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Evaluating Nicotine Replacement Therapy and Stage-Based Therapies in a Population-Based Effectiveness Trial

Wayne F. Velicer
University of Rhode Island

Robert H. Friedman
Boston University Medical Center

Joseph L. Fava
University of Rhode Island

Suzy B. Gulliver
Veterans Affairs Medical Center, Boston

Stefan Keller
University of Hawaii

Xiaowu Sun
University of Rhode Island

Harley Ramelson
Boston University Medical Center

James O. Prochaska
University of Rhode Island

Pharmacological interventions for smoking cessation are typically evaluated using volunteer samples (efficacy trials) but should also be evaluated in population-based trials (effectiveness trials). Nicotine replacement therapy (NRT) alone and in combination with behavioral interventions was evaluated on a population of smokers from a New England Veterans Affairs Medical Center. Telephone interviews were completed with 3,239 smokers, and 2,054 agreed to participate (64%). Participants were randomly assigned to one of four conditions: stage-matched manuals (MAN); NRT plus manuals (NRT + MAN); expert system plus NRT and manuals (EXP + NRT + MAN); and automated counseling plus NRT, manuals, and expert system (TEL + EXP + NRT + MAN). Assessments were completed at baseline, 10, 20, and 30 months. The point prevalence cessation rates at final follow-up (30 months) were MAN, 20.3%; NRT + MAN, 19.3%; EXP + NRT + MAN, 17.6%; and TEL + EXP + NRT + MAN, 19.9%. Stage-matched manuals provided cessation rates comparable with previous studies. The addition of NRT, expert system interventions, and automated telephone counseling failed to produce a further increase in intervention effectiveness.

Keywords: effectiveness trial, expert system, nicotine replacement therapy, smoking cessation, telecommunications

Of the people alive in the world today, 500,000,000 are predicted to die from the use of tobacco, with an average loss of 10 years of life (Peto & Lopez, 1990). Consequently, 5 billion years of human life will be lost because of one behavior. A breakthrough in developing an intervention with even a modest impact on populations of smokers could prevent millions of premature deaths and billions of lost years of life.

Wayne F. Velicer, Joseph L. Fava, Xiaowu Sun, and James O. Prochaska, Cancer Prevention Research Center, University of Rhode Island; Robert H. Friedman and Harley Ramelson, Medical Information Systems Unit, Boston University Medical Center; Suzy B. Gulliver, Outpatient Clinic, Veterans Affairs Medical Center, Boston; Stefan Keller, Department of Public Health Sciences and Epidemiology, University of Hawaii.

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Correspondence concerning this article should be addressed to Wayne F. Velicer, Cancer Prevention Research Center, 2 Chaffee Road, University of Rhode Island, Kingston, RI 02881. E-mail: velicer@uri.edu

Transdermal nicotine replacement therapy (NRT or the "patch") has been one of the most widely studied and most frequently used smoking cessation interventions. Multiple trials have supported the efficacy of this intervention (Fiore, Smith, Jorenby, & Baker, 1994; Hughes, Shiffman, Callas, & Zhang, 2003; Po, 1993; Silagy, Mant, Fowler, & Lodge, 1994; Tang, Law, & Wald, 1994). However, the vast majority of clinical trials to date have been efficacy trials (i.e., studies that involve highly select volunteer samples). A recent epidemiological study found no evidence supporting NRT in reducing smoking rates at the population level (Pierce & Gilpin, 2002). Other general population studies have not supported this finding (Alberg et al., 2004; Hasford, Fagerstrom, & Haustein, 2003; Miller et al., 2005).

To promote general implementation of an intervention and resolve these conflicting results, an effectiveness trial can provide critical empirical support. A particular strength of effectiveness trials is the attempt to recruit a representative sample from a defined population, allowing an inference of the generalizability of the results to similar populations. The aim of this study was to perform an effectiveness trial of NRT in combination with three low-cost behavioral therapies (manuals, tailored expert system interventions, and an automated counseling intervention). Proactive recruitment was used to recruit a large proportion of a defined

population of smokers. We also conducted an extended follow-up to assess the sustainability of the intervention.

The first goal of the study was to recruit a large proportion (i.e., > 75%) of the identified smokers in a defined population. The second goal was to recruit a representative sample of the population of eligible smokers on the basis of (a) demographic variables, (b) smoking history, and (c) stage of change. The third goal was to prepare the maximum proportion of the population for NRT use through application of the behavioral interventions. In a general population, a large proportion will not be ready to quit smoking (Velicer et al., 1995) and, therefore, not likely to use the NRT intervention. We anticipated that more than 40% of the sample would receive NRT. The fourth goal was to maximize retention at final follow-up (30 months), which we defined as more than 70% of the sample. A fifth goal was to evaluate the differential effectiveness of four combinations of behavioral and pharmacological interventions.

The study was an additive (i.e., each condition adds a component to the previous condition) four-group design with four assessments (baseline, Month 10, Month 20, and Month 30). The first intervention was the comparison condition used of stage-matched manuals (MAN) only. The second intervention condition (NRT + MAN) added NRT to the stage-matched manuals. The third intervention condition (EXP + NRT + MAN) added expert system tailored print reports (EXP) to MAN and NRT. The fourth intervention condition (TEL + EXP + NRT + MAN) added automated telephone counseling (TEL) to MAN, NRT, and EXP. The telecommunications system was developed for this study.

Effectiveness Versus Efficacy

Clinical trials are sometimes classified as efficacy trials or effectiveness trials (Flay, 1986; Glasgow, Lichtenstein, & Marcus, 2003). The efficacy trial relies on a volunteer sample that is randomly assigned to an intervention condition. In contrast, the effectiveness trial attempts to recruit a large representative proportion of a target population, which is similarly randomly assigned to an intervention condition. One of the advantages of an effectiveness trial is that the impact of an intervention (Velicer & DiClemente, 1993; Velicer & Prochaska, 1999) can be estimated. Population impacts of programs are defined as the recruitment rate times the efficacy rate. Producing high impacts begins with recruiting large percentages of eligible populations. For example, if 80% of the population can be recruited for an intervention with an efficacy rate of .10, the impact will be four times larger than an intervention with an efficacy rate of .40 that recruits 5%.

Recruitment and Representativeness

The most common approach for recruitment in efficacy trials has been a reactive approach, that is, subjects are informed about the availability of an intervention program and must initiate contact to participate. This volunteer sample is typically highly motivated to quit smoking and likely to adhere to the treatment protocol. Volunteer samples are also more likely to be female, White, and well educated (Prochaska, Velicer, Fava, Rossi, & Tsoh, 2001). In contrast, effectiveness trials typically rely on a proactive recruitment approach, that is, the subjects are contacted directly and the services are offered to them. The samples should reflect the general population. Two recent smoking cessation effectiveness studies (Prochaska, Velicer, Fava, Ruggiero, et al., 2001; Velicer, Prochaska, Fava, Laforge, & Rossi, 1999) achieved recruitment rates of 82% and 85%, and the samples were demographically similar to the defined population. In contrast, efficacy studies typically recruit 1% to 5% of the population at best (Schmid, Jeffrey, & Hellerstedt, 1989).

