Predictors of Sustained Smoking Cessation: A Prospective Analysis of Chronic Smokers From the Alpha-Tocopherol Beta-Carotene Cancer Prevention Study

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Despite significant progress in smoking prevalence reduction within the United States since the mid-1990s, in the past 15 years, rates of smoking have remained virtually unchanged.[1–3] Smoking continues to be a significant public health issue with a substantial associated cancer[4] and health care burden.[5] In the United States, current smoking rates are reported to be 21.6% of the adult population, with 440 000 deaths per year attributable to smoking.[3] These unchanged smoking rates have occurred within a context of widely marketed cessation medications and consistent reports of strong motivation by smokers to quit smoking, which speaks to the difficulty of successfully achieving cessation for many smokers. Approximately 40% of current smokers attempt to quit in any given year, but only 5% sustain abstinence for more than a few weeks, and most relapse within a week.[6] To effectively reduce the burden of tobacco use, there needs to be a better understanding of the factors associated with successful cessation.

Smoking is a complex behavior that encompasses social, economic, environmental, behavioral, and physiological factors.[7] A comprehensive model of smoking should account for as many of these dimensions or factors as possible. Like other substance abuse and dependence behaviors, smoking occurs along a trajectory from experimentation and initiation to cessation attempts (and relapse). Therefore, to understand factors associated with smoking behavior along that trajectory, researchers must compare 2 groups who have similar histories—that is, groups in which both have reached a prerequisite "stage" before diverging on the behavior of interest. This allows any differences in the 2 groups to be more

Objectives. Because US smoking rates have not declined during the past decade, there is a renewed need to identify factors associated with smoking cessation. Using a nested case–control design, we explored the association between ability to sustain cessation over an extended period and demographic, smoking, medical, and behavioral variables.

Methods. We selected a sample of 1379 sustained quitters (abstinent from smoking for at least 40 months) and 1388 relapsers (abstinent for more than 8 months before relapse) from participants in the Alpha-Tocopherol Beta-Carotene Cancer Prevention Study, a nutritional intervention study involving Finnish men aged 50 to 69 years at baseline. Contingency table and multiple regression analyses were used to evaluate potential differences between the 2 groups on baseline variables.

Results. Compared with sustained quitters, relapsers were more likely to report symptoms of emotional distress and higher levels of nicotine dependence, to drink more alcohol, and to report more medical conditions.

Conclusions. Factors associated with both tobacco use and comorbid conditions impact an individual's ability to maintain long-term smoking cessation. Understanding the underlying mechanisms of action and potential common pathways among these factors may help to improve smoking cessation therapies. (*Am J Public Health.* 2008; 98:549–555. doi:10.2105/AJPH.2005.084137)

precisely attributed to the differences in the behavior of interest.

To illustrate this point, consider that to compare participants' responses to a stimulus first requires participant exposure to the stimulus. Likewise, to compare smokers' progression from 1 stage of the smoking trajectory to the next, the smokers must be "exposed" to the previous stage on the continuum. For example, to assess liability to dependence, researchers are now effectively arguing that comparison groups must be exposed to nicotine,[8] or, in other words, individuals must progress through the cigarette-experimentation stage of the trajectory before liability to dependence can be assessed.

In the case of smoking cessation, there are 2 relevant behaviors. The first is initiating a quit attempt and the second is sustaining that quit attempt. If the behavior of interest is sustained cessation, then a proper study design

requires that all participants have made a quit attempt. In other words, smokers must progress to making a quit attempt before factors associated with quit length can be assessed. Individuals who have not made a quit attempt are not informative regarding their liability to relapse, and their inclusion in a study of sustained cessation presents a potential problem of misclassification bias. As an example, it has been suggested that a history of major depression may influence initiation of cessation but not maintenance of cessation.[9–10] To directly assess the impact of depression on the ability to sustain cessation (behavior of interest), individuals with and without a history of major depression who have all made a quit attempt (necessary exposure) should be compared.

