E-Cigarettes: Risks and Benefits

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Disclosure Information

• No financial relationships to disclose
What’s Coming

• History
• What is an e-cigarette?
• Use and uptake
• Vapor and second-hand vapor analyses
• Health effects
• Potential for harm reduction
  – Cessation aid?
  – Smokers switching/dual use?
• Product regulation
• Summary pros and cons
History of E-Cigarette Development

- RJR Tobacco
  - Premiere cigarette 1980s
  - Eclipse cigarette 1990s

- “Non-combustible cigarettes” delivered low levels of nicotine that evolved into the nicotine inhaler 1990s

- Chinese pharmacist Hon Lik developed the 1st marketable e-cigarette 2004

- Patented by the RUYAN Group (now Dragonite International), Beijing, China in 2004

- First appeared in the U.S. in 2007

- FDA declined to regulate until April 24, 2014
Tobacco Industry In the Market

• Lorillard
  ▪ Acquired blu e-cigs in April 2012 for $135M

• Reynolds American
  ▪ Vuse supposedly has technology that improves the vaping experience, unique digital design features and will be manufactured in the U.S.

• Altria Group (previously Philip Morris)
  ▪ Launched MarkTen this year

• NJOY (privately held)
  ▪ One of the first retail entrants to the e-cig market; personnel includes several ex-Altria execs.
Sales (Millions of Dollars) of E-cigarettes in the U.S., 2008-2013
(Source: UBS)

Projected

$1.9B
What is an e-cigarette?
3 Major Components

- Battery
- Atomizing unit
- Cartridge (contains nicotine)
Where Do You Get E-Cigarettes?
Widely Available through the Internet

- Affiliate marketing schemes
  - Product users can become distributors and earn profits from recruiting customers
  - In less than 5 minutes someone can becomes a sales person on commission, with an ad library and Web forum
  - Podcasts advise on search engine optimization
  - It works: 8 of top 10 results of a Google search on e-cigs link to shops

- Advertised as a ‘smoking sensation’ (not cessation) product
What to Buy?

Advanced Personalized Vaporizer (APV)

“Cig-a-Likes”
Percentage of adults (≥18 years) who have heard of and used electronic nicotine delivery systems (ENDS)—2009 and 2010 ConsumerStyles.

- 2013: 46% (Adkison)
- 2011: 6.2%

Regan AK et al. Tob Control 2013
Youth Uptake
Among Middle and High School Students
National Youth Tobacco Survey

• In 2012 more than 1.78 million middle and high school students nationwide had tried e-cigarettes
• 76.3% of who used e-cigarettes within the past 30 days also smoked conventional cigarettes in the same period
• CDC Director Tom Frieden: “Many teens who start with e-cigarettes may be condemned to struggling with a lifelong addiction to nicotine and conventional cigarettes”

<table>
<thead>
<tr>
<th></th>
<th>2011</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ever used</td>
<td>4.7%</td>
<td>10.0%</td>
</tr>
<tr>
<td>Used in past 30 days</td>
<td>1.5%</td>
<td>2.8%</td>
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</table>

MMWR, CDC, 2013
Electronic Cigarettes and Conventional Cigarette Use Among US Adolescents: A Cross-sectional Study