Generalizability

Beyond demonstrating the potential impact of an intervention, effectiveness trials increase confidence in the generalizability of the results (Prochaska & Velicer, 2004). Interventions are often less efficacious in effectiveness trials than in efficacy trials. Several reasons might explain these results: (a) Effectiveness trials evaluate treatments in the settings where they will commonly be applied, whereas efficacy trials employ optimal conditions; (b) implementation in a real-world setting must employ available personnel rather than personnel hired especially for the study; (c) some part of the intervention costs may have to be borne by the participants; (d) the intervention may be appropriate only for a small proportion of the population; and (e) effectiveness trials have a lower level of control over the timing of the intervention.

Method

Procedure

As a first step of proactive recruitment, approximately 33,962 letters were sent to potential recruits who were listed as members of a large northeastern U.S. Veterans Affairs Medical Center (VAMC). The letter introduced the study as a collaboration between the University of Rhode Island and the VA and informed the potential recruits about an upcoming telephone survey. Informed consent materials for the phone survey were included in the letter. VA members could return a postcard (postage prepaid) to decline to be contacted for the phone survey. A total of 5,022 returned the refusal card (14.8%). (This was an unusually high number compared with other studies and was attributed to the fact that many VA members had alternative health care providers that were viewed as their primary provider.) Approximately 2 weeks later, all members who did not decline participation (passive consent) were screened for study eligibility via a telephone survey. A total of 4,369 could not be contacted because of nondeliverable mail, a nonworking phone number, currently residing out of the country, or were deceased. Seventy-five were duplicate subjects. We eliminated 2,011 members for health or language issues. A total of 1,429 could not be contacted in 15 attempts (answering machines, not home, etc.), and the attempt to contact was terminated. A total of 2,664 were in the calling queue when recruitment for the study was terminated. Of the 18,392 potential subjects, 3,332 refused to participate in the phone survey when contacted (22.1%).

The screening survey was completed on a total sample of 15,060. Screening continued until the total sample size required for the study was recruited (N = 2,000). Any spouses of VAMC members who smoked were also recruited. The eligibility criteria included self-identification as a smoker who regularly smoked 10 or more cigarettes per day and, therefore, met the requirements for using NRT. Subjects in the action or maintenance stages were excluded.

After completing the survey, all eligible smokers were randomized by computer-based random number generator to one of four intervention conditions. The four intervention conditions were (a) MAN (Velicer, Rossi, Ruggiero, & Prochaska, 1994), (b) NRT + MAN, (c) EXP + NRT + MAN (Velicer et al., 1993), and (d) TEL + EXP + NRT + MAN (Friedman, 1998; Friedman et al., 1996; Ramelson, Friedman, & Ockene,

1999). Subjects were blinded to their treatment condition until they received the first intervention material; thus, awareness of the treatment condition could not influence the readiness for study participation. However, subjects were aware that several of the possible treatment conditions included NRT and that up to four follow-up assessments by telephone were scheduled over the following 30 months. All subjects were assessed at baseline, Month 10, Month 20, and Month 30. The survey center staff was blind to treatment condition. Two groups (EXP + NRT + MAN and TEL + EXP + NRT + MAN) received a limited additional assessment at Month 6 only on those variables needed to generate the expert system progress report.

Recruitment

A total of 3,239 smokers were identified as eligible and completed the full assessment during the telephone survey. Of this group, 324 subjects (10%) declined any further participation in the study after completing the initial phone survey; they are defined as the "survey-only" group. Written informed consent materials were mailed to the 2,915 subjects (90%) who provided verbal informed consent during the telephone survey. Up to 15 telephone contacts were made to participants who did not return the signed informed consent within a 2-month period. Overall, 861 subjects (29.5%) failed to return their written informed consent after having given verbal consent during the telephone interview ("verbal-consent" group). The remaining 2,054 smokers (63.4% of all eligible subjects) who sent back their written consent form constitute the "full-consent" group (see Figure 1). All information for the study was completely confidential.

Measures

The baseline assessment was completed on all subjects in all four groups and included sociodemographic variables, smoking history, and history of NRT use. Also included were the variables of the Transtheoretical Model (TTM) for smoking cessation: stages of change, 10 processes of change (Prochaska, Velicer, DiClemente, & Fava, 1988), pros and cons or decisional balance (Velicer, DiClemente, Prochaska, & Brandenberg, 1985), and situational temptations (Velicer, DiClemente, Rossi, & Prochaska, 1990). These measures were used to generate the expert system progress reports in the EXP + NRT + MAN and TEL + EXP + NRT + MAN groups. The stage variable was needed for the manuals in all four groups.

Three primary outcome measures (24-hr point prevalence, 7-day point prevalence, and 6-month prolonged abstinence) were assessed on the last three occasions (Months 10, 20, and 30). Because self-report is extremely accurate in a low-demand study like this, no biochemical validation was performed (Benowitz et al., 2002; Glasgow et al., 1993; Patrick et al., 1994).

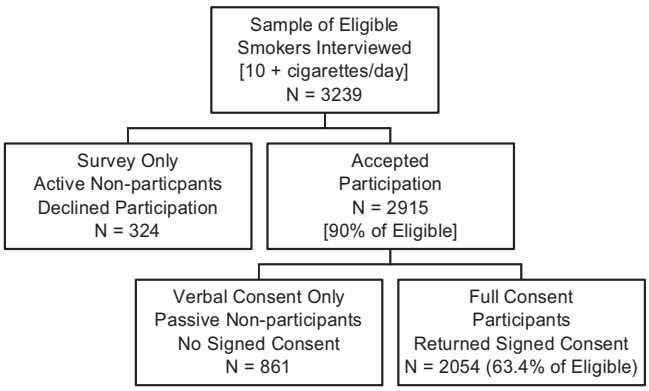

Figure 1. Flowchart for recruitment of eligible smokers classified as one of two nonparticipant groups (survey only and verbal consent only) or the participant group (full consent).

NRT Readiness

The design of the study was to provide NRT only to smokers judged to be ready for use in the immediate future. The decision to provide NRT was based on the smokers' stage of change and their decisional balance at baseline, Month 6, and Month 10 assessments. We projected that the baseline distribution would be 40% in precontemplation, 40% in contemplation, and 20% in preparation. The smokers in preparation and smokers in contemplation who had more pros of quitting than cons of smoking were immediately provided with NRT. On the basis of previous studies, we estimated that 25% would receive NRT at baseline. The remaining smokers were provided with intervention materials designed to promote stage movement and, therefore, eligibility for NRT. We estimated that 10% would receive NRT after the 6-month assessment and an additional 5% after the 10-month assessment, for a total of 40% of the smokers in the three NRT-eligible groups.

Interventions

MAN. The MAN group received the stage-based self-help manuals (Velicer et al., 1994) following baseline contact. The manuals inform users about their particular stage of change and the processes they can use to progress to the next stage. On the basis of their baseline assessment scores, treatment participants were sent the manual matched to their current stage of change and the stage beyond their current stage. Each smoker in each different stage at baseline received the same package of materials; the only difference was the number of manuals received on each occasion. This was viewed as representing a minimal intervention condition. This group served as a comparison group for the other three groups.