Previous literature has identified a number of factors that are likely to impact smoking cessation. Few studies, however, have clearly

differentiated initiating versus sustaining cessation,[11] so the impact of those factors on quit attempts versus sustained cessation is unknown. Demographic variables that have been reported to positively influence cessation include male gender, older age, higher education, and indicators of higher socioeconomic status.[11–17] A number of smoking-related factors, including those associated with nicotine dependence, are related to increased difficulty with cessation. These include higher numbers of cigarettes per day, earlier age of smoking onset, few to no previous quit attempts, and indicators of nicotine dependence, such as shorter time to first cigarette in the morning.[18–21] Comorbid conditions have also been demonstrated to impact cessation, including behavioral symptoms and psychiatric disorders[22–24] and medical conditions.[25–29] Despite this seemingly comprehensive list, a limited body of research has considered the impact of these types of factors longitudinally or has addressed the contribution of more than 1 domain of factors within a single study. This is because, at least in part, of the lack of available longitudinal data that encompass a wide range of potential factors.

To address this gap, we performed a nested case–control study on a sample drawn from a large, randomized longitudinal clinical trial of male smokers that contained a number of relevant variables including smoking use and history, demographics, comorbid medical conditions, and comorbid behavioral symptoms. In a selected sample of individuals who had made at least 1 quit attempt, we evaluated differences between those individuals who were able to sustain abstinence from smoking for at least 40 months (sustained quitters) to individuals who relapsed within 8 months (relapsers). These intervals were chosen a priori in an effort to maximize differences between our groups on the behavior of interest—sustained cessation.

METHODS

Data Source

The sample for this study was drawn from the Alpha-Tocopherol Beta-Carotene (ATBC) Cancer Prevention Study.[30] Between 1985 and 1993, this longitudinal, population-based chemoprevention trial enrolled 29 133 Finnish, male, current smokers aged between 50 and 69 years into a randomized primary prevention trial to assess whether alpha-tocopherol or beta-carotene would reduce cancer incidence. At baseline, all individuals in the ATBC Cancer Prevention Study smoked at least 5 cigarettes per day and were generally in good health. Median age at entry into the study was 57 years, and the median number of cigarettes smoked per day was 20 with a reported median years smoked of 36 years. Exclusion criteria included a history of cancer, significant cardiac diagnoses, cirrhosis, chronic alcoholism, and significant psychiatric diagnoses. By the end of the trial, 20 072 were still actively participating in the nutritional intervention. Of those not participating by the end, 3570 had died. For details please see ATBC Cancer Prevention Study Group, 1994.[30]

The ATBC Cancer Prevention Study was initially conducted from 1985 to 1993, although outcome data continue to be collected for vital status, cause-specific mortality, cancer incidence, and hospitalization-related morbidities. Extensive data of medical history based on participant self-report and medical examination were collected at baseline and participants were followed for 5 to 8 years with 3 scheduled follow-up visits per year (i.e., every 4 months). At each follow-up, participants were queried about health and smoking status since their previous visit. Annually, additional medical questions regarding cardiovascular and respiratory symptoms were asked and a basic medical examination was performed.

Defining Cases and Controls

We utilized a nested case–control design. Individuals who were diagnosed with lung cancer during the trial were excluded from our sample because of lung cancer's impact on smoking cessation[25,31] and high mortality. Eligibility criteria for this nested study required a reported cessation attempt during the trial. In addition, we excluded men with missed visits during the timeframe that was used to define their quit status.

All individuals selected for our nested case–control sample were exposed to the key behavior of having made at least 1 quit attempt during the trial. Approximately 30% (n=8605) of the participants in the ATBC Cancer Prevention Study made 1 quit attempt during the trial; that is, they reported that they either stopped smoking at some point during at least 1 follow-up interval or did not smoke at all during at least 1 follow-up interval. Of these, 1379 men met the definition of a sustained quitter and 1388 met the definition of a relapser and were therefore included in our analysis.

Smoking status was determined by the following question (translated from Finnish), which was asked at each follow-up visit: "Have you smoked since your last visit?" Three response options allowed participants to indicate that during the previous 4 months they had not smoked at all (i.e., 4 full months of not smoking), had smoked but had stopped at some time during the interval (i.e., <4 months of not smoking), or had smoked continuously (i.e., 4 full months of smoking). Sustained quitters were defined as men who reported not smoking at all for at least 10 consecutive follow-up visits, equal to 40 months or more of abstinence. Relapsers were men who reported that they either stopped smoking or did not smoke at all during a follow-up interval but sustained no more than 1 consecutive "not smoked at all" interval and had a confirmed relapse—that is, a visit where they reported smoking continuously. The maximum quit length of the majority of our relapsers was less than 4 months; most relapsers (n=1104; 79.5%) were unable to stop for even 1 full interval.

