

Tobacco Regulation Across the Continuum of Harm

Tracy T. Smith, Ph.D.



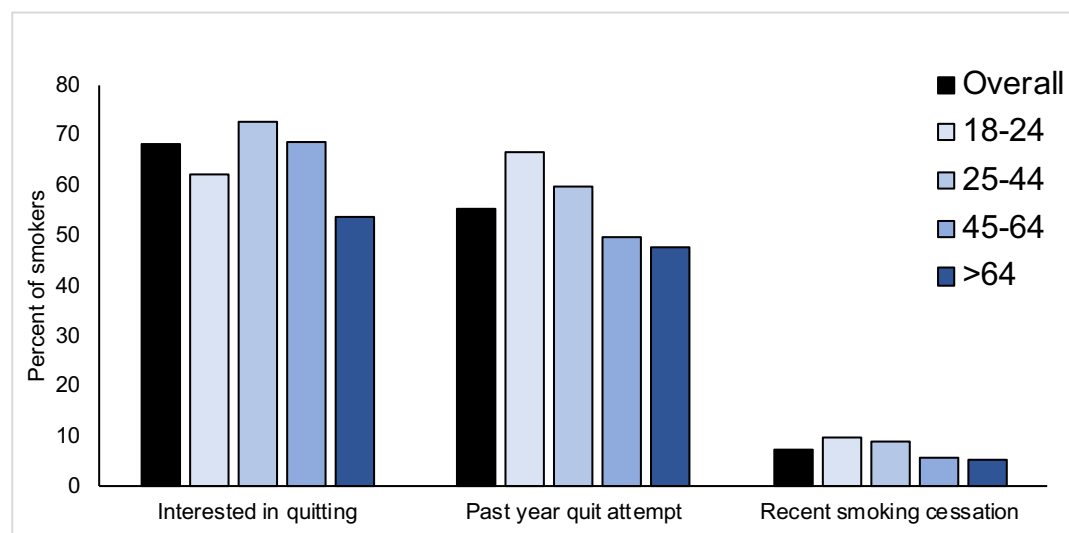
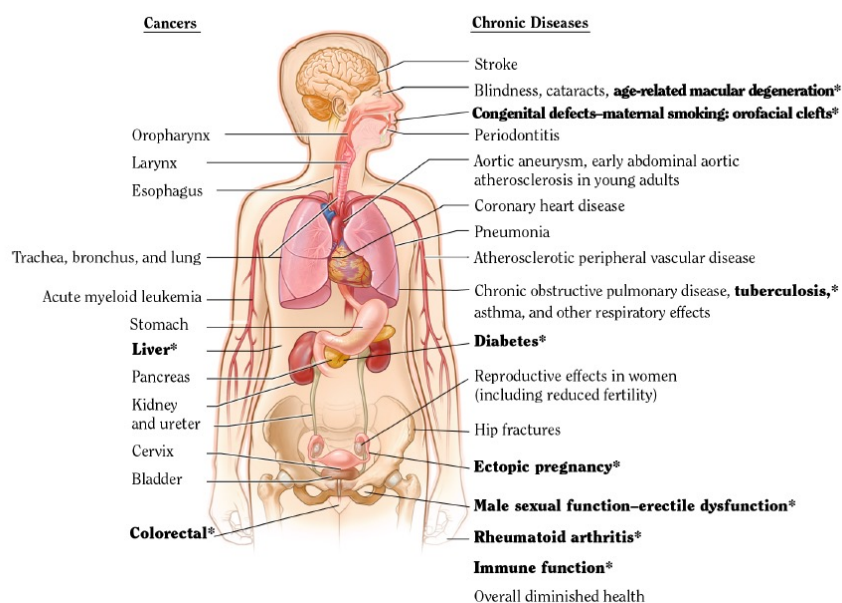
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Cigarettes are deadly and most smokers want to quit

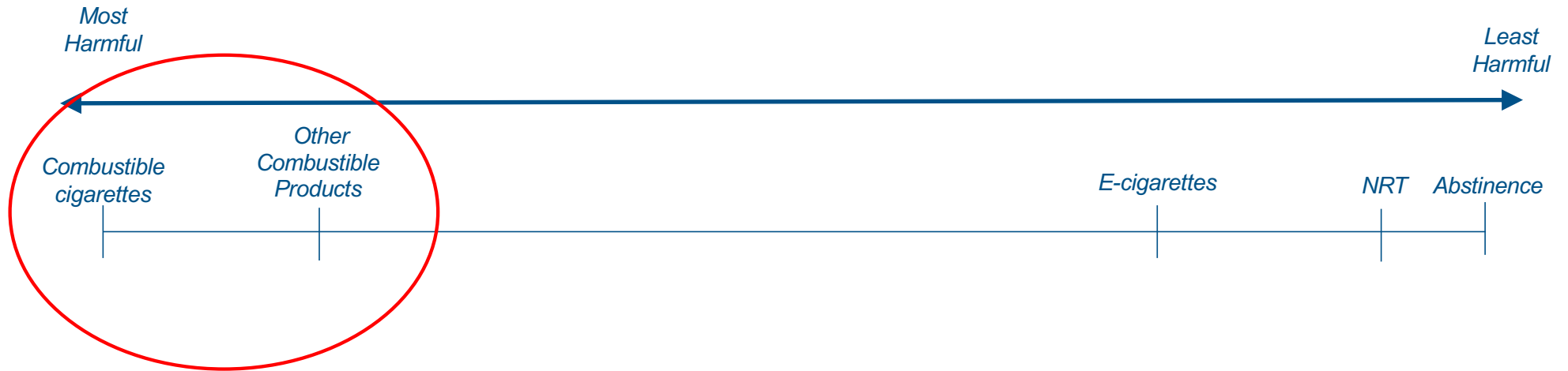
Figure 1.1A The health consequences causally linked to smoking



Babb et al., 2017 *MMWR*



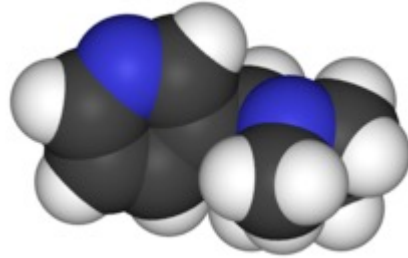
Continuum of Harm



Bulk of the harm, Most opportunity for impact



Why do people smoke?



Family Smoking Prevention and Tobacco Control Act

Set proc

› Curr
› Naiv
Product

FDA NEWS RELEASE

FDA Announces Plans for Proposed Rule to Reduce Addictiveness of Cigarettes and Other Combusted Tobacco Products

Potential Rule Would Propose to Establish a Maximum Level of Nicotine in Cigarettes with the Goal of Reducing Youth Use, Addiction and Death

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For Immediate Release: June 21, 2022

Content

 **MUSC Health**
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**How would a mandated reduction in nicotine
content impact smoking behavior?**



Human Clinical Trial Design

Assigned to either receive:



