

Nicotine Reduction Policy to Reduce Youth Tobacco Use: Promise and Pitfalls

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Agenda

- Part 1:
 - Overview of my work on policy and youth, focusing on nicotine reduction as an exemplar of a tobacco control policy
- Part 2:
 - Potential challenges and opportunities for this policy that my work has uncovered
 - Menthol Ban
 - Areas for future work across disciplines



Nicotine Reduction

A Nicotine-Focused Framework for Public Health

Scott Gottlieb, M.D., and Mitchell Zeller, J.D.

Despite extraordinary progress in tobacco control and prevention, tobacco use remains the leading cause of preventable disease and death in the United States. Combustible cigarettes cause the overwhelming majority of tobacco-related disease and are responsible for more than 480,000 U.S. deaths each year. Indeed, when used as intended, combustible cigarettes kill half of all long-term users.¹

N ENGL J MED 377:12 NEJM.ORG SEPTEMBER 21, 2017

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- Reducing the level of nicotine in cigarettes has been proposed as way to make cigarettes less addictive and reduce the harm from these products
- Clinical trials with adults have shown that smokers asked to switch to lower nicotine content cigarettes reduce their cigarette consumption
- What about youth?

Apelberg et al., 2018; Donny et al., 2015; Gottlieb & Zeller, 2017

Young People & Nicotine Reduction

- While adolescent daily smoking is at historic lows, many continue to use tobacco products
 - The age of smoking initiation is rising to college-aged young adults
 - Exacerbates health disparities, as smoking is concentrated among marginalized youth
- Compared to adults, youth tend to be lighter and more intermittent smokers, with much shorter histories of nicotine exposure
 - With different motivations for smoking, may respond differently to this policy
- What do we know about potential effects of a nicotine reduction policy on young people?

Barrington-Trimis et al., 2020; Terry-McElrath & O'Malley, 2015; Colby et al., 2000a,b; Colby, Cassidy et al., 2021

Overview of studies modeling this policy in youth

- Studies of this policy in adolescents (15-19 year olds)
 - Acute laboratory study of adolescents (Cassidy et al., 2018, 2019)
 - Longer-term trial in adolescents (Cassidy et al., 2022)
- Studies of this policy in young adults (18-24 year olds)
 - Longer-term trials in young adults compared to older adults (Cassidy et al., 2018; 2021)

VLNC= Very Low Nicotine Content, NNC= Normal Nicotine Content (Control)

Do very low nicotine content cigarettes reduce withdrawal and craving?

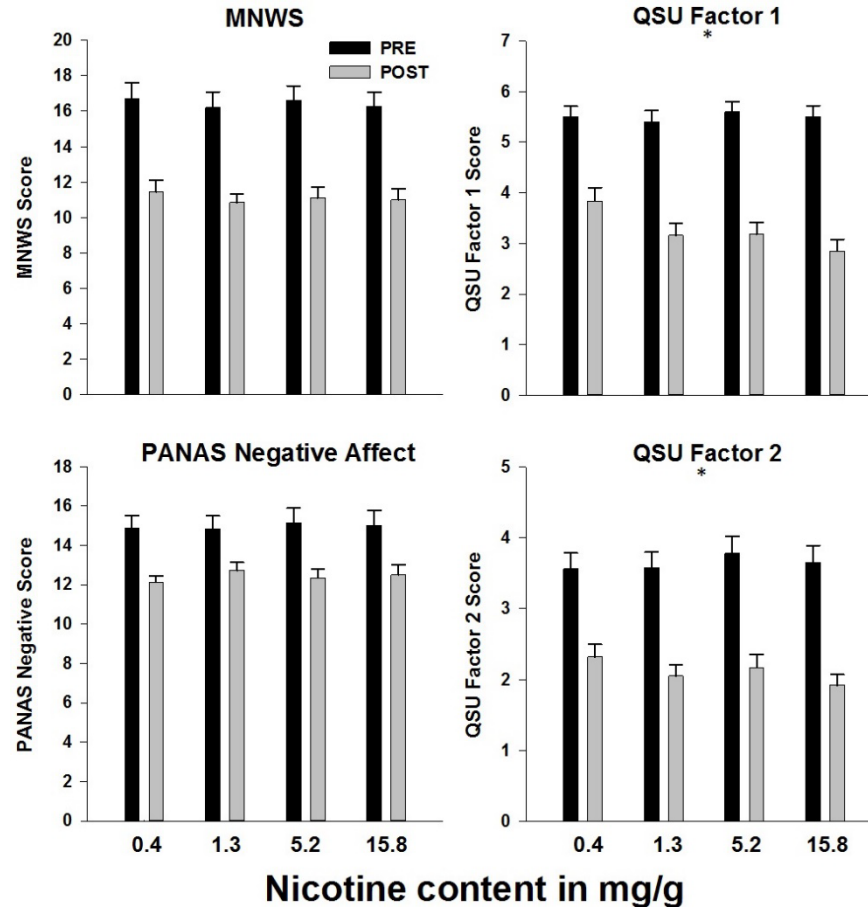
- Tested this using a within-subject study of N=50 15-19 year old daily smokers who came in to the lab following overnight abstinence

Method

- Adolescent daily smokers aged 15-19
 - Smoking daily for at least 6 months
 - Smoking status confirmed biochemically
 - Not currently intending to quit
 - Not currently endorsing SI or pregnant
- Doses of nicotine administered via cigarettes in four counter-balanced laboratory sessions using a within-subjects design
 - Subjects were abstinent from smoking overnight
- Doses: Normal nicotine content (15.8 mg), 5.2 mg, 1.3 mg and 0.4 mg yield per cigarette (Very Low)