NRT. The NRT group received the stage-based self-help manuals following baseline contact. Those subjects for whom NRT was appropriate (preparation stage or contemplation stage with pros > cons) also received NRT. Six months after the initial assessment, the subjects who received only the manuals were recontacted. If they had progressed, NRT was provided. At the Month 10 assessment, subjects who had not received NRT were reevaluated, and those who had progressed received NRT. Subjects who received NRT at one of the early assessments but had relapsed received a second NRT intervention. The patch used was the 16-hr/15-mg patch (Nicotrol) with a 6-week course of treatment. The company provided the NRT replacement therapy at cost.

EXP. The third group (EXP + NRT + MAN) received the stage-based manuals, one expert system feedback report, and NRT when indicated. The expert system report provided feedback on the basis of normative comparisons. The 14 variables of the TTM were assessed as part of the baseline interview, and the responses of each subject were compared with peers in the same stage who were successful in progressing to the next stage. Detailed descriptions of this intervention are available elsewhere (Velicer et al., 1993; Velicer & Prochaska, 1999; Velicer, Prochaska, & Redding, 2006). Participants for whom NRT was not appropriate at baseline were reassessed at Month 6 and again at Month 10. If they had progressed, they were provided with NRT at that time.

TEL. The fourth group (TEL + EXP + NRT + MAN) received the stage-based manuals, the expert system progress report at baseline, and NRT. In addition, they received regular telecommunications contacts via an automated counseling intervention. The interactive telecommunications system was developed for this study and employs a series of prerecorded voice files assembled in the form of a conversation that is tailored to the responses of the smoker. The telecommunications contacts served to both complete the assessment of progress on the 14 TTM variables and provide instant automated feedback. Material similar to that in the written paragraphs of the expert system progress reports was presented during the call

and reproduced verbally. To limit the length of the call to 15 to 20 min, two telecommunications calls were needed to cover the same material as a single progress report. The responses to the assessment questions were entered using the telephone keypad.

There were two different frequency rates for the telecommunication contacts. In each case, the smoker was free to initiate additional contacts at any time and for as many times as desired. However, if a participant did not call in a set period, proactive calls were initiated automatically. The *lean* contact rate was monthly and applied to those smokers who had not received NRT (precontemplators, contemplators with pros > cons). The *dense* contact rate applied to smokers who received NRT and was weekly for the first month, biweekly the second month, and monthly for Months 3–6. The two rates of contact were used because we have observed that early-stage smokers change more slowly and are more likely to develop reactance against the intervention when pressed too hard. In each case, the rate automatically changed from lean to dense for any smoker who progressed and received NRT.

The total length of contact was designed to be 6 months. However, for those smokers who progressed to NRT status later in the study or at the Month 10 assessment, the telecommunications option was available for a 2-month period after receiving NRT.

Results

Sample

A total of 2,054 smokers participated in the study. Table 1 presents the demographic characteristics and stage of change for each group and the total sample. The average age was 50.5 years ($SD = 11.0$), and 77% were men. The mean education level was 13.0 years ($SD = 2.5$), 48.2% were currently married, and the sample was predominantly White (89.4%). Compared with the general population of smokers (Hughes, 2004), the sample included a larger proportion of White non-Hispanics (89.4% vs. 77.9%), men (77.0% vs. 52.6%), and was older (50.5 years vs. 40.8 years). For those who shared a household, 57.6% lived with another smoker. The stage distribution included fewer smokers in precontemplation and more smokers in preparation than other population-based samples (Velicer et al., 1995; Velicer, Prochaska, Fava, et al., 2006): Distributions for five U.S. samples are approximately 40% in precontemplation, 40% in contemplation, and 20% in preparation. As a randomization check, tests of significance ($p < .01$) were performed to determine whether there were any differences between the four groups. All tests were nonsignificant.

Table 1 also presents the comparison of the four groups on smoking history and NRT use. As a randomization check, tests of significance ($p < .01$) were performed to determine whether there were any differences between the four groups. All tests were nonsignificant. The average number of cigarettes smoked per day was 24.5, and the time to first daily cigarette was 35.3 min. The sample demonstrated significant quitting activity ($M = 2.5$ quit attempts during the past year), and 48.9% reported having previously used NRT, many in the past year (45.6%).

Velicer et al. (2005) provided a detailed comparison of the characteristics of the group that participated in this study and two groups of nonparticipants. The participants (full consent) differed significantly from both nonparticipant groups (survey only and verbal consent only). Participants were more likely to be married, young, female, living with others, and to have used NRT previously or considered using NRT. The survey-only group was more likely to be in precontemplation (54%), whereas the full-consent group was more likely to be in contemplation (46%) or preparation (35%). The recruitment procedure resulted in a sample that was not completely representative of the sample of smokers.

Retention

Attrition was classified as lost to follow-up or refused. The overall retention rate at the Month 30 assessment was 61% (1,249/2,054). There were no significant differences between the four groups (see Figure 2). The overall refusal rate was 8.1%.

Preparation for NRT

The proportion of the sample that received NRT on each of the three assessment occasions for each of the groups that were NRT eligible was higher than predicted. We initially estimated that 40% of the sample in the three conditions would receive the intervention. The proportion receiving NRT was 80% in NRT + MAN, 77% in EXP + NRT + MAN, and 79% in TEL + EXP + NRT + MAN. There was no significant difference between the three groups (see Figure 3). There were no adverse events reported.

Comparison of Treatment Conditions

Table 2 presents the results for three outcome measures (24-hr point prevalence, 7-day point prevalence, and 6-month prolonged abstinence) assessed on the final three occasions (Month 10, Month 20, and Month 30). The same pattern of results was observed for all three measures as would be expected given the extremely high correlation between the measures (Velicer & Prochaska, 2004). In this section, we focus on 24-hr point prevalence (see Figure 4) because it is the most sensitive outcome measure (Velicer, Prochaska, Rossi, & Snow, 1992).

The SAS PROC GENMOD (SAS Institute, 1997) procedure was used to perform the GEE analyses for the point prevalence outcome data. This analytic model included parameter estimates for the intercept, treatment effects (MAN, NRT + MAN, EXP + NRT + MAN, TEL + EXP + NRT + MAN), temporal effects at each follow-up assessment (Month 10, Month 20, and Month 30), and a term for the patterns of missing data ("missing"). The intention-to-treat analysis was conducted on the entire sample of 2,054 subjects identified as at risk for smoking and randomized to condition, including individuals with missing data for one or more of the follow-up time points. One parameter beyond the intercept was significant: time ($p < .01$). For the analysis of the time effects, the Month 10 assessment served as the referent because all respondents were smoking at baseline. The significant time effect indicates that there were small treatment effects over time between Month 10 and Month 20, $\chi^2(1) = 3.28$, $p < .10$, and big effects between Month 10 and Month 30, $\chi^2(1) = 20.21$, $p < .0001$. Overall smoking cessation rates increased from Month 10 (13.25%) to Month 20 (15.67%) and again to Month 30 (19.30%). Different patterns of missing data were modeled. The missing data parameter and the interactions of the missing data parameter and intervention parameters were not significant.

