



MASSACHUSETTS
GENERAL HOSPITAL

PSYCHIATRY ACADEMY

The New Frontier of Adolescent Nicotine Use

Substance Use Disorders Conference 2021

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Disclosures

Neither I nor my spouse/partner has a relevant financial relationship with a commercial interest to disclose.

Tobacco Use is a Pediatric Disease



Most Tobacco Users Start Before the Age of 21

95% of U.S. adult smokers start before age 21 (IOM Report, 2015)

Tobacco use during youth:

- Has immediate health consequences
- Accelerates development of chronic diseases over the lifespan



People who have not used tobacco by age 21 are unlikely to ever start.



Nicotine and the Developing Adolescent Brain

- Prefrontal cortex still developing through age 25
 - Decision making, impulse control, executive functioning
- Adolescent brain uniquely vulnerable to nicotine addiction
 - Become addicted more quickly, at lower levels of use
- Early use of nicotine associated with:
 - Earlier addiction
 - Greater risk of progressing to daily smoking
 - Difficulty quitting



Adolescents and Poor Quit Rates

- Treatment for adolescents shows reduction in the amount smoked, but overall abstinence rates are low
- More than half of adolescent smokers think seriously about quitting and make a quit attempt each year
- However, only 4% of adolescent smokers successfully quit smoking each year
 - Starting smoking at a younger age is associated with lower quit rates

Adolescents are Uniquely Vulnerable to Effects of Nicotine

- Nicotine acts on nicotinic acetylcholine receptors (nAChRs) widely distributed throughout the brain
- Neurochemical effects of nicotine are greatest in young users
 - Immaturity of NACRs (e.g., heightened expression and binding)
 - Greater sensitivity to nicotine, particularly in regions central to reward and cognition

Adolescents are Uniquely Vulnerable to Effects of Nicotine

- Behavioral response to nicotine is also distinct during adolescence
 - Greater sensitivity to the rewarding effects of nicotine (which is predictive of chronic use)
 - Blunted responsivity to negative effects of nicotine and less prominent withdrawal

Adolescent Nicotine Use and Cognitive Functioning

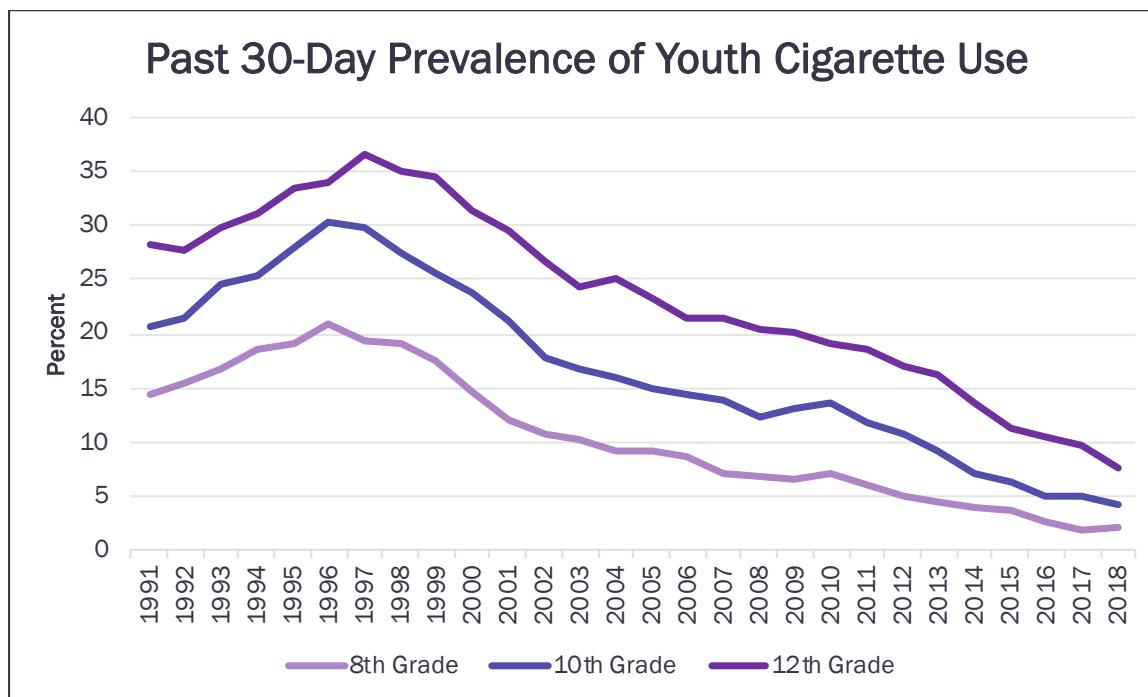
- Nicotine withdrawal related to deficits in working



