# Juul, Suorin, Vaping-the new nicotine

Asha N. Chesnutt, MD

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# **EVALI**

E-cigarette or Vaping Associated Lung Injury

#### **Disclosures**

I have no disclosures

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#### **New Yorker**

• The Promise of Vaping and the Rise of Juul

Teens have taken a technology that was supposed to help grownups stop smoking and invented a new kind of bad habit, molded in their own image

New Yorker May 14,2018

 "you're expected to Juul, but you're expected to not depend on it. If you're cool then you Juul with other people, and you post about it, so everyone will see that you are social and ironic and funny. But if you are addicted, you go off by yourself and Juul because you need it, and everyone knows."

#### **Outline**

- Terminology of e-cigarette devices
- Chemistry behind the flavorings
- VAPI/EVALI
- Vaping cannabis
- TIMELINE -how did we get here?
- The rise of Juul
- Adolescent vaping

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#### **E-cigarettes**

- The term "electronic cigarettes" covers a wide variety of products like cigarettes, pens or USB drives
- Battery powered devices which heat a solution to create a vapor.
- Heating element is activated electronically which vaporizes the liquid and the vapor condenses to form an aerosol
- NO combustion
- ENDS (electronic nicotine delivery system) contain flavors +/- nicotine

#### Comparison

#### cigarettes

- Carbon monoxide
- Cyanide
- Nicotine
- Formaldehyde
- Arsenic
- Nitrosamines
- Cadmium
- OTHER (Hoffman list)

#### **E-cigarettes**

- Propylene glycol
- Glycerin
- Nicotine
- Water
- Flavorings
- OTHER

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#### Nicotiana tabacum

- Dates back to 1000BC
- Major industry in Europe by 1700



• Harvested then cured



#### **Nicotine**

- Not carcinogenic
- Highly addictive
- Reaches brain within 15 secs of inhalation
- This rapid increase in nicotine levels in the brain, faster than with intravenous administration, leads to activation of the dopaminergic reward system and produces rapid behavioral reinforcement (craving)
- Withdrawal causes anxiety and stress

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#### Combustible cigarettes

- 7000 chemicals in the smoke by lighting tobacco leaves on fire
- >70 known carcinogens
- Average smoker inhales 1-2 mg nicotine/cig
- 10 puffs over the 5 min cigarette is lit
- 1 pack (20 cigs) is 200 hits of nicotine (20-40 mg nicotine)
- Rush followed by feelings of withdrawal (positive feedback)

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#### Chemicals in **Every Tobacco Plant**

It is a fact that cigarettes contain dangerous chemicals.2 But how do these chemicals get into cigarettes? Are most of the harmful chemicals added during the manufacturing process?

Fact: Some of the toxic chemicals in tobacco are present in the plant itself.<sup>3</sup> Watch the tobacco carcinogens occur growth video to uncover



#### Chemicals in **Every Cigarette Product**

Ok, so harmful chemicals are in the tobacco plant. What happens during manufacturing? Is that when more dangerous chemicals are added?

Fact: Not all of the harmful chemicals created cigarette smoke.2 More during cigarette manufacturing are manmade. Some of the naturally as tobacco is cured.3 Watch the video about cigarette manufacturing.

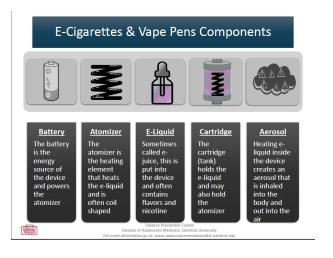


#### Chemicals in **Every Puff of Cigarette Smoke**

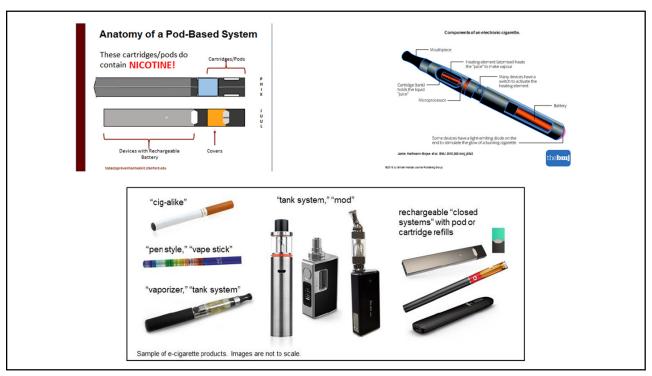
How many harmful and potentially harmful chemicals are in a cigarette? Is there more than nicotine and tar?

