

Table s1: List of clinically relevant PGx variants

Gene	Allele	Array Type	Data source	Allele Functional Status^	Activity Score*	TPMI_AF	Sensitivity ^{\$}	Specificity ^{\$}
ABCG2	c.421 C>A	TPM/TPM2	Genotype	Decreased function	N/A	31.7%	99.9%	100.0%
CYP2B6	decrease variants	TPM/TPM2	Genotype	Decreased function	N/A	19.1%	99.8%	100.0%
CYP2C9	*3	TPM/TPM2	Genotype	Decreased function	0.5	3.2%	100.0%	100.0%
	*16	TPM/TPM2	Genotype	Decreased function	0.5	0.5%	100.0%	100.0%
CYP2C19	*2	TPM/TPM2	Genotype	No function	N/A	32.3%	100.0%	100.0%
	*3	TPM/TPM2	Genotype	No function	N/A	5.2%	100.0%	100.0%
	*6	TPM/TPM2	Genotype	No function	N/A	0.2%	100.0%	100.0%
	*17	TPM/TPM2	Imputation	Increased function	N/A	0.5%	100.0%	100.0%
CYP3A5	*1	TPM/TPM2	Genotype	Normal function		28.6%	100.0%	100.0%
CYP4F2	*3	TPM/TPM2	Genotype	Decreased function		23.6%	100.0%	100.0%
G6PD	Canton/Taiwan-Hakka	TPM/TPM2	Imputation/Genotype	Deficient function	II	1.41%	100.0%	100.0%
	Chinese-3/taipei	TPM/TPM2	Genotype	Deficient function	III	0.20%	100.0%	100.0%
	Chinese-5	TPM/TPM2	Genotype	Deficient function	II	0.25%	100.0%	100.0%
	Gaohe	TPM/TPM2	Genotype	Deficient function	II	0.17%	100.0%	100.0%
	Kaiping	TPM/TPM2	Genotype	Deficient function	II	0.61%	100.0%	100.0%
	QuingYan	TPM/TPM2	Genotype	Deficient function	III	0.17%	100.0%	100.0%
HLA-A	*31:01	TPM/TPM2	HiBag	Risk		2.3%	100.0%	100.0%
HLA-B	*15:02	TPM/TPM2	HiBag	Risk		4.2%	100.0%	99.9%
	*57:01	TPM/TPM2	HiBag	Risk		0.2%	100.0%	100.0%
	*58:01	TPM/TPM2	HiBag	Risk		10.6%	100.0%	100.0%
HLA-DQA1	*02:01	TPM/TPM2	HiBag	Risk		2.4%	100.0%	100.0%
HLA-DRB1	*07:01	TPM/TPM2	HiBag	Risk		2.3%	96.3%	100.0%
IFNL3	rs12979860	TPM/TPM2	Genotype	Unfavorable response		5.8%	99.4%	100.0%
MTRNR1	m.1095T>C	TPM/TPM2	Genotype	Risk		0.2%	100.0%	100.0%
	m.1555A>G	TPM/TPM2	Genotype	Risk		0.2%	100.0%	100.0%
NAT2	*5	TPM/TPM2	Genotype	Decreased Function		3.9%	100.0%	100.0%
	*6	TPM/TPM2	Genotype	Decreased Function		26.5%	100.0%	100.0%
	*7	TPM/TPM2	Genotype	Decreased Function		16.1%	100.0%	100.0%
NUDT15	*2/*3	TPM/TPM2	Imputation/Genotype	No Function		11.0%	99.7%	100.0%
SLCO1B1	*5/*15	TPM/TPM2	Genotype	No function		11.2%	100.0%	100.0%
TPMT	*3C	TPM/TPM2	Genotype	No Function		1.4%	100.0%	100.0%
UGT1A1	*6	TPM/TPM2	Genotype	Decreased Function		15.3%	100.0%	100.0%
	*27	TPM/TPM2	Genotype	Decreased Function		2.1%	100.0%	100.0%
	rs887829	TPM/TPM2	Genotype	Decreased Function		12.1%	100.0%	100.0%
VKORC1	-1639G>A	TPM/TPM2	Genotype	Require warfarin dose reduction		89.3%	100.0%	100.0%

^ PharmGKB Gene-specific Information Tables <https://www.pharmgkb.org/page/pgxGeneRef>

PharmVar 5.0.1 <https://www.pharmvar.org/>

* PharmGKB Gene-specific Information Tables <https://www.pharmgkb.org/page/pgxGeneRef>

^{\$} Evaluated the concordance of genotype and imputation calls with NGS or Sanger sequencing data

Table s2: Distribution of PGx phenotype, actionable phenotypes, and risk drug exposure

