

Public Health Implications of E-Cigarettes: What does the evidence show?

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Outline

- Achieving Context: Harms of Smoking
- E-cigarettes: constituents
- E-cigarettes: health effects
- E-cigarettes in relation to cigarette smoking among youth and adults
- Summary

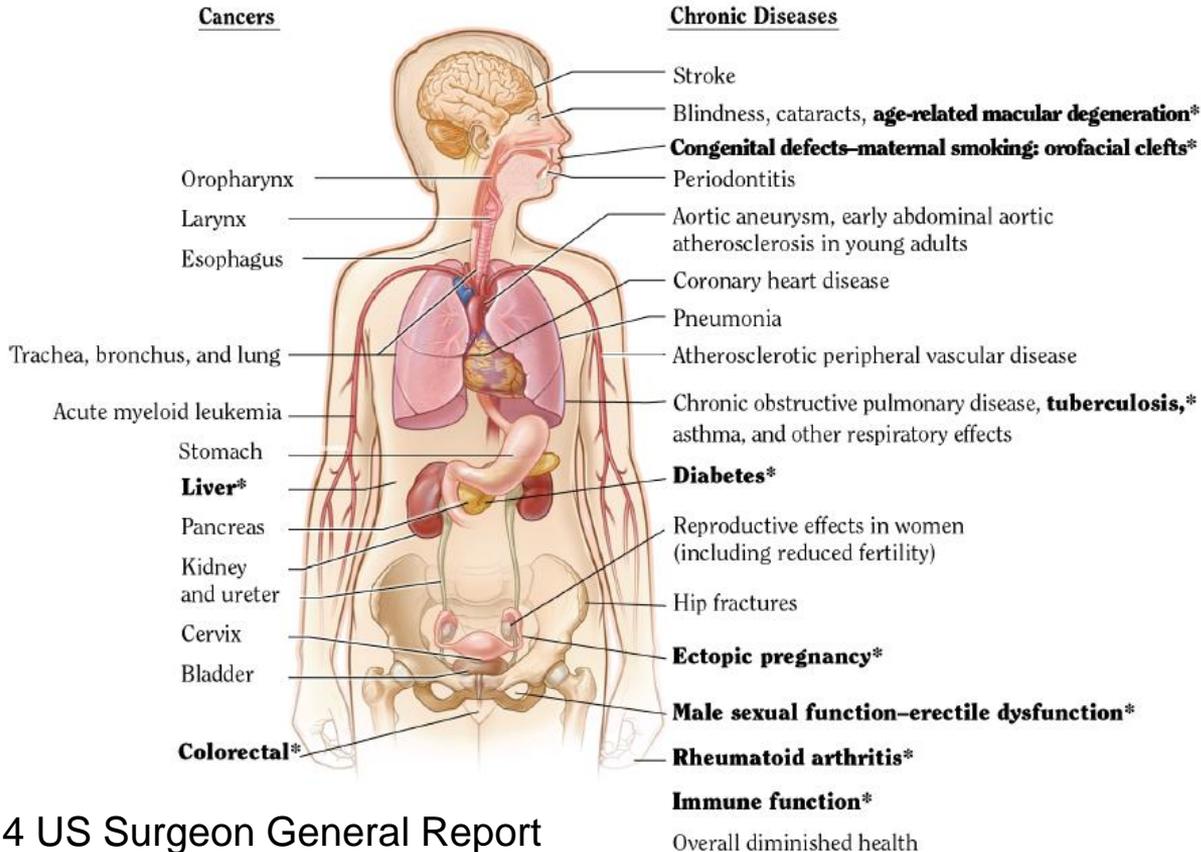
Achieving Context: Review of the Harms of Combustible Tobacco Cigarettes

To guide prudent, evidence-based policy on e-cigarettes one needs a firm understanding of the health effects of combustible tobacco cigarette smoking.

Cigarette Smoke: A Highly Toxic Mixture

- **>7000 constituents in cigarette smoke**
 - Tobacco plant constituents
 - Large number of additives
 - enhance absorption, increase flavor, increase addiction
 - Pyrolysis products
 - **60+ known carcinogens**
 - including aldehydes, benzene, metals, nitrosamines, polycyclic aromatic hydrocarbons

Health Consequences Causally Linked to Active Cigarette Smoking



Cigarette smoking: a cause of 12 types of cancer

- **Lung**
- **Oral cavity**
- **Larynx**
- **Esophagus**
- **Pancreas**
- **Bladder**
- **Kidney**
- **Cervix**
- **Acute Myeloid
Leukemia**
- **Stomach**
- **Colorectal**
- **Liver**

