e-Cigarettes: Can we use them to make combusting of tobacco obsolete - end the “cigarette century” and its preventable deaths?

David B. Abrams

The Schroeder Institute For Tobacco Research And Policy Studies at Legacy.
The Johns Hopkins Bloomberg School of Public Health
Georgetown University Medical Center / Lombardi Comprehensive Cancer Center

AAHB Laureate award
Charleston SC March, 2014.
In the United States, smoking tobacco is the only legal method of being killed.
The Health Consequences of Smoking—50 Years of Progress

A Report of the Surgeon General

Executive Summary

Citation

• Worse – 480,000+ deaths - 20 million overall
• More diseases: colon, arthritis, blindness…
• Greater cost: $289 billion
• 5.6 million children alive will die prematurely
• CTP Youth & CDC TIPS campaigns, movies
• 2014 budget - 94c tax hike
• Affordable Care Act: access coverage
• Vulnerable groups
• Progress slow/stalled.. Need a breakthrū?
Setting a Challenging Yet Realistic Smoking Prevalence Target for Healthy People 2020: Learning From the California Experience.


Note. The bottom 2 lines depict corresponding scenarios assuming that the United States as a whole achieves California’s 2005 rates (20% initiation rate and 3.33% cessation rate). The dotted line reflects the assumption that such rates are attained instantaneously (in 2006), whereas the solid line reflects the more plausible scenario that such rates will be achieved gradually (by 2010). The status quo initiation rate is 25% and the cessation rate is 2.59%.

Harm Reduction: Policy and Practice Proportional to HARM

• Evidence incontrovertible: inhaling combustion compounds in smoke is deadly. Cigarette is defective product – *unreasonably* dangerous, and addictive by design.

Zeller at FDA – Reduce *appeal, addiction, harm* of combusteds
- Product standards: for ingredients, Menthol, additives, carcinogenicity
- Reduce the nicotine content to make cigarettes less addictive/appealing;
- Greater restrictions at state, local level - time, place and manner

**AND**

*Adopt harm reduction*: Support cleaner, appealing nicotine products to compete / win over cigarettes

• The *enemy is not nicotine* per se: its burning tobacco = lethal tars toxins CO₂ & nicotine in *most addictive form.*
Emerging Tobacco & Nicotine Products: DISRUPTIVE: Evolution / Revolution? Ending the cigarette century before 100th SGR
Industry Comments

March 25, 2013 Interview:
“At NJOY, we are proud to be a leader in this process and believe our products have the potential to render traditional cigarettes obsolete,” said Craig Weiss, CEO of NJOY.

June 21, 2012
“...we believe the elimination of combustion via tobacco heating and other innovative systems for aerosol generation is the most promising path to secure risk reduction.” Andre Calantaopoulos, COO of PMI
Appeal, satisfaction, addiction. harm-
“abuse liability” decontructed
Appeal, Addiction, Harm: A Framework

Addiction Liability - Nicotine +?

Combusted Tobacco: Cigarettes, Cigars, Pipe, Hookah...

Appeal - satisfaction

Abuse liability, toxicity - harmfulness
Appeal, Addiction, Harm: A 3-d Framework

Addiction Liability - Nicotine +?

Abuse liability, toxicity - harmfulness

Combusted Tobacco: Cigarette, Cigar, Pipe, Hookah...
Addiction Liability – Nicotine +?

Flavored NRT’s in small packs in grocery stores (Zonnic)

Unflavored NRT’s:

Unflavored E-cigs

Flavored E-cigs

Combusted Tobacco:
Cigarette, Cigar, Pipe, Hookah...>
Public Health Impact: Zero Tolerance and Harm Reduction Ideology: Data vs Dogma

Combusted Tobacco:
Cigarettes, Cigars, Pipe, Hookah.....

Non-Combusted Tobacco and Nicotine Products:

?? Next Generation: Pyruvate

e-cigs ENDS

Cessation Behav, NRT's: inhaler, patch, gum...

