Emerging Tobacco Products & Policies

DONA UPSON, MD, MA

PROFESSOR OF MEDICINE
PULMONARY, CRITICAL CARE & SLEEP
UNIVERSITY OF NEW MEXICO
NEW MEXICO VETERANS AFFAIRS HEALTH CARE SERVICES

Policy - collaboration is essential

- Non-profit organizations
- Grassroots groups
- Professional societies
- Legislators
- Other government officials

Non-profit organizations

- National level
  - Determine priorities, strategies, resources
  - Collaborate with other national groups
  - Communicate with local organizations
- Local level
  - Determine priorities, strategies, resources
  - Collaborate with other local groups
  - Communicate with grassroots
  - Obtain media coverage

Grassroots activists/ advocates

- Educate the community
- Inform legislators of desired outcomes
  - Meet with elected officials
- Show support – especially constituents
  - Phone calls
  - Letters, emails, faxes
  - Attend hearings, press events

Professional societies

- Provide scientific evidence, credibility
- Clinicians and scientists:
  - Testify at hearings
  - Media interviews
  - Letters to the editor
  - Patient stories
  - Focus on health effects

Communication is key

- Organized strategy between groups
- Keep local activists/advocates informed
- Especially regarding committee hearings

Why does the American Thoracic Society (ATS) advocate?

Public policy impacts:

Causes of disease

- Tobacco laws
- Clean air & climate change
- Occupational health standards

Advancement of health

- Research for better treatments and cures
- Respiratory /CC/ sleep disease surveillance

Delivery of medical services

- Public health insurance programs (Medicare, Medicaid, VA)
- Medicare coverage and reimbursement
- Review and approval of new drugs and devices

AMERICAN THORACIC SOCIETY · 1905 · ATS®
We help the world breathe
PULMONARY • CRITICAL CARE • SLEEP

How does the ATS advocate?

Congress

- Support/oppose legislation (ACA, tobacco taxes, clean air roll back bills, cigar bill)
- Fund programs (NIH, CDC, EPA, VA)
- Urge the Administration to take action (language on TB, COPD, clean air reports)

Administration

- Support/oppose policy (OMB, EPA, OSHA)
- Develop/implement regulatory policy (EPA, NIH)
- Fund programs (eNIH, CDC, EPA, VA)

Courts

- Rule in support/opposition to law or regulatory policy (ex Ozone NAAQS, Cross State Air Pollution Rule, Silica Standard, TPSAC committee, ACA)

ATS advocacy committees (Chair/co-Chairs)

- Environmental Health Policy (Thurston & Rice)
- Health Equality and Diversity (Roman & Pakhale)
- Health Policy (Upson & Lyons)
- Research Advocacy (Antony & Gerald)
- Tobacco Action (Farber and Neptune)

AMERICAN THORACIC SOCIETY · 1905 · ATS
We help the world breathe
PULMONARY • CRITICAL CARE • SLEEP

ATS member involvement - 2017

- 165 participated in the March and May Capitol Hill Days
- 250+ participated in the May Capitol Hill Rally
- 5 testified before Congress or Administrative hearings
- 3 presented at Congressional briefings
- 2 at state meetings & several LTEs

AMERICAN THORACIC SOCIETY · 1905 · ATS®
We help the world breathe
PULMONARY • CRITICAL CARE • SLEEP

ATS advocacy process - 2017

- 8 Court Actions
- 5 Congressional Hearings
- 6 Administrative Hearings
- 7 Congressional Policy Briefings
- 7 Policy publications (+2 under review)
- 14 Administration meetings
- 160+ Congressional offices visited by staff

AMERICAN THORACIC SOCIETY · 1905 · ATS
We help the world breathe
PULMONARY • CRITICAL CARE • SLEEP

ATS advocacy successes - 2017

- FY17 NIH Increase
- FY17 VA Increase
- Defeat of Methane Rule CRA
- New ICD-10 code for Pulmonary Hypertension
- Defeat of House/Senate Repeal Replace bills
- Court action to defeat EPA 1-year ozone delay
- FY17 bills free of tobacco riders
- Burn Pits language in DOD re-authorization bill
- TB funding Dear Colleague letter support

AMERICAN THORACIC SOCIETY · 1905 · ATS
We help the world breathe
PULMONARY • CRITICAL CARE • SLEEP

What are ATS members doing?

- Advocating to:
  - Expand access to health care
  - Increase research funding for Pulmonary, Critical Care & Sleep
  - Strengthen laws and regulations regarding tobacco
  - Improve air quality, outdoors/ indoors
  - Adequately fund national/ global TB efforts

Reasons to get involved

- Personal satisfaction – a way to make a difference in people's lives on societal levels
- Policy affects large numbers of people at once
- A different kind of challenge than our usual work
- It's interesting and rewarding

Federal policy

- Important to have state approval first
- Builds grassroots support
- Demonstrates constituent approval

Tobacco 21 – Congress

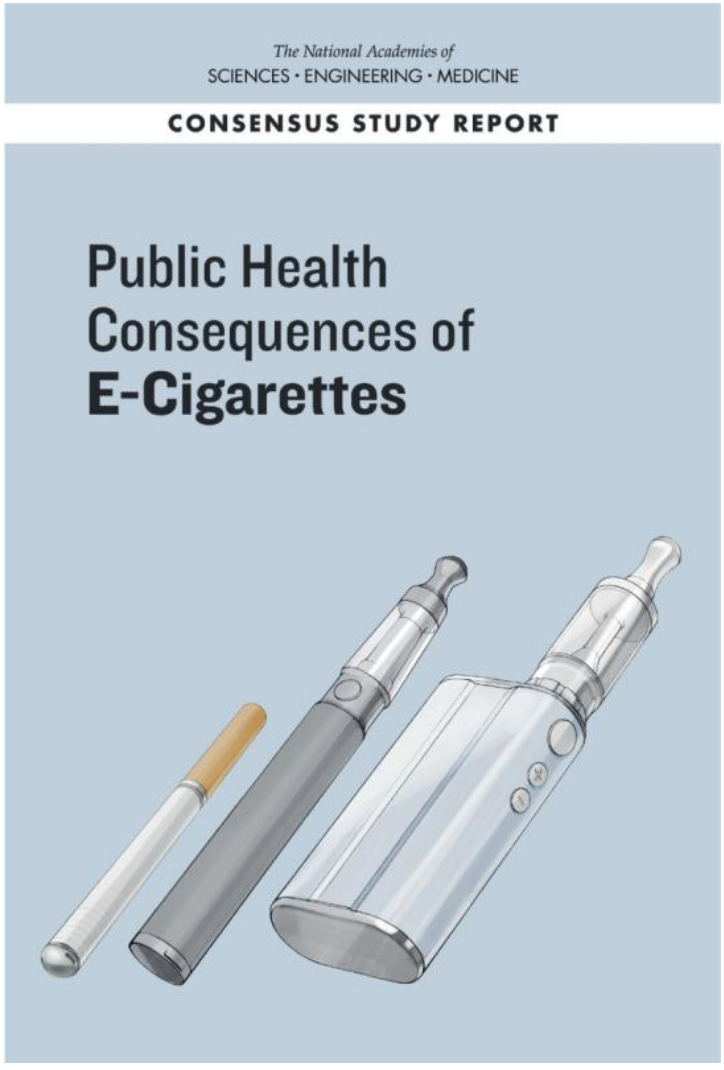
- Last week - bipartisan legislation to raise the minimum federal age for purchasing tobacco to 21 introduced in House and Senate
  - S. 1258 – sponsored by Sens. Schatz (D-HI) and Young (R-IN)
  - H.R. 2411 – sponsored by Reps. DeGette (D-CO) and Stewart (R-UT)
- Raises minimum age for all tobacco products, including cigars and e-cigarettes
- Prohibits retailers from selling tobacco products to anyone under age 30 without age verification

Reversing the Youth Tobacco Epidemic Act

- Being introduced by House Energy and Commerce Chair Frank Pallone (D-NJ) and Rep. Donna Shalala (D-FL)
- Bans flavored tobacco products
  - Including flavored ENDS, flavored cigars, menthol cigarettes
  - Over 1/2 of youth smokers – including 7/10 African-American youth smokers – smoke menthol cigarettes
    - increases smoking initiation and progression to regular smoking
    - increases nicotine dependence (addiction)
    - reduces success in quitting smoking

