

# Vaping and lung disease

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**UKCTAS**

UK Centre for Tobacco & Alcohol Studies

# Some reported constituents of electronic cigarette vapour

## From intended contents

- Nicotine
- Propylene [ethylene] glycol
- Glycerine
- Flavours \*

## From contaminants/ heating/vapourisation

- Oxidant species \*
- Metal particles (Ag, Cu, Ca, Ni, Zn, Cr, Sn)
- Tobacco-specific nitrosamines
- Polycyclic aromatic hydrocarbons
- Formaldehyde
- Acetaldehyde
- Propionaldehyde
- Acrolein
- Acetone
- Cresol
- Xylene
- Toluene
- Others

Range and levels <<< tobacco smoke

# Likely real and potential harms of e-cigarettes to users:

Expect modest increases in risk of:

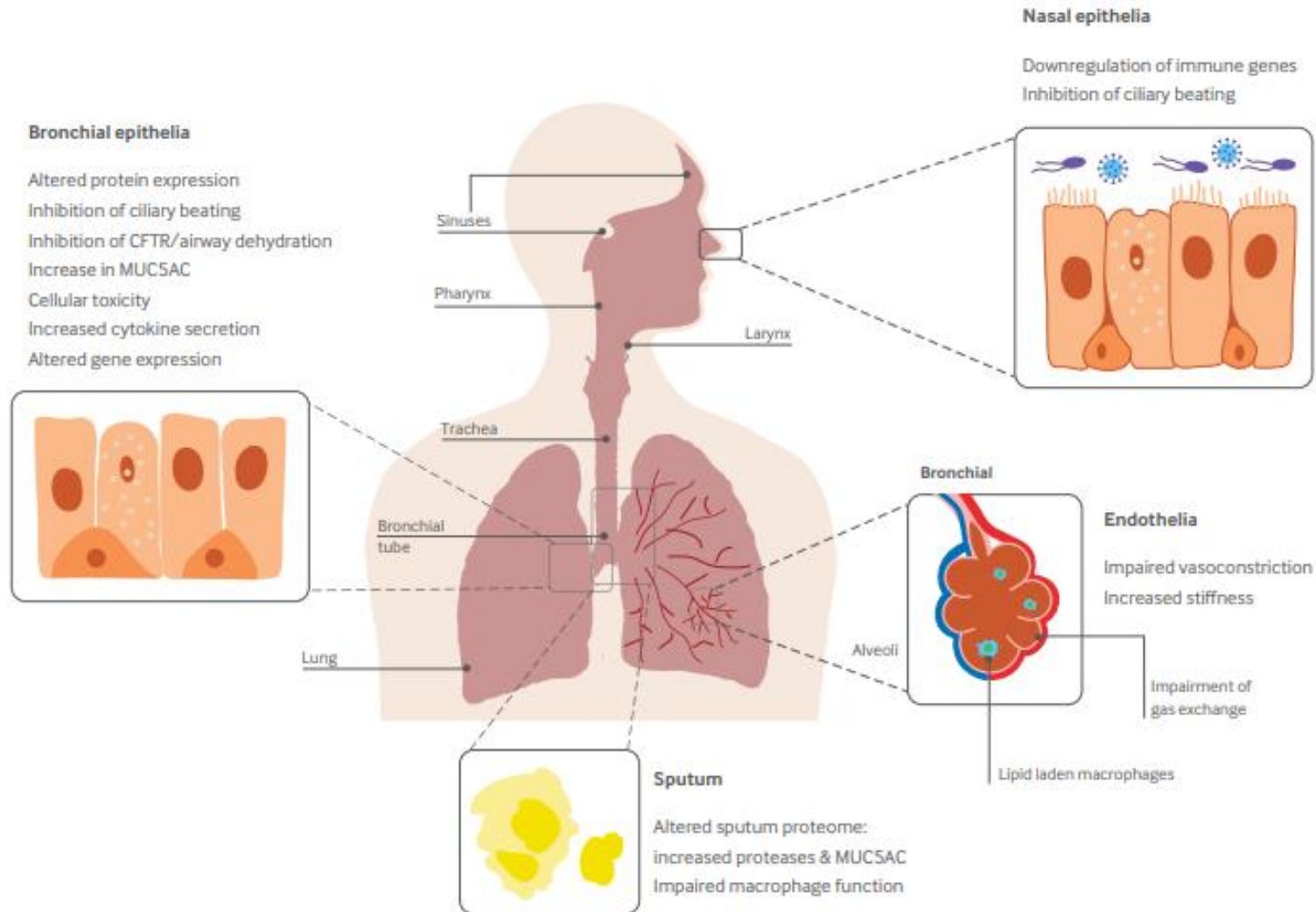
- Lung cancer
- Emphysema/COPD
- Pulmonary infection
- Cardiovascular events
- Pulmonary fibrosis
- (Hypersensitivity pneumonias)

