

The number of prescriptions for proton pump inhibitors exceeds 82 million at an annual cost of 11.56 billion dollars. The comparative per-prescription price differential for a thirty day supply of a proton pump inhibitor and a histamine-2 receptor blocker is 51 dollars, based on the average wholesale price. In 2003, SUNY Upstate Medical University, Syracuse, NY, in an effort to stimulate a national discussion, linked population-based pharmacogenomics with treatment response by the use of standard cost-benefit modeling techniques. This model used a common disease state, duodenal ulcer and a high volume and expensive class of drugs, the proton pump inhibitors, as a representative example: Lehmann DF, Medicis JJ, Franklin PD. Polymorphisms and the Pocketbook: The Cost-Effectiveness of Cytochrome P450 2C19 Genotyping in the Eradication of *Helicobacter pylori* Infection Associated with Duodenal Ulcer, as discussed in the following abstract:

The clinical outcome of duodenal ulcer treated with proton pump inhibitor (PPI)-based, anti-Helicobacter pylori (H.p.) regimens varies according to cytochrome P450 2C19 (CYP2C19) genotype. CYP2C19 genotypes differ markedly in peoples of Pacific Rim descent compared with another ethnicity. The authors sought to determine the specific impact that these factors have on the cost-effectiveness of duodenal ulcer management. Their model consisted of two patient cohorts with Helicobacter pylori and duodenal ulcer, trichotomized into CYP2C19 homozygous extensive metabolizers (EMs), heterozygous EMs, and poor metabolizers (PMs), altering the anti-H.p. regimen in the genotyped cohort only. The authors took the perspective of a third-party payer, and the denominator was ulcer episode prevented. In the reference case, the use of CYP2C19 genotyping prior to initiating anti-H.p. therapy was dominant (costs were saved with each ulcer episode prevented) in all geographic regions

of the United States. The subsequent break-even analysis showed a range of \$89.20 to \$118.96—from Hawaii to the Midwest, respectively—required to eliminate the cost-savings from each genotype test performed. Using probabilities most unfavorable to genotyping, the variation of peoples with Pacific Rim origins from 0% to 100% altered the cost-effectiveness from \$495 to \$2125 per ulcer event prevented, respectively. The results suggest that treatment decisions for H.p. infection that are based on a patient's CYP2C19 genotype decreases expenses for health plans implementing testing. This analysis provides an economic basis to support recent calls to expand this technology into routine clinical care to prevent toxicity of narrow therapeutic index drugs.

Keywords: CYP2C19 genotype; duodenal ulcer; cost-effectiveness; genotyping; polymorphism
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Five further exhibits accompany this response that identify our cost-effectiveness model, provide justification for our model assumptions, and offer a more graphic outline of our results.

This analysis helped to stimulate negotiations that are underway between SUNY Upstate Medical University and the main third party payer, Excellus BCBS of Central New York, to investigate optimal ways to operationalize these results in our region.