performance than non-users

Shifting Landscape of Adolescent Nicotine Use

Prevalence of past-month cigarette use among youth has been nearly eradicated, with rates dropping from ~21% (1991) to ~4% (2018) among 8th-12th graders.



Miech, R. A., Schulenberg, J. E., Johnston, L. D., Bachman, J. G., O'Malley, P. M., & Patrick, M. E. (December 17, 2018).

"National Adolescent Drug Trends in 2018." Monitoring the Future: Ann Arbor, MI. Retrieved MM/DD/YYYY from

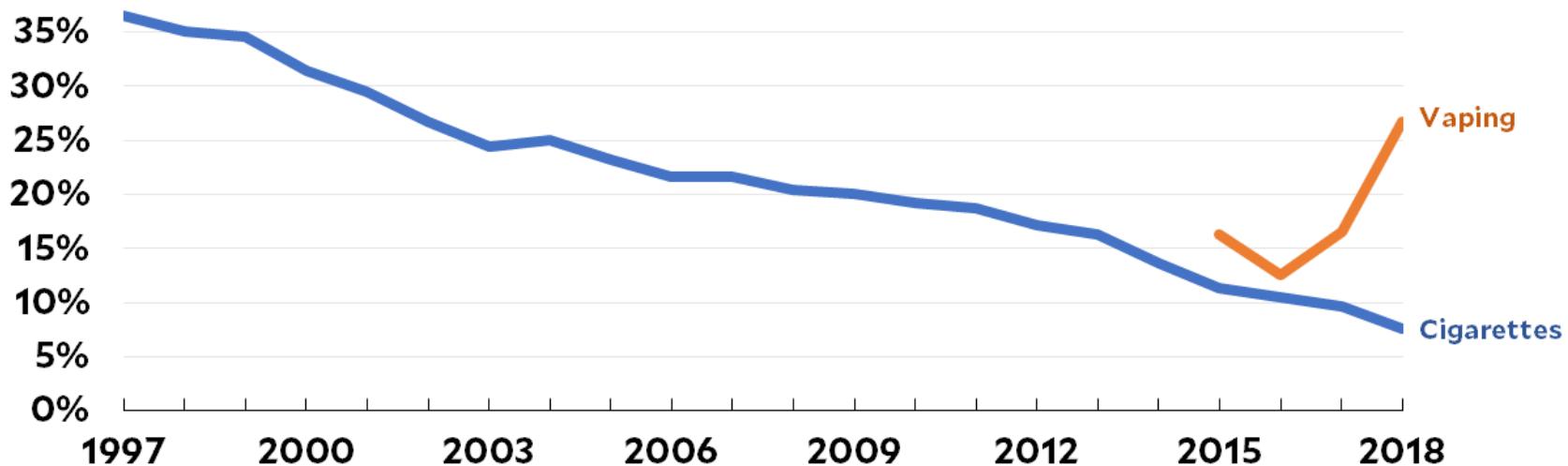
<http://www.monitoringthefuture.org>

www.mghcme.org

Shifting Landscape of Adolescent Nicotine Use

However, while cigarette use has been falling, prevalence of vaping use among youth has increased substantially

Trends in Vaping and Cigarette Use 12th Graders



Data source: Miech, R. A., Schulenberg, J. E., Johnston, L. D., Bachman, J. G., O'Malley, P. M., & Patrick, M. E. (December 17, 2018).

"National Adolescent Drug Trends in 2018." Monitoring the Future: Ann Arbor, MI. Retrieved MM/DD/YYYY from <http://www.monitoringthefuture.org>

Graph source: <https://www.motherjones.com/kevin-drum/2018/12/the-juul-fad-is-far-bigger-than-i-ever-would-have-guessed/> www.mghcme.org

What is Vaping?

