Barriers to Translating Emerging Genetic Research on Smoking into Clinical Practice

Perspectives of Primary Care Physicians

Alexandra E. Shields, PhD,¹ David Blumenthal, MD, MPH,^{2,3} Kevin B. Weiss, MD, MPH,^{4,5} Catherine B. Comstock, MPH,¹ Douglas Currivan, PhD,⁶ Caryn Lerman, PhD^{7,8}

¹Health Policy Institute, Georgetown Public Policy Institute, Georgetown University, Washington, DC, USA; ²Institute for Health Policy, Massachusetts General Hospital/Partners HealthCare System, Boston, MA, USA; ³Departments of Medicine and Health Care Policy, Harvard Medical School, Boston, MA, USA; ⁴Midwest Center for Health Services and Policy Research, Hines VA Medical Center, Hines, IL, USA; ⁵Center for Healthcare Studies and Division of General Medicine, Department of Medicine, Northwestern Feinberg School of Medicine, Chicago, IL, USA; ⁶Survey Research Division, RTI International, Research Triangle Park, NC, USA; ⁷Department of Psychiatry, University of Pennsylvania Abramson Cancer Center, Philadelphia, PA, USA; ⁸Annenberg Public Policy Center, Philadelphia, PA, USA.

OBJECTIVE: Smoking remains the leading cause of preventable death nationally. Emerging research may lead to improved smoking cessation treatment options, including tailoring treatment by genotype. Our objective was to assess primary care physicians' attitudes toward new genetic-based approaches to smoking treatment.

DESIGN AND SETTING: A 2002 national survey of primary care physicians. Respondents were randomly assigned a survey including 1 of 2 scenarios: a scenario in which a new test to tailor smoking treatment was described as a "genetic" test or one in which the new test was described as a "serum protein" test.

PARTICIPANTS: The study sample was randomly drawn from all U.S. primary care physicians in the American Medical Association Masterfile (e.g., those with a primary specialty of internal medicine, family practice, or general practice). Of 2,000 sampled physicians, 1,120 responded, yielding a response rate of 62.3%.

MEASUREMENTS AND MAIN RESULTS: Controlling for physician and practice characteristics, describing a new test as "genetic" resulted in a regression-adjusted mean adoption score of 73.5, compared to a score of 82.5 for a nongenetic test, reflecting an 11% reduction in physicians' likelihood of offering such a test to their patients.

CONCLUSIONS: Merely describing a new test to tailor smoking treatment as "genetic" poses a significant barrier to physician adoption. Considering national estimates of those who smoke on a daily basis, this 11% reduction in adoption scores would translate into 3.9 million smokers who would not be offered a new genetic-based treatment for smoking. While emerging genetic research may lead to improved smoking treatment, the potential of novel interventions will likely go unrealized unless barriers to clinical integration are addressed.

KEY WORDS: physicians; genetic screening; smoking cessation; attitude of health personnel.

DOI: 10.1111/j.1525-1497.2005.30429.x

J GEN INTERN MED 2005; 20:131-138.

Despite decades of clinical research and concentrated public health efforts, tobacco use remains the leading cause of preventable death in the United States, accounting for approximately \$157 billion annually in health-related costs.¹ Although nicotine replacement therapy and non-nicotine medications such as bupropion are effective treatments for tobacco dependence, there is significant individual variability in treat-

ment outcome² and little empirical data to guide individualized treatment.³

Research in genetics has the potential to provide an empirical foundation for the tailoring of pharmacological treatment for individuals with tobacco dependence.⁴ Data from twin studies have firmly established that inherited factors account for about 50% of the variability in smoking initiation and about 70% of the variance in liability to nicotine dependence.⁵⁻⁸ Although the identification of specific genetic variants has proved to be a daunting task,⁹ there is initial evidence for the role of polymorphisms in nicotine-metabolizing enzymes,¹⁰ as well as genes important in the regulation of dopamine and serotonin, two neurotransmitters important in reward and mood regulation.¹¹⁻¹⁶ Building upon genetic association studies of smoking status, pharmacogenetic investigations are identifying genetic polymorphisms that predict response to different medications for tobacco dependence treatment.^{17,18} The basic premise of this approach is that inherited differences in drug metabolism and drug targets have important effects on treatment toxicity and efficacy.^{19,20} The clinical value of this information is thus potentially far reaching, as treatment approaches could be tailored to genotype in order to minimize toxicity and improve outcomes for individual patients.²¹

Research into the genetic basis of nicotine dependence and response to pharmacologic treatment is in the early stages. Although the variants that putatively increase susceptibility to nicotine dependence are relatively common (e.g., approximately 35% of smokers carry at least 1 DRD2 Taq1 A1 allele¹¹), the effects of individual genes on predisposition to smoking are quite small and the results of these studies have not been replicated consistently (see Lerman and Berrettini, 2003⁹ for a review). Nonetheless, the pace of scientific discovery in genetics and genomics threatens to outstrip our knowledge of factors affecting successful translation of research into clinical practice.^{22,23} As a result of advances in molecular neurobiology and genomics, genetically tailored tobacco dependence treatment may emerge as one of the first major areas in which primary care physicians confront genetic testing for tailoring pharmacotherapeutic choices for a common health problem. Given the potential importance and revolutionary nature of genetically tailored treatments, it is important to ascertain *in advance* what challenges might be involved in clinical integration whether specific barriers to their adoption may exist that do not pertain to other nongenetic technologies.²⁴ This article attempts to explore this question.