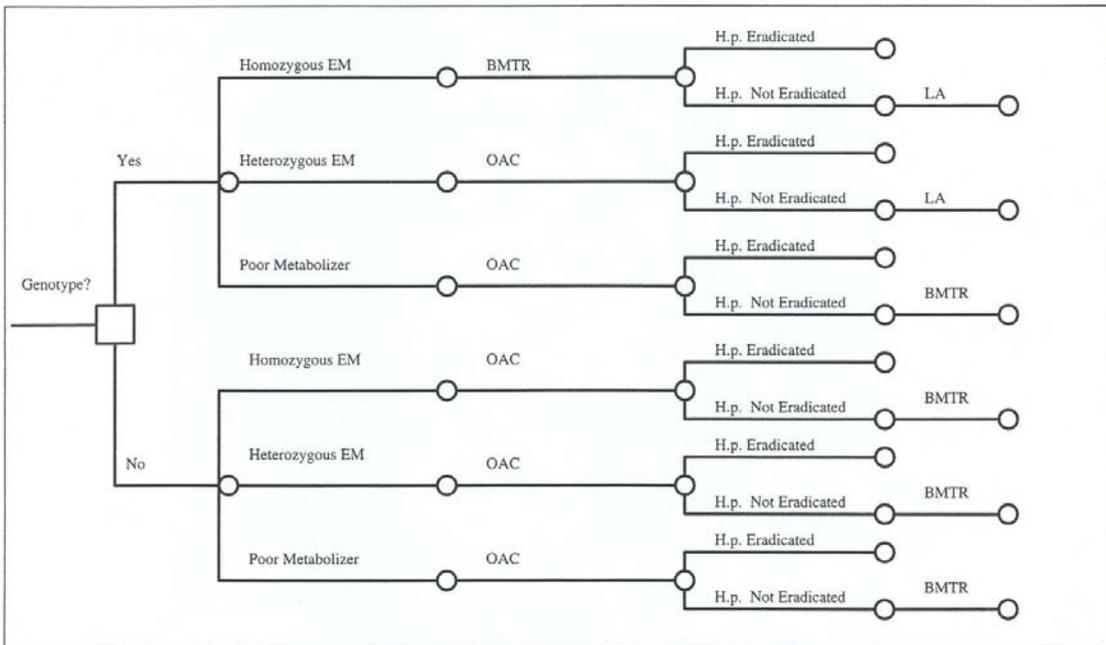


Figure 1. Decision model. Cohorts with newly diagnosed duodenal ulcer (DU) and *Helicobacter pylori* (H.p.) infection. Decisions regarding duodenal ulcer recurrences are not shown (see text). EM, extensive metabolizer; BMTR, bismuth, metronidazole, tetracycline, and ranitidine; OAC, omeprazole, amoxicillin, and clarithromycin; LA, lansoprazole and amoxicillin.

Table I Model Probabilities

Probabilities	Value (Range Used for Sensitivity Analysis)			Reference
	PMs	Heterozygous EMs	Homozygous EMs	
<i>H.p.</i> eradication rate according to treatment regimen				2, 15, 16, 21, 22
OAC	0.98	0.92	0.73	
BMTR	0.86 (0.80, 0.91)	0.86 (0.80, 0.91)	0.86 (0.80, 0.91)	
LA	—	1.0 (0.7)*	1.0 (0.7)*	
Ethnic distribution of (CYP2C19) genotype				24-31, 33-38
Asian/Pacific Islander	0.17	0.48	0.35	
Other ethnic groups	0.03	0.30	0.67	
		Asian/Pacific Islander	Other Ethnic Groups	Reference
Regional U.S. ethnic distribution (2000 census)				32
Northeast		.040	.960	
Midwest		.019	.981	
South/Mountain		.020	.980	
Pacific Coast/Alaska		.098	.902	
Hawaii		.51	.49	
		<i>H.p.</i> Eradication Successes	<i>H.p.</i> Eradication Failures	Reference
Duodenal ulcer recurrence rate		.02 (.03)	0.85 (.86)	17, 18
Duodenal ulcer complication rate (requiring hospitalization)			.027 (.02, .05)	17, 18

H.p., *Helicobacter pylori*; PM, poor metabolizer of *S*-mephenytoin 4' hydroxylase (CYP2C19); EM, extensive metabolizer of *S*-mephenytoin 4' hydroxylase (CYP2C19); OAC, omeprazole, amoxicillin, and clarithromycin; BMTR, bismuth, metronidazole, tetracycline, and ranitidine; LA, lansoprazole and amoxicillin. Asian/Pacific Islander = Americans with ethnic origins in Asia and the Pacific Islands; other ethnic groups = Native Americans and Americans of European, African, and Hispanic descent.

**p* = 1.0, derived from "nonintention to treat" in Figure 2 (Furuta et al¹⁹).

Table II Model Costs

Per DU Recurrence Episode	\$/Resource #	Times Resource Used	Total \$
Endoscopy (facility + physician)	716.51	1	716.51
Primary physician (PCP) office visit (level 3)	52.98	3	158.94
Gastroenterologist (GI) office visit (level 3)	52.98	1	52.98
Hospitalization (DRG 174; ALOS = 6.1 days)	6450.91	1	6450.91
Inpatient initial visits (1 PCP and 1 GI)	121.76	2	243.52
Inpatient follow-up visits (5 PCP and 3 GI)	59.38	8	475.04
Total associated with a complication			7169.47
Drug Regimens	\$/Week	# Weeks	Total \$
Ranitidine	20.83	52	1083.16
BMTR	32.25	1	32.25
OAC	75.54	1	75.54
LA	105.86	2	211.72

Utilization values are derived from Nakamura et al²⁶ Resource utilization costs are based on the 2001 Medicare reimbursement schedule. Pharmaceutical costs are based on the 2002 average wholesale price (AWP). DU, duodenal ulcer; PCP, primary care provider; GI, gastroenterologist; DRG, diagnosis-related group; ALOS, average length of stay.

