E-Cigarettes: A Solution to Nicotine Addiction? Or Just Nicotine in Solution?

Laura E. Crotty Alexander, MD
Assistant Professor of Medicine
Division of Pulmonary & Critical Care
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Disclosures

• I have nothing to disclose.

• Advertisements are contained in this presentation, but companies were chosen at random for educational purposes.
The real reason dinosaurs became extinct
Tobacco Cigarette Smoking

- 19% of all adults (44 million) in the U.S. smoke cigarettes
- Leading preventable cause of death in the U.S.
  - >480,000/yr
  - 1 of every 5
- 289 billion in healthcare costs per year
- Causes 90% (Males) and 80% (Females) of lung cancers
- 90% of COPD-related deaths
- Increases risk of coronary artery disease (CAD) and stroke by 2-4x
1930s
Researchers in Cologne, Germany, epidemiologic correlation

1938
Dr. Raymond Pearl, Johns Hopkins

1952
Reader’s Digest published “Cancer by the Carton”
Tobacco Cigarette Smoking Cessation

• Success rates

  • Cold turkey (<10%)
  • Nicotine replacement therapy (NRT) only (<15%)
  • Oral medication (~28%)
  • Medication + Counseling (~38%)
  • Medication + NRT + Counseling (~40%)
Methicillin resistant *Staphylococcus aureus*

MRSA
MRSA Pneumonia

8 hours

MRSA Surviving in Lung (CFU x10⁶)

Control 75% CSE

Bacterial Treatment

20 hours

Mortality

Control MRSA

CSE-MRSA

Survival (%)

Time (d)

McEachern et al, Infection and Immunity 2015
Shunting cellular energy to defense/offense?
Electronic Cigarettes

E-cigarettes were invented by pharmacist Hon Lik in 2003 in China, and entered the international market in 2007. 3.5 million sold in 2012

- Drug delivery device which does not require combustion
- How they work: a battery is activated to heat a metal coil (atomizer) that creates a fine suspension of particles of liquid or solid or both, in a gas
- E-juice is the liquid inside the cartridge, and is heated to a maximum temperature of 55°C (?) for aerosolization
- Can be activated either manually or pneumatically
E-Cigarettes

- Drug delivery device which does not require combustion
- How they work: a battery is activated to heat a metal coil (atomizer) that creates a fine suspension of particles of liquid or solid or both, in a gas
- E-juice is the liquid inside the cartridge, and is heated to a maximum temperature of 55°C (?) for aerosolization
- Can be activated either manually or pneumatically
E-cigarette use is:

- Quadrupling in the adult U.S. population annually
- Tripling in middle-school and high-schoolers annually (25% of Californian kids have tried them)
- Cigarette smokers are the largest population of adult vapers
No offensive odors
No ash or cigarette butts
High vapor volume

* Patented two part design
* Produces most vapor

Click Here To Try GreenSmoke Now
10% off coupon code (orders over $100) - disc10-12103
5% off coupon code - disc5-12103

Hello, I thought you'd be interested in this great new product - the Green Smoke® electronic cigarette. To declare the Green Smoke® e-cigarette as the finest in the market would be an understatement. This elegant e-cigarette has a patent-pending 2 part design that is effortless to assemble and easy to maintain. Not only that, but Green Smoke® e-cigarettes emit an incredibly high smoke volume.

What people like most about Green Smoke is their commitment to high quality and to their customers. While the Green Smoke® Starter Kit costs more than many other brands, you really get what you pay for. Their e-cigarette batteries are sturdy and guaranteed to last for an entire year. If your battery dies within a year, just call Green Smoke customer service and they'll send you a replacement.

Green Smoke® cartridges are also top-of-the-line. Each cartridge lasts about one day for the average vaper, that's a lot of puff! Green Smoke® also offers a large variety of flavors and nicotine levels, so you can really customize your e-cigarette exactly to your liking.

And the Green Smoke customer service department is top-notch - their representatives are all very friendly and knowledgeable. You can call them for any e-cigarette related question and they'll be happy to assist.