We conducted a national survey of primary care physicians' attitudes toward genetic testing in this context. Using a randomized scenario-based assessment,²⁵⁻²⁷ we investigated

Accepted for publication July 1, 2004

None of the authors has any conflicts of interest related to this study.

Address correspondence and requests for reprints to Dr. Shields: Health Policy Institute, Georgetown University, 2233 Wisconsin Avenue, NW, Suite 525, Washington, DC 20007 (e-mail: shieldsa@georgetown.edu).

physicians' reports of the likelihood that they would adopt a new genetic test to match patients who smoke to optimal treatment, compared with a new, nongenetic (protein) test designed for the same purpose. We hypothesized that primary care physicians would be less likely to adopt a new genetic test to tailor treatment compared to a nongenetic test. We further hypothesized that physicians with a personal history of smoking would be more sensitive to the difficulty of quitting, and thus more open to novel treatment modalities.

METHODS

Sample Selection

The study sample of 2,000 primary care physicians was randomly drawn from all U.S. primary care physicians in the American Medical Association (AMA) Masterfile with a primary specialty of internal medicine, family practice, or general practice, through one of its authorized vendors (Synavant, Fairhaven, NJ; 2002). While there were significant differences between the population and sample figures for internal medicine and family practice, based on one-sample *t* tests of these proportions (Table 1), these differences were within the range of sampling variation. Our respondents also included significantly fewer younger physicians (age 27–44) and women relative to national estimates.

Survey Design and Administration

Development of the survey instrument was informed by 5 focus groups with primary care physicians in Washington, DC and Chicago, Illinois, 20 semistructured interviews with primary care physicians, comments from key physician organizations and tobacco experts, and a review of the literature. Focus groups were used to develop credible scenarios and identify key concerns physicians may have about offering a new genetic test to their patients who smoke. Given that this study seeks to identify and anticipate issues likely to arise in

translating new genetic research into clinical practice, rather than assess adoption of an already available test, we relied on realistic scenarios, based on published genetic data, to measure physicians' anticipated behavior. Previous research has demonstrated that physician responses to patient scenarios or vignettes are closely associated with actual physician practice,^{25–27} with one study finding vignette scores to closely reflect standardized patient visits (the gold standard) and more accurately reflect physician behavior than chart abstraction.²⁷

To address our primary research question regarding the effect on physician adoption of describing a new test as genetic versus nongenetic, physicians were randomly assigned to receive a survey including a scenario in which the new test was presented as a "genetic test" or one in which the new test was presented as a "serum protein test." All other elements in the scenario were identical. The survey also addressed physicians' knowledge, training, and attitudes with respect to clinical genetics, smoking treatment practices, and other physician characteristics.

The draft instrument was further refined in response to comments from representatives of the American Academy of Family Physicians and American College of Physicians—American Society of Internal Medicine. The final survey instrument was pretested by senior staff from the Center for Survey Research at the University of Massachusetts-Boston (UMASS-Boston) for ease of understanding and accuracy of response through semistructured, cognitive interviews with 20 primary care physicians. The final 39-item questionnaire was designed to take approximately 20 minutes to complete.

Data collection was conducted between May and November 2002. Survey participants were provided 20 dollars in cash with the mailing to compensate for their time to complete the survey.^{28,29} Nonrespondents were sent a reminder postcard approximately 10 to 14 days and follow-up calls commencing 17 to 20 days after the initial mailing. This protocol was approved by the Institutional Review Boards of Georgetown University and UMASS-Boston.

Given our interest in surveying the attitudes of primary care physicians engaged primarily in clinical practice, we required respondents to practice a minimum of 20 hours per week in direct patient care. The final response rate, adjusted for ineligible cases, was 62.3%. We calculated the number of ineligible respondents based upon information from respondents who returned the survey and estimates of ineligibility rates among nonrespondents. Among ineligible respondents, 182 physicians were in clinical practice fewer than 20 hours/week, 11 practiced in a non-primary care specialty, and 8 had retired.

Sample Weights

Because the respondents represented a simple random sample of physicians practicing in primary care specialties, we did not need to weight the sample to account for differential probabilities of selection. However, we considered 2 weighting adjustments to enhance the representativeness of our final study population. First, to adjust for differences in response rates across specialties (65.9% for family practice, 66.1% for general practice, and 57.1% for internal medicine), we calculated a nonresponse weight equal to the inverse of the response rate for each specialty, to be applied in our analysis. Second, to account for the slight differences in the distribution of primary

Table 1. Characteristics of Study Respondents Versus AMA National Data

Physician Demographics	Total Respondents [†] (%)	AMA National Data [‡] (%)
Age, y		
27–44*	33.5	47.4
45–64*	52.5	40.6
65+	11.4	10.5
Gender*		
Male	79.5	70.0
Female	19.8	30.0
Region		
Northeast*	21.1	23.6
South	31.7	31.7
Midwest	26.0	23.8
West	21.3	20.9
Primary specialty		
Internal medicine*	45.0	49.6
Family practice*	47.5	44.0
General practice	7.5	6.3

*Difference between respondents and national data is statistically significant at $P < .05$.

[†]Numbers may not sum to 100% due to missing observations.

