



# EVALI: E-Cigarette or Vaping-Associated Lung Injury

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Managed Care APPE Rotation  
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# Objectives



Define EVALI



Epidemiology



Recognize key signs and symptoms



Discuss diagnosis and management



Familiarize with key updates and how to prevent EVALI

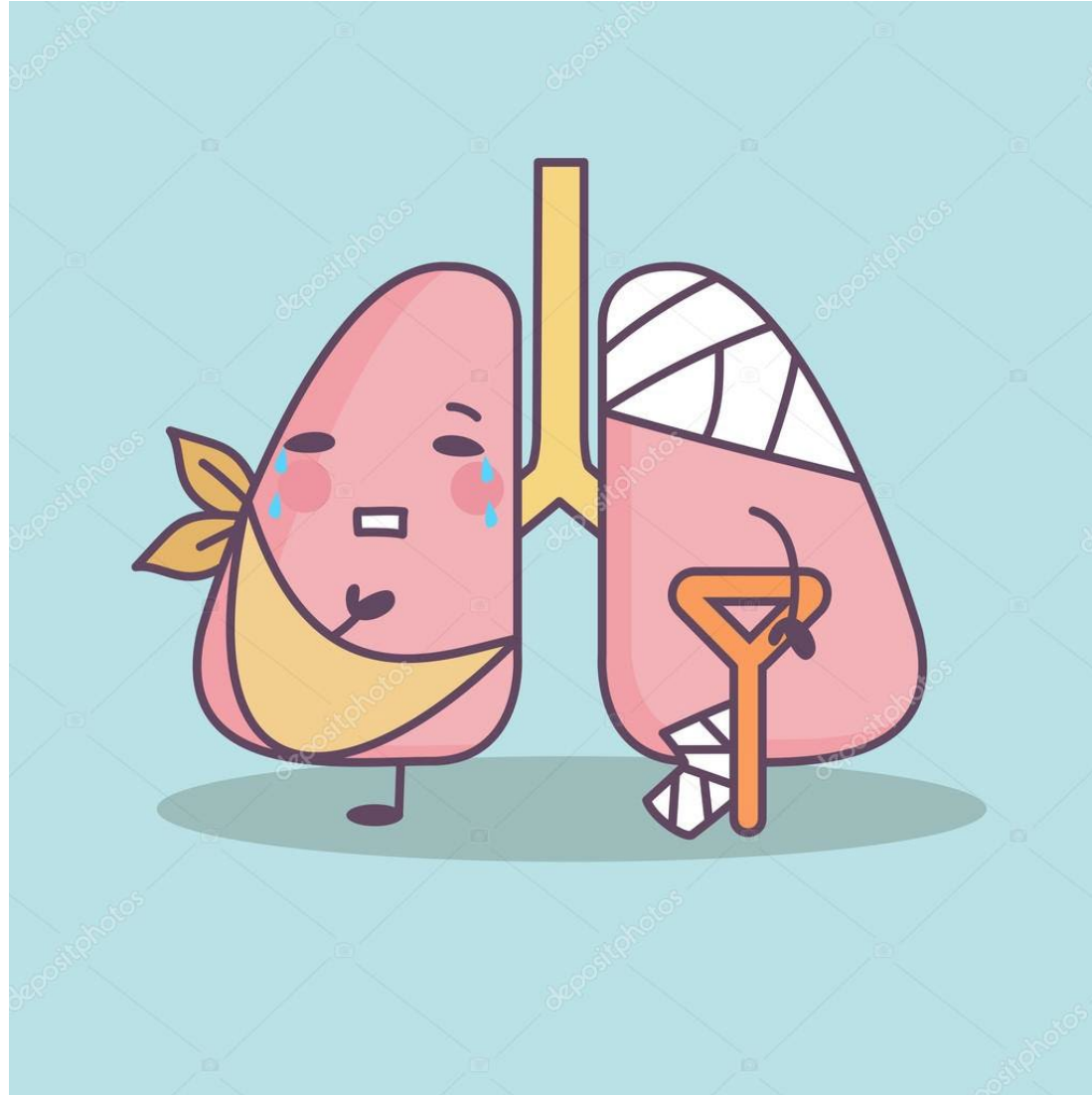
# Background





# What is EVALI?

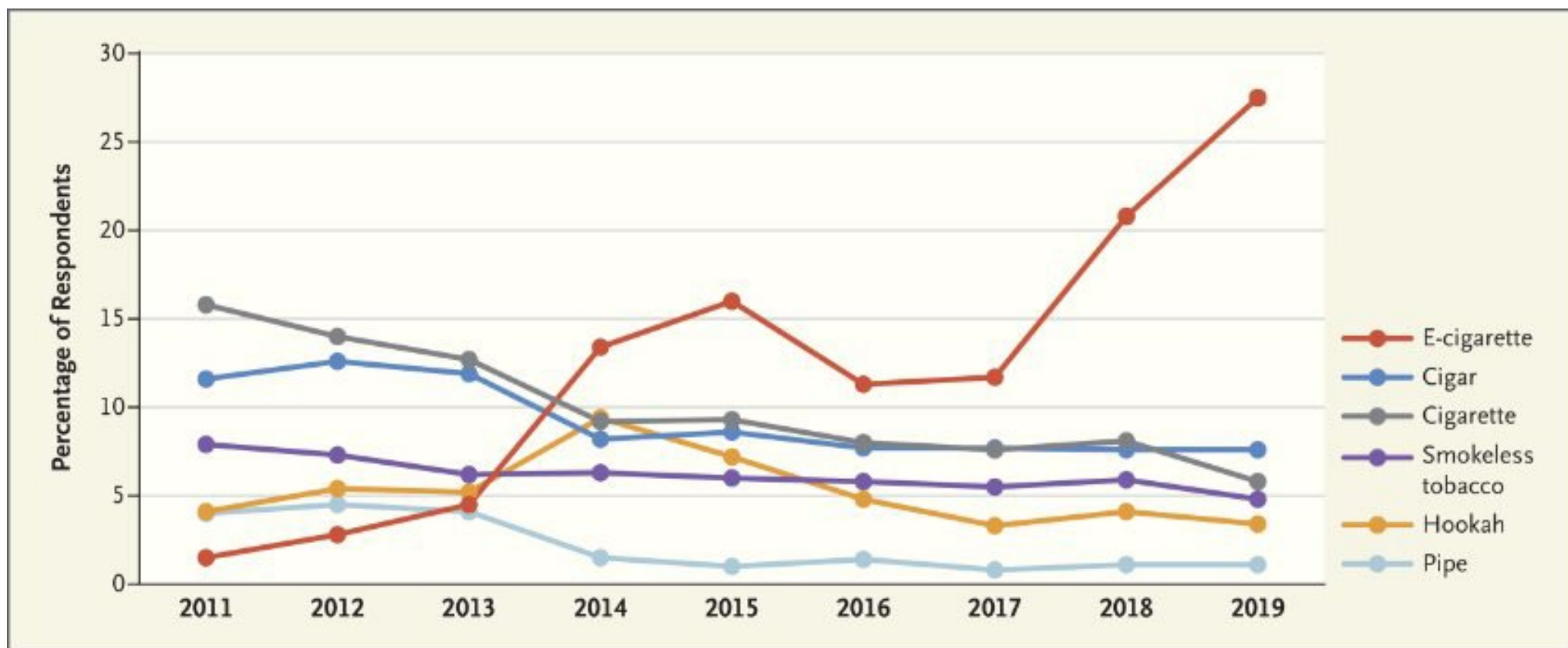
- EVALI: E-cigarette or Vaping-Associated Lung Injury
- Identified in 2019 following a cluster of cases linked to the use of e-cigarettes and vaping products (CDC)
- Characterized by lung inflammation



