How to Identify and Interpret Quality Science

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History, Health, Science and Regulation

- Tobacco has long been used in the Americas, with some cultivation sites in Mexico dating back to 1400-1000 BC. In 1559, it was introduced to Europe. The Social-Economic Factor.

- The FDA approval is a science driven process. Therefore, data and analysis must be adequate. Not everything is useful to draw conclusions. The Regulatory-Health-Science Factor.

- FDA policies may not be able to completely balance social elements for the regulated subject because its policies are driven by health and science.

- How relevant are social variables in a health-science exercise?

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Why not everything is useful?

- Many articles and studies have a disconnect between their objective and the quality of data, collection, method, analysis and conclusions. The deficiencies disqualify them as relevant and material.

- When using articles or designing studies to test a hypothesis ask yourself:
  - Are data elements adequate?
  - Are data collection tools adequate?
  - Is the statistical or analytical method chosen adequate?
  - Is the method used correctly?
  - Is the conclusion driven by the findings?

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We Must Avoid Bias

- Cognitive bias – it refers to perceiving a distorted reality due to personal preferences, beliefs or other subjective influences.

- Confirmation bias – the emphasis on data that supports the expectations, and the downplay or ignorance of opposing results.

- There is a difference between designing a study to test a hypothesis, and the design with a pre-determined conclusion in mind.

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What's the RELEVANT EQUATION?

Adequate (Data + Method + Interpretation) = Conclusions

Failure in any equation variable leads to inaccurate conclusions:

Inadequate (Data + Method + Interpretation) ≠ Conclusions

Bias ≠ Conclusions

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Truths, half truths and barriers to finding common ground:

7 examples of deceptive or misleading practices in the science that misinforms regulation, policy and the public

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Disclosures

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- **NIH-NCI: R01 CA 155369; R01 CA 155489**
- **Truth Initiative**
- **Georgetown University**

No financial, consulting or other contracts from any tobacco product, pharma, or nicotine product (e-cigarettes, Nicotine Replacement Therapy) entity.

I am a grandfather of a 14.5 year old girl and 11 year old boy … I fiercely protect them

It is a capital mistake to theorize before one has data. Insensibly one begins to twist facts to suit theories, instead of theories to suit facts.

Sherlock Holmes. Sir Arthur Conan Doyle (1891). *A Scandal in Bohemia*

- We all fall short to some degree on occasions
- The aim is not to ascribe blame but to provide a framework for improving the quality of and interpreting of science

All are biased: how do best practices minimize bias for  consensus?

At stake: 38 million smokers and potential smokers lives.

Contents lists available at ScienceDirect

Preventive Medicine

journal homepage: www.elsevier.com/locate/ypmed

Are we guilty of errors of omission on the potential role of electronic nicotine delivery systems as less harmful substitutes for combusted tobacco use?

Jack E. Henningfield[a,*], Stephen T. Higgins[b], Andrea C. Villanti[c]

Decision-making research: humans have a bias towards avoidance of commission errors and an insensitivity to omission errors.

- This bias may contribute to lack of common ground and deceptive misuse of science
- **Omitting beneficial contributions** of ENDS to eliminate deaths from combusted smoke
- Avoiding commission error by promoting ENDS **despite some risk.**

Problems with the reporting of research: Adapted from Dr. Robert West.

Over-interpreting: Attributing causal connections when there are plausible alternatives

Overstating: Creating a misleading impression about the nature, size or importance of effects

Overgeneralizing: Unwarranted generalization beyond the study conditions

Cherry picking: Select findings to report or highlight according to a specific viewpoint

Double standards: Apply different standards to research that supports or conflicts with a given view

False equivalence of weak science and strong science. Exaggerations and Omissions.

MUST READ: 'Critics guide to bad vaping science' – Clive Bates

https://www.clivebates.com/documents/BadScienceBriefing1.pdf

It is never a good idea to mislead anyone especially youth.
Breach of trust diminishes integrity of the source and backfires

NASEM Report. USA 2018

Framework for Public Health Effects

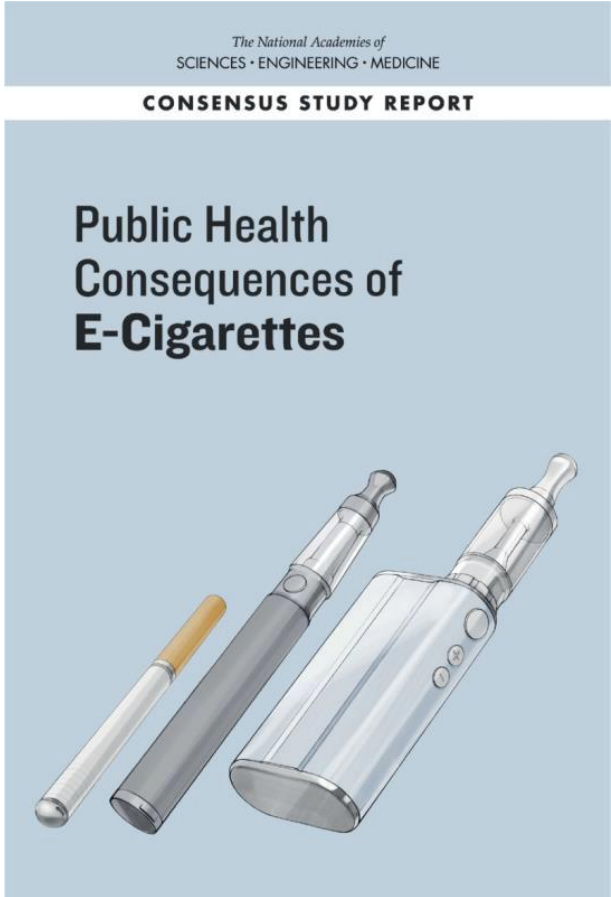
•The net public health effect of e-cigarettes will depend on the balance of 3 factors:

–Potential to increase the uptake of ***combustible tobacco use***

–Inherent toxicity Absolute ***and relative to combustible tobacco***

–Potential to help current ***smokers to quit***

nationalacademies.org/eCigHealthEffects

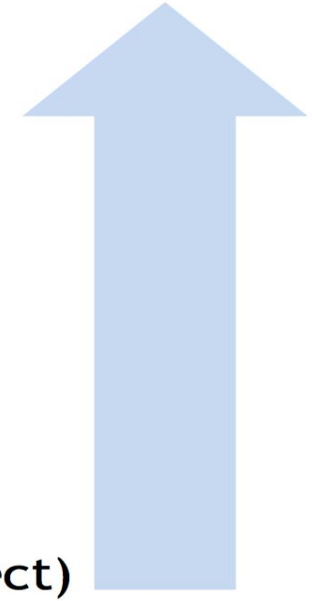


NASEM Report. USA 2018

Levels of Evidence Framework

- Conclusive
- Substantial
- Moderate
- Limited
- Insufficient
- No available

(≠ evidence of no effect)



