

# Informing Tobacco Policy through Laboratory and Field Experiments



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*The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Food and Drug Administration.*

**I have no conflicts of interest to report.**

# Centering us and our work

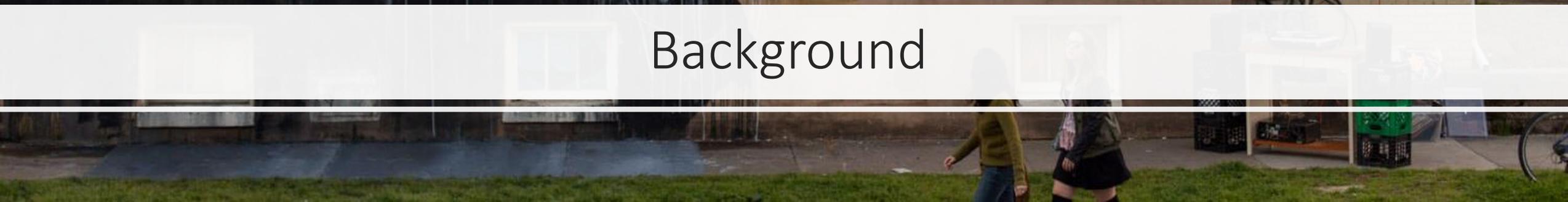
- Co-PI Health Equity Disclosure: We are white, affluent, cisgender researchers. We do not intend to be health equity tourists. We are committed to improving the health of groups who are disproportionately affected by tobacco products.
- Our research team is led by a health economist (Barnes) and a health psychologist (Cobb) and has 10+ ongoing or completed experimental studies in the laboratory and in the field.

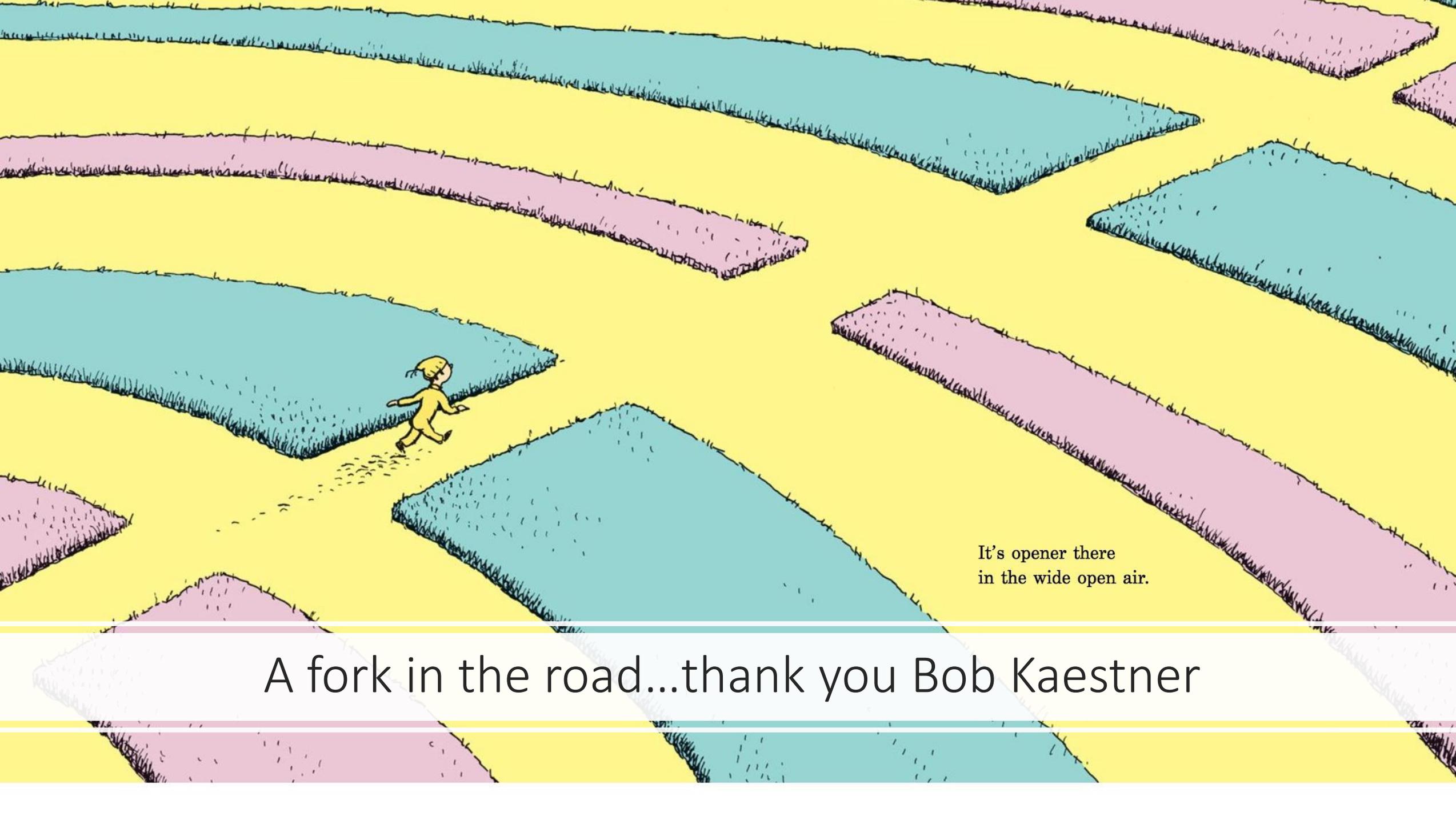
# In case you leave early...

- Economic models of demand for tobacco products play a pivotal role in assessing the efficacy of price and non-price policies aimed at internalizing the consequences of tobacco use behaviors.
- Such approaches typically rely on historical consumer and policy data presenting challenges for predicting potential policy effects on tobacco use behavior *ex ante*, particularly in a tobacco market undergoing rapid innovation and differentiation.
- In such cases, laboratory and field experiments permit experimental examination of how an array of potential regulatory policies, sometimes operating in concert, may affect demand across or within classes of tobacco products.
- Our work provides opportunities for a prospective analysis of the potential impact of tobacco policies on own- and cross-product demand.



Background





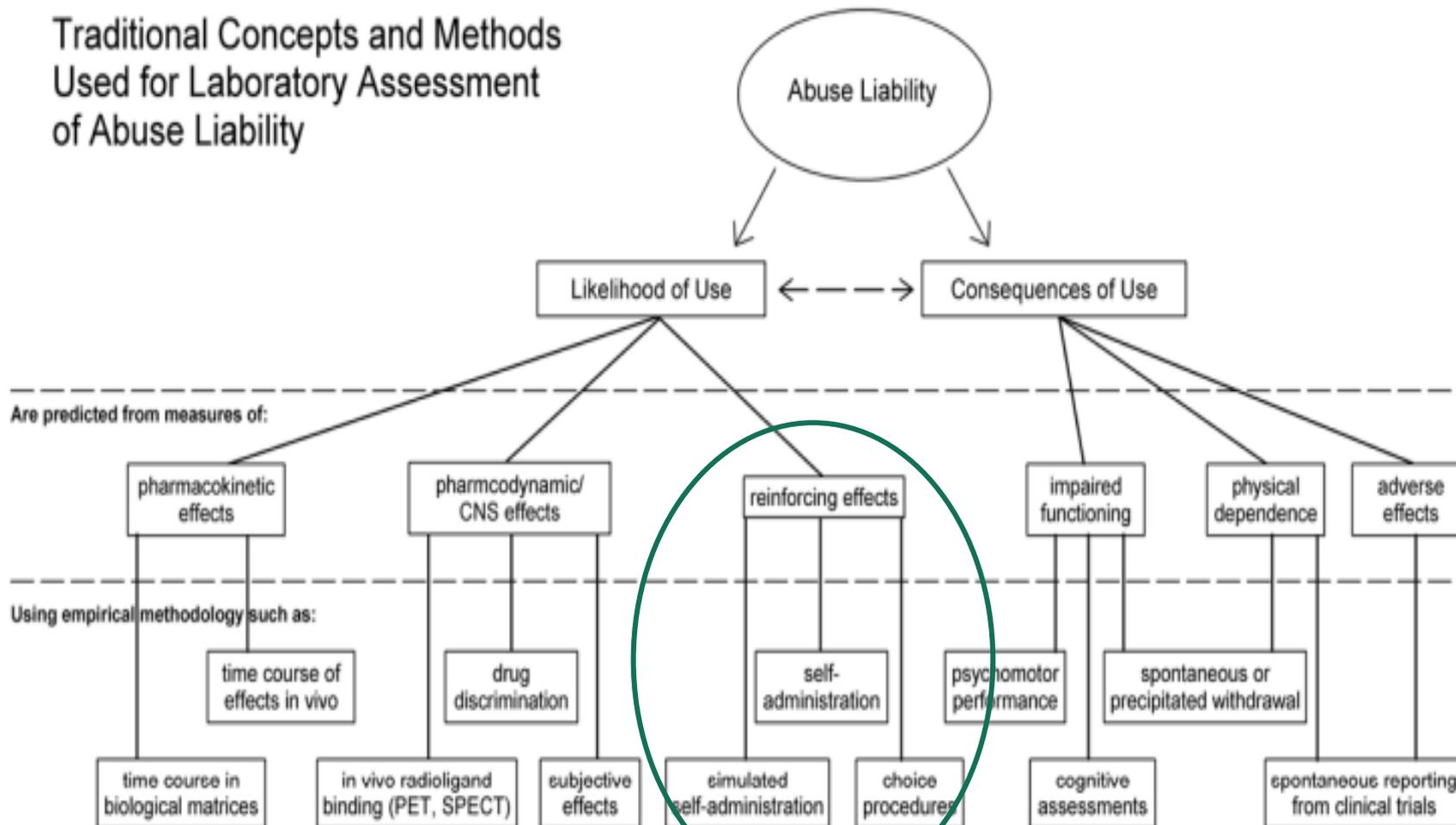
It's opener there  
in the wide open air.