[‡]National data on all physicians with a designated specialty of family practice, general practice, or internal medicine (Synavant, 2002). AMA, American Medical Association.

care specialties in our study population relative to the AMA universe (Table 1), we calculated a poststratification weight that adjusts the cases in each specialty to match the “true” proportion in the universe. Using a combined nonresponse-adjusted, post-stratification weight had no impact on the results of the data analysis. Results from the weighted analysis are reported.

Measures and Variables

Likelihood of Offering a New Test to Tailor Smoking Treatment. The outcome variable measured physicians’ self-reported likelihood of offering a new test to match patients to optimal smoking cessation treatment. Following a scenario (Fig. 1) describing characteristics of a new test useful for matching patients to optimal nicotine replacement therapy and presenting a short description of the patient, physicians were asked to score (on a scale of 0 to 100) the likelihood that they would offer the test described in the scenario to the patient (“How likely would you be to offer the new test to this patient?”). Physicians were randomly assigned to receive a survey with scenarios that presented the new test as either a “genetic” test or a “serum protein” test.

Received “Genetic Test” Scenario. The primary independent variable of interest was a binary variable indicating whether respondents were in the study group that completed the genetic or nongenetic version of the scenario (genetic test scenario = 1).

Additional Variables. Several factors were considered as control variables in the analysis. Physician characteristics included age, gender, region in which a physician practiced, primary specialty, self-identified race/ethnicity, year of graduation from medical school, whether the physician had a full-time medical school faculty appointment, personal smoking history, and training in clinical genetics.

Our assessment of physicians’ personal smoking history was based on 2 questions, namely, “Do you currently smoke cigarettes?” and “Have you ever smoked cigarettes daily?” Given our interest in identifying physicians with personal experience with smoking and difficulties in trying to quit, we identified physicians with a personal history of smoking—either currently or formerly—as having “ever smoked.”

We assessed physicians’ knowledge of the most current smoking treatment guidelines and level of focus on smoking treatment through an aggregate variable constructed from several smoking practice questions. Physicians who “always” or “often” prescribe the nicotine patch, gum, or bupropion for patients wishing to quit smoking were coded as 1. Similarly, we identified those physicians who “always” or “often” refer their patients who smoke to a formal smoking cessation program or smoking expert.

Physicians’ practice setting was controlled for by identifying those physicians in independent practices, as opposed to those practicing in a health maintenance organization, hospital-based practice, community health center, or other setting. Size and geographic location of a physician’s practice was also determined. Urban/rural locations were based on mapping practice zip codes to Metropolitan Statistical Areas designated in the Area Resource File.³⁰

We assessed physicians’ attitudes toward new technologies and treatments. Physicians who said they “tended to offer new diagnostic tests before most of their peers” were identified as early adopters. Optimism about clinical genetics was determined by asking physicians, “How optimistic are you that genetic research will lead to significant improvements in the treatment of complex traits such as smoking behavior?” (very optimistic, somewhat optimistic, only a little optimistic, or not at all optimistic; 1 = very optimistic). Familiarity with research on the role of genetics in smoking behavior was assessed using an empirical question: “How much of individual variation in smoking behavior do you think is determined by: 1) genetic factors? and 2) social, environmental, or other factors?” Re-

Assume new smoking cessation research demonstrates to your satisfaction that:

- among individuals who express a particular [protein/genotype], the nicotine nasal spray yields a clinically meaningful improvement in smoking quit rates over the nicotine patch,
- a [serum protein/genetic] test with acceptable sensitivity, specificity, and predictive value can detect this particular [protein/genotype], and
- this particular [protein/genotype] is fairly prevalent in the population.

Assume further that you have a patient who:

- is a 35-year-old African-American female,
- smokes 1 pack of cigarettes per day,
- wants to quit smoking,
- has tried to quit smoking on her own several times and failed,
- has no known smoking-related illnesses, and
- has full insurance coverage for the [serum protein/genetic] test.

FIGURE 1. Scenario.*

*Genetic/protein versions of this scenario were identical with the exception of scenario-specific language [in brackets].

sponses indicating that 50% or more of variation in smoking behavior is due to genetic factors were coded as 1. Finally, we controlled for physicians' level of comfort with genetic testing by asking, "How prepared do you feel to counsel patients considering a genetic test?" (1=very prepared).

Analysis

Bivariate analyses were conducted to identify factors associated with adoption of the new test to individually tailor smoking treatment. Factors associated with the dependent variable at a significance level of $P < .10$ or greater, as well as factors suggested by the literature, were included in the final linear regression model predicting physician adoption of the new test. Our dependent variable was a continuous variable reflecting physicians' self-scored likelihood, on a scale of 0 to 100, that they would offer the new test to their patient, as presented in the scenario. We explored the explanatory power of all physician characteristics presented in Tables 1 and 2, tested model assumptions regarding linearity and normality of the data, and assessed correlation among independent variables. Our dependent variable was not normally distributed. Transforming the dependent variable using Logit transformation and the Box-Cox transformation improved normality assumptions, but produced very similar results. We therefore present the linear regression results for ease of interpretation and convenience with respect to calculating regression-adjusted means and corresponding standard errors.

Our final model included gender, race/ethnicity, year of graduation from medical school, appointment to a medical school faculty, having ever smoked, smoking treatment practices, practice setting, being an early adopter of new technologies, level of optimism about the promise of genetic research, beliefs regarding the genetic contribution to smoking behavior, and preparedness to counsel patients considering genetic testing.

