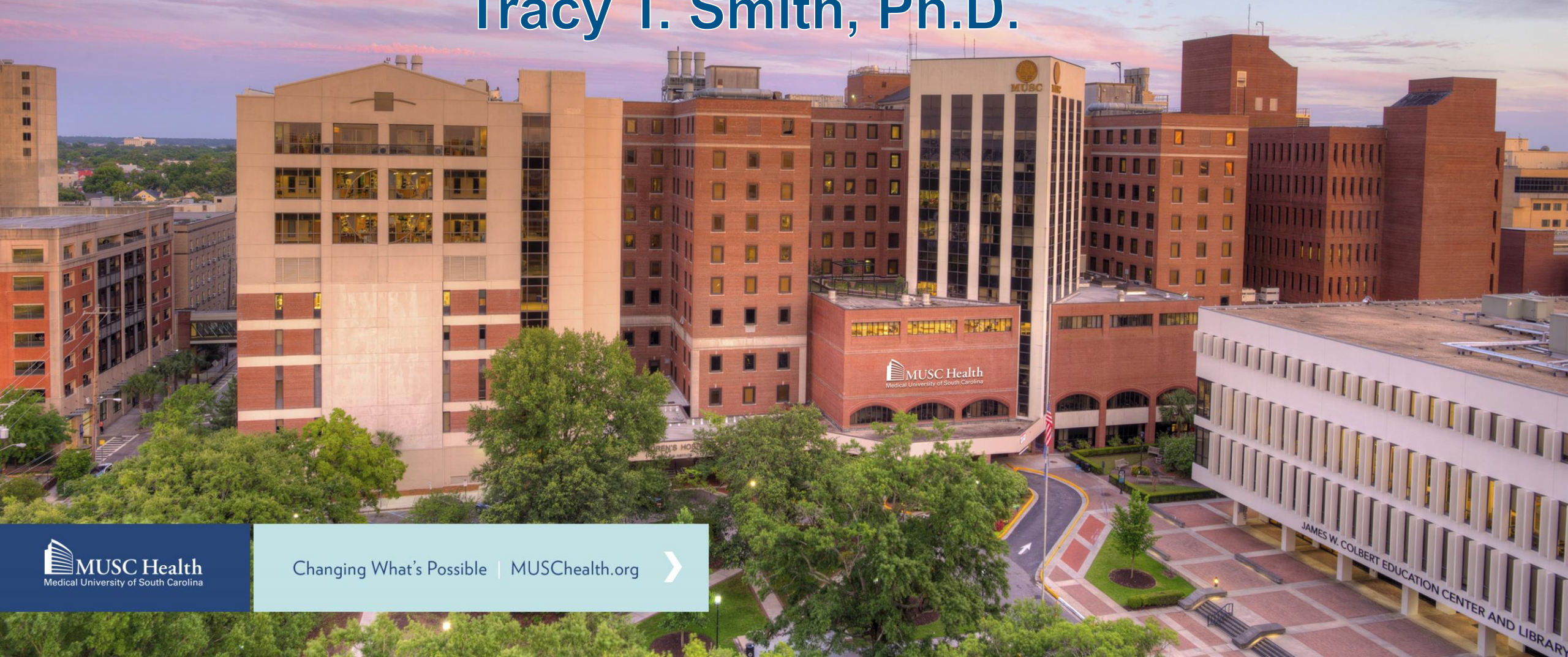


Research to inform tobacco regulation: moving people down the continuum of harm

Tracy T. Smith, Ph.D.



Funding and Disclosures

Current funding: Projects in **Red** are the trials I will be talking about today

- P01 CA200512 (Cummings)
- R01 CA246729 (Carpenter)
- **R01DA057327 (Smith and Wagener)**
- **R01DA055985 (Smith)**
- R01CA284649 (Smith and Carpenter)
- R01DA056445 (Smith)
- K01 DA047433 (Smith)

Disclosures:

- Research reported in this publication was supported by the National Institute On Drug Abuse of the National Institutes of Health and the Food and Drug Administration under Award Numbers R01DA055985 and R01DA057327. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.
- I have no conflicts of interest



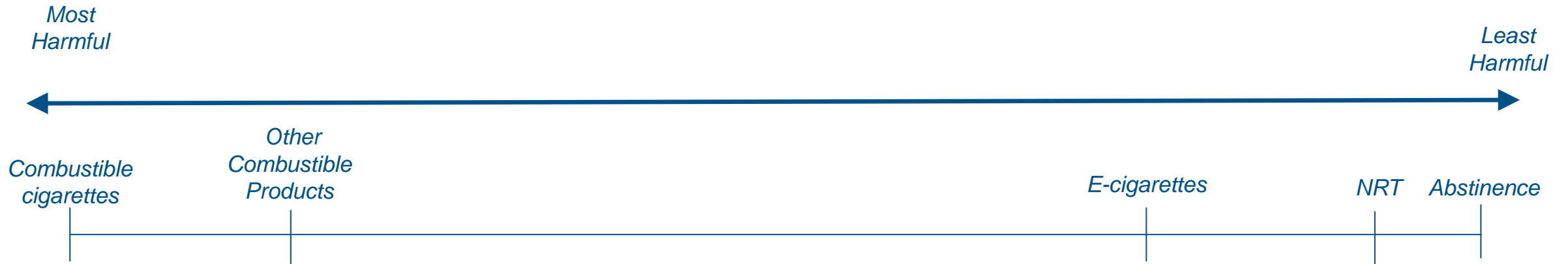
Family Smoking Prevention and Tobacco Control Act

Set product standards for the improvement of public health considering both:

- › Current users
- › Naive individuals



Continuum of Harm



How should we regulate non-combustible products?



Background: Relative risks of vaping nicotine

- No data on long-term health effects
- NAESM report found conclusive evidence that complete switching reduces exposure to toxicants and carcinogens
- Vaping may worsen asthma, bronchitis, cough among nonsmokers
- However, smokers with asthma or COPD see improvements after switching e-cigarettes
- Smokers who switch to e-cigarettes show improved lung and vascular function. Exclusive users of e-cigarettes report fewer respiratory symptoms
- **Not safe, but can safely say it is safer than smoking and people who smoke would reduce harm by complete switching**
- **23 products authorized by FDA for commercial sale based on public health standard**



Background: Vaping impact on smoking cessation

Randomized trials

- › Smoking cessation at 1 year (18%) compared to nicotine replacement (9.9%), Hajek et al. 2019
 - › 80% of those who quit with e-cigarettes were still vaping
- › Multiple clinical trials have now shown higher rates of cigarette abstinence from e-cigarettes than NRT
- › Cochrane review: high-certainty evidence that EC with nicotine increase quit rates compared to NRT

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized Trial of E-Cigarettes versus Nicotine-Replacement Therapy

Peter Hajek, Ph.D., Anna Phillips-Waller, B.Sc., Dunja Przulj, Ph.D., Francesca Pesola, Ph.D., Katie Myers Smith, D.Psych., Natalie Bisal, M.Sc., Jinshuo Li, M.Phil., Steve Parrott, M.Sc., Peter Sasieni, Ph.D., Lynne Dawkins, Ph.D., Louise Ross, Maciej Goniewicz, Ph.D., Pharm.D., Qi Wu, M.Sc., and Hayden J. McRobbie, Ph.D.