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>Ever&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Current&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Ever&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Current&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2011 (n = 5169)</td>
<td>2012 (n = 5681)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever e-cigarette use&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted</td>
<td>7.66 (5.44-10.79)</td>
<td>5.99 (5.02-7.16)</td>
<td>5.61 (4.66-6.76)</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>1.33 (1.23-1.44)</td>
<td>1.24 (1.17-1.33)</td>
<td>1.25 (1.16-1.35)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>0.37 (0.23-0.57)</td>
<td>0.44 (0.29-0.69)</td>
<td>0.47 (0.31-0.72)</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic other</td>
<td>0.72 (0.54-0.97)</td>
<td>0.73 (0.58-0.92)</td>
<td>0.77 (0.60-0.99)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.39 (1.13-1.70)</td>
<td>1.53 (1.26-1.86)</td>
<td>1.44 (1.18-1.74)</td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>8.52 (6.06-11.98)</td>
<td>6.97 (5.76-8.44)</td>
<td>6.52 (5.37-7.93)</td>
<td></td>
</tr>
<tr>
<td>Current e-cigarette use&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted</td>
<td>7.46 (4.12-13.49)</td>
<td>7.41 (5.41-10.14)</td>
<td>8.24 (6.04-11.23)</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>1.35 (1.25-1.46)</td>
<td>1.29 (1.22-1.37)</td>
<td>1.30 (1.22-1.39)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>0.31 (0.20-0.47)</td>
<td>0.32 (0.21-0.50)</td>
<td>0.35 (0.23-0.53)</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic other</td>
<td>0.67 (0.50-0.89)</td>
<td>0.61 (0.48-0.77)</td>
<td>0.64 (0.49-0.84)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.38 (1.13-1.70)</td>
<td>1.55 (1.27-1.90)</td>
<td>1.45 (1.19-1.77)</td>
<td></td>
</tr>
<tr>
<td>Unadjusted</td>
<td>6.84 (4.01-11.67)</td>
<td>7.52 (5.69-9.93)</td>
<td>8.31 (6.28-11.00)</td>
<td></td>
</tr>
</tbody>
</table>
Electronic Nicotine Delivery Systems: International Tobacco Control Four-Country Survey
n=5939 (Canada, U.S., U.K., Australia)

Percentage of current ENDS users who stated that they used ENDS for various reasons

- Use in smokefree zones
- Help me reduce
- Less-harmful
- Help me quit

Fluid Composition

• Contain
  – Humectants for vapor production
    • Propylene glycol
    • Glycerin
  – Nicotine
  – Flavoring
Propylene Glycol

• A humectant used to produce aerosol
• FDA approved food additive (humectant, solvent for colors and flavors), cosmetics, and medicines
• Used in theatrical fog/smoke machines
• Can cause airway irritation in some individuals
Nicotine

- Range of concentration in refill fluid 0-100 mg/ml
- Large amounts are lethal
  - 60 mg adult
  - 6 mg child
- Labeling not necessarily accurate: nicotine concentrations were measured in 35 different brands (but may be improving)
- Absence of product standards impedes research agenda

<table>
<thead>
<tr>
<th># Brands</th>
<th>Accuracy of Label</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>More nicotine</td>
</tr>
<tr>
<td>10</td>
<td>Accurate</td>
</tr>
<tr>
<td>18</td>
<td>Less nicotine</td>
</tr>
</tbody>
</table>

Goniewicz MJ. Tob Control 2013
Plasma Nicotine Concentrations for Nicotine Containing Products

![Graph showing plasma nicotine concentrations for different nicotine-containing products over time. The graph includes lines for cigarette, moist snuff, nasal spray, inhaler, lozenge (2mg), gum (2mg), and patch.](image-url)
Mean (±1 SEM) plasma nicotine (top panel; assay's limit of quantitation=2 ng/ml) and response to a visual analogue scale item assessing ‘craving for a cigarette/nicotine’ (bottom panel; 0–100 scale) from 16 cigarette smoking participants who each abstained from tobacco/nicotine for at least 12 h before completing each of the study's 4 conditions.

Eissenberg T. Tob Control 2010
Learning Curve

- More complex than cigarettes due to different components
- Myriad of replacement options
- Often start with device that looks like cigarette and move on
- “Priming” and “vaping” puffs – puff harder

McQueen A et al. N&TR 2011
Experienced users customize e-cigs to improve nicotine delivery – “Mods”

<table>
<thead>
<tr>
<th>Used a….</th>
<th>Total sample (n=98)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modified battery housing PV (3.7/6 v) (e.g. Omega, Silver Bullet, Helix)</td>
<td>39%</td>
</tr>
<tr>
<td>5 v Regulated battery modification PV (e.g. Triple V, Tekk Mod)</td>
<td>6%</td>
</tr>
<tr>
<td>Variable voltage modification PV (e.g. Provari, Eclipse)</td>
<td>6%</td>
</tr>
<tr>
<td>Large/long-life proprietary PV (eGo, Joye, Riva)</td>
<td>38%</td>
</tr>
<tr>
<td>Standard 3.7 v e-cig (e.g. Njoy, Magma)</td>
<td>8%</td>
</tr>
<tr>
<td>Multiple voltage battery compatible modified PV (3.7/5/6/7.4 v) (e.g. Megalodon)</td>
<td>3%</td>
</tr>
</tbody>
</table>

