Electronic Cigarettes and Harm Reduction

Peter Hajek

Declaration of interest

- I have no links with any e-cigarette manufacturers

- My research into safety and effects of EC is funded by National Institute of Health Research, UK Centre for Tobacco and Alcohol Studies and UK Medicines Regulatory Agency
E-cigarette – cig-a-likes (first generation)

E-cigarettes – tank systems (second generation)
E-cigarettes – variable power (third generation)

Changing terminology: Goodbye e-cig, hello vaping
Cig-a-likes vs tanks

- Most vapers start with cig-a-likes
  - Cheaper; Easier to use; Better promotion – tobacco industry
- Successful quitters use tank systems
- Tobacco industry lobbies to ban them
  - Promotes weak cig-a-likes
  - Exception: Vuse (Reynolds) 45mg/ml
  - NJOY King 45mg/ml as well – the only large non-TI company, the rest are small producers

EC use in UK (ASH 2016)

- 2.8 million vapers, virtually all smokers or ex-smokers (0.2% never smokers)
- 1.3 million (47%) stopped smoking

- Since 2014, EC adoption slowed down
  - 2013, 7% thought EC=>harmful than CC
  - 2016: 25% think so !!!
EC use in UK

- 12% of 11-16 year olds ever tried EC
- Most of them also tried cigarettes
- 2% vape regularly – virtually all have already used tobacco

Review four areas

- Health risks
- Evidence for the gateway hypothesis
- Nicotine delivery
- Effects on smoking cessation
Safety of EC

Adverse effects

- No serious adverse effect in any study
- Some irritation and cough, same in control conditions and on online forums
- FDA monitoring: 47 reports, 8 serious, 2 linked to EC (infant choking on EC cartridge and burns from exploding EC)
- Case study of lipoid pneumonia
- Cochrane review: No safety concerns emerged with use over short to mid-term
What is in EC liquid?

- Propylene glycol and/or vegetable glycerol, nicotine, flavourings
- Also impurities and potential toxicants
- Concentrations of these however are very small, much lower than in smoke, and unlikely to affect health
- Long-term use can only pose dangers if toxicants are present in doses that can harm health

Sola dosis facit venenum

(only the dose makes the poison)
### Tobacco Specific Nitrosamine Levels

<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>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 (full)</td>
<td>2900</td>
<td>960</td>
<td>2300</td>
<td>100</td>
<td>6260</td>
</tr>
</tbody>
</table>

Cahn, Siegel et al Journal of Public Health Policy 2010

### Aldehydes

<table>
<thead>
<tr>
<th></th>
<th>Formaldehyde</th>
<th>Acetaldehyde</th>
</tr>
</thead>
<tbody>
<tr>
<td>EC at 10W</td>
<td>1.1</td>
<td>0.2</td>
</tr>
<tr>
<td>EC at 15W</td>
<td>4.7</td>
<td>0.4</td>
</tr>
<tr>
<td>Cig 4mg tar</td>
<td>9</td>
<td>240</td>
</tr>
<tr>
<td>Cig 10mg tar</td>
<td>25-35</td>
<td>420</td>
</tr>
</tbody>
</table>

* Micrograms per 15 puffs on EC or per cigarette

Notes: Popular cigs have usually >10mg tar and higher aldehydes levels. EC at 20W produce aldehydes too, but this is unpalatable to smokers. Formaldehyde levels from EC are only 5x lower than in cigs, but this is several times below short-term irritation threshold. Geiss et al. (2016) Int J Hygiene Envir Health
Other toxicants

- Free radicals >1,000 lower than in cigs
- CO, phenolic compounds etc: none
- 156 volatile organic compounds in smoke, none or negligible levels in EC aerosol, e.g.