GREEN SMOKE® E-CIGARETTE

LED Puff indicator
Smart Chip Controller
Operating Mode Sensor
Lithium Ion Battery
Heating Vapor Coil
Atomization Chamber
E-cigarettes

Use in minors is more than doubling annually (p<0.05), with 17% of high-schoolers using. 20% use e-cigarettes alone (no conventional tobacco). 1 million adolescents purchased some form of cigarette online in 2012.

“14-year-old boy left blinded after e-cigarette explodes at Brooklyn mall”
FOX News, April 14, 2016

“Three million American teens used e-cigarettes in 2015”
The Verge, April 14, 2016

“Teen vapers have easy time buying supplies online”
Reuters, April 7, 2016
E-cigarette use among youth is rising as e-cigarette advertising grows

Dollars spent on e-cigarette advertising

Past 30-day e-cigarette use among youth

2011 2012 2013 2014

Dollars spent on e-cigarette advertising (in millions)

Past 30-day e-cigarette use among youth (%)

E-liquid / E-juice

- Components: humectant(s) + nicotine + flavor(s)
  - Propylene glycol
  - Vegetable glycerin
  - Nicotine – anywhere from 6 to 26 mg/mL
  - >450 brands
- Vapers tend to vape 2-20x as much as they would smoke

Depending on the nicotine concentration chosen, one e-juice cartridge can equal 15 or more cigarettes
Flavors of E-juice

- eLiquid - Hillington Tobacco
  - Price: $4.99
  - Rating: ★★★★★ (83)

- eLiquid - Impulse
  - Price: $4.99
  - Rating: ★★★★★ (34)

- eLiquid - Joye M/USAMIX
  - Price: $4.99
  - Rating: ★★★★★ (1)

- eLiquid - Joye Tobacco
  - Price: $4.99
  - Rating: ★★★★★ (49)
1986 Juicebox (PG/VG Blend)
$3.95

An orange punch flavor that brings you back to your favorite childhood juicebox! Available in 3 different nicotine strengths and multiple sizes. This product page is for the 50/50 PG/VG Blend version of this E-Liquid...

Choose Options  Compare

Bedrock Blast (PG/VG Blend)
$3.95

A Pineapple and Orange refreshing drink Vape. Yabba dabba do try this flavor! Available in 3 different nicotine strengths and multiple sizes. This product page is for the 50/50 PG/VG Blend version of this E-Liquid...

Choose Options  Compare

Blue Demon (PG/VG Blend)
$3.95

Just like a refreshing energy drink! Available in 3 different nicotine strengths and multiple sizes. This product page is for the 50/50 PG/VG Blend version of this E-Liquid flavor. Learn About VG E-Liquids vs PG/VG...

Choose Options  Compare

Cereal Killer (PG/VG Blend)
$3.95

A delicious berry breakfast cereal. Available in 3 different nicotine strengths and multiple sizes. This product page is for the 50/50 PG/VG Blend version of this E-Liquid flavor. Learn About VG E-Liquids vs PG/VG...

Choose Options  Compare

Holy Water (PG/VG Blend)
$3.95

A delicious drink flavor familiar of coconut rum, one vape of our Holy Water and you will know why we consider it holy! For fans of our Strawberry Champagne and Screamin' Mimo, this vape is a must-try! Available in 3...

Choose Options  Compare
Manufacturing

- Highly variable quality control
- Lack of uniform manufacturing standards
- Huge differences between brands in all studies to date, including ours (Goniewicz 2013, Czogala 2014)
- Labels do not include full chemical composition, and when they include nicotine concentration information, the measured levels do not match up (Goniewicz 2013)
# Labeling vs. Reality?

Table 1  Nicotine reported in refill solutions, cartridges, aerosols and environmental emission of e-cigarette products

