Presenter's Bio

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Dr. Michael Ong is Professor in Residence of Medicine & Public Health at UCLA and the Associate Chief of Staff for Research and Development at the VA Greater Los Angeles Health Care System. His research has focused on health system-based care, technology evaluation, mental health, and tobacco control.

Dr. Ong was previously the Hospitalist Chief at the VA Greater Los Angeles Health Care System from 2018-2022. He has been Chair of the State of California Tobacco Education and Research Oversight Committee since 2009, which, among other activities, oversees the California Tobacco Control Program.

Vaping:
What Providers Should Know

Saturday, October 1, 2022

Directly Provided CME/CE Activity by L.A. Care Health Plan

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Disclosures

The following CME planners and faculty do not have relevant financial relationships with ineligible companies:

- Leilanie Mercurio, L.A. Care PCE Program Manager, CME Planner
- Alex Li, MD, L.A. Care Deputy Chief Medical Officer, CME Planner
- Michael Brodsky, MD, L.A. Care Senior Medical Director, Behavioral Health Department, CME Planner
- Michael Ong, MD, PhD, Professor in Residence of Medicine & Public Health at UCLA and Associate Chief of Staff for Research and Development, VA Greater Los Angeles Health Care System, CME Planner and Faculty

An ineligible company is any entity whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

Commercial support was not received for this CME activity.

Learning Objectives:

- Recognize prevalence of vaping and products used for vaping.
- Discuss vaping and potential for tobacco cessation.
- Examine, identify and list physical health effects related to vaping, including e-cigarette and vaping-induced acute lung injury.
- Summarize behavioral and brain health effects related to vaping, including addiction and adolescent brain development.

Surgeon General: e-cigarette youth epidemic

- E-cigarette use among high school students increased from 1.5% in 2011 to 11.7% in 2017
- Current e-cigarette use among high school students rose from 11.7% in 2017 to 20.8% in 2018
- Current e-cigarette use among high school students is now at 11.3% in 2021.
  - Current cigarette use among high school students is now at 1.9% in 2021.

"I am officially declaring e-cigarette use among youth an epidemic in the United States"
Surgeon General Jerome Adams
December 2018

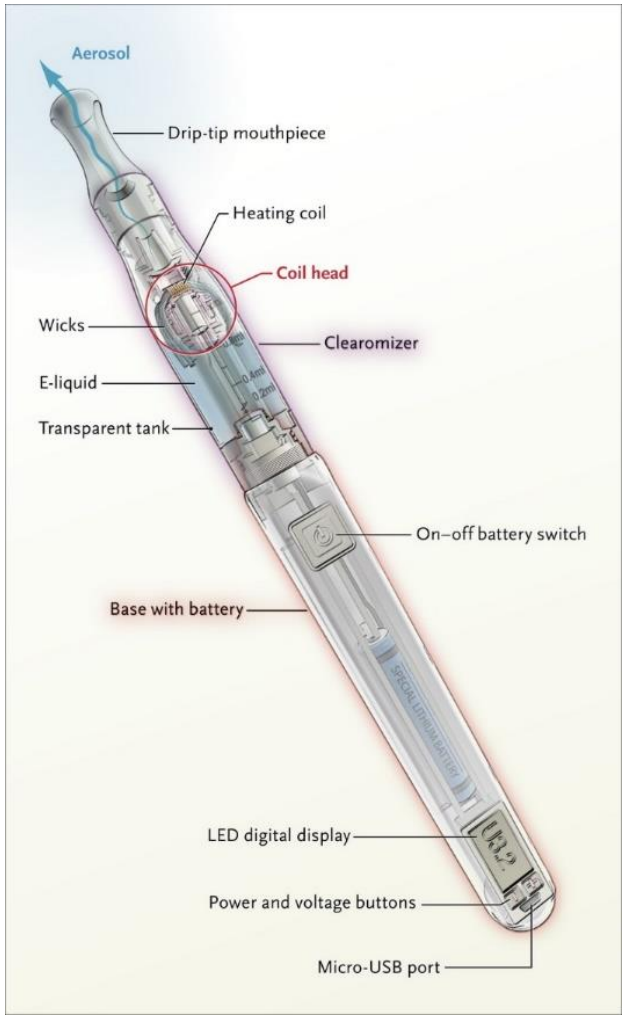
Wang et al., MMWR, 2018;
Cullen et al., MMWR, 2018;
Gentzke et al., MMWR, 2022

Question 1: What is this?

Question 1: What is this? Vaping

Product
Disposable e-cigarette 
Rechargeable e-cigarette 
Pen-style, medium-sized rechargeable e-cigarette 
Tank-style, large-sized rechargeable e-cigarette 

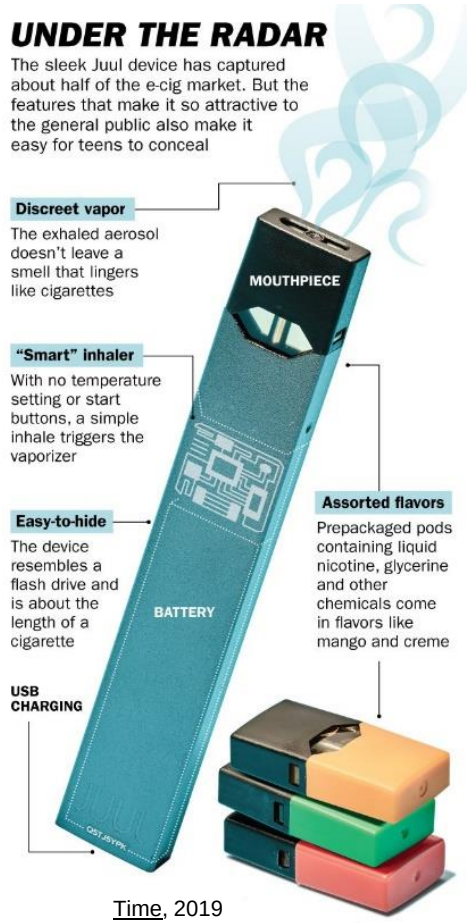
- AKA e-cigarettes
  - Electronic nicotine delivery systems (ENDS)
  - Combination of disposable nicotine cartridge and aerosolizing device
- US FDA classified as “tobacco product” April 2011
  - Manufacturers finally submitted premarket tobacco product applications Sept 2020
    - >6 million applications received
    - To date 8 products have been approved to be marketed



