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Extended cognitive behavior therapy for cigarette smoking cessation

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Abstract

Primary aim—Examine the effectiveness of extended cognitive behavior therapy (CBT) in promoting longer-term smoking abstinence.

Design—Open-label treatment phase followed by extended treatment phase. Randomization conducted prior to entry into open-label treatment phase; analysis based on intention-to-treat to avoid threat of selection bias.

Setting—Community smoking cessation clinic.

Participants—A total of 304 adult smokers (18 years of age; 10 cigarettes/day).

Intervention—Open-label (8 weeks): all participants received bupropion SR, nicotine patch, CBT. Extended treatment (12 weeks): participants received either CBT + voicemail monitoring and telephone counseling or telephone-based general support.

Measurements—Seven-day point prevalence abstinence, expired-air carbon monoxide.

Results—At week 20 follow-up, CBT produced a higher 7-day point prevalence abstinence rate: 45% versus 29%, $P = 0.006$; at 52 weeks the difference in abstinence rates (31% versus 27%) was not significant. History of depression was a moderator of treatment. Those with a positive history had a better treatment response at 20 weeks when assigned to the less intensive telephone support therapy ($P < 0.05$).

Conclusion—The superiority of CBT to 20 weeks suggests that continued emphasis on the development of cognitive and behavioral strategies for maintaining non-smoking during an extended treatment phase may help smokers to maintain abstinence in the longer term. At present, the minimum duration of therapy is unknown.

Keywords

Abstinence; bupropion SR; Cognitive behavior therapy; extended treatment; nicotine dependence; smoking cessation; telephone support

Introduction

Smoking cessation therapy is provided typically for 8–12 weeks. This paper presents the results of an investigation of the efficacy of smoking cessation therapy when extended beyond the standard 8–12-week treatment regimen. Adult smokers received 9 weeks of open-label treatment that combined cognitive behavioral skills training (CBT), nicotine replacement and bupropion SR followed by 12 weeks of extended treatment with CBT or brief telephone support.

This investigation is interesting for several reasons. First, most cigarette smokers relapse following treatment [1,2]. In one representative meta-analysis, abstinence rates for nicotine patch users averaged 27% at end of treatment and 22% at 24-week follow-up [3]. Thus, treatments that can produce more durable effects are needed.

Secondly, developments in the treatment of alcoholism, cocaine and opioid dependence reflect the view that drug addictions are chronic, relapsing disorders requiring extended therapy and follow-up [4]. However, only a few extended smoking cessation treatment studies have been conducted.

The Collaborative European Anti-Smoking Evaluation trial examined the efficacy of nicotine patch therapy given for 8 or 22 weeks. Both regimens produced similar sustained abstinence rates at 52 weeks (15% versus 14%) [5].

Three controlled trials of the effectiveness of extended treatment with bupropion SR have been published. In the first trial, 461 of 784 participants (59%) achieved abstinence after 7 weeks of open-label cessation therapy with bupropion SR. Of the 461 successful quitters, 429 were then randomized to receive either 45 weeks of therapy with bupropion or placebo. At week 52, abstinence rates for this subsample were significantly different (bupropion SR 55%; placebo 42%), but the effect had vanished by final follow-up at week 104 (42% versus 40%) [6].

In the second bupropion trial, 181 of 578 participants (31%) stopped smoking after 8 weeks of nicotine patch therapy. Of this group, 176 were assigned to extended treatment with bupropion or placebo for an additional 26 weeks. At the end of extended treatment, 28% and 25% were not smoking for bupropion and placebo, respectively [7].

In a previous trial conducted by our research group, 362 smokers completed 11 weeks of open-label treatment (nicotine patch, bupropion SR and cognitive behavior therapy) followed by 14 weeks of extended treatment with either bupropion SR or matching placebo. Randomization occurred prior to study entry and all participants were included in intention-to-treat analyses. Although bupropion was not superior to placebo, overall abstinence rates exceeded 40% at 24-week follow-up and 30% at 52-week follow-up [8].

Hall and colleagues gave all participants behavioral group therapy, 8 weeks of nicotine patch and 12 weeks of nortriptyline or placebo. Therapy ended at week 12 for half the participants. The remainder took either placebo or nortriptyline to 52 weeks and received additional 9 monthly individual behavioral treatment sessions. Abstinence rates at week 52

were placebo brief treatment: 30%; placebo extended treatment: 42%; active brief treatment: 18% and active extended treatment: 50%. Extended behavioral therapy produced a better response at end of treatment but there was no effect of nortriptyline beyond week 12 [9].