Reversing the Youth Tobacco Epidemic Act

- Tobacco 21 nationwide
- Prohibits online sales of tobacco products
- Extends advertising restrictions (currently cigarettes, smokeless tobacco) to other tobacco products, inc. ENDS
  - Prohibitions on brand-name sponsorships of sports, music or other events, and distribution of non-tobacco items (such as shirts and hats) with tobacco brand names
- Requires FDA to issue a final rule to implement graphic health warnings on cigarette packs and advertising, as required by the 2009 Tobacco Control Act



The National Academies of

SCIENCES • ENGINEERING • MEDICINE

1/23/2018

Download report:

nationalacademies.org/eCigHealthEffects

#eCigHealthEffects

Net public health effect

Depends on 3 factors:

- Potential to increase the uptake of combustible tobacco product use (initiation)
- Potential to help current smokers quit
  - 14% prevalence of tobacco smoking in U.S.
  - Exceeds 25% among high-risk subgroups
- Inherent toxicity

Electronic nicotine delivery systems

- Increase the risk of youth initiating smoking of combustible cigarettes
- May help adults who smoke combustible tobacco cigarettes quit smoking, but more research needed
- Have health risks, likely to be less harmful than combustible tobacco
  - Fewer numbers and lower levels of toxic substances than conventional cigarettes
  - Long-term health effects unknown

Diverse group of devices


AVAILABLE IN 6 COLORS

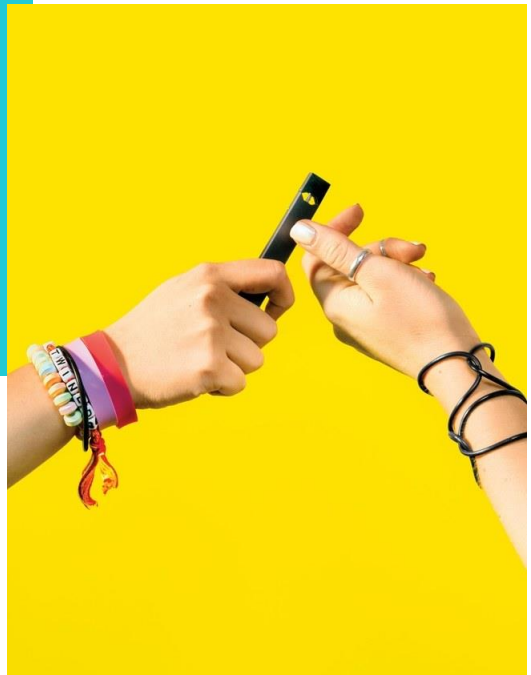
Over 15,000 flavors

“Teenagers embrace JUUL, saying it’s discreet enough to vape in class”

NPR 12/4/17

The Promise of Vaping and the Rise of Juul

The New Yorker 5/14/18



- Nicotine liquid refills called “pods”
- Cool Cucumber, Fruit Medley, Mango, Mint

Juul

- Uses nicotine salts – allow high levels of nicotine to be inhaled more easily and with less irritation than the free-base nicotine traditionally used in tobacco products, including e-cigarettes
- Easier to initiate nicotine use and to progress to regular e-cigarette use/ nicotine dependence
- 2/3 of JUUL users aged 15-24 do not know that JUUL always contains nicotine

https://e-cigarettes.surgeongeneral.gov

Question #1

During 2017–2018, current e-cigarette use in high school students increased by

a) 21%

b) 34%

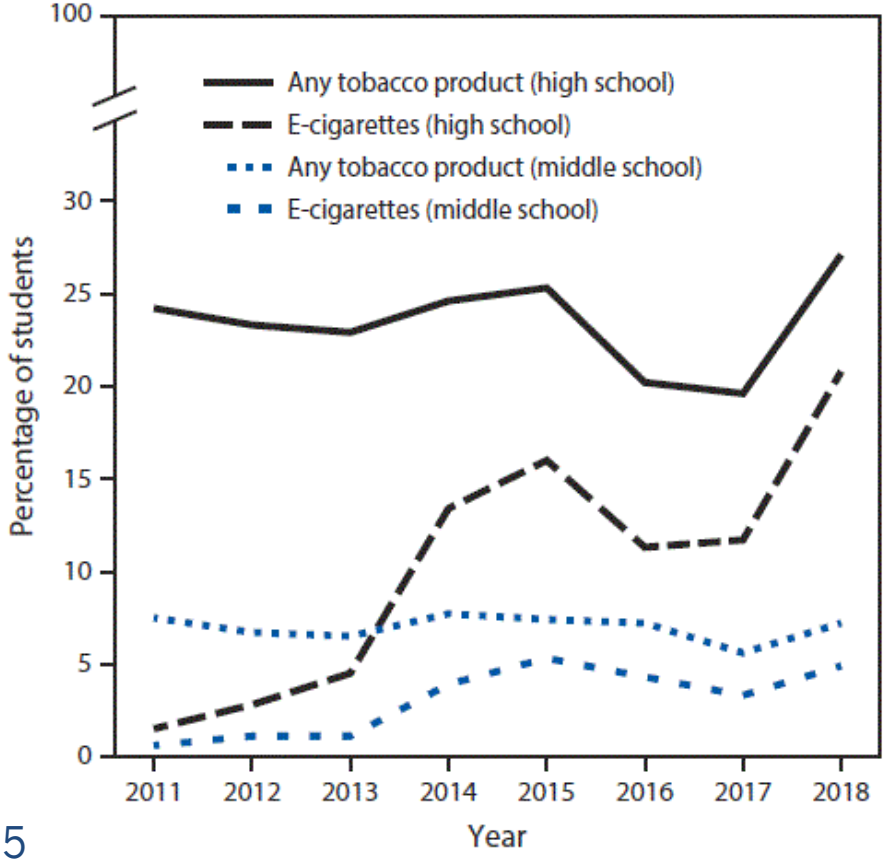
c) 78%

d) 90%

Use of e-cigarettes among youth

High school students

- E-cigarette use increased from 1.5% (220,000 students) in 2011 to 20.8% (3.05 million) in 2018 ($p<0.001$)
- During 2017–2018, current e-cigarette use increased by 78%
  - From 11.7% to 20.8%, $p<0.001$
- Proportion of current e-cigarette users who reported use on ≥20 of the past 30 days increased from 20.0% in 2017 to 27.7% in 2018 ($p = 0.008$)