Fact: There are more than 7,000 chemicals in than 70 of those chemicals are linked to cancer.4,5,6,7 Watch the video on cigarette smoke to learn more about what happens when you light

# **Terminology**



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#### **Humectants**



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#### Nicotine in E-Liquids

- 27 clinical studies
- Product, nicotine content (16-48mg/ml), puffing protocol, biomarkers
- E Cig Naïve users ecigs deliver lower levels of nicotine c/w combustible tobacco
- Experienced e-cig users ecigs can deliver nicotine in range of combustible cigarettes

#### Flavorings

• Banana: isoamyl acetate

• Cinnamon: cinnamaldehyde

• Almond or cherry: benzaldehyde

• Vanilla: vanillin

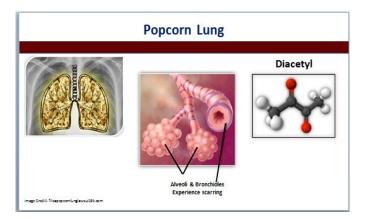
• Butter flavor : diacetyl

• Meant to be eaten not INHALED



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# Diacetyl



# Vape clouds





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## Vaping topography

- Puff duration
- Interpuff interval
- # puffs in a vaping session
- Longer puff duration is associated with higher nicotine yield
- User experience (throat hit)
- 3<sup>rd</sup> generation products (pods) have more watts

#### T3 website (UK lifestyle)

- Vegetable glycerin is a thick, sticky, sweet liquid that produces maximum vapour at the expense of throat grip and flavour.
- higher VG to PG ratios are preferred by ardent cloud chasers
- PG liquid, on the other hand, provides a much better throat hit similar to that of a tobacco cigarette.
- VG50/PG50 mix is best for those who like an intense flavour as well as a throat hit,
- PG20/VG80 provides a much smoother inhale with bigger clouds and a mild flavour.
- Nicotine is the final ingredient (3-18 mg e-liquid)

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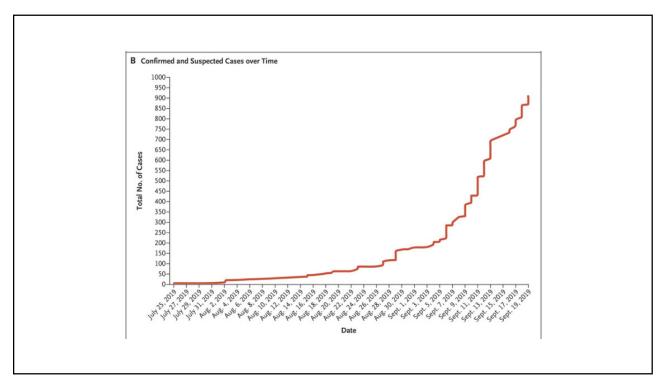
# EVALI VAPI

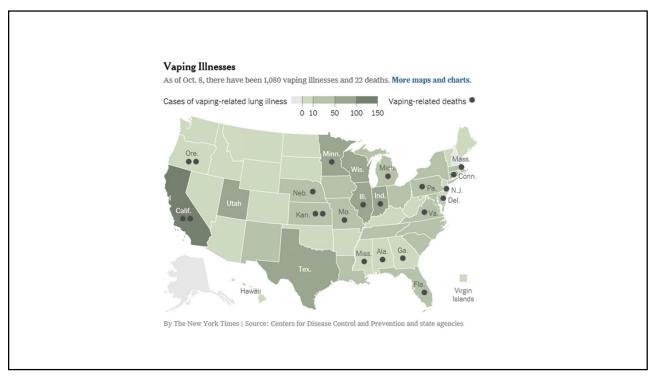
Ecig or Vaping Associated Lung Injury Vaping Associated Pulmonary Illness

#### **Timeline**

- April IL and WI state health departments
- Aug 23 first death in IL. 200 cases in 22 states
- OR first death due to a store bought product (marijuana oil)
- Oct 14 first teenage death 17 yr old in Bronx
- Oct 11 MMWR 1299 VAPI and 26 deaths
- Oct 22 CDC 1604 EVALI cases, 34 deaths (2.1%)

