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Time-varying Effects of 'Optimized Smoking Treatment' on Craving, Negative Affect, and Anhedonia

Nayoung Kim, Ph.D.[1,*], **Danielle E. McCarthy, Ph.D.**[1], **Jessica W. Cook, Ph.D.**[1], **Megan E. Piper, Ph.D.**[1], **Tanya R. Schlam, Ph.D.**[1], **Timothy B. Baker, Ph.D.**[1]

[1]Center for Tobacco Research and Treatment, University of Wisconsin School of Medicine and Public Health, Madison, WI 53711, USA

Abstract

Aims: To identify when smoking cessation treatments affect craving, negative affect and anhedonia, and how these symptoms relate to abstinence, to help evaluate the effects of particular intervention components in multicomponent treatments and accelerate treatment refinement.

Design: Secondary analysis of data from a 2-arm randomized controlled trial.

Setting: Seven primary care clinics in Wisconsin, USA.

Participants: Adult primary care patients who smoked daily (N=574).

Intervention and comparator: Intervention was Abstinence-Optimized Treatment (A-OT, n=276) comprising 3 weeks of nicotine mini-lozenges pre-target quit day (TQD), 26 weeks of combination nicotine patch and mini-lozenges post-TQD, and extensive psychosocial support. Comparator was Recommended Usual Care (RUC, n=298) comprising brief counseling and 8 weeks of nicotine patch post-TQD.

Measurements: Time-varying effect models examined dynamic effects of A-OT (versus RUC) on the primary outcomes of nightly cigarette craving, negative affect, and anhedonia from 1 week pre- to 2 weeks post-TQD. Exploratory models examined within-person relations between nicotine medication use and same-day symptom ratings. Secondary logistic regression analyses examined associations between post-TQD craving, negative affect and anhedonia and 1-month post-TQD abstinence.

Findings: A-OT significantly suppressed pre- and post-TQD craving (β=−0.27 to −0.46 across days) and post-TQD anhedonia (β=−0.24 to −0.38 across days), relative to RUC. Within persons, using patches was associated with lower negative affect in RUC (β=−0.42 to −0.52), but not in A-OT. Using more mini-lozenges was associated with greater craving (β=0.04 to 0.07) and negative

[*]**Corresponding Author**: Nayoung Kim, Ph.D., Center for Tobacco Research and Intervention, Department of Medicine, University of Wisconsin School of Medicine and Public Health, 1930 Monroe St., Suite 200, Madison, WI 53711 USA, Telephone: (608) 265-4447, Fax: (608) 265-3102, nkim86@ctri.wisc.edu.

All authors can be reached at the Center for Tobacco Research and Treatment, University of Wisconsin-Madison, 1930 Monroe Street, Suite 200, Madison, WI 53711.

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affect (β=0.03 to 0.05) early, and with lower anhedonia (β=−0.06 to −0.12) later. Greater post-TQD craving (OR=0.68) and anhedonia (OR= 0.85) predicted lower odds of abstinence 1 month post-TQD.

Conclusion: Time-varying effect models showed that a multicomponent treatment intervention for smoking cessation suppressed significant withdrawal symptoms better than recommended usual care among daily adult smokers motivated to quit. The intervention reduced craving pre- and post-target quit day (TQD) and anhedonia post-TQD.

Keywords

Smoking cessation; withdrawal; time-varying effect modeling; multiphase optimization strategy; nicotine replacement therapy

Even with intensive smoking cessation treatment, long-term abstinence rates rarely exceed 30% [1, 2]. In addition, treatments often have modest effects on the symptoms that prompt relapses [3–5]. Thus, there is still substantial room for improvement in smoking cessation therapy. Better understanding of how and when treatments achieve their effects on particular targets predictive of abstinence may accelerate treatment refinement.

Baker and colleagues [6] have proposed using engineering principles [7] to design treatments that effectively target phase-specific challenges in the multi-phase smoking cessation process. The Phase-Based Model of Smoking Intervention [6] holds that different phases of treatment (i.e., motivation, precessation, cessation, and maintenance) may require different interventions. Informed by this model and the Multiphase Optimization Strategy (MOST) for intervention development [7, 8], factorial screening experiments identified effective phase-specific intervention components [9–11] that were then tested in a randomized controlled trial of a multicomponent treatment (RCT) [12]. The RCT compared an Abstinence-Optimized Treatment (A-OT) comprising promising precessation, cessation, and maintenance intervention components with lower-intensity Recommended Usual Care (RUC) [12]. In A-OT, participants received 3 weeks of precessation treatment involving fast-acting nicotine replacement therapy (NRT: nicotine mini-lozenges) and in-person counseling (Figure 1). Cessation-phase treatment comprised combination NRT (C-NRT: patch and mini-lozenge), 6 counseling sessions, and 7 automated calls through 8 weeks post-target-quit-day (TQD). Maintenance-phase treatment included C-NRT through 26 weeks post-TQD, 4 maintenance counseling calls, and 4 automated adherence reminders (for those still smoking 8 weeks post-TQD). A-OT was compared with RUC comprising brief counseling (a single clinic visit and referral to the state quit line and a stop-smoking app) and 8 weeks of nicotine patch therapy (Figure 1). Six-month post-TQD biochemically confirmed point-prevalence abstinence rates were 16% in A-OT and 6% in RUC [12]. Thus, A-OT is relatively effective, but needs improvement.