Category	Gene	Phenotype	Actionable Phenotype	Case number	Phenotype Freq		Risk drug	Risk drug exposure freq in each phenotype	Individuals encountered following risk drugs in each phenotype group
Phase 1 Metabolic Enzymes	CYP2B6	Total		486,956			13,118	2.7%	Efavirenz Sertraline 258 4,786 179 3,086 73 1,507 6 189 0 4
		EM	v	318,276	65.4%	318879	8,539	2.7%	
		IM	v	149,998	30.8%	168,077	4,082	2.7%	
	PM	v	18,079	3.7%		487	2.7%		
	Indetermined		603	0.1%		10	1.7%		
	CYP2C9	Total		486,956			92,103	18.9%	Celecoxib Flurbiprofen Fluvastatin Ibuprofen Meloxicam Nateglinide Phenytoin Piroxicam Tenoxicam Warfarin 50,200 28,989 4,219 6,681 10,174 227 670 13,933 23 6,113 46,570 26,807 3,903 6,135 9,447 210 623 12,841 23 5,665 3,556 2,122 302 529 715 17 46 1,061 - 439 52 37 9 12 7 1 17 7 22 23 5 5 5 14 2
EM		v	451,020	92.6%	451,393	85,301	18.9%		
IM		v	35,032	7.2%	35,563	6,639	19.0%		
PM	v	531	0.1%		97	18.3%			
Indetermined		373	0.1%		66	17.7%			
Phase 2 Metabolic Enzymes	CYP2C19	Total	v	486,956			116,120	23.8%	Abrocitinib Brivaracetam Citalopram Clobazam Clopidogrel Dexlansoprazol Doxepin Escitalopra Imipramin Lansoprazol Omeprazole Pantoprazol Sertraline Voriconazole 11 28 6,942 1,283 33,664 19,147 6,773 6,845 9,636 44,378 33,407 28,138 4,786 343 51 6 229 122 44 51 46 284 210 185 30 3 4 13 2,714 478 12,872 7,387 2,588 2,677 3,802 17,063 12,807 10,889 1,821 133 5 12 3,196 611 15,667 8,866 3,157 3,146 4,393 20,613 15,453 12,967 2,222 159 2 3 964 188 4,850 2,738 974 954 1,374 6,342 4,891 4,057 706 48 17 46 34 10 17 21 76 46 40 7
		UM	v	17	0.0%	187,877		0.0%	
		RM	v	3,183	0.7%	299,079	751	23.6%	
		EM	v	187,095	38.4%		44,657	23.9%	
		IM	v	226,301	46.5%		53,742	23.7%	
		PM	v	69,578	14.3%		16,787	24.1%	
	CYP3A5	Total		486,956			3,299	0.7%	Tacrolimus 3,299 1,668 1,341 289 1
		PM	v	248,453	51.0%	248,578	1,668	0.7%	
		IM	v	198,492	40.8%	238,378	1,341	0.7%	
	CYP4F2	Total		486,956			6,113	1.3%	Warfarin 6,113 3,578 2,174 352 9
		EM	v	284,173	58.4%	285,017	3,578	1.3%	
		IM	v	174,577	35.8%	201,939	2,174	1.2%	
Phase 2 Metabolic Enzymes	NAT2	PM	v	104,942	21.5%		4,205	4.0%	Isoniazid Sulfamethoxazole and Trimethoprim Sulfasalazine 2,918 7,699 9,777 854 2,172 2,803 1,415 3,844 4,876 646 1,666 2,082 3 17 16
		Indetermined		682	0.1%		36	5.3%	
	NUDT15	Total		486,956			8,523	1.8%	Azathioprine Mercaptopurine 8,486 37 6,789 31 1,590 5 70 1 37 1
		EM	v	384,231	78.9%	386,050	6,820	1.8%	
		IM	v	95,046	19.5%	100,906	1,595	1.7%	
TPMT	Total		486,956			8,523	1.8%	Azathioprine Mercaptopurine 8,486 37 8,243 36 240 1 1 1 2 1	
	EM	v	473,144	97.2%	473,360	8,279	1.7%		
	IM	v	13,479	2.8%	13,596	241	1.8%		
Phase 2 Metabolic Enzymes	UGT1A1	PM	v	117	0.0%		1	0.9%	Atazanavir Irinotecan Nilotinib Pazopanib 56 596 73 120 31 324 38 54 19 208 28 49 6 56 6 16 - 8 1 1
		Indetermined		216	0.0%		2	0.9%	
	ABCG2	Total		486,956			46,617	9.6%	Rosuvastatin 49,032 22,702 21,384 4,932 14
		Normal		227,345			21,588	9.5%	
		Decreased		210,293			20,314	9.7%	
Poor		v	49,162	10.1%	49,162	4,703	9.6%		
Indetermined			156	0.0%		12	7.7%		
SLCO1B1	Total		486,956			127,197	26.1%	Atorvastatin Fluvastatin Lovastatin Pitavastatin Pravastatin Rosuvastatin Simvastatin 73,078 4,219 4,154 32,334 7,786 49,032 11,558 57,718 3,314 3,248 25,416 6,140 38,557 9,000 14,440 847 839 6,498 1,540 9,817 2,391 915 58 67 419 106 655 166 5 - - 1 - 3 1	
	Normal		383,660			100,390	26.2%		
	Decreased	v	97,031	19.9%	383,711	25,163	25.9%		
	Poor	v	6,214	1.3%		1,637	26.3%		
	Indetermined		51	0.0%		7	13.7%		
HLA	HLA-A*3101	Total		486,956			1,319	0.3%	Carbamazepine 1,319 1,278 41
		Negative		467,890	96.1%		1,278	0.3%	
	Positive	v	19,066	3.9%		41	0.2%		
HLA-B*1502	Total		486,956			3,961	0.8%	Carbamazepin Oxcarbazepine Phenytoin 1,319 2,229 670	