- Number of studies
- Quality of studies
  - Study design
  - Ability to rule out chance, bias, confounding

#eCigHealthEffects

The National Academies of SCIENCES ENGINEERING MEDICINE

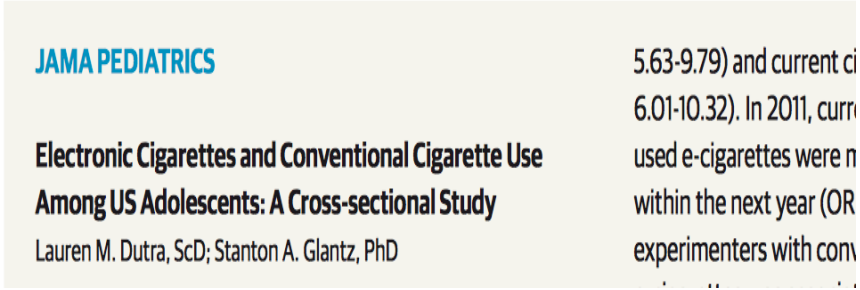
1. False Equivalence: Exaggeration and / or Omission

Dutra & Glantz : JAMA Pediatrics and JAMA: Aug, 2014 Vol 312, No 6

From The JAMA Network

Youth Experimentation With e-Cigarettes
Another Interpretation of the Data

Raymond S. Niaura, PhD; Thomas J. Glynn, PhD; David B. Abrams, PhD



JAMA PEDIATRICS

Electronic Cigarettes and Conventional Cigarette Use Among US Adolescents: A Cross-sectional Study

Lauren M. Dutra, ScD; Stanton A. Glantz, PhD

5.63-9.79) and current ci
6.01-10.32). In 2011, curr
used e-cigarettes were n
within the next year (OR
experimenters with conv

CLAIMED CONCLUSION: Use of e-cigarettes does not discourage, and may encourage, conventional cigarette use among US adolescents. (implies causal gateway ?)

? WHOLE TRUTH: There are at least 3 possible explanations for their findings: use of e-cigarettes. causes use of conventional cigarettes; use of conventional cigarettes causes use of e-cigarettes; or there are as-common causes of e-cigaretteandlethalcombustible cigarette use. **The study cannot rule out any of these explanations.**

2. False Equivalence: Exaggeration and / or Omission

Watkins S, Gantz, SA, Chaffee BW. Association of noncigarette tobacco …with future cigarette smoking…youth in the Population Assessment of Tobacco and Health (PATH) Study20182013-2015. **JAMA Pediatrics**. 2018;172(2):181-187

CLAIMED CONCLUSIONS: Any use of e-cigarettes, hookah, noncigarette combustible tobacco, or smokeless tobacco **was independently associated with cigarette smoking 1 year later**. Use of more than 1 product increased the odds of progressing to cigarette use."

? Half TRUTH:

There was little collinearity among baseline tobacco use variables (all variance inflation factors <1.4). Sensitivity analyses yielded similar findings to the main analyses (eTables 1-7 in the Supplement). Associations decreased in magnitude with adjustment for marijuana use (eTable 4 in the Supplement). The ORs not adjusted for other noncigarette tobacco products were consistently larger than the ORs with simultaneous control for other products (eTable 5 and eTable 6 in the Supplement).

eTable 4. Associations of Noncigarette Tobacco Single-Product Ever Use and Polyuse With Subsequent Cigarette Use: Sensitivity to Adjustment For Baseline Cigarette Susceptibility or Marijuana Ever Use

	Outcome: Cigarette ever use			Outcome: Cigarette past 30-day use		
Predictors:	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
e-cigarettes	4.62 (3.10, 6.89)	2.21 (1.42, 3.44)	2.62 (1.65, 4.18)	2.98 (1.55, 5.74)	1.49 (0.75, 2.98)	1.69 (0.79, 3.61)
hookah	4.52 (2.90, 7.05)	2.30 (1.39, 3.79)	1.84 (1.06, 3.22)	4.31 (2.31, 8.04)	2.36 (1.19, 4.69)	1.98 (0.93, 4.18)
other combustables	3.52 (1.94, 6.40)	1.95 (1.03, 3.69)	2.45 (1.15, 5.21)	5.25 (2.61, 10.58)	2.90 (1.34, 6.25)	3.33 (1.28, 8.64)
smokeless	3.44 (1.74, 6.80)	1.42 (0.65, 3.08)	1.70 (0.75, 3.86)	4.34 (1.74, 10.80)	1.59 (0.59, 4.30)	1.83 (0.63, 5.26)
polyuse	8.55 (5.96, 12.26)	3.67 (2.45, 5.51)	3.41 (2.03, 5.75)	9.03 (5.64, 14.45)	3.65 (2.10, 6.34)	2.80 (1.35, 5.78)
cigarette susceptibility		2.84 (2.22, 3.63)			2.45 (1.73, 3.48)	
marijuana ever use			2.61 (1.79, 3.81)			2.54 (1.52, 4.24)
N	9909	9189	8940	9907	9187	8938

Abbreviations: OR = odds ratio; CI = confidence interval

Notes: All models additionally adjusted for gender, age, race/ethnicity, parents' education, sensation-seeking score, ever use of alcohol, living with another tobacco user, noticing cigarette warnings score, having a favorite tobacco ad, and baseline interview conducted in the summer. Models are listwise deletion models with sample weights.

