

***e-Cigarettes:
Can we use them to make
combusting of tobacco obsolete -
end the “cigarette century” and its
preventable deaths?***

David B. Abrams

*The Schroeder Institute For Tobacco Research And Policy
Studies at Legacy.*

*The Johns Hopkins Bloomberg School of Public Health
Georgetown University Medical Center / Lombardi
Comprehensive Cancer Center*

AAHB Laureate award
Charleston SC March, 2014.

THE GAS-CHAMBER OF THE 21ST CENTURY



In the United States, Smoking Tobacco is the only legal method of being killed.

The Health Consequences of Smoking—50 Years of Progress

A Report of the Surgeon General



Executive Summary



Citation

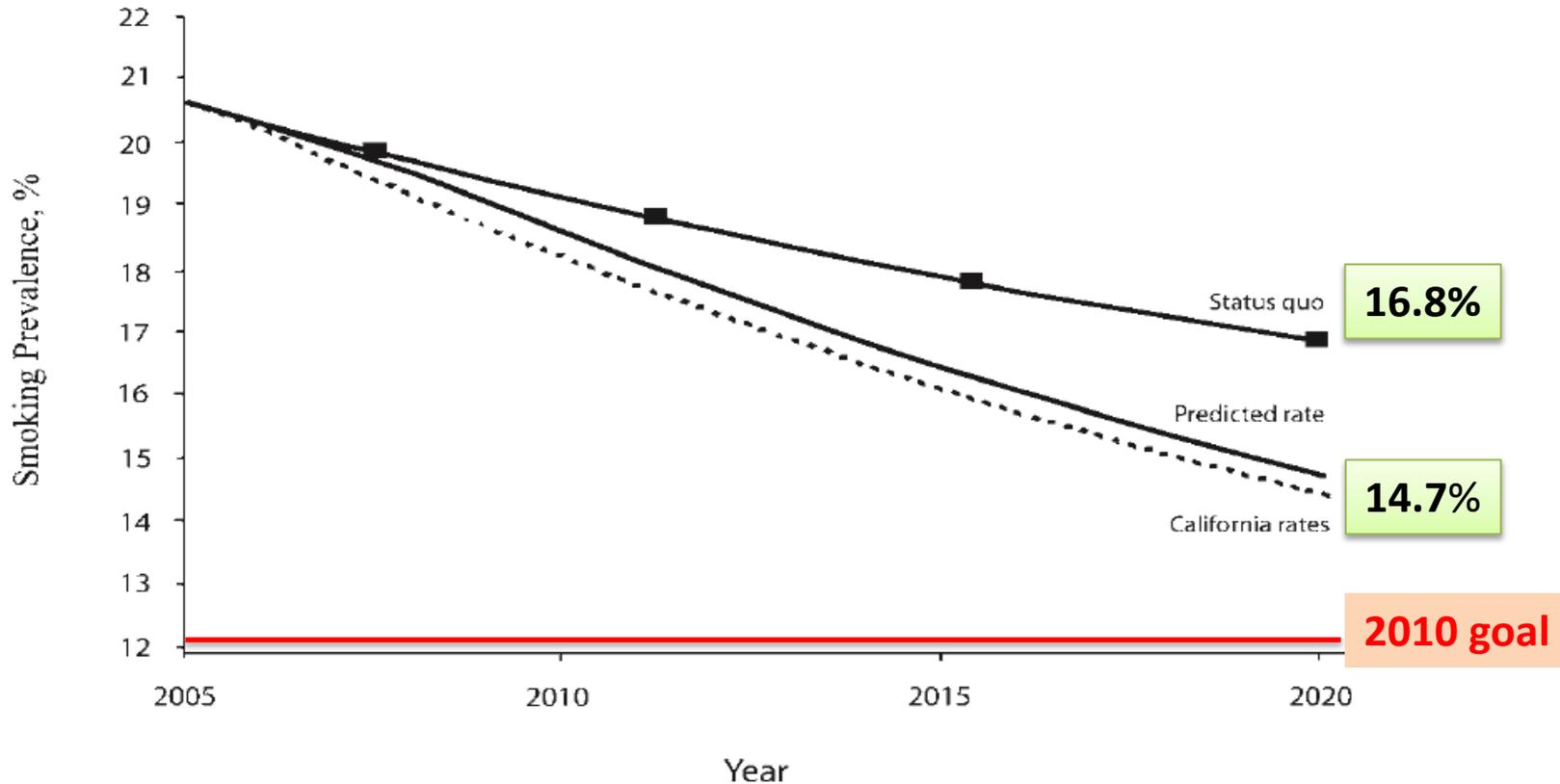
U.S. Department of Health and Human Services. *The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General*. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014.

50 Years of Progress: A Report of the Surgeon General 2014.

- Worse – 480,000+ deaths - 20 million overall
- More diseases: colon, arthritis, blindness...
- Greater cost: \$289 billion
- 5.6 *million* children alive will die prematurely
- CTP Youth & CDC TIPS campaigns, movies
- 2014 budget - 94c tax hike
- Affordable Care Act: access coverage
- Vulnerable groups
- **Progress slow/stalled.. Need a breakthrough?**

Setting a Challenging Yet Realistic Smoking Prevalence Target for Healthy People 2020: Learning From the California Experience.

Mendez, D, Warner, KE. *Am J Public Health.* 2008;98:556–559.



Note. The bottom 2 lines depict corresponding scenarios assuming that the United States as a whole achieves California's 2005 rates (20% initiation rate and 3.33% cessation rate). The dotted line reflects the assumption that such rates are attained instantaneously (in 2006), whereas the solid line reflects the more plausible scenario that such rates will be achieved gradually (by 2010). The status quo initiation rate is 25% and the cessation rate is 2.59%.

FIGURE 2—Projections of US adult smoking prevalence rates under status quo scenario and California rate scenarios: 2005–2020.

Harm Reduction: Policy and Practice Proportional to HARM

- Evidence incontrovertible: inhaling combustion compounds in smoke is deadly. Cigarette is defective product – *unreasonably* dangerous, and addictive by design.

Zeller at FDA – Reduce **appeal, addiction, harm** of combusteds

- Product standards: for ingredients, Menthol, additives, carcinogenicity
- Reduce the nicotine content to make cigarettes less addictive/appealing;
- Greater restrictions at state, local level - time, place and manner

AND

Adopt harm reduction: Support cleaner, appealing nicotine products to compete / win over cigarettes

- The **enemy is not nicotine** per se: its burning tobacco = lethal tars toxins CO₂ & nicotine in **most addictive form.**

Emerging Tobacco & Nicotine Products:
DISRUPTIVE: Evolution / Revolution?
Ending the cigarette century before 100th SGR



Industry Comments

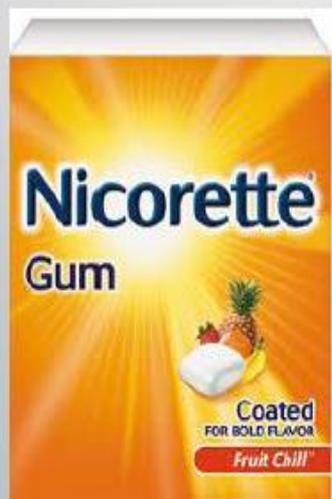
March 25, 2013 Interview:

“At NJOY, we are proud to be a leader in this process and **believe our products have the potential to render traditional cigarettes obsolete**,” said Craig Weiss, CEO of NJOY.

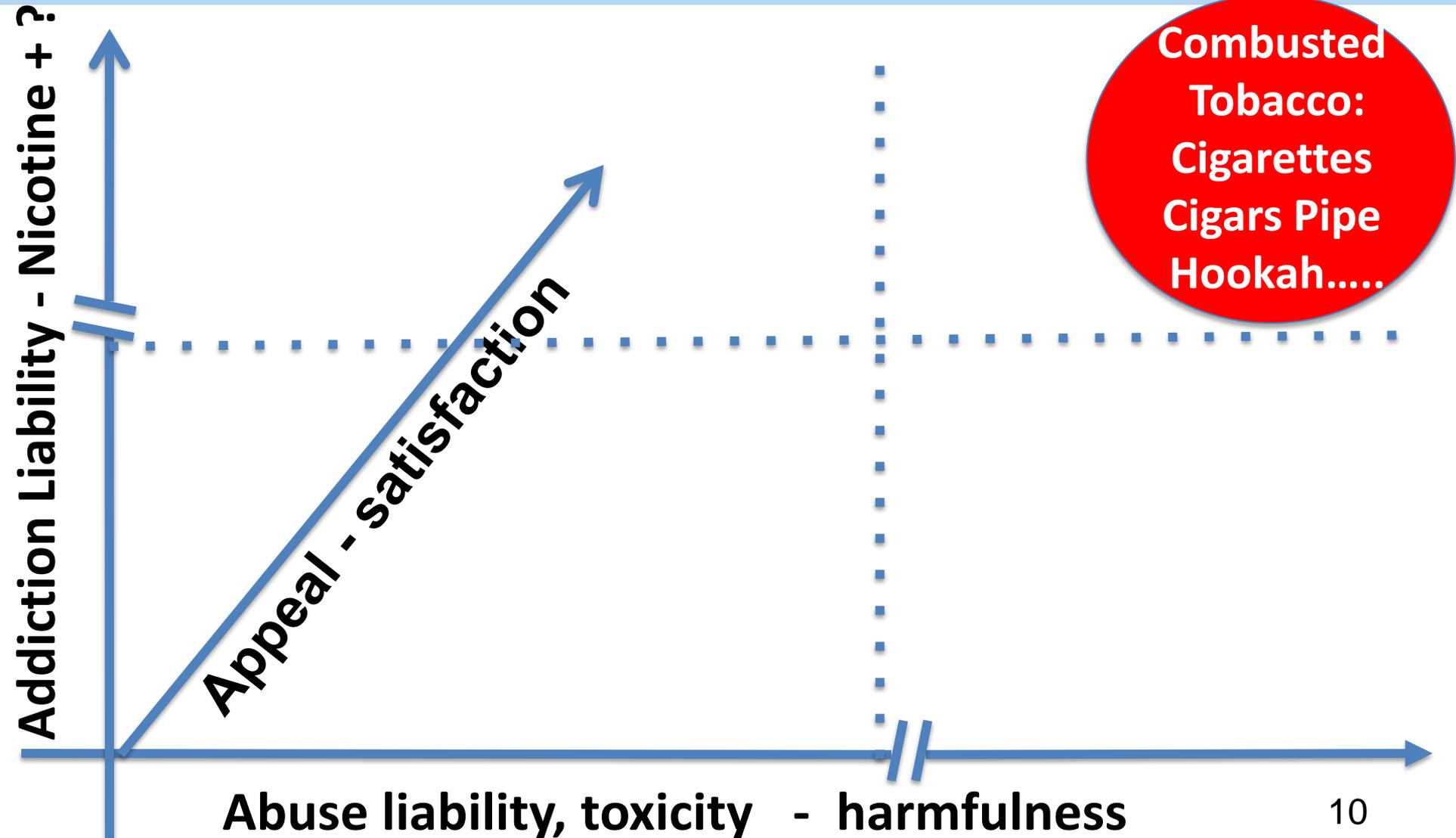
June 21, 2012

“...we believe the **elimination of combustion** via tobacco heating and other innovative systems for aerosol generation is the **most promising path to secure risk reduction.**” Andre Calantaopoulos, COO of PMI

