

Cannabis and derivatives in lung disease

Samuel K Evans, MD

Assistant Professor of Medicine, Clinician Educator

Brown University, Alpert School of Medicine

Newport Pulmonary Medicine/LPG

ALA Lung Force Expo

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Disclosures

None

Key take home point



Learning objectives

- Briefly assess the known risks of smoking traditional combustible cannabis
- Explore the EVALI outbreak

Brief background of cannabis

- Cannabis, AKA marijuana, contains, among others, three psychoactive substances:
 - THC - 9-tetrahydrocannabinol
 - CBN - cannabinol
 - CBD - cannabidiol
- Most widely used illicit drug worldwide, 2.6-5% of the world's population
- Consumed in many ways but we are going to focus on smoking/inhalation
 - Joint, pipe, blunt*, vape
- Smoked in a different manner than tobacco
 - Larger volumes, longer inspiration/hold, smoked without a filter (↑ particulate matter and temp)
- Hard to study - the joint-year, information bias, variable tobacco consumption

Pulmonary health effects of smoking cannabis (epi level)

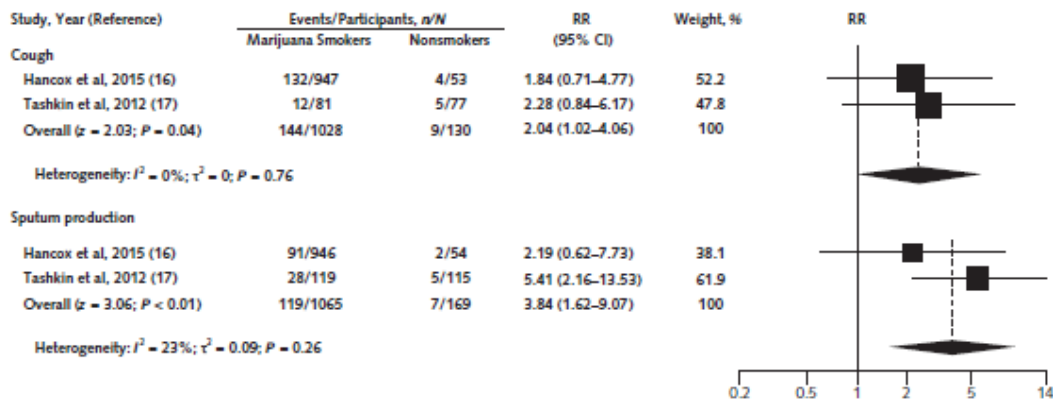
- Lung cancer
- Other chronic respiratory illness
 - COPD, chronic bronchitis, etc

Marijuana Use, Respiratory Symptoms, and Pulmonary Function

A Systematic Review and Meta-analysis

Mehmaz Ghasemiesfe, MD; Divya Ravi, MD, MPH; Marzieh Vali, MSc; Deborah Korenstein, MD; Mehrdad Arjomandi, MD; James Frank, MD; Peter C. Austin, PhD; and Salomeh Keyhani, MD, MPH

Figure 2. Association between marijuana use and cough and sputum production in prospective cohort studies.

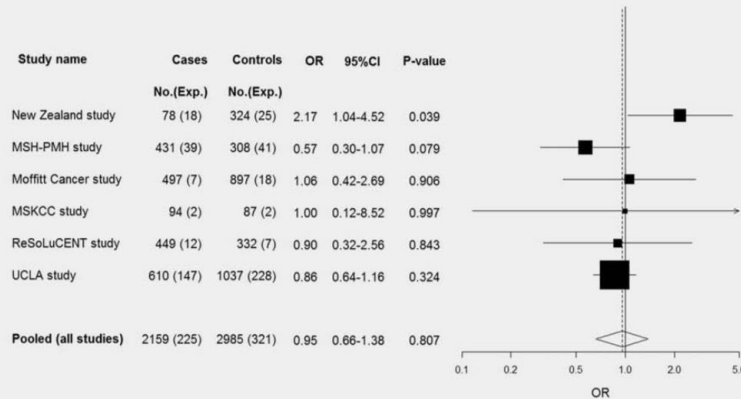


We used the Paule-Mandel method for estimating τ^2 . The squares indicate RRs from primary studies, and size reflects the statistical weight of the studies. The horizontal lines indicate 95% CIs. The diamonds represent the subtotal and overall RR and 95% CI. The vertical solid line shows the line of no effect (RR = 1). The pooled RR was not significant after the Knapp-Hartung small-sample adjustment for cough ($P = 0.10$) and sputum production ($P = 0.20$). RR = risk ratio.