Whole Truth: Actually the effect is **NOT diminished .. IT DISAPPEARS and is NOT SIGNIFICANT**

DANGER No one observational study can be relied on to make major policy decisions

3. False Equivalence: Exaggeration and / or Omission

Chaffee BW, Watkins SL, Glantz SA. Electronic cigarette… progression… ***Pediatrics.*** **2018;141(4): e20173594**

Studied 1,295 12-17 year olds in PATH Waves 1 to 2 data. FDA-NIH-Westat public use file:

CLAIMED CONCLUSION: Among adolescents…. **using e-cigarettes was positively and independently associated with progression to current established smoking,** suggesting that **e-cigarettes do not divert from, and may encourage, cigarette smoking in this population**

? WHOLE TRUTH: …omitted lifetime cigarette consumption at Wave 1…a profoundly important variable relevant to progression. Results for e-cigarette users **substantially reduced and not statistically significant after adjusting**. Conclusion e-cigarette use is "independently associated" with progression to established smoking **is incorrect.**

Substantial revision or retraction of this study is warranted …

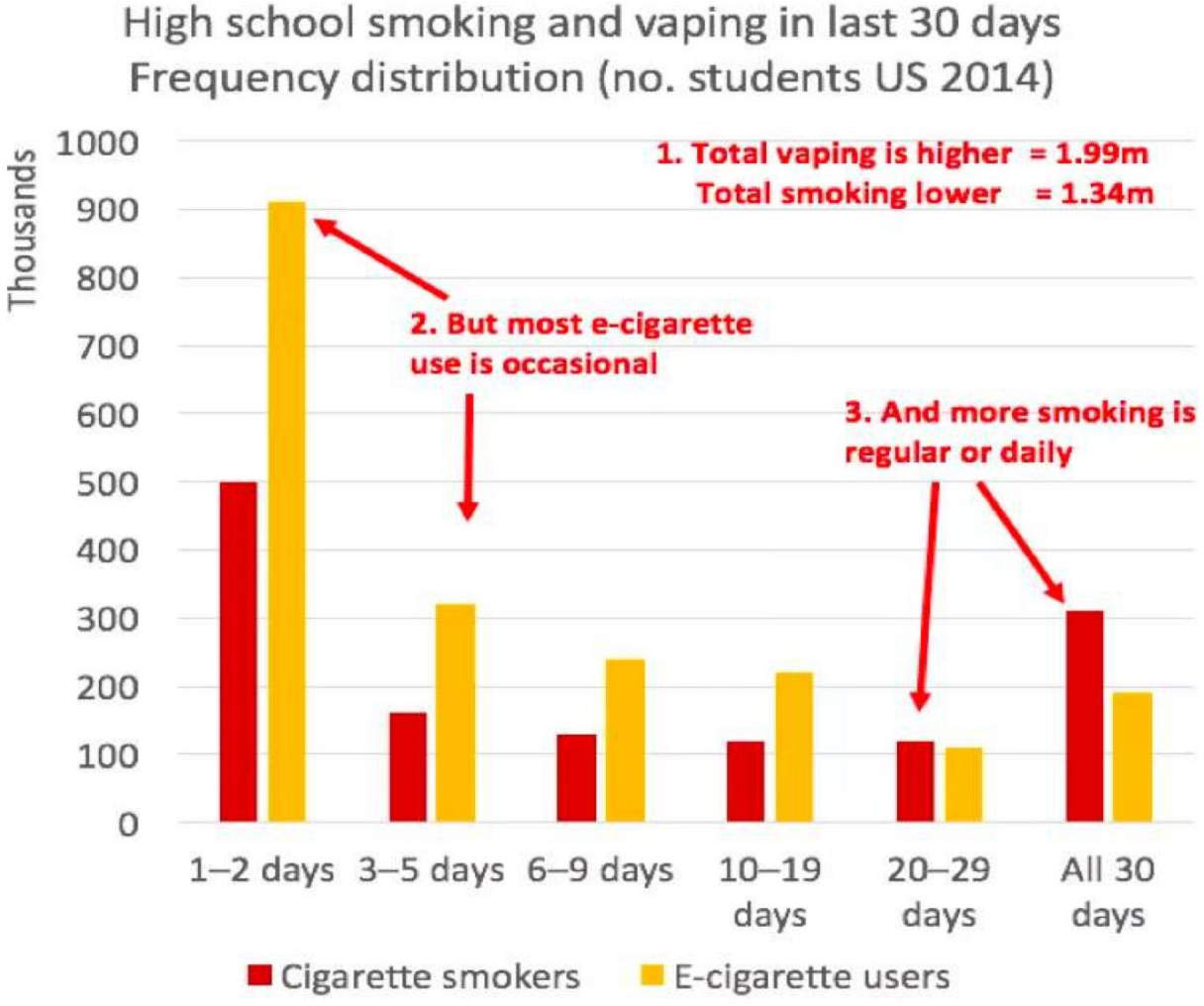
Rodu B, Plurphanswat N. RE: ***Pediatrics.***

Frequency of Youth E-Cigarette and Tobacco Use Patterns in the United States: **Measurement Precision Is Critical to Inform Public Health**

Villanti, Pearson, Glasser, Johnson, Collins, Niaura, & Abrams.
Nicotine & Tobacco Research, 2016, 1–6 doi:10.1093/ntr/ntw388

