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A randomized, controlled trial of NRT-aided gradual vs. abrupt cessation in smokers actively trying to quit

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ABSTRACT

Most smoking cessation programs advise abrupt rather than gradual cessation. We conducted a randomized, controlled trial of gradual cessation ($n = 297$) vs. abrupt cessation ($n = 299$) vs. minimal treatment ($n = 150$) among smokers who wanted to quit now and preferred to quit gradually. Participants were recruited via newspaper and radio advertisements. The gradual and abrupt conditions received five phone calls (total = 90 min) and the minimal treatment condition received two calls (25 min total). The gradual condition received nicotine lozenge (via mail) to reduce smoking prior to their quit date. After the quit day, all participants received lozenge. The primary outcome was prolonged abstinence from 2 weeks post-quit day through 6 months. Prior to the quit day, the gradual condition decreased cigarettes/day by 54%, whereas the other two conditions decreased by 1% and 5%. Prolonged abstinence rates (CO < 10 ppm) did not differ among gradual, abrupt and minimal treatment conditions (4%, 7% and 5%), nor did 7-day point prevalence rates (7%, 11% and 11%). Fewer smokers in the gradual condition (48%) made a quit attempt than in the abrupt (64%) or minimal (60%) conditions ($p < .001$). In the gradual condition, every week delay to the quit date increased the probability of lapsing by 19% ($p < .001$). We conclude that among smokers who want to stop gradually in the near future, gradual cessation with nicotine pre-treatment does not produce higher quit rates than abrupt cessation. One liability of gradual reduction may be that it allows smokers to delay their quit date.

1. Introduction

Often alcohol and illegal drug abusers decide to quit when an urgent drug-related problem occurs and, thus, they are urged to stop abruptly as soon as possible (Kleber et al., 2006). In contrast, urgent problems are often not occurring when cigarette smokers decide to quit (Larabie, 2005). As a result, many wish to stop via "gradual cessation"; i.e., reducing the number of cigarettes/day (CPD) over several days or weeks prior to quitting. In recent surveys, 48–83% of those planning to quit wanted to quit gradually (Hughes et al., 2007; Shiffman et al., 2006), 39–51% had reduced in the last year (Meyer et al., 2003; Shiffman et al., 2006), and 43–57% of these reducers were trying to quit (Meyer et al., 2003; West et al., 2001). The most common rationales for gradual cessation are: (a) reduction is an intermediary step toward quitting (Skinner, 1969), (b) reduction increases self-efficacy (Bandura, 1977), (c) reduction breaks up conditioned responses to smoke (Bouton and Swartzentruber, 1991), and (d) reduction decreases nicotine dependence (Hughes and Carpenter, 2006).

Current guidelines, meta-analyses and reviews either explicitly recommend abrupt rather than gradual cessation or do not mention gradual cessation as a potential treatment (Fiore et al., 2008; West et al., 2000; Silagy et al., 2004; Law and Tang, 1995; Stead et al., 2008). However, the evidence for whether gradual cessation is as effective as abrupt cessation is unclear. In case–control studies, smokers who quit gradually have lower abstinence rates than those who quit abruptly; however, this may be because those who chose gradual cessation are more dependent and have failed more in the past (Peters et al., 2007; Hughes, 2007; Cheong et al., 2007).

Nine randomized, control trials (RCTs) have compared gradual vs. abrupt cessation in smokers actively trying to quit (Table 1). Although most (7/9) of these showed numerically superior abstinence rates for gradual cessation, most had small sample sizes such that only one showed statistically significant results (Cinciripini et al., 1994). The nine studies used a variety of designs and methods. Two studies examined combined instructed gradual reduction and nicotine replacement therapy (NRT) pre-treatment and compared this to abrupt cessation; i.e., a design similar to that of the current study. The first study using an internet-based treatment and nicotine gum showed no advantage for gradual over abrupt (Etter et al., 2009). The second used transdermal nicotine and reported

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Table 1
Prior randomized, controlled trials of gradual cessation or nicotine pre-treatment.

Study	N/gradual condition	Psycho-social Tx	Pre-cessation medication	Percent reduction active/control	Placebo control	Percent quit active/control	OR[a] (95% CI) gradual > abrupt
Etter et al. (2009)	~157	Internet	Gum × 4 weeks	Not stated	No	21/20	1.1 (0.6–1.9)
Rezaishiraz et al. (2007)	47–51	In person	Patch × 2 weeks + denic cigarettes	Not stated	No	28/21	1.4 (0.6–3.6)
Cinciripini et al. (1994)	17	In person	None	−75/−26	No	41/6	11.2 (1.2–105.1)
Cinciripini et al. (1995)	63–65	In person	None	−76/−47	No	31/27	1.2 (0.6–2.6)
Cummings et al. (1988)	252–257	Written	None	Not stated	No	9/6	1.6 (1.0–2.5)
Flaxman (1978)	16	In person	None	−23/−13	No	38/56	0.8 (0.3–2.2)
Gunther et al. (1992)	55	In person	None	Not stated	No	25/22	0.9 (0.3–2.2)
Rose et al. (1998)	~40	In person	Patch × 4 weeks ± mecamylamine	57/13	Yes	30/15	2.4 (0.8–7.3)
Schuurmans et al. (2004)	100	In person	Patch × 2 weeks	−3/−3	Yes	22/12	2.1 (1.0–4.5)

CI = confidence interval; denic = denicotinized; OR = odds ratio; Tx = treatment.
[a] OR > 1.0 if quit rate with gradual > quit rate with abrupt; OR < 1.0 if gradual < abrupt.

an advantage for gradual, but this study was confounded by the use of a denicotinized cigarette in the gradual cessation condition (Rezaishiraz et al., 2007). Five RCTs compared gradual and abrupt cessation among smokers actively trying to quit but did not use NRT to aid in reduction and reported widely varying results (Cinciripini et al., 1994, 1995; Cummings et al., 1988; Flaxman, 1978; Gunther et al., 1992). Two RCTs examined "pre-treatment" with NRT prior to the quit date and did not instruct smokers to reduce but reported some smokers spontaneously reduced prior to their quit date (Rose et al., 1998; Becker et al., 2008; Schuurmans et al., 2004). In one of these, smokers who reduced more prior to the quit date were more likely to achieve abstinence than smokers who did not (Rose et al., 1998; Becker et al., 2008).