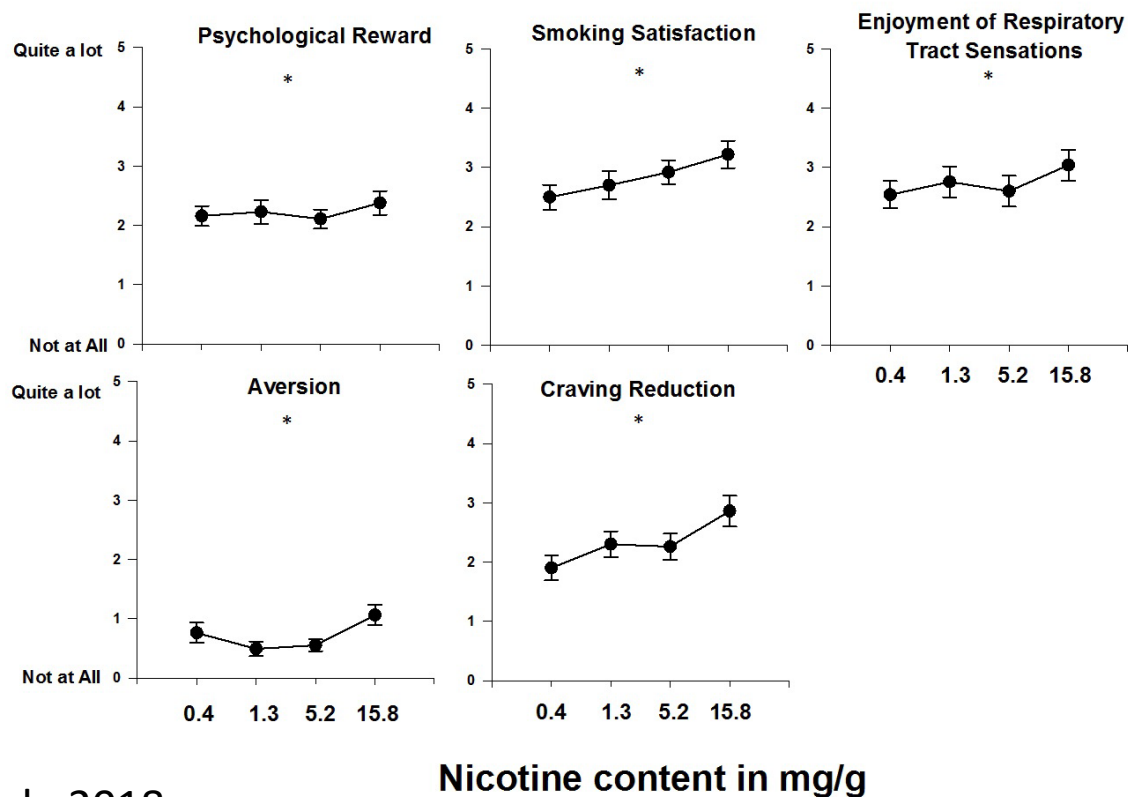


Abstinence Effects



Cassidy et al., 2018

Subjective Effects

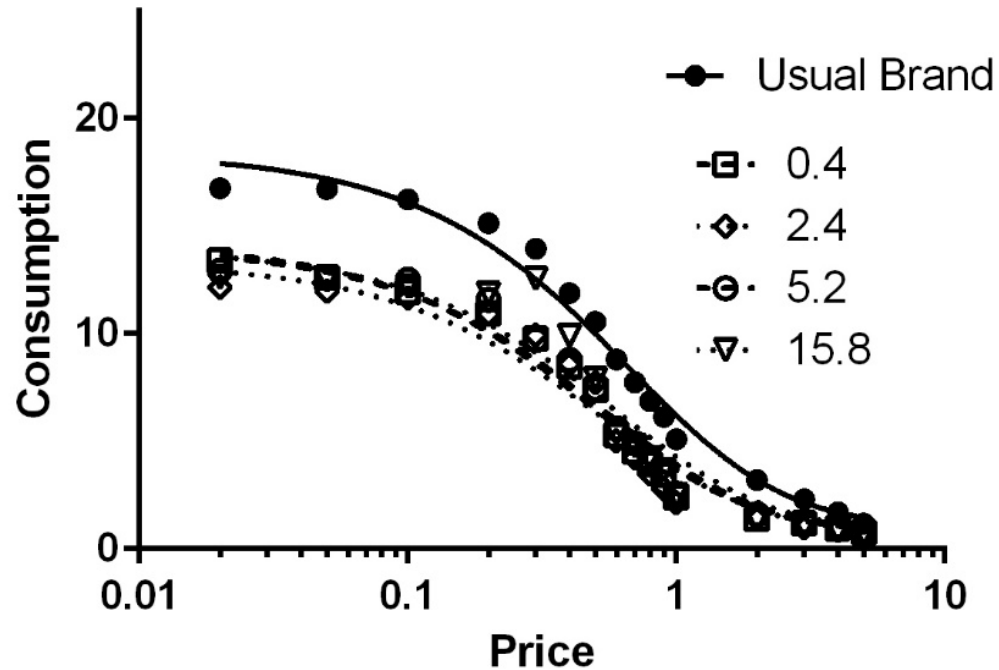


Cassidy, Colby et al., 2018

Nicotine content in mg/g

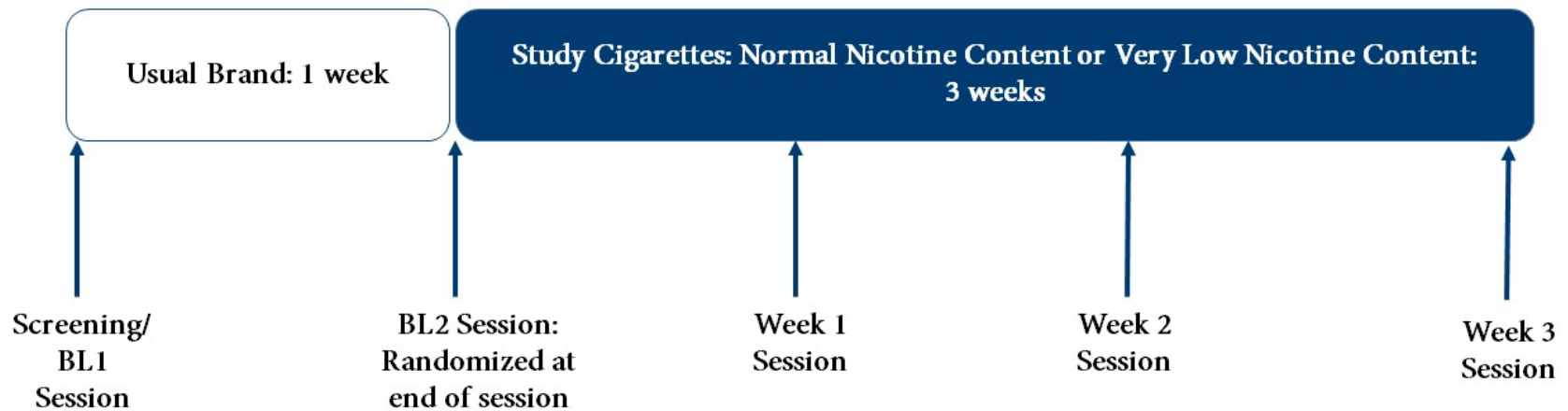


Demand for study cigarettes



Cassidy et al., 2019

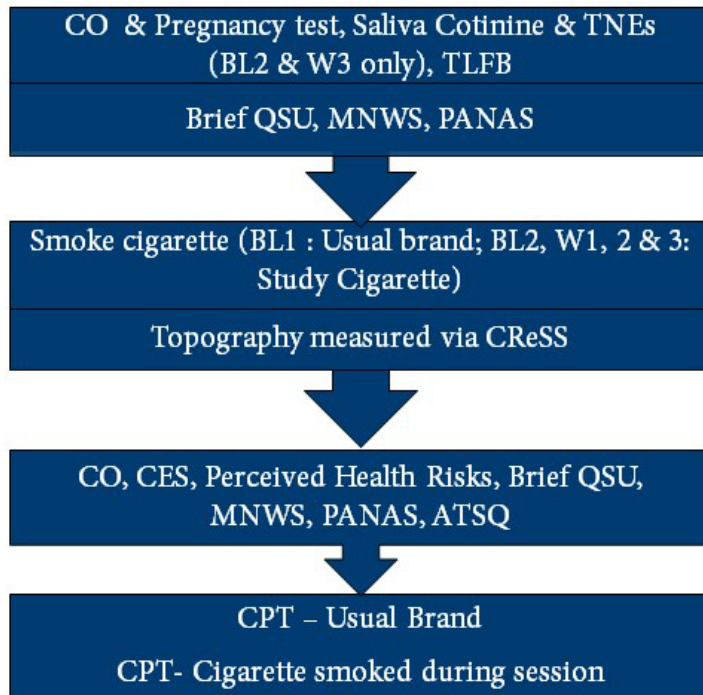
Does extended exposure to very low nicotine cigarettes reduce smoking?



Does extended exposure to very low nicotine cigarettes reduce smoking?

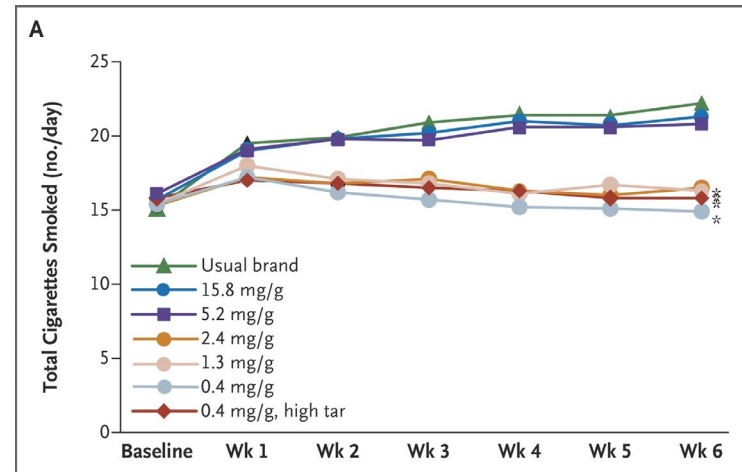
