



HEALTH AND MEDICINE DIVISION

# Public Health Consequences of E-Cigarettes

January 23, 2018

# Committee

- *David L. Eaton (Chair)*
- Anthony J. Alberg
- *Maciej Goniewicz*
- *Adam Leventhal*
- José E. Manatou
- Sharon McGrath-Morrow
- *David Mendez*
- Richard Miech
- Ana Navas-Acien
- Kent E. Pinkerton
- *Nancy A. Rigotti*
- *David A. Savitz*
- Gideon St.Helen



# Statement of Task

- Evaluate the available evidence of the health effects related to the use of electronic nicotine delivery systems (ENDS)
- Identify future federally funded research needs



# Terminology: What are E-Cigarettes?

- Heterogeneous group of products that are referred to using a widely variably terminology (e.g., ENDS, electronic cigarettes, vaporizers, mods, tanks)
- May or may not contain nicotine\*
- Excludes heat-not-burn products\*



# Report Organization

Section I: E-Cigarette Devices,

Constituents, and Exposures

Section II: Effects of E-Cigarettes on Health

Section III: Public Health Implications of  
E-Cigarettes

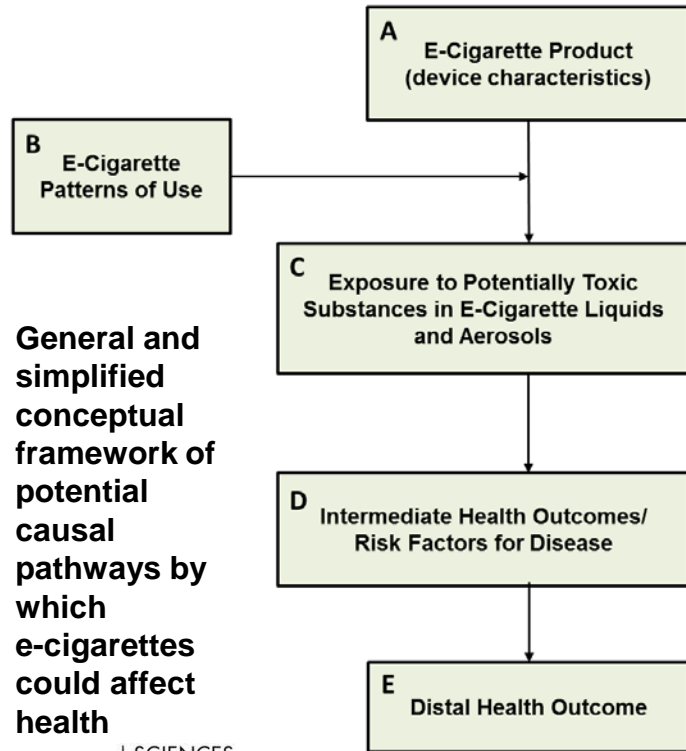


# Committee Approach

- Literature Search
  - February 1, 2017 to August 31, 2017
  - 6 databases
  - Approximately 4,200 unique results identified; over 800 reviewed for the report
- Literature Review and Quality Assessment
- Approach to Assessing Causality
  - Evidence Synthesis (Hill's criteria)
- Levels of Evidence and Conclusions



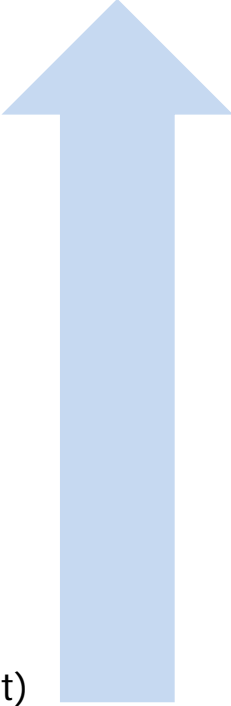
# Approach to Assessing Causality



Source: Figure 2-1

- First examined evidence on distal health outcomes [E], then moved up the causal chain to intermediate/short-term outcomes, mechanisms/modes of action, and exposures
- Considered human data most relevant and animal data supportive
- In vitro data useful for hypothesis generation and understanding mechanisms, but relevance for establishing human health risk uncertain

