Alternative Nicotine Delivery Systems (ANDS):
FRIEND, FRENEMY, OR ENEMY?
Disclosures: David Abrams

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- No other financial relationships to disclose
Big Picture: Reduce Death and Disease Burden from Deadly Combusted Smoke

“Death is Overwhelmingly Caused By Cigarettes and Other Combustibles...

Promotion of E-cigarettes and Other Innovative Products Is...Likely To Be Beneficial...

Where The Appeal, Accessibility and Use of Cigarettes Are Rapidly Reduced.”

50th Anniversary Surgeon General’s Report, 2014, Executive Summary, Pages 14-17
OPERATIONALIZE POPULATION IMPACT: BENEFITS AND HARMS


- **Harms**: relative - to deadly smoke & absolute - to nothing

- **State of The Science: Uptake** by non-tobacco users, especially youth and young adults and former smokers

- **State of The Science: Cessation** by current tobacco users, primarily smokers of deadly cigarettes.
Markov Model

All states & Trajectories for population impact:

- **Enemy**
- **Frenemy?**
- **Friend**

1. informing impact: harms

RELATIVE & ABSOLUTE - PRODUCT QUALITY VARIES

**Relative:** vape to combusted smoke and passive exposure to smoke.

**Absolute:** not harmless: No / variable nicotine; humectants (aerosol vapor); additives, flavors… some more harmful than others

**Absolute:** compared to no use: (fetus, accidental poisoning, passive exposure, indoor air, youth and young adult never users).

**Regulation:** needed to ensure quality and make as low in harm as possible

**Common Sense Regulation:** Goldilocks Rule, not too much and not too little

**Core Principle:**

Policy and Regulation proportional to the harm of the product class...
Relative harms of different product classes.

EXTREME Toxicity
Cigs - Combustibles

MUCH Less Harm

No Harm
No use at all

non-combustible

Cigarettes
Small cigars
Pipes
Cigars
Water pipe
Smokeless unreﬁned
Smokeless reﬁned
Snus
ENDS
Nasal sprays
Oral products
Patch


Public Health England (PHE)
2. informing impact: patterns of uptake

Enemy, Frenemy, Friend?

- **Uptake of E-cigarette** use by non-users of tobacco products, especially minors: vigilance and no use enforced

- **Progression:** either into or a deflection out of deadly lifetime combustible / cigarette use

- **Appeal and Addiction:** when decoupled from deadly smoke from combustion?
Past 30-Day Use among High School Students

Past 30-Day Cigarette Use 8, 10, & 12 Graders

Source: Monitoring the Future, 2015 - Table 1
## Progression: Frequency of Use

**Frequency of Past 30-Day Use of E-Cigarettes and Cigarettes (NYTS, 2014)**

<table>
<thead>
<tr>
<th>Days used/month</th>
<th>% high school users</th>
<th>% high school population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Of ENDS</td>
<td>Of Cigarettes</td>
</tr>
<tr>
<td>1-2 days</td>
<td>45.4</td>
<td>37.0</td>
</tr>
<tr>
<td>3-5 days</td>
<td>16.2</td>
<td>12.3</td>
</tr>
<tr>
<td>6-9 days</td>
<td>12.0</td>
<td>9.7</td>
</tr>
<tr>
<td>10-19 days</td>
<td>10.9</td>
<td>9.4</td>
</tr>
<tr>
<td>20-29 days</td>
<td>5.8</td>
<td>9.0</td>
</tr>
<tr>
<td>All 30 days</td>
<td>9.7</td>
<td>22.6</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>100.0</td>
<td>100.0</td>
</tr>
</tbody>
</table>
past 30-Day e-Cig use leveled off / dropped slightly

BY GRADE AND YEAR

<table>
<thead>
<tr>
<th>Grade</th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>8th Grade</td>
<td>8.7%</td>
<td>9.5%</td>
</tr>
<tr>
<td>10th Grade</td>
<td>16.2%</td>
<td>14.0%</td>
</tr>
<tr>
<td>12th Grade</td>
<td>17.1%</td>
<td>16.2%</td>
</tr>
</tbody>
</table>

Source: Monitoring the Future, 2015 (Table 3)
Substance Vaporized the Last Time e-Cigarette Used

![Bar chart showing the percentage of different substances used the last time an e-cigarette was used, by grade level.](chart)

- **Nicotine**: Lower percentages across all grades.
- **Marijuana or hash oil**: Very low usage, especially in 8th grade.
- **Just flavoring**: Significantly higher usage, especially in 12th grade.
- **Other**: Minimal usage.
- **Don't know**: Minimal usage.