<table>
<thead>
<tr>
<th>Literature</th>
<th>Matrix</th>
<th>Units</th>
<th>Nicotine level</th>
<th>Deviation from label*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goniewicz et al</td>
<td>Refill solution</td>
<td>mg</td>
<td>0±0.0 to 25±1.1</td>
<td>−75 to 28%</td>
</tr>
<tr>
<td></td>
<td>Cartridge</td>
<td>mg</td>
<td>0±0.0 to 19±0.5</td>
<td>−89 to 25%</td>
</tr>
<tr>
<td></td>
<td>Aerosol</td>
<td>mg/150 puffs</td>
<td>0.3±0.2 to 8.7±1.0</td>
<td>N.A.</td>
</tr>
<tr>
<td>Etter et al</td>
<td>Refill solution</td>
<td>mg/mL</td>
<td>N.D. to 29.0</td>
<td>−15 to 21%†</td>
</tr>
<tr>
<td>Kirschner et al</td>
<td>Refill solution</td>
<td>mg/mL</td>
<td>14.8±0.2 to 87.2±2.7</td>
<td>−50 to 40%†</td>
</tr>
<tr>
<td>Cameron et al</td>
<td>Refill solution</td>
<td>mg/mL</td>
<td>8.5±0.16 to 22.2±0.62</td>
<td>−66 to 42%†</td>
</tr>
<tr>
<td>Pellegrino et al</td>
<td>Cartridge</td>
<td>% W/W</td>
<td>&lt;0.001 to 0.25</td>
<td>N.A.</td>
</tr>
<tr>
<td></td>
<td>Aerosol</td>
<td>mg/m³</td>
<td>&lt;0.01 to 6.21</td>
<td>N.A.</td>
</tr>
<tr>
<td>McAuley et al</td>
<td>Indoor air</td>
<td>ng/L</td>
<td>538 to 8770</td>
<td>N.A.</td>
</tr>
<tr>
<td>Cheah et al</td>
<td>Cartridge</td>
<td>mg/cartridge</td>
<td>0.00 to 15.3</td>
<td>−89 to 105%†</td>
</tr>
<tr>
<td>Trehy et al</td>
<td>Refill solutions</td>
<td>mg/mL</td>
<td>0 to 25.6</td>
<td>−100 to 100%†</td>
</tr>
<tr>
<td></td>
<td>Cartridge</td>
<td>mg/cartridge</td>
<td>0 to 21.8</td>
<td>−100 to 100%†</td>
</tr>
<tr>
<td></td>
<td>Aerosol</td>
<td>μg/100 mL puff</td>
<td>0 to 43.2</td>
<td>N.A.</td>
</tr>
<tr>
<td>Cobb et al</td>
<td>Cartridge</td>
<td>mg/cartridge</td>
<td>3.23±0.5 to 4.07±0.54</td>
<td>−80 to −77%†</td>
</tr>
<tr>
<td></td>
<td>Aerosol</td>
<td>μg/35 mL puff</td>
<td>0.3 for puffs 11 to 50 to 1.0</td>
<td>N.A.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>for puffs 1 to 10</td>
<td>N.A.</td>
</tr>
<tr>
<td>Westenberger</td>
<td>Cartridge</td>
<td>mg/cartridge</td>
<td>0.00 to 6.76</td>
<td>N.A.</td>
</tr>
<tr>
<td></td>
<td>Aerosol</td>
<td>μg/100 mL puff</td>
<td>0.35 to 43.2</td>
<td>N.A.</td>
</tr>
<tr>
<td>Westenberger</td>
<td>Refill solution</td>
<td>μg/mL</td>
<td>N.D. to 25.6</td>
<td>N.A.</td>
</tr>
</tbody>
</table>

*Deviation from label=(measured value – labelled value) * 100/labelled value.  
†Calculation performed by this analysis based on reported data in each study.  
N.A., not available; N.D., not detected.
Table 2  Aldehydes reported in refill solutions and aerosols of e-cigarettes

<table>
<thead>
<tr>
<th>Literature</th>
<th>Matrix</th>
<th>Units</th>
<th>Formaldehyde</th>
<th>Acetaldehyde</th>
<th>Acrolein</th>
<th>o-Methyl benzaldehyde</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goniewicz et al(^{20})</td>
<td>Aerosol</td>
<td>μg/150 puffs</td>
<td>3.2±0.8 to</td>
<td>2.0±0.1 to</td>
<td>N.D. to</td>
<td>1.3±0.8 to</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>56.1±1.4</td>
<td>13.6±2.1</td>
<td>41.9±3.4</td>
<td>7.1±0.4</td>
</tr>
<tr>
<td>Lim and Shin(^{25})</td>
<td>Refill solution</td>
<td>mg/L</td>
<td>0.02 to 10.09</td>
<td>0.10 to 15.63</td>
<td>N.D.</td>
<td>N.T.</td>
</tr>
<tr>
<td>Ohta et al(^{22})</td>
<td>Aerosol</td>
<td>mg/m(^3)</td>
<td>260</td>
<td>&lt;LOQ</td>
<td>&lt;LOQ</td>
<td>N.T.</td>
</tr>
<tr>
<td>Uchiyama et al(^{24})</td>
<td>Aerosol</td>
<td>mg/m(^3)</td>
<td>8.3</td>
<td>11</td>
<td>9.3</td>
<td>N.T.</td>
</tr>
<tr>
<td>Laugesen(^{22})</td>
<td>Aerosol</td>
<td>ppm/38 mL puff</td>
<td>0.25</td>
<td>0.34</td>
<td>N.D. to 0.33</td>
<td>N.T.</td>
</tr>
</tbody>
</table>