We used all available data at each assessment ("available"). Given the results of the GEE missing data analysis, this approach is appropriate for this study. Table 3 presents the 24-hr point

Table 1
Comparison of Four Intervention Groups on Demographic, Nicotine Replacement Therapy (NRT), and Smoking History Variables

	Intervention group														
	MAN (n = 523)			NRT + MAN (n = 522)			EXP + NRT + MAN (n = 509)			TEL + EXP + NRT + MAN (n = 500)			Total (N = 2,054)		
Variable	%	*M*	*SD*	%	*M*	*SD*	%	*M*	*SD*	%	*M*	*SD*	%	*M*	*SD*
Stage															
Precontemplation	19.12			17.62			19.65			19.00			18.84		
Contemplation	46.85			43.49			47.15			46.40			45.96		
Preparation	34.03			38.89			33.20			34.60			35.20		
Gender															
Men	78.78			77.59			75.64			75.80			76.97		
Race/ethnicity															
White	89.87			91.35			88.58			87.53			89.36		
Black	4.59			4.23			6.30			5.23			5.08		
Asian	0.00			0.00			0.39			0.20			0.15		
Native American	1.15			1.73			1.77			1.81			1.61		
Other	4.40			2.69			2.95			5.23			3.81		
Hispanic															
Yes	3.08			0.96			2.55			2.40			2.25		
Marital status															
Married	50.10			49.33			47.05			46.09			48.17		
Living with partner	9.56			11.95			10.04			9.62			10.30		
Not married	12.43			12.33			14.37			16.23			13.81		
Separated	5.93			5.39			5.51			4.21			5.27		
Divorced	18.16			18.11			18.70			20.64			18.89		
Widowed	3.82			2.89			4.33			3.21			3.56		
No. in household															
1	21.31			22.20			23.61			21.13			22.06		
≥2	78.69			77.80			76.39			78.87			77.94		
Other smoker in household															
No	44.01			43.18			44.42			38.11			42.44		
Yes	55.99			56.82			55.58			61.89			57.56		
Age (years)		50.52	10.55		50.89	10.11		50.6	10.62		49.93	10.7		50.49	10.5
Education (years)		12.98	2.72		12.98	2.36		13.16	2.49		13.1	2.42		13.05	2.5
Ever used NRT?															
Yes	50.19			51.44			46.17			47.60			48.88		
No	49.81			48.56			53.83			52.40			51.12		
Used for recommended time?															
Yes	42.86			40.84			38.70			39.15			40.45		
No	57.14			59.16			61.30			60.85			59.55		
Used NRT in past year?															
Yes	45.00			45.52			45.53			46.64			45.65		
No	55.00			54.48			54.47			53.36			54.35		
Ever considered using NRT?															
Yes	66.28			68.11			67.65			72.52			68.64		
No	33.72			31.89			32.35			27.48			31.36		
Quit attempts in past 3 months (n)		1.19	2.08		1.45	2.36		1.21	2.03		1.15	2.05		1.25	2.14
Quits in past 12 months (n)		2.46	3.01		2.75	3.16		2.49	3.03		2.25	2.87		2.49	3.02
No. cigarettes smoked per day		25.18	12.87		24.55	12.96		24.31	11.39		23.85	12.74		24.48	12.51
Length of last quit attempt (days)		356.32	693.13		323.71	654.7		335.93	649.72		323.24	618.73		334.94	654.68
Days without smoking in past year (n)		19.38	54.00		15.80	39.51		12.93	35.60		15.92	40.79		16.02	43.13
Time until first daily cigarette (minutes)		31.43	49.85		36.84	66.05		33.35	58.54		39.71	85.27		35.29	66.04

Note. MAN = stage-matched manuals; EXP = expert system intervention; TEL = telecommunications.

prevalence estimates for four different missing data mechanisms (complete case, available, expectation maximization [EM], and intention to treat). The method labeled "intention to treat" represents the widely employed ad hoc procedure in which the status of smoker is assigned for all missing observations. This procedure makes the unreasonable assumption that smoking status is the only reason that an observation is missing and leads to extreme distortions of the data when an extended follow-up is employed (Hall et

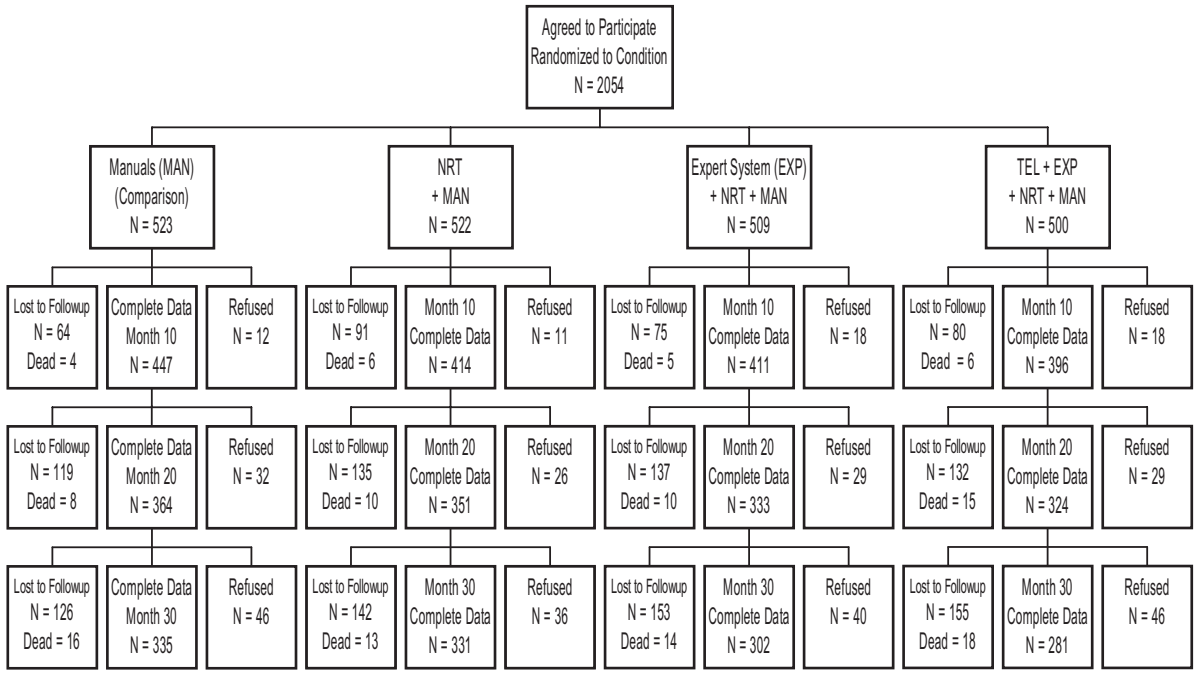

Figure 2. Retention rates for the four groups with dropouts classified as lost to contact or refusals. MAN = stage-matched manuals; NRT = nicotine replacement therapy; EXP = expert system intervention; TEL = telecommunications.

al., 2001). The complete case procedure (i.e., only participants whose data are available on each occasion) is another widely employed ad hoc procedure that is reasonable only when the observations can be assumed to be missing at random. The EM algorithm is one recommended statistical procedure for accurately estimating parameters in the presence of missing data and provides a maximum likelihood estimate of the parameters using all available data to estimate the missing values (Schafer & Graham, 2002). The same pattern of results was observed for all four methods.