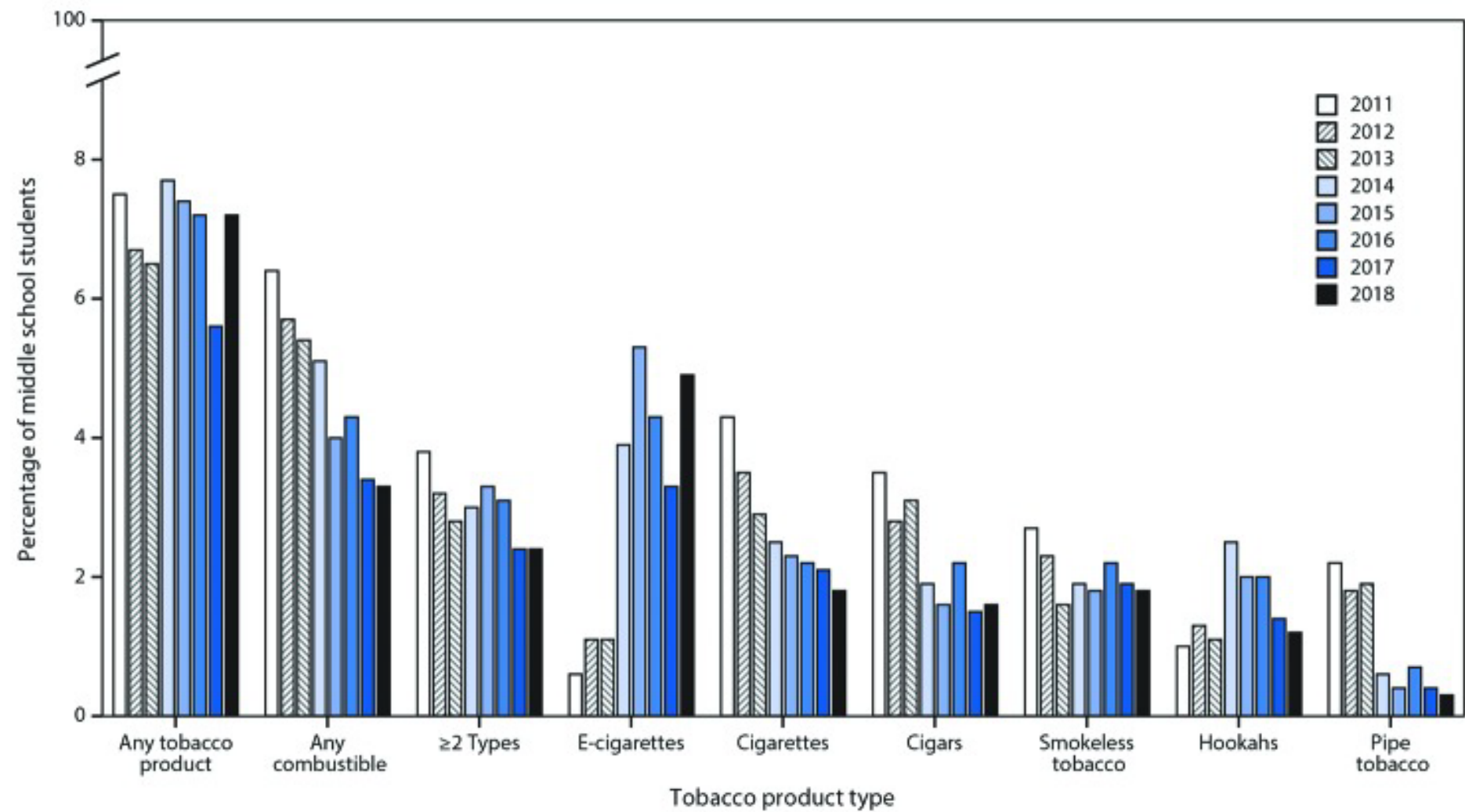
# Epidemiology



- Over 2,800 cases and 68 deaths reported in the U.S
- Predominately affects adolescent and young adults



