Continuous associations of urinary tobacco exposure biomarker concentrations and transitions between cigarette and e-cigarette use in the Exhale cohort

TCORS | Center for the Assessment of Tobacco Regulations [CAsToR]

Andrew F. Brouwer[1], Fatema Shafie-Khorassani[1], Douglas E. Jorenby[2], Timothy B. Baker[2], Neal L. Benowitz[3], Todd Hayes-Birchler[2], Megan E. Piper[2]
Contact: brouweaf@umich.edu

Background

- Understanding how people transition between cigarettes, e-cigarettes, and dual use is important for designing effective regulations and interventions that reduce harm to people who use cigarettes.
- Tobacco smoke and nicotine exposure biomarkers may provide more accurate estimates of product use and dependence and be predictive of transitions.
- Regulating nicotine concentrations in tobacco products could change biomarker concentrations and thus transitions. We need a method to estimate those changes.

Data

- The Exhale Study: a longitudinal cohort study in Wisconsin from 2015-2017.
- Cohort: adult who used cigarettes daily, with or without e-cigarettes, who were not intending to quit.
- Participants were followed up every two months for two years
- 380 participants had at least 2 visits.
- Urine was collected every 4 months for biomarker analysis
- Tobacco product use states were determined by self-reported abstinence in the past 30 days, and participants were categorized into four categories:
  - Non-current use, cigarette-only use, e-cigarette-only use, or dual use of cigarettes and e-cigarettes.

Key Findings

1. Lower **NNAL:creatinine** (a tobacco smoke biomarker), **NE2:creatinine** (an all-nicotine-use biomarker), **NNAL:NE2** (a biomarker of how much nicotine comes from combustible tobacco) ratios were associated with a higher rate of stopping the use of cigarettes for both cigarette-only and dual users.
2. Lower **NNAL:NE2 ratios** were associated with reduced rate of transitioning from dual to cigarette-only use.
3. The ratio **3HC:cotinine** (a biomarker of the rate of nicotine metabolism) was not associated with any transitions.

Results may support models predicting the potential public health impact of regulations limiting nicotine concentration in the manufacture of tobacco products.
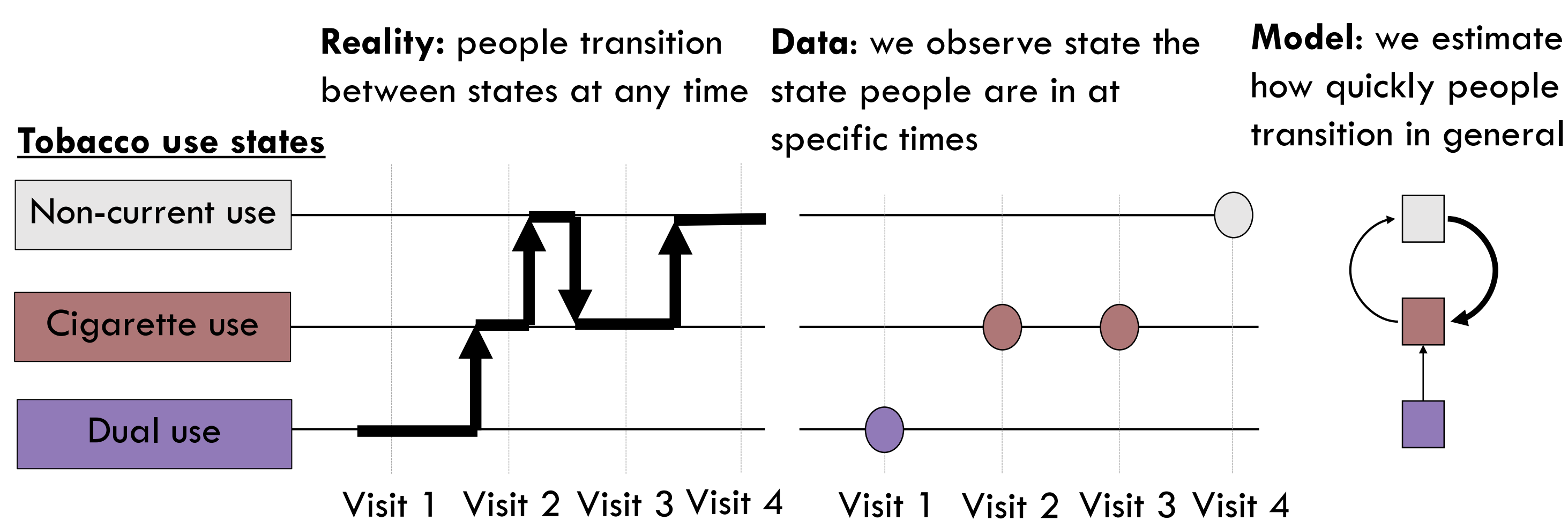
Methods

Biomarkers

- Four biomarkers were assayed: NNAL (tobacco smoke biomarker), cotinine and 3HC (nicotine metabolites, NE2 = cotinine + 3HC), and creatinine (a control biomarker).
- We estimated associations between transition rates and each of the following measures.