Cigarette smoking: a major cause of cancer

- Lung
- Oral cavity
- Larynx
- Esophagus
- Pancreas
- Kidney
- Cervix
- Acute myeloid leukemia
- Stomach
- Colorectal
- Liver

48% of all cancer deaths

Cigarette smoking: a major cause of cardiometabolic and cardiovascular disease

- **Coronary heart disease**
- **Aortic aneurysm**
- **Subclinical atherosclerosis**
- **Cerebrovascular disease**
- **Type 2 diabetes**

Cigarette smoking: a major cause of cardiometabolic and cardiovascular disease

20% of all cardiovascular and metabolic disease deaths

- Coronary artery disease
- Atherosclerosis
- Type 2 diabetes

Cigarette smoking: a major cause of pulmonary disease

- **COPD**
- **Acute illnesses: pneumonia,
influenza**
- **Tuberculosis**
- **Reduced lung function**
- **Asthma symptoms (wheeze)**

Cigarette smoking: a major cause of pulmonary disease

- COPD
- Acute illnesses: pneumonia, influenza
- Tuberculosis
- Reduced lung function
- Asthma symptoms (wheeze)

62% of all pulmonary deaths

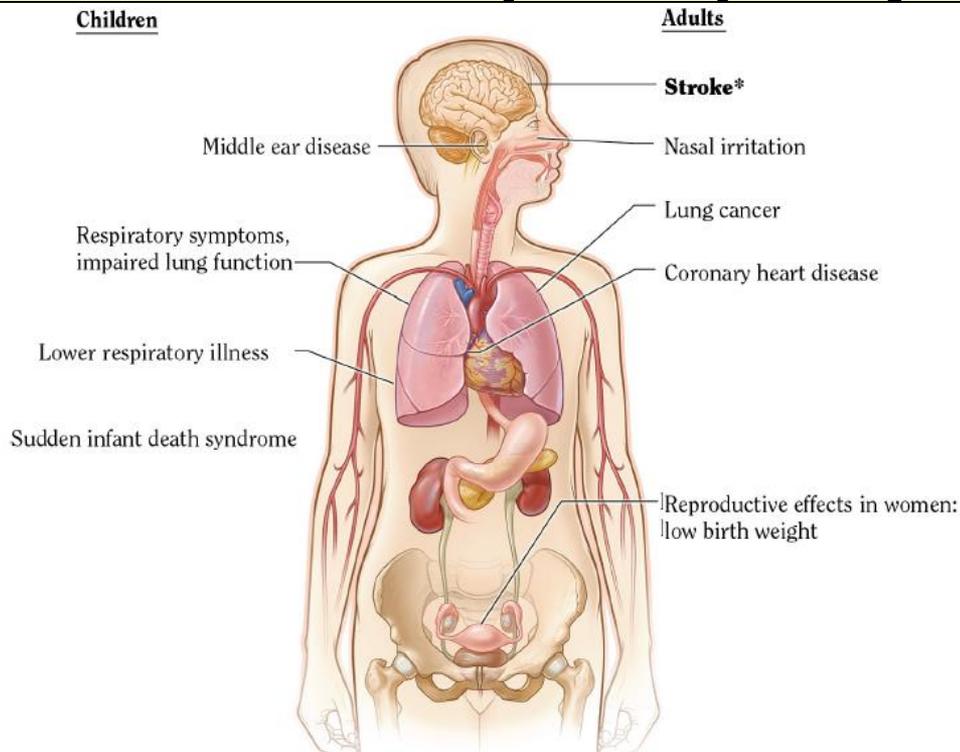
Cigarette smoking: a cause of adverse reproductive effects

- **Reduced fertility (women)**
- **Male sexual function—erectile dysfunction**
- **Preterm delivery, shortened gestation**
- **Ectopic pregnancy**

Cigarette smoking: other health effects

- **Hip fractures, bone density**
- **Periodontitis**
- **Blindness, cataracts, ARMD**
- **Rheumatoid arthritis**
- **“Diminished health status”**

Health consequences caused by secondhand smoke (SHS) exposure



US Surgeon General Report, 2014

**What about exposure
to secondhand smoke?**

41,000 deaths/year in US

Cigarette Smoking: A Major Public Health Problem

- **Leading cause of preventable disease and premature death in the US**
- **Causes 480,000 deaths per year**
 - **About 1 in 5 of all deaths**