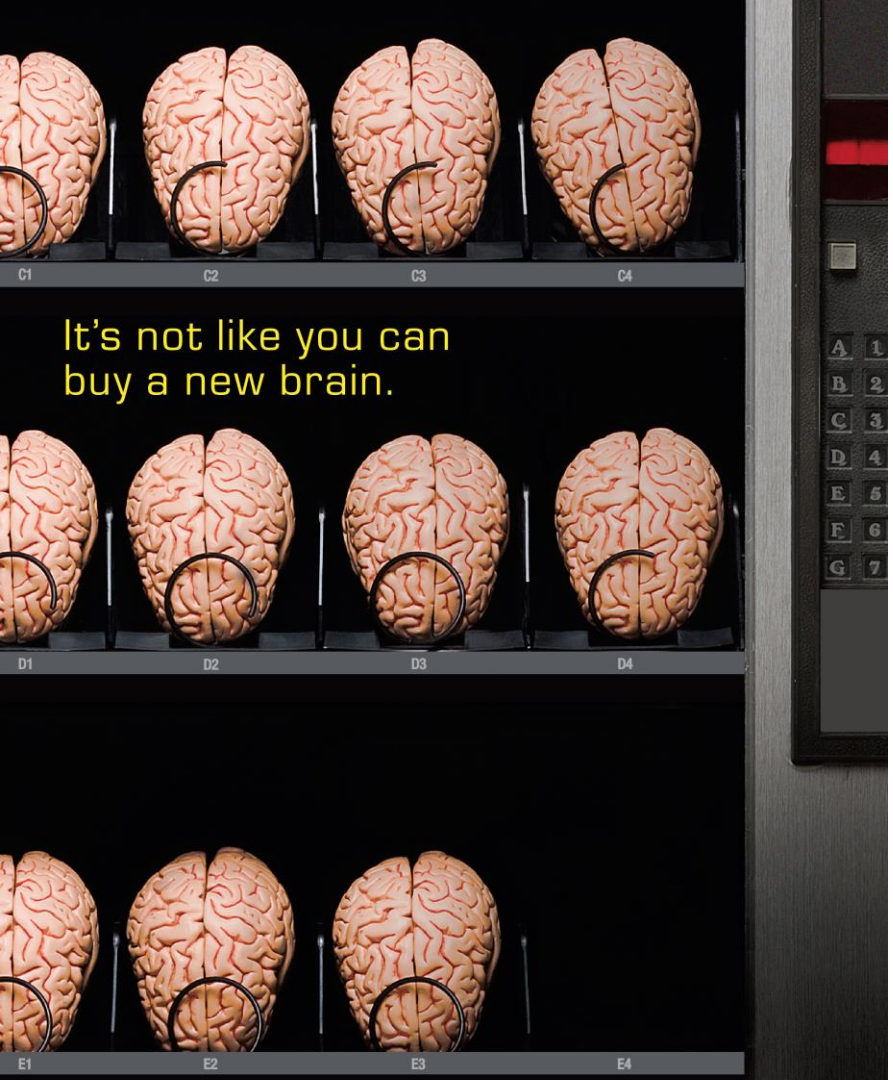


Cullen KA et al. MMWR 11/16/18;Vol. 67;No. 45

Epidemic of youth e-cigarette use

- FDA Commissioner Scott Gottlieb & Surgeon General Jerome Adams blame Juul
  - Others blame inaction by federal/ state governments
- Juul captured 75% of e-cigarette market in 3 years
  - Juul valued at $38 billion
- Juul has high nicotine concentrations
  - A pod has as much nicotine as a pack of 20 cigarettes
- Adolescent use of nicotine can harm brain areas that control attention, learning, mood & impulse control

Farber et al. Ann Am Thorac Soc Vol 16, No 1, pp 44–48, Jan 2019; https://www.hhs.gov/news; https://surgeongeneral.gov



A MESSAGE FROM THE U.S. SURGEON GENERAL

The human brain is the last organ to fully develop, at around age 25.

Nicotine in e-cigarettes can harm brain development and lead to addiction in youth and young adults.

Let's protect our kids: e-cigarettes.surgeongeneral.gov

NICOTINE CONTENT

Retail Price: **$14.99**

No tax

2019 $ 0.50 tax/cartridge = $16.99

Retail Price: **$32.00**

Tax @ $1.66 each **$ 6.64**

Total **$38.64**

2019 $ 2.00 tax/pack = $40.00

ENDS aerosols

- Contain potentially harmful compounds
  - including nicotine, volatile organic compounds, heavy metals, and ultrafine particulates
- Nonusers can be exposed through inhalation, ingestion, or dermal contact

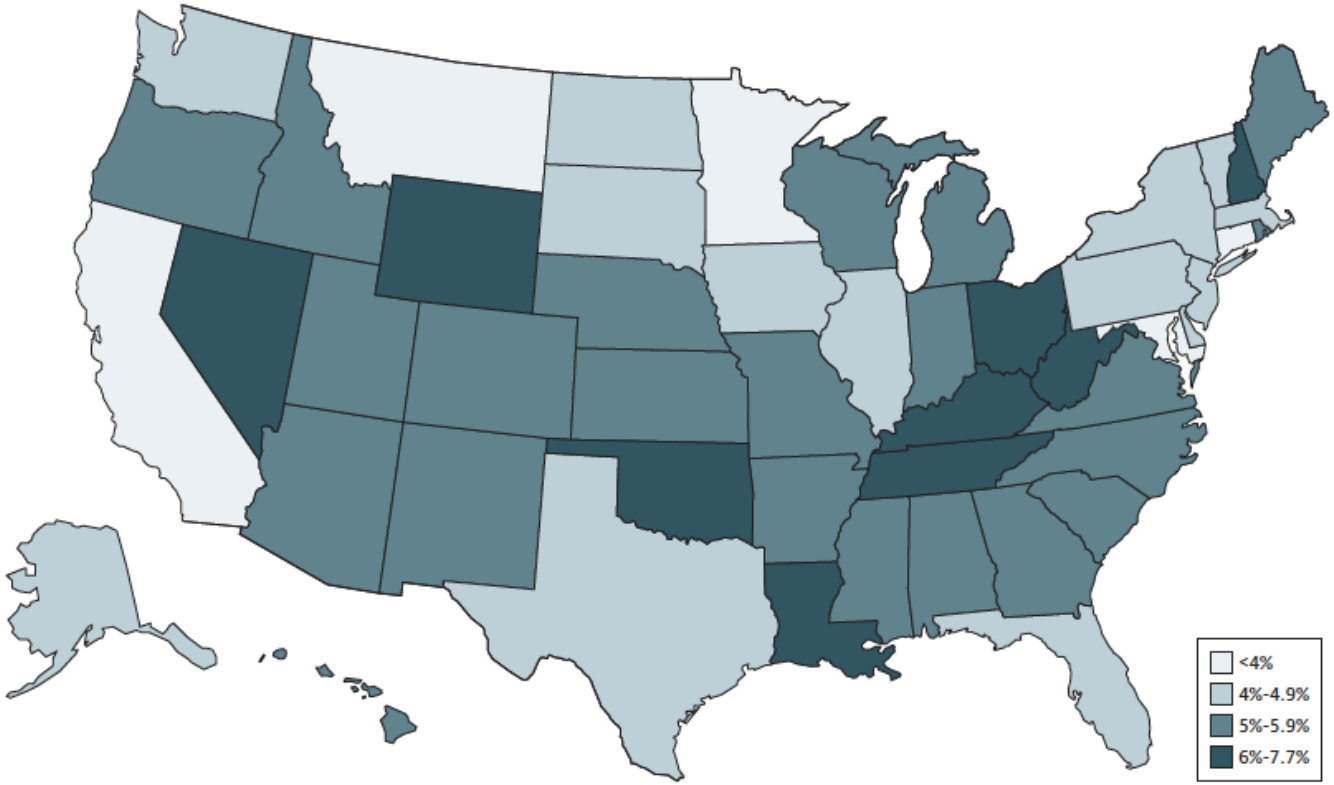
Secondhand exposure

- US Surgeon General recommends prohibiting ENDS use in enclosed areas to avoid probable harm because of secondhand exposure

Among US adults, 2016-2017:

- 4.4% (95%CI, 4.3-4.5) reported current use
- 4.9% (95%CI, 4.7-5.1) if a child in the home
- 5.6% if living with a child with vs without (4.8%) asthma
  - prevalence difference 0.8%;95%CI,−0.05 to1.7

Figure 1. Prevalence of Electronic Cigarette Use Among US Adults With at Least 1 Child in the Household by State, Behavioral Risk Factor Surveillance System, 2016 to 2017



In the continental United States, prevalence ranged from 2.3% (95% CI, 1.5-3.4) in the District of Columbia to 7.7% (95% CI, 6.5-9.0) in Oklahoma. Data not shown: Puerto Rico, 0.85%; US Virgin Islands, 1.3%; and Guam, 8.4%.