In contrast to the above studies, a separate literature has examined smoking reduction among smokers who do not plan to quit in the near future. These studies consistently found reduction increases the probability of making a quit attempt later and of subsequent abstinence (Hughes and Carpenter, 2006).

Although many of these studies suggest gradual cessation is at least as efficacious as abrupt cessation, the above trials had one or more methodological or reporting problems; e.g., small sample sizes, no matching on treatment contact time, confounding by including other interventions, no verification of reduction in the gradual condition and non-reduction in the abrupt condition prior to the quit date, or no biochemical verification of abstinence. Given this, we believed a large, stringent RCT test of gradual cessation vs. abrupt cessation was indicated. We hypothesized that gradual cessation would produce higher quit rates than abrupt cessation if (a) participants were smokers who wanted to quit gradually and (b) NRT was used to aid pre-treatment reduction.

2. Methods

2.1. Design

We recruited only smokers who preferred to quit gradually for three reasons. First, we thought that this would be the group most likely to benefit from gradual cessation. Second, in recent studies, over half of smokers who wished to quit, planned to do so gradually (Peters et al., 2007; Shiffman et al., 2006). Third, our anecdotal observation is that many treatment programs encourage smokers who wish to quit gradually to quit abruptly, and we wondered if abrupt cessation might actually be less efficacious in this group of smokers.

Smokers who wished to stop gradually were randomly assigned in a 2:2:1 ratio to a gradual cessation intervention, an abrupt cessation intervention, or a minimal treatment control condition. We included a minimal treatment condition, so that if both the outcomes of gradual and abrupt conditions were equivalent, we could know if both were effective (i.e., both had quit rates greater than the minimal treatment) or both were ineffective (both had quit rates similar to minimal treatment). All counseling was delivered via phone. The gradual cessation condition used nicotine lozenge to aid in reduction prior to their quit day. The major outcome was prolonged abstinence between 2 weeks and 6 months post-quit day.

The study methods and gradual intervention were designed to represent an intervention that might be used in clinical settings or a telephone quit-lines. Most gradual cessation interventions in clinical settings and in the RCTs in Table 1 differ from abrupt cessation interventions on several aspects other than gradual vs. abrupt cessation. For example, because the gradual treatment is usually a more extended treatment, the time between the start of treatment and the quit date is often longer than in the abrupt treatment, and the gradual treatment can have more sessions prior to the quit date and involve more treatment time. In the current study, we equated abrupt and gradual treatments on total treatment time because we believed this was the variable most likely to confound outcomes if it varied between treatments. We considered making the time between treatment entry and the quit date the same in abrupt vs. gradual treatments, but this would require the abrupt group to wait for several weeks, and we thought this was not externally valid and might unfairly disadvantage the abrupt treatment; thus, we allowed the abrupt condition to quit sooner after study entry than the gradual condition. We had those in the gradual condition use NRT for several weeks prior to the quit date to aid in reduction. We considered having the abrupt group also use NRT prior to the quit date but not reduce, but did not do so because this is currently not approved nor standard use of NRT. The resultant design, although equating for number of sessions and treatment time across abrupt and gradual groups, allowed abrupt and gradual groups to have different distributions of pre-cessation vs. post-cessation sessions; i.e., the gradual condition had four calls pre-cessation and one post-cessation call whereas the abrupt had two pre- and three post-cessation (the minimal had one pre- and one post-cessation call). As a result of these decisions, our study is *not* a test of reducing cigarettes/day per se, but rather is a comparison of gradual cessation and abrupt cessation treatments likely to be used in a clinical or quit-line setting.

2.2. Recruitment

To obtain a substantial number of minority smokers, we recruited in Columbia, SC, Albuquerque, NM and Florence, SC with newspaper and radio ads that stated "Want to quit smoking gradually? Receive free nicotine lozenges and confidential telephone support without leaving your home." Major inclusion criteria were: (a) ≥18-year-old daily smoker of ≥15 cigarettes/day, (b) want to quit smoking in the next 30 days and prefer to quit gradually rather than abruptly, (c) no change in cigarettes/day by ±20% or more in the last month, (d) willing to use nicotine lozenge, and (e) no FDA caution for use of lozenge requiring physician contact. We included only those who smoked ≥15 cigarettes/day because we believed that those who smoked less would be less likely to undertake a reduction program. We included those who wished to quit in the next 30 days because this indicates a serious intention to quit (DiClemente et al., 2004). About half of those screened were eligible, and about 75% of those eligible consented (Fig. 1). The study was approved by the University of Vermont Committees on Human Research.

2.3. Participants

Compared to population-based samples of US smokers (Giovino, 2002; Etter and Perneger, 2001; Fagerstrom and Furgerg, 2008; Hughes, 2004), our smokers were more likely to be women (54% vs. 48%), were older (48 vs. 39 years old), were as likely to be African American (10% vs. 12%) but were somewhat more likely to be Hispanic (13% vs. 8%), and were more likely to have completed high school (91% vs. 79%). The mean cigarettes/day upon entry was greater (23 vs. 15), the prevalence of use of light or ultra-light cigarettes was lower (58% vs. 87%), and the mean Fagerstrom Test for Nicotine Dependence (FTND) score was higher than the national sample (5.9 vs. 4.3–4.6). The above differences are likely due to our inclusion criteria and the fact that smokers who seek treatment are heavier and more dependent smokers (Haviland et al., 2003).

