Table 1. Descriptive Statistics of Study Variables for Placebo, Monotherapy, and Combination Therapy Groups

	Placebo, *M* (*SD*)	Monotherapy, *M* (*SD*)	Combination Therapy, *M* (*SD*)
Craving	4.6 (3.6)	4.4 (3.5)	4.0 (3.4)
Negative affect	1.7 (1.7)	1.5 (1.5)	1.4 (1.4)
Baseline dependence	5.3 (2.1)	5.2 (2.2)	5.4 (2.0)
Number of cigarettes	0.4 (2.0)	0.2 (1.7)	0.2 (1.3)

Note. Craving, negative affect and number of cigarettes was assessed using EMA data and represent means scores across time and individuals; baseline dependence was measured once at baseline, and it represents the mean across individuals; $N = 1{,}106$ individuals.

the other predictors. The choice of parameterization should be driven by ease of interpretation of the results. For each group, the following model was specified for predicting craving from the time-varying covariate negative affect (NA) and baseline dependence (FTND), controlling for any cigarette use (CIGUSE) during the 2-week time period:

$$\begin{aligned}\text{Craving}_{ij} = {} & \beta_0(t) + \beta_1(t) \times \text{NA}_{ij} + \beta_2(t) \times \text{FTND}_i \\ & + \beta_3(t) \times \text{CIGUSE}_{ij} + \varepsilon_{ij}\end{aligned} \tag{2}$$

where Craving_{ij}, NA_{ij}, and CIGUSE_{ij} are intensively measured longitudinal variables for individual i from assessment j measured at time t_{ij} and FTND_i represents baseline nicotine dependence for individual i. In this model, $\beta_0(t)$ represents mean craving over time for individuals with values of zero on all other predictors. Similarly, $\beta_1(t)$ is a slope function describing the time-varying association between negative affect and craving, $\beta_2(t)$ is a slope function describing the time-varying association between baseline dependence and craving, and $\beta_3(t)$ is a slope function describing the time-varying association between cigarette use and craving.

To prepare data for the analysis, we stacked the data so that each record contained one EMA assessment for an individual (i.e., each individual had j records in the dataset). In addition to the predictor and outcome variables described above, two additional variables were necessary to run the TVEM. First, a time variable was created, representing the time at which a given EMA took place (this is t_{ij}). Given that assessment times were random and differed for each person, the time scale can be considered as nearly continuous. Second, to enable the program to calculate the intercept function (see Supplementary Appendix; Yang et al., 2012), we created a variable that was coded 1 for every record. Readers who wish to study technical details are referred to the study by Tan et al. (2012).

Software

The SAS macro %TVEM_normal was used to estimate the model. This macro is available free for download at methodology.psu.edu. See the Supplementary Appendix for the SAS syntax used to specify the final model for each treatment group.

RESULTS

Figure 1 presents the intercept functions separately for the placebo group (solid line) and each treatment group (dashed lines), along with the corresponding 95% pointwise confidence intervals. At any point in time, the level on this curve represents the mean level of craving for nonsmoking individuals in that treatment group with average negative affect and baseline dependence (i.e., for individuals with values of 0 on all covariates). If at a particular time point a confidence interval does not include 0, there is a nonzero mean level of craving, that is, there is a significant urge to smoke. Further, if at a particular time the confidence intervals for two of the groups do not overlap, craving is statistically significant between those groups at that specific time. The TVEM SAS macro does not provide simultaneous confidence intervals, which are appropriate for overall group comparisons across the entire period of time; this is an important topic for future research. The 95% pointwise confidence intervals, however, are appropriate for comparing groups at a particular time. Figure 1 shows that, among nonsmoking individuals with average negative affect and baseline dependence, craving decreased over time for all treatment groups; between Days 5 and 8, those in the combination therapy group had significantly lower mean craving.

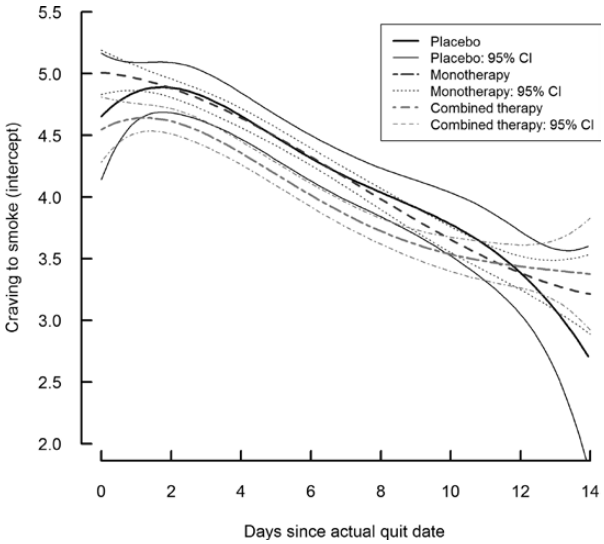

Figure 1. Intercept function (i.e. time-varying mean craving during first 2 weeks of quit attempt) by treatment group.