		Negative Positive	v	446,907 40,049	91.8% 8.2%		3,675 286	0.8% 0.7%	1,247 72	2,056 173	616 54			
	HLA-B*5701	Total Negative Positive	v	486,956 485,071 1,885	99.6% 0.4%		692 691 1	0.1% 0.1% 0.1%	692 691 1	Abacavir				
	HLA-B*5801	Total Negative Positive	v	486,956 389,717 97,239	80.0% 20.0%		5,251 4,373 878	1.1% 1.1% 0.9%	5,251 4,373 878	Allopurinol				
	DRB1*0701	Total Negative Positive	v	486,956 464,494 22,462	95.4% 4.6%		27 27	0.0% 0.0% 0.0%	27 27	Lapatinib				
	DQA1*0201	Total Negative Positive	v	486,956 464,545 22,411	95.4% 4.6%		27 27	0.0% 0.0% 0.0%	27 27	Lapatinib				
	Others	G6PD	Total normal variable deficient Indetermined	v v v	486,956 446,940 14,095 6,258 19,663	91.8% 2.9% 1.3% 4.0%	466,603 20,353	144 129 6 3 6	0.0% 0.0% 0.0% 0.0% 0.0%	108 96 5 2 5	5 4 1	31 29		
		VKORC1	Total Indetermined	0 v 1 v 2	486,956 388,233 92,927 5,676 120	79.7% 19.1% 1.2% 0.0%	5,796 481,160	6,113 4,803 1,237 70 3	1.3% 1.2% 1.3% 1.2% 2.5%	6,113 4,803 1,237 70 3	Warfarin			
									Peginterferon alfa-2a	Peginterferon alfa-2b	Ribavirin			
IFNL3		Total Favored Unfavored Indetermined	v	486,956 431,219 55,385 352	88.6% 11.4% 0.1%	431,571 55,385	4,255 3,692 562 1	0.9% 0.9% 1.0% 0.3%	576 504 72	218 181 37	1,873 1,591 282			
									Amikacin	Gentamicin	Kanamycin	Paromomycin n	Streptomycin n	Tobramycin
MT-RNR1		Total Normal Risk Indetermined	v	486,956 484,521 1,897 538	99.5% 0.4% 0.1%	485,059 1,897	27,595 27,441 121 33	5.7% 5.7% 6.4% 6.1%	635 631 3 1	23,953 23,816 109 28	5 5	15 15	59 59	4,190 4,168 16 6

Table s3: The distribution of TPML participants exposed to high-risk PGx drugs

Number of drug prescribed per person	Case number	Accumulated count	Accumulated %
0	249796		
1	98724	237160	48.7%
2	60111	138436	28.4%
3	33926	78325	16.1%
4	19251	44399	9.1%
5	10596	25148	5.2%
6	6114	14552	3.0%
7	3550	8438	1.7%
8	2124	4888	1.0%
9	1133	2764	0.6%
10	673	1631	0.3%
11	440	958	0.2%
12	242	518	0.1%
13	132	276	0.1%
14	78	144	0.0%
15	42	66	0.0%
16	14	24	0.0%
17	9	10	0.0%
18	1	1	0.0%

Table s4: The demography of clopidogrel-related MACE cohort

Clopidogrel Users	no MACE		MACE		OR (95% CI)	P value
No. of subjects	24578		3477			
Male	8208	33.4%	1179	33.9%	0.98 (0.91-1.06)	5.49E-01
Age (years, mean±SD)	72.0±9.5		71.24±10.4			1.50E-01
Comorbidity						
DM	13700	55.7%	1910	54.9%	0.97 (0.9-1.04)	3.7E-01
HC	15803	64.3%	2219	63.8%	0.98 (0.91-1.06)	5.8E-01
HTN	11503	46.8%	1625	46.7%	1 (0.93-1.07)	9.1E-01
CKD	8852	36.0%	1209	34.8%	0.95 (0.88-1.02)	1.5E-01
Concurrent medications						
aspirin	2231	9.1%	324	9.3%	1.03 (0.91-1.16)	6.4E-01
warfarin	1253	5.1%	190	5.5%	1.08 (0.92-1.26)	3.6E-01
PPI	8670	35.3%	1420	40.8%	1.27 (1.18-1.37)	1.56E-10
statin	10061	40.9%	1458	41.9%	1.04 (0.97-1.12)	2.8E-01