- Battery operated devices that heat up liquids to an aerosol. E-liquids generally contain nicotine (or marijuana), vegetable glycerin, propylene glycol, and other chemicals and additives such as flavorings.
 - a.k.a. e-cigs, vape pens, JUUL, Puff Bar, e-hookahs, e-pipes, tanks, mods, vapes, electronic nicotine delivery systems (ENDS)
- Many shapes and sizes
 - Some made to look like regular cigarettes, cigars, or pipes
 - Some made to resemble pens, small electronic devices such as USB sticks





Many Different Vape Systems: Some are Meant to Deceive

How Do Vape Devices Work?

- Vape devices are powered by a battery, which activates a heating element
- This heating element heats the vape “juice,” vaporizing it and allowing it to be breathed in through the mouthpiece
- Cartridges can be changed out, and may contain nicotine, THC, and/or CBD, and flavors, among other chemicals

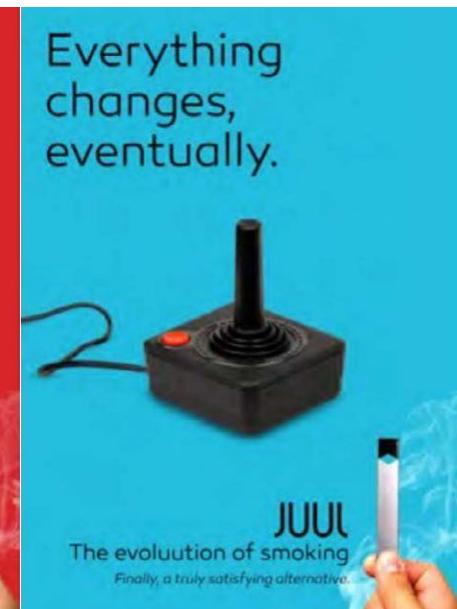


What Are the Ingredients Found in E-Cigarette Solutions (E-Juice)?

- Humectant (propylene glycol and glycerin)
- Flavoring
- Nicotine (can be present even when listed as 0 mg/ml)
- Toxicants
- Carcinogens
- Cytotoxic metallic nano-particles (from the coil/heating element)
- Silicates
- Other psychoactive ingredients (added by users)