All risks much lower than for tobacco smoking: probably <5%

Could be reduced by product standards regulation or improved technology

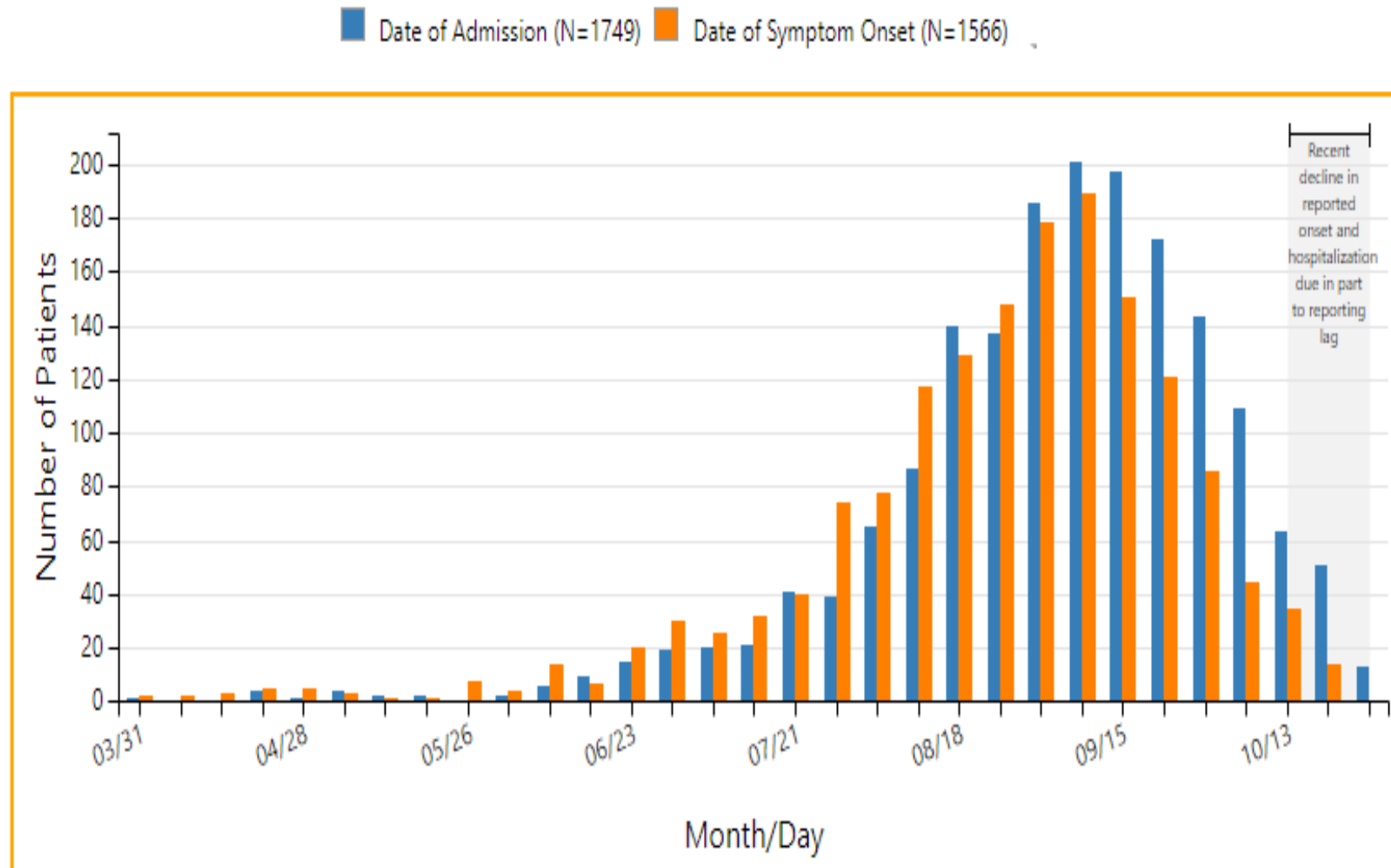
# Reported human pulmonary effects of vaping

*Gotts et al, BMJ 2019;366:l5275*



# Vaping-associated lung injury cases, USA (to 2.11.19)

[https://www.cdc.gov/tobacco/basic\\_information/e-cigarettes/severe-lung-disease.html](https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html)



## Pulmonary Lipid-Laden Macrophages and Vaping

Maddock et al, N Engl J Med 2019;381:15

The NEW ENGLAND JOURNAL of MEDICINE

### ORIGINAL ARTICLE

## Pulmonary Illness Related to E-Cigarette Use in Illinois and Wisconsin — Preliminary Report

Jennifer E. Layden, M.D., Ph.D., Isaac Ghinai, M.B., B.S., Ian Pray, Ph.D., Anne Kimball, M.D., Mark Layer, M.D., Mark Tenforde, M.D., Ph.D., Livia Navon, M.S., Brooke Hoots, Ph.D., Phillip P. Salvatore, Ph.D., Megan Elderbrook, M.P.H., Thomas Haupt, M.S., Jeffrey Kanne, M.D., Megan T. Patel, M.P.H., Lori Saathoff-Huber, M.P.H., Brian A. King, Ph.D., M.P.H., Josh G. Schier, M.D., Christina A. Mikosz, M.D., M.P.H., and Jonathan Meiman, M.D.

New Engl J Med 2019; DOI: 10.1056/NEJMoa1911614

Morbidity and Mortality Weekly Report

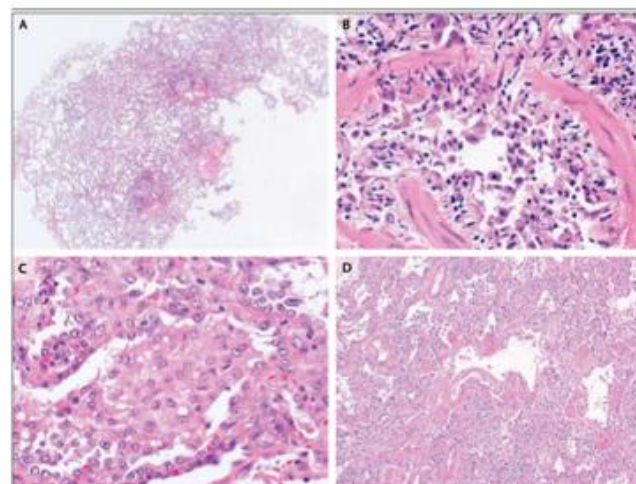
## Outbreak of Electronic-Cigarette–Associated Acute Lipoid Pneumonia — North Carolina, July–August 2019

Kevin Davidson, MD<sup>1</sup>; Alison Brancato, MS<sup>1</sup>; Peter Heetderks, MD<sup>1</sup>; Wissam Mansour, MD<sup>1</sup>; Edward Matheis, MD<sup>1</sup>; Myra Nario, MS<sup>1</sup>; Shrinivas Rajagopalan, MD, PhD<sup>2</sup>; Bailey Underhill, MS<sup>1</sup>; Jeremy Wininger, MS<sup>1</sup>; Daniel Fox, MD<sup>1</sup>

