



Electronic Nicotine Delivery Systems

Part II: Adult Smoker Cessation and Harm Reduction

Aruni Bhatnagar, Professor of Medicine and Distinguished University Scholar,
University of Louisville and Fellow, American Heart Association

Katherine Ciambrone, Legal, Regulatory & External Affairs – US, Fontem
Ventures

Gregory Conley, President, American Vaping Association

Moderated by **Robyn Gougelet**, Senior Associate, Pinney Associates, Inc.



Electronic Nicotine Delivery Systems Part II: Adult Smoker Cessation and Harm Reduction

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Senior Associate
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Speakers

- **Katherine Ciambrone**, Legal, Regulatory & External Affairs – US, Fontem Ventures
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Financial Disclosures

PinneyAssociates provides consulting services on tobacco harm minimization to Reynolds American Inc. and British American Tobacco. We do not work on combustible tobacco.

IN THE ROOM WHERE IT HAPPENS



FDA's Comprehensive Plan for Tobacco and Nicotine Regulation

- Lowering nicotine in cigarettes to a minimally- or non-addictive level
- Provide an array of noncombustible alternatives for those who need or want to continue using nicotine
 - Nicotine replacement therapies
 - Consumer nicotine and tobacco products (including e-cigarettes)
- Push-Pull strategy to move smokers from smoke to noncombustible sources of nicotine



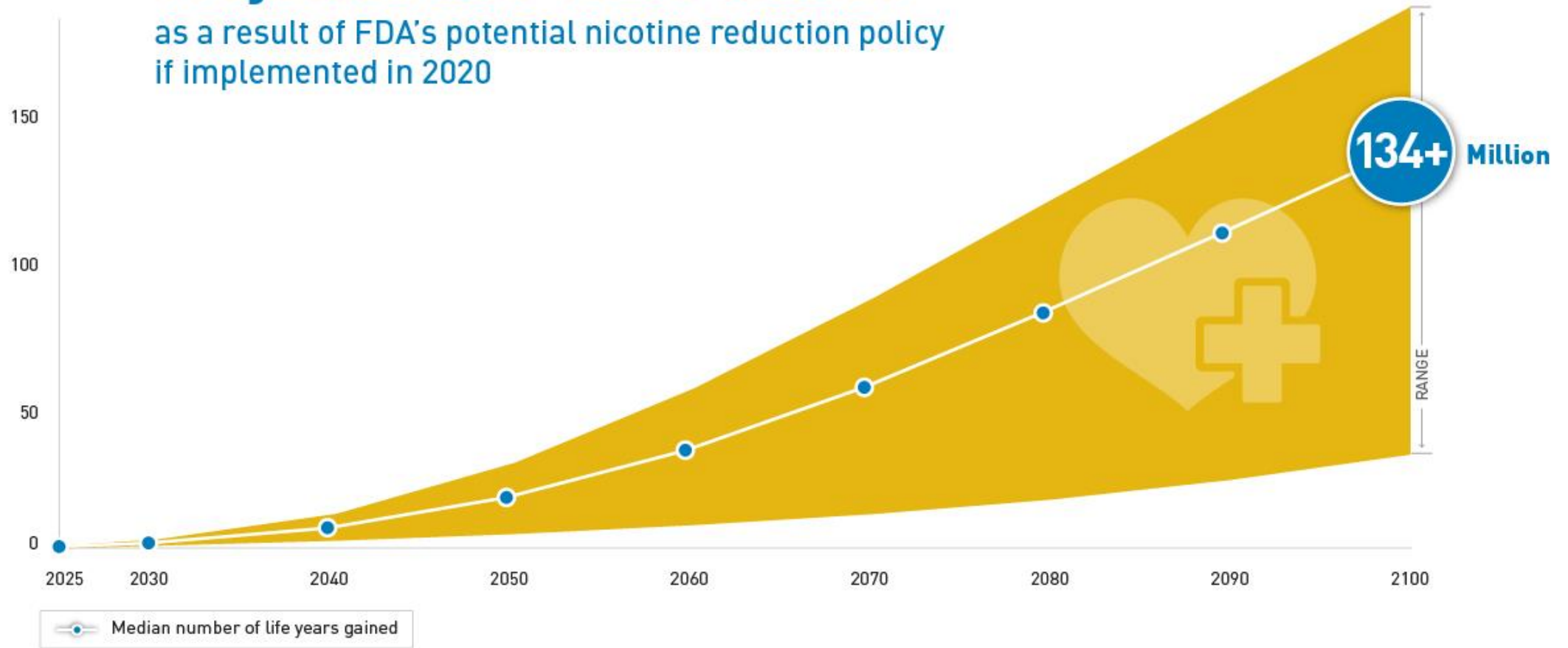


(Don't) let it
burn

FDA's Population Modeling – a Look at What Could Be

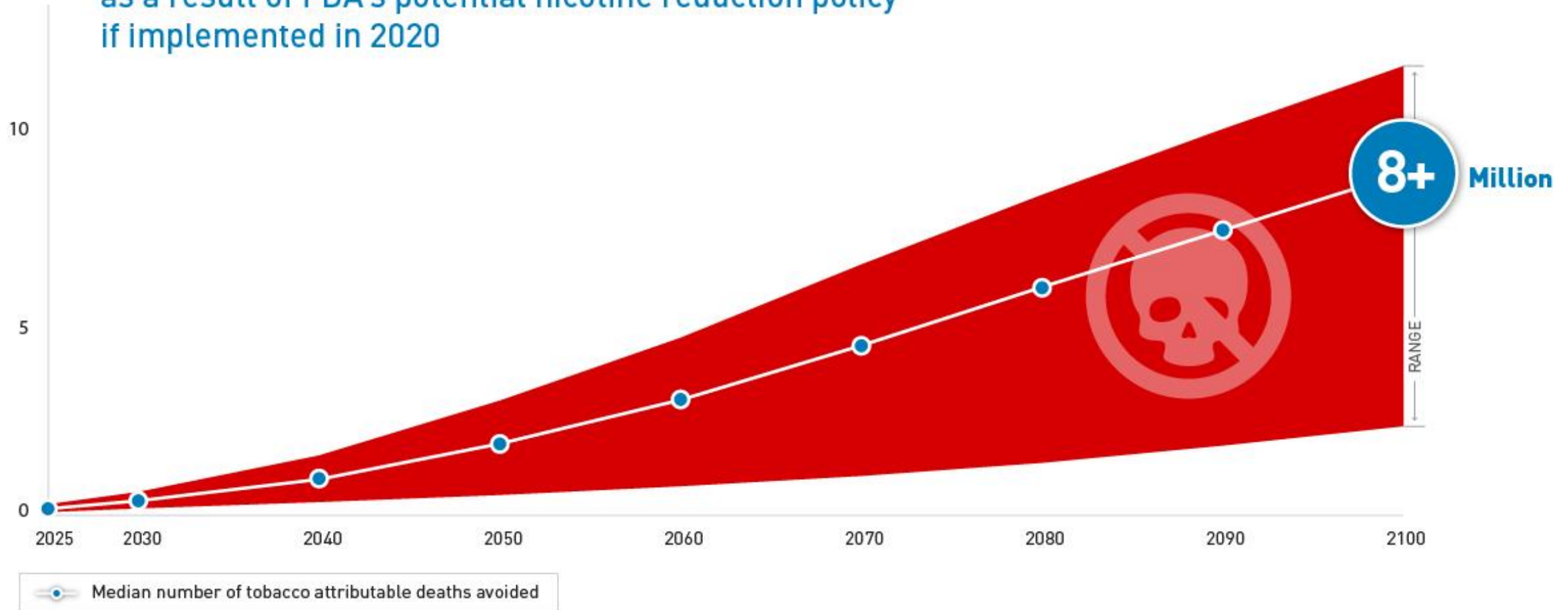
Projected Life Years Gained

as a result of FDA's potential nicotine reduction policy
if implemented in 2020



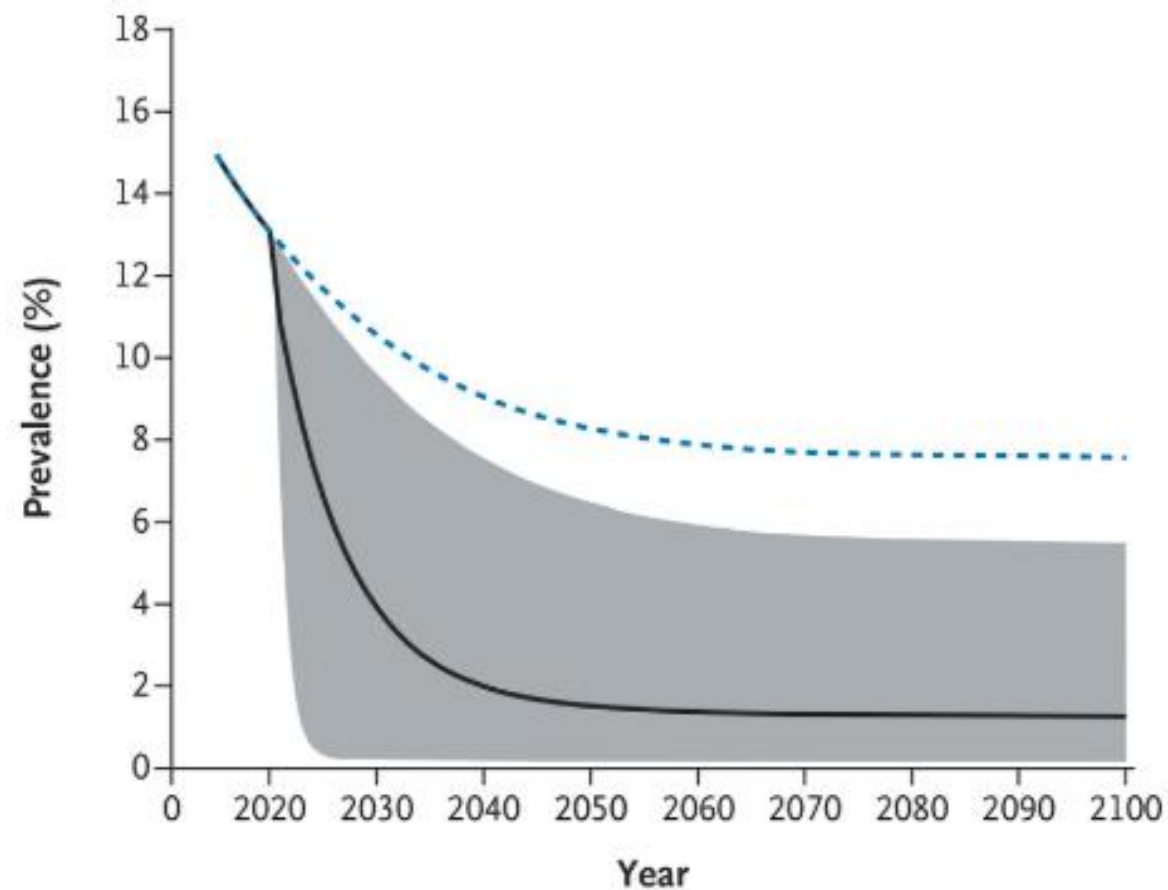
Projected Tobacco Attributable Deaths Prevented