<LOQ, below the limit of quantitation but above the limit of detection; N.D., not detected; N.T., not tested by the study.

Table 3  Tobacco-specific nitrosamines reported in aerosols, refill solutions and cartridges of e-cigarettes

<table>
<thead>
<tr>
<th>Literature</th>
<th>Matrix</th>
<th>Units</th>
<th>NNN</th>
<th>NNK</th>
<th>NAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goniewicz et al(^{20})</td>
<td>Aerosol</td>
<td>μg/150 puffs</td>
<td>N.D. to 4.3±2.4</td>
<td>N.D. to 28.3±13.2</td>
<td>N.T.</td>
</tr>
<tr>
<td>Kim and Shin(^{21})</td>
<td>Refill solution</td>
<td>μg/L</td>
<td>0.34 to 60.08</td>
<td>0.22 to 9.84</td>
<td>0.09 to 62.19</td>
</tr>
<tr>
<td>Westenberger et al(^{9})</td>
<td>Cartridge</td>
<td>mg/cartridge</td>
<td>N.D. to &lt;LOQ</td>
<td>N.D. to &lt;LOQ</td>
<td>N.D. to &lt;LOQ</td>
</tr>
<tr>
<td>Laugesen(^{22})</td>
<td>Cartridge</td>
<td>ng/cartridge</td>
<td>BDL to 3.87</td>
<td>0.26 to 1.46</td>
<td>BDL to 2.16</td>
</tr>
</tbody>
</table>

<LOQ, below the limit of quantitation but above the limit of detection; BDL, below detection limit; N.D., not detected; N.Q., not quantifiable; N.T., not tested | NNN, N-nitrosornicotine; NNK, 4-(N-nitrosomethylamino)-1-(3-pyridyl)-1-butane; NAT, N-nitrosoanatabine; NAB, N-nitrosoanabasine. |
Fig. 1. The pyrolytic reactions of glycerol to produce formaldehyde, acetaldehyde and acrolein. Radical intermediates for steps involving loss of water are omitted for simplicity.

I.G. Gillman et al. / Regulatory Toxicology and Pharmacology 75 (2016) 58–65
Hidden Formaldehyde in E-Cigarette Aerosols

![Graph showing daily intake of formaldehyde in different scenarios.]

- **Cigarettes (Miyake and Shibamoto, 1995)**: 20 Cigarettes/day
- **Cigarettes (Counts et al., 2005)**: Not detected
- **Low voltage E-Cigarettes from Formaldehyde Gas Phase (Kosmider et al., 2014)**: 0.0033 mg/day
- **High voltage E-Cigarettes from Formaldehyde Gas Phase (Kosmider et al., 2014)**: 0.48 mg/day
- **Low voltage E-Cigarettes from Aerosol Particles Containing FRAs (Our Study)**: Not detected
- **High voltage E-Cigarettes from Aerosol Particles Containing FRAs (Our Study)**: 14 mg/day
From: Electronic Cigarettes: Heating Filament and Lung Toxicity of E-Cigarettes: The Resistance Value of the Heating Filament Could Be the Key to Lung Toxicity


Figure Legend:

Power of 3.3- and 5-V electronic cigarettes, depending on the filament used.
E-cigarette Hypothesis #1

• E-cigarette vapor exposure will alter pathogenic bacteria in the airways
EVE effect on bacterial growth kinetics

**Growth Curves**

- control
- Nicotine 0.4 mg/mL
- Nicotine 2 mg/mL
- Propylene glycol (PG)
- PG+N
- Vegetable glycerin (VG)
- VG+N

