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Genotype-Guided Dosing of Vitamin K Antagonists

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TO THE EDITOR

Kimmel and colleagues note that a genotype-guided dosing algorithm using *CYP2C9*2, CYP2C9*3*, and *VKORC1* (–1639G→A) is statistically inferior to a clinical-dosing algorithm in patients of African descent. However, the single-nucleotide polymorphisms (SNPs) used in the study's pharmacogenetic dosing algorithm are known to occur at significantly lower frequencies in persons of African descent than in persons of European descent (Table 1).[1–4] The authors' ability to draw appropriate conclusions about the usefulness of genetics when determining dosages of warfarin for patients of African descent is thus very limited, and the benefits for this population have not been adequately tested. Physicians should not assume that self-reported race is an accurate proxy for the influence of genetic ancestry.[5] Rather, studies testing the usefulness of pharmacogenetics in a specific population should test variants with high frequency and measurable effect in that population.

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Table 1

Frequencies of Tested Warfarin Variants in Persons of European and African Descent.*

Variant	Genotype Frequencies		P Value*
	Persons of European Descent	Persons of African Descent	
*CYP2C9*2*†	TT = 0.0175 TC = 0.227 CC = 0.756	TT = 0.00182 TC = 0.0499 CC = 0.948	$P<2.2\times10^{-16}$
*CYP2C9*3*†	CC = 0.00349 CA = 0.125 AA = 0.872	CC = 0.000454 CA = 0.0277 AA = 0.972	$P<2.2\times10^{-16}$
VKORC1 (3673G→A)‡	AA = 0.195 GA = 0.407 GG = 0.398	AA = 0.061 GA = 0.082 GG = 0.857	$P = 1.564\times10^{-7}$

*P values were calculated for the comparison of genotype distributions with the use of Fisher's exact test and the R Statistical Package, version 2.15.3.

†Data are from the GO Exome Sequencing Project and are based on 4300 persons of European descent and 2203 persons of African descent. See the project home page.[3]

‡Data are from the HapMap Project as reported by the dbSNP and are based on 113 persons of European descent and 49 persons of African descent. See the International HapMap 3 Consortium.[4]