Nicotine Electronic Cigarettes: What Does The Scientific Evidence Tell Us?

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What are electronic cigarettes?

What are the harms of electronic cigarettes?

Do e-cigs help smokers to quit smoking?

How addictive are e-cigs?

Can e-cigs produce a public health benefit?

Major Smoking-caused Diseases

- **Cancer (lung and many other sites)**
- Many carcinogens (e.g. BaP, NNK, measured as urine NNAL) cause DNA damage, inflammation, oxidative stress which promote initiation and growth of tumors.
- **Cardiovascular disease (MI, stroke etc)**
- Volatile gases cause inflammation (e.g. carbon-monoxide), platelet aggregation, nicotine stimulates BP,HR. CO impairs oxygen transport
- **Chronic respiratory diseases (COPD)**
- Deposition of tar, blocks airways, ox stress (3-HPMA (acrolein), NO etc) damage cilia,and inflammation stimulates muccus, reduces elastin.
- **Smoking adversely affects virtually every organ of the body**
- **Causes over 450,000 premature deaths and 10 million serious illnesses each year in USA alone**

Cigarette smoke contains over 7000 chemicals, including dozens of carcinogens.

But people smoke for the psychopharmacological effects of nicotine.

“If it were not for the nicotine in tobacco smoke, people would be little more inclined to smoke than they are to blow bubbles.” (Prof. Michael Russell, 1974)

Definitions: Electronic Cigarettes

E-cigs include a diverse group of devices that include an electrical power supply (typically a battery) that heats a liquid, which typically contains nicotine, flavorings and other additives, to produce an aerosol that is intended to be inhaled by the user.

Different types of e-cigs are sometimes referred to by companies and consumers by other names, such as "cigalikes", "e-hookahs", "mods", "vape pens", "tank systems" or simply by their brand names, e.g. "Blue", "Njoy", "Juul" or "Ego".

There are hundreds of different types of electronic cigarettes. They vary by size, battery power, atomizer resistance, number of coils, liquid nicotine strength, liquid flavor, liquid type (PPG/VG) etc etc. Two broad categories are (a) First Generation/cigalikes (bottom) and Second Generation/Advanced (top)

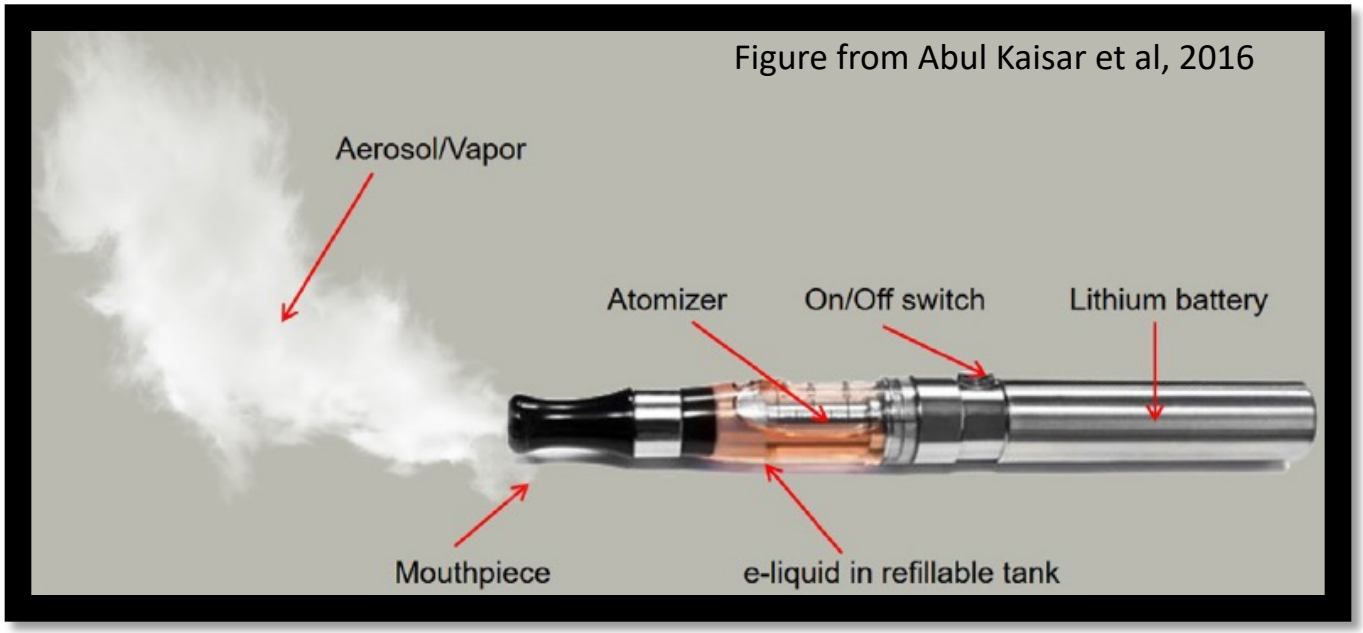
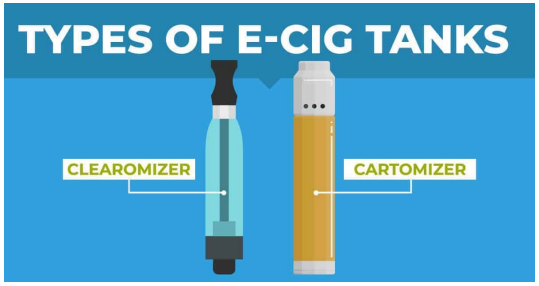