Dinakar & O’Connor, NEJM, 2016; MMWR, 2016; Grana et al, Circulation, 2014; FDA, 2022

Question 1: What is this? JUUL

- Introduced 2015, dominated e-cigarette market
  - Appeal of USB lookalike device, easy to hide
- Nicotine salt concentrated formulation
  - One pod = 20 cigarettes
  - A standard 5% JUUL pod use a concentrated nicotine salt formulation so that a standard JUUL pod nicotine content is 59 mg/mL of nicotine, or about 40 mg of nicotine
- Multiplicity of Pods
  - Multiple flavors: Mango, fruit, mint were top flavors prior to flavored sales restriction
  - Non JUUL pods, including THC-filled pods
- December 2018: Altria (U.S. spinoff of Phillip Morris) purchased 35% stake in company

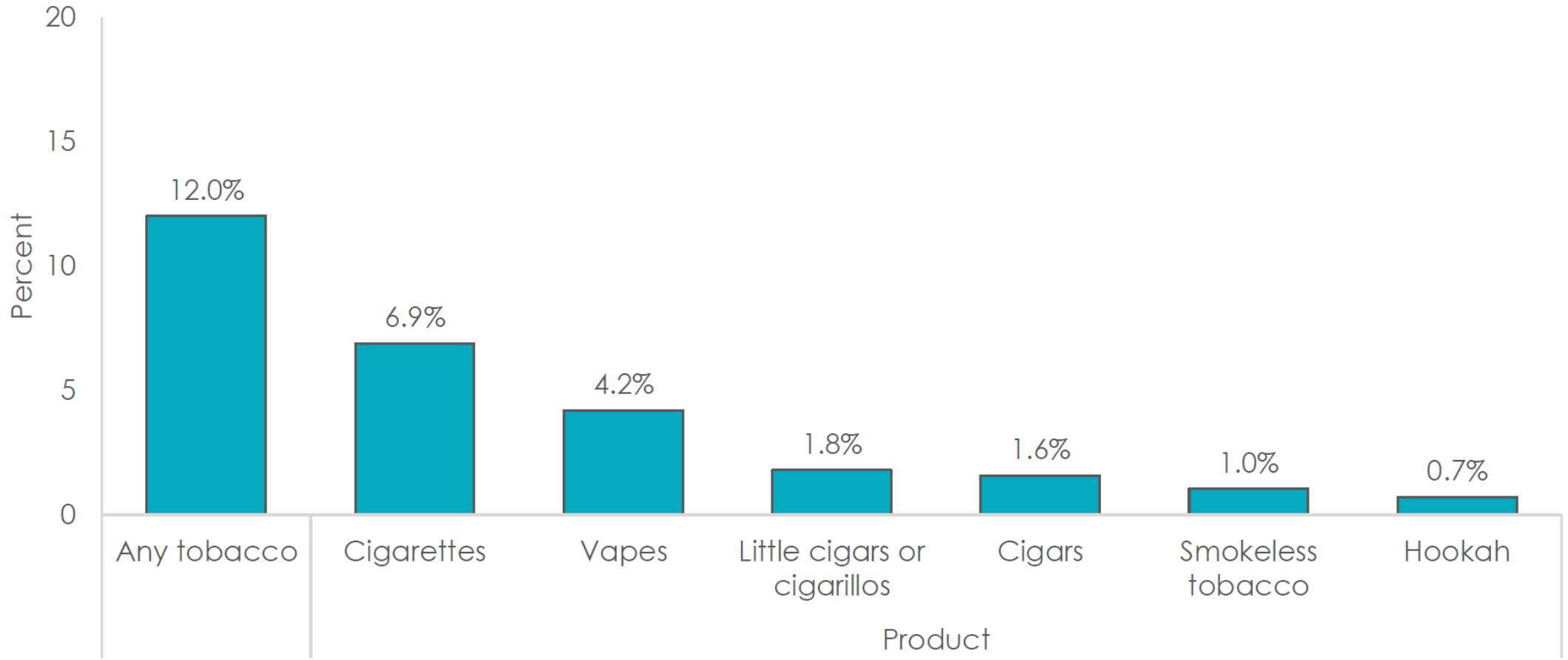


Time, 2019

Question 1: What is this? Other products

- IQOS and VUSE
  - Heat-not-burn products
  - IQOS has been authorized by FDA as modified risk tobacco product in 2020
    - Indicates that it has lower risks compared to cigarettes due to not generating carcinogens from burning tobacco
  - Other modified risk tobacco products are Swedish Match snus and very low nicotine cigarettes from 22nd Century Group