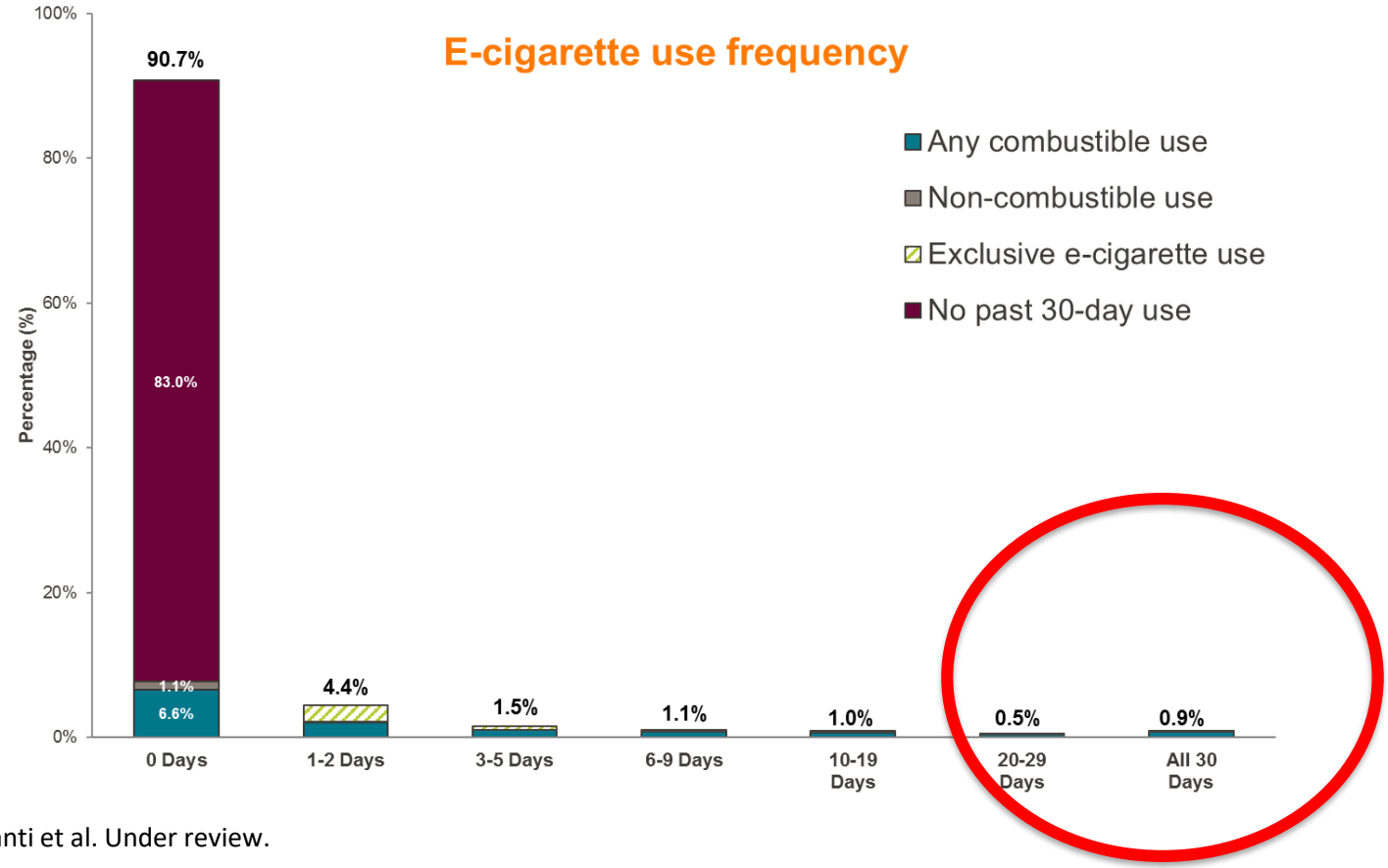
Update: Collins et al … Nicotine & Tobacco Research, 2017, 1–2
doi:10.1093/ntr/ntx073

Measurement Precision Is Critical to Inform Public Health…



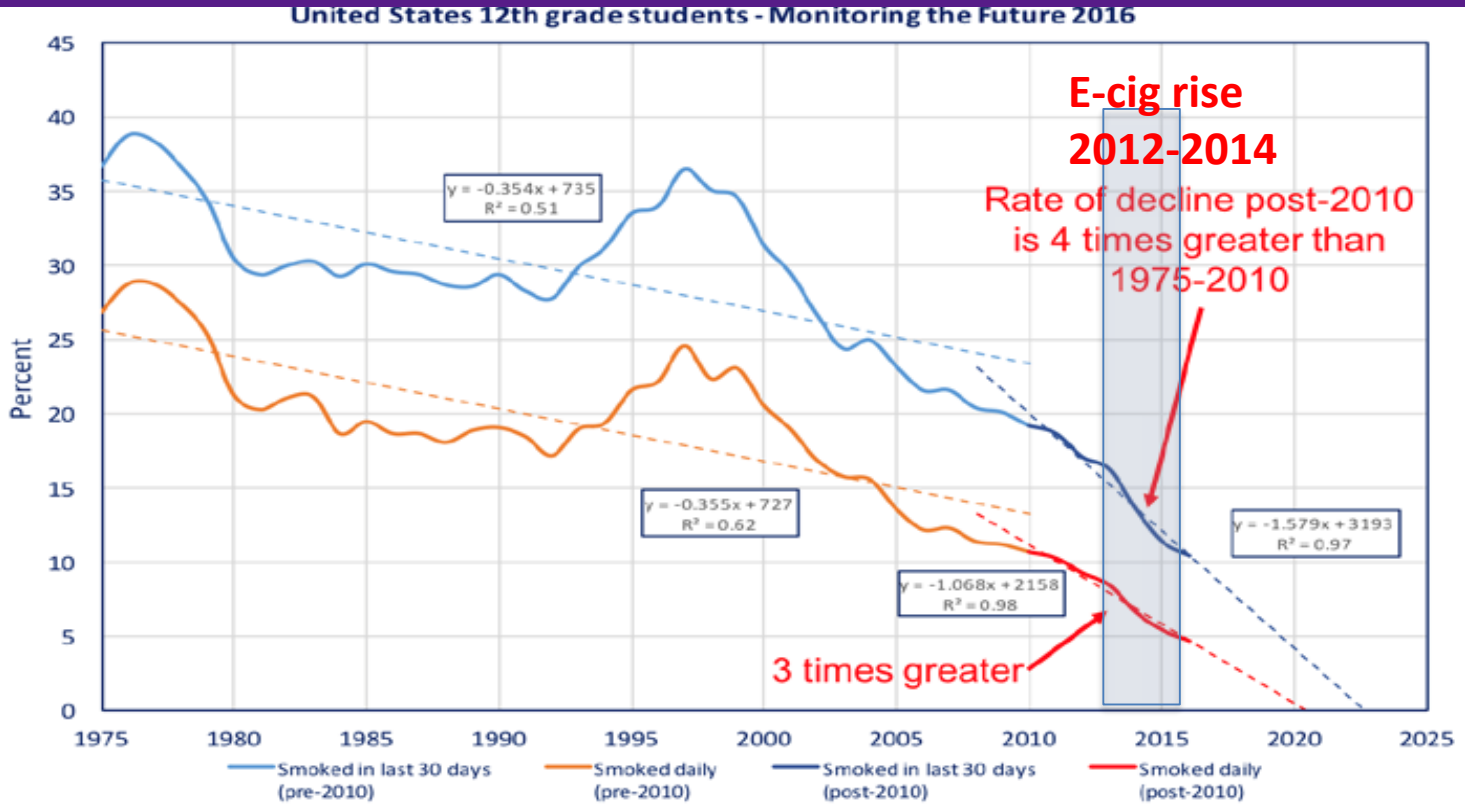
CDC Frequency of Tobacco Use Among Middle and High School Students – United States, 2014

Distribution of tobacco and e-cigarette co-use among U.S. middle and high school students (weighted); NYTS, 2014….15..16….17…..18???



Villanti et al. Under review.