Appeal, satisfaction, addiction. harm- “abuse liability” deconstructed

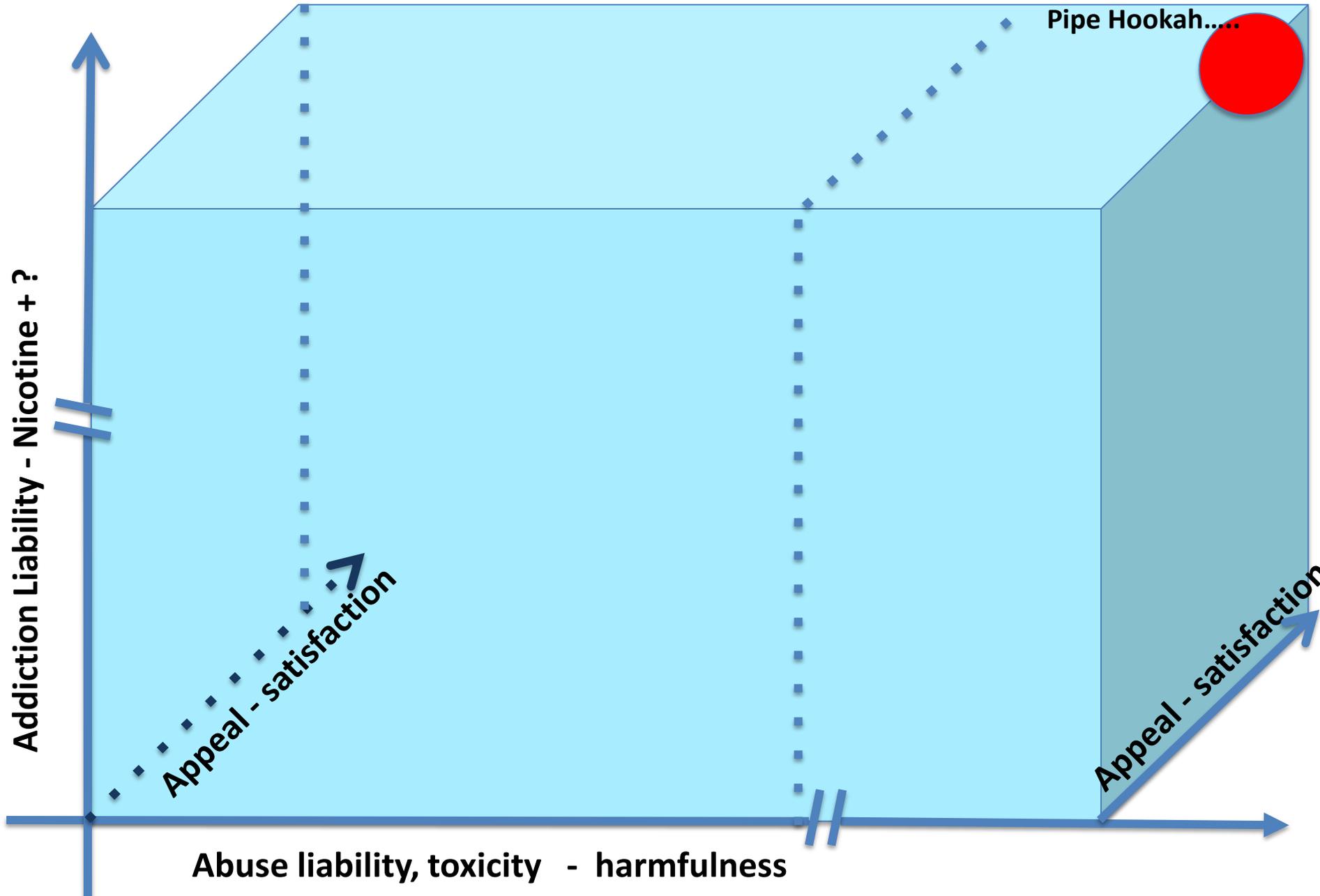


Appeal, Addiction, Harm: A Framework



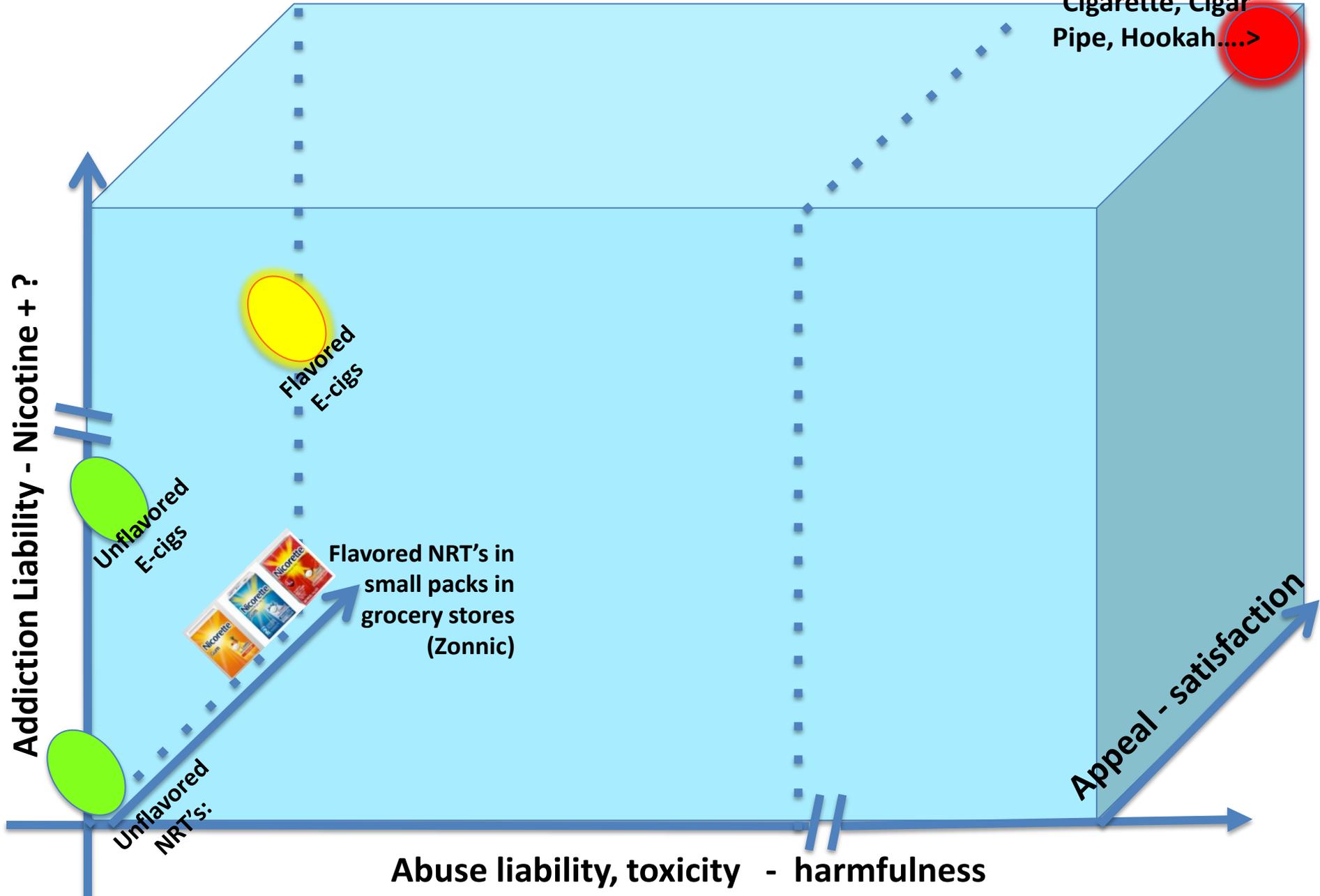
Appeal, Addiction, Harm: A 3-d Framework

Combusted Tobacco:
Cigarette, Cigar
Pipe Hookah.....

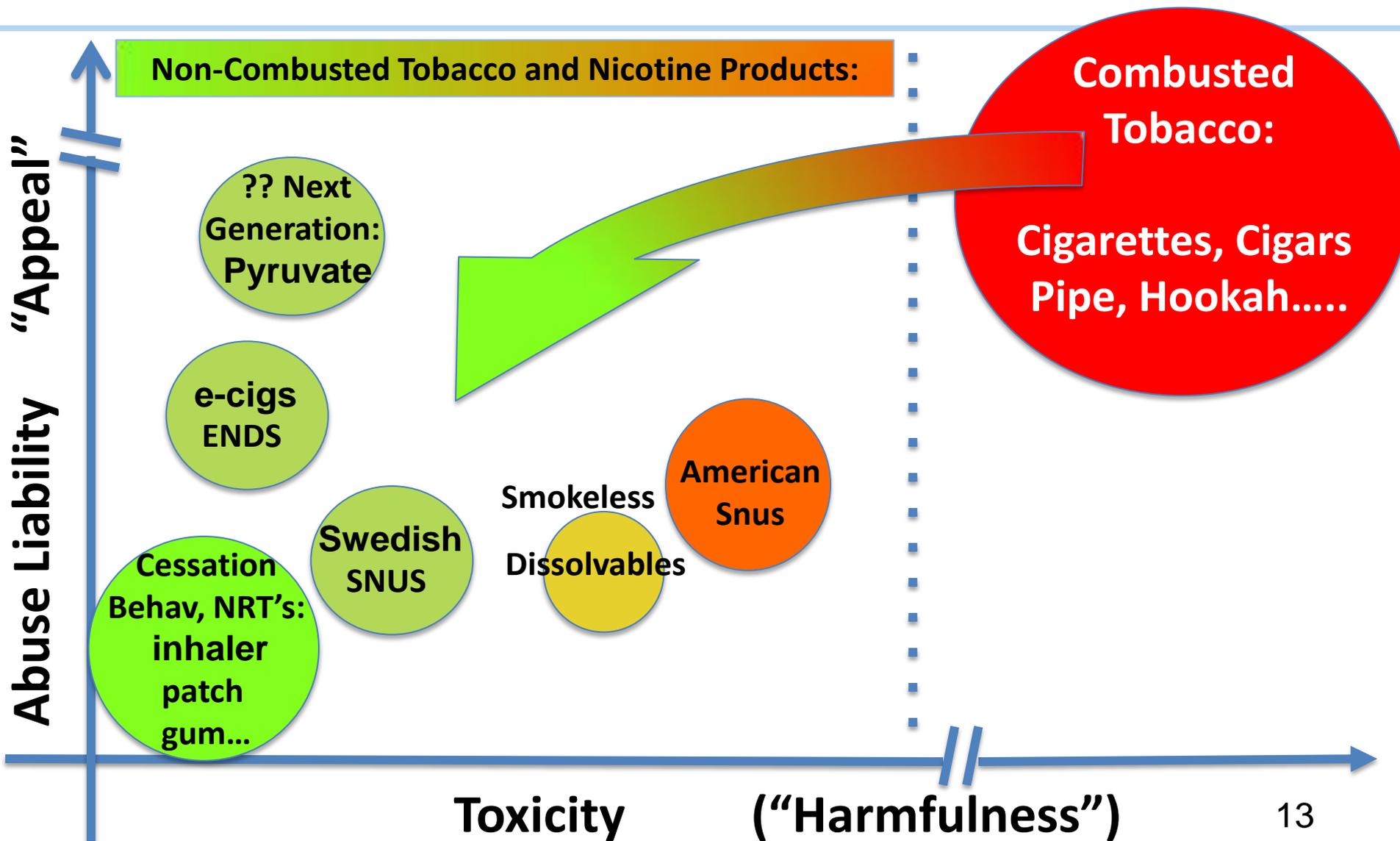


Appeal, Addiction, Harm: A 3-d Framework

Combusted Tobacco:
Cigarette, Cigar
Pipe, Hookah....>



Public Health Impact: Zero Tolerance and Harm Reduction Ideology: Data vs Dogma



EMERGING PRODUCTS. POLY-USE

NON-Combusted Products versus Combusted Products

E-cigs:
Electronic
Nicotine
Delivery
Systems
(ENDS) –
flavored.



Dissolvable
Tobacco
Products –
flavored.



SNUS,
smokeless
Products -
Flavored.



Cigarettes (with or without menthol),
Little cigars (flavored), Hookah ...



Dual / Poly-use: A new norm? Blurring differences between lethal combusted, less harmful non-combusted, and safest medicinal forms of nicotine delivery.

A game changer for tobacco control?

