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Warfarin dose	
Median	32.5 mg/week
Interquartile range	24.0-42.5 mg/week
VKORC1 genotype	
G/G	38 (37)
A/G	46 (44)
A/A	16 (15)
NA	4 (4)
CYP2C9 genotype	200
*1/*1	61 (59)
*1/*2	17 (16)
*3/*18	10 (10)
*2/*2	4 (4)
*1/*6	2 (2)
*1/*11	2 (2)
*1/*12	2 (2)
*6/*7	1 (1)
*1/*9	1 (1)
*2/*12	1 (1)
*3/*12/*18	1 (1)
NA OVER 150	2 (2)
CYP4F2 genotype	55 (50)
C/C	55 (53)
T/C	40 (38)
T/T	6 (6)
NA	3 (3)
Age	0.4
Mean, median	64 years, 67 years
Interquartile range	53-75.3 years
Height Mean, median	172 cm, 173 cm
	163-180 cm
Interquartile range	163-180 cm
Weight Mean, median	91 79 9
	81 kg, 78.8 kg
Interquartile range Race	64.9-90.7 kg
White	78 (75)
Asian	18 (17)
Black	8 (8)
Sex	0 (0)
Male	60 (58)
Female	44 (42)
Inducers use	44 (42)
	1 (1)
Number (percent) Amiodarone use	1 (1)
Number (percent)	5 (5)

Extending and evaluating a warfarin dosing algorithm that includes CYP4F2 and pooled rare variants of CYP2C9.

Sagrieya, Hersh; Berube, Caroline; Wen, Alice; Ramakrishnan, Ramesh; Mir, Alain; Hamilton, Amy; Altman, Russ

Pharmacogenetics and Genomics. 20(7):407-413, July 2010.

DOI: 10.1097/FPC.0b013e328338bac2

Table 1 Characteristics of the patient population (N=104) Inducers included carbamazepine, rifampin, and phenytoin.



Fig. 1

Model F	Pharmacogenetic Clinical		Fixed
Mean AE (mg/week)	8.1 ± 0.9	10.4 ± 1.0	12.2 ± 1.0
Adjusted R ² (%)	46	19	NA
Within 1 mg/day of actual dose (%)	63	54	38
> 1 mg/day over actual dose (%)	13	14	34
> 1 mg/day under actual dose (%)	23	32	29
50 - 60 - 50 - 50 - 50 - 50 - 50 - 50 -			
20 -			
10			
0			
Pgx within Pgx > Pgx > 1 mg/day 1 mg/day 1 mg/day 1 mg/day of actual over under actual		Clinical > Fixed 1 mg/day within under 1 mg/day actual of actual	Fixed > Fixed > 1 mg/day 1 mg/day over under actual actual

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Fig. 1 (a) Performance of the three different dosing models: pharmacogenetic, clinical, and fixed. Includes all patients who reached stable dose (N=104). (b) Percentage of patients who were either within 1 mg/day of the actual dose, more than 1 mg/day over the actual dose, or more than 1 mg/day under the actual dose for the three different dosing models: pharmacogenetic, clinical, and fixed.



CYP2C9 SNP	Number	Average dose ± SE	
*12 C/C	87	36.3 ± 1.7	
*12 T/C	4	19.6 ± 2.6	
*12 NA	13	34.1 ± 5.1	
*18 A/A	87	36.5 ± 1.7	
*18 T/A	11	27.2 ± 3.3	
*18 NA	6	35.3 ± 8.1	
CYP2C9 regression	Adjusted R ²	P value	
*12	3.9%	0.034	
*18	2.5%	0.064	

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Table 2 Analysis of rare CYP2C9 variants. Analysis of the *12 and *18 alleles alone SNP, single nucleotide polymorphism.



CYP2C9 (*6-*18)	Number	Average dose ± SE	Comparison	Value
Homozygous WT at all SNPs	82	37.6 ± 1.8	P value	0.0065
Heterozygous at any	20	27.0 ± 2.1	Adjusted R ²	6%

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Table 3 Comparison of individuals who were either wildtype for *6, *7, *9, *11, *12, and *18, or had a variant genotype at any of these alleles SNP, single nucleotide polymorphism; WT, wild-type.



CYP2C9 (*2-*3)	Number	Average dose ± SE	Comparison	Value
Homozygous WT at all SNPs	69	38.6 ± 2.1	P value	0.0034
Heterozygous at any	33	28.9 ± 1.7	Adjusted R2	7%

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Table 4 Comparison of individuals who were either wildtype for *2 and *3, or had a variant genotype at either *2 or *3 SNP, single nucleotide polymorphism; WT, wildtype.



CYP2C9 (*2-*18)	Number	Average dose ± SE	Comparison	Value
Homozygous WT at all SNPs	61	40.2 ± 2.2	P value	0.00018
Heterozygous at any	41	28.5 ± 1.5	Adjusted R ²	12%

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Table 5 Comparison of individuals who were either wildtype for *2, *3, *6, *7, *9, *11, *12, and *18, or had a variant genotype at any of these alleles SNP, single nucleotide polymorphism; WT, wild-type.



Model	MAE±SE (mg/week)	Adjusted R ² (%)
IWPC Pgx. (2009) [29]	7.80 ± 0.84	50
IWPC clinical (2009) [29]	10.14 ± 1.04	22
Gage et al. [23]	7.79 ± 0.83	49
Sconce et al. [25]	8.98 ± 0.94	47
Zhu et al. [28]	8.98 ± 0.95	39
Tham et al. [26]	9.72 ± 0.95	33
Herman et al. [24]	9.73 ± 0.89	47
Wu et al. [27]	9.98 ± 0.95	35

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Table 6 Comparison of model performance This analysis was restricted to the 95 patients who had all the variables necessary for the eight different dosing equations.IWPC, International Warfarin Pharmacogenetics Consortium; MAE, mean absolute error.