Risks to children of ENDS users

- ENDS users generally perceive secondhand aerosols as safe for children
- Only 1/5 of users voluntarily prohibit use in their home or vehicle
- Children in the same household as users are more likely to initiate use, may be more likely to accidentally ingest refill liquid and experience burn injuries

Youth & young adult smoking

Substantial evidence

- E-cigarette use increases risk of ever using combustible tobacco cigarettes
  - Consistent evidence from longitudinal cohort studies of a strong association between e-cigarette use and transition from never to ever combustible tobacco cigarette smoking
  - Across different methodologies, age ranges, research groups & locations
- Longitudinal association stronger in low-risk youth

Youth & young adult smoking

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

Moderate evidence

- E-cigarette use increases the frequency and intensity of subsequent combustible cigarette smoking

Limited evidence

- E-cigarette use increases, in the near term, the duration of subsequent combustible cigarette smoking

Association of Non-cigarette Tobacco Product Use With Future Cigarette Smoking Among Youth in the Population Assessment of Tobacco and Health (PATH) Study, 2013-2015

Adjusted odds of past 30-day cigarette use at follow-up about twice as high among baseline ever users of:

- E-cigarettes (AOR 1.87; 95%CI 1.15-3.05)
- Hookah (AOR 1.92; 95%CI 1.17-3.17)
- Non-cigarette combustible tobacco (AOR 1.78; 95%CI 1.00-3.19)
- Smokeless tobacco (AOR 2.07; 95%CI 1.10-3.87)

Youth who had tried >1 type of tobacco product at baseline had 3.81 (95%CI 2.22-6.54) greater adjusted odds of past 30-day cigarette smoking at follow-up than did baseline never-tobacco users

JAMA Pediatr. 2018;172(2):181-187. doi:10.1001/jamapediatrics.2017.4173

E-cigarette use as a predictor of cigarette smoking: results from a 1-year follow-up of a national sample of 12th grade students

Richard Miech, Megan E Patrick, Patrick M O'Malley, Lloyd D Johnston

What this paper adds

This paper contributes to the growing body of evidence that e-cigarette use is an independent risk factor for future smoking, both among youth who are non-smokers and also among youth with past smoking experience. Results support a desensitisation process, whereby youth who vape lower their perceived risk of cigarette smoking.

Miech R, *et al*. *Tob Control* 2017;**0**:1–6.

E-cigarette Use and Subsequent Smoking Frequency Among Adolescents

WHAT'S KNOWN:

- Electronic cigarette use is associated with cigarette initiation

WHAT THIS STUDY ADDS:

- Adolescent e-cigarette users appear to follow similar trajectories of cigarette smoking frequency as nonusers
- Exclusive cigarette or dual product users are more likely to continue using cigarettes than to transition away from smoking to exclusive e-cigarette use or to nonuse

Barrington-Trimis JL, Kong G, Leventhal AM, et al. Pediatrics. 2018;142(6):e20180486

E-cigarette use predicts subsequent marijuana use among youth

Marijuana Never Users at Wave 1	Marijuana P12M Use at Wave 2		Marijuana Heavy Use at Wave 2	
No. E-cigs and/or Cartridges Used at Wave 1	n	aOR	n	aOR
All adolescents, n = 10,364	897	1.3 (1.1–1.5)**	286	1.2 (1.0–1.5)
Aged 12–14 y (n = 5901)	373	1.7 (1.3–2.0)**	128	1.6 (1.2–2.2)*
Aged 15–17 y (n = 4463)	524	1.2 (1.0–1.4)	158	0.9 (0.7–1.3)
Interaction between e-cig use and age group	n/a	1.5 (1.2–1.9)*	n/a	1.8 (1.2–2.6)*

Age-stratified analysis of the temporal association between the number of E-cigarettes and/or cartridges used at Wave 1 and marijuana use at Wave 2 among baseline marijuana never users, PATH Study, 2013–2015

* $P < .01$
** $P < .001$

Dai H, Catley D, Richter KP, et al. Electronic Cigarettes and Future Marijuana Use: A Longitudinal Study. Pediatrics. 2018;141(5):e20173787

“Tobacco giant Altria buys 35% of Juul”

- Altria - largest tobacco company in the US
- Invested $12.8 billion cash (plus $2 billion bonus)
- Gives Juul top-shelf space alongside Marlboro
- Helps with distribution & logistics
  - 230,000 retail locations
- Lobbying and legal expertise
- Bought 45% of Canadian cannabis company Cronos

www.cnbc.com/2018/12/20/altria-takes-stake-in-juul-a-pivotal-moment-for-the-e-cigarette-maker.html

FDA plan – November 2018

- Banning sales of flavored products other than mint, menthol & tobacco at most convenience stores, gas stations
- Halting online sales until websites have heightened age-verification standards
- Pull products entirely if companies continue to market them in ways that increase their appeal to adolescents

https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements

Food & Drug Administration

- FDA Commissioner Gottlieb resigned
- Acting commissioner Ned Sharpless, former director of the National Cancer Institute
- Proposed rule/action limiting flavored e-cig sales at gas stations & convenience stores
- Proposed rule to ban menthol & mint cigarettes

Question #2

There is substantial evidence that use of electronic nicotine delivery systems (i.e. e-cigarettes)

a) results in symptoms of dependence

b) works as well as FDA-approved medications for treatment of tobacco dependence

c) decreases short-term adverse health outcomes in several organ systems

d) improves clinical cardiovascular outcome

Adult smoking cessation

E-cigarettes have the potential for large public health benefit if they help smokers to quit, especially those who are unwilling or unable to quit using existing treatments

Limited evidence that e-cigarettes may be effective aids to promote smoking cessation overall

- Very little data from randomized controlled trials
- Results of trials and observational studies often differ
- >20 systematic reviews - evidence is slim to make definitive conclusions

Adult smoking cessation

- Moderate evidence - randomized controlled trials
  - E-cigs with nicotine are more effective than those without
- Moderate evidence - observational studies
  - More frequent use of e-cigarettes is associated with increased likelihood of cessation
- Insufficient evidence - randomized controlled trials
  - about their effectiveness as cessation aids compared with no treatment or to FDA–approved pharmacotherapy

E-cigarettes and smoking cessation in real-world and clinical settings: a systematic review and meta-analysis

- Odds of quitting 28% lower in those who used e-cigarettes compared with those who did not (OR 0.72; CI 0.57–0.90)
- Association of e-cigarette use with quitting did not differ among studies of all smokers (irrespective of interest in quitting) compared with studies of only those interested in cessation (OR 0.63; CI 0.45–0.86 vs 0.86; CI 0.60–1.23)
- 577 unique records (up to 6/2015)
  - 38 included in qualitative synthesis, 20 in meta-analysis

Kalkhoran S, Glantz SA. The Lancet Respiratory Medicine 2016;4:116-128 DOI:10.1016/S2213-2600(15)00521-4

A Randomized Trial of E-Cigarettes versus Nicotine-Replacement Therapy (NRT)

- Multicenter, pragmatic, randomized trial of e-cigarettes, as compared with NRT
- Nicotine-replacement products of their choice, including combinations, for ≤3 months
- E-cigarette starter pack – second generation, refillable e-cigarette, 1 bottle of nicotine e-liquid
  - Recommendation to purchase further e-liquids of flavor & strength of their choice
- Weekly behavioral support for ≥4 weeks

Hajek P et al. DOI: 10.1056/NEJMoa1808779; published 1/30/19

A Randomized Trial of E-Cigarettes versus Nicotine-Replacement Therapy (NRT)

886 participants (2045 screened)

1-year abstinence rate

- 18.0% e-cigarette group
- 9.9% NRT group
  - Relative risk, 1.83; 95% confidence interval 1.30-2.58; P<0.001

Use of assigned product at 52 weeks

- 80% e-cigarette group
- 9% NRT group

Hajek P et al. DOI: 10.1056/NEJMoa1808779; published 1/30/19

A Randomized Trial of E-Cigarettes versus Nicotine-Replacement Therapy (NRT)

- E-cigarettes were more effective in alleviating nicotine withdrawal symptoms
  - Less severe urges to smoke at week 4
  - May have allowed better tailoring of nicotine dose to individual needs (user decides how and when to puff)
- Greater declines in incidence of cough and phlegm than the NRT group
- No excess wheezing or dyspnea
- More oropharyngeal irritation (65.3% vs 51.2%)

Hajek P et al. DOI: 10.1056/NEJMoa1808779; published 1/30/19

Limitations of the study

- 75% of sample had already failed NRT
- Not blinded
  - Possible that behavioral counselors may have influenced patient expectations
  - If NRT was seen as an inferior option, that group may have put less effort into quit attempt
  - NRT & bupropion 20% abstinence at 1 year
- Did not compare e-cigarettes to the best treatment for tobacco dependence
  - Varenicline 26% rate at 24 weeks

Hajek P et al. DOI: 10.1056/NEJMoa1808779; Borrelli B, O'Connor GT. DOI: 10.1056/NEJMe1816406