A fork in the road...thank you Bob Kaestner

# What is abuse liability

- Abuse liability refers to the likelihood that a product will be used persistently despite consequences (Carter et al., 2009)

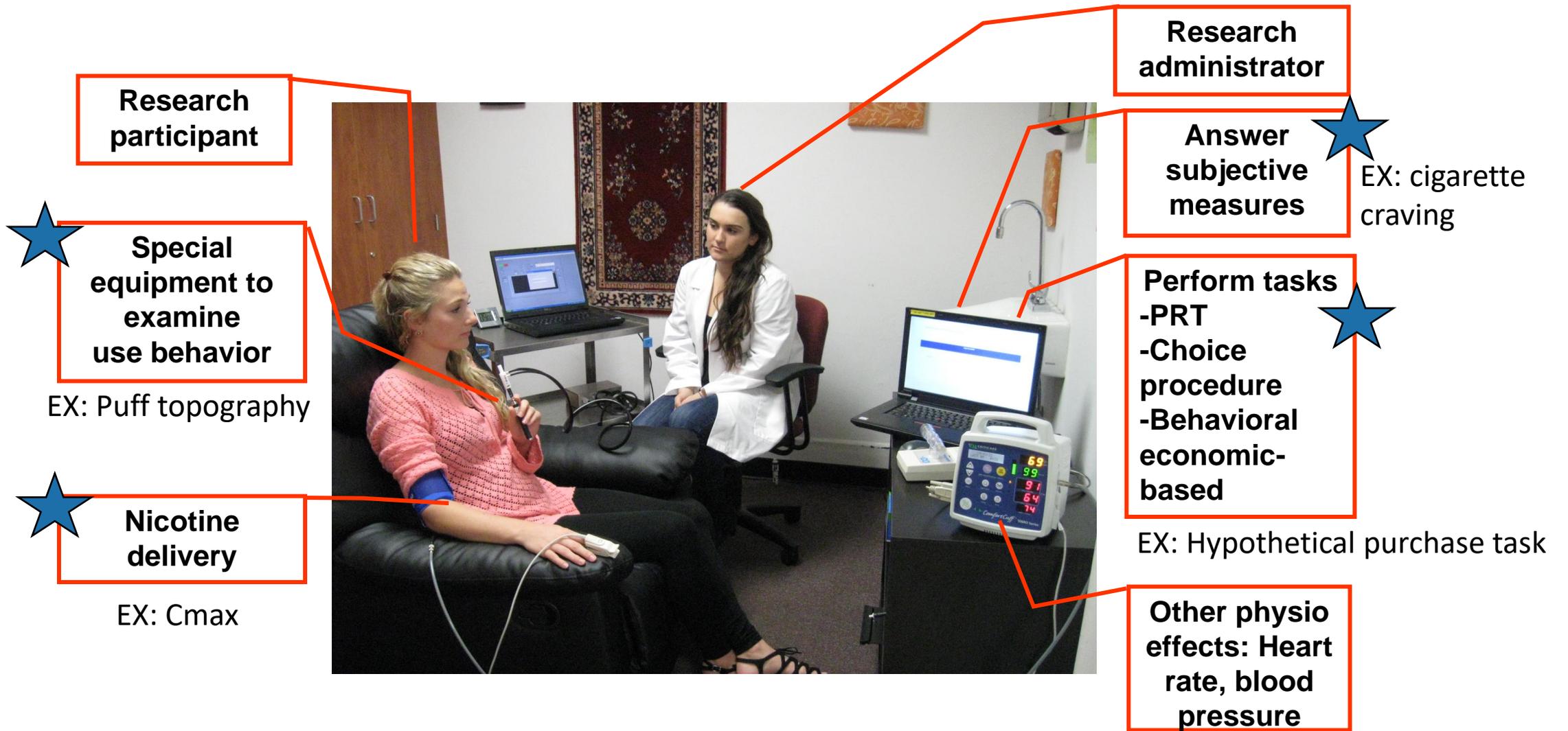
Traditional Concepts and Methods  
Used for Laboratory Assessment  
of Abuse Liability



**FDA needs to know how regulatory targets influence abuse liability:**

- 1) Nicotine delivery
- 2) Flavors
- 3) Product design (E.g., ENDS device power)
- 4) Other constituents of tobacco products
- 5) User experiences
- 6) Substitution to lower harm products