**Different Brands**

- control
- Cali Blues
- Highlander Grog
- Treasury
- Vapure
- Pure Smoke

Hwang et al, Journal of Molecular Medicine 2016
EVE-MRSA

Biofilm Formation

Hydrophobicity

Adherence to Epithelial

Invasion of Epithelial Cells

Hwang et al, Journal of Molecular Medicine 2016
EVE-MRSA

LL-37 Susceptibility

Surface Charge

Hwang et al, Journal of Molecular Medicine 2016
MRSA Pneumonia – Day 4

**Pneumonia Mortality**

Survival (%)

<table>
<thead>
<tr>
<th>Time (days)</th>
<th>control</th>
<th>EV-SA</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time (days)</th>
<th>control</th>
<th>EV-SA</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
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<tr>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**MRSA Pneumonia – Day 4**

SA (CFU/Lung)

<table>
<thead>
<tr>
<th>Time (days)</th>
<th>control</th>
<th>EV-SA</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>100</td>
<td></td>
</tr>
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</tr>
<tr>
<td>3</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

**EV-SA Gene Expression**

mRNA copies (relative to control SA)

<table>
<thead>
<tr>
<th>Gene</th>
<th>coa</th>
<th>pvl</th>
<th>icaA</th>
<th>agrA</th>
<th>spa</th>
<th>hla</th>
<th>psm_a</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>EV-SA</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

Hwang et al, Journal of Molecular Medicine 2016
E-cigarette vapor extract (EVE) exposure (1-2 hours) decreases bactericidal capacity of epithelial cells, alveolar macrophages, and neutrophils.
Toxins in E-cigarette Vapor

- Present, but lower than in smoke
  - Ethylbenzene
  - Benzene
  - Toluene
  - Acetone
  - Formaldehyde
  - Acetaldehyde
  - TSNA – tobacco specific nitrosamines
  - Nicotine
  - DEG – diethylene glycol

- Same level as in smoke: Benzo(a)pyrene
- Higher in vapor than in smoke: Glycols

Regulation

- **Availability** – completely banned in Australia, Mexico, Brazil, Argentina and Colombia.
- **Purchase** – online, gas stations, Vape shops
- **Use**
- **Advertising**: TV, Billboards, Magazines, Computer Ads

FDA announced in April 2014 that it would regulate e-cigarettes, but regulations have not been enacted.
E-cigarette vapor exposure of mice
The figure illustrates BAL (Bronchoalveolar Lavage) Cellularity and Cytospin of BAL from E-cigarette and Air control groups. The bar graph shows a comparison of total cells in BAL between the two groups, with E-cigarette showing a significantly higher cell count. The Cytospin images depict the cellular composition at 40x magnification, with Giemsa Wright staining for E-cigarette and Air control. The histological slides at 10x magnification and Trichrome staining further highlight the differences and patterns observed in the BAL samples from the E-cigarette and Air control groups.

Hwang et al, Journal of Molecular Medicine 2016
E-cigarette

Epihelial Cell

Hydrophobicity
+Surface charge
Biofilm
Adherence
Invasion
AMP resistance
Virulence

S. aureus

Pulmonary vessels

Alveolar Macrophage

↑ Necrosis
↓ Bactericidal function

Neutrophil

↑ Necrosis
↓ Bactericidal function

Epihelial Cell

↑ IL-1ra
↑ KC
↑ TREM-1
↑ Pentraxin 3
↓ IL-3
↓ GM-CSF

↑ Replication
↑ Hydrophobicity
+Surface charge
Biofilm
Adherence
Invasion
AMP resistance
Virulence

Hwang et al, Journal of Molecular Medicine 2016
MRSA Pneumonia

4 days

MRSA Surviving (CFU/Lung)

Control

Nicotine 2mg/mL

EVE w/ high nicotine

Laura, Carola, and John Hwang
Why are people using e-cigarettes?