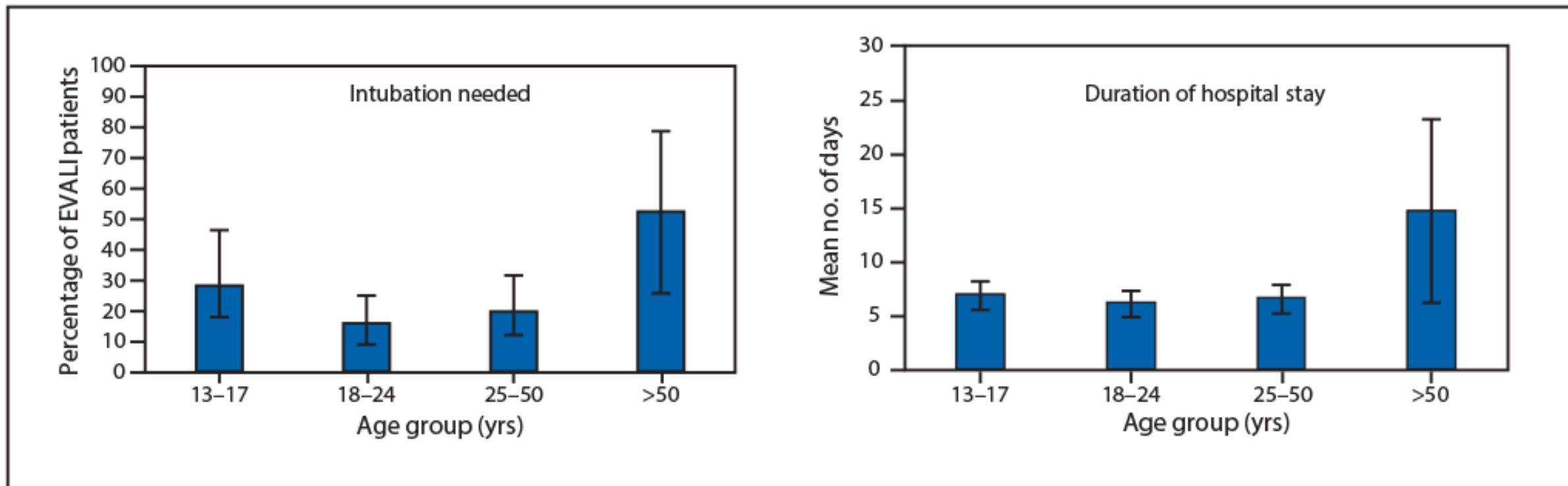
# Case Trends



# CDC 2019 Statistics



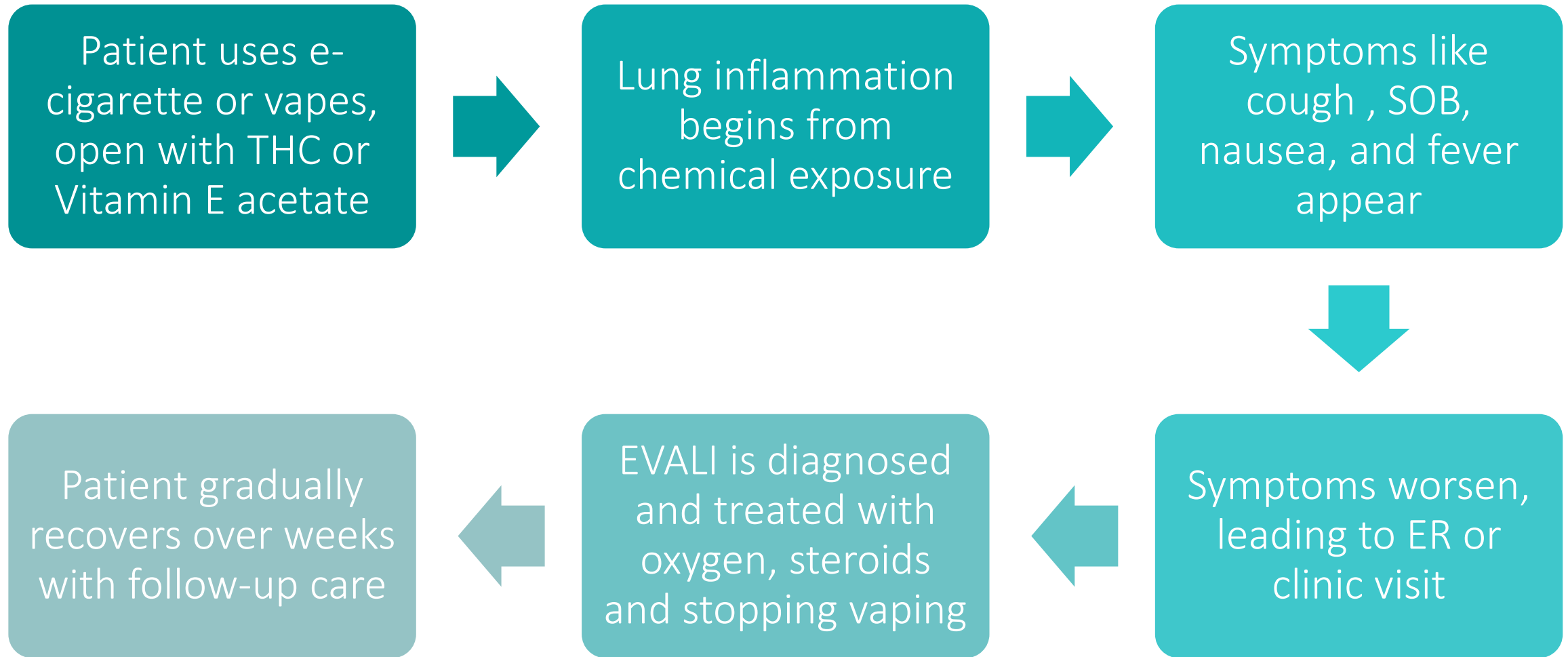
## CDC 2019 EVALI Statistics:



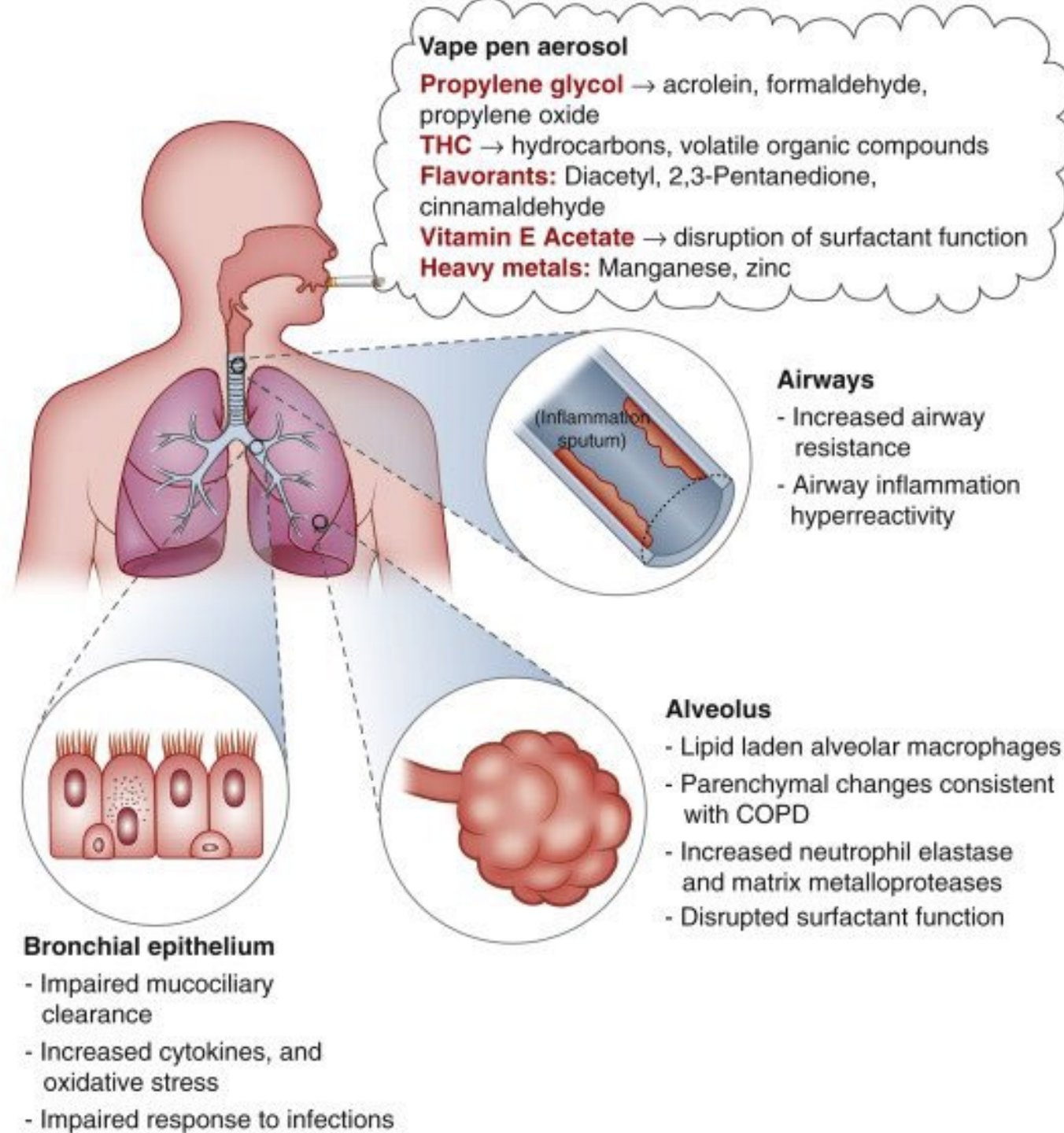
**Percentage of persons needing intubation (N = 338) and hospitalization (N = 242) among patients with e-cigarette, or vaping, product use associated lung injury (EVALI), by age of patient — United States, February 1–October 3, 2019\***



# Development of EVALI



# Pathophysiology



# How vaping works?

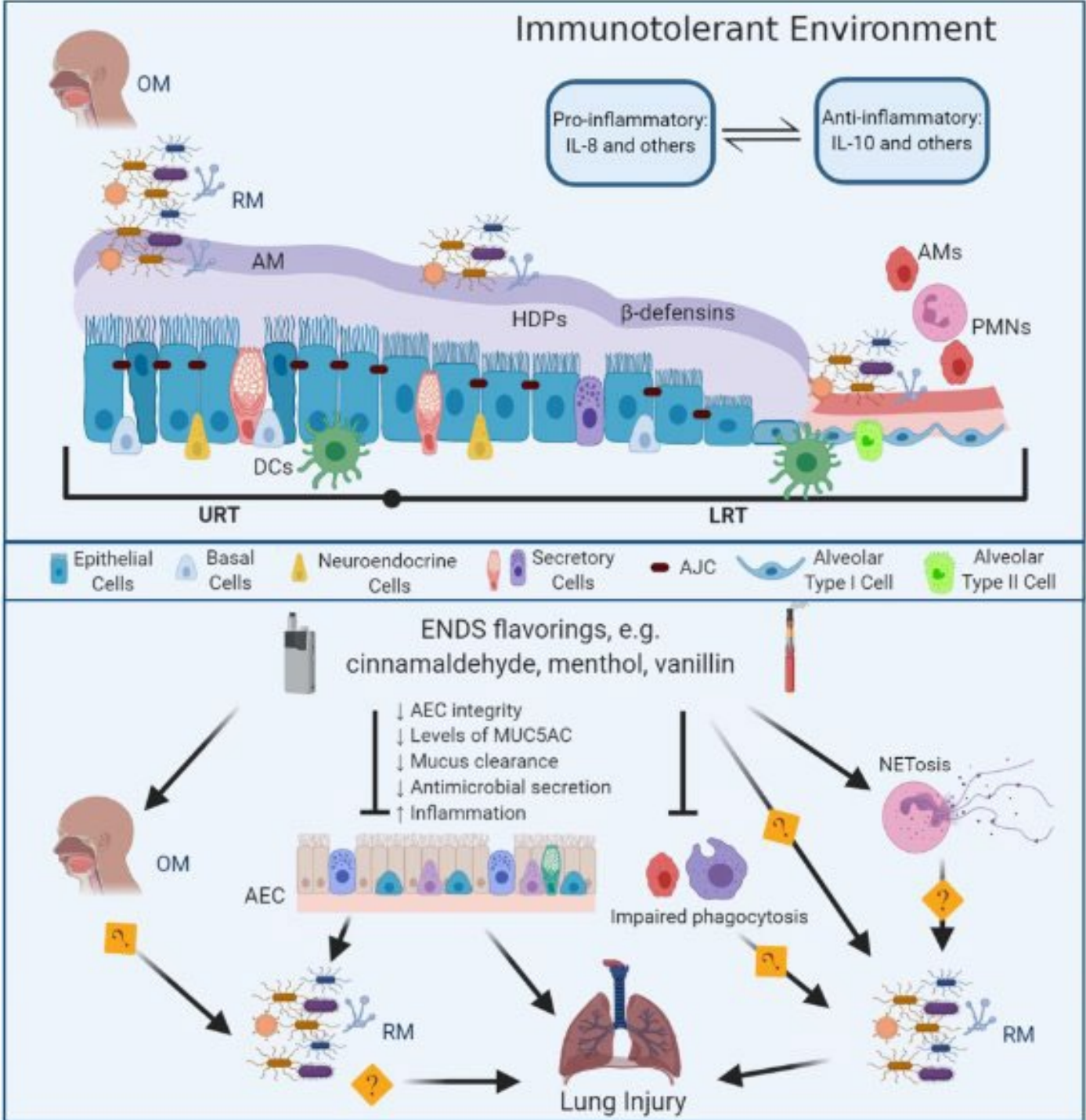
- Direct chemical injury happens from inhaled toxins causing disrupted lung surfactant and cell integrity
- Alveolar permeability
- Fluid, proteins and immune cells leak into alveoli
- May trigger cytokine release IL-6, IL-8, TNF-alpha, worsening the inflammation
- Can mimic or progress to ARDS (Acute Respiratory Distress Syndrome)