15.8 mg nicotine / g tobacco

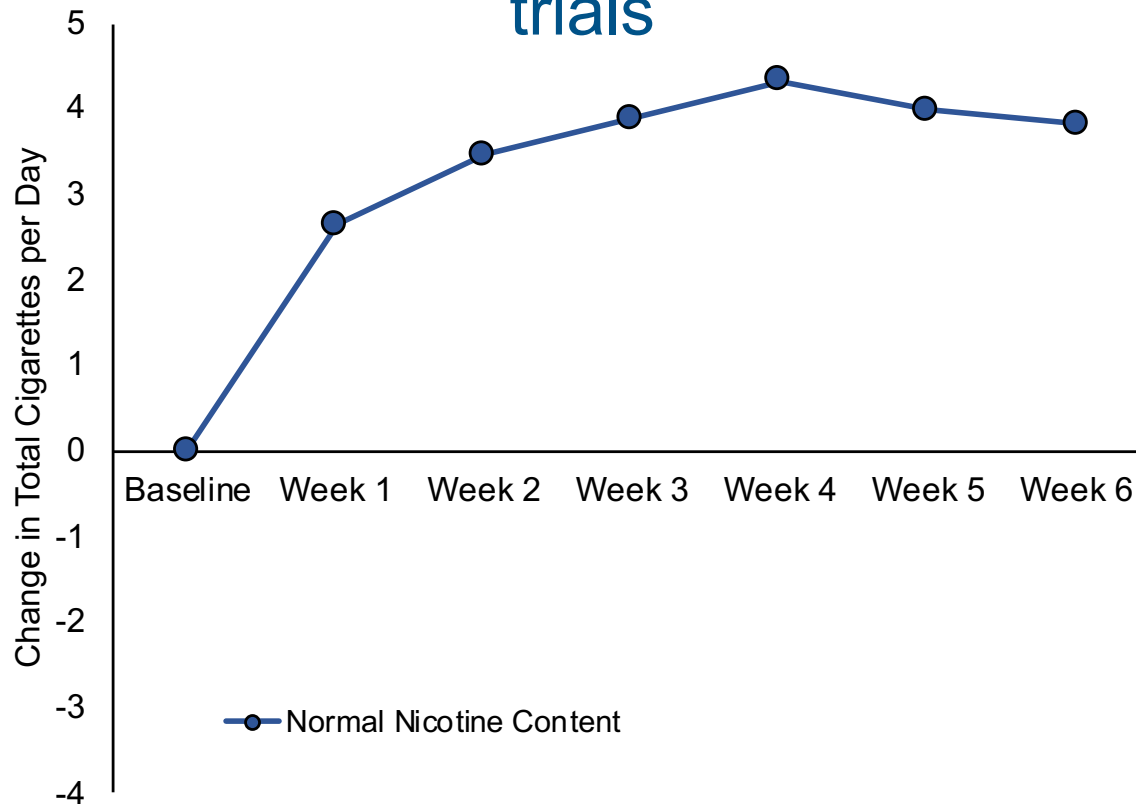


0.4 mg nicotine / g tobacco
>97% reduced

Smith et al., 2019 AJPM



Impact of nicotine reduction on smoking behavior in clinical trials



Eric Donny, PhD

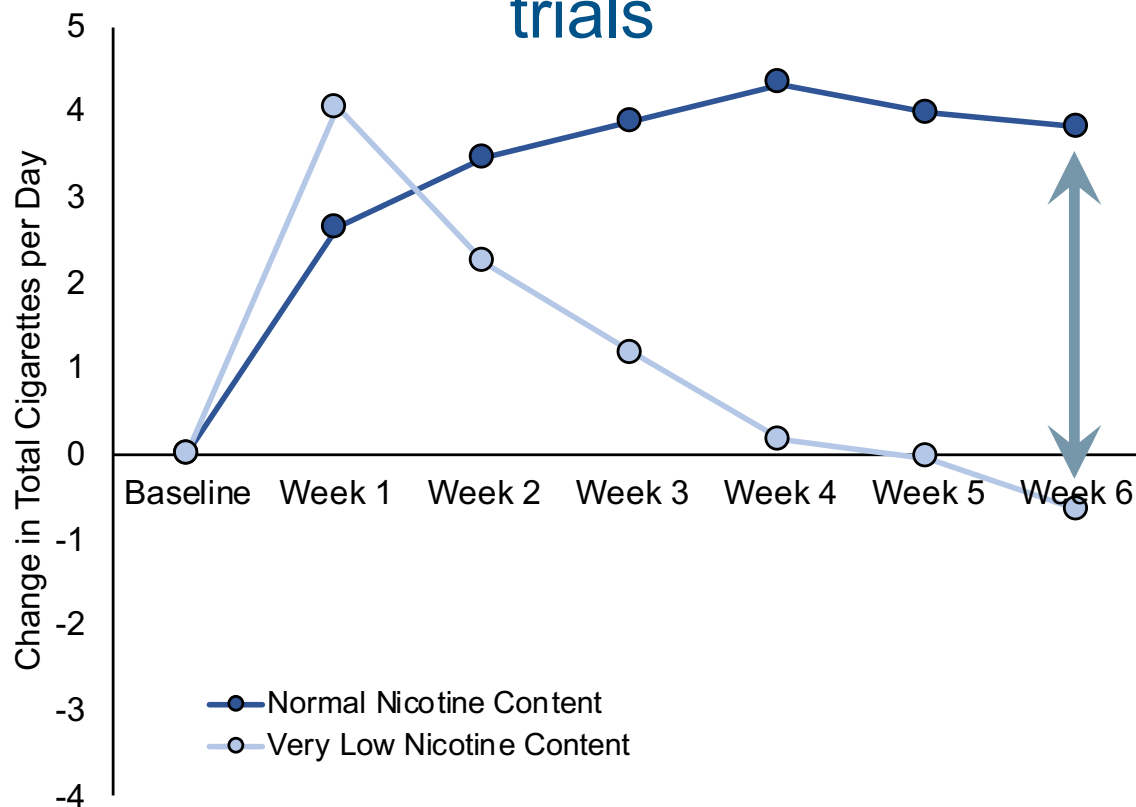


N=120

Smith et al., 2019 AJPM



Impact of nicotine reduction on smoking behavior in clinical trials



Eric Donny, PhD



N=120

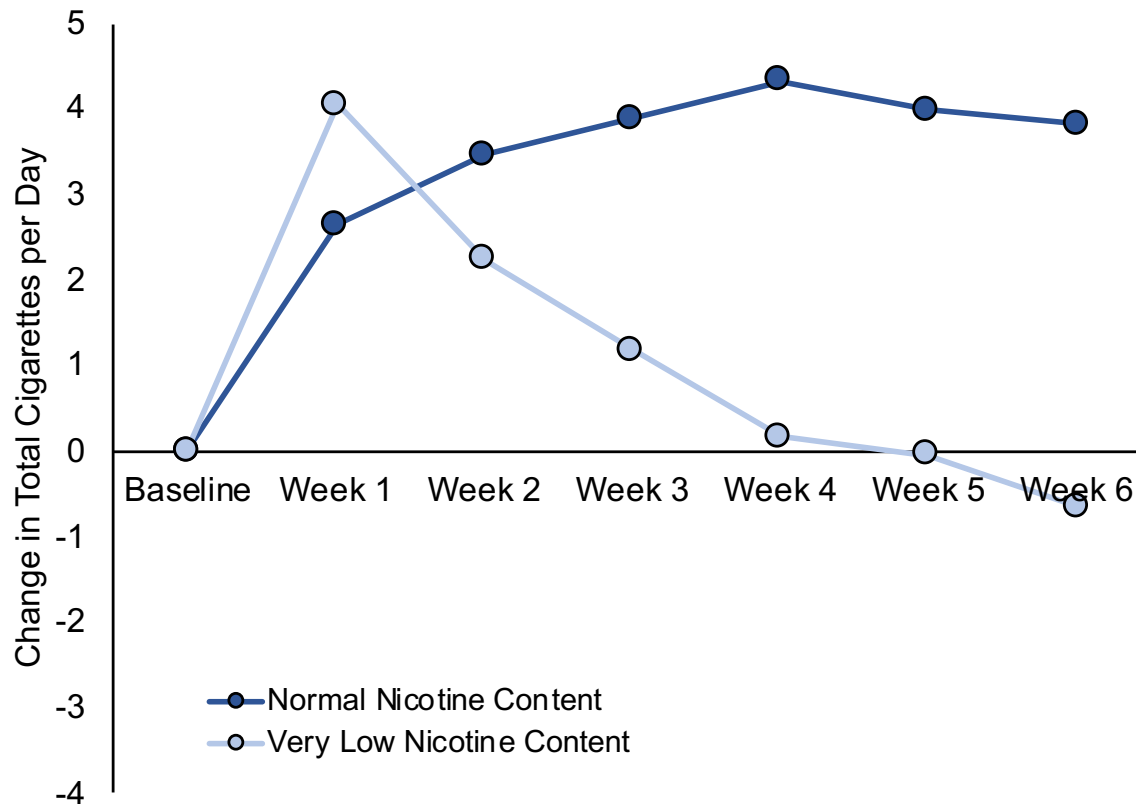
Smith et al., 2019 AJPM



Will smokers compensate for a reduction in nicotine content?



Clinical trials do not show sustained increase in CPD

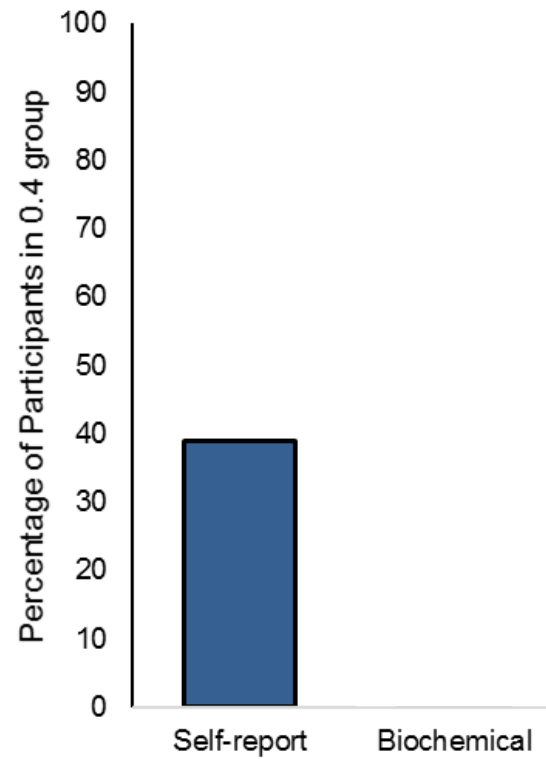


N=120

Smith et al., 2019 AJPM



Many smokers are noncompliant



Nardone et al., 2016



Would smokers compensate if they were unable to access normal nicotine content cigarettes?





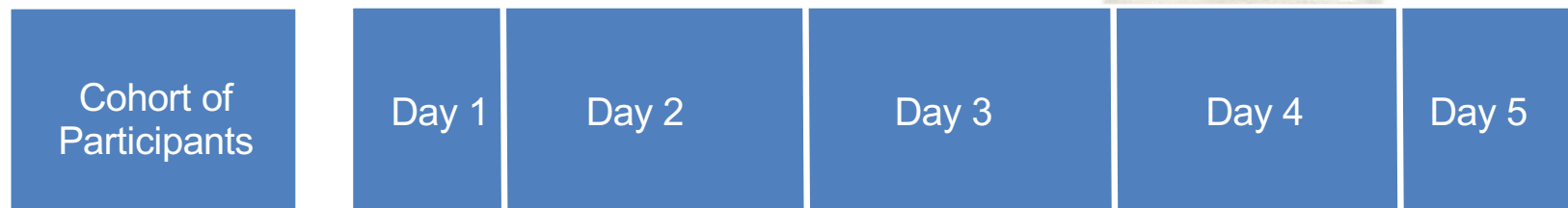
Hotel Inpatient Study

Normal Nicotine Content Cigarettes



Washout week

Very Low Nicotine Content Cigarettes



N=16



Cigarettes for Purchase

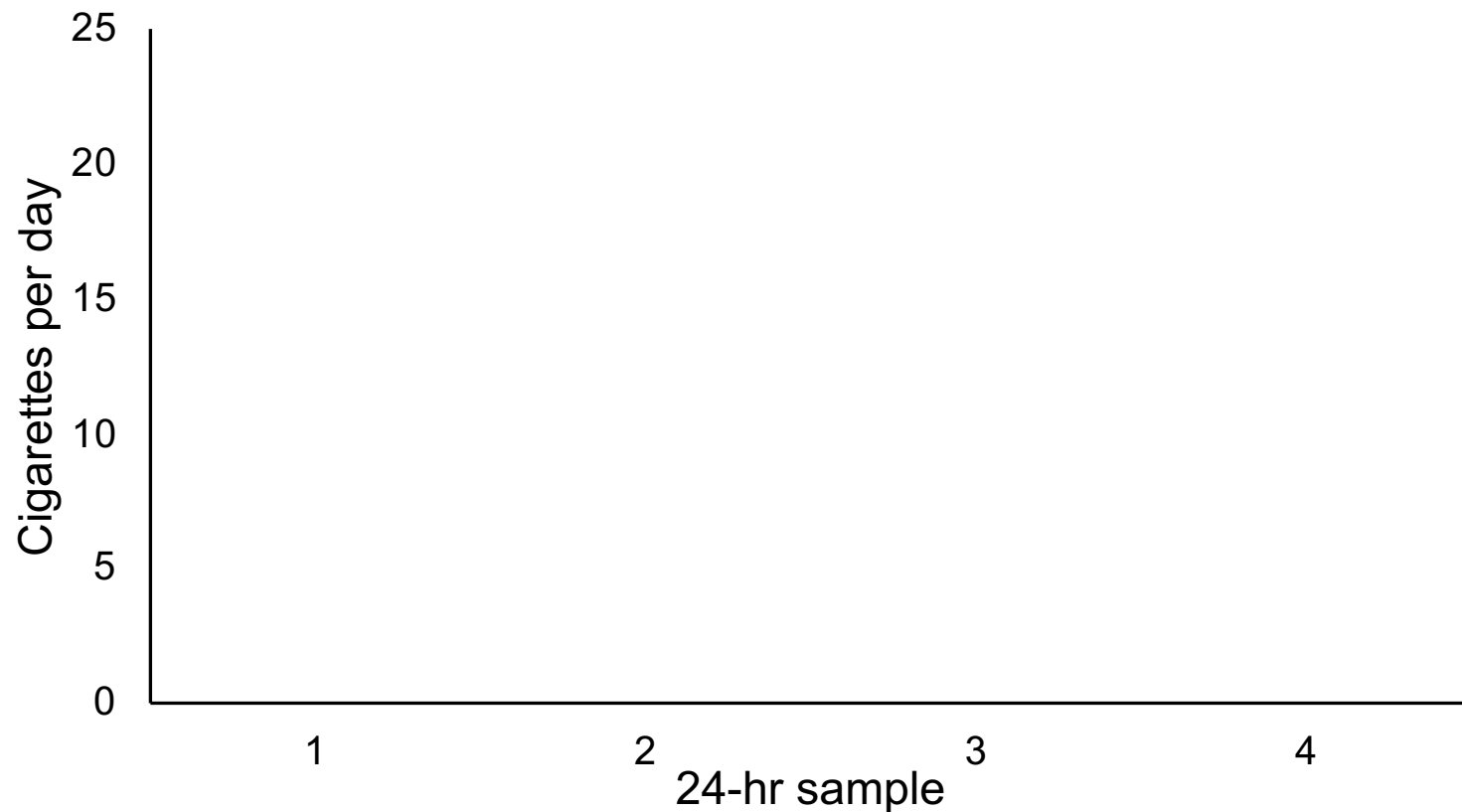


Cigarettes for Purchase

- Any money left in participants' accounts was provided to them at the end of the week



