210G>A
CYP2C9	*3	rs1057910	NC_000010.10:g.96741053A>C
	*2	rs1799853	NC_000010.10:g.96702047C>T
	*11	rs28371685	NC_000010.10:g.96740981C>T
	*5	rs28371686	NC_000010.10:g.96741058C>G
CYP2D6	*10	rs1065852	NC_000022.10:g.42526694G>A
	*17	rs28371706	NC_000022.10:g.42525772G>A
	*41	rs28371725	NC_000022.10:g.42523805C>T
	*3	rs35742686	NC_000022.10:g.42524244delT
	*4	rs3892097;	NC_000022.10:g.42524947C>T;
		rs1065852	NC_000022.10:g.42526694G>A
	*6	rs5030655	NC_000022.10:g.42525086delA
	*9	rs5030656	NC_000022.10:g.42524176_42524178delCTT
	*8	rs5030865	NC_000022.10:g.42525035C>A
	*14B	rs5030865	NC_000022.10:g.42525035C>T
	*14A	rs5030865;	NC_000022.10:g.42525035C>T;
		rs1065852	NC_000022.10:g.42526694G>A
CYP3A5	*6	rs10264272	NC_000007.13:g.99262835C>T
	*7	rs41303343	NC_000007.13:g.99250393_99250394insA
	*3	rs776746	NC_000007.13:g.99270539C>T
DPYD	*2	rs3918290	NC_000001.10:g.97915614C>T
	*13	rs55886062	NC_000001.10:g.97981343A>C
	1236G>A	rs56038477	NC_000001.10:g.98039419C>T
	2846A>T	rs67376798	NC_000001.10:g.97547947T>A
F5L	FvL	rs6025	NC_000001.10:g.169519049T>C
SLCO1B1	*5	rs4149056	NC_000012.11:g.21331549T>C
TPMT	*3A	rs1142345;	NC_000006.11:g.18130918T>C;
		rs1800460	NC_000006.11:g.18139228C>T
	*3C	rs1142345	NC_000006.11:g.18130918T>C
	*3B	rs1800460	NC_000006.11:g.18139228C>T
	*2	rs1800462	NC_000006.11:g.18143955C>G
UGT1A1	*27	rs35350960	NC_000002.11:g.234669619C>A
	*6	rs4148323	NC_000002.11:g.234669144G>A
	*36	rs8175347[5]	NC_000002.11:g.234668881_234668882TA[5]
	*28	rs8175347[7]	NC_000002.11:g.234668881_234668882TA[7]
	*37	rs8175347[8]	NC_000002.11:g.234668881_234668882TA[8]
VKORC1	1173	rs9934438	NC_000016.9:g.31104878G>A

Table S2: Haplotype frequencies of the prospective cohort. There were no significant differences in haplotype frequencies between the parents and children (χ^2, $p<0.001$) with the exception of VKORC1 ($p = 0.48$).

Gene	Haplotype assignment	Parents only (prospective)		Children only (prospective)	
		N	Frequency	N	Frequency
CYP2B6		226		110	
	*1	165	73.0%	86	78.2%
	*4	13	5.8%	3	2.7%
	*6	46	20.4%	21	19.1%
	*9	2	0.88%		
CYP2C19		0		0	
CYP2C9		226		110	
	*1	189	83.6%	94	85.5%
	*2	25	11.1%	11	10%
	*3	12	5.3%	5	4.5%
CYP2D6		224		110	
	*1	129	57.6%	57	51.8%
	*10	10	4.5%	5	4.5%
	*3	8	3.6%	2	1.8%
	*4	41	18.3%	26	23.6%
	*41	23	10.3%	12	10.9%
	*6	2	0.9%	1	0.9%
	*9	11	4.9%	7	6.4%
CYP3A5		192		88	
	*1	9	4.7%	5	5.7%
	*3	181	94.3%	82	93.2%
	*6	2	1.0%	1	1.1%
DPYD		226		110	
	*1	217	96.0%	106	96.4%
	*2A	2	0.88%	1	0.91%
	1236G>A	6	2.7%	3	2.7%
	2846A>T	1	0.44%	0	
FVL		226		110	
	F5 positive	7	3.1%	3	2.7%
	F5 negative	219	96.9%	107	97.3%
SLCO1B1		226		110	
	*5	31	13.7%	18	16.4%
	wt	195	86.3%	92	83.6%
TPMT		224		106	
	*3A	11	4.9%	5	4.7%
	wt			1	0.94%
		213	95.1%	100	94.3%
VKORC1		226		106	
	1173T	93	41.2%	48	45.3%
	wt	133	58.8%	58	54.7%

Table S3: Manually assigned diplotype for calls that could not be phased automatically. Diplotype assignments are based on linkage and adapted from the Ubiquitous pharmacogenomics consortium translation tables.