Swedish SNUS

Smokeless Dissolvables

American Snus

Toxicity
(“Harmfulness”)
NON-Combusted Products versus Combusted Products

Dissolvable Tobacco Products – flavored.
SNUS, smokeless Products - Flavored.

Cigarettes (with or without menthol), Little cigars (flavored), Hookah ...

Dual / Poly-use: A new norm? Blurring differences between lethal combusted, less harmful non-combusted, and safest medicinal forms of nicotine delivery.

A game changer for tobacco control?
1. It’s the deaths, stupid, not the nicotine addiction

2. Nicotine is a good drug?

3. Do we care if many current smokers use cleaner nicotine even if it’s an addictive form of nicotine? What about youth update???

4. ... and even if more youth take up e-cigs -- than are now using cigarettes, little cigars, hookah, marijuana and alcohol?

5. Is nicotine in cleaner forms just like caffeine or close enough?

6. Can we support harm reduction? After all, it includes zero tolerance/total abstinence as its first premise = Its not “us versus them” not a battle over extremist ideologies...and is there a differences among independents vs big tobacco companies
Family Smoking Prevention And Tobacco Control Act (2009)

Public Health Standard

Calls for the review of the scientific evidence regarding:

1. Risks and benefits to the population as a whole, including both users and non-users of tobacco products;

2. Whether there is an increased or decreased likelihood that existing users of tobacco products will stop using such products; and

3. Whether there is an increased or decreased likelihood that those who do not currently use tobacco products, most notably youth, will start to use tobacco products

4. Individual safety and efficacy and public health IMPACT
Benefits vs. Downside to individuals and to public health

Can cleaner, appealing tobacco products be supported, while minimizing their downsides:

• Youth starter and progression to combusted products
• Undermining de-normalization - indoor air policy
• Dual / poly use when one can’t smoke without harm
• Delaying / Promoting cessation of cigarettes.
• Undermining clear messages about SOME tobacco dangers – blurring risk perception of harms, addiction,
• Impact of Internet and social media marketing and KABB
• BUT the genie is out of the bottle, can we capitalize?
Patterns of Use and Harm Reduction:
Behavioral transitions from combustibles to dual use of combustible and non-combustibles; exclusive use of non-combustibles and desistence of all or of combustibles.
State of the science:

- **Product design**: Variety. less harmful than cigarettes. Quality?

- **Nicotine**: doses vary, mislabel. Can deliver nicotine effectively, reduces craving. Appeal and Abuse liability less than cigarettes. Future?

- **Liquid/propylene glycol**: liquids and vapor, not studied for long-term inhalational safety in humans, local irritant

- **Secondhand Vapor**: Health effects not well-studied. Mainstream and secondhand vapor produces ultrafine and fine particulate matter.

- **Other toxicants** (VOCs, TSNAs, heavy metals, flavoring, additives): Fewer constituents at much lower levels than in cigarette smoke but higher in poor quality products.
Tobacco Specific Nitosamines in e-cigs are basically similar to “unregulated” NRT.

<table>
<thead>
<tr>
<th>Product</th>
<th>NNN</th>
<th>NNK</th>
<th>NAT</th>
<th>NAB</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicorette gum</td>
<td>2.00</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>2.00</td>
</tr>
<tr>
<td>Nicoderm CQ patch</td>
<td>ND</td>
<td>8.00</td>
<td>ND</td>
<td>ND</td>
<td>8.00</td>
</tr>
<tr>
<td>E-cigarettes</td>
<td>3.87</td>
<td>1.46</td>
<td>2.16</td>
<td>0.69</td>
<td>8.18</td>
</tr>
<tr>
<td>Swedish Snus</td>
<td>980</td>
<td>180</td>
<td>790</td>
<td>60</td>
<td>2010</td>
</tr>
<tr>
<td>Marlboro (Ultra-light)</td>
<td>2900</td>
<td>750</td>
<td>1100</td>
<td>58</td>
<td>4808</td>
</tr>
<tr>
<td>Marlboro (Red)</td>
<td>2900</td>
<td>960</td>
<td>2300</td>
<td>100</td>
<td>6260</td>
</tr>
</tbody>
</table>

Cahn et al. J Pub Health Pol 2010
Plasma nicotine concentrations for some nicotine and tobacco products.