- No clear link to airway obstruction by spirometry (but maybe subtle measures - sRaw)
- Chronic cough and sputum production appear to be associated

Cannabis smoking and lung cancer risk: Pooled analysis in the International Lung Cancer Consortium

- 2,159 cases and 2,985 controls in six studies that met criteria
- Habitual use: 1 joint-year (1 joint daily for 1 year)
 - Including non-tobacco users (370 cases and 1,358 controls)



cision was low at high exposure levels. Results from our pooled analyses provide **little evidence for an increased risk** of lung cancer among habitual or long-term cannabis smokers, although the possibility of potential adverse effect for heavy consumption cannot be excluded.

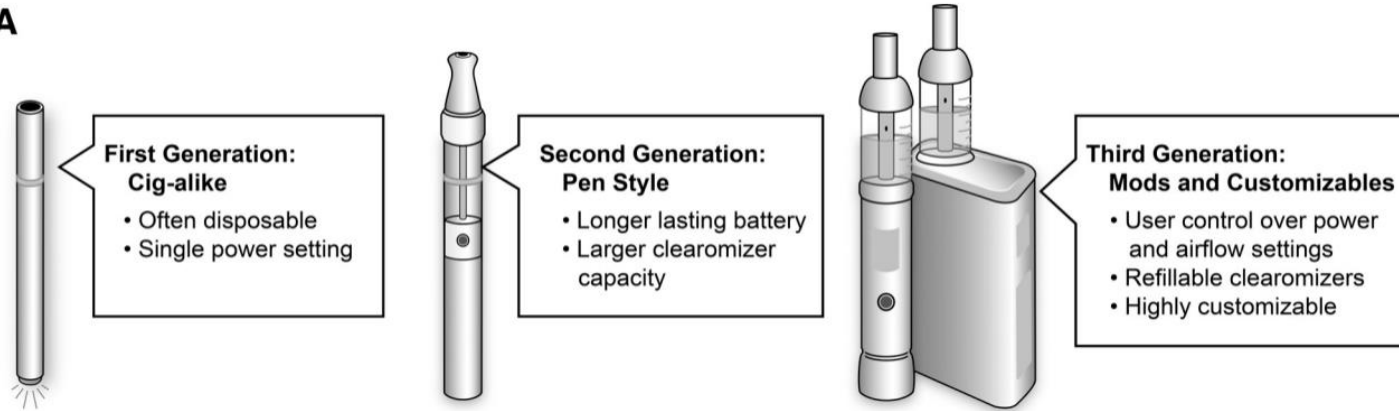
EVALI



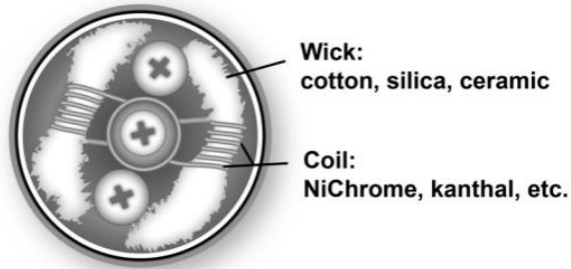
DAVE GRANLUND © www.davegranlund.com

Basic anatomy of e-cig devices

