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Primary Care Physicians' Willingness to Offer a New Genetic Test to Tailor Smoking Treatment, According to Test Characteristics

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Abstract

Emerging pharmacogenetics research may improve clinical outcomes for common complex conditions typically treated in primary care settings. Physicians' willingness to offer genetically-tailored treatments to their patients will be critical to realizing this potential. According to recent research, it is likely that genotypes used to tailor smoking will have pleiotropic associations with other addictions and diseases, and may have different frequencies across populations. These additional features may pose an additional barrier to adoption. To assess physicians' willingness to offer a new test to individually tailor smoking treatment according to specific test characteristics, we conducted a national mailed survey of 2000 U.S. primary care physicians (response rate: 62.3%). Physicians responded to a baseline scenario describing a new test to tailor smoking treatment, and 3 additional scenarios describing specific test characteristics based on published research; there was random assignment to one of two survey conditions in which the test was described as a genetic or non-genetic test. Our findings indicate physicians' self-reported likelihood (0–100 scale) that they would offer a new test to tailor smoking cessation treatment ranged from 69–78% across all scenarios. Relative to baseline scenario responses, physicians were significantly less likely to offer the test when informed that the same genotypes assessed for treatment tailoring: (1) may also identify individuals predisposed to become addicted to nicotine ($p < .001$); (2) differ in frequency by race ($p < .004$); and (3) may have associations with other conditions (e.g., alcohol and cocaine addiction, ADHD and Tourette's Syndrome) ($p < .01$). Describing a new test to individually tailor smoking treatment as a "genetic" versus non-genetic test significantly reduced physicians' likelihood of offering the test across all scenarios, regardless of specific test characteristics ($p < .0007$). Effective education of primary care physicians will be

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critical to successful integration of promising new pharmacogenetic treatment strategies for smoking.

INTRODUCTION

In the anticipated future of personalized medicine, clinical care may be tailored to patients' individual profiles, including patients' genetic profiles and environmental exposures (Collins, 1999; Collins, Green, Guttmacher, & Guyer, 2003). While several pharmacogenetic applications are already in use to match patients to safer, more effective pharmacotherapy (Collins, Green, Guttmacher, & Guyer, 2003; Roses, 2000), genomic medicine may yield the greatest benefits when applied to highly prevalent chronic conditions (e.g., tobacco dependence, diabetes, hypertension).

The genetics of complex traits, however, raises several challenges likely to affect physicians' likelihood of offering genetically-tailored treatments to their patients (Shields, Lerman, & Sullivan, 2004). First, many genetic polymorphisms have pleiotropic associations with other, potentially more stigmatized illnesses or behaviors (Shields, Blumenthal, Weiss, Comstock, Currihan, & Lerman, 2005; Wachbroit, 1998; Wilfond, Geller, Lerman, Audrain-McGovern, & Shields, 2002). Polymorphisms useful for tailoring smoking cessation treatment, for example, have also been linked to susceptibility to nicotine, cocaine, and alcohol addiction (Comings, Gade, Wu, Chiu, Dietz, Muhleman, Saucier, Ferry, Rosenthal, Lesieur, Rugle, & MacMurray, 1997; Comings, Muhleman, Ahn, Gysin, & Flanagan, 1994), compulsive gambling (Comings, Gade, Wu, Chiu, Dietz, Muhleman, Saucier, Ferry, Rosenthal, Lesieur, Rugle, & MacMurray, 1997), depression (Bellivier, Henry, Szoke, Schurhoff, Nosten-Bertrand, Feingold, Launay, Leboyer, & Laplanche, 1998), and a host of other psychiatric conditions (Billett, Richter, Sam, Swinson, Dai, King, Badri, Sasaki, Buchanan, & Kennedy, 1998; Comings, Muhleman, & Gysin, 1996; Muglia, Jain, Macciardi, & Kennedy, 2000). This issue is complicated further by differences in the frequency of risk alleles across populations of different geographical ancestry (Goldstein, Tate, & Sisodiya, 2003), where such differences are almost always interpreted in a clinical context as "racial" differences. While differences in populations defined by geographical ancestry are highly correlated with self-identified racial groups, the less precise use of racial categories in the clinical context has important social and clinical implications (Shields, Fortun, Hammonds, King, Lerman, Rapp, & Sullivan, 2005). Such "racial" differences in the frequency of alleles associated with increased risk of developing a highly stigmatized condition will require physicians to balance the potential clinical benefits of genetically-tailored treatment against the potential for stigma or discrimination that may accrue to their patients.