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#### **EVALI**

- Clinical: fever, cough, vomiting, diarrhea, HA, dizziness, chest pain following use of a vaping device
- Subacute: days to weeks before seeking healthcare
- Labs: nonspecific, elevated WBC, ESR, CRP
- CXR/CT scan: bilateral pulmonary infiltrates (alveolar)
- BAL: neutrophilia, no infection,

#### Clinical MMWR 10.11.19

- 95% resp sx (cough, sob, chest pain)
- 77% GI sx (abd pain, N/V/D)
- 85% constitutional sx (fever, chills, wt loss)
- Demographics
  - Median age 23 yrs
  - 80% < 35 yrs
  - 15% < 18 yrs
- DX of EXCLUSION
- In IL and WI 72% had outpatient or ED visit before the hospitalization

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#### Clinical (MMWR)

- Tachycardia in 55% (169/310)
- Tachypnea in 45% (77/172)
- Pulse oximetry O2sat <95% at rest on RA in 57% (m(143/253)
- Mean first recorded saturation of
  - Pts requiring intubation 87%
  - Pts not requiring intubation 92%
- 47% admitted to ICU (159/342)
- 22% were intubated (74/338)

Early Release

TABLE. Characteristics of patients with electronic cigarette (e-cigarette), or vaping, product use-associated lung injury (EVALI) reported to CDC — United States, August-October 2019\*

	No. /Total No. (%†)		
Characteristic	EVALI patients who survived	EVALI-associated deaths	All EVALI patients
Sex			
Male	947/1,349 (70)	17/29 (59)	964/1,378 (70)
Female	402/1,349 (30)	12/29 (41)	414/1,378 (30)
Age group (yrs)			
13-17	735/1,335 (55) <sup>§</sup>	2/29 (7) <sup>5</sup>	196/1,364 (14)
18-24			541/1,364 (40)
25-34	339/1,335 (25)	5/29 (17)	344/1,364 (25)
35-44	165/1,335 (12)	7/29 (24)	172/1,364 (13)
45-64	79/1,335 (6)	8/29 (28)	87/1,364 (6)
65-75	17/1,335 (1)	7/29 (24)	24/1,364 (2)
Median age, yrs (range)			
Overall	23 (13-72)	45 (17-75)	24 (13-75)
Male	23 (13-68)	55 (17-71)	23 (13-71)
Female	25 (13-72)	43 (27-75)	25 (13-75)
Race/Ethnicity¶			
White	283/365 (78)	15/18 (83)	298/383 (78)
Black or African American	22/365 (6)**	1/18 (6)**	9/383 (2)
American Indian or Alaska Native			4/383 (1)
Asian, Native Hawaiian, or other Pacific Islander			5/383 (1)
Other			5/383 (1)
Hispanic	60/365 (16)	2/18 (11)	62/383 (16)
Substances used in e-cigarette, or vaping, products <sup>++</sup> ,55			
THC-containing products, any use	733/848 (86)	16/19 (84)	749/867 (86)
Nicotine-containing products, any use	545/848 (64)	7/19 (37)	552/867 (64)
Both THC- and nicotine-containing products, any use	451/848 (53)	4/19 (21)	455/867 (52)
THC-containing products, exclusive use	282/848 (33)	12/19 (63)	294/867 (34)
Nicotine-containing products, exclusive use	94/848 (11)	3/19 (16)	97/867 (11)
No THC- or nicotine-containing products reported	21/848 (2)	0/19 (0)	21/867 (2)

Abbreviation: THC = tetrahydrocannabinol.

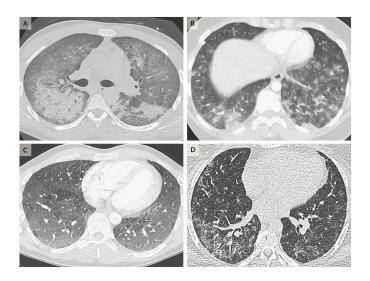
Reported as of October 15, 2019.
Percentages might not add up to 100% because of rounding.

Data for the 13–17 and 18–24 age groups were combined to protect patient identity.