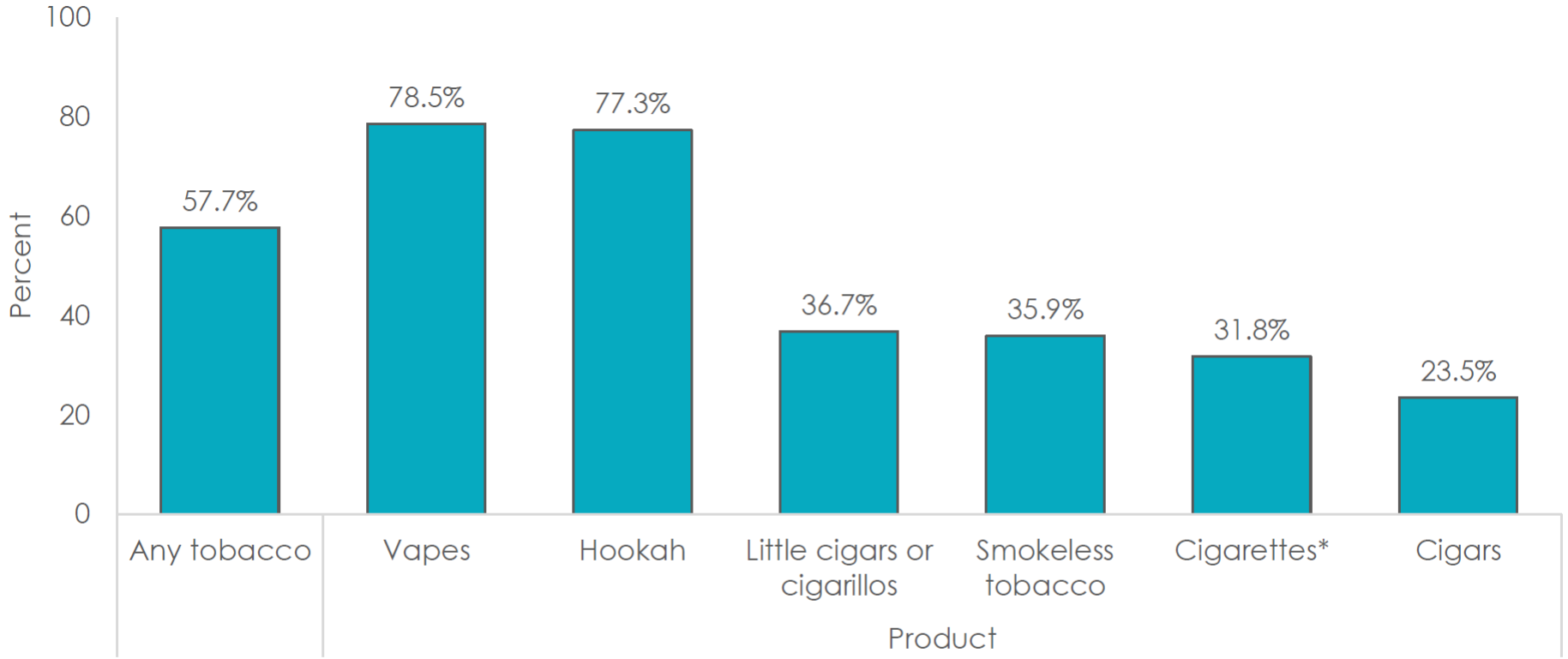
Prevalence of Vaping Among California Adults



Tobacco use includes cigarettes, cigars, hookah, little cigars or cigarillos, smokeless tobacco, or vapes. See Additional Notes section for more information.

Source: California Health Interview Survey. CHIS 2019 Adult Files. Los Angeles, CA: UCLA Center for Health Policy Research; October 2020.

Prevalence of Flavored Vaping Products Among California Adults

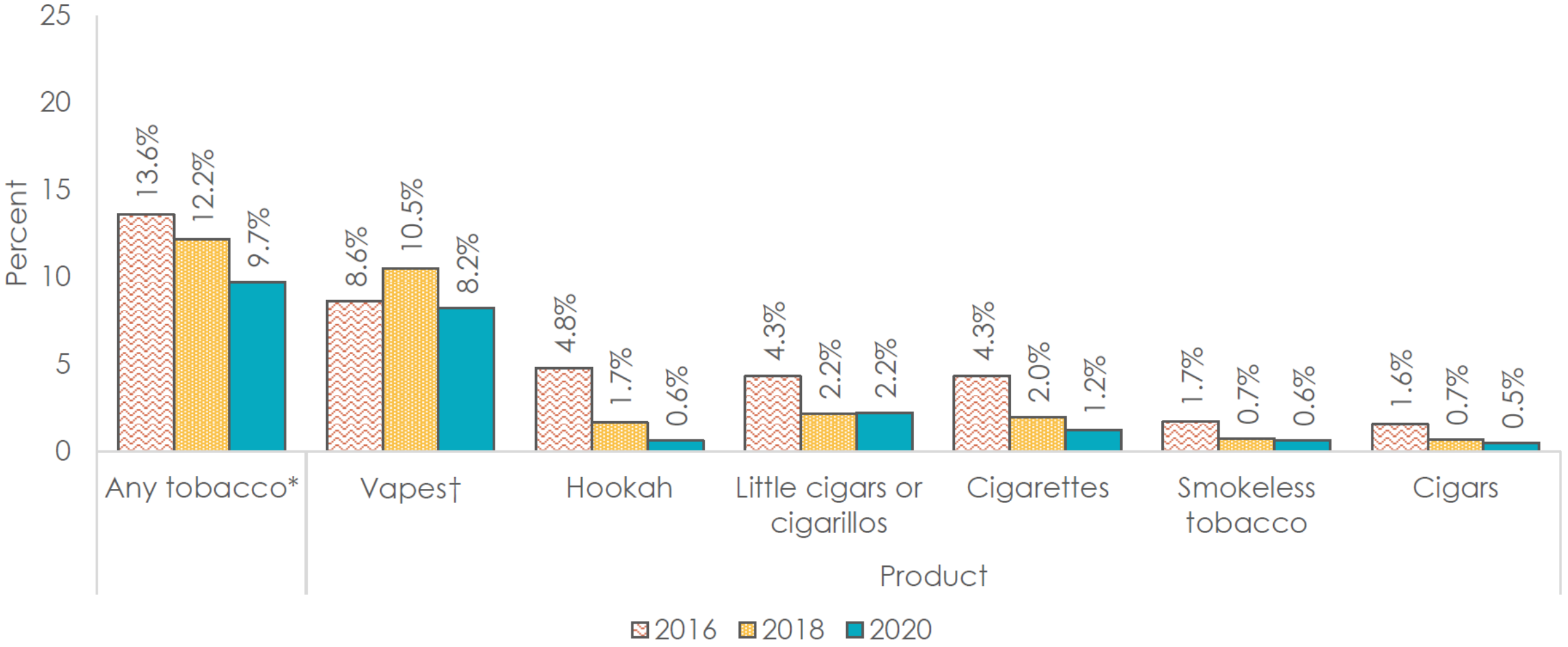


Tobacco use includes cigarettes, cigars, hookah, little cigars or cigarillos, smokeless tobacco, or vapes. See Additional Notes section for more information.

* The question used to assess menthol cigarette use was based on usual use and not any use.