as a result of FDA's potential nicotine reduction policy
if implemented in 2020

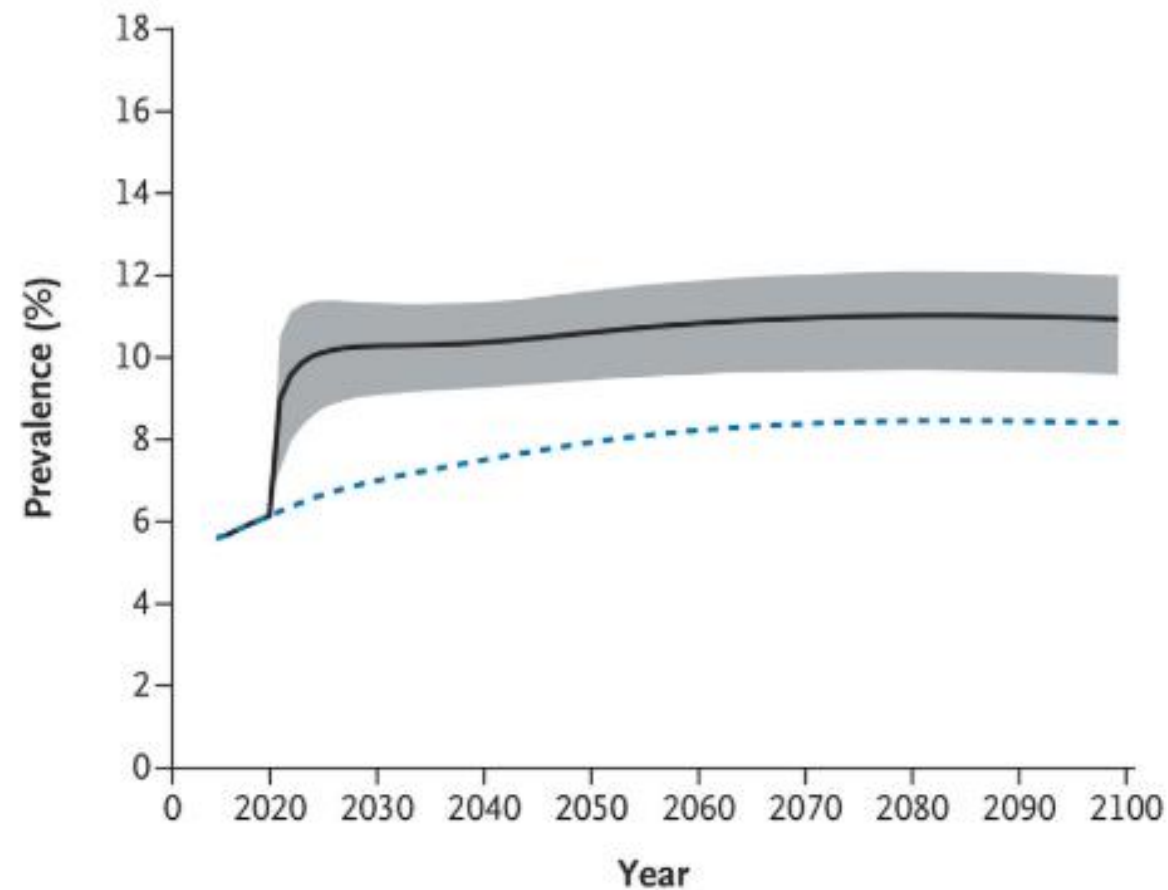


--- Baseline scenario ■ Policy scenario: 5th to 95th percentile — Policy scenario: Median

A Cigarette Smoking



B Noncombusted Tobacco Use



AWESOME!
WOW!

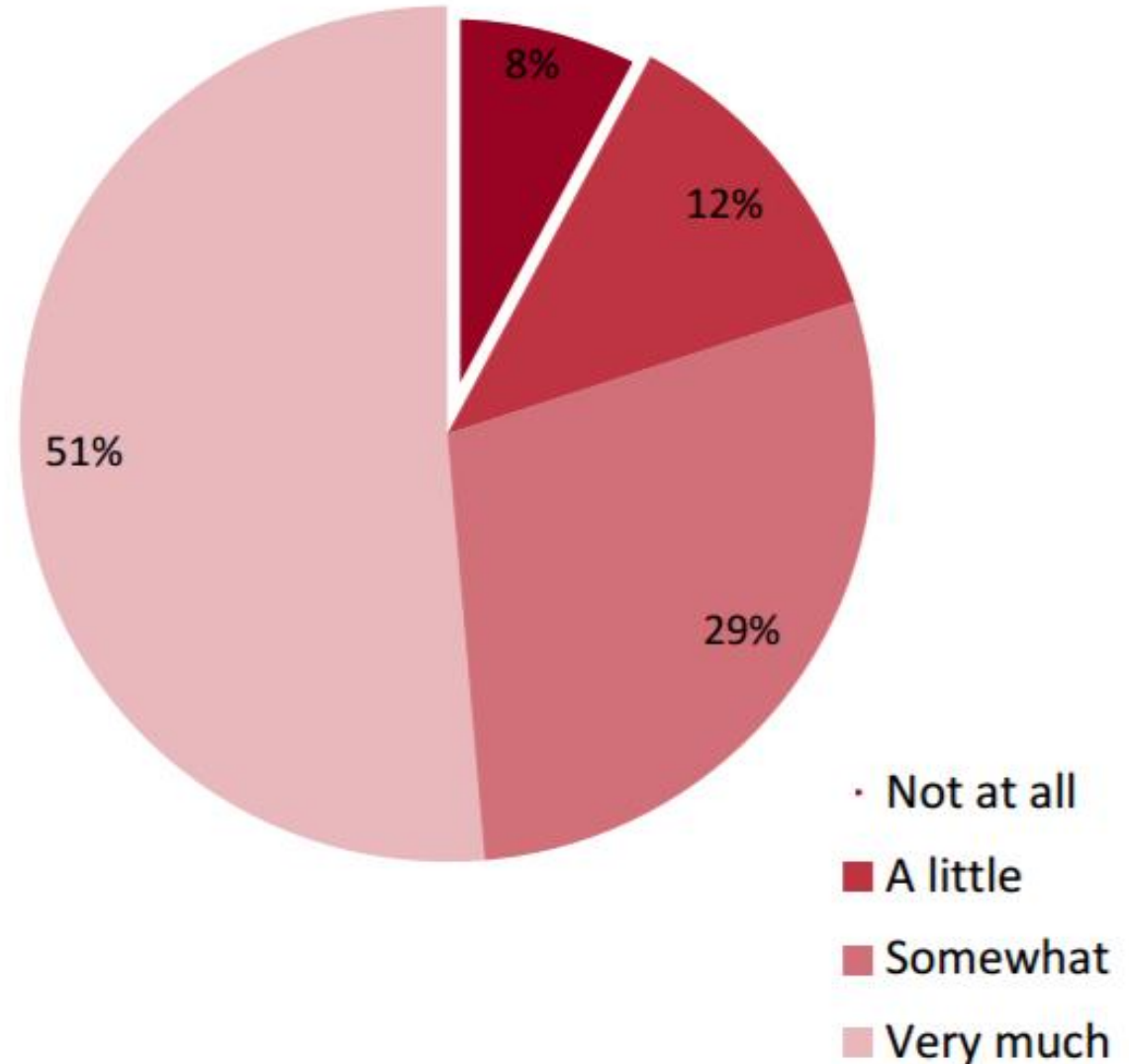


PATH STUDY

FINDINGS: NICOTINE AND CANCER

To what extent, if at all, do you believe the nicotine in cigarettes to be the chemical that causes most of the cancer caused by smoking?

The majority (80%) believe (*very much* or *somewhat*) that nicotine causes cancer.