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## Vaping history

- Among 865 pts with available data (MMWR 11/1/19)
- 86% used THC
- 64% nicotine containing products
- 52% both



TS Henry et al. N Engl J Med 2019. DOI: 10.1056/NEJMc1911995

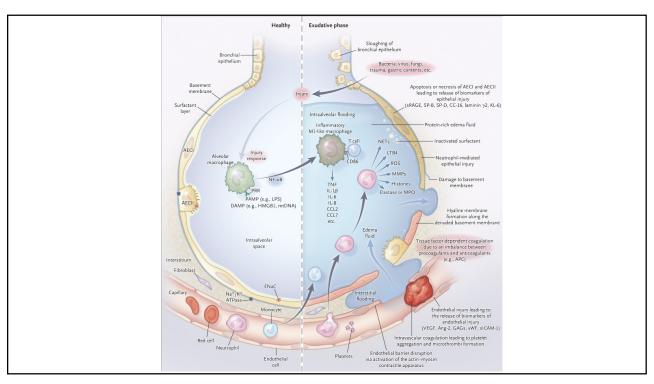
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# **VAPI**: Differential Diagnosis

- Community acquired pneumonia
- Acute eosinophilic pneumonia
- ARDS /Lung Injury
- Hypersensitivity pneumonitis
- Organizing pneumonia
- Respiratory bronchiolitis-associated pneumonia
- Lipoid pneumonia

Criteria	Rationale	
Onset within 7 days after a known clinical insult or new or worsening respiratory symptoms	Observational data suggest that ARDS will develop within 72 hr in the majority of patie at risk for the syndrome and within $1\mathrm{wk}$ in nearly all patients at risk	
Bilateral opacities that are "consistent with pul- monary edema" on chest radiographs or chest CT	There is poor interobserver reliability in interpreting the chest radiograph for the presence of edema. To address this issue, the Berlin definition offers more explicit criteria (e.g. opacities should not be fully explained by effusions, lobar or lung atelectasis, or no ules or masses), with illustrative radiographs provided	
Categorization of ARDS severity	A patient-level meta-analysis validated three thresholds for hypoxemia, all consisting of a Pao $_2$ :Fio $_2$ ratio $\le$ 300 mm Hg	
Mild	Pao <sub>2</sub> :Fio <sub>2</sub> , 201 to 300 mm Hg; mortality, 27% (95% CI, 24–30)	
Moderate	Pao <sub>2</sub> :Fio <sub>2</sub> , 101 to 200 mm Hg; mortality, 32% (95% CI, 29–34)	
Severe	Pao <sub>2</sub> :Fio <sub>2</sub> , ≤100 mm Hg; mortality, 45% (95% CI, 42–48)	
Minimum PEEP setting or CPAP, 5 cm of water; Pao <sub>2</sub> :Fio <sub>2</sub> assessed on invasive mechanical ventilation (CPAP criterion used for the diag- nosis of mild ARDS)	Estimates of Fio <sub>2</sub> are not accurate with oxygen-delivery systems other than invasive or no invasive ventilation (with a tight-fitting mask), with the exception of nasal high-flow ox gen delivery systems (at flow rates 245 liters per minute); requiring higher PEEP setting does not increase predictive validity of the Berlin severity strata and adds complexit	

\* The definition and the quotation about opacities are from Ferguson et al.<sup>6</sup> CI denotes confidence interval, CPAP continuous positive airway pressure, Pao<sub>2</sub>:Fio<sub>2</sub> ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen, and PEEP positive end-expiratory pressure.

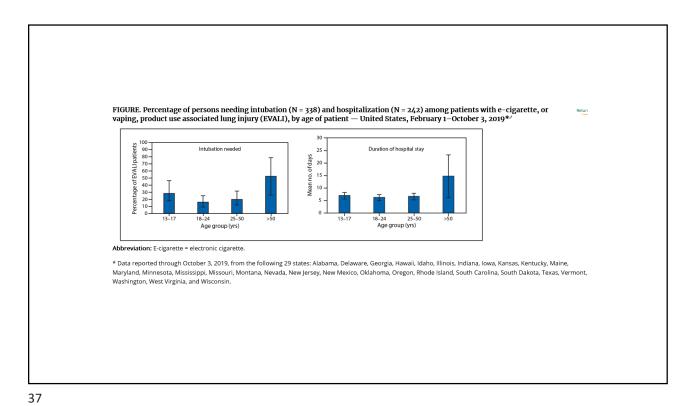




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#### **Treatment**

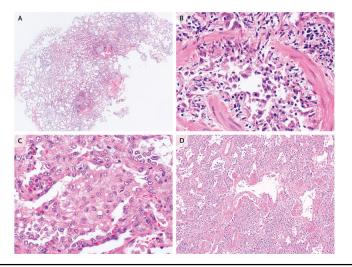
- Natural progression is not known
- Treat patients for CAP initially
- 92% of 50 pts in IL and WI got steroids
- Some pts have relapsed during taper so followup 1-2 weeks after discharge is recommended
- Influenza will complicate the picture if infected simultaneously