Discussion

The overall results of the study demonstrate that a large percentage of a defined sample can be recruited to participate in a smoking cessation study. The overall recruitment rate (63.4%) was lower than comparable studies using the same method. The sample was less representative of the defined population than expected, with an underrepresentation of early-stage smokers. The retention rate of 61% at Month 30 was lower than expected. The proportion of the sample that received NRT was very large (80%), perhaps as a result of the failure to recruit early-stage smokers. All four interventions were equally effective, resulting in an almost 20% reduction in smoking at the final assessment. However, there were no differences between the four intervention conditions, and the absence of a control group limits our ability to conclude that any of the interventions were effective.

Manuals

Manuals are sometimes used to represent a minimal or no-intervention condition. In this case, stage-based manuals represent an active treatment condition. In previous research (Prochaska, DiClemente, Velicer, & Rossi, 1993), stage-matched manuals outperformed standard manuals (18.5% cessation rate at 24 months vs. 11%). A similar cessation rate (16.5%) was reported by Velicer et al. (1999). In this study, the MAN condition resulted in a slightly higher cessation rate than in previous studies (20.3% current vs. 18.5% in Prochaska et al., 1993, and 16.5% in Velicer et al., 1999). The higher rate may be due to the longer follow-up in this study (30 vs. 18 or 24 months).

NRT

The point prevalence cessation rate in the NRT condition produced cessation rates below the rates reported in efficacy studies. The most direct comparison is the 10-month rate because most previous efficacy studies fail to conduct an extended follow-up. The rate at 10 months was 11.4% compared with 19.5% at Month 6 in a meta-analysis. There are no comparable extended outcome data available for other NRT studies.

There are several potential explanations for the difference reported in efficacy trials and our current estimate and the results of over-the-counter (OTC or nonprescription) trials. First, only a proportion of our sample received NRT (80%), and all smokers receive NRT in efficacy studies. Second, there was no selectivity and only limited contacts; therefore, the compliance rate was much lower than expected in typical efficacy trials. Third, the VA sample represents a unique sample that may represent a more difficult challenge than the typical volunteer sample in an efficacy trial. For example, subjects were not screened for comorbid conditions, and the sample was older than most samples. However, a more appropriate comparison is the recent meta-analysis on seven

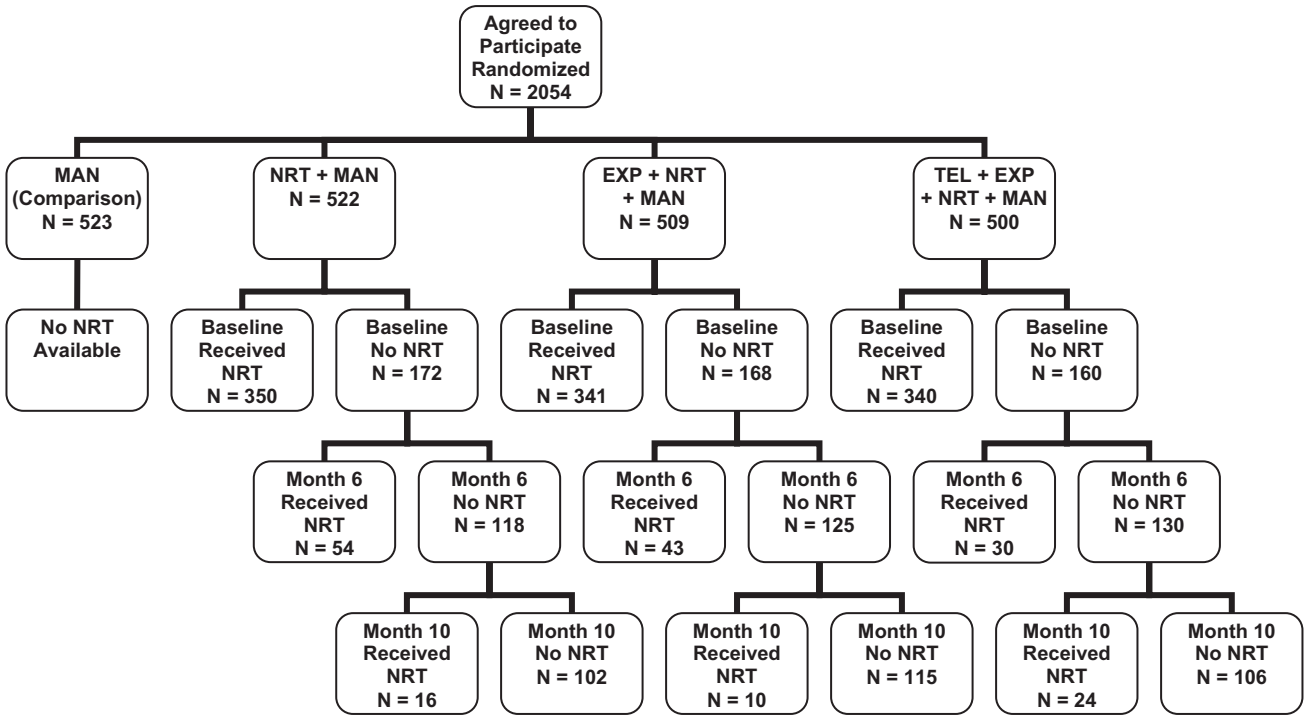

Figure 3. Proportion of each group receiving nicotine replacement therapy (NRT) on each assessment occasion. MAN = stage-matched manuals; EXP = expert system intervention; TEL = telecommunications.

studies of OTC NRT that reported a rate of 7% at 6-month follow-up (Hughes et al., 2003). The reported rate of 7.3% is very similar.

Expert System Intervention

The point prevalence cessation rate (17.6%) at Month 30 was below what would be expected on the basis of previous studies. The expert system intervention alone, typically combined with stage-tailored manuals, has resulted in cessation rates of 22–26% at 18 or 24 months across seven studies (Velicer, Prochaska, & Redding, 2006). The expectation was that the combination of NRT and EXP would outperform EXP alone by about 7%. Instead, the combination underperformed EXP alone from previous studies by about 7%.

There are several potential explanations. The expert system intervention used here departed from the usual three-report protocol, providing only a single expert system report. Velicer et al. (1999) compared three reports and a single report and found no significant difference. A second explanation is that the inclusion of

Table 2
Point Prevalence and Prolonged Abstinence Measures for the Four Intervention Groups at Months 10, 20, and 30

	Intervention group				
Assessment	MAN (n = 523)	NRT + MAN (n = 522)	EXP + NRT + MAN (n = 509)	TEL + EXP + NRT + MAN (n = 500)	Total (N = 2,054)
Month 10					
24-hr point prevalence	12.1	11.4	15.3	14.4	13.3
7-day point prevalence	6.7	7.3	9.7	11.1	8.6
6-month prolonged abstinence	3.6	4.1	5.4	6.6	4.9
Month 20					
24-hr point prevalence	15.1	12.8	17.7	17.3	15.7
7-day point prevalence	11.8	10.8	12.3	13.0	11.9
6-month prolonged abstinence	8.5	8.3	11.1	9.3	9.3
Month 30					
24-hr point prevalence	20.3	19.3	17.6	19.9	19.3
7-day point prevalence	14.9	15.1	15.2	15.0	15.1
6-month prolonged abstinence	12.5	10.0	13.6	15.0	12.7

Note. All data entries represent percentage of abstinent participants. MAN = stage-matched manuals; NRT = nicotine replacement therapy; EXP = expert system intervention; TEL = telecommunications.