Table s5: Influence of CYP2C19 for incidence of MACE

1. Clopidogrel users with one or two CYP2C19 LoF vs with non-LoF

MACE	Univariate analysis				Multivariate analysis			
	OR	Lower95%CI	Upper95%CI	Pvalue	OR	Lower95%CI	Upper95%CI	Pvalue
Stroke	1.007	1.004	1.011	7.30E-05	1.007	1.004	1.011	7.10E-05
MI	1.023	1.019	1.026	8.30E-37	1.023	1.019	1.026	2.56E-37
UA	1.014	1.010	1.018	2.21E-13	1.014	1.010	1.018	1.61E-13
HF	1.014	1.009	1.019	1.31E-07	1.014	1.009	1.019	8.20E-08
TLR	1.009	1.004	1.013	1.28E-04	1.009	1.004	1.014	1.16E-04
CV death	1.001	0.999	1.002	2.35E-01	1.001	0.999	1.002	2.36E-01
MACE	1.045	1.036	1.053	2.10E-27	1.045	1.037	1.053	7.98E-28

2. Clopidogrel users with one CYP2C19 LoF vs with non-LoF

MACE	Univariate analysis				Multivariate analysis			
	OR	Lower95%CI	Upper95%CI	Pvalue	OR	Lower95%CI	Upper95%CI	Pvalue
Stroke	1.007	1.003	1.011	2.77E-04	1.00706	1.00326	1.01088	2.69E-04
MI	1.022	1.019	1.026	1.83E-34	1.02242	1.01883	1.02602	6.11E-35
UA	1.013	1.010	1.017	1.40E-11	1.01355	1.00963	1.01748	1.03E-11
HF	1.012	1.007	1.018	5.00E-06	1.01260	1.00727	1.01796	3.37E-06
TLR	1.008	1.004	1.013	5.76E-04	1.00839	1.00363	1.01318	5.45E-04
CV death	1.001	0.999	1.002	3.19E-01	1.00077	0.99924	1.00230	3.22E-01
MACE	1.042	1.034	1.051	6.97E-23	1.04262	1.03407	1.05125	3.28E-23

3. Clopidogrel users with two CYP2C19 LoF vs with non-LoF

MACE	Univariate analysis				Multivariate analysis			
	OR	Lower95%CI	Upper95%CI	Pvalue	OR	Lower95%CI	Upper95%CI	Pvalue
Stroke	1.008	1.003	1.014	1.62E-03	1.008	1.003	1.014	1.62E-03
MI	1.024	1.020	1.028	6.71E-28	1.024	1.020	1.028	4.27E-28
UA	1.016	1.011	1.022	6.04E-10	1.017	1.011	1.022	5.45E-10
HF	1.018	1.011	1.026	1.00E-06	1.018	1.011	1.026	1.00E-06
TLR	1.011	1.004	1.017	1.65E-03	1.011	1.004	1.017	1.58E-03
CV death	1.001	0.999	1.003	2.54E-01	1.001	0.999	1.003	2.56E-01
MACE	1.053	1.041	1.064	8.38E-19	1.053	1.041	1.065	5.74E-19

Table s6: Patient characteristics of azathioprine users in TPMI

Azathioprine Users	no ADR		ADR		OR (95% CI)	P value
No. of subjects	6948		1503			
Male	2140	30.8%	434	28.9%	0.91 (0.8-1.03)	1.40E-01
Age (years, mean±SD)	46.2±15		42.5±14.7			9.43E-02
Comorbidity						
DM	763	11.0%	170	11.3%	1.03 (0.86-1.23)	7.10E-01
HC	1329	19.1%	305	20.3%	1.08 (0.94-1.24)	3.00E-01
HTN	1304	18.8%	309	20.6%	1.12 (0.97-1.37)	1.10E-01
IHD	484	7.0%	115	7.7%	1.11 (0.9-1.37)	3.50E-01
HF	138	2.0%	34	2.3%	1.14 (0.76-1.67)	4.90E-01
CVD	292	4.2%	72	4.8%	1.15 (0.88-1.5)	3.10E-01
Concurrent medications						
aspirin	327	4.7%	61	4.1%	0.86 (0.65-1.14)	2.80E-01
allopurinol	67	1.0%	29	1.9%	2.02 (1.3-3.13)	1.37E-03
corticosteroids	5262	75.7%	1164	77.4%	1.1 (0.96-1.26)	1.60E-01
methotrexate	1030	14.8%	217	14.4%	0.97 (0.83-1.14)	7.00E-01

Table s7: Influence of NUDT15 and TPMT for azathioprine discontinuation due to ADR