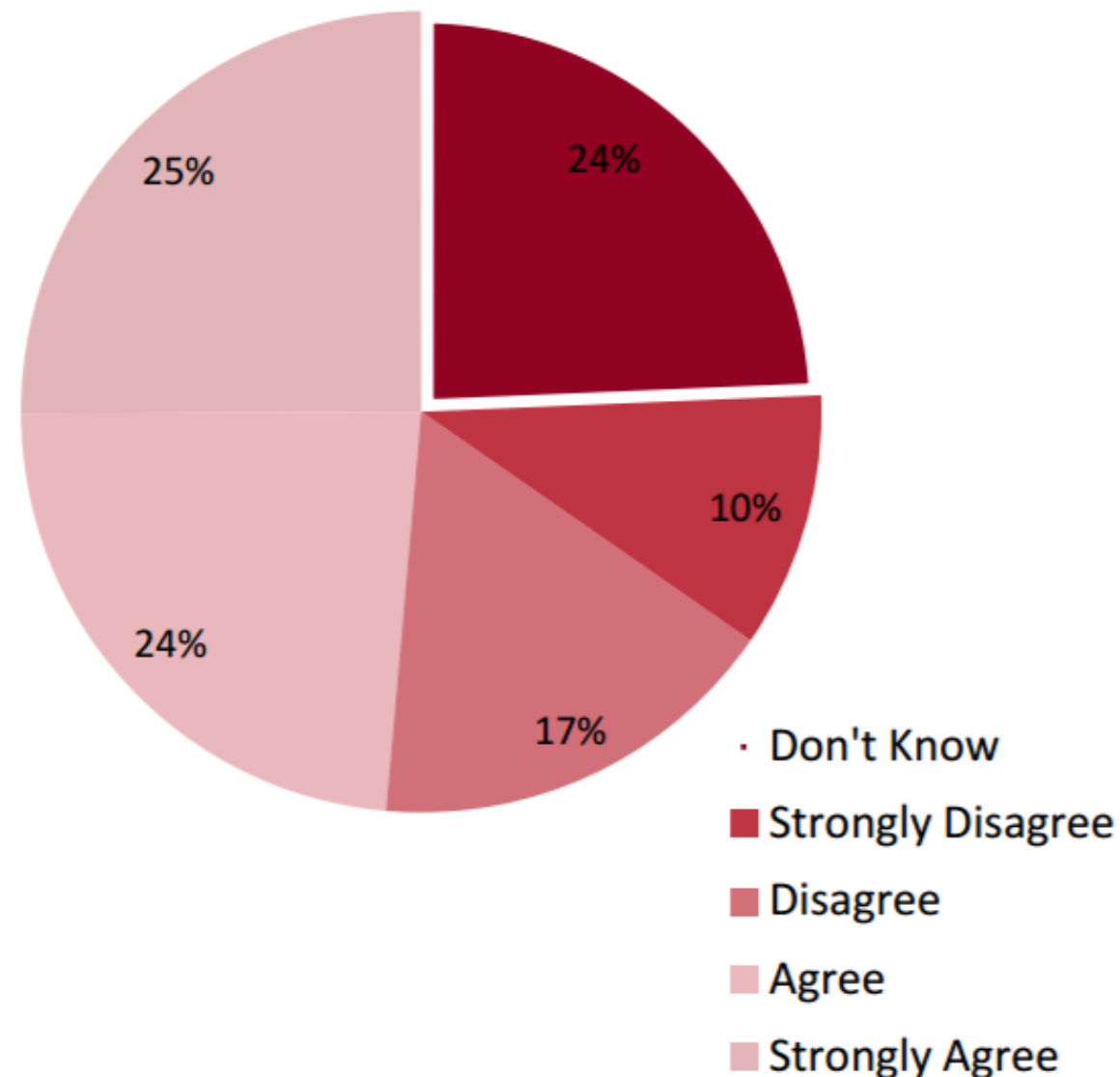
HINTS-FDA

FINDINGS: NICOTINE AND CANCER

The nicotine in cigarettes is the substance that causes most of the cancer caused by smoking.

Just under half (49%) agreed (*strongly agree* and *agree*) nicotine causes cancer.

24% selected *don't know*.

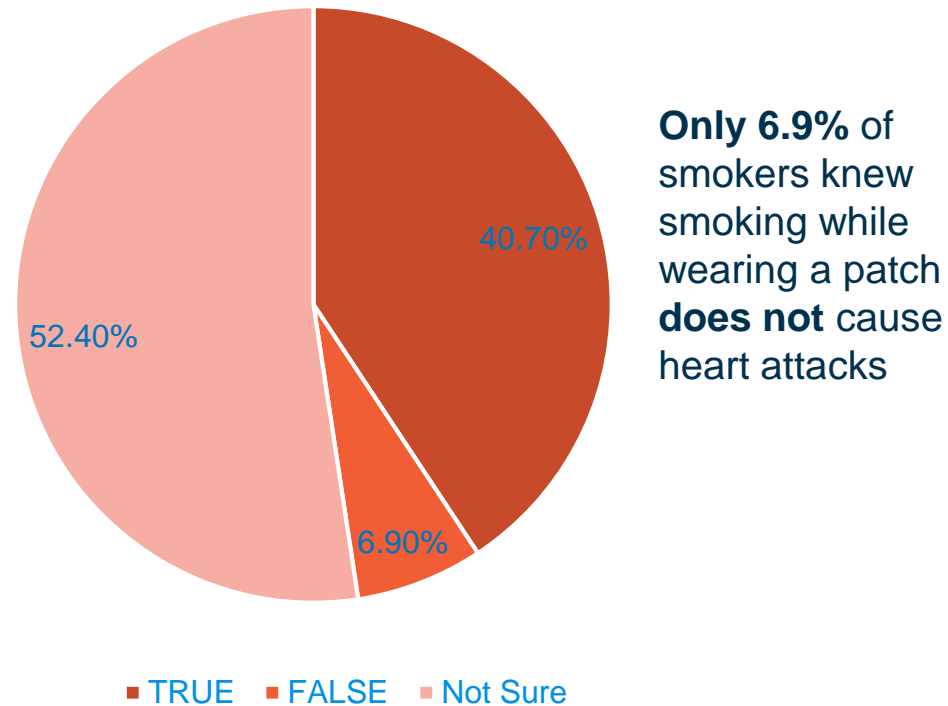




REVOLUTION

revelation

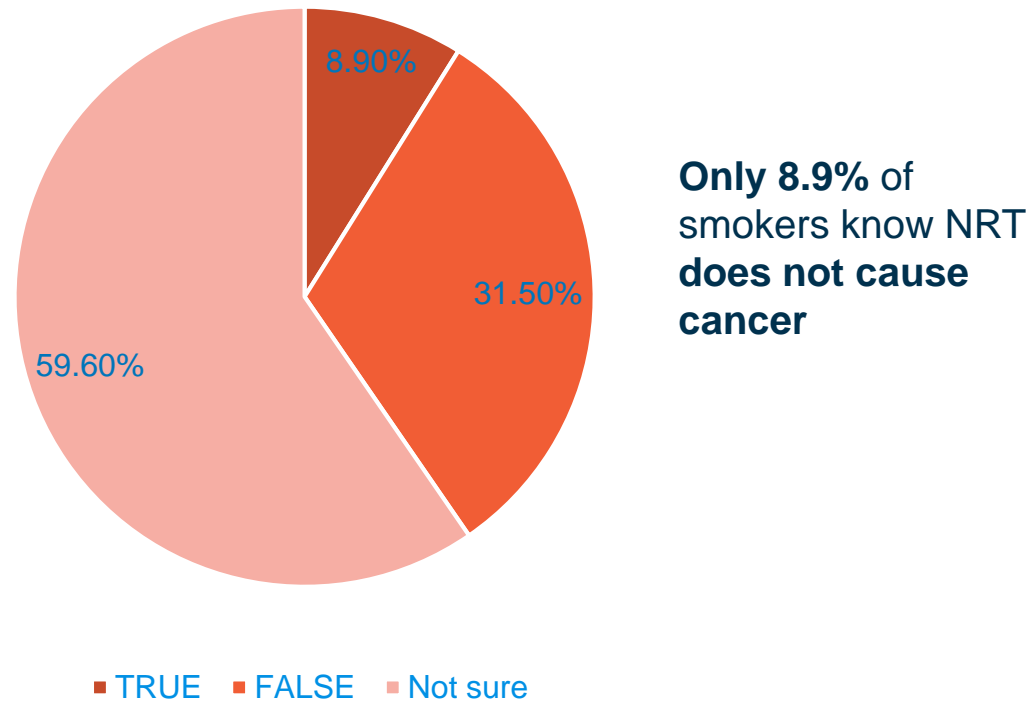
Nicotine while wearing the nicotine patch can cause heart attacks (false)



Only 6.9% of smokers knew smoking while wearing a patch **does not** cause heart attacks

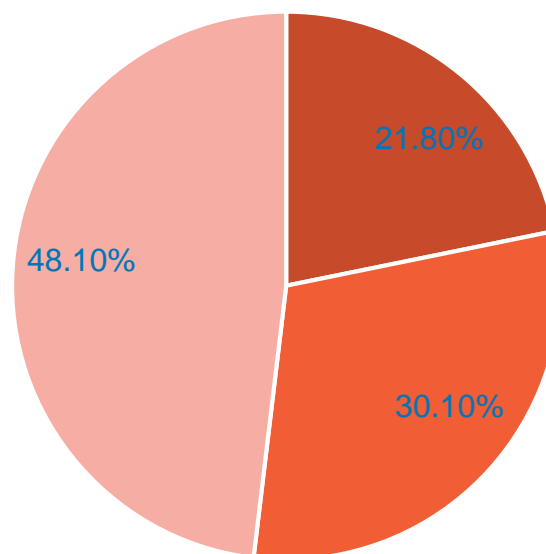
Ferguson et al., 2011

Nicotine patch, gum, and lozenge can cause cancer (false)



Ferguson et al., 2011

NRT products are designed to make you feel sick if you slip and have a cigarette (false)

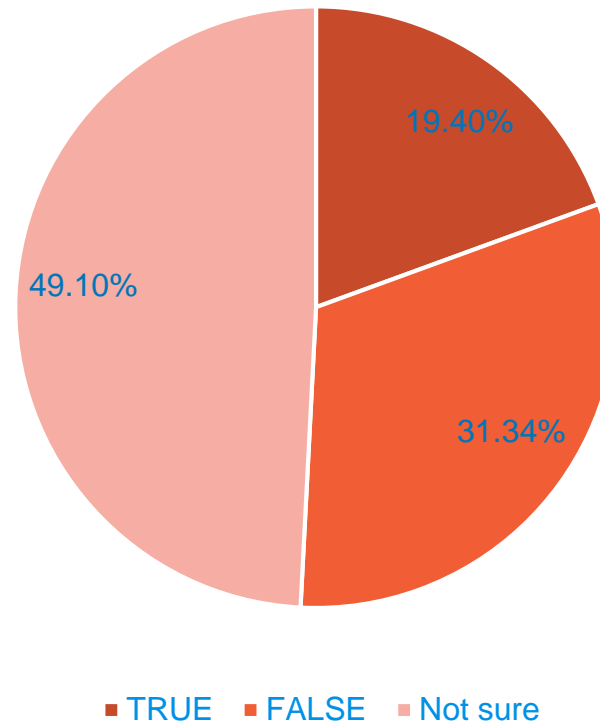


Only 30.1% of smokers know NRT not designed to make you sick

■ TRUE ■ FALSE ■ Not sure

Ferguson et al., 2011

NRTs are just as harmful as cigarettes (false)