Marital status and confidence in quitting via gradual reduction statistically differed across experimental conditions (Table 2). When we entered these as covariates

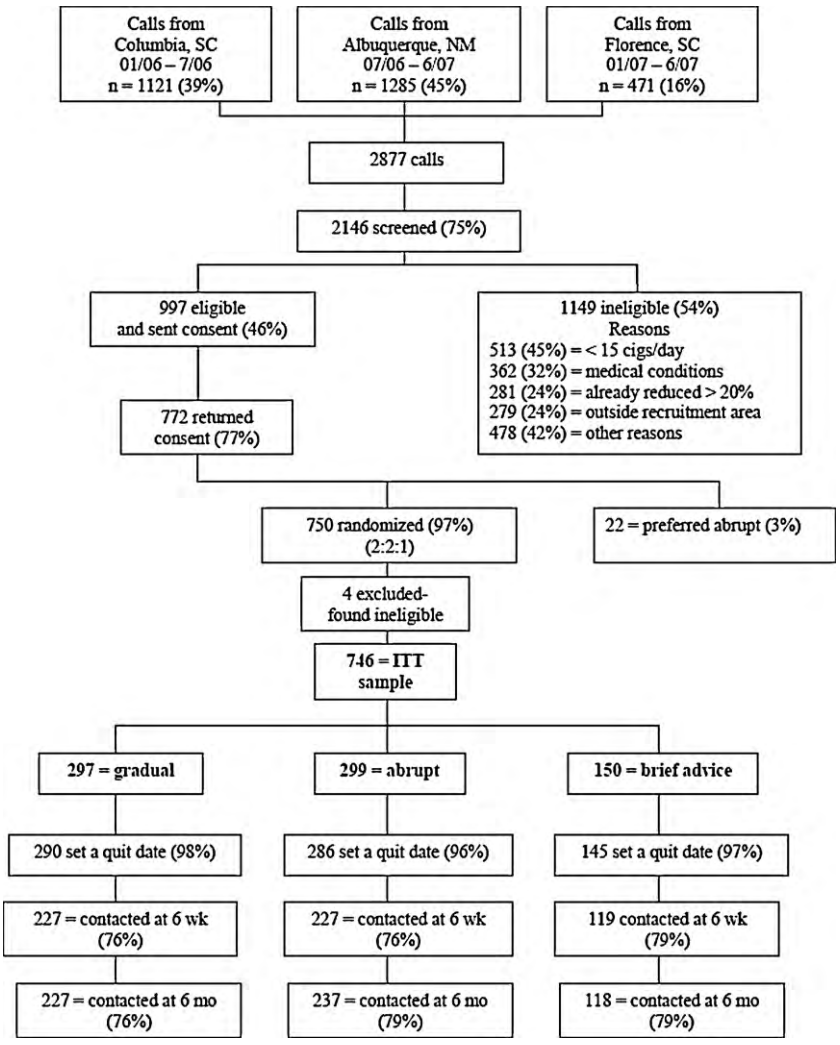

Fig. 1. Recruitment and retention flow chart. ITT = intent-to-treat.

in the analyses below, the results did not change to any appreciable extent; thus, we present unadjusted results. Our intended sample size of 300 in the abrupt and 300 in the gradual condition was based on an a priori hypothesis that the abstinence rate through 26 weeks would be 25% in the gradual condition vs. 15% in the abrupt condition vs. 10% in the minimal treatment condition. These rates were based on the results in Table 1 and our belief that the use of NRT pre-quit date in the gradual group (Shiffman and Ferguson, 2008), and the use of free NRT to all participants post-quit date (Stead et al., 2008), would substantially increase quit rates.

Upon receipt of consent, our statistician generated a concealed allocation sequence and randomized participants to the gradual, abrupt, or minimal treatment conditions in a 2:2:1 ratio using blocked randomization (stratified by city and counselor) based on the SAS procedure PLAN (Cary, NC: SAS Institute, Inc.).

The number of sessions (5) and treatment time (90 min total) were identical for the gradual and abrupt conditions, but were greater than in the minimal treatment control condition (2 sessions, 20 min total). The schedule of calls and timing of the quit dates were intended to mimic the typical practice of smoking cessation programs and are outlined in Fig. 2 (McEwen et al., 2006; Abrams et al., 2003). All participants set a quit day at the first session but this varied between those in the gradual condition (3–5 weeks later to allow reduction) and abrupt/minimal treatment condition (1–3 weeks later, as is typical in abrupt smoking cessation treatments (Abrams et al., 2003; McEwen et al., 2006)).

The phone counseling was delivered by counselors who had a bachelor's degree in psychology or counseling. All counselors delivered all treatments, and participants had the same counselor for the duration of the intervention. Counselors received 7 h of training and used a detailed treatment manual for each intervention. Sessions were not taped but were monitored by one of us (LS) listening to randomly chosen calls and providing feedback to counselors monthly during the study. The treatment manuals for all three conditions are available at www.uvm.edu/~hbpl. There were no effects of counselor nor counselor by treatment condition interactions on our major outcomes.

2.4. Gradual cessation intervention

We recommended participants in the gradual condition reduce by 25% in the first week, 50% in the second week, and 75% in the third week; however, each smoker chose his/her own goal and rate of progress. We described three different reduction methods from which the participant could choose: (a) scheduled reduction (SR) in which smokers gradually increase the time between cigarettes (Cinciripini et al., 1997), (b) hierarchical reduction-easiest first (HR-E) in which smokers eliminate cigarettes from easiest to hardest to give up (Levinson et al., 1971), and (c) hierarchal reduction-hardest first (HR-H) in which they eliminated the hardest to give up cigarettes first. Sixty percent of smokers chose SR, 25% chose HR-E, 11% chose HR-H, and in 4% it was unclear which method they chose. Reduction and abstinence results did not appear to differ across the initially chosen methods. Our clinical observation was that the large majority of smokers did not exclusively use their chosen method of reduction, but instead used several methods or reduced without using any of the above methods. Thus, the initial choice of methods may not be a valid description of actual behavior and this may be why the outcomes of different methods did not differ. As a result, we have pooled results across the initially chosen reduction methods.