We then calculated regression-adjusted means for all variables in the model, with all analyses adjusted as described above. We used SAS version 8.2 (SAS Institute, Cary, NC) to construct the analytic file and conduct all analyses. Descriptive analyses included all respondents, but may not always be based on the same number of respondents due to a small number of missing observations. For all variables, there were fewer than 2.7% missing observations. Only those respondents for whom there were complete data (92.1%) were included in the regression analysis ($N=1,031$).

RESULTS

Characteristics of Respondents

Physician Characteristics. The final study population included 1,120 physicians. Bivariate analyses revealed no significant differences between physicians who received the "genetic" scenario compared with those who received the nongenetic scenario on any variable. As shown in Tables 1 and 2, the majority of our study population was age 45 to 64, male, and white, with a fairly even distribution across regions of the country. Approximately 16% of respondents graduated from medical school in 1990 or more recently, and fewer than 10% had a full-time faculty appointment in a medical school. Approximately 22% of respondents were current or former smokers.

Table 2. Characteristics of the Study Population ($N=1,120$)*

Physician Characteristics		%
Race/ethnicity	White	74.5
	Black	2.6
	Hispanic	3.7
	Asian	16.0
	Other	3.2
Year of graduation	Before 1990	84.2
	1990 or later	15.8
Full-time faculty appointment	Yes	9.3
	No	90.7
Personal smoking history	Current or former smoker	22.1
	Never smoked	77.9
Training in clinical genetics	Formal courses/training in medical school	56.8
	Clinical rotation in genetics in medical school	15.5
	Genetics rotation in residency	4.0
	Continuing medical education	46.6
	Any of the above	75.8
Smoking treatment practices	Often/always prescribes pharmacological treatment (bupropion, nicotine patch, nicotine gum) to patients who wish to quit smoking	83.6
	Often/always refers smokers to a smoking cessation program or expert	27.9
	Has trained staff available to advise patients who want to quit smoking	22.2
Practice characteristics		
Practice setting	Independent practice	62.2
	Group/staff model HMO	8.6
	Hospital OPD	7.5
	Hospital-licensed CHC/clinic	6.1
	Freestanding CHC/clinic	6.8
	Other	8.8
Size of practice (number of physicians)	1	24.7
	2–4	31.0
	5–9	19.0
	10+	25.3
Urban/rural location	Urban location	78.8
	Rural location	21.2
Physician attitudes/beliefs		
Early adopter	Offers new diagnostic tests before peers	14.5
	Offers new diagnostic tests after or at the same time as their peers	85.5
Optimistic that genetic research will lead to significant clinical improvements	Very optimistic	13.9
	Somewhat, only a little, or not at all optimistic	86.1
Believes that 50% or more of variation in smoking behavior is due to genetics	Yes	24.2
	No	75.8
Preparedness to counsel patients considering a genetic test	Very prepared	4.2
	Somewhat, only a little, or not at all prepared	95.8

*Based on responses with complete data. Missing rate was less than 2.7% for all variables.

OPD, Outpatient Department; CHC, community health clinic.

Primary Care Physicians' Training in Clinical Genetics. More than 75% of respondents reported having had some formal training in clinical genetics, with most having received training

in medical school (57%) or continuing medical education courses (47%). Only 4% had a genetics rotation in residency; fewer than 16% reported a clinical rotation in genetics during medical school.

Smoking Treatment Practices. Nearly 84% of respondents reported that they often or always prescribe bupropion (Zyban) and/or a nicotine patch or nicotine gum for their patients who smoke. Approximately 28% reported that they often or always refer smokers to a smoking cessation program or expert, although only 22% reported having trained staff, other than physicians, available to advise patients who want to quit smoking.

Practice Setting. More than 62% of respondents worked in independent practices, as opposed to managed care organizations, hospital-based clinics, or other settings. More than half of all respondents were in practices comprised of fewer than 5 physicians, and close to 80% practiced in urban locations.

Physician Attitudes/Beliefs. Approximately 15% of respondents reported that they typically adopt new tests or procedures before their peers. About the same proportion (14%) rated themselves “very optimistic” that genetics will lead to significant clinical improvements in the treatment of complex traits, such as smoking. Fewer than 25% of respondents believed that genetic factors accounted for 50% or more of individual variation in smoking behavior, as compared with social and environmental factors. Only about 4% reported feeling “very prepared” to counsel patients considering genetic testing.

Anticipating Physician Adoption of a New Test to Tailor Smoking Treatment

Overall, respondents’ average self-reported likelihood (on a scale of 0 to 100) that they would offer the new test to tailor smoking treatment to their patients, as described in the scenario, was 73.7% (standard deviation [SD], 26.6). Among respondents who received the “genetic” test scenario, the unadjusted mean adoption score was 69.2% (SD, 28.8), compared to 78.1% (SD, 23.5) among physicians who received the nongenetic scenario.

Linear regression results estimating physicians’ self-scored likelihood that they would offer the described new test to their patients are summarized in Table 3. Those who received the “genetic” test scenario were significantly less likely ($P < .001$) to offer the test relative to those who received the scenario in which the new test was described as a “serum protein” test, controlling for all covariates. Specifically, as indicated by the negative parameter estimate, physicians responding to the genetic scenario were 9% less likely than those responding to the nongenetic scenario to offer the test to the patient. The regression-adjusted mean adoption score among those responding to a “genetic” test scenario was 73.5, versus 82.5 among those responding to the nongenetic scenario, controlling for all the above covariates (Table 4).

