

Smoking Reduction Trajectories and their Associations with Smoking Cessation

VCBH Retreat

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Disclosures

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- The University of Oxford and NHS Greater Manchester Integrated Care
- Gemma Taylor works for a scientific consulting company offering statistical services for projects unrelated to this research.
- The current authors were not involved in the design, conduct, analysis, write-up or dissemination of the original trials, and the funder of these trials (McNeil AB) had no involvement in the planning, analysis, or interpretation of this secondary analysis.



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- Smoking is the leading cause of premature death and preventable illness worldwide.

World Health Organization 2011.
Reid et al. 2019; Hewers et al. 2003.

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- Smoking is the leading cause of premature death and preventable illness worldwide.
- Treatment is often designed for people motivated to quit now, but many are not

World Health Organization 2011.
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- Smoking is the leading cause of premature death and preventable illness worldwide.
- Treatment is often designed for people motivated to quit now, but many are not
- A common suggestion is smoking reduction.

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Smoking reduction interventions for smoking cessation (Review)

Lindson N, Klemperer E, Hong B, Ordóñez-Mena JM, Aveyard P

However ...

- A prior Cochrane review found that reduction interventions are no more or less effective than quitting abruptly.

Lindson N, Klemperer E, Hong B, Ordóñez-Mena JM, Aveyard P
Smoking reduction interventions for smoking cessation.
Cochrane Database of Systematic Reviews 2020, Issue 9. Art. No.: CD001262.
DOI: 10.1002/14651858.CD001262.pub2

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Smoking reduction interventions for smoking cessation [Review]
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Lindson et al. 2019.

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Smoking reduction interventions for smoking cessation [Review]
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However ...

- A prior Cochrane review found that reduction interventions are no more or less effective than quitting abruptly.
- Little is known about how people reduce their smoking and which smoking reduction patterns predict better cessation outcomes.
 - Many ways to reduce
 - What is the best way?

Lindson et al. 2019.

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- When people (who are not motivated to quit) are asked to reduce smoking, how do people choose to do so?

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- When people (who are not motivated to quit) are asked to reduce smoking, how do people choose to do so?
- Are there smoking or demographics associated with certain reduction patterns?

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- When people (who are not motivated to quit) are asked to reduce smoking, how do people choose to do so?
- Are there smoking or demographics associated with certain reduction patterns?
- Which patterns of reduction are associated with better cessation outcomes?

Methods

Combine data from 5 RCTs of nicotine replacement therapy (NRT) in people not looking to quit smoking (the “McNeil Trials”):

- Baseline and follow-up (weeks 2, 10, 18, and 26) CPD

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Wennike et al. 2003; Rennard et al. 2006; Bolliger 2000; Batra et al. 2005; Haustein 2001.

Combine data from 5 RCTs of nicotine replacement therapy (NRT) in people not looking to quit smoking (the “McNeil Trials”):

- Baseline and follow-up (weeks 2, 10, 18, and 26) CPD
 - Measures of anxiety, depression, and nicotine dependence



Wennike et al. 2003; Rennard et al. 2006; Bolliger 2000; Batra et al. 2005; Haustein 2001.

Methods

Combine data from 5 RCTs of nicotine replacement therapy (NRT) in people not looking to quit smoking (the “McNeil Trials”):

- Baseline and follow-up (weeks 2, 10, 18, and 26) CPD
- Measures of anxiety, depression, and nicotine dependence
- Biochemically-verified smoking cessation at week 52



Wennike et al. 2003; Rennard et al. 2006; Bolliger 2000; Batra et al. 2005; Haustein 2001.

Methods

Participants in each of the included trials were:

- enrolled if they
 - smoked ≥ 15 CPD

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References

Participants in each of the included trials were:

- enrolled if they
 - smoked ≥ 15 CPD
 - made a serious quit attempt within the past 2 years

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Participants in each of the included trials were:

- enrolled if they
 - smoked ≥ 15 CPD
 - made a serious quit attempt within the past 2 years
 - were currently unmotivated to quit

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Participants in each of the included trials were:

- enrolled if they
 - smoked ≥ 15 CPD
 - made a serious quit attempt within the past 2 years
 - were currently unmotivated to quit
 - wanted to reduce their smoking using NRT

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Participants in each of the included trials were:

