

# SMOKING REDUCTION TRAJECTORIES AND THEIR ASSOCIATION WITH SMOKING CESSATION

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## Introduction

- Smoking is the leading cause of premature death and preventable illness worldwide [9].
- A prior Cochrane review found that reduction interventions are no more or less effective than quitting abruptly [5].
- However, little is known about how people reduce their smoking and which smoking reduction patterns predict better cessation outcomes.

## Methods

### Data

- Smoking and demographic information from 5 clinical trials of NRT [1, 2, 4, 7, 8]
- Baseline and follow-up (weeks 2, 10, 18, and 26) CPD were recorded
- CPD and expired breath carbon monoxide (CO) collected at week 56
- Anxiety and depression (from SCQoL[6]), and nicotine dependence (FTND[3]) were recorded at baseline
- Participants in the included trials were:
  - enrolled if they smoked  $\geq 15$  CPD, made a recent quit attempt, were currently unmotivated to quit, and wanted to reduce their smoking.
  - randomly assigned to receive active or placebo NRT (gum or inhaler)
  - told to reduce their smoking as much as possible.

Table 1: Baseline demographic, smoking, and behavioral characteristics.				
	Overall	Class 1	Class 2	Class 3
N (%)	1783 (100)	186 (10.4)	803 (45.0)	794 (44.5)
Study Site (%)				
Australia	360 (20.2)	32 (17.2)	159 (19.8)	169 (21.3)
Denmark	340 (19.1)	35 (18.8)	175 (21.8)	130 (16.4)
Germany	353 (19.8)	60 (32.3)	153 (19.1)	140 (17.6)
Switzerland	301 (16.9)	29 (15.6)	139 (17.3)	133 (16.8)
USA	429 (24.1)	30 (16.1)	177 (22.0)	222 (28.0)
Active NRT (%)	900 (50.5)	125 (67.2)	413 (51.4)	362 (45.6)
Sex = Male (%)	798 (44.8)	96 (51.6)	357 (44.5)	345 (43.5)
Age (m(sd))	44.10(10.72)	45.79 (11.41)	44.26 (10.52)	43.53 (10.73)
FTND (m(sd))	6.14 (2.00)	5.60 (2.13)	6.11 (2.01)	6.30 (1.94)
CPD (m(sd))	27.32 (9.73)	25.65 (10.37)	27.42 (9.78)	27.62 (9.50)
SCQoL Anxiety (m(sd))	0.45 (0.85)	0.41 (0.83)	0.41 (0.82)	0.51 (0.90)
SCQoL Depression (m(sd))	0.29 (0.69)	0.29 (0.69)	0.26 (0.67)	0.32 (0.71)

### Analysis

1. We estimated smoking trajectories using latent class analysis (LCA) as a function of percent reduction in CPD. Participants were assigned to the most likely latent class.
2. We used regularized regression (i.e., elastic net) under a nested cross validation scheme to predict latent class using baseline and demographic characteristics (see Table 1).
3. We predicted biochemically-verified smoking status (CO < 6ppm) at week 52 using baseline and demographic characteristics, plus latent class.

- Pre-registered protocol: <https://osf.io/qh378/>
- Analytical code: <https://github.com/ajbarrows/mcneil-lca>

