

# Incorporating Genetic Susceptibility Feedback into a Smoking Cessation Program for African-American Smokers with Low Income<sup>1</sup>

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## Abstract

**Purpose:** Markers of genetic susceptibility to tobacco-related cancers could personalize harms of smoking and motivate cessation. Our objective was to assess whether a multicomponent intervention that included feedback about genetic susceptibility to lung cancer increased risk perceptions and rates of smoking cessation compared with a standard cessation intervention.

**Experimental Design:** Our design was a two-arm trial with eligible smokers randomized in a 1:2 ratio to Enhanced Usual Care or Biomarker Feedback (BF). Surveys were conducted at baseline, 6, and 12 months later. The setting was an inner city community health clinic. African-American patients who were current smokers ( $n = 557$ ) were identified by chart abstraction and provider referral. All smokers received a self-help manual and, if appropriate, nicotine patches. Smokers in the BF arm also were offered a blood test for genotyping the GST<sup>3</sup> gene (*GSTM1*), sent a test result booklet, and called up to four times by a health educator. Prevalent abstinence was assessed by self-report of having smoked no cigarettes in the prior 7 days at the 6- and 12-month follow-ups and sustained abstinence, *i.e.*, not smoking at either follow-up or in-between.

**Results:** Smoking cessation was greater for the BF arm than the Enhanced Usual Care arm (19% versus 10%, respectively;  $P < 0.006$ ) at 6 months but not at 12 months.

**Conclusions:** Smokers agreed to genetic feedback as part of a multicomponent cessation program. Although the program increased short-term cessation rates

compared with standard intervention, genetic feedback of susceptibility may not benefit smokers with high baseline risk perceptions.

## Introduction

Tobacco smoke is the most significant human carcinogen. One of every five deaths among adults in the United States is attributable to cigarette smoking (1). Unfortunately, 24% or 47 million Americans are current cigarette smokers (2). Smoking cessation has substantial health benefits with a 2-fold reduction in risk of lung cancer (3) and even greater and more immediate benefits for heart disease (4). Increasing rates of smoking cessation is essential to reduce smoking-related morbidity and mortality.

Although the prevalence of smoking has declined steadily over the past two decades, smoking rates remain relatively high among those with low income and low education (2). Prevalence of smoking is high, particularly among those with less than a high school education (37%) and those living below the poverty level (32%; Ref. 2). Ethnic differences remain as well. Although the prevalence of smoking has declined equally among Whites and African Americans, cessation rates remain lower among African Americans, despite their more frequent quit attempts and greater reported confidence to quit (5, 6). These lower rates of cessation are disturbing, because African Americans bear a disproportionate burden of tobacco-related cancers of the lung, esophagus, larynx, and buccal cavity (6, 7). Thus, it has been argued that African-American smokers with low income and education are an important target group for smoking cessation interventions (8).

Multicomponent, proactively delivered and self-directed interventions have shown great promise for promoting smoking cessation in clinical settings (7, 9). Components that personalize risk, enhance motivation, build skills, and provide ongoing support all have been demonstrated to increase smoking cessation. However, an acknowledged challenge for these interventions when proactively delivered has been to engage smokers to use intervention components (10).

Feedback of genetic susceptibility to tobacco-related cancers (11, 12) could be an attractive intervention strategy to encourage participation for a number of reasons. Smokers might find the opportunity to learn about their personal vulnerability to the harms of smoking compelling. Thus, the novelty of genetic markers might engage a broader spectrum of smokers to participate in smoking-related assessments and programs. Although smokers acknowledge the general harms of smoking and cite health concerns as a reason for quitting (11, 13), they also hold optimistic biases about the likelihood of experiencing negative health outcomes themselves (14). Test results could be used to personalize health communications and in so doing, increase the salience of smoking risks and motivate cessation. In our prior work with community health clinic patients, smokers with heightened perceptions of their own lung cancer risk

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<sup>3</sup> These abbreviations used are: GST, glutathione S-transferase; EUC, enhanced usual care; BF, biomarker feedback; PIA, preintervention assessment; LCHC, —.

were two times as likely to be contemplating smoking cessation (15). Similarly, other studies of low-income African-American smokers have reported a strong association of perceived personal susceptibility to and worry about lung cancer with increased desire and plans to quit smoking (16). Thus, genetic feedback interventions about susceptibility to tobacco-related health risks might increase rates of participation and ultimately, smoking cessation.

Alternatively, smokers, especially those with low levels of education, might be intimidated by genetic testing and related consent procedures or resistant to learning more about personal vulnerability, if they have no desire to quit smoking. Some African-American smokers may hesitate to agree to genetic testing because of concerns about the potential for discrimination (12, 17). Our prior work that evaluated receptivity to genetic testing for breast cancer among African-American women suggested that about half were interested (18). Other studies of African-American women have reported even higher levels of interest in genetic risk assessment for breast cancer (19, 20). However, these were small studies ( $n = 36-70$ ) of well-educated African-American women with family histories of breast or ovarian cancer who perceived themselves to be at increased risk. It is unclear whether African Americans with low income who smoke would agree to genetic susceptibility testing.