Varenicline, a nicotinic acetylcholine partial agonist developed specifically for smoking cessation, has been examined in one trial. Of 1927 cigarette smokers treated with varenicline and brief counseling for 12 weeks, 1210 (63%) were randomized to receive active medication or placebo for an additional 12 weeks. The 7-day point prevalence abstinence at week 52 was significantly higher for those receiving varenicline [odds ratio (OR) = 1.33, $P = 0.01$] [10].

Thirdly, in their review of factors influencing the durability of treatment response, Ockene and colleagues suggested that treatment efficacy could be enhanced by combining more intensive interventions with self-help approaches, telephone counseling and methods for the rapid identification and treatment of 'slips' [1]. Each of these components was incorporated into the multi-factor treatment approach tested in the randomized clinical trial reported in this paper.

An analysis of moderators of treatment response was also included in this trial. A 'moderator' of treatment is a pre-randomization factor (hence uncorrelated with treatment in a randomized clinical trial [RCT]) that has an interactive effect with treatment on outcome [11]. Subgroups of the population sampled in an RCT, identified by strata of a moderator variable, may have different treatment effect sizes. Moderators may help clinicians to develop better treatment targeting algorithms, can be used by researchers to identify appropriate study inclusion/exclusion criteria and can serve as factors on which a study may be stratified to amplify power. Thus, for example, in an examination of the effects of message tailoring on smoking cessation, Strecher and colleagues found that presence of non-smoking children in the household, tobacco-related illness and higher alcohol consumption moderated short-term (12-week) treatment response and suggested that these variables might be used to instruct the tailoring of cessation messages [12].

Gender was used to stratify randomization in this trial and examined specifically as a potential moderator of treatment response. Gender is of interest because some *post-hoc* analyses indicate that cessation therapy may work better for men [13-16] although the effect, if present, would appear to be small [17]. However, men and women may respond differently to different types of cessation interventions [18]. Thus, although mediators or moderators of the hypothesized association between gender and abstinence remain to be identified, efforts to uncover such factors might be warranted if a differential treatment response is finally confirmed because such research might lead to the development of more tailored and effective treatment protocols.

Method

Study design

A total of 304 cigarette smokers (18–65 years of age; smoking 10 cigarettes per day or 3.5 packs a week) were randomized between 28 February 2004 and 3 March 2006. The final

sample size available for analyses was 301, because three participants received the wrong treatment and were excluded from the analysis. The Stanford University Panel for the Protection of Human Subjects in Medical Research approved the study protocol. The trial was funded by the National Institute on Drug Abuse and registered with clinicaltrials.gov.

The trial included open-label treatment and a randomized extended treatment phase with follow-ups conducted at 20 and 52 weeks. Randomized extended treatment assignments were generated prior to study entry rather than at the end of open-label treatment and analyses were based on intention-to-treat to avoid the threat of selection bias [19].

Randomization to extended treatment condition was conducted using a permuted block method (block size = 4 to obtain balance between groups) and stratified on gender. When participants were assigned to the next available ID number in the corresponding gender, they associated with their treatment group. The research team and participants were blinded to extended treatment assignment to the end of the open-label phase.

Open-label treatment—All participants received 8 weeks of cognitive and behavioral cessation and relapse prevention skills training (CBT) and nicotine patch therapy combined with 9 weeks of bupropion SR therapy.

Extended treatment—Following open-label treatment, half the participants ($n = 154$) received an additional 12 weeks of CBT that combined clinic-based skills training sessions, voicemail monitoring and telephone counseling and half ($n = 147$) received general supportive therapy delivered via four telephone calls made to participants over a 12-week period.

Primary hypothesis—Extended CBT should produce higher expired-air carbon monoxide (CO)-confirmed 7-day point prevalence abstinence rates at 20- and 52-week follow-ups than telephone-based general support. With 150 participants per condition the trial had, in general, 80% power at a two-tailed alpha of 0.05 to detect a difference in abstinence rates of at least 15% over a range of success probabilities [20].