A third challenge to clinical integration of pharmacogenetic applications for complex diseases is that many such illnesses are treated in primary care settings, suggesting that primary care physicians will play a central role in offering new genetic-based treatments to patients (Burke, 2004; Collins, 1999). Yet several studies have suggested that most primary care physicians do not have the knowledge, willingness, or resources needed to play such a role (Emery & Hayflick, 2001; Escher & Sappino, 2000; Mountcastle-Shah & Holtzman, 2000; Park, Kleimann, Pelan, & Shields, 2007; Wideroff, Vadaparampil, Greene, Taplin, Olson, & Freedman, 2005).

In this study, we investigate primary care physicians' attitudes toward the integration of pharmacogenetic treatment strategies in primary care practice through the anticipated case of a novel pharmacogenetic test to tailor smoking cessation treatment. Smoking is the leading cause of death in the U.S. (Mokdad, Marks, Stroup, & Gerberding, 2004). Available smoking

cessation treatments are only somewhat effective, with 1-year quit rates averaging 7–30%, depending on the intensity of counseling accompanying pharmacotherapy (Fiore, Bailey, Cohen, & et al, 2000; National Institute for Clinical Excellence, March 2002; Nides, Oncken, Gonzales, Rennard, Watsky, Anziano, & Reeves, 2006). Data from twin studies indicate that individual differences in nicotine dependence and the ability to quit smoking are attributable, in part, to inherited factors (Heath & Martin, 1993; Kendler, Neale, Sullivan, Corey, Gardner, & Prescott, 1999; Sullivan & Kendler, 1999; Xian, Scherrer, Madden, Lyons, Tsuang, True, & Eisen, 2003). Current pharmacogenetics research may lead to the future tailoring of pharmacotherapy to improve treatment outcomes for tobacco dependence (Ho & Tyndale, 2007; Munafo, Shields, Berrettini, Patterson, & Lerman, 2005) and identify patients most likely to experience adverse side effects of treatment (Swan, Valdes, Ring, Khroyan, Jack, Ton, Curry, & McAfee, 2005). Emerging data suggest that polymorphisms in drug metabolizing enzymes and central nervous system genes predict successful smoking cessation with nicotine replacement therapy (David SP, Munafo MR, Murphy MFG, Walton RT, & Johnstone EC, 2007; Johnstone, Yudkin, Hey, Roberts, Welch, Murphy, Griffiths, & Walton, 2004; Lerman, Jepson, Wileyto, Epstein, Rukstalis, Patterson, Kaufmann, Restine, Hawk, Niaura, & Berrettini, 2006; Malaiyandi, Lerman, Benowitz, Jepson, Patterson, & Tyndale, 2006) and bupropion (Berrettini WH, Wileyto EP, Epstein L, Restine S, Hawk L, Shields P, Niaura R, & Lerman C, 2007; David, Niaura, Papandonatos, Shadel, Burkholder, Britt, Day, Stumpff, Hutchison, Murphy, Johnstone, Griffiths, & Walton, 2003; Lee AM, Jepson C, Hoffmann E, Epstein L, Hawk LW, Lerman C, & Tyndale RF, 2007). While these findings have not yet been sufficiently reproduced to warrant clinical use, the pace of developments in genomic and bioinformatic technologies are likely to yield novel efficacious applications in the near future, underscoring the importance of parallel analyses to understand and address challenges to anticipated clinical integration.