A

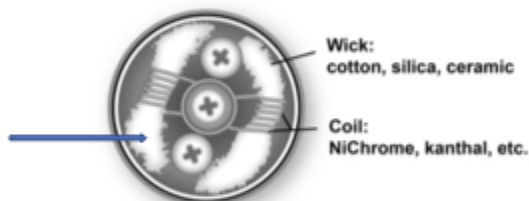


B



E-cig risk from the device

- Plastic mouthpiece – probably the least harmful part of the apparatus
- Wick

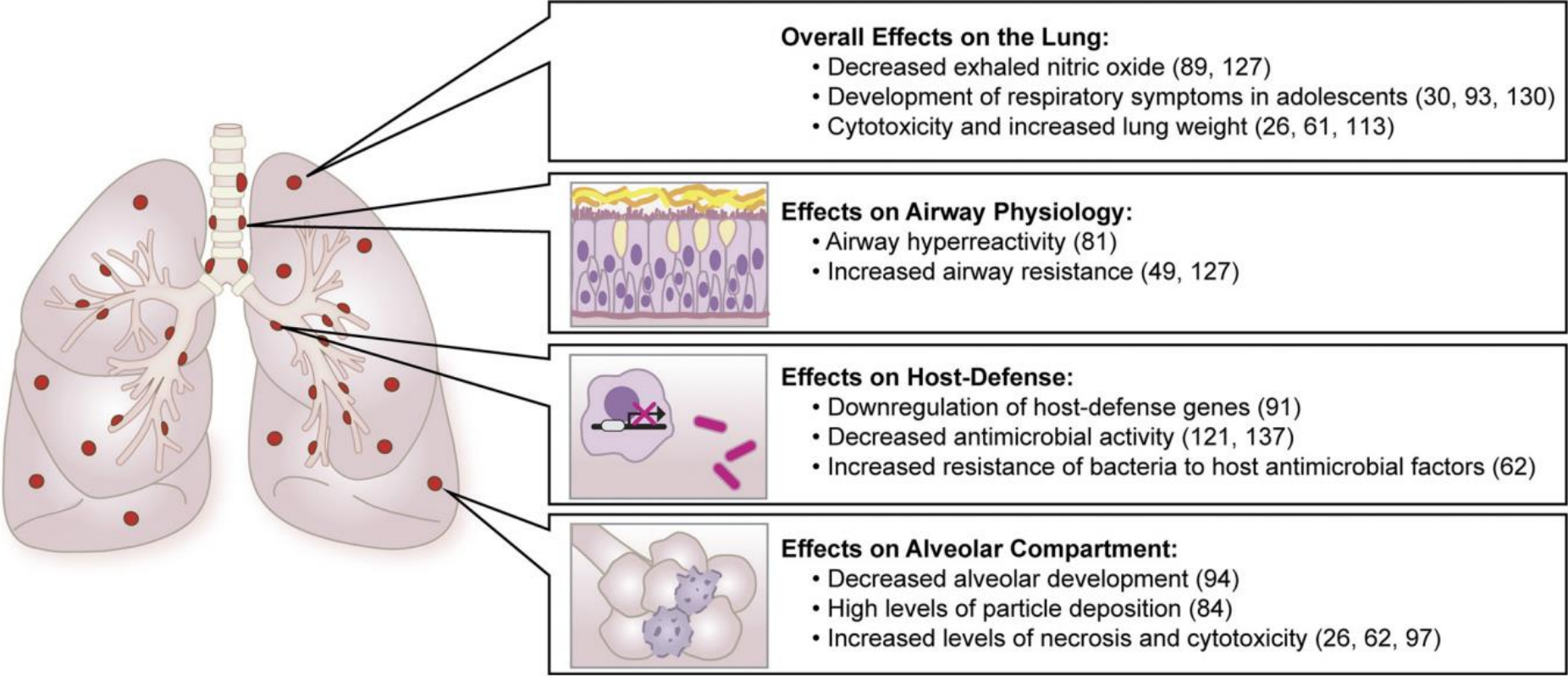


Material	Known Risks
Silica	Silicosis
Nickel	Carcinogenesis, lung injury, immune suppression
Chromium	Carcinogenesis, lung injury, immune suppression, reproductive toxicity

- Lithium ion battery – thermal burns
- Coil – remember $\text{power} = \text{voltage}^2 / \text{resistance}$
 - User can the material and energy to vary the experience
 - Varies the heat and downstream inhaled material (metallic fumes, leaches into vape liquid)

E-cig risk from the liquid

- Vegetable glycerin or propylene glycol (stage smoke)
 - GRAS by the FDA for ORAL CONSUMPTION but no long term studies on lung health
 - Different puffing topography
- Nicotine
- Additives
- Leach from coil