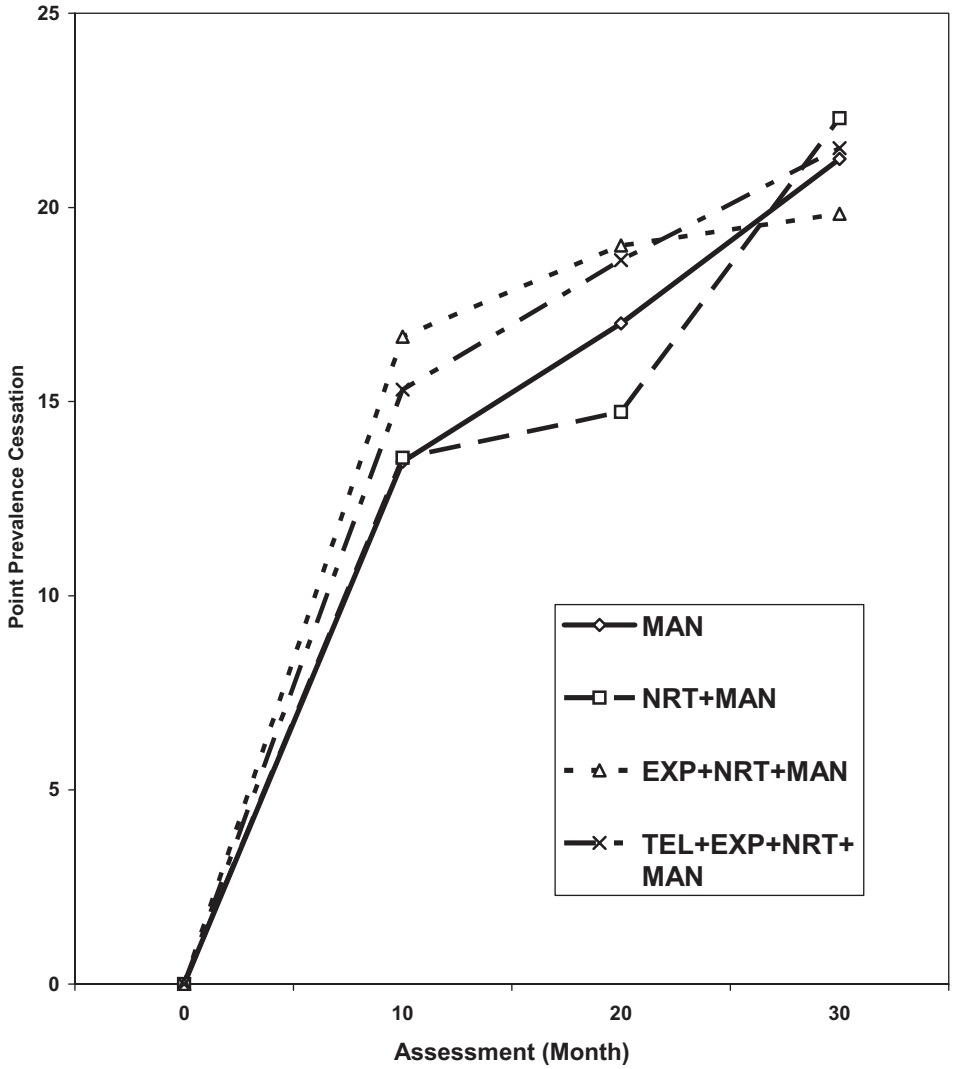

Figure 4. Point prevalence smoking cessation for the four intervention conditions at baseline, Month 10, Month 20, and Month 30. MAN = stage-matched manuals; NRT = nicotine replacement therapy; EXP = expert system intervention; TEL = telecommunications.

NRT resulted in overreliance on the pharmacological component, resulting in a failure to engage in the necessary behavior changes for successful cessation. This explanation gains some support from the fact that the expert system did not demonstrate the delayed treatment effects, that is, an increasing proportion quitting after treatment is completed, which have been observed with other stage-matched interventions. There was a slight increase from Month 10 (15.3%), the end of intervention, to Month 20 (17.7%), but no further increase occurred at Month 30 (17.6%). In contrast, the MAN condition went from 12.1% at Month 10 to 15.1% at Month 20 to 20.3% at Month 30. Previous reviews have reported that behavioral therapy and pharmacotherapy are likely to be more effective than pharmacotherapy alone (Hughes, 1995). A third possible explanation is that this was a unique sample that presents a more difficult challenge for the intervention.

Telecommunications

The inclusion of the telecommunication intervention represents a unique intervention that has not been evaluated previously in this context. The study failed to provide evidence of added value for this intervention. Telecommunication interventions have been effective with other behaviors, including adherence to medical procedures (Friedman et al., 1996), increasing exercise (King et al., 2003; Pinto et al., 2002), and improving diet (Delichatsios et al., 2001).

The effects of the telecommunication intervention are difficult to evaluate in the context of the other interventions. As with the EXP intervention, the inclusion of NRT could have resulted in an overreliance on the pharmacological intervention. Some qualitative utilization data indicate that subjects may have viewed the TEL intervention as an option rather than an expectation. The

Table 3
Point Prevalence Abstinence Estimates (24 hr) for Four Treatment Groups at Months 10, 20, and 30 for Four Missing Data Procedures

		Time					
		Month 10		Month 20		Month 30	
Group	Procedure	*n*	%	*n*	%	*n*	%
MAN	Complete case	297	12.79	297	16.50	297	19.87
	Available	447	12.08	364	15.11	335	20.30
	EM algorithm	523	13.45	523	17.01	523	21.25
	Intention to treat	523	10.33	523	10.52	523	13.00
NRT + MAN	Complete case	273	11.36	273	12.45	273	16.12
	Available	414	11.35	351	12.82	331	19.34
	EM algorithm	522	13.55	522	14.73	522	22.30
	Intention to treat	522	9.00	522	8.62	522	12.26
EXP + NRT + MAN	Complete case	250	16.40	250	18.80	250	19.20
	Available	411	15.33	333	17.72	302	17.55
	EM algorithm	509	16.67	509	19.02	509	19.84
	Intention to treat	509	12.38	509	11.59	509	10.41
TEL + EXP + NRT + MAN	Complete case	241	15.77	241	18.67	241	21.16
	Available	396	14.39	324	17.28	281	19.93
	EM algorithm	500	15.31	500	18.64	500	21.53
	Intention to treat	500	11.40	500	11.20	500	11.20

Note. Baseline predictors used were as follows: 24-hr quit in the past year, time to first daily cigarette, cigarettes per day in past week, gender, weight, education, age, and stage membership. MAN = stage-matched manuals; NRT = nicotine replacement therapy; EXP = expert system intervention; TEL = telecommunications; EM algorithm = expectation-maximization algorithm.

utilization rates were lower than in other telecommunications trials. Approximately 30% used the telecommunication on multiple occasions, 30% used it on a single occasion, and the remaining 40% did not use it at all. A study evaluating TEL alone for smoking is needed.