ABSTRACT

Hartmann-Boyce, J., Lindson, N., Butler, A. R., McRobbie, H., Bullen, C., Begh, R., Theodoulou, A., Notley, C., Rigotti, N.A., Turner, T., Fanshawe, T. R., Hajek, P. (2022). Electronic cigarettes for smoking cessation. *Cochrane Library*



We have done some of this work ourselves!

Our intent: Within randomized design (minimizing selection bias), across a range of smokers (both motivated and unmotivated to quit), provision of ecigs to use as self-determined; i.e., naturalistic.

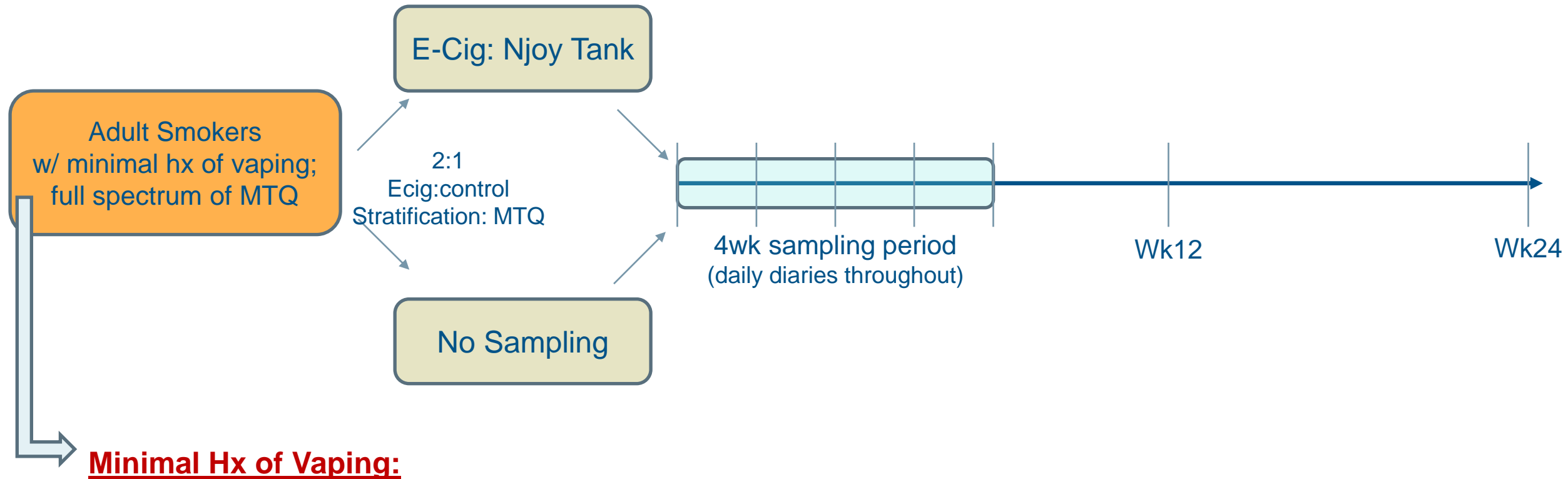
- Adults who smoke randomized, (2:1) provision of e-cig (NJoy Tank; 3ml pre-filled tanked, 15mg/ml of nicotine) or not, for self-determined use, with follow-up thru 6 months
 - Up to 30 days (tanks) provided; multiple flavors available
 - ~"Use (or not use) as you wish, to reduce, quit, or during smoking restrictions. It's completely up to you"
- Product supplied to us, at cost, by NJoy. No financial or other support from e-cig industry



Matthew Carpenter, PhD

MUSC HOLLINGS CANCER CENTER

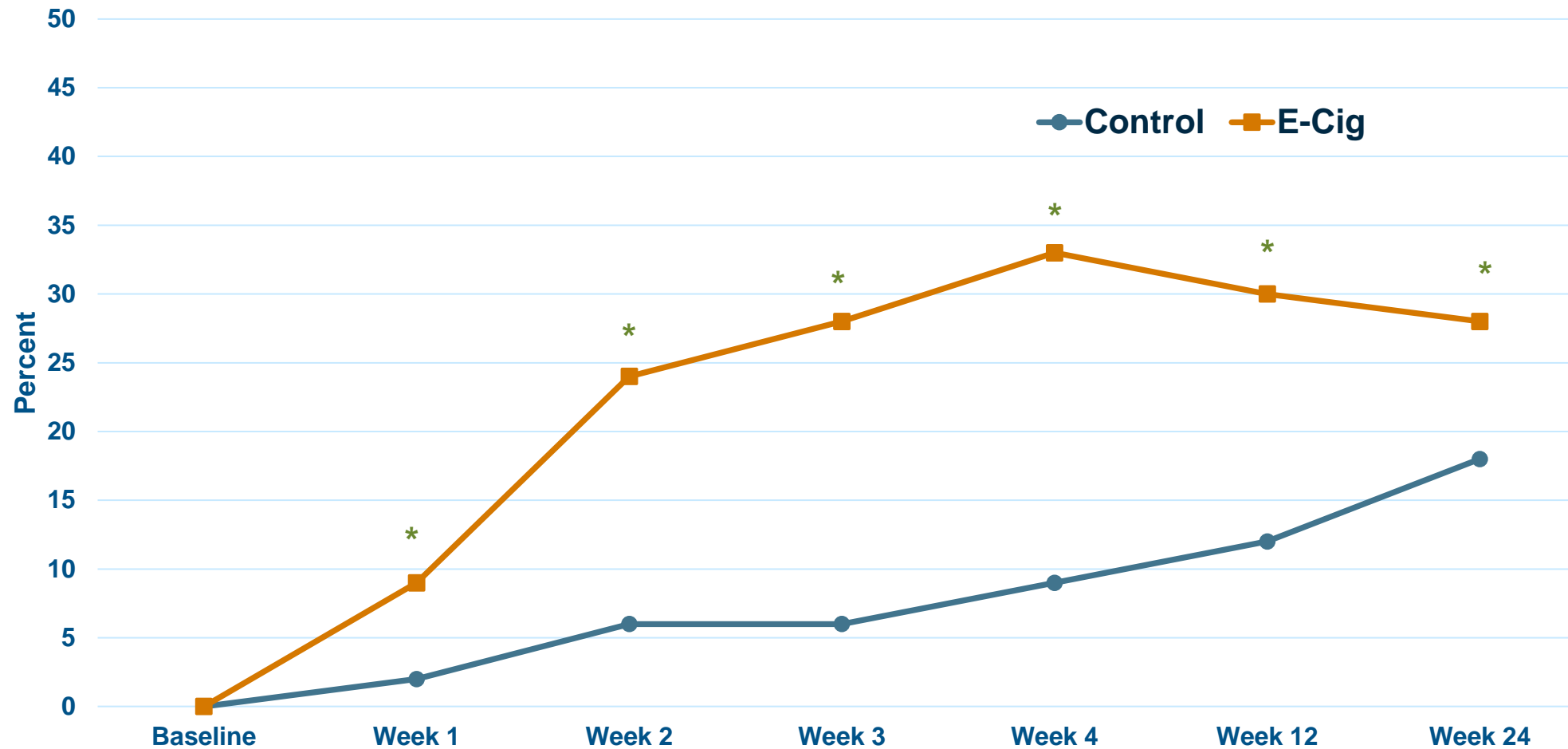
Carpenter, M. J., Wahlquist, A. E., Dahne, J., Gray, K. M., Cummings, K. M., Warren, G., Wagener, T. L., Goniewicz, M. L., **Smith, T. T.** in press. Effect of unguided e-cigarette provision on uptake, use, and smoking cessation among adults who smoke in the USA: A naturalistic, randomized, controlled clinical trial. eClinical Medicine.