Varenicline – EAGLES trial

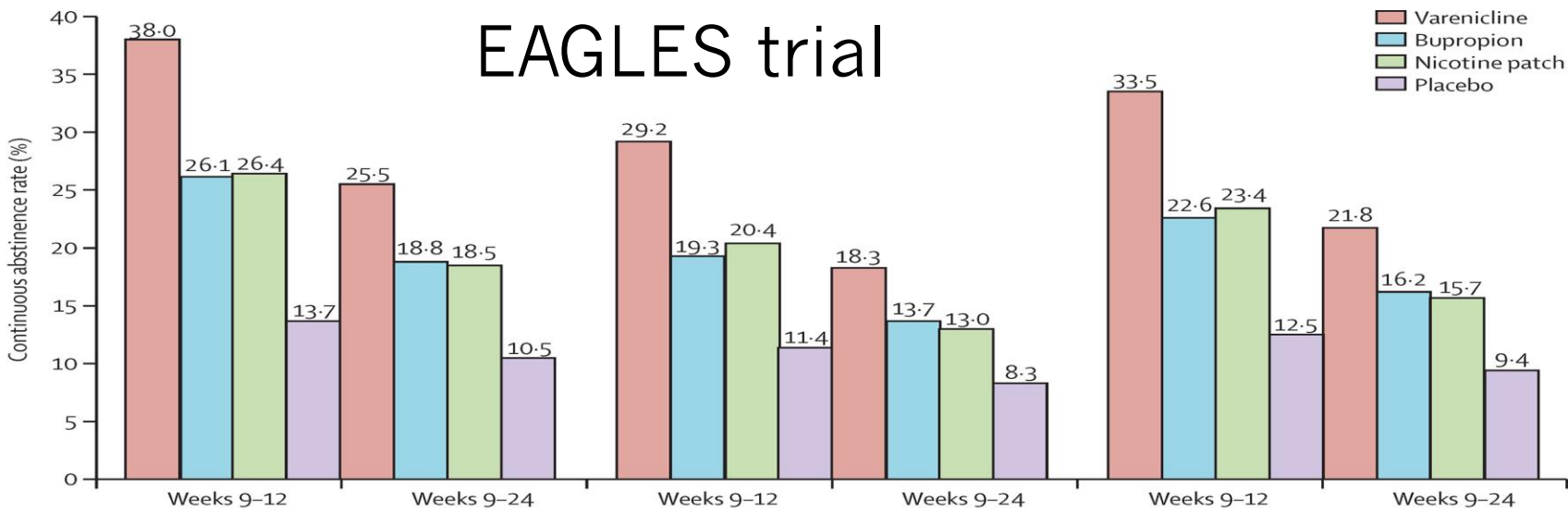
Boxed warning removed 12/16/16

- Large clinical trial that FDA required of drug companies
- Risk of serious side effects on mood/ behavior lower than previously suspected (also true for bupropion)
- Still risk, especially with depression, anxiety, schizophrenia
  - Not statistically different than placebo
  - Most did not require hospitalization

Confirmed benefits of quitting outweighed risks of meds

Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. Anthenelli RM et al. Lancet 2016: 387:2507-2520.

EAGLES trial



Non-psychiatric cohort (n=4028)
Varenicline (n=1005)
Bupropion (n=1001)
Nicotine patch (n=1013)
Placebo (n=1009)

Psychiatric cohort (n=4116)
Varenicline (n=1032)
Bupropion (n=1033)
Nicotine patch (n=1025)
Placebo (n=1026)

Overall (n=8144)
Varenicline (n=2037)
Bupropion (n=2034)
Nicotine patch (n=2038)
Placebo (n=2035)

OR (95% CI) p value	Weeks 9–12	Weeks 9–24	Weeks 9–12	Weeks 9–24	Weeks 9–12	Weeks 9–24
Primary comparisons						
Varenicline *vs* placebo	4·00 (3·20–5·00) p<0·0001	2·99 (2·33–3·83) p<0·0001	3·24 (2·56–4·11) p<0·0001	2·50 (1·90–3·29) p<0·0001	3·61 (3·07–4·24) p<0·0001	2·74 (2·28–3·30) p<0·0001
Bupropion *vs* placebo	2·26 (1·80–2·85) p<0·0001	2·00 (1·54–2·59) p<0·0001	1·87 (1·46–2·39) p<0·0001	1·77 (1·33–2·36) p<0·0001	2·07 (1·75–2·45) p<0·0001	1·89 (1·56–2·29) p<0·0001
Secondary comparisons						
Nicotine patch vs placebo	2·30 (1·83–2·90) p<0·0001	1·96 (1·51–2·54) p<0·0001	2·00 (1·56–2·55) p<0·0001	1·65 (1·24–2·20) p=0·0007	2·15 (1·82–2·54) p<0·0001	1·81 (1·49–2·19) p<0·0001
Varenicline *vs* nicotine patch	1·74 (1·43–2·10) p<0·0001	1·52 (1·23–1·89) p=0·0001	1·62 (1·32–1·99) p<0·0001	1·51 (1·19–1·93) p=0·0008	1·68 (1·46–1·93) p<0·0001	1·52 (1·29–1·78) p<0·0001
Bupropion *vs* nicotine patch	0·98 (0·80–1·20) p=0·8701	1·02 (0·81–1·28) p=0·8645	0·94 (0·75–1·16) p=0·5467	1·07 (0·83–1·39) p=0·5824	0·96 (0·83–1·11) p=0·5797	1·04 (0·88–1·24) p=0·6002
Varenicline vs bupropion	1·77 (1·46–2·14) p<0·0001	1·49 (1·20–1·85) p=0·0003	1·74 (1·41–2·14) p<0·0001	1·41 (1·11–1·79) p=0·0047	1·75 (1·52–2·01) p<0·0001	1·45 (1·24–1·70) p<0·0001

Combination NRT better

Cochrane Review 2019

- Using nicotine patch and another type of NRT (gum or lozenge) together: 15%-36% more likely that a person would quit than if only one used
- More likely to quit with higher-dose NRT patches 21 mg (worn for 24 hours) compared to 14 mg
- Using NRT before a quit day as well as after may help more people to quit than only using it after, but more evidence needed

Other concerns

- Americans trying to quit smoking use e-cigarettes more frequently than FDA-approved cessation aids
- Differential pattern of long-term use raises concerns about the health consequences of e-cigarette use
- Nicotine patch use during pregnancy associated with higher rates of smoking cessation & better child development outcomes than placebo – no such data for e-cigarettes

Borrelli B, O'Connor GT. DOI: 10.1056/NEJMe1816406

Other concerns

- Models addictive behavior
- Exposes children to e-cigarette vapor
  - Associated with increased likelihood of reporting an asthma attack (adjusted OR, 1.27%; CI 1.11 to 1.47)

Borrelli B, O'Connor GT. DOI: 10.1056/NEJMe1816406 Bayly JE et al. Chest 1/2019

The Dangerous Flavors of E-Cigarettes

- Since smoking is not a natural behavior, like eating or drinking, manufacturers commonly add flavoring
- Flavoring enhances appeal to first-time users — especially teenagers
- Nicotine is as addictive as heroin
- The creation of a generation of nicotine-addicted teens will lead to a resurgence in use of combustible tobacco in the decades to come

Drazen JM, Morrissey S, Campion EW. DOI: 10.1056/NEJMe1900484; Dai H. JAMA Pediatrics: published online 1/7/19; Ambrose BK, Day HR, Rostron B, et al. JAMA. 2015;314(17):1871-1873. doi:10.1001/jama.2015.13802

The Dangerous Flavors of E-Cigarettes

- Creation of a large cohort of nicotine-addicted adults has consequences beyond the adverse physiological effects of nicotine
- Gateway drug that lowers the threshold for addiction to other agents - including cocaine, opioids
- We think the FDA should simply ban the sale of flavored nicotine products for use in e-cigarettes

Drazen JM, Morrissey S, Campion EW. DOI: 10.1056/NEJMe1900484

Harm reduction – complete switching

Conclusive evidence - cross-sectional & longitudinal studies

- Significantly reduced levels of biomarkers of exposure to potentially toxic chemicals

Substantial evidence

- Significant short-term improvements in health outcomes

E-cigarette vapor

- Contains many toxins & exerts potentially adverse biologic effects on human cells in vitro or in animal models
- Toxin levels and biologic effects lower than those of tobacco smoke
- Humans – altered bronchial epithelial proteome, including some protein alterations also seen in tobacco smokers
- Mice – inhaling e-cigarette vapor results in distal airspace enlargement consistent with pulmonary emphysema
- Consensus that e-cigarettes safer than combustible cigarettes