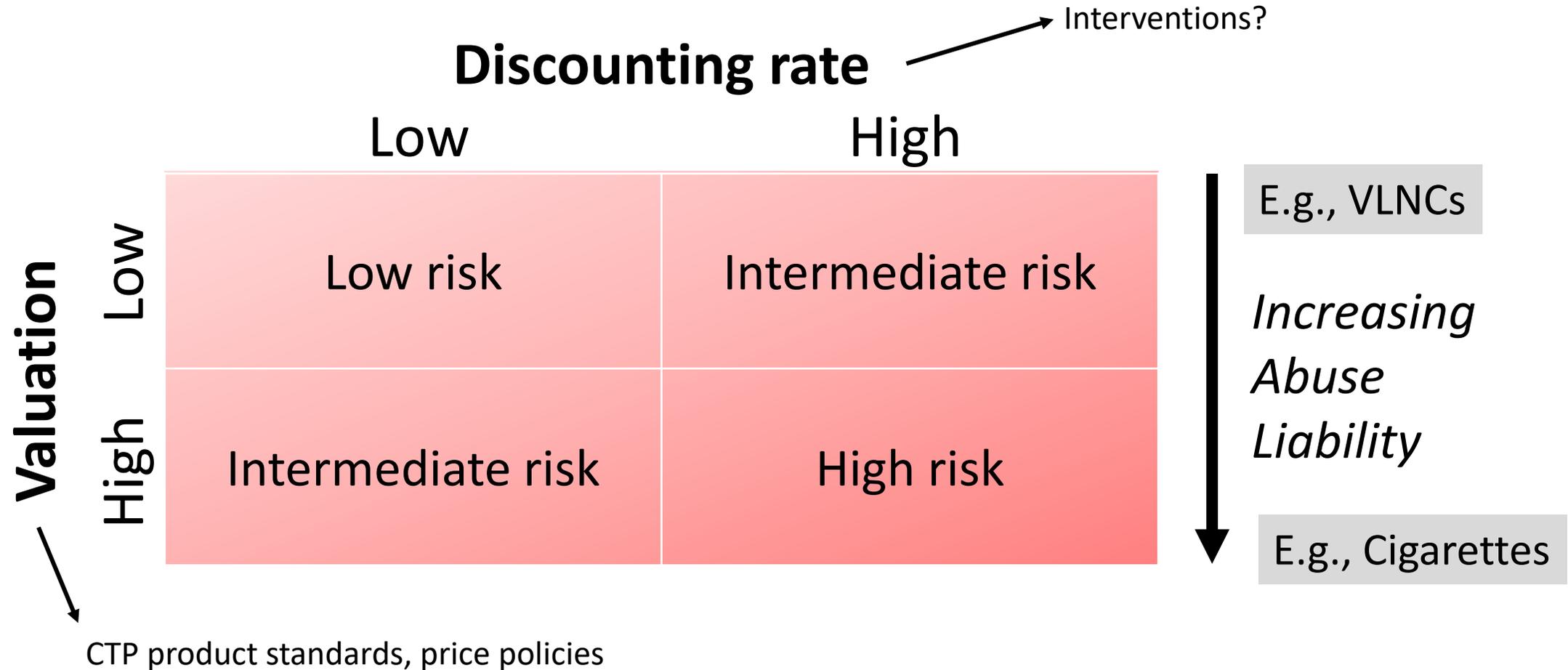
# CSTP Methods



★ = Key Abuse Liability Outcomes

+ Naturalistic assessments of tobacco use!

# Can consider abuse liability in a reinforcer pathology model of drug abuse



# What are (behavioral) economic assessments of abuse liability

- These are NOT nudges or that kind of behavioral economics
- But rather methods used in behavioral labs in psychology to assess abuse potential of various drugs with several outcomes informed by neoclassical consumer theory
- *Own-Price Elasticity of Demand* - Drug self-administration can be uniquely understood with behavioral economics. The basis of this unique understanding is through assessment of a drug's *own-price elasticity* of demand, or sensitivity of consumption of a commodity (e.g., cigarettes) to increases in unit price. When applied to drugs of abuse, measures of elasticity reflect one component of abuse liability ([Carter et al., 2009](#)).
- *Cross-Price Elasticity of Demand* - Measures of *cross-price elasticity* describe the interaction between the reductions in consumption of one price-manipulated product (e.g., cigarettes) and the consumption of one or more constant-priced alternative products (e.g., ENDS). For one product to substitute with another, their abuse liability profiles need to be congruent (Pacek et al., 2019)

# Why use (behavioral) economic methods to assess tobacco product abuse liability?

- **Predict** policy impact in a heterogenous and evolving market
- Forecast **unintended consequences** of policies and regulations
- Examine **interactions** of multiple potential policies
- **Contextualize** other clinical, survey, and economic data

# Behavioral economic measures of abuse liability

- These tasks can help determine:
  - How much a participant values a tobacco product (choice procedures, purchase tasks)
  - How hard a participant will work to obtain a tobacco product (progressive ratio tasks)
  - Relative strength of preferences, substitution, and likelihood of poly use of competing products (cross-price purchase tasks, experimental tobacco marketplaces)

# Some behavioral economic tools in and out of the lab

## For assessing abuse liability

- Multiple choice procedure (MCP)\*
- Purchase tasks
  - Own-price purchase task
  - Cross-price purchase task
- Progressive ratio tasks (PRT)\*
  - Own-price PRT
  - Cross-price PRT
- Experimental tobacco marketplaces (ETM)\*
  - Legal and Illegal ETMs

## For assessing economic preferences

- Delay discounting tasks
  - Minute discounting task
- Risk-taking measures
  - Balloon Analog Risk Task\*

*\*choices are reinforced*

# Multiple choice procedure (MCP)

For each choice below, please select whether you prefer to receive 10 puffs from the ECIG or to receive money.

After you make your decisions, one choice will be drawn at random and you will either receive money or be given time to take 10 puffs from the ECIG.

Please Circle Your Choices:

1. 10 puffs from ECIG	\$0.01
2. 10 puffs from ECIG	\$0.02
3. 10 puffs from ECIG	\$0.04
4. 10 puffs from ECIG	\$0.08
5. 10 puffs from ECIG	\$0.16
6. 10 puffs from ECIG	\$0.32
7. 10 puffs from ECIG	\$0.64
8. 10 puffs from ECIG	\$1.28
9. 10 puffs from ECIG	\$2.56
10. 10 puffs from ECIG	\$5.12
11. 10 puffs from ECIG	\$10.24



Crossover value =  
measure of the  
reinforcing efficacy  
of a drug

# ENDS purchase task

- Imagine a TYPICAL DAY during which you use e-cigarettes.
- The following questions ask how many times you would buy 10 puffs of your own brand e-cigarettes if they cost various amounts of money.
- The only available e-cigarettes are your own brand.
- Assume that you have the same income/savings that you have now and NO ACCESS to any e-cigarettes or nicotine products other than those offered at these prices.
- In addition, assume that you would consume the puffs that you request on that day; that is, you cannot save or stockpile puffs for a later date.
- Please respond to these questions honestly.

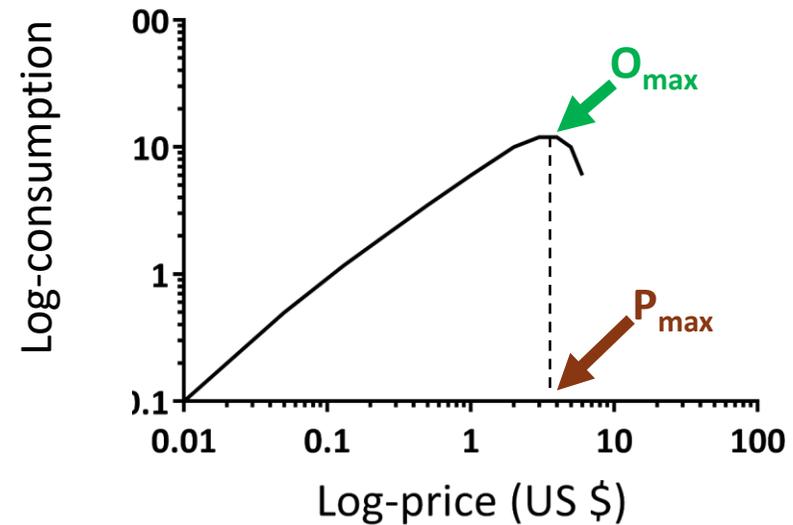
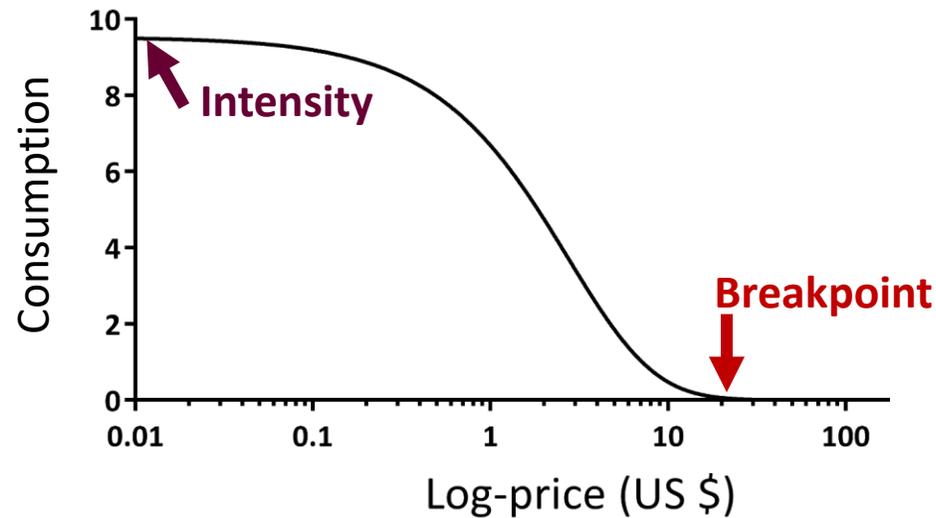
-If 10 puffs of your own brand e-cigarettes cost **X**:

-How many **times** would you buy 10 puffs of your own brand e-cigarettes to consume in one day?