Provocations ... adapted from Clive Bates . UK

1. It's the deaths, stupid, not the nicotine addiction
2. Nicotine is a good drug ?
3. Do we care if many current smokers use cleaner nicotine even if it's an addictive form of nicotine? What about youth update ???
4. ... and even if more youth take up e-cigs -- than are now using cigarettes, little cigars, hookah , marijuana and alcohol ?
5. Is nicotine in cleaner forms just like caffeine or close enough?
6. Can we support harm reduction ? After all, it includes zero tolerance/total abstinence as its first premise = Its not " us versus them" not a battle over extremist ideologies...and is there a differences among independents vs big tobacco companies

Family Smoking Prevention And Tobacco Control Act (2009)

Public Health Standard

Calls for the review of the scientific evidence regarding:

1. Risks and benefits **to the population as a whole**, including both users and non-users of tobacco products;
2. Whether there is an increased or decreased likelihood that existing users of tobacco products will **stop** using such products; and
3. Whether there is an increased or decreased likelihood that those who do not currently use tobacco products, most notably youth, will **start** to use tobacco products
4. Individual safety and efficacy and public health IMPACT

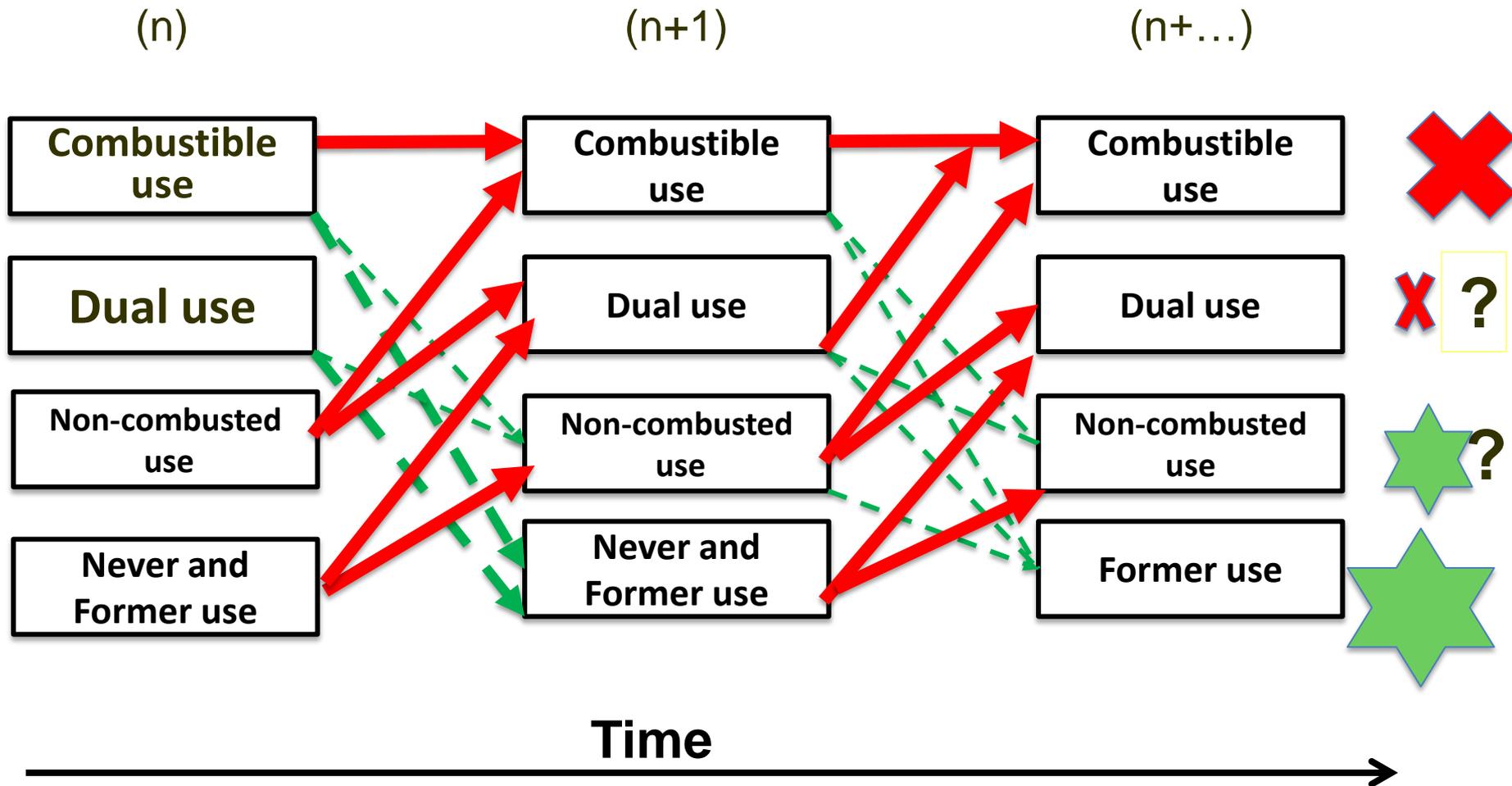
Benefits vs. Downside to individuals and to public health

Can cleaner, appealing tobacco products be supported, while minimizing their downsides:

- Youth starter and progression to combusted products
- Undermining de-normalization - indoor air policy
- Dual / poly use when one can't smoke without  harm
- Delaying / Promoting cessation of cigarettes.
- Undermining clear messages about SOME tobacco dangers – blurring risk perception of harms, addiction,
- Impact of Internet and social media marketing and KABB
- BUT the genie is out of the bottle, can we capitalize? ₁₇

Patterns of Use and Harm Reduction:

Behavioral transitions from combustibles to dual use of combustible and non-combustibles; exclusive use of non-combustibles and desistence of all or of combustibles.

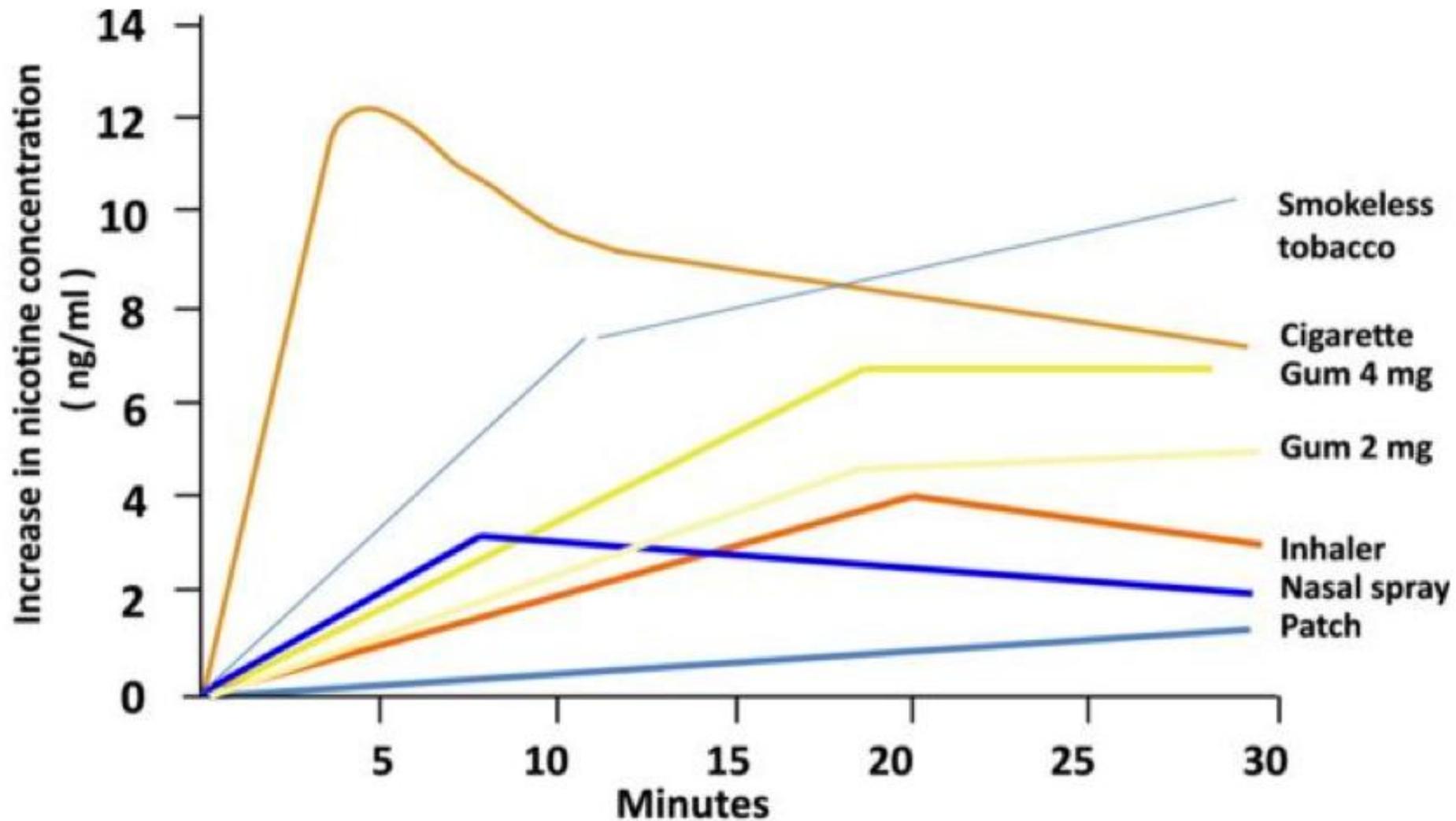


State of the science:

- **Product design:** Variety. less harmful than cigarettes. Quality ?
- **Nicotine:** doses vary, mislabel. Can deliver nicotine effectively, reduces craving. Appeal and Abuse liability less than cigarettes. Future ?
- **Liquid/propylene glycol:** liquids and vapor, not studied for long-term inhalational safety in humans, local irritant
- **Secondhand Vapor:** Health effects not well-studied. Mainstream and secondhand vapor produces ultrafine and fine particulate matter.
- **Other toxicants** (VOCs, TSNAs, heavy metals, flavoring, additives): Fewer constituents **at much lower levels than in cigarette smoke** but higher in poor quality products.

Tobacco Specific Nitosamines in e-cigs are basically similar to “unregulated”

Product	NNN	NNK	NAT	NAB	Total
Nicorette gum	2.00	ND	ND	ND	2.00
Nicoderm CQ patch	ND	8.00	ND	ND	8.00
E-cigarettes	3.87	1.46	2.16	0.69	8.18
Swedish Snus	980	180	790	60	2010
Marlboro (Ultra-light)	2900	750	1100	58	4808
Marlboro (Red)	2900	960	2300	100	6260



Source: Balfour DJ & Fagerström KO. *Pharmacol Ther* 1996 72:51-81.

Plasma nicotine concentrations for some nicotine and tobacco products.