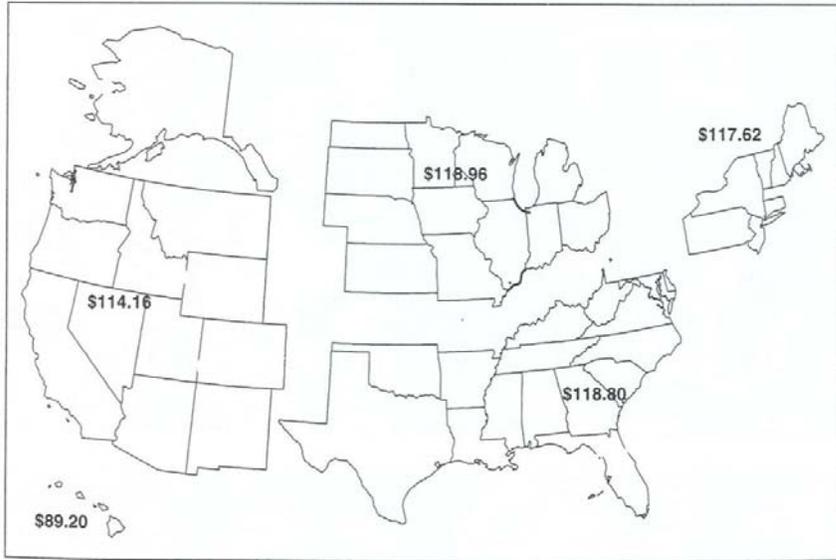


Figure 2. Effect of ethnicity on cost-effectiveness of CYP2C19 genotyping. Probability data used were those most unfavorable to CYP2C19 genotyping in the homozygous extensive metabolizer subgroup portion of the model.

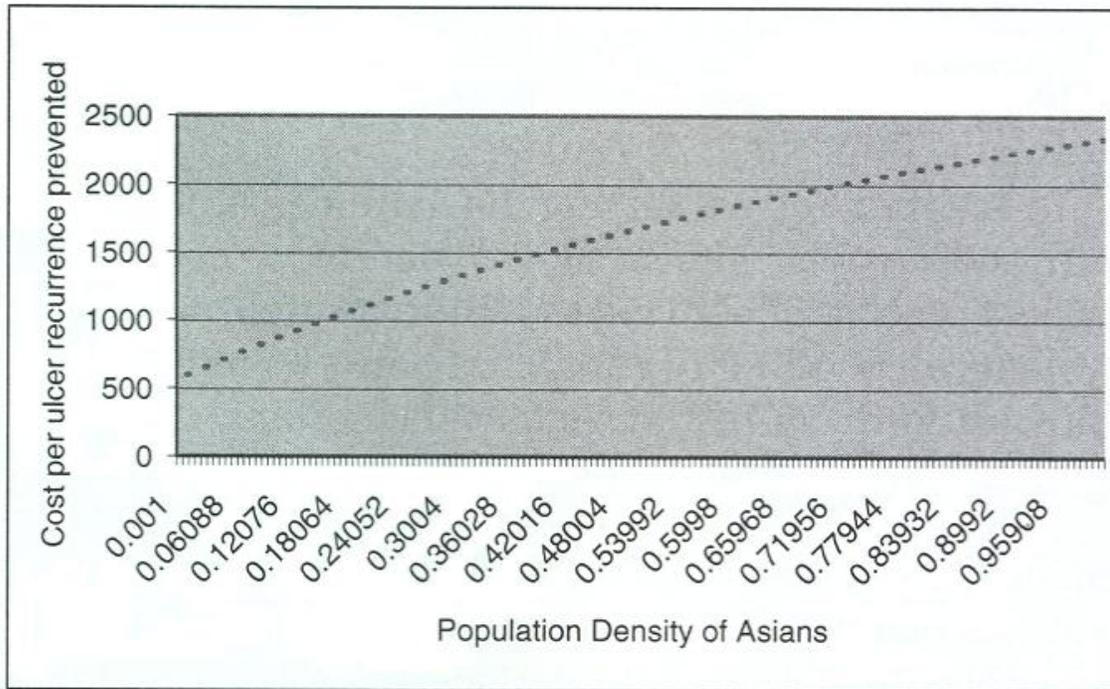


Figure 3. Cost break-even point for genotyping. Dollar amounts for cost per CYP2C19 genotype test to eliminate the cost savings (dominance) in the reference case. Variability in dollar amounts is derived from the variability of Oriental/Pacific Islander population density. Regional population data are based on the 2000 U.S. census.

Respectfully Submitted,

David F. Lehmann M.D., Pharm.D.
 Professor of Medicine and Pharmacology
 SUNY Upstate Medical University
 Syracuse, NY
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