With that context,
let's move on to e-cigarettes

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

CONSENSUS STUDY REPORT

Public Health
Consequences of
E-Cigarettes



National Academies of Science, Engineering and Medicine 2018 Report

[nationalacademies.org/
eCigHealthEffects](https://nationalacademies.org/eCigHealthEffects)

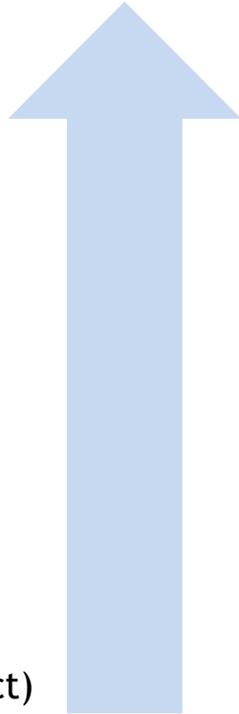
to download the full report

[#eCigHealthEffects](https://twitter.com/eCigHealthEffects)



Levels of Evidence Framework

- Conclusive
- Substantial
- Moderate
- Limited
- Insufficient
- No available
(not evidence of no effect)



- More, higher quality studies (e.g., randomized and non-randomized controlled studies)
- Conclusions can be made
- Greater confidence that limitations (including chance, bias, and confounding factors can be ruled out)



E-cigarettes: Constituents

Constituents of E-liquids

- Humectants
- Flavorants
- Nicotine

Constituents

- Humectants
 - Propylene glycol

Constituents

- Humectants
 - Propylene glycol



Constituents

- Humectants
 - Propylene glycol



Constituents

- Humectants
 - Propylene glycol
- Flavorants
 - Generally recognized as safe (GRAS) for ingestion but health effects unknown when vaporized and inhaled into the respiratory tract

Constituents

- Humectants
 - Propylene glycol
- Flavorants
 - Generally recognized as safe (GRAS) for ingestion but health effects unknown when vaporized and inhaled into the respiratory tract
- **Nicotine**

Toxicology of Constituents

- *Conclusive evidence that ...*
 - *most EC products contain and emit numerous potentially toxic substances. [5-1]*
 - *the number, quantity, and characteristics of substances emitted ... is highly variable. [5-2]*



Number of constituents in e-cigarettes vs. cigarettes

- >7000 constituents in combustible tobacco cigarette smoke
- Constituents of e-cigarette vapor number in the hundreds

Toxicology of Constituents

- *Substantial evidence that ... under typical conditions of use, exposure to potentially toxic substances from ECs is significantly lower compared with cigarettes. [5-3]*



Nicotine

- ***Conclusive evidence that exposure to nicotine from ECs is highly variable [4-1]***
- ***Substantial evidence that nicotine intake from EC devices among experienced adult users can be comparable to cigarettes.[4-2]***



Rapidly Evolving Nicotine Marketplace

- Pod systems with nicotine salts vs. free-base nicotine
 - E.g., Juul

Metals

- ***Substantial evidence that EC aerosol contains metals [5-4]***
- ***Limited evidence that the number of metals in EC aerosol could be greater than the number of metals in cigarettes.* [5-5]***



Secondhand Vape Exposure

- ***Conclusive evidence that e-cigarette use increases airborne concentrations of particulate matter and nicotine in indoor environments compared with background levels [3-1]***
- ***Moderate evidence that secondhand exposure to nicotine and particulates is lower from e-cigarettes compared with combustible tobacco cigarettes [18-5]***



Consideration of the health effects of e-cigarettes

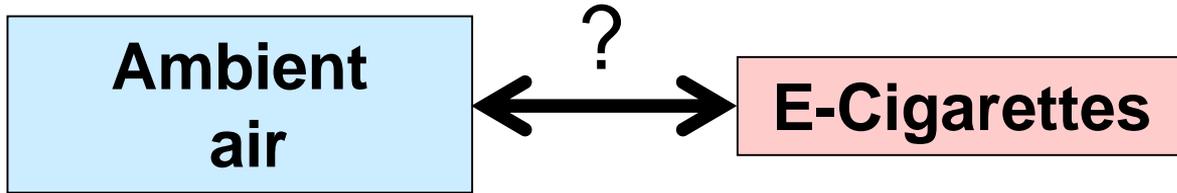
Key issue

Exposure variability

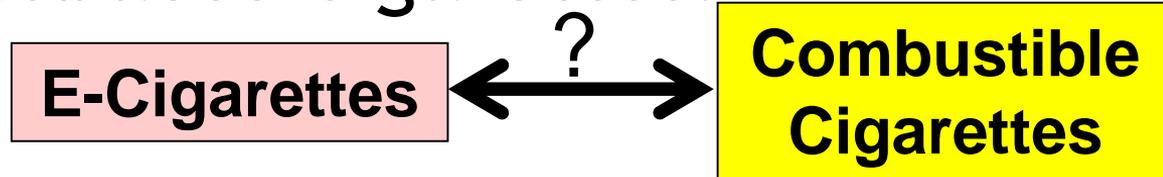
- variability between products
- variability between users

Key issue: E-cigarettes compared to what?

