The Impact of E-cigarettes on Smoking Cessation:
Results from a Large, Randomized, Nationwide Clinical Trial in the United States

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Medical University of South Carolina
Hollings Cancer Center
A One-Sided Presentation

My Presentation:
Focused on Adult Smoking Cessation
That’s Not the Entire Story!

My Presentation:
A clinical presentation (RCT)
But with policy implications

My Presentation:
Includes a few slides with ~Main Outcome
Data (denoted). Please do not share.

Funding:
NCI R01 210625

Disclosures from Past 10yrs:
• E-cigarette product purchased from NJoy
• 2018-2019: Consulting for Pfizer
• 2020: Consulting to Frutarom, Inc.
• Multiple NIH Grants as PI
Most but not all research(ers) agree: E-cigarettes offer a reduced harm alternative to individual users, as compared to combustible cigarettes.

- Reduced carcinogen exposure, reduced morbidity (mortality?), particularly for those who completely switch.
- E-cigarettes may not be safe. But they are safer.

E-cigarettes suppress nicotine withdrawal and craving in ways that NRT cannot.

The best, most direct evidence (RCTs) generally suggest that e-cigarettes can help smokers quit and may be superior to NRT.\(^1\)\(^-\)\(^2\)

Much of the debate is based on distorted interpretations of science.\(^3\)

But most (if not all?) of these RCTs are instructional, purposeful, guided intervention studies of e-cigarettes for cessation/reduction.

1. Hartmann-Boyce et al (2022) Cochrane Database of Systematic
Clinical Outcomes for a Nationwide, Naturalistic, E-Cigarette Trial

Funding:
NCI R01 210625

With acknowledgements to my collaborators:
Tracy Smith, Mike Cummings, Jen Dahne, Kevin Gray, Graham Warren (MUSC)
Amy Wahlquist (East Tennessee State Univ)
Ted Wagener (Ohio St)
Maciej Goniewicz (Roswell Park Cancer Institute)

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Liz Hawes
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Karolina Kazlauskaite
Tatiana Myers
Gabby Mullins

And Interns/Postdocs: Elly Leavens & Margaret Fahey

Always get a study logo
**General Rationale:**

- The best evidence to date (RCTs) generally suggest that e-cigarettes could help smokers quit.
- Most of this evidence comes from outside the US, and most of this evidence is based on prescribed/instructional use, for a limited range of smokers (e.g., “use this e-cigarettes to quit/reduce”).
- Very few large scale RCTs, even fewer in US, and even fewer with naturalistic intent.
- Building on our prior pilot study (Carpenter et al. CEBP 2017).

**Our intent:**
Within randomized design (minimizing selection bias), across a range of all comers (both motivated and unmotivated to quit smoking), we offer smokers the opportunity to use ecigs as they wish, for whatever purpose they wish.
General Methods

• Randomized, (2:1) provision of e-cig (NJoy Tank; 3ml pre-filled tanked, 15mg/ml of nicotine) or not, for self-determined use, with follow-up thru 6 months

• E-cig group sent up to 30 days (split over 2 shipments) with choice (up to 2) among 5 flavors: tobacco, menthol, blue/blackberry, apple melon, iced fruit
  - ~"Use (or not use) as you wish, to reduce, quit, or during smoking restrictions. It's completely up to you"
  - To be clear: providing ecigs for free is not naturalistic. We’re focused on naturalistic outcomes when cost is not a barrier

• Daily diaries for first 30 days; Phone-based follow-up periodically for deeper assessment

• Product supplied to us, at cost, by NJoy. No financial or other support from e-cig industry

• 11 Cities recruited

Outcomes (some of which presented today):

• Uptake, and patterns of it: trajectories, frequency/quantity of use, adoption (independent purchase)
• Attitudinal & subjective responses: liking, reward, dependence
• Behavioral: Smoking Reduction, Quit attempts, Cessation
• Biological*: cotinine, NNAL, CO
Target N: 660
of which n=120 will be local (biomarker collection)

Actual N: 638 (97%)
of which n=105 were local, *but still very limited biomarker collection (COVID shutdowns)

Minimal Hx of Vaping:
• no purchase in past 6 months,
• no ever regular use (daily or weekly) of tank/mod/advanced personal vaporizer (regular cig-a-like usage ok)
• no regular use (daily or weekly) of any e-cig (including cig-a-likes devices) in past 6 months
### Baseline Characteristics (N=638) - Demographics