In previous work, we demonstrated that merely describing a new test to tailor smoking treatment as a genetic test as opposed to a non-genetic test significantly reduced primary care physicians' likelihood of offering their patients the test in a simple baseline scenario, with anticipated offer rates of 78% when the test was presented as nongenetic versus 70% when the test was described as genetic (Shields, Blumenthal, Weiss, Comstock, Currivan, & Lerman, 2005). In this follow-up analysis, we assess the impact of specific additional test characteristics (e.g., pleiotropic associations, racial differences in allele frequencies), drawn from published literature, on physicians' likelihood of offering their patients a new genetic test to tailor smoking cessation treatment relative to that baseline case. We hypothesized that physicians' likelihood of offering the test would decrease when informed of these additional, likely test characteristics.

METHODS

Sample Selection

An initial sample of 2000 primary care physicians was randomly drawn from all U.S. primary care physicians in the AMA Masterfile with a primary specialty of internal medicine, family practice, or general practice, through an authorized vendor (Synavant, 2002). Differences in the distribution of internal medicine, family practice, age and sex between the population and the sample were within the range of sampling variation (Shields, Blumenthal, Weiss, Comstock, Currivan, & Lerman, 2005). Respondents were required to practice a minimum of 20 hours per week in direct patient care. The final response rate, adjusted for ineligible cases, was 62.3%. The sample of respondents included significantly fewer females and younger physicians (27–44) compared to national estimates. Further details of survey design and administration are available elsewhere (Shields, Blumenthal, Weiss, Comstock, Currivan, & Lerman, 2005). The study protocol was approved by the

Institutional Review Board of Georgetown University, where the principal investigator was on faculty at the time the survey was fielded.

Survey Design and Administration

Data collection was conducted via a mailed survey over a 7-month period and completed in November 2002. Design of the survey instrument was informed by focus groups and semi-structured interviews with primary care physicians, and comments from national physician organizations and tobacco experts (Shields, Blumenthal, Weiss, Comstock, Currivan, & Lerman, 2005). Scenarios describing likely characteristics of a hypothetical new test to tailor smoking cessation treatment were developed by the research team based on published scientific data and revised via focus groups for inclusion in the survey.

In this two by four study design, physicians were asked to respond to four different scenarios, with respondents randomly assigned to receive a survey in which the new test to tailor smoking treatment was described in the scenarios as a “genetic” or non-genetic (“serum protein”) test. All other elements in the scenarios were identical. A baseline scenario described characteristics of a patient who wanted to quit smoking and characteristics of a new test to individually tailor smoking treatment (Figure 1). Three additional scenarios followed, presenting different characteristics of the new test. After reading each scenario, physicians were asked to report how likely (on a scale from 0–100 percent) they would be to offer the test described in the scenario.

In the first non-baseline scenario, physicians were told that in addition to predicting treatment outcomes, this particular genotype/protein “has also been shown to predict an increased risk of becoming addicted to nicotine in the first place.” In the second scenario, physicians were told that “research further demonstrates to your satisfaction that the prevalence of this particular genotype/protein is approximately 43% among white smokers and 53% among African-American smokers.” In the third scenario, physicians were told that “several credible, replicated studies further demonstrate that this same genotype/protein is also associated with an increased risk of addiction to alcohol and cocaine, as well other conditions, such as attention deficit hyperactivity disorder (ADHD) and Tourette’s Syndrome.” The three scenarios were presented in the same order for all respondents. Physicians’ self-reported likelihood of offering the test across scenarios and how these reports differed among physicians responding to the genetic versus non-genetic version of the survey are the main outcomes of interest.

Several additional factors were considered as control variables in our analyses. Physician characteristics included age, sex, region in which a physician practiced, primary specialty, self-identified race/ethnicity, year of graduation from medical school, full-time medical school faculty appointment, personal smoking history, and training in clinical genetics. Given our interest in identifying physicians with personal experience with smoking and challenges associated with quitting, we identified physicians with a personal history of smoking, currently or formerly, as having “ever smoked.”

Based on prior research (Schnoll, Rukstalis, Wileyto, & Shields, 2006), we assessed physicians’ knowledge of smoking treatment guidelines and intensity of focus on smoking treatment through aggregate variables constructed from several smoking treatment practice questions. Physicians who “often” or “always” prescribe the nicotine patch, gum, or bupropion for patients wishing to quit smoking were coded as 1, as were physicians who “often” or “always” refer their patients who smoke to a formal smoking cessation program or smoking expert.