With respect to our secondary hypothesis regarding the impact of physicians’ personal smoking history, physicians who were current or former smokers themselves were significantly more likely to offer the new test to their patients

Table 3. Factors Affecting Physician Adoption of a New “Genetic” Test Versus Nongenetic Test to Tailor Smoking Treatment

Variable	Parameter Estimate*	P Value
Received genetic scenario [†]	− 9.0	.001
Physician characteristics		
Black	7.0	.20
Hispanic [‡]	− 8.4	.05
Asian	1.6	.47
Other race/ethnicity	− 3.9	.39
Year of graduation from medical school	0.1	.23
Full-time medical school faculty appointment	− 3.9	.16
Smoking Treatment Variables		
Current or former smoker [§]	5.7	.004
Often/always recommends pharmacological treatment (nicotine patch, gum and bupropion) [§]	6.5	.003
Often/always refers patients to a smoking cessation program or expert [‡]	3.9	.03
Female	1.9	.35
Practice characteristics		
Independent practice	2.8	.11
Physician attitudes/beliefs		
Early adopter (offers new diagnostic tests before most peers) [‡]	4.8	.03
Very optimistic that genetic research will lead to significant clinical improvements [‡]	9.4	.001
Believes that 50% or more of variation in smoking behavior is due to genetics	3.6	.06
Feels very prepared to counsel patients considering a genetic test	5.3	.18

Adjusted R², 0.08.

*Given that the dependent variable (physician likelihood of adoption score) ranged from 0 to 100, parameter estimates may be interpreted as percent change.

[†] $P < .001$.

[‡] $P < .05$.

[§] $P < .01$.

($P < .01$), with a regression-adjusted mean adoption score of 80.6, compared to 75.4 among physicians who had never smoked. Several additional factors also significantly affected physician likelihood of adoption of the new test. Physicians who routinely recommend pharmacological treatment ($P < .01$) and smoking cessation programs or counseling ($P < .05$) to their patients who smoke, those who adopt new treatments before most of their peers ($P < .05$), and those who judged themselves “very optimistic” that genetic research will lead to significant clinical improvements ($P < .001$) were all significantly more likely to offer a novel test to tailor smoking treatment to their patients who smoke. Finally, Hispanic physicians were significantly less likely to offer the new test to their patients, controlling for whether the test was described as “genetic” or nongenetic, and all other covariates, with a regression-adjusted mean adoption score of 73.2 versus 82.8 for white physicians ($P < .05$).

Comment

Using the case of genetic-based smoking treatment as a case study, this analysis provides the first national estimates of primary care physicians’ willingness to adopt genetic versus nongenetic tests to tailor treatment decisions. Confirming our main hypothesis, our findings suggest that the mere fact that a new test to tailor smoking cessation treatment is described as

Table 4. Regression-adjusted Mean Adoption Scores (Scale 0 to 100) for Factors Significantly Affecting Physician Adoption of a New Test to Tailor Smoking Treatment*

Variable	Mean Adoption Score
Scenario received [†]	
New test presented as genetic test	73.5
New test presented as protein test	82.5
Physician characteristics	
Physician of Hispanic origin [‡]	
Yes	73.2
No	82.8
Physician's smoking status [§]	
Current or former smoker	80.6
Never smoked	75.4
Recommends pharmacological treatment (bupropion, nicotine patch, and/or gum) [§]	
Often/always	80.9
Never/sometimes	75.1
Refers patients to a smoking cessation program or expert [‡]	
Often/always	79.9
Never/sometimes	76.0
Physician attitudes/beliefs	
Early adopter [‡]	
Yes	80.7
No	75.3
Optimistic that genetic research will lead to significant clinical improvements [†]	
Very optimistic	82.4
Not very optimistic	73.6

*Only variables significantly associated with physician adoption in our linear regression model (Table 3) are presented. Notation of significance based on P values on parameter estimates in regression model.

[†]P < .001.

[‡]P < .05.

[§]P < .01.

"genetic" poses a significant barrier to adoption among primary care physicians in the United States. If we consider a new, nongenetic test designed for the same purpose to be the standard against which a new genetic test ought to be compared, then describing a new test as "genetic" results in an 11% reduction in anticipated take-up rates. While the appropriate target population for any future genetic-based treatment intervention for smoking has not yet been defined, it seems reasonable to assume that daily smokers would be likely candidates for new treatment strategies. The most recent data estimate that more than 35.4 million Americans smoke cigarettes on a daily basis.³¹ Based on these figures, the seemingly modest 11% reduction in physicians' self-reported take-up rates of a new genetic test to tailor smoking treatment relative to a new nongenetic test would translate into as many as 3.9 million smokers who would not be offered a promising new treatment strategy.