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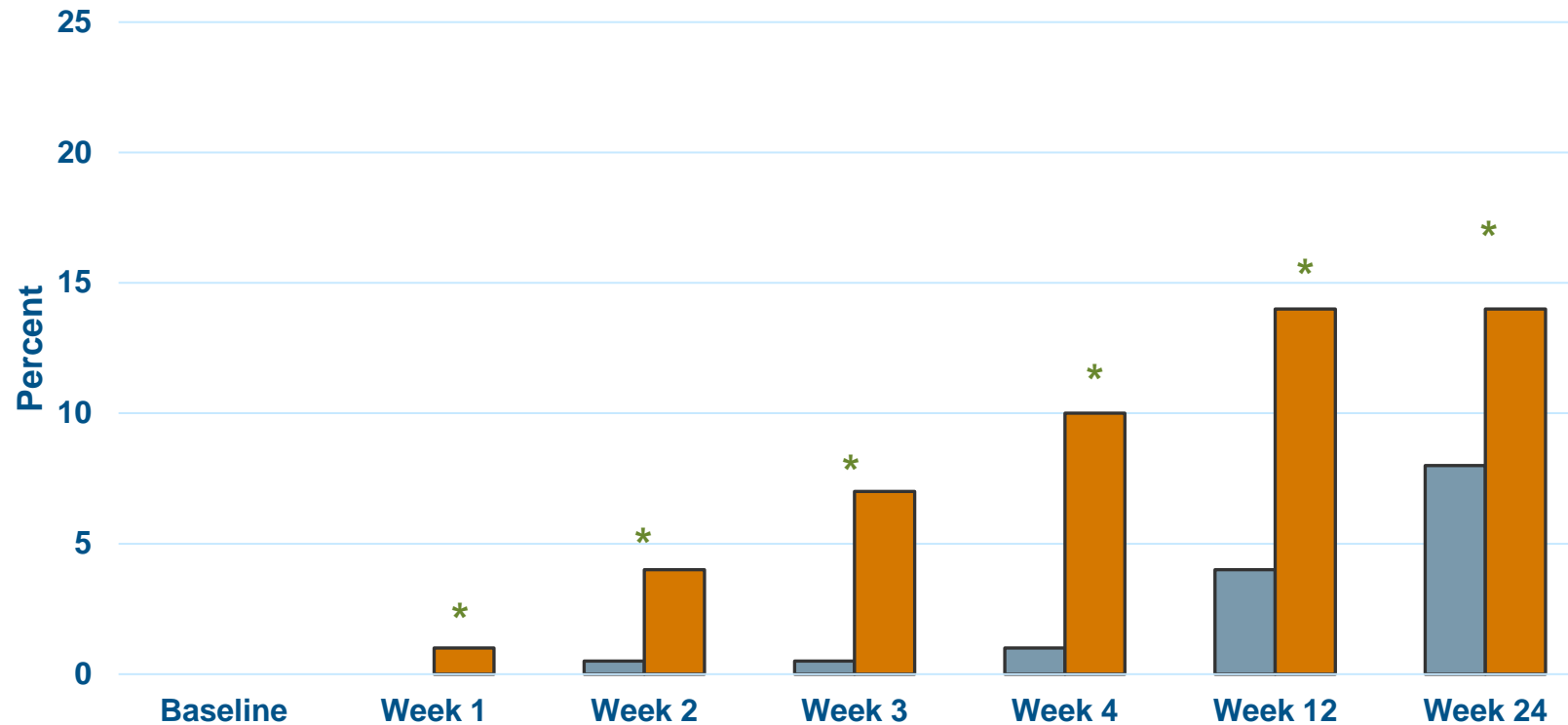
Smoking Reduction

Reduction $\geq 50\%$ Reduction in CPD, Since Baseline



Carpenter, M. J., Wahlquist, A. E., Dahne, J., Gray, K. M., Cummings, K. M., Warren, G., Wagener, T. L., Goniewicz, M. J., **Smith, T. T.** in press. Effect of unguided e-cigarette provision on uptake, use, and smoking cessation among adults who smoke in the USA: A naturalistic, randomized, controlled clinical trial. eClinical Medicine.

Self-Reported Cigarette Cessation



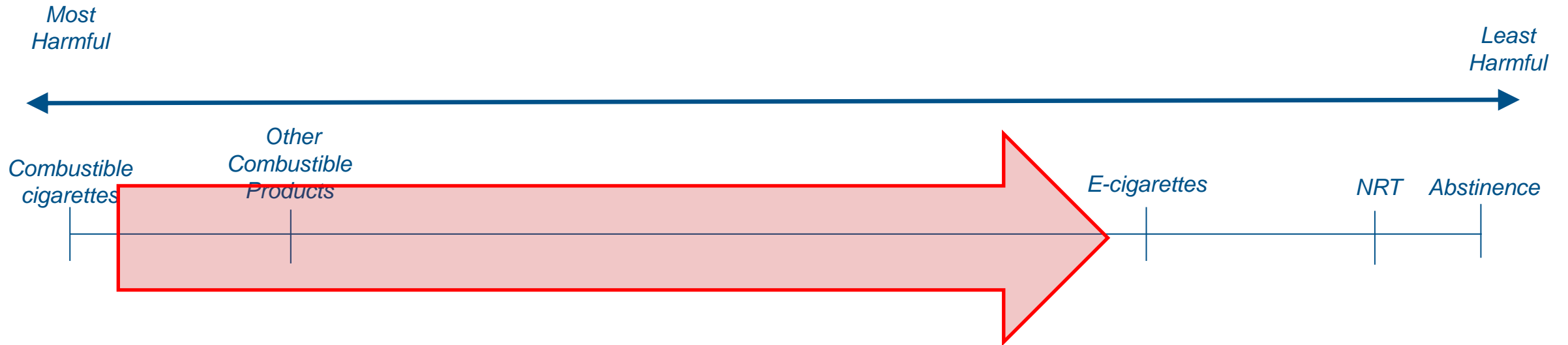
Carpenter, M. J., Wahlquist, A. E., Dahne, J., Gray, K. M., Cummings, K. M., Warren, G., Wagener, T. L., Goniewicz, M. J., **Smith, T. T.** in press. Effect of unguided e-cigarette provision on uptake, use, and smoking cessation among adults who smoke in the USA: A naturalistic, randomized, controlled clinical trial. eClinical Medicine.