We identified those physicians in independent practices, as opposed to those practicing in a health maintenance organization, hospital-based practice, community health center, or other setting. Practice size and geographical location were also determined. Urban/rural locations were derived by mapping practice zip codes to Metropolitan Statistical Areas designated in the Area Resource File (National Center for Health Workforce Information & Analysis, 2001).

We also assessed physicians' knowledge, attitudes, and beliefs about genetics. 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, somewhat, only a little, or not at all optimistic) (1="very optimistic"). Familiarity with research on the role of genetics in smoking behavior was assessed using the question: "How much of individual variation in smoking behavior do you think is determined by: (a) genetic factors? and (b) social, environmental, or other factors?" Responses indicating that 50% or more of variation in smoking behavior is due to genetic factors, as indicated in twin studies (Heath & Martin, 1993; Kendler, Neale, Sullivan, Corey, Gardner, & Prescott, 1999; Sullivan & Kendler, 1999; True, Xian, Scherrer, Madden, Bucholz, Heath, Eisen, Lyons, Goldberg, & Tsuang, 1999), were coded as 1. We controlled for physicians' sense of preparedness to counsel their patients about genetic testing by asking, "How prepared do you feel to counsel patients considering a genetic test?" ("very prepared" = 1). Finally, we identified physicians who said they tended to offer new diagnostic tests "before" most of their peers, as opposed to "at about the same time as" or "after" most of their peers, as early adopters.

Analysis

Bivariate analyses were conducted to identify factors associated with anticipated likelihood of offering the new test to individually tailor smoking treatment. We explored the explanatory power of all characteristics presented in Table 1, assessed plausibility of the normality assumption of the response variable by examining QQ plots and conducting Kolmogorov-Smirnov tests, and assessed collinearity among independent variables using Pearson's correlation coefficient. Unadjusted offer rates and statistical tests for significant differences in unadjusted offer rates were estimated using generalized least squares to account for the correlations in error terms within individuals across the four scenarios, assuming an unstructured covariance matrix. The same type of regression model was used in the adjusted case with the inclusion of our covariates. Because the dependent variable was not normally distributed, we ran models transforming the outcomes using a logit transformation and the Box-Cox transformation. These transformations made the normality assumption of the error terms more plausible, but comparisons of the model predictions from the transformed and untransformed models indicated that the untransformed models fit the data well. We therefore present the untransformed linear regression results for ease of interpretation.

In addition to the scenario variables and indicator for receipt of the genetic/non-genetic version of the survey, our final model included sex, race/ethnicity, year of graduation from medical school, appointment to a medical school faculty, practice setting, having ever smoked, smoking treatment practices, being an early adopter of new technologies, level of optimism about the promise of genetics research to improve clinical care, beliefs regarding the genetic contribution to smoking behavior, and preparedness to counsel patients considering genetic testing. We also estimated the final regression model with the scenario variables recoded to capture the marginal change in likelihood of offering the test relative to the previous scenario presented.

Data were weighted to account for slight differences in response rates across specialties (65.9% for family practice, 66.1% for general medicine and 57.1% for internal medicine) and in the distribution of primary care specialties in our study population relative to the AMA universe (Shields, Blumenthal, Weiss, Comstock, Currivan, & Lerman, 2005). Weighting had no impact on findings. Results from the weighted analysis are reported. We used SAS version 9.1 (SAS, 2004) 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 any given variable, there were fewer than 2.7% missing observations. Only those respondents for whom there were complete data on all variables included in the final model (89%) were included in the regression analysis (N=997).

RESULTS

Characteristics of the study population (sample N = 1120) are summarized in Table 1. Bivariate analyses revealed no significant differences on any baseline measure between physicians randomly assigned to complete surveys in which the new test was described as a genetic versus non-genetic test.