**Source**: University of Michigan, 2015 Monitoring the Future Study
3. Informing impact: use in current and former smokers

Enemy, Frenemy, Friend?

- **Impact**: on use of cigarettes:
  - at scale: reach x efficacy, cost, appeal
  - do e-cigs speed or slow population cessation?

- **Dual use**: concern if get stuck on path to exclusive use (a sticky versus a transitional state)?

- **Relapse**: prevention or promotion in former smokers?
Appeal as a Cessation Aid: IMPACT at Scale: (Reach x Efficacy / Cost Efficiency)


**SMOKING TOOLKIT STUDY: ROBERT WEST et al. USE TO QUIT: RECENT EX SMOKERS:**

N=10078 adults who smoke and tried to stop or who stopped in the past year

Factors Associated with Odds of Success in Most Recent Quit Attempt

Odds ratio

Base: 14,813 smokers who tried to quit in past 12 months
Findings from meta-analysis of smoking cessation studies with six-month outcomes in “Treating Tobacco Use and Dependence”

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Number of arms</th>
<th>Estimated abstinence rate (95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Among smokers not willing to quit (but willing to change their smoking patterns or reduce their smoking)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>5</td>
<td>3.6</td>
</tr>
<tr>
<td>Nicotine replacement (gum, inhaler, or patch)</td>
<td>5</td>
<td>8.4 (5.9–12.0)</td>
</tr>
<tr>
<td><strong>Nicotine E-cigarette (Caponnetto 2013)</strong></td>
<td>2</td>
<td>11.0</td>
</tr>
<tr>
<td><strong>Among smokers interested in quitting</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>80</td>
<td>13.8</td>
</tr>
<tr>
<td>Nicotine Patch (6–14 weeks)</td>
<td>32</td>
<td>23.4 (21.3–25.8)</td>
</tr>
<tr>
<td>Long-Term Nicotine Patch (&gt; 14 weeks)</td>
<td>10</td>
<td>23.7 (21.0–26.6)</td>
</tr>
<tr>
<td>Nicotine Inhaler</td>
<td>6</td>
<td>24.8 (19.1–31.6)</td>
</tr>
<tr>
<td><strong>Nicotine E-cigarette (Bullen 2013)</strong></td>
<td>1</td>
<td>21.1</td>
</tr>
<tr>
<td><strong>Patches (Bullen 2013)</strong></td>
<td>1</td>
<td>15.6</td>
</tr>
</tbody>
</table>
observational studies: with better measurement of exposure and use specific to quit intentions.

<table>
<thead>
<tr>
<th>Study</th>
<th>Follow-up period</th>
<th>Cigarette smoking abstinence (%)</th>
<th>Other outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biener Hargrave (2014)</td>
<td>2 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensive e-cigarette users at baseline</td>
<td>20.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermittent e-cigarette users at baseline</td>
<td>8.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E-cigarette non-users/triers at baseline</td>
<td>12.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brose (2015)</td>
<td>1 year</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily e-cigarette use at baseline</td>
<td>8.1</td>
<td>13.9</td>
<td>64.9%</td>
</tr>
<tr>
<td>Non-daily e-cigarette use at baseline</td>
<td>9.5</td>
<td>5.5</td>
<td>52.5%</td>
</tr>
<tr>
<td>Non-use of e-cigarettes at baseline</td>
<td>12.9</td>
<td>5.7</td>
<td>43.7%</td>
</tr>
<tr>
<td>Brown (2014)</td>
<td>Cross-sectional</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E-cigarettes used in last serious quit attempt</td>
<td>20.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRT used in last serious quit attempt</td>
<td>10.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No aid in last serious quit attempt</td>
<td>15.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
device type may matter

Adapted Table 3. E-cigarette use, product type, and quit smoking at follow-up

<table>
<thead>
<tr>
<th>E-cigarette type and frequency at follow up</th>
<th>% quit smoking</th>
<th>AOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-daily cigalike</td>
<td>5.2%</td>
<td><strong>0.35 (0.20, 0.60)</strong></td>
</tr>
<tr>
<td>Non-daily tank</td>
<td>8.6%</td>
<td>0.70 (0.29, 1.68)</td>
</tr>
<tr>
<td>Daily cigalike</td>
<td>10.6%</td>
<td>0.74 (0.39, 1.42)</td>
</tr>
<tr>
<td>No e-cigarette use</td>
<td>13.5%</td>
<td>1.0</td>
</tr>
<tr>
<td>Daily tank</td>
<td>27.5%</td>
<td><strong>2.69 (1.48, 4.89)</strong></td>
</tr>
</tbody>
</table>

Source: Hitchman, Sara C., et al. (2015) Associations between e-cigarette type, frequency of use, and quitting smoking: findings from a longitudinal online panel survey in Great Britain." Nicotine & Tobacco Research. [epub ahead of print]
device type: improved satisfaction?