Foulds J. Intl J Clin Practice 2011
E-Liquids

Vapor Town E-liquid (E-juice) is specialized for E cigarette. It is made with or without nicotine. The e-liquid is extract from naturally tobacco, tastier and healthier than any other synthetic E-liquid. The cigarette e-liquid does not contain any harmful substances and it doesn’t produce second hand smoke.

2 Bottle Sizes:
15mL & 30mL

5 Strengths:
0mg | 6mg | 18mg | 24mg

Some of our popular flavors
## Some of our popular flavors

### Beverages
- Amaretto
- Apple Cider
- Black Raspberry
- Champagne
- Butter Rum
- Cherry Limeade
- Chocolate Malt
- Cream Soda
- Island Punch
- JD and Cola
- Mojito
- Peach Bellini
- Raspberry Lemonade
- Root Beer
- Strawberry Daiquiri
- Vanilla Cola
- Vanilla Latte

### Fruity
- Cherries n Cream
- Cherry Blossom
- Cinnamon Pear
- Coconut Cream Pie
- Coconut Twist
- Dreamsicle
- Grape Tart
- Hawaiian Delight
- Melon Explosion
- Peaches n Cream
- Pineapple Ice
- Strawberry Shortcake
- Triple Zest
- Tropical Splash
- Watermelon
- Wild Berry

### Miscellaneous & Tobacco
- Banana Bread
- Banana Split
- Bubble Gum
- Butterscotch
- Caramel Cream
- Caramel Tobacco
- Cherry Tobacco
- Cookies and Cream
- Cotton Candy
- Fire and Ice
- French Vanilla
- Grandpa’s Mix
- Lemon-Blueberry
- Cotton Candy
- Mad Plasma
- Mad Tobacco
- Menthol Tobacco
- Maple Cream
- Pound Cake
- S’mores
- Spearmint
- Tobacco
- Waffle
- Wild Berry Tobacco
## When Do You Finish an e-Cigarette?

<table>
<thead>
<tr>
<th>Brand</th>
<th>Total smokable puffs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liberty Stix</td>
<td>197 ± 64</td>
</tr>
<tr>
<td>Smoking Everywhere</td>
<td>177 ± 15</td>
</tr>
<tr>
<td>Crown Seven</td>
<td>208 ± 34</td>
</tr>
<tr>
<td>NJOY</td>
<td>313 ± 115</td>
</tr>
<tr>
<td>VapCigs</td>
<td>30 ± 43</td>
</tr>
<tr>
<td>Merit Ultra Lights</td>
<td>11 ± 0</td>
</tr>
<tr>
<td>Marlboro Ultra Lights</td>
<td>7 ± 0</td>
</tr>
<tr>
<td>Camel Lights</td>
<td>8 ± 0</td>
</tr>
<tr>
<td>Marlboro Lights</td>
<td>7 ± 0</td>
</tr>
<tr>
<td>Camel Regular</td>
<td>10 ± 1</td>
</tr>
<tr>
<td>Marlboro Reds</td>
<td>7 ± 0</td>
</tr>
<tr>
<td>Camel Unfiltered</td>
<td>7 ± 0</td>
</tr>
<tr>
<td>Pall Mall Unfiltered</td>
<td>11 ± 0</td>
</tr>
</tbody>
</table>

Trtchounian A et al. N&TR 2010
Vapor Composition

- Nicotine
- Propylene glycol
- Flavorants
- Heavy metals
- Volatile organic compounds
- Tobacco specific nitrosamines

Challenge: analyzing vapor in the absence of product standards - cartridges contain variable levels so generalizing among different brands and within the same brand is problematic.
Levels of selected carcinogens and toxicants in vapor from electronic cigarettes