- enrolled if they
 - smoked ≥ 15 CPD
 - made a serious quit attempt within the past 2 years
 - were currently unmotivated to quit
 - wanted to reduce their smoking using NRT
- randomly assigned to receive active or placebo NRT

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Participants in each of the included trials were:

- enrolled if they
 - smoked ≥ 15 CPD
 - made a serious quit attempt within the past 2 years
 - were currently unmotivated to quit
 - wanted to reduce their smoking using NRT
- randomly assigned to receive active or placebo NRT
- were told to reduce their smoking as much as possible

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

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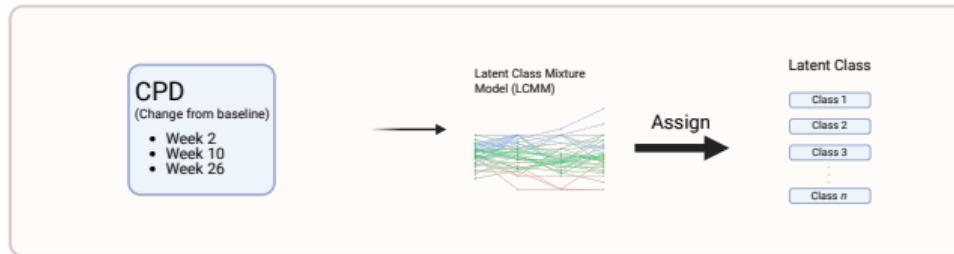
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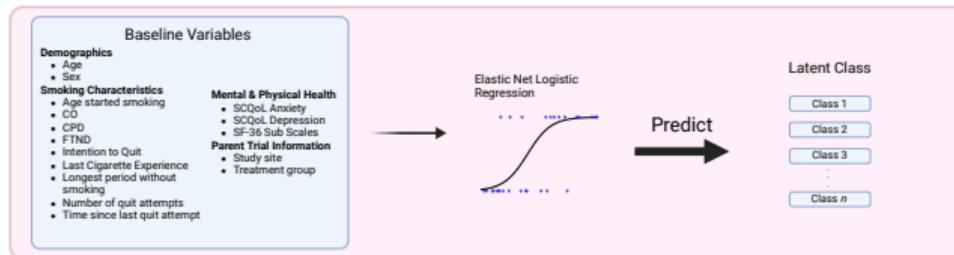
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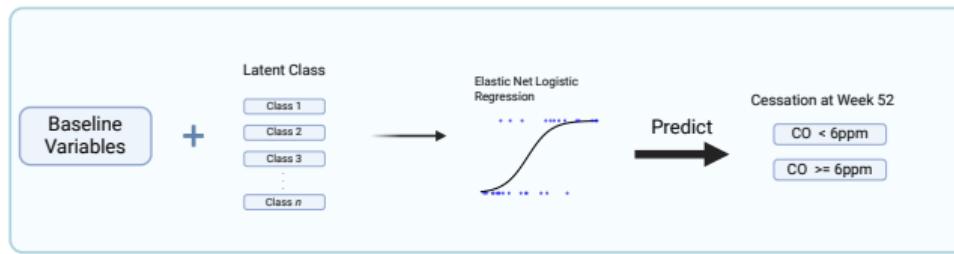
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Baseline Variables

Demographics

- Age
- Sex

Parent Trial Information

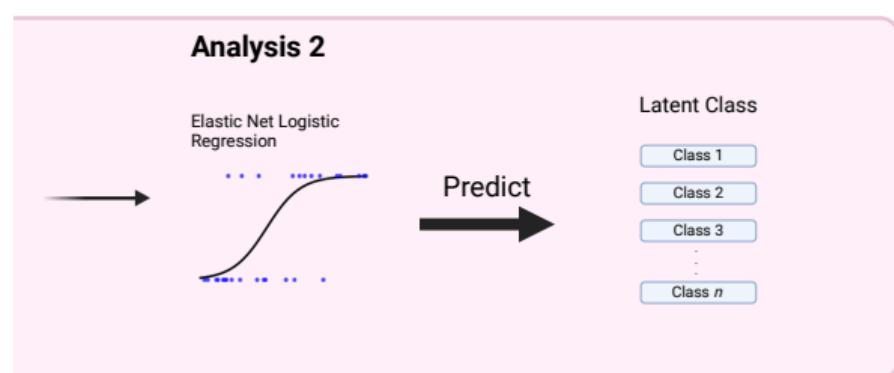
- Study site
- Treatment group

Mental and Physical Health

- SCQoL Anxiety, Depression
- SF-36 Sub Scales

Smoking Characteristics

- Age started smoking
- CO
- CPD
- FTND
- Intention to quit
- Last cigarette experience
- Longest period without smoking
- Number of quit attempts
- Time since last quit attempt