#### Histopathology

- Mayo Clinic NEJM (Oct 2 correspondence)
- 17 lung biopsies; h/o vaping (71% cannabis oils)
- 11/17 confirmed diagnosis of VAPI
- All cases with patterns of acute lung injury
  - · Diffuse alveolar damage
  - · Organizing pneumonia
  - Acute fibrinous pneumonitis
- No case had lipid laden macrophages (lipoid pna)

# Histopathology

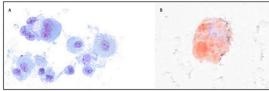


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#### Lipoid Pneumonia

Classic is inhalation of mineral oil in a elderly patient
Cause of Acute lung injury
CHEST 2012 Legacy Good Sam: case report of a pt developing lipoid
pneumonia from recurrent exposure to glycerin based oils in ecigs
5 patients North Carolina with BAL with lipid laden macrophages

 $FIGURE\ 2.\ Microscopy\ of\ a\ bronchoal veolar\ lavage\ sample\ (Papanicolaou\ stain\ (A)^*\ and\ oil\ red\ O\ stain\ (B)')\ lung\ injury\ associated\ with\ vaping\ —\ North\ Carolina,\ July-August\ 2019$ 



\*Papanicolaou stain demonstrating alveolar macrophages laden with vacuoles

'Oil red O stain showing lipid deposits staining red (400x magnification).

#### **CDC**

- Clinical evaluation for patients with recent history of use of e-cigarette, or vaping, products and suspected lung injury
- Ask about respiratory, gastrointestinal, and constitutional symptoms (e.g., cough, chest pain, shortness of breath, abdominal pain, nausea, vomiting, diarrhea, and fever) for patients who report a history of use of e-cigarette, or vaping, products.
- Ask all patients about recent use of e-cigarette, or vaping, products.
  - Types of substances used (e.g., tetrahydrocannabinol [THC], cannabis [oil, dabs], nicotine, modified products or the addition of substances not intended by the manufacturer); product source, specific product brand and name; duration and frequency of use, time of last use; product delivery system, and method of use (aerosolization, dabbing, or dripping).

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#### **EVALI**

- Type of e-device
- Specific type of liquid (nicotine, flavor, THC)
- Were devices, liquids, shared with others?
- Were old cartridges or pods reused with homemade or other online items?
- Were devices used to inhale drugs that were concentrated by heating prior to vaping? (called dabbing, dripping
- Details of vaping behavior (cloud volume, puff frequency, zero or stealth vaping)

#### Current hypothesis

- Aerosolization of flavoring compunds of e-cigarette liquids
- Adulteration of devices with THC
- Black market THC with oils, contaminants
- Lipid emulsion
- Vitamin E used to extract THC
- None of above are mutually exclusive

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#### FDA STATEMENT

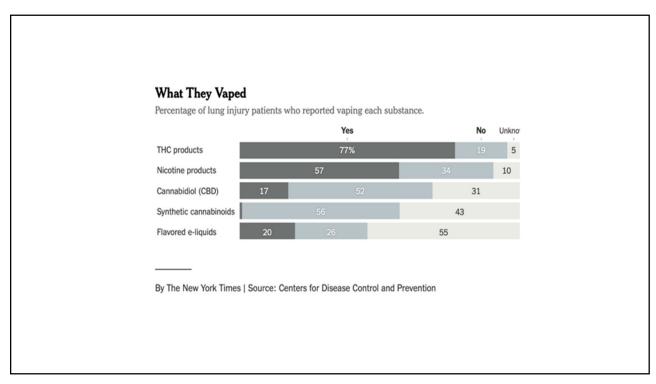
# Statement on consumer warning to stop using THC vaping products amid ongoing investigation into lung illnesses