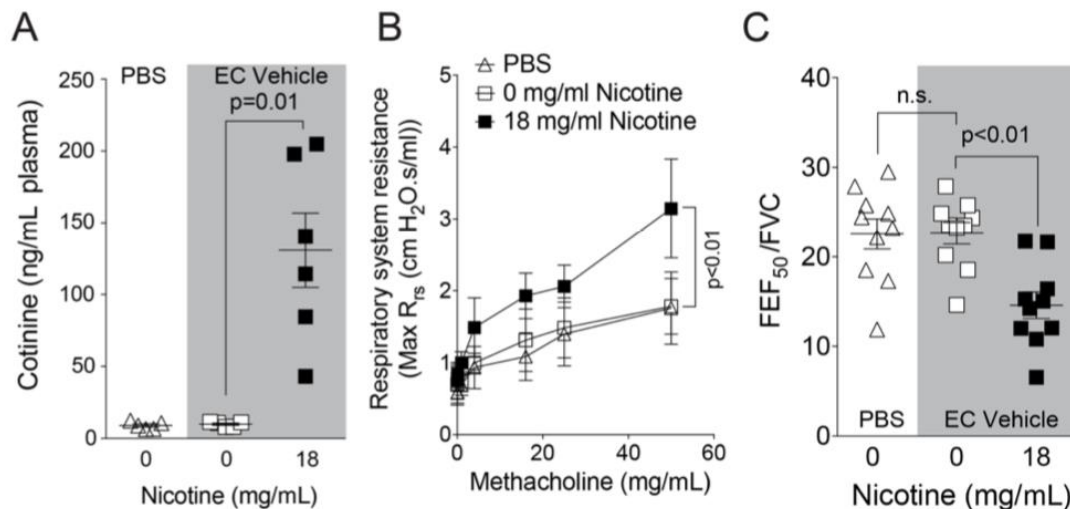


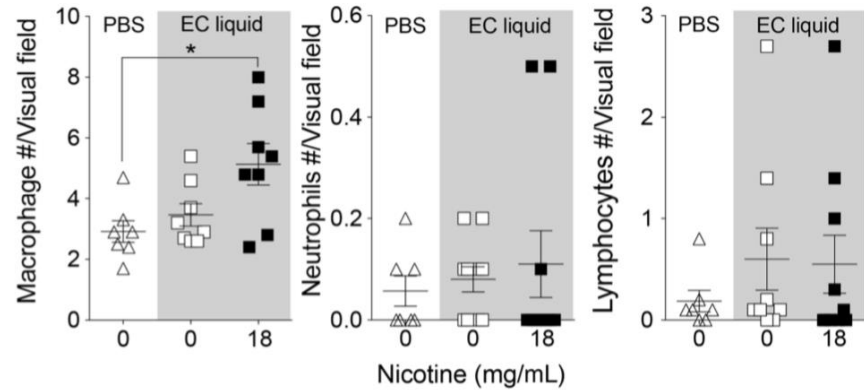
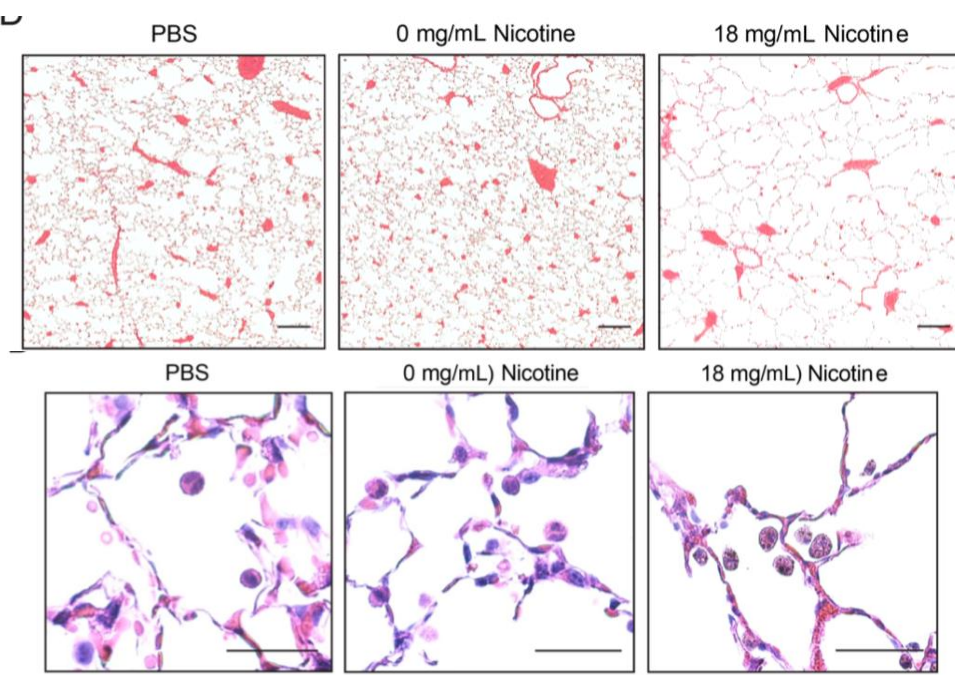
OPEN ACCESS