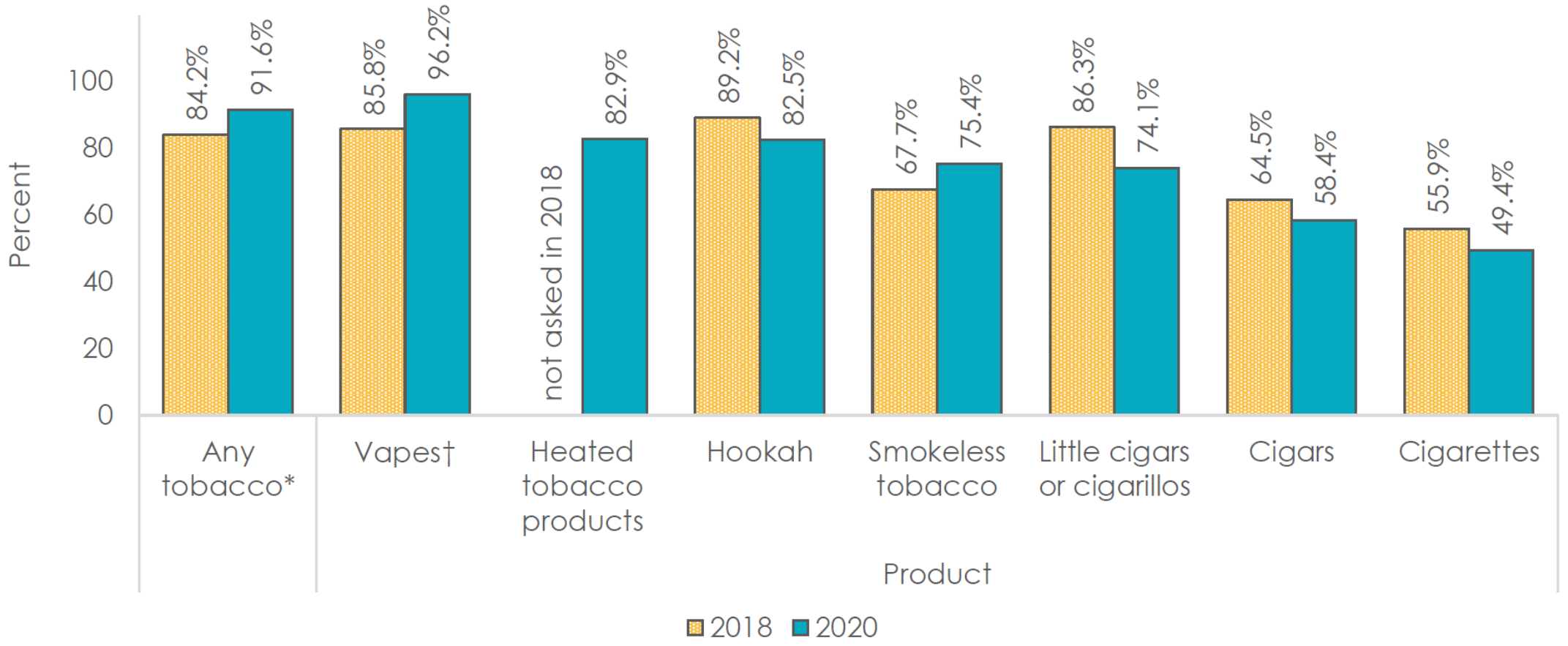
Source: California Health Interview Survey. CHIS 2019 Adult Files. Los Angeles, CA: UCLA Center for Health Policy Research; October 2020.

Prevalence of Vaping Among California Youth



Source: California Student Tobacco Survey. CSTS 2016 to CSTS 2020. San Diego, CA: University of California, San Diego, Center for Research and Intervention in Tobacco Control; 2021.

Prevalence of Flavored Vaping Products Among California Youth



Source: California Student Tobacco Survey. CSTS 2016 to CSTS 2020. San Diego, CA: University of California, San Diego, Center for Research and Intervention in Tobacco Control; 2021.

Question 2: Can vaping help a smoker quit?

Question 2: Can vaping help a smoker quit?

- Ongoing debate whether these could be used for cessation or harm reduction products
  - USPSTF 2015 review: insufficient evidence to recommend for cessation
    - Meta-analysis published in 2016 shows reduced likelihood of quitting (OR 0.72) if using electronic cigarettes
    - Observational U.S. study published in 2018 showed reduced likelihood of quitting (OR 0.30) for those using electronic cigarettes.
  - Should we focus on cessation or transfer to products with “safer” profile?
    - Don’t we have these already with NRT?

Siu et al. Ann Intern Med, 2015; Patnode et al., Ann Intern Med, 2015; Kalkoran & Glantz, Lancet Resp Med, 2016; Weaver et al., PLOS ONE, 2018; Grana et al., Circulation, 2014; Benowitz & Goniewicz, JAMA, 2013

Question 2: Can vaping help a smoker quit?

- Randomized Controlled Clinical Trials (RCT) at UK free smoking cessation clinics
  - 886 patients randomized to e-cigarette or Nicotine-Replacement Therapy (NRT)
  - 1 year abstinence rate from smoking
    - E-cigarette: 18.0%
    - NRT: 9.9%
  - Of those who quit in each arm, 80% still using e-cigarettes, 4% still using NRT
  - 1 year abstinence rate from nicotine
    - E-cigarette: 3.7%
    - NRT: 9.0%

Hayek et al, NEJM, 2019

Question 3 & 4: Is vaping safe?

Question 3: Is vaping safe? Physical Health

- Nicotine has an LD_{50}
  - Amount for humans is anecdotal
  - Increase in poisoning exposure cases from 2010-2018
  - Nicotine has cardiovascular effects

- Generated vapor is not just water vapor due to additives
  - Propylene glycol and glycerin are common additives
  - Flavorings are also common additives
  - When heated, these products can generate volatile organic compounds that are carcinogenic

Mayer, Arch Toxicol 2014; Wang et al., Clin Toxicol 2020; Benowitz & Burbank, Trends in Cardiovascular Med, 2016; Sassano et al. PLOS Biology, 2018; Sleiman et al., Environmental Science & Technology, 2016; Allen et al., Environmental Health Perspectives, 2016

Question 3: Is vaping safe? Physical Health

Chapter 5: Nicotine

1. The evidence is sufficient to infer that at high-enough doses nicotine has acute toxicity.

2. The evidence is sufficient to infer that nicotine activates multiple biological pathways through which smoking increases risk for disease.