Background conclusions

- Cigarettes are by far the most harmful tobacco product
- E-cigarettes are harmful, but smokers who switch completely are likely to substantially reduce their long-term harms
- E-cigarettes can promote abstinence from cigarettes better than NRT and better than no intervention



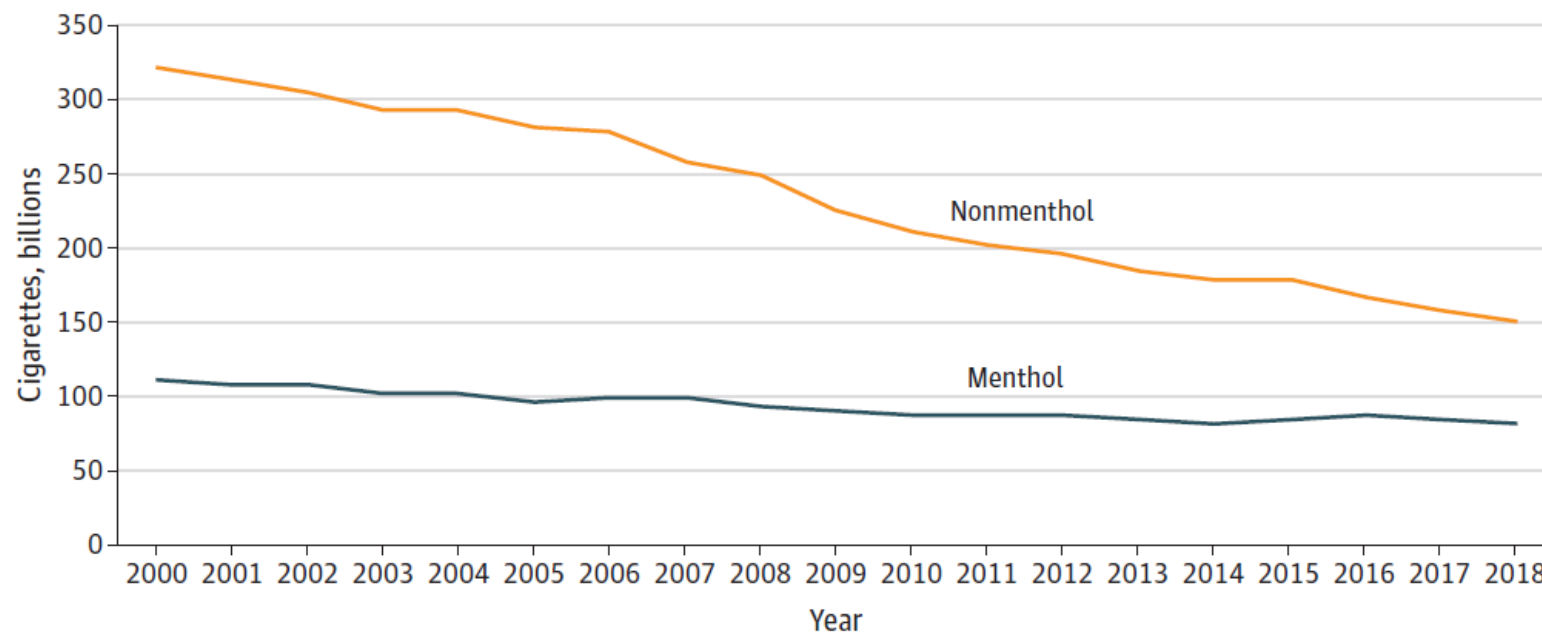
Continuum of Harm



Trial 1= R01DA055985 (Smith)



Menthol: A broader definition of harm



Delveno et al., 2020



Menthol: A broader definition of harm

- A. Menthol may increase smoking initiation
 - i. Youth and new smokers are more likely to smoke menthol cigarettes
- B. Menthol may increase cigarette dependence and hinder quitting
 - i. Menthol smokers are more likely to try to quit and less likely to be successful
- C. Menthol contributes to tobacco use disparities. Menthol is more used among vulnerable groups including African Americans, women, members of the LGBT community, individuals with low income and low education, and those with comorbid mental illness
 - i. African Americans make up 30% of menthol smokers, but 80% of African American smokers use menthol cigarettes



FDA NEWS RELEASE

FDA Commits to Evidence-Based Actions Aimed at Saving Lives and Preventing Future Generations of Smokers

Efforts to ban menthol cigarettes, ban flavored cigars build on previous flavor ban and mark significant steps to reduce addiction and youth experimentation, improve quitting, and address health disparities

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Incements

For Immediate Release: April 29, 2021



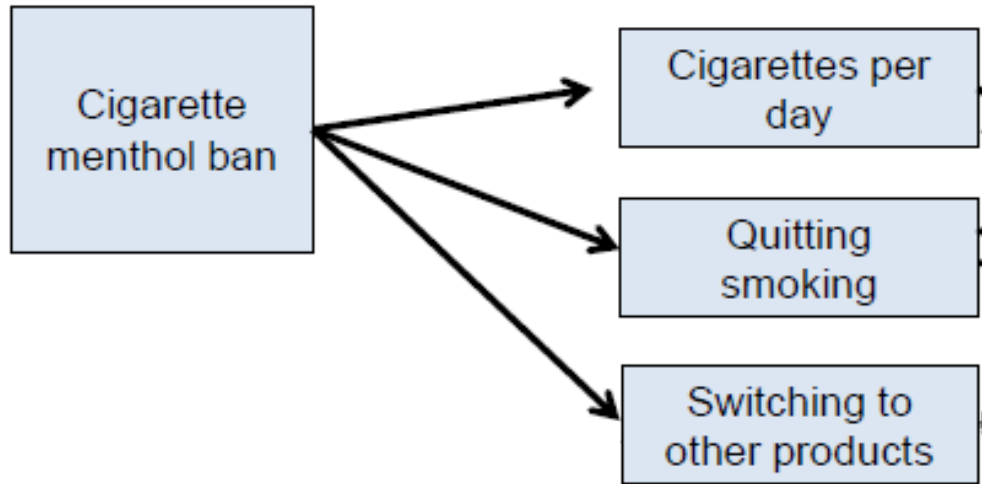


Figure 1. Conceptual framework illustrating the impact of a cigarette and e-cigarette menthol ban on tobacco use outcomes for menthol smokers. Once treatment effects have been estimated in a clinical trial sample, it is critical to model their impact in the population. These policies are likely to also impact nonsmokers, including e-cigarette users, but those pathways are not the focus of this trial and not displayed in Figure 1.