ORIGINAL ARTICLE

Chronic electronic cigarette exposure in mice induces features of COPD in a nicotine-dependent manner

Itsaso Garcia-Arcos,^{1,2} Patrick Geraghty,^{1,2} Nathalie Baumlin,³ Michael Campos,³ Abdoulaye Jules Dabo,^{1,2} Bakr Jundi,⁴ Neville Cummins,⁵ Edward Eden,⁵ Astrid Grosche,³ Matthias Salathe,³ Robert Foronjy^{1,2}

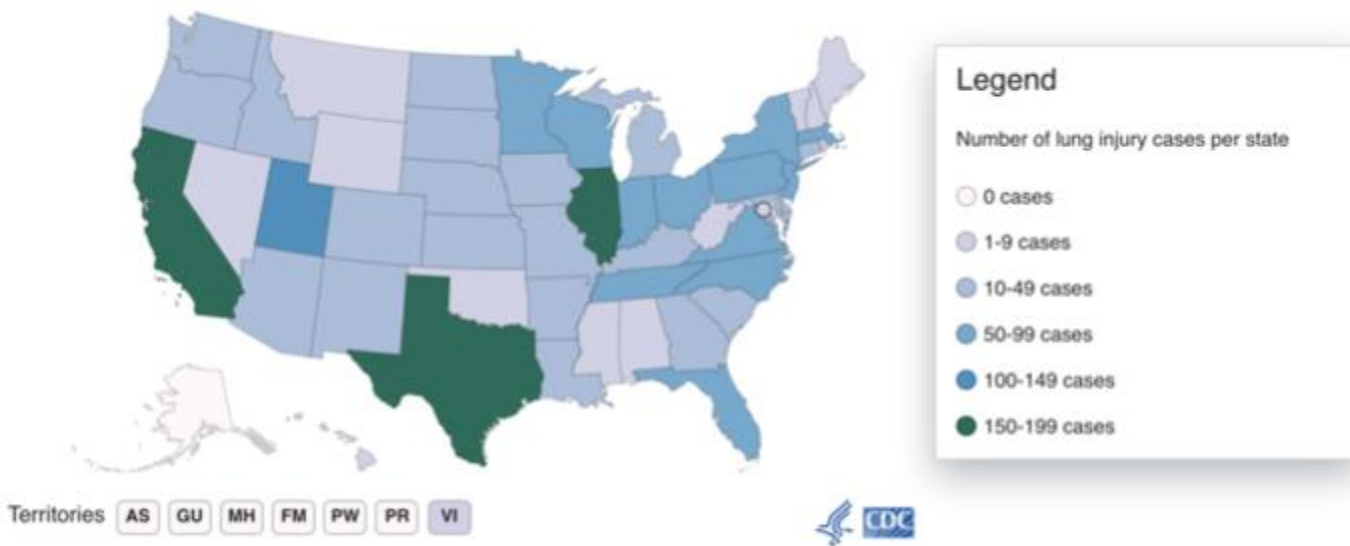




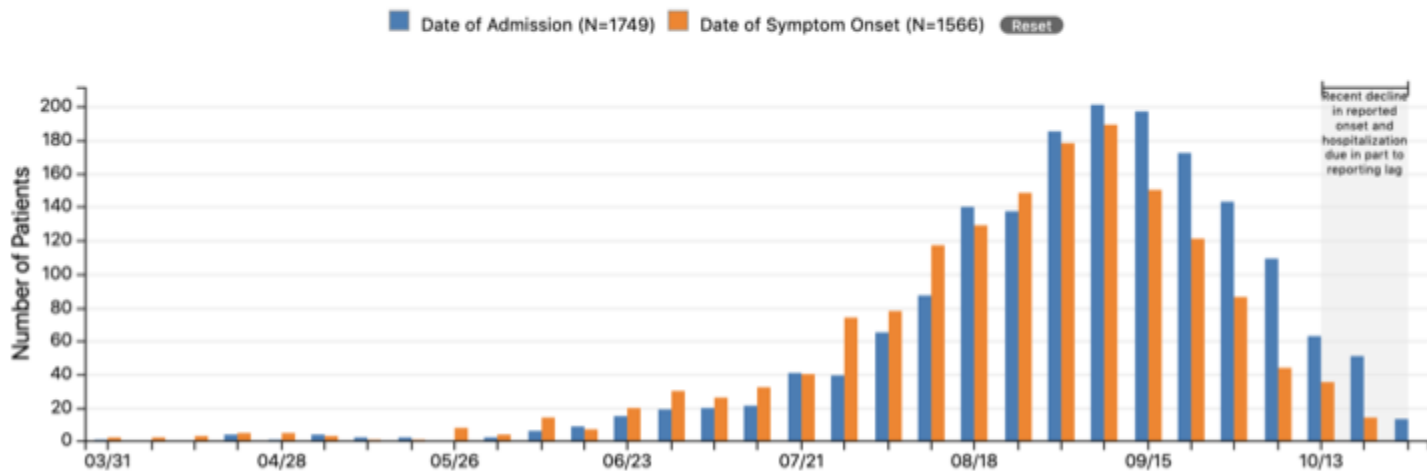
Epidemiology of EVALI outbreak (as of Nov 5)