Physicians' Likelihood of Offering a New Genetic Test to Tailor Smoking Treatment Unadjusted Results

Overall, the anticipated likelihood of offering a new test to tailor smoking treatment was relatively high, ranging from 69–78% across scenarios reflecting specific test characteristics (Table 2). Anticipated offer rates among physicians responding to scenarios in which the new test was described as genetic were flat, while physicians responding to scenarios in which the new test was described as a non-genetic test were far more sensitive to additional information about test characteristics.

Adjusted Analyses

As shown in Table 3, controlling for all covariates, each additional scenario led to a statistically significant reduction in physicians' anticipated likelihood of offering the test relative to the baseline scenario. When physicians were informed that the same genotype/protein that predicted treatment response (Baseline Scenario) also was associated with an increased risk of becoming addicted to nicotine in the first place, physicians' self-reported likelihood of offering the test was reduced by 3 percentage points ($p<.001$) relative to the baseline case. Self-reported likelihood of offering the test was reduced by more than 2 percentage points relative to baseline in response to information that the same genetic variants/proteins used to tailor treatment also had a higher frequency among Blacks relative to whites ($p<.001$), and similarly by 2 percentage points relative to baseline when physicians were informed that these same genetic variants/proteins were also associated with increased risk of developing other addictions (e.g., alcohol and cocaine) and various psychiatric conditions (e.g., Tourette's Syndrome, ADHD) ($p=.002$).

Additional analyses (not shown) assessing the marginal impact of the information in successive scenarios showed that informing physicians that the genotype/protein used to individually tailor treatment was also associated with an increased risk of becoming addicted to nicotine in the first place had a statistically significant dampening effect on physicians' likelihood of offering the test. The marginal impacts of the scenarios describing the racial distribution and pleiotropic associations of the genetic variant were not statistically significant after the genetic association with the risk of nicotine addiction was mentioned.

Controlling for specific test characteristics, physicians responding to scenarios in which the new test to tailor smoking treatment was described as a genetic test were on average 5 percentage points less likely to offer the new test to their patients compared than those responding to scenarios in which the new test was described as a non-genetic test ($p=.001$).

Several other factors were significantly associated with physicians' likelihood of offering a new test to tailor smoking treatment to their patients who smoke (Table 3). Physicians who were current or former smokers (+4 percentage points, $p=.03$), routinely prescribe state-of-the-art pharmacotherapy for their patients who smoke (+5 percentage points, $p=.01$), were early adopters of new tests and procedures (+7 percentage points, $p=.001$), and were "very optimistic" that genetics research will lead to significant improvements in the treatment of complex traits such as smoking behavior (+12 percentage points, $p<.001$) were all more likely than comparison groups to offer their patients a new test to individually tailor smoking cessation treatment. Those with a full-time medical school faculty appointment were less likely to offer the new test to their patients (−6 percentage points, $p=.01$).

DISCUSSION

This study provides the first national estimates of primary care physicians' self-reported likelihood of offering a new genetic test to tailor smoking treatment according to specific, likely test characteristics. In particular, we assessed the impact of three potential features of a new test, via scenarios in which physicians were told that the same genotype or protein identified to tailor treatment had also been associated with increased risk of nicotine addiction, as well as alcohol, cocaine and various psychiatric diseases, and that the frequency of these particular genotypes were somewhat higher among Black versus white populations. Each of these test characteristics is based on published research on polymorphisms implicated in smoking behavior and response to treatment, and reflects the kind of complex information that primary care physicians will have to process in deciding if, when and how to use such emergent pharmacogenetic applications. These data provide the first documented evidence that specific test characteristics likely to be present in many pharmacogenetic tests for highly prevalent complex traits (e.g. racial differences in allele frequencies, pleiotropic associations with other conditions) are likely to modestly reduce physicians' likelihood of offering such tests to their patients.

In general, physicians responding to the survey in which the test was described as genetic were insensitive to specific test characteristics; when the test is described as "genetic," the additional information provided in the subsequent scenarios did not change the likelihood of offering the test. By contrast, physicians to whom the test was described as a non-genetic "serum protein" test expressed a higher initial likelihood of offering the test, but once the nicotine scenario was introduced, their average likelihood fell close to that of the "genetic" group respondents. Our findings suggest that physicians may be assuming that there is an inherent level of complexity in "genetic" tests, such that specific details regarding this complexity will have little further impact on adoption. When a test is described as a non-genetic test, physicians' initial enthusiasm is dampened as additional test characteristics typical of genetic tests are revealed, thereby bringing their responses in line with those responding to the "genetic" test scenario.