Independent Variables

We examined the relationship of baseline variables to sustained cessation. The variables we included in this analysis were those associated with chronic medical conditions, behavioral or psychological symptoms, alcohol use, demographic variables, and smoking history. Participants reported their lifetime history of chronic medical conditions at baseline from a list of physician-diagnosed conditions. We included the following diagnoses in our analysis: cirrhosis of the liver, degenerative joint disease, rheumatoid arthritis, other arthritis, chronic bronchitis, myocardial infarction, coronary heart disease, heart failure, and diabetes mellitus.

In addition, participants indicated at baseline whether they had experienced a variety

of medical or behavioral symptoms within the previous 4 months. We included the following symptoms for analysis: back pain resulting in at least 1 day of bed rest, walking pain in the knees, joint ache, muscle ache, walking pain in the hips, leg cramps, and headache. Psychological symptoms were self-reported "symptoms or troubles with" anxiety, depression, poor memory, difficulty concentrating, fatigue, poor appetite, or insomnia during the previous 4 months. Alcohol use (mean g/day) during the past 12 months was coded as a categorical variable (0 g/day, 0.1–15 g/day, 15.1–30 g/day, >30 g/day). Caffeine intake during the past 12 months was coded as a continuous variable (mean g/day). Demographics included in the analyses were age at enrollment, marital status, education, employment status, and physical activity. Smoking history included self-report of inhaling when smoking, total cigarettes per day at baseline, age of smoking onset, years smoked, and pack years. Pack years were defined as years smoked multiplied by cigarettes smoked per day.

Statistics

Analyses were performed with SAS version 8.2 (SAS Institute Inc, Cary, NC). We initially compared sustained quitters to relapsers with standard contingency table analysis and univariate analyses. Reported P values were based on the Pearson χ^2 test for categorical variables or the Student t test for continuous variables. A multivariate analysis was performed with logistic regression to assess predictors of relapse versus sustained cessation. Variables that were significant in the unadjusted analyses were included for consideration in the multiple regression model. Age of smoking onset and number of years smoked, despite not reaching significance in the univariate analysis, were included because of their potential theoretical importance.[32] In addition, to control for potential differences between the groups in the number of completed follow-up assessments, we controlled for number of follow-up intervals as a measure of time in trial. Variables that were not significant in the full model were dropped from the analysis with the exception of marital status, anxiety, depression, and age of smoking onset. Although not significant, these variables

were retained in the model because of potential theoretical importance. Variables included in the final model were report of always inhaling, cigarettes per day, years smoked, insomnia, alcohol use, marital status, age of smoking onset, age enrolled in the study, time in trial, and self-report of anxiety and depression.

RESULTS

Characteristics of sustained quitters and relapsers at baseline are shown in Table 1. Relapsers were younger at entry into the trial ($P<.001$) and were less likely to be married ($P<.001$). No differences were noted for education level or employment status.

The results for the smoking variables are presented in Table 1. No differences between sustained quitters and relapsers were noted for age of smoking onset or years smoked. However, relapsers reported smoking more cigarettes per day ($P<.001$), were more likely to always inhale when smoking ($P=.001$), and had greater pack years of smoking ($P<.001$).

A number of differences between the sustained quitters and relapsers were found for medical conditions (Table 2). Relapsers were also more likely to report a history of myocardial infarction ($P=.02$) and reported higher rates of back ($P<.01$) and joint pain ($P=.02$). No differences were noted for other pain symptoms, diabetes, or chronic bronchitis. In addition, no differences were found for other chronic heart, liver, lung, or kidney functions (data not shown).

Relapsers were more likely than sustained quitters to report baseline symptoms of anxiety (23.7% vs 19.9%; $P=.014$) and depression (15.0% vs 11.2%; $P=.003$), although no significant differences were noted for cognitive complaints or fatigue (Table 3). Relapsers also reported higher levels of insomnia (19.7% vs 13.6%; $P<.001$). Mean grams per day of alcohol differed significantly between the groups, with relapsers being more likely to report drinking amounts larger than 15 grams per day ($P<.001$), with no significant difference found for mean daily caffeine intake.