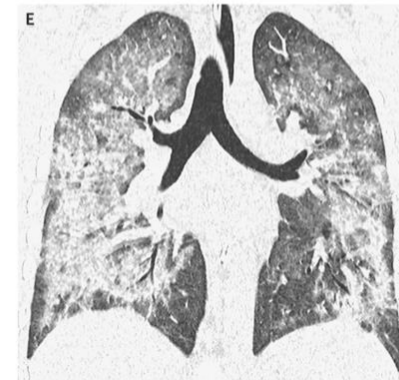
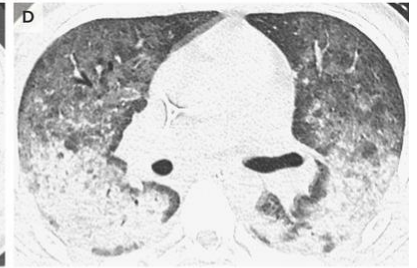
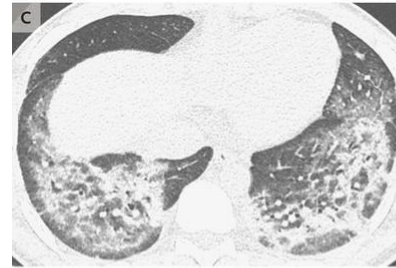
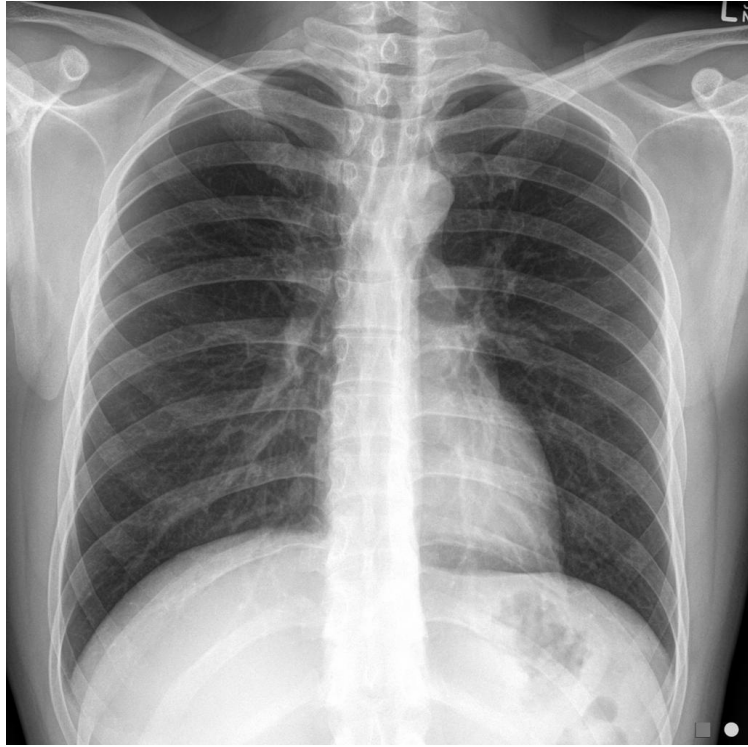
- 2,051 cases as of Nov 5, 2019, may be decreasing
- 39 deaths (2% fatality rate)
- 70% male
- 79% are under 35 years old (14% under 18 years old)
- 86% reported using THC-containing products; 34% exclusively
- 64% reported using nicotine-containing products; 11% exclusively