## Lipid-Laden Macrophages:

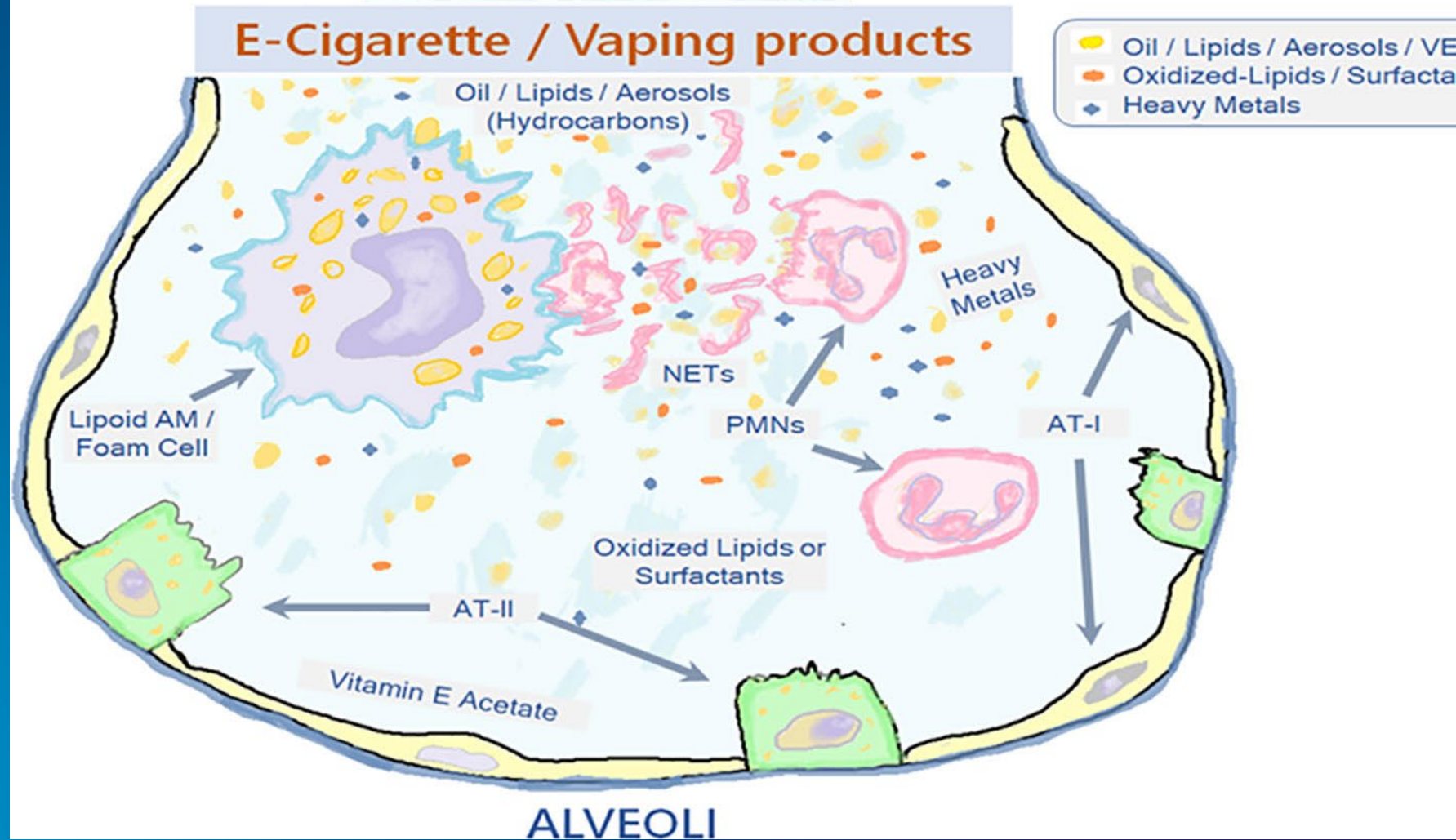
- Vitamin E acetate and oils are poorly cleared by the lung
- Macrophages engulf these lipids, forming "foamy" macrophages
- These are key markers in bronchoalveolar lavage fluid (BAL)
- May contribute to oxidative stress and impaired microphage function