### CORRESPONDENCE

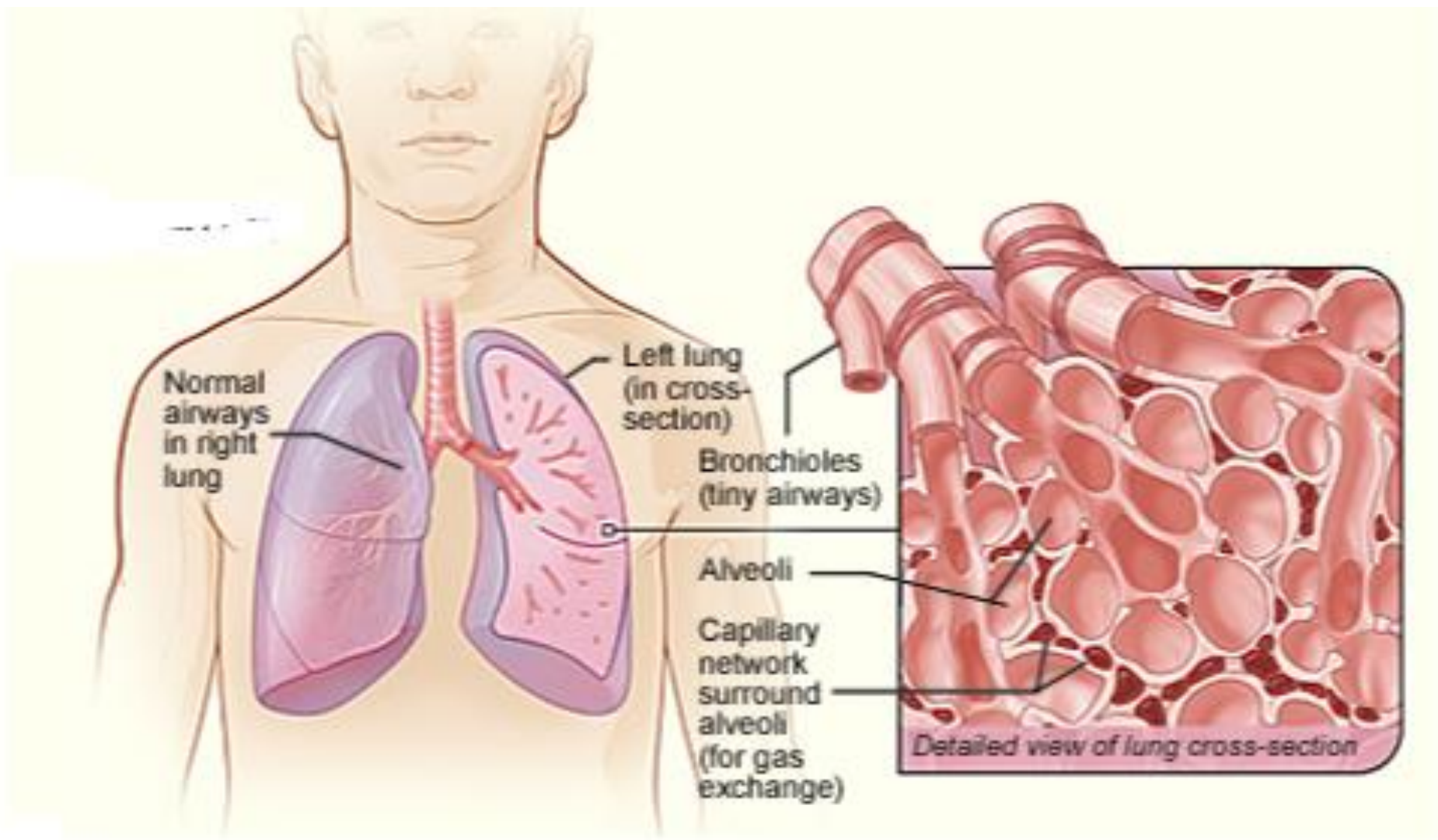
#### Pathology of Vaping-Associated Lung Injury

Butt et al, N Engl J Med 2019; 381:1780-1781



**Figure 1. Histopathology of Acute Lung Injury Associated with Vaping.**

Most cases showed airway-centered acute lung injury (Panel A), often with severe bronchiolitis accompanied by marked mucosal edema, sloughing of bronchiolar epithelium, and peribronchiolar organization (Panel B). All cases showed accumulation of foamy or vacuolated macrophages in peribronchiolar airspaces with pneumocyte vacuolization (Panel C). Four cases showed severe injury, with diffuse alveolar damage and hyaline membranes (Panel D); two of these patients died.



# What is vaping-associated lung injury?

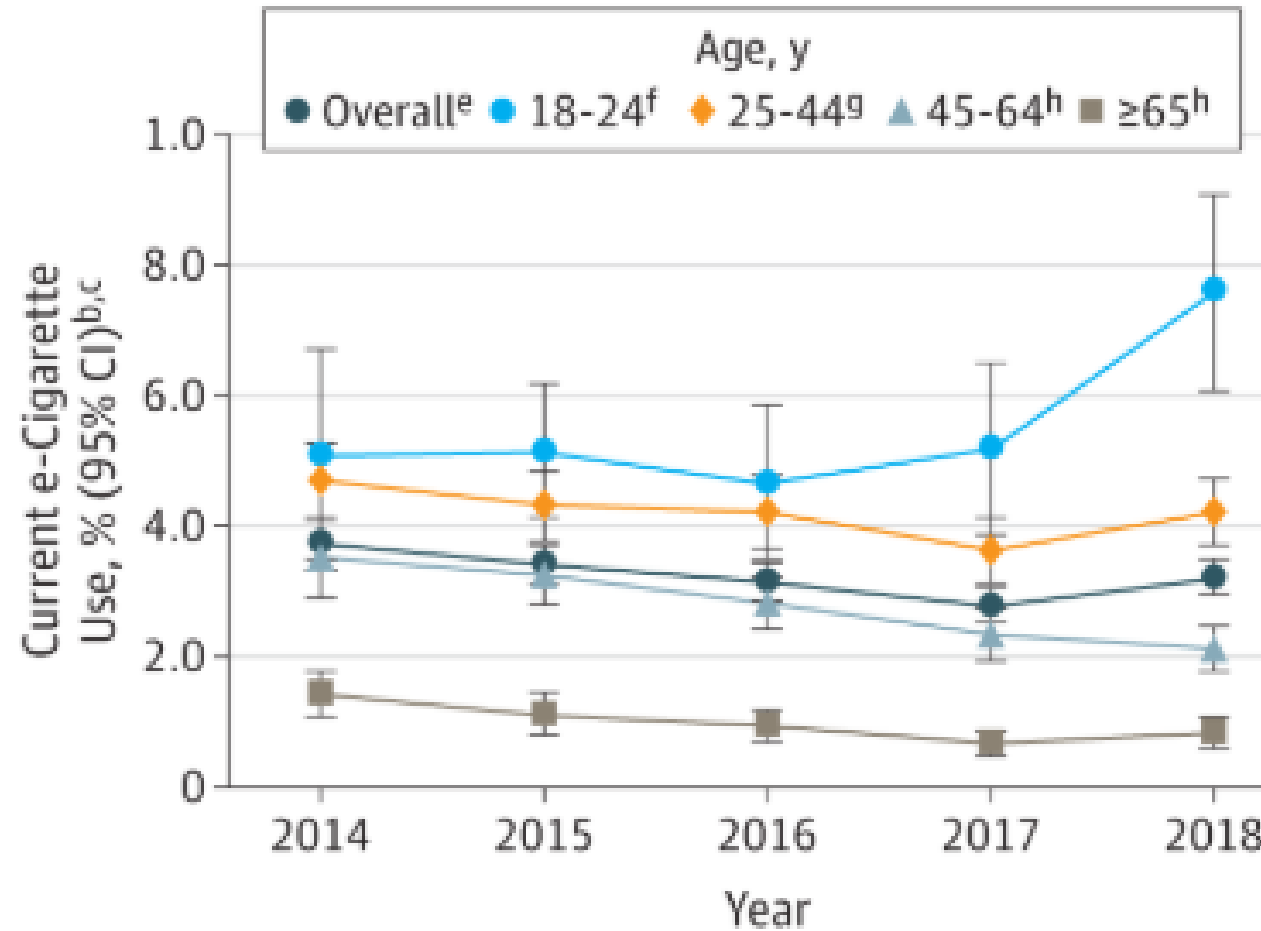
Heterogeneous group of diseases with consistent theme of acute lung damage, manifesting as