The current study aimed to generate hypotheses about ways to refine A-OT by examining the time course of its effects on distinct symptoms thought to motivate smoking [13]. The goal of this approach is to identify how and when A-OT affects cravings to smoke, negative affect, and anhedonia (i.e., reduced responsivity to reward) in the critical pericessation period. Although craving, negative affect, and anhedonia do not occur only in the context of

nicotine withdrawal [14–19], these symptoms are sensitive to nicotine deprivation [14, 20–22], predictive of difficulty quitting smoking [4, 23–25], and mediate pharmacotherapy effects on abstinence [4, 26, 27]. In addition, drug motivation theory identifies negative affect (from withdrawal or other sources) as the dominant driver of smoking motivation [28], and identifies craving as subjective awareness of high levels of such motivation [28, 29]. As such, these constructs are identified by theory as key predictors of smoking. Anhedonia, on the other hand, was recently identified as a nicotine withdrawal symptom and predictor of smoking [23, 25, 30–32] and has not been adequately assessed as a mediator of smoking cessation interventions. The current study seeks to address this gap by exploring the responsivity of anhedonia to pericessation treatment [33–35].

Treatment relations with abstinence are strongest during the pericessation period, as lapse and relapse survival curves show maximal differentiation by treatment immediately after the TQD [36]. We therefore examined treatment-symptom relations in the week preceding and two weeks following the TQD, and symptom relations with abstinence 1-month post-TQD (undiluted by distal stressors or other relapse precipitants). Although these effects will be imperfectly related to longer-term (e.g., 6-month) abstinence outcomes of public health importance, understanding which symptoms are sensitive to treatment during the pericessation period may generate hypotheses about ways to refine treatment packages such as A-OT by adjusting the dose, targets, or timing of particular intervention components. Clinically, this knowledge could help determine when to evaluate treatment responsivity and consider alternative or adaptive treatments.

Time-varying effect modeling (TVEM) is an analytical tool that can identify the periods of greatest treatment effect through graphical displays of relations between treatment and outcomes over time [37]. These models showed that the magnitude of NRT effects (versus placebo) on smoking declines after the first week post-TQD, and that craving and negative affect have different relations with smoking over the first two weeks of quitting [38]. The current study applied TVEM to data from the RCT of A-OT versus RUC [12] to examine the time course of treatment effects on pericessation craving, negative affect, and anhedonia, assessed nightly via interactive voice response (IVR) system. We also examined relations between these ratings and later (1-month post-TQD) point-prevalence abstinence via logistic regression analyses. Finally, we examined within-person relations between deviations in medication use from each individual’s average use [39] and craving, negative affect, and anhedonia severity to explore temporal patterns in within-person medication effects and identify when treatment use was most tightly associated with symptom severity.

Method

Data came from an RCT [12] in which 623 adult daily smokers motivated to quit smoking and recruited from primary care clinics were randomized to either A-OT (n=308) or RUC (n=315). Participants in both conditions completed 4 clinic visits and 6 phone follow-up assessments through 12-months post-TQD; those in A-OT completed 3 additional visits for cessation counseling.

Participants

Participants were recruited from 7 primary care clinics in two Wisconsin healthcare systems. During clinic visits, clinic staff were prompted by the electronic health record (EHR) to invite patients who smoked to participate in a smoking treatment study. Patients who accepted this offer were referred to study staff who called patients to screen them for eligibility. Inclusion criteria required participants be: over age 18, English-literate, smoking at least 5 cigarettes per day in the previous 6 months, motivated to quit smoking in the next 30 days, willing to refrain from using non-study medication during the study, and reachable by telephone. Study exclusion criteria included: current use of bupropion; history of stroke, heart attack, transient ischemic attack, or an abnormal electrocardiogram in the past 4 weeks; diagnosis or treatment of serious mental illness (schizophrenia, a psychotic disorder, bipolar disorder) in the past 10 years; and pregnancy or unwillingness to use an approved method of birth control during treatment. After the phone screen, individuals were invited to their clinic to confirm eligibility and provide written informed consent. Study procedures were approved by the University of Wisconsin Health Sciences Institutional Review Board.

Treatment

As shown in Figure 1, the experimental treatment, A-OT, comprised 3 weeks of pre-TQD mini-lozenges; 26 weeks of post-TQD C-NRT with nicotine patches and mini-lozenges; 3 in-person and 8 phone counseling sessions; and 7–11 automated calls to promote medication use (7 calls for those who reported abstinence by week 8, and 11 for those still smoking at week 8). As recommended by the 2008 PHS Guideline [2], 15–20 minute A-OT counseling sessions were designed to help participants prepare to quit, develop knowledge and skills to cope with craving and withdrawal, identify and avoid or mitigate triggers to smoke, and provide social support. Counseling protocols for both conditions are included in the supplementary material online.

RUC participants received less intensive treatment comprising: 8 weeks of nicotine patch starting on the TQD; a single, 10-min face-to-face counseling session; faxed referral to the Wisconsin Tobacco Quit Line (WTQL) for phone counseling; and instructions for installing a free smoking cessation mobile app (QUITNOW).

Measures

At an initial research visit, participant demographics (gender, ethnicity, age, marital status, education, and employment), smoking history, and exhaled carbon monoxide (CO) were assessed. Tobacco dependence was assessed with the Fagerström Test of Cigarette Dependence (FTCD; [40, 41]). Additional baseline assessments will not be discussed further.

Daily craving, negative affect and anhedonia.—Participants provided ecological momentary assessment (EMA) data nightly via IVR [42]. Participants were prompted to complete a report every night an hour before going to bed from 1 week pre-TQD through 2 weeks post-TQD to assess daily smoking, medication use (patch and mini-lozenge use), and how they felt in general over the day in terms of craving, negative affect, and anhedonia.