Figure 3.3
Concentration of PM$_{2.5}$ ($\mu$g/m$^3$) in indoor air before and after using an e-cigarette and a conventional cigarette. Blue line: WHO air quality guideline value for PM$_{2.5}$ for short term exposure (24 hour mean).
Source: Pellegrino et al.
YOUTH Patterns of USE. (Experimenting only and over 90% already use conventional cigs).

- **Adults**: Awareness (76%) and use (21%) is growing fast among current smokers and young adults. Perceived as less harmful.

- **Youth** (CDC MMWR 2013)

![Bar chart showing the increase in use among all students, middle school students, and high school students from 2011 to 2012.](image)

- Use doubled middle and high school students 2011–2012, estimated 1.78 million students ever used.
FIGURE 1
Cigarettes: Trends in 30-Day Use, Risk, Disapproval, and Availability
Grades 8, 10, and 12

Use
% who used in last 30 days

Risk
% seeing "great risk" in smoking a pack or more per day
E-cigarette advertising: consumer patterns of use, beliefs, perceptions

Dear Smoking Ban,

WHY QUIT?
SWITCH TO BLU

Visit blucigs.com

blu ELECTRONIC CIGARETTE

Take back your freedom to smoke anywhere with blu electronic cigarettes. blu produces no smoke and no ash, only vapor, making it the smarter alternative to regular cigarettes. It's the most satisfying way to tell the smoking bans to kiss off. Okay, maybe the second-most satisfying way.

New blu Smart Pack

blucigs.com

18+ only.

CALIFORNIA PROPOSITION 65 Warning: This product contains nicotine, a chemical known to the state of California to cause birth defects or other reproductive harm.
State of the science: cessation

- New Zealand-based study 2011-2013 (Bullen et al., 2013)
  - N=657 current smokers motivated to quit. No difference in abstinence between treatment arms at 6 months between NRT and e-Cigs
    - Nicotine e-cig=7.3%, Placebo e-cig=4.1%, NRT patch=5.8%
    - Rates of smoking reduction (≥50%) were higher for nic e-cig (57%) relative to the NRT.

- Italy-based study 2010-2011 (Caponnetto et al., 2013)
  - N=300, current smokers curious about trying e-cigs (not motivated to quit)
  - No difference (nicotine or placebo e-cigs) at 52 weeks. 8.7% quit and 10.3% reduced their smoking by ≥50% Those who at first dual used were likely to relapse.

- Among quitline callers from 6 states in 2011-2012 (Vickerman et al., 2013)
  - E-cig groups (used for 1 mo or more than 1 mo) were less likely to be abstinent at 7-months compared with participants who had never tried e-cigs. 21.7%, 16.6% vs. 31.3%

- In 2011 a nationally rep. study of U.S. adults (Popova & Ling, 2013):
  - E-cig ever users were 78% more likely to be an unsuccessful quitter compared with non-users of e-cigs (OR: 1.78, p<.05). INCONCLUSIVE ...

Population impact ? : these studies have MAJOR methods limitations. E.g. observational, indication bias: Could be the users are more addicted smokers / have harder time to start with (like limits of Alpert, Connolly, Biener NRT study )
Caponnetto et al.. Unmotivated smokers quit at 12\% continuous abst, ITT at 12 months