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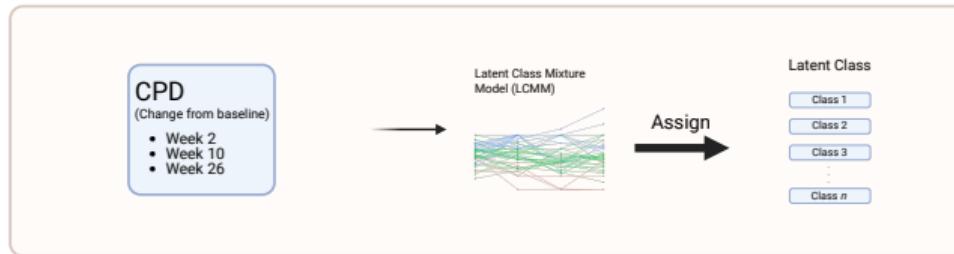
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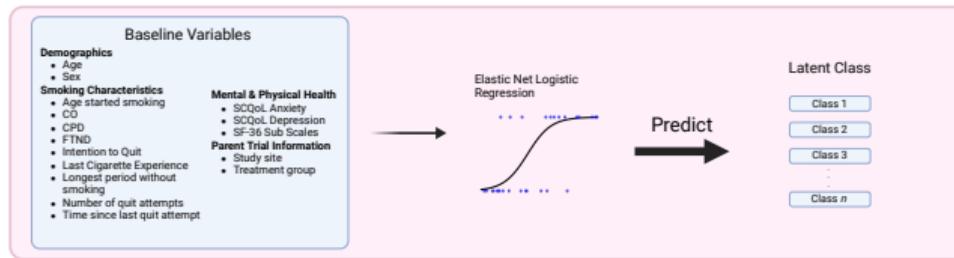
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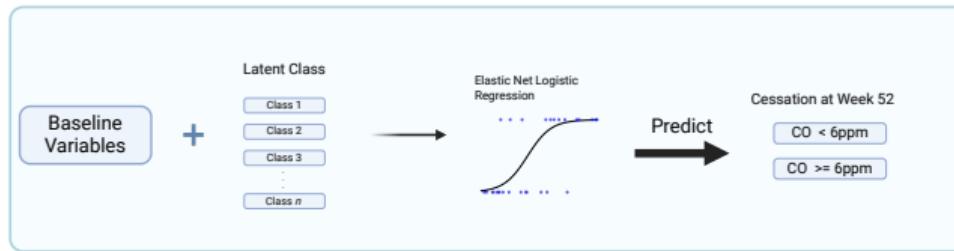
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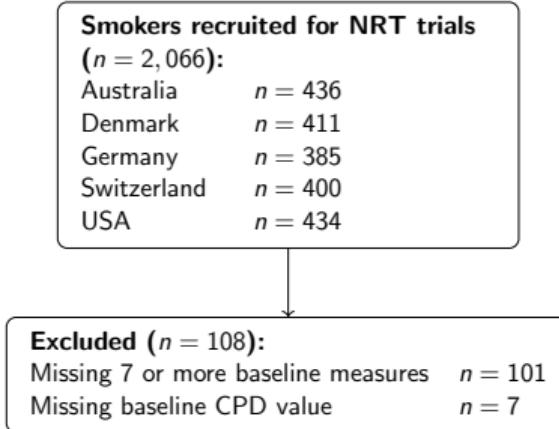
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	Overall
N (%)	1783 (100)
Study Site (%)	
Australia	360 (20.2)
Denmark	340 (19.1)
Germany	353 (19.8)
Switzerland	301 (16.9)
USA	429 (24.1)
Active NRT (%)	900 (50.5)
Sex = Male (%)	798 (44.8)
Age (m(sd))	44.10(10.72)
FTND (m(sd))	6.14 (2.00)
CPD (m(sd))	27.32 (9.73)
SCQoL Anxiety (m(sd))	0.45 (0.85)
SCQoL Depression (m(sd))	0.29 (0.69)