Study population

Participants were recruited through advertisements in local newspapers, via radio, on a community website and by notices distributed through various local organizations. Interested smokers were instructed to telephone the study clinic in San Jose, California to complete an eligibility interview. Eligible smokers were scheduled for a baseline clinic visit where they signed written consent forms, were administered a structured clinical interview designed to detect current and past depression, completed a questionnaire assessment battery, received instructions on use of the study medications and participated in an initial CBT session. Each participant set a quit date for approximately 7 days after his or her baseline visit. Subsequent appointments were calculated based on expired-air CO confirmed quit date.

Screening

Individuals were excluded for pregnancy, current lactation, epilepsy, bipolar disorder, schizophrenia, receiving active treatment for or reporting current depression or substance abuse, history of heart problems in the previous 6 months, head trauma leading to unconsciousness in the past year, history of severe head injury resulting in brain surgery or specific neurological problems, current use of bupropion or nicotine replacement therapy (NRT) or medication use that could interact with bupropion or NRT. Written permission from the participant's primary medical provider was required in order to be enrolled in the study. Those without a medical provider were referred to local clinics for physical examinations paid for by the trial.

Treatments

Open-label: pharmacotherapy—All participants attended clinic sessions at baseline, quit week and weeks 1, 2, 4 and 6. All participants received bupropion SR (Zyban) for 9 weeks and nicotine patch therapy for 8 weeks. During their first week, participants continued to smoke while taking bupropion SR (150 mg/day on days 1–3, then 300 mg/day on days 4–7) in order to establish therapeutic blood levels prior to quitting. Nicotine patch (21 mg) was added to treatment with bupropion (300 mg) on the target quit date if the participant succeeded. After 1 month, participants were tapered to 14 mg nicotine patch for 2 weeks and then 7 mg for 2 weeks.

Open-label: CBT—At each clinic session, staff met with participants individually for 30 minutes to develop cognitive and behavioral skills to resist urges to smoke. Staff used self-efficacy questionnaires to assess participants' confidence in their abilities to resist urges to smoke in specific situations and behavioral worksheets to help participants articulate treatment plans to be used in managing their behavior in these situations without smoking. All treatment sessions were led by one of three staff interventionists trained and supervised by the study psychologist and psychiatrist who had previous training in behavioral therapy.

Extended CBT—Those participants randomized to extended CBT continued to work with treatment staff individually on the development and use of cognitive and behavioral cessation and relapse prevention skills. Treatment sessions, lasting approximately 30 minutes, were conducted at the San Jose clinic site at weeks 8, 12, 16 and 20. Between clinic-based treatment sessions, participants made weekly 'check-in' telephone calls to a voicemail system to report progress and to answer the following two questions: 'Have you had a cigarette, even a puff, in the past 7 days?' and 'Have you experienced increased cravings and/or urges to smoke in the past 7 days?'. An affirmative response to either question triggered a return telephone call from a member of the treatment team for telephone-based skills training. Telephone treatment sessions focused upon identifying early relapse warning signs and assisting the participant in gaining cognitive and behavioral skills necessary to avoid relapse. Staff worked with those participants who had relapsed to set new cessation goals and plans.

Support telephone calls—Those participants randomized to general support participated in 5-minute telephone calls in weeks 8, 12, 16 and 20. These calls included standardized

questions regarding participants' smoking status, cravings, urges and withdrawal symptoms, general support for those experiencing difficulty in maintaining abstinence and encouragement and affirmation for successful quitters.

Measures

Primary study end-point—The primary study end-point was expired-air CO-confirmed 7-day point prevalence abstinence evaluated at both 20 and 52 weeks. This end-point measure is defined as a report of non-smoking (not even a puff) for 7 consecutive days prior to contact plus an expired-air CO level below 10 parts per million (ppm). At all clinic and telephone contacts smoking status was determined via the query: 'Have you smoked a cigarette, even a puff, in the past week?'. Expired-air CO was measured at all clinic visits with the Bedfont EC50 Smokerlyzer (<http://www.Bedfont.com/>).

Measures of nicotine dependence—The five-question modified Fagerström Tolerance Questionnaire (mFTQ), an instrument designed to assess tobacco dependence, was administered at the initial telephone contact [21,22].

Craving and withdrawal symptoms were measured at baseline and at all clinic and telephone appointments. Craving was measured with the following two questions: 'Have you felt cravings for a cigarette?' and 'Have you felt strong urges to smoke?'. Participants rated on six-point scales how upsetting cravings and urges had been in the past 24 hours. A craving score was obtained by averaging the two items. The measure of craving has been shown to be a useful predictor of smoking relapse in previous research [23].