State of the science: SECOND HAND VAPOR: HEALTH AND SAFETY

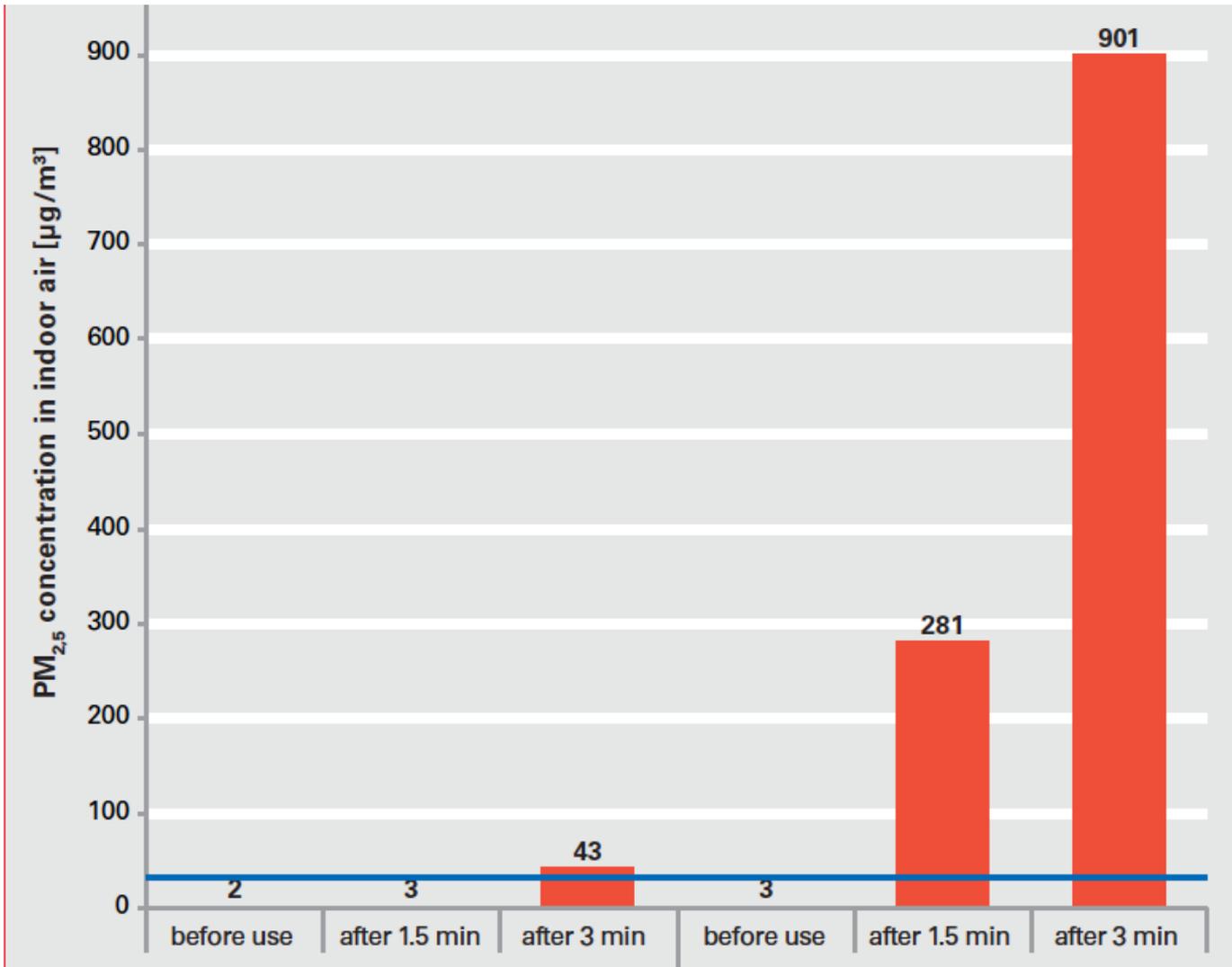
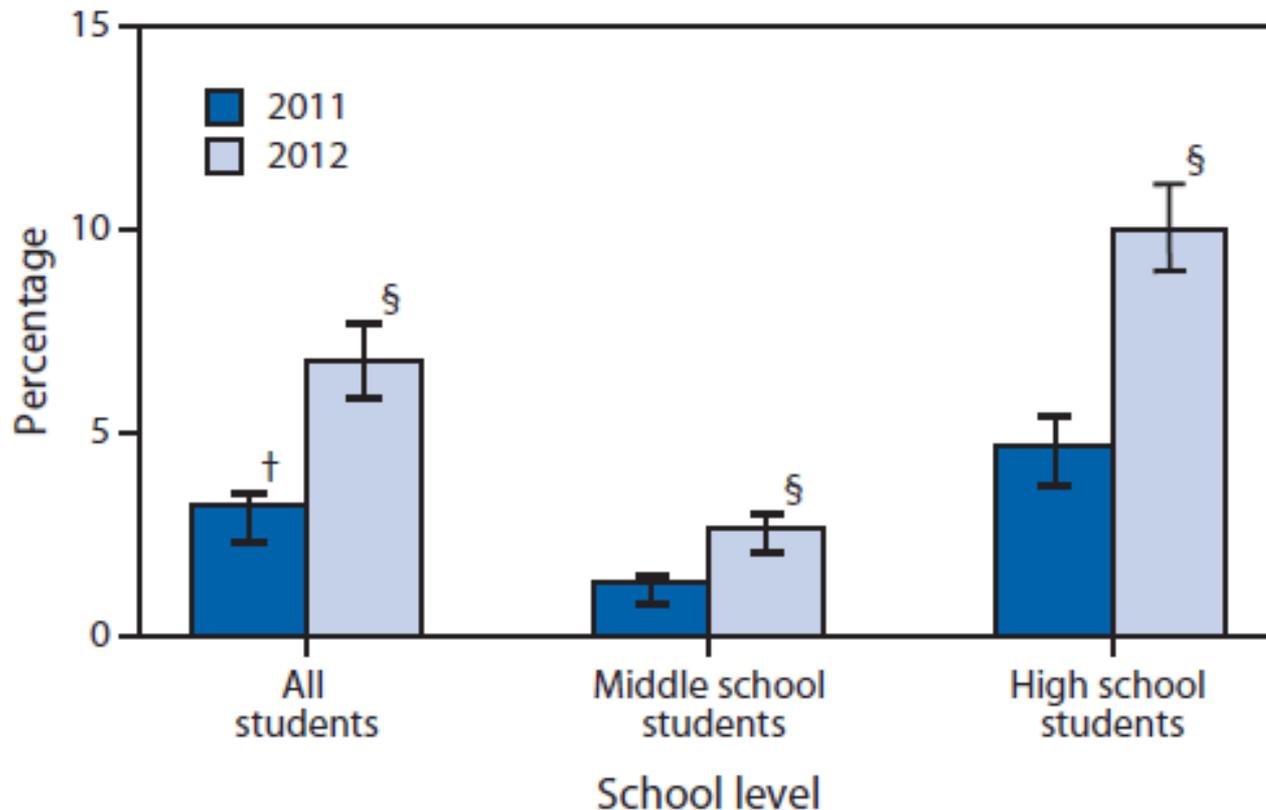


Figure 3.3
Concentration of PM_{2.5} (µg/m³) in indoor air before and after of using an e-cigarette and a conventional cigarette. Blue line: WHO air quality guideline value for PM_{2.5} for short term exposure (24 hour mean).
Source: Pellegrino et al.

YOUTH Patterns of USE. (Experimenting only and over 90% already use conventional cigs).

- **Adults:** Awareness (76%) and use (21%) is growing fast among current smokers and young adults. Perceived as less harmful.
- **Youth** (CDC MMWR 2013)

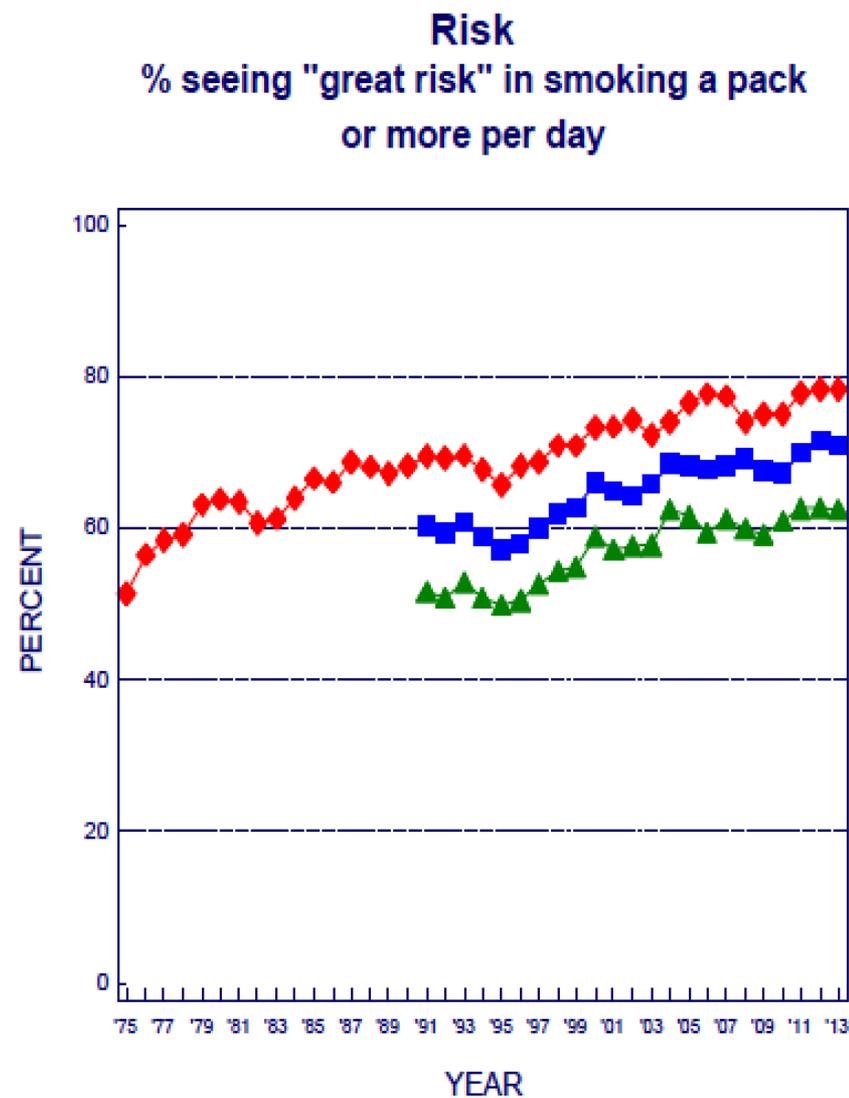
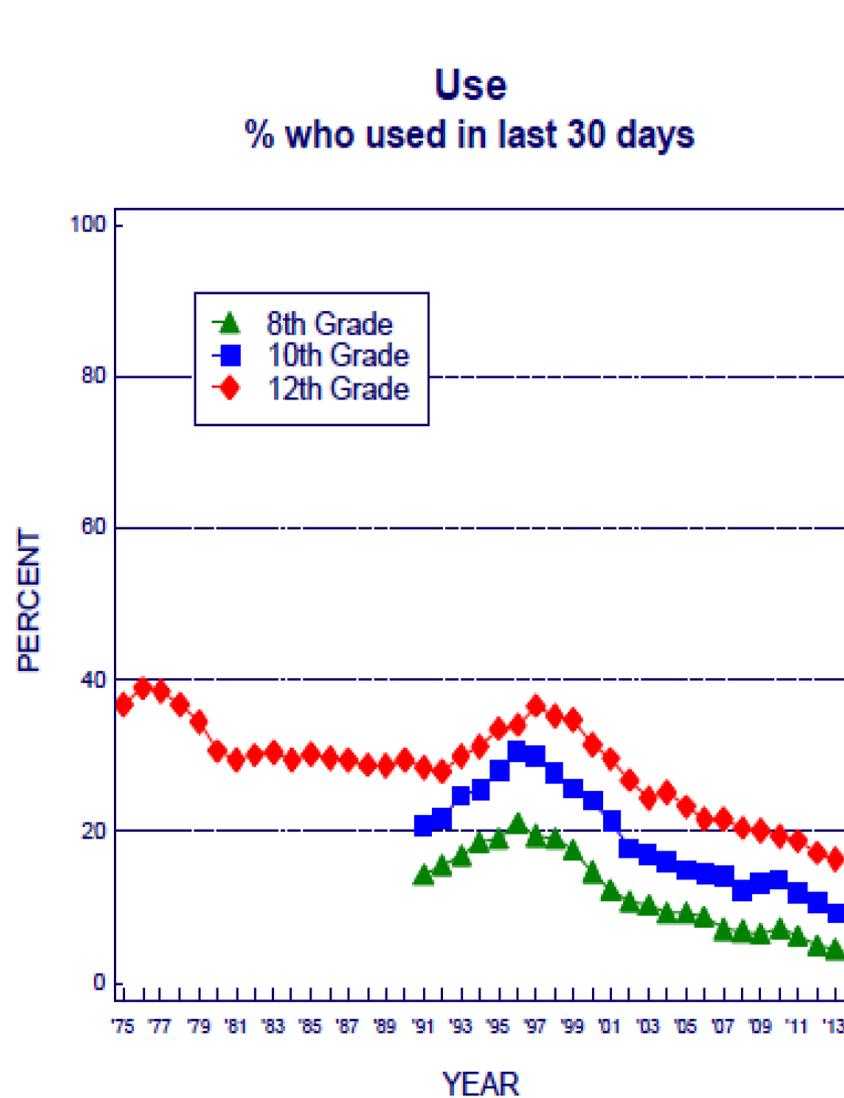


- Use doubled middle and high school students 2011–2012, estimated 1.78 million students ever used.

FIGURE 1

Cigarettes: Trends in 30-Day Use, Risk, Disapproval, and Availability

Grades 8, 10, and 12



E-cigarette advertising: consumer patterns of use, beliefs, perceptions

WHY QUIT? SWITCH TO BLU

blu is the smart choice for smokers wanting a change. Take back your freedom to smoke when and where you want without ash or smell. blu is everything you enjoy about smoking and nothing else. Nobody likes a quitter, so make the switch today. Visit blucigs.com




PREMIUM ELECTRONIC CIGARETTE

18+ only. CALIFORNIA PROPOSITION 65 Warning: This product contains nicotine, a chemical known to the state of California to cause birth defects or other reproductive harm.

DEAR SMOKING BAN,



blu ELECTRONIC CIGARETTE

Take back your freedom to smoke anywhere with blu electronic cigarettes. blu produces no smoke and no ash, only vapor, making it the smarter alternative to regular cigarettes. It's the most satisfying way to tell the smoking bans to kiss off. Okay, maybe the second-most satisfying way.



New blu Smart Pack

blucigs.com

18+ only. CALIFORNIA PROPOSITION 65 Warning: This product contains nicotine, a chemical known to the state of California to cause birth defects or other reproductive harm.