Incorporating genetic markers of susceptibility to motivate smoking cessation raises a number of other important questions and challenges as well. Genetic feedback provided along with smoking cessation interventions could increase cessation rates. Alternatively, being told that one is not highly susceptible (even with appropriate caveats) could inadvertently encourage continued smoking (21). One earlier trial reported that genetic feedback initially increased fear and depression without associated benefits for cessation (22). However, the genetic marker used (a *CYP2D6* polymorphism) categorized 92% of the sample in the high-risk group. Thus, the impact of "non-susceptible" status on affect, motivation, and cessation could not be evaluated.

There are now genetic markers that are amenable for use as feedback in health communications that enable us to address some of these questions. One of these is a polymorphism in the *GSTM1* gene that encodes a glutathione *S*-transferase isoenzyme, a phase II enzyme that detoxifies a number of environmental carcinogens including those found in cigarette smoke. In meta-analyses of case control studies, individuals with lung cancer have been significantly more likely to be missing *GSTM1* than matched controls (23, 24). *GSTM1* has several characteristics that make it optimal for generating BF. Two distinct susceptibility classes are distinguished, those who are missing *GSTM1* and not able to detoxify carcinogens via the *GSTM1* metabolic pathways and those who have *GSTM1*. Estimates from case control studies suggest that 35% of African Americans may be missing the *GSTM1* enzyme, permitting comparisons of those who do and do not have the enzyme (25). *GSTM1* genotyping also relies on relatively inexpensive PCR analysis that enables feedback in 1 day. Finally, the test is highly accurate with a misclassification rate of <1%.

In 1996, we initiated a trial to evaluate the potential of genetic markers of susceptibility to motivate African-American smokers who received care in a community health clinic to consider cessation. Because of important and lingering questions about participation in genetic testing and the acknowledged difficulties of recruiting smokers in these settings (8), we evaluated genetic feedback in the context of a multicomponent cessation intervention and compared it to enhanced usual care

in a two-arm design. This design and the selected genetic marker (*GSTM1*) were intended to extend on previous work and to address the following questions: (a) would African-American smokers who received care at a community health clinic agree to genetic testing for susceptibility to lung cancer?; (b) would the multicomponent intervention increase cessation rates over a minimal clinic-based cessation program among this important target group?; and (c) would feedback of increased genetic susceptibility result in greater increases in perceived risk, negative affect, and cessation rates than feedback of non-susceptibility?

## Patients and Methods

### Overview of Study Design

Eligible smokers were randomized in a 1:2 ratio to EUC or BF that additionally included tailored feedback of genetic susceptibility to lung cancer based on the presence or absence of *GSTM1* and telephone counseling (Fig. 1). African-American smokers were screened for eligibility during their clinic visit. Those who were eligible and agreed to participate were called within 7 days of their visits to complete a PIA. Trial participants were recontacted at 6- and 12-month follow-ups. Biochemical validation of smoking status was attempted at the 12-month follow-up.

### Setting

The study was conducted at LCHC, an inner city community health clinic that provides health care to low-income residents of an urban county in North Carolina. African Americans comprised 83% of the patients during the time the study was conducted. Approximately 70% of the patients had household incomes that fell below the poverty line. Most patients were uninsured or participants in entitlement programs. Our prior work at LCHC showed that rates of smoking were 25% overall; among the African-American patients, 40% of the males and 25% of the females reported current smoking (15).

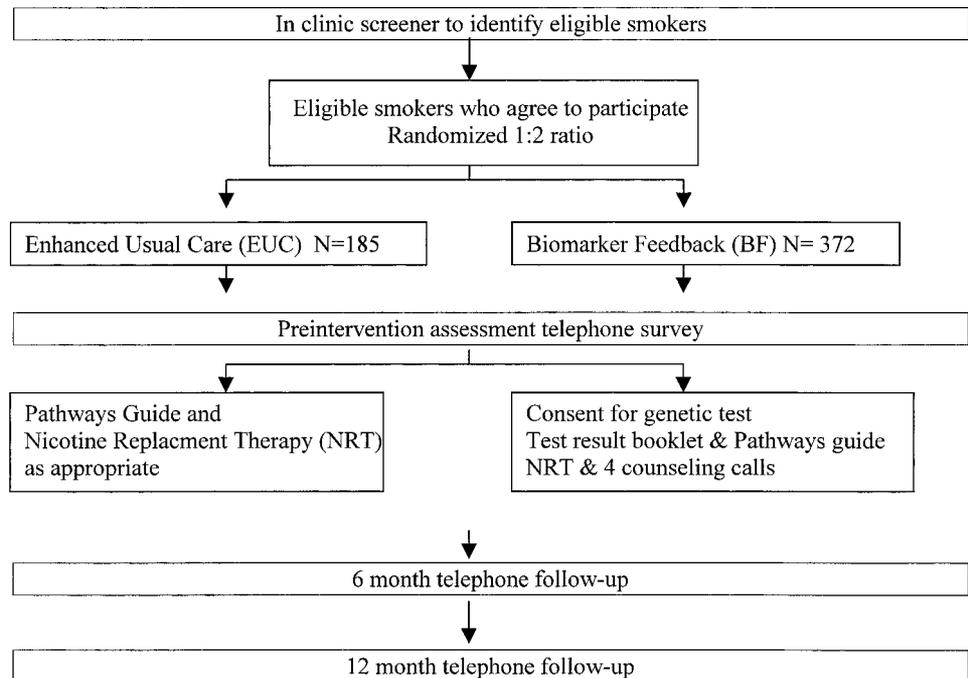
### Identification and Recruitment of Eligible Smokers