Image from www.fda.gov

Abul Kaisar, Prasad, Liles, Cucullo, 2016

Electronic Cigarettes are Diverse



Many Liquids & Flavors Too

Contents

- Propylene glycol and/or

  Vegetable glycerine (glycerol)
- Nicotine (in mg/ml; ranging from 0-60), sometimes as a nicotine salt
- Flavourings (e.g. tobacco, mint, fruit, menthol, unicorn fart etc)
- Additives

How harmful are electronic cigarettes to health?

(a) Compared to fresh air

(b) Compared to cigarettes

(a) E-cigs contain PG, VG, flavors, additives, nicotine and heating can cause other chemicals to be formed. These substances are inhaled into the lungs.

It therefore seems obvious that e-cigs are not harmless, that non-smokers (particularly children) should be strongly discouraged from trying e-cigs, and that it should be illegal to sell them to children.

Hecht et al (2015) Comparison of toxicant and carcinogen biomarkers in the urine of exclusive cigarette smokers and exclusive e-cig users.

E-cig aerosol contains a variety of potentially harmful compounds, generally around 10-500 times less than in cigarette smoke.

- **Compared concentration in urine of 28 e-cig users with over 200 cigarette smokers.**
- **Assessed 6 carcinogen biomarkers and one marker of nicotine intake (cotinine).**
- **All the carcinogen biomarkers were much lower in e-cig users compared to cigarette smokers. In fact the e-cig users were in the same range or lower than typically found in non smokers.**

This provides strong evidence that e-cigs, as typically used, are likely to be far less harmful than cigarettes, as typically used.

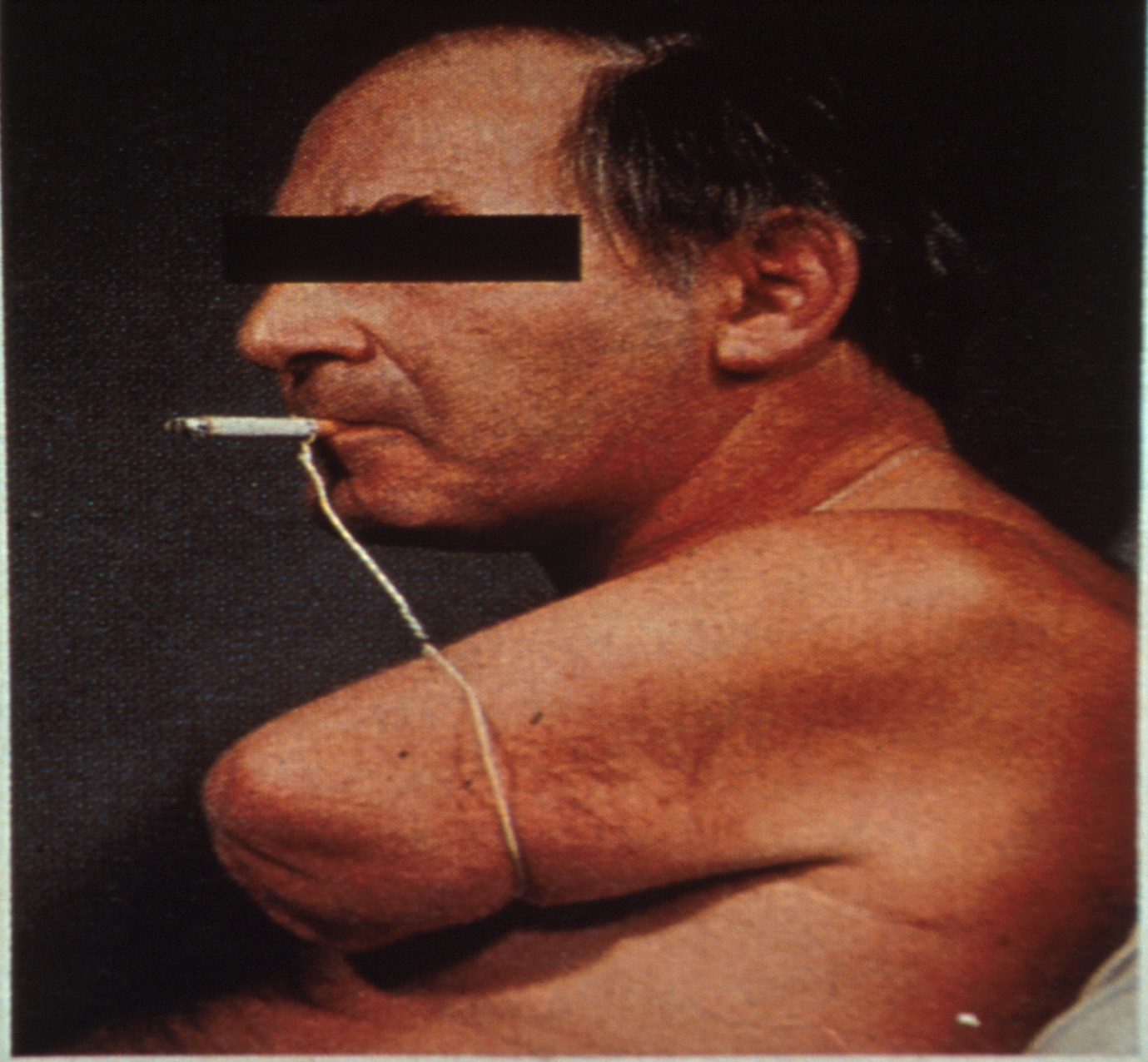
Cigarette are highly addictive.