Initially Designed To Be a Safer Alternative to Smoking

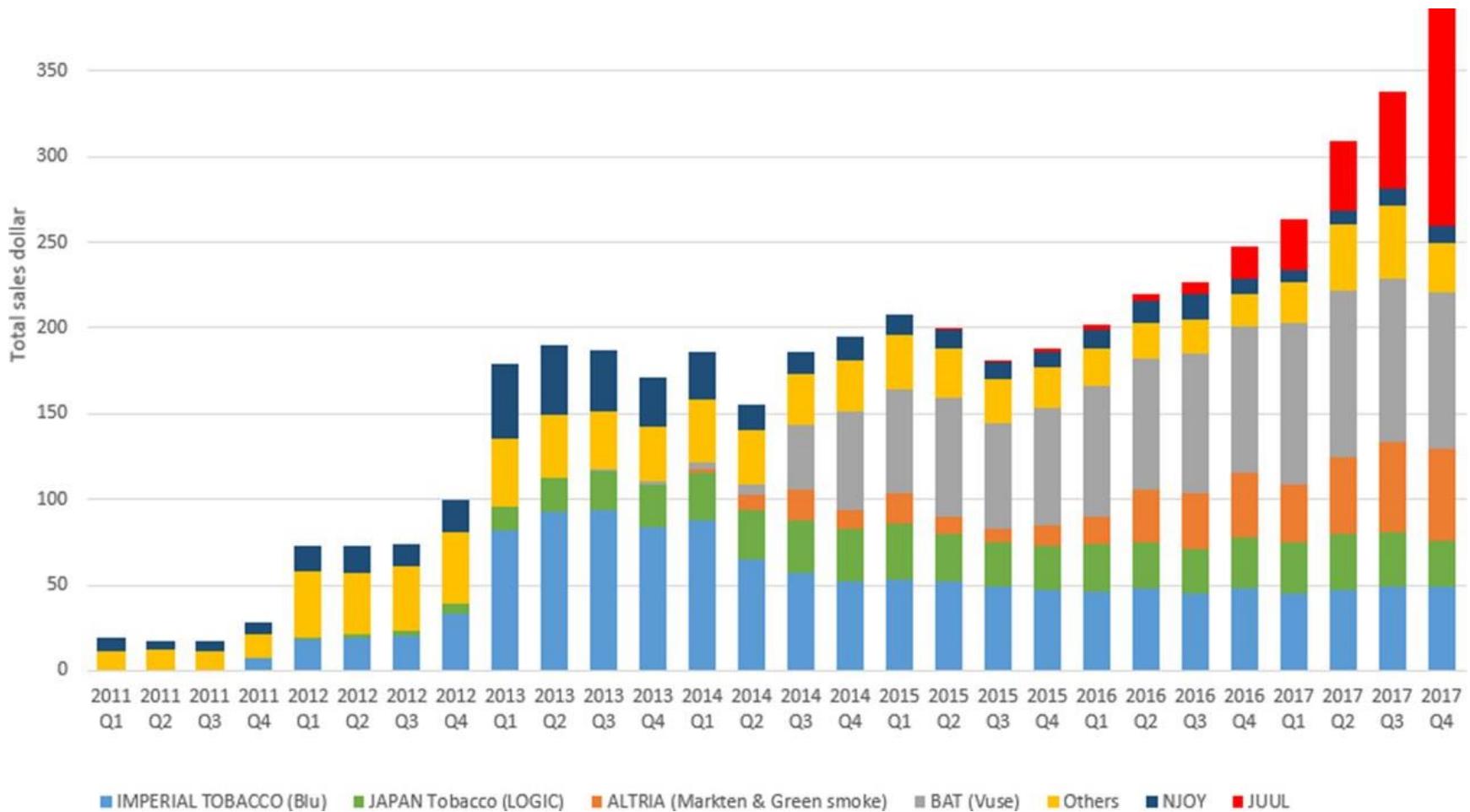
- JUUL initially hired a marketing firm, Cult Collective, which targeted branding for adult smokers and framed JUUL as a technology company
- This marketing strategy contained images of old technology next to a JUUL, with the slogans “Everything changes, eventually” and “The evolution of smoking”
- JUUL rejected this campaign in favor of “Vaporized,” their campaign marketing JUUL as a cool lifestyle product, featuring bright colors and young models