Craving was assessed by taking the average of 2 craving items, “Wanting to smoke” and “Bothered by urges to smoke” (r=.70) adapted from the Wisconsin Smoking Withdrawal Scale (WSWS; [43]) and rated on a scale from 1 (not at all) to 7 (extremely). Negative affect was assessed by taking the average of 3 adapted WSWS items, “Feeling anxious, worried or stressed,” “Feeling angry or irritated,” and “Feeling sad or unhappy” (Cronbach’s α=.81) rated on the same 7-point scale. Craving and negative affect scores were moderately correlated both pre-TQD (r=.40) and post-TQD (r=.52). Anhedonia was assessed with 3 EMA items [32] assessing pleasure experienced that day in 3 domains (social contact, school/work, and recreation) (α=.84) used in validated anhedonia scales [44, 45]. These items were rated on a scale ranging from 1 (no pleasure) to 7 (extreme pleasure), reverse coded so that higher scores indicated greater anhedonia. Anhedonia scores were weakly correlated with craving (r=−.02 pre-TQD, r=.10 post-TQD) and negative affect (r=.18 pre-TQD, r=.19 post-TQD).

Patch and mini-lozenge use.—Patches were available for at least 8 weeks post-TQD in both treatment conditions. Patch use was assessed nightly as a binary variable (1=used a patch, 0=no patch) from the TQD through 2 weeks post-TQD. The number of mini-lozenges used (range 0–25) was assessed nightly in the A-OT condition from 1 week pre- to 2 weeks post-TQD.

Cigarette counts.—The number of cigarettes smoked each day was assessed nightly from 1 week pre- to 2 weeks post-TQD in both conditions.

7-day point-prevalence abstinence 1-month post-TQD.—Abstinence was coded as binary (1= abstinent, 0=smoking or missing) based on self-reported smoking over the past 7 days collected via timeline follow-back interview [46].

Data analyses

Time-varying effects models were fit using SAS macro suite %TVEM, version 3.1.1 [47]. Parameter coefficients were estimated using maximum likelihood estimation and the p-spline method, which selects optimal regression coefficient functions with an optimal number of knots [48]. We examined time-varying effects of randomly assigned treatment condition (A-OT versus RUC) separately on craving, negative affect, and anhedonia from 1 week pre-TQD (when mini-lozenges and psychosocial treatment were available in A-OT) to 2 weeks post-TQD. Next, we explored within-person time-varying relations between patch use and symptoms in the combined sample, and the interaction between treatment condition and within-person patch effects post-TQD (patch use started on the TQD). In the A-OT condition only, we explored within-person relations between mini-lozenge use and symptoms, and the interaction between mini-lozenge and patch use over 2 weeks post-TQD (to see if mini-lozenge-symptom relations differed depending on patch use). To disaggregate within- and between-person effects, we person-mean-centered patch and mini-lozenge use variables and controlled for person-level averages of patch or mini-lozenge use in models. Exploratory models examining interactions between within-person patch or mini-lozenge use and smoking status in TVEM models are presented in supplementary material online.

Models were conducted both with and without the following covariates: baseline FTCD total score, clinical site (0=Milwaukee, 1=Madison), a binary indicator of assessment epoch (pre- vs. post-quit), a time-varying binary indicator of EMA-assessed daily smoking (1=smoked, 0=abstinent), and a post-quit indicator by daily smoking status interaction term. Model results are displayed graphically with 95% confidence intervals (CI) around daily average intercepts or coefficients (slopes). Slopes for a particular day are significantly different from 0 at α=0.05 if the 95% CI does not include 0. Models with and without covariates yielded similar results. We present models adjusted for FTCD and daily smoking status in the results and note where the adjusted and unadjusted models differed.

Logistic regression models separately tested relations between mean craving, negative affect, anhedonia, patch use, and mini-lozenge use rates in the first 2 weeks post-TQD and later intent-to-treat (with missing abstinence imputed as smoking), 7-day point prevalence abstinence 1-month post-TQD. Participants who provided at EMA data on at least one of the 21 days of interest were included in analyses to make use of all of available observations [48].

Results

Participant characteristics

A total of 11,038 EMA reports (90.4% of those scheduled) from the 574 participants with at least one EMA report (92.1% of the 623 randomized) were included in TVEM analyses. Table 1 presents demographics and baseline smoking history variables for the study sample, by treatment condition. The analyzed sample differed from those without sufficient data (n=49) in gender composition and age. More men (n=28, 10.5% of 266 enrollees) than women (n=21, 5.9% of 357 enrollees) failed to provide EMA data (χ2(1, N=623)=4.54, p=.03). Those retained were significantly older (M=50.1, SD=12.7 years) than those who attrited (M=45.2, SD=12.4 years, t(620)=2.58, p=.01).

Time varying effects of A-OT versus RUC Time-varying effects of A-OT on symptoms, with baseline FTCD and daily smoking covariates, are shown in Figure 2. Relative to RUC, A-OT significantly suppressed craving from 6 days pre-TQD through 10 days post-TQD (β=−0.27 to −0.46). A-OT treatment did not significantly affect negative affect in models with covariates, but suppressed negative affect from 2 days pre- to 3 days post-TQD in unconditional models (not shown). A-OT significantly suppressed anhedonia on days 1–12 post-TQD (β=−0.24 to −0.38) relative to RUC. Site was associated with symptoms, such that Madison participants reported greater post-TQD craving and negative affect (not shown), but including site did not change the pattern of treatment effects. The indicators of site, assessment epoch (pre- vs. post-TQD), the non-significant interaction between epoch and daily smoking status were pruned from this and all subsequent models without changing the pattern of results.