Most people who ever smoke 60 cigarettes go on to become daily smokers for years.

The average middle aged smoker has made over 20 serious attempts to quit.

When an average smoker decides they are going to try to quit, there is a 95% chance they will still be smoking a year later.

When an average smoker who has had difficulty quitting on their own gets professional help (counseling plus FDA-approved medication), there is an 80% chance they will still be smoking a year later.



Self mutilation by smoking—this patient had all four limbs amputated for a Buerger's type

What is in e-cigarette liquid, and what is in the aerosol users inhale?

E-liquid contents:
Propylene glycol, vegetable glycerine, nicotine, flavors, additives

E-cig aerosol contains:
The same potentially harmful toxicants, but when these are subject to heat this can result in decomposition to create additional harmful toxicants including formaldehyde, acetaldehyde and acrolein

E-cig aerosol contains a variety of potentially harmful compounds, generally delivering lower levels of nicotine and up to 400 times less for some of the most harmful toxicants than in cigarette smoke.
However, very few e-liquids have undergone a complete toxicological assessment.

Chemical Research in Toxicology

Rapid Report

pubs.acs.org/crt

Highly Reactive Free Radicals in Electronic Cigarette Aerosols

Reema Goel,[†] Erwann Durand,[‡] Neil Trushin,[§] Bogdan Prokopczyk,[§] Jonathan Foulds,[†] Ryan J. Elias,[‡] and John P. Richie, Jr.*[,†]

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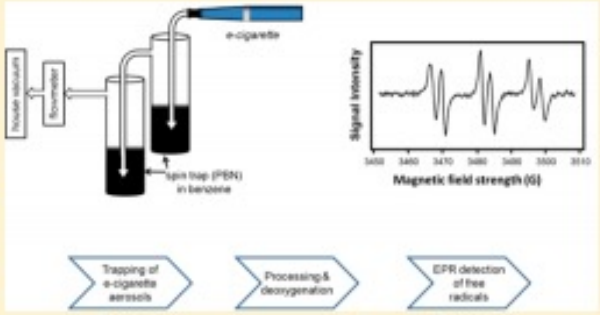
Supporting Information

ABSTRACT: Electronic cigarette (EC) usage has increased exponentially, but limited data are available on its potential harmful effects. We tested for the presence of reactive, short-lived free radicals in EC aerosols by electron paramagnetic resonance spectroscopy (EPR) using the spin-trap phenyl-*N*-*tert*-butylnitrone (PBN). Radicals were detected in aerosols from all ECs and eliquids tested (2.5×10^{13} to 10.3×10^{13} radicals per puff at 3.3 V) and from eliquid solvents propylene glycol and glycerol and from "dry puffing". These results demonstrate, for the first time, the production of highly oxidizing free radicals from ECs which may present a potential toxicological risk to EC users.