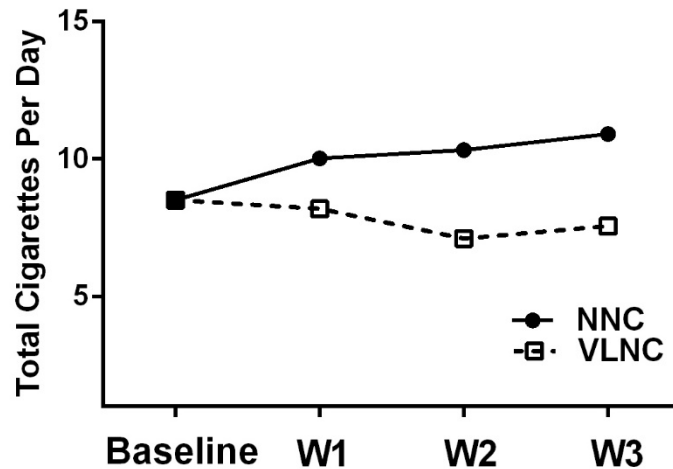
Laboratory Sessions: Baseline 1 & 2, Weeks 1, 2, & 3

N= 66



Variable	M (SD)
Age	18.5 (0.08)
Gender	50% Female
Race	65.3% White, 13.5% Hispanic, .01% Black, 13.4% Asian, Native American or Pacific Islander, 19.2% More than one race or other
Menthol Status	45% Menthol
Average Cigarettes per Day	8.1 (7.4)
mFTQ score	3.5 (0.2)
Salivary cotinine (ng/mL)	227.5 (196.9)
CESD score	12.4 (1.1)
CO (ppm)	11.0 (8.1)
Age of Onset, Daily Smoking (years)	16.5 (0.2)