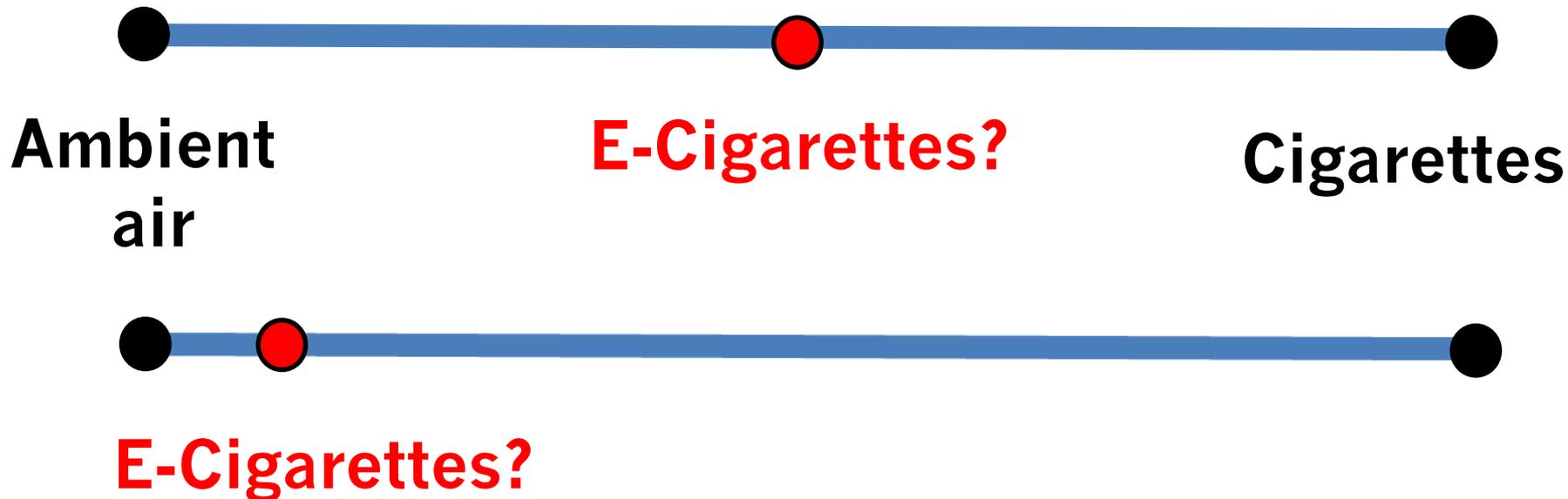
-No tobacco products at all?



-Combustible tobacco cigarettes?



The Big Question: How Much Less?



New Exposure

Long-term Health Effects Unknown for:

- **Cardiovascular Diseases:** clinical outcomes, atherosclerosis [9-1]
- **Cancers and intermediate endpoints** [10-2]
- **Respiratory Diseases** [11-1]
- **Reproductive & Developmental Effects** [13-1]



Cardiovascular Diseases

- *Substantial evidence that heart rate increases after nicotine intake from ECs [9-2]*
- *Moderate evidence that diastolic blood pressure increases after nicotine intake from ECs [9-3]*



Cancers

- *Substantial evidence that some chemicals present in EC aerosols are capable of causing DNA damage and mutagenesis* ... Whether the levels of exposure are high enough to contribute to human carcinogenesis remains to be determined [10-4]*



Modes of Action: *Substantial evidence that e-cigarette aerosols can...*

- *induce acute endothelial cell dysfunction, (long-term consequences are uncertain) [7-1]*
- *promote formation of reactive oxygen species (ROS)/oxidative stress [7-2]*
 - *generation of ROS and oxidative stress induction is generally lower from e-cigarettes than cigarettes*



Dependence & Abuse Liability

- *Substantial evidence that EC use results in symptoms of dependence on ECs[8-1]*



Respiratory Diseases

- *Moderate evidence for increased cough and wheeze in adolescents who use EC and an association with EC use and an increase in asthma exacerbations [11-4]*



Injuries & Poisonings

Conclusive evidence that...