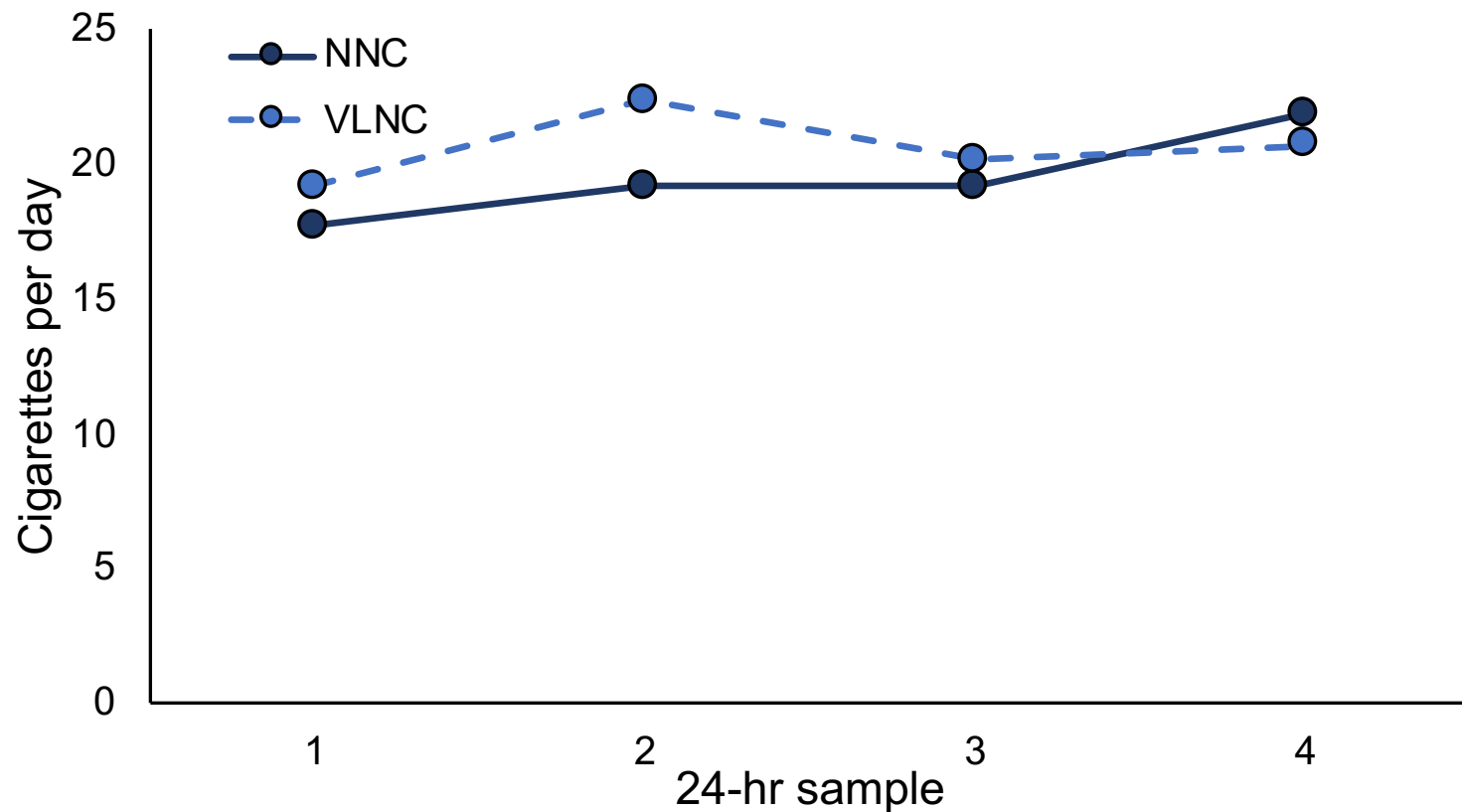
Cigarettes per day



Smith et al., 2020 CEBP



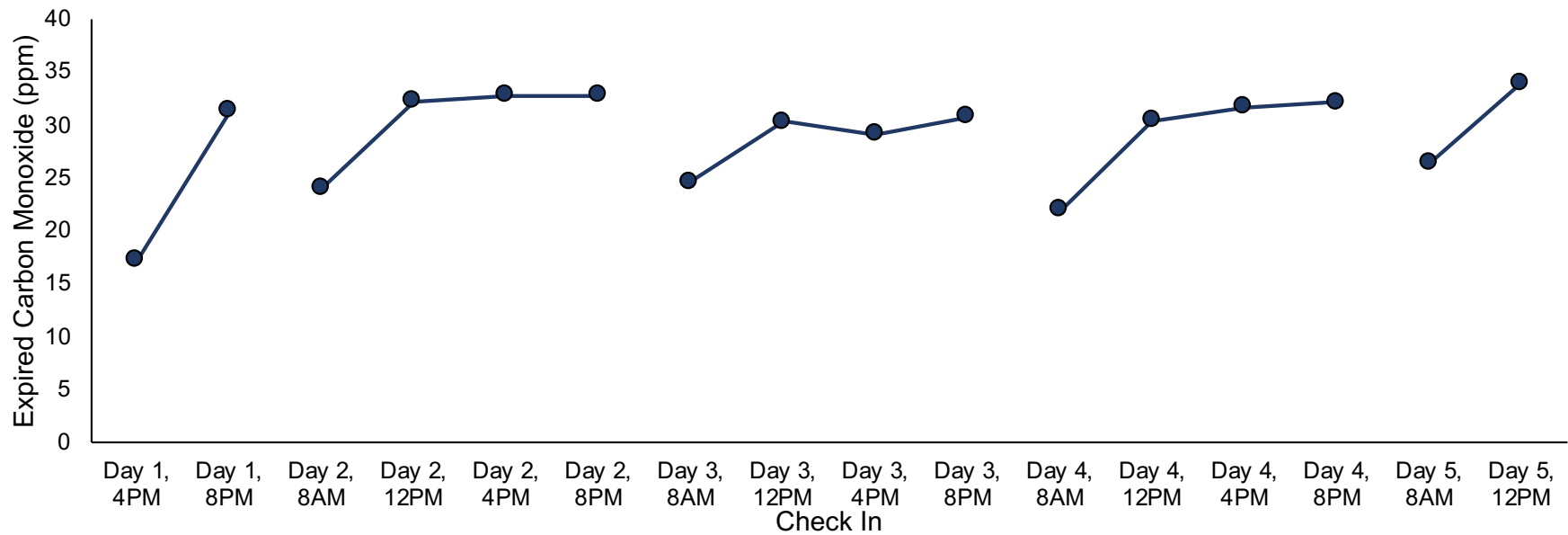
Cigarettes per day



Smith et al., 2020 CEBP



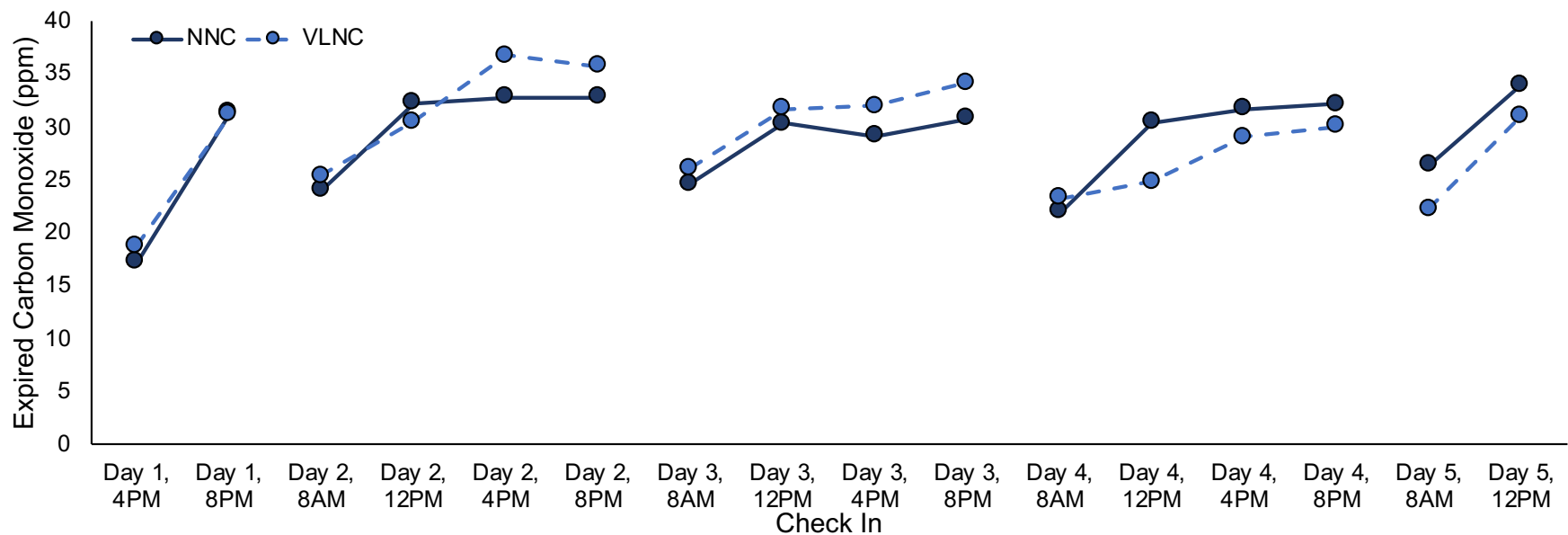
Expired Carbon Monoxide



Smith et al., 2020 CEBP



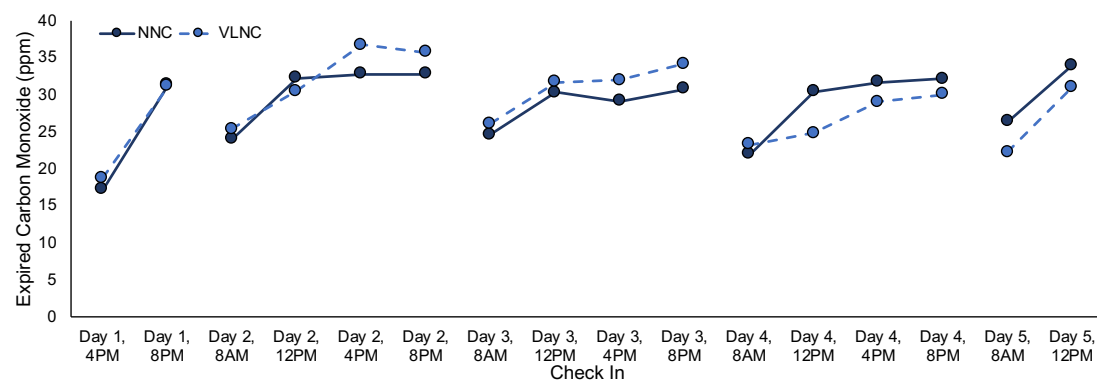
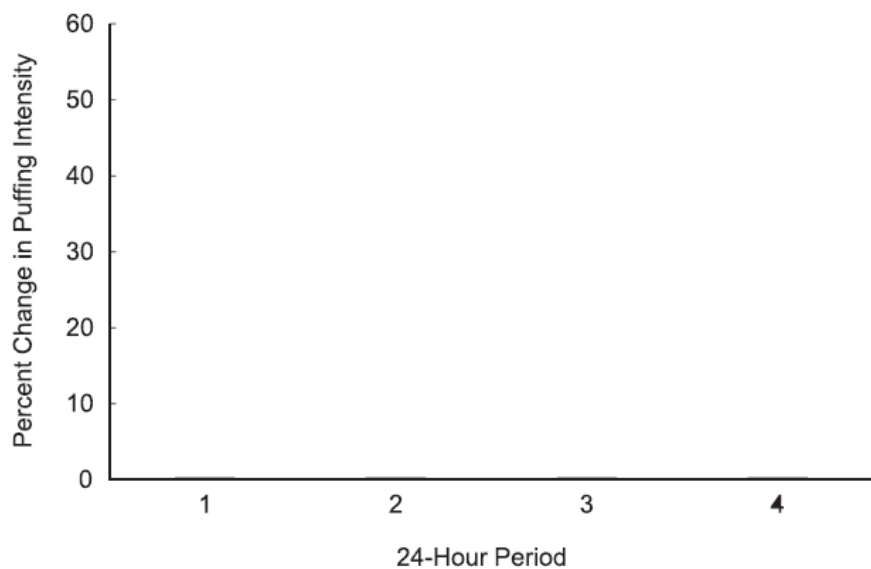
Expired Carbon Monoxide



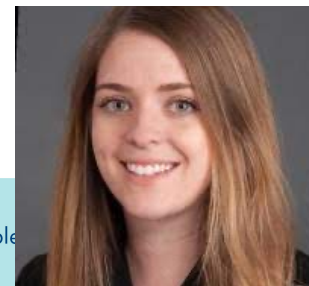
Smith et al., 2020 CEBP



What about changes in smoking intensity within each cigarette?



