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

- Reducing the level of nicotine in cigarettes has been proposed as a 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
Demand for study cigarettes

Cassidy et al., 2019
Does extended exposure to very low nicotine cigarettes reduce smoking?

Usual Brand: 1 week

Screening/BL1 Session

BL2 Session: Randomized at end of session

Study Cigarettes: Normal Nicotine Content or Very Low Nicotine Content: 3 weeks

Week 1 Session

Week 2 Session

Week 3 Session
Does extended exposure to very low nicotine cigarettes reduce smoking?

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

- CO & Pregnancy test, Saliva Cotinine & TNEs (BL2 & W3 only), TLFB
- Brief QSU, MNWS, PANAS
- Smoke cigarette (BL1: Usual brand; BL2, W1, 2 & 3: Study Cigarette)
- Topography measured via CReSS
- CO, CBS, Perceived Health Risks, Brief QSU, MNWS, PANAS, ATSQ
- CPT – Usual Brand
- CPT- Cigarette smoked during session

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

<table>
<thead>
<tr>
<th>Usual Brand</th>
<th>Baseline 2 weeks</th>
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<tbody>
<tr>
<td>Randomized to one of 6 groups: Usual Brand, Normal-Nicotine Cigarettes (0.8 mg) Reduced Nicotine (0.26mg, 0.12 mg) or Very Low Nicotine Cigarettes (0.03 mg/0.07 mg) for 6 weeks; assessed at the lab weekly</td>
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- Week 2 Assessment
- Week 6 Assessment

BROWN
School of Public Health
Center for Alcohol & Addiction Studies

CENIC
Center for the Evaluation of Nicotine in Cigarettes
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

<table>
<thead>
<tr>
<th>Usual Brand Baseline 2 weeks</th>
<th>Gradual Reduction (Monthly reduction: 15.8 mg/g, 11.7 mg/g, 5.3 mg/g, 2.4 mg/g, 0.4 mg/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Immediate Reduction (0.4 mg/g)</td>
</tr>
<tr>
<td></td>
<td>Control Group (Normal nicotine content, 15.8 mg/g)</td>
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</table>

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
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 ($p \leq .05$) 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.

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.

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### Reactions to a Hypothetical Nicotine Reduction Policy

<table>
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<tr>
<th>Expectations to change smoking behavior</th>
<th>Expectations to cut down or quit smoking</th>
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<tbody>
<tr>
<td></td>
<td>150: “Honestly over a period of like a month or two, I’d probably quit.”</td>
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<td></td>
<td>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.”</td>
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<table>
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<tr>
<th>Predicted use of alternative tobacco products</th>
<th>E-cigarettes</th>
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<td>176: “Um, I would probably like just use an e-cigarette just for like the nicotine.”</td>
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|                                               | Other Tobacco Products |
|                                               | 121: “Like I would try rolling the cigs.” |
|                                               | 156: “Yeah, possibly I might smoke more cigars than cigarettes if this is really the only option.” |
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
Study Protocol

Study Cigarettes: Randomized to Normal Nicotine Content or Very Low Nicotine Content

- Usual Brand: 1 week
- BL2 Lab Session: Randomized to NNC OR VLNC
- Week 1 Safety & Product Dispensation Visit
- Week 2 Lab Session
- Week 3 Safety & Product Dispensation Visit
- Week 4 Lab Session; Return all cigarettes
- 30 Days

Daily EMA surveys
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

Cigarettes
Little Cigars
Cigars
iQOS
E-Cigarettes
Smokeless Tobacco
Nicotine Gum

Cigarettes
0.12 - Cigarette Menthol

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

0.12 - Cigarette Menthol
Product Code: 0.12 Cigarette Menthol
Availability: In Stock

$0.12

Qty

1

Add to Cart
Alternative Products

Project SIREN

Cigarettes  Little Cigars  Cigarillos  E-Cigarettes  Smokeless Tobacco  Nicotine Gum

Juul Pods

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?