Nicotine Reduction is Likely to Reduced Smoking in Adolescents



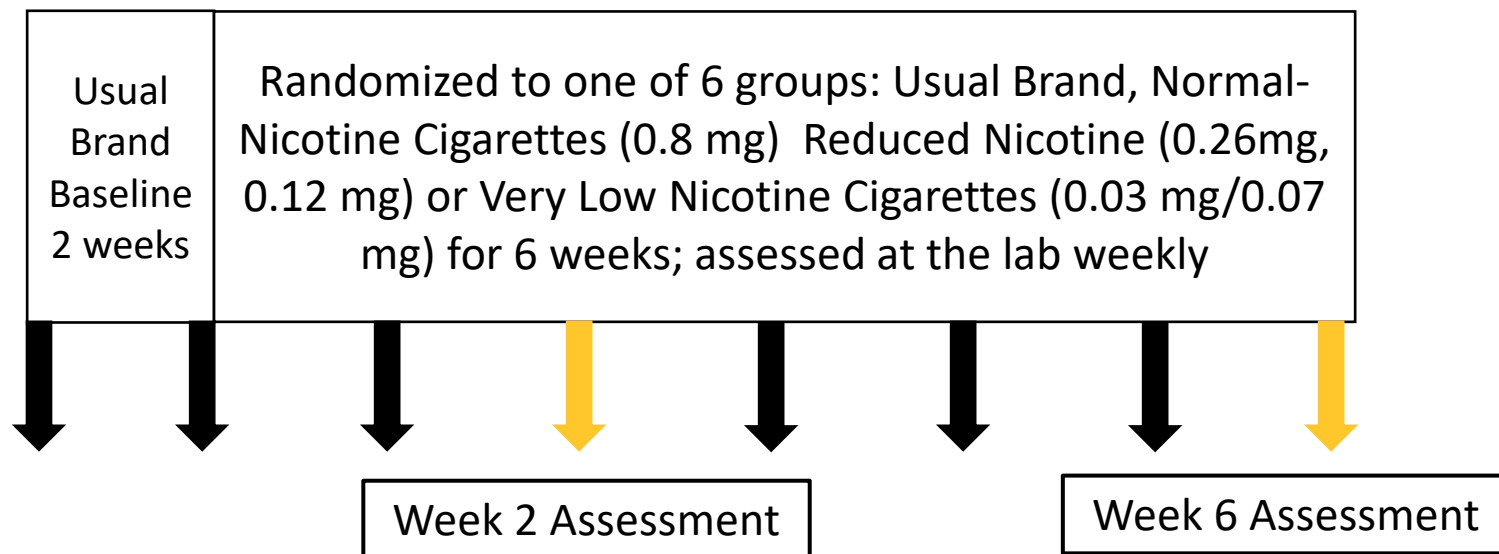
Cassidy et al., 2022

Summary of Results in Adolescents

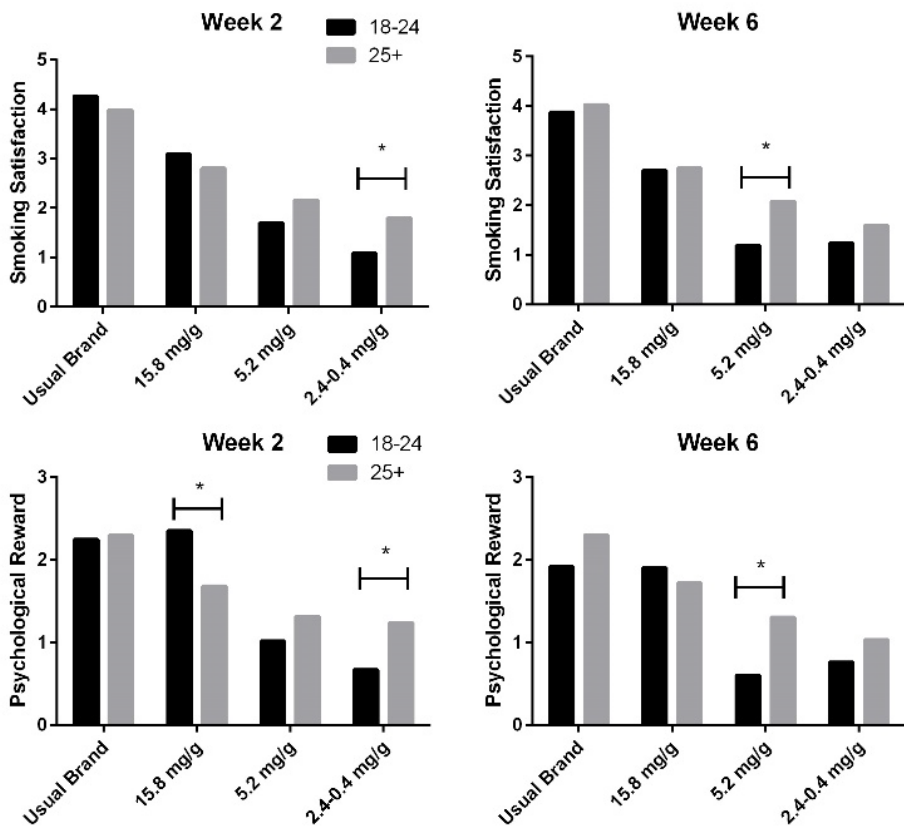
- Acutely, all of the research cigarettes significantly reduced indicators of abuse liability
 - Adolescents reported lower reinforcement from all research cigarettes relative to their own brand
- Over time, VLNC exposure reduced smoking
 - But biomarkers suggest 'cheating'/other sources of nicotine, as with adults (e.g., Benowitz et al., 2015; Nardone et al., 2016)
- Reinforcing efficacy and subjective effects show dislike of all the research cigarettes complicates the picture somewhat
 - Adolescents are somewhat less driven by nicotine differences

In the same trial, would young adults respond differently to a VLNC policy than older adults?