White et al., 2022 *Nicotine and Tobacco Research*



Expectancies

“My initial reaction was I'm gonna have to smoke probably two to one or three to one just to get the same amount.” –47 yo, M

“What my thoughts were and what the reality was is two totally different ideas. You know my thought was they're going to be nasty. You're not going to even taste anything. I'm going to smoke like a freight train to try to make up for the nicotine my body is craving, and it didn't even come out that way.” –38 yo, F

“I was just thinking I would have to keep lighting up cigarettes back-to-back just to get-like five cigarettes, I was thinking, just to feel like I smoked one. But then, and after trying them, it wasn't like that at all.” –33yo, M

“Oh sh*t” –51 yo, F

Denlinger-Apte et al., 2021 Drug and Alcohol Dependence



Withdrawal?

“I’ve been like—I’m not freaking out, I’m not upset, I’m not depressed, I feel fine. I feel kinda tired though, you know, kinda drained.” 51 yo, F

“I would say I feel about the same as I always do....if anything, I’ve been more—maybe more hungry.” –33 yo, M

”Slightly more irritated about it.” –50 yo, M

Denlinger-Apte et al., 2021 Drug and Alcohol Dependence



Dependence

“when I go home now I’m thinking. “Do I just not even smoke when I get back in that car with my husband?” you know. Should I do that you know, or do I actually pick up another cigarette, you know... Cause I think I can actually quit now.” –51 yo, F

“I find I’m able to play cards without dying for a cigarette, to go and read a book without having that cigarette in my hand. I’m not having the urge to literally keep that cigarette pack next to me.”—36 yo, F

“I smoked more on Monday, I still smoked a decent amount on Tuesday, but once Wednesday got here it’s like my cravings for wanting to smoke and my really need to smoke has really come down a whole lot. It’s like the desire of I need a cigarette is not as strong.” –38 yo, F

Denlinger-Apte et al., 2021 Drug and Alcohol Dependence



A mandated reduction in nicotine content is likely to...

- Reduce cigarettes smoked per day among smokers unmotivated to quit
- Unlikely to produce sustained compensation
- Reduce initiation of cigarette smoking among individuals who are naïve to nicotine
- Increase cessation among smokers motivated to quit
- Similar effects observed a variety of vulnerable subpopulations



There are other interventions aimed at reducing appeal and addictiveness....more on this later.

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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Announcements

For Immediate Release: April 29, 2021

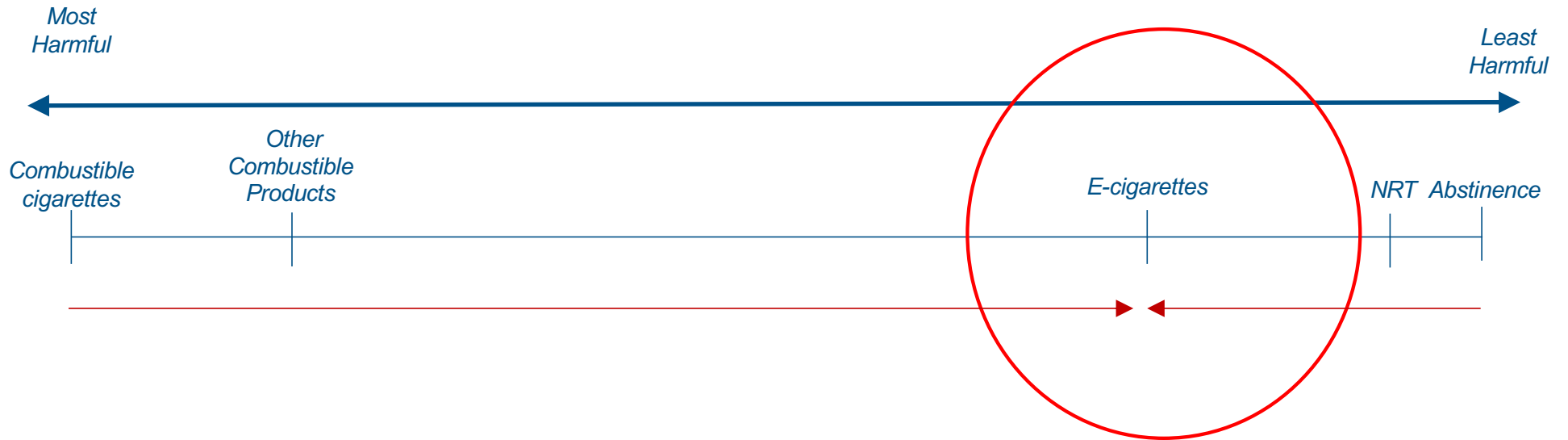
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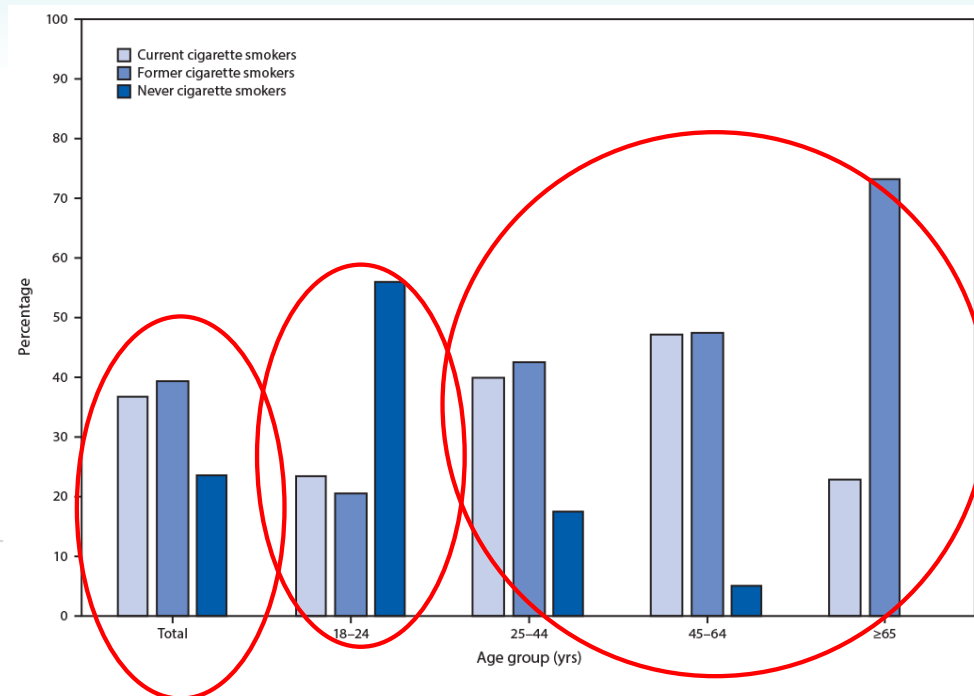
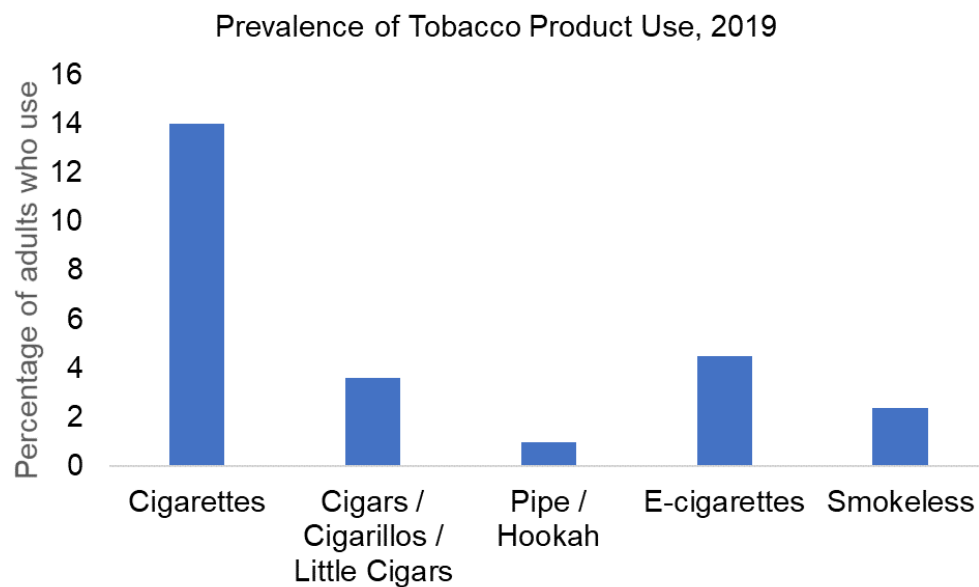
Continuum of Harm



How should we regulate non-combustible products?



Prevalence of E-cigarette Use Among Adults



Cornelius et al., 2020 *MMWR*



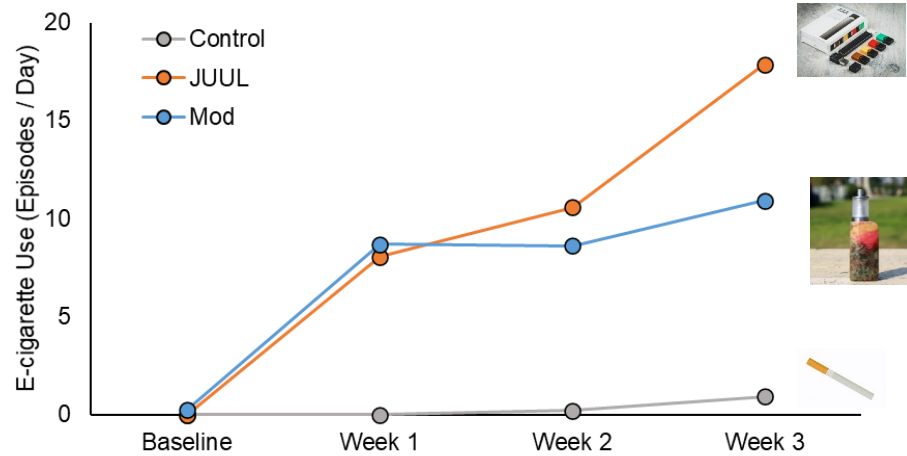
What is the impact of e-cigarette use on cigarette smoking for adults?