From March 1998 through October 1999, smokers were identified from the Adult Medicine, Dental, Urgent Care, and Specialty Clinics of LCHC. Smoking status was assessed for all patients as part of standard intake. Random chart abstraction conducted prior to the trial indicated that smoking status was noted in 90% of the charts.<sup>4</sup> Providers (physicians, physician assistants, and nurse practitioners) referred smokers identified by chart notation or during their clinic visit to a "smoking specialist" hired by the study team. Baseline data were collected in two surveys, a screening survey and the PIA (Fig. 1). The screening survey was administered by the smoking specialist immediately after the smoker's clinic visit. The screener was intentionally brief and included the critical variables associated with smoking cessation and those needed to generate the tailored test result booklet. Smokers were eligible if they self-identified as African American and smoked at least one cigarette/day in the prior 7 days. The PIA was administered to participants by a project research assistant within 7 days after the clinic visit and included a broader array of questions.

Consent for blood testing was obtained in a two-step process. All smokers were informed that as part of their par-

<sup>4</sup> M. Baldwin, personal oral communication, February 6, 1998.

Fig. 1. Study flow diagram. Effects of feedback of genetic susceptibility on smoking cessation.



participation in the trial, they might be asked to give a blood sample. Those who agreed were randomized to the EUC arm or the BF arm. A second level of consent was obtained from those randomized to the BF arm for provision of the blood sample to be tested for *GSTM1*. Smokers in the BF arm continued participation in the trial, even if they declined to provide a blood sample.

#### Intervention Arms

**EUC.** Consistent with recommendations of the Agency for Health Research Quality for clinic-based smoking cessation programs, smokers in the EUC arm received provider advice to quit smoking and were referred to the smoking specialist who assessed stage of readiness to quit and the appropriateness of nicotine replacement therapy. Within 2 weeks after the clinic visit, all smokers were sent a self-help smoking cessation guide especially designed for African-American smokers, “Pathways to Freedom,” and if eligible (smoked at least five cigarettes/day and in the preparation stage of readiness to quit), a 14-day supply of 15-mg nicotine patches. Refill kits that included a 7-day supply of patches were provided as needed. Participants were allowed to request up to eight refills over the study period (for a total of 10 weeks of therapy).

#### BF

**Obtaining Consent for the Blood Test.** Smokers in the BF arm were given the opportunity to have their blood tested for the  $\mu$  isoenzyme of GST (*GSTM1*). As part of the consent procedure, the smoking specialist explained the role of *GSTM1* in “cleaning up cancer-causing chemicals in cigarette smoke” using a flip chart of graphically displayed information. Smokers could accept or decline the blood test. Those who agreed to provide a blood sample were escorted by the smoking specialist to LCHC’s phlebotomist. Peripheral venous blood was collected in sodium-heparin Vacutainer tubes and immediately stored at 4°C.

**Tailored Test Result Booklet.** Within 2 weeks after the clinic visit, all participants were priority mailed an eight-page test result booklet written at a fifth grade reading level. The booklet included the test result, information about the chemical constituents of tobacco smoke and the harms of exposure, regardless of genetic make-up. Using graphical displays identical to those in the consent process, the booklet described whether the result indicated greater susceptibility to lung cancer than other smokers (*GSTM1* missing) or the same risk as other smokers (*GSTM1* present). (Fig. 2). Also included was text that described the risks of smoking and benefits to quitting for heart and other diseases tailored to the participant’s gender, age, and number of years smoked. Those who declined the test were sent an identical booklet that included the same graphical displays along with a generic description of the test and a question mark in the result box.