Figures 2 and 3 show the time-varying association between craving and two covariates for the placebo group (solid line) and two treatment groups (dashed lines), along with the corresponding 95% confidence intervals. The time-varying effect of negative affect is depicted in Figure 2, and the time-varying effect of baseline dependence is depicted in Figure 3. At any point in time, the level on a curve represents that time-specific

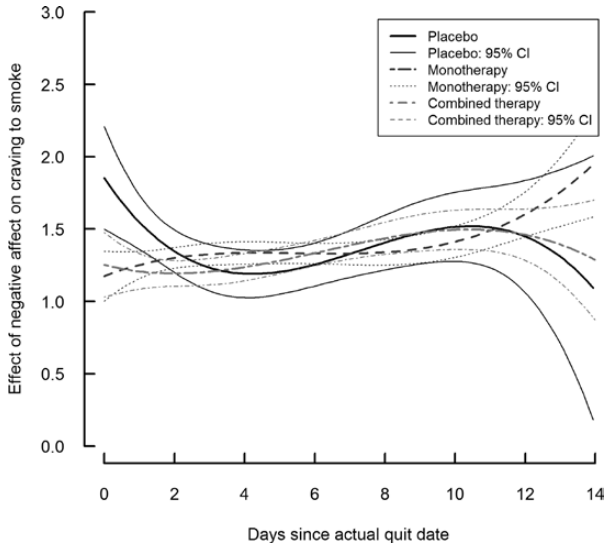

Figure 2. Time-varying effect of negative affect on craving by treatment group.

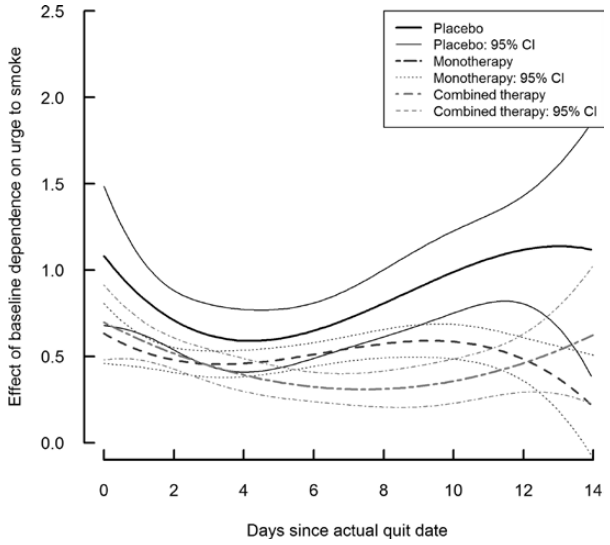

Figure 3. Time-varying effect of baseline nicotine dependence on craving by treatment group.

association between the covariate and craving. If at a particular time point a confidence interval does not include 0, there is significant effect of the covariate on craving. Further, if at a particular time the confidence intervals for two of the groups do not overlap, the effect of the covariate on craving is significantly different between those groups.

Figure 2 shows that immediately upon quitting (Days 0 and 1), the association between negative affect and craving was significantly stronger among individuals in the placebo group, suggesting that monotherapy and combination therapy both had a positive impact early in the quit attempt. However, by Day 2 the association within the placebo group weakened to match that of the treatment group, and from Day 2 to Day 14, there was a significant positive association between negative affect and craving that did not differ between groups. This association increased slightly over the time period although it never reached the original strength observed in the placebo group. To further interpret the slight increase over time in association within the monotherapy and combination therapy groups, an increase of 1 *SD* on negative affect was associated with about a 1.2-unit increase in craving at the TQD, whereas a 1 *SD* increase in negative affect was associated with a 1.5-unit increase in craving at Day 12. The association between negative affect and craving increased over the entire time period in a roughly linear manner in the groups receiving treatment, whereas for the placebo group, there was a sharper decline during Days 0–4, followed by a somewhat sharper increase through Day 10.

Figure 3 represents the time-varying association between baseline dependence and craving, showing that they were significantly correlated at all points during the study for all three treatment groups (although this associated approached nonsignificance at Day 14 for the monotherapy group). This association was relatively stable over time for the monotherapy and combination therapy groups, with 1 *SD* higher baseline dependence associated with approximately a 0.5-unit higher craving. During Days 6–10, combination therapy resulted in a significantly weaker association compared with the monotherapy group. In the placebo group, the association doubled with time between Days 4–14. For these individuals, 1 *SD* higher baseline dependence was associated with 0.6-unit higher craving at Day 4 and 1.2-unit higher craving at Day 12. The difference between placebo and combination therapy groups was significant from Days 6 to 13, when the association between baseline dependence and craving was stronger for the placebo group. The difference between placebo and monotherapy groups was less pronounced and only present from Days 9 to 13.