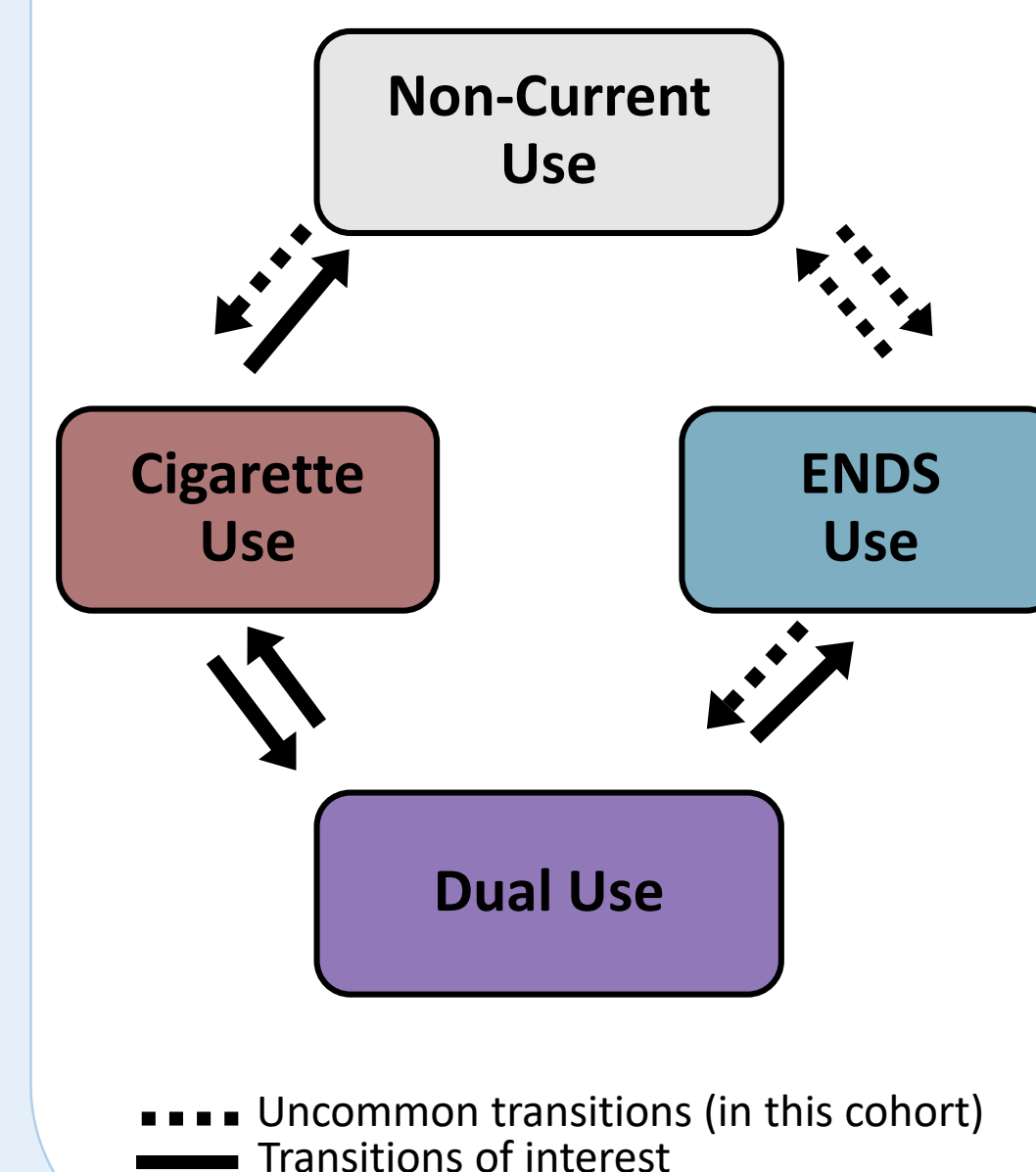| Biomarker ratio	Description
NNAL:creatinine	Lower values associated with less exposure to combustible tobacco smoke
NE2:creatinine	Lower values associated with less exposure to all nicotine
NNAL:cotinine	Lower values indicate more of the nicotine exposure comes from non-combustible tobacco
3HC:cotinine	Lower values indicate slower nicotine metabolism