It seems clear that primary care physicians are likely to be more deliberate and cautious when considering novel treatments or protocols that involve genetic testing. Previous studies have documented physicians' concerns regarding the potential for genetic discrimination, problematic family dynamics, confusion, or other adverse consequences resulting from genetic testing.^{32,33} Such caution is not inappropriate. Despite some modest protections provided by the privacy regulations promulgated by the Department of Health and Human Services under the Health Insurance Portability and Accountability Act of 1996 (HIPAA), current privacy law in

the United States fails to protect patients from unauthorized use of genetic information. With respect to genetic discrimination statutes, the 1990 Americans with Disabilities Act (ADA) prohibits certain uses of genetic information, yet no federal law in the United States currently bans genetic discrimination in the general population. State laws remain the primary source of protection, yet only 41 states currently ban genetic discrimination in group health insurance and only 31 states have passed laws that ban the misuse of genetic information by employers.³⁴ Failure to address the inadequacy of current privacy and anti-discrimination protections will seriously undermine any future efforts to integrate genetic testing into smoking treatment.

Overall, physicians across the board were positively disposed to offering a new test to tailor smoking treatment to their patients. The average self-reported adoption rate for all respondents was approximately 74% (out of 100). Among those physicians who received the genetic test scenario, the regression-adjusted mean adoption score was 69%, despite the small proportion of physicians (4%) who reported feeling "very prepared" to counsel patients considering a genetic test. We interpret this as reflecting the importance primary care physicians ascribe to developing improved treatment options for smoking. These results are similar to a small pilot study that surveyed family physicians regarding their willingness to use a hypothetical commercially available genetic test to identify patients most likely to quit smoking using transdermal nicotine replacement.³⁵

As we had hypothesized, physicians who were current or former smokers themselves were significantly more receptive to novel treatment approaches. Physicians who routinely prescribed pharmacological treatment to their patients and who routinely referred them to a smoking cessation program or expert were also more likely to offer the new test to their patients, controlling for whether they were responding to the genetic or nongenetic version of the scenario. We hypothesize that these variables identify a group of physicians who are more focused on smoking as an important health concern and who, through personal experience or experience with their patients, have a particular appreciation for the difficulty involved in quitting. Self-described early adopters were also more likely to offer the new test to their patients. This finding supports the seminal study by Rogers on the role of individual characteristics with respect to the adoption of emergent technologies in numerous fields, including medicine.³⁶ We did not replicate previous research showing recent graduation from medical school to significantly affect physician adoption of.³⁷

Finally, physicians who identified themselves as Hispanic were significantly less likely than white physicians to offer the new test to their patients ($P < .05$). Differing attitudes toward the adoption of new tests and treatments—particularly new genetic tests—across physicians from different racial and ethnic communities is an area for further study.

This study has several limitations that should be noted. First, while patient scenarios or vignettes have been widely used to assess physicians' knowledge^{38–41} and decision making^{42–48} and have been demonstrated to closely reflect physicians' actual clinical practice,^{25–27} their use in predicting physicians' future behavior has not been as extensively studied. Scenarios have been used, however, to measure patients' anticipated take-up rates of potential predictive genetic tests for Alzheimer's disease according to different hypothesized test

characteristics and treatment options.⁴⁹ While the use of scenarios to predict physician decision making regarding tests or treatments that may become available in the future remains an area for further study, we believe it is essential to begin trying to anticipate and identify issues likely to affect the translation of emerging genetic research into clinical practice.

With respect to the representativeness of our sample, primary care physicians with a specialty of internal medicine had a lower response rate than family practice physicians. While we attempted to control for this differential response rate through statistical adjustments, there may remain some residual bias in research results.

Smoking remains the leading cause of preventable death in the United States, accounting for more than 440,000 deaths per year.¹ Thus far, efforts to prevent smoking and to help smokers quit have had mixed success, underscoring the need for broader, transdisciplinary approaches^{50,51} to understand the etiology of smoking behavior and the mechanisms of response to treatment. As emerging genetic research continues to increase our understanding of the multifactorial etiology of smoking behavior and leads to new smoking treatment strategies, it is essential that concomitant efforts address primary care physicians' knowledge of and comfort with clinical genetics. Indeed, the findings of this study regarding current barriers to primary care physicians' adopting genetic testing in the context of smoking treatment are likely to apply to other conditions as well, underscoring the need for additional support and education to prepare primary care physicians for genomic medicine, as well as the importance of broader policy concerns related to privacy and antidiscrimination protections for patients undergoing genetic testing.

Several initiatives aimed at improving physicians' knowledge of genetics through the development of educational coalitions, medical school curricula, and Internet-based resources have been implemented.⁵²⁻⁵⁴ Such programs have focused primarily on developments in our understanding of the genetic basis of major diseases and will need to be extended to address new and more complicated issues related to the genetics of complex behaviors, such as smoking. Additional educational opportunities in bioethics may also be useful to physicians.⁵⁵ A recent study of physician attitudes toward genetic testing for cancer susceptibility also emphasizes the importance of developing physician guidelines on genetic testing.⁵⁶ Further efforts to educate and support primary care physicians will likely prove essential to realizing potential future benefits of genetic research on tobacco dependence treatment—and indeed of genetic research more broadly—in patients' lived experience.

This work is supported by The Robert Wood Johnson Foundation (AES) and a Transdisciplinary Tobacco Use Research Center grant (CL), funded by the National Cancer Institute and National Institute on Drug Abuse (P50 CA/DA84718). The authors would like to thank the American Academy of Family Physicians, the American College of Physicians—American Society of Internal Medicine, Drs. Gail Geller, Nancy Rigotti, Eric Campbell, and Elyse Park for comments on early drafts of the survey instrument, as well as members of the Georgetown Ethics Research Consortium on Smoking and Genetics, of which Drs. Weiss, Lerman, and Shields are members. We are indebted to Dr. Recai Yucel for expert statistical advice, and Julie Pelan, Keira Fuener, and John Orwat provided superb research assistance.