Borrelli B, O'Connor GT. DOI: 10.1056/NEJMe1816406

Used primarily to deliver nicotine

Conclusive evidence

- Nicotine has adverse health effects
- Nicotine exposure from e-cigarettes is highly variable
  - Product characteristics (e-liquid content, electrical power)
  - User characteristics & vaping behavior (experience, puff duration)

Substantial evidence

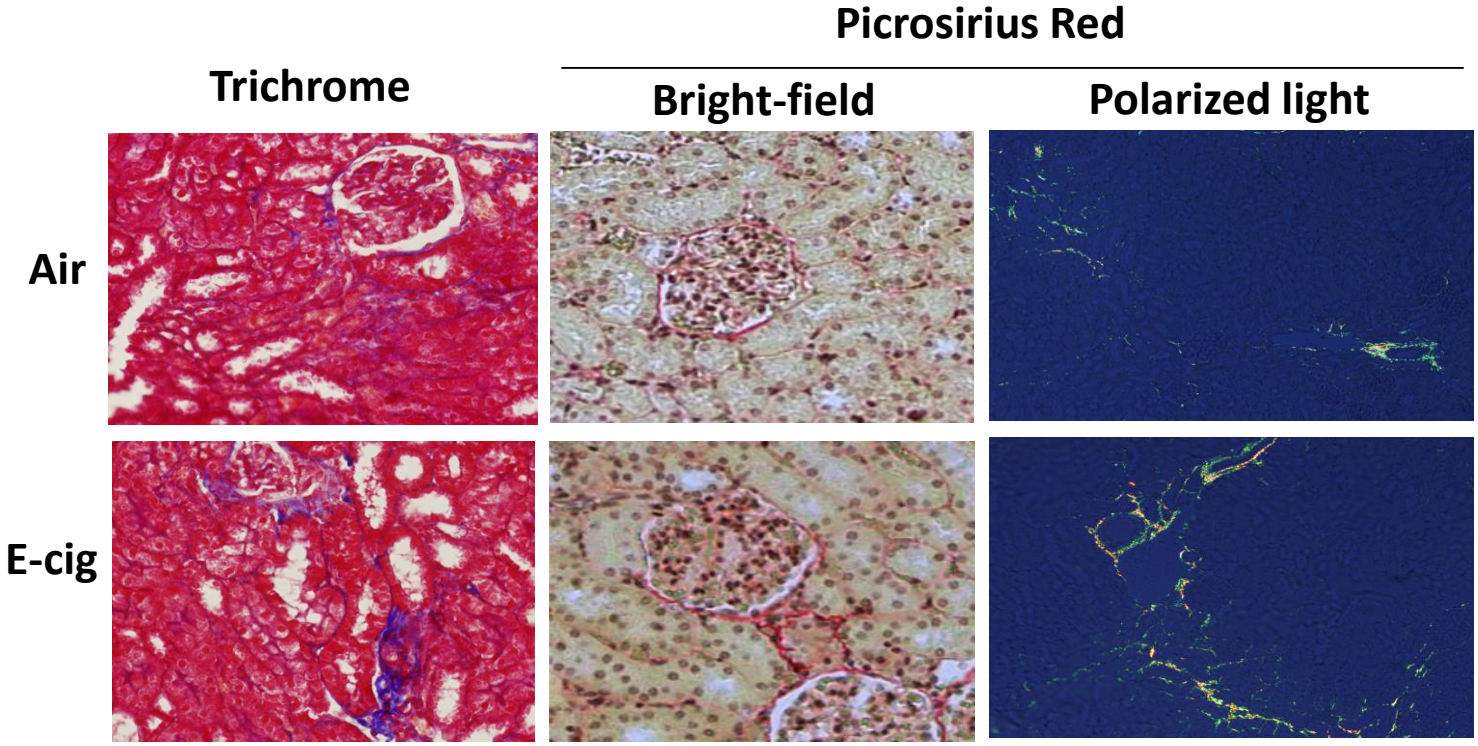
- Nicotine intake can be comparable to that from combustible tobacco cigarettes
- E-cigarette use results in symptoms of dependence

Health effects are related to exposure to toxins

Conclusive evidence

- Most e-cigarette products contain and emit numerous potentially toxic substances
- Many at lower levels than from combusted tobacco
  - Most not listed on the labels
  - Toxic aldehydes, other VOCs, flavorants, fine particles
    - » Benzene, toluene, formaldehyde, acetaldehyde, tobacco-specific nitrosamines, benzopyrene*
  - Metals: chromium, lead, manganese, aluminum, tin, iron**
    - » Wide variability in concentrations of metals
    - » Likely derived from coils and other parts of the devices

Multi-organ fibrosis seen in mice exposed to e-cigarette vapor



Kidney

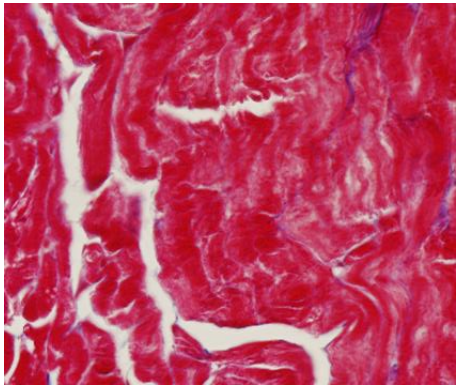
Slide courtesy of Laura Crotty Alexander. AJP Regulatory, Integrative, and Comparative Physiology, 2018

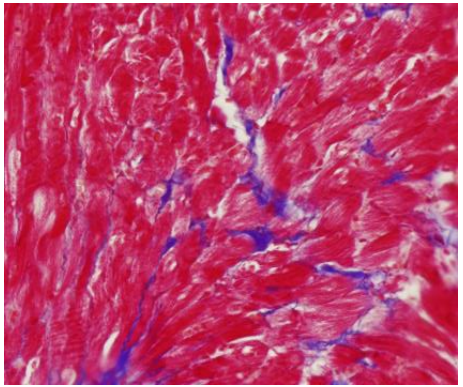
Multi-organ fibrosis seen in mice exposed to e-cigarette vapor

Air Control

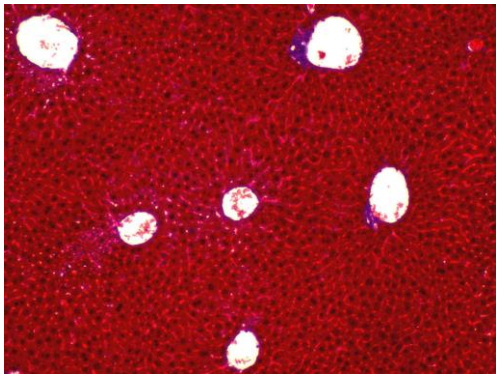
E-cigarette

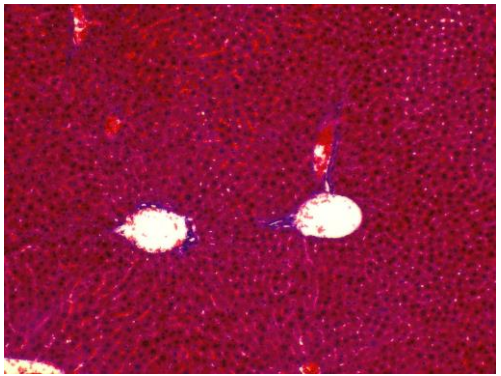
Heart





Liver





Slide courtesy of Laura Crotty Alexander

AJP Regulatory, Integrative, and Comparative Physiology,

Heart - collaboration with Joan Heller Brown

Chronic E-Cigarette Exposure Alters the Human Bronchial Epithelial Proteome

- Research bronchoscopies on healthy nonsmokers, cigarette smokers, and e-cigarette users (vapers)
  - Vaper airways appeared friable and erythematous
- Epithelial cells from bronchial brush biopsies: ~300 proteins were differentially expressed in smoker and vaper airways
- Chronic vaping exerts marked biological effects on the lung, may in part be mediated by propylene glycol/vegetable glycerin base
- Changes are likely harmful, may have clinical implications for development of chronic lung disease