- Lipoid pneumonia
- Diffuse Alveolar Damage
- Acute eosinophilic pneumonia
- Organising pneumonia
- Diffuse alveolar haemorrhage
- Hypersensitivity pneumonitis
- Giant-cell interstitial pneumonia



# Current vaping prevalence by age, USA 2014-18

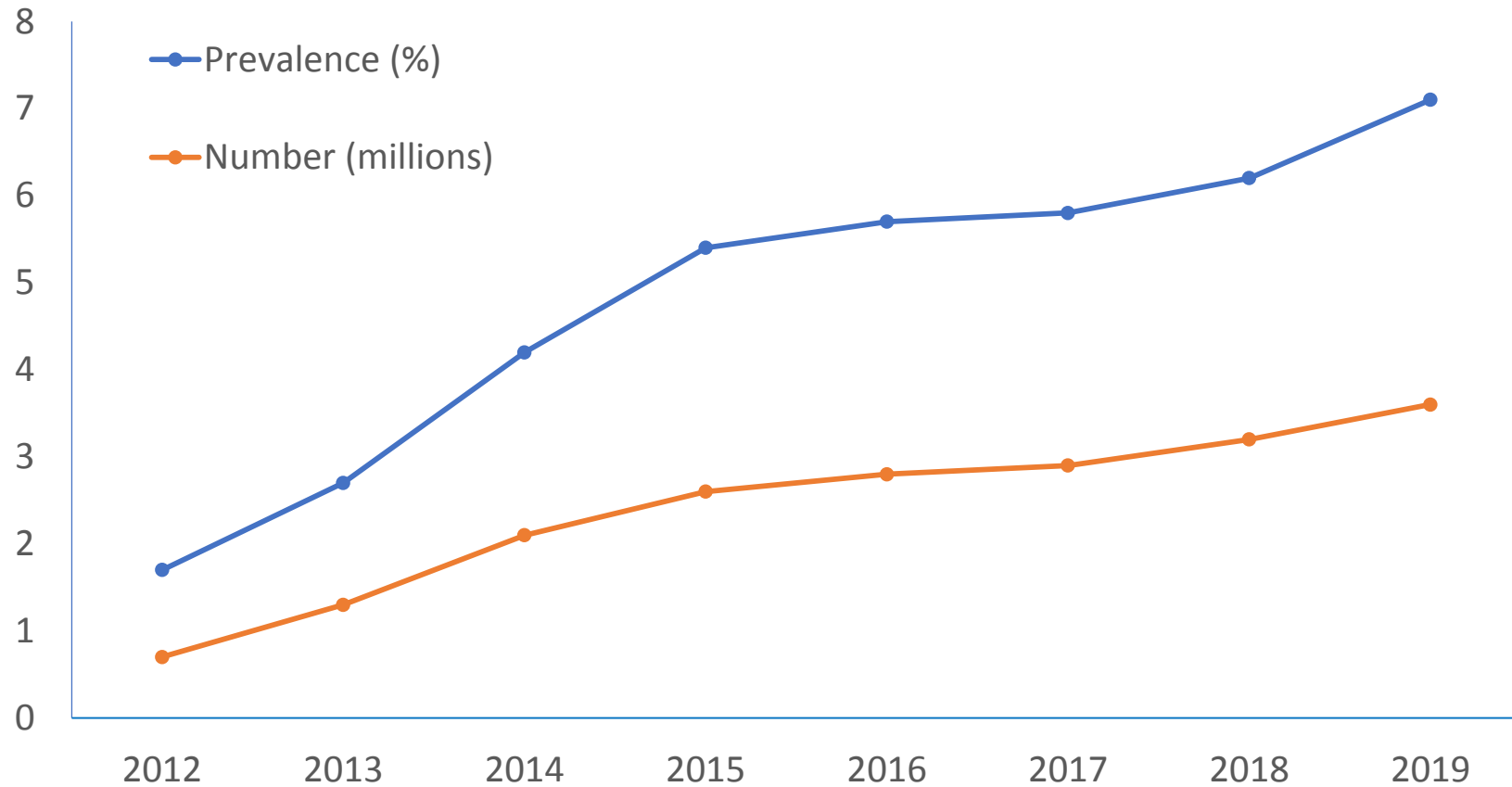
*Dai et al, JAMA 2019 doi:10.1001/jama.2019.15331*



Approx 9 million vapers in US; 3.6 million in UK; global total 41 million

# Vaping in the UK 2012-19

<https://ash.org.uk/wp-content/uploads/2019/09/Use-of-e-cigarettes-among-adults-2019.pdf>



# Characteristics of USA outbreak cases (as of 5.11.19)

[https://www.cdc.gov/tobacco/basic\\_information/e-cigarettes/severe-lung-disease.html](https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html)

- 2,051 cases, 39 deaths
- Affecting all US States except Alaska
- 70% male
- Median age 24 (range 13-75); 79% aged under 35
- Mortality median age 53 (range 17-75)
- ~ 86% report using THC products (34% exclusively)
- ~ 64% report using nicotine products (11% exclusively)

*The latest ... findings suggest products containing THC, particularly those obtained off the street or from other informal sources (e.g. friends, family members, illicit dealers), are linked to most of the cases and play a major role in the outbreak.*

# Outbreak of Lung Injury Associated with the Use of E-Cigarette, or Vaping, Products

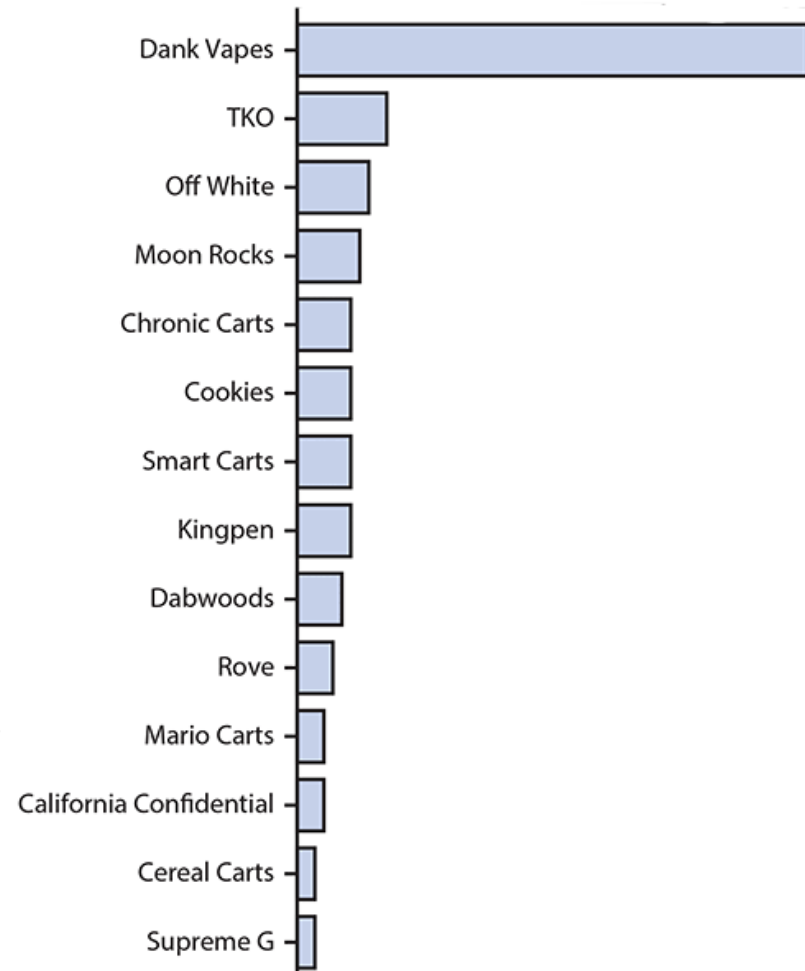
*Updated November 8, 2019, at 1:00 PM EST*