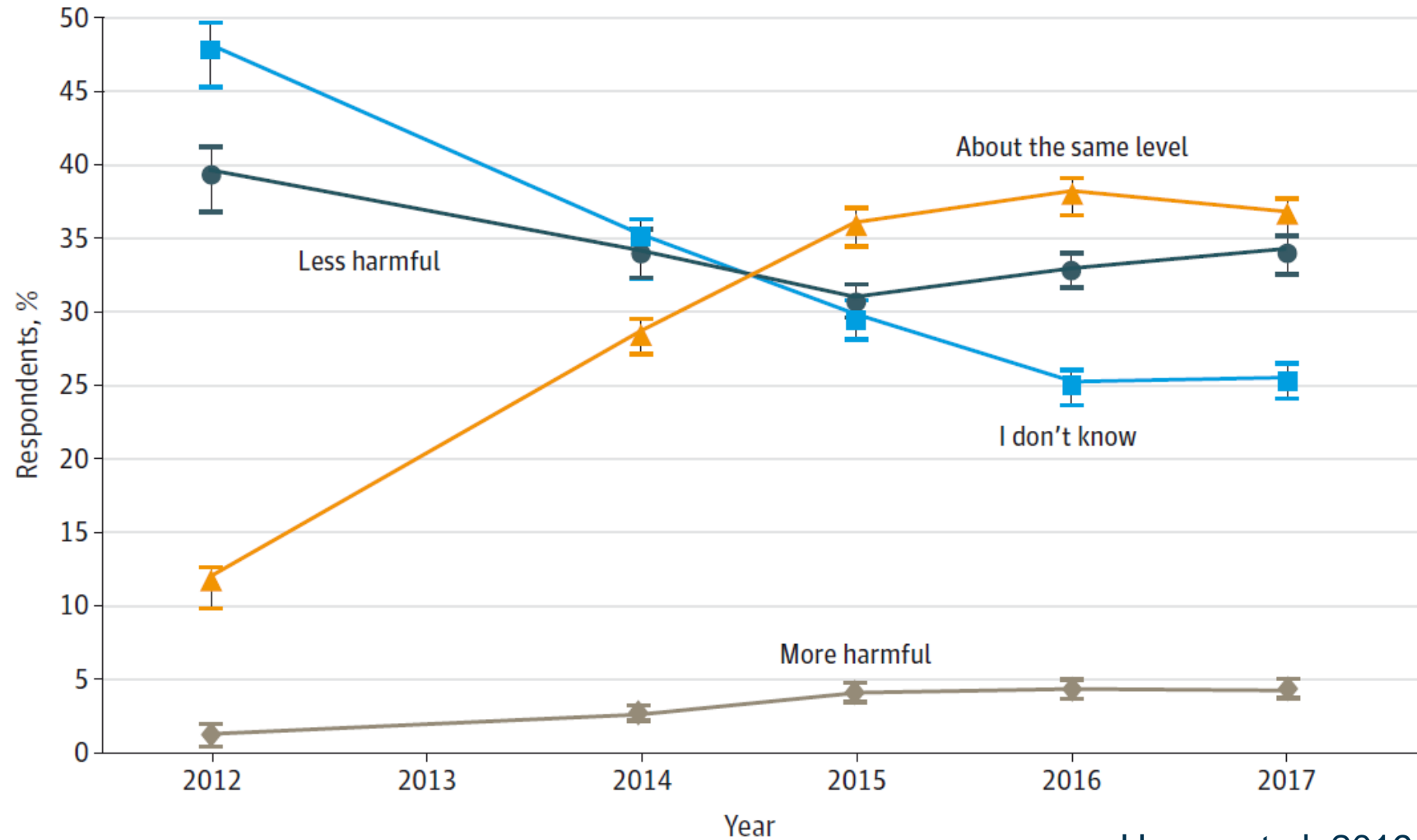
Only 31.4% of smokers know NRTs are not as dangerous as cigarettes

Ferguson et al., 2011



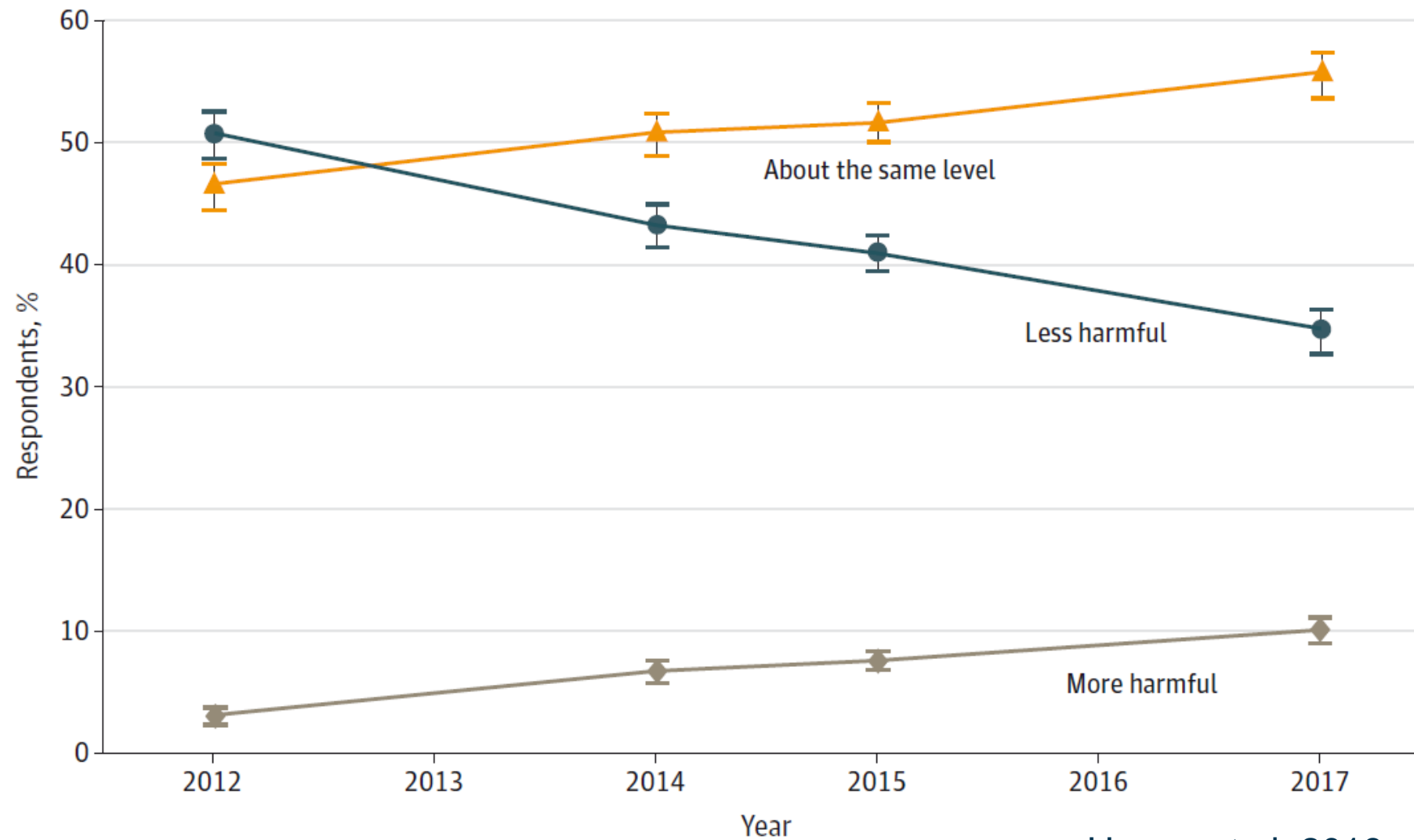
Let's Have Another Round (of Misperceptions Data)

Figure 1. Perceived Harm of Electronic Cigarettes Relative to Combustible Cigarettes in the Tobacco Products and Risk Perceptions Surveys



Huang et al, 2019

Figure 2. Perceived Harm of Electronic Cigarettes Relative to Combustible Cigarettes in the Health Information National Trends Surveys