Time varying effects of within-person daily patch use—Figure 3 shows the rates of patch use by day through 2 weeks post-TQD in each treatment condition. Patch use rates exceeded 70% every day in both conditions, but were higher in A-OT than in RUC. Greater patch use predicted abstinence 1-month post-TQD in logistic regression (B=2.21, SE=0.42,

Wald=28.21, OR=9.13, 95% CI=4.04–20.66, p<.001), and the relation between patch use and abstinence did not differ by condition (B=−0.06, SE=0.85, Wald=0.01, OR=0.93, 95% CI=0.18–4.89, p=0.93).

Figure 4 illustrates time-varying relations between within-person daily patch use and craving, negative affect, and anhedonia over 2 weeks post-TQD in the combined sample, controlling for baseline FTCD and daily smoking status. Within-person daily patch use was not significantly related to craving, negative affect, or anhedonia, meaning that symptom levels did not differ on days participants deviated from their usual patch use behavior (e.g., wearing one when this was rare for them). Patch use interacted significantly with treatment condition (on days 5–8), however (Figure 5). Patch use was associated with significantly lower negative affect 5–8 days post-TQD in RUC (β=−0.42 to −0.52), but not in A-OT (β=0.30 to 0.58).

Time varying effects of within-person mini-lozenge use in A-OT—Daily means of self-reported number of mini-lozenges used are shown by day in Figure 3. Mini-lozenge count averages were below recommended levels (9–20 lozenges per day) throughout the assessment period, but increased post-TQD. Using more mini-lozenges on average did not significantly predict abstinence 1-month post-TQD in a bivariate logistic regression analysis (B=0.06, SE=0.04, Wald=2.47, OR=1.07, 95% CI=0.99–1.15, p=0.12). Within-persons (Figure 6), using more mini-lozenges than average was associated with greater craving from 1 day pre-TQD to day 5 post-TQD (β=0.04 to 0.07), greater negative affect in the first 4 days post-TQD (β=0.03 to 0.05), but reduced anhedonia on days 10–13 post-TQD (β=−0.06 to −0.12). Wearing a patch moderated relations between mini-lozenge use and symptoms at times. Spikes in mini-lozenge use were more strongly associated with worse craving (β=0.12 to 0.17) and anhedonia (β=0.03 to 0.06) on days 2–3 post-TQD if patch use was above average (i.e., was worn that day, but not all others), and more weakly associated with negative affect 8–10 days post-TQD (β=0.12 to 0.15) if patch use was below average (Figure 7).

Craving, negative affect, and anhedonia relations with abstinence—In multiple logistic regression analyses, mean post-TQD craving (B=−0.39, SE=0.08, Wald=26.59, OR=0.68, 95% CI=0.58–0.79, p<.001) and anhedonia (B=−0.16, SE=0.07, Wald=5.02, OR=0.85, 95% CI=0.74–0.98, p=.03) significantly predicted lower odds of abstinence 1-month post-TQD, but negative affect did not (B=−0.05, SE=0.09, Wald=0.32, OR=0.95, 95% CI=0.80–1.14, p=.57), despite a significant bivariate relation with abstinence (B=−0.30, SE=0.07, Wald=17.44, OR=0.74, 95% CI=0.64–0.85, p<.001). Abstinence odds were significantly higher in Madison than in Milwaukee (B=0.51, SE=.19, Wald=6.93, OR=1.66, 95% CI=1.14–2.42, p=.009).

Discussion

This secondary analysis of pericessation craving, negative affect, and anhedonia detected significant benefits of an effective multi-component smoking cessation treatment [12] in terms of craving and anhedonia suppression, in comparison with usual care. Craving suppression was evident in A-OT versus RUC in the week preceding the TQD, when

psychosocial treatment was available in both conditions but mini-lozenges were available only in A-OT. A-OT suppression of craving continued through 10 days post-TQD, a period when A-OT received intensive psychosocial support and C-NRT, while RUC received patch monotherapy and much less psychosocial support. Anhedonia was significantly lower for the first 12 days of the quit attempt in A-OT versus RUC, as well. Negative affect was not significantly improved by A-OT, and an interaction showed that within-person patch use was associated with reduced negative affect only in RUC (not A-OT), and only when smoking (not abstinent). Mini-lozenge use was generally positively related to symptom severity, particularly if abstinent before the TQD. These results suggest that precessation medication may enhance craving control and that C-NRT and/or intensive psychosocial support may improve control of pericessation craving and anhedonia, motivationally significant symptoms that predict later abstinence. Although formal mediation analyses were not conducted, these results are consistent with previous research [4, 27, 32, 35, 49, 50].

Improved management of craving and anhedonia may be attributable to psychosocial components in A-OT, nicotine mini-lozenges, and/or higher rates of patch use in A-OT than in RUC. Between persons, higher rates of nicotine patch use, but not nicotine mini-lozenge use, predicted abstinence at 1-month post-TQD. Within participants, however, nicotine patch use was not associated with lower symptom ratings in A-OT. In RUC, using a patch when this was rare was associated with lower negative affect on days 5–8 post-TQD, but this was not true in A-OT, where daily patch use rates were high. In the first few days of the quit attempt, patch use was associated with lower symptoms levels only if a person was smoking; patch use was associated with higher symptoms on abstinent days. As such, differences in within-person acute patch use relations with symptoms do not seem to account for greater reductions in craving and anhedonia in A-OT than RUC.