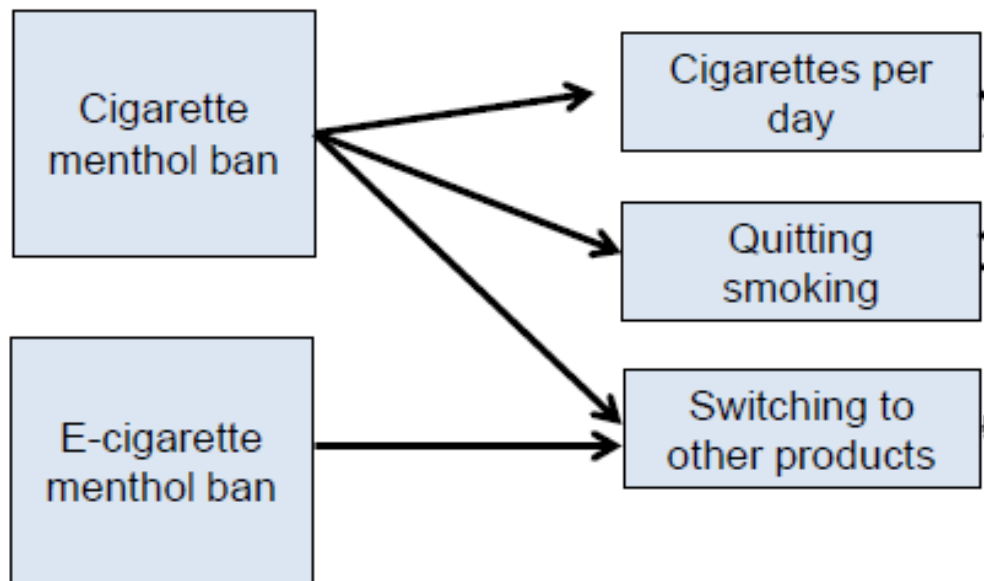


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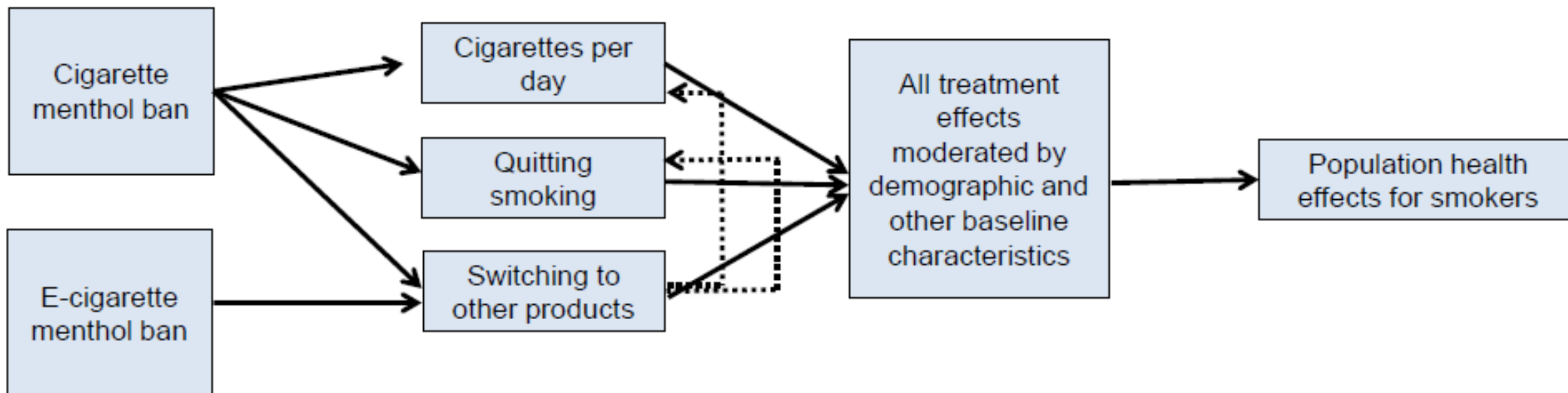


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How would a menthol ban impact smoking behavior, switching to e-cigarettes, and quitting?



Trial Design

Current
Menthol
Smokers
(N=240)