<table>
<thead>
<tr>
<th>Toxic compound</th>
<th>Conventional cigarette (µg in mainstream smoke) 35</th>
<th>Electronic cigarette (µg per 15 puffs)</th>
<th>Average ratio (conventional vs electronic cigarette)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formaldehyde</td>
<td>1.6–52</td>
<td>0.20–5.61</td>
<td>9</td>
</tr>
<tr>
<td>Acetaldehyde</td>
<td>52–140</td>
<td>0.11–1.36</td>
<td>450</td>
</tr>
<tr>
<td>Acrolein</td>
<td>2.4–62</td>
<td>0.07–4.19</td>
<td>15</td>
</tr>
<tr>
<td>Toluene</td>
<td>8.3–70</td>
<td>0.02–0.63</td>
<td>120</td>
</tr>
<tr>
<td>NNN</td>
<td>0.005–0.19</td>
<td>0.000008–0.00043</td>
<td>380</td>
</tr>
<tr>
<td>NNK</td>
<td>0.012–0.11</td>
<td>0.00011–0.00283</td>
<td>40</td>
</tr>
</tbody>
</table>

Goniewicz MJ et al. Tob Control 2013
Some E-Cigarettes Deliver a Puff of Carcinogens

By MATT RICHTEL  May 3, 2014

- Tank systems + batteries
- Vapor composition changes with temperature
- Trickle drops of liquid directly on the atomizer – “dripping”
- Especially high levels of formaldehyde
Does e-cigarette consumption cause passive vaping?

Data support the idea that EC users’ exhale contains a number of chemicals: far lower concentrations than SHS
Health Effects

- In vitro studies
- Animal studies
- Human studies
- Epidemiological studies
# Cytotoxicity for 41 Refill Fluids

## Related to Flavors, not Nicotine

Bahl V et al. Reprod Toxicol 2012

<table>
<thead>
<tr>
<th>Electronic cigarette refill fluid name</th>
<th>Company</th>
<th>Nicotine (mg/ml)</th>
<th>hESC IC₅₀</th>
<th>hESC NOAEL</th>
<th>mNSC IC₅₀</th>
<th>mNSC NOAEL</th>
<th>hPF IC₅₀</th>
<th>hPF NOAEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propylene Glycol</td>
<td>FS-USA²</td>
<td>24mg</td>
<td>&gt;1</td>
<td>0.3</td>
<td>&gt;1</td>
<td>0.3</td>
<td>&gt;1</td>
<td>&gt;1</td>
</tr>
<tr>
<td>Vegetable Glycerin</td>
<td>FS-USA²</td>
<td></td>
<td>&gt;1</td>
<td>&gt;1</td>
<td>&gt;1</td>
<td>&gt;1</td>
<td>&gt;1</td>
<td>&gt;1</td>
</tr>
<tr>
<td>Ethanol</td>
<td>FS-USA</td>
<td>24mg</td>
<td>&gt;1</td>
<td>0.3</td>
<td>&gt;1</td>
<td>0.3</td>
<td>&gt;1</td>
<td>&gt;1</td>
</tr>
<tr>
<td>Butterscotch</td>
<td>FS-USA</td>
<td>0mg</td>
<td>&gt;1</td>
<td>0.3</td>
<td>&gt;1</td>
<td>0.3</td>
<td>&gt;1</td>
<td>&gt;1</td>
</tr>
<tr>
<td>Butterscotch</td>
<td>FS-USA</td>
<td>6mg</td>
<td>&gt;1</td>
<td>0.1</td>
<td>&gt;1</td>
<td>0.1</td>
<td>&gt;1</td>
<td>&gt;1</td>
</tr>
<tr>
<td>Caramel</td>
<td>FS-USA</td>
<td>0mg</td>
<td>&gt;1</td>
<td>0.3</td>
<td>&gt;1</td>
<td>0.3</td>
<td>&gt;1</td>
<td>&gt;1</td>
</tr>
<tr>
<td>Caramel</td>
<td>FS-USA</td>
<td>6mg</td>
<td>&gt;1</td>
<td>0.3</td>
<td>&gt;1</td>
<td>0.3</td>
<td>&gt;1</td>
<td>&gt;1</td>
</tr>
<tr>
<td>Caramel</td>
<td>FS-USA</td>
<td>6mg</td>
<td>&gt;1</td>
<td>0.3</td>
<td>&gt;1</td>
<td>0.3</td>
<td>&gt;1</td>
<td>&gt;1</td>
</tr>
<tr>
<td>Chocolate Biscotti</td>
<td>FS-USA</td>
<td>24mg</td>
<td>&gt;1</td>
<td>0.3</td>
<td>&gt;1</td>
<td>0.3</td>
<td>&gt;1</td>
<td>&gt;1</td>
</tr>
</tbody>
</table>