<table>
<thead>
<tr>
<th></th>
<th>Smoking</th>
<th>Vaping</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoprene</td>
<td>2,700</td>
<td>none</td>
</tr>
<tr>
<td>Benzene</td>
<td>1,100</td>
<td>0.6-same as indoor air</td>
</tr>
<tr>
<td>Toluene</td>
<td>1,400</td>
<td>none</td>
</tr>
</tbody>
</table>

Particulates and glycols

- EC release droplets of aerosol
- Presented as particulates(p)=dangerous, p from diesel engines, power stations=risks
- Different physically and chemically
- P in boiling water or shower are harmless

- ‘Bad glycols’ (diethylene glycol, 1,3-butanediol) absent
Recent health scares

- Acetaldehyde from overheated EC liquid
- Only released with ‘dry puffs’ aversive to vapers (Jensen et al., NEJM 2015; Farsalinos Addiction 2015)

- Mice in EC fog 1.5h twice a day for 2 weeks, toxic nicotine levels, distress. Loss of weight, when infected by viruses and bacteria, reduced immunity, more death
- Not relevant for vapers (Sussan et al. PLOS One 2015)

Diacetyl in some flavourings

- Popcorn lung (bronchiolitis obliterans) in 8 popcorn plant workers, very high doses
- Headlines on vaping risks
- Levels in EC vapour >100 times lower than in cigarette smoke
- Smoking never linked to popcorn lung
- Another agenda-driven scare
- BUT flavours need testing, some may pose avoidable risks even if none found yet
The Oscar for the Worst Misreport: Neck cells study

- Cells in extract from smoke or EC vapour, no relevance for human exposure (cells discarded, repair and detox enzymes etc.)
- Cells still alive in EC medium after 8 weeks, but some damaged
- Smoke extract killed all cells in 24 hours: EC effects negligible compared to cigs
- Authors’ and media conclusion: EC are as dangerous as cigs and cause cancer
  
  Yu et al. Oral Oncology 2015.10.018

And some brand new ones

- Vapers exhale through nose, nicotine affects cells in nose, but no link to health
  
  E-cigarettes 'increase risk of infection by damaging hundreds of genes in immune system'

- Cells 24h in EC extract-"Details elsewhere [11]“ and reference to unpublished report; no comparison with smoke!
  
  HEALTH + BEHAVIOR
  E-cigarette vapors could be toxic to oral cavity, UCLA study finds

Concern that dual users increase toxin intake

- 40 smokers wanting to quit
- At baseline urine samples for 3-HPMA (metabolite of acrolein), cotinine and CO
- Given a cig-a-like EC (2.4% nicotine)
- Followed up at 4 weeks, tests repeated
- 6 dropped out, 16 abstinent; 18 ‘dual users’


Smokers using EC for 4 weeks and smoking (dual users)
Transition from dual use to vaping (ASH 2016)

Quitters need time to complete the switch via dual use

- 111 vapers who quit smoking
- Dual use for 1M on average
- EC dependence significantly lower than cig dependence
- Significant reduction in nicotine content over time (no objective measure though)
- 23% needed e-liquid > 20mg/ml to quit!

Farsalinos et al. Subst Abuse Res Treatment 2013,7,139-146
Other studies of dual users

- 26% quit at 2-year f-u (23% of smokers not using EC – good result as successful vapers already gone – 61% still abstinent at 2 years) Manzoli et al. Tobacco Control 2016

- Our study, preliminary results: 63 dual users at 3M: 32% quit smoking (16% quit vaping as well); 23 reached 6M: 43% quit smoking (17% quit vaping as well)

Passive vaping?

- Unlike smoking, exhaled vapour does not expose bystanders to carbonyls or phenolics (Long 2014) or volatile compounds (Marco 2015)

- Particulates: smoker’s home=576; vaper’s =10; smoke/vape free homes=10+9 (Fernandes 2015) – plus of course P content differs

- Negligible nicotine on surfaces (Goniewitz 2014), a baby would need to lick 30m² of floor to ingest 1mg of nicotine
Toxicity of nicotine

- Common claim: 30-60mg lethal if ingested
- Traced to 19th century made-up figure*
- Suicide attempts by up to 1,500 mg in e-liquid: ‘Voluminous vomiting’ and full recovery in a few hours. Recent suicide >3,000 mg, anti-emetics?
- Nicotine from tobacco, NRT, EC: Millions exposed, fatal poisonings extremely rare

* Mayer, Arch Toxicol 2014

Is nicotine 100% safe?