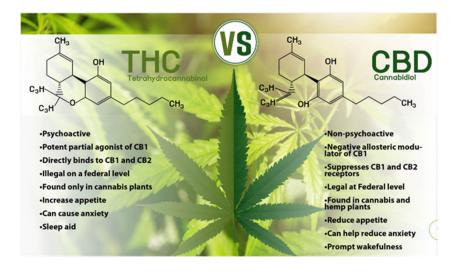
#### **VAPING THC**

- In Colorado, 78% increase in number of marijuana concentrates (inc vape products) sold from 2017 to 2018
- THC is suspended in a oil solution which also includes chemicals
- FDA does not regulate THC vaping products (regulatory vacuum)
- Products containing <0.3% THC do not fall under DEA
- Black market (Wisconsin brothers NYT 9/16/2019)
- 14% of US adults report marijuana use in previous year; 1/3 report vaping it

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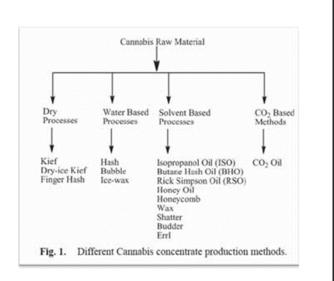
#### **Cannabis**



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#### **Cannabis**

- Cannabis oil vs plant
- Can vaporize the flower bud
- Contaminated by solvent residuals (70%) such as isopentane and propane and pesticides (30%)
- Vitamin E acetate

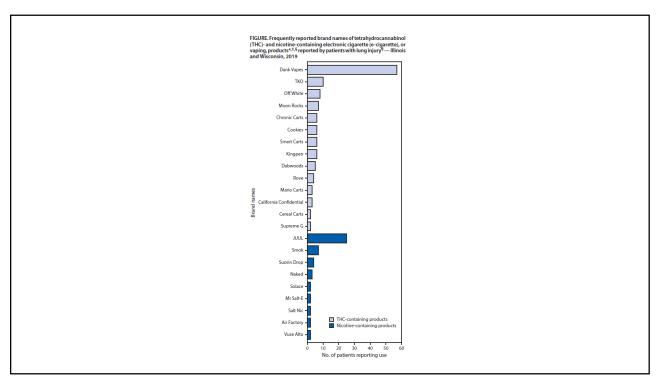


## **DANK VAPES**



Empty Dank Vapes packaging.

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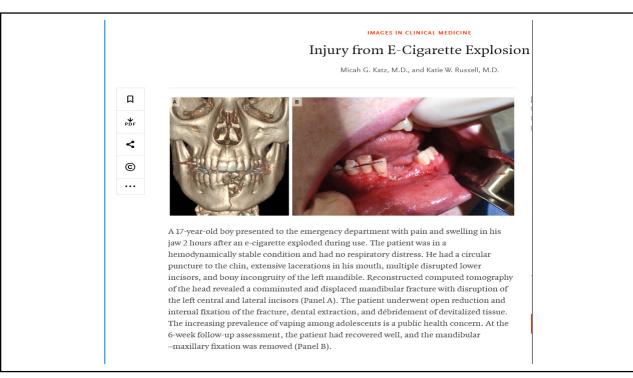


#### Vaping Lung Injury

- CDC Warns People Not To Use Vaping Supplies Bought On The Street And To Stop Modifying E-Cigarettes
- The New York Times (8/30, Kaplan) reported that in response to "more than 200 cases of respiratory illnesses possibly related to vaping," the CDC "warned people not to use vaping ingredients bought on the street and to stop modifying either nicotine or cannabis e-cigarette device in an effort to curb the vaping-related lung sicknesses that have alarmed health officials in more than two dozen states this summer."

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# FDA to investigate reports of seizures possibly linked to e-cigarette use The agency has received 35 reports of seizures among e-cigarettes users, mainly in teens and young adults, since 2010. DUS. FOOD & DRUG ADMINISTRATION Redict PDA Wedget FDA Commetics Commetics Wedget FDA Commetics Commetics Wedget FDA Commetics Commetics Commetics Fobacco Products Fobacco Products Fobacco Products Commetics Commeti



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# How did we get here?