Within persons in A-OT, use of more mini-lozenges was associated with greater craving and negative affect early in the quit attempt if abstinent, and with greater symptoms later in the quit attempt if not using a patch. This pattern of results indicates that spikes in mini-lozenge use might occur in response to more severe withdrawal. More mini-lozenge use was associated with reduced anhedonia during the end of the second week post-TQD, at least among those smoking or using patches. This may reflect a benefit of intensifying rather than tapering mini-lozenge use, but the clinical significance of this delayed effect is unclear. More use of ad lib NRT may sometimes quell symptoms or may sometimes reflect greater abstinence motivation or distress.

The following limitations should be considered when interpreting these results. First, we are not able to attribute the effects of A-OT on craving and anhedonia to specific components of A-OT, as this was a comparison of multicomponent treatments rather than a factorial or dismantling study that permits isolation of the effects of specific intervention components. The psychosocial components of A-OT treatment may have cumulative effects that cannot be pinpointed to specific days, particularly given that the dynamic effects of such components on mediators were not assessed. Medication use is also self-selected and likely related to smoking status [51], which also limits inferences that can be drawn from within-person medication use analyses. Second, we did not conduct formal mediation analyses or analyses of treatment effects on prolonged abstinence of more clinical significance (e.g., 6

months post-TQD) due to the complexity of examining treatment-mediator effects that vary by day. Third, the clinical significance of the roughly 0.2–0.4-point reductions observed in craving and anhedonia is difficult to state, although lower mean levels of craving and anhedonia were predictive of abstinence. Fourth, we did not account for random effects of clinics or site in computing standard errors [52]. However, treatment randomization and treatment delivery by research staff rather than clinic personnel possibly mitigate the confounding effects of clinics. Despite site differences in craving, negative affect, and abstinence, controlling for site did not change the pattern of results. Finally, the %TVEM macro does not yet support integration across multiple imputed datasets. Instead, maximum likelihood estimation was used to handle missing EMA data.

Despite these limitations, results demonstrate benefits of A-OT (versus RUC) in reduced craving and anhedonia. These results suggest that craving and anhedonia are sensitive to intensive treatment at both the precessation and cessation phases of treatment [6] and predictive of abstinence. More broadly, the time-varying effects observed highlight the value of a phase-based approach to smoking treatment, and of examining time as a moderator of treatment effects. Treatments may have different functional relations with smoking motivation at different points in time; understanding this may facilitate development of treatment packages aimed at varying targets (e.g., craving, anhedonia) to maximize benefits.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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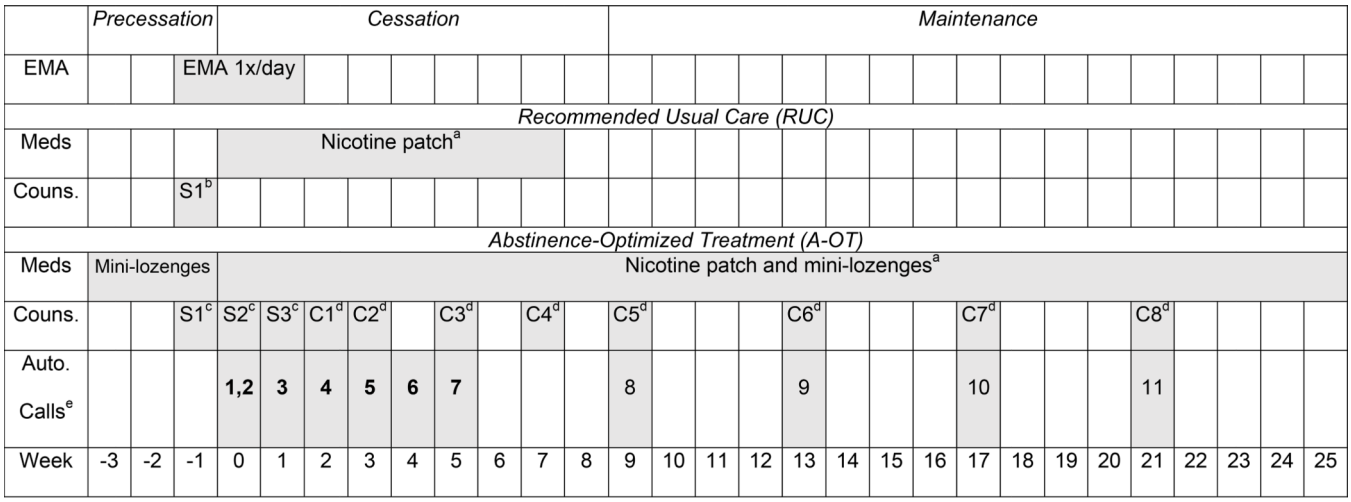

Figure 1. Timeline of study phases, ecological momentary assessment, and treatments by treatment condition

[a] Participants were encouraged to use the full-course of medication, regardless of whether they had returned to smoking (unless they experienced intolerable side effects).

[b] In RUC, Session 1 (S1) involved a face-to-face counseling session of 10 minutes, fax referral to the Wisconsin Tobacco Quit Line, and instruction in downloading the QuitNow smartphone app.

[c] In A-OT, Session 1–3 (S1-S3) were 20-minute face-to-face counseling sessions.

[d] In A-OT, Calls 1–8 (C1-C8) were 15-minute counseling calls.

[e] In A-OT, all participants received the first 7 automated calls to promote medication adherence (shown in bold); only those who were still smoking at week 8 received automated calls 8–11.