Number of Lung Injury Cases Reported to CDC as of November 5, 2019



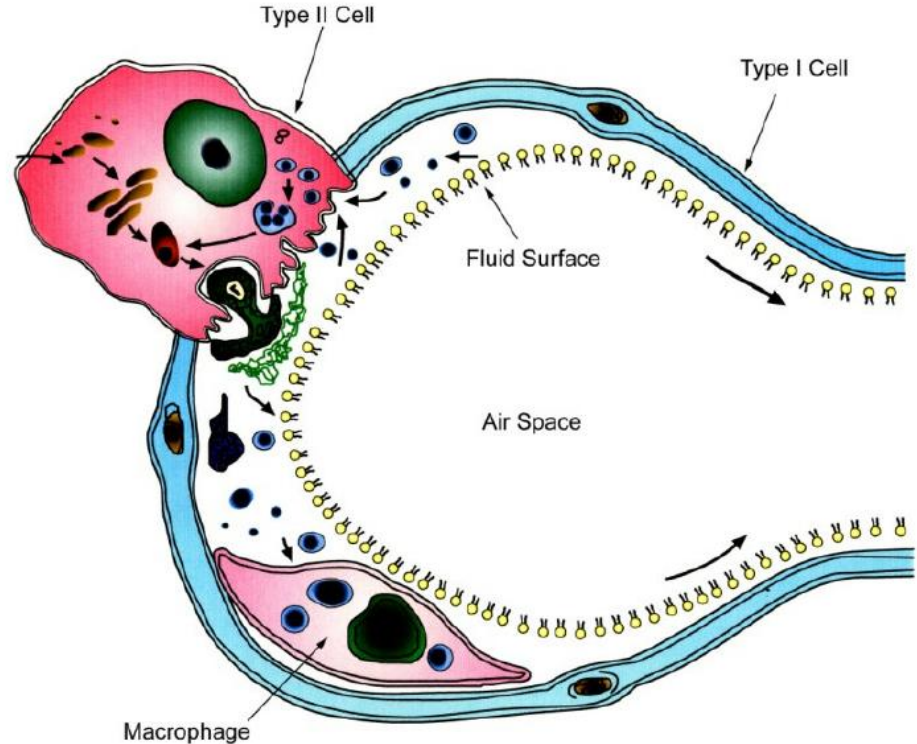
Dates of symptom onset and hospital admission for patients with lung injury associated with e-cigarette use, or vaping — United States, March 31–November 2, 2019