DISCUSSION

Implications of Results for Theory and Practice

Consistent with previous literature, we found that overall craving levels decrease over the first 2 weeks postquit (Hughes, 2007). This demonstrates that regardless of treatment condition, craving does decrease over the first 2 weeks of a quit attempt.

It is important to disentangle the finding that negative affect becomes more strongly associated with craving over time, given that both craving and negative affect may be related to relapse risk, with craving perhaps being a more influential predictor (Chandra, Scharf & Shiffman, 2011; Piper et al., 2011; Van Zundert, Ferguson, Shiffman, & Engels, 2012). The mechanisms and direction of this association are unclear. It may be that smokers are initially able to cope with negative affect using limited alternate coping strategies, but over time, the ability to use such strategies, or the effectiveness of such strategies, may diminish, leaving smokers with less and less ability to resist the urge to smoke. Conversely, given that the association between craving and negative affect is likely bidirectional, it may be that smokers are able to tolerate cravings initially, but over time the cravings come to elicit an increasingly stronger negative affective response. This may, in turn, increase the smokers' urges to smoke in order to alleviate such negative affect. While there was an initial effect of treatment on the association between

Shiffman, S., Scharf, D. M., Shadel, W. G., Gwaltney, C. J., Dang, Q., Paton, S. M. & Clark, D. B. (2006). Analyzing milestones in smoking cessation: illustration in a nicotine patch trial in adult smokers. *Journal of Consulting and Clinical Psychology*, *74*, 276–285. doi:10.1037/0022-006X.74.2.276

Shiyko, M. P., Lanza, S. T., Tan, X., Li, R., & Shiffman, S. (2012). Using the time-varying effect model (TVEM) to examine dynamic associations between negative affect and self confidence on smoking urges: differences between successful quitters and relapsers. *Prevention Science*, *13*, 288–299. doi:10.1007/s11121-011-0264-z

Siegel, S. (1983). Classical conditioning, drug tolerance, and drug dependence. In R. G. Smart, F. B. Glaser, Y. Israel, R. Kalant, E. Popham & W. Schmidt (Eds.), *Research advances in alcohol and drug problems* (7th ed.), New York, NY: Plenum. *7*, 207–246.

Smyth, J. M., & Stone, A. A. (2003). Ecological assessment research in behavioral medicine. *Journal of Happiness Studies*, *4*, 35–52.

Solomon, R. L., & Corbit, J. D. (1974). An opponent-process theory of motivation. I. Temporal dynamics of affect. *Psychological Review*, *81*, 119–145. doi:10.1037/h0036128

Stone, A. A., & Shiffman, S. (1994). Ecological momentary assessment (EMA) in behavorial medicine. *Annals of Behavioral Medicine*, *16*, 199–202.

Stone, A. A., & Shiffman, S. (2002). Capturing momentary, self-report data: a proposal for reporting guidelines. *Annals of Behavioral Medicine*, *24*, 236–243. doi:10.1207/S15324796ABM2403_09

Tan, X., Shiyko, M., Li, R., Li, Y., & Dierker, L. (2012). Intensive longitudinal data and model with varying effects. *Psychological Methods*, *17*, 61–77. doi:10.1037/a0025814

Van Zundert, R. M., Ferguson, S. G., Shiffman, S., & Engels, R. (2012). Dynamic effects of craving and negative affect on adolescent smoking relapse. *Health Psychology*, *31*, 226–234. doi:10.1037/a0025204

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: the PANAS scales. *Journal of Personality and Social Psychology*, *54*, 1063–1070. doi:10.1037/0022-3514.54.6.1063

Welsch, S. K., Smith, S. S., Wetter, D. W., Jorenby, D. E., Fiore, M. C., & Baker, T. B. (1999). Development and validation of the Wisconsin Smoking Withdrawal Scale. *Experimental and Clinical Psychopharmacology*, *7*, 354–361. doi:10.1037/1064-1297.7.4.354

Wikler, A. (1980). *Opioid dependence*. New York, NY: Plenum.

Yang, J., Tan, X., Li, R., & Wagner, A. (2012). *TVEM (time-varying effect model) SAS macro suite users' guide* (Version 2.0.0). University Park, PA: The Methodology Center, Penn State. Retrieved from http://methodology.psu.edu

Zhou, X., Nonnemaker, J., Sherrill, B., Gilsenan, A. W., Coste, F., & West, R. (2009). Attempts to quit smoking and relapse: factors associated with success or failure from the ATTEMPT cohort study. *Addictive Behaviors*, *34*, 365–373.