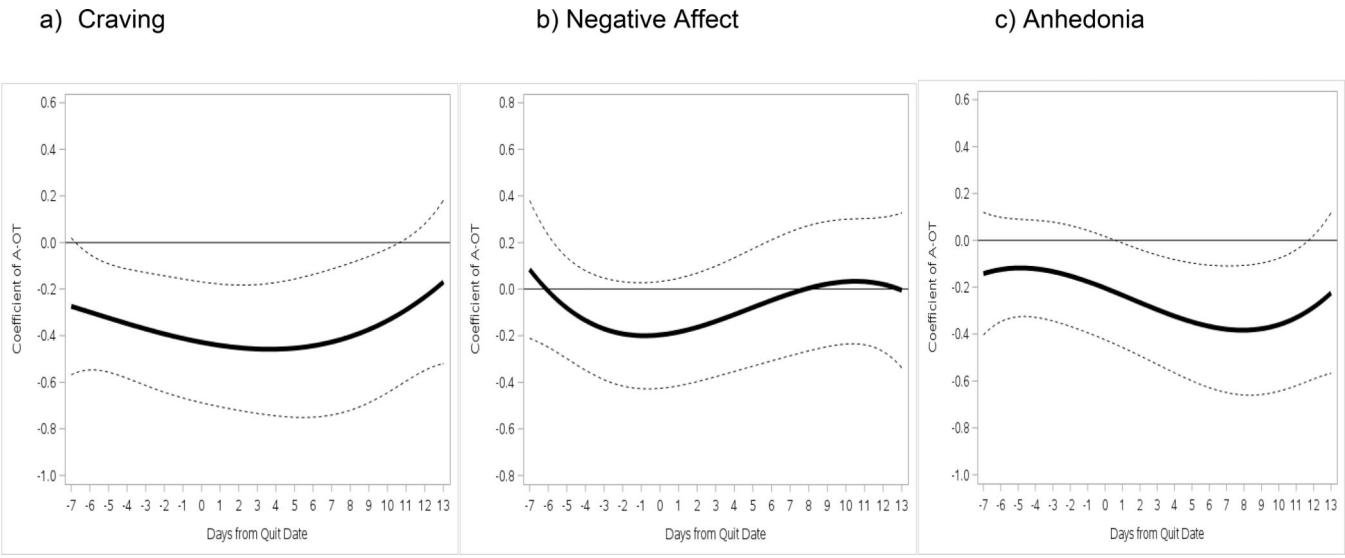

Figure 2.

Time-varying associations between Abstinence-Optimized Treatment (A-OT) vs. Recommended Usual Care (RUC) and (a) craving, (b) negative affect, and (c) anhedonia, with corresponding 95% confidence intervals (dotted lines) from 1 week pre-TQD to 2 weeks post-TQD.

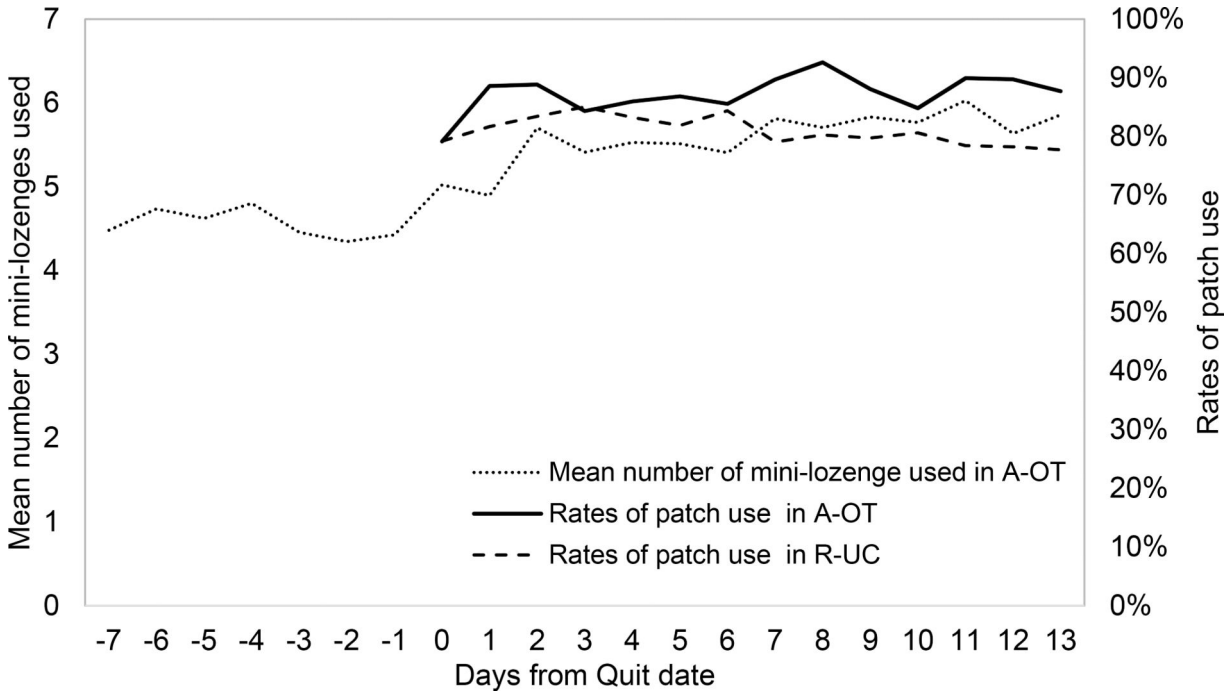

Figure 3.
Mean number of mini-lozenge used in A-OT during 1 week pre-TQD and 2 weeks post-TQD and rates of patch use in A-OT and RUC during 2 weeks post-TQD.