# 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)





# Devices, Uses, and Exposures

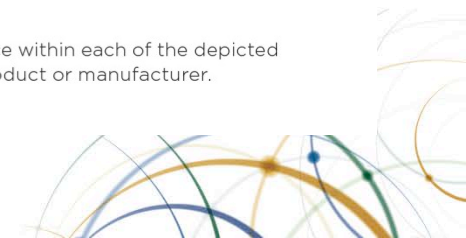


*\* shown to demonstrate approximate scale*

- a.** Generic Combustible Tobacco Cigarette
- b.** First Generation E-Cigarette
- c.** Second Generation E-Cigarette
- d.** Third Generation E-Cigarette

## **DISCLAIMER**

These illustrations are intended to be generic representations of a device within each of the depicted categories. They are not meant to represent or endorse any specific product or manufacturer.



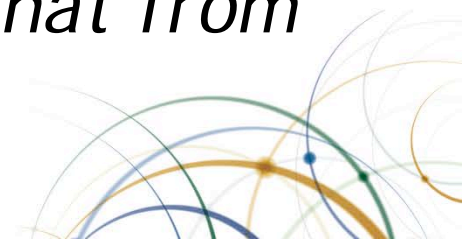
# Toxicology of Constituents

- *Conclusive evidence that ...*
  - *most e-cigarette products contain and emit numerous potentially toxic substances. [5-1]*
  - *the number, quantity, and characteristics of [these] substances emitted ... is highly variable and depends on product characteristics ... and how the device is operated. [5-2]*
- *Substantial evidence that ... under typical conditions of use, exposure to potentially toxic substances from e-cigarettes is significantly lower compared with combustible tobacco cigarettes. [5-3]*



# Nicotine

- *Conclusive evidence that exposure to nicotine from e-cigarettes is highly variable and depends on product characteristics ... and how the device is operated. [4-1]*
- *Substantial evidence that nicotine intake from e-cigarette devices among experienced adult e-cigarette users can be comparable to that from combustible tobacco cigarettes.[4-2]*



# Metals

- *Substantial evidence that e-cigarette aerosol contains metals [5-4]*
- *Limited evidence that the number of metals in e-cigarette aerosol could be greater than the number of metals in combustible tobacco cigarettes.\* [5-5]*



# Health Effects Evaluated

- Modes of Action
  - Endothelial Cell Dysfunction
  - Oxidative Stress
- Dependence & Abuse Liability
- Cardiovascular Diseases
- Cancers
- Respiratory Diseases
- Oral Diseases
- Reproductive & Developmental Effects
- Injuries & Poisonings



# Approach to Evaluation of Health Effects

- Characterization of Disease Endpoints and Intermediate Outcomes
- Optimal Study Design
- Questions Addressed by the Literature
  - Considered comparisons to unexposed and to smokers as appropriate
- Evidence Review
- Synthesis and Conclusions
- Vulnerable/Susceptible Populations



# Dependence & Abuse Liability

- *Substantial evidence that e-cigarette use results in symptoms of dependence on e-cigarettes[8-1]*
- *Moderate evidence that*
  - *risk and severity of dependence are lower for e-cigarettes than combustible tobacco cigarettes [8-2]*
  - *variability in e-cigarette product characteristics ... is an important determinant of risk and severity [8-3]*



# Cardiovascular Diseases

- *No available evidence whether or not e-cigarette use is associated with clinical cardiovascular outcomes ... and subclinical atherosclerosis [9-1]*
- *Substantial evidence that heart rate increases after nicotine intake from e-cigarettes [9-2]*
- *Moderate evidence that diastolic blood pressure increases after nicotine intake from e-cigarettes [9-3]*