**Telephone Counseling.** Within 1 week after we mailed the test result booklet, the smoker was called to discuss the *GSTM1* test and their result. The counselors attempted a total of four calls with each participant over a 12-week period. Between the first and second calls, the participant was sent the “Pathways” self-help guide and nicotine patches, if appropriate. Four calls were selected to maintain the salience of the *GSTM1* test and encourage the smoker to take steps toward quitting. Counselors received 15 h of training related to the *GSTM1* enzyme, tobacco dependence, motivational interviewing, social cognitive theory, and also made practice calls with staff members. Calls were monitored on an ongoing basis for a random sample of 10% of the participants in the BF arm to maintain counselors’ adherence to study protocols.

Counselors used a standardized protocol for the counseling calls. Each call was based on motivational interviewing techniques and tailored to be stage appropriate (23, 26). The objective of the first call was to discuss the smoker’s blood test result and its importance for smoking cessation. During the call,

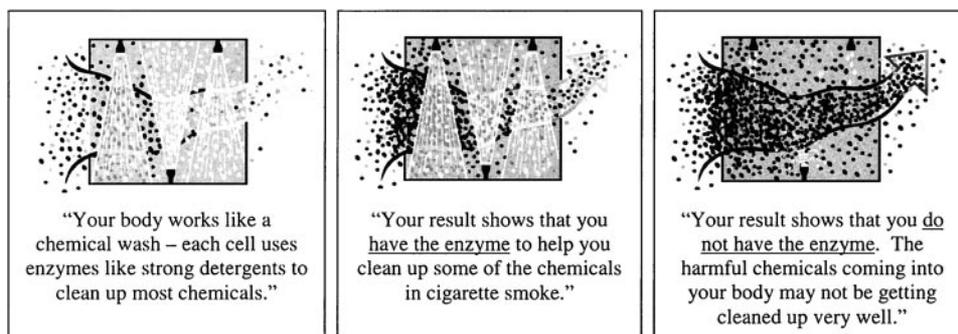


Fig. 2. How chemicals are “cleaned up” by *GSTM1*. Effects of feedback of genetic susceptibility on smoking cessation.

smokers were asked to have their test result booklet open and to follow along as the counselor reviewed the contents, page by page. Counselors reviewed the smoker’s test result, asked the smoker to indicate their interpretation of the result, and addressed any misunderstanding of the feedback. Via reflective listening techniques, counselors segued to discussion of smoking by asking the participant how the test result had influenced his/her thinking about smoking. Calls two through four focused on encouraging steps toward quitting, and counselors continued to reinforce the test result as an important reason for quitting. For example, smokers who had the enzyme missing were reminded of the concern they felt after learning of their result and their awareness that they could benefit greatly from smoking cessation.

### Measures

**Screening and PIA Surveys.** The screener and PIA surveys obtained baseline data on demographics, health status, amount smoked, prior serious quit attempts, perceptions of personal risk (5-point scales: very likely, likely, 50/50, unlikely, very unlikely) for lung cancer and other smoking-related diseases in the lifetime and compared with other smokers and nonsmokers, level of worry about getting lung cancer (not at all, slightly, somewhat, or very), desire [1 (none) to 10 (strong)], and stage of readiness to quit smoking (Ref. 27; combination of intentions to quit in the next 6 months and the next 30 days), and depression (10-item Centers for Epidemiological Studies Depression Scale,  $\alpha = 0.76$ ). Surveys are available upon request from the corresponding author.

**Follow-Up Surveys.** Self-reported smoking status was assessed at the 6- and 12-month follow-ups with the question, have you smoked any cigarettes in the prior 7 days? Risk perceptions, worry, desire, and stage of readiness to quit and a shortened four-item Centers for Epidemiological Studies Depression Scale were reassessed at each follow-up. Use of the intervention materials (e.g., Pathway’s guide, nicotine patches, and biomarker test result booklet) was assessed at the 6-month follow-up (~3 months after the intervention).

**Blood Analysis.** Genomic DNA was extracted from 5 ml of whole blood using an affinity resin chromatography procedure according to the manufacturer’s instructions (Qiagen, Santa Clarita, CA). For *GSTM1* genotypes resulting from the presence or absence of the  $\mu$ -class GST isoenzyme, the forward primer CTGCCCTACTTGATGATGGG (5’ region of exon 4) and the reverse primer CTGGATTGTAGCAGATCATGC (3’ region of exon 5) were used (28). Reactions were performed in a total volume of 20  $\mu$ l containing 10 ng of template DNA, 1 unit of Taq polymerase, 200  $\mu$ M of each deoxynucleotide triphosphate, and 1  $\mu$ M of each primer. Cycling conditions were 94°C

denaturation, 55°C annealing, and 72°C extension for 40 cycles. A homozygous deletion of this gene resulted in an absence of an amplification product and presence of this gene on one or both alleles resulted in a detectable PCR product of 273 bp. Two genotypes resulted from this analysis: presence or absence of *GSTM1*. To ensure that absence of the *GSTM1* PCR product (indicative of increased susceptibility) was not the result of technical error, specimens were amplified for two additional genes, *DRD4* and *CYP2A6*, with gene-specific primer pairs. Only those with a positive amplification product for these additional genes and an absent product for *GSTM1* were considered valid results.