Crude and adjusted odds ratios are presented in Table 4. After we controlled for age at enrollment, age of onset for smoking, and

TABLE 1—Baseline Demographics and Smoking Variables of Male Sustained Quitters and Relapsers of Smoking: Alpha-Tocopherol Beta-Carotene Cancer Prevention Study, Finland, 1985–1993

	Sustained Quitters (n = 1379)	Relapsers (n = 1388)	P^a
Demographics			
Age, mean, y[b]	57.3	56.6	<.001
Marital status, %			<.001
Married	88.0	82.6	
Never married	4.3	5.1	
Divorced	5.1	9.4	
Widowed	2.6	2.9	
Education,[c] %	17.5	19.3	.37
Smoking characteristics			
Always inhale, % yes	44.2	50.2	.001
Total no. cigarettes per day, %[d]			<.001
1–9	17.7	10.8	
10–19	35.8	31.0	
≥20	46.5	58.2	
Age started, y, mean	20.3	20.0	.13
Years smoked, mean	33.4	33.9	.21
Pack years,[e] mean	29.2	33.0	<.001

Note. Sustained quitters were defined as men who reported not smoking at all for at least 10 consecutive follow-up visits, equal to 40 months or more of abstinence. Relapsers were men who reported that they either stopped smoking or did not smoke at all during a follow-up interval (4 months) but sustained no more than 1 consecutive "not smoked at all" interval and had a confirmed relapse—that is, a visit where they reported smoking continuously.
[a]P values are based on χ^2 analyses for categorical variables and analysis of variance for continuous variables.
[b]Age at enrollment in the Alpha-Tocopherol Beta-Carotene Cancer Prevention Study trial.
[c]Percentage with 2 years or more of advanced training beyond basic education.
[d]Cigarettes per day including manufactured and handmade.
[e]Pack years was defined as years smoked multiplied by cigarettes smoked per day.

time in the trial, several key variables remained significant. Relapsers were more likely to demonstrate potential markers for nicotine dependence, because they were more likely to always inhale when smoking (odds ratio [OR]=1.14; 95% confidence interval [CI]=1.00, 1.35) and to smoke more cigarettes per day (10 to 19 [OR=1.36; 95% CI=1.05, 1.77] and 20 or more [OR=1.78;

TABLE 2—Baseline Medical Comorbid Variables of Male Sustained Quitters Versus Relapsers of Smoking: Alpha-Tocopherol Beta-Carotene Cancer Prevention Study, Finland, 1985–1993

Comorbid Medical Variable, % Yes	Sustained Quitters (n = 1379)	Relapsers (n = 1388)	P^a
Degenerative joint disease[b]	30.2	32.7	.13
Chronic bronchitis[b]	5.5	6.9	.13
Myocardial infarction[b]	5.4	7.6	.02
Diabetes[b]	4.3	4.9	.43
Severe back pain[c]	14.7	18.5	<.007
Knee pain[c]	2.3	1.8	.22
Joint pain[c]	27.0	31.2	.02
Headaches[c]	19.5	19.4	.94

Note. Sustained quitters were defined as men who reported not smoking at all for at least 10 consecutive follow-up visits, equal to 40 months or more of abstinence. Relapsers were men who reported that they either stopped smoking or did not smoke at all during a follow-up interval (4 months) but sustained no more than 1 consecutive "not smoked at all" interval and had a confirmed relapse—that is, a visit where they reported smoking continuously.
[a]P values are based on χ^2 analyses.
[b]Lifetime history.
[c]Problem occurring within at least the past 4 months.

TABLE 3—Baseline Behavioral Comorbid Variables of Male Sustained Quitters Versus Relapsers of Smoking: Alpha-Tocopherol Beta-Carotene Cancer Prevention Study, Finland, 1985–1993

	Sustained Quitters (n = 1379)	Relapsers (n = 1388)	P^a
Behavioral symptoms, % yes			
Anxiety[b]	19.9	23.7	.014
Depression[b]	11.2	15.0	.003
Insomnia[b]	13.6	19.7	<.001
Poor memory[b]	25.5	27.7	.18
Poor concentration[b]	9.3	11.4	.07
Fatigue[b]	21.5	23.9	.12
Alcohol and caffeine intake			
Alcohol consumption per day,[c] %			
None	12.7	10.2	<.001
0.1 g to 15 g	57.9	49.0	
15.1 g to 30 g	18.3	23.7	
>30 g	11.2	17.2	
Caffeine, mean g/day[c]	604.1	597.4	.61

Note. Sustained quitters were defined as men who reported not smoking at all for at least 10 consecutive follow-up visits, equal to 40 months or more of abstinence. Relapsers were men who reported that they either stopped smoking or did not smoke at all during a follow-up interval (4 months) but sustained no more than 1 consecutive "not smoked at all" interval and had a confirmed relapse—that is, a visit where they reported smoking continuously.
[a]P values are based on χ^2 analyses for categorical variables and analysis of variance for continuous variables.
[b]Problem occurring within at least the past 4 months.
[c]During the past 12 months.