## *New CDC Laboratory Findings (summarised):*

- Vitamin E acetate found in **all** bronchoalveolar lavage samples from 29 patients from 10 states
- THC identified in 82% of samples and nicotine in 62%
- Other compounds found in or added to THC products (plant oils, mineral oil, medium-chain triglyceride oil and terpenes) **not** found
- first time a potential chemical of concern [detected] in biologic samples from patients with these lung injuries
- Findings provide direct evidence of vitamin E acetate at the primary site of injury within the lungs.

# Frequently reported brand names of tetrahydrocannabinol (THC)- and nicotine-containing electronic cigarette products reported by patients with lung injury — Illinois and Wisconsin, 2019

[https://www.cdc.gov/mmwr/volumes/68/wr/mm6839e2.htm?s\\_cid=mm6839e2\\_w#F1\\_down](https://www.cdc.gov/mmwr/volumes/68/wr/mm6839e2.htm?s_cid=mm6839e2_w#F1_down)



## Maricopa County Sheriff's Office Busts Illegal THC Vape Cartridges Operation

September 18, 2019 Arizona Daily Independent News Service



Over \$380,000 worth of illegal drugs, firearms and cash. [Photo courtesy MCSO]

According to the Maricopa County Sheriff's Office, detectives also located approximately 1,100 "Dank" brand packaged vape cartridges and 8 jars of narcotic distillate. These cartridges have been located throughout the country and have been associated with recent vaping deaths, were being manufactured in the residence.

<https://arizonadailyindependent.com/2019/09/18/maricopa-county-sheriffs-office-busts-illegal-thc-vape-cartridges-operation/>

# MHRA e-liquid content database (Nov 2017) analysis

*Nyakutsikwa et al, submitted for publication*

- 41 809 products, comprising cartridges and refill containers
- Searched for
  - vitamin E acetate
  - vitamin E acetate synonyms listed on PubChem
  - all potential Chemical Abstract Service (CAS) numbers for Vitamin E acetate (58-95-7, 7695-91-2, 52225-20-4)
- Vitamin E acetate not listed as an ingredient or emission in any of the provided products
- 854 (2%) of products listed flavours but not specific ingredients; their composition therefore unknown.

## Gateshead doctor calls for research into 'e-cigarettes'

🕒 28 March 2011



**A doctor from Tyneside has called for more research into "electronic" cigarettes following the death of one of his patients.**

It comes after an inquest recorded an open verdict into the death of Terence Miller from Gateshead.

Mr Miller, who used large quantities of the substitutes, had suffered from a



Dr Rob Allcock, who treated him at the Queen Elizabeth Hospital, believes this could be associated with his use.

The "e-cigarettes" are battery-powered and contain a cartridge of liquid nicotine.

This is heated and the user inhales vaporised droplets of the drug and breathes out a mist rather than smoke.

Supporters describe them as a healthy alternative to real cigarettes because their users can inhale nicotine without tar, tobacco or carbon monoxide.

Dr Allcock said that the brand Mr Miller had been using seemed to involve a mixture of nicotine and some oil.

<https://www.bbc.co.uk/news/uk-england-12887335>



## An Unexpected Consequence of Electronic Cigarette Use

*Lindsay McCauley, DO; Catherine Markin, MD, FCCP; and Danielle Hosmer, MD*

*CHEST 2012; 141(4):1110–1113*



FIGURE 1. Representative CT images show the “crazy paving” pattern of patchy ground glass superimposed on interlobular septal thickening. A, Bilateral upper lobes. B, Bilateral lower lobes.