Participants also rated on six-point scales how upsetting a variety of physiological and psychological withdrawal symptoms had been in the past 24 hours. Symptoms included in the Smokers Complaint Scale and the Shiffman–Jarvik withdrawal scale comprised the withdrawal symptoms assessment [24,25].

Major depressive disorder (MDD)—A screen for MDD was administered at the baseline visit using the mood disorders portion of the Structured Clinical Interview for the *Diagnostic and Statistical Manual of Mental Disorders* (SCID), fourth edition (DSM-IV) [26]; both the current and past depression sections were administered, as well as sections for differential diagnosis (i.e. bereavement and substance-induced depression). Those whose interview answers indicated current depression were excluded from participation, encouraged to seek treatment and, upon request, given help in obtaining treatment.

Depression symptoms were measured at all clinic visits during open-label treatment with the 20-item Center for Epidemiological Studies depression instrument (CES-D) [27].

Physiological measures—Heart rate and blood pressure were measured twice at each clinic visit during the open-label phase with an automated blood pressure device (DINAMAP Procare 120; <http://www.gehealthcare.com/>). If a difference greater than 10 was found between the two diastolic and/or systolic readings, a third reading was collected. The two readings closest to each other were used in analysis. At the baseline visit, participants with blood pressure exceeding 160 (systolic) or 100 (diastolic) were asked to

see their physicians for treatment before they could enter the trial. All blood pressure levels were reported to participants and those with elevated levels were advised to see their physicians.

Height was measured on a wall-mounted stadiometer and weight was recorded on a Scale-Tronix 5600 electronic scale (<http://www.scale-tronix.com/>) at baseline, and at weeks 6, 20 and 52. Participants removed shoes, jackets and any additional heavy clothing prior to measurement.

Adverse events—Occurrence, duration and severity of adverse events were assessed at all clinic visits. Adverse events deemed to be serious were sent to a consulting Stanford physician for review. Decisions on continuation of medication were made according to physician review.

Medication compliance—At each assessment during open-label treatment, participants were asked if they were ‘wearing a patch now’, if they had ‘taken [their] Zyban in the morning’ and if they had ‘taken [their] Zyban every day in the past week’. Any deviations in medication compliance from protocol were recorded including date of and reason for deviation.

Results

Screening

A total of 770 smokers were screened to yield the analysis sample of 301 (180 men and 121 women). The ethnic distribution of the sample was: white: 82%; Asian: 6%; black: 5%; multiple ethnicity: 3%; other: 4%.

Of those not randomized, 234 were not eligible, 155 declined to participate after screening and 77 did not participate for a variety of other reasons. Smokers failed the eligibility screen for the following principal reasons: too few cigarettes (44); taking exclusionary medication (45); residence outside target sample geographic area (30); failed depression screen (24); current alcohol/drug abuse (21); and age > 65 years (21) (Fig. 1).

Comparability of treatment groups

As is evident from Table 1, differences between treatment groups on various baseline measures were not statistically significant.

Reclassification

Of self-reported non-smokers, 99%, 91% and 83% provided biochemical confirmation of abstinence at 6, 20 and 52 weeks. Those reporting abstinence but failing to provide breath samples for carbon monoxide verification were reclassified as smokers with the following exceptions. At week 6, self-reports of abstinence were accepted from one participant traveling in Europe and one participant recovering from surgery. At week 20, one participant reported abstinence but was no longer living in the Bay Area. At week 52, an additional 10 participants reported abstinence in response to staff telephone calls but were living outside the Bay Area.

Point prevalence abstinence

Open-label—At the end of open-label treatment, the abstinence rate for those participants who then went on to receive supportive therapy via telephone calls was 56% (83 of 147); the abstinence rate for those who then went on to receive CBT during the extended treatment phase was also 56% (87 of 154).

Test of primary hypothesis—Logistic regression analysis was used to test the primary hypothesis. Because gender was used to stratify the randomization, gender and the gender $\times$ treatment interaction were examined along with treatment in the model. The interaction term was included in the main effects model because when an existing interaction is omitted from the model, at best the error variance is exaggerated, thus decreasing the precision of estimation and the power to detect clinically significant effects. At worst, some of the interaction effect is also re-mapped into the main effect, thus sacrificing accuracy of estimation as well [28].