95% CI=1.38, 2.30]). Relapsers also more frequently reported insomnia (OR=1.32; 95% CI=1.05, 1.68). In addition, relapsers were more likely to drink between 15 grams and 30 grams per day of alcohol (OR=1.58; 95% CI=1.17, 2.13) and more than 30 grams per day of alcohol (OR=1.79; 95% CI=1.29, 2.48).

DISCUSSION

In this nested case–control study, we compared smokers who sustained smoking cessation for 40 or more months to smokers who made a quit attempt but relapsed in less than 8 months on a variety of baseline variables. Consistent with the findings in previous literature,[11,19–21,33] we found that prior smoking history and potential indicators of nicotine dependence were associated with ability to sustain cessation. At baseline, relapsers smoked more cigarettes per day and were more likely to always inhale. Age at smoking initiation and number of years smoked were

not significantly different between the groups in the adjusted analyses. The number of cigarettes smoked per day was significant in the multivariate model, with marginal significance found for self-report of always inhaling when smoking. Although the number of cigarettes smoked per day and inhalation are not optimal measures of dependence, this pattern suggests that behaviors associated with higher levels of nicotine dependence at baseline are important in predicting ability to sustain cessation attempts.

Previous research has shown that medical conditions often provide the impetus for initiating and maintaining cessation attempts.[25–29] Contrary to previous results that individuals

with more health problems were more likely to quit, we found the opposite: relapsers had more medical conditions at baseline than sustained quitters. Although no significant difference at baseline was found for self-report of severe, chronic conditions, the results indicated that a baseline history of myocardial infarction as well as self-reported difficulties with back and joint pain were associated with relapse during the subsequent ATBC Cancer Prevention Study. These differences suggest that relapsers may have been in poorer health overall.

Previous literature indicates that for many smokers poorer health often serves as a "wake-up call" to make lifestyle changes. Our findings indicate that experiencing generally poorer health may also negatively impact a smoker's ability to rally needed resources to sustain a quit attempt or may discourage smokers from even attempting to make such changes. The difference in findings may also be associated with a potentially important difference between our study and others in that most of this literature has been based on clinical samples diagnosed with severe medical conditions. Our nested case–control study drew on data from generally healthy men with no history of severe medical conditions. It may be that the impact of a medical event is at least partially related to its severity. However, the results with regard to the impact of the medical conditions should be considered tentative because none of the medical conditions were significant in the multivariate model.

We found a number of behavioral symptoms were associated with sustained cessation. Self-reported anxiety, depressed mood, insomnia, and alcohol use at baseline predicted later ability to sustain a quit attempt. A solid literature base supports the negative impact of alcohol use on the duration of smoking cessation.[6,34–36] It is interesting to note that the level of alcohol use in our sample was relatively low and yet alcohol use still differentiated sustained quitters from relapsers, even after adjusting for other factors in the multivariate model.

Previous literature has also strongly associated psychological conditions such as anxiety and depression with smoking, but the role of these types of comorbid conditions in sustaining cessation is unclear, with most studies failing to

TABLE 4—Unadjusted and Adjusted Odds Ratios for Male Sustained Quitters Versus Relapsers of Smoking: Alpha-Tocopherol Beta-Carotene Cancer Prevention Study, Finland, 1985–1993

	Crude Odds Ratio (95% CI)	Odds Ratio (95% CI)
Always inhale	1.28 (1.10, 1.49)	1.14 (1.00, 1.35)
Total no. cigarettes per day[b]		
1–9	1.0	1.0
10–19	1.38 (1.08, 1.77)	1.36 (1.05, 1.77)
≥20	1.95 (1.54, 2.46)	1.78 (1.38, 2.30)
Years smoked	1.00 (1.00, 1.01)	1.01 (1.00, 1.02)
Insomnia[c]	1.52 (1.23, 1.88)	1.32 (1.05, 1.68)
Alcohol (g/day)[d]		
None	1.0	1.0
0.1 g to 15 g	1.05 (0.82, 1.35)	1.27 (0.86, 1.47)
15.1 g to 30 g	1.61 (1.21, 2.13)	1.58 (1.17, 2.13)
>30 g	1.90 (1.40, 2.59)	1.79 (1.29, 2.48)