EVALI: potential mechanisms

- VG/PG
- Nicotine
- Heat
- Coil
- THC formulations
- Other?
- Interactions



**Evaluation of Bronchoalveolar Lavage Fluid from Patients in an Outbreak of
E-cigarette, or Vaping, Product Use–Associated Lung Injury — 10 States,
August–October 2019**

- Bronchoalveolar lavage (BAL) fluid from 29 patients in 10 states
- Looked for: vitamin- E-acetate, medium chain triglycerides. Plant oils, petroleum distillates, (including mineral oil), diluent terpenes. Cannabinoids, and nicotine
- Controlled for dipalmitoylphosphatidylcholine (*DPPC, primary lipid in lung surfactant)

Bronchoalveolar lavage



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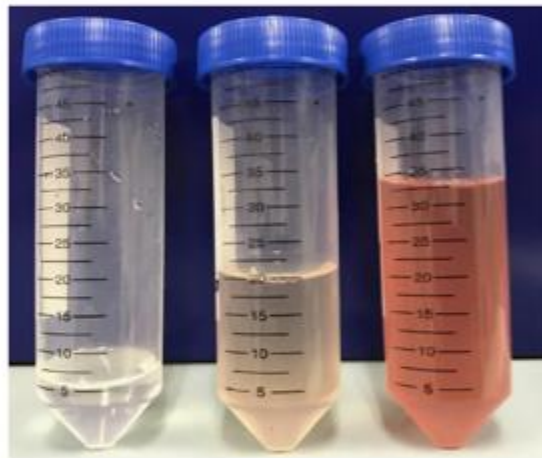


Figure 3 The bronchoalveolar lavage fluid gradually became bloody from the left tube to the right tube.

CDC findings suggest vitamin E-acetate may be culprit

- 27 Samples analyzed
- Median age 23 year (range 16-67)
- Vitamin E detected in all samples (with negligible levels of the other compounds in question)

Pathology reports range widely

- Diffuse alveolar damage
- Lipoid pneumonia
- Acute necrotizing pneumonitis
- Organizing pneumonia with lipid-laden macrophages
- Non-specific inflammation
- Hypersensitivity pneumonitis
- Eosinophilic pneumonia

Which is the culprit(s)? Take a good exposure hx!



A collection of Dank Vapes products, including Diamond OG, Jack Herer, Diablo, Blue Dream, Jetfuel OG, Gelato, Family Pebbles, Zucchini Popcorn, and Jack Herer, displayed on a wooden surface.

Dank Vapes : What's Their Real Background and Are They Reliable?

By Francisco - February 19, 2019 88

Hearing about this at first did surprise me and lowered their credibility. They've failed multiple times in lab tests, containing several types of pesticides. Also, they ranked as low as 65% *THC*. Shown below are their most recent [lab results](#);

[illegible]

To sum up, we hope Dank Vapes to return stronger than ever

Dank Vapes were fast to react to their last counterfeit situation. Now they have to stay consistent with building their brand reputation. As of now, what they're doing is calling out people selling fake cartridges through their Instagram. If you ever encounter people selling fakes, you can just notify them and they will take care of the rest.

In the meantime, I personally won't be picking these up until I know they are authentic or not. I really do believe all of these problems really will go away once marijuana becomes recreational in most states. Then, all this will become irrelevant, having trademarks and more lab results. Meanwhile, I recommend you as always to pick up from a licensed

how reliable this company really is. Despite how good each flavor taste, Dank Vapes have been suspicious because of how many fakes are out. This issue has been hurting their company negatively, loosing credibility and trustworthy.

EVALI management notes

- Much like ARDS
 - Lung protective ventilation
 - Supportive care (pressors, etc)
 - Rule out infection
 - ECMO if needed

Conclusions

- Nothing but air should go into the lungs
- Smoking combustible cannabis causes chronic bronchitis but lung cancer risk much less clear than with tobacco
- Maintain a high index of suspicion in patients presenting with acute respiratory complaints
- Take a good exposure history
- EVALI may be due to the diluent vitamin-E acetate but very little is known with certainty
- If cessation is the only (maybe....) legitimate use for ENDS, perhaps require a prescription?

Thank you

- All of you for standing up for sensible tobacco/nicotine control policy
- Dr. Carolyn Calfee, UCSF