Cigarette Assignment

Menthol

Non menthol



Trial Design

Cigarette Assignment

Menthol

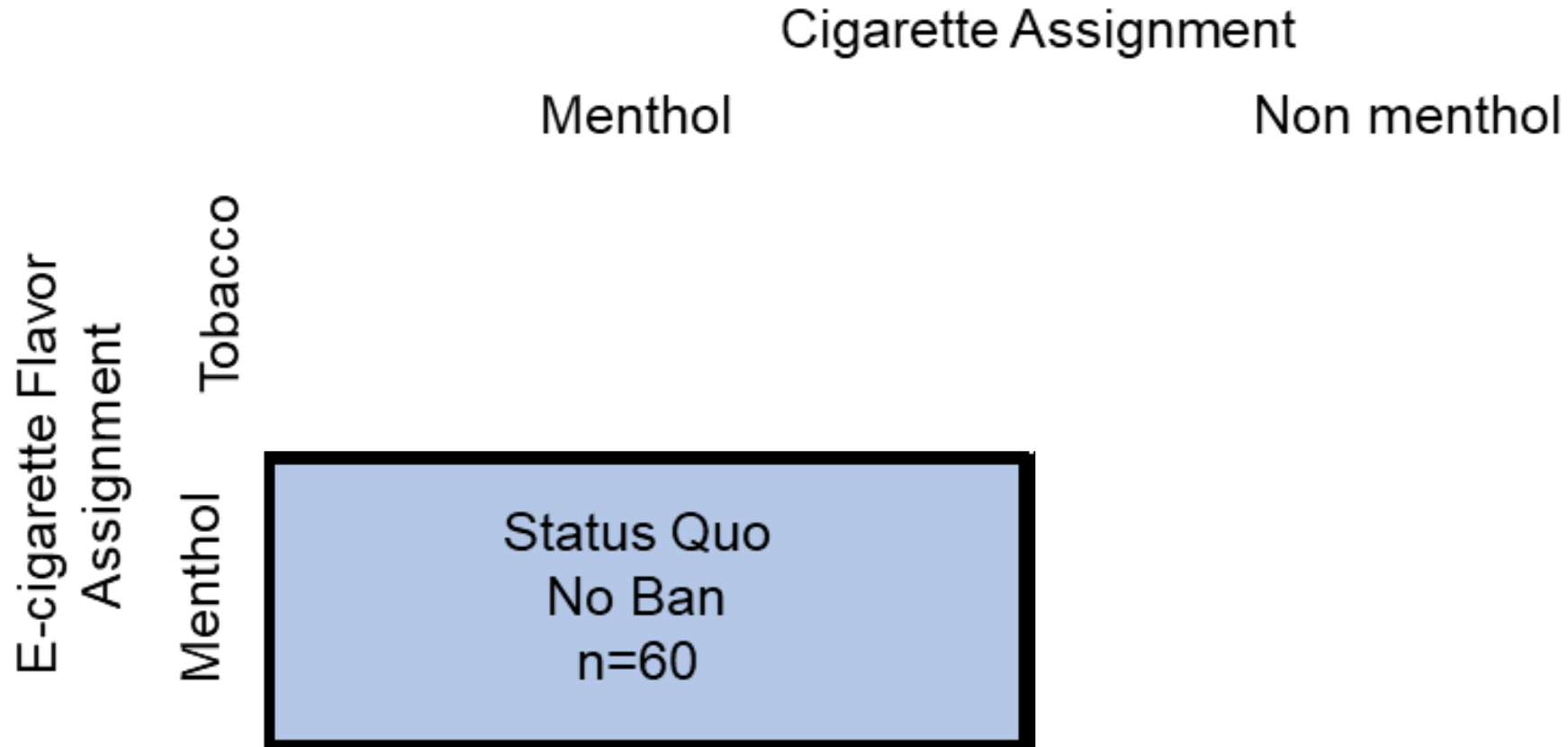
Non menthol

E-cigarette Flavor
Assignment

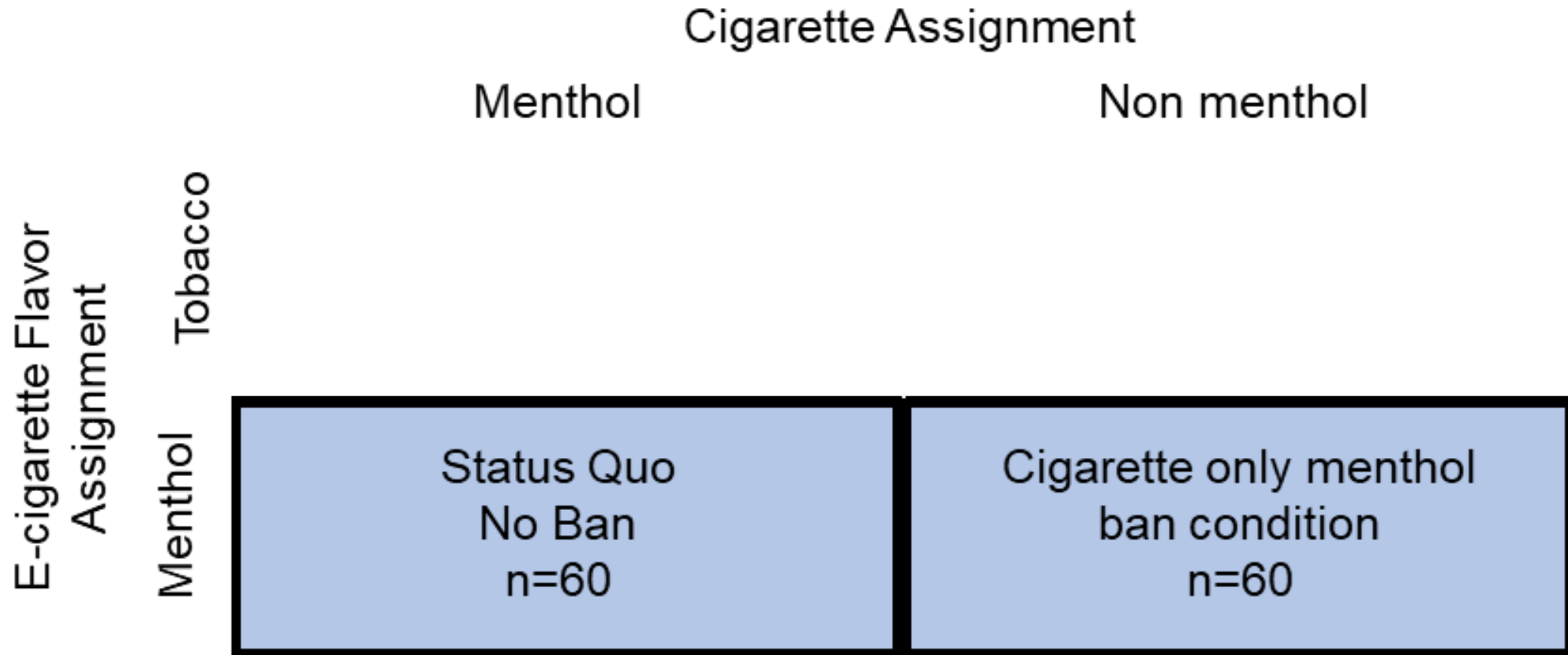
Menthol Tobacco



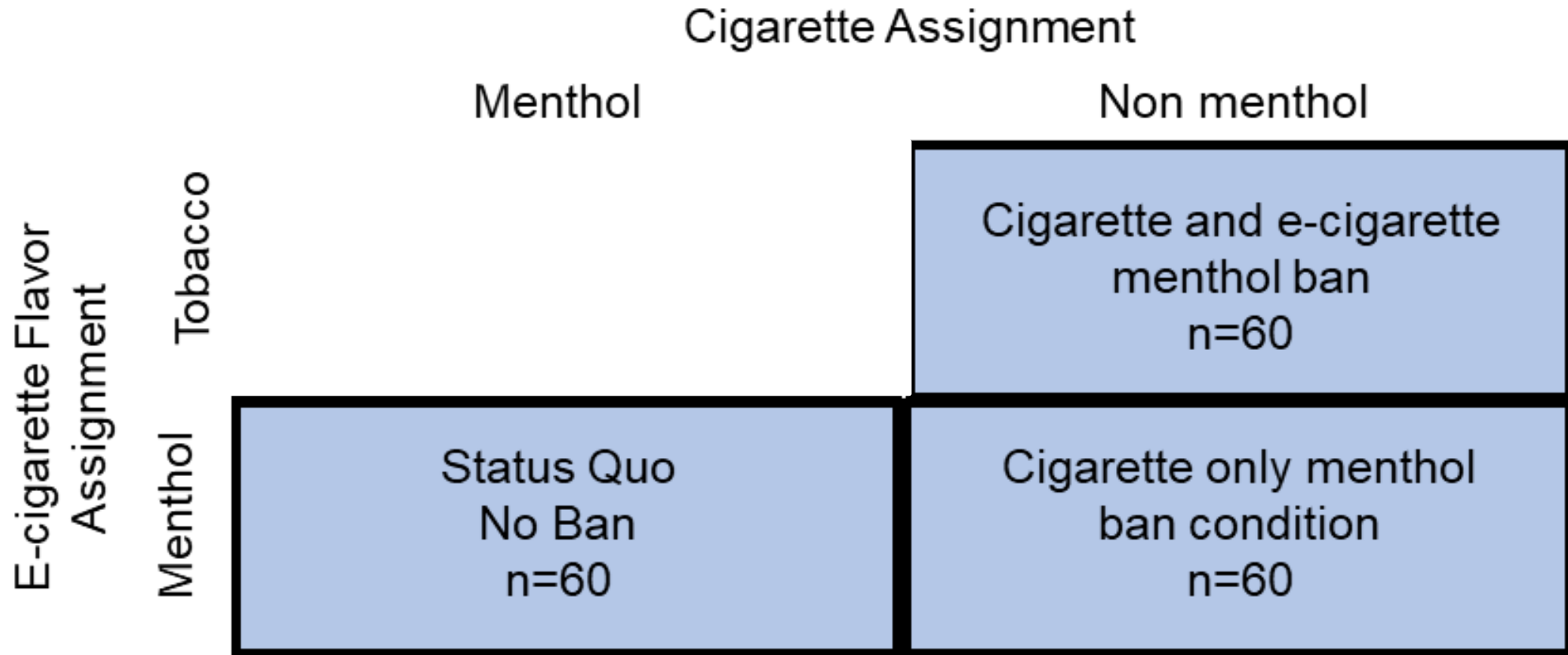
Trial Design



Trial Design



Trial Design



Trial Design

		Cigarette Assignment	
		Menthol	Non menthol
E-cigarette Flavor Assignment	Tobacco	E-cigarette only menthol ban condition n=60	Cigarette and e-cigarette menthol ban n=60
	Menthol	Status Quo No Ban n=60	Cigarette only menthol ban condition n=60



Baseline



Usual
Brand
Provided

Recruitment of 240 people who smoke menthol cigarettes

- Charleston
- Florence
- Lancaster





Usual
Brand
Provided

Study product provided free of charge
Participants complete daily diaries and return to the lab every 2 weeks for a breath sample and urine collection





Usual
Brand
Provided

Study product provided free of charge
Participants complete daily diaries and return to the lab
every 2 weeks for a breath sample and urine collection



Practice Quit Attempt

- Participants will be asked to try to abstain from smoking for a one-week period as part of a Practice Quit Attempt
- Submit two breath samples to us each day to confirm they have not smoked
- Goal is to ask whether a menthol cigarette ban or menthol e-cigarette regulation might affect someone's ability to quit smoking *when motivated to do so*
- Participants can continue to use their assigned e-cigarette or NRT
- Participants are compensated for each day they are abstinent from cigarettes
 - Day 1: \$80
 - Day 2: \$40
 - Day 3: \$20
 - Day 4: \$10
 - Day 5: \$5
 - Day 6: \$2.50
 - Day 7: \$0

When does the participant lapse and return to smoking? = how valuable smoking is to them

Might depend on whether they are assigned to menthol or nonmenthol cigarettes and whether they have menthol e-cigarettes available



Outcomes and Significance

- Cigarettes per day
- E-cigarette use (including switching)
- Cessation related outcomes including quit attempts, NRT use, sustained abstinence, and time to lapse during Week 7
- ***Provide FDA with information about the impact of a menthol ban for cigarettes and e-cigarettes on public health***
- ***Modeling in Year 5 will report the number of life years saved and deaths averted by each of the 4 policy scenarios***
 - *No menthol ban*
 - *Menthol cigarette ban, Menthol e-cigarettes available*
 - *Menthol cigarette ban, Menthol e-cigarettes removed from market*
 - *No menthol cigarette ban, Menthol e-cigarettes removed from market*



Continuum of Harm



Trial 2=R01DA057327 (Smith and Wagener)



What about other e-cigarette flavors?