3. The evidence is sufficient to infer that nicotine exposure during fetal development, a critical window for brain development, has lasting adverse consequences for brain development.

4. The evidence is sufficient to infer that nicotine adversely affects maternal and fetal health during pregnancy, contributing to multiple adverse outcomes such as preterm delivery and stillbirth.

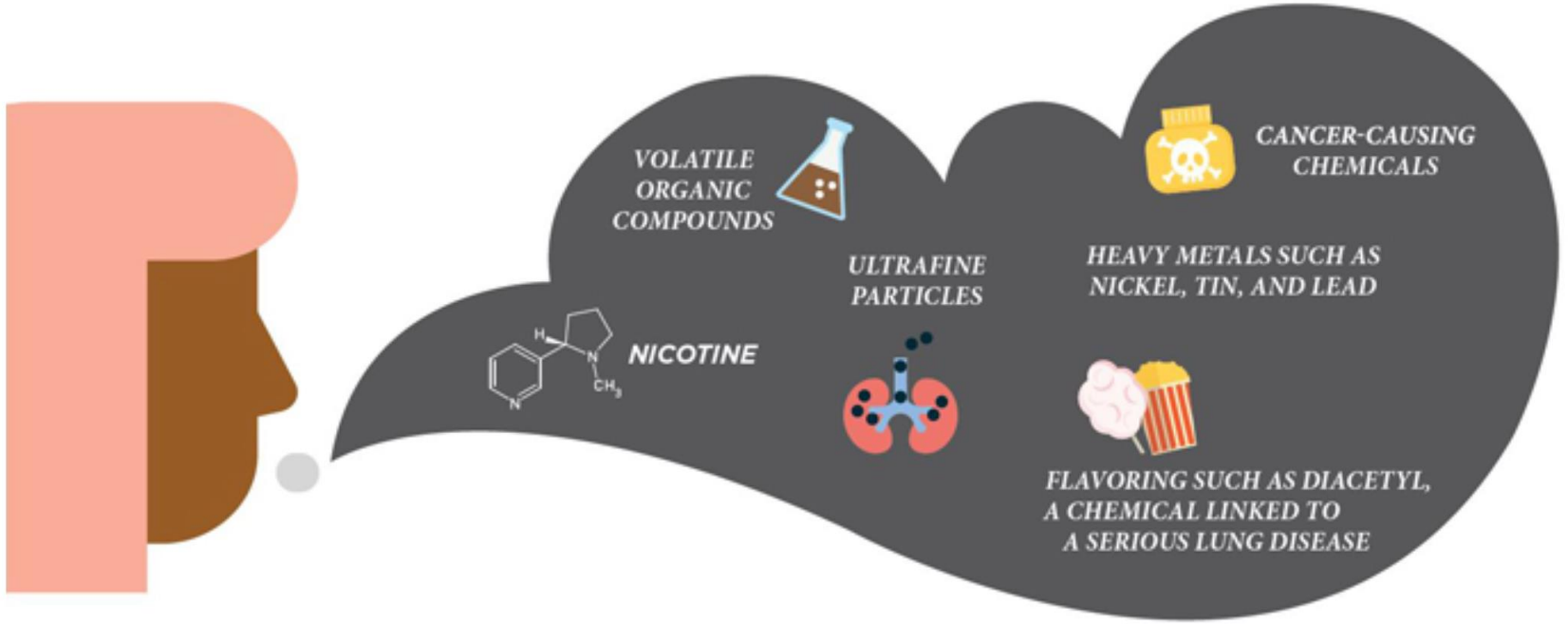
- Nicotine and Disease Risk
  - "The potential role of nicotine in atherogenesis and in triggering acute coronary eents has been discussed extensively in the medical literature"
  - "there is compelling evidence that nicotine affects cellular immunity"
  - "Smoking has been linked to diverse adverse health outcomes for the developing fetus and … nicotine specifically has a role in causing them"

Surgeon General Report 2014: The Health Consequences of Smoking

Question 3: Is vaping safe? Physical Health

Secondhand vaping can include

- Nicotine
- Ultrafine particles that can be inhaled deep into the lungs
- Flavorings such as diacetyl, a chemical linked to a serious lung disease
- Volatile organic compounds
- Cancer-causing chemicals
- Heavy metals such as nickel, tin, and lead

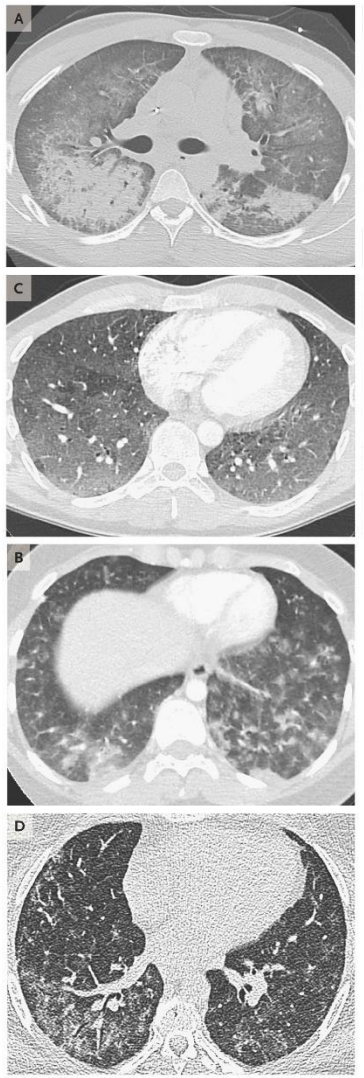


Marynak et al, American Journal of Public Health, 2017, CDC.gov

Question 3: Is vaping safe? EVALI

E-Cigarette and/or Vaping Product Associated Lung Injury (EVALI)