1. Azathioprine users with one or two NUDT15 LoF vs with non-LoF

ADR	Univariate analysis				Multivariate analysis			
	OR	Lower95%CI	Upper95%C	Pvalue	OR	Lower95%CI	Upper95%C	Pvalue
Leukopenia	1.0669	1.0494	1.0848	0.0000	1.0668	1.0493	1.0847	2.14E-14
Thrombocytopen	1.0103	0.9967	1.0241	0.1390	1.0117	0.9981	1.0255	9.17E-02
Hepatitis	0.9991	0.9879	1.0105	0.8820	0.9994	0.9883	1.0107	9.23E-01
Allergy	1.0009	0.9968	1.0050	0.6710	1.0003	0.9961	1.0046	8.77E-01
GI	1.0028	0.9973	1.0083	0.3140	1.0037	0.9982	1.0092	1.89E-01
HairLoss	1.0014	0.9970	1.0058	0.5440	1.0010	0.9966	1.0055	6.42E-01
ADR	1.0461	1.0248	1.0679	0.0000	1.0478	1.0264	1.0696	9.28E-06

2. Azathioprine users with one NUDT15 LoF vs with non-LoF

ADR	Univariate analysis				Multivariate analysis			
	OR	Lower95%CI	Upper95%C	Pvalue	OR	Lower95%CI	Upper95%C	Pvalue
Leukopenia	1.0568	1.0393	1.0746	0.0000	1.0574	1.0399	1.0752	6.33E-11
Thrombocytopen	1.0066	0.9929	1.0205	0.3459	1.0084	0.9947	1.0223	2.30E-01
Hepatitis	0.9980	0.9691	1.0227	0.7426	0.9981	0.9868	1.0096	7.44E-01
Allergy	1.0006	0.9964	1.0047	0.7950	0.9999	0.9957	1.0042	9.78E-01
GI	1.0021	0.9966	1.0077	0.4559	1.0030	0.9974	1.0086	2.94E-01
HairLoss	0.9986	0.9943	1.0029	0.5097	0.9988	0.9944	1.0031	5.75E-01
ADR	1.0348	1.0135	1.0566	0.0013	1.0376	1.0161	1.0595	5.39E-04

3. Azathioprine users with two NUDT15 LoF vs with non-LoF

ADR	Univariate analysis				Multivariate analysis			
	OR	Lower95%CI	Upper95%C	Pvalue	OR	Lower95%CI	Upper95%C	Pvalue
Leukopenia	1.327	1.238	1.423	2.26E-15	1.312	1.223	1.408	3.55E-14
Thrombocytopen	1.098	1.035	1.165	2.04E-03	1.091	1.028	1.158	4.04E-03
Hepatitis	1.027	0.976	1.079	3.04E-01	1.032	0.981	1.085	2.24E-01
Allergy	1.009	0.991	1.027	3.45E-01	1.010	0.991	1.029	3.19E-01
GI	1.019	0.995	1.044	1.15E-01	1.021	0.997	1.045	9.37E-02
HairLoss	1.068	1.047	1.090	9.89E-11	1.056	1.035	1.077	1.05E-07
ADR	1.342	1.228	1.468	1.09E-10	1.316	1.203	1.440	2.33E-09

4. Azathioprine users with one or two TPMT LoF vs with non-LoF

ADR	Univariate analysis				Multivariate analysis			
	OR	Lower95%CI	Upper95%C	Pvalue	OR	Lower95%CI	Upper95%C	Pvalue
Leukopenia	1.006	0.967	1.046	0.778	1.003	0.964	1.043	8.96E-01
Thrombocytopen	0.994	0.963	1.027	0.727	0.999	0.967	1.031	9.39E-01
Hepatitis	0.995	0.969	1.022	0.733	0.994	0.968	1.021	6.69E-01
Allergy	0.998	0.988	1.008	0.717	0.998	0.988	1.008	7.21E-01
GI	0.998	0.985	1.011	0.743	0.998	0.985	1.012	8.09E-01
HairLoss	1.006	0.995	1.016	0.273	1.002	0.991	1.012	7.35E-01
ADR	0.988	0.941	1.037	0.624	0.988	0.941	1.038	6.40E-01

5. Azathioprine users with one TPMT LoF vs with non-LoF

ADR	Univariate analysis				Multivariate analysis			
	OR	Lower95%CI	Upper95%C	Pvalue	OR	Lower95%CI	Upper95%C	Pvalue
Leukopenia	1.006	0.967	1.047	0.761	1.003	0.964	1.044	8.76E-01
Thrombocytopen	0.995	0.963	1.027	0.739	0.999	0.967	1.032	9.47E-01
Hepatitis	0.996	0.969	1.023	0.743	0.994	0.968	1.021	6.77E-01
Allergy	0.998	0.988	1.008	0.720	0.998	0.988	1.008	7.24E-01
GI	0.998	0.985	1.011	0.747	0.998	0.985	1.012	8.13E-01
HairLoss	1.006	0.995	1.017	0.269	1.002	0.991	1.012	7.28E-01
ADR	0.988	0.941	1.038	0.644	0.989	0.942	1.039	6.59E-01