- 1053 (59.1%) were enrolled in trial that used NRT gum
- n=730 (40.9%) used inhalers

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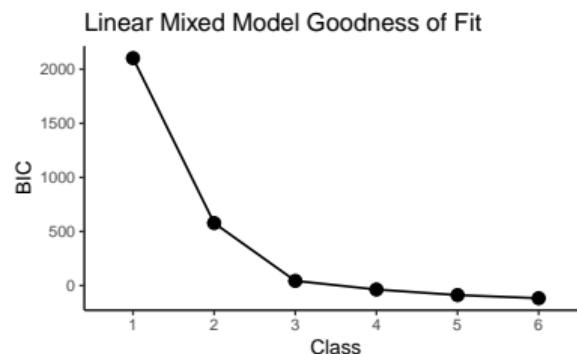
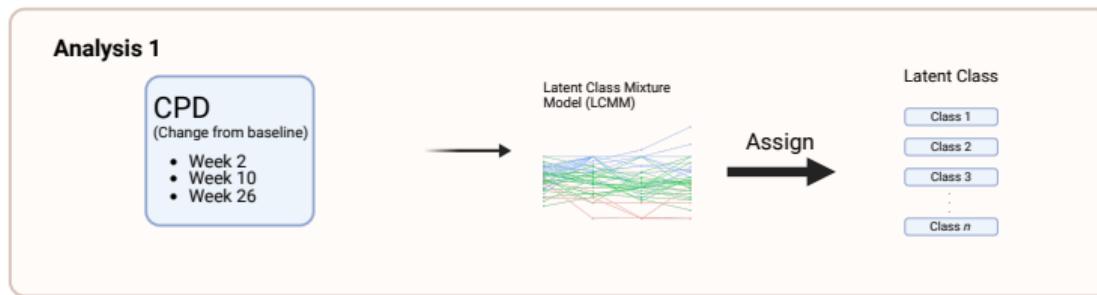
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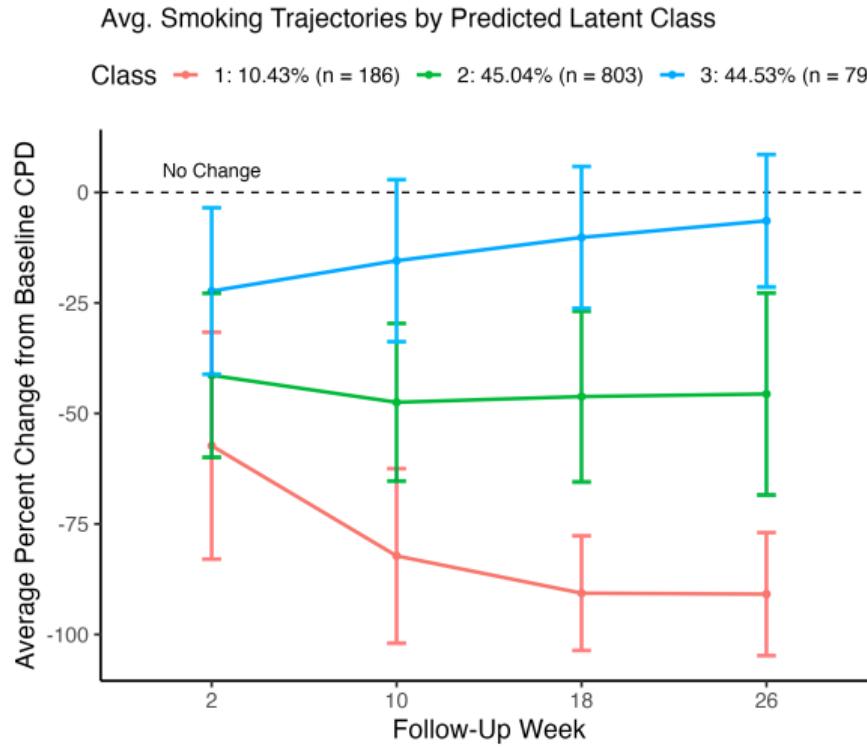
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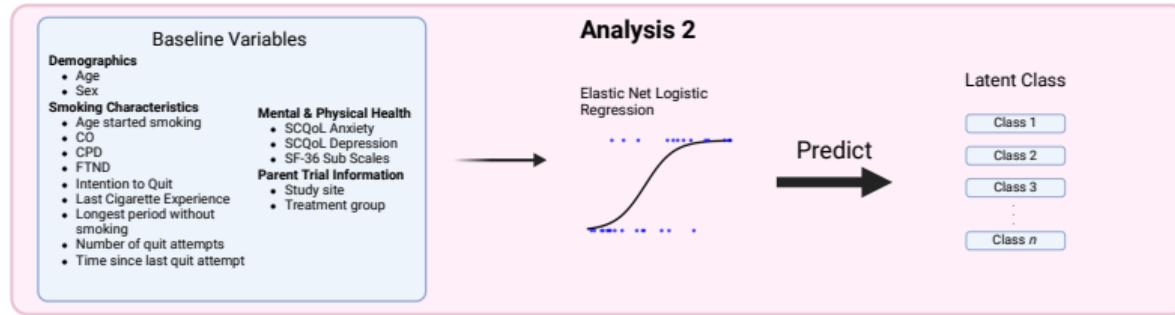
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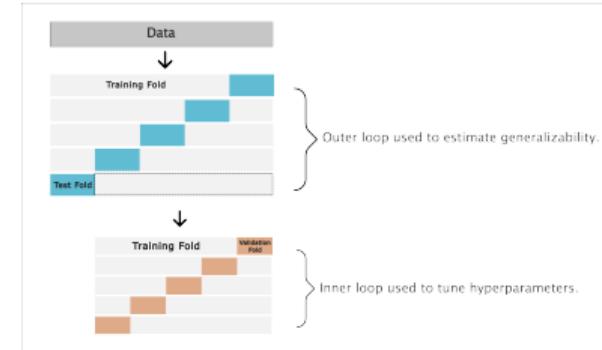
- **Class 1 (substantial reducers):** 10.43% initially reduced and nearly eliminated smoking
- **Class 2 (moderate reducers):** 45.04% reduced by nearly 50% and remained
- **Class 3 (minimal reducers):** 44.53% initially reduced but reverted to their baseline smoking