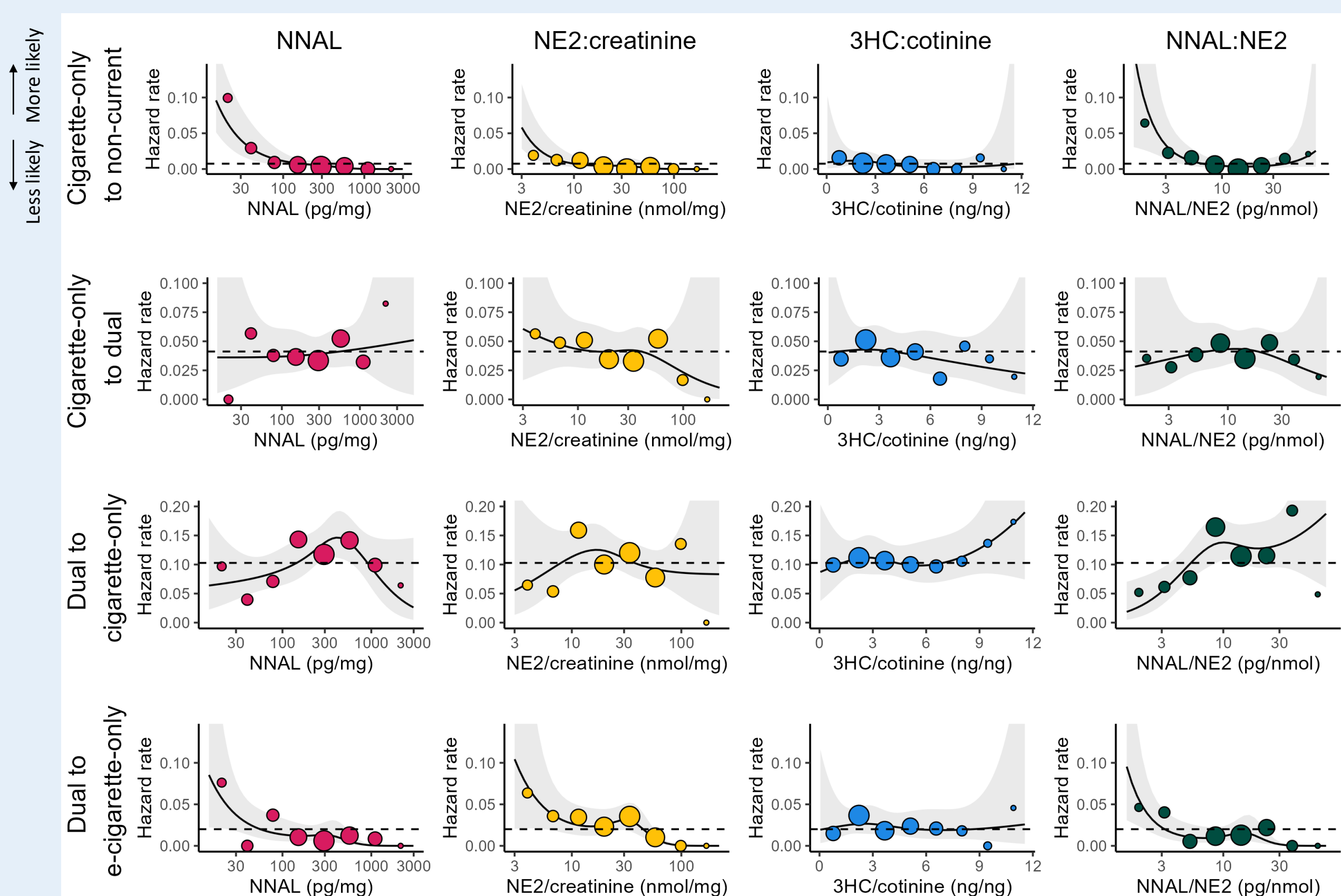Markov transition models are continuous time stochastic processes models.

Reality: people transition between states at any time
Data: we observe state the state people are in at specific times
Model: we estimate how quickly people transition in general

Tobacco use states: Non-current use, Cigarette use, Dual use
Visit 1, Visit 2, Visit 3, Visit 4

Multistate Markov Transition Model Framework

State Transitions

We consider these transitions in our model.