From: **Comparison of Nicotine and Toxicant Exposure in Users of Electronic Cigarettes and Combustible Cigarettes** JAMA Netw Open. 2018;1(8):e185937. doi:10.1001/jamanetworkopen.2018.5937

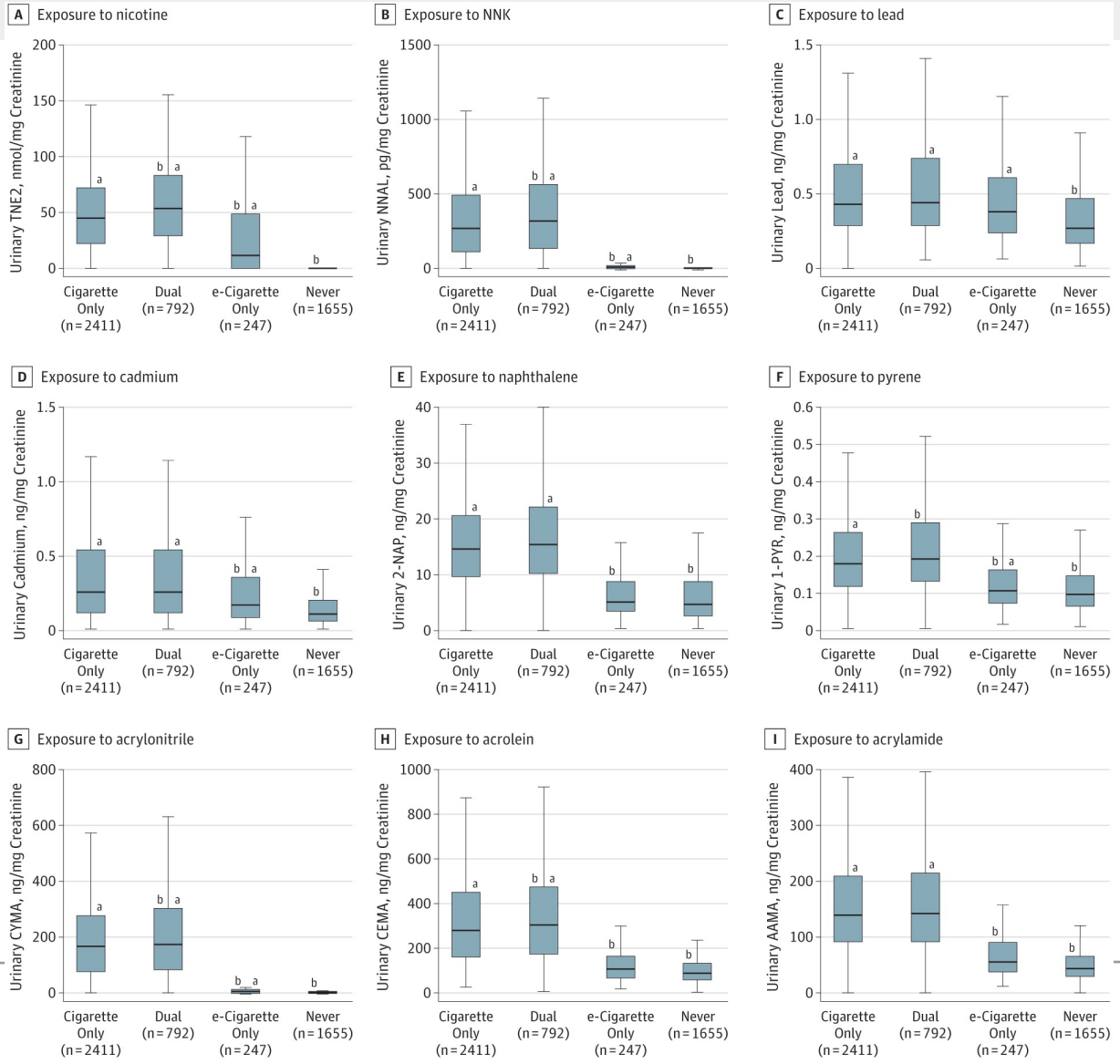
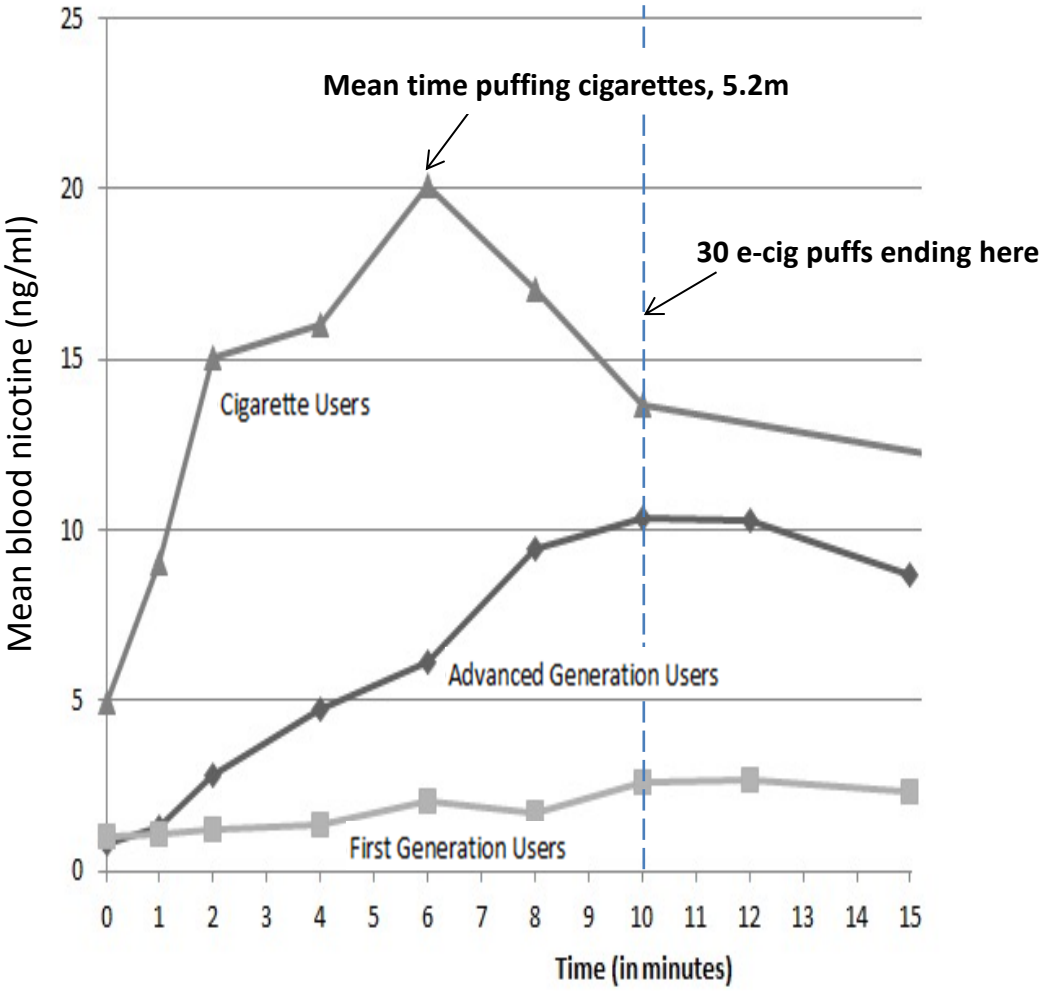