Note. CI = confidence interval. Sustained quitters were defined as men who reported not smoking at all for at least 10 consecutive follow-up visits, equal to 40 months or more of abstinence. Relapsers were men who reported that they either stopped smoking or did not smoke at all during a follow-up interval (4 months) but sustained no more than 1 consecutive "not smoked at all" interval and had a confirmed relapse—that is, a visit where they reported smoking continuously.
[a]Cigarettes per day including manufactured and handmade.
[b]Problem occurring within at least the past 4 months.
[c]During the past 12 months.

find evidence to support an association between comorbid psychological disorders and the ability to maintain a quit attempt.[22–24,37–39] The results of our study suggest that reported anxiety and depression, even at baseline, may impact subsequent cessation, although neither of these was significant in the adjusted model. Insomnia did remain significant in the multivariate model. Note that this was insomnia reported at baseline, so it was distinct from potential sleep disturbances commonly associated with nicotine withdrawal during cessation attempts.[40] This may represent an important finding because previous studies have typically not assessed insomnia as a key behavior of interest, despite its clear association with many behavioral disorders.[41]

Strengths and Limitations

Although our findings are promising, there were several limitations that should be noted when considering these results. First, although the outcome is defined as cessation sustained across a substantial interval, the predictors were based on baseline data. How these factors may vary across the trial was not assessed in this analysis. Future analysis of the predictors across the follow-up intervals is planned. Second, the questions about smoking history and smoking patterns were not detailed enough to provide information for a fine-grained analysis of variation in smoking patterns. For example, fluctuations in number of cigarettes per day were not assessed nor was any information available as to whether any formal treatment for smoking cessation was sought by, or provided to, ATBC Cancer Prevention Study participants. Next, because the parent study excluded individuals with significant comorbid medical or psychiatric conditions, the impact of these factors could not be assessed. This is a problem that occurs in most studies of smoking behavior and is an area in much need of further research. Last, the ability to generalize our findings from a sample of male, Finnish smokers aged older than 50 years obtained between 1985 and 1993 to other samples is limited. Therefore we were unable to assess important potential gender and age differences as well the possible impact of social and cultural factors.

This study was unique in a number of ways. First, we made a distinction between initiation and maintenance of cessation. By only including individuals who had made a quit attempt during the ATBC Cancer Prevention Study, we ensured that all of the individuals in our sample had been exposed to the prerequisite behavior of having made a quit attempt so that we could then focus analyses on the relevant outcome—sustained cessation. Next, this study was based on a sample drawn from a trial in which a large number of smokers were followed at 4-month intervals for a median follow-up of more than 6 years. This allowed us to assess factors associated with the ability to maintain cessation over a much longer term than is usual in most clinical trials. In addition, extensive medical and psychological and behavioral data were collected, allowing for the consideration of the potential impact of a wide range of variables. An additional strength of this study was that the parent ATBC Cancer Prevention Study was a population-based cancer prevention trial, not a smoking cessation treatment trial, and it was not based on a clinical population. Thus, results of this study are more likely to be generalizable to male smokers in the population.

Another important strength of this study is that compliance rates were extremely high for the parent cohort study as well as within our sample, avoiding possible bias related to missing data. The high rate of compliance may have been attributable to the extensive screening used in selecting the parent cohort for the ATBC Cancer Prevention Study but also to the substantial efforts to retain study participants made by the ATBC Cancer Prevention Study research team. The high compliance rate also suggests that the individuals in our sample may have been more compliant with respect to medical advice than is typical in longitudinal studies. It is interesting to note that even in this sample of highly compliant individuals (approximately 98% compliance with the nutritional intervention in our sample; data not shown), less than 5% of the whole ATBC Cancer Prevention Study sample was able to successfully sustain smoking cessation, and we were able to identify a number of significant differences between sustained quitters and relapsers.

Conclusions

Our results suggest that a cluster of factors associated both directly (nicotine dependence) and indirectly (medical and behavioral comorbid conditions) with smoking behavior are involved in the maintenance of

smoking cessation. Exploration of the nature and possible explanatory mechanisms that link these features may represent the next steps toward the improvement of smoking cessation interventions. ∎

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Contributors

E.M. Augustson originated the study, performed the primary statistical analyses, synthesized the results, and led the writing. K.L. Wanke participated in all stages of the project from conceptualization of the study to the final article. S. Rogers contributed to the conceptual development of the study, synthesis of results, and assisted with writing the article. A.W. Bergen contributed to the conceptualization of the study, reviewed results, and edited the article. N. Chatterjee provided statistical guidance and edited drafts of the article. K. Synder provided data management expertise and assisted with analyses. D. Albanes and P.R. Taylor developed and ran the original Alpha-Tocopherol Beta-Carotene Cancer Prevention Study and provided editorial feedback on the article. N.E. Caporaso contributed to the conceptual development of the study, participated in interpretation and synthesis of results, and assisted in the writing of the article.