**Saliva Collection and Analysis.** Participants who reported not having smoked any cigarettes in the prior 7 days at 12-month follow-up were asked to provide saliva samples for cotinine analysis. Samples were collected by mail using a method that has been validated previously (29). Participants were offered a \$10 incentive for returning the sample. Those who did not return a sample within 2 weeks were sent a reminder postcard and contacted by a staff person after an additional 10 days to encourage return of the sample. Samples were analyzed at the American Health Foundation.

### Statistical Analysis

Baseline characteristics of the study participants were compared by intervention arm with the  $\chi^2$  statistic for discrete variables and *t* tests for normally distributed continuous and ordinal variables. The Wilcoxon test statistic was used when variables were not normally distributed. Logistic regression was used for the main binary outcomes of the trial, abstinence from smoking in the prior 7 days at the 6- and 12-month follow-ups, and continuous abstinence (not smoking at both the 6- and 12-month follow-ups). All analyses were done twice, first unadjusted and then adjusted by adding baseline variables that differed ( $P < 0.05$ ) by arm and were known to be associated with smoking cessation. These included number of chronic illnesses (0 versus 1 or more), smoking within 30 min of rising (no versus yes), and desire to quit (below or equal to the median versus above the median). The unadjusted and adjusted intervention effects were similar. We report the unadjusted proportions and unadjusted and adjusted *P*s to compare the two arms.

Comparisons of outcomes were assessed consistent with an intent-to-treat approach. When data on smoking status were missing for a participant because of nonresponse, either to a follow-up survey or to that item, the participant was included in the analysis with status set equal to smoker. These analyses were replicated excluding participants with missing follow-up data. Both outcomes are presented. Changes over time in risk perceptions, worry, and depression were compared by arm with

Table 1 Characteristics of smokers who participated by intervention arm

Baseline characteristics	Total (n = 557)	EUC (n = 185)	BF (n = 372)	P
Demographics and health				
Age, mean (SD)	44.5 (12.3)	45.5 (12.4)	44.0 (12.2)	0.17
Male (%)	40	44	38	0.20
Current health fair to poor (%)	48	45	50	0.25
One or more chronic illnesses (%)	64	70	61	0.03
Completed preintervention assessment (%)	87	90	86	0.15
Smoking-related				
Cigarettes/day, mean (SD)	15.5 (10.4)	16.1 (9.8)	15.3 (10.7)	0.13
Desire to quit (mean/SD) <sup>a</sup>	7.5 (2.5)	7.2 (2.6)	7.6 (2.4)	0.03
Smoke within 30 min of waking (%)	78	84	75	0.01
Have made a serious quit attempt in the prior 12 months (%)	59	55	61	0.25
Precontemplator/contemplator (%)	32	32	32	0.95
Risk perceptions/affect				
Likely to get lung cancer in lifetime if continue to smoke (%) <sup>a</sup>	68	64	70	0.30
Likely to get lung cancer in lifetime if quit smoking (%) <sup>b</sup>	9	9	10	0.81
Worried about lung cancer in lifetime (%) <sup>c</sup>	52	50	53	0.53
Depression, mean (SD)	11.9 (6.2)	11.4 (6.2)	12.2 (6.2)	0.16

<sup>a</sup> Response range from 1 (no desire to quit) to 10 (strong desire to quit).

<sup>b</sup> Includes those who reported likely or very likely.

<sup>c</sup> Includes those who reported worried or very worried, PIA only.

repeated measures analyses adjusted for the same covariates described above.

## Results

**Recruitment Outcomes.** Of the 869 smokers referred for recruitment to the study, 307 were ineligible (163 were not African American, 58 were being treated for substance abuse, 26 did not smoke a minimum of seven cigarettes/week, 27 did not have a telephone, 26 had medical conditions that contraindicated their participation, *e.g.*, Alzheimer's disease, alcohol dependence, and 7 for other reasons, *e.g.*, non-English speaking, <18 years of age). An additional 5 eligible patients refused to participate in the study. None of the participants declined to consider genetic testing (a condition required for participation). A total of 557 smokers completed the in-clinic screener, of whom 487 (87%) completed the PIA.

Rates of participation in the 6- and 12-month follow-ups were 74 and 64%, respectively. Baseline, 6-, and 12-month follow-up data are available for 57% ( $n = 316$ ) of the sample. The primary reason for loss to follow-up was that participants lost telephone access during the course of the trial (21%). Rates of attrition did not differ by study arm (EUC, 38% *versus* BF, 37%). However, as compared with those retained in the study, smokers lost to follow-up were younger (mean ages, 46 *versus* 41, respectively), male (36% *versus* 47%), more likely to have declined the blood test (14% *versus* 24%), and less likely to have a chronic illness (66% *versus* 57%).