Ghosh A et al. Am J Respir Crit Care; 2018; DOI: 10.1164/rccm.201710-2033O

E-cigarettes may increase risk of pneumonia

J Mol Med
DOI 10.1007/s00109-016-1378-3

JMolMed CrossMark

ORIGINAL ARTICLE

Electronic cigarette inhalation alters innate immunity and airway cytokines while increasing the virulence of colonizing bacteria

John H. Hwang[1,2] · Matthew Lyes[1,8] · Katherine Sladewski[1] · Shymaa Enany[3,1] · Elisa McEachern[1,7] · Denzil P. Mathew[1] · Soumita Das[4] · Alexander Moshensky[1] · Sagar Bapat[5] · David T. Pride[4] · Weg M. Ongkeko[6] · Laura E. Crotty Alexander[1,2]

E-cigarette vapor damages DNA & cells

Oral Oncology 52 (2016) 58–65

Contents lists available at ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

Electronic cigarettes induce DNA strand breaks and cell death independently of nicotine in cell lines

Vicky Yu [a], Mehran Rahimy [a], Avinaash Korrapati [a], Yinan Xuan [a], Angela E. Zou [a], Aswini R. Krishnan [a], Tzuhan Tsui [b], Joseph A. Aguilera [c], Sunil Advani [c], Laura E. Crotty Alexander [b,d], Kevin T. Brumund [a], Jessica Wang-Rodriguez [e,1], Weg M. Ongkeko [a,1,*]

Question #3

Components of e-cigarette aerosols can promote formation of reactive oxygen species and oxidative stress, which

a) enhances the likelihood of becoming addicted to nicotine

b) supports the biological plausibility of tissue injury and disease

c) increases the odds that youth who vape will initiate marijuana use

d) elevates systolic and diastolic blood pressure

Cardiovascular system

Substantial evidence

- Heart rate increases after nicotine intake from e-cigs
- Aerosol components can promote formation of reactive oxygen species and oxidative stress
  - supports biological plausibility of tissue injury & disease
  - generally lower than from combustible cigarette smoke

Moderate evidence

- Diastolic blood pressure increases
  - short term increases similar to combustible cigarettes

Cardiovascular system

Limited evidence

- Short-term increase in systolic blood pressure, changes in biomarkers of oxidative stress, increased endothelial dysfunction and arterial stiffness

Insufficient evidence

- Long-term changes in heart rate, blood pressure, and cardiac geometry and function

No evidence

- Whether or not use is associated with clinical cardiovascular outcome and subclinical atherosclerosis

Respiratory system

Moderate evidence

- Increased cough and wheeze in adolescents
- Association with an increase in asthma exacerbations

Limited evidence among adult smokers who switch to e-cigarettes completely or in part (dual use)

- Improvement in lung function and respiratory symptoms in those with asthma
- Reduction in COPD exacerbations in those with COPD

Respiratory system

Limited evidence – animals exposed to nicotine-containing e-cig vapor

- Impaired lung growth in new born babies
- Impaired bacterial clearance from lungs of adult mice

No evidence yet on whether or not e-cigarettes cause respiratory disease in humans

Cancers & immune dysregulation

Substantial evidence

- Components of e-cigarette aerosols can promote formation of reactive oxygen species and oxidative stress - generally lower than from combustible tobacco smoke

Limited evidence

- Supports the biological plausibility of tissue injury and disease
- In vivo animal studies using intermediate biomarkers of cancer support the hypothesis that long-term use could increase the risk of cancer

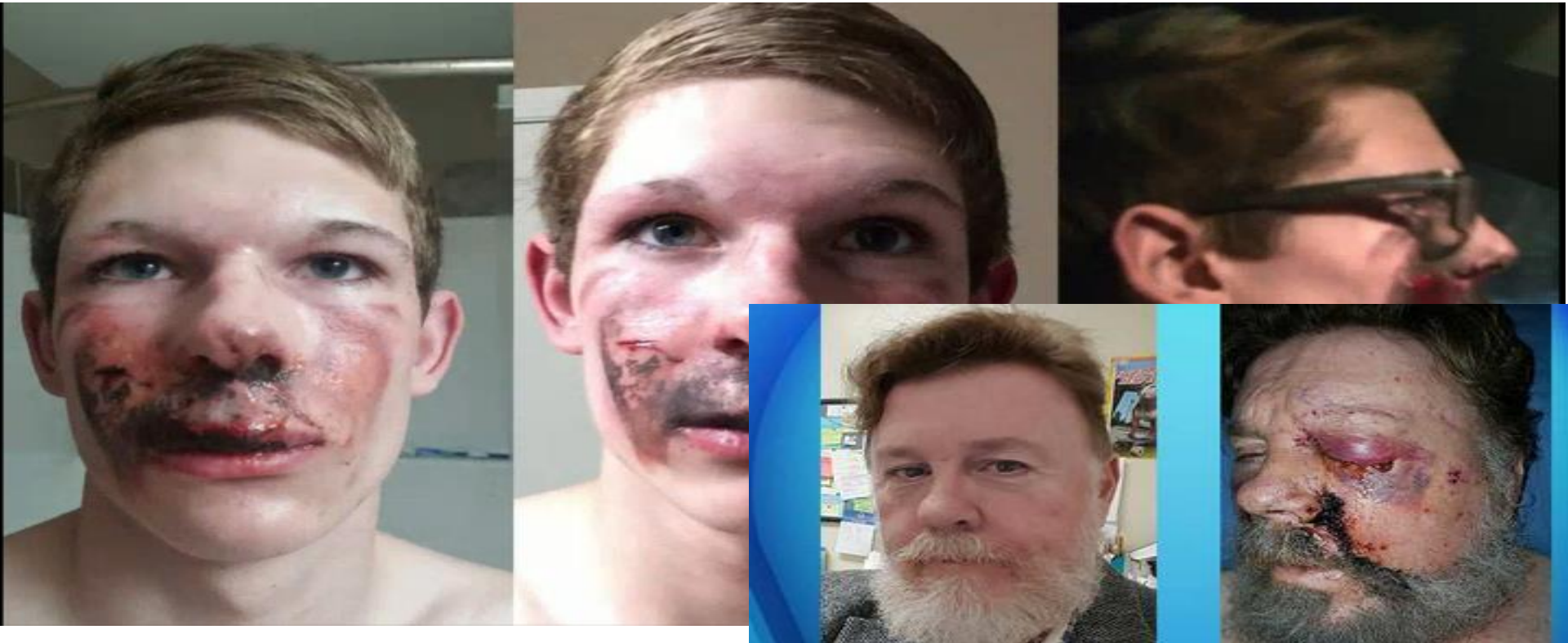
Modeling of e-cigarette use

- If e-cigarettes increase smoking cessation rates: 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
- For long-range projections (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 smoking cessation rates: net public health harm in the short and long term

BMJ Case Rep. 2016 Apr 5;2016. pii: bcr2016214964. doi: 10.1136/bcr-2016-214964.