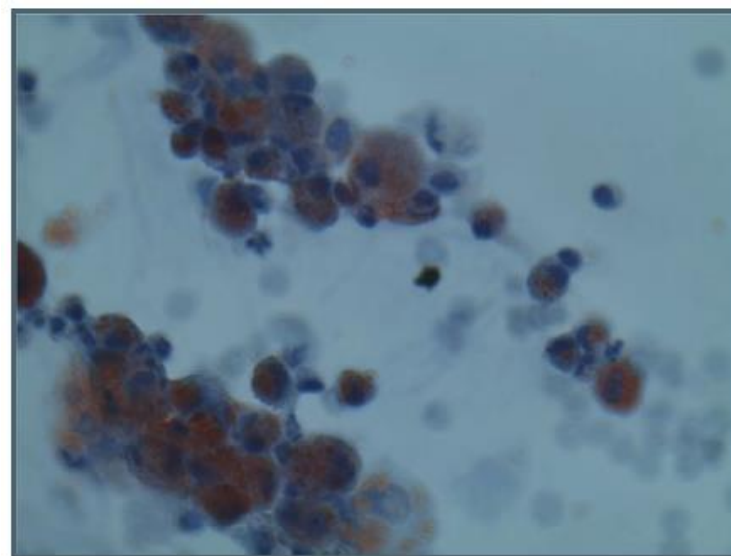
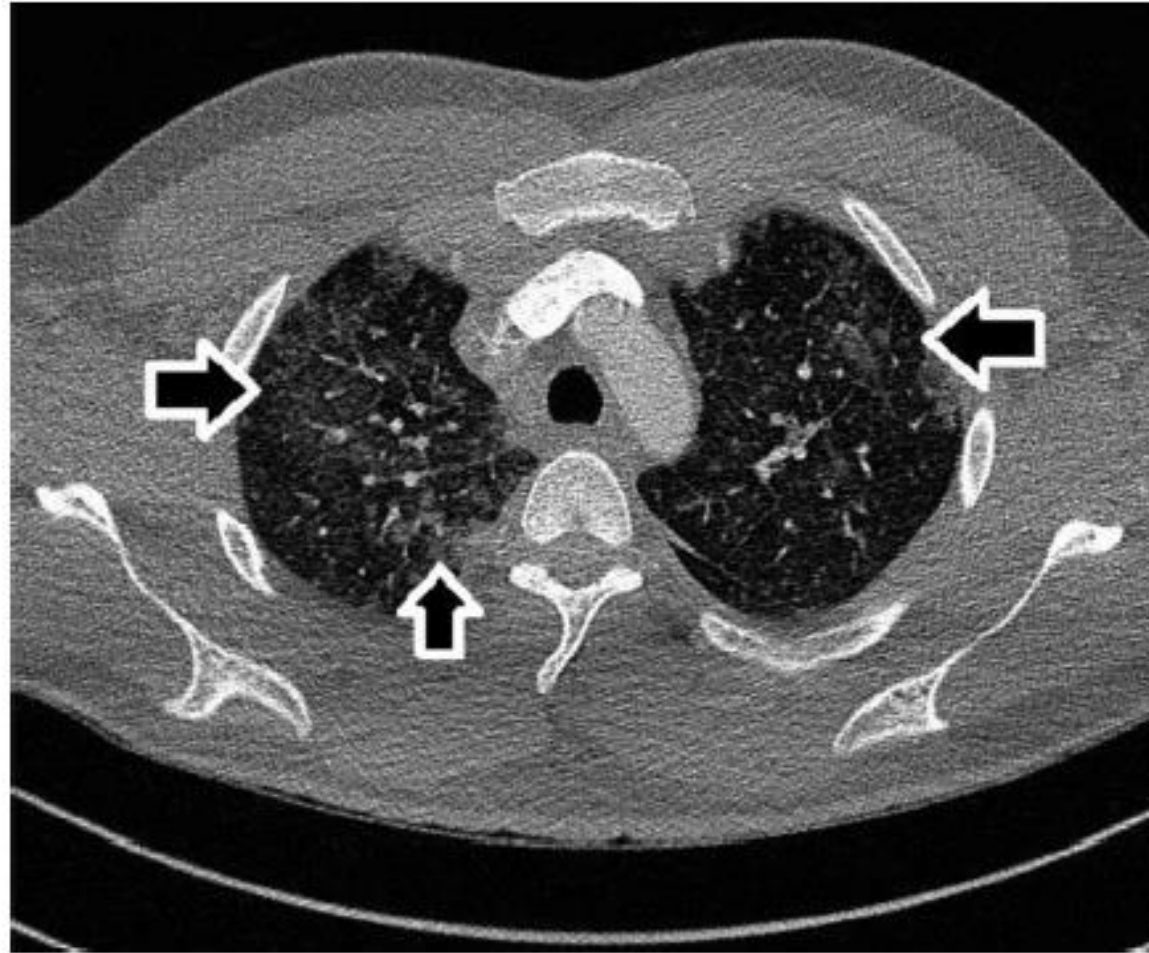


FIGURE 2. Photomicrograph of BAL sample shows lipid-laden macrophages (Oil-Red-O stain, original magnification  $\times 100$ ).



# Eosinophilic pneumonia in otherwise healthy young man

*Thota J Emerg Med 2014;47:15-17*



**Figure 2.** Chest computed tomography showing apical ground glass opacities.

## Bilateral Pneumonia and Pleural Effusions Subsequent to Electronic Cigarette Use

Kendall Moore, Henry Young II, Matthew F. Ryan\*

- 43 year-old man
- Three days of intense vaping
- Presented with pneumonia, raised inflammatory markers, normal blood count
- Recovered over 48 hours with antibiotics and bronchodilators





CASE BASED DISCUSSION

## A case report of subacute bronchial toxicity induced by an electronic cigarette

José Hureaux,<sup>1,2,3,4</sup> Martine Drouet,<sup>1,2</sup> Thierry Urban<sup>1,2,3,4</sup>

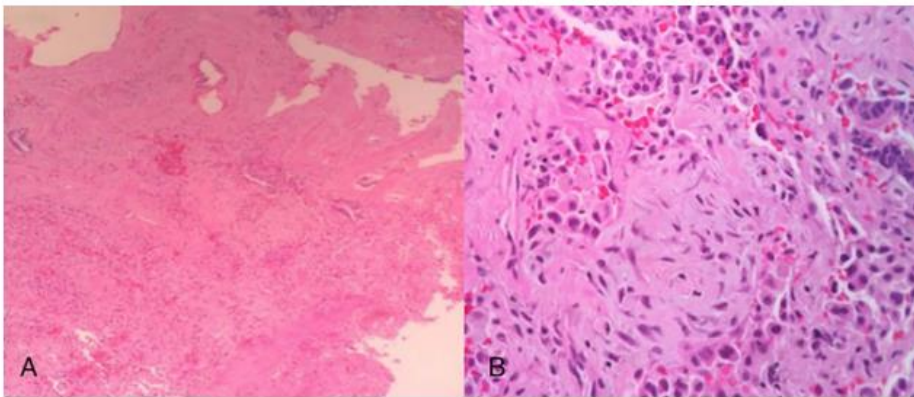
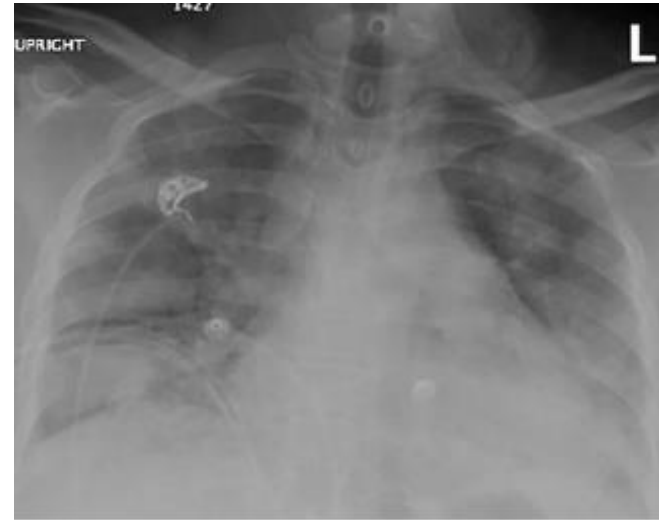
Thorax 2014;69:596–597

- 43 year-old man with chronic obstructive pulmonary disease and disseminated lung cancer, post chemotherapy
- Former heavy smoker, switched to e-cigarettes
- Productive cough within 48 hours, breathlessness from one week
- Wheezing on examination, chest X-ray unchanged
- No signs of infection
- Diagnosis of non-infective bronchiolitis
- Improved within days of stopping vaping