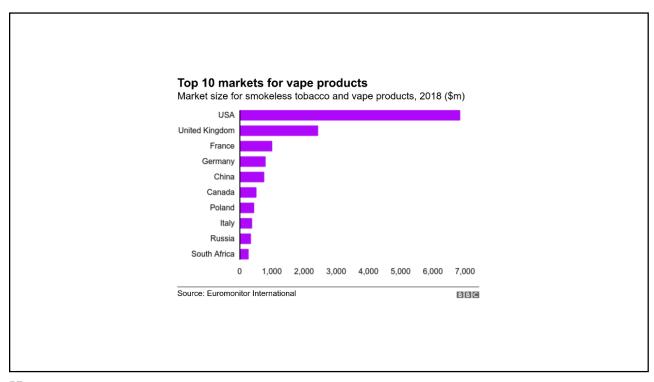
## **Global View**

- EU no THC tighter regulations; restrict marketing to children,, lower limit nicotine content; UK cannot target teens, cannot depict users who are <25</li>
- UJ 3.6 million regular e-cigarette users
- India banned all e cigarette products
- China Juul went live in September for 2 weeks then Alibaba took it off its online market

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Where is vaping banned or restricted around the world?



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# E-Cigarettes Went Unchecked in 10 Years of Federal Inaction

A decade after Congress gave the F.D.A. the power to regulate tobacco products like e-cigarettes, the federal government has repeatedly delayed or weakened efforts that could have protected teenagers.

2007	Earliest forms of ecigs arrive in US
2009	FDA declared ecigs illegal drug-device combination and
	halted imported Companies sued
2010	FDA lost suit
2010-	slowly developed regulations ; market became flooded FDA struggled
2015	FDA sent proposed rule for oversight of all ecigs and tobacco products 468pages to OMB; White House deleted flavor ban
2017	Gottlieb handed ecig industry a 4 yr extension to comply with new rules
2018	FDA investigated Juul



One girl on his dorm hall sold Juul pods from stock she had bought from a guy who ordered armloads on the internet. Unlike back home in high school, college students vaped in public everywhere — in lecture halls, at hockey games, in the dorm common rooms.

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#### Juul

- Monsees and Bowen 2007
- Came to market it had 5% nicotine c/w 1-3 % in competition
- In US-Juul now has 75% market share
- Now most vape pen cartridges have 5-7% nicotine
- Salt based nicotine (protonated form, less acidic, less harsh)

#### Juul



#### **JUULPOD BASICS**

Our disposable, snap-in pods make it easy to customize your experience while you find what works for you. No messy refills, just snap the pod into the top of your device and puff.

We offer a variety of JUULpod flavors, with some flavors



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#### JUUL

#### PROPYLENE GLYCOL AND **GLYCERINE (30/60MIX)**

(UP TO 90%)

Propylene glycol and glycerine are clear liquids that are used to create a visible vapor, and are commonly used by the medical, beauty and food industries. A majority, if not all e-liquids, contain propylene glycol (PG).

#### **BENZOIC ACID**

Benzoic acid is a naturally occurring ingredient, found in tobacco and other substances. When combined with nicotine as which provide the specific taste profile for part of our nicotine salts formulation, it helps each flavor. provide cigarette-like satisfaction.

#### NICOTINE

Nicotine is a stimulant that comes from the tobacco plant. We use highly purified/USP grade/pharmaceutical grade nicotine.

#### **FLAVOR**

JUUL flavors consist of both naturally occurring and artificial flavor ingredients

# JUUL pod



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#### JUUL website



#### JUUL social MEDIA

#### Images for vaping



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#### You tube

#### Why is the JUUL so popular? - YouTube

https://www.youtube.com/watch?v=rearlzdaXEk



Jul 6, 2018 - Uploaded by DashVapes https://www.dashvapes.com/juul The JUUL by Pax has taken the industry by storm and revolutionized the ...

#### Helpful Tips & Tricks for the JUUL - YouTube

https://www.youtube.com/watch?v=-LH9N-nvG5Q



Sep 23, 2018 - Uploaded by Donny Vapes (+18) Content is intended for adults I think it's finally time that I help all of your out with a few helpful tips to ...

#### JUUL by PAX Review - YouTube

https://www.youtube.com/watch?v=GKhgncyDwnM 🔻



Jun 6, 2015 - Uploaded by Lenny Vaknine
Hey everyone. I just got my JUUL today and I wanted to take 5 minutes to review it for you and give you my ...