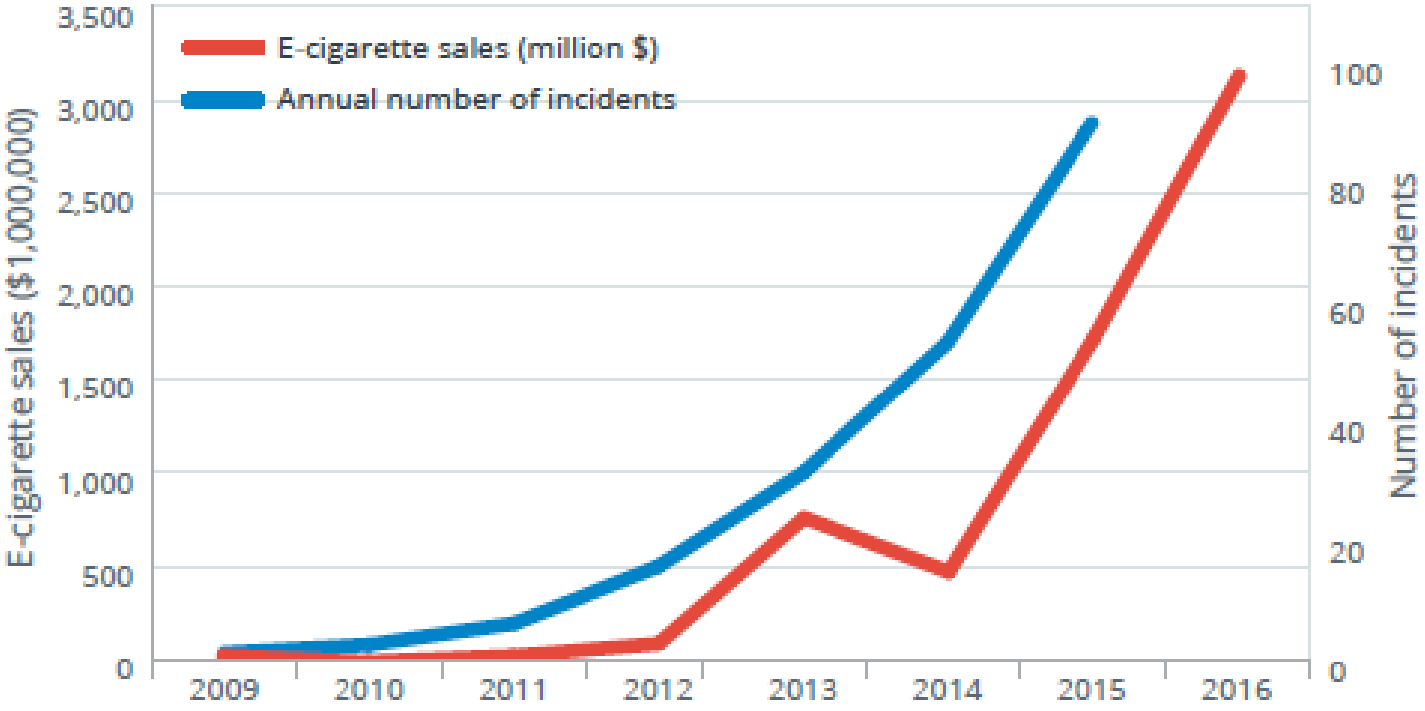
Front to back ocular injury from a vaping-related explosion.

Khairudin MN[1], Mohd Zahidin AZ[1], Bastion ML[1].



Fires & Explosions

January 2009 to December 31, 2016



E-cigarette sales data from http://www.statisticbrain.com/electronic-cigarette-statistics/ on 3/27/2017.

Fires & Explosions

- Combination of an electronic cigarette and a lithium-ion battery – new and unique hazard
  - Events are due to the lithium-ion batteries
- Severe, acute injury
  - Uncommon; can be devastating
  - May 2018 – 1st reported death in U.S.
  - February 2019 – "Texas man dies after exploding vape pen severs carotid artery"
  - Likely that the number of incidents and injuries will continue to increase
- January 2009 to December 31, 2016:
  - 195 separate incidents of explosion/ fire involving an electronic cigarette reported by the U.S. media.
  - 133 acute injuries, 38 (29%) were severe.
- Shape, construction of e-cigarettes can make them (more than other products with lithium-ion batteries) behave like "flaming rockets" when battery fails

American Medical Association urges policy changes for e-cigarettes

"We are concerned that consumers have an inaccurate reflection of the amount of nicotine and type of substances they're inhaling when using e-cigarettes," AMA President Barbara L. McAneny, MD. "The AMA will continue to advocate for more stringent policies to help keep all harmful tobacco products, including e-cigarettes, out of the hands of our nation's youth."

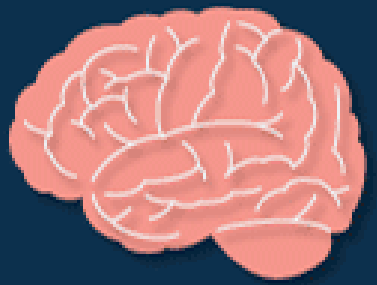
AMA Wire 6/15/18

Centers for Disease Control and Prevention
MMWR

YOUTH E-CIGARETTE USE IS RISING

E-CIGARETTES TYPICALLY DELIVER NICOTINE

YOUTH NICOTINE EXPOSURE CAN:



- CAUSE ADDICTION
- HARM THE DEVELOPING BRAIN

E-CIGARETTE USE SURGED DURING 2017-2018

IN 2018:

1 IN 5 HIGH SCHOOL KIDS

1 IN 20 MIDDLE SCHOOL KIDS

CURRENTLY USE E-CIGARETTES

HELP PREVENT YOUTH E-CIGARETTE USE

- KNOW THE RISKS OF E-CIGARETTES
- TALK TO YOUTH ABOUT THESE DANGERS
- BE TOBACCO FREE

National Youth Tobacco Survey as reported in Cullen et al., MMWR 2018
http://bit.ly/CDCVA18

WWW.CDC.GOV

Talk with teens

- Know the facts.
- Get credible information about e-cigarettes and young people at E-cigarettes.SurgeonGeneral.gov.
- Be patient and ready to listen.
- Avoid criticism and encourage an open dialogue.
- Goal is to have a conversation, not deliver a lecture.
- OK for your conversation to take place over time, in bits and pieces.
- Set a positive example by being tobacco-free.
- If you use tobacco, it’s never too late to quit.

https://e-cigarettes.surgeongeneral.gov

Recommendations (Drazen et al)

- Consider our guiding ideology of Do No Harm
- Have we found anything that is safe to inhale besides clean air?
- Compared to cigarettes, newer generation devices (Mods) may be harm reducing
- Inhalation of e-cigarette vapor will alter lung and systemic inflammation and host defenses

Drazen JM, Morrissey S, Campion EW. DOI: 10.1056/NEJMe1900484

Recommendations – cessation

- Only use e-cigarettes when FDA-approved treatments (combined with behavioral counseling) fail
- Advise patients to use lowest dose needed to manage cravings
- A clear timeline and “off ramp” for use
- Monitored by health care providers
- Further research needed on health consequences of long-term e-cigarette use

Borrelli B, O’Connor GT. DOI: 10.1056/NEJMe1816406

Summary

- Use rising dramatically among youth
- Increases the risk of youth initiating smoking of combustible cigarettes
- Cessation benefits not proven; less than evidence-based treatment for tobacco dependence
- Long-term safety unknown – growing evidence of toxicity
- Health effects of second-hand exposure are unknown
  - Emission of fine and ultrafine inhalable liquid particles, nicotine & cancer-causing substances

Heat-not-burn (HNB) cleared by FDA

- Hybrid between e-cigarettes & traditional cigarettes
- Uses electric element to heat tobacco
  - Produces smoke that contains nicotine, tar, other chemicals & particulates
- No evidence of a lower health risk
  - Potential to increase oxidative stress and inflammation, infections, airway remodeling and initiate changes in the airways of users
- Agreement for Altria to commercialize IQOS in the U.S.
  - >50% people interested in IQOS are never-smokers

Philip Morris International's heated tobacco product, IQOS

https://truthinitiative.org/news/what-are-heat-not-burn-cigarettes

Sohal SS et al. IQOS exposure impairs human airway cell homeostasis: direct comparison with traditional cigarette and e-cigarette. ERJ Open Res 2019; 5:00159-2018 [https://doi.org 10.1183/23120541.00159-2018].

We know what works to reduce use of tobacco

Evidence-based strategies that reduce the number of youth who start using tobacco, help more adults quit & decrease exposure to secondhand smoke:

1. Increasing the price of all tobacco products through regular and significant tobacco tax increases
2. Comprehensive smoke- and tobacco-free policies
3. Fund and sustain evidence-based, statewide tobacco use prevention and treatment programs
4. Tobacco 21 laws

Resources

- Center for Disease Control and Prevention (CDC)
  - https://www.cdc.gov/tobacco/index.htm
- Office of the Surgeon General
  - https://e-cigarettes.surgeongeneral.gov
- Truth Initiative – https://truthinitiative.org/
- Campaign for Tobacco Free Kids – http://www.tobaccofreekids.org/
- American Thoracic Society – https://www.thoracic.org
- Tobacco 21–An Important Public Policy to Protect our Youth
  - https://www.thoracic.org/patients/patient-resources/resources/ tobacco-21.pdf
- American Lung Association
  - https://www.lung.org/our-initiatives/tobacco/reports-resources/sotc/
- American Academy of Pediatrics – https://www.aap.org