N=595 older adults, N=93 18-24 year old young adults

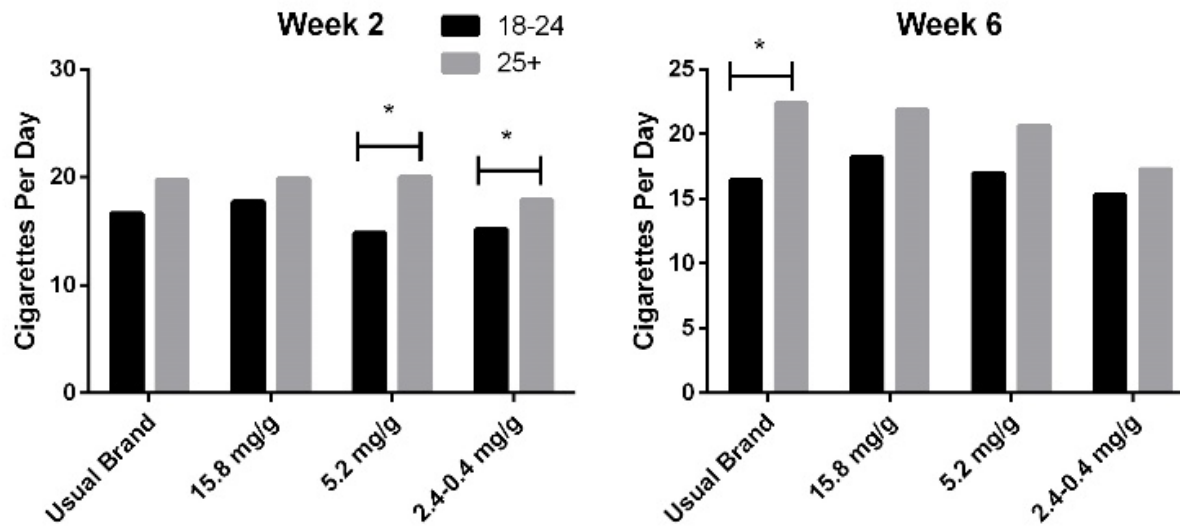


Subjective effects post-smoking in the laboratory



Cassidy, Tidey et al., 2018, *NTR*

Cigarettes per day



Cassidy, Tidey et al., 2018;
NTR

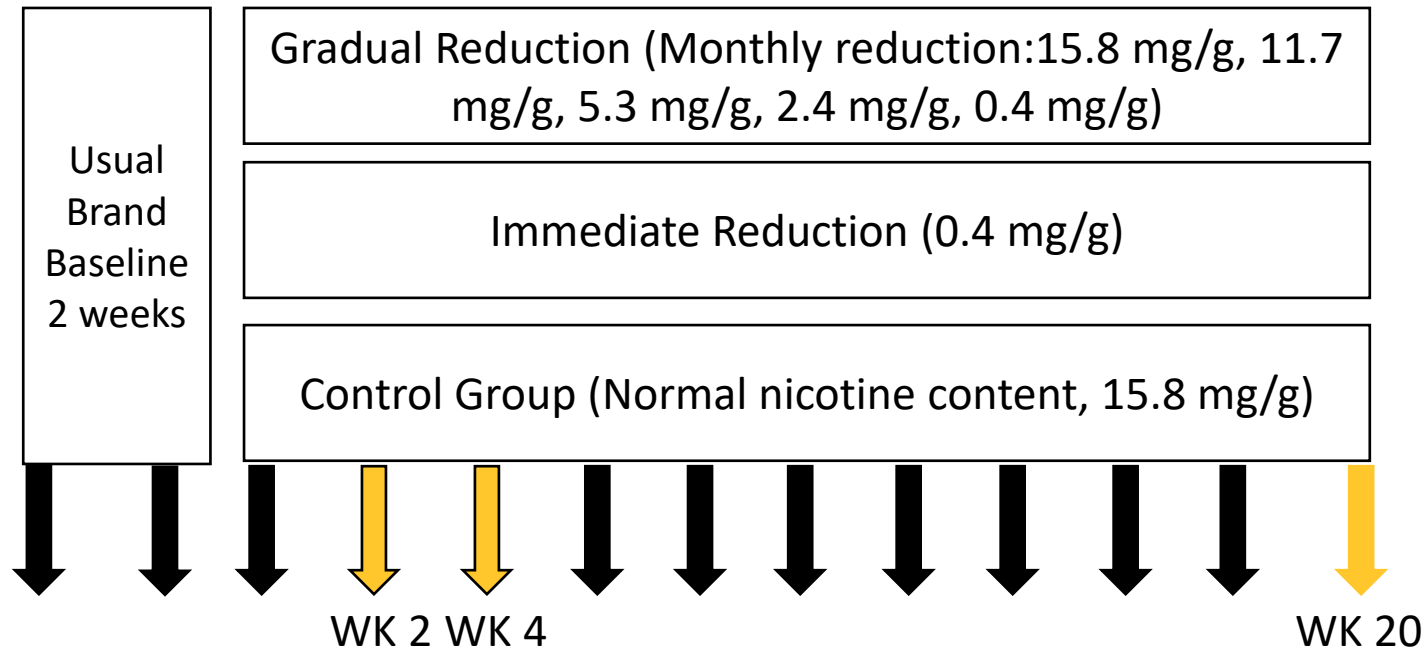
Policy implementation

- Should a nicotine product standard be implemented, should nicotine be reduced immediately or gradually?
 - And would young people respond differently than older adults to an immediate vs a gradual policy implementation?



Young adults: Gradual vs. Immediate Reduction in Nicotine

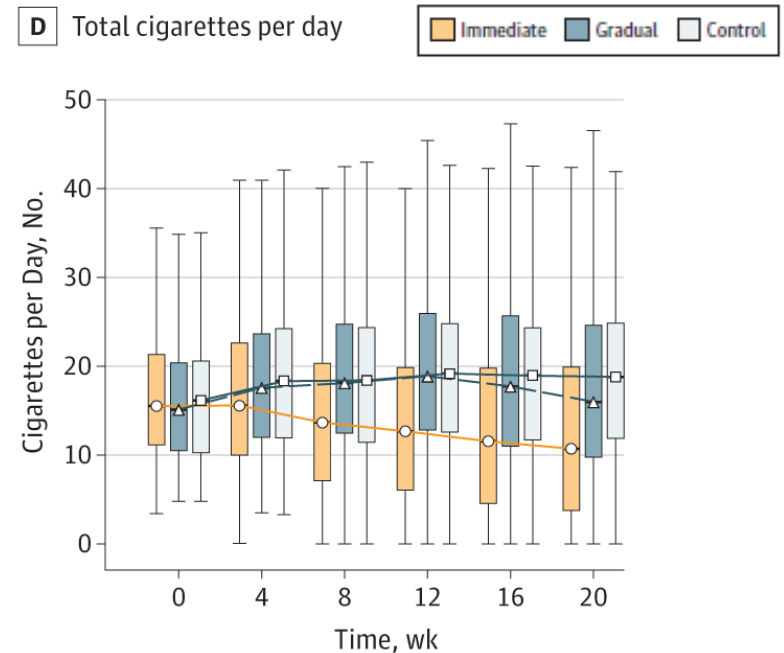
- Compared over 20 weeks, N= 1250



- Data from the CENICP2 trial (Hatsukami et al., 2018)

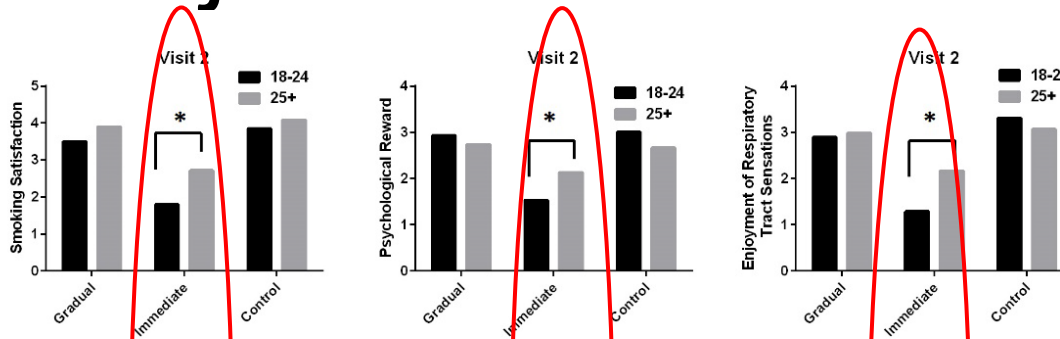
Gradual vs. Immediate Reduction in Nicotine

- Overall results showed a significant decrease in cigarettes per day for the immediate group, but not the gradual or control groups
- What about young adults?