#### Juuling: What It Is and How It Works - YouTube

https://www.youtube.com/watch?v=sYQM0tkVs4s



Mar 30, 2018 - Uploaded by AAMCNews

## Twitter #JUUL



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# JUUL is cool





mages for juul instagram





# Vaping websites

# Best vape 2019: vape pens and e cigarettes for the discerning vapeur

Is vaping bad for you? Well, it's not as bad as smoking. So enjoy the biggest clouds of fruity or herb-tinged vapour possible with the best vape pens



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#### Altria 12.8 billion for 35%



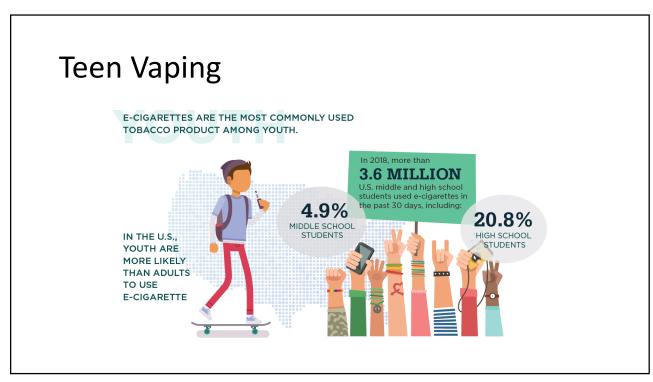
#### The industry



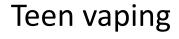
- Vuse owned by RJ Reynolds
- Markten owned by Altria (parent company of Phillip Morris)
- Blu owned by Imperial brands
- Juul by Altria

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# Big Smoke While tobacco alternatives have huge potential, cigarettes are still the main driver of the industry \$713.7 billion Global cigarette market 2018 Source: Euromonitor International Note: Tobacco alternatives include smokeless tobacco, electronic cigarettes and devices that heat, rather than burn tobacco. BloombergOpinion



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#### Adolescent Vaping and Nicotine Use in 2017–2018 — U.S. National Estimates

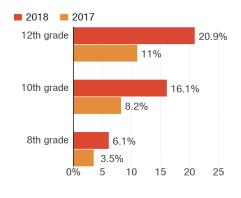
TO THE EDITOR: A rapid increase in the preva-nicotine use with any nicotine product. (For all survey measures and question wording see the

Jessica L. Barrington-Trimis, Ph.D., and Adam M. Leventhal, Ph.D.

dolescents' use of electronic cigarettes initially took the public health community by surprise. In 2011, less than 2% of U.S. high school students reported having used e-cigarettes in the previous month. But by 2015, a popular pod mod brand, high-the percentage had jumped to 16%. light anecdotal reports from

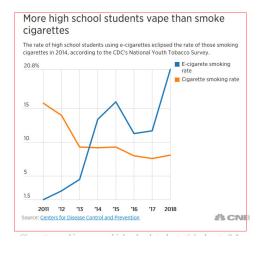
# **Adolescent Vaping stats**

#### **Prevalence Of Nicotine Vaping**



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#### CDC 2019 data



#### Our mission

 "I will not allow a generation of children to become addicted to nicotine through e-cigarettes," Scott Gottlieb, commissioner of the Food and Drug Administration, said in a statement.

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#### **ATS Advocacy**

- ATS involvement in the larger cigarette/tobacco issue has been extensive and is ongoing. During both the Obama and Trump administrations, the ATS called upon the FDA to strictly regulate all tobacco products, including e-cigarettes, in the following ways:
- Ban the use of menthol as a characterizing flavor agent in all tobacco products
- Ban the use of sweet, fruity and other child-luring flavors in all tobacco products
- • Require disclosure of all ingredients in e-cigarette products
- Require the testing of flavoring agents with known or suspected respiratory toxicity
- •Require graphic warning labels on all tobacco products including e-cigarettes
- Urge stricter regulation of online sales of e-cigarette products
- Ban advertising and other marketing techniques intended to appeal to youth

#### TAKE HOME POINTS

- EVALI nonspecific resp/gi/const symptoms
- Ask detailed questions about vaping history
- Dx of exclusion
- Influenza season challenges (can have 2 diseases)
- Remember that a O2 sat of 95% is a PaO2 of 80
- Talk to patients about the dangers of vaping