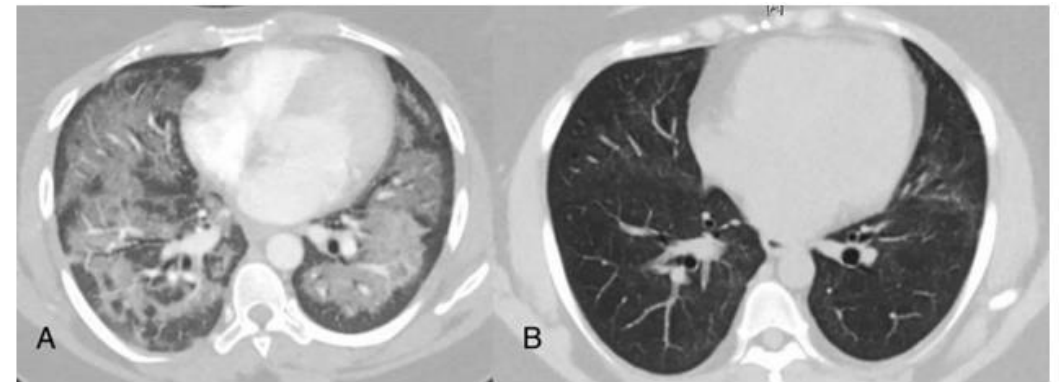
# Organizing pneumonia related to electronic cigarette use

*Khan et al, Clin Respir Journal 2018;12:1295–1299*

- Female, 40 years
- One month of chest pain and breathlessness
- Started on switching from tobacco to electronic cigarettes



**FIGURE 3** (A) Low power view of organizing pneumonia showing several rounded and elongated nodules of fibrous tissue compressing adjacent lung. (B) High power view shows nodules of fibroblasts and myofibroblasts arranged in whorls with pale grey matrix (Masson bodies) within the airspace



**FIGURE 2** (A) CT of the chest showed multifocal discrete and confluent ground glass opacities diffusely involving bilateral lung lobes. (B) Follow up CT of chest 2 months later showing complete resolution of ground glass opacities

# Diffuse alveolar damage and e-cigarettes: Case report and review of literature

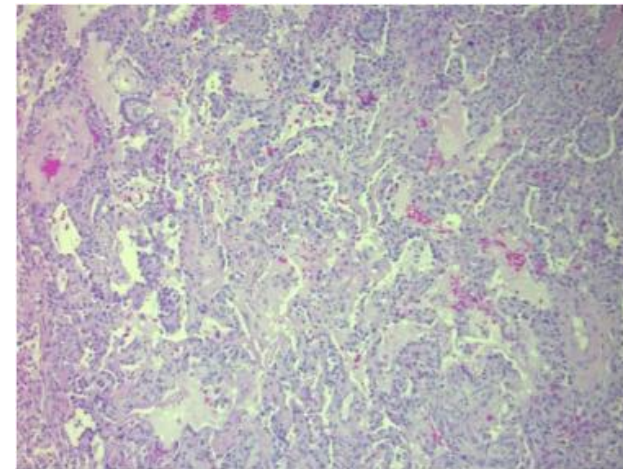
Sulaimon A. Bakre<sup>a,\*</sup>, Tariq S. Al-Farra<sup>b</sup>, Sherif Al-Farra<sup>c</sup>

Respiratory Medicine Case Reports 28 (2019) 100935

- 47 year-old woman
- 3 years vaping history



Fig. 1. Computed Tomography (CT) of the chest showing diffuse opacities.

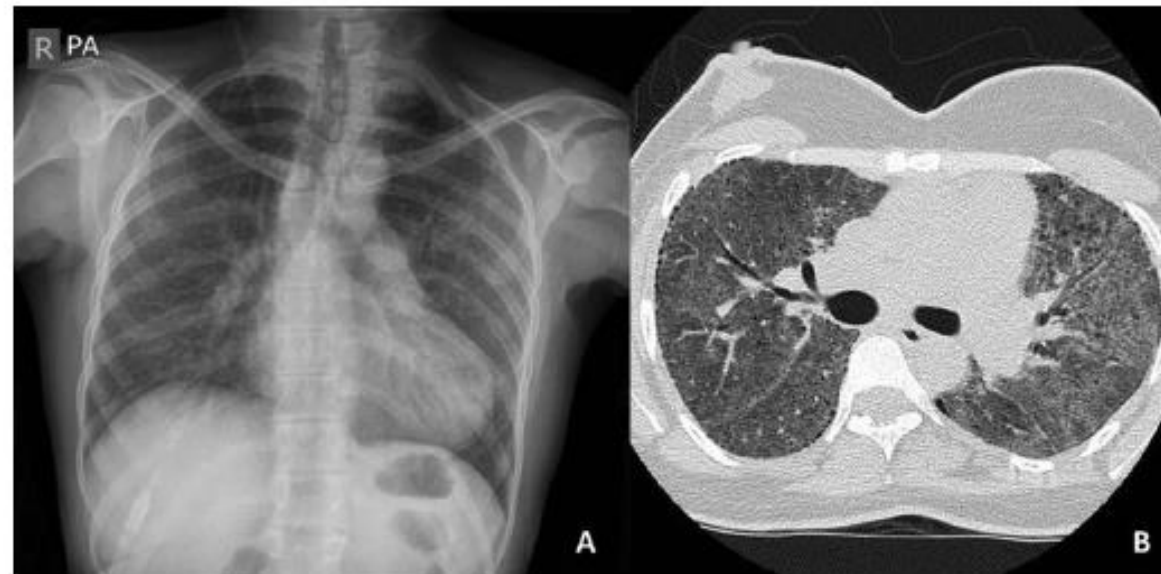




# Respiratory failure caused by lipoid pneumonia from vaping


*Viswam et al, BMJ Case Reports 2018 doi:10.1136/bcr-2018-224350*

- 34 year old UK woman
- Vaping 3 years, ex smoker
- 3 months increasing breathlessness and cough
- Improved with steroid therapy

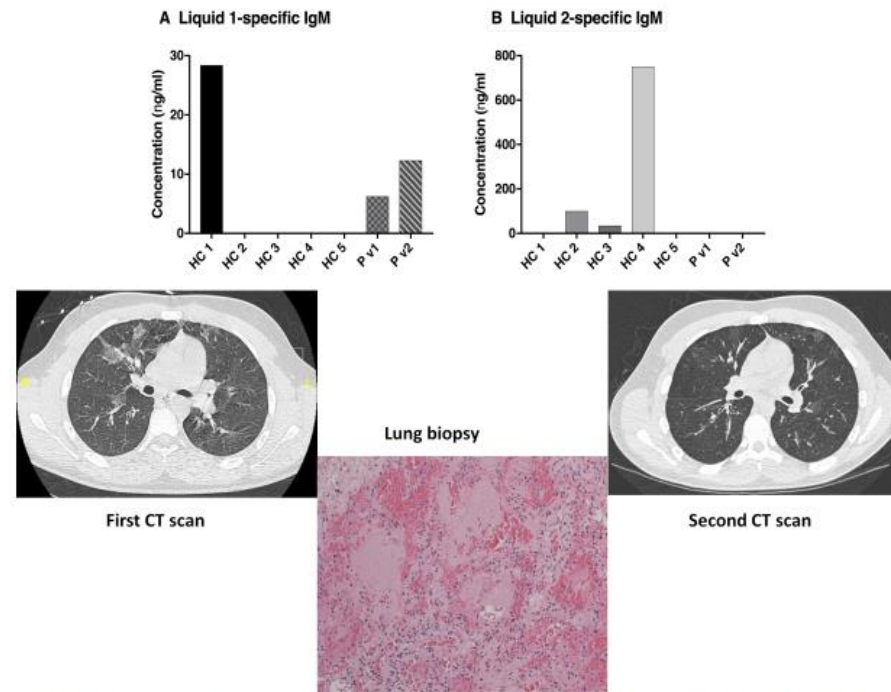


**Figure 1** (A) Chest radiograph showing bilateral diffuse infiltrates throughout both lung fields. (B) High-resolution CT slice from upper lobes showing diffuse ground-glass opacity and subpleural cysts bilaterally.