Submit Tobacco Product Applications for Deemed Tobacco Products

Resources for Applicants Required to Submit by September 9, 2020



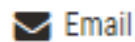
Share



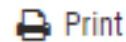
Tweet



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Email



Print

Applications for many e-cigarettes and other new deemed tobacco products that were on the market as of Aug. 8, 2016 were required to be submitted to FDA by **Sept. 9, 2020**. The deadline has now passed. If you have submitted an application and are looking for information on next steps, visit the [“What Happens After I Submit the Application?”](#) section on this page. If you are looking for information on FDA compliance and enforcement, visit the [“Why Must I Comply?”](#) section on this page.

On Sept. 9, 2021, CTP Director Mitch Zeller [provided an update on FDA's progress on tobacco product application review and related enforcement](#).



FDA Denies Marketing Applications for About 55,000 Flavored E-Cigarette Products for Failure to Provide Evidence They Appropriately Protect Public Health

Action Marks First Marketing Denial Order
Orders Must be Removed from the US Market

We've made [significant progress](#) in the months since, working diligently to better understand these products and, as of today, taking action on about 93% of the total timely-submitted applications. This includes issuing Marketing Denial Orders (MDO) for more than 946,000 flavored ENDS products because their applications lacked sufficient evidence that they have a benefit to adult smokers sufficient to overcome the public health threat posed by the well-documented, alarming levels of youth use of such products.

FDA Makes Significant Progress in Science-Based Public Health Application Review, Taking Action on Over 90% of More Than 6.5 Million 'Deemed' New Tobacco Products Submitted

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FDA Denies Authorization to Market JUUL Products

Currently Marketed JUUL Products Must Be Removed from the US Market

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For Immediate Release: June 23, 2022

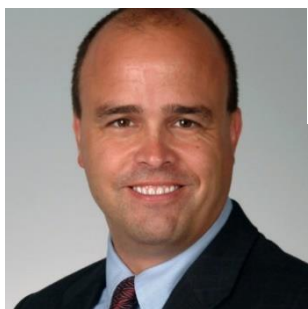
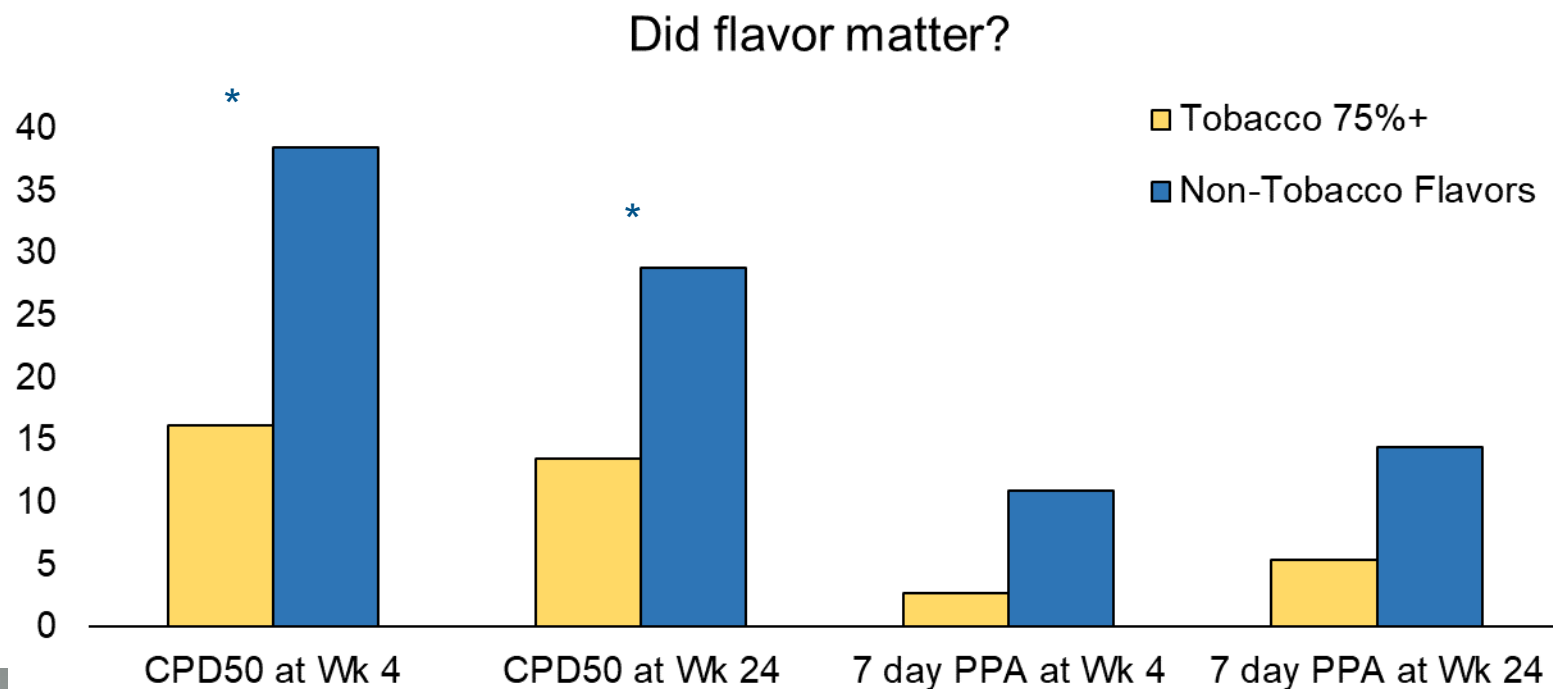
E-Cigarette Products, as Kind by the

emonstrate that
f Public Health

Do non-tobacco flavors in e-cigarettes better promote switching than tobacco flavors?