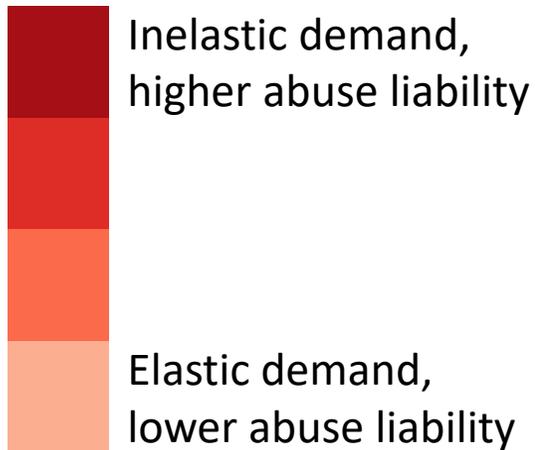
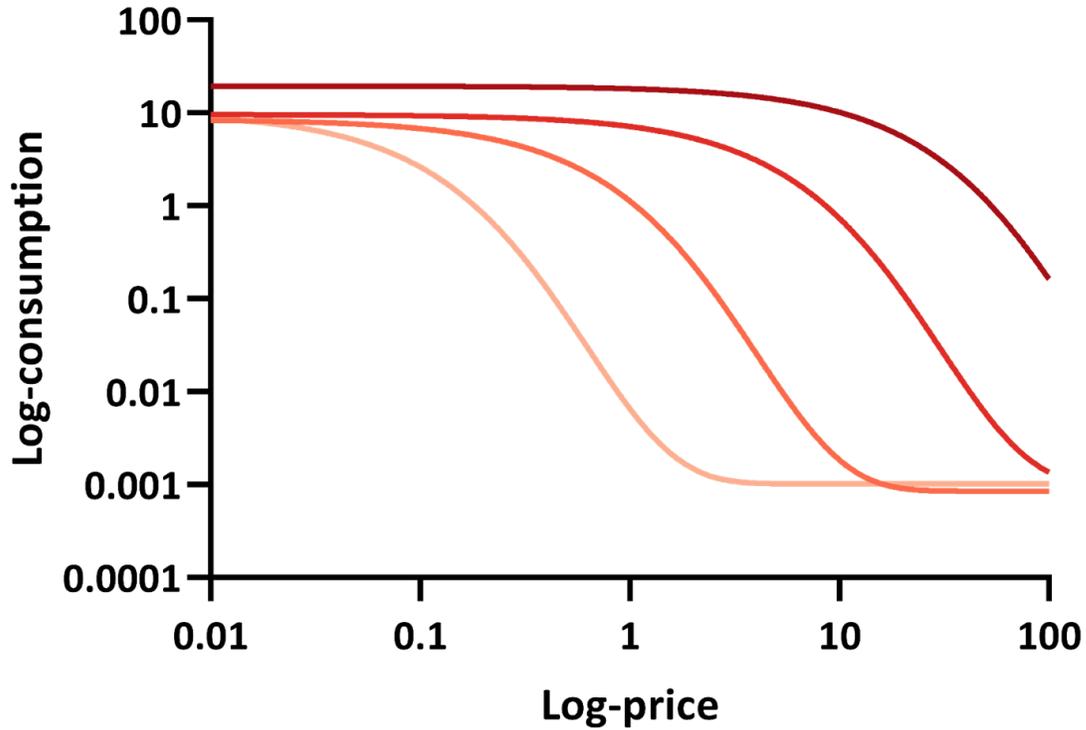
Y times (numeric response by participant)	X (price)
	\$0 (free)
	\$0.01
	\$0.02
	\$0.04
	\$0.08
	\$0.16
	\$0.32.... \$10.24

# Purchase task outcomes

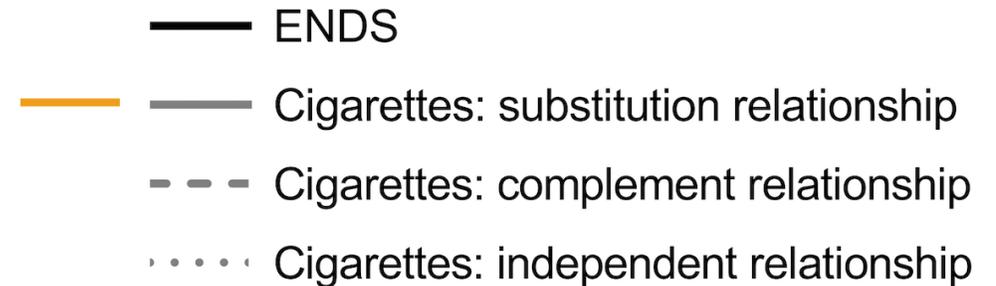
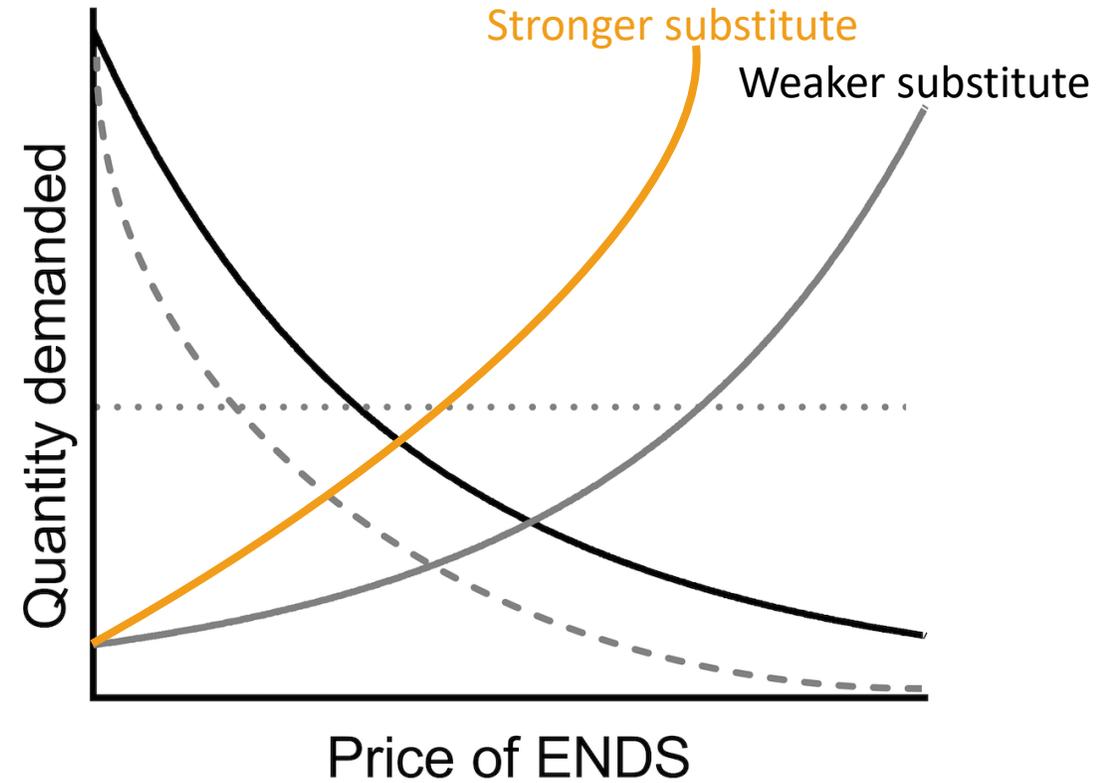
- **Intensity**: consumption at \$0
- **Breakpoint**: price at which participants would no longer purchase a product
- $P_{max}$ : price after which consumption falls disproportionately with increases in price, or the price associated with  $O_{max}$
- $O_{max}$ : maximum daily expenditure



# Own price elasticity



# Cross price elasticity



# Progressive Ratio Task (PRT)

- Participants click a space bar 4 times to earn 1 puff of the session product.
- Work requirement doubles after each puff earned until the participant makes no responses for 5 minutes.
- Outcomes:
  - Puffs earned
  - Presses