Limitations

The study has two important limitations. First, the inclusion of a pure control group would have served to exclude the interpretation that none of the interventions was effective and that the observed differences were the result of secular trends. The observed quit rate was far in excess of the 2–5% that has been observed in monitoring studies, but the population was unusual; therefore, this explanation cannot be confidently excluded. Second, the use of the VA sample represents both a strength and a weakness. The sample is clearly in need of services. The VA organization provided the opportunity to perform the proactive recruitment. However, it is an unusual sample with a much higher average age and higher rates of psychiatric problems and is predominantly male, which make generalization to other samples of smokers difficult.

Future Directions

In this effectiveness trial with a defined population, NRT was not more effective than stage-based manuals alone. Furthermore, NRT was not more effective than manuals alone, regardless of which behavioral interventions were combined with NRT.

We cannot determine the effects of NRT on EXP because EXP alone was not tested. In previous trials, adding counselors to EXP made no difference, even when the EXP alone was effective (Prochaska et al., 1993; Prochaska, Velicer, Fava, Ruggiero, et al., 2001). On the other hand, adding nicotine-fading computers (Lifesign) to EXP was significantly less effective than EXP alone (Prochaska, Velicer, Fava, Ruggiero, et al., 2001). We would predict that EXP + NRT < EXP alone.

It is tempting to conclude that NRT is not effective with populations of smokers. However, recent innovative applications of NRT have been designed to use NRT to reduce the number of cigarettes smoked in unmotivated smokers. These interventions have produced significantly more cessation than did a control condition (Carpenter, Hughes, Solomon, & Callas, 2004). This was true for NRT reduction counseling and motivational interviewing plus NRT. These results suggest that NRT may be effective with populations of smokers when used innovatively to reduce smoking rather than as historically applied to produce more immediate cessation.

Conclusions

The study had five primary goals. The first goal was to recruit a large proportion (75%) of the sample of identified smokers. The study recruited 63.4% of the sample of identified smokers, which is smaller than has been reported in other studies. However, the initial rate of 90% was higher than in other studies. The focus in the informed consent process on the potential use of NRT may explain the lower and highly selective recruitment rate (Velicer et al., 2005). Another potential explanation is the unique nature of the sample of VA members.

The second goal was to recruit a representative sample of the identified smokers. Several segments of the population were underrepresented in the final sample, particularly smokers in the precontemplation stage.

The third goal was to prepare early-stage smokers for NRT and deliver NRT to the maximum proportion of the sample possible. This goal was exceeded. The NRT utilization rate was projected to be 40%. The actual rate in the study was 80%. One explanation is that the self-selection that occurred during recruitment produced a sample that was more ready to use NRT.

The fourth goal was to retain 70% of the sample at long-term follow-up. This study had one of the longest follow-up rates in any NRT study and provides evidence of the extended effects of the intervention. The retention rate at 30 months was 61%. This is below the 70% at 24 months reported in comparable studies. The lower retention rate is probably due to the additional 6 months involved in this study.

The fifth goal was to examine the differential effectiveness of NRT alone and in combination with three behavioral interventions. No significant differences were observed between the four conditions. Stage-matched manuals provided point prevalence cessation rates comparable to two previous studies. The addition of NRT, EXP, and TEL failed to produce a further increase in intervention effectiveness.

References

Alberg, A. J., Margalit, R. S., Burke, A., Rasch, K. A., Stewart, N., Kline, J. A., et al. (2004). The influence of offering free transdermal nicotine patches on quit rates in a local health department's smoking cessation program. *Addictive Behaviors, 29,* 1763–1768.

Benowitz, N. L., Jacob, P., III, Ahijevych, K., Jarvis, M. J., Hall, S., LeHouezec, J., et al. (2002). Biochemical verification of tobacco use and cessation. *Nicotine and Tobacco Research, 4,* 149–159.

Carpenter, M. J., Hughes, J. R., Solomon, L. J., & Callas, P. W. (2004). Both smoking reduction with nicotine replacement therapy and motivational advice increase future cessation among smokers unmotivated to quit. *Journal of Consulting and Clinical Psychology, 72,* 371–381.

Delichatsios, H. K., Friedman, R. H., Glanz, K., Tennstedt, S., Smigelski, C., Pinto, B. M., et al. (2001). Randomized trial of a "talking computer" to improve adult's eating habits. *American Journal of Health Promotion, 15,* 215–224.

Fiore, M. C., Smith, S. S., Jorenby, D. E., & Baker, T. B. (1994). The effectiveness of the nicotine patch for smoking cessation: A meta-analysis. *Journal of the American Medical Association, 266,* 3139–3144.

Flay, B. R. (1986). Efficacy and effectiveness trials (and other phases of research) in the development of health promotion programs. *Preventive Medicine, 15,* 451–474.

Friedman, R. H. (1998). Automated telephone conversations to assess health behavior and deliver behavioral interventions. *Journal of Medical Systems, 22,* 95–102.

Friedman, R. H., Kazis, L. E., Jette, A., Smith, M. B., Stollerman, J., Torgerson, J., & Carey, K. (1996). A telecommunications system for monitoring and counseling patients with hypertension: Impact on medication adherence and blood pressure control. *American Journal of Hypertension, 9,* 285–292.

Glasgow, R. E., Lichtenstein, E., & Marcus, A. C. (2003). Why don't we see more translation of health promotion research to practice? Rethinking the efficacy-to-effectiveness transition. *American Journal of Public Health, 93,* 1261–1267.

Glasgow, R. E., Mullooly, J. P., Vogt, T. M., Stevens, V. J., Lichtenstein, E., Hollis, J. F., et al. (1993). Biochemical validation of smoking status in public health settings: Pros, cons and data from four low-intensity intervention trials. *Addictive Behaviors, 18,* 504–527.

Hall, S. M., Delucchi, K. L., Velicer, W. F., Kahler, C. W., Ranger-Moore, J., Hedeker, D., et al. (2001). Statistical analysis of randomized trials in tobacco treatment: Longitudinal designs with dichotomous outcome. *Nicotine and Tobacco Research, 3,* 193–202.

Hasford, J., Fagerstrom, K. O., & Haustein, K.-O. (2003). A naturalistic cohort study on effectiveness, safety and usage pattern of an over-the-counter nicotine patch. *European Journal of Clinical Pharmacology, 59,* 443–447.

Hughes, J. R. (1995). Combining behavioral therapy and pharmacotherapy for smoking cessation: An update. In L. S. Onken, J. D. Blaine, & J. J. Boren (Eds.), *Integrating behavior therapies with medication in the treatment of drug dependence* (NIDA Research Monograph; pp. 92–109). Washington, DC: U.S. Government Printing Office.