# Cardiovascular Diseases

- *Limited evidence that e-cigarette use is associated with a short-term increase in systolic blood pressure, changes in biomarkers of oxidative stress, increased endothelial dysfunction and arterial stiffness, and autonomic control. [9-4]*
- *Insufficient evidence that e-cigarette use is associated with long-term changes in heart rate, blood pressure, and cardiac geometry and function. [9-5]*



# Cancers

- *Limited evidence from in vivo animal studies using intermediate biomarkers of cancer to support the hypothesis that long-term e-cigarette use could increase the risk of cancer [but] no available evidence whether or not e-cigarette use is associated with intermediate cancer endpoints in humans\* [10-1, 10-2]*



# Cancers

- *No available evidence from adequate long-term animal bioassays of e-cigarette aerosol exposures to inform cancer risk [10-2]*
- *Limited evidence that e-cigarette aerosol can be mutagenic or cause DNA damage in humans, animal models, and human cells in culture [10-3]*
- ***Substantial evidence that some chemicals present in e-cigarette aerosols are capable of causing DNA damage and mutagenesis\* ... Whether or not the levels of exposure are high enough to contribute to human carcinogenesis remains to be determined [10-4]***



# Respiratory Diseases

- *No available evidence whether or not e-cigarettes cause respiratory diseases in humans [11-1]*
- *Moderate evidence for increased cough and wheeze in adolescents who use e-cigarettes and an association with e-cigarette use and an increase in asthma exacerbations [11-4]*
- *Limited evidence of adverse effects of e-cigarette exposure on the respiratory system from animal and in vitro studies [11-5]*



# Respiratory Diseases

- *Limited evidence for*
  - *improvement in lung function and respiratory symptoms among adult smokers with asthma who switch to e-cigarettes completely or in part (dual use) [11-2]*
  - *reduction of COPD exacerbations among adult smokers with COPD who switch to e-cigarettes completely or in part (dual use) [11-3]*



# Injuries & Poisonings

- *Conclusive evidence that ...*
  - *e-cigarette devices can explode and cause burns and projectile injuries ... [especially] when batteries are of poor quality, stored improperly, or are being modified by users [14-1]*
  - *intentional or accidental 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]*



# Public Health Implications of E-Cigarettes

- Smoking among Youth and Young Adults
- Smoking Cessation among Adults
- Harm Reduction
- Modeling of E-Cigarette Use



# Youth & Young Adult Smoking: Ever Use

- *Substantial evidence that e-cigarette use increases risk of ever using combustible tobacco cigarettes among youth and young adults [16-1]*





# Youth & Young Adult Smoking: Smoking Progression

*Among youth and young adult e-cigarette users who ever use combustible tobacco cigarettes:*

- *Moderate evidence that e-cigarette use increases the frequency and intensity of subsequent combustible tobacco cigarette smoking [16-2]*
- *Limited evidence that e-cigarette use increases, in the near term, the duration of subsequent combustible tobacco cigarette smoking [16-3]*



# Adult Smoking Cessation

*Limited evidence that e-cigarettes may be effective aids to promote smoking cessation overall<sup>a,b</sup> [17-1]*

*<sup>a</sup>Very little data from randomized controlled trials*

*<sup>b</sup>Results of trials and observational studies often differ*



# Adult Smoking Cessation

- *Moderate evidence from randomized controlled trials that e-cigarettes with nicotine are more effective than e-cigarettes without nicotine for smoking cessation [17-2]*
- *Insufficient evidence from randomized controlled trials about the effectiveness of e-cigarettes as cessation aids compared with no treatment or to FDA-approved smoking cessation treatments [17-3]*
- *Moderate evidence from observational studies that more frequent use of e-cigarettes is associated with increased likelihood of cessation [17-4]*