Figure Legend:

Biomarkers of Exposure Among Dual Users, Cigarette-Only **Smokers, e-Cigarette–Only Users, and Never Users, Population Assessment of Tobacco and Health Study, Wave 1, 2013-2014**

Blood Nicotine Levels in Cigarette and E-cigarette Users



First generation e-cigs deliver very little nicotine.

Advanced e-cigs deliver a higher blood nicotine concentration typically less than a cigarette

Some advanced e-cigs can deliver nicotine as rapidly as cigarettes.

Nicotine & Tobacco Research, 2015, 186–192
doi:10.1093/ntr/ntu204
Advance Access publication October 19, 2014
Original investigation

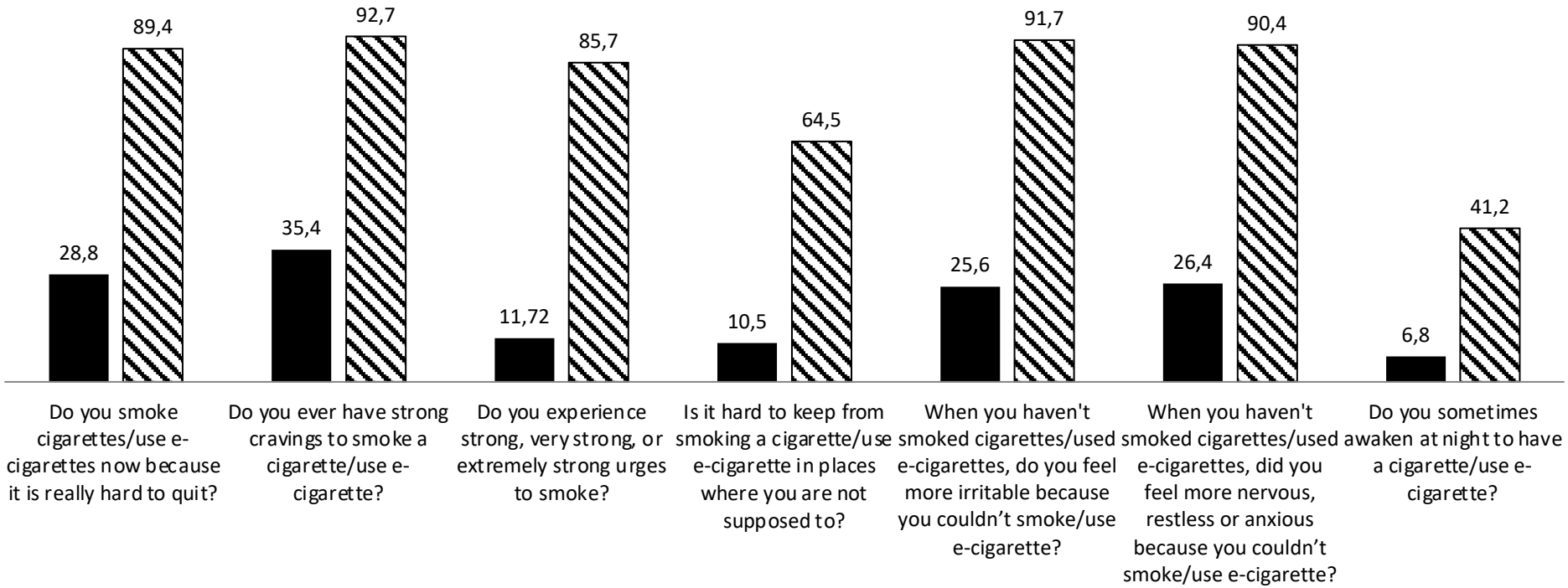
OXFORD

Original investigation

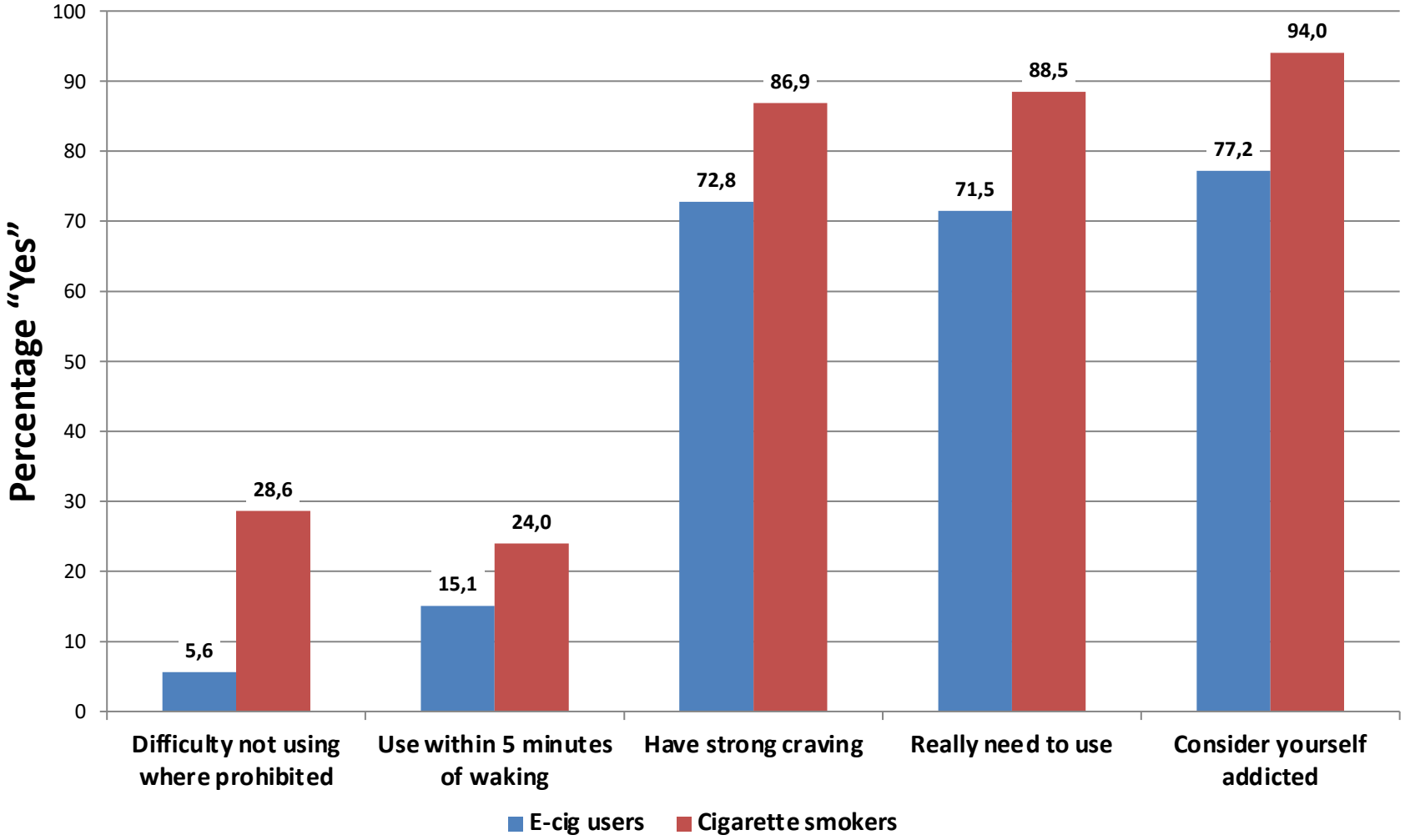
Development of a Questionnaire for Assessing Dependence on Electronic Cigarettes Among a Large Sample of Ex-Smoking E-cigarette Users