# Life-threatening hypersensitivity pneumonitis secondary to e-cigarettes

Nisha Nair,<sup>1</sup> Matthew Hurley,<sup>2</sup> Simon Gates,<sup>1</sup> Patrick Davies,<sup>3</sup> I-Ling Chen,<sup>4</sup> Ian Todd,<sup>4</sup> Lucy Fairclough,<sup>4</sup> Andrew Bush ,<sup>5</sup> Jayesh Mahendra Bhatt <sup>2</sup>

*Arch Dis Child* 2019;0:1–3. doi:10.1136/archdischild-2019-317889



**Figure 1** Radiology—immunology—histopathology correlation in a case of hypersensitivity pneumonitis: concentration of liquid 1 specific IgM. Concentration of liquid 2 specific IgM. First CT scan: day 6 from first presentation. Second CT scan: day 44 from first presentation. Lung biopsy showing inflammation and hyaline membrane formation.

# MHRA e-cigarette yellow card reports of respiratory disease (1<sup>st</sup> January 2010 to 27<sup>th</sup> September 2019)

Name: E-cigarette Yellow Card reports		
Report Run Date: 30-Sep-2019		
Earliest Reaction Date: 01-Jan-2010		
Data Lock Date: 27-Sep-2019 19:00:05		
MedDRA Version: MedDRA 22.0		
Reaction Name	Total	Fatal
<b>Respiratory disorders</b>		
<i>Breathing abnormalities</i>		
Dyspnoea	13	0
Dyspnoea at rest	2	0
Respiratory distress	1	0
<i>Bronchospasm and obstruction</i>		
Asthma	3	0
Chronic obstructive pulmonary disease	1	0
Wheezing	3	0
<i>Conditions associated with abnormal gas exchange</i>		
Asphyxia	1	0
<i>Coughing and associated symptoms</i>		
Cough	13	0
Productive cough	1	0
Sputum increased	1	0
<i>Lower respiratory tract inflammatory and immunologic conditions</i>		
Pneumonia lipoid	2	1
Pneumonitis	1	0
<i>Nasal congestion and inflammations</i>		
Nasal congestion	1	0
<i>Parenchymal lung disorders NEC</i>		
Pulmonary alveolar haemorrhage	1	0
Pulmonary fibrosis	1	0
<i>Pharyngeal disorders (excl infections and neoplasms)</i>		
Pharyngeal swelling	2	0
<i>Pulmonary oedemas</i>		
Pulmonary congestion	1	0
<i>Respiratory tract disorders NEC</i>		
Allergic respiratory disease	1	0
<i>Upper respiratory tract signs and symptoms</i>		
Choking	1	0
Dry throat	1	0
Dysphonia	2	0
Oropharyngeal pain	6	0
Rhinalgia	1	0
Rhinorrhoea	4	0
Sneezing	1	0
Throat irritation	3	0
<b>Respiratory disorders SOC TOTAL</b>	<b>68</b>	<b>1</b>

Plus ? one case pulmonary haemorrhage + lipoid pneumonia, ? one of ARDS



# Likely respiratory effects of vaping nicotine:

Chronic disease: expect modest increases in risk of:

- Lung cancer
- Emphysema/COPD
- Pulmonary fibrosis

Acute disease: expect rare cases of

- Lipoid pneumonia
- Hypersensitivity pneumonitis
- Lung infection (pneumonia)
- Other acute lung injury as per US outbreak

Balance of risk strongly favours vaping over smoking

# Annual health consequences of tobacco smoking in the UK

*ASH 2019, NHS Digital 2017, RCP 2010*

## *To adults:*

- ~ 100,000 deaths, average 10 year loss of life

## *To the unborn child:*

- 5300 fetal/perinatal deaths
- 2,200 premature births; 19,000 low birth weight babies
- Increased risk of developmental anomalies

## *To children:*

- 40 sudden infant deaths
- 165,000 new cases of asthma, bronchitis, ear disease, meningitis
- Twice as likely to become a smoker if parents smoke

## *To wider society:*

- £3.1 billion in NHS and social care costs
  - – includes 474,000 admissions, 35% higher GP use
- Nearly £10 billion in wider societal costs

# Practical consequences for vaping: PHE recommendations (summarised)

<https://publichealthmatters.blog.gov.uk/2019/10/29/vaping-and-lung-disease-in-the-us-phes-advice/>

- **For smokers:**
  - stop smoking completely.
- **For people who vape nicotine:**
  - if you are still smoking, switch completely to vaping
  - come off nicotine when you are confident you won't relapse to smoking.
- **If you have never smoked:**
  - Don't vape.
- **For people who vape CBD or THC:**
  - if you experience symptoms or are concerned you should stop.
  - If you feel unwell or have any difficulty breathing after vaping THC, go to A&E and tell them precisely what the product was you were using.

## VAPE ALERT Teenage boy, 16, nearly died after vaping triggered ‘catastrophic’ lung damage – in just 5 months

Shaun Wooller  
11 Nov 2019, 23:30 | Updated: 12 Nov 2019, 7:37

## Boy, 17, is first to have double lung transplant because of vaping damage



Richard Hartley-Parkinson Wednesday 13 Nov 2019 6:29 am

## Study suggests vaping causes inflammation linked to lung cancer just a MONTH after non-smokers start heavily using devices linked to nearly 30 US deaths

By NATALIE RAHHAL DEPUTY HEALTH EDITOR FOR DAILYMAL.COM  
PUBLISHED: 15:07, 16 October 2019 | UPDATED: 17:27, 16 October 2019

VIDEO

## Watchdog dossier reveals 200 health problems linked to vaping

As experts call for a national system to record all ill-effects reported, the head of the vape giant Juul has resigned

Andrew Gregory and Jon Ungood-Thomas

September 29 2019, 12:01 am,  
The Sunday Times

United States Health



Medical authorities say there is no proof problems suffered by vapers are due to the e-cigarettes themselves but scrutiny is growing.  
DAVID BARNALL

## Smoking in the UK, Australia and USA 2011-18