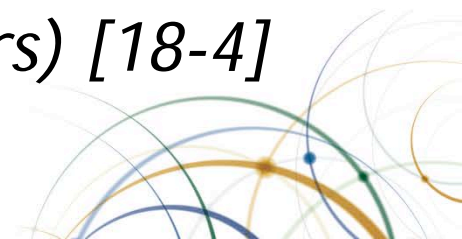
# Harm Reduction: Complete Switching

- *Conclusive evidence that completely substituting e-cigarettes for combustible tobacco cigarettes reduces users' exposure to numerous toxicants and carcinogens present in combustible tobacco cigarettes [18-1]*
- *Substantial evidence that completely switching from regular use of combustible tobacco cigarettes to e-cigarettes results in reduced short-term adverse health outcomes in several organ systems [18-2]*



# Harm Reduction: Dual Use

- *No available evidence whether or not long-term e-cigarette use among smokers (dual use) changes morbidity or mortality compared with those who only smoke combustible tobacco cigarettes [18-3]*
- *Insufficient evidence that e-cigarette use changes short-term adverse health outcomes in several organ systems in smokers who continue to smoke combustible tobacco cigarettes (dual users) [18-4]*



# Secondhand 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]*
- *Limited evidence that e-cigarette use increases levels of nicotine and other e-cigarette constituents on a variety of indoor surfaces compared with background levels. [3-2]*



# Modeling of E-cigarette Use

- Mendez-Warner model of smoking prevalence and health effects
- Range of assumptions about e-cigarette effects on:
  - Smoking initiation rate (0, 5, 10, 25, and 50% increase),
  - Smoking cessation rate (-5, 0, 5, 10, and 15% increase), and
  - Relative harm of e-cigarettes compared to combustible tobacco cigarettes (0, 10, 25, and 50% as harmful)
- Period: 2015-2050 and 2015-2070
- Outcomes: life years lost/gained because of e-cigarettes compared to the status-quo (no e-cigarette effects)



# Modeling of E-cigarette Use

**2015-2050** Life-years lost due to e-cigs (in Millions)  
E-cigs = 10% x risk of combustibles

		Cessation Increases by				
		-5%	0%	5%	10%	15%
Initiation Increases by	0%	1.4	0.0	(1.1)	(2.2)	(3.2)
	5%	1.5	0.1	(1.0)	(2.1)	(3.1)
	10%	1.5	0.1	(1.0)	(2.1)	(3.1)
	25%	1.7	0.3	(0.8)	(1.9)	(2.9)
	50%	2.1	0.7	(0.5)	(1.5)	(2.6)

**2015-2070** Life-years lost due to e-cigs (in Millions)  
E-cigs = 10% x risk of combustibles

		Cessation Increases by				
		-5%	0%	5%	10%	15%
Initiation Increases by	0%	2.4	0.0	(2.3)	(4.5)	(6.6)
	5%	3.1	0.7	(1.7)	(3.9)	(6.0)
	10%	3.8	1.4	(1.0)	(3.2)	(5.3)
	25%	5.9	3.4	1.0	(1.2)	(3.3)
	50%	9.3	6.8	4.4	2.1	(0.0)



# Modeling of E-cigarette Use

**2015-2050** Life-years lost due to e-cigs (in Millions)  
E-cigs = 10% x risk of combustibles

		Cessation Increases by				
		-5%	0%	5%	10%	15%
Initiation Increases by	0%	1.4	0.0	(1.1)	(2.2)	(3.2)
	5%	1.5	0.1	(1.0)	(2.1)	(3.1)
	10%	1.5	0.1	(1.0)	(2.1)	(3.1)
	25%	1.7	0.3	(0.8)	(1.9)	(2.9)
	50%	2.1	0.7	(0.5)	(1.5)	(2.6)

If e-cigarettes increase smoking initiation by 5% and smoking cessation by 15% from 2015 on, there would be a net 3.1 million cumulative life-years saved by the year 2050