Table s8: Influence of ABCG2, CYP2C9 and SLCO1B1 for statin-associated myopathy

1. Atorvastatin users with decreased or poor function ABCG2 vs with normal function ABCG2

	ADR(non LOF)	ADR(LOF)	no ADR (non LOF)	no ADR (LOF)	OR	Upper 95%CI	Lower 95%CI	p value
HighCPKonly	2	1	33787	39264	0.43	4.74	0.04	4.78E-01
myalgia	368	466	33421	38799	1.09	1.25	0.95	2.15E-01
myositis	38	52	33751	39213	1.18	1.79	0.78	4.43E-01
rhabdomyolysis	7	15	33782	39250	1.84	4.51	0.75	1.74E-01
SAM	415	534	33374	38731	1.11	1.26	0.98	1.17E-01
sSAM	45	67	33744	39198	1.28	1.87	0.88	1.97E-01

2. Atorvastatin users with decreased function ABCG2 vs with normal function ABCG2

	ADR(non LOF)	ADR(LOF)	no ADR (non LOF)	no ADR (LOF)	OR	Upper 95%CI	Lower 95%CI	p value
HighCPKonly	2	1	33787	31738	0.53	5.85	0.05	5.36E-01
myalgia	368	375	33421	31364	1.09	1.26	0.94	2.25E-01
myositis	38	33	33751	31706	0.92	1.47	0.58	5.19E-01
rhabdomyolysis	7	15	33782	31724	2.28	5.59	0.93	1.03E-01
SAM	415	424	33374	31315	1.09	1.25	0.95	1.47E-01
sSAM	45	48	33744	31691	1.14	1.71	0.76	2.82E-01

3. Atorvastatin users with poor function ABCG2 vs with normal function ABCG2

	ADR(non LOF)	ADR(LOF)	no ADR (non LOF)	no ADR (LOF)	OR	Upper 95%CI	Lower 95%CI	p value
HighCPKonly	2	0	33787	7526				5.04E-01
myalgia	368	91	33421	7435	1.11	1.4	0.88	3.69E-01
myositis	38	19	33751	7507	2.25	3.9	1.3	3.09E-03
rhabdomyolysis	7	0	33782	7526				2.12E-01
SAM	415	110	33374	7416	1.19	1.47	0.96	1.02E-01
sSAM	45	19	33744	7507	1.9	3.25	1.11	1.73E-02

6. Atorvastatin users with decreased or poor function SLCO1B1 vs with normal function SLCO1B1

	ADR(non LOF)	ADR(LOF)	no ADR (non LOF)	no ADR (LOF)	OR	Upper 95%CI	Lower 95%CI	p value
HighCPKonly	2	1	57716	15354	1.88	20.74	0.17	6.00E-01
myalgia	625	209	57093	15146	1.26	1.48	1.08	3.91E-03
myositis	67	23	57651	15332	1.29	2.07	0.8	2.90E-01
rhabdomyolysis	17	5	57701	15350	1.11	3.01	0.41	8.44E-01
SAM	711	238	57007	15117	1.26	1.46	1.09	1.97E-03
sSAM	84	28	57634	15327	1.25	1.92	0.81	3.00E-01

7. Atorvastatin users with decreased function SLCO1B1 vs with normal function SLCO1B1

	ADR(non LOF)	ADR(LOF)	no ADR (non LOF)	no ADR (LOF)	OR	Upper 95%CI	Lower 95%CI	p value
HighCPKonly	2	1	57716	14439	2	22.06	0.18	5.70E-01
myalgia	625	190	57093	14250	1.22	1.44	1.04	1.24E-02
myositis	67	22	57651	14418	1.31	2.12	0.81	2.69E-01
rhabdomyolysis	17	5	57701	14435	1.18	3.2	0.44	7.65E-01
SAM	711	218	57007	14222	1.23	1.43	1.06	5.73E-03
sSAM	84	27	57634	14413	1.29	1.99	0.84	2.62E-01

8. Atorvastatin users with poor function SLCO1B1 vs with normal function SLCO1B1

	ADR(non LOF)	ADR(LOF)	no ADR (non LOF)	no ADR (LOF)	OR	Upper 95%CI	Lower 95%CI	p value
HighCPKonly	2	0	57716	915				
myalgia	625	19	57093	896	1.94	3.08	1.22	4.22E-03
myositis	67	1	57651	914	0.94	6.78	0.13	9.52E-01
rhabdomyolysis	17	0	57701	915				
SAM	711	20	57007	895	1.79	2.81	1.14	9.87E-03
sSAM	84	1	57634	914	0.75	5.39	0.1	7.75E-01