A total of 185 smokers were randomized to EUC, and 372 were randomized to the BF arm. Among those randomized to the BF arm, 83% ( $n = 308$ ) agreed to have their blood tested for the *GSTM1* enzyme. There were no differences in gender, age, amount smoked, perceived risk, or worry related to lung cancer for those who accepted or declined the test ( $n = 64$ ).

**Participant Characteristics.** All participants were African American; the mean age was 44 (SD, 12), 40% were men, and the majority had at least one chronic illness (Table 1). Participants reported smoking an average of 15 cigarettes/day, 78% smoked within 30 min of waking, and 59% reported having made a serious quit attempt in the prior 12 months. Most of the participants (68%) perceived their risk for lung cancer to be

somewhat or very likely if they continued to smoke, with only 9% perceiving lung cancer to be likely if they quit smoking; 52% were worried about getting lung cancer in their lifetime. Smokers in the EUC arm had significantly more chronic illnesses, less desire to quit smoking, and were more likely to smoke within 30 min of waking than those in the BF arm.

**Use of Self-Help Materials and Nicotine Patches by Study Arm.** Recall of receiving the "Pathways" self-help guide was significantly greater among smokers in the BF arm than the EUC arm (BF, 96% *versus* EUC, 86%;  $P = 0.0002$ ; Table 2). Similarly, reports of having read some or all of the guide (BF, 74% *versus* EUC, 64%;  $P = 0.04$ ) and followed suggestions in the guide (BF, 76% *versus* EUC, 62%;  $P = 0.008$ ) as well as rated helpfulness of the guide (mean helpfulness: BF, 7.5 *versus* EUC, 6.1;  $P = 0.0001$ ) were significantly greater among smokers in the BF arm compared with EUC. There was no difference between the two arms in use of nicotine patches (BF, 48% *versus* EUC, 46%), although helpfulness of the nicotine patches was rated significantly greater among smokers in the BF arm (means: BF, 8.1 *versus* EUC, 7.0;  $P = 0.01$ ).

**Use of the Biomarker Test Result Booklet.** There were no differences in use of the *GSTM1* booklet between those who had a result that indicated heightened susceptibility to lung cancer (*GSTM1* missing,  $n = 104$ ) and those whose result indicated they were not "susceptible" (*GSTM1* present,  $n = 204$ ). About half of the smokers reported having read the test result booklet (*GSTM1* present, 51% *versus* missing, 56%). Smokers in the two test result groups were equally likely to accurately interpret the meaning of the test result, having the enzyme present indicated their risk for lung cancer was equal to other smokers and missing the enzyme indicated their risk was greater compared with other smokers (53 and 56% accurate, respectively). Compared with those with the enzyme present, those who were missing the enzyme were significantly more likely to say that based on their test result it was likely that they would get lung cancer in their lifetime (23% *versus* 53%, respectively;  $P = 0.0002$ ). Among those in the BF arm, 13% could not be reached for any of the calls, 87% participated in at least one counseling call, 76% in two calls, 64% in three calls, and 38% participated in all four calls.

Table 2 Use of "Pathways" self-help guide and nicotine replacement therapy (NRT) by intervention arm

Materials	Total (n = 557)	EUC (n = 185)	BF (n = 372)	P
Recalled receiving "Pathways" guide (%)	92	86	96	0.0002
Read some or all of "Pathways" (%)	71	64	75	0.04
Followed any suggestions in "Pathways" (%)	71	63	76	0.008
Helpfulness of "Pathways" <sup>a</sup> (mean/SD)	7.0 (2.6)	6.1 (2.8)	7.5 (2.4)	0.0001 <sup>b</sup>
Requested NRT and used it (%)	47	46	48	0.72
Helpfulness of NRT, <sup>a</sup> mean (SD)	7.7 (2.8)	7.0 (3.0)	8.1 (2.5)	0.01 <sup>b</sup>

<sup>a</sup> Response range from 0 (not at all helpful) to 10 (extremely helpful).

<sup>b</sup> P from nonparametric test because of nonnormal data.

Table 3 Unadjusted and adjusted logistic models to predict primary cessation outcomes

Outcome	EUC (n = 185)	BF (n = 372)	P <sup>a</sup>	P <sup>b</sup>
6 months (%)				
Intent to treat <sup>c</sup>	10	19	0.006	0.03
Missing deleted <sup>d</sup>	13	27	0.0009	0.009
12 months				
Intent to treat <sup>c</sup>	10	15	0.12	0.34
Missing deleted <sup>d</sup>	16	24	0.09	0.28
Continuous abstinence				
Intent to treat <sup>c</sup>	5	11	0.02	0.08
Missing deleted <sup>d</sup>	8	19	0.01	0.07

<sup>a</sup> Unadjusted.