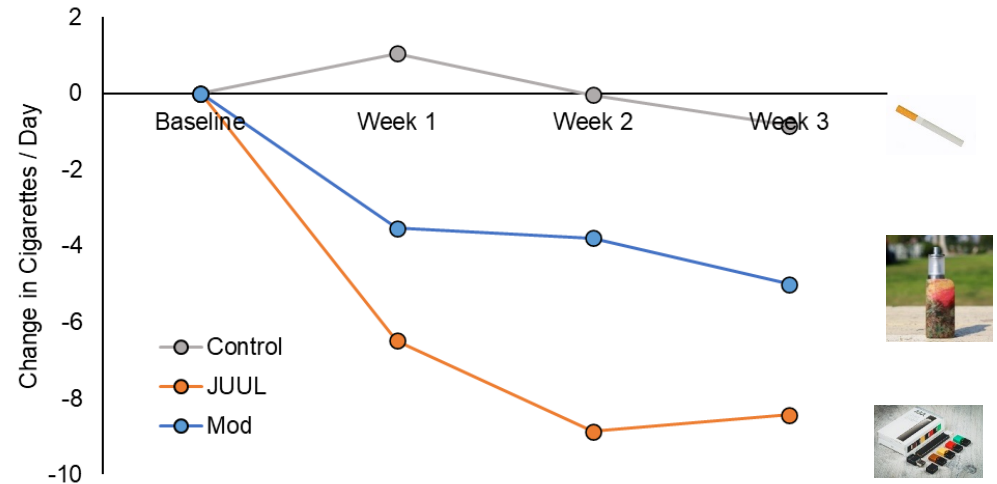
Pilot trial investigating impact of e-cigarettes on smoking



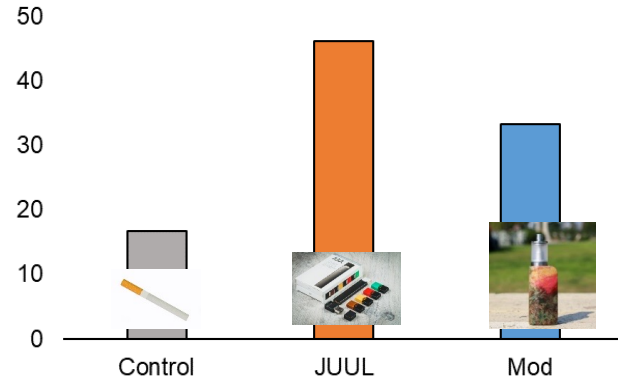
E-cigarette Use



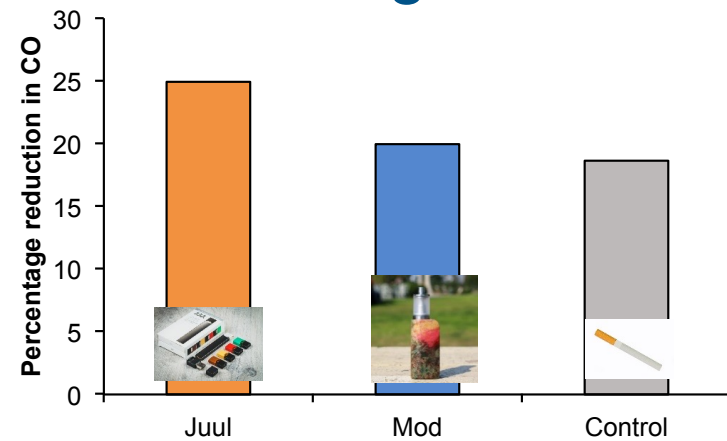
Change in CPD



% Trying to Quit Smoking



Change in CO



E-cigarettes can reduce cigarette smoking, even among smokers not instructed to switch

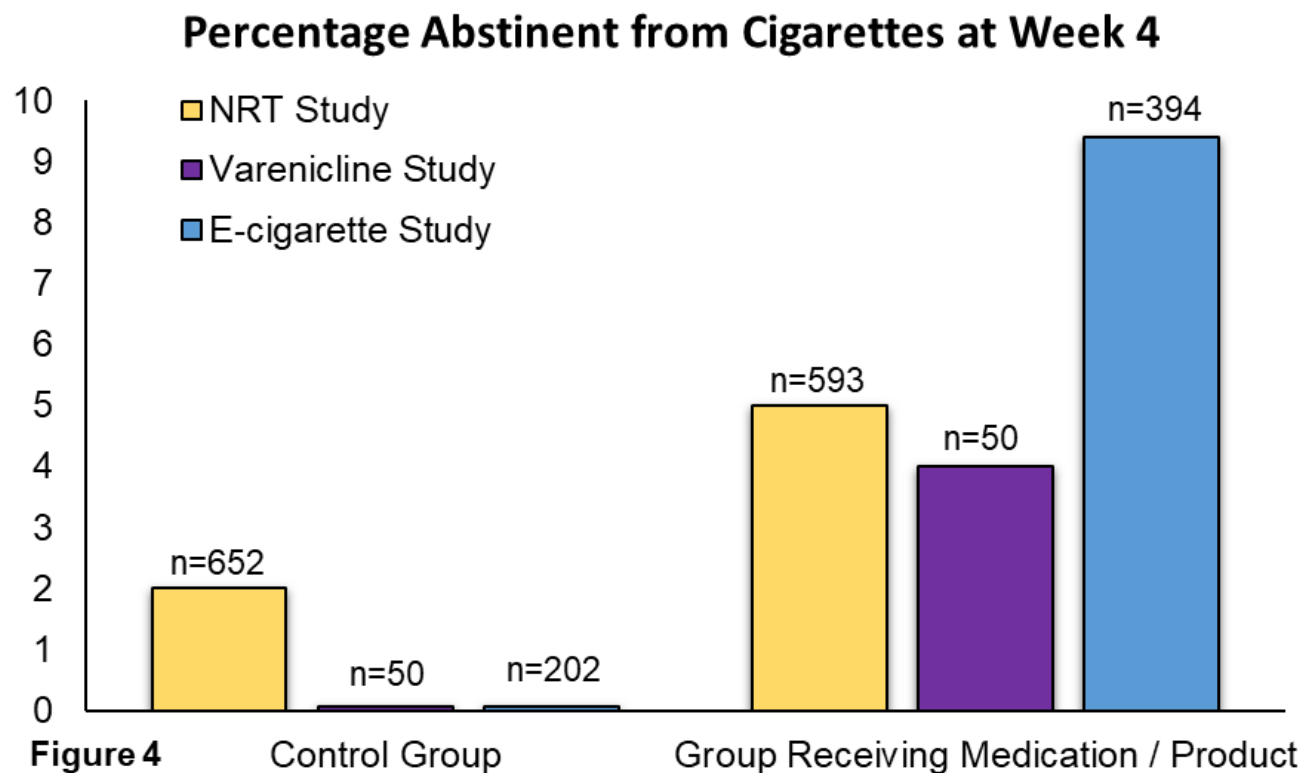


Figure 4

Dr. Matt Carpenter



Can e-cigarettes help smokers abstain from smoking better than FDA-approved medications?

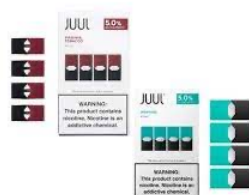


Daily diaries reporting tobacco use and tobacco/medication use throughout.





N=150 OR



OR

N=75



1 week
pre-switch

Target Switch
Date

8 weeks, switch
completely

Follow up to 6-mo,
encouraged to get
more as desired

*Outcomes: Self-reported tobacco and medication use,
expired carbon monoxide, urinary NNAL, respiratory
function (self-reported and spirometry)*

1 week
pre-quit

Target Quit
Date

8 weeks, quit
completely

Follow up to 6-mo,
encouraged to get
more as desired

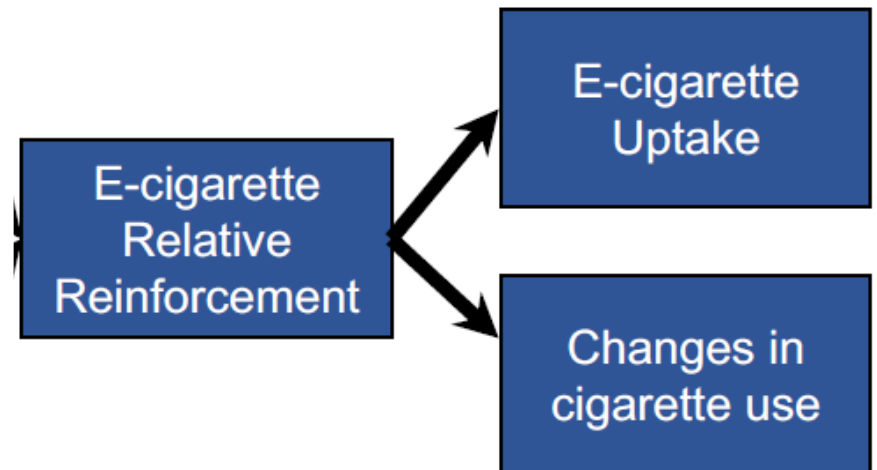
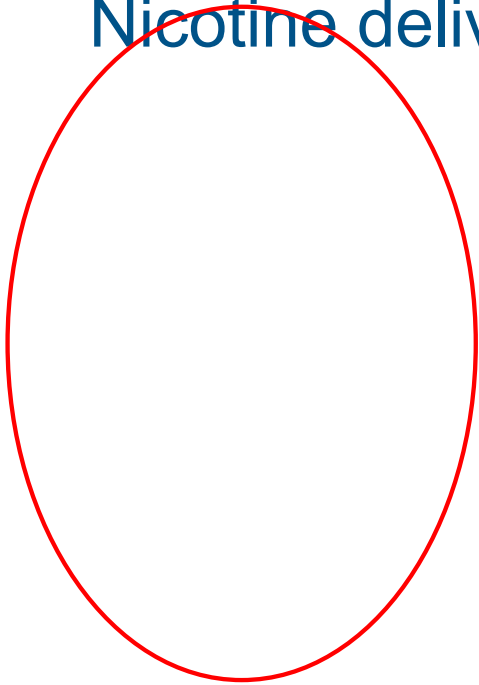
Smokers who
have already
tried to quit
and failed
with FDA-
approved
medications
N=225



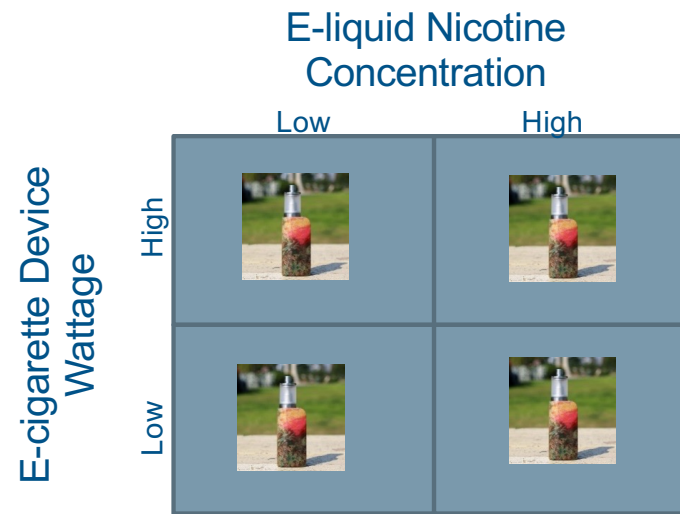
What are determinants of “successful” switching to e-cigarettes?