Instead, Marketed to Youth



\$6.6 BILLION Industry Since 2007

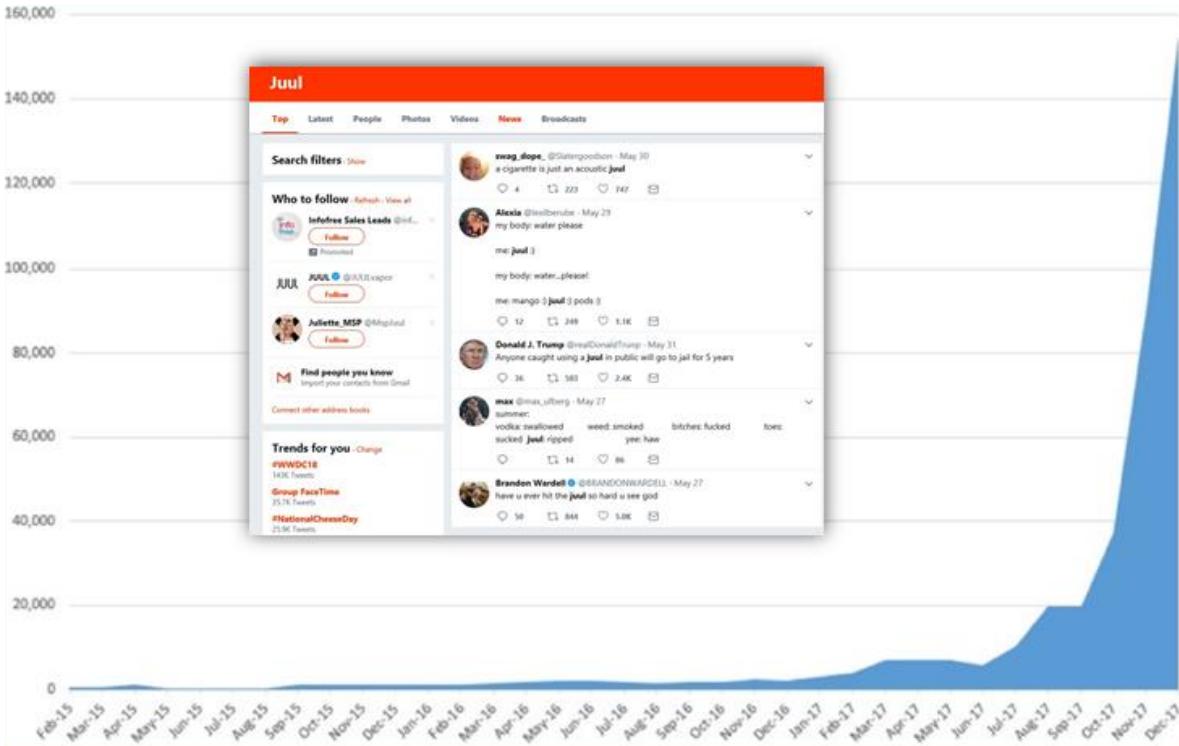


Jidong Huang et al. Tob Control doi:10.1136/tobaccocontrol-2018-054382

Social Media Has Fueled This Fire



Number of JUUL-related Tweets on Twitter 2015- 2017



Source: Huang J, Duan Z, Kwok J, et al Vaping versus JUULing: how the extraordinary growth and marketing of JUUL transformed the US retail e-cigarette market *Tobacco Control* Published Online First: 31 May 2018. doi: 10.1136/tobaccocontrol-2018-054382



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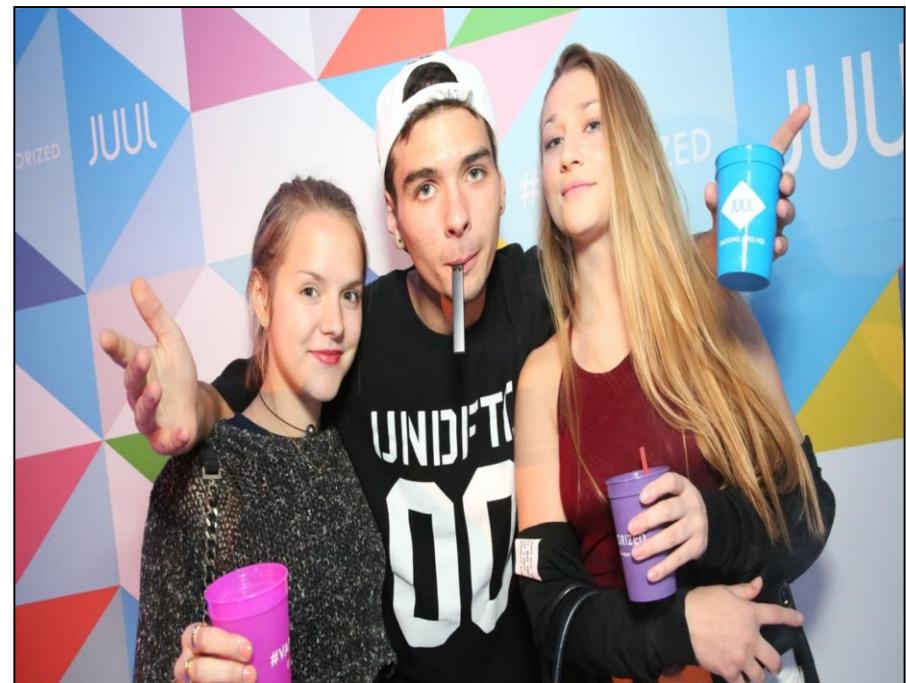
Social Media Has Fueled This Fire

JUUL  @JUULvapor · 4 Jun 2015
Having way too much fun at the #JUUL launch party #LightsCameraVapor #NYC



Q T 1 M

June 4, 2015 <https://twitter.com/JUULvapor/status/606656253885038592>



<http://ads.gawkerassets.com/creative/ads/live/Juul/Launch%20Party/carousel/carousel.html>

What Are The Health Harms of Vaping?