We mailed smokers either 2 or 4 mg nicotine lozenges (Stead et al., 2008) (COMMIT, GlaxoSmithKline Consumer Healthcare) according to the recommended labeling for abrupt cessation (4 mg for those who smoked within <30 min of arising and 2 mg for others) throughout the pre-quit period. We recommended smokers substitute one lozenge for each cigarette foregone and use more lozenges to combat urges to smoke. Each counseling or data call asked about adverse events (AEs). The first three calls focused on reduction. The fourth call at 2 days prior to the quit day discussed common preparation strategies (e.g., making it difficult to get access to a cigarette), and reviewed the proper use of nicotine lozenges for cessation. The fifth call at 2 days post-quit day focused on relapse prevention with an emphasis on problem-solving high-risk-for-smoking situations.

Table 2
Participant characteristics.

	All (n = 746)	Condition			Statistic (df)	p-Value*
		Abrupt (n = 299)	Gradual (n = 297)	Minimal treatment (n = 150)		
Recruitment site						
Columbia	36%	35%	36%	35%	$\chi^2_{(4)} = 0.06$	1.00
Albuquerque	51%	51%	51%	51%		
Florence	14%	14%	13%	14%		
Demographics						
Gender						
Male	46%	45%	46%	47%	$\chi^2_{(2)} = 0.21$	0.90
Age						
Mean (sd)	46 (13)	48 (12)	48 (13)	47 (13)	$F_{(2,743)} = 0.08$	0.92
Hispanic						
Yes	13%	13%	14%	11%	$\chi^2_{(2)} = 0.58$	0.75
Race						
White	82%	79%	85%	81%	$\chi^2_{(4)} = 3.57$	0.47
Black or African American	10%	12%	8%	12%		
Other	8%	9%	7%	8%		
Marital status						
Married	47%	44%	50%	45%	$\chi^2_{(4)} = 10.74$	0.03
Divorces/widowed/separated	38%	38%	39%	34%		
Never married	16%	18%	10%	21%		
Highest education						
<High school	9%	10%	9%	9%	$\chi^2_{(4)} = 1.23$	0.87
High school	60%	61%	58%	60%		
College graduate	31%	29%	33%	30%		
Smoking history						
Cigarettes/day						
Mean (sd)	23 (9)	23 (9)	23 (8)	24 (9)	$F_{(2,740)} = 0.45$	0.64
Cigarette type						
Regular	42%	42%	41%	47%	$\chi^2_{(4)} = 6.61$	0.16
Lights	43%	43%	42%	45%		
Ultra-lights	15%	15%	17%	8%		
Age started smoking						
Mean (sd)	18 (5)	18 (6)	17 (5)	18 (5)	$F_{(2,738)} = 1.66$	0.19
# Prior quit attempts						
Mean (sd)	5.0 (7.9)	5.1 (8.4)	5.1 (8.7)	4.5 (4.2)	$F_{(2,717)} = 0.39$	0.68
Median	3	3	3	3	KW $\chi^2_{(2)} = 0.58$	0.75
Prior treatments**						
Called quit-line	6%	5%	6%	6%	$\chi^2_{(2)} = 0.42$	0.81
Used any medication	68%	65%	72%	64%	$\chi^2_{(2)} = 4.32$	0.12
Tried but none of above	37%	35%	37%	39%	$\chi^2_{(2)} = 0.77$	0.68
Plan to quit next month (0–10)						
Mean (sd)	8.3 (2.2)	8.1 (2.4)	8.4 (2.1)	8.4 (2.0)	$F_{(2,734)} = 1.70$	0.18
Preference for gradual vs. abrupt (0–10)						
Mean (sd)	4.0 (2.5)	4.0 (2.6)	3.9 (2.4)	4.3 (2.4)	$F_{(2,717)} = 1.09$	0.34
Confident can stop gradually (1–5)						
Mean (sd)	3.8 (0.9)	4.0 (0.9)	3.8 (0.9)	3.7 (1.0)	$F_{(2,740)} = 4.25$	0.01
Confident can stop abruptly (1–5)						
Mean (sd)	2.4 (1.2)	2.4 (1.2)	2.5 (1.2)	2.4 (1.2)	$F_{(2,740)} = 0.73$	0.48
FTND						
Mean (sd)	5.9 (1.8)	5.8 (1.8)	5.9 (1.8)	5.9 (1.7)	$F_{(2,717)} = 0.09$	0.91
Minutes to first cigarette						
Mean (sd)	16 (25)	18 (33)	16 (19)	15 (15)	$F_{(2,739)} = 0.81$	0.45

FTND = Fagerstrom Test for Nicotine Dependence; sd = standard deviation.
* Chi-square test for categorical variables, ANOVA for means, Kruskal-Wallis test for nonparametric.
** Among those who tried to quit in past (n = 702).

2.5. Abrupt cessation intervention

The abrupt cessation intervention mimicked a typical behavioral therapy (Abrams et al., 2003; McEwen et al., 2006). The first call in the abrupt condition reviewed reasons for wanting to quit, prior quit attempt strategies, and possible barriers to cessation. Participants were explicitly instructed not to change their cigarettes/day prior to the quit date. The second call immediately prior to the quit day had the same content as the pre-quit day preparation call in the gradual condition. The third, fourth and fifth calls after the quit day focused on relapse prevention; e.g., problem-solved ways to manage high-risk-for-smoking situations.