Table s9: Patient characteristics of NSAID users in TPMI

NSAID Users	no ADR		ADR		OR (95% CI)	P value
No. of subjects	9471		529			
Male	3288	34.7%	205	38.8%	1.19 (0.99-1.42)	6.00E-02
Age (years, mean±SD)	61±14		61.8±14.3			1.10E-01
Dose_first (DDD)	1.1±0.84		1.22±0.4			6.00E-02
Comorbidity						
HTN	1857	19.6%	213	40.3%	2.76 (2.3-3.31)	3.62E-30
HC	1940	20.5%	178	33.6%	1.97 (1.63-2.38)	5.51E-13
DM	1466	15.5%	159	30.1%	2.35 (1.94-2.85)	9.15E-19
CVD	500	5.3%	65	12.3%	2.51 (1.91-3.3)	1.09E-11
IHD	817	8.6%	80	15.1%	1.89 (1.47-2.42)	3.60E-07
PVD	23	0.2%	11	2.1%	8.72 (4.23-17.99)	1.64E-12
COPD	43	0.5%	14	2.6%	5.96 (3.24-10.96)	7.09E-11
HF	122	1.3%	35	6.6%	5.43 (3.69-7.99)	8.50E-22
HP	6	0.1%	0	0.0%		5.63E-01
Concurrent medications						
aspirin	769	8.1%	88	16.6%	2.26 (1.78-2.87)	9.80E-12
antibiotics	3	0.0%	5	0.9%	30.11 (7.18-126.34)	4.76E-13
ACEI/ARB	20	0.2%	9	1.7%	8.18 (3.71-18.05)	5.55E-10
diuretics	66	0.7%	80	15.1%	25.39 (18.08-35.65)	1.25E-159
anticoagulants	45	0.5%	5	0.9%	2 (0.79-5.06)	1.36E-01
immunosuppressants	36	0.4%	11	2.1%	5.57 (2.82-11.01)	2.68E-08
CYP2C9						
EM	8757	92.5%	499	94.3%		
IM	693	7.3%	28	5.3%	0.71 (0.48-1.05)	8.13E-02
PM	12	0.1%	2	0.4%	2.92 (0.65-13.08)	1.41E-01
Indetermined	9	0.1%	0	0.0%		4.74E-01