## Cytotoxicity

- **Low (IC₅₀ > 1%)**
- **Moderate** (0.1% < IC₅₀ < 1%)
- **High (IC₅₀ < 0.1%)**

Bahl V et al. Reprod Toxicol 2012
Acute effects of electronic and tobacco cigarette smoking on complete blood count

- Cigarette smoking
- E-cig smoking
- Control

Blood cell count increased in those actively or passively smoking tobacco cigarettes.

Blood cell count was not significantly affected in those actively or passively using EC.

Flouris et al. Food and Chem Tox 2012
Short-term Pulmonary Effects +/- Results

Using an e-cigarette for 5 min led to an immediate decrease in FENO within the experimental group by 2.14 ppb ($P = .005$) but not in the control group ($P = .859$). Total respiratory impedance at 5 Hz in the experimental group was found to also increase by 0.033 kPa/(L/s) ($P < .001$), and flow respiratory resistance at 5 Hz, 10 Hz, and 20 Hz also statistically increased.

N=15
Flouris AD et al. Inhal Tox 2013

N=30
Vardavas CI et al. Chest 2012
Representative CT images show the “crazy paving” pattern of patchy ground glass superimposed on interlobular septal thickening. A, Bilateral upper lobes. B, Bilateral lower lobes.
Reduce the risk of lung cancer?

- Possibly, but not known
- It will depend on
  - Long-term toxicity
  - The extent to which they are used with cigarettes
Adverse Events Reported to the

8 SAEs - Hospitalization for:
- pneumonia
- congestive heart failure
- disorientation
- seizure
- hypotension
- aspiration pneumonia
- second degree burns to face (explosion)
- chest pain and rapid heart beat
- possible infant death secondary to choking on EC cartridge
- loss of vision requiring surgery

39 Other complaints
- False advertising
- Headache/migraine
- Chest pain
- Cough/sputum
- Nausea/vomiting
- Dizziness
- Sleepy/tired
- Feeling sick
- Confusion/stupor
- Sore throat
- Shortness of breath
- Abdominal pain
- Pleurisy
- Blurry vision

https://www.accessdata.fda.gov/scripts/medwatch/

Chen I. N&TR 2012
Electronic cigarette explodes in man's mouth, causes serious injuries

(CBS/AP) So much for being safer. An electronic cigarette blew up in a Florida man's face, leaving him in a hospital with severe burns, missing his front teeth and a chunk of his tongue.

Fire officials said Wednesday that the man had switched to electronic cigarettes to try and quit smoking, and that the scary situation was caused by a faulty battery.

"The best analogy is like it was trying to hold a bottle rocket in your mouth when it went off," said Joseph Parker, division chief for the North Bay Fire Department. "The battery flew out of the tube and set the closet on fire."