# Mechanism of e-liquid flavorings



# Pathophysiology

THC containing  
counterfeit  
ENDS cartridges



# Immune Response Shift

## - EVALI

- High neutrophil counts CD163 (-) M1 macrophages - pro-inflammatory
- Increase in inflammatory markers:
  - IL-6, IL-8
  - TNF- $\alpha$
  - CCL2
  - Serum Amyloid A



# What are IL and TNF markers and how do they work?

- IL-6: Interleukin-6 is a pro-inflammatory cytokine
  - Mediates acute phase response
  - Fever
  - Stimulates immune response
  - Produced by T cells, macrophage, other
- IL-8: Interleukin-8 Chemokine CXCL8
  - Attracts neutrophils to sites of infection/inflammation
  - Secreted by macrophages, epithelial cells, airway smooth muscle cells
- TNF-alpha: Tumor Necrosis Factor Alpha
  - Key mediator for systemic inflammation, fever, apoptotic cell death
  - Macrophages, some T cells/mast cells



# What are IL and TNF markers and how do they work?

- ELISA (Enzyme-Linked Immunosorbent Assay)
  - Most common for cytokine in blood
- Polymerase Chain Reaction (PCR)
  - Used for mRNA expression of cytokines in tissues
- Flow cytometry
  - Cytokine-producing cells using intracellular staining
- Immunohistochemistry
  - localization
- Multiplex bead assays:
  - detects several cytokines at once



# Role in EVALI?

- Elevated IL-6, IL-8, TNF-alpha indicate intense inflammation and immune activation
- It specifically attracts neutrophils to the lungs correlating with neutrophilic alveolitis seen in EVALI cases
- The IL-6 and TNF promote a cytokine storm and alveolar damage
- They recruit inflammatory cells and lead to lung tissue injury
- Amplify immune response -> more damage
- Associated with severe disease and possible hospitalization



# Triggers for EVALI?

## Vitamin E

- Used as a thickening agent in vape cartridges
- Disrupts lung surfactant
- Triggers inflammatory response



## Other additives:

- THC: can be counterfeit cartridges
- MCT: medium chain triglycerides
- Propylene glycol
- Flavorings (toxic when vaporized)

# How long does it take to develop EVALI?

- Most cases: few days to a few weeks of frequent use
- First exposure: some cases develop after a few uses of high-risk products (THC cartridges with vitamin E acetate)
- Chronic users: some developed after months or years of regular use
- There is no amount of use that is deemed "safe", risk depends on product content



# Timeline for discovery of EVALI



2019

First cluster of lung injury cases reported, CDC investigation is initiated



October 2019

Vitamin E acetate identified as key chemical culprit in lung injury



November 2019

Outbreak peaks: over 2,000 cases and increasing, CDC issues national health alerts



January 21st 2020

2,711 cases of hospitalized EVALI or deaths were reported by all 50 states, District of Columbia, and 2 U.S territories

- 60 deaths had been confirmed



2021-2022

Focus shifted to long-term effects, youth vaping, and lung recover research



2023-2024 -> present

Continued prevention efforts, regulation and small isolated cases, most information has been archived on CDC website



# Rise of E-cigarettes and Vapes:

- Early E-cigarettes invented in China (early 2000's)
- Designed as a "smokeless" nicotine delivery system
- Mid-2000's, early brands marketed as safer alternative to smoking



- Large brand name JUUL Labs launches JUUL in 2015 with a sleek USB-like design (appealing to youth, discreet)
- Nicotine salt technology with flavored pods (mango, mint)
- Social media aggressive marketing and influence campaigns, youth friendly imagery and flavors

- E-cigarette use among high schoolers from 1.5% in 2011 to 27% in 2019
- The further restrict FDA flavored pods and advertising
- JUUL removes certain flavors