<sup>b</sup> Adjusted for desire to quit, chronic illness, and smoking within 30 min of waking.

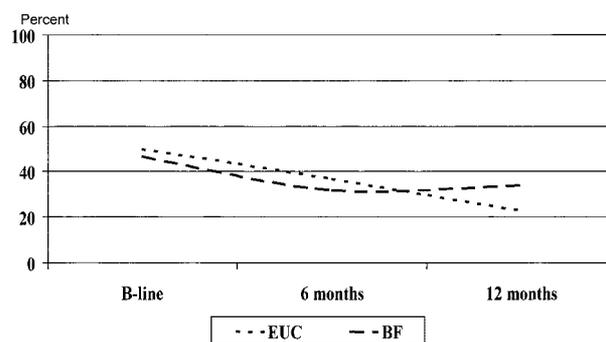
<sup>c</sup> Smokers with missing follow-up data were coded as continuing smokers.

<sup>d</sup> Smokers with missing follow-up data were omitted from analyses.

**Cessation Outcomes by Study Arm.** Efforts to biochemically confirm self-reported cessation were unsuccessful. Only 39% (24 of 61) of those who reported abstinence and agreed to provide a saliva sample returned one. Rates of return did not differ between the two arms ( $P = 0.78$ ). Thus, trial outcomes are based on self-reported cessation.

The proportion who reported not having smoked any cigarettes in the prior 7 days (prevalent abstinence) at each follow-up and who reported not having smoked at both the 6- and 12-month follow-ups (sustained abstinence) was compared by arm (Table 3). At 6-month follow-up, the rate of prevalent abstinence was significantly greater among those in the BF arm than for those in the EUC arm (19% versus 10%, respectively;  $P < 0.006$ ). Rates of prevalent abstinence were not significantly different at 12-month follow-up (15% versus 10%, respectively;  $P = 0.12$ ). The rate of sustained abstinence was significantly higher among those in the BF arm compared with those in the EUC arm (11% versus 5%, respectively;  $P = 0.02$ ). However, adjustment for baseline covariates diminished the significance of this result ( $P = 0.08$ ). Outcome analyses that excluded those with missing follow-up data were similar at each time point.

**Association between Test Result and Cessation among Smokers in the BF Arm.** Cessation rates among those with heightened susceptibility to lung cancer (*GSTM1* missing,  $n = 104$ ) were compared with those with results that indicated they were not "susceptible" (*GSTM1* present,  $n = 204$ ). Rates of prevalent and sustained abstinence for those with the enzyme missing or present did not differ significantly at follow-up: 6 months, 17 and 23%, respectively; 12 months, 18 and 15%; sustained, 12 and 12%. Among those who declined the test, rates of prevalent abstinence at 6 and 12 months and sustained



$p = .06$

Fig. 3. Percent worried about lung cancer by time & arm.

abstinence were substantially lower (11, 11, and 5% for each outcome and time point, respectively).

**Comparison of Risk Perceptions and Affect Over Time by Arm.** Proportions who perceived lifetime risk of lung cancer to be likely were worried about lung cancer, and mean depression levels were compared by intervention arm over time in repeated measures analyses adjusting for baseline covariates. There were no time-by-arm interactions for changes in perceived risk of lung cancer or depression ( $P = 0.60$  and  $0.46$ , respectively). Between baseline and 12-month follow-ups, the proportion who perceived lung cancer risk to be likely and level of depression decreased steadily among smokers in both arms. However, for worry, the time-by-arm interaction was marginally significant ( $P = 0.06$ ). The proportion who were worried about lung cancer leveled off among those in the BF arm and steadily declined among the EUC arm (Fig. 3).

#### Cost Effectiveness of the Multicomponent Intervention.

The cost effectiveness of the BF intervention was evaluated using standard health cost accounting techniques to categorize cost components as either labor or capital and account for their distribution between the EUC and BF study arms. Labor unit prices were estimated for the smoking specialist, health educator, telephone counselors, and lab technician. Capital unit prices were collected for telephone usage, distribution of the self-help and test result booklets, provision of nicotine replacement therapy, and analysis of the blood test. These unit costs were multiplied by their respective resource utilization in each arm and then aggregated to derive the total cost incurred by arm. The main incremental costs attributable to the BF arm were consent for and analysis of the blood test and the telephone counseling. Using 6-month intent-to-treat as the effectiveness measure, the average cost effectiveness of BF was \$1,719.00 (cost per quit) and the incremental cost effectiveness of BF over

EUC (cost per additional quit above usual care) was \$3,210.00. Assuming 1.97 quality-adjusted life years are saved per quitter, the incremental cost effectiveness of BF is \$1,629.00 per quality-adjusted life years saved (30).