Application

# How would people who smoke respond to ENDS flavors **and** modified risk messages?

- Study 1 (n=17):

Own-brand cigarette	No message
Tobacco-flavored ENDS	No message
Tobacco-flavored ENDS	Message: “Reduced harm relative to cigarettes”
Menthol-flavored ENDS	No message
Menthol-flavored ENDS	Message: “Reduced harm relative to cigarettes”

- Study 2 (n=19):

Own-brand cigarette	No message
Unflavored ENDS	No message
Unflavored ENDS	Message: “Reduced exposure to carcinogens relative to cigarettes”
Cherry-flavored ENDS	No message
Cherry-flavored ENDS	Message: “Reduced exposure to carcinogens relative to cigarettes”

Both studies:

- Participants age 18–55, smoked  $\geq 5$  cigarettes/day for  $\geq 1$  year, strong preference for either menthol or non-menthol, race self-identified as Black or White, no regular ENDS use, no desire to quit smoking, healthy
- Own-brand cigarettes assessed at baseline lab visit, followed by 4 lab visits (Latin-square ordered) for ENDS conditions
- 12 hours nicotine abstinence before each session (48 hours minimum between sessions)

# How would people who smoke respond to ENDS flavors **and** modified risk messages?

## Main Takeaways

1. Both flavors and messages are potentially important policy levers and the interaction of the two could have a powerful influence on abuse liability (e.g., unflavored ENDS + “reduced exposure” message had the lowest abuse liability of any condition)
2. Differences between the tasks highlight the need for multiple methods to assess abuse liability

Own-brand  
cigarette

Tobacco  
ENDS

Tobacco  
ENDS  
+ message

Menthol  
ENDS

Menthol  
ENDS  
+ message

Own-brand  
cigarette

Unflavored  
ENDS

Unflavored  
ENDS  
+ message

Cherry  
ENDS

Cherry  
ENDS  
+ message

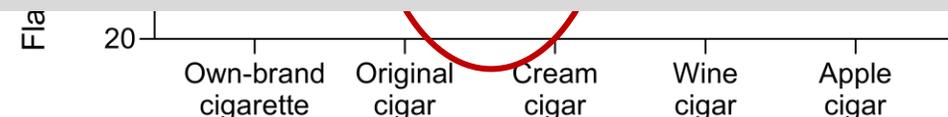
# How do characterizing flavors in cigars shape abuse liability among young adult smokers?

- For cigarettes, characterizing flavors other than menthol were banned in 2009. In April 2022, FDA proposed new product standards that would ban characterizing flavors for cigars as well
- Clinical laboratory study of n=25 people who smoke age 18–25 with limited cigar experience
  - Across 5 lab visits, assessed 5 products: own-brand cigarettes + 4 flavors of Black & Mild cigars (original, cream, wine, apple)
  - Triangulated abuse liability through behavioral, physiological and subjective effects measures

# How do characterizing flavors in cigars shape abuse liability among young adults who smoke?

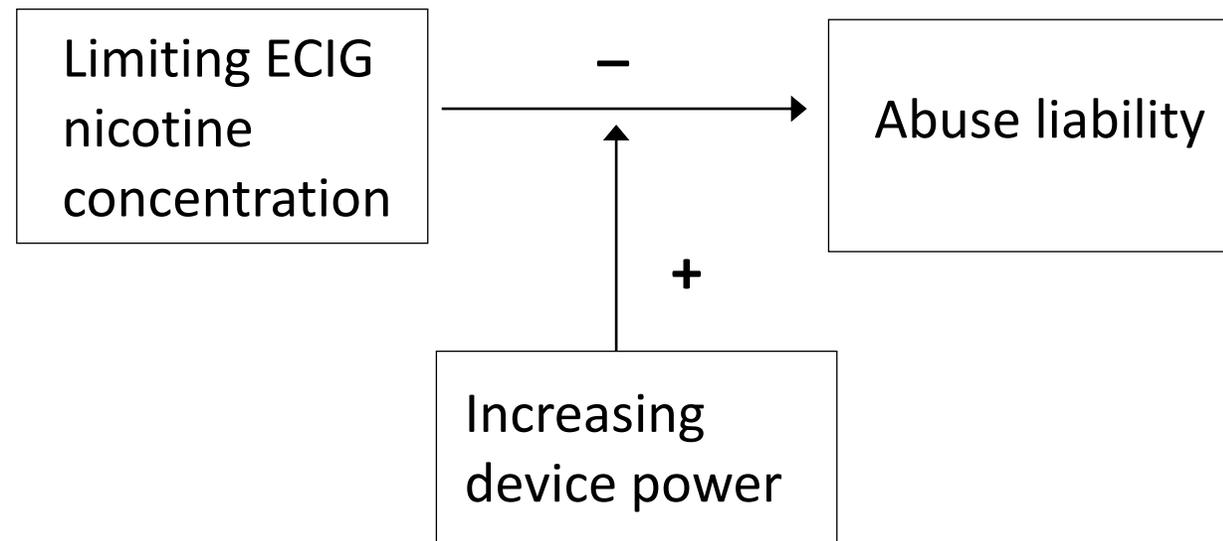
## Main Takeaways

1. Original and cream cigars appear to have the highest abuse liability of the four cigar flavors tested and their abuse liability profiles were most like own-brand cigarettes
2. Findings support FDA's proposed product standards for cigars, which cover implicit and explicit flavor descriptors as well as the presence and amount of flavor additives



# How do ENDS nicotine concentration **and** device power affect abuse liability?

- 2014 EU TPD regulations limited ENDS liquid nicotine concentration to 20 mg/mL to reduce abuse liability.
- However, this reduction can be offset by increasing ECIG device power.



# How do ENDS nicotine concentration **and** device power affect abuse liability? **And, what is the role of individual economic preferences?**

- Clinical laboratory study of n=19 people who exclusively use ENDS and n=17 people who dual use cigarettes and ENDS

- Evaluated abuse liability across five ENDS conditions

- Also measured risk-taking, delay discounting, and dependence at baseline

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Own-brand ENDS	
ENDS with low nicotine concentration (10 mg/mL)	Low device power (15 W)
ENDS with low nicotine concentration (30 mg/mL)	High device power (30 W)
ENDS with high nicotine concentration (10 mg/mL)	Low device power (15 W)
ENDS with high nicotine concentration (30 mg/mL)	High device power (30 W)

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How do ENDS nicotine concentration **and** device power affect abuse liability? **What is the role of individual economic preferences?**

Dual users

Exclusive ENDS users

## Main Takeaways

1. ENDS regulations should consider device characteristics (e.g., power) in tandem with liquid nicotine concentration in markets with open-system devices, or consider restricting sales of ENDS to closed-system devices
2. Recall the reinforcer pathology model, individual economic preferences like risk-taking and delay-discounting shape dependence and ratings of product abuse liability

- Among dual users, lower discount rates associated with higher cigarette dependence

# How does nicotine flux shape abuse liability?

- Nicotine flux: rate of nicotine emission from the device ( $\mu\text{g/s}$ )
  - ENDS nicotine flux is governed by device power and nicotine concentration
  - Given a specific nicotine flux, puff duration (s) controls the dose of nicotine delivered to the user
- 2 clinical laboratory studies of  $n=24$  people who use ENDS and/or smoke cigarettes and  $n=21$  people who smoke cigarettes
  - Five total sessions: own-brand cigarettes + four experimental ENDS:

<b>ENDS condition</b>	<b>[nicotine]</b>	<b>Wattage</b>	<b>Flux</b>	<b>Duration</b>
No flux	0 mg/mL	30W	0 mg/s	2s
Low flux	6 mg/mL	30W	36.01 mg/s	2s
Cigarette-like flux	15 mg/mL	30W	90.03 mg/s	2s
High flux	30 mg/mL	30W	180.06 mg/s	2s

# How does nicotine flux shape abuse liability?

## Main Takeaways

1. ENDS nicotine dose can be controlled by limiting nicotine flux + puff duration and is a potential regulatory target.
2. Limiting nicotine dose helps prevent people who use ENDS from receiving more nicotine than is delivered by a combustible cigarette use (even in high flux conditions).
3. ENDS with high nicotine flux appear to have lower abuse liability than cigarettes, with the fewest puffs earned, relatively greater harshness, and worse taste profile. However, high flux ENDS were more effective in suppressing cigarette cravings than no flux ENDS.