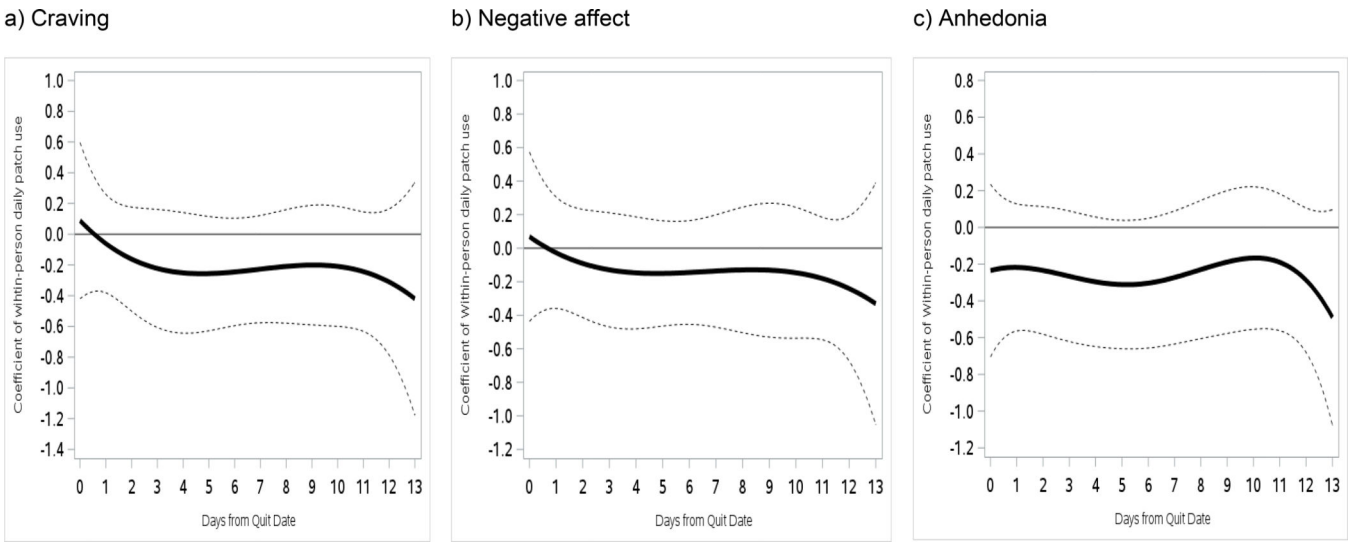

Figure 4.

Time-varying main effects of within-person daily patch use on (a) craving, (b) negative affect, and (c) anhedonia from the TQD to 2 weeks post-TQD. 95% confidence intervals are indicated by dotted lines in all panels.

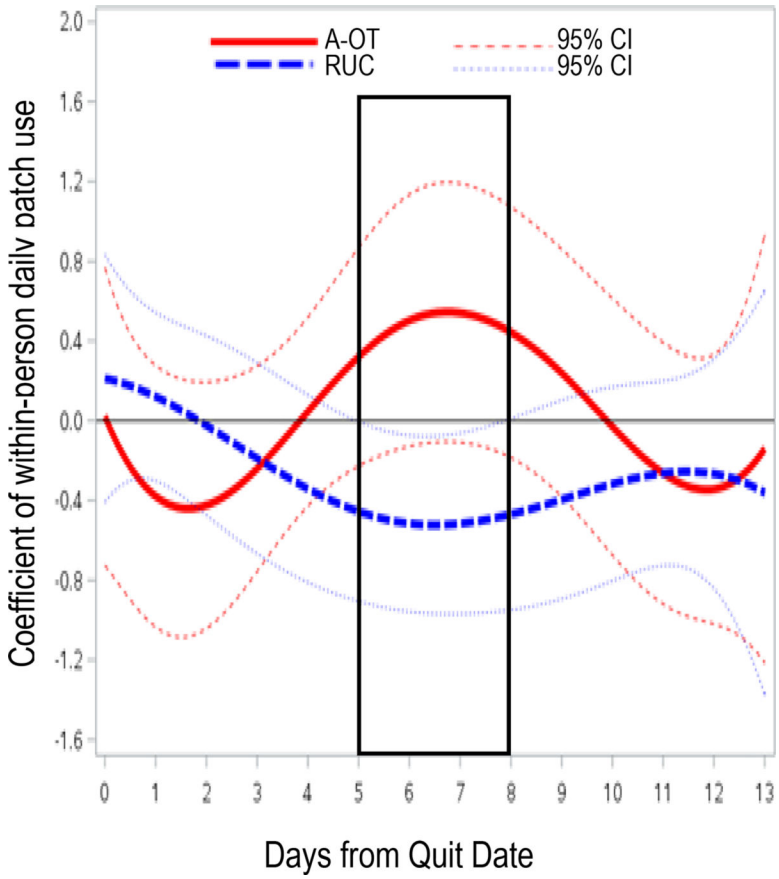

Figure 5.

Simple time-varying main effects of patch use on negative affect by treatment condition. Days on which there were significant interaction effects are the days within the black rectangle. 95% confidence intervals are indicated by dotted lines.