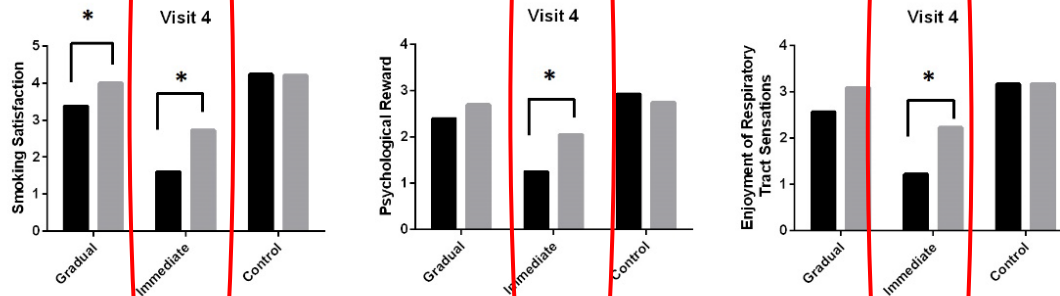


Positive Subjective Effects

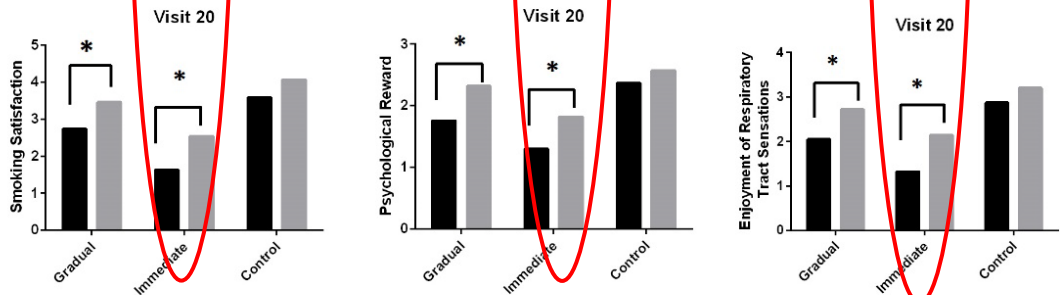
Visit 2:
Gradual group
15.8 mg/g



Visit 4:
Gradual group
15.8 mg/g



Visit 20:
Gradual group
0.4 mg/g



All Visits:
Control Group
15.8 mg/g
Immediate
Group 0.4 mg/g

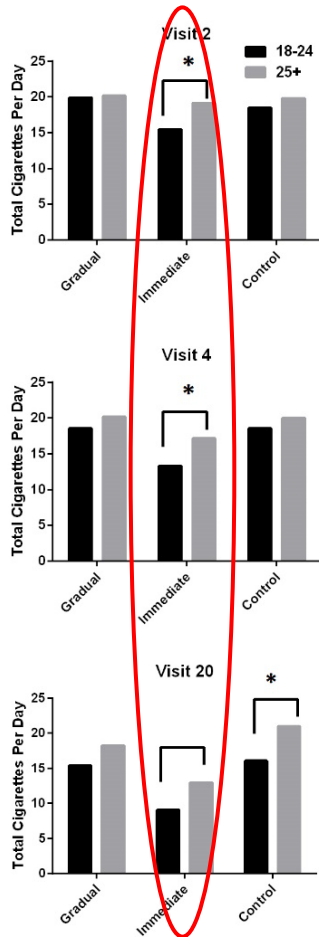
Cassidy, Tidey et al., 2021; NTR

Gradual or Immediate nicotine reduction?

Visit 2:
Gradual group
15.8 mg/g

Visit 4:
Gradual group
15.8 mg/g

Visit 20:
Gradual group
0.4 mg/g



All Visits:
Control Group
15.8 mg/g
Immediate
Group 0.4 mg/g

- Replicated findings of differences between young adults and older adults in this trial

Cassidy et al., 2021; Hatsukami et al., 2019

Summary of Young Adult Results

- Compared to older adults, younger smokers (ages 18–24) showed greater dislike for and lower use of low nicotine cigarettes across two studies
 - Suggests that a reduced nicotine standard for cigarettes may reduce the abuse potential of cigarettes to a greater extent among young adult smokers
- Both young and older adults who were switched immediately to the lowest content of nicotine smoked fewer CPD and had lower nicotine intake than those in the gradual condition
 - Suggests that immediate implementation would be better than gradual for both age groups

Potential Pitfalls and Areas for Future Work



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What about risk perceptions?

- We assessed perceived risk for addiction in our lab study
 - “Compared to my usual brand of cigarettes, my risk for the following disease by using my study cigarettes is lower/higher/the same”
 - Double-blind administration; no specific information given about the cigarettes
- Participants reported lower risk of developing lung cancer, other cancers, emphysema, bronchitis, and heart disease ($ps \leq .05$) when smoking VLNC cigarettes relative to NNC cigarettes (Denlinger-Apte, Cassidy et al. 2019)
- **Concern: Nicotine Reduction May Lead to Lower Cigarette Health Risk Perceptions in Adolescent Smokers**

Qualitative Reactions

- Young participants were exposed to VLNC cigarettes in the lab, and then the policy was described to them
- Participants expressed a lot of concerns about the policy
- And some expressed that they would switch to other products

Switch to other nicotine or tobacco products

“Wherever the nicotine is, I’ll go there...I’d probably just do Juul again.” (Female, 18; VLNC)

“I would definitely use those nicotine pack pouches that you put under your lip. I think those are called...ZYN?...also shisha, hookah.” (Female, 19; VLNC)

Will not address smoking-related stigma

“I believe it’s harmful because...there is sort of a stigma of people who use different substances as a way to cope. So when we see a person smoking outside of work or something like that, people look down upon them, even though this may be their only break for the day, and then they have to go home to a toxic work environment, toxic home environment. Reducing the amount of nicotine won’t decrease, the amount of smokers that exist.” (Male, 18; NNC)

Counterintuitive since the government benefits from cigarette sales

“I feel like putting things on like restriction is kind of dumb because I feel like you could eventually like benefit from like, like, not like so much you smoking them, but like the government, like it could tax on it.” (Female, 19; VLNC)

Ineffective
Will lead to increased smoking

“It sounds good on paper, but...I’ve read studies about like people smoking light cigarettes. And that they end up consuming the same amount of nicotine in the day and they just smoke more of them.” (Male, 18; VLNC)

Will lead to illicit markets

“It’s just going to create a black market of higher nicotine products that are unregulated or unscientifically confirmed to have a certain amount of percentage.” (Male, 18; NNC)

Nicotine is not the only reason to smoke

“I feel like addiction is more broad than the nicotine itself. You know, it’s also the act of going outside, sitting in our lawn for example, smoking the cigarettes for five minutes where you’re doing nothing, but you’re smoking that cigarette. I think...you have a very limited view of what addiction is.” (Male, 18; VLNC)

Denlinger-Apte, Cassidy et al., 2023

Qualitative Reactions

- Similarly, in the previously discussed study in which adolescents actually used their study cigarettes for 3 weeks, participants were asked what they would do if those were the only cigarettes available
- Some expressed an expectation that they would quit, while others would continue smoking
- And some expressed that they would switch to other products

Reactions to a Hypothetical Nicotine Reduction Policy	
Expectations to change smoking behavior	<p><i>Expectations to cut down or quit smoking</i></p> <p>150: “Honestly over a period of like a month or two, I’d probably quit.”</p> <p>201: “I think it would just lead to me stop smoking over time, like I would probably like smoke those for a bit and then just stop smoking.”</p> <p><i>Expectations to continue smoking</i></p> <p>149: I’d probably still smoke them, depending on the price.”</p>
Predicted use of alternative tobacco products	<p><i>E-cigarettes</i></p> <p>176: “Um, I would probably like just use an e-cigarette just for like the nicotine.”</p> <p><i>Other Tobacco Products</i></p> <p>121: “Like I would try rolling the cigs.”</p> <p>156: “Yeah, possibly I might smoke more cigars than cigarettes if this is really the only option.”</p>

Reed et al., Under Review

What about other product use?