- First reported by CDC in August 2019
- 2,807 cases and 68 deaths through February 18, 2020
- 95% cases hospitalized (of 2,016 cases through November 5)
- Median age 24, deaths generally among older individuals (median age 53)
  - 2% of all EVALI patients were aged 65-75 years, 24% of deaths
  - Age range 17-75



Moritz et al, MMWR 2019, Henry et al., NEJM, 2019

https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html

Question 3: Is vaping safe? EVALI

- EVALI: Diagnosis of exclusion
- 83% associated with THC use
  - 35% THC use only
- 61% nicotine use
  - 13% nicotine only
- 48% both THC/nicotine use
  - 4% no THC/nicotine use
- Based on 1,184 cases through 11/5 with complete information on substances used

https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html

Cummings, CDPH, 2019

Case definition: confirmed vs. probable

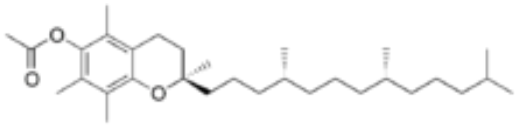
Confirmed	Probable
Respiratory illness requiring hospitalization	
Using an e-cigarette ("vaping") or dabbing* in 90 days prior to symptom onset	
Pulmonary infiltrate (such as opacities on plain film chest radiograph or ground-glass opacities on chest CT)	

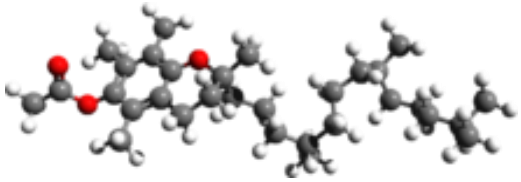
Absence of pulmonary infection on initial workup
Minimum criteria:
• Negative respiratory viral panel and influenza PCR rapid test.
• All other clinically indicated respiratory ID testing must be negative. E.g.:
  ▪ Urine strep pneumo/legionella/mycoplasma
  ▪ Sputum culture if productive cough
  ▪ BAL culture if done, blood culture
  ▪ HIV-related opportunistic respiratory infections if appropriate
	Infection identified by culture or PCR but clinical team believes this is not the sole cause of the underlying respiratory disease process
	-OR-
	No evidence of pulmonary infection but minimum criteria to rule out pulmonary infection not performed.

No evidence in medical record of alternative plausible diagnosis (e.g., cardiac, rheumatologic, or neoplastic process)	

Question 3: Is vaping safe? EVALI

- No single compound or ingredient emerged as the cause of EVALI
  - Not just THC: some cases are nicotine only, some with no THC/nicotine, but based on self report
  - Not much residue to test in used devices
- Vitamin E acetate: Ester of vitamin E (alpha-tocopherol) and acetic acid
  - Used in dermatologic preparations, antioxidant effects
  - Used as thickening agent for THC vaping devices
  - Associated with BAL fluid of 48/51 EVALI patients
- Multiple problems?
  - Additive? Vitamin E associated with some but not all cases
  - Different patterns of injury – chemical burn vs. lipoid pneumonia
  - Product? Multiple products used





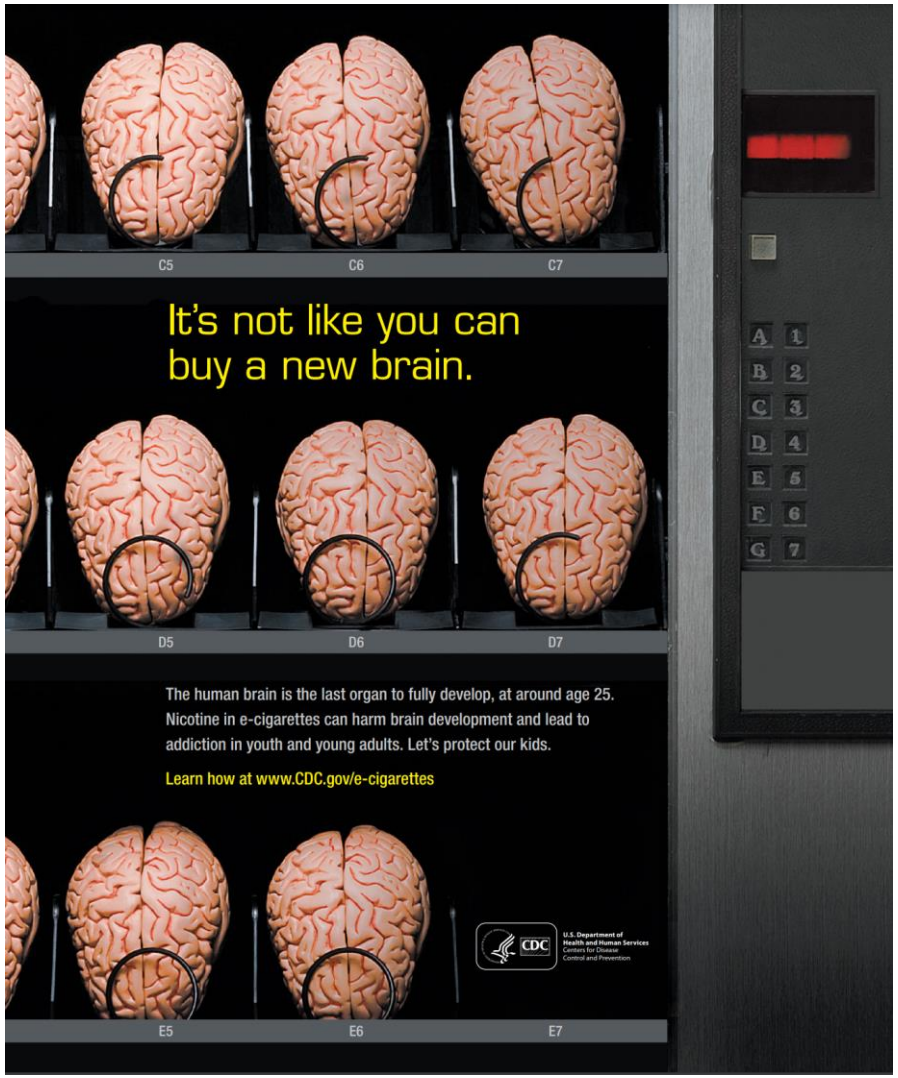
Blount et al., NEJM, 2020

https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html

Question 3: Is vaping safe? Mental Health

Chapter 5: Nicotine

5. The evidence is suggestive that nicotine exposure during adolescence, a critical window for brain development, may have lasting adverse consequences for brain development.