- Probably not: Adverse effects in pregnancy in animal studies (but none from nicotine patches in humans). Dependence (in tobacco)
  - But no contribution to lung disease, cancer, or heart disease in long-term NRT and snus users

- Nicotine also has positive effects
  - Lowers BMI
  - May prevent Parkinsons’ disease
  - May prevent ulcerative colitis

- The comparator is not nothing but smoking
Exploding batteries

- A few cases with a wide media coverage
- Lithium batteries in laptops and mobiles and even alkaline batteries do this
- Rare risk, negligible compared to fires from tobacco
- In 2011, 90,000 smoking-material fires in the U.S., 540 civilian deaths, 1,640 civilian injuries and $621 million in direct property damage. Similar for previous years.

Summary of EC safety

- There is no known passive exposure risk
- Little risk of nicotine poisoning for users (but e-liquid should be in child-proof containers)
- Effects of long-term use, especially on users with asthma/lung diseases are not known. Main ingredients unlikely to pose risks, but some flavourings/contaminants or materials used in EC manufacture may do so
Summary of EC safety

- Monitoring is needed to detect and remove any emerging risk
- The estimate that EC are at least 95% safer than cigarettes takes this future uncertainty into account
- Smokers need not wait for further proofs to switch to vaping

Smokers are being misled
Harm perception is going the wrong way

- EU 2012 – 2014 (Special Eurobarometer for Tobacco Survey)
- Perception that EC are harmful increased from 27% to 52% !!!

Harm perceptions among adults
(Internet cohort survey 2012-14)

Harm perceptions among adults
(ASH YouGov adult surveys 2013-15)

Other things in the pipeline: PM products

RRPs: Our Product Platforms

Heated Tobacco Products

Nicotine-Containing Products

Platform 1
iQOS

Platform 2

Platform 3

Platform 4

Note: Reduced Risk Products (RRPs) is the term the company uses to refer to products with the potential to reduce individual risk and population harm in comparison to smoking cigarettes. The products depicted are subject to ongoing development and therefore the visuals are illustrative and do not necessarily represent the latest stages of product development.
BAT products

- ePen = EC
- iFuse = heated tobacco

Also likely much safer than cigs, but only TI data so far

Aerosol emission abundance compared against a 3R4F reference cigarette (% per puff)
Re-normalisation/gateway concerns
EC use by non-smokers

- As EC use spreads, more non-smokers have an opportunity to try vaping

- Strikingly, this leads to little further use. So far, EC have been unattractive to non-smokers

- Anti-EC activists and media keep mis-reporting experimentation as regular use

How is the trick done (US surveys)

- Did you ever use an EC = EC USER
  - Smoker=>100 cigs ever and currently smokes

- Have you used EC at least once in the past 30 days = CURRENT USER
  - Current smoker => 90 cigarettes over the past 30 days!!!

- ‘EC user’ and ‘Current EC user’ = tried EC once; but this is sold to media and regulators as regular daily use
UK surveys using honest methods

- If Yes to Have you ever tried an EC?
- How often if at all, do you currently use an EC?
  - Daily
  - Less than daily, but at least once a week
  - Less than weekly, but at least once a month
  - Less than monthly
  - Not at all

EC use among adolescents is confined to smokers

Scottish Health Survey 2014

Amongst never smokers, only 1 person had ever used EC, there was no current use

Comparison to smoking

- Some 50% of adolescents who try a cigarette become daily smokers
- Despite increasing experimentation with EC, few if any non-smoking adolescents became daily vapers of nicotine EC
- So far, EC are not a gateway even to vaping, and may even deter those who would otherwise smoke
- However, vigilance is needed
Smoking experimenters progressing to daily use