Biomarkers are often under genetic control and are correlated with the presence of specific genetic variants, but a test to identify these biomarkers is not technically a genetic test (Secretary's Advisory Committee on Genetics Health and Society, 2006). Recent research has shown, for example, that the ratio of 3-hydroxycotinine to cotinine estimated from a blood test predicts smokers' ability to quit smoking with a standard dose of the nicotine patch (Lerman, Tyndale, Patterson, Wileyto, Shields, Pinto, & Benowitz, 2006). Since the

conversion of nicotine to its metabolites is mediated by CYP2A6 enzyme, this measure correlates with CYP2A6 genotype (Malaiyandi, Lerman, Benowitz, Jepson, Patterson, & Tyndale, 2006), but the correlation is imperfect, so the biomarker test does not have the same attributes as a genetic test to assess one's CYP2A6 status (e.g. pleiotropic associations with other conditions). Our data suggest that, where such options exist, promoting tailored treatment based on biomarkers rather than genotype may accelerate physician adoption of efficacious new treatment strategies.

Although the issues raised in the study scenarios have crucial policy significance, there were other measures in our survey that had equal importance in determining the likelihood of offering the test. The effect sizes for physicians self-identifying as early adopters and those deeming themselves very optimistic that genetics research will lead to significant clinical improvements in treatment for complex diseases such as smoking were of similar or greater magnitude than the scenario effects. These two groups account for 14.5% and 13.9% of the primary care physician population, respectively, with an overlap of 2.8% of physicians who fell into both groups. This subset of physicians is far more likely to adopt novel pharmacogenetic treatment regimens, and may be important thought leaders to engage in outreach efforts to other physicians.

Results should be viewed in the context of study limitations. Due to constraints on the number of physicians we were able to survey, the scenarios we presented were described sequentially and in a fixed order. Thus, we were unable to measure the later scenarios' effects independent of the earlier scenarios. Future surveys of this type could randomly assign the scenario order and parse out the effects of each scenario separately. Since we examined physicians' anticipated responses to a newly available genetic test rather than adoption of a currently available test, we relied on realistic scenarios describing characteristics of a new test to tailor smoking treatment to assess physicians' anticipated take-up rates for such a test. While previous work has validated the use of physician self-reported data, and the use of clinical vignettes or scenarios in particular, as reliable proxies for physicians' actual past behavior (Carey & Garrett, 1996; Mandelblatt, Berg, Meropol, Edge, Gold, Hwang, & Hadley, 2001; Peabody, Luck, Glassman, Dresselhaus, & Lee, 2000), other studies have documented the tendency of physicians to overestimate their self-reported provision of preventive, health promotional services (Leaf, Neighbor, Schaad, & Scott, 1995; Montano & Phillips, 1995; Roter & Russell, 1994). The validity of physicians' self-reported likelihood of future behavior has not been assessed and is an important area for future research. We believe this approach is warranted at this time due to the importance of anticipating and addressing barriers to integrating new efficacious treatment strategies for such a high priority condition. Our models control for a number of factors identified through our focus group work, but there remains the possibility that our findings are biased by omitted variables.

The promise of genomic medicine to improve population health cannot be realized without the active engagement and support of primary care physicians. Few high quality studies addressing barriers to physician adoption of genetic tests are available. A comprehensive review of the literature addressing barriers to primary care physician provision of genetic services from 1991–2001 identified only 18 English language peer-reviewed studies (Suther & Goodson, 2003). Only 8 of these were based on representative random samples; only two employed multivariate analyses. The most recent literature cites a few studies that include national randomized samples and more rigorous methods (Freedman, Wideroff, Olson, Davis, Klabunde, Srinath, Reeve, Croyle, & Ballard-Barbash, 2003; Wideroff, Vadaparampil, Greene, Taplin, Olson, & Freedman, 2005), but these are restricted to cancer genetics. More systematic investigations are needed to better understand factors affecting primary care physicians' likelihood of offering new genetic tests to their patients and

resources needed to facilitate clinical integration of promising pharmacogenetic interventions into primary care practice.