REFERENCES

1. **Centers for Disease Control and Prevention.** Cigarette smoking among adults—United States, 2000. *MMWR*. 2002;51:642–5.
2. **Silagy C, Lancaster T, Stead L, Mant D, Fowler G.** Nicotine replacement therapy for smoking cessation. *Cochrane Database Syst Rev*. 2002; 3:CD000146.
3. **Hughes JR, Goldstein MG, Hurt RD, Shiffman S.** Recent advances in the pharmacotherapy of smoking. *JAMA*. 1999;281:72–6.
4. **Lerman C, Niaura R.** Applying genetic approaches to the treatment of nicotine dependence. *Oncogene*. 2002;21:7412–20.
5. **Heath AC, Martin NG.** Genetic models for the natural history of smoking: evidence for a genetic influence on smoking persistence. *Addict Behav*. 1993;18:19–34.
6. **Kendler KS, Neale MC, Sullivan P, Corey LA, Gardner CO, Prescott CA.** A population-based twin study in women of smoking initiation and nicotine dependence. *Psychol Med*. 1999;29:299–308.
7. **Sullivan PF, Kendler KS.** The genetic epidemiology of smoking. *Nicotine Tob Res*. 1999;1(suppl 2):S51–S57.
8. **True WR, Xian H, Scherrer JF, et al.** Common genetic vulnerability for nicotine and alcohol dependence in men. *Arch Gen Psychiatry*. 1999; 56:655–61.
9. **Lerman C, Berrettini W.** Elucidating the role of genetic factors in smoking behavior and nicotine dependence. *Am J Med Genet*. 2003;118B: 48–54.
10. **Xu C, Goodz S, Sellers EM, Tyndale RF.** CYP2A6 genetic variation and potential consequences. *Adv Drug Deliv Rev*. 2002;54:1245–56.
11. **Lerman C, Caporaso NE, Audrain J, et al.** Evidence suggesting the role of specific genetic factors in cigarette smoking. *Health Psychol*. 1999;18:14–20.
12. **Lerman C, Caporaso NE, Bush A, et al.** Tryptophan hydroxylase gene variant and smoking behavior. *Am J Med Genet*. 2001;105:518–20.
13. **Noble EP, St Jeor ST, Ritchie T, et al.** D2 dopamine receptor gene and cigarette smoking: a reward gene? *Med Hypotheses*. 1994;42:257–60.
14. **Sabol SZ, Nelson ML, Fisher C, et al.** A genetic association for cigarette smoking behavior. *Health Psychol*. 1999;18:7–13.
15. **Spitz MR, Shi H, Yang F, et al.** Case-control study of the D2 dopamine receptor gene and smoking status in lung cancer patients. *J Natl Cancer Inst*. 1998;90:358–63.
16. **Sullivan PF, Jiang Y, Neale MC, Kendler KS, Straub RE.** Association of the tryptophan hydroxylase gene with smoking initiation but not progression to nicotine dependence. *Am J Med Genet*. 2001;105:479–84.
17. **Lerman C, Shields PG, Wileyto EP, et al.** Pharmacogenetic investigation of smoking cessation treatment. *Pharmacogenetics*. 2002;12:627–34.
18. **Lerman C, Wileyto EP, Patterson F, et al.** The functional mu opioid receptor (OPRM1) Asn40Asp variant predicts short-term response to nicotine replacement therapy in a clinical trial. *Pharmacogenomics J*. 2004; 4:184–92.
19. **Evans WE, Relling MV.** Pharmacogenomics: translating functional genomics into rational therapeutics. *Science*. 1999;286:487–91.
20. **Poolsup N, Li Wan Po A, Knight TL.** Pharmacogenetics and psychopharmacotherapy. *J Clin Pharm Ther*. 2000;25:197–220.
21. **Roses AD.** Pharmacogenetics and the practice of medicine. *Nature*. 2000;405:857–65.
22. **Contopoulos-Ioannidis DG, Ntzani E, Ioannidis JP.** Translation of highly promising basic science research into clinical applications. *Am J Med*. 2003;114:477–84.
23. **Crowley WF Jr.** Translation of basic research into useful treatments: how often does it occur? *Am J Med*. 2003;114:503–5.
24. **Shields AE, Lerman C, Sullivan PF.** Translating emerging research on the genetics of smoking into clinical practice: ethical and social considerations. *Nicotine Tobacco Res*. 2004;6:675–88.
25. **Carey TS, Garrett J.** Patterns of ordering diagnostic tests for patients with acute low back pain. The North Carolina Back Pain Project. *Ann Intern Med*. 1996;125:807–14.
26. **Mandelblatt JS, Berg CD, Meropol NJ, et al.** Measuring and predicting surgeons' practice styles for breast cancer treatment in older women. *Med Care*. 2001;39:228–42.
27. **Peabody JW, Luck J, Glassman P, Dresselhaus TR, Lee M.** Comparison of vignettes, standardized patients, and chart abstraction: a prospective validation study of 3 methods for measuring quality. *JAMA*. 2000; 283:1715–22.
28. **Church AH.** Estimating the effect of incentives on mail survey response rates: a meta-analysis. *Public Opin Q*. 1993;57:62–79.