<table>
<thead>
<tr>
<th>Survey</th>
<th>% ever tried a cigarette</th>
<th>% ever smoked daily</th>
<th>% experimenters progressing to daily use</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Adult Tobacco Survey USA 2009-10</td>
<td>75</td>
<td>39</td>
<td>53%</td>
</tr>
<tr>
<td>Adult Tobacco Survey Poland 2009-2010</td>
<td>74</td>
<td>45</td>
<td>63%</td>
</tr>
<tr>
<td>Opinion and Lifestyle Survey UK 2013</td>
<td>55</td>
<td>42</td>
<td>76%</td>
</tr>
</tbody>
</table>

(11%, 28% and 19% currently smoke daily – most daily smokers quit)

Rise of vaping does not promote smoking !!!

Figure 8.1. Prevalence of current cigarette smoking among adults aged 18 and over: United States, 1997–2015

% high school students who used EC, hookah and cigs in the past 30 days

Increased EC use does not increase and may be decreasing smoking

Ever tried cigarettes:
2011 – 29%
2012 – 26%
2013 – 25%
2014 – 22%

Result of misreporting

- Over-regulation of EC is presented as a measure that may harm smokers, but is necessary to protect children from ‘nicotine addiction’
A cautionary tale

Swedish snus
Snus use and cancer risk

Proof of concept

- Swedish Snus was banned in Europe on the same pre-cautionary principle invoked for EC regulation (gateway to smoking and residual risk)

- Allowed in Sweden and Norway, enabling a natural experiment
Daily smoking and snus use in men aged 35-44, Sweden
Statistics Sweden/SCENIHR 2008

Smoking prevalence in European Union 2015

Q. Regarding cigarettes, cigars, sigarettes or a pipe, which of the following applies to you? In this question smoking cigarettes does not include the use of e-cigarettes
A. You currently smoke
Effect on health

- Removing tobacco smoke leads to the removal of risks of smoking even if nicotine use continues.
- Snus use has been associated with substantial decline in smoking-related morbidity and mortality.


Respiratory cancers in men aged 45-64,
EU 2001-3, Eurostat 2006

[Bar chart showing respiratory cancer deaths per 100,000 across EU countries, with countries listed vertically and deaths shown horizontally.]
What does it mean?

- If snus was not banned and there was only 50% of Swedish adoption rate in Europe, over 20,000 lung cancers per year would be avoided, plus a big chunk of other smoking related diseases.
- People responsible for the ban are responsible for 100,000’s of avoidable deaths. They did not know this when the ban was first implemented, but they do now.

And Yet !!!

- Despite the overwhelming evidence of benefits and no evidence of harm, the European Commission renewed the ban on snus in 2014.
- It also imposed drastic anti-EC regulation to start in 2016.
Hostile EU regulations will harm EC march on smoking

- Notification much tougher/more costly than for cigs, each model and e-liquid!!!
- 6 month wait before sale (not for cigs)
- Power to ban flavours and internet sales - worse for EC than cigs
- ‘Consistent dose’ onerous and vague, not required from cigs
- Only low nicotine and small containers
- Warnings=cigs disproportionate
- Ban on true info on relative risk, etc.

EC and nicotine delivery
Nicotine in e-liquids

- Over a dozen studies tested >400 different e-liquids to check accuracy of labelling
- ‘Ready made’ liquids labelled up to 36 mg/ml, highest recorded 36.6 mg/ml
- DIY liquids (150mg/ml) can pose danger
- Levels lower than labelled in older samples
- With some early exceptions, nicotine in ‘zero’ liquids only at trace levels

Conclusions

- Poor labelling poses little risk to users; labelling accuracy now mostly acceptable
- From consumers’ perspective, a general indication of e-liquids strength (mild, moderate, strong) provides sufficient information
- DIY liquid for dilution may become an issue with the ill-advised EU ruling
Nicotine delivery to users

- How much nicotine users get
- Effects of practice
- Differences between EC products

Novice users do not get much nicotine from cig-a-likes

- 20 smokers
- 6 x 10 puff

Vansickle et al, Addiction 2012
Experienced users on tank systems get more

* 8 experienced vapers abstained overnight
* Smoked 10 