Results

Predicting Latent Class



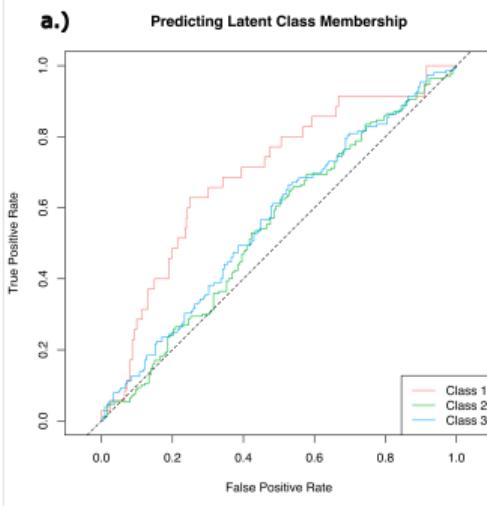
- Dataset initially divided into 80% training and 20% testing partitions
- 5-fold cross-validation performed with training set
 - Each fold further divided into 5 “inner folds” for selecting optimal hyperparameters



Results

Predicting Latent Class

Predictive performance assessed using unseen data (i.e., 20% held-out testing partition)



- substantial reducers (Class 1) test AUC = 0.766, $p < .001$
- moderate reducers (Class 2) test AUC = 0.569, $p = .008$
- minimal reducers (Class 3) test AUC = 0.523, $p < .001$

Note: Statistical significance determined with respect to $ROCAUC = 0.5$ and concordance its with the Mann-Whitney U statistic:

$$AUC = \frac{U}{n_1 n_2}$$

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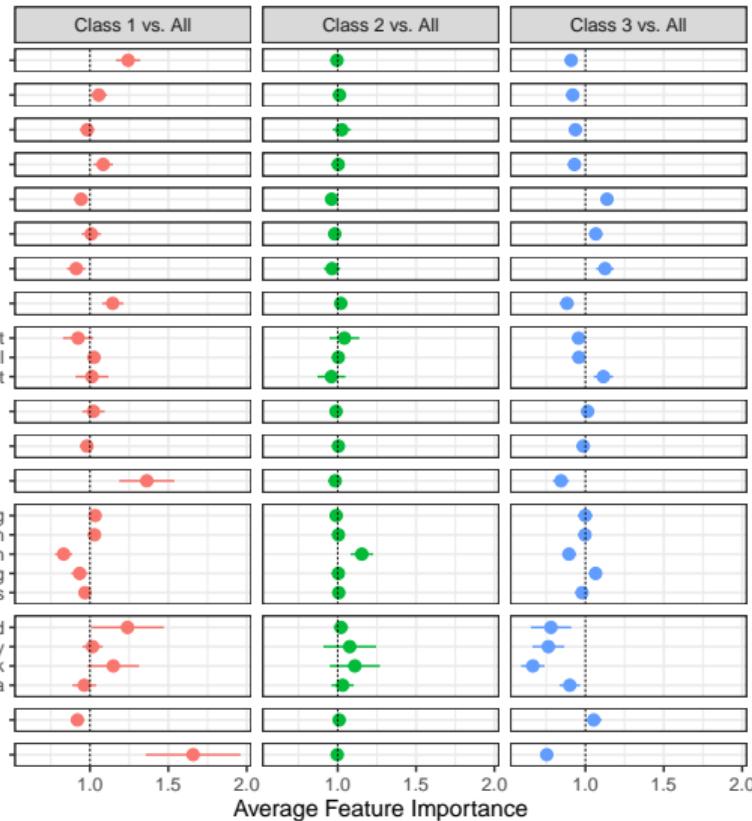
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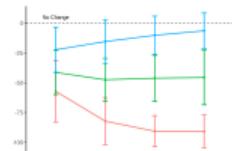
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Age
Age Started Smoking
Anxiety
Average CPD
CO
Depression
FTND
Intention to Quit
Last Cigarette Experience
Longest Period Without Smoking
Number of Quit Attempts
Sex (Male)
SF-36 Subscales
Study Site
Time Since Last Quit Attempt
Treatment Group (Active)



- **substantial reducers (Class 1):** Older, anxiety + FTND ↓
- **moderate reducers (Class 2):** No clear pattern
- **minimal reducers (Class 3):** Inverse of Class 1



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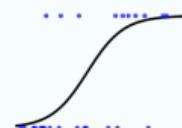
Latent Class

- Class 1
- Class 2
- Class 3
- ⋮
- Class n



Baseline
Variables

Elastic Net Logistic
Regression



Predict

Cessation at Week 52

- CO < 6ppm
- CO \geq 6ppm

Results

Predicting Smoking Cessation

Smokers recruited for NRT trials

($n = 2,066$):

Australia	$n = 436$
Denmark	$n = 411$
Germany	$n = 385$
Switzerland	$n = 400$
USA	$n = 434$

Excluded ($n = 108$):

Missing 7 or more baseline measures	$n = 101$
Missing baseline CPD value	$n = 7$

Assigned latent class ($n = 1783$):

Class 1	$n = 186$
Class 2	$n = 803$
Class 3	$n = 794$

1-year CO values available:

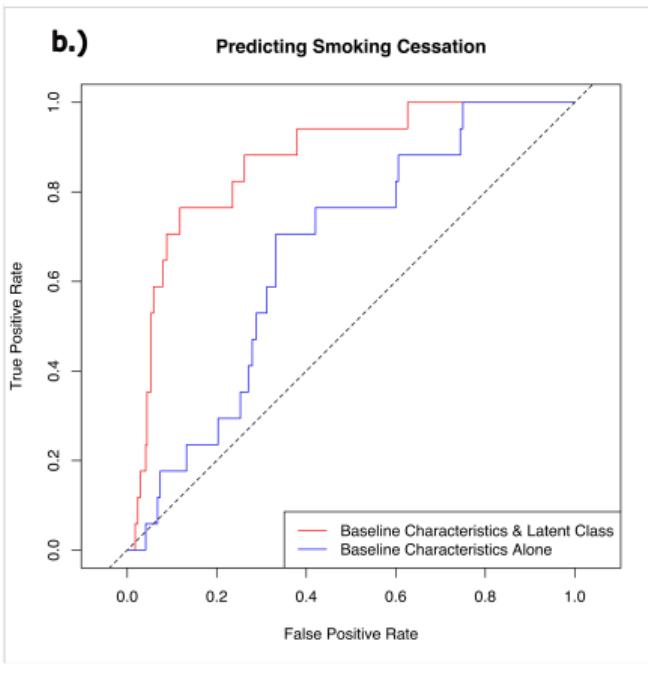
Class 1	$n = 143/186 (76.9\%)$
Class 2	$n = 500/803 (62.3\%)$
Class 3	$n = 285/794 (35.9\%)$