# EVALI

## Diagnosis and Symptoms



# ICU Admission Criteria

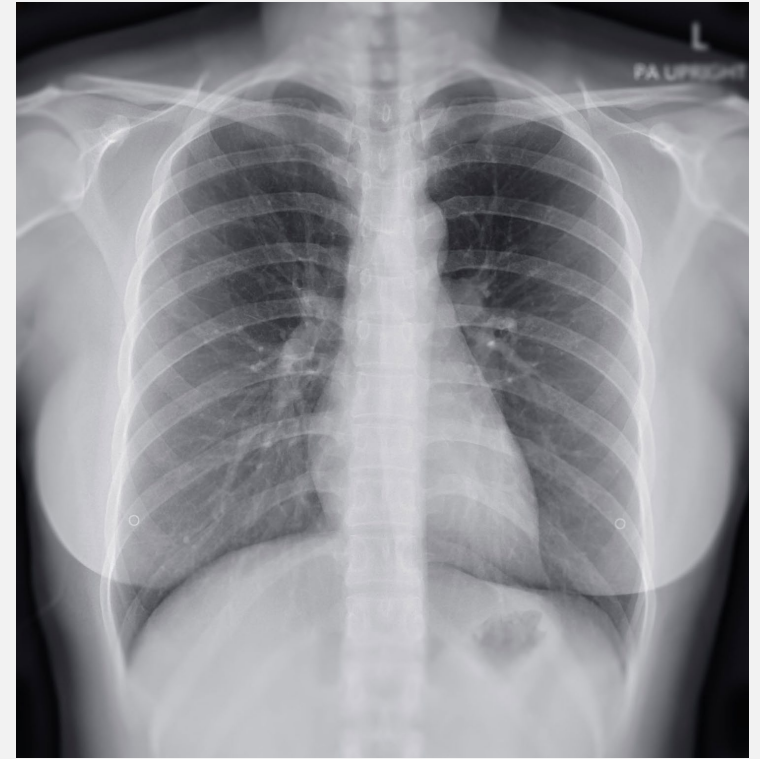


- Severe hypoxia ( $\text{SpO}_2 < 90\%$ )
- Tachypnea, altered mental status
- Hemodynamic instability
- Multisystem symptoms  
(GI + respiratory + fever)



# Imaging and Diagnosis

- CT showed ground-glass opacities  
pleural effusions
- BAL cytology: lipid-laden macrophages
- Infectious disease workup negative
- Diagnosis: confirmed EVALI per CDC  
definition



# Clinical Presentation

Cough, shortness of  
breath, chest  
tightness



Nausea, vomiting,  
diarrhea



Fever, fatigue,  
malaise



Commonly mimics  
pneumonia

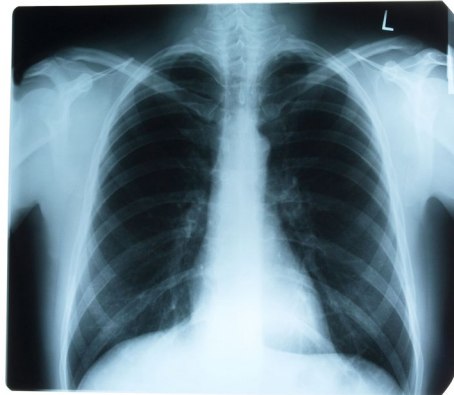


# CDC Diagnostic Criteria

History of vaping/e-cigarette use within 90 days of symptom onset



Pulmonary infiltrates upon imaging



Negative infectious workup



No more plausible alternative diagnosis



# E-Cig Use Associated with Immune Response

- High neutrophil counts, CD163 (+) M2 macrophages - involved in tissue repair, anti- inflammation
- Minimal inflammation - similar to healthy controls



# Pharmacologic Interventions

- Systemic corticosteroids (e.g., prednisone or methylprednisolone)
  - IV preferred for hospitalized patients
    - > IV prednisone 60 mg Q6H
  - Oral taper post-discharge
- Empiric antibiotics if bacterial infection can't be excluded
- Supportive medications:
  - Antiemetics
  - Antipyretics
  - Bronchodilators (esp. with asthma history)



# EVALI Case Study



# Case Study: HG

- 18-year-old male soldier, history of asthma
- Presents with fever, cough, chest pain
- Initial diagnosis: community-acquired pneumonia
- Symptoms worsened despite treatment



# EVALI Prevention



# Vaping Cessation



- Strong recommendation for cessation of all vaping products
- Education on risks (Vitamin E acetate, THC additives)
  - Behavioral counseling
  - Military tobacco cessation programs
  - Follow-up support



# Recovery

- Improvement typically within 4-7 days of steroid therapy
- Some symptoms persistent:
  - Chest discomfort with activity
  - General weakness and fatigue
- Follow-up imaging resolves in around 3 weeks after therapy.



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# Prevention Strategies



- Expand access to vaping cessation programs
- Regulate ingredients and labeling in vaping products
- Increase awareness for youth and servicemembers



# Unanswered Questions



- Is there genetic susceptibility? Does environment affect EVALI risk?
- Is there a reliable diagnostic biomarker?
- How do you prevent minors from accessing vapes?



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# Thank You.