**2015-2070** Life-years lost due to e-cigs (in Millions)  
E-cigs = 10% x risk of combustibles

		Cessation Increases by				
		-5%	0%	5%	10%	15%
Initiation Increases by	0%	2.4	0.0	(2.3)	(4.5)	(6.6)
	5%	3.1	0.7	(1.7)	(3.9)	(6.0)
	10%	3.8	1.4	(1.0)	(3.2)	(5.3)
	25%	5.9	3.4	1.0	(1.2)	(3.3)
	50%	9.3	6.8	4.4	2.1	(0.0)

# Modeling of E-cigarette Use

**2015-2050** Life-years lost due to e-cigs (in Millions)  
E-cigs = 10% x risk of combustibles

		Cessation Increases by				
		-5%	0%	5%	10%	15%
Initiation Increases by	0%	1.4	0.0	(1.1)	(2.2)	(3.2)
	5%	1.5	0.1	(1.0)	(2.1)	(3.1)
	10%	1.5	0.1	(1.0)	(2.1)	(3.1)
	25%	1.7	0.3	(0.8)	(1.9)	(2.9)
	50%	2.1	0.7	(0.5)	(1.5)	(2.6)

If e-cigarettes increase smoking initiation by 50% and decrease smoking cessation by 5% from 2015 on, there would be a net 9.3 million cumulative life-years lost by the year 2070

If e-cigarettes increase smoking initiation by 5% and smoking cessation by 15% from 2015 on, there would be a net 3.1 million cumulative life-years saved by the year 2050

**2015-2070** Life-years lost due to e-cigs (in Millions)  
E-cigs = 10% x risk of combustibles

		Cessation Increases by				
		-5%	0%	5%	10%	15%
Initiation Increases by	0%	2.4	0.0	(2.3)	(4.5)	(6.6)
	5%	3.1	0.7	(1.7)	(3.9)	(6.0)
	10%	3.8	1.4	(1.0)	(3.2)	(5.3)
	25%	5.9	3.4	1.0	(1.2)	(3.3)
	50%	9.3	6.8	4.4	2.1	(0.0)

# Modeling of E-cigarette Use

**2015-2050** Life-years lost due to e-cigs (in Millions)  
E-cigs = 25% x risk of combustibles

		Cessation Increases by				
		-5%	0%	5%	10%	15%
Initiation Increases by	0%	1.4	0.0	(0.8)	(1.7)	(2.4)
	5%	1.5	0.1	(0.8)	(1.6)	(2.4)
	10%	1.5	0.1	(0.7)	(1.5)	(2.3)
	25%	1.7	0.3	(0.5)	(1.3)	(2.1)
	50%	2.1	0.7	(0.2)	(1.0)	(1.8)

**2015-2070** Life-years lost due to e-cigs (in Millions)  
E-cigs = 25% x risk of combustibles

		Cessation Increases by				
		-5%	0%	5%	10%	15%
Initiation Increases by	0%	2.4	0.0	(1.7)	(3.3)	(4.8)
	5%	3.1	0.7	(1.0)	(2.6)	(4.1)
	10%	3.8	1.4	(0.3)	(1.9)	(3.4)
	25%	5.9	3.4	1.7	0.1	(1.4)
	50%	9.3	6.8	5.1	3.4	1.9

# Modeling of E-cigarette Use

- In all scenarios where e-cigarettes increase the smoking cessation rate, the modeling projects that use of these products will generate a net public health benefit at least in the short run (by 2050)
- The harms from increased initiation by youth will take time to manifest, occurring decades after the benefits of increased cessation are seen



# Modeling of E-cigarette Use

- For long-range projections (e.g., 50 years out), the net public health benefit is substantially less, and is negative under some scenarios due to the harms from increased initiation.
- If e-cigarette use does not increase the smoking cessation rate, the model projects that there would be net public health harm in the short and long term