<table>
<thead>
<tr>
<th>Groups</th>
<th>Reduction rates (%)</th>
<th>Quit rates (%)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
<td>B</td>
<td>C</td>
</tr>
<tr>
<td>Week-2</td>
<td>29.0</td>
<td>38.0</td>
<td>36.0</td>
</tr>
<tr>
<td>Week-4</td>
<td>29.0</td>
<td>33.0</td>
<td>29.0</td>
</tr>
<tr>
<td>Week-6</td>
<td>24.0</td>
<td>26.0</td>
<td>25.0</td>
</tr>
<tr>
<td>Week-8</td>
<td>23.0</td>
<td>21.0</td>
<td>20.0</td>
</tr>
<tr>
<td>Week-10</td>
<td>26.0</td>
<td>15.0</td>
<td>19.0</td>
</tr>
<tr>
<td>Week-12</td>
<td>26.0</td>
<td>20.0</td>
<td>21.0</td>
</tr>
<tr>
<td>Week-24</td>
<td>17.0</td>
<td>19.0</td>
<td>15.0</td>
</tr>
<tr>
<td>Week-52</td>
<td>10.0</td>
<td>9.0</td>
<td>12.0</td>
</tr>
</tbody>
</table>
New Zealand-based RCT Cessation study 2011-2013 (Bullen et al., 2013). At 6 months 7 day pp for e-cigs is very good and > compared to Patch: 21.1% vs 15.5%

<table>
<thead>
<tr>
<th></th>
<th>16 mg e-cig (N=289)</th>
<th>Patches (N=295)</th>
<th>P-value</th>
<th>Rel Risk (95% CI)</th>
<th>Risk Diff (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Continuous abstinence</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One month</td>
<td>67 (23.2%)</td>
<td>47 (15.9%)</td>
<td>0.03</td>
<td>1.46 (1.04-2.04)</td>
<td>7.25 (0.84-13.66)</td>
</tr>
<tr>
<td>Three months</td>
<td>38 (13.1%)</td>
<td>27 (9.2%)</td>
<td>0.12</td>
<td>1.44 (0.90-2.33)</td>
<td>4.00 (-1.10-9.10)</td>
</tr>
<tr>
<td>Six months (primary outcome)</td>
<td>21 (7.3%)</td>
<td>17 (5.8%)</td>
<td>0.46</td>
<td>1.26 (0.68-2.34)</td>
<td>1.51 (-2.49-5.51)</td>
</tr>
<tr>
<td><strong>7-day point prevalence</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One month</td>
<td>69 (23.9%)</td>
<td>51 (17.3%)</td>
<td>0.05</td>
<td>1.38 (1.00-1.91)</td>
<td>6.59 (0.05-13.13)</td>
</tr>
<tr>
<td>Three months</td>
<td>62 (21.5%)</td>
<td>50 (17.0%)</td>
<td>0.17</td>
<td>1.27 (0.91-1.77)</td>
<td>4.50 (-1.88-10.88)</td>
</tr>
<tr>
<td>Six months</td>
<td>61 (21.1%)</td>
<td>46 (15.6%)</td>
<td>0.09</td>
<td>1.35 (0.96-1.91)</td>
<td>5.52 (-0.75-11.79)</td>
</tr>
</tbody>
</table>
Latest trends on smoking in England: from the Smoking Toolkit Study

Robert West
Jamie Brown

Last updated: 2\textsuperscript{nd} Sept 2013

www.smokinginengland.info
jamie.brown@ucl.ac.uk
Harm reduction? Using e-cigs to cut down

% of cigarettes smokers (3 month moving average)

- Cutting down
- Using NRT to cut down
- Using ecigs to cut down
Support used in quit attempts

% of those trying to stop in the past year who used support

NRT OTC: Nicotine replacement therapy bought over the counter; Med Rx: Prescription medication; NHS: NHS Stop Smoking Service; E-cig: Electronic cigarette
People smoke because they are addicted to nicotine, but nicotine itself is not especially hazardous; it is the other constituents of **tobacco smoke** that cause most of the harm.

Use of smoke-free nicotine would benefit smokers directly by reducing the personal harm caused by nicotine addiction.