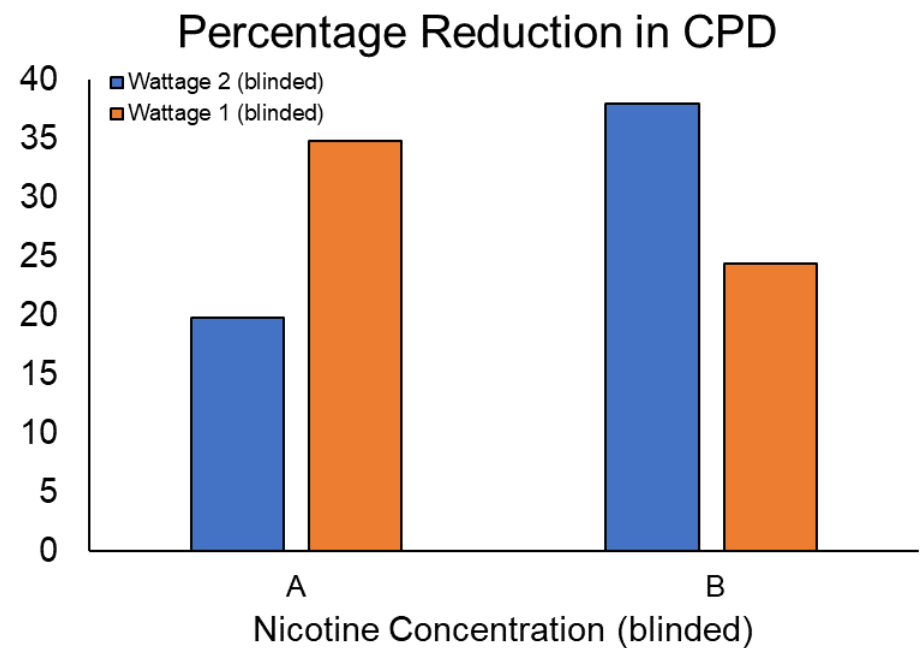
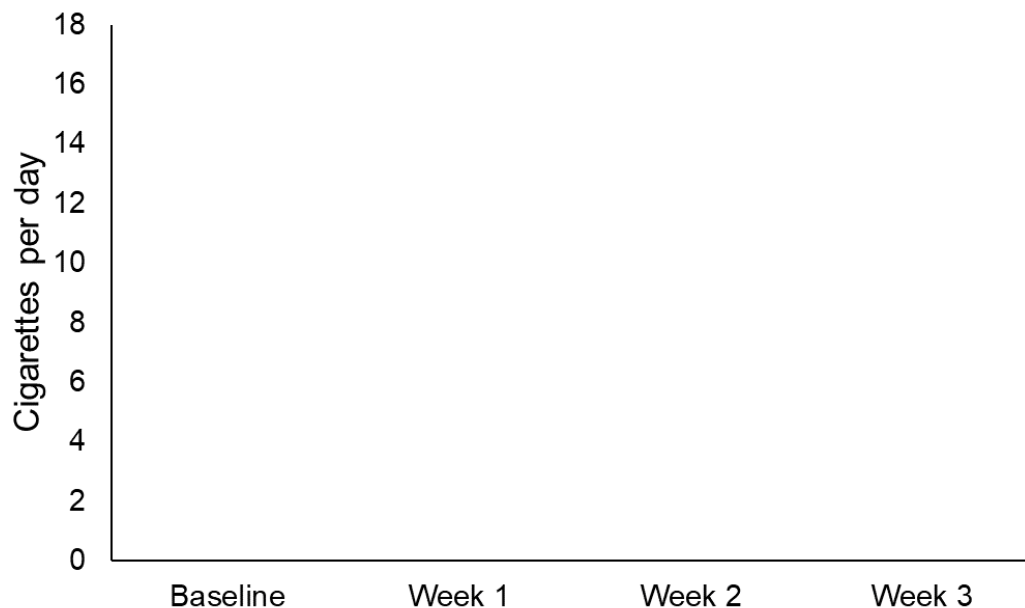
Nicotine delivery and sensorimotor cues are likely important



Impact of Nicotine Concentration and Device Wattage



Impact of Nicotine Concentration and Device Wattage



Ongoing, N=74



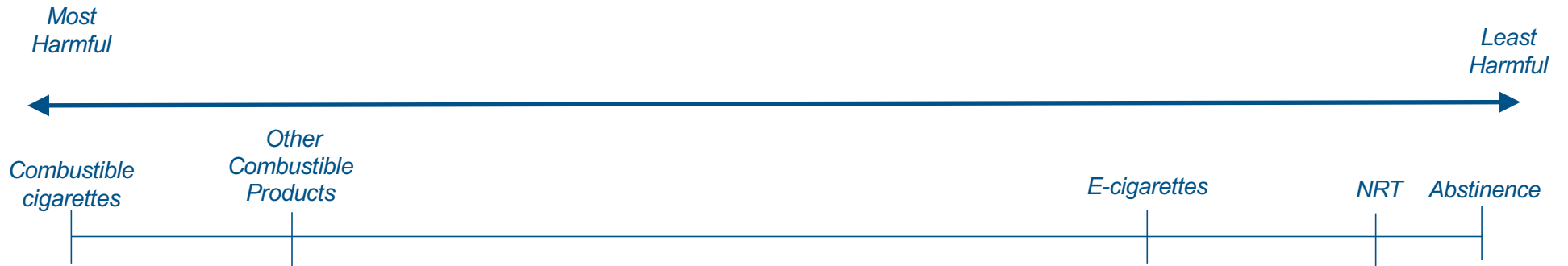
E-cigarettes....

- Among adults, are most used in current and former smokers
- Have the potential to reduce cigarette smoking and dependence in adult smokers, even without explicit instructions to switch
 - Future research should investigate intentional switching
- Device characteristics likely important, nicotine is critical determinant in all tobacco products
 - What level of nicotine is required? How does this compare to the level adolescents find appealing?
- Are popular among non-smoking youth
 - Many youth want to quit vaping and future studies should develop and test interventions

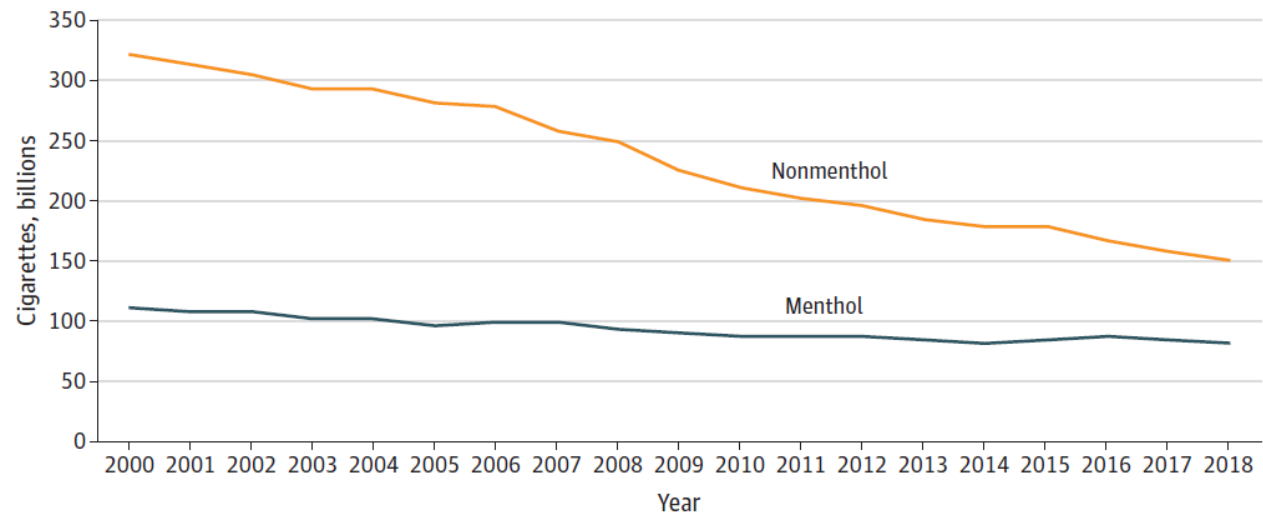




Continuum of Harm



Menthol: A broader definition of harm



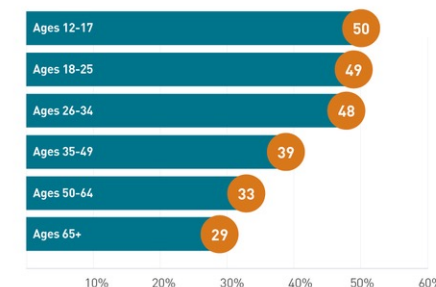
Delveno et al., 2020



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

Menthol cigarette preference among cigarette smokers in the U.S by age, 2018



Source: Tobacco control?



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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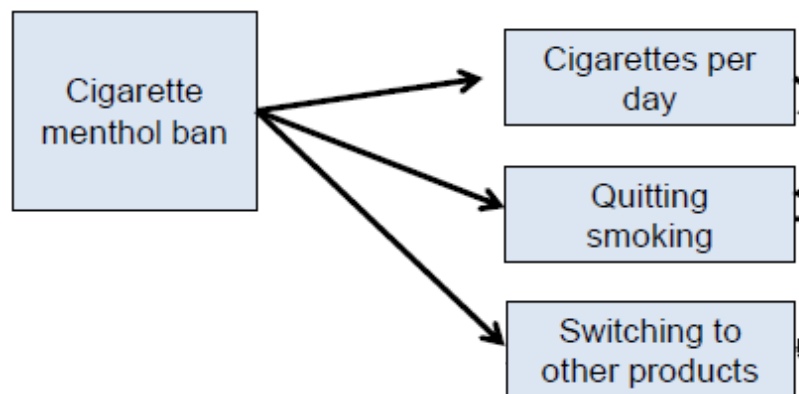


Figure 1. Conceptual framework illustrating the impact of a cigarette and e-cigarette menthol ban on tobacco use outcomes for menthol smokers. Once treatment effects have been estimated in a clinical trial sample, it is critical to model their impact in the population. These policies are likely to also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

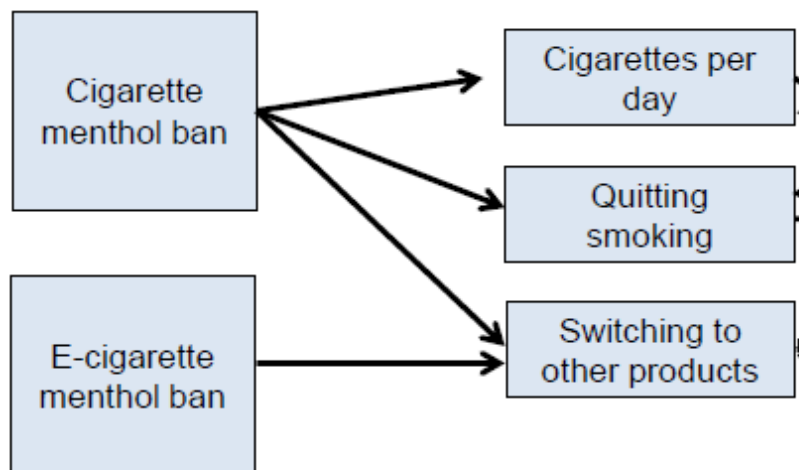


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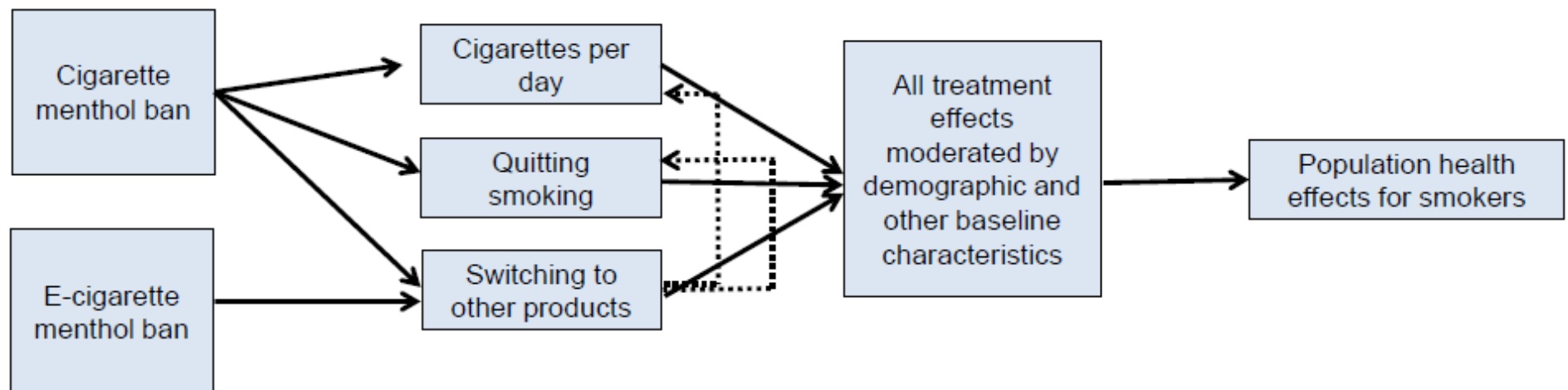