- Bigger battery = better nicotine delivery
- exclusive users: use open (tank/Mod) systems; flavors help them to extinguish tobacco/menthol cue reminders of cigs.

Summary: friend of cessation / switching?

• More rigorous studies and randomized trials needed.

• Uninformative studies must be excluded entirely

• Promising when intended for cessation and used regularly. Likely at least as good as and more impact/reach than NRT

• Dual use not desirable, except if like NRT, used for a limited time on a trajectory to cessation or exclusive use (reduce to quit)?
formal markov model

need all states & trajectories for net population impact:

Enemy?

Frenemy

Friend

summary: can nicotine in less harmful delivery modes be a friend or frenemy to speed the obsolescence of combustible tobacco?

1. **Youth**: Despite dramatic declines in cigarette use, total combustible tobacco use (cigars and hookah) is of great concern – most toxic, appealing, addictive and overwhelming cause of progression and death.

2. **Increases in youth trial use has leveled off**: Current data cannot confirm whether a pathway in or out of combustible use. Trajectory to regular use >20 days is miniscule. No sign of progression to cigarettes.

3. **Larger than usual drops** in youth and adult cigarette prevalence: e-cigs?

4. **Use for cessation/switching promising**: RCTs and real world trials needed with the newer, better products and with treatment support.

5. **Blind People and Elephants**: ALL moving parts, not one aspect. Big picture – relative harm - combustibles cause the deaths. Longitudinal Data + Modeling to capture dynamic interplay and net population impact.

6. **Goldilocks: just right regulation**: data (science) not dogma (ideology).
Thank You

Dabrams@truthinitiative.org
Past 30-Day E-Cigarette Use Among 8th, 10th, and 12th Graders – MTF, 2015

<table>
<thead>
<tr>
<th>Grade</th>
<th>Non-Nicotine E-Cigarette Use</th>
<th>Nicotine E-Cigarette Use</th>
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<tbody>
<tr>
<td>8th Grade</td>
<td>9.5%</td>
<td>1.7%</td>
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<td>10th Grade</td>
<td>14.0%</td>
<td>2.8%</td>
</tr>
<tr>
<td>12th Grade</td>
<td>16.2%</td>
<td>3.6%</td>
</tr>
<tr>
<td>Combined</td>
<td>13.2%</td>
<td>2.6%</td>
</tr>
</tbody>
</table>

Source: Monitoring the Future, 2015
E-cigarette Use Frequency
Past 30-day users

Figure 1 inset: Detail of e-cigarette frequency among past 30-day users
Youth Patterns of Use

DISTRIBUTION OF TOBACCO AND E-CIGARETTE USE AMONG U.S. MIDDLE AND HIGH SCHOOL STUDENTS (WEIGHTED); NATIONAL YOUTH TOBACCO SURVEY, 2014

Figure 1 inset: Detail of e-cigarette frequency among past 30-day users
Regulatory Implications

The swirl of data on trial e-cigarette uptake, dual use and use for cessation **does not** change many policy recommendations –

- Prudent Product standards to ensure safety and quality BUT without over burden – favors big tobacco
- Integrated Fast Track nicotine regulation: maximize benefits for cigarette cessation (CDER) and harm minimization (CTP)
- Accurate Education on harms and benefits of e-cigarettes
- Prevent sales, marketing, flavors or targeting to appeal to youth of any and all tobacco and nicotine products
Regulatory Tools: Complement Traditional T.C.

FDA-Center for Tobacco Products (CTP) can: Regulate and Educate:

- Product Standards: Individual Safety & Efficacy
- New Product and Substantial equivalence applications
- Modified Risk Reduced Harm Product (MRTP) designations
- Public Education: Correct Misperceptions
- Pre- and post-market surveillance: PATH patterns, trajectories
- CTP separate from CDER (Therapeutics for Cessation Tx)
- Need for Comprehensive Nicotine Policy

KEY ISSUE: Rethinking Nicotine in light of new delivery modes