- Health concerns of smokers
- Increased cost of tobacco cigarettes
- Indoor and outdoor smoking restrictions (Etter 2011)
- Relieve smoking withdrawal symptoms due to workplace smoking restrictions
Smoking Cessation Tool

• Act of “smoking” that mimics conventional smoking
  • physical hand-to-mouth motion is more similar than gum, lozenges or patches

• E-cigarettes reduce cravings for smokers

• E-cigarette use reduces relapses in quitters

Successful smoking cessation with electronic cigarettes in smokers with a documented history of recurring relapses: a case series

Pasquale Caponnetto¹*, Riccardo Polosa¹², Cristina Russo¹, Carmelo Leotta³ and Davide Campagna¹²

Abstract

Introduction: Smoking cessation programs are useful in helping smokers to quit, but smoking is a very difficult addiction to break and the need for novel and effective approaches to smoking cessation interventions is unquestionable. The E-cigarette is a battery-powered electronic nicotine delivery device that may help smokers to remain abstinent during their quit attempt. We report for the first time objective measures of smoking cessation in smokers who experimented with the E-cigarette.

Case presentation: Three Caucasian smokers (two men aged 47 and 65 years and one woman aged 38 years) with a documented history of recurring relapses were able to quit and to remain abstinent for at least six months after taking up an E-cigarette.

Conclusions: This is the first time that objective measures of smoking cessation are reported for smokers who quit successfully after using an E-cigarette. This was accomplished in smokers who repeatedly failed in previous attempts with professional smoking cessation assistance using the usual nicotine dependence treatments and smoking cessation counselling.
Electronic cigarettes for smoking cessation: a randomised controlled trial

Christopher Bullen, Colin Howe, Murray Laugesen, Hayden McRobbie, Varsha Parag, Jonathan Williman, Natalie Walker

Findings 657 people were randomised (289 to nicotine e-cigarettes, 295 to patches, and 73 to placebo e-cigarettes) and were included in the intention-to-treat analysis. At 6 months, verified abstinence was 7·3% (21 of 289) with nicotine e-cigarettes, 5·8% (17 of 295) with patches, and 4·1% (three of 73) with placebo e-cigarettes (risk difference for nicotine e-cigarette vs patches 1·51 [95% CI −2·49 to 5·51]; for nicotine e-cigarettes vs placebo e-cigarettes 3·16 [95% CI −2·29 to 8·61]). Achievement of abstinence was substantially lower than we anticipated for the power calculation, thus we had insufficient statistical power to conclude superiority of nicotine e-cigarettes to patches or to placebo e-cigarettes. We identified no significant differences in adverse events, with 137 events in the nicotine e-cigarettes group, 119 events in the patches group, and 36 events in the placebo e-cigarettes group. We noted no evidence of an association between adverse events and study product.

Interpretation E-cigarettes, with or without nicotine, were modestly effective at helping smokers to quit, with similar achievement of abstinence as with nicotine patches, and few adverse events. Uncertainty exists about the place of e-cigarettes in tobacco control, and more research is urgently needed to clearly establish their overall benefits and harms at both individual and population levels.
• May have failed 2/2 poor nicotine delivery. Newer generation devices could be different, or having people use higher nicotine concentration e-juices.

• May have failed without intensive counseling support – but most subjects picking up e-cigs to help them quit do not also seek intensive counseling support.

• E-cigarettes are an alternative to nicotine patches – cheaper, don’t require a prescription, less burden on the healthcare system
E-cigarettes and smoking cessation in real-world and clinical settings: a systematic review and meta-analysis

Sara Kalkhoran, Stanton A Glantz

Summary

Background Smokers increasingly use e-cigarettes for many reasons, including attempts to quit combustible cigarettes and to use nicotine where smoking is prohibited. We aimed to assess the association between e-cigarette use and cigarette smoking cessation among adult cigarette smokers, irrespective of their motivation for using e-cigarettes.

Methods PubMed and Web of Science were searched between April 27, 2015, and June 17, 2015. Data extracted included study location, design, population, definition and prevalence of e-cigarette use, comparison group (if applicable), cigarette consumption, level of nicotine dependence, other confounders, definition of quitting smoking, and odds of quitting smoking. The primary endpoint was cigarette smoking cessation. Odds of smoking cessation among smokers using e-cigarettes compared with smokers not using e-cigarettes were assessed using a random effects meta-analysis. A modification of the ACROBAT-NRSI tool and the Cochrane Risk of Bias Tool were used to assess bias. This meta-analysis is registered with PROSPERO (number CRD42015020382).