## Results

### Participants

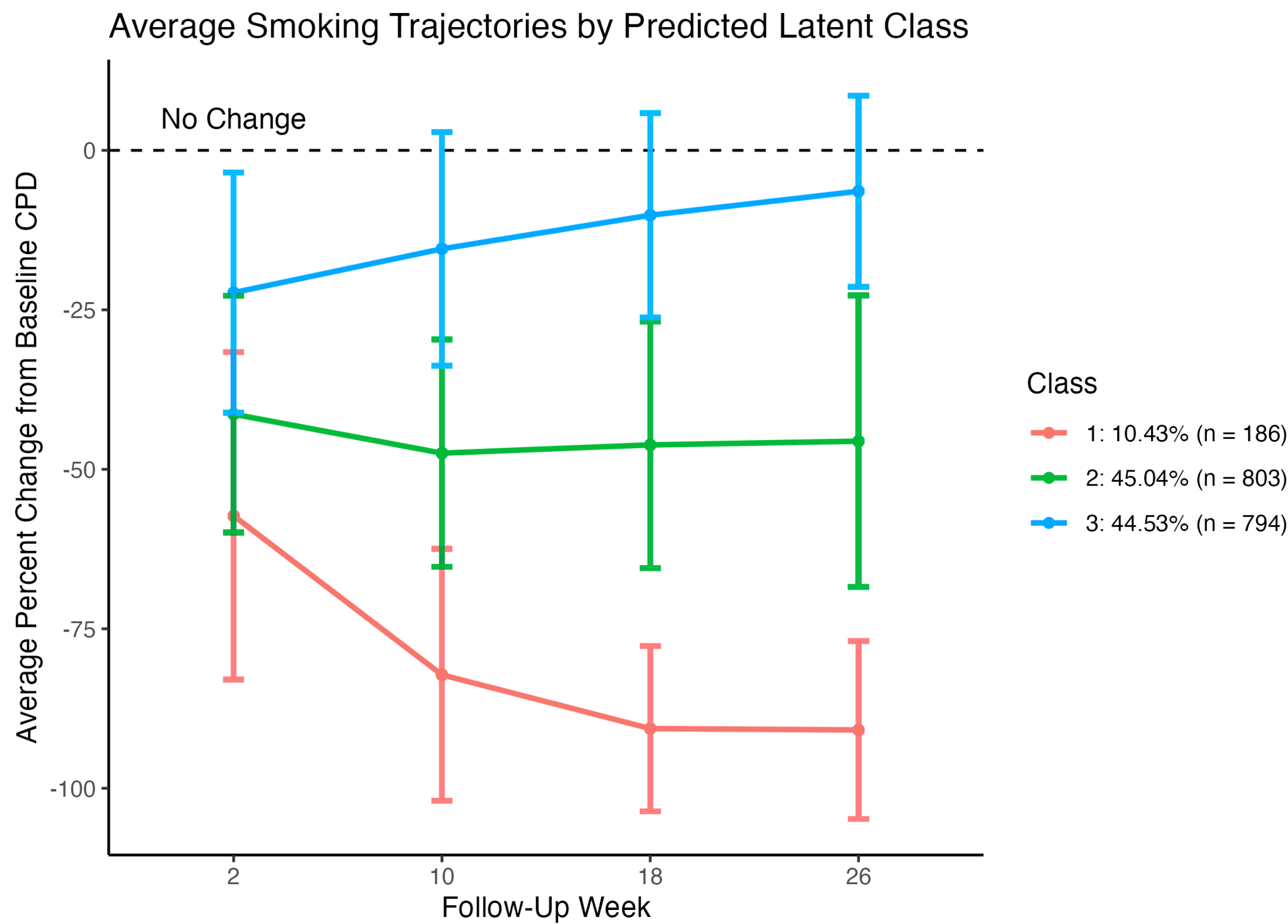
- 108/2066 participants were excluded for missing values.
- Resulting  $n = 1783$ :
  - From five countries
  - 44.8% male, mean age  $44.10 \pm 10.72$  years
  - Smoked an average of  $27.32 \pm 9.73$  CPD

### Latent Class Analysis

- Class 1:  $\sim 10\%$  initially reduced and nearly eliminated smoking
- Class 2:  $\sim 45\%$  reduced by nearly 50% and remained
- Class 3:  $\sim 45\%$  initially reduced but reverted to their baseline smoking

### Predicting Latent Class

- Demographic data and baseline characteristics (e.g., smoking and quit behavior, FTND, SF-36, trial treatment group) were used as independent variables
- Latent class was used as the dependent variable
- One cross-validated elastic net logistic regression for each latent class (i.e., one-versus-all)
- All models performed better than chance:
  - Class 1 test AUC = 0.766,  $p < .001$ . Tended to be older with lower anxiety and nicotine dependence, more likely to have received active NRT.
  - Class 2 test AUC = 0.569,  $p = .008$  No clear pattern of characteristics.
  - Class 3 test AUC = 0.523,  $p < .001$  Inverse of class one: higher nicotine dependence, more likely to have received placebo NRT.