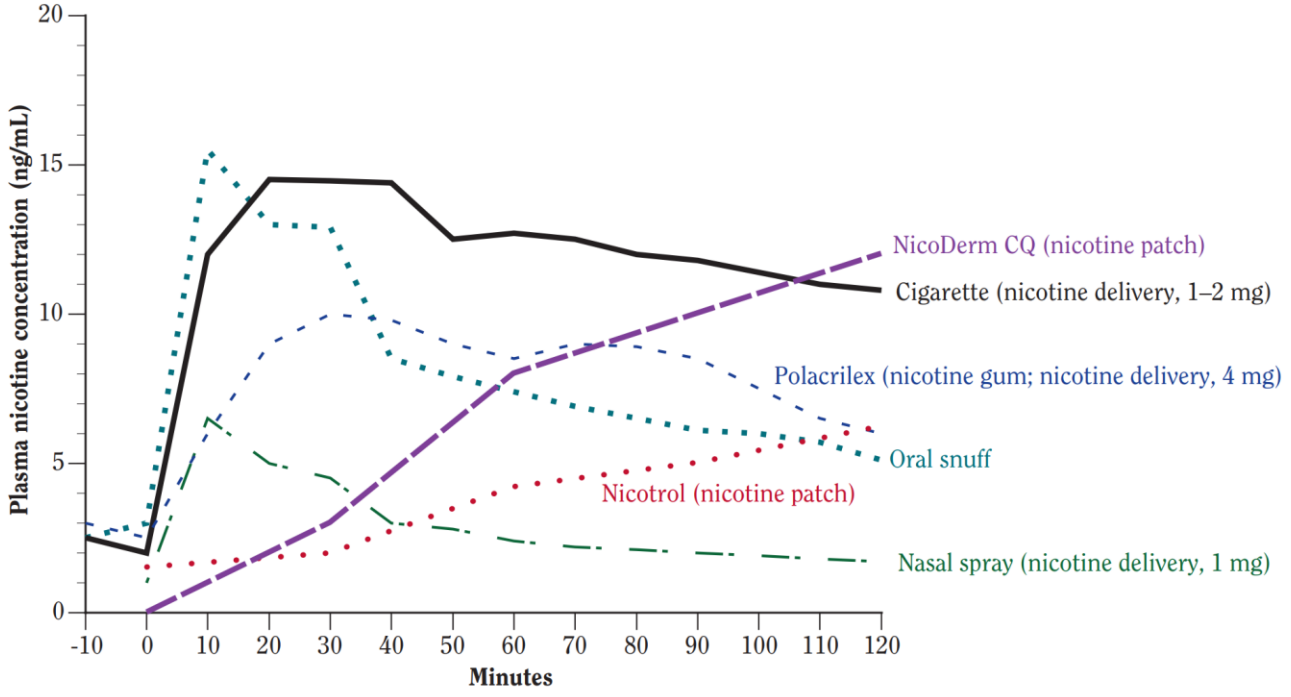


Surgeon General Report 2014: The Health Consequences of Smoking

Question 4: Is vaping safe? Mental Health

- Nicotine addiction
  - Nicotine binds to nAChR
  - Widespread release of neurotransmitters, particularly dopamine in ventral tegmental area, nucleus accumbens, prefrontal cortex

- Longitudinal research shows that addiction (transition to regular smoking) happens with nicotine from 100 cigarettes



Source: Adapted from Fant et al. 1999 with permission from Elsevier, ©1999.
Note: **mg** = milligrams; **ng/mL** = nanograms per milliliter.

Surgeon General Report 2014: The Health Consequences of Smoking

Question 4: Is vaping safe? Mental Health

- Smoking during adolescence
  - Lasting cognitive and behavioral impairments including effects on working memory and attention
  - Functional MRI show reduced prefrontal cortex activation during attentional tasks when compared with nonsmoking controls
    - Diminished activity correlates with duration of smoking

- Animal studies for mechanisms
  - Nicotine induces changes in gene expression in the brain to a greater degree during adolescent exposure vs at other times
  - Persistent upregulation of nAChRs in midbrain, cerebral cortex, and hippocampus

Goriunova & Mansvelder, Cold Spring Harbor Perspectives in Medicine 2012, Musso et al, Psychopharmacology 2007; Surgeon General Report 2014: The Health Consequences of Smoking

So: How do you quit vaping?

So: How do you quit vaping?

- No RCT data on vaping cessation
- Most studies focus on behavioral assistance, particularly for youth
- Pharmacotherapy should be beneficial, use in youth not well studied
  - Nicotine Replacement Therapy
    - Gum, patch, lozenge, nasal spray, inhaler
  - Bupropion
  - Varenicline

Berg et al., Addict Behav, 2021; Hadland & Chadi, Journal of Adolescent Health, 2020

Treating Tobacco Use and Dependence: 2008 Update

So: How do you quit vaping?

- Combination pharmacotherapy recommended for heavy smokers, equivalent nicotine for some vaping devices
- NRT
  - Long-acting formulation (patch) produces relatively constant levels of nicotine
  - Short-acting formulation (gum, lozenge, inhaler, nasal spray) allows for acute dose titration
  - Combination with bupropion or varenicline effective
- Counseling with all medication approaches
  - California has https://novapes.org aka https://kickitca.org/quit-vaping with texting cessation programs, associated with Kick-It California (formerly the California Smokers' Helpline)

So: How do you quit vaping? NRT

Nicotine Gum & Lozenge		
Weeks 1–6	Weeks 7–9	Weeks 10–12
1 piece q 1–2 h	1 piece q 2–4 h	1 piece q 4–8 h

Nicotine Patch	
Light Smoker	**≤10 cigarettes/day** Step 2 (14 mg x 6 weeks) Step 3 (7 mg x 2 weeks)
Heavy Smoker	**>10 cigarettes/day** Step 1 (21 mg x 6 weeks) Step 2 (14 mg x 2 weeks) Step 3 (7 mg x 2 weeks)

So: How do you quit vaping?