Findings 38 studies (of 577 studies identified) were included in the systematic review; all 20 studies with control groups (15 cohort studies, three cross-sectional studies, and two clinical trials) were included in random effects meta-analysis and sensitivity analyses. Odds of quitting cigarettes were 28% lower in those who used e-cigarettes compared with those who did not use e-cigarettes (odds ratio [OR] 0.72, 95% CI 0.57–0.91). Association of e-cigarette use with quitting did not significantly differ among studies of all smokers using e-cigarettes (irrespective of interest in quitting cigarettes) compared with studies of only smokers interested in cigarette cessation (OR 0.63, 95% CI 0.45–0.86 vs 0.86, 0.60–1.23; p=0.94). Other study characteristics (design, population, comparison group, control variables, time of exposure assessment, biochemical verification of abstinence, and definition of e-cigarette use) were also not associated with the overall effect size (p=0.77 in all cases).

Interpretation As currently being used, e-cigarettes are associated with significantly less quitting among smokers.
Known effects of E-cigarettes on humans
Data are Sparse

- No change in peripheral white blood count after 1 hour (WBC; Flouris 2012)
- Acute vaping did not change cardiac function – LV function is impaired in tobacco smokers (Farsalinos 2012)
- Vaping causes upper airway irritation (Vardavas 2011)
- Second-hand vapor leads to the same nicotine levels as conventional cigarettes in secondhand recipients (Flouris 2013)
- Nicotine has adverse effects on brain development (U.S. Surgeon General 2014)

Many small papers, most funded by e-cigarette companies in some way, and authors involved with e-cigarette companies as well.
Conventional Tobacco Cigarettes

- Deliver nicotine and > 4,000 chemicals via combustion and inhalation of smoke
- 100 chemicals are known carcinogens
- 900 chemicals have cancer-causing potential (WHO)
- Some examples: arsenic, polonium, carbon monoxide
- Second-hand smoke is composed of *sidestream* smoke from the burning cigarette plus exhaled smoke. Is responsible for >600,000 deaths per year worldwide and 40% of children are exposed
- 23% of high-school students currently use a tobacco product

Could they be made safer?

- Change propylene glycol to water
- Consistent heating temp, as low as possible (consistent batteries and microprocessors)
- Use clean materials in the manufacturing process
E-cigarettes, The good

- May theoretically assist smokers trying to quit by delivering nicotine into the bloodstream as effectively as other nicotine replacements.
- Simulates behavioral and sensory dimensions of smoking

E-cigarettes, The bad

- Dual use may reinforce nicotine addiction
- Observing vaping makes current and ex-smokers desire a real cigarette
- They have been proven to contain toxins
Recommendations

1. We need to be aware of the epidemic of e-cigarette use. Ask patients specifically about e-cigarettes:
   - how much liquid used per day (mLs)?
   - what wattage is applied to the e-liquid (battery Voltage plus resistance)?
   - what nicotine concentration (16 mg/mL)?

2. Cigarette smoke has well defined toxicities, and e-cigarettes could theoretically facilitate smoking cessation.

3. Well designed longitudinal clinical trials are needed!

4. Basic science may help inform clinical research and could be clinically directive until definitive human studies can be completed.
Thank you!

**Mentors**
Victor Nizet
Atul Malhotra

**Collaborators**
Christopher Drummond, U of Toledo
Weg Ongkeko, UCSD Head and Neck Surgery
David Pride, UCSD Department of Pathology
Ross Corriden, UCSD Department of Pediatrics

**My awesome vapers**
Denzil Matthew (senior)
Zach Yong (sophmore)
Kevin Vega (junior)

**The Lab crew**
Alex Moshensky (junior)
Soumita Das, Ph.D. (Asst Prof)
Marina Ahn (Masters student)
Jisha Joshua, M.D. (I.M. resident)
Anuja Vyas, M.D. (PCC fellow)
John Hwang, M.S. (post-bac researcher)
Carola Dewitz, M.S. (PhD student)
Katie Sladewski (post-bac researcher)
Matthew Lyes (Duke med student)
Elisa McEachern (Cornell med student)
Shymaa Enany, Ph.D. (visiting Prof)

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LCA Lab 2015
In e-cigarette vapor we trust