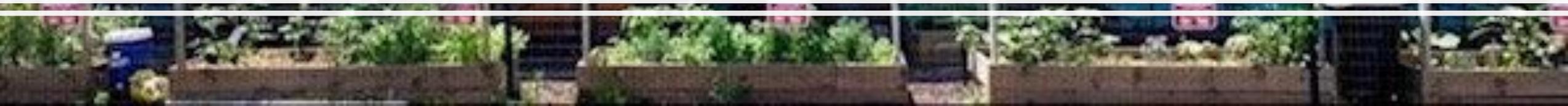


# Discussion 1





The roads ahead



# Refining our methods

- Choosing the best price frames
- Exploring heterogenous substitution responses to raising ENDS prices among people who exclusively use ENDS and those who dual use

# Choosing the best price frame

- In the purchase task, the “price frame” is the unit of the commodity being purchased (e.g., 1 cigarette)
- Added complexity with ENDS, a heterogenous class of products
  - Do responses differ for “10 puffs” vs. “1 mL of e-liquid”?

Correlation in Outcomes Between Price-Frames (10 puffs vs. 1 mL of liquid)							
	Intensity (1 mL)	alpha (1 mL)	P <sub>max</sub> (1 mL)	O <sub>max</sub> (1 mL)	Breakpoint (1 mL)	Persistence (1 mL)	Amplitude (1 mL)
★ Intensity (10 puffs)	0.5721 (0.0003)	-0.3312 (0.0519)	0.1601 (0.3582)	0.2329 (0.1782)	0.2105 (0.2248)	0.2353 (0.1738)	0.4069 (0.0153)
alpha (10 puffs)	-0.0065 (0.9706)	0.7175 ( $<0.0001$ )	-0.5932 (0.0002)	-0.7269 ( $<0.0001$ )	-0.7022 ( $<0.0001$ )	-0.7304 ( $<0.0001$ )	-0.0325 (0.8530)
P <sub>max</sub> (10 puffs)	0.1132 (0.5172)	-0.5866 ( $<0.0002$ )	0.5274 (0.0011)	0.6403 ( $<0.0001$ )	0.6584 ( $<0.0001$ )	0.6491 ( $<0.0001$ )	0.0712 (0.6845)
O <sub>max</sub> (10 puffs)	0.0994 (0.5699)	-0.7581 ( $<0.0001$ )	0.7003 ( $<0.0001$ )	0.7784 ( $<0.0001$ )	0.7917 ( $<0.0001$ )	0.8114 ( $<0.0001$ )	0.0960 (0.5834)
Breakpoint (10 puffs)	0.1780 (0.3064)	-0.6872 ( $<0.0001$ )	0.6147 (0.0001)	0.6708 ( $<0.0001$ )	0.7448 ( $<0.0001$ )	0.7413 ( $<0.0001$ )	0.1427 (0.4135)
Persistence (10 puffs)	0.1143 (0.5133)	-0.7360 ( $<0.0001$ )	0.6401 ( $<0.0001$ )	0.7823 ( $<0.0001$ )	0.7741 ( $<0.0001$ )	0.7858 ( $<0.0001$ )	0.0919 (0.5996)
★ Amplitude (10 puffs)	0.6082 (0.0001)	-0.2818 (0.1010)	0.1160 (0.5069)	0.1704 (0.3277)	0.1732 (0.3198)	0.1953 (0.2610)	0.3606 (0.0334)

Correlations for people who exclusively use ENDS (N=19) tended to be higher than for people who dual use (N=17)

★ Significantly correlated with ENDS dependence

# Expanding on the cross-product purchase task: Comparing substitution to cigarettes as ENDS prices increase



Preferred  
product  
available at a  
fixed price

AND



Alternative  
product  
varies in price

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If 10 puffs of your own brand of cigarettes cost \$0.00 (free) and 10 puffs of your own brand of e-cigarettes cost \$1:  
How many times would you buy 10 cigarette puffs and/or 10 e-cigarette puffs to consume in one day?

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If 10 puffs of your own brand of cigarettes cost \$0.01 (free) and 10 puffs of your own brand of e-cigarettes cost \$1:  
How many times would you buy 10 cigarette puffs and/or 10 e-cigarette puffs to consume in one day?

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If 10 puffs of your own brand of cigarettes cost \$0.02 (free) and 10 puffs of your own brand of e-cigarettes cost \$1:  
How many times would you buy 10 cigarette puffs and/or 10 e-cigarette puffs to consume in one day?

...

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If 10 puffs of your own brand of cigarettes cost \$8.96 (free) and 10 puffs of your own brand of e-cigarettes cost \$1:  
How many times would you buy 10 cigarette puffs and/or 10 e-cigarette puffs to consume in one day?

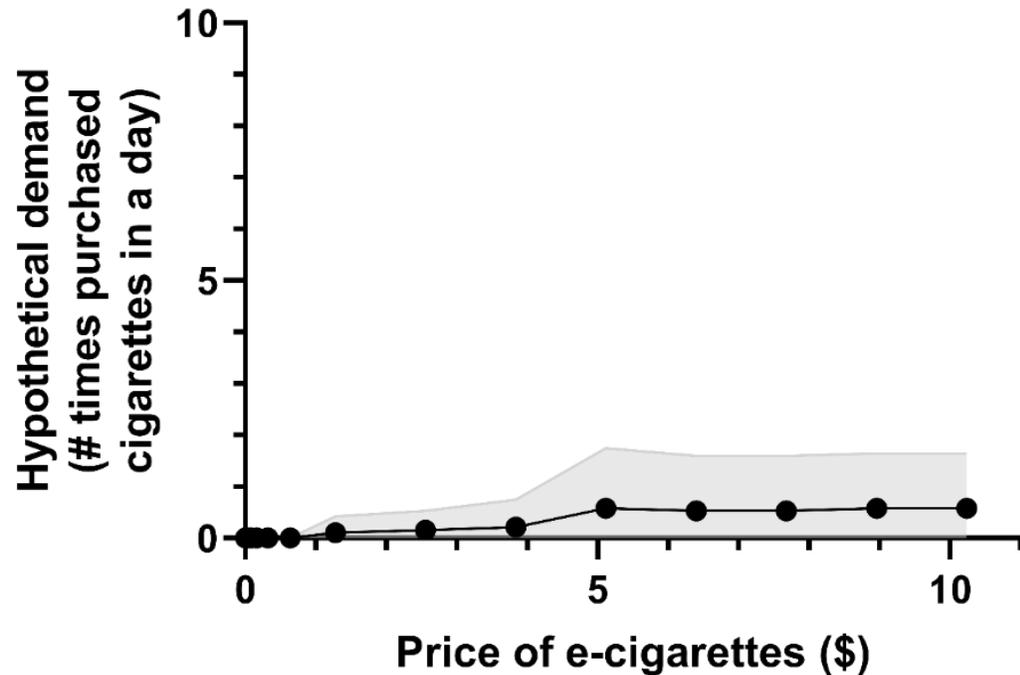
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If 10 puffs of your own brand of cigarettes cost \$10.24 (free) and 10 puffs of your own brand of e-cigarettes cost \$1:  
How many times would you buy 10 cigarette puffs and/or 10 e-cigarette puffs to consume in one day?