Monitoring the Future Survey: 1975 – 2016 for 12th grade smoking. **Unusually rapid decline** 2011-2016



SUMMARY: YOUTH UPTAKE & PROGRESSION
Very Concerning 2018 data - in scientific context …

- **NASEM report 2018 ; UK, PHE Report 2018; Soneji et al.** Meta analysis 2017; Abrams et al. Annual Review of Public Health. Feb 2018.. **Largely consistent**
- Longitudinal studies, show as expected: SOME youth ever e-cigarette users will **TRY cigarettes**.
- Raising concern about so-called "gateway" effects (i.e., e-cigarette use leading directly to smoking).
- **Soneji et al.** Meta analysis 2017 **duly note that** finding such an association, even in longitudinal studies**, does not imply causality**. Confounding influences, such as shared vulnerability factors that predispose youth to try alcohol, marijuana, other drugs and risky experiences, cannot be easily ruled out. They TRAVEL TOGETHER.
- Progression of use beyond experimentation has not been established.
- Even if there was a gateway effect, **Kozlowski and Warner (2017); Warner 2018, others conclude:** while society must be vigilant, fears of hypothesized harms due to gateway effects among youth **are unlikely to undermine the much larger benefits of discouraging smoking behavior in the whole population.**
- Simulation modeling with sensitivity analyses shows that **the purported gateway effect would have to be implausibly large to increase the net public health harm over benefits…**

NASEM Report: YOUTH Initiation and ?? Progression

Substantial evidence *that e-cigarette use increases risk of* ***ever using combustible*** *tobacco cigarettes among youth and young adults*

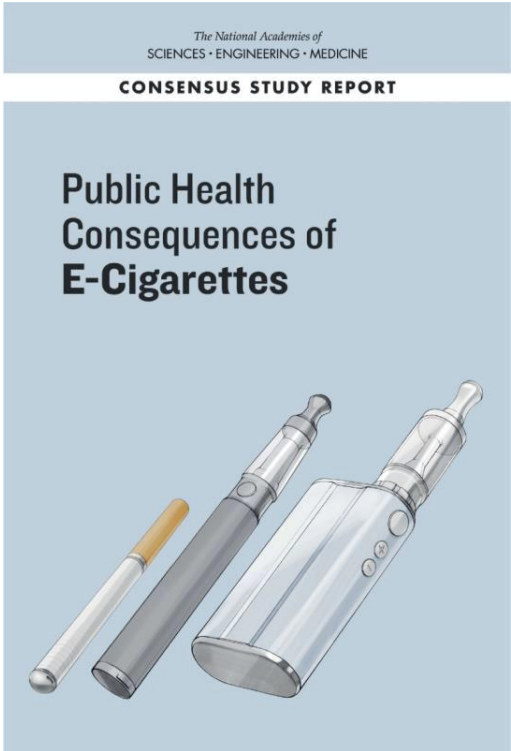
Limited evidence *that e-cigarette use increases,* ***in the near term****, the duration of subsequent combustible tobacco cigarette smoking*

Note: No evidence e-cig experimentation ***causes progression to daily cigarette use, let alone a lifetime of use***

Daily use about 1% and majority among already tobacco users

In some youth e-cigs can be displacing smoking *mitigating fears*

New evidence ENDS use is unstable unless followed for > 2 years…



How do we determine the impact of e-cigarettes on cigarette smoking cessation?

Review and recommendations for answering the research question with scientific rigor.

Villanti AC[1,2,3], Feirman SP[1], Niaura RS[1,2], Pearson JL[1,2], Glasser AM[1], Collins LK[1], Abrams DB[1,2,4].

Addiction. 2017 Oct 3. doi: 10.1111/add.14020.

4. False Equivalence: Exaggeration and / or Omission

’ **Kalkhoran & Glantz** Lancet Respir Med. 2016 Feb;4(2):116-28

and Updated in Glantz & Bareham. 2018

CLAIMED CONCLUSIONS: ‘Odds of quitting cigarettes were 28% lower in those who used e-cigarettes compared with those who did not use e-cigarettes (odds ratio [OR] 0·72, 95% CI 0·57-0·91). …Currently being used, e-cigarettes are associated with significantly less quitting among smokers. E-cigarettes may **INHIBIT CESSATION……**

? The WHOLE TRUTH: The Cochrane Handbook warns: ‘meta-analyses of studies that are at risk of bias may be seriously misleading. If bias is present in each (or some) of the individual studies, meta-analysis will simply compound the errors, and produce a ‘wrong’ result that may be interpreted as having more credibility’ ([135], p. 247).

5. False Equivalence: Exaggeration and / or Omission

Alzahrani, T., Pena, I., Temesgen, N., & Glantz, S. A. Prev. Med (2018). **E-cigarettes and myocardial infarction**

Table 2. Univariate and Multivariable Associations Between E-cigarette Use and Myocardial Infarction of NHIS 2014 and 2016 Combined

	Unadjusted model		Adjusted model	
Characteristics	**OR (95% CI)**	***p*-value**	**OR (95% CI)**	***p*-value**
E-cigarette use				
Never	ref		ref	
Former	**0.79 (0.67, 0.94)**	**0.009**	1.06 (0.86, 1.30)	0.608
Some days	1.06 (0.79, 1.44)	0.665	1.16 (0.83, 1.62)	0.392
Daily	**1.69 (1.19, 2.39)**	**0.003**	**1.79 (1.20, 2.66)**	**0.004**

CLAIMED CONCLUSIONS ***(authors):*** *"Daily e- cigarette use, adjusted for smoking conventional cigarettes as well as other risk factors, is associated with increased risk of myocardial infarction (double?) ."* The study also found that the risks compound, so that daily **use of both e-cigarettes and conventional cigarettes raises the heart attack risk five-fold**

THE WHOLE TRUTH? The two data sets that cannot be combined. Implies a causal link but temporal definition of events (e-cigarettes preceding infarction CANNOT be determined from cross sectional study. Selection bias, duration of use not long …NOT replicated with latest data available.. i.e ?? Another ?? **Flawed study grossly misleads.**

6. Harms: False Equivalence: Exaggeration and / or Omission

PLOS ONE

RESEARCH ARTICLE

Benzene formation in electronic cigarettes

James F. Pankow[1,2]*, Kilsun Kim[1], Kevin J. McWhirter[2], Wentai Luo[1,2], Jorge O. Escobedo[1], Robert M. Strongin[1], Anna K. Duell[1], David H. Peyton[1]

Three e-cigarette devices were used: ….**the JUULTM ªpodº** system (provides no user accessible settings other than flavor cartridge choice) …

…Benzene formation was ND (not detected) in the JUUL system

(from the same folks who brought us the (debunked?) formaldehyde scares

The acrolein and popcorn lung damage exaggerations …. also debunked?