Figure 1. Conceptual framework illustrating the impact of a cigarette and e-cigarette menthol ban on tobacco use outcomes for menthol smokers. Once treatment effects have been estimated in a clinical trial sample, it is critical to model their impact in the population. These policies are likely to also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

How would a menthol ban for cigarettes and/or e-cigarettes 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

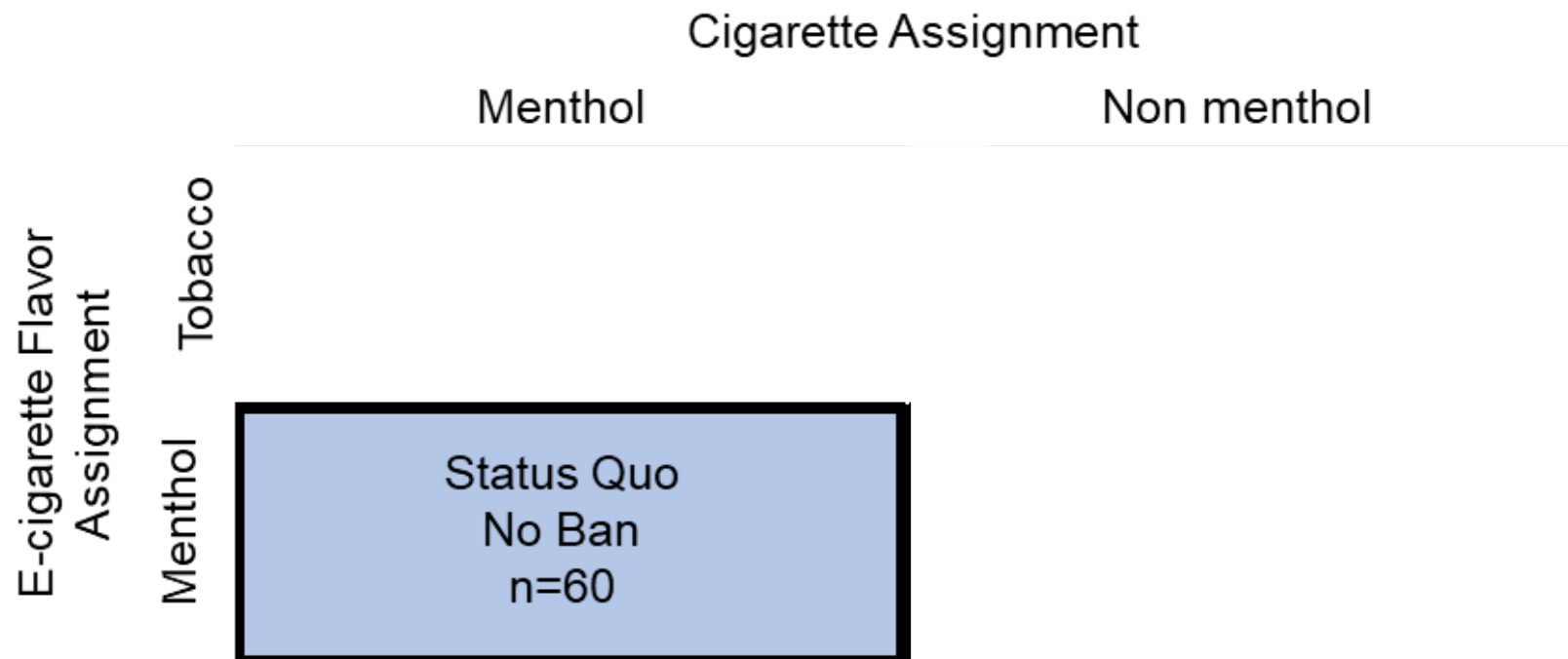
Non menthol

E-cigarette Flavor
Assignment

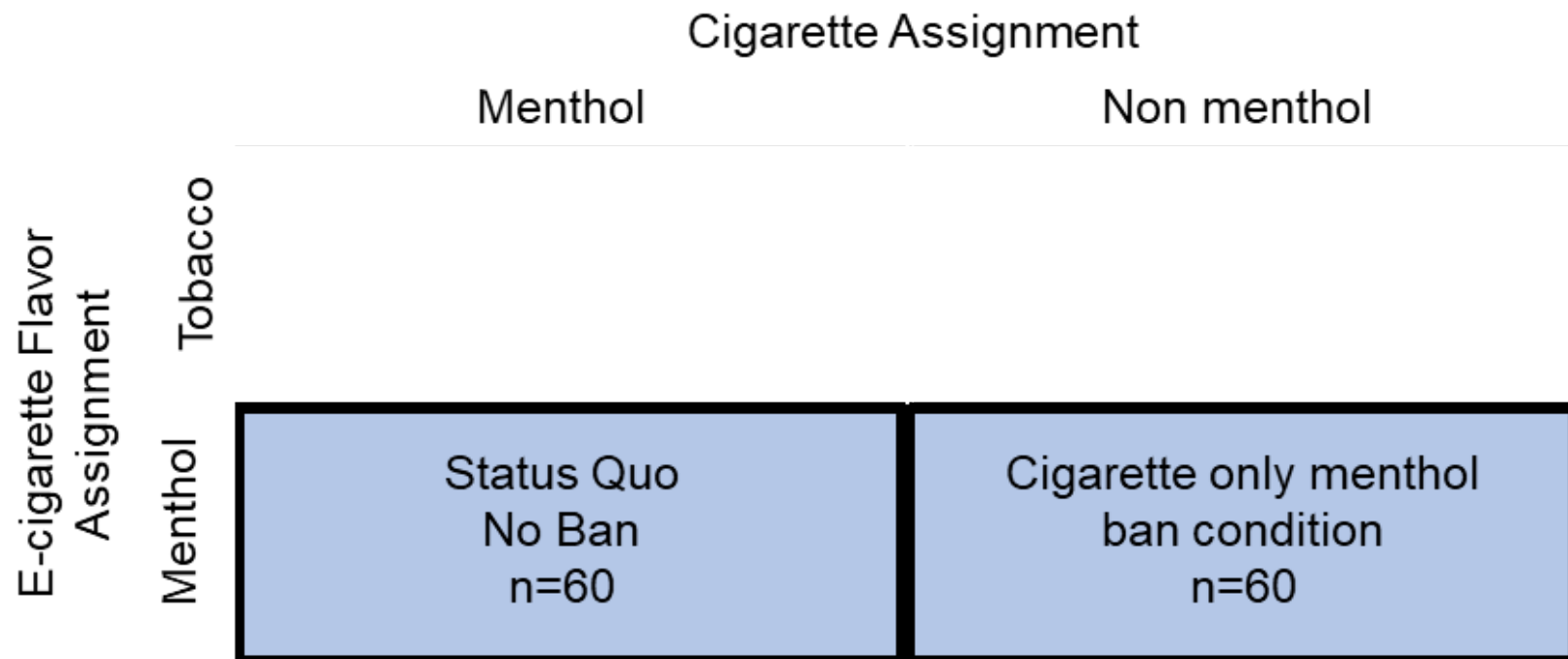
Menthol Tobacco



Trial Design



Trial Design



Trial Design

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



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





Usual
Brand
Provided

Study product provided free of charge

... everyone also has the option to take home NRT each week.





... everyone also has the option to take home NRT each week.

Outcomes: Cigarettes per day, e-cigarette use (including switching), ability to remain abstinent in Week 7, NRT use, quit attempts, subjective effects, cigarette and e-cigarette dependence

Aim 3 will describe the heterogeneity, calibrate the effect to the US adult menthol population, and model the impact on death and life years lost.

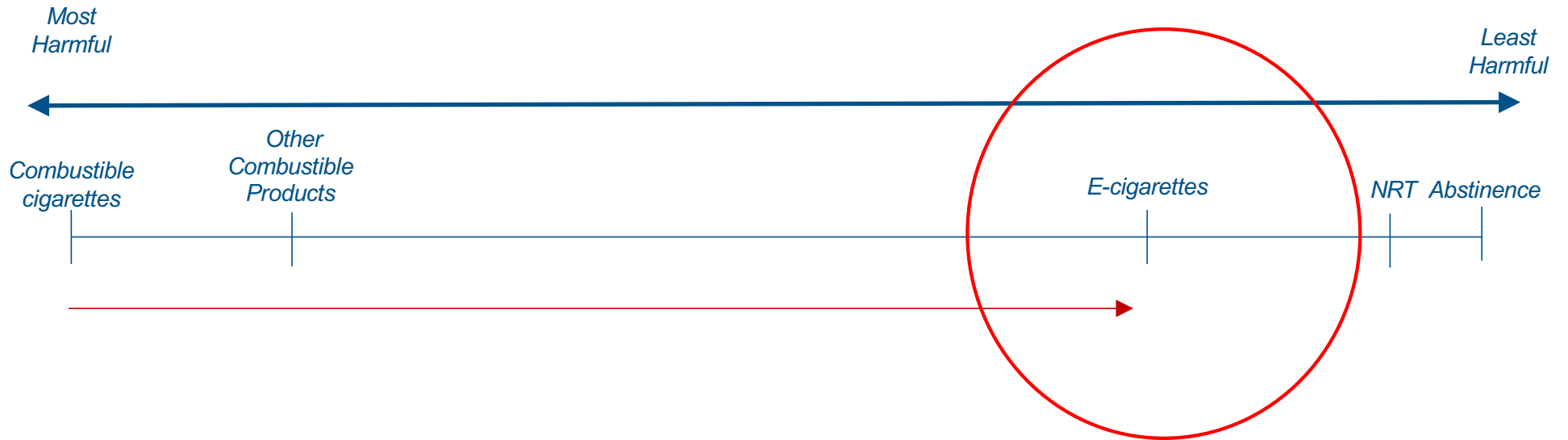


Joe Koopmeiners, PhD



David Levy, PhD

Continuum of Harm



How should we regulate non-combustible products?



What about flavors?