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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.

Baseline Scenario Depicting a New Test to Individually Tailor Smoking Treatment*

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

Table 1Characteristics of the Study Population (N=1120)⁴

Characteristic	%
Race / Ethnicity	
White	74.5
Black	2.6
Hispanic	3.7
Asian	16.0
Other race	3.2
Year of Graduation from Medical School	
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/Resources	
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 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	
1	24.7
2-4	31.0
5-9	19.0

Characteristic	%
10+	25.3
Practice Location	
Urban location	78.8
Rural location	21.2
Physician Attitudes / Beliefs Regarding Genetics	
Early Adopter of new genetic tests	14.5
Very optimistic that genetics research will lead to significant clinical improvements	13.9
Believes 50% or more of variation in smoking is due to genetics	24.2
Very prepared to counsel patients considering a genetic test	4.2

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

Table 2

Average Likelihood Score Across Scenarios, by Genetic versus Non-Genetic Version of Scenarios

Scenarios	Genetic	Non-Genetic	Significance ^A
Baseline Scenario	69.8 %	77.9%	$p < 0.001$
Increased Risk of Nicotine Addiction	69.4%	72.3%	$p < 0.001$
Racial Differences in Allele Frequencies	69.2%	74.5%	$p = 0.005$
Pleiotropic Associations	71.6%	72. 6%	$p < 0.001$

^A Comparison of responses of those randomly assigned to receive a version of the survey in which the new test to tailor treatment was described as a genetic versus non-genetic test, based on generalized linear model unadjusted for covariates.

Table 3

Anticipating Physician Likelihood of Offering a New Genetic Test to Tailor Smoking Treatment, According to Test Characteristic

Variable	Parameter Estimate ^A	95% Confidence Interval
Test Characteristics		
Nicotine scenario (same genotypes used to tailor tx also associated with increased risk of addiction)	-0.03 [†]	(-0.04, -0.02)
Race scenario (racial differences in frequency of key risk alleles)	-0.02 [†]	(-0.03, -0.01)
Pleiotropy scenario (same genotypes used to tailor treatment have also been associated with other addictions and certain psychiatric conditions)	-0.02 ^{**}	(-0.04, -0.01)
Received genetic version of the survey instrument	-0.05 ^{**}	(-0.08, -0.02)
Physician Characteristics		
Female	0.01	(-0.03, 0.04)
Race		
White	REF	-
Black	0.04	(-0.06, 0.14)
Hispanic	-0.07	(-0.15, 0.002)
Asian	0.03	(-0.01, 0.07)
Other race / ethnicity	0.03	(-0.06, 0.11)
Year of graduation from medical school	0.00	(-0.001, 0.002)
Full-time medical school faculty appointment	-0.06 [*]	(-0.11, -0.01)
Current or former smoker	0.04 [*]	(0.003, 0.07)
Smoking Treatment Practice		
Often/always recommends pharmacological treatment (nicotine patch, gum and bupropion)	0.05 ^{**}	(0.01, 0.09)
Often/always refers patients to a smoking cessation program or expert	0.03	(-0.01, 0.06)
Practice Setting		
Independent practice	0.02	(-0.01, 0.06)
Physician Attitudes / Beliefs Regarding Genetics		
Early adopter (offers new diagnostic tests)	0.07 ^{**}	(0.03, 0.11)
Very optimistic that genetic research will lead to significant clinical improvements	0.12 [†]	(0.08, 0.17)
Believes that 50% or more of variation in smoking behavior is due to genetics	0.03	(-0.001, 0.07)
Feels very prepared to counsel patients considering a genetic test	0.03	(-0.04, 0.11)

^A Given that the dependent variable (physician likelihood to offer test) ranged from 0 – 100, parameter estimates may be interpreted as absolute percentage point changes.

* $p < 0.05$

^{**}
 $p < 0.01$

[†]
 $p < 0.00$