Achieved cessation (CO < 6ppm):

Class 1	$70/186 (37.6\%)$
Class 2	$34/803 (4.2\%)$
Class 3	$18/776 (2.3\%)$
Overall	$122/1783 (6.8\%)$

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Predicting Smoking Cessation



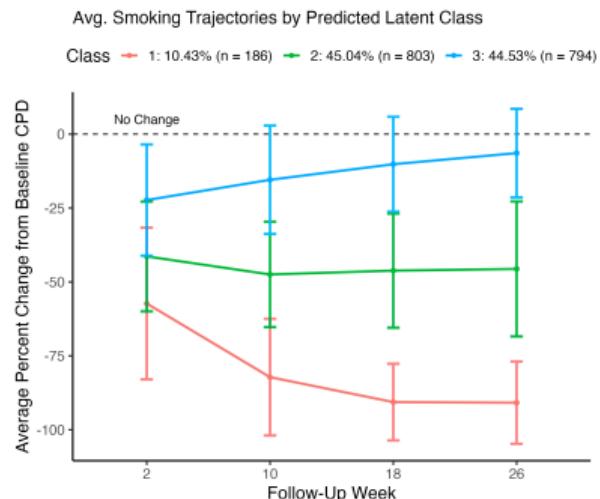
Elastic net logistic regression predicting smoking cessation using

- 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%

- Examining latent trajectories in smoking behavior among people not motivated to quit revealed three distinct patterns

Conclusions

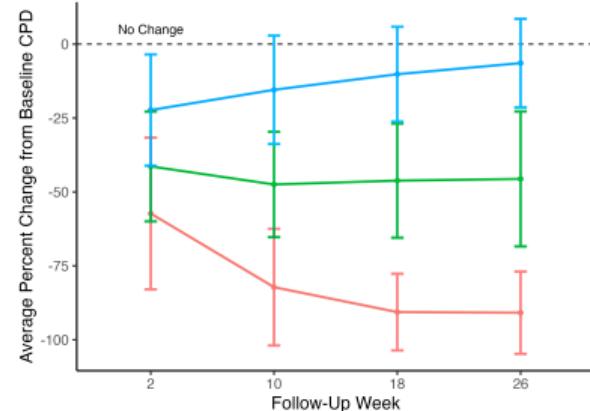


- Examining latent trajectories in smoking behavior among people not motivated to quit revealed three distinct patterns
- Those who reduced their smoking by $\geq 50\%$ in the first two weeks were more than twice as likely to quit

Conclusions

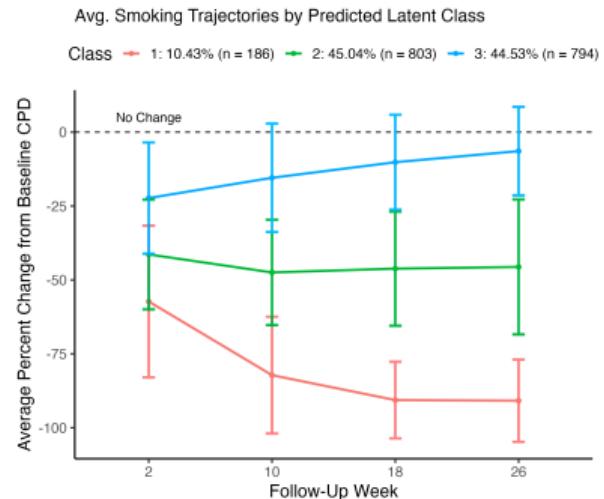
Avg. Smoking Trajectories by Predicted Latent Class

Class 1: 10.43% (n = 186) Class 2: 45.04% (n = 803) Class 3: 44.53% (n = 794)



- Examining latent trajectories in smoking behavior among people not motivated to quit revealed three distinct patterns
- Those who reduced their smoking by $\geq 50\%$ in the first two weeks were more than twice as likely to quit
- First study to date to use rigorous machine learning-based methods to predict latent smoking reduction behavior

Conclusions



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- Lots of early reduction is most likely to encourage cessation

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- Lots of early reduction is most likely to encourage cessation
- 50% reduction is often considered the threshold for successful smoking reduction
 - We validate this analytically