Mom: 3-Old-Son Severely Burned After Exploding E-cigarette Ignites Car Seat. I never heard of a nicotine patch doing that. Forget the FDA. Where is the Consumer Product Safety Commission?
Poison Control Reports

- Vomiting, nausea, eye irritation
- One suicide from IV administration
- 51% 0-5 years, 42%>20 years

*Kirschner RI, et al. Clinical Toxicology 2013
Ordonez J et al. Clinical Toxicology 2013
Cantrell L. Clinical Toxicology 2013*
Number of calls to poison centers for cigarette or e-cigarette exposures, by month — United States, September 2010–February 2014
E-Cigarettes for Smoking Cessation?
Smoking Cessation
2 clinical trials published

<table>
<thead>
<tr>
<th></th>
<th>Caponnetto 2013 (PlosOne)</th>
<th>Bullen 2013 (Lancet)</th>
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<tbody>
<tr>
<td>Population</td>
<td>Unmotivated to quit</td>
<td>Motivated to quit</td>
</tr>
<tr>
<td>Inclusion criteria</td>
<td>≥10cpd</td>
<td>≥10cpd</td>
</tr>
<tr>
<td>Brand</td>
<td>Categoria</td>
<td>Elusion</td>
</tr>
<tr>
<td>Sample size</td>
<td>300</td>
<td>657</td>
</tr>
<tr>
<td>Intervention</td>
<td>7.2 mg E-cig</td>
<td>16mg E-cig</td>
</tr>
<tr>
<td></td>
<td>7.2-5.4 mg E-cig</td>
<td>21mg NRT patch</td>
</tr>
<tr>
<td></td>
<td>0 mg E-cig</td>
<td>0mg E-cig</td>
</tr>
<tr>
<td></td>
<td>No behavioral support</td>
<td>Minimal behavioral support</td>
</tr>
<tr>
<td>Intervention period</td>
<td>12 weeks</td>
<td>13 weeks</td>
</tr>
<tr>
<td>Follow-up</td>
<td>12 months</td>
<td>6 months</td>
</tr>
<tr>
<td>Power</td>
<td>75%</td>
<td>80%</td>
</tr>
<tr>
<td>Primary outcome</td>
<td>Verified continuous abstinence at 6 months</td>
<td>Verified continuous abstinence at 6 month</td>
</tr>
</tbody>
</table>
ECLAT Study (Italy): Efficacy and safety of an electronic cigarette (intention-to-treat analysis)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Reduction rates (%)</th>
<th>Quit rates (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>Week-2</td>
<td>29.0</td>
<td>38.0</td>
</tr>
<tr>
<td>Week-4</td>
<td>29.0</td>
<td>33.0</td>
</tr>
<tr>
<td>Week-6</td>
<td>24.0</td>
<td>26.0</td>
</tr>
<tr>
<td>Week-8</td>
<td>23.0</td>
<td>21.0</td>
</tr>
<tr>
<td>Week-10</td>
<td>26.0</td>
<td>15.0</td>
</tr>
<tr>
<td>Week-12</td>
<td>26.0</td>
<td>20.0</td>
</tr>
<tr>
<td>Week-24</td>
<td>17.0</td>
<td>19.0</td>
</tr>
<tr>
<td>Week-52</td>
<td>10.0</td>
<td>9.0</td>
</tr>
</tbody>
</table>

*p values are relevant to the differences in frequency distribution in reduction and quit rates among groups at each Study Visits (χ² test).
doi:10.1371/journal.pone.0066317.t002

Caponnetto P et al. PLoS ONE 2013
New Zealand RCT

Kaplan-Meier analysis of time to relapse. EC=e-cigarettes.

<table>
<thead>
<tr>
<th>Number at risk</th>
<th>Duration between quit date and relapse date (days)</th>
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</thead>
<tbody>
<tr>
<td>Nicotine EC</td>
<td>289</td>
</tr>
<tr>
<td>Patches</td>
<td>295</td>
</tr>
<tr>
<td>Placebo EC</td>
<td>73</td>
</tr>
</tbody>
</table>

Contabst Nic E-Cig Patches P-value Placebo e-Cig P-value

<p>| | | | | | |</p>
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>1M</td>
<td>23%</td>
<td>16%</td>
<td>0.03</td>
<td>16%</td>
<td>0.21</td>
</tr>
<tr>
<td>3M</td>
<td>13%</td>
<td>9%</td>
<td>0.12</td>
<td>7%</td>
<td>0.14</td>
</tr>
<tr>
<td>6M</td>
<td>7%</td>
<td>6%</td>
<td>0.46</td>
<td>4%</td>
<td>0.44</td>
</tr>
</tbody>
</table>

Bullen C et al. Lancet 2013
Long-term (≥6 month) Quit Rates for Smoking Cessation Medications

Do e-cigs inhibit quitting?