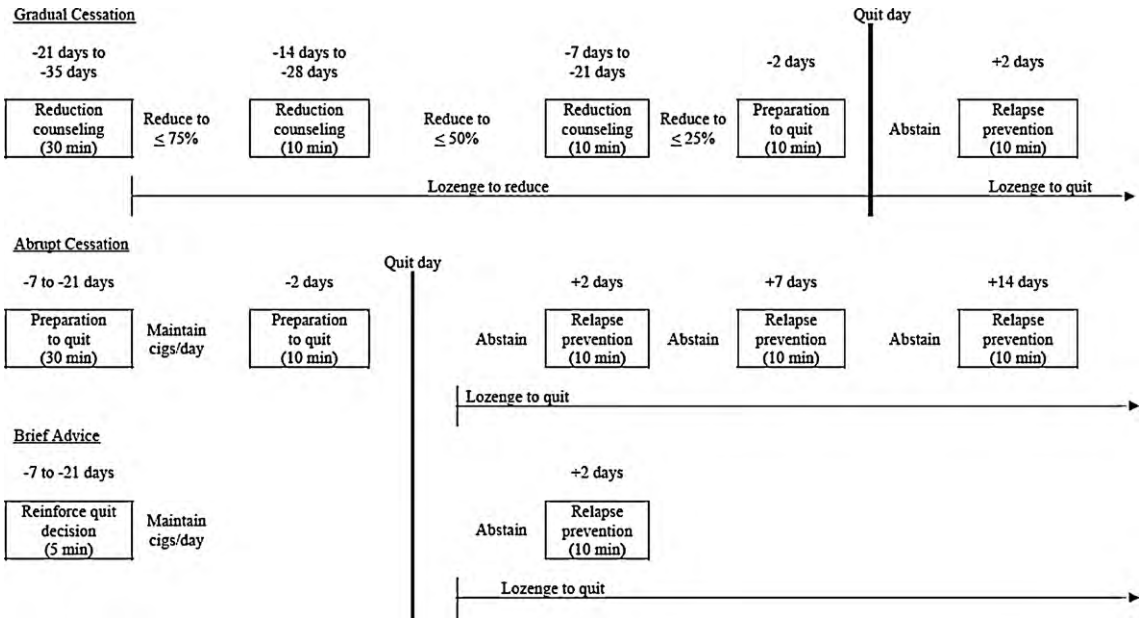

Fig. 2. Treatment schedule.

2.6. Minimal treatment intervention and treatment common to all conditions

This condition was intended to mimic a minimal intervention done in a primary care practice (Fiore et al., 2008). In the first session, we reviewed their plans to quit, encouraged them to set a quit date, and advised them to use nicotine lozenges according to label instructions. In the second session, which was 2 days post-quit date, we did the same relapse prevention problem-solving counseling we did in the last session of the gradual condition.

In all conditions, participants were sent the US National Cancer Institute's *Clearing the Air* booklet (www.smokefree.gov/pubs/clearing_the_air.pdf), as well as nicotine lozenges to use starting on their quit date. All participants were advised to use the lozenges following package recommendations for up to 12 weeks post-quit date, contingent upon abstinence.

2.7. Assessments

Descriptive data were collected at study entry. We used mailed questionnaires at study entry and immediately pre-quit date in the gradual and abrupt conditions to examine whether gradual cessation would have the beneficial effects outlined in the introduction; i.e., decreased dependence, disrupted pattern of smoking, and/or increased self-efficacy. We examined nicotine dependence via the total score on the 7-item Fagerstrom Test for Nicotine Dependence (FTND), as well as time-to-first cigarette, and a previously validated, single-item visual analog scale of self-reported addiction (Hughes et al., 2004b), where 0 = I am not addicted to cigarettes at all and 100 = I am extremely addicted to cigarettes. We examined disruption of the regularity of smoking using the stereotypy subscale of the Nicotine Dependence Syndrome Scale (Shiffman et al., 2004) where smokers rate from "not at all true" to "extremely true" on two 5-point Likert scales (total score 0–10) the following two statements: "I smoke just about the same number of cigarettes from day to day" and "my smoking is not much affected by other things." We examined self-efficacy using the short form of Velicer's scale (Velicer et al., 1990) that asks ability to resist smoking in 9 situations. We examined motivation to quit using 11-point motivation ladders we previously validated (Hughes et al., 2005), where 0 = definitely do not plan to quit in the next month and 10 = definitely plan to quit in next month. We included Likert scales of confidence in ability to quit (1 = not at all to 5 = very confident) and of perceived difficulty in quitting (1 = quitting would be impossible to 5 = quitting would be very easy). We also examined preference for quitting method on an 11-point ladder with 0 = only want to quit if I can do it by gradual reduction, 5 = willing to quit either gradually or abruptly, and 10 = only want to quit if I can do it abruptly.

To verify reduction and non-reduction, we hired a local research assistant to visit smokers in the gradual and abrupt conditions at study entry and immediately before the quit day to obtain a breath carbon monoxide (CO) level. This research assistant also obtained CO levels among those who reported abstinence at 6-month follow-up in all three conditions. The time of day of the CO collection was uncontrolled.

All follow-ups were tied to the set quit date and post-quit day outcomes were collected via phone by research assistants who were blind to study condition and had no role in the intervention. Assessments occurred 2 weeks, 4 weeks, 6 weeks, 3 months, and 6 months after the quit date set by the participant at study onset. We reached about three-quarters of participants for the 6-month follow-up (Fig. 1). At the 6-month call, those who reported no smoking in the last week were visited to obtain a CO sample to verify abstinence. Across the three cities, we obtained CO samples from 52% in the gradual condition, 66% in the abrupt condition, and 51% in the minimal treatment condition.