Human Participant Protection

No human participant protection was sought for this secondary data analysis. The original Alpha-Tocopherol Beta-Carotene Cancer Prevention Study research protocol was reviewed and approved by the National Cancer Institute's institutional review board.

References

1. Centers for Disease Control and Prevention. Tobacco use—United States, 1900–1999. *MMWR Morb Mortal Wkly Rep.* 1999;48:986–993.

2. Centers for Disease Control and Prevention. Cigarette smoking among adults—United States, 1997. *MMWR Morb Mortal Wkly Rep.* 1999;48:993–996.

3. Centers for Disease Control and Prevention. Cigarette smoking among adults—United States, 2004. *MMWR Morb Mortal Wkly Rep.* 2005;54:1121–1124.

4. Vineis P, Alavanja M, Buffler P, et al. Tobacco and cancer: recent epidemiological evidence. *J Natl Cancer Inst.* 2004;96:99–106.

5. Barendregt JJ, Bonneux L, van der Maas PJ. The health care costs of smoking. *New Engl J Med.* 1997;337:1052–1057.

6. Hughes JR, Keely J, Naud S. Shape of the relapse curve and long-term abstinence among untreated smokers. *Addiction.* 2004;99:29–38.

7. Morgan GD, Kobus K, Gerlach KK, et al. Facilitating transdisciplinary research: the experience of the transdisciplinary tobacco use research centers. *Nicotine Tob Res.* 2003;5(suppl 1):S11–S19.

8. Etter JF, Sutton S. Assessing 'stage of change' in current and former smokers. *Addiction.* 2002;97:1171–1182.

9. Dilsaver SC, Pariser SF, Churchill CM, Larson CN. Is there a relationship between failing effects to stop smoking and depression? *J Clin Psychopharmacol.* 1990;10:153–154.

10. Zhu SH, Sun J, Billings SC, Choi WS, Malarcher A. Predictors of smoking cessation in U.S. adolescents. *Am J Prev Med.* 1999;16:202–207.

11. Hymowitz N, Cummings KM, Hyland A, Lynn WR, Pechacek TF, Hartwell TD. Predictors of smoking cessation in a cohort of adult smokers followed for five years. *Tob Control.* 1997;6(suppl 2):S57–S62.

12. Burns DM, Anderson CM, Johnson M, et al. Cessation and cessation measures among adult daily smokers: national and state-specific data. In: *Population Based Smoking Cessation: Smoking and Tobacco Control Monograph No. 12.* Burns D, Amacher R, Ruppert W, eds. Bethesda, Md: US Dept of Health and Human Services, National Cancer Institute; 1997. NIH publication 97-4213.

13. US Department of Health and Human Services. *Reducing Tobacco Use: A Report of the Surgeon General.* Atlanta, Ga: National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2000.

14. US Department of Health and Human Services. *Tobacco Use Among US Racial/Ethnic Minority Groups; African Americans, American Indians and Alaska Natives, Asian Americans and Pacific Islanders and Hispanics: A Report of the Surgeon General.* Atlanta, Ga: National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 1998.

15. Bang KM, Kim JH. Prevalence of cigarette smoking by occupation and industry in the United States. *Am J Ind Med.* 2001;40:233–239.

16. Gilpin EA, Pierce JP. Demographic differences in patterns in the incidence of smoking cessation: United States 1950–1990. *Ann Epidemiol.* 2002;12:141–150.

17. Levy DT, Romano E, Mumford E. The relationship of smoking cessation to sociodemographic characteristics, smoking intensity, and tobacco control policies. *Nicotine Tob Res.* 2005;7:387–396.

18. Coambs RB, Li S, Kozlowski LT. Age interacts with heaviness of smoking in predicting success in cessation of smoking. *Am J Epidemiol.* 1992;135:240–246.

19. Shiffman S, Hickcox M, Paty JA, Gnys M, Kassel JD, Richards TJ. Progression from a smoking lapse to relapse: prediction from abstinence violation effects, nicotine dependence, and lapse characteristics. *J Consult Clin Psychol.* 1996;64:993–1002.