“In Sweden, the availability and use by men of an oral tobacco product called snus, one of the less hazardous smokeless tobacco products, is widely recognised to have contributed to the low prevalence of smoking in Swedish men and consequent low rates of lung cancer.”
probably: yes,
because the major harmful toxins in cigarette smoke are formed during the combustion and consequently absent in smokeless tobacco products.

still, some smokeless tobacco products are very harmful, but there is a very wide variation between products at the lower and the upper end of the scale.
For example, there were concerns that...

- snus may lead to dual use rather than replace cigarettes.

- nicotine addiction may be strengthened by snus use.

- snus use may lead to fewer attempts to quit smoking.

- snus may serve as a gateway to smoking and thereby increase smoking.
Initiation of daily tobacco use. Swedish men in different birth cohorts.

- **Never any daily tobacco use**
- **Snus, never smoking**
- **First snus, later smoking**
- **First smoking, later snus**
- **Smoking, never snus**
Does primary snus use make young people more or less likely to start smoking???

NO all fears were NOT confirmed
Smokers who have started subsequent snus use appear to make MORE efforts to quit smoking than those who have not.
Choice of aid at "Self-help" quit-attempts among Swedish men, and outcome of the quit-attempt

Proportion of different types of aid use

<table>
<thead>
<tr>
<th>Aid Type</th>
<th>Continued smoking</th>
<th>Quit smoking</th>
<th>Completely (quit rate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine gum only</td>
<td>0.43</td>
<td>(0.71)</td>
<td></td>
</tr>
<tr>
<td>Nicotine patch only</td>
<td>0.34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Snus only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other single aids</td>
<td>0.43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined aid use</td>
<td>0.58</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source:
Lars Ramström,
ITS (Institute for Tobacco Studies) Special analysis of FSI: database "Your Country and Your Life"
CASE STUDY SWEDEN

Smoking rate in Sweden and snus consumption

Source: Snus Consumption - Swedish Match
Whole bar: Relative risk of death for male tobacco users

Green sector: Never-smokers' death risk (reference)
Red sector: Excess risk (above Never-smokers)

Cigarette smokers
Snus users
Never-smokers

Less than 9% of

Data derived from:
Not the cleanest— but clean enough?
Behavioral transitions: combusted, dual use, non-combusted, none

TIME 01

Combustible use
Dual use
Non-combustible use
Never Use / Former Use

TIME 02

Combustible use
Dual use
Non-combustible use
Never use / Former use

TIME...N+1

Combustible use
Dual use
Non-combustible use
Never / Former use

Time
Regulatory Landscape: Need overall Nicotine Regulation Policy that bridges CTP and CDER

Center for Tobacco Products
- Cigarettes
- Roll-your-own tobacco
- Smokeless tobacco
- Hookah tobacco
- Cigars/cigarillos/LCCs
- E-cigs for harm reduction

Center for Drug Evaluation & Research
- Pharma – NRT, Chantix, Buprion
- Other medications for cessation
- RJR Zonnic: Package, Price, Placement
- ? E-cigs for cessation

Next Generation Products (Aerosol, Pyruvate, Cleaner Nicotine)
Trends in Per Capita Consumption of Various Tobacco Products – United States, 1880-2005 and Beyond.

Back To The Future? (based on Giovino article)

Source: Tobacco Situation and Outlook Report, U.S. Department of Agriculture, U.S. Census

Note: Among persons > 18 years old.

Beginning in 1982, fine-cut chewing tobacco was reclassified as snuff.

Source: US Department of Agriculture

Non-combusteds: NRT’s, E-cigs, Swedish Snus…

Combusteds: Cigarettes, all cigars, hookah…

Source: US Department of Agriculture
State of the science: Policy & regulation, federal and state

- Product classification (medicinal, recreational, other)
- Product safety standards – regulation - light or heavy?
- Claims of modified risk / reduced harm.
- Use in public places (indoor air laws, de-normalization)
- Youth protection (24 states restrict sales to minors)
- Taxation ?
- FTC: correction of misleading labels and claims
Proportionate to Harm Policies