## Discussion

Results suggest that African-American smokers in this inner-city community health clinic were receptive to genetic testing and related feedback. No smokers approached to participate were unwilling to consider genetic testing. Moreover, the majority of those randomized to the BF arm agreed to be tested (83%). Although we questioned whether the novelty of the biomarker might attract a broad group of smokers, those who participated were generally in the preparation or greater stage of readiness (68%) and reported a relatively strong desire to quit smoking (7.5 on a 10-point scale). However, this may have been attributable, in part, to use of provider referral for recruitment. Similar to other clinic-based studies, participants were on average older and had more chronic illnesses (31). It is open to question whether in other settings the offer of genetic testing would engage younger healthier smokers to participate in cessation activities.

The multicomponent intervention that included BF resulted in significantly greater rates of smoking cessation at 6-month follow-up than the minimal program. Cessation rates at 12 months and sustained cessation favored the multicomponent intervention but were not significant. As has been suggested by others (9), longer term or booster interventions may be needed to promote enduring cessation.

In contrast to the previous study (20), there were no arm differences in risk perceptions or levels of depression. However, levels of worry about lung cancer stabilized over time among smokers in the BF arm, whereas they continuously declined among those in the EUC arm. Thus, the multicomponent intervention that included serialized contacts may have sustained participants' concern about the harms of smoking.

Although we attempted biochemical confirmation of abstinence for all self-reported quitters, return rates were poor in both arms. Self-reported cessation has been argued to be highly accurate, particularly when demand effects are relatively weak (32). Accordingly, all follow-up assessments of smoking status occurred after the intervention had been completed. Moreover, self-reported cessation rates were comparable with those reported in other similar interventions (33).

Our two-arm study design did not allow us to disentangle the independent contribution of the BF from the telephone counseling. The ideal study design would have included a telephone counseling arm without BF. However, when this trial was started, questions concerning smokers' receptivity to genetic feedback, the feasibility of communicating test results to target groups with low education, whether telephone follow-up was appropriate for genetic test results (34, 35), and difficulties recruiting low-income smokers (8) together suggested the need to evaluate a multicomponent approach that could be disaggregated in later studies.

Low-income smokers were receptive to the free smoking cessation aids. About two-thirds reported using the self-help materials, and half used nicotine replacement patches. Use and ratings of the helpfulness of these aids, and in all likelihood cessation, was increased by the telephone counseling. The doubling of cessation rates among smokers in the BF arm is comparable with our previous trial that evaluated customized intervention approaches (36) and telephone counseling interventions with smokers of higher socioeconomic status (33, 37).

However, other trials with low-income populations have shown lower rates of cessation (11%) and participation in telephone counseling (33%; Ref. 8). In this trial, telephone counseling participation was relatively high; 76% completed at least two calls. Whether receiving the initial call about the genetic test result engaged smokers to participate in more of the telephone counseling warrants further study. In any case, provision of free or low-cost and state-of-the-science cessation aids such as telephone counseling could have important public health benefit for smokers with low income. Moreover, the cost of \$1,600.00 per quality-adjusted life year for the BF intervention suggests that these approaches may be cost effective when compared with other preventive health services (31, 35).

Consideration of the impact of susceptibility status on risk perceptions and smoking cessation among the biomarker arm lends some insight into the independent effects of the feedback. Feedback of increased susceptibility to lung cancer was not associated with significant increases in smoking cessation, risk perceptions, or levels of depression in the short or long term. On the other hand, feedback of not being susceptible did not undermine success at smoking cessation. That increased susceptibility was not a powerful inducement may have been attributed to characteristics of the participants, the majority of whom already were experiencing health effects of their smoking and had high baseline levels of perceived risk for lung cancer and high motivation to quit. These ceiling effects reduced the possibility of further increasing risk perceptions. Future genetic feedback interventions may have greater impact with younger, healthier smokers who do not yet perceive their own vulnerability to smoking-related disease. However, whether notification of not being susceptible will operate differently in these healthier and younger smokers is unclear.

Feedback of genetic susceptibility also may not have had a powerful impact because 45% of the smokers did not fully understand the test result. In our pilot study (38), 55% of the smokers accurately comprehended the meaning of the test result (38). The low education level of our target group suggested that we provide multiple telephone counseling sessions to help smokers understand the meaning and limitations of the test result and give them the necessary support to quit smoking. However, multiple calls resulted in the same rate of accurate comprehension (55%). Future trials should evaluate other graphical approaches for communicating results, the optimal content and number of counseling sessions needed to explain results and potential cognitive biases such as denial responses that might undermine retention of test results.

The rapid advancement of genetics augurs the eventual availability of biomarkers of susceptibility for numerous diseases and behaviors. Development and evaluation of related feedback and communication approaches that might motivate adoption of risk-reducing health behaviors are needed. Focusing these intervention approaches on populations of smokers who might be particularly susceptible to smoking-related health outcomes, such as African Americans, women, relatives of patients who have lung cancer, or other smoking-related illnesses, might be a fruitful focus for future research.

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