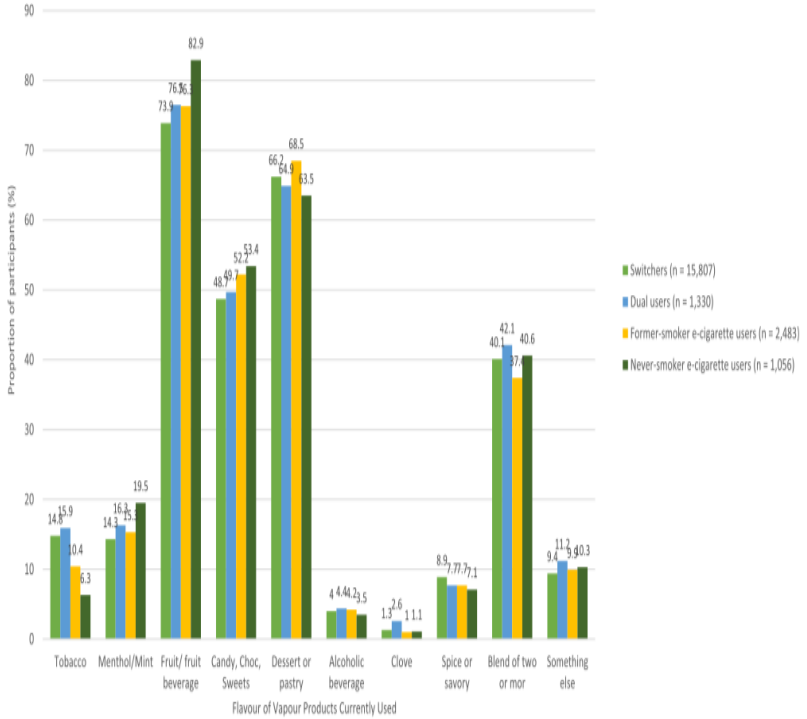
Prudent Product standards can readily take care of any of these concerns

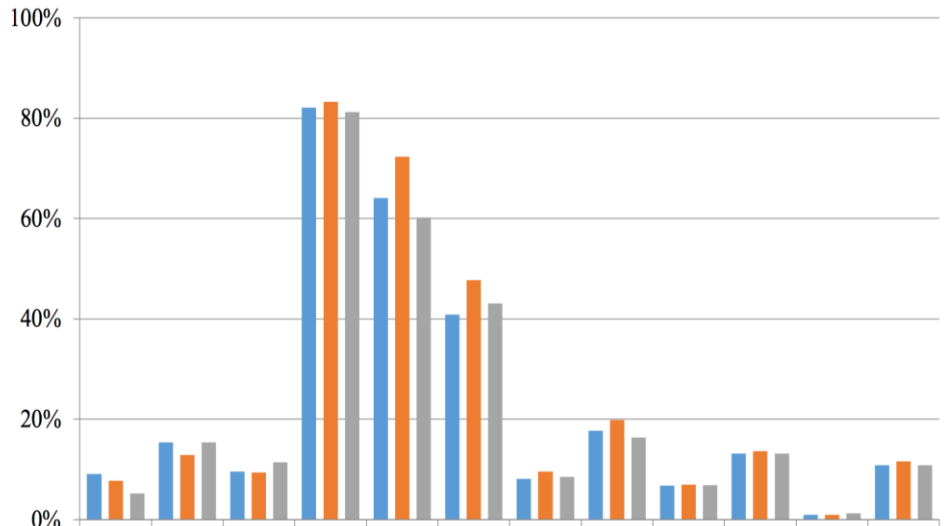
7. Successful switchers: 2 studies +/-90,000 respondents:

Russell et al. Harm Reduction Journal (2018) 15:33 doi.org/10.1186/s12954-018-0238-6

K Farsalinos et al..: FDA Docket on Flavors No. FDA-2017-N-6565… 2018….

Tobacco; Menthol/mint; Fruit/beverage; candy/choc/sweet; dessert/pastry;..Blend. consistent