### Predicting Smoking Status

- 122/1783 (6.8%) achieved biochemically-verifiable smoking cessation at week 52:
  - Class 1: 70/186 (37.6%); Class 2: 34/803 (4.2%); Class 3: 18/776 (2.3%)
- Elastic net logistic regression predicting smoking cessation using
  - baseline characteristics alone: AUC =  $0.632 \pm 0.006$ ,  $p < .001$
  - baseline characteristics plus latent class: AUC =  $0.776 \pm 0.010$ ,  $p < .001$
- **Adding latent class as an independent variable improved cessation prediction by 14.4%**

## References

- [1] A. Batra, K. Klingler, B. Landfeldt, H. Friederich, A. Westin, and T. Danielsson. Smoking reduction treatment with 4-mg nicotine gum: A double-blind, randomized, placebo-controlled study. *Clinical Pharmacology & Therapeutics*, 78(6):689–696, Dec. 2005. ISSN 00099236. doi: 10.1016/j.clpt.2005.08.019.
- [2] C. T. Bolliger. Smoking reduction with oral nicotine inhalers: Double blind, randomised clinical trial of efficacy and safety. *BMJ*, 321(7257):329–333, Aug. 2000. ISSN 09598138. doi: 10.1136/bmj.321.7257.329.
- [3] K. O. Fagerstrom, T. F. Heatherton, and L. T. Kozlowski. Nicotine addiction and its assessment. *Ear, Nose, & Throat Journal*, 69(11):763–765, Nov. 1990. ISSN 0145-5613.
- [4] K. Haustein. A double-blind, randomized, placebo-controlled multicentre trial of a nicotine chewing gum in smoking reduction. *Study ID 980-CHC-9021-0013. Unpublished data.*, 2001.
- [5] N. Lindson, E. Klemperer, B. Hong, J. M. Ordóñez-Mena, and P. Aveyard. Smoking reduction interventions for smoking cessation. *Cochrane Database of Systematic Reviews*, 2019(9), Sept. 2019. ISSN 14651858. doi: 10.1002/14651858.CD013183.pub2.
- [6] A. O. Olufade, J. W. Shaw, S. A. Foster, S. J. Leischow, R. D. Hays, and S. J. Coons. Development of the Smoking Cessation quality of life questionnaire. *Clinical Therapeutics*, 21(12):2113–2130, Dec. 1999. ISSN 01492918. doi: 10.1016/S0149-2918(00)87242-2.
- [7] S. Rennard, E. Glover, S. Leischow, D. Daughton, P. Glover, M. Muramoto, M. Franzon, T. Danielsson, B. Landfeldt, and Å. Westin. Efficacy of the nicotine inhaler in smoking reduction: A double-blind, randomized trial. *Nicotine & Tobacco Research*, 8(4):555–564, Aug. 2006. ISSN 1462-2203. doi: 10.1080/14622200600789916.
- [8] P. Wenneke, T. Danielsson, B. Landfeldt, Å. Westin, and P. Tønnesen. Smoking reduction promotes smoking cessation: Results from a double blind, randomized, placebo-controlled trial of nicotine gum with 2-year follow-up: Smoking reduction with nicotine gum. *Addiction*, 98(10):1395–1402, Oct. 2003. ISSN 09652140. doi: 10.1046/j.1360-0443.2003.00489.x.
- [9] World Health Organization. WHO report on the global tobacco epidemic, 2011: Warning about the dangers of tobacco. 2011. ISSN 9789244564264.

## Conclusions

- **Examining latent trajectories in smoking behavior among people not motivated to quit revealed three distinct patterns**
- **One of these trajectories was nearly twice as likely as the others to achieve cessation**
- **Smoking reduction in the first two weeks after intervention by  $\geq 50\%$   $\rightarrow$  substantially increased cessation likelihood**

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