- Relative to smoked tobacco, **less harmful**
- Relative to NO tobacco or medical NRT:
 - Growing concerns for decreased lung function (aldehydes)
 - Poor quality control – explosions, anti-freeze
 - Safety of flavor when heated and inhaled is unknown
- Real hazards of nicotine and toxins to bystanders
- Non- and former smokers may become addicted
- Renormalizing and glamourizing “smoking”
- Poisoning risk to children
- May decrease chances of quitting tobacco—vape when you can’t smoke

Nicotine is Highly Addictive

- Nicotine binds to nAChRs, which leads to the release of dopamine in the brain
- Dopamine signals a pleasurable experience to the brain, which reinforces the behavior and can cause the user to become addicted
- Smoking and vaping are highly efficient methods of use, delivering nicotine to the brain almost instantaneously, and rapidly inducing reward
- Repeated nicotine use quickly builds tolerance and induces withdrawal when not using, further reinforcing the addiction cycle of nicotine

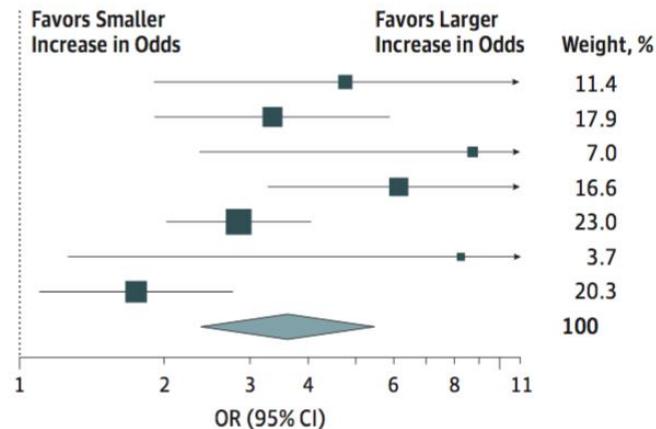
E-Cigarettes: A Gateway?

Figure 2. Meta-analysis of Adjusted Odds of Cigarette Smoking Initiation Among Never Cigarette Smokers at Baseline and Ever e-Cigarette Users at Baseline Compared With Never e-Cigarette Users at Baseline

Source	Probability of Cigarette Smoking Initiation, %		Unadjusted OR (95% CI)	Adjusted OR (95% CI)
	Ever e-Cigarette Users	Never e-Cigarette Users		
Miech et al, ¹⁰ 2017	31.1	6.8	6.23 (1.57-24.63)	4.78 (1.91-11.96)
Spindle et al, ⁹ 2017	29.4	10.6	3.50 (2.41-5.09)	3.37 (1.91-5.94)
Primack et al, ²² 2016	37.5	9.0	6.06 (2.15-17.10)	8.80 (2.37-32.69)
Barrington-Trimis et al, ⁸ 2016	40.4	10.5	5.76 (3.12-10.66)	6.17 (3.29-11.57)
Wills et al, ⁷ 2016	19.5	5.4	4.25 (2.74-6.61)	2.87 (2.03-4.05)
Primack et al, ⁶ 2015	37.5	9.6	5.66 (1.99-16.07)	8.30 (1.19-58.00)
Leventhal et al, ⁵ 2015	31.8	5.6	7.78 (6.15-9.84)	1.75 (1.10-2.78)
Total	30.4	7.9	5.12 (4.41-5.95)	3.62 (2.42-5.41)

Heterogeneity: $\tau^2=0.15$; $Q_6=15.04$; $P=.02$; $I^2=60\%$

Test for overall effect: $z=6.25$; $P<.001$



The odds ratios (OR) for the studies^{5-10,22} are adjusted for a study-specific set of demographic, psychosocial, and behavioral risk factors. The size of the point estimate (black square) is proportional to the weight of the study in the

random-effects meta-analysis model. The weights add to 99.9% and not 100% because of rounding. Q indicates Cochrane Q.