Huang et al, 2019

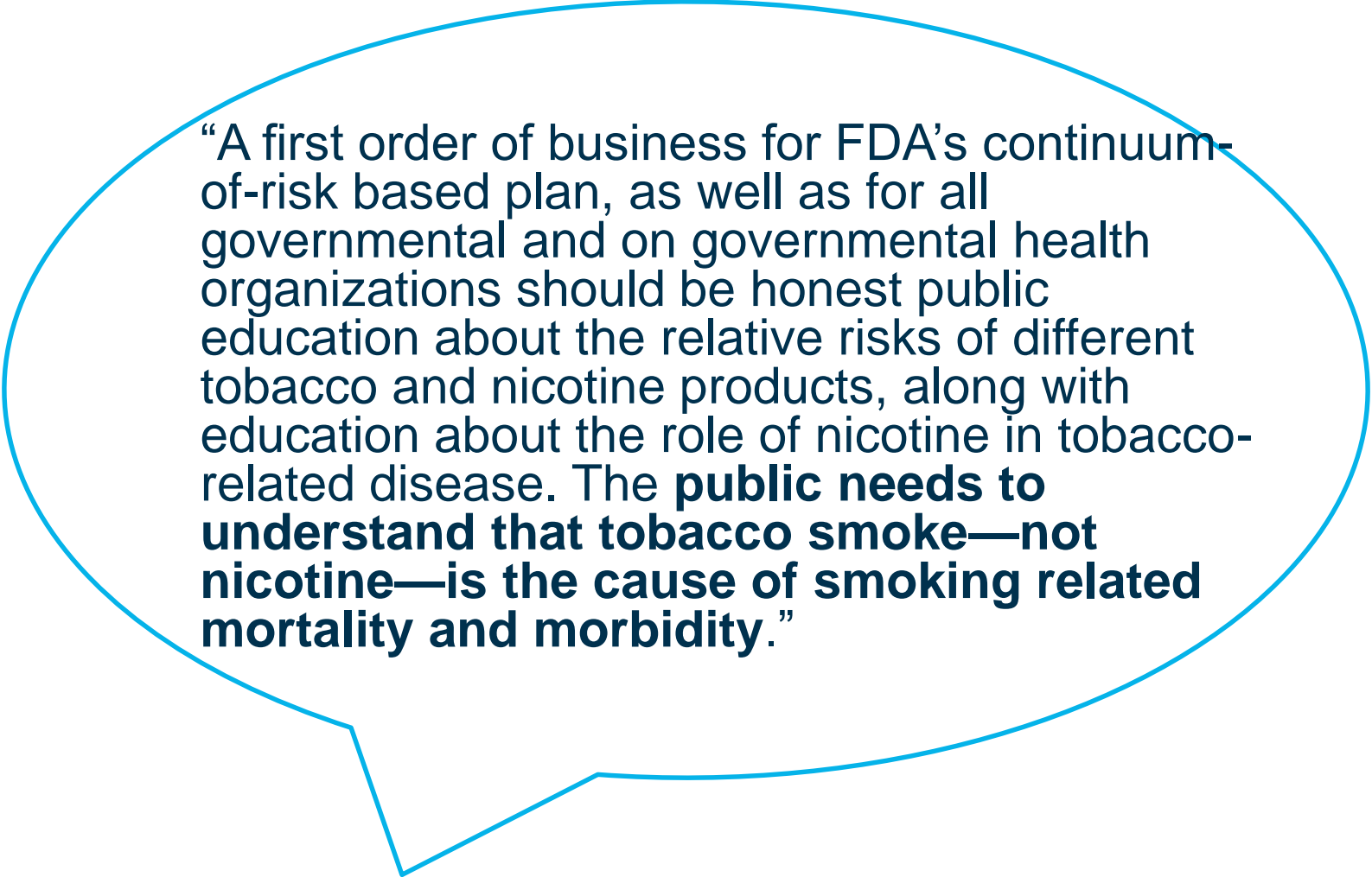


**We're in dire need of
some assistance**

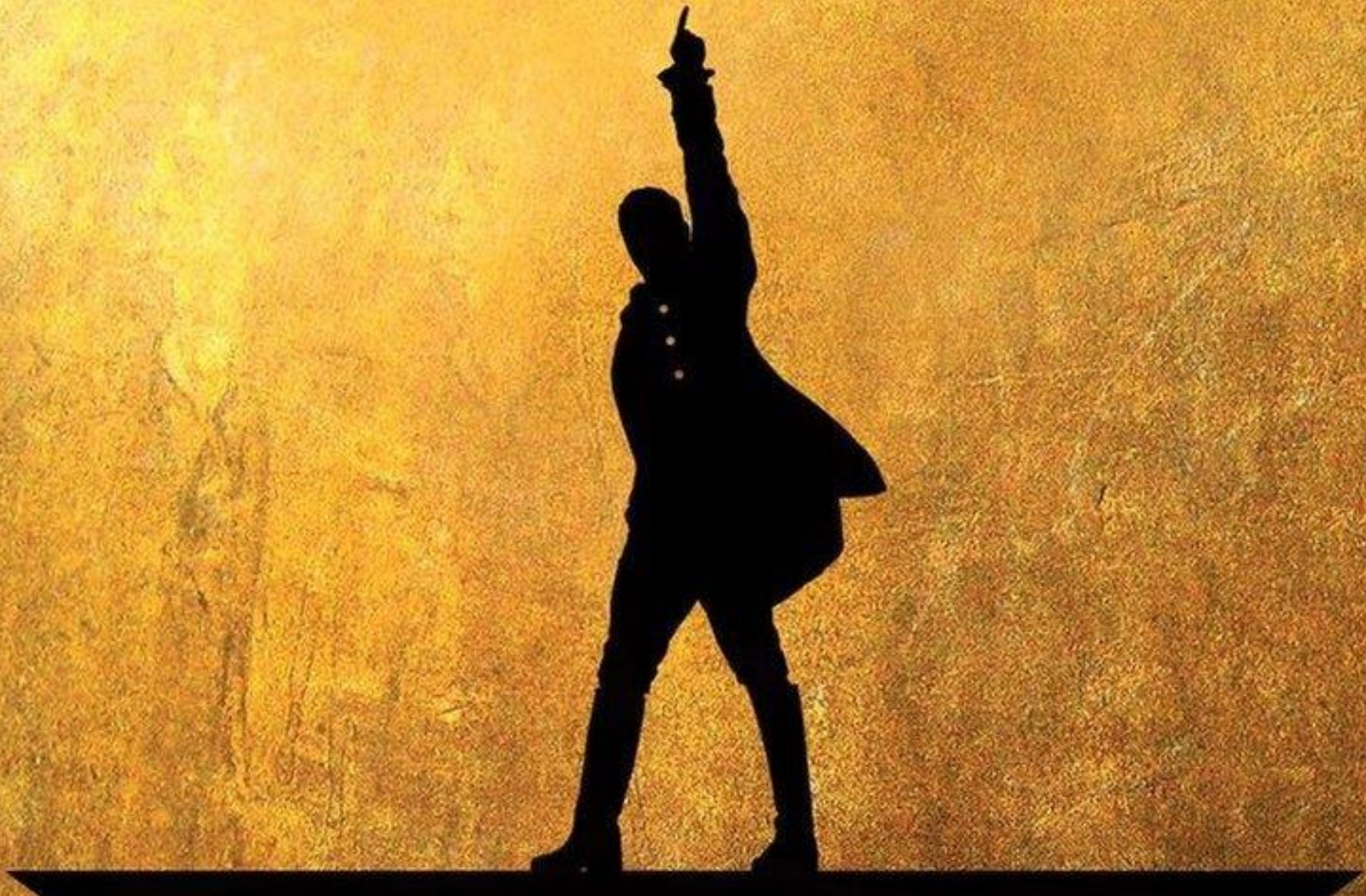
Huang et al. – JAMA Commentary

“[C]onfusion between relative risk and absolute risk of e-cigarettes may contribute to framing bias in risk communication and result in media reports and press releases in which absolute harm is overstated and relative harm is downplayed. **Lack of accurate, consistent, and proactive risk communications to the public from scientists may also contribute to the confusion about the health risks of e-cigarettes.**”

Warner and Schroeder – JAMA Commentary



“A first order of business for FDA’s continuum-of-risk based plan, as well as for all governmental and on governmental health organizations should be honest public education about the relative risks of different tobacco and nicotine products, along with education about the role of nicotine in tobacco-related disease. The **public needs to understand that tobacco smoke—not nicotine—is the cause of smoking related mortality and morbidity.**”



Time to Revisit the Risk Continuum and Communication?

Ka
EVP, Legal,



fontem US, inc.

ron
xternal Affairs

These concepts are merely an example of how an improved approach to considering risk, communicating risk and mitigating risk could be achieved by broadening the scope and integrating assets. The examples used are not validated.

Current Dilemma: 39 million smokers are confused. For Manufacturers, our hands are tied... *No Market Order = No Information?*



(-)

FDA to investigate reports of seizures possibly linked to e-cigarette use

The agency has received 35 reports of young adults, since 2010.

FDA launches investigation into reports of

APRIL 3, 2019 / 01:13

Scientific Conference: Opioid and Nicotine Use, Dependence, and Recovery: Influences of Sex and Gender

SHARE TWEET LINKEDIN PIN IT EMAIL PRINT



Tobacco company Philip Morris launches life insurance ...



CNBC

1 day ago · Philip Morris International, the tobacco company that sells Marlboro cigarettes, is getting into the life insurance business. Called Reviti, the wholly owned subsidiary will initially sell life ...



Scott Gottlieb, M.D. @SGottliebFDA · Jan 18

I still believe e-cigarettes present an opportunity for adult smokers to transition off cigarettes and onto nicotine delivery products that may not have the same level of risks. However, if the youth use continues to rise, the entire category will face an existential threat

(+)

San Francisco considers new law to ban e-cigarette sales ...

<https://finance.yahoo.com/video/san-francisco-considers-law-ban...>



Mar 20, 2019 · San Francisco considers new law to ban e-cigarette sales. CNBC Videos. March 20, 2019. The "Squawk Box" news team discusses the potential impact of the proposed ban.



Why are lawmakers more concerned with youth vaping than opioid abuse?

BY LINDSEY STROUD, OPINION CONTRIBUTOR — 03/31/19 06:00 PM EDT
THE VIEWS EXPRESSED BY CONTRIBUTORS ARE THEIR OWN AND NOT THE VIEW OF THE HILL

138 COMMENTS

Juul is pitching its e-cigarette as an anti-smoking tool to employers and insurers

- Juul wants to sell employers and insurers on using its e-cigarettes to help their workers stop smoking cigarettes.
- Juul built a business on helping employers and insurers.
- The e-cigarette is a health-care tool.

Angelica LaVigne
Published 11:46 AM
CNBC

Juul launches 'make the switch' TV campaign aimed at adult smokers

Jordan Crook @jordancrook / 4 months ago

Comment



U.S. FDA @US_FDA · 11h
Aerosol produced by some e-cigarettes can contain high amounts of some toxic substances, which can pose a risk to the lungs, lower the body's defense against pathogens and mimic metastatic cancer.