Separate models were fitted for each follow-up point (20 and 52 weeks) using expired-air CO verified reported 7-day point prevalence smoking status as the dependent variable. Abstinence rates are presented in Table 2. At week 20, extended CBT produced a higher abstinence rate: 45% versus 29% [χ^2 (1, n = 301) = 7.50, P = 0.006, odds ratio (OR) = 1.98, 95% confidence interval (CI) = 1.2 – 3.2]. Tests for the effects of gender and the interaction did not meet criterion for statistical significance. At week 52, main effects and interaction tests did not meet criteria for statistical significance.

Repeated 7-day point prevalence abstinence and continuous abstinence were also examined in secondary analyses. Twenty-five per cent (25%) of participants receiving CBT and 22% of participants receiving telephone-based support were abstinent at both 20-and 52-week assessments. Continuous abstinence was defined as no smoking (not even a puff) after quit date. By this definition, 22% of those receiving extended CBT and 18% of those receiving support via the telephone were continuously abstinent through the 52-week follow-up.

Moderator analysis

In an RCT, treatment assignment is independent of all pre-randomization factors. Thus, pre-randomization factors are orthogonal in the analytical model. A statistically significant interaction between treatment and a pre-randomization factor is an indication of a moderator effect. If there is a main effect of the pre-randomization factor, but no interaction with treatment, this indicates that the pre-randomization factor is a predictor of treatment response independent of treatment [11].

The analytical approach is based on recommendations made by Kraemer *et al.* in their paper describing the approach to the analysis of moderators of treatment effects in randomized clinical trials [29]. As these authors indicate, the linear model to be used for moderator analysis comparing a treatment group (T) versus a control or comparison group includes the independent variables T, M (the possible moderator or mediator) and the T $\times$ M interaction.

As noted, randomization was stratified on gender so that we might examine gender specifically as a moderator of treatment response. In addition, putative moderators explored

in the analysis were depression [history of MDD, CES-D score], nicotine dependence (cigarettes/day expired-air CO, modified FTQ, immediate post-cessation craving), body mass index [weight (kg)/height(m²)] and age. For each variable, a logistic model was formed with treatment, the putative moderator and the treatment × putative moderator interaction as independent factors and smoking cessation status at weeks 20 and 52 as the dependent variables. At week 20, history of depression, as measured by structured clinical interview, was a moderator of treatment response ($\chi^2_{(1)} = 4.4$ $P = 0.03$; OR = 0.19, 95% CI = 0.04, 0.90). Those positive for a history of depression ($n = 31$) had an abstinence rate of 50% if assigned to brief telephone support and an abstinence rate of 32% if assigned to CBT. Conversely, those negative for a history of depression ($n = 270$) had an abstinent rate of 26% if assigned to telephone support compared to 47% if assigned to extended CBT. The moderator effect was not present at 52 weeks (Fig. 2).

Medication compliance

Medication compliance was assessed on five occasions during open-label treatment; 53% of participants responded 'yes' on all occasions when asked if they had taken their Zyban pill that morning; about 6% responded 'no' on all occasions. With respect to patch use, 50% responded 'yes' on all occasions when asked if they were currently wearing a patch; 6% responded 'no' on all occasions.

Treatment session attendance/calls completed

During open-label treatment, the average number of treatment sessions attended was 4.3 (of five sessions) [standard deviation (SD) = 1.1]. During extended treatment, the average number of treatment sessions attended and calls completed by those receiving extended CBT equaled 2.9 (of four sessions) (SD = 1.5) and 7.7 (of 12 sessions) (SD = 3.8), respectively. The average number of calls completed by those in the telephone support condition was 3.3 (of four sessions) (SD = 1.2).

Safety and tolerability

Mean (SD) blood pressure and heart rate at baseline were: systolic: 127.8 (15.0), diastolic: 74.4 (10.2), heart rate (HR): 75.7 (10.7). Mean (SD) blood pressure and heart rate during open-label treatment were: systolic: 128.0 (16.9), diastolic: 74.5 (10.1), HR: 74.3 (10.9).

Adverse events reported by 5% or more of the participants during open-label treatment are listed in Table 3.

Sleep disturbance was the most commonly reported adverse event, with 58% of participants reporting insomnia and 14% reporting the experience of vivid dreams.

