Supplement to:

Smoking reduction trajectories and their association with smoking cessation: A secondary analysis of longitudinal RCT data

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## Latent Class Analysis Model Fit Information

Smoking trajectories were fit to percent change in cigarettes per day (CPD) from baseline using the distributions shown in sFigure 1 for each trial follow-up point except Week 52, which was reserved for smoking cessation prediction.

## Updated Smoking Cessation Verification Guidelines

Using <=11ppm CO as the threshold for biochemically verified smoking cessation, 135/1784 (7.5%) meet abstinence criteria (40.8% of Class 1, 4.7% of Class 2, and 2.6% of Class 3), compared with 122/1784 (6.8%) using <6ppm CO (37.6% of Class 1, 4.2% of Class 2, and 2.3% of Class 3. Using <11ppm CO as a verification threshold, participants in Classes 2 and 3 were substantially less likely to achieve smoking cessation 6 months following the trial compared to those in Class 1 (Class 2 OR = 0.112 ± 0.057, Class 3 OR = 0.066 ± 0.007).

Given the relatively small impact of reducing the verification threshold, we used <6ppm for smoking cessation predictive modeling, which is consistent with the most recent guidance.(1)

## Variable Coding

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Name | | | Type | Values |
| Age | | | Numeric | Years |
| Sex | | | Categorical | * Male * Female |
| Age Started Smoking | | | Numeric | Years |
| Carbon Monoxide (CO) | | | Numeric | Parts Per Million (ppm) |
| Cigarettes Per Day (CPD) | | | Numeric | Self-report Average |
| Fagerstrom Test for Nicotine Dependence | | | Numeric | Summary Score (0-10) |
| Intention to Quit\* | | | Categorical | * Not at all * A little * Somewhat * A lot |
| Last Cigarette Experience (Relief from Smoking Questionnaire) | | Overall | Categorical | * Very unpleasant * Somewhat unpleasant * Neutral * Somewhat pleasant * Very pleasant |
| Pepping-Up Effect |
| Calming Effect |
| Longest Period Without Smoking | | | Categorical | * <1 week * 1 week – 1 month * >1 month – 3 months * >3 months |
| Number of Quit Attempts | | | Categorical | * Never * Once * 2 to 5 times * 6 to 10 times * More than 10 times |
| Time Since Last Quit Attempt | | | Categorical | * Never quit * >12 months * >12-24 months * >6-12 months * 0-6 months |
| Smoking Cessation Quality of Life (SCQoL) | Anxiety | | Categorical | * Not at all * Somewhat * Moderately so * Very much so * Extremely so |
| Depression | |
| RAND 36-Item short-form survey | | Emotional Problems | Numeric | See (2) |
| Emotional Wellbeing |
| Pain |
| Physical Health |
| Social Functioning |
| Study Site | |  | Categorical | * Australia * Denmark * Germany * Switzerland * USA |
| Treatment Group | |  | Categorical | * Active * Placebo |

\*Four of the five included trials captured intention to quit smoking using continuous variables (i.e., “Rate the likelihood that you will quit smoking in the next 6 months,” or “How motivated are you to quit smoking?”), recorded from 0 to 10. In those cases, the continuous scales divided evenly into the four categories described above.

# Supplemental Tables

**sTable 1** Latent class model fit comparison (n = 1783). \*Selected model. BIC = Bayesian Information Criterion, AIC = Akaike Information Criterion.

| Number of Classes | BIC | AIC | Maximum Log-Likelihood |
| --- | --- | --- | --- |
| 1 | 2102.42 | 2085.97 | -1039.98 |
| 2 | 577.95 | 545.04 | -266.52 |
| 3\* | 43.75 | -5.62 | 11.81 |
| 4 | -36.02 | -101.85 | 62.92 |
| 5 | -87.61 | -169.90 | 99.95 |
| 6 | -116.79 | -215.54 | 125.77 |

**sTable 2** \*Average AUC across five-fold cross-validation SEM. \*\*AUC using unseen data. p values represent the probability that the test AUC value is greater than the average computed null AUC value for the test data.

|  | Mean CV AUC\* | Test AUC\*\* |  |
| --- | --- | --- | --- |
| Class 1 vs. All |  | 0.766 |  |
| Class 2 vs. All |  | 0.569 |  |
| Class 3 vs. All |  | 0.585 |  |
| Class 1 vs. Class 2 |  | 0.784 |  |
| Class 1 vs. Class 3 |  | 0.788 |  |
| Class 2 vs. Class 3 |  | 0.523 |  |
| Class 1 vs. All (Placebo NRT Only) |  | 0.717 |  |

# Supplemental Figure Legends

**sFigure 1.** Distributions of changes in cigarettes per day (CPD) as a percentage of baseline smoking rates (Total N = 1783). A value of 0 represent no change in smoking rate from baseline.

A graph of different colored lines

Description automatically generated with medium confidence

**sFigure 2**. Latent class mixture model BIC curve (n = 1783).

A graph with a line

Description automatically generated

**sFigure 3.** 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 ± 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 ± 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).

A comparison of a graph

Description automatically generated

# References

1. Benowitz NL, Bernert JT, Foulds J, Hecht SS, Jacob P, Jarvis MJ, et al. Biochemical Verification of Tobacco Use and Abstinence: 2019 Update. Nicotine Tob Res. 2020 Jun 12;22(7):1086–97.

2. Hays RD, Morales LS. The RAND-36 measure of health-related quality of life. Ann Med. 2001 Jan;33(5):350–7.