Association with Other Substance Use

- Animal studies show that nicotine primes for other substances, increasing vulnerability to drug effects and addictive liability
- Effects are unidirectional
- In our data, we see that high school students who vape have 25-40 times greater odds of using marijuana or alcohol regularly than non-users
 - Same odds for daily vapers and daily smokers
- Not surprising as a single vaporizing device can be used to consume multiple products via switching cartridges to use cannabis concentrates that can exceed potencies of dried cannabis by 4 to 30 times

Vaping Related Lung Injury: An Epidemic of Severe Respiratory Distress

With acute, severe lung illness rising, often in healthy youth, health investigators call this an epidemic, warn people to stop vaping

- 2,807 vaping-related lung injury cases in 50 states, the District of Columbia, and two U.S. territories
- 68 deaths in 29 states and the District of Columbia
- Many in otherwise healthy young people
 - 15% of cases in those younger than 18
 - 76% have been under age 35

Vaping Related Lung Injury: An Epidemic of Severe Respiratory Distress

- Definitive cause unknown
 - ~80% used THC-containing vapes 30% exclusively THC, 'dank vapes' common, vitamin E acetate diluent
 - ~60% used nicotine-containing vapes 10% exclusively nicotine, JUUL most common
 - ~20% involved CBD-containing vapes
 - Mixing of multiple primary ingredients, contaminants, and heat may produce new compounds that may be toxic
 - A specific device, type of vaping liquid, flavoring, frequency or pattern of use may be important

Vaping Related Lung Injury: An Epidemic of Severe Respiratory Distress

- Shortness of breath most common chief complaint
 - Progressive dyspnea, hypoxemia
 - Cough, fatigue, GI symptoms: nausea/vomiting/diarrhea, fever/chills/weight loss
 - History positive for vaping in past 90 days, 94% within one week of hospitalization
- Bilateral infiltrates on Chest Imaging: 'ground glass opacities'
 - Oxygenation compromised
 - ICU for respiratory failure common
 - Intubation and mechanical ventilation in one third of cases, ECMO
- Extensive infectious, rheumatologic and oncologic workups negative
 - Lipid pneumonia?
 - Acute Toxic Lung Injury: Pathology resembles severe chemical injury with dense infiltrate



Layden et al, NEJM 2019

Public Health Harm: Renormalizing Smoking

- Allowed in places where smoking is not allowed
- Advertising is completely unrestricted, with TV ads for the first time since 1971
- Advertising is indistinguishable from cigarettes



Cigarette and Vape Ads: Strikingly Similar



Cigarette and Vape Ads: Strikingly Similar



King, 16 mg "tar", 11 mg nicotine av. per cigarette by FTC method
© 2016 JUUL Labs, Inc.
SURGEON GENERAL'S WARNING: Smoking By Pregnant Women May Result in Fetal Injury, Premature Birth, And Low Birth Weight.