2.8. Data analysis

We used the SRNT recommended outcomes for clinical trials (Hughes et al., 2003). Unless otherwise stated, all analyses are based on those randomized and not later found to be ineligible; i.e., a modified intent-to-treat (ITT) sample. Smoking cessation trials typically count those lost to follow-up as smokers and we did so (Hall et al., 2001; SRNT Subcommittee on Biochemical Verification, 2002). No statistical corrections were made for the number of tests because many statisticians believe such corrections are not necessary (Feise, 2002). Baseline characteristics were compared for the three study conditions using chi-square tests for categorical variables and analysis of variance or the Kruskal–Wallis test for continuous variables (Siegel, 1956). Abstinence outcomes and quit attempts were analyzed bivariately using chi-square tests, with assessment of possible confounding variables and interactions performed via logistic regression. Proportional hazards modeling was used for time-to-lapse analyses.

3. Results

3.1. Internal validity/compliance

Almost all (90%) of the smokers in the gradual condition were assigned 4 mg lozenge because they smoked within 30 min of arising. Prior to the quit date, 93% of smokers in the gradual condition used at least one nicotine lozenge and 86% used lozenges for 1 week or more. They used a median of 83% of days and used an average of 18.6 mg/day (i.e., 4–5 lozenges) on the days they used. In the week after the quit attempt, the mean number of days NRT was used was 6.5 in the gradual, 6.2 in the abrupt condition and 6.0 in the minimal treatment ($F_{(2,419)} = 2.01$, $p = 0.14$). The incidence of AEs rated severe was small and similar across gradual, abrupt, and minimal treatment conditions (3% vs. 5% vs. 3%), and the incidence of discontinuation due to AEs was <1% for all three groups. Most participants completed ≥4/5 treatment calls in the gradual (79%) and abrupt (78%) conditions or completed 2/2 calls in the minimal treatment (83%) condition.

The mean decrease in CPD between study entry and the week prior to the quit date among the subset of participants with no missing data was 54% (13 CPD) in the gradual vs. 1% (0.3 CPD) in the abrupt and 5% (1 CPD) in the minimal treatment condition. The decrease in CO was 21% (6 ppm) in the gradual vs. 0% (0 ppm) in the

abrupt condition. As expected, the mean time until the designated quit date was greater in the gradual than in the abrupt or minimal treatment conditions (27 vs. 15 vs. 15 days, $F_{(2,718)} = 358.7$, $p < .001$).

3.2. Abstinence

The three conditions did not differ statistically on any measure of abstinence at 6-month follow-up (Table 3); however, the gradual condition had a consistent, non-significant trend for lower abstinence rates. Because the incidence of 6-month contacts and of CO sampling differed somewhat across groups, we re-ran the analyses in Table 3 using only those contacted at 6 months. Although the quit rates were higher, the odds ratio across the groups were very similar to the results in Table 3.

Smokers in the gradual condition were less likely to make a quit attempt, defined as ≥1 day of not smoking, than those in the abrupt and minimal treatment conditions (48% vs. 64% vs. 60%, $\chi^2_{(2)} = 15.9$, $p < .001$). In a survival analysis of lapses in the first 6 weeks (the time period in which we collected daily data), the time-to-lapse was non-significantly longer for abrupt than gradual conditions (proportional hazard ratio (HR) = 1.2, $\chi^2_{(1)} = 3.35$, $p = .07$), and for abrupt vs. minimal treatment conditions (HR = 1.2, $\chi^2_{(1)} = 2.52$, $p = .11$), but did not differ between gradual and minimal treatment conditions (HR = 1.0, $\chi^2_{(1)} = 0.00$, $p = .96$) (Fig. 3).

3.3. Effects of gradual reduction on self-efficacy, dependence and regularity of smoking

We measured whether gradual cessation prior to the quit date had the anticipated effects on self-efficacy, dependence and regularity of smoking by examining the results of the baseline and pre-quit questionnaires. The outcomes of these results must be interpreted cautiously for two reasons. First, we were not able to verify that the pre-quit questionnaire was completed immediately prior to cessation. Secondly, the rate of completion of both the baseline and pre-quit surveys differed across conditions, with 57% completion in the gradual, 82% in the abrupt, and 70% in the minimal treatment condition ($\chi^2_{(2)} = 44.3$, $p < .001$); thus, the outcomes reported below are based on this self-selected subsample.

As anticipated, participants in the gradual condition increased self-efficacy more (mean score at baseline = 18 vs. at pre-quit = 23) than in the other two conditions (18 at pre-cessation to 19 at pre-quit for each, $F_{(2,502)} = 45.67$, $p < .0001$). A similar effect occurred with the 5-point confidence in quitting scale ($F_{(2,510)} = 2.97$, $p = .05$) and the 5-point perceived difficulty in quitting scale ($F_{(2,504)} = 24.63$, $p < .0001$). Participants in the gradual condition also decreased dependence; i.e., increased time-to-first cigarette (15–28 min), but participants in the other two conditions did not ($F_{(2,509)} = 21.29$, $p < .0001$). Similar outcomes occurred with the dependence measures of FTND ($F_{(2,487)} = 12.15$, $p < .0001$) and self-rated addiction ($F_{(2,512)} = 62.13$, $p < .0001$). Participants in the gradual condition decreased the regularity of smoking (from 6.9 to 5.3 on the 1–10 scale) indicating smoking became more disrupted, but the regularity of smoking did not change in participants in the other two conditions ($F_{(2,507)} = 30.26$, $p < .0001$). Craving decreased in the gradual condition (4.5–4.0 on 1–5 scale) from baseline to pre-quit, but did not do so in the other two conditions (4.5–4.4, $F_{(2,508)} = 9.16$, $p < .0001$).