4 15 21

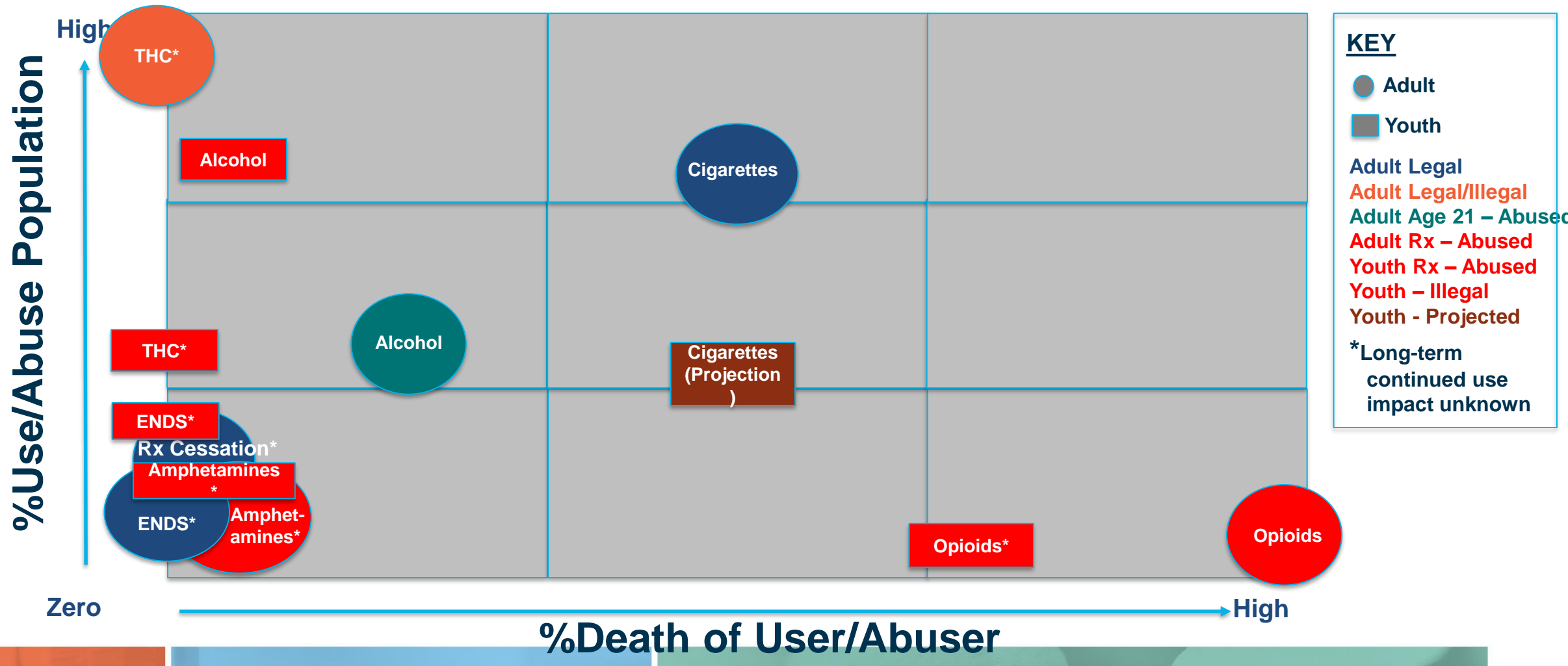
What is the real risk continuum?

Product	Opioids	Stimulants	Prescription Cessation Aids	NRT	Cigarettes	ENDS	THC/CBD?	Alcohol AGE 21
Type	~21-29% Prescription Illegal trade	Prescription Illegal trade	Prescription	OTC	Behind Counter/Age Gated Illegal trade	Behind Counter Age Gated Illegal Trade	Age Gated Illegal Trade	Age 21 ALREADY IN PLACE 7.7m Youth using 5.1 binging 5k deaths per year 210,000 ER visits per year
Est Adult Users	57,000,000 use 1,700,000 abuse (2017)	16,000,000 use 5,000,000 illegal 1,700,000 abuse	11,000,000 (2016)		1,000,000	10,800,000	55,000,000 current 35,000,000 regular (2017)	
Est Adult Deaths (per year)	47,600 deaths (2017)	7,662 (2017)	deaths. (2018)		480,000 smokers per year +41,000 second hand smoke related fires	1 (2017)	0	
Reported Youth Use	5,700 first time users in 2014 (SAMHSA)	3,500,000 use (2013) 1.8 million abuse (2017)	Not recommended Recent Pheny Study compared to different placebo	?	3,000,000 High School (2017) Middle School	10,000 (2017) Increase in 2018	4,000,000	
Est Youth Deaths (per year)	Illegal: >3,400 deaths Prescription: 1,050 (2017)	10,000 (2017)		?	At current rate 1.5 million of today's American youth will be 18 years of age expected to die prematurely.	1 (2018)	Maybe 1	
AEs/SAEs	~250,000 ER Visits	156,000 exposure calls (2000-2013) 19,000 reports (2013->)	Chantix bled for 3,063 serious injuries (2010-2013)		millions of disease caused by smoking.	~1,000 battery burns (2016)	?	

These numbers are collected from a varying number of sources, some may or may not be validated.

Example: Population Risk Spectrum

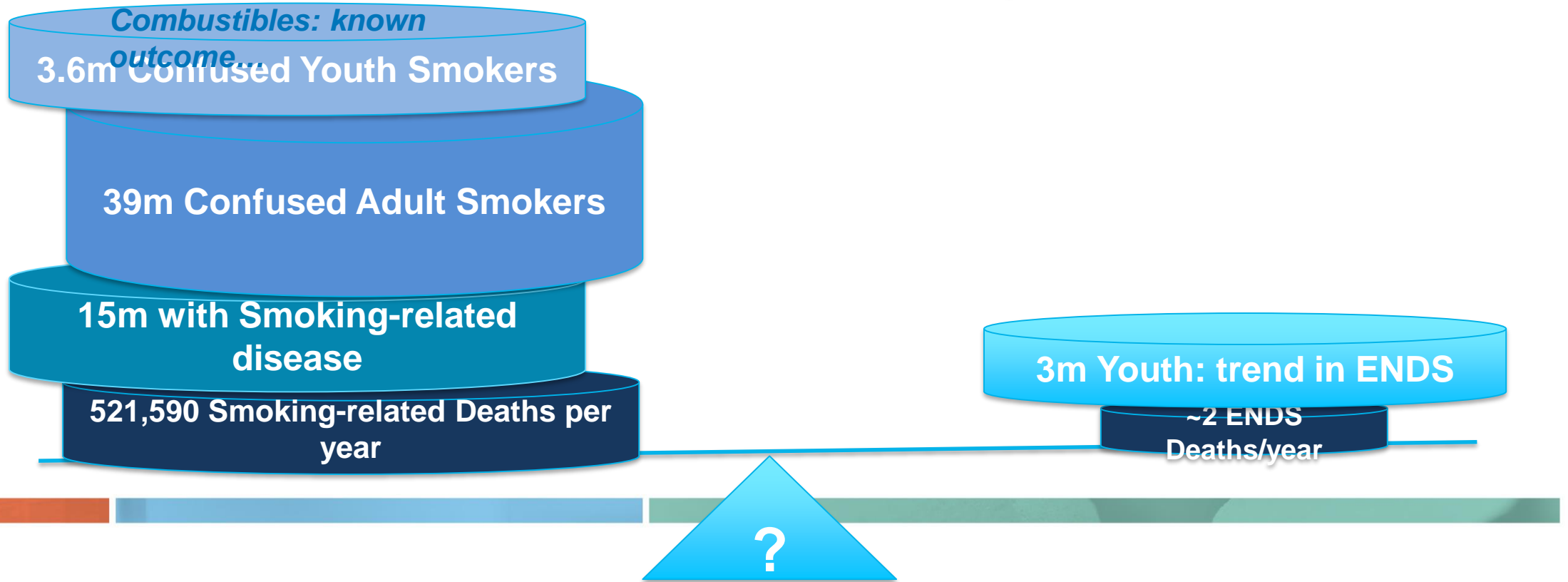
FOR EXAMPLE ONLY - A VALIDATED ANALYSIS SHOULD BE PERFORMED



Focus and Balance...?

- FDA CTP Budget-User Fees: \$626,000,000 (2018)
 - Cigarette Tax Revenue: \$13,800,000,000 (2018)
 - Annual MSA Payments: \$ 8,200,000,000 (2018)
- \$ 22,626,000,000 a YEAR!**

*Surely we
can do
better!*



Conclusion

- “Youth addiction” is the concern. Efforts and assets should be combined to create **ONE** incentive/education campaign.
- Ensure risk models **differentiate** between legal use and illegal/abuse of products
- **NOW**: Communicate harm reduction options to cigarette smokers in a responsible manner.



Sources

Tobacco

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- <https://www.cdc.gov/mmwr/volumes/67/wr/mm6745a5.htm>
- **Youth users** https://www.cdc.gov/mmwr/volumes/67/wr/mm6722a3.htm#T1_down
- [HTTPS://WWW.REUTERS.COM/ARTICLE/US-HEALTH-ECIGS-US-ADULTS/ALMOST-ONE-IN-20-U-S-ADULTS-NOW-USE-E-CIGARETTES-IDUSKCN1LC2DN](https://www.reuters.com/article/us-health-ecigs-us-adults/almost-one-in-20-u-s-adults-now-use-e-cigarettes-idUSKCN1LC2DN)
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- <https://www.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/alcohol-facts-and-statistics>
- <https://www.niaaa.nih.gov/news-events/news-releases/nih-study-shows-steep-increase-rate-alcohol-related-er-visits>

Marijuana

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Stimulants

- **Adult Use** <https://www.washingtontimes.com/news/2018/apr/16/16-million-us-adults-prescription-stimulants-study/>
- **Death** <https://www.webmd.com/mental-health/addiction/news/20180403/experts-warn-of-emerging-stimulant-epidemic>
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Tobacco \$

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- **User Fees:** <https://www.hhs.gov/about/budget/fy2018/budget-in-brief/fda/index.html>



E-cigarettes: Cessation and Harm Reduction?

Aruni Bhatnagar, PhD, FAHA

Director, American Heart Association Tobacco Regulation Center

Department of Medicine

University of Louisville, Louisville, KY

Are E-cigarettes reduced harm products?