IN STYLE

Cigarettes

Control when and where you smoke with blu e-cigarettes. blu produces no smoke and no ash, only vapor, making it the ultimate choice to tell the smoking bans to kiss off. Okay, maybe the second-most satisfying way.



blucigs.com

18+ only. CALIFORNIA PROPOSITION 65 Warning: This product contains nicotine, a chemical known to the state of California to cause birth defects or other reproductive harm.

State of the science: cessation

- **New Zealand-based study 2011-2013 (Bullen et al., 2013)**
 - N=657 current smokers motivated to quit. **No difference in abstinence between treatment arms at 6 months between NRT and e-Cigs**
 - **Nicotine e-cig=7.3%, Placebo e-cig=4.1%, NRT patch=5.8%**
 - Rates of smoking reduction ($\geq 50\%$) were higher for nic e-cig (57%) relative to the NRT.
- **Italy-based study 2010-2011 (Caponnetto et al., 2013)**
 - N=300, current smokers curious about trying e-cigs (not motivated to quit)
 - **No difference (nicotine or placebo e-cigs) at 52 weeks. 8.7% quit and 10.3% reduced their smoking by $\geq 50\%$ Those who at first dual used were likely to relapse.**
- **Among quitline callers from 6 states in 2011-2012 (Vickerman et al., 2013)**
 - E-cig groups (used for 1 mo or more than 1 mo) **were less likely to be abstinent** at 7-months compared with participants who had never tried e-cigs. 21.7%, 16.6% vs. 31.3%
- **In 2011 a nationally rep. study of U.S. adults (Popova & Ling, 2013):**
 - **E-cig ever users were 78% more likely to be an unsuccessful quitter** compared with non-users of e-cigs (OR: 1.78, $p < .05$). **INCONCLUSIVE ...**

Population impact ? : these studies have MAJOR methods limitations. E.g. observational, indication bias: Could be the users are more addicted smokers / have harder time to start with (like limits of Alpert, Connolly, Biener NRT study)

Bullen C, Howe C, Laugesen M, McRobbie H, Parag V, Williman J, Walker N. Electronic cigarettes for smoking cessation: a randomised controlled trial. *Lancet*. September 9 2013.

Caponnetto P, Campagna D, Cibella F, et al. Efficiency and Safety of an eElectronic cigAreTte (ECLAT) as tobacco cigarettes substitute: a prospective 12-month randomized control design study. *PloS one*. 2013;8(6):e66317.

Caponnetto et al.. Unmotivated smokers quit at 12 % continuous abst, ITT at 12 months

Groups	Reduction rates (%)			Quit rates (%)			p value*
	A	B	C	A	B	C	
Week-2	29.0	38.0	36.0	20.0	12.0	5.0	0.02
Week-4	29.0	33.0	29.0	14.0	14.0	6.0	0.25
Week-6	24.0	26.0	25.0	11.0	15.0	2.0	0.03
Week-8	23.0	21.0	20.0	9.0	12.0	4.0	0.31
Week-10	26.0	15.0	19.0	7.0	15.0	3.0	0.01
Week-12	26.0	20.0	21.0	11.0	17.0	4.0	0.04
Week-24	17.0	19.0	15.0	12.0	10.0	5.0	0.39
Week-52	10.0	9.0	12.0	13.0	9.0	4.0	0.24

New Zealand-based RCT Cessation study 2011-2013 (Bullen et al., 2013). At 6 months 7 day pp for e-cigs is very good and > compared to Patch: 21.1% vs 15.5%

	16 mg e-cig (N=289)	Patches (N=295)	P-value	Rel Risk (95% CI)	Risk Diff (95% CI)
Continuous abstinence					
One month	67(23.2%)	47 (15.9%)	0.03	1.46 (1.04-2.04)	7.25 (0.84-13.66)
Three months	38 (13.1%)	27 (9.2%)	0.12	1.44 (0.90-2.33)	4.00 (-1.10-9.10)
Six months (primary outcome)	21 (7.3%)	17 (5.8%)	0.46	1.26 (0.68-2.34)	1.51 (-2.49-5.51)
7-day point prevalence					
One month	69 (23.9%)	51 (17.3%)	0.05	1.38 (1.00-1.91)	6.59 (0.05-13.13)
Three months	62 (21.5%)	50 (17.0%)	0.17	1.27 (0.91-1.77)	4.50 (-1.88-10.88)
Six months	61 (21.1%)	46 (15.6%)	0.09	1.35 (0.96-1.91)	5.52 (-0.75-11.79)

Latest trends on smoking in England: from the Smoking Toolkit Study



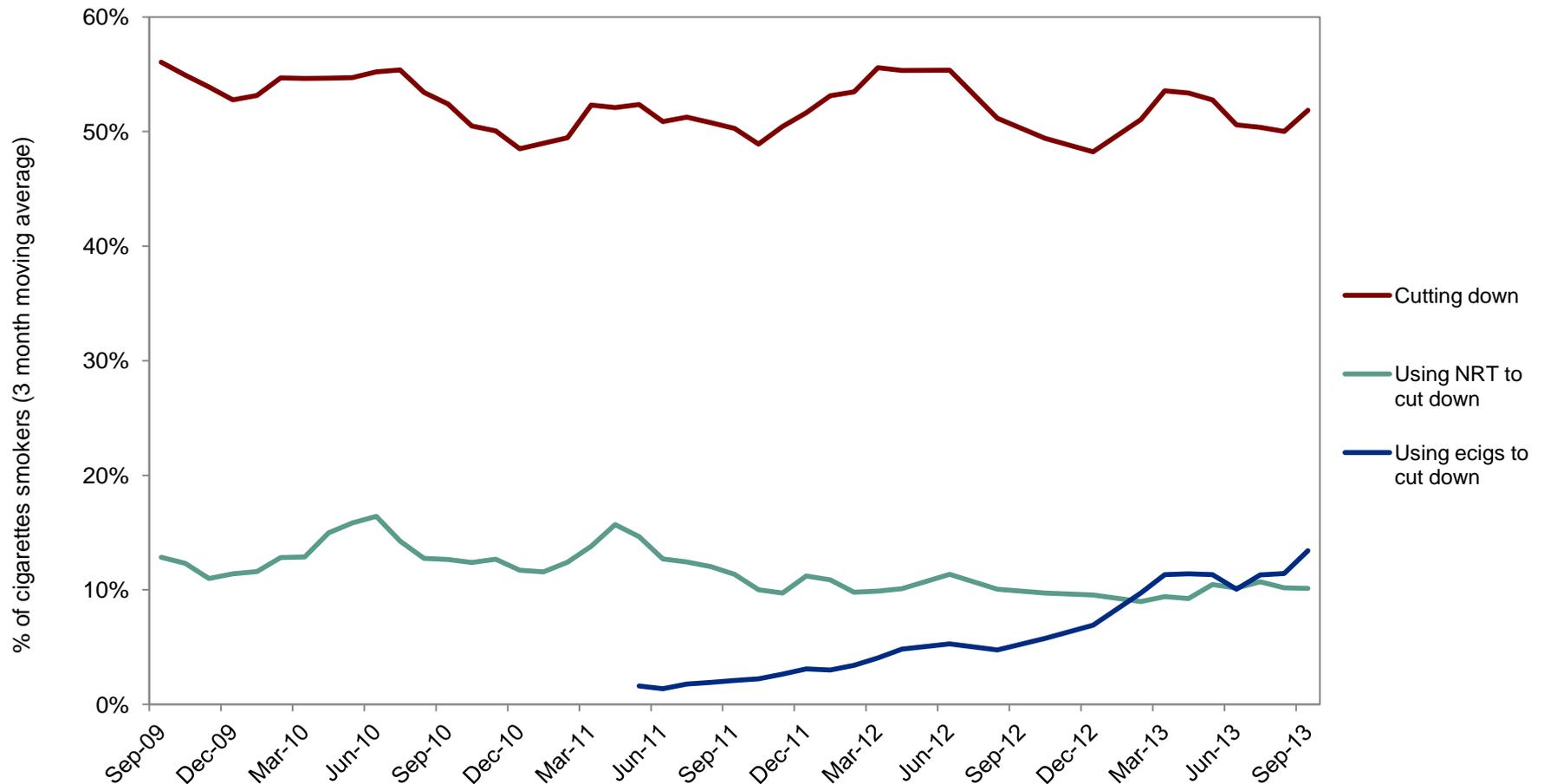
***Robert West
Jamie Brown***

Last updated: 2nd Sept 2013

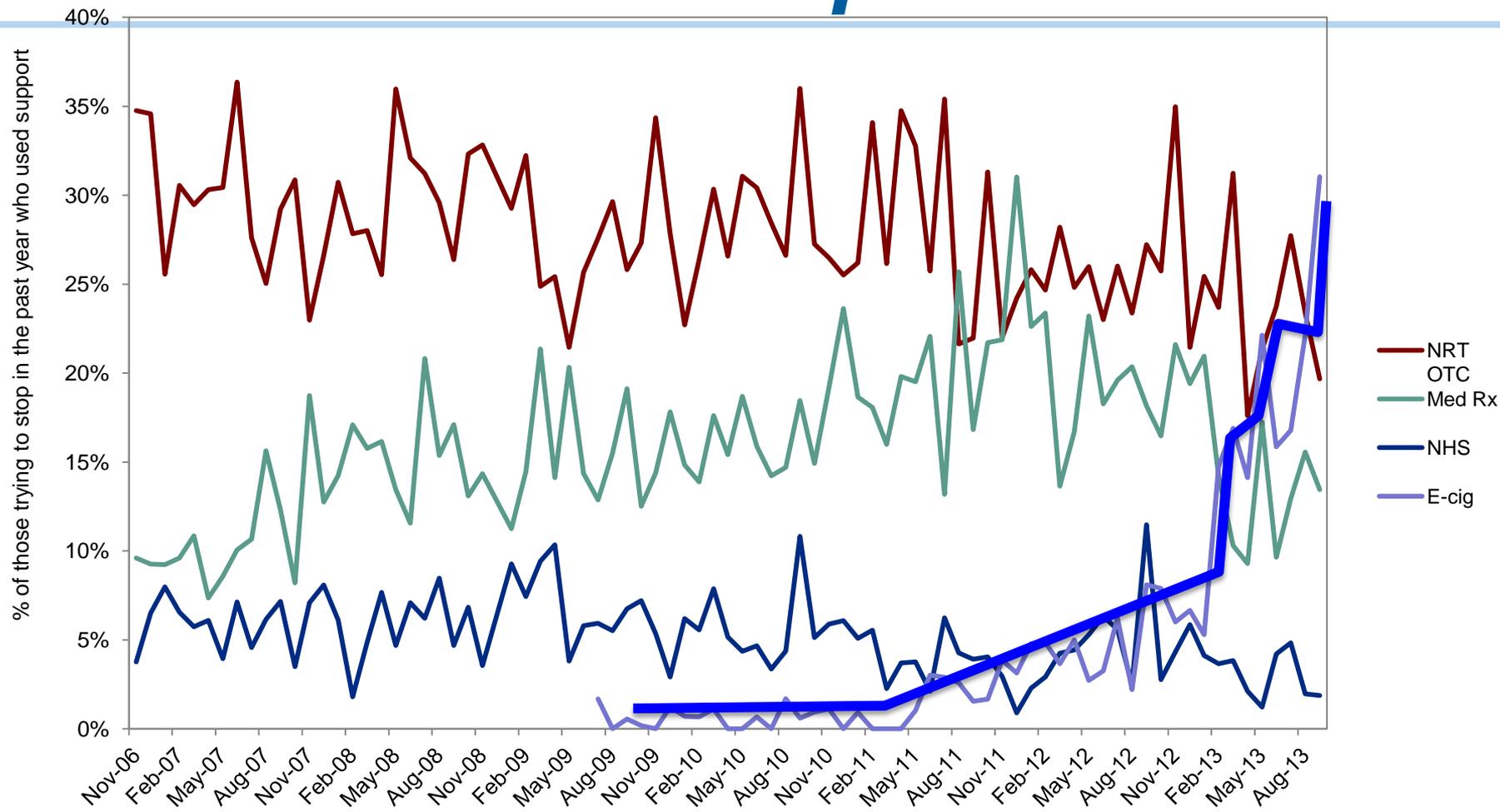
***www.smokinginengland.info
jamie.brown@ucl.ac.uk***



Harm reduction? Using e-cigs to cut down



Support used in quit attempts



NRT OTC: Nicotine replacement therapy bought over the counter; Med Rx: Prescription medication; NHS: NHS Stop Smoking Service; E-cig: Electronic cigarette

Excerpts from: **Ending tobacco smoking in Britain; Radical strategies for prevention and harm reduction in nicotine addiction**

Royal College of Physicians of London, 2008.