Jonathan Foulds PhD[1], Susan Veldheer MS[1], Jessica Yingst MS[1], Shari Hrabovsky MSN[1], Stephen J. Wilson PhD[2], Travis T. Nichols MS [2], Thomas Eissenberg PhD[3]

Penn State Nicotine Dependence Questions (% yes)



Indicators of Dependence Among Exclusive Daily E-cig Users (n=156) and Exclusive Daily Cigarette Smokers (n=3430) in the PATH Wave 1 Survey*



*All e-cig and cigarette differences p<0.0001 after adjusting for covariates.

Liu, Wasserman, Kong, Foulds. Preventive Medicine 2017.

The National Academies of
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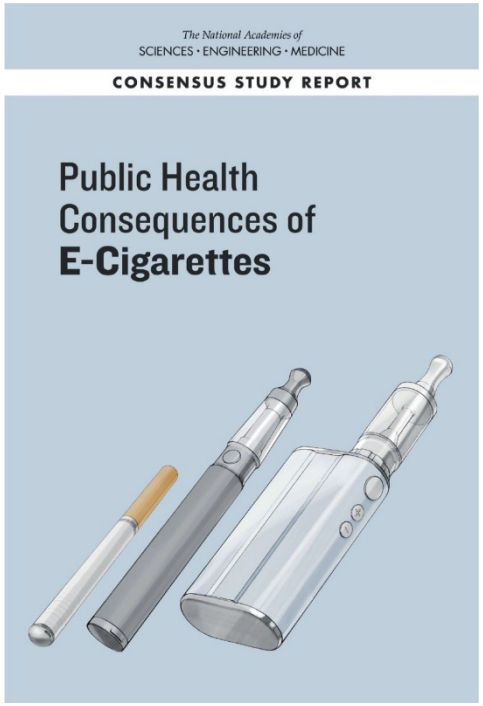


Public Health Consequences of E-Cigarettes

#eCigHealthEffects

Summary, NAS Report 2018

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: NAS Report 2018.

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.

Hajek et al 2019. E-cigs v NRT (both with counseling). At one year, E-cigs 18% quit smoking, NRT 10% quit smoking.

Table 2. Abstinence Rates at Different Time Points and Smoking Reduction at 52 Weeks.*

Outcome	E-Cigarettes (N=438)	Nicotine Replacement (N=446)	Primary Analysis: Relative Risk (95% CI)†	Sensitivity Analysis: Adjusted Relative Risk (95% CI)
Primary outcome: abstinence at 52 wk — no. (%)	79 (18.0)	44 (9.9)	1.83 (1.30–2.58)	1.75 (1.24–2.46)‡
Secondary outcomes				
Abstinence between wk 26 and wk 52 — no. (%)	93 (21.2)	53 (11.9)	1.79 (1.32–2.44)	1.82 (1.34–2.47)§
Abstinence at 4 wk after target quit date — no. (%)	192 (43.8)	134 (30.0)	1.45 (1.22–1.74)	1.43 (1.20–1.71)¶
Abstinence at 26 wk after target quit date — no. (%)	155 (35.4)	112 (25.1)	1.40 (1.14–1.72)	1.36 (1.15–1.67)‡
Carbon monoxide–validated reduction in smoking of ≥50% in participants without abstinence between wk 26 and wk 52 — no./total no. (%)	44/345 (12.8)	29/393 (7.4)	1.75 (1.12–2.72)	1.73 (1.11–2.69)‖