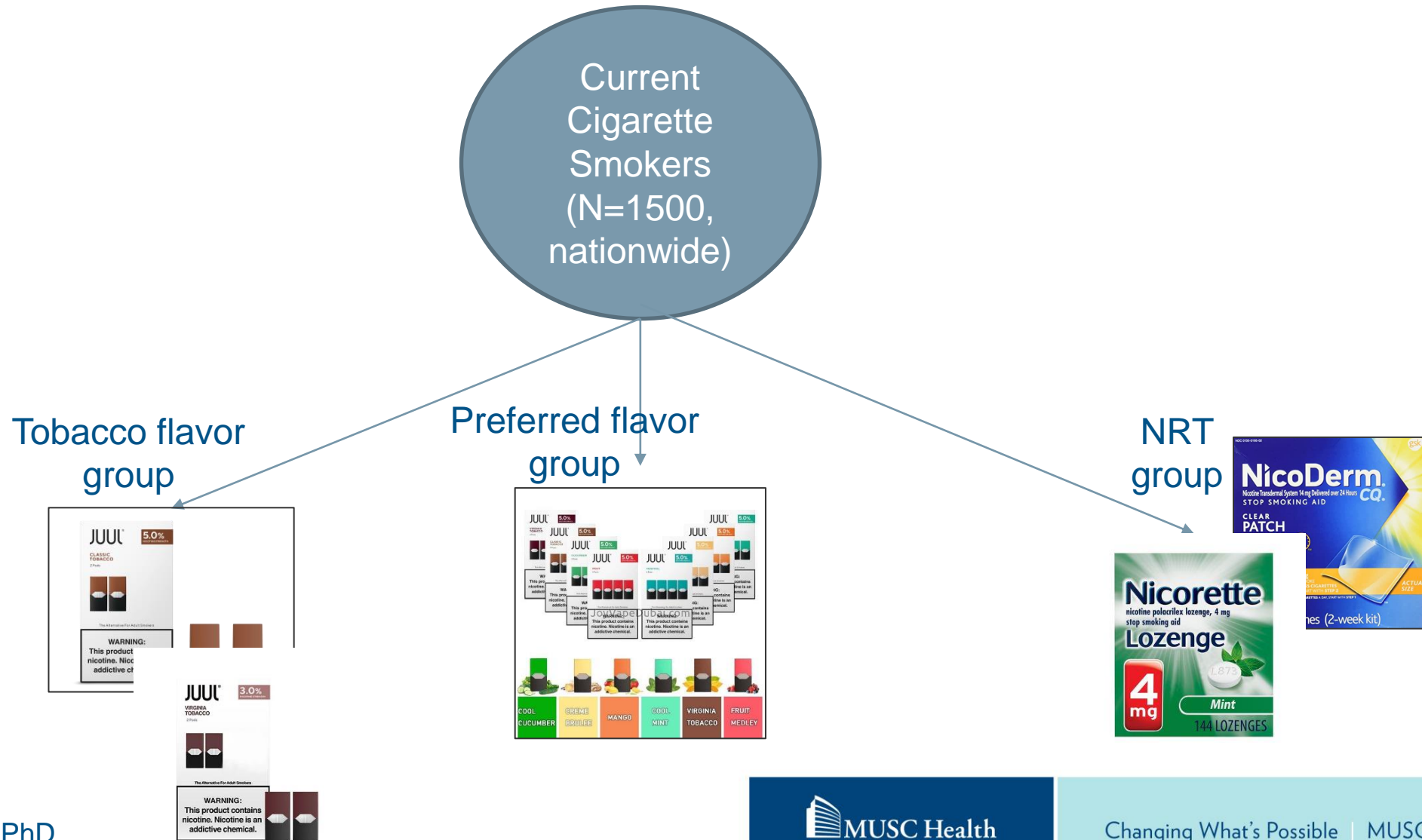
Non-tobacco flavors: What do we already know?



Matthew Carpenter, PhD



Randomized trial to test the impact of e-cigarette flavoring on switching from cigarettes to e-cigarettes



Theodore Wagener, PhD
Ohio State University





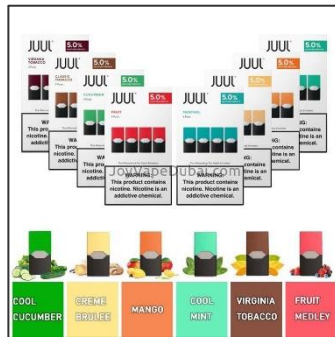
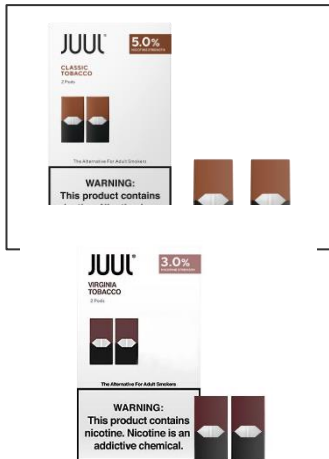
Orientation Call
and Baseline
Assessment /
Randomization
/ Mail Study Kits

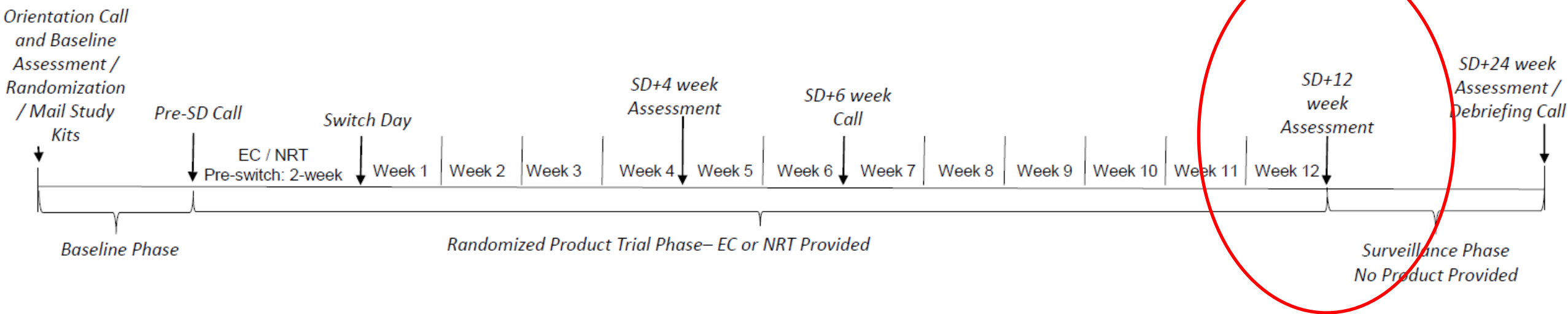
Pre-SD Call

Switch Day

EC / NRT
Pre-switch: 2-week

Baseline Phase





Outcomes and Significance

- Cigarette smoking, e-cigarette use, complete switching (abstinence from smoking)
- **Is the rate of complete switching higher among the PEC group?**
- *Provide information to FDA about the potential benefit (or not) of non-tobacco flavored e-cigarettes for adult smokers*



Summary

- FDA has the authority to regulate tobacco products to improve public health, and these regulations need to consider both users and non-users
- Regulations that reduce the appeal and addictiveness of combusted tobacco are likely to have the biggest impact
 - Nicotine reduction, if it can get done, is likely the most effective possible intervention
 - Upcoming RCT on menthol (planned start 11/1/2023)
- Regulations that reduce the appeal of non-combusted products, like e-cigarette flavoring regulations, are complicated because they impact both users and non-users
 - Upcoming RCT on flavors (planned start 10/1/2023)



Thank You and Questions

Thank you to collaborators!

- Theodore Wagener, PhD
- Matthew Carpenter, PhD
- K. Michael Cummings, PhD
- Amy E. Wahlquist, MS
- Joseph Koopmeiners, PhD
- Andrea Villanti, PhD
- Neal Benowitz, MD
- David Levy, PhD
- Darren Mays, PhD

Thank you to staff!

- Merritt McDonald
- Amy Boatright
- Yunuen Lupian
- J'Neice Hunter
- Dale Kiss
- Kaila Norton
- Neil Molina
- Susan Match
- Alice Hinton