Within the gradual condition, we examined predictors of time-to-lapse via a series of bivariate analyses. The following were not predictors of survival time in the first 6 weeks: greater reductions in CPD, time-to-first cigarette, confidence in quitting, motivation to quit, self-efficacy, craving, dependence, and regularity of smoking. However, for every extra week between study entry and the quit day within the gradual condition, the probability of lapsing increased by 19% (HR = 1.19; $\chi^2_{(1)} = 4.80$, $p = .03$). Within the gradual condition, the amount of use of NRT was not related to survival time.

3.4. Possible moderators

We tested whether the following baseline characteristics interacted with the effect of gradual vs. abrupt treatment on survival time: age, sex, race, CPD, FTND, self-rated addiction, confidence in ability to quit, intention to quit in the next month, confidence could quit gradually, confidence could quit abruptly, and their ratio, desire to quit gradually vs. abruptly, self-efficacy, and regularity of smoking. Among smokers who rated their dependence as low on the visual analog scale at study onset, the abrupt condition had a better outcome than the gradual condition (i.e., had a longer time-to-lapse); however, among smokers who rated themselves as highly dependent, the abrupt condition did not have a better outcome than the gradual condition ($\chi^2_{(1)} = 3.91$, $p = .05$). A similar, but non-significant, interaction occurred with the other two dependence measures of FTND and CPD. Among smokers with high self-efficacy, the abrupt condition out-performed the gradual condition but among smokers with low self-efficacy, the abrupt condition did not out-perform the gradual condition ($\chi^2_{(1)} = 4.98$, $p = .03$). A similar, but non-significant, interaction occurred with self-rated confidence in quitting. Surprisingly, relative preference for gradual vs. abrupt cessation did not predict response to treatment. Also, those who did not return the pre-quit questionnaire were more likely to relapse (HR = 1.23, 1.01–1.49) but this effect did not interact with experimental conditions. None of the above moderators influenced point prevalence or prolonged outcomes.

4. Discussion

4.1. Summary of results

Our major finding is that, among smokers who preferred to quit gradually, gradual cessation was not superior to abrupt cessation nor minimal treatment treatments. In fact, there was a non-significant trend for outcomes to be worse in the gradual cessation condition. Thus, we failed to confirm our hypotheses that, among smokers who preferred to reduce and then quit and who received NRT to reduce, gradual cessation would produce more abstinence than abrupt cessation. A post hoc finding suggested gradual cessation might be equivalent to abrupt cessation in more dependent smokers; however, given this only occurred in time-to-relapse analyses but not in dichotomous abstinence outcomes, it requires replication.

Our failure to find statistical differences among the conditions could be interpreted to mean none of our interventions were efficacious or all were efficacious. We believe the later is more likely given that NRT, phone counseling and minimal treatment interventions very similar to ours have been validated as treatments, even when delivered over the phone or via mail (Fiore et al., 2008). In addition, our incidence of 6-month prolonged abstinence is higher than would be expected among self-quitters not receiving any treatment (Hughes et al., 2004a).

4.2. Study assets and limitations

Assets of this study included that the sample size was larger than prior studies; participants in the abrupt and gradual conditions received the same amount of counseling; and similar results occurred across several outcome measures. Also, prior to the quit day, the gradual condition used NRT on most days in substantial amounts, had a large, biochemically confirmed decline in CPD that did not occur in the abrupt group, decreased their nicotine depen-

Table 3
Abstinence outcomes at 6-month follow-up[a].

	Percent abstinent gradual condition	Percent abstinent abrupt condition	Percent abstinent minimal treatment condition	Odds ratio gradual vs. abrupt
Prolonged abstinence[b]				
3-Month self-report	13 (10,18)	20 (16,25)	11 (7,18)	0.6 (0.4,1.0)
6-Month self-report	9 (6,13)	13 (9,17)	12 (7,18)	0.7 (0.4,1.1)
6-Month CO-verified	4 (2,7)	7 (4,10)	5 (2,9)	0.6 (0.3,1.2)
7-Day abstinence				
3-Month self-report	30 (25,36)	37 (32,43)	27 (20,35)	0.7 (0.5,1.0)
6-Month self-report	24 (19,29)	31 (26,36)	31 (24,39)	0.7 (0.5,1.0)
6-Month CO-verified	7 (4,10)	11 (8,15)	11 (6,17)	0.6 (0.3,1.0)

CO = carbon monoxide.
[a] Mean 95% confidence interval in parentheses.
[b] With 2-week grace period.

dence, increased their self-efficacy, and disrupted their smoking more than the abrupt condition.

Our study had several limitations. As discussed above, our experimental conditions varied in several ways other than reduction pre-quit date. One could hypothesize that these other differences prevented a benefit of gradual cessation; e.g., if we had not matched the treatments on time and allowed the gradual treatment to spend as much time on traditional behavioral techniques as the abrupt group, then the gradual treatment may have shown a benefit. Another possibility is that the parameters for reduction were less-than-optimal; e.g., perhaps we should have used patch rather than lozenge or used a longer reduction period. Also, our projected incidence of abstinence was over-optimistic and, thus, our power was less than expected. A comparison of the second vs. third rows and fifth vs. sixth rows of Table 2 indicates that about half of participants who reported abstinence either did not agree to a CO test or had a test with a high value. This raises questions about the validity of the self-reports in our study. However, many studies of phone-based treatments (Stead et al., 2006), obtain response rates for biochemical verification of <50%.

4.3. Possible explanations of our results

Recent retrospective surveys indicate that smokers who chose to quit immediately have better outcomes than those who quit later, and some have suggested this is because smokers who delay lose motivation to quit (Larabie, 2005; West and Sohal, 2006; Ferguson et al., 2009). Our finding that, within the gradual condition, a longer delay to the quit date was associated with more lapse is consistent with these findings.