- Adolescents commonly use other tobacco products, including e-cigarettes
- As a nicotine reduction policy would reduce the reinforcing efficacy of cigarettes, its possible that adolescents would switch to other tobacco products

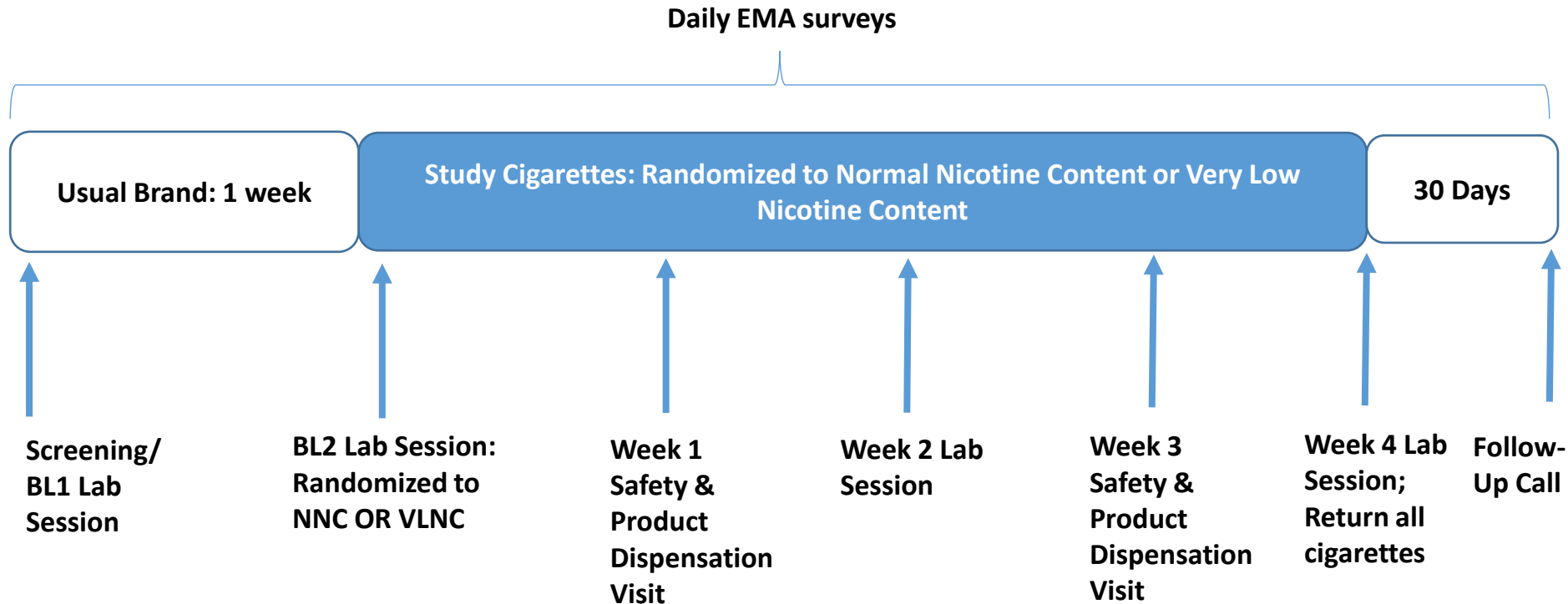


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Study Protocol



Experimental Tobacco Marketplace

- In the ETM, the only cigarette available was their study cigarette
 - Other products included cigarillos, little cigars, smokeless tobacco JUUL, disposable e-cigarettes, e-liquid, and nicotine replacement gum
 - Flavors available based on current market
- Study cigarette prices increased across trials
 - \$0.12, \$0.25, \$0.50, \$1, \$2, \$4, \$8, \$16
 - Alternative product prices stayed the same
 - Purchased products for one week
- Participants were given an experimental budget that was based on their current tobacco product consumption for 1 week

Experimental Tobacco Marketplace


Project SIREN

Search

0 item(s) - \$0.00

Cigarettes Little Cigars Cigarillos E-Cigarettes Smokeless Tobacco Nicotine Gum

Cigarettes > 0.12 - Cigarette Menthol



0.12 - Cigarette Menthol

Product Code: 0.12 Cigarette Menthol
Availability: In Stock

\$0.12

Qty

Description

Your study cigarettes with menthol flavor. This is the price per **INDIVIDUAL CIGARETTE**.

- 5 cigarettes = \$0.60
- 10 cigarettes = \$1.20
- 15 cigarettes = \$1.80
- 20 cigarettes (1 pack) = \$2.40
- 40 cigarettes (2 packs) = \$4.80
- 60 cigarettes (3 packs) = \$7.20

Alternative Products

\$ Currency ▾ 123456789 My Account ▾ Wish List (0) Shopping Cart Checkout

Project SIREN Search 0 item(s) - \$0.00


Cigarettes Little Cigars Cigarillos E-Cigarettes Smokeless Tobacco Nicotine Gum

Home E-Cigarettes Juul Pods

Cigarettes (15)
Little Cigars (6)
Cigarillos (8)
E-Cigarettes (11)
- Disposable E-Cigarettes (4)
- E-liquid (6)
- Juul Pods (1)
Smokeless Tobacco (10)
Nicotine Gum (6)