# Modeling of E-cigarette Use

- While there is uncertainty about the relative harm of e-cigarettes compared to combustible tobacco and their effect on smoking initiation and cessation, the available evidence suggests that:
  - E-cigarettes are likely to be substantially less harmful than combustible tobacco
  - E-cigarette use is not likely to increase the smoking initiation rate by more than 10%
  - E-cigarette use is likely to increase the smoking cessation rate within the 5% - 15% range



# Modeling of E-cigarette Use

**2015-2050** Life-years lost due to e-cigs (in Millions)  
E-cigs = 10% x risk of combustibles

		Cessation Increases by					
		-5%	0%	5%	10%	15%	
Initiation Increases by	0%	1.4	0.0	(1.1)	(2.2)	(3.2)	
	5%	1.5	0.1	(1.0)	(2.1)	(3.1)	
	10%	1.5	0.1	(1.0)	(2.1)	(3.1)	
	25%	1.7	0.3	(0.8)	(1.9)	(2.9)	
	50%	2.1	0.7	(0.5)	(1.5)	(2.6)	

**2015-2070** Life-years lost due to e-cigs (in Millions)  
E-cigs = 10% x risk of combustibles

		Cessation Increases by					
		-5%	0%	5%	10%	15%	
Initiation Increases by	0%	2.4	0.0	(2.3)	(4.5)	(6.6)	
	5%	3.1	0.7	(1.7)	(3.9)	(6.0)	
	10%	3.8	1.4	(1.0)	(3.2)	(5.3)	
	25%	5.9	3.4	1.0	(1.2)	(3.3)	
	50%	9.3	6.8	4.4	2.1	(0.0)	

# Modeling of E-cigarette Use

- The modeling results suggest that, under likely scenarios, the use of e-cigarettes in the population will result in a net public health benefit.
- Under extreme adverse assumptions, the modeling projects a net public health loss





# Moving Forward

- More and better research is needed to clarify the short-and long-term health effects of e-cigarettes in individuals and populations
- The committee's approach to evaluating the health effects of e-cigarettes provides a generalizable template for future evaluations of the evidence

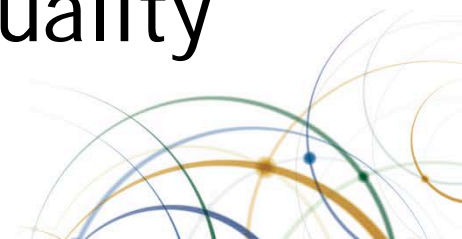


# Research Needs

This is not an intractable problem; See Handout

Each of the three major sections of the report ends with a chapter on research needs with specific suggestions to:

1. Address Gaps in Substantive Knowledge
2. Improve Research Methods and Quality



# Research Needs, for example

- Research into e-cigarette device and liquid characteristics to inform product standards
- Cohort studies to compare clinical and subclinical health outcomes among e-cigarette users vs. combustible tobacco users
- Observational studies to assess the relationship between youth use of e-cigarettes and subsequent progression to regular smoking of combustible tobacco products
- Randomized controlled trials of the effectiveness of e-cigarettes as cessation aids, especially compared with FDA-approved smoking cessation aids



# Summary

- While e-cigarettes are not without health risks, they are likely to be far less harmful than combustible tobacco cigarettes.
- E-cigarettes contain fewer numbers and lower levels of toxic substances than conventional cigarettes
- The long-term health effects of e-cigarettes are not yet clear.



# Summary

- Using e-cigarettes may help adults who smoke combustible tobacco cigarettes quit smoking, but more research is needed.
- Among youth, e-cigarette use increases the risk of initiating smoking combustible tobacco cigarettes.



# Visit

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

to download the full report

For more information,  
Kathleen Stratton  
(kstratton@nas.edu)

# Thank you!

## CONSENSUS STUDY REPORT

### Public Health Consequences of **E-Cigarettes**