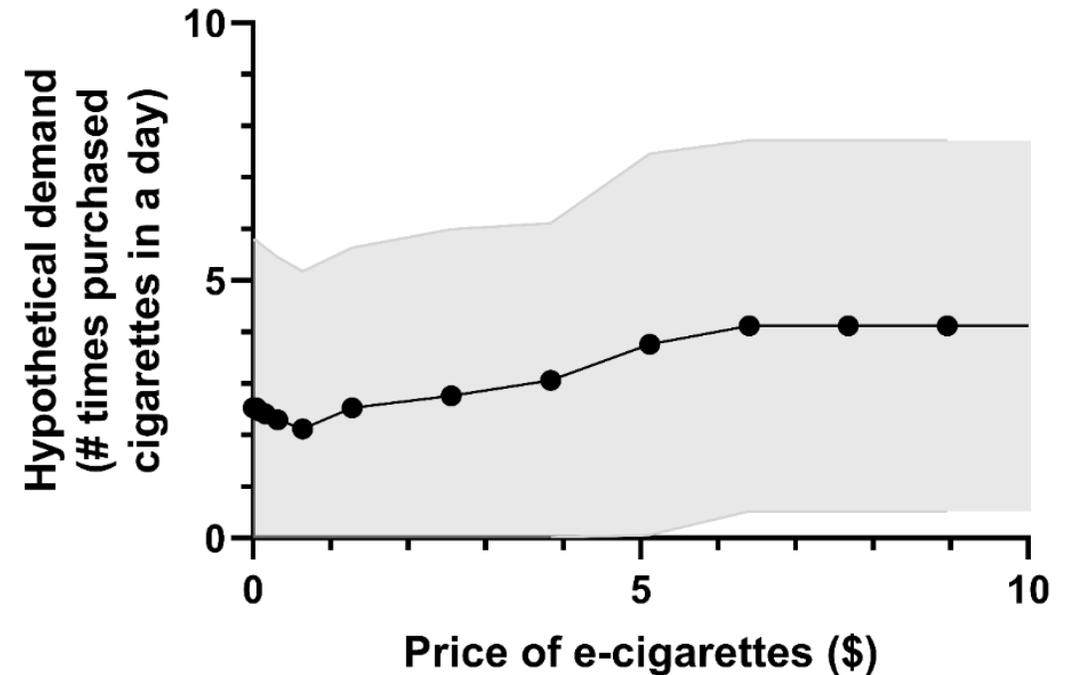
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Overall, cigarettes would be a substitute for ENDS both people who dual use and who exclusively use ENDS

- Exclusive ENDS users:  $B=0.29$ ,  $p<0.001$

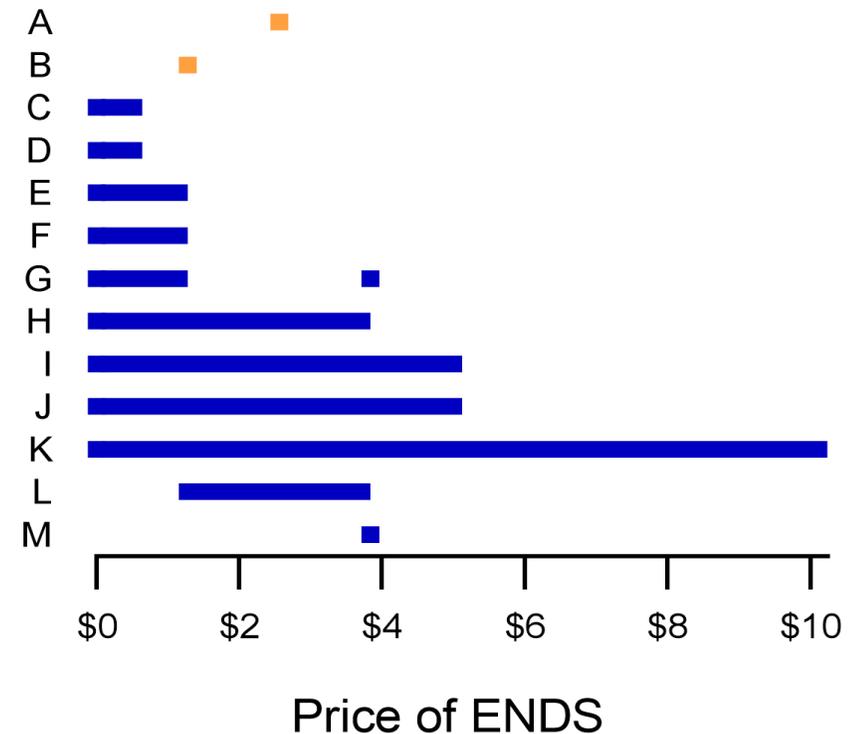


- Dual users:  $B=0.29$ ,  $p<0.001$



# Despite equal CPEs, there remain important differences between people who are dual and exclusive users ....

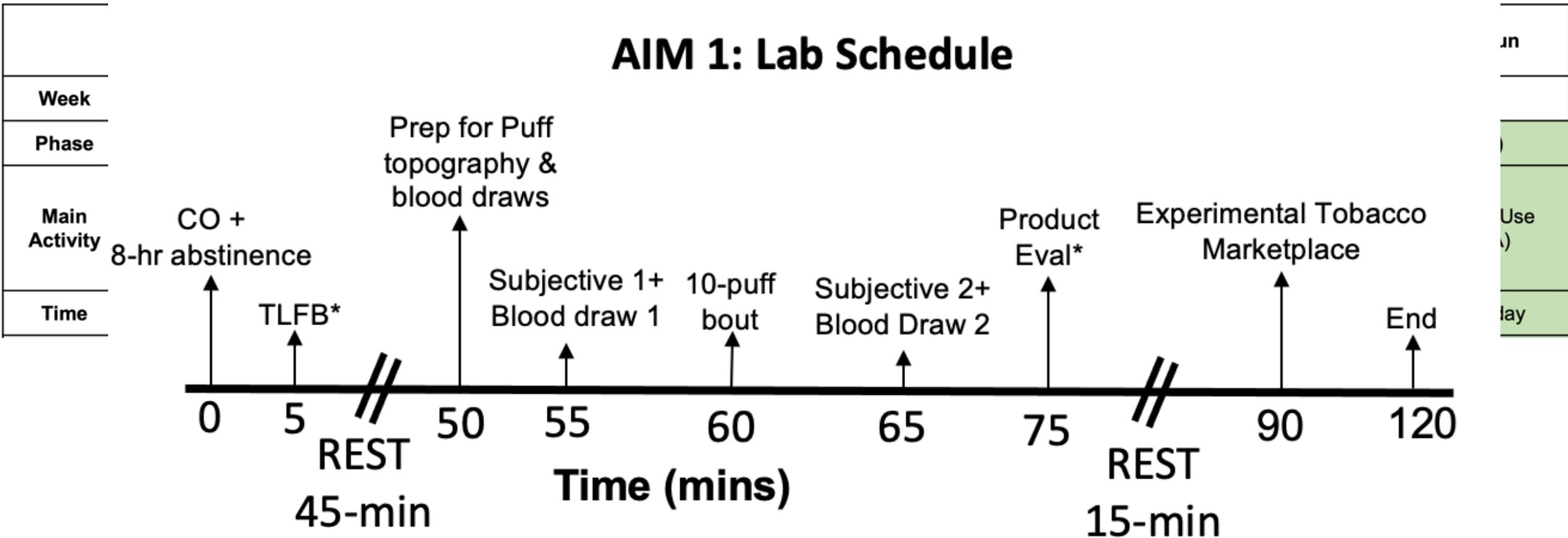
- A majority (59%) of people who dual use would still buy cigarettes if ENDS were free
- People who dual use purchased both products simultaneously in 35% of price scenarios but people who exclusively use ENDS did not (<1%)
- For those most at risk of dual use, raising the price of ENDS to be 3-4X the price of cigarettes may promote complete substitution from ENDS to cigarettes
- ENDS taxes may not steer people who exclusively use ENDS toward cigarette use, but could prompt some people who dual use to completely substitute cigarettes while others will continue to dual use



■ Exclusive ENDS users  
■ Dual users

# IQOS Study

Do flavors (e.g., “tobacco” vs. “menthol”) alter the abuse liability of Heated Tobacco Products and their ability to substitute for menthol cigarettes?