- *EC devices can explode and cause burns & projectile injuries ... [especially] when batteries are of poor quality,... or are being modified by users [14-1]*
- *...exposure to e-liquids (from drinking, eye contact, or dermal contact) can result in adverse health effects ... and can be fatal [14-2, 14-3]*



Health Effects: Bottom Line

- E-cigarettes contain fewer numbers and lower levels of toxic substances than cigarettes
- The health risks of e-cigarettes are likely to be substantially less than cigarettes
- **E-cigarettes have health risks**
 - **Safer does not mean safe**
- The long-term health effects of e-cigarettes are uncertain

E-cigarettes in relation to cigarette smoking in youth and adults

To assess the *public health consequences* of e-cigarettes, two key questions are:

- What is the impact on uptake of cigarette smoking in *youth and young adults*?
- What is the impact on smoking cessation among *addicted smokers*?

Prospective cohort study of e-cigarette use in relation to the uptake of smoking in youth

All never cigarette smokers at baseline

E-cigarette use

No E-cigarette use

Cigarette smoking

No cigarette smoking

Cigarette smoking

No cigarette smoking

EC and Youth Smoking: Ever Use

- *Substantial evidence that among never smokers, e-cigarette use increases risk of ever smoking cigarettes among youth and young adults [16-1]*



EC and Youth Smoking: Ever Use

Table 1. Summary of 10 prospective cohort studies of the association between ever use of e-cigarettes and subsequent risk of ever smoking combustible tobacco cigarettes.

Location	n	Ages at baseline	Follow-up duration	RR (95% CI) ¹
S. California, USA	298	17.4 yrs. (med)	16 mos.	5.5 (2.7-11.2)
Scotland, UK	2,125	11-18 yrs.	12 mos.	2.4 (1.6-3.6)
England, UK	1,726	13-14 yrs.	12 mos.	4.1 (2.9-5.6)
Los Angeles, CA, USA	2,530	14 yrs. (mean)	12 mos.	2.7 (2.0-3.7)
Texas (24 colleges)	2,558	19.7 yrs. (mean)	18 mos.	1.4 (1.01-1.8)
USA (MTF)	347	12 th grade	13 mos.	4.8 (1.9-12.0)
USA (MAH Study)	694	20 yrs. (mean)	12 mos.	8.3 (1.2-58.6)
USA (sample)	915	23.5 yrs. (mean)	18 mos.	6.8 (1.2-58.6)
VCU	3,757	18.5 yrs. (mean)	12 mos.	3.4 (1.9-5.9)
Oahu, Hawaii, USA	1,141	14.7 yrs. (mean)	12 mos.	2.9 (2.0-4.1)

EC and Youth Smoking: Smoking Progression

Among youth and young adult e-cigarette users who never used combustible tobacco cigarettes before:

- ***Moderate evidence that e-cigarette use increases the frequency and intensity of subsequent combustible tobacco cigarette smoking [16-2]***



ECs and Adult Smoking Cessation

- *Strong evidence from randomized controlled trials that electronic cigarettes with nicotine are as or more effective than nicotine replacement therapy products for smoking cessation*

Randomized Trials of ECs vs. NRTs for Adult Smoking Cessation

Author (yr.)	Follow-up	RR (95% CI)
Bullen (2013)	6 mos.	1.3 (0.7 - 2.3)
Hajek (2019)	12 mos.	1.8 (1.3 - 2.6)

Refs: Bullen C, et al. Lancet 2013; Hajek P, et al. N Engl J Med 2019

ECs for smoking cessation in adults: Current clinical advice?

- **Not yet part of evidence-based guidelines**
- **Smokers willing to quit by any means:**
front-line therapy remains evidence-based medications
- **Smokers only willing to quit using ECs:**
support use of ECs

Bottom Line

- Among youth: *substantial evidence* that e-cigarette use increases the risk of transitioning to cigarette smoking
- Among adults: *strong evidence* that e-cigarettes can be efficacious for helping adults quit cigarette smoking



Summary

- E-cigarettes contain toxic substances
- Exposures to toxic substance less for e-cigarettes than cigarettes
- E-cigarettes have health risks
- The long-term health effects of e-cigarettes are not yet clear, but the health risks of e-cigarettes are likely substantially less than the risks of cigarettes

Summary-2

- A major known concern is that youth who use e-cigarettes have a much greater risk of going on to use combustible tobacco cigarettes

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