Hughes, J. R. (2004). Data to estimate the similarity of tobacco research samples to intended populations. *Nicotine and Tobacco Research, 6,* 177–179.

Hughes, J. R., Shiffman, S., Callas, P., & Zhang, J. (2003). A meta-analysis of the efficacy of over-the-counter nicotine replacement. *Tobacco Control, 12,* 21–27.

King, A. C., Friedman, R. H., Marcus, B., Napolitano, M., Castro, C., & Forsyth, L. (2003). Increasing regular activity via humans or automated technology: The CHAT trial. *Annals of Behavioral Medicine, 25*(Suppl.), S111.

Miller, N., Frieden, T. R., Liu, S. Y., Matte, T. D., Mostashari, F., Deitcher, D. R., et al. (2005). Effectiveness of a large scale distribution programme of free nicotine patches: A prospective evaluation. *Lancet, 365,* 1849–1854.

Patrick, D. L., Cheadle, A., Thompson, D. C., Diehr, P. M. Koepsell, T., & Kinne, S. (1994). The validity of self-reported smoking: A review and meta-analysis. *American Journal of Public Health, 84,* 1086–1093.

Peto, R., & Lopez, A. (1990). World-wide mortality from current smoking patterns. In B. Durstone & K. Jamrogik (Eds.), *The global war: Proceedings of the Seventh World Conference on Tobacco and Health* (pp. 62–68). East Perth, Western Australia: Organizing Committee of Seventh World Conference on Tobacco and Health.

Pierce, J. P., & Gilpin, E. A. (2002). Impact of over-the-counter sales on effectiveness of pharmaceutical aids for smoking cessation. *Journal of the American Medical Association, 288,* 1260–1264.

Pinto, B. M., Friedman, R. H., Marcus, B. H., Kelly, H., Tennstedt, S., & Gillman, N. W. (2002). Effects of computer-based telephone counseling systems on physical activity. *American Journal of Preventive Medicine, 23,* 113–120.

Po, A. L. W. (1993). Transdermal nicotine in smoking: A meta-analysis. *European Journal of Clinical Pharmacology, 45,* 519–528.

Prochaska, J. O., DiClemente, C. C. Velicer, W. F., & Rossi, J. S. (1993). Standardized, individualized, interactive and personalized self-help programs for smoking cessation. *Health Psychology, 12,* 399–405.

Prochaska, J. O., & Velicer, W. F. (2004). Integrating population smoking cessation policies and programs. *Public Health Reports, 119,* 244–252.

Prochaska, J. O., Velicer, W. F., DiClemente, C. C., & Fava, J. L. (1988). Measuring the processes of change: Applications to the cessation of smoking. *Journal of Consulting and Clinical Psychology, 56,* 520–528.

Prochaska, J. O., Velicer, W. F., Fava, J. L., Rossi, J. S., & Tsoh, J. Y. (2001). Evaluating a population-based recruitment approach and a stage-based expert system intervention for smoking cessation. *Addictive Behaviors, 26,* 583–602.

Prochaska, J. O., Velicer, W. F., Fava, J. L., Ruggiero, L., Laforge, R. G., & Rossi, J. S. (2001). Counselor and stimulus control enhancements of a stage-matched expert system intervention for smokers in a managed care setting. *Preventive Medicine, 32,* 23–32.

Ramelson, H. R., Friedman, R. H., & Ockene, J. K. (1999). An automated telephone-based smoking cessation education and counseling system. *Patient Education and Counseling, 36,* 131–144.

SAS Institute. (1997). *SAS/STAT software: Changes and enhancements through release 6.12.* Cary, NC: Author.

Schafer, J. L., & Graham, J. W. (2002). Missing data: Our view of the state of the art. *Psychological Methods, 7,* 147–177.

Schmid, T. L., Jeffrey, R. W., & Hellerstedt, W. L. (1989). Direct mail recruitment to house-based smoking and weight control programs: A comparison of strengths. *Preventive Medicine, 18,* 503–517.

Silagy, C., Mant, D., Fowler, G., & Lodge, M. (1994). Meta-analysis on efficacy of nicotine replacement therapies in smoking cessation. *Lancet, 343,* 139–142.

Tang, J. L., Law, M., & Wald, N. (1994). How effective is nicotine replacement therapy in helping people to stop smoking? *British Medical Journal, 308,* 21–26.

Velicer, W. F., & DiClemente, C. C. (1993). Understanding and intervening with the total population of smokers. *Tobacco Control, 2,* 95–96.

Velicer, W. F., DiClemente, C. C., Prochaska, J. O., & Brandenberg, N. (1985). A decisional balance measure for assessing and predicting smoking status. *Journal of Personal and Social Psychology, 48,* 1279–1289.

Velicer, W. F., DiClemente, C. C., Rossi, J. S., & Prochaska, J. O. (1990). Relapse situations and self-efficacy: An integrative model. *Addictive Behaviors, 15,* 271–283.

Velicer, W. F., Fava, J. L., Prochaska, J. O., Abrams, D. B., Emmons, K. M., & Pierce, J. (1995). Distribution of smokers by stage in three representative samples. *Preventive Medicine, 24,* 401–411.

Velicer, W. F., Keller, S., Friedman, R. H., Fava, J. L., Gulliver, S. B., Ward, R. M., et al. (2005). Comparing participants and nonparticipants recruited for an effectiveness study of nicotine replacement therapy. *Annals of Behavioral Medicine, 21,* 181–191.

Velicer, W. F., & Prochaska, J. O. (1999). An expert system intervention for smoking cessation. *Patient Education and Counseling, 36,* 119–129.

Velicer, W. F., & Prochaska, J. O. (2004). A comparison of four self-report smoking cessation outcome measures. *Addictive Behaviors, 29,* 51–60.

Velicer, W. F., Prochaska, J. O., Bellis, J. M., DiClemente, C. C., Rossi, J. S., Fava, J. L., & Steiger, J. H. (1993). An expert system intervention for smoking cessation. *Addictive Behaviors, 18,* 269–290.

Velicer, W. F., Prochaska, J. O., Fava, J. L., Laforge, R. G., & Rossi, J. S. (1999). Interactive versus non-interactive interventions and dose-response relationships for stage-matched smoking cessation programs in a managed care setting. *Health Psychology, 18,* 1–8.

Velicer, W. F., Prochaska, J. O., Fava, J. L., Redding, C. A., Rossi, J. S., Rossi, S. R., et al. (2006). *Stage distributions for three risk factors in three large USA samples*. Manuscript submitted for publication.

Velicer, W. F., Prochaska, J. O., & Redding, C. A. (2006). Tailored communications for smoking cessation: Past successes and future directions. *Drug and Alcohol Review, 25,* 47–55.

Velicer, W. F., Prochaska, J. O., Rossi, J. S., & Snow, M. (1992). Assessing outcome in smoking cessation studies. *Psychological Bulletin, 111,* 23–41.

Velicer, W. F., Rossi, J. S., Ruggiero, L., & Prochaska, J. O. (1994). Minimal interventions appropriate for an entire population of smokers. In R. Richmond (Ed.), *Interventions for smokers: An international perspective* (pp. 69–92). Baltimore: Williams & Wilkins.

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