Juul Pods

Product Compare (0) Sort By: Default Show: 15



JUUL Pods Virginia Tobacco Flavor

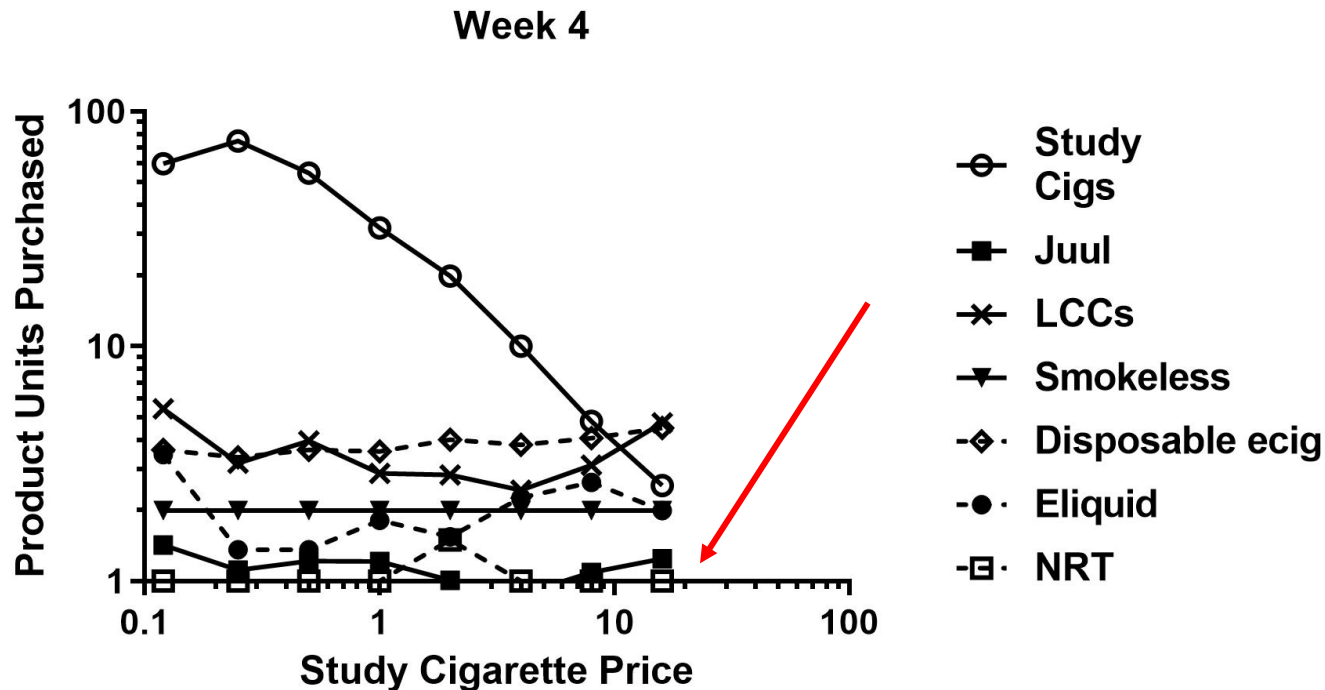
One pack contains 2 Virginia Tobacco flavored pods to be used with the JUUL Vaping Device (not ...)

\$10.00

Summary of Results

- VLNCs were still purchased at high prices
- Combustible products were the most frequently purchased alternative products
 - We did not model a policy extension to other combustible products; this may or may not be the case in the real world
 - Provides support for extending the nicotine reduction policy to include all combustible products
- There was no indication of increased combustible purchasing in the VLNC group over time

What about NRT use among youth?



What about flavor bans?

- In an Experimental Marketplace Study conducted by a mentee, we enrolled adults who smoked menthol cigarettes
 - They completed an ETM task with and without other combustible products available
 - The increasing price represents more difficulty in obtaining menthol cigarettes, to see what would be the product that would be most commonly substituted for menthol cigarettes

What about flavor bans?

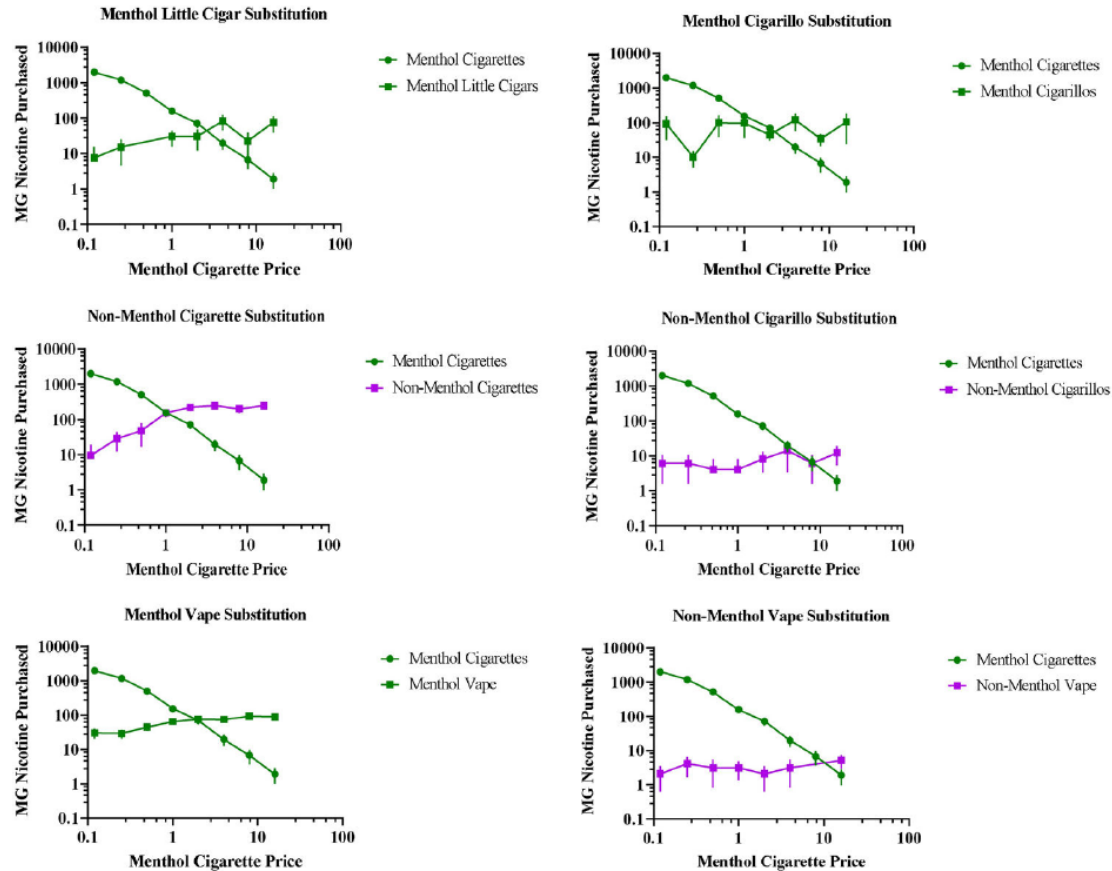


Figure 1. Demand graphs comparing menthol cigarettes and alternative products purchased when the ETM includes menthol LCCs

Demand graphs displaying menthol cigarette and alternative product purchasing when the ETM includes menthol LCCs. Green lines represent menthol products while purple lines represent non-menthol products. The x and y axes were log-transformed for better visual display.

Summary of Results

- Confirms the need for careful messaging about the risks of VLNC cigarettes and the relative risk of alternative tobacco products
 - We need to encourage cessation and provide support for young adults in the event of a nicotine reduction policy standard
 - NRT use is rare in youth
- Flavor bans will need to be carefully thought out and potentially extended to all products

Thank you!

Questions?



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