A total of 14 participants (5%) discontinued nicotine patch and 30 participants (10%) discontinued bupropion because of adverse events experienced during open-label treatment. One participant experienced a serious adverse event during open-label treatment (hospitalization for depression).

Discussion

Three results merit attention. First, at 20-week follow-up, extended CBT produced a better treatment response than brief supportive therapy. The superiority of CBT suggests that continued emphasis on the development of cognitive and behavioral relapse prevention strategies during an extended treatment phase may help smokers to maintain abstinence.

This result may shed light on findings obtained in our previous trial [8]. In that study, participants received either bupropion SR or placebo for 14 weeks following open-label treatment. At 25 weeks, bupropion was not superior to placebo but the overall abstinence rate of 40% represented a higher-than-average treatment response. However, in addition to bupropion or placebo, all participants in the previous trial received additional sessions of CBT during extended treatment. The findings from our current trial suggest that the provision of CBT during extended treatment may have been a key factor contributing to the comparatively high abstinence rates achieved in both studies.

The effect of CBT in this trial was not sustained through 52 weeks. Clearly, the timetable for producing longer-term maintenance and generalization of behavior change is not deduced easily. In this instance, the optimal duration of such treatment to produce longer-term abstinence appears to be longer than 20 weeks. The accurate identification of environmental triggers, the specific skills chosen for training, the time allotted to training and practice, the individual's perceived level of personal mastery and adjustments in training schedule required to match individuals' performance accomplishments are just some of the variables that influence skill acquisition and performance [30]. Sufficient guidance, time and effort are required to produce durable effects. Thus, for example, Hall and colleagues were able to achieve abstinence rates exceeding 40% by extending therapist-guided behavioral treatment over a 52-week period [9].

Secondly, gender did not moderate treatment response. As noted, some investigations, based on *post hoc* analyses, have concluded that men are more successful than women at quitting smoking. Other studies, also based on *post hoc* analyses, have failed to replicate this finding [31–33].

The reliance on *post hoc* analyses is problematic [34,35]. *Post hoc* subgroup analyses of clinical trial results can be very misleading and should be interpreted with caution. If researchers wish to examine the hypothesized gender effect in smoking cessation in a methodologically sound manner, they must power studies accordingly and stratify randomization on gender.

We have now examined the question of whether men are more successful in quitting than women in five cessation trials [8,14]. In each trial, randomization was stratified on gender so that we might examine the data specifically for potential gender $\times$ treatment effects. In one trial, gender was a predictor of treatment response [8]. In none of the trials was gender a moderator of treatment. In this trial, although men performed marginally better if assigned to CBT, as before we conclude that there may be little value added in diverting research funds from efforts to develop more effective treatments for both men and women, to efforts to explain a very small gender effect associated with existing treatments. While it may be

appropriate to make gender comparisons for new therapies for nicotine dependence, we recommend against analyses of gender differences in studies that do not account for gender in their research designs.

Thirdly, history of depression moderated treatment response at 20 weeks. Those with a positive history were more successful at 20 weeks if they received telephone-based general support rather than the more intensive and focused CBT. The finding is difficult to explain because a positive history was not correlated with response during the open-label phase when all participants received CBT. Although exploratory, the finding is interesting given that few moderators of smoking cessation therapy have been identified and the resulting possibility for improved treatment targeting.

History of depression was examined in our trial, given evidence that smoking and depression co-occur more frequently than would be expected by chance [36–38]. However, because the number of participants with a previous history was small and because we did not stratify randomization on history of depression, this interesting result will require replication in future research that employs a larger sample size and appropriate randomization design.

Regarding the primary analysis, perhaps the treatment effect at 20 weeks is the result of resentful demoralization. This seems an unlikely rival hypothesis. All participants received the same open-label treatment and the abstinence rates at end of open-label treatment for those who would receive differential treatment later were impressive (56%) and identical. Compliance in the minimal contact condition was good; 75% of telephone calls conducted during extended treatment were completed and there was no difference between treatment groups in number of participants available at follow-ups; further, the 20-week abstinence rate of 29% achieved in the minimal contact group compares favorably with the results of meta-analyses of pharmacotherapy trials.