29. **Singer E, Groves RM, Corning AD.** Differential incentives: beliefs about practices, perceptions of equity, and effects on survey participation. *Public Opin Q.* 1999;63:251-60.
30. **Area Resource File (ARF).** February 2003. U.S. Department of Health and Human Services, Health Resources and Services Administration, Bureau of Health Professions, Rockville, MD. Available at: <http://www.arfsys.com>. Accessed January 2004.
31. **Substance Abuse and Mental Health Services Administration.** Results from the 2001 National Household Survey on Drug Abuse. Volume 1: Summary of National Findings. U.S. Department of Health and Human Services, Rockville, MD; 2002.
32. **Emery J, Watson E, Rose P, Andermann A.** A systematic review of the literature exploring the role of primary care in genetic services. *Fam Pract.* 1999;16:426-45.
33. **Suchard MA, Yudkin P, Sinsheimer JS.** Are general practitioners willing and able to provide genetic services for common diseases?. *J Genet Couns.* 1999;8:301-11.
34. **National Human Genome Research Institute.** Search the NHGRI Policy and Legislation Database by U.S. State. Available at: <http://222.genome.gov/policyEthics/LegDatabase/pubMapSearch.cfm>. Accessed June 2004.
35. **Stamp MJ, David SP.** Are family physicians willing to use pharmacogenetics for smoking cessation therapy? *Fam Med.* 2003;35:83.
36. **Rogers E.** *Diffusion of Innovations.* New York, NY: Free Press of Glencoe; 1962.
37. **Hofman KL, Tambor ES, Chase GA, Geller G, Faden RR, Holtzman NA.** Physicians' knowledge of genetics and genetic tests. *Acad Med.* 1993;68:625-32.
38. **Demmer LA, O'Neill MJ, Roberts AE, Clay MC.** Knowledge of ethical standards in genetic testing among medical students, residents, and practicing physicians. *JAMA.* 2000;284:2595-6.
39. **Ford CA, Millstein SG.** Delivery of confidentiality assurances to adolescents by primary care physicians. *Arch Pediatr Adolesc Med.* 1997;151:505-9.
40. **Hayflick SJ, Eiff MP, Carpenter L, Steinberger J.** Primary care physicians' utilization and perceptions of genetics services. *Genet Med.* 1998;1:13-21.
41. **James C, Geller G, Bernhardt BA, Doksum T, Holtzman NA.** Are practicing and future physicians prepared to obtain informed consent? The case of genetic testing for the susceptibility to breast cancer. *Community Genet.* 1998;1:203-12.
42. **Carnes M, Howell T, Rosenberg M, Francis J, Hildebrand C, Knuppel J.** Physicians vary in approaches to the clinical management of delirium. *J Am Geriatr Soc.* 2003;51:234-9.
43. **Hagbin Z, Streltzer J, Danko GP.** Assisted suicide and AIDS patients. A survey of physicians' attitudes. *Psychosomatics.* 1998;39:18-23.
44. **Hodges MO, Tolle SW, Stocking C, Cassel CK.** Tube feeding. Internists' attitudes regarding ethical obligations. *Arch Intern Med.* 1994;154:1013-20.
45. **Mallory MD, Shay DK, Garrett J, Bordley WC.** Bronchiolitis management preferences and the influence of pulse oximetry and respiratory rate on the decision to admit. *Pediatrics.* 2003;111:e45-e51.
46. **Menasha JD, Schechter C, Willner J.** Genetic testing: a physician's perspective. *Mount Sinai J Med.* 2000;67:144-51.
47. **Slome LR, Mitchell TF, Charlebois E, Benevedes JM, Abrams DI.** Physician-assisted suicide and patients with human immunodeficiency virus disease. *N Engl J Med.* 1997;336:417-21.
48. **Swarztrauber K, Vickrey BG, Mittman BS.** Physicians' preferences for specialty involvement in the care of patients with neurological conditions. *Med Care.* 2002;40:1196-209.
49. **Roberts JS.** Anticipating response to predictive genetic testing for Alzheimer's disease: a survey of first-degree relatives. *Gerontologist.* 2000;40:43-52.
50. **Baker TB, Hatsukami DK, Lerman C, O'Malley SS, Shields AE, Fiore MC.** Transdisciplinary science applied to the evaluation of treatments for tobacco use. *Nicotine Tob Res.* 2003;5:S89-S99.
51. **Clayton RR, Scutchfield FD, Wyatt SW.** Hutchinson Smoking Prevention Project: a new gold standard in prevention science requires new transdisciplinary thinking. *J Natl Cancer Inst.* 2000;92:1964-5.
52. **American Society of Human Genetics Social Issues Subcommittee on Familial Disclosure.** ASHG statement: professional disclosure of familial genetic information. *Am J Hum Genet.* 1998;62:474-83.
53. **Collins FS.** Preparing health professionals for the genetic revolution. *JAMA.* 1997;278:1285-6.
54. **Stephenson J.** As discoveries unfold, a new urgency to bring genetic literacy to physicians. *JAMA.* 1997;278:1225-6.
55. **Malek JI, Geller G, Sugarman J.** Talking about cases in bioethics: the effect of an intensive course on health care professionals. *J Med Ethics.* 2000;26:131-6.
56. **Freedman AN, Wideroff L, Olson L, et al.** US physicians' attitudes toward genetic testing for cancer susceptibility. *Am J Med Genet.* 2003;120A:63-71.