<table>
<thead>
<tr>
<th></th>
<th>Control (n=211)</th>
<th>E-Cigarette (n=427)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>43.1%</td>
<td>48.0%</td>
<td>.24</td>
</tr>
<tr>
<td>Race</td>
<td>.17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>69.2%</td>
<td>68.2%</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>15.2%</td>
<td>20.1%</td>
<td></td>
</tr>
<tr>
<td>Age, Mean (SD)</td>
<td>42.0 (11.9)</td>
<td>42.4 (11.2)</td>
<td>.63</td>
</tr>
<tr>
<td>Education</td>
<td>.12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HS or less</td>
<td>36.0%</td>
<td>28.3%</td>
<td></td>
</tr>
<tr>
<td>Some+ college</td>
<td>64.0%</td>
<td>71.7%</td>
<td></td>
</tr>
<tr>
<td>% Married or Partnered</td>
<td>33.2%</td>
<td>28.1%</td>
<td>.54</td>
</tr>
<tr>
<td>Income</td>
<td>.43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; $25,000 USD</td>
<td>31.0%</td>
<td>33.0%</td>
<td></td>
</tr>
<tr>
<td>$25 - $50,000 USD</td>
<td>40.0%</td>
<td>33.7%</td>
<td></td>
</tr>
<tr>
<td>Ever Dx’d with Mental Health Disorder</td>
<td>19.9%</td>
<td>19.9%</td>
<td>.99</td>
</tr>
<tr>
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</tr>
<tr>
<td>------------------------------------</td>
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</tr>
<tr>
<td>CPD, Mean (SD)</td>
<td>14.8 (7.2)</td>
<td>14.8 (7.2)</td>
<td>.88</td>
</tr>
<tr>
<td>Age start smoking, Mean (SD)</td>
<td>17.6 (5.5)</td>
<td>17.7 (5.9)</td>
<td>.76</td>
</tr>
<tr>
<td>% w Smoker in home</td>
<td>41.2%</td>
<td>37.9%</td>
<td>.63</td>
</tr>
<tr>
<td>% QA in past year</td>
<td>27.5%</td>
<td>22.5%</td>
<td>.61</td>
</tr>
<tr>
<td>% Ever used e-cigarette</td>
<td>36.5%</td>
<td>42.4%</td>
<td>.15</td>
</tr>
<tr>
<td>% Ever purchased e-cigarette</td>
<td>22.3%</td>
<td>25.5%</td>
<td>.37</td>
</tr>
<tr>
<td>% w E-Cigarette user in home</td>
<td>5.2%</td>
<td>4.0%</td>
<td>.47</td>
</tr>
<tr>
<td>Motivation to Quit Smoking (0-10)</td>
<td>4.5 (3.1)</td>
<td>4.3 (3.3)</td>
<td>.31</td>
</tr>
<tr>
<td>Confidence to Quit Smoking (0-10)</td>
<td>3.3 (2.9)</td>
<td>3.3 (2.9)</td>
<td>.90</td>
</tr>
</tbody>
</table>
**E-Cigarette Uptake**

### # times/day using e-cig (asked only among users)

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<th>Control</th>
<th>E-Cig</th>
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<tbody>
<tr>
<td>Week 1</td>
<td>8.15 (6.9)</td>
<td>6.13 (5.3)</td>
<td>All n.s.</td>
</tr>
<tr>
<td>Week 2</td>
<td>6.48 (5.9)</td>
<td>7.31 (7.9)</td>
<td></td>
</tr>
<tr>
<td>Week 3</td>
<td>8.27 (10.3)</td>
<td>8.36 (9.7)</td>
<td></td>
</tr>
<tr>
<td>Week 4</td>
<td>8.70 (9.9)</td>
<td>7.74 (6.5)</td>
<td></td>
</tr>
<tr>
<td>Week 12</td>
<td>7.17 (5.7)</td>
<td>6.85 (6.1)</td>
<td></td>
</tr>
<tr>
<td>Week 24</td>
<td>6.58 (9.4)</td>
<td>6.96 (7.6)</td>
<td></td>
</tr>
</tbody>
</table>

* Non-Users included (0 days)

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* MUSC HOLLINGS CANCER CENTER
**E-Cigarette Uptake**

### Percent Using E-Cigs (bars)

- **Control**
- **E-Cig**

### # Days Using E-Cigarettes (lines)

- **CONTROL**
- **E-CIG**

### # times/day using e-cig (asked only among users)

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* Non-Users included (0 days)

** Users only
Interest in Tobacco & Menthol is low, and diminishing

Interest in Fruit Flavors (3 options) is high, and increasing
Other Outcomes

Significant Time x Group Interactions

- Motivation to Quit Cigarettes
- Confidence to Quit Cigarettes
- CPD
- HSI
- Penn State Dependence (cigarettes)

Interaction: n.s.; Time: p=0.012; Group: n.s.