- For both bupropion and varenicline: patients should begin therapy 1 to 2 weeks PRIOR to their quit date.

Bupropion	Dose
Day 1 to day 3	150 mg qam
Day 4 to end of treatment*	150 mg bid

* Up to 7 to 12 weeks

Varenicline	Dose
Day 1 to day 3	0.5 mg qd
Day 4 to day 7	0.5 mg bid
Day 8 to end of treatment*	1 mg bid

* Up to 12 weeks

Question 4: How do you quit vaping?

	Standard Dose/Administration[f,g]	Duration
Combination NRT (preferred)	• Begin with 21-mg patch + short-acting NRT[h] ▸ If 21-mg patch is not effective, consider using more than one patch to increase the dose to 35 or 42 mg • Short-acting NRT: 2 or 4 mg ▸ 2 mg preferred if time to first cigarette is >30 minutes after waking; or 4 mg preferred if time to first cigarette is ≤30 minutes after waking ▸ Every 1 h (while awake), or more often as needed	Minimum of 12 weeks of pharmacotherapy is recommended. However, therapy may be substantially extended to promote continued cessation
Varenicline[e] (preferred)	• Initiate dosing 1–6 wks prior to quitting • Days 1–3: 0.5 mg orally, once daily • Days 4–7: 0.5 mg orally, twice daily • Day 8 to end of treatment: 1 mg orally, twice daily (if tolerated) ▸ Consider increase to 3 mg per day (if tolerated) for those who cut back by ≥50% but have not quit at 6 wks ▸ If severe renal impairment (estimated creatinine clearance <30 mL/min): Begin with 0.5 mg once daily and titrate to 0.5 mg twice daily ▸ For patients with end-stage renal disease undergoing hemodialysis, 0.5 mg maximum daily, if tolerated	
Bupropion[e]	• Initiate dosing 1–2 wks prior to quitting • Days 1–3: 150 mg orally, once daily • Day 4 – end of treatment: ▸ Sustained release: 150 mg orally, twice daily, if tolerated; or ▸ Extended release: 300 mg, once daily, if tolerated • Maximum 300 mg per day • Adjust dose or frequency for: ▸ Renal impairment[g] ▸ Hepatic impairment: Maximum dose 150 mg every other day for moderate/severe hepatic impairment (Child-Pugh score 7–15); For mild hepatic impairment (Child-Pugh score 5–6), consider reducing the dose and/or frequency adjustment.	

[e] Same dosing/administration when used in combination with other pharmacotherapy options.
[f] Dose adjustments may be considered if clinically indicated.
[g] See drug labels and full prescribing information for varenicline, bupropion, and NRT products.
[h] Gradually decrease dose over 10 weeks or more. Dose reduction may not be appropriate for patients with limited life expectancy.

Adverse Effects and Contraindications

NCCN, 2021

Vaping Resources

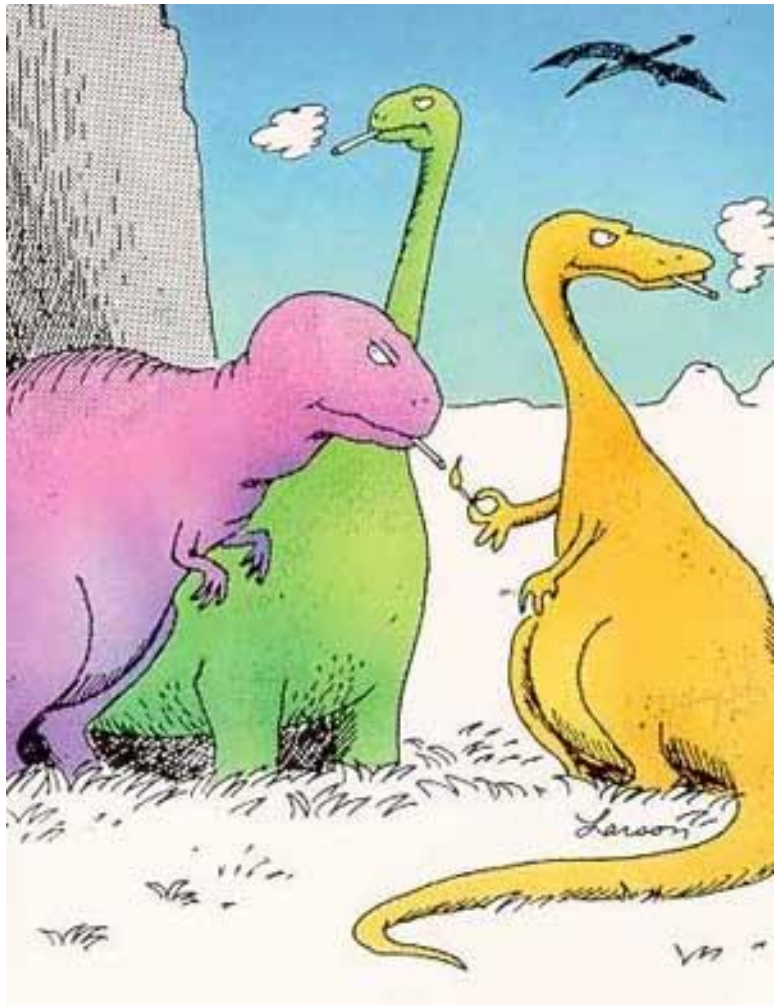
Informational websites on electronic cigarettes / vaping devices

- https://www.cdc.gov/tobacco/basic_information/e-cigarettes/index.htm
- https://www.fda.gov/tobacco-products/products-ingredients-components/e-cigarettes-vapes-and-other-electronic-nicotine-delivery-systems-ends

electronic cigarettes / vaping cessation resources

- https://kickitca.org/quit-vaping

The real reason dinosaurs became extinct….



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