

# SMOKING REDUCTION TRAJECTORIES AND THEIR ASSOCIATION WITH SMOKING CESSATION: A SECONDARY ANALYSIS OF LONGITUDINAL CLINICAL TRIAL DATA

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Character count (with spaces): 2490/2500

## Significance

Tobacco smoking remains the leading cause of preventable death worldwide, with quitting the only cure. Smoking reduction (SR) can be recommended to people unmotivated to quit, but evidence on reduction outcomes is mixed, and little is known about how people reduce their smoking without receiving specific instructions. Despite a range of available behavioral SR strategies, there is no clear evidence to support one method over others.

## Methods

In a pre-registered secondary analysis of five randomized, placebo-controlled trials of nicotine replacement therapy (NRT), we determined latent smoking trajectories using cigarettes per day (CPD) at four time points across 26 weeks. Participants were adults who smoked daily and were unmotivated to quit. All were instructed to reduce their cigarettes as much as possible. We used predictive modeling to identify associations between smoking trajectories and participant characteristics at baseline (e.g., sex, age, nicotine dependence, depression, anxiety). Finally, we assessed whether smoking trajectories improved prediction of smoking cessation at trial follow-up week 52.

## Results

Participants (N=2066) smoked a mean  $27.26 \pm 9.74$  CPD at baseline. Of these, 1783 had CPD values for at least two time points and were included in analyses. We selected a three-class trajectory model: Class 1 (n=186) achieved the greatest reduction in CPD from baseline (57-90%), mostly within the first two weeks; Class 2 (n=803) reduced by ~50%; Class 3's (n=794) CPD remained stable.

Older, male participants with lower baseline anxiety were most likely to reduce their smoking (cross-validated AUCs = 0.520-0.684,  $p$ 's < .01).

Latent class improved prediction of smoking cessation at the 52-week follow-up by 14.4% over prediction using baseline characteristics alone (AUC =  $0.776 \pm 0.010$ ,  $p = 0.002$ ). Those who reduced their smoking by more than 50% were nearly 90% more likely to quit than those who reduced minimally (ORs compared to Class 1: Class 2 =  $0.111 \pm 0.013$ , Class 3 =  $0.070 \pm 0.005$ ).

## Conclusions

Our findings quantified the level of SR (more than 50%) most associated with smoking cessation and identified participant characteristics that predicted greater magnitudes of reduction among people unmotivated to quit at baseline. We emphasize the importance of reducing smoking within the first two weeks of an intervention, as this group was nearly twice as likely to achieve complete cessation. This work may help clinicians identify patients most likely to quit and those in need of additional support.

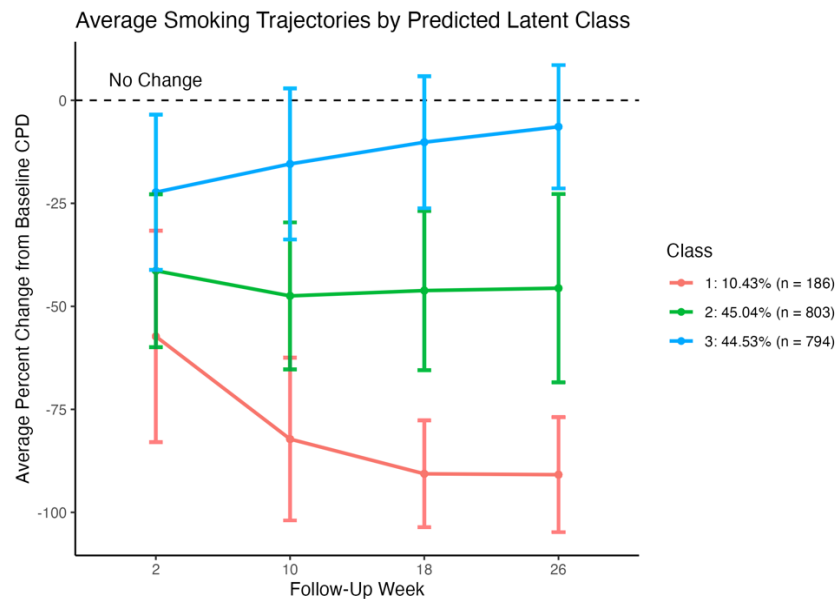


Figure 1 Average smoking trajectories for the 3-class model (i.e., change from baseline smoking rate) ( $n = 1783$ ). Error bars represent SD from average CPD at each trial follow-up point.

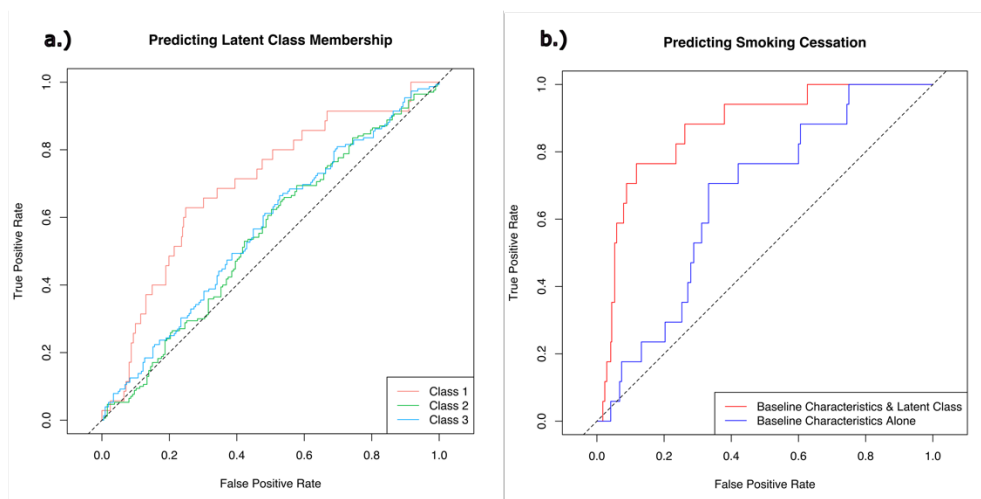


Figure 2 Receiver operating characteristic (ROC) curves for regularized binary logistic regression predictive models. **a.)** Prediction of smoking trajectories as a proportion of baseline smoking during the trial. Each curve represents one-versus-all prediction to latent trajectories 1, 2, and 3 in turn. The model predicting membership to Class 1, the group who reduced the most, performed best ( $AUC = 0.657 \pm 0.027$ ). All three models performed better than classification using a permuted null distribution ( $p$ 's  $< .001$ ).

**b.)** Smoking cessation prediction 6 months after the trial using participant baseline characteristics alone (blue) and baseline characteristics plus latent class as a predictor (red). Adding latent class as a predictor improved classification performance by an average of 14.4% ( $AUC = 0.776 \pm 0.010$ ,  $p = 0.002$ ), suggesting smoking trajectories among people not looking to quit may be meaningful for long-term cessation outcomes. Each model performed better than classification using a permuted null distribution ( $p$ 's  $< .001$ ).