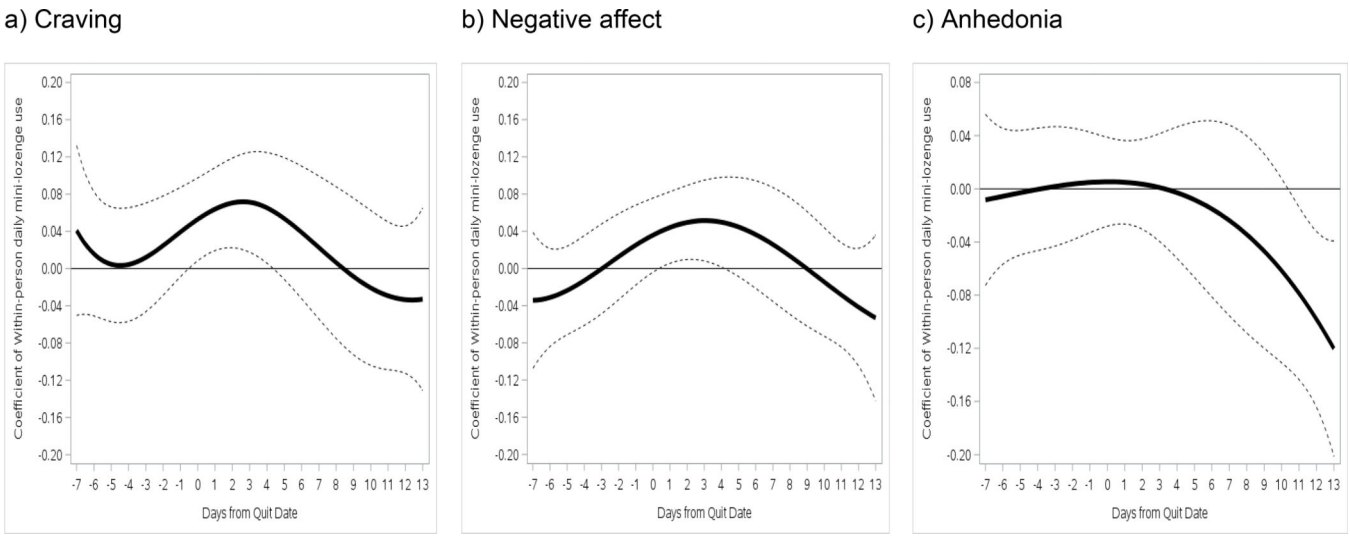

Figure 6.

Time-varying main effects of within-person daily mini-lozenges use on (a) craving, (b) negative affect, and (c) anhedonia from 1 week pre-TQD to 2 weeks post-TQD. 95% confidence intervals are indicated by dotted lines in all panels.

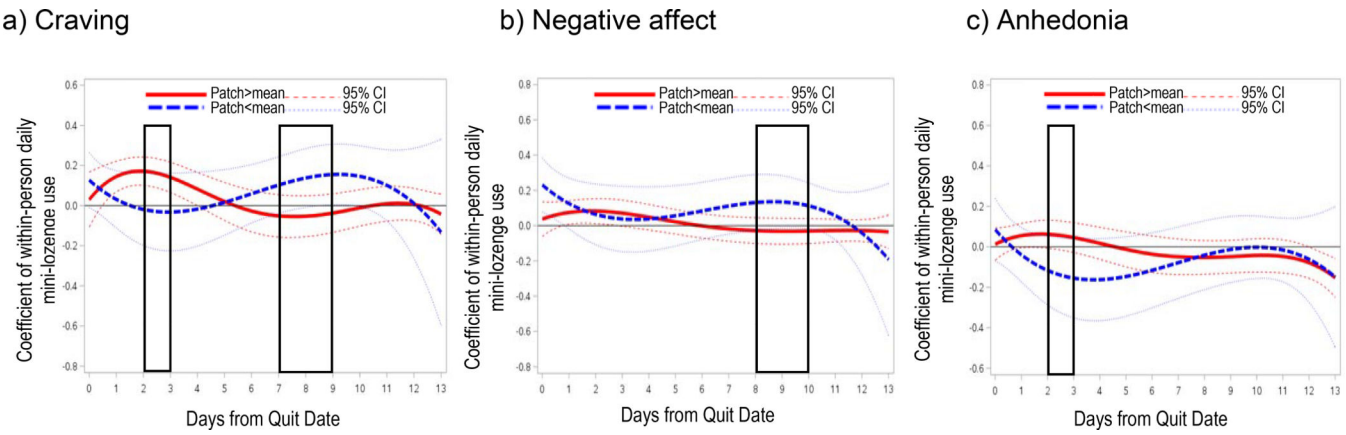

Figure 7.

Simple time-varying main effects of within-person daily mini-lozenge use in A-OT on (a) craving, (b) negative affect, and (c) anhedonia by patch use over 2 weeks post-TQD. Days on which there were significant interaction effects are the days within the black rectangles. 95% confidence intervals are indicated by dotted lines.

Table 1.

Sample characteristics by treatment condition

	Total sample (n=574)	Recommended Usual Care (n=298)	Abstinence-Optimized Treatment (n=276)
		n (%)	
Gender (Female)	336 (58.5)	179 (60.1)	157 (56.9)
Race			
White	396 (69.1)	200 (67.1)	196 (71.3)
Minority group	177 (30.9)	98 (32.9)	79 (28.7)
Education			
Less than college	315 (55.0)	176 (59.3)	139 (50.4)
College or more	258 (45.0)	121 (40.7)	137 (49.6)
Annual household income			
Less than $24,999	275 (53.2)	139 (51.3)	136 (55.3)
$25,000 or more	242 (46.8)	132 (48.7)	110 (44.7)
		Mean (SD)	
Age	50.1 (12.7)	49.6 (12.9)	50.7 (12.5)
Cigarettes per day	16.8 (9.3)	17.1 (9.8)	16.4 (8.7)
FTCD score	4.8 (2.2)	4.9 (2.2)	4.7 (2.2)
Quitting motivation (1–7)	6.4 (1.0)	6.4 (1.0)	6.4 (1.0)
Quitting confidence (1–7)	5.6 (1.4)	5.5 (1.5)	5.7 (1.4)

FTCD: Fagerström Test of Cigarette Dependence.