Another possible explanation for the failure to find gradual cessation superior is that the counseling time in the gradual condition was spent mostly on teaching gradual reduction, not on problem-solving ways to cope with high-risk-for-smoking situations. This deficit could have caused the gradual condition to do worse. Also, although the number of calls was similar in the gradual and abrupt condition, the gradual condition received more pre-cessation calls and fewer post-cessation calls than the abrupt condition. Massing treatment sessions early in abstinence, when smokers are struggling, rather than pre-cessation, may be important in establishing abstinence.

A prior study found that smoking reduction via systematically increasing the time between cigarettes; i.e., scheduled reduction (SR), increased abstinence compared to abrupt cessation, but other methods of reducing did not (Cinciripini et al., 1995). However, we found no differences in abstinence outcomes between SR and other methods.

4.4. Failure to replicate efficacy of pre-treatment and the reduce-to-quit indication

Most, but not all, studies suggest pre-treatment with NRT increases abstinence (Shiffman and Ferguson, 2008). Although our

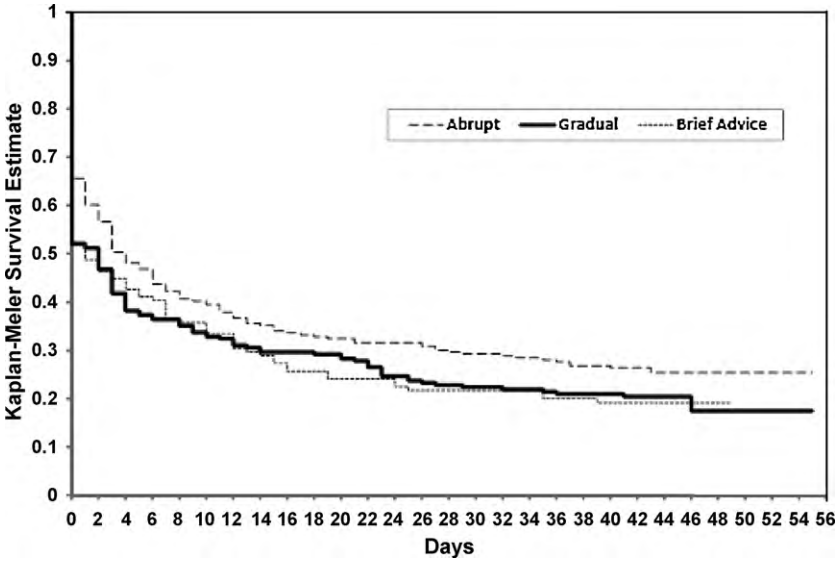

Fig. 3. Survival curve of time-to-self-reported first lapse among quit attempters. For those who did not quit or relapsed on the first day of abstinence, we assigned a value of zero. Due to the timing of calls, we sometimes did not inquire about smoking on every day of the study. When post-cessation smoking status was missing due to the study design, we believed using last observation carried backwards was more accurate and more conservative than using last observation carried forward.

study was not specifically designed to test pre-treatment, because our gradual condition used NRT prior to the quit date and our abrupt did not and we found no difference between the two, our trial failed to confirm a beneficial effect of pre-treatment. The two prior studies that failed to find pre-treatment with NRT increased quit rates were similar to our study in that they did not deliver treatment in person; i.e., they provided treatment via internet (Etter et al., 2009) or phone (Bullen et al., 2008). In addition, most of the pre-treatment studies used nicotine patches. The other two trials that, like our study, used oral NRT, failed to find positive results (Etter et al., 2009; Herrera et al., 1995). These results suggest in person contact or use of transdermal nicotine may be essential to increase sufficient compliance to observe beneficial pre-treatment effects.

A "reduce-to-quit" indication for NRT has been approved in several countries for smokers who plan to quit (Wang et al., 2008). Our results appear to be inconsistent with these findings as well. However, the reduce-to-quit indication was based on studies of smokers who did *not* plan to quit in the near future. Among such smokers, reduction consistently increases the probability of later quit attempts and abstinence (Hughes and Carpenter, 2005). Thus, one interpretation is that reduction is efficacious in ambivalent smokers who do not plan to quit in the near future, but not in motivated smokers who want to quit soon.

4.5. Summary

Given that many smokers want to quit gradually and given that many countries now have a reduce-to-quit indication, we believe our study's unexpected negative results increase the need for further RCTs of gradual vs. abrupt cessation.

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Contributors

Drs Callas, Hughes, and Solomon designed the study and obtained the funding. Dr Hughes, Ms Livingston and Dr Peters participated in data collection. Drs Callas, Hughes, Peters and Solomon participated in data analysis. All authors participated in interpretation of results, writing of the paper and approved the final draft of the manuscript.

Conflict of interest

Since 1/1/2007, Dr Hughes has received research grants from the National Institute on Health and Pfizer. Pfizer develops and sells smoking cessation medications. During this time, he has accepted honoraria or consulting fees from several non-profit and for-profit organizations and companies that develop, sell or promote smoking cessation products or services or educate/advocate about smoking cessation: Abbot Pharmaceuticals; Acrux; Aradigm; American Academy of Addiction Psychiatry; American Psychiatric Association; Begbies Traynor; Cambridge Hospital, Cline, Davis and Mann; Constella Group; Consultants in Behavior Change; Dean Foundation, DLA Piper, EPI-Q, European Respiratory Society, Evotec; Exchange Limited; Fagerstrom Consulting; Free and Clear; Glaxo-Smith Kline; Golin Harris; Healthwise; Insyght; Informed, Invivodata; Johns Hopkins University; JL Reckner; Maine Medical Center; McNeil Pharmaceuticals; Novartis Pharmaceuticals; Oglivy Health PR, Ottawa Heart Institute, Pfizer Pharmaceuticals; Pinney Associates; Propagate Pharmaceuticals. Reuters; Scientia, Selecta; Temple University of Health Sciences; University of Arkansas; University of California-San Francisco; University of Cantabria; University of Kentucky, US National Institutes on Health; Wolters Publishing, and Xenova. All other authors have nothing to declare.

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