- ▶ People smoke because they are addicted to nicotine, but nicotine itself is not especially hazardous; it is the other constituents of **tobacco smoke that cause most of the harm.**
- ▶ Use of smoke-free nicotine would benefit smokers directly by reducing the personal harm caused by nicotine addiction.
- *“In Sweden, the availability and use by men of an oral tobacco product called snus, one of the less hazardous smokeless tobacco products, is widely recognised to have contributed to the low prevalence of smoking in Swedish men and consequent low rates of lung cancer.”*

SWEDISH EXPERIENCE OVER 50 YEARS

Can switching from burned to unburned tobacco result in any substantial risk reduction?

Probably: YES,

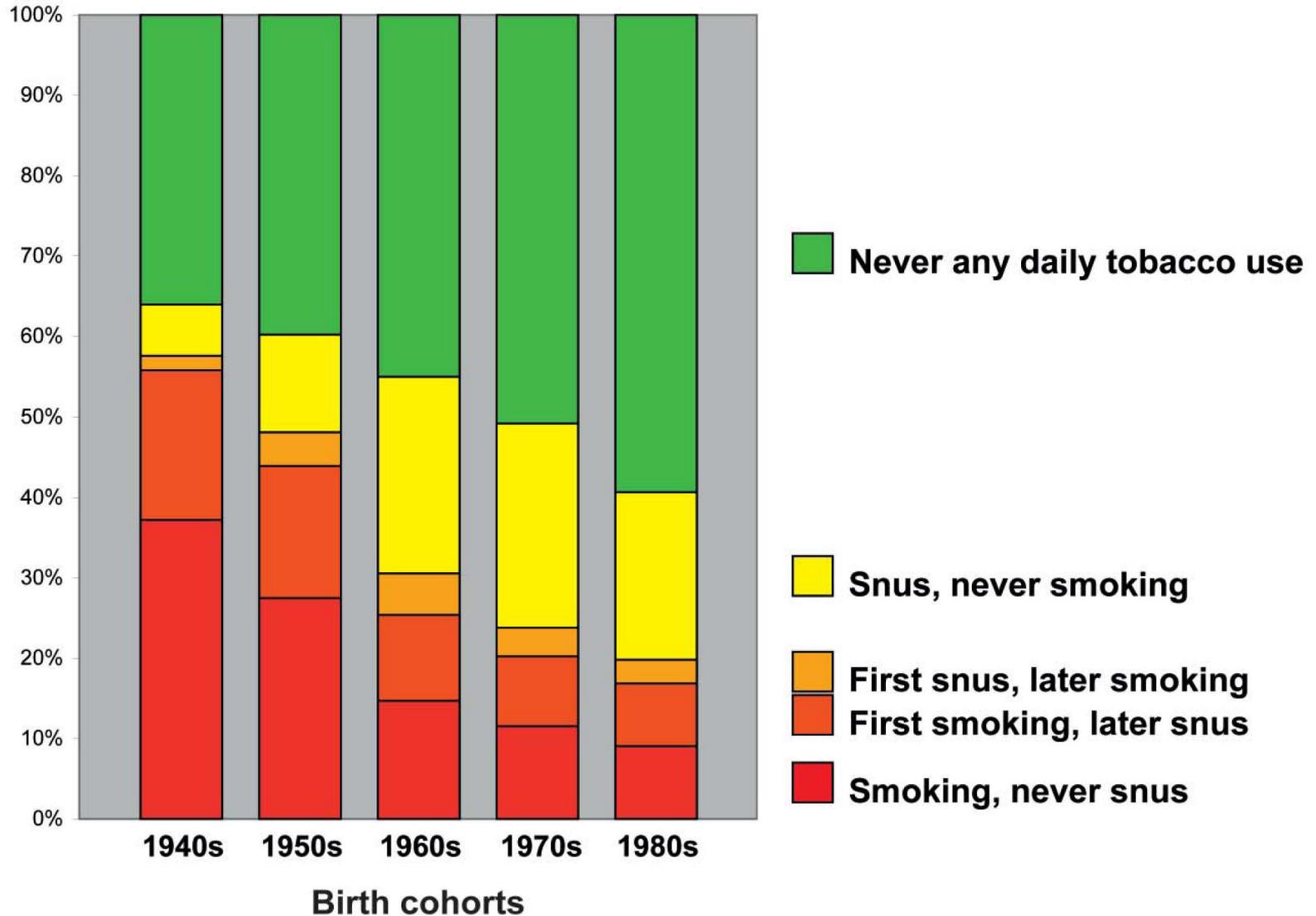
because the major harmful toxins in cigarette smoke are formed during the combustion and consequently absent in smokeless tobacco products.

Still, some smokeless tobacco products are very harmful, but there is a very wide variation between products at the lower and the upper end of the scale.

For example, there were concerns that...

- **snus may lead to dual use rather than replace cigarettes.**
- **nicotine addiction may be strengthened by snus use.**
- **snus use may lead to fewer attempts to quit smoking.**
- **snus may serve as a gateway to smoking and thereby increase smoking**

Initiation of daily tobacco use. Swedish men in different birth cohorts.



**Does primary snus use make
young people
more or less likely to start
smoking???**

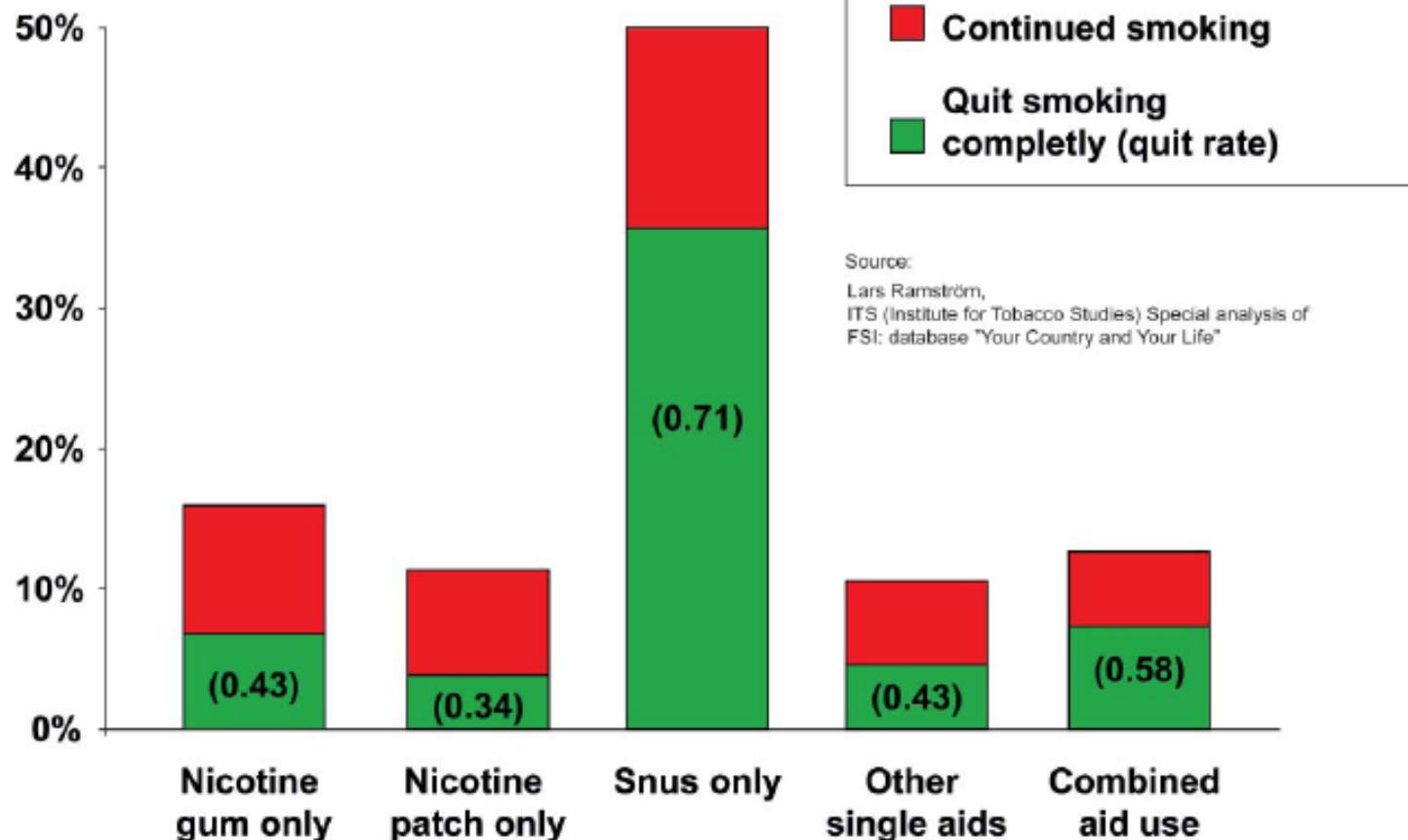
NO all fears were NOT confirmed

**Smokers who have started subsequent snus
use appear**

**to make MORE efforts to quit smoking than
those who
have not.**

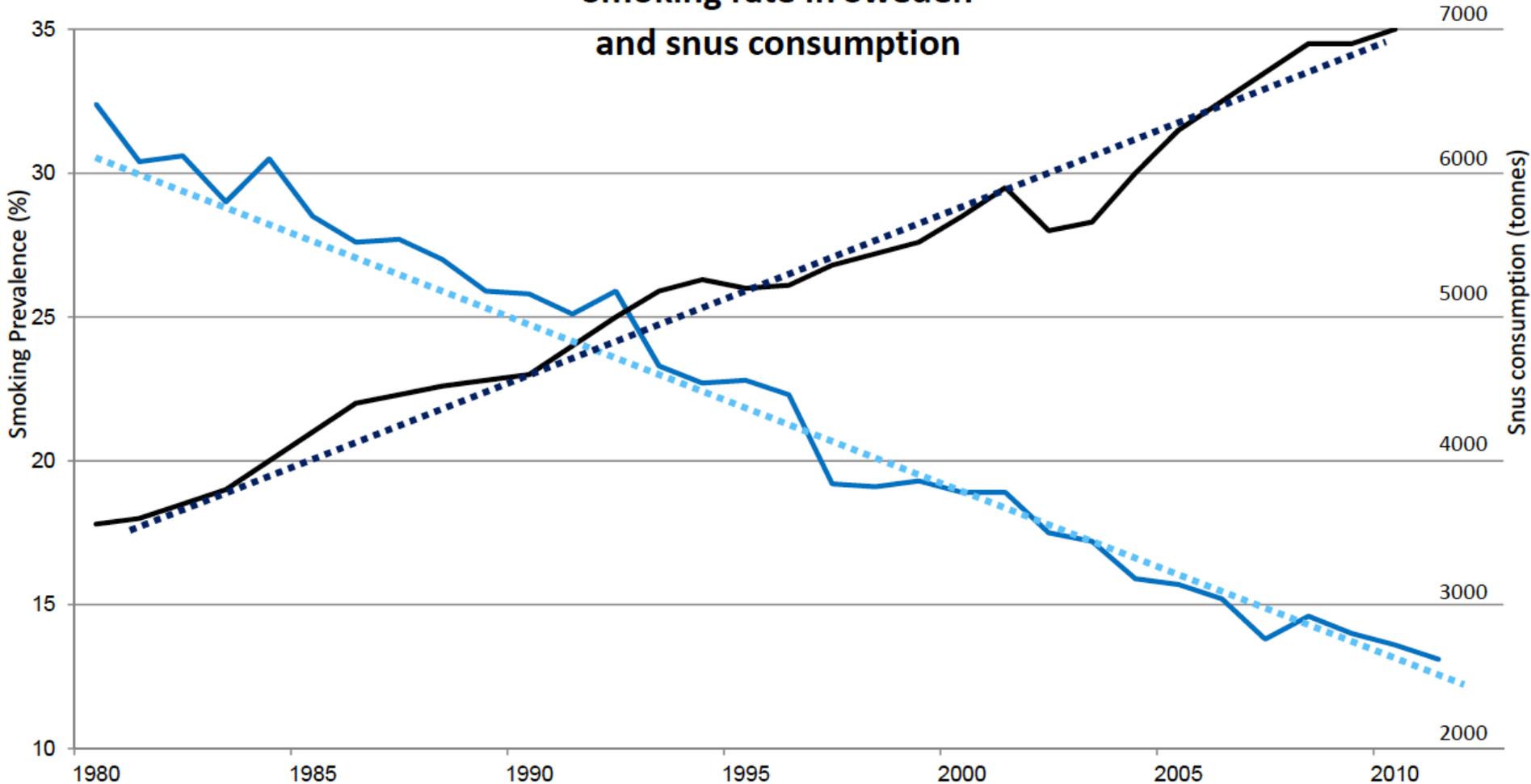
Choice of aid at "Self-help" quit-attempts among Swedish men, and outcome of the quit-attempt