#SMOKINGEV

JUULva

Cigarette and Vape Ads: Strikingly Similar

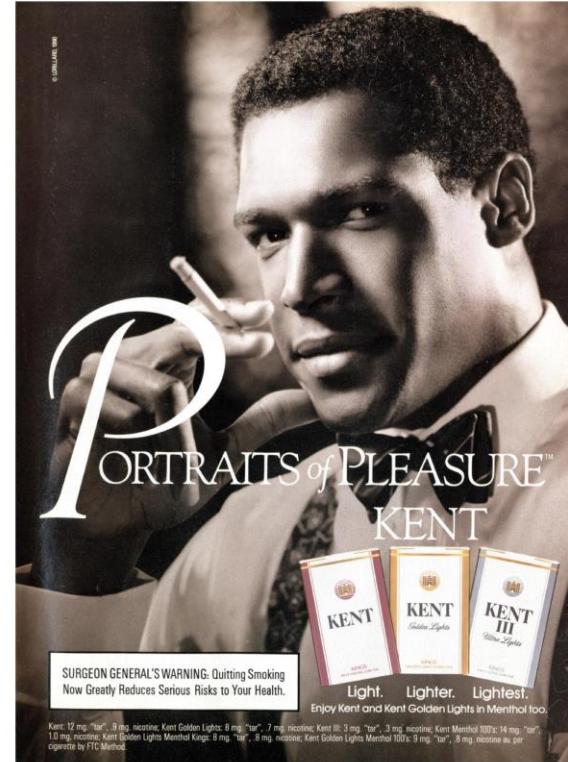
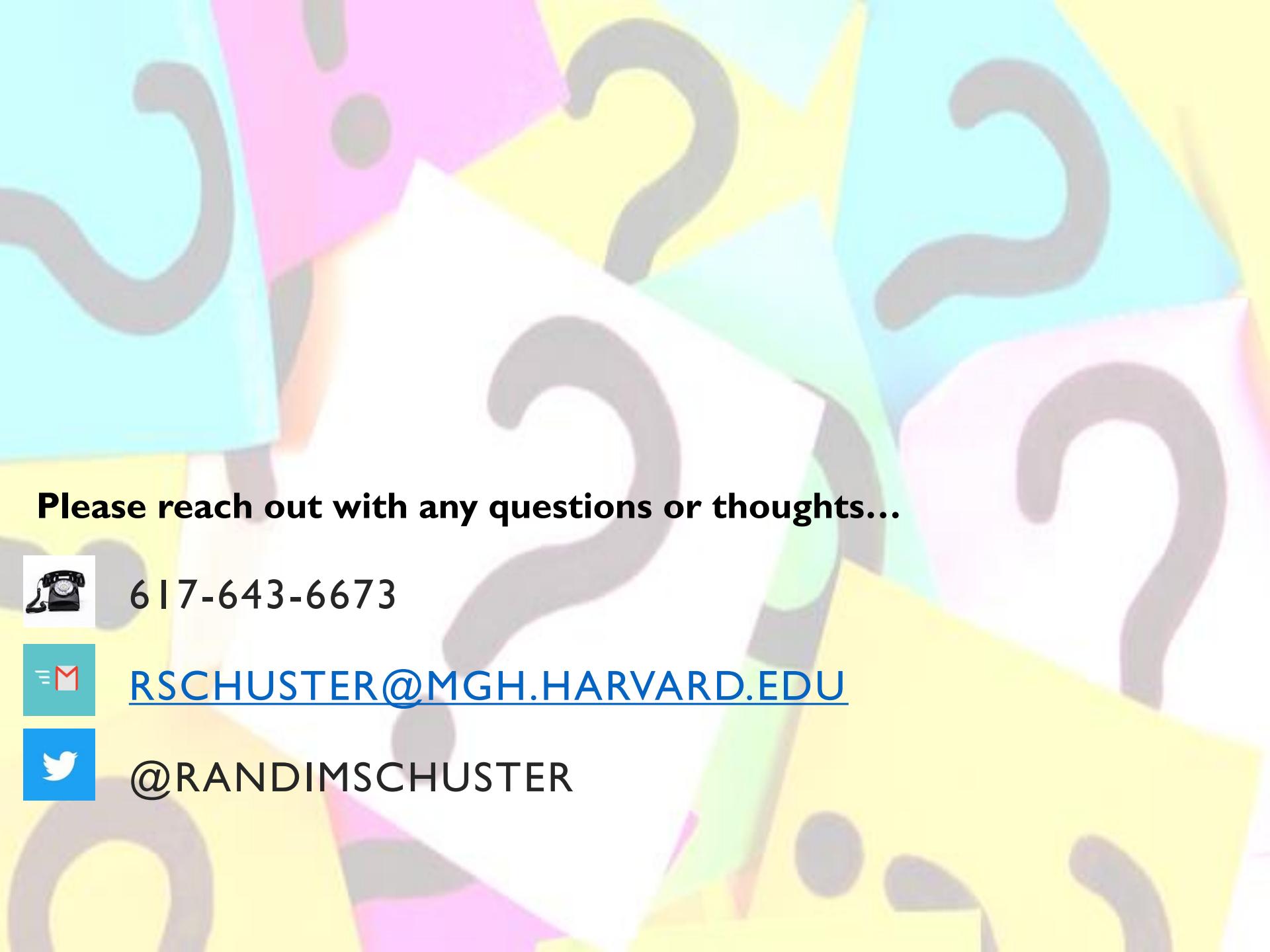


Image credit: <https://www.dispatch.com/news/20191118/vape-companies-borrow-from-big-tobacco-ad-playbook/1>

www.mghcme.org



Please reach out with any questions or thoughts...



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