- Least harm is not to use any tobacco product at all
- No sales or advertising targeted at youth for any product
- Indoor air policy - restrict all use
- Tax combusted at much higher rates than non-combusted, same or higher differential if we do tax e-cigarettes
- Make combusted unappealing, expensive, ?less addictive - restrict and regulate strictly
- Prudent regulation of non-combusted – quality controls, advertising and marketing practices (support responsible companies not affiliated with combusted tobacco (verify good behavior with aggressive post approval surveillance. Warner et al a gold star
- Educate public to highlight the lethality of combusted in any form. Contrast with reduced harm with safer nicotine products - non-combusted being much less harmful (FDA approved NRT best, then Swedish Snus and e-cigs – then other smokeless products
Cancer Death Rates* Among Men, US, 1930-2009

*Age-adjusted to the 2000 US standard population.
e-Cigarettes: Can we use them to make combusting of tobacco obsolete - end the cigarette century and its preventable deaths?

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## E-cigarettes: Belief propositions and what is known

<table>
<thead>
<tr>
<th>Proponents</th>
<th>Opponents</th>
<th>Facts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ecig use is increasing</td>
<td>Ecig use is increasing</td>
<td>Ecig use is increasing but it is still a small fraction of cigarette market Mostly smokers are trying ecigs</td>
</tr>
<tr>
<td>Ecigs save lives:</td>
<td>Ecigs do not save lives:</td>
<td>Unknown</td>
</tr>
<tr>
<td>(smokers will quit all tobacco or smokers will switch to ecigs)</td>
<td>(smokers will not quit or smokers will dual use)</td>
<td>Ecigs do not help smokers quit (sparse evidence) Most smokers who try ecigs dual use</td>
</tr>
<tr>
<td>Ecigs are safe</td>
<td>Ecigs are not safe</td>
<td>Unknown</td>
</tr>
<tr>
<td>Ecigs are safer than cigarettes</td>
<td>Ecigs are safer than cigarettes</td>
<td>Ecigs are safer than cigarettes</td>
</tr>
<tr>
<td>Secondhand vapor is safe</td>
<td>Secondhand vapor is unsafe</td>
<td>Secondhand vapor is safer than secondhand smoke</td>
</tr>
<tr>
<td>Ecigs are not a gateway to smoking:</td>
<td>Ecigs are a gateway to smoking:</td>
<td>Unknown</td>
</tr>
<tr>
<td>(among never smokers - youth)</td>
<td>(among never smokers - youth)</td>
<td>Unknown</td>
</tr>
<tr>
<td>(among former smokers – relapse)</td>
<td>(among former smokers – relapse)</td>
<td>Unknown</td>
</tr>
<tr>
<td>Over-regulation is a risk</td>
<td>Under-regulation is a risk</td>
<td>Unknown</td>
</tr>
<tr>
<td>This problem is too important to worry about getting it right</td>
<td>This problem is too important to worry about getting it right</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
Risk reduction by products like snus: some policy considerations (1)

- Snus use entails nicotine dependence and some health risks, but risk levels are closer to those of no-tobacco-use than to those of cigarette smoking.
- Primary snus use is associated with reduced likelihood for onset of smoking.
- Increase of initiation of snus use is associated with an even greater decrease of initiation of smoking.
- Secondary snus use is associated with increased likelihood of stopping smoking.
- When used as smoking cessation aid, snus is more effective than nicotine gum or patch.
- Switching from cigarettes to snus may be a first step towards no-tobacco-use.
- In Sweden snus appears to be a contributing factor behind the low level of tobacco-related mortality.
Risk reduction by products like snus: some policy considerations (2)

- Regulations are needed to safeguard product quality.
- Strict legislation is needed to prevent sales to minors and restrain manufacturers from using misleading claims or other undue marketing practices.
- Labelling of packages should give consumer information regarding product content and characteristics including additives.
- Public education campaigns should point out actual risks while avoiding the kind of scaremongering that has sometimes been seen in the past.
- It should be kept in mind that experience from Sweden may not be immediately applicable in other countries.