* Abstinence at 52 weeks was defined as a self-report of smoking no more than five cigarettes from 2 weeks after the target quit date, validated biochemically by an expired carbon monoxide level of less than 8 ppm at 52 weeks. Abstinence between week 26 and week 52 was defined as a self-report of smoking no more than five cigarettes between week 26 and week 52, plus an expired carbon monoxide level of less than 8 ppm at 52 weeks. Abstinence at 4 weeks was defined as a self-report of no smoking from 2 weeks after the target quit date, plus an expired carbon monoxide level of less than 8 ppm at 4 weeks. Abstinence at 26 weeks was defined as a self-report of smoking no more than five cigarettes from 2 weeks after the target quit date to 26 weeks; there was no validation by expired carbon monoxide level.

† The analysis was adjusted for trial center only.

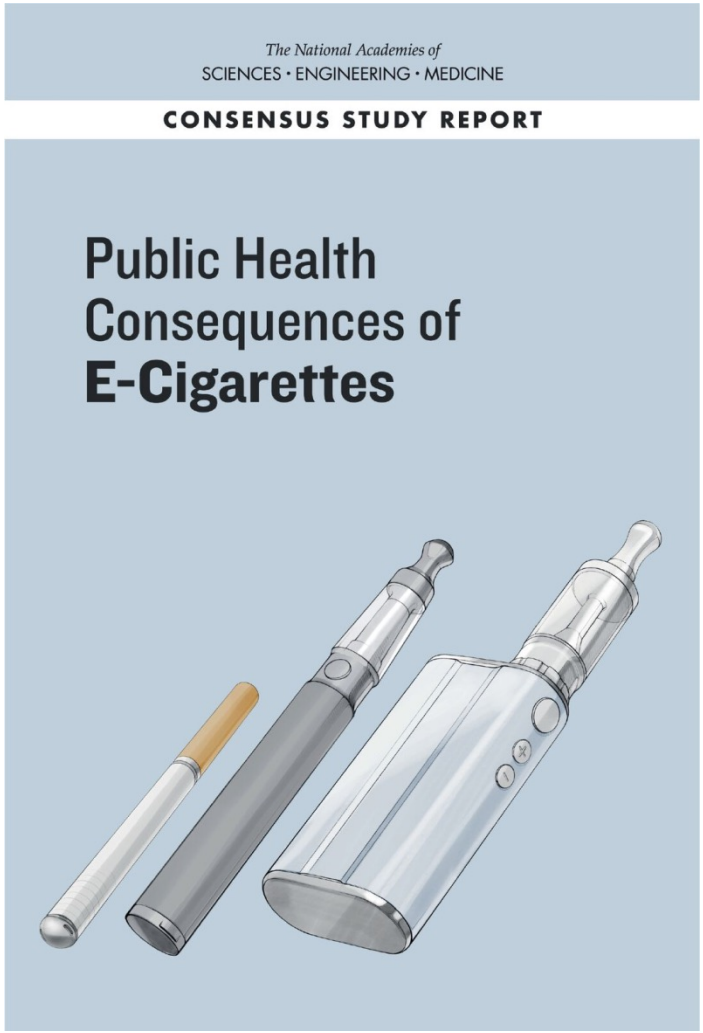
‡ The analysis was adjusted for trial center, marital status, age at smoking initiation, and score on the Fagerström Test for Cigarette Dependence.

§ The analysis was adjusted for trial center, age, score on the Fagerström Test for Cigarette Dependence, and age at smoking initiation.

¶ The analysis was adjusted for trial center, education level, partner who smokes (yes or no), and score on the Fagerström Test for Cigarette Dependence.

‖ The analysis was adjusted for trial center, sex, age, and partner who smokes (yes or no).

P Hajek et al. N Engl J Med 2019;380:629-637.



Visit

nationalacademies.org/eCigHealthEffects

to download the full report

Also see 2016 US Surgeon General's report on e-cigs in young people: https://www.surgeongeneral.gov/library/2016ecigarettes/index.html

Summary

1. If you are not currently a smoker, don't start using any nicotine or vaping product.

2. If you are a smoker, then switching completely to an e-cig will likely be much less harmful to your health than smoking. But remember that the evidence is better that medicines like varenicline will help you quit.

3. If you have already successfully quit smoking by switching completely to an e-cig then that is positive, and when you are ready you should wean yourself off the e-cigs.

4. I believe e-cigs, if appropriately regulated, can produce a public health benefit by replacing the cigarette industry completely.