Acute exposure increases dynamic air resistance (18%) and decreased NO (16%) after puffing on e-cigarettes for 5 min

No significant decrease in expired lung volume

No change in white cell count or coronary reserve

Elevated levels of NO – attributed to pulmonary inflammation

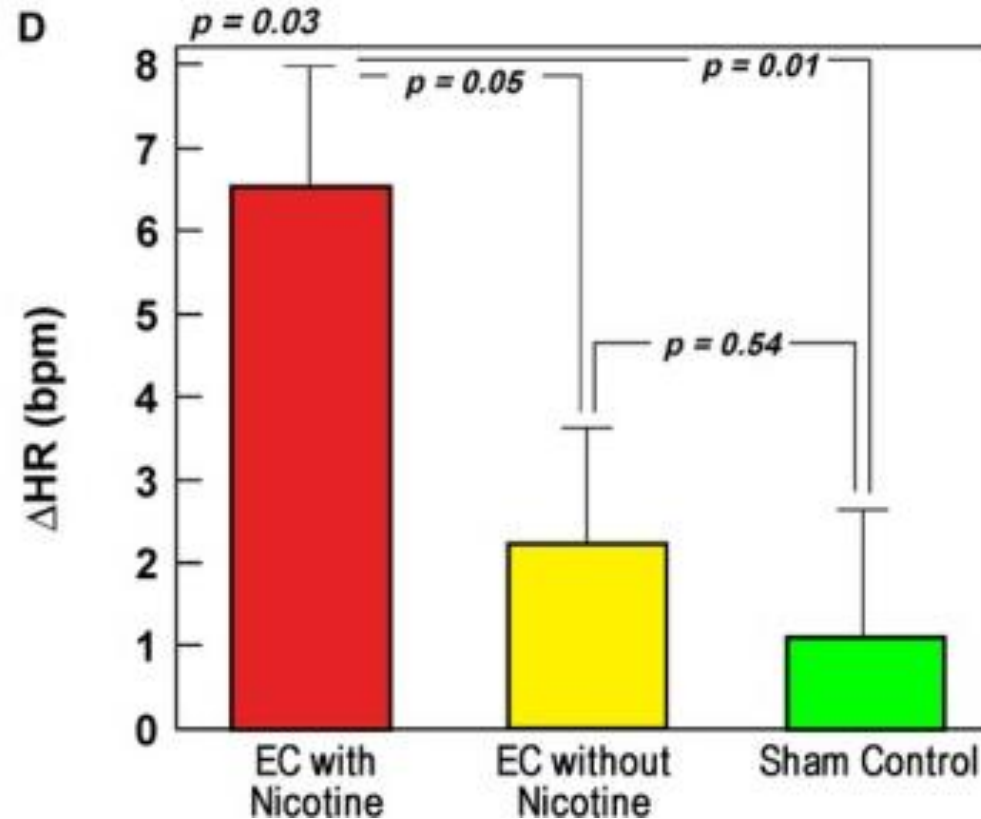
Increased arterial stiffness

Increased plasma myeloperoxidase

E-CIGARETTES AND BLOOD PRESSURE

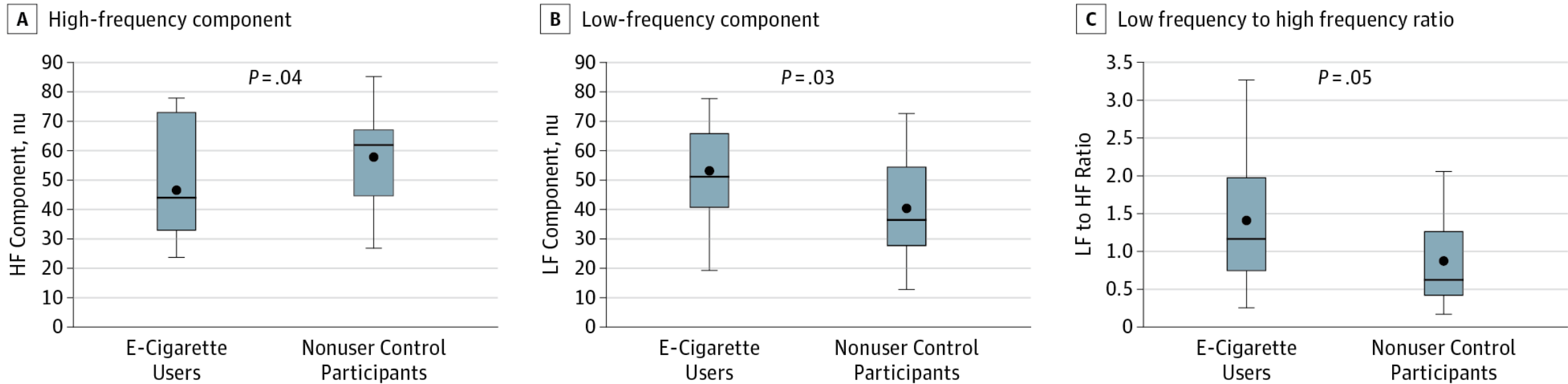
- In young healthy nonsmokers, acute inhalation of e-cigarette aerosol increases both systolic and diastolic blood pressure and heart rate
- In habitual smokers - increased arterial blood pressure after e-cigarette use, less than conventional cigarettes
- In young normotensive nonsmokers, e-cigarette inhalation increases both resting and exercise diastolic blood pressure after nicotine inhalation
- In 3.5 years observational study, there was no changes in blood pressure in young users compared with healthy never smokers and non e-cigarette users

Sympathomimetic Effects of E-Cigarettes



The acute sympathomimetic effect of e-cigarettes is attributable to the inhaled nicotine

E-Cigarettes and Heart Rate Variability



Habitual use associated with a shift in cardiac autonomic balance towards sympathetic predominance and increased oxidative stress

E-cigarettes and Flow Mediated Dilation

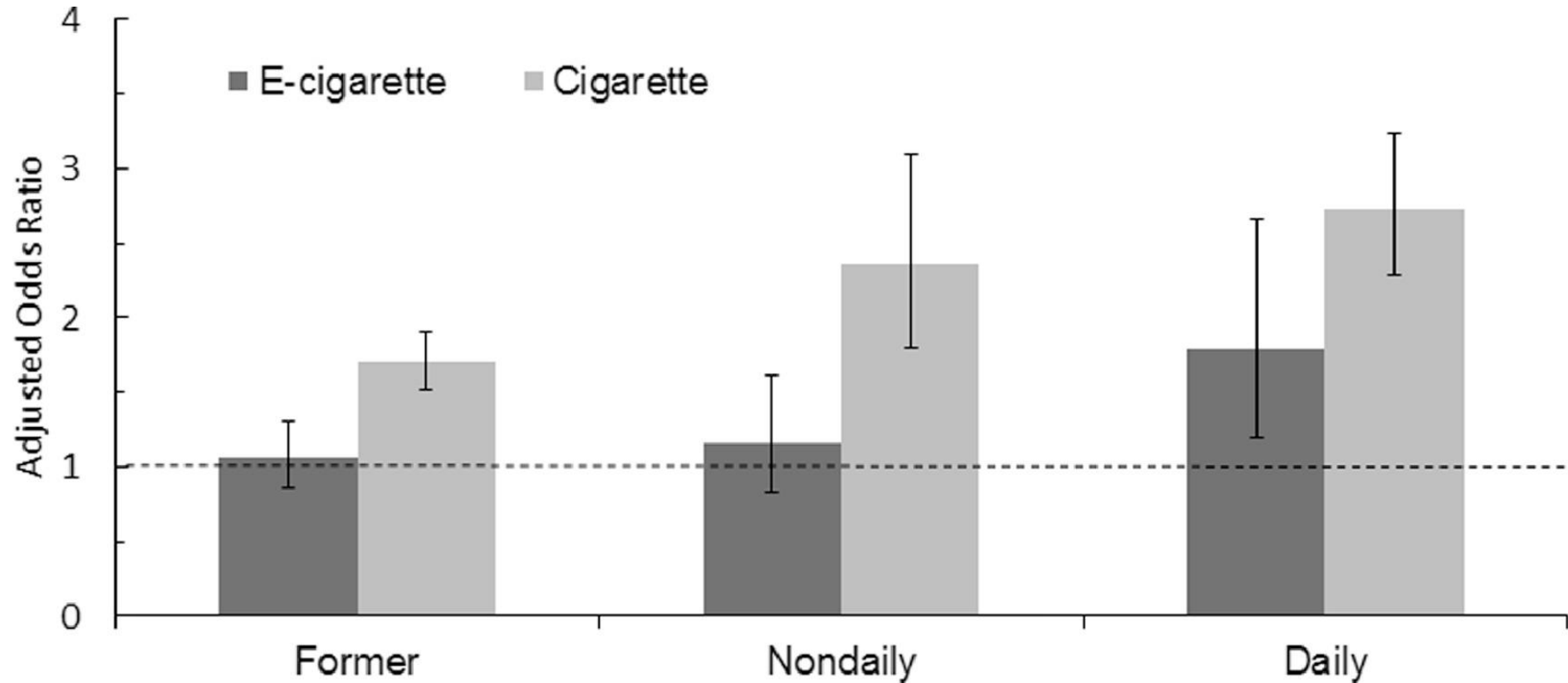
TABLE 2] Overall Results

Variable	Time	Descriptive Analysis			Exploratory Inferential Analysis ^a		
		Overall (N = 40)	Nonsmokers Only (n = 20)	Smokers Only (n = 20)	Overall (N = 40)	Nonsmokers Only (n = 20)	Smokers Only (n = 20)
sNOX2-dp, pg/mL	Before tobacco cigarette	23.6 ± 7.8	19.4 ± 7.6	27.8 ± 5.3	< .001	< .001	< .001
	After tobacco cigarette	38.2 ± 9.9	32.4 ± 7.4	44.1 ± 8.7			
	Before e-Cigarette	21.6 ± 6.8	17.6 ± 4.9	25.6 ± 6.1	< .001	< .001	< .001
	After e-Cigarette	30.2 ± 6.2	26.4 ± 3.18	34.1 ± 6.1			
FMD, %	Before tobacco cigarette	6.73 ± 4.34	7.83 ± 5.22	5.62 ± 2.96	< .001	< .001	.002
	After tobacco cigarette	3.39 ± 3.85	3.96 ± 4.09	2.82 ± 3.59			
	Before e-Cigarette	6.68 ± 3.62	7.48 ± 3.89	5.88 ± 3.23	.001	.026	.017
	After e-Cigarette	4.27 ± 2.22	4.56 ± 2.42	3.99 ± 2.02			

Both combustible and electronic cigarettes have unfavorable effects on markers of oxidative stress and FMD after single use, although e-cigarettes have lesser impact