**Epidemiological data**

- N= 1836 current smokers/recent quitters
  - Ever use of e-cigarettes not associated with being a successful quitter (OR 1.09; 95% CI 0.72-1.65) but was associated with being an unsuccessful quitter (OR=1.78, 95% CI 1.25-2.53) compared to people who had never tried to quit.

- N=2758 quitline users
  - E-cig users less likely to be abstinent at the 7-month survey compared with participants who had never tried e-cig (30-day point prevalence quit rates: 22% and 17% vs. 31%, \( p < .001 \)).

Vickerman KA et al. N&TR 2013
Dual Use is Common

• Most common pattern of use

• **ITC Four country survey** (n=5,939)
  – 75% to reduce cpd
  – But dual users may smoke fewer CPD when vaping

<table>
<thead>
<tr>
<th>CPD baseline</th>
<th>CPD when vaping</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>15</td>
<td>Etter, Addiction 2011</td>
</tr>
<tr>
<td>50% &gt; 20 CPD</td>
<td>2% &gt;20 CPD</td>
<td>Goniewicz, Drug Alc Rev 2013</td>
</tr>
</tbody>
</table>

Pearson L. *Am J Pub Health* 2012
Implications of Lack of Regulation
“It’s a Wild West”

• No product standards
• No minimum/maximum for nicotine or other constituents
• No indoor air regulations
• No advertising restrictions
• No restrictions for sales to minors
Proposed Regulation April 2014
Open for public comment for 75 days

What It Does
• Restrict sales to minors
• Warning labels: contains the addictive drug nicotine
• Ingredient disclosure
• Require registration with FDA & disclosure of manufacturing processes
• No free samples
• Can not claim less harm than combusted cigarettes without submitting data

What It Does Not Do
• Ban use of flavorants
• Halt online sales
• Curb advertising
• Restrict marketing
• (At least 2 years until implementation)
1998 – Tobacco Billboards Die in MN

photo courtesy of Jaime Martinez
Currently...

• Assortment of local and state ordinances, laws and regulations
• Duluth Ely, Mankato have updated their clean indoor air ordinance to include e-cigarettes
• Not included in MN indoor air law, but...
  – Banned in government owned buildings (including schools)
  – No longer can be sold in kiosks
  – Child-resistant packaging required
  – Must be behind the counter in stores
  – Penalties for selling to minors
Advocacy

- Vocal about potential bans, clean indoor air legislation
- Some anti-China, pro-American sentiments
- Enthusiasm for research
Research Agenda

• Pre-clinical studies
  – Refill liquid composition
  – Vapor composition
  – Product quality

• Animal studies
  – Toxicology
  – Long-term exposure

• Clinical studies
  – PK
  – Abuse liability
  – Puff topography, dose & duration preferences
  – SC efficacy
  – Efficacy for delivery of other drugs

• Epidemiological studies
  – Surveillance, sales
  – 2nd hand vapor
  – Economic studies
  – Impact on smoking behavior
  – Impact of regulation
Summary of Pros & Cons

Potential Benefits
• Reduced toxicity (cigarette for cigarette)
• Harm reduction
• Smoking cessation
• Safer use in public places
• Current laws allow nicotine only in tobacco (deadly) and in medications (gum, patch), which are not appealing, not very effective
• Increased reach

Potential Harms
• Dual use – less cessation
• Initiation among non-smokers - “Gateway”
• Skirting smoke-free indoor air laws
• Potential toxicities may not be identified
• Persistent nicotine addiction
Warning Signs

• Tobacco company involvement
• Wide-spread and rapidly growing popularity
• Persistent culture and acceptability of smoking
• Use of technology to deliver other drugs
Spectrum of Harm

- Conventional cigarettes
- Modified tobacco cigarettes
- Smokeless tobacco products
- LTSNA oral tobacco products
- Nicotine replacements
- Smoking cessation

Electronic cigarettes?
Questions?