Penn State Dependence (ecigs)
What About Dependence?

Penn St Dependence Scale (0-20)

- Cig Dependence: CONTROL group
- Cig Dependence: ECIG group
- E-Cig Dependence: ECIG group

Significant Time x Group interaction
Example: Trajectories of Use Buckets over Time

- All “buckets” defined by product use in past 7 days
E-cigarette Group
Completed Week 4
Now at Week 24

Smokers at baseline
N=427

Smoke Only
N=68 (16%)
N=59 (87%)
N=1 (1%)
N=8 (12%)
N=0 (0%)

Vape Only
N=43 (10%)
N=7 (16%)
N=25 (58%)
N=3 (7%)
N=8 (19%)

Dual Users
N=315 (74%)
N=54 (17%)
N=22 (7%)
N=231 (73%)
N=8 (3%)

Quitters
N=1 (<1%)
N=1 (100%)
N=1 (100%)

Of W4 dual users:
- 91 (28.9%) relapsed to mono-smoking
- 19 (44.2%) still mono vapers
- 2 (4.7%) dual users (went back to smoking)
- 13 (30.2%) achieved complete abstinence
- i.e., 74.4% not smoking

By Week 24:

Of W4 mono smokers:
- 60 (88.2%) maintained mono smoking
- 1 (1.5%) became a mono-vaper
- 5 (7.3%) became dual users
- 2 (2.9%) achieved complete abstinence
- i.e., 4.4% not smoking

Of W4 mono vapers:
- 9 (20.9%) relapsed to mono-smoking
- 19 (44.2%) still mono vapers
- 5 (7.3%) became dual users
- 2 (2.9%) achieved complete abstinence
- i.e., 74.4% not smoking

All percents based on denominator from previous step
For individuals with missing data, the last observation reported was carried forward
### Among Dual Users at Week:

<table>
<thead>
<tr>
<th>Week</th>
<th>Reduction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 4</td>
<td>32%</td>
</tr>
<tr>
<td>Week 12</td>
<td>33%</td>
</tr>
<tr>
<td>Week 24</td>
<td>32%</td>
</tr>
</tbody>
</table>

### Among Ever Dual Users throughout Follow-Up

- **40%**
- **36% mean reduction in CPD (31% -- 41%)**

### Among Ever Dual Users NOT Achieving >50% CPD reduction (n=199)

- **14% mean reduction in CPD (9% -- 19%)**

… Dual Users had substantial reductions in CPD
### Outcomes at Week 24:

<table>
<thead>
<tr>
<th></th>
<th>Mono Smokers</th>
<th>Mono E-Cig Users</th>
<th>Dual Users</th>
<th>Achieved Completed Abstinence (of both)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Within E-CIG Group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mono Smokers (n=68)</td>
<td>60 (88.2%)</td>
<td>1 (1.5%)</td>
<td>5 (7.3%)</td>
<td>3 (4.4%)</td>
</tr>
<tr>
<td>Mono E-Cig Users (n=43)</td>
<td>9 (20.9%)</td>
<td>19 (44.2%)</td>
<td>2 (4.7%)</td>
<td>13 (30.2%)</td>
</tr>
<tr>
<td>Dual Users (n=315)</td>
<td>91 (28.9%)</td>
<td>19 (6.0%)</td>
<td>187 (59.4%)</td>
<td>18 (5.7%)</td>
</tr>
<tr>
<td><strong>Total: 426</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(1ppt quit at week 4; Total N in E-CIG Group = 427)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

... Dual Users had substantial reductions in CPD
... Greater Proportion of Dual Users achieved abstinence than the entirety of the control group

If missing: LOCF
Conclusions; Moving Forward

- Study findings complement existing RCTs of e-cigarettes, which were primarily cessation focused & supported.
- Our results show that unstructured/unguided e-cigarette use leads to increase quitting, across a range of outcomes.
- Effect sizes were comparable among those who were and were not ready to quit.
- Dual use was the predominant outcome, but moderate reduction in CPD exist even among dual users.

Limitations: Lack of bioverification (the curse of covid)

Manuscript(s) in development:
- Main outcomes
- Impact of flavors relative to outcomes
- Reasons for Use → Actual Use
- Remote recruitment process
- Invitation to others!

SRNT Symposium (Thurs, 3/2): Podium Session #2
ALL e-cig cessation trials should be balanced with public health needs and science focused on prevention of youth initiation.

**Us vs. Them:** Only 1 side wins

**Balance:** How do we get e-cigarettes in the right hands of smokers, **AND** out of the hands of kids?

Slide credit: Tracy Smith
Thank you!

Questions?

carpente@musc.edu