20. Augustson E, Marcus S. Use of the current population survey to characterize subpopulations of continued smokers: a national perspective on the "hardcore" smoker phenomenon. *Nicotine Tob Res.* 2004;6:621–629.

21. Hyland A, Li Q, Bauer JE, Giovino GA, Steger C, Cummings KM. Predictors of cessation in a cohort of current and former smokers followed over 13 years. *Nicotine Tob Res.* 2004;6(suppl 3):S363–S369.

22. Goldsmith JR, Knapp J. Towards a broader view of recovery. *J Subst Abuse Treat.* 1993;10:107–111.

23. Black DW, Zimmerman M, Coryell WH. Cigarette smoking and psychiatric disorder in a community sample. *Ann Clin Psychiatry.* 1999;11:129–136.

24. Lasser K, Boyd JW, Woolhandler S, Himmelstein DU, McCormick D, Bor DH. Smoking and mental illness: a population-based prevalence study. *JAMA.* 2000;284:2606–2610.

25. Gritz ER, Nisenbaum R, Elashoff RE, Holmes EC. Smoking behavior following diagnosis in patients with stage I non-small cell lung cancer. *Cancer Causes Control.* 1991;2:105–112.

26. Gritz ER, Carr CR, Rapkin D, et al. Predictors of long-term smoking cessation in head and neck cancer patients. *Cancer Epidemiol Biomarkers Prev.* 1993;2:261–270.

27. Freund KM, D'Agostino RB, Belanger AJ, Kannel WB, Stokes J III. Predictors of smoking cessation: the Framingham Study. *Am J Epidemiol.* 1992;135:957–964.

28. Schnoll RA, James C, Malstrom M, et al. Longitudinal predictors of continued tobacco use among patients diagnosed with cancer. *Annals Behav Med.* 2003;25:214–222.

29. Cox LS, Africano NL, Tercyak KP, Taylor KL. Nicotine dependence treatment for patients with cancer. *Cancer.* 2003;98:632–644.

30. The ATBC Cancer Prevention Study Group. The alpha-tocopherol, beta-carotene lung cancer prevention study: design, methods, participant characteristics, and compliance. *Ann Epidemiol.* 1994;4:1–10.

31. Sanderson Cox L, Patten CA, Ebbert JO, et al. Tobacco use outcomes among patients with lung cancer treated for nicotine dependence. *J Clin Oncol.* 2002;20:3461–3469.

32. Emery S, Gilpin EA, Ake C, Farkas AJ, Pierce JP. Characterizing and identifying "hard-core" smokers: implications for further reducing smoking prevalence. *Am J Public Health.* 2000;90:387–394.

33. Nordstrom BL, Kinnunen T, Utman CH, Krall EA, Vokonas PS, Garvey AJ. Predictors of continued smoking over 25 years of follow-up in the normative aging study. *Am J Public Health.* 2000;90:404–406.

34. Hughes JR. Treating smokers with current or past alcohol dependence. *Am J Health Behav.* 1996;20: 286–290.

35. Hays JT, Schroeder DR, Offord KP, et al. Response to nicotine dependence treatment in smokers with current and past alcohol problems. *Ann Behav Med.* 1999;21:244–250.

36. Kalman D, Tirch D, Penk W, Denison H. An investigation of predictors of nicotine abstinence in a smoking cessation treatment study of smokers with a past history of alcohol dependence. *Psychol Addict Behav.* 2002;16:346–349.

37. Breslau N, Novak SP, Kessler RC. Psychiatric disorders and stages of smoking. *Biol Psychiatry.* 2004; 55:69–76.

38. Breslau N, Peterson EL, Schultz LR, Chilcoat HD, Andreski P. Major depression and stages of smoking. A longitudinal investigation. *Arch Gen Psychiatry.* 1998;55:161–166.

39. Hitsman B, Borrelli B, McChargue DE, Spring B, Niaura R. History of depression and smoking cessation outcome: a meta-analysis. *J Consult Clin Psychol.* 2003; 71:657–663.

40. Colrain IM, Trinder J, Swan GE. The impact of smoking cessation on objective and subjective markers of sleep: review, synthesis and recommendations *Nicotine Tob Res.* 2004;6:913–925.

41. Smith MT, Huang MI, Manber R. Cognitive behavior therapy for chronic insomnia occurring within the context of medical and psychiatric disorders. *Clin Psychol Rev.* 2005;25:559–592.