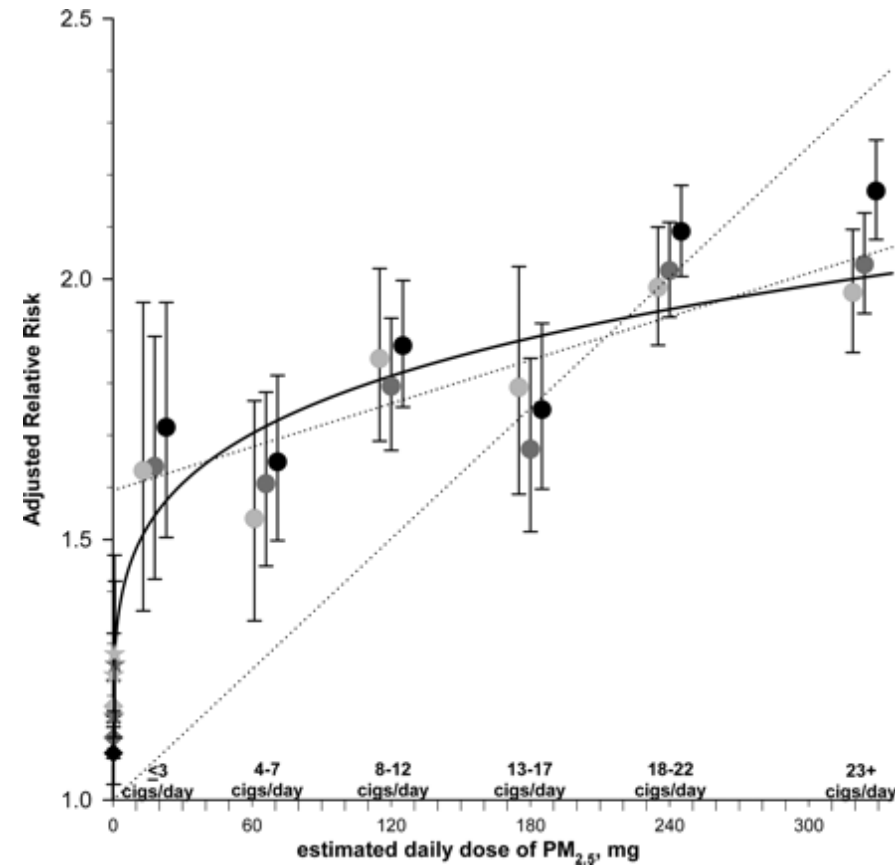
Carnevale et al., *Chest* (2016) 150:606

E-Cigarette Use and Myocardial Infarction



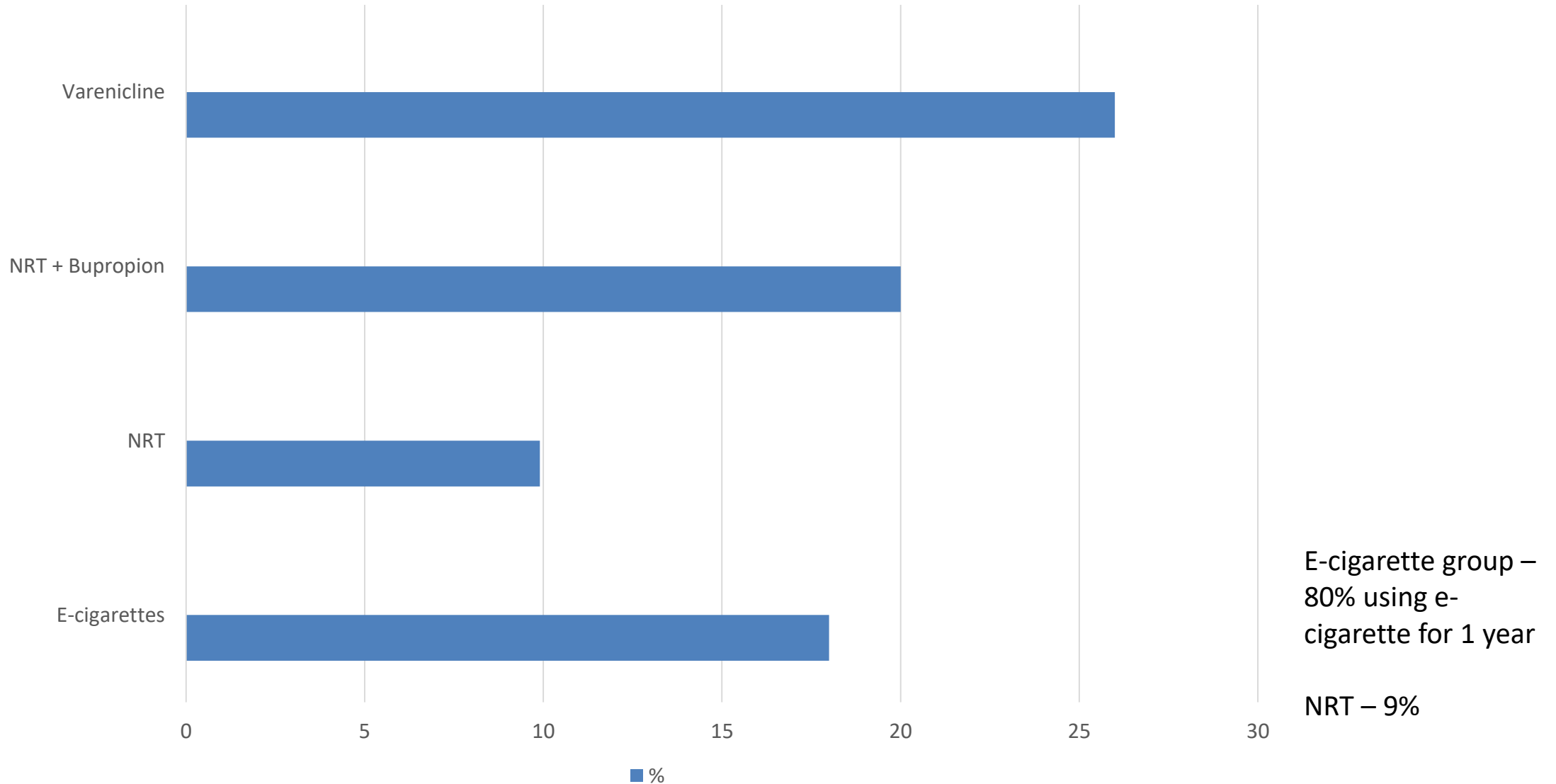
National Health Interview Survey

Reduction in exposure is not proportional to reduction in harm



Most of the risk of smoking is at low doses: 80 % of the harm at <3 cigarettes/day

E-Cigarettes and Smoking Cessation



A large, stylized torch logo in a lighter shade of red, positioned on the right side of the image. The torch has a circular bowl and a flame with several curved, flame-like shapes rising from it.

life is why™

es por la vida™

全為生命™



Present & Future Barriers to Adult Smoking Cessation Using EVPs

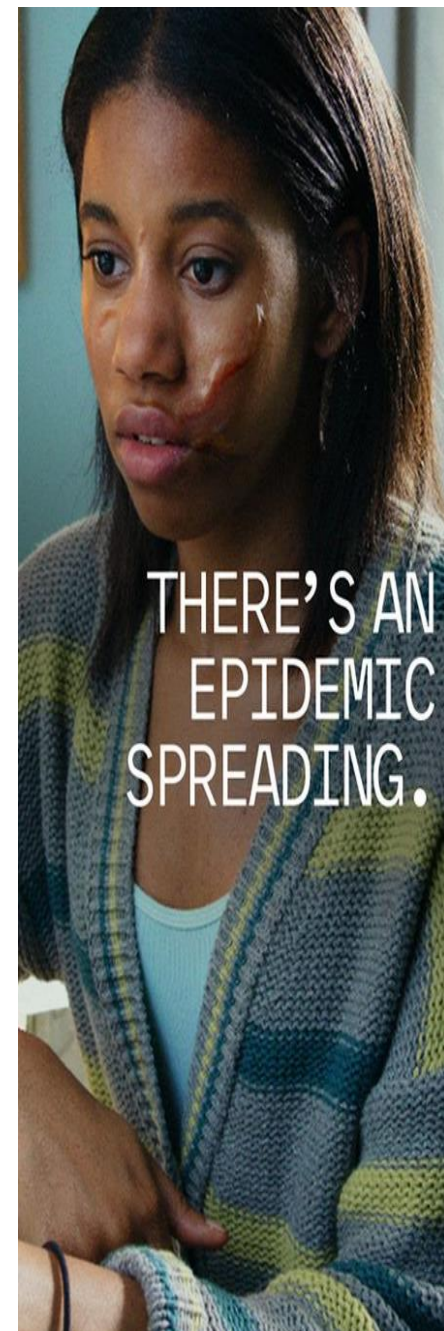
Gregory Conley

President, American Vaping Association



Misinformation Kills

- “... may pose just as much or even higher risk as smoking tobacco for worsening a stroke” – AHA
- “... there is no reason to believe that they will significantly reduce the risks for these diseases” – National Center for Health Research
- ‘... vapors contain a chemical that can cause popcorn lung.’ – ACSCAN IA



PMTAs Won't Stop Innovation

- August 8, 2021 – doomsday for much of vaping industry
- Open systems stand little chance
- Terminally slow PMTA process – U.S. is still waiting for IQOS
- But worldwide innovation won't stop.



Smoking Endgame vs. Nicotine Endgame

- FDA ANPRM sought comments on reducing nicotine in only cigarettes.
- What constitutes an ‘end’?
- What prevalence, if any, can we accept?
- The term ‘prohibition’ isn’t just rhetoric – it’s what some activists are striving for
 - Beverly Hills, CA – total tobacco and nicotine sales ban (minus cigar lounges and NRT)
 - Open hostility to harm reduction arguments



“Are you steering?”

FDA's Nicotine Education Campaign

- Mitch Zeller has said:
 - “The continuum is real...”
 - “It's not the nicotine that kills half of all long-term smokers, its the delivery mechanism.”
 - “It's everyone's responsibility to educate public about misconceptions...”

FDA's Nicotine Education Campaign STILL WAITING



Barriers Will Only Get Worse

- The millions of middle-aged smokers whose lives can be saved should be our focus
- Taxes and flavor bans at the state local level will negatively affect switching
 - Total flavor ban proposed in California and other states
 - States with some of the worst smoking rates are proposing high taxes on vaping products with support of health activists
 - Arkansas (67% of wholesale), Indiana (24% of retail), Michigan (81% of wholesale)
- FDA restrictions on where flavored vaping products can be sold do nothing to help adult smokers switch
- Existing tech-savvy vapers will continue to access “new” products, but what about those who are still smoking?