Proportion of different types of aid use



CASE STUDY SWEDEN

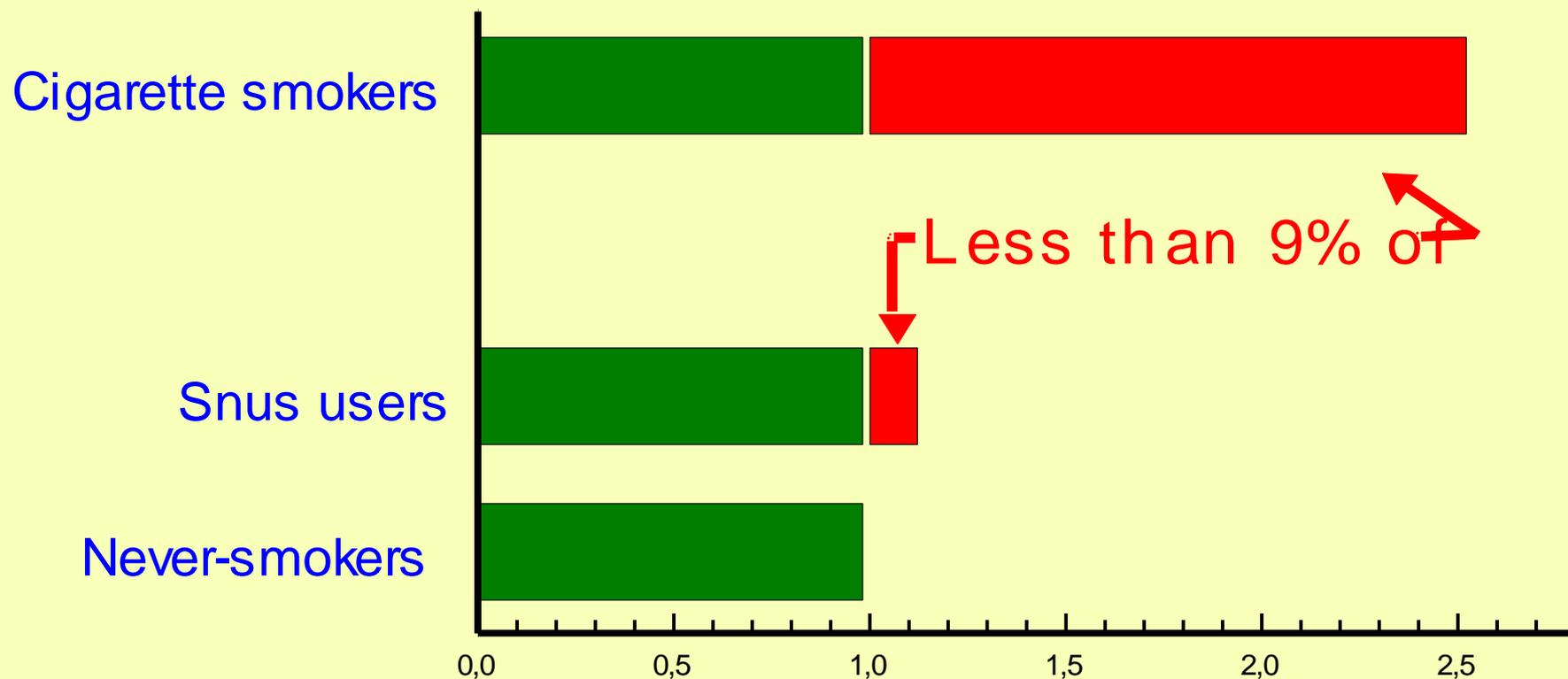
Smoking rate in Sweden
and snus consumption



Whole bar: Relative risk of death for male tobacco users

Green sector: Never-smokers' death risk (reference)

Red sector: Excess risk (above Never-smokers)



Data derived from:

Bjartveit K, Tverdal A. Health consequences of smoking 1-4 cigarettes per day.

Tobacco Control 2005; 14:315-320.

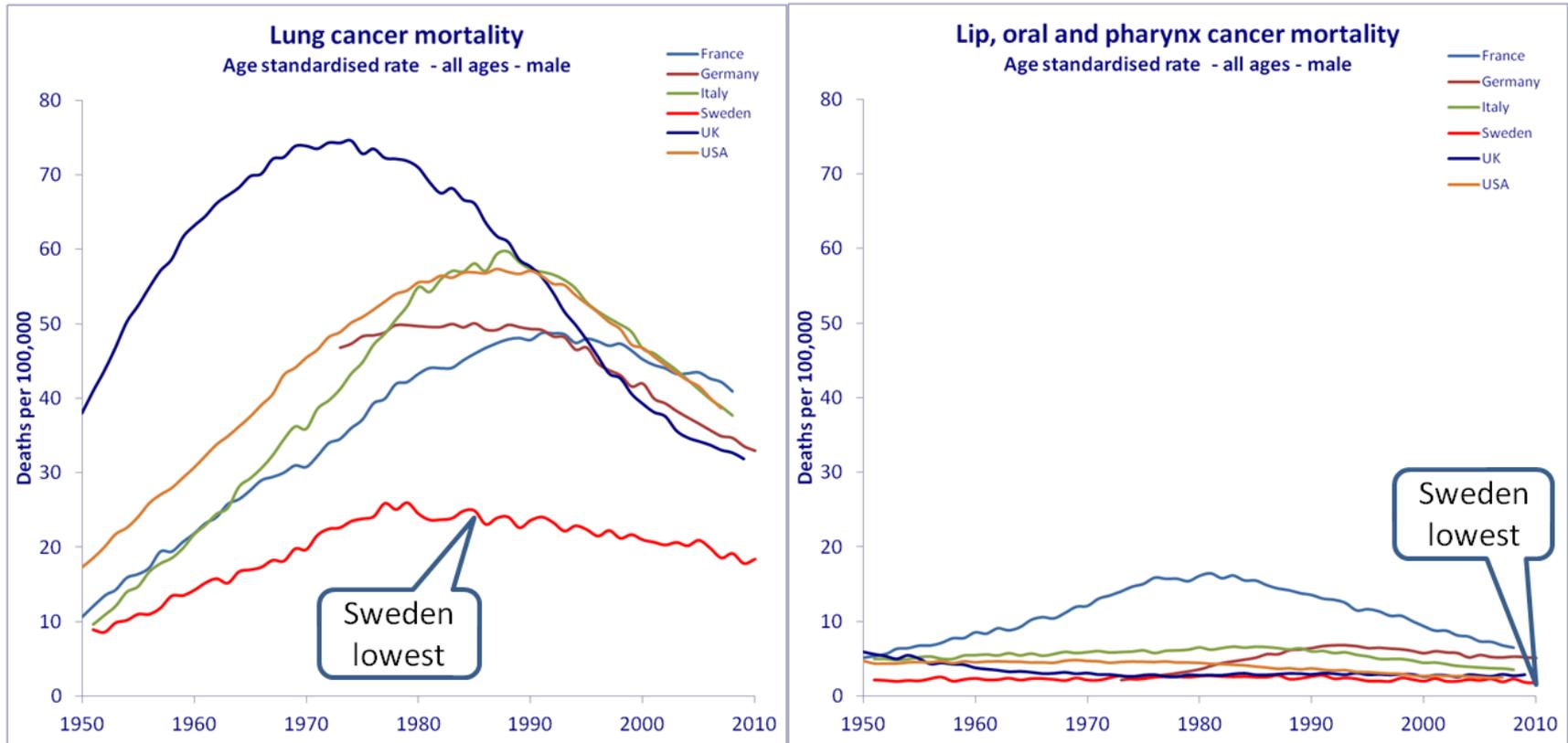
Levy D T et.al. The Relative Risks of a Low-Nitrosamine Smokeless Tobacco Product Compared with Smoking

Cigarettes: Estimates of a Panel of Experts.

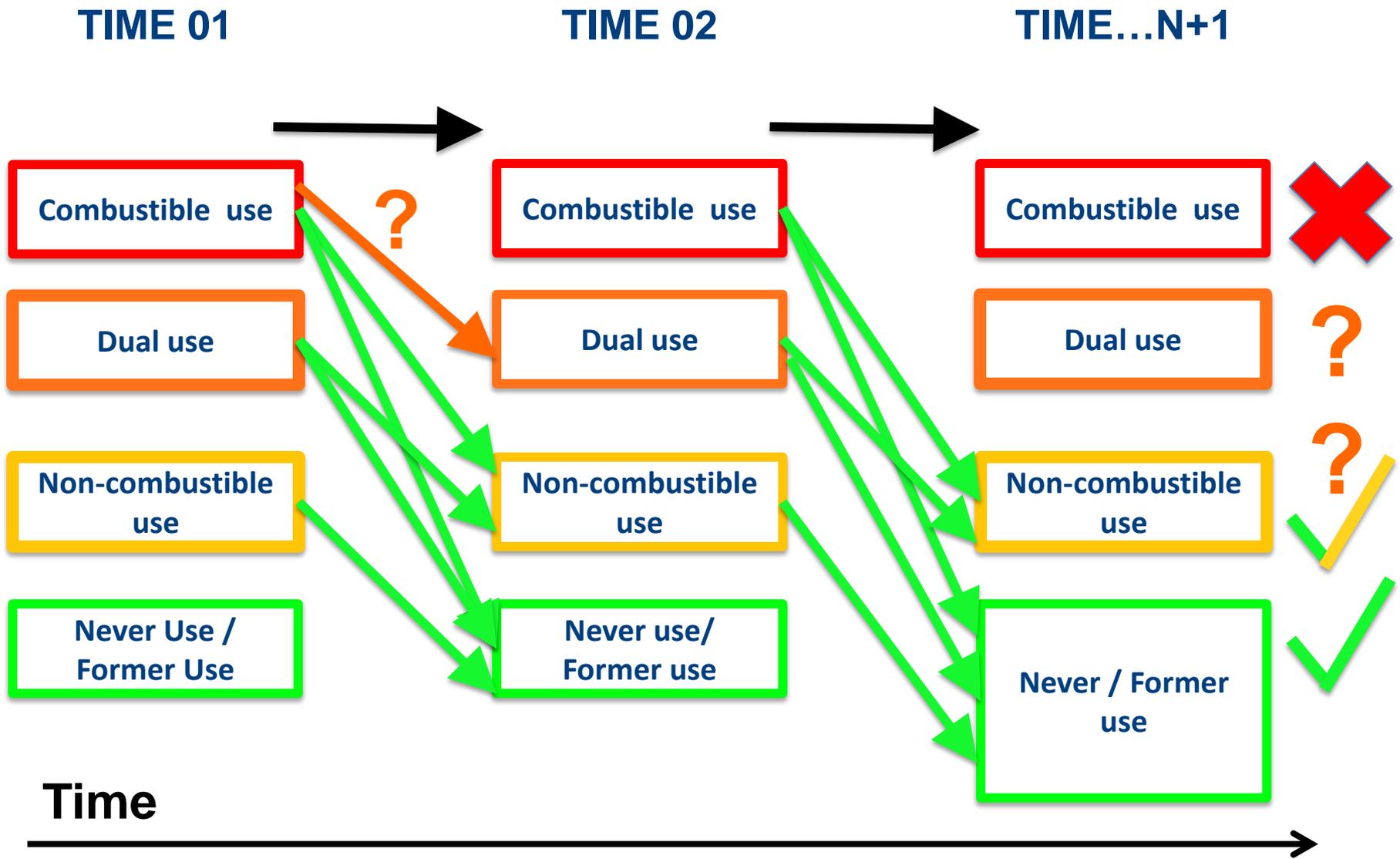
Cancer Epidemiol Biomarkers Prev

2004; 13(12):2035-2041.

Not the cleanest– but clean enough?