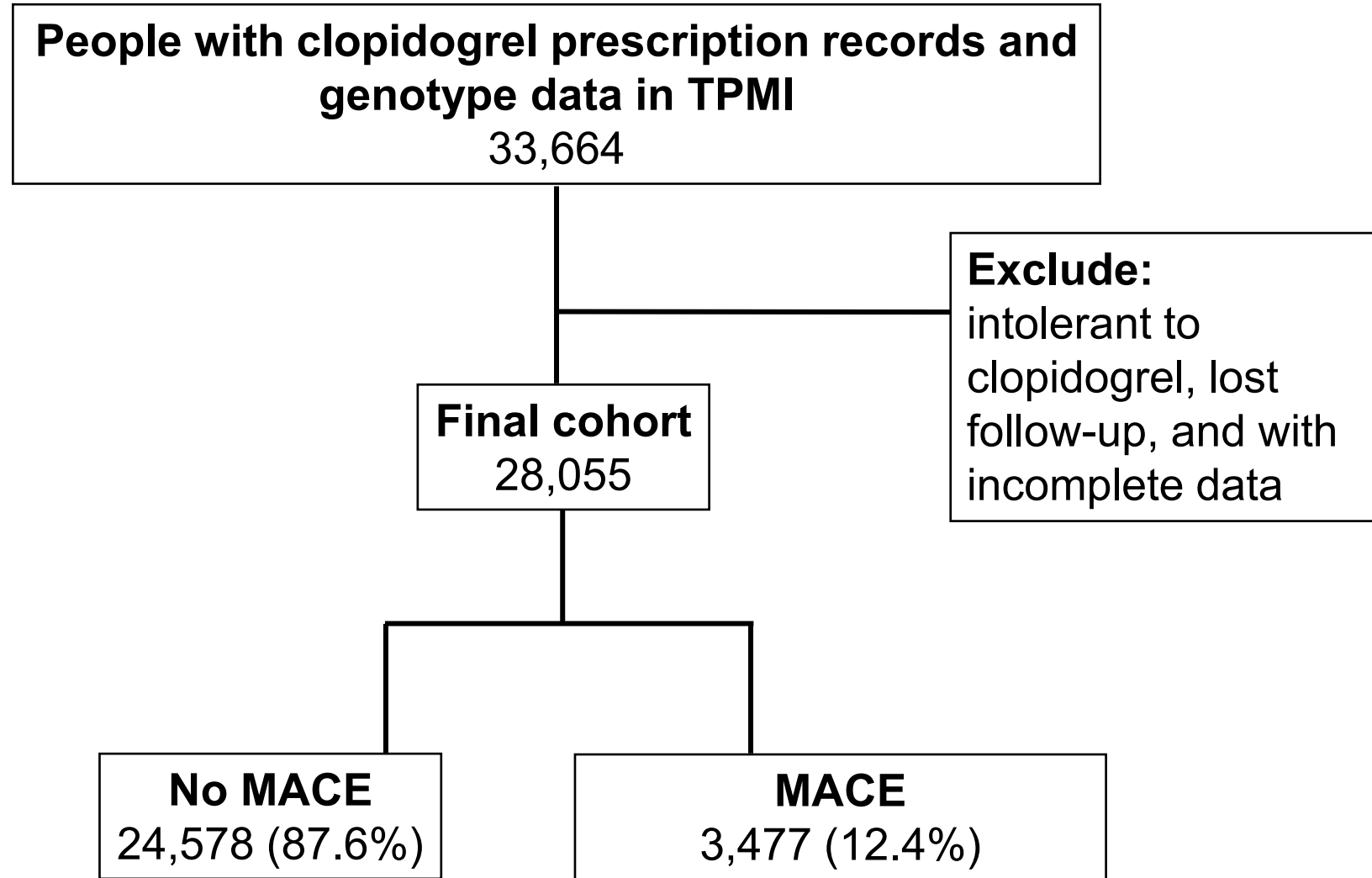


Figure s1: study design for clopidogrel-related adverse drug reactions

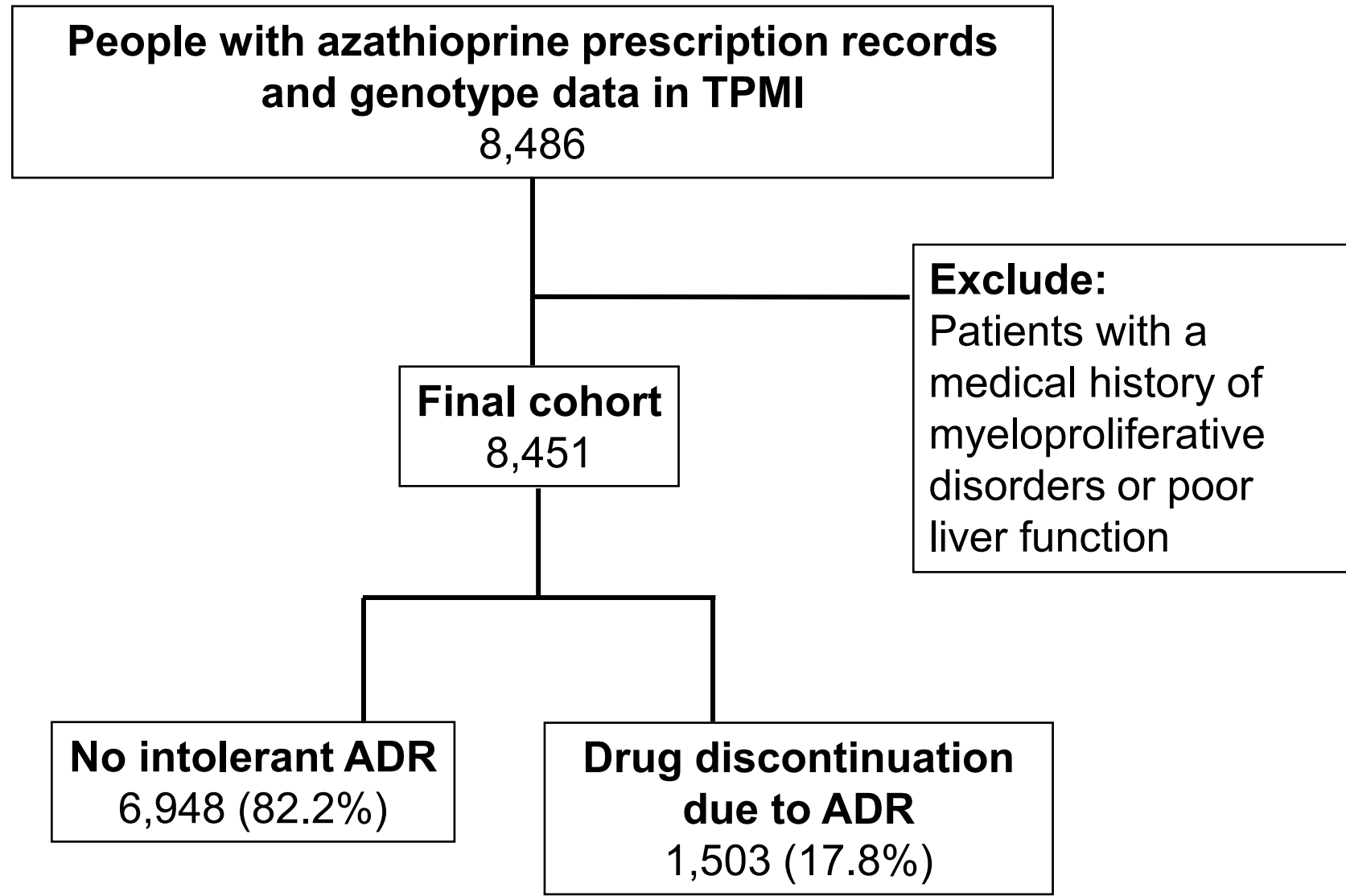


Figure s2: study design for azathioprine-related adverse drug reactions