Submit Tobacco Product Applications for Deemed Tobacco Products


Resources for Applicants Required to Submit by September 9, 2020

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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 NEWS RELEASE

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

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

FDA NEWS RELEASE

FDA Permits Marketing of E-Cigarette Products, Marking First Authorization of Its Kind by the Agency

FDA STATEMENT

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

*demonstrate that
of Public Health*

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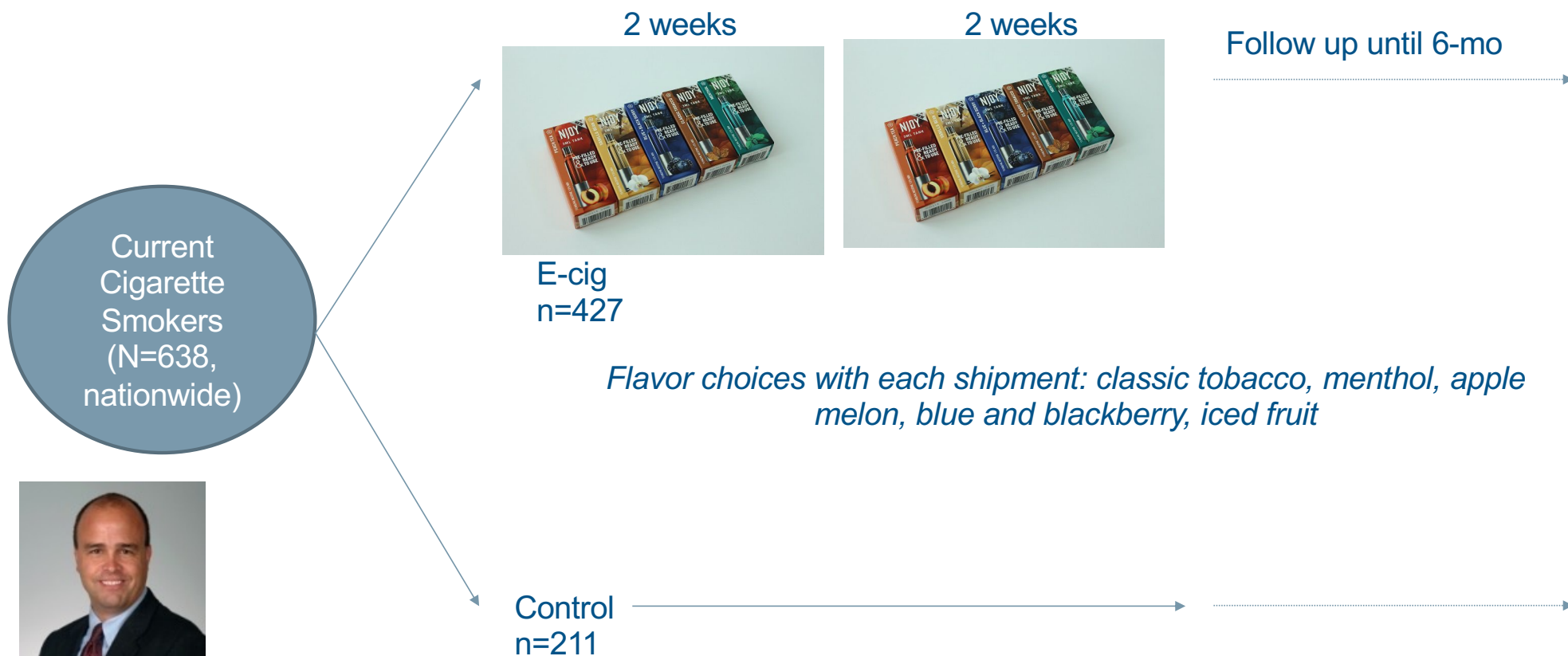
We've made significant progress in the months since, working diligently to better understand these products and, as of today, taking action on about 93% of the total timely-submitted applications. This includes issuing Marketing Denial Orders (MDO) for more than 946,000 flavored ENDS products because 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.



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



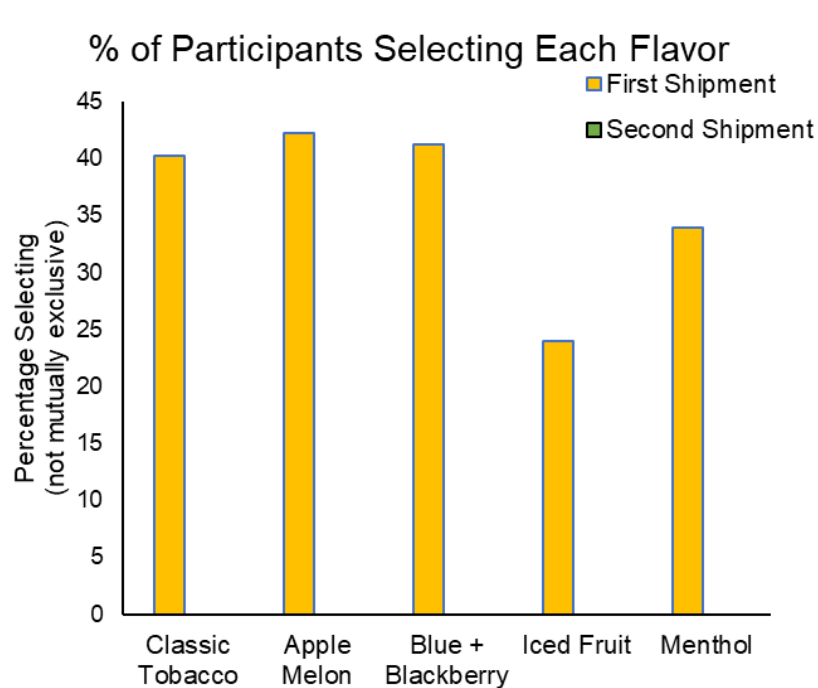
Preliminary data—CONNECT STUDY



Dr. Matt Carpenter



Reason to believe they may be important for switching



Data are preliminary

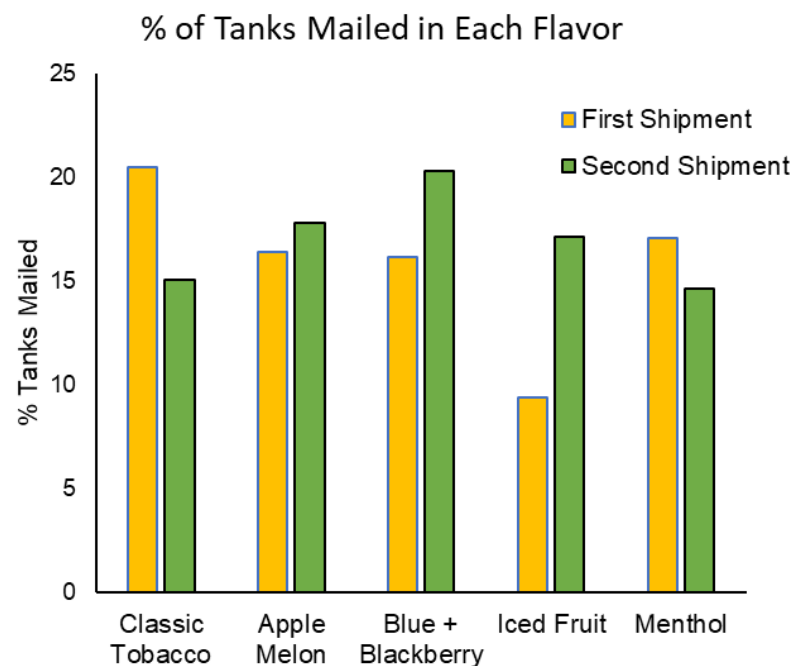
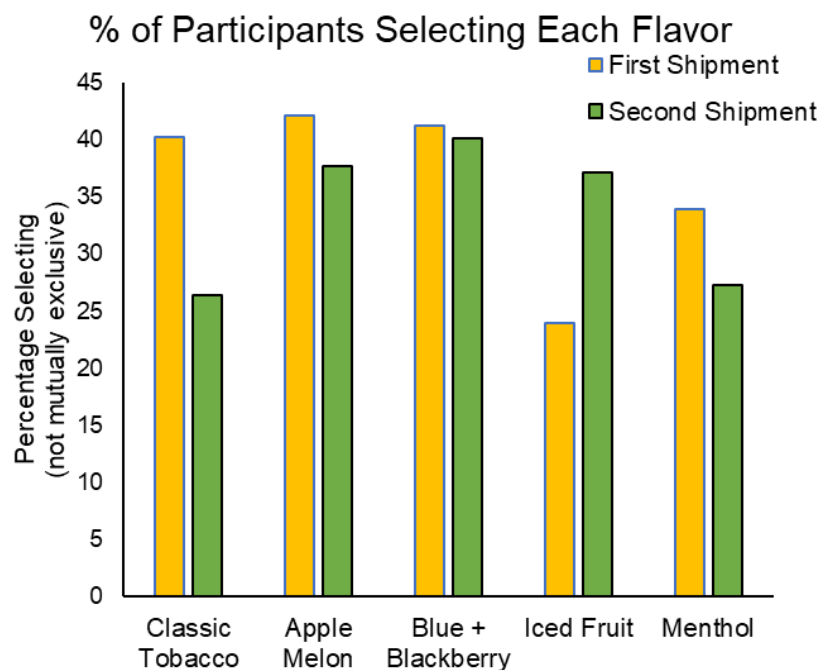
Dr. Matt Carpenter



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Reason to believe they may be important for switching

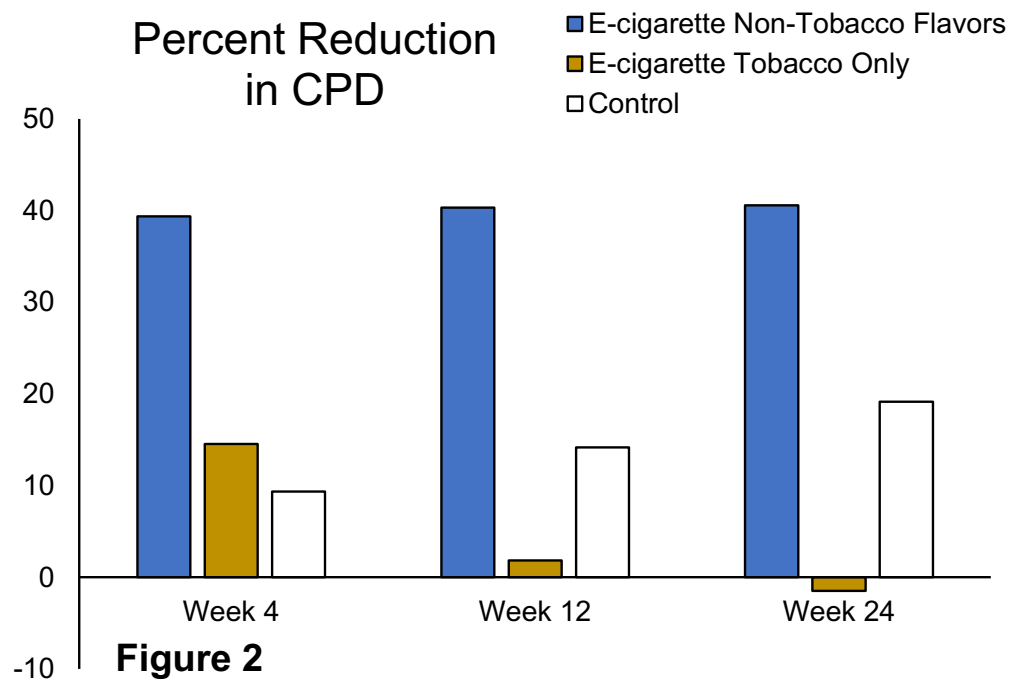


Data are preliminary

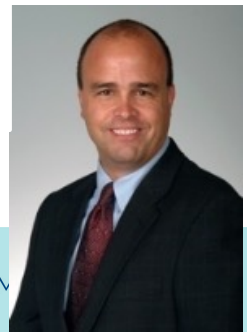
Dr. Matt Carpenter



Did flavor matter?



Data are preliminary



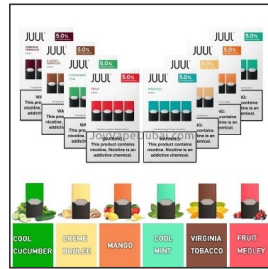


Theodore Wagener, PhD
Ohio State University

Current
Cigarette
Smokers
(N=1500,
nationwide)

SWITCH
DAY

2 weeks pre-switch



12 weeks, switch completely

12 weeks follow up

Outcomes: Cigarettes per day, e-cigarette use (including switching), expired carbon monoxide



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
 - Menthol is also likely to impact outcomes for current menthol users. Upcoming RCT on menthol
- 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, Upcoming intervention trial for smokers who can't quit



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- Lisa Coles
- J'Neice Hunter

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Thank You and Questions