A difference in contact time between the more intensive counseling provided via CBT and the brief counseling provided via telephone support might also explain the result. Again, this seems unlikely for the reasons mentioned above. However, if extra contact trumps CBT as an explanation, the treatment effect at week 20 remains of more than passing interest. Lancaster & Stead recently reviewed the literature on the efficacy of individual behavioral treatment for smoking cessation. As might be expected, behavioral treatment was found to be superior to no treatment control. However, the review failed to detect a greater effect of intensive counseling compared to brief counseling. The review concluded that the identification of effective and cost-effective intensity and duration of treatment remains an important area for research [39].

Finally, as noted previously, smoking cessation treatments are given typically for 8–10 weeks. As yet, relatively few trials have recognized the call for longer-term treatment and monitoring. The fact that 45% met abstinence criteria at end of extended CBT is encouraging and suggests, along with results from previous extended treatment trials [8,9], that recent recommendations for more effective cessation treatments made by several investigators are on target [1,4].

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Figure 1. Flowchart showing attrition of smokers over 52 weeks

Figure 2. Abstinence rates by history of major depressive disorder (MDD)/treatment group. CBT: cognitive behaviour therapy

Table 1

Participant characteristics.

Variable	Telephone support				Cognitive behavior therapy							
	Male		Female		Male				Female			
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Tx P	Gender P
Cigarettes smoked/day	21.19	7.78	19.92	6.66	20.61	8.82	18.13	6.52	0.19	0.03	0.51	
Expired-air CO (ppm)	28.03	12.83	26.41	14.80	25.29	12.92	24.21	11.94	0.11	0.38	0.86	
mFTQ (5–25)	16.69	3.74	16.83	3.54	16.33	3.87	16.27	3.85	0.30	0.92	0.83	
CES-D (0–60)	6.86	6.87	6.01	5.23	7.25	7.20	6.21	7.27	0.71	0.23	0.91	
BMI (kg/m ²)	29.39	6.20	27.21	6.37	28.09	4.46	26.66	5.54	0.16	0.007	0.58	
Age (years)	46.56	11.31	44.59	10.15	45.90	11.38	46.23	10.44	0.70	0.52	0.37	
Education (years)	14.61	2.46	13.58	2.03	14.46	2.45	13.69	1.93	0.94	0.0009	0.61	
History of MDD (%)	9.10%		6.80%		14.10%		9.60%		0.27	0.34	0.77	
Married (%)	54.50%		44.10%		56.50%		37.10%		0.67	0.01	0.44	
Sample size	88		59		92		62					

BMI: body mass index; CES-D: Center for Epidemiological Studies–Depression scale; MDD: major depressive disorder; mFTQ: modified Fagerström Tolerance Questionnaire; ppm: parts per million; SD: standard deviation.

Table 2

Point prevalence abstinence rates.

Treatment phase	No. abstinent	% abstinent	
Open-label (6 weeks)	170	56%	
Male	111	62%	
Female	59	49%	
20 weeks			Tx: $\chi^2 (1) = 7.5; P = 0.006$
Telephone support	42	29%	Gender $P = 0.38$
Male	25	28%	Tx $\times$ gender $P = 0.34$
Female	17	29%	
CBT	70	45%	
Male	46	50%	
Female	24	39%	
52 weeks			Tx: $P = 0.71$
Telephone support	40	27%	Gender $P = 0.32$
Male	24	27%	Tx $\times$ gender $P = 0.34$
Female	16	27%	
CBT	47	31%	
Male	32	35%	
Female	15	24%	

CBT: cognitive-behavioral therapy.

Table 3
Adverse events reported by at least 5% of participants during open-label treatment.

Adverse event	All	Men	Women	P-value	OR (CI) Male : female
Insomnia	58%	54%	64%	0.08	1.5 (0.9, 2.4)
Headache	37%	30%	46%	0.004	2.0 (1.2, 3.2)
Skin rash	19%	17%	22%	0.27	1.4 (0.8, 2.5)
Vivid dreams	14%	12%	17%	0.29	1.4 (0.7, 2.7)
Dry mouth	13%	15%	10%	0.20	0.6 (0.3, 1.3)
Anxiety	13%	11%	16%	0.19	1.6 (0.8, 3.1)
Nausea	7%	5%	11%	0.06	2.3 (0.9, 5.5)
Dizziness	6%	4%	7%	0.27	1.7 (0.6, 4.6)
Racing heart	5%	3%	8%	0.06	2.6 (0.9, 7.4)

No adverse events were reported during extended treatment by as many as 5% of participants. CI: confidence interval; OR: odds ratio.