# IQOS – Experimental Tobacco Marketplace (ETM)

CIGARETTES	
	
Own-Brand Cigarettes (Flavor: Menthol)	Cigarettes (Flavor: Tobacco)
Description: A single menthol cigarette in your normal brand.	Description: A single tobacco-flavored (i.e., non-menthol) cigarette.
Price: \$0.12/cigarette	Price: \$0.40/cigarette
Quantity: <input type="text" value="0"/> cigarettes	Quantity: <input type="text" value="0"/> cigarettes
Cost: \$0	Cost: \$0

HEATED TOBACCO PRODUCTS	
	
IQOS HeatSticks (Flavor: Menthol)	IQOS HeatSticks (Flavor: Tobacco)
Description: A single HeatStick (14 puffs). Assume you already have the heating device required or that it is available for free.	Description: A single HeatStick (14 puffs). Assume you already have the heating device required or that it is available for free.
Price: \$0.30/HeatStick	Price: \$0.30/HeatStick
Quantity: <input type="text" value="0"/> HeatSticks	Quantity: <input type="text" value="0"/> HeatSticks
Cost: \$0	Cost: \$0

The ETM is an extension of the Cross-Product Purchase Task that gives the participant the choice between a price-varying preferred product (e.g., OB cigarettes) and **MULTIPLE** fixed-price alternatives (e.g., IQOS, ENDS) subject to a **budget constraint**. Participants can also purchase: **cigars, cigarillos, two types of ENDS, nicotine pouches, chewing tobacco, and NRT.**

# RVA Flavors

*Predicting effects of ENDS flavor regulations on tobacco use behavior, toxicity, and abuse liability among African American menthol smokers*

Three-arm, 6-week, parallel group RCT among Black/African American people who smoke menthol cigarettes with a follow-up at 30 days post intervention.

**Study Arms** differ by potential FDA regulations restricting ENDS flavor availability:

- 1) Menthol+Tobacco
- 2) Tobacco
- 3) Unflavored

# RVA Flavors

- Aim 3: Test the effect of ENDS flavor availability on addiction/abuse liability using validated behavioral economic instruments at multiple time points during the trial.
  - H3: African American/Black people who smoke menthol cigarettes will be (a) willing to pay more money for ENDS in the M+T\_Reg condition and (b) willing to substitute from cigarettes to ENDS earlier in the M+T\_Reg condition.
- Primary endpoint: Willingness to substitute from cigarettes to ENDS (at Week 6)
- Secondary outcome: Willingness to pay for ENDS (at Week 6).

	<u>Screening /Baseline</u>	<u>Rand</u>	<u>Weekly study visits</u>						<u>30-d FU</u>
<b>Study Week</b>	<b>-1</b>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>~10</b>
<b>Tobacco use behavior (Aim 1)</b>									
Daily Tobacco Use (daily text surveys)		x	x	x	x	x	x	x	
7-day Tobacco Use TLFB		x	x	x	x	x	x	x	x
ENDS liquid consumed (weight via products returned)					x			x	
<b>Cigarette/ENDS (Aim 2)</b>									
Expired air CO	x*	x			x			x	
Urinary cotinine, NNAL, PG	x*	x			x			x	
<b>Abuse liability/addiction (Aim 3)</b>									
Cigarette/ENDS purchase tasks (n=3)		x (cigarette-only)			x			x	

Outcomes and study timeline

N=17 randomized/210

# P3 Taste – launch January 2023

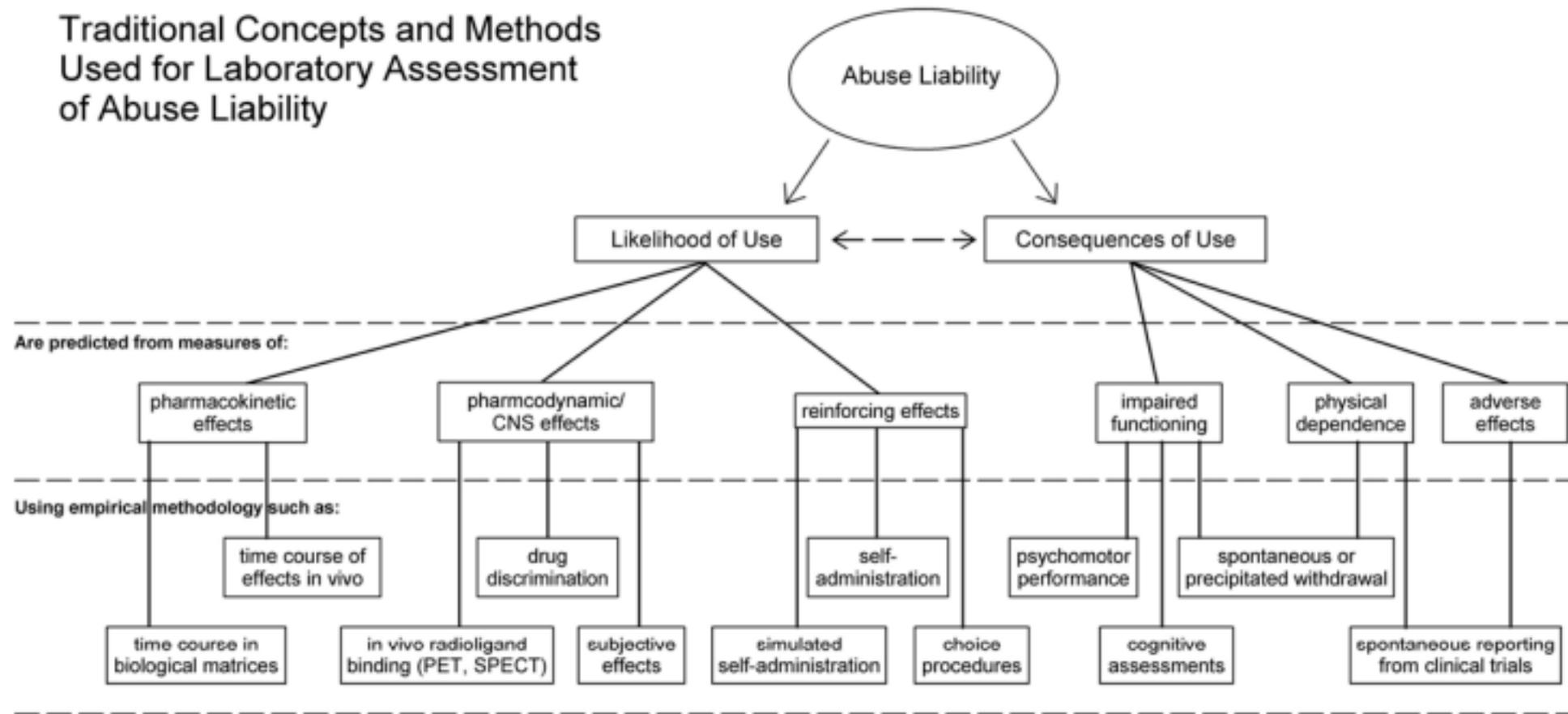
- Compare abuse liability indices between three FDA authorized ENDS products that vary in nicotine flux (but are all tobacco flavor) and own brand cigarettes.
  - We hypothesize that as nicotine flux is lowered, abuse liability indices will be lowered.
- Test the influence of ENDS flavor availability (tobacco vs. menthol) within three ENDS product classes.
  - We also hypothesize that across ENDS product classes, abuse liability indices will be higher for menthol-flavored products.
- Measures – purchase tasks, experimental tobacco marketplace, minute discounting task, subjective effects, urine (cotinine, NNAL, PG)

# P3 Taste – launch January 2023

- 40 people who smoke cigarettes will complete 4, within-subject, lab sessions differing by the product used:
  - Own brand cigarette
  - NJOY Ace 2.4% nicotine ECIG (Menthol and Classic Tobacco flavor)
  - NJOY Ace 5.0% nicotine ECIG (Menthol and Classic Tobacco flavor)
  - NJOY Daily ECIG 6% nicotine (Menthol and Extra Rich Tobacco).
- First condition for all subjects will be their OB cigarette
- Subsequent three sessions will be randomly assigned following enrollment and within each session participants will sample and evaluate two flavors of each session's product.

In 2023, we hope to begin a series of papers fitting some of these pieces together – abuse liability, demand, dependence, drug delivery

### Traditional Concepts and Methods Used for Laboratory Assessment of Abuse Liability





## Discussion 2





Thank you  
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