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- Lots of early reduction is most likely to encourage cessation
- 50% reduction is often considered the threshold for successful smoking reduction
 - We validate this analytically
- Not all reduction interventions are equally likely to result in cessation

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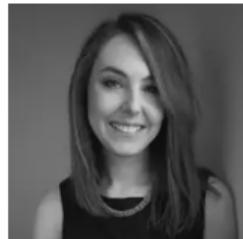
Hugh Garavan, PhD
University of Vermont



Nick Allgaier, PhD
University of Vermont



Nicola Lindson, PhD
University of Oxford



Gemma Taylor, PhD
University of Bath



Thank You

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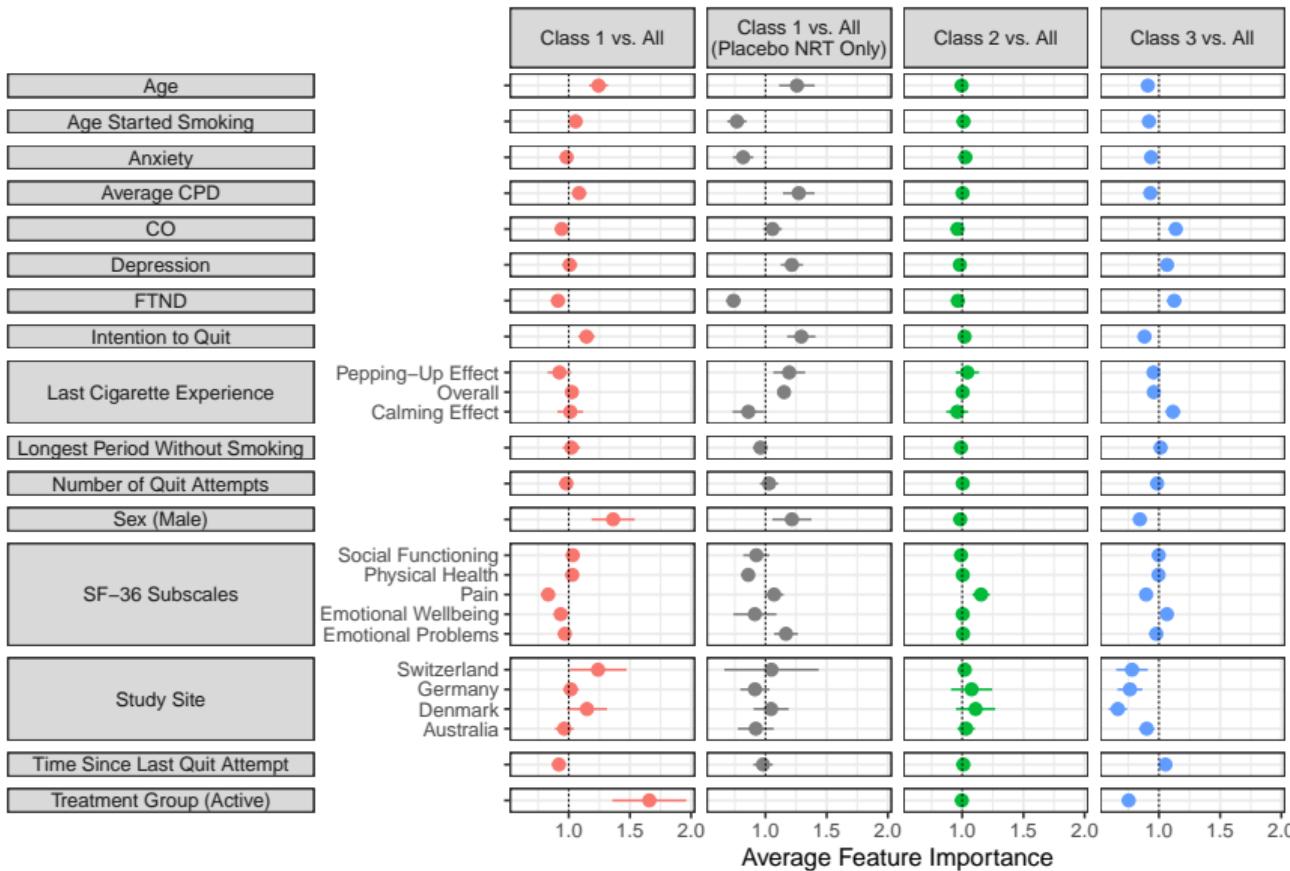
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