Gene	Assigned diplotype	Variant on allele A	Variant on Allele B	Unphased variants	Frequency
CYP2B6	*1/*6	-	-	41515263A>G; 41512841G>T	81
	*1/*6	-	41515263A>G	41512841G>T	3
	*1/*6	-	41512841G>T	41515263A>G	7
	*1/*6	41515263A>G	-	41512841G>T	8
	*4/*6	41515263A>G	41515263A>G	41512841G>T	3
	*6/*9	41512841G>T	41512841G>T	41515263A>G	1
CYP2C9	*2/*3	-	96741053A>C	96702047C>T	2
CYP2D6	*4/*1	42526694G>A	-	42524947C>T	2
	*4/*1	42524947C>T	-	42526694G>A	2
	*4/*3	42524947C>T; 42526694G>A	-	42524244delT	1
	*3/*4	-	42526694G>A; 42524947C>T	42524244delT	1
	*9/*4	42524178_ 42524180delTCT	-	42526694G>A; 42524947C>T	1
	*41/*4	42523805C>T	-	42526694G>A; 42524947C>T	2
	*41/*4	-	42526694G>A; 42524947C>T	42523805C>T	1
	*1/*4	-	42524947C>T	42526694G>A	2
	*1/*4		42526694G>A	42524947C>T	1
	*41/*4	42523805C>T	42524947C>T	42526694G>A	1
	*4/*41	-	-	42526694G>A; 42523805C>T; 42524947C>T	2
	*4/*41	-	42523805C>T	42526694G>A; 42524947C>T	3
	*10/*41	-	42523805C>T	42526694G>A	1
	*10/*41	42526694G>A	-	42523805C>T	2
	*4/*41	-	-	42523805C>T; 42526694G>A; 42524947C>T	1
	*9/*41	42524178_ 2524180delTCT	-	42523805C>T	1
	*4/*9	-	42524178_ 42524180delTCT	42526694G>A; 42524947C>T	1
	*17/*41	42523805C>T	-	42525772G>A	1
	*17/*41	-	42523805C>T	42525772G>A	1
	*41/*9	-	42524178_ 42524180delTCT	42523805C>T	1
CYP3A5	*3/*7	-	99250394_ 99250395insA	99270539C>T	1
TPMT	wt/*3A	-	-	18130918T>C; 18139228C>T	18

Table S4: Phenotype frequencies and actionability based on CPIC guidelines. Phenotypes are based on the U-PGx translation tables, actionability is based on the Clinical Pharmacogenomics implementation consortium (CPIC) guidelines, where actionable is defined as a phenotype accompanied by at least one dosing advise. Guidelines for Factor V Leiden are not available.

Gene	Phenotype	Number of subjects	Frequency	Actionable
CYP2B6		1577		
	PM	105	6.7%	Yes
	IM	528	33.5%	Yes
	EM	944	59.9%	
CYP2C19		15		
	PM	-		Yes
	IM	4	26.7%	Yes
	EM	7	46.7%	
	RM	4	26.7%	Yes
	UM	-		Yes
CYP2C9		1583		
	PM	59	3.7%	Yes
	IM	487	30.2%	Yes
	EM	1037	65.5%	
CYP2D6		1576		
	PM*	66	4.2%	Yes
	Not assigned	1510	95.8%	
CYP3A5		1163		
	PM	882	75.8%	
	IM	263	22.6%	Yes
	EM	18	1.5%	Yes
DPYD		1581		
	AS: 0	-		Yes
	AS: 0.5	-		Yes
	AS: 1	21	1.3%	Yes
	AS: 1.5	95	6.0%	Yes
	AS: 2	1465	92.7%	
SLCO1B1		1579		
	Normal Function	1172	74.2%	
	Decreased function	371	23.5%	Yes
	Poor function	36	2.3%	Yes
TPMT		1562		
	PM	1	0.1%	Yes
	IM	139	8.9%	Yes
	EM	1421	91.0%	
VKORC1		1549		
	Normal Function (1173CC)	564	36.4%	
	Decreased Function (1173CT)	723	46.7%	
	Poor Function (1173TT)	262	16.9%	Yes

PM: Poor metabolizer, IM: Intermediate Metabolizer, EM: Extensive Metabolizer, RM: Rapid Metabolizer, UM: ultra-rapid Metabolizer, AS: Activity Score, * Based on Single Nucleotide Variants (2 null-alleles), as Copy Number variants could not be determined.