Behavioral transitions: combusted, dual use, non-combusted, none



Regulatory Landscape: Need overall Nicotine Regulation Policy that bridges CTP and CDER



U.S. Food and Drug Administration

Protecting and Promoting *Your* Health



Center for Tobacco Products

- ✓ Cigarettes
- ✓ Roll-your-own tobacco
- ✓ Smokeless tobacco
- ☐ Hookah tobacco
- ☐ Cigars/cigarillos/LCCs
- ☐ E-cigs for harm reduction

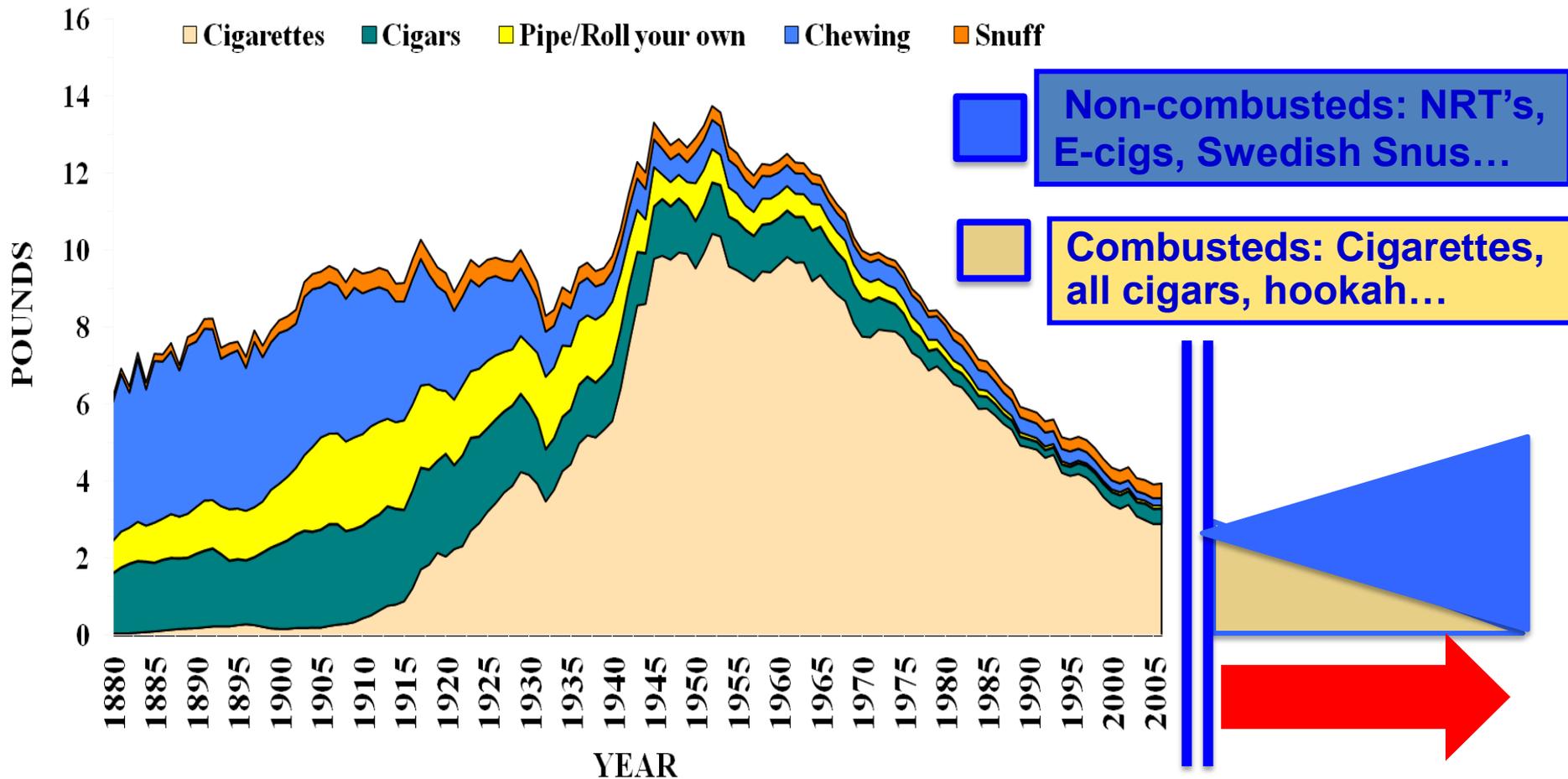
Center for Drug Evaluation & Research

- ✓ **Pharma** – NRT, Chantix, Buprorion
- ✓ Other medications for cessation
- ✓ **RJR Zonnic: Package, Price, Placement**
- ✓ **? E cigs for cessation**

Next Generation Products (Aerosol, Pyruvate, Cleaner Nicotine)

Trends in Per Capita Consumption of Various Tobacco Products – United States, 1880-2005 and Beyond.

Back To The Future ? (based on Giovino article)



Source: US Department of Agriculture

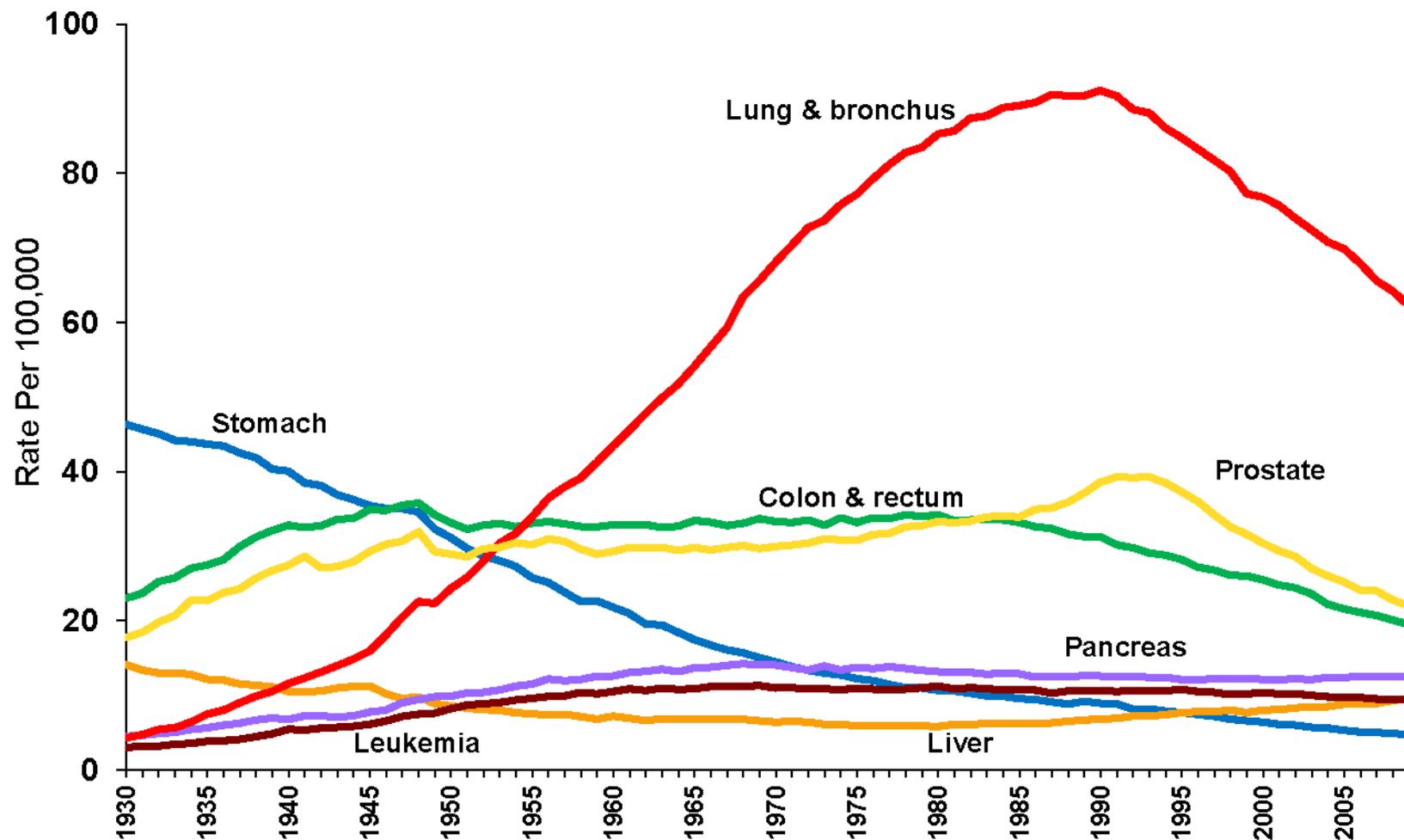
State of the science: Policy & regulation, federal and state

- Product classification (medicinal, recreational, other)
- Product safety standards – regulation - light or heavy?
- Claims of modified risk / reduced harm.
- Use in public places (indoor air laws, de-normalization)
- Youth protection (24 states restrict sales to minors)
- Taxation ?
- FTC: correction of misleading labels and claims

Proportionate to Harm Policies

- Least harm is not to use any tobacco product at all
- No sales or advertising targeted at youth for any product
- Indoor air policy - restrict all use
- Tax combusteds at much higher rates than non-combusteds, same or higher differential if we do tax e-cigarettes
- Make combusteds unappealing, expensive , ?less addictive - restrict and regulate strictly
- Prudent regulation of non-combustibles – quality controls, advertising and marketing practices (support responsible companies not affiliated with combusteds tobacco (verify good behavior with aggressive post approval surveillance.. **Warner et al a gold star**
- Educate public to highlight the lethality of combusteds in any form. Contrast with reduced harm with safer nicotine products - non-combusteds being much less harmful (FDA approved NRT best, then Swedish Snus and e- cigs – then other smokeless products

Cancer Death Rates* Among Men, US, 1930-2009



*Age-adjusted to the 2000 US standard population.

Source: US Mortality Data 1960-2009, US Mortality Volumes 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention.

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AAHB Laureate award
Charleston SC March, 2014.

 **LEGACY** | **The Schroeder Institute**
FOR TOBACCO RESEARCH AND POLICY STUDIES

From Dr. Ray Niaura : Draft Table

E-cigarettes: Belief propositions and what is known

Proponents

Ecig use is increasing

Ecigs save lives:
(smokers will quit all tobacco or
smokers will switch to ecigs)

Denormalizes smoking

Normalizes “vaping”

Ecigs are safe

Ecigs are safer than cigarettes

Secondhand vapor is safe

Ecigs are not a gateway to smoking:
(among never smokers - youth)
(among former smokers – relapse)

Over-regulation is a risk

This problem is too important to
worry about getting it right

Opponents

Ecig use is increasing

Ecigs do not save lives:
(smokers will not quit or
smokers will dual use)

Ecigs perpetuate nicotine
addiction

Normalizes smoking

Glamorizes smoking

Ecigs are not safe

Ecigs are safer than cigarettes

Secondhand vapor is unsafe

Ecigs are a gateway to smoking:
(among never smokers - youth)
(among former smokers – relapse)

Under-regulation is a risk

This problem is too important to
worry about getting it right

Facts

Ecig use is increasing but it is still
a small fraction of cigarette market
Mostly smokers are trying ecigs

Unknown
Ecigs do not help smokers quit (sparse evidence)
Most smokers who try ecigs dual use

Unknown

Unknown

Unknown

Unknown

Ecigs are safer than cigarettes

Secondhand vapor is safer than secondhand smoke

Unknown

Unknown

Unknown

Unknown

Unknown

Risk reduction by products like snus: some policy considerations (1)

- Snus use entails nicotine dependence and some health risks, but risk levels are closer to those of no-tobacco-use than to those of cigarette smoking.
- Primary snus use is associated with reduced likelihood for onset of smoking.
- Increase of initiation of snus use is associated with an even greater decrease of initiation of smoking.
- Secondary snus use is associated with increased likelihood of stopping smoking.
- When used as smoking cessation aid, snus is more effective than nicotine gum or patch.
- Switching from cigarettes to snus may be a first step towards no-tobacco-use.
- In Sweden snus appears to be a contributing factor behind the low level of tobacco-related mortality.

Risk reduction by products like snus: some policy considerations (2)

- Regulations are needed to safeguard product quality.
- Strict legislation is needed to prevent sales to minors and restrain manufacturers from using misleading claims or other undue marketing practices.
- Labelling of packages should give consumer information regarding product content and characteristics including additives.
- Public education campaigns should point out actual risks while avoiding the kind of scaremongering that has sometimes been seen in the past.
- It should be kept in mind that experience from Sweden may not be immediately applicable in other countries.