Non-Current Use, Cigarette Use, ENDS Use, Dual Use

····· Uncommon transitions (in this cohort)
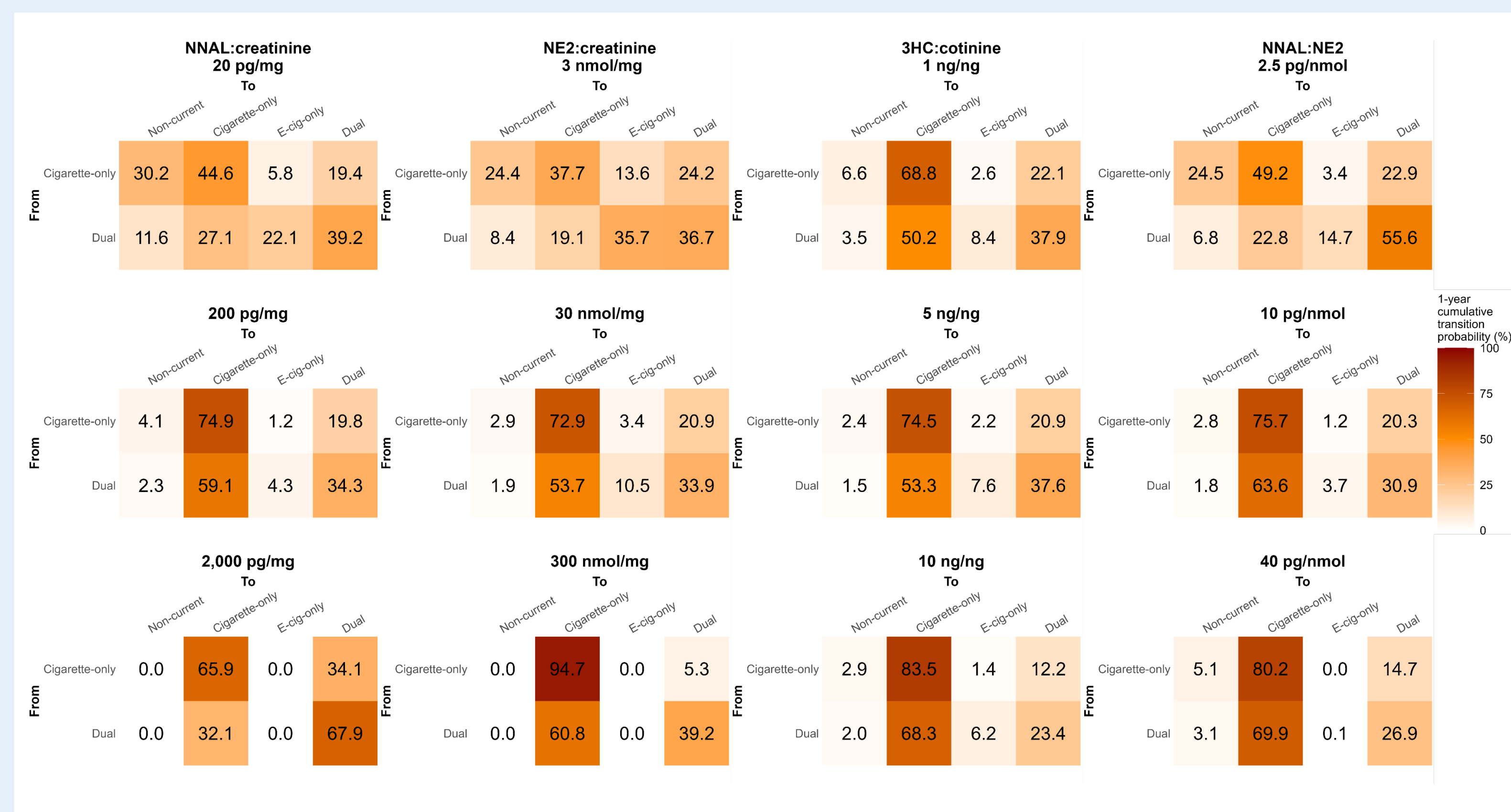—— Transitions of interest

Results

Associations of biomarkers with transition propensity

Predicting transition probabilities at different biomarker values

Disclosures

Affiliations
1 — SCHOOL OF PUBLIC HEALTH, UNIVERSITY OF MICHIGAN
2 — UW Center for Tobacco Research and Intervention, UNIVERSITY OF WISCONSIN, SCHOOL OF MEDICINE AND PUBLIC HEALTH
3 — UCSF Center for Tobacco Control Research and Education

	Tobacco Industry	E-cigarette & nicotine product industry	Pharma Industry
The work being presented has received funding or other means of support from any of the following sources:	NO	NO	NO
Any of the authors have received funding (including consultancy) from any of the following sources in the past 5 years:	NO	NO	YES*

Disclosure: NLB has previously been a consultant to Pfizer and Achieve Life Sciences*, companies that market or are developing smoking cessation medications, and has served as an expert witness in litigation against tobacco companies.