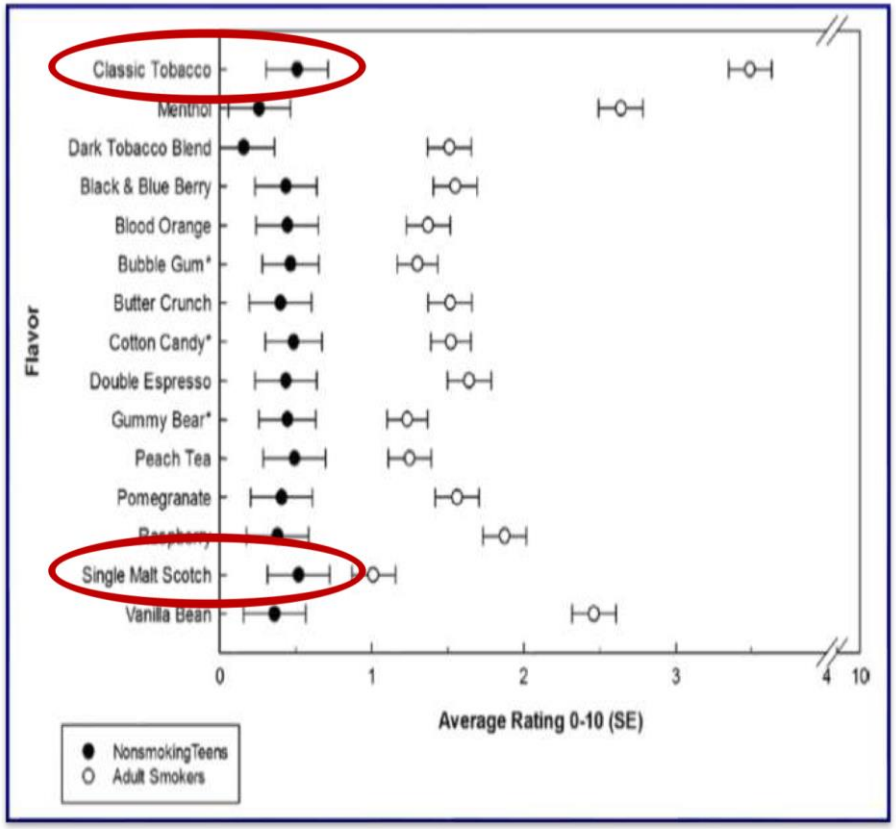




	Tobacco	Menthol	Mint / wintergreen	Fruit	Dessert / pastry / bakery	Candy / chocolate / sweet	Spice	Coffee	Alcohol / cocktail	Non alcoholic / non coffee drink	Unflavored	Other
Current smokers	9.1%	15.4%	9.5%	82.1%	64.1%	40.8%	8.1%	17.7%	6.7%	13.1%	0.9%	10.8%
Former smokers	7.7%	12.8%	9.4%	83.2%	72.3%	47.7%	9.5%	19.8%	6.9%	13.6%	0.9%	11.6%
Never smokers	5.2%	15.4%	11.4%	81.2%	60.2%	43.1%	8.5%	16.3%	6.8%	13.1%	1.2%	10.8%

garette/e-liquid flavors currently used by 20,676 US adult frequent e-cigarette users stratified by Tobacco Use Pathway (for) group

Shiffman, Sembower…Gitchell NTR 2015



Shiffman S, Sembower MA, Pillitteri JL, Gerlach KK, Gitchell JG. The impact of flavor descriptors on nonsmoking teens' and adult smokers' interest in electronic cigarettes. Nicotine Tob Res 2015
Participants indicated their interest (0-10 scale) in e-cigarettes paired with various flavor descriptors

Ambrose et al, JAMA, 2015

	% (95% CI) e-Cigarettes (n = 418)[c]
I use [product] because they come in flavors I like	81.5 (77.9-85.0)
I use [product] because they are affordable	47.8 (42.9-52.6)
I use [product] because I can smoke/use them at times when or in places where smoking cigarettes isn't allowed	58.9 (54.1-63.7)
I use [product] because I like socializing while using them	40.3 (34.9-45.8)
I use [product] because it doesn't bother non-tobacco users	53.9 (48.1-59.8)
I use [product] because they might be less harmful to me than cigarettes	79.1 (75.2-83.0)
I use [product] because they might be less harmful to people around me than cigarettes	78.1 (74.3-81.8)
I use [product] because they don't smell	58.7 (54.2-63.2)
I use [product] because they help people to quit smoking cigarettes	59.5 (54.6-64.5)
I use [product] because people who are important to me use them	34.9 (30.6-39.2)
I use [product] because people in the media or other public figures use them	36.1 (31.5-40.7)

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Managing nicotine without smoke to save lives now: Evidence for harm minimization

David B. Abrams[a,*], Allison M. Glasser[a], Andrea C. Villanti[b], Jennifer L. Pearson[c], Shyanika Rose[d], Raymond S. Niaura[a]

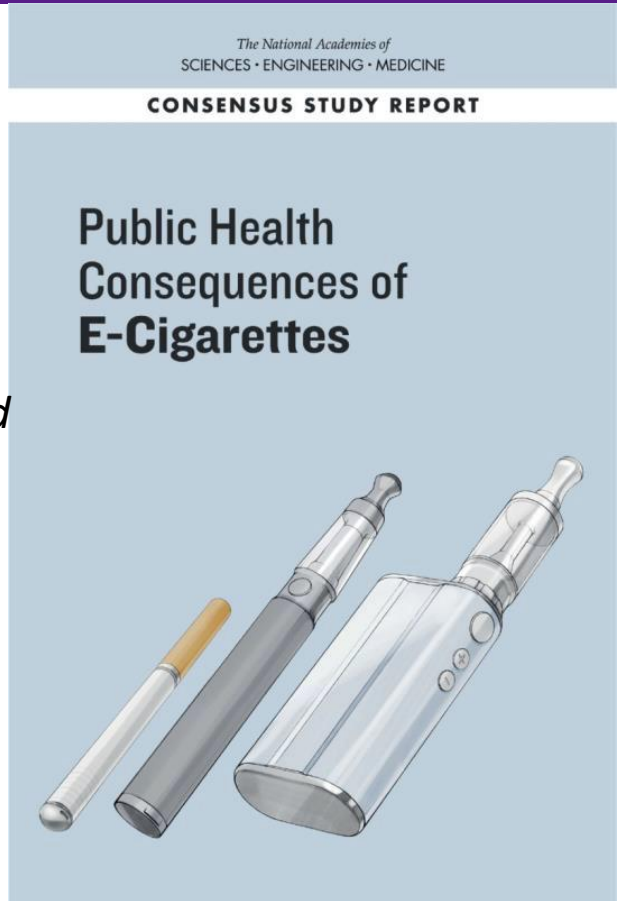
- In summary, the accumulating evidence does not support the contention that e-cigarettes **either inhibit cessation or are undermining historical "tobacco control" cessation efforts.** Rather, the stronger studies suggest e-cigarettes are increasing cessation rates and quit attempts …
- … based on a **misleading negative correlation between e-cigarettes and smoking cessation from a meta-analysis (Kalkhoran and Glantz,2016) … has been debunked (Villanti et al., 2017a).**

NASEM Report: Harms & Help smokers to quit

- ***Conclusive evidence*** *that completely substituting e-cigarettes for combustible tobacco cigarettes reduces users' exposure to numerous toxicants and carcinogens present in combustible tobacco cigarettes [18-1]*

- ***Substantial evidence*** *that completely switching from regular use of combustible tobacco cigarettes to e-cigarettes results in reduced short-term adverse health outcomes in several organ systems [18-2]*

Largely Consistent with Public Health England 2018, Royal College of Physicians 2018 and many recent content specific systematic reviews and knowledge syntheses papers…



Josh Stein, Attorney General

PRESS RELEASE

Dangers of E-cigarettes

Juul Investigation

 Health Risks Associated with Nicotine:

o Daily e-cigarette users have **twice the risk of a heart attack…vape and smoke... Risk 5 times**

o Vaping leads to increased levels of DNA-damaging chemicals in saliva – which increases the risk of **oral cancer.**

- The U.S. Surgeon General estimates that 5.6 million young people alive today will **die prematurely from tobacco use.**
- E-cigarettes contain toxic chemicals including **formaldehyde, arsenic, and acetone.**
- Vaping leads to lung tissue inflammation and harm to lungs' protective cells, making people susceptible to allergens and may even lead to **COPD, respiratory disorders, and other health problems.** (University of Birmingham)
- The brain does not finish developing until a person is about 25 years old. **Exposure to a highly addictive drug like nicotine can dramatically change the brain**, making kids get more addicted to nicotine more quickly than adults.

o CDC research shows that teens who vape are **7 times more likely to smoke regular cigarettes**.

"I just feel fortunate to live in a world with so much disinformation at my fingertips."

False Equivalence: Exaggeration and / or Omission

- Scientists more willing to look for problems rather than benefits
  - A lot of research about e-cigarettes being gateway TO smoking
  - Little research about e-cigarettes being gateway FROM smoking
- Funding focused mostly on searching for problems
  - Further motivation for scientists to look for problems
- Abstinence-only approach, denial for harm reduction potential
  - This approach has still not solved the smoking problem globally
  - Harm reduction as a strategy has been accepted in other areas
- Predisposition
  - It looks like smoking, it is used like smoking, so it must be bad
  - Associations assumed to have causal link

Prejudice in tobacco and nicotine product science:

? More bias against harm reduction and in looking for harms rather than benefits in funded research, in journal reviews and publications..?

Adapted from Dr. K. Farsalinos

The Tobacco and Nicotine Science Misinformation Mess: What can be done?

Efforts should focus on making FDA, tobacco and nicotine regulatory scientists and professionals

More sensitive to the limitations of the evidence

More critical appraisal, and enhancing communication skills to accurately summarize evidence to improve decision-making.

Similar efforts to target journal editors and reviewers, tobacco and nicotine product consumers, journalists, policy makers, the lay public and any other stakeholders.

Adapted from Ray Niaura, adapted from: Ioannidis JPA, Stuart ME, Brownlee S, Strite SA. How to survive the medical misinformation mess. Eur J Clin Invest 2017, Nov;47(11):795-802.

Gottlieb S, Zeller M. A Nicotine-Focused Framework for Public Health. N Engl J Med. 2017;377(12):1111- 1114.

The availability of potentially less harmful tobacco products could reduce risk while delivering satisfying levels of nicotine for adults who still need or want it."8 (p.1).

Nicotine, though not benign, is not directly responsible for the tobacco-caused cancer, lung disease and heart disease that kill hundreds of thousands of Americans each year" (p.1)

QUESTION: Do we all have the courage to correct misperceptions, stay the course on the whole plan, emphasize truth, in balanced way ?

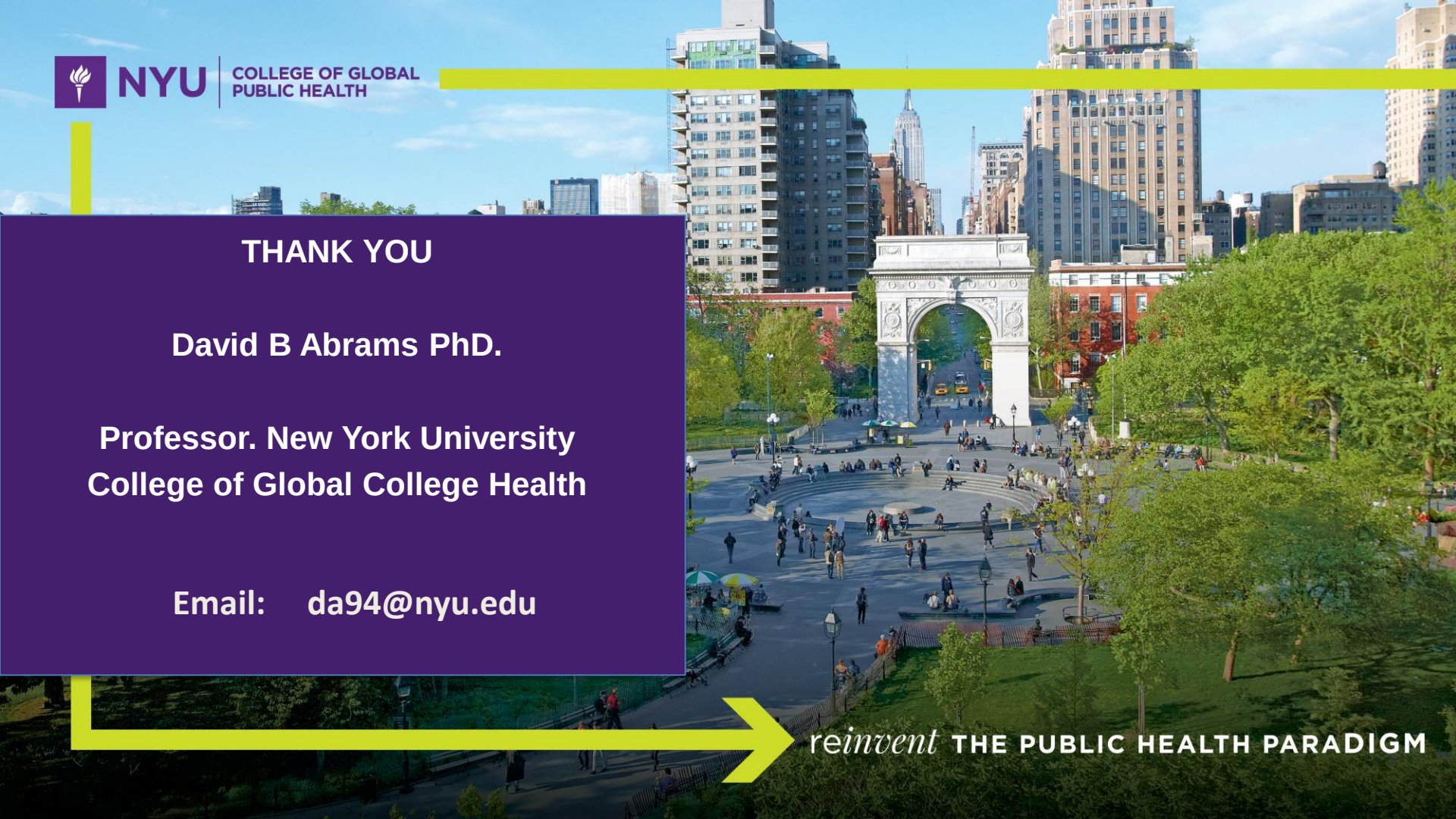
WARNING: Confusion and misinformation about the substantially less harms of noncombusted nicotine only keeps the incumbent deadly cigarette's dominance for longer than would otherwise be the case.

Even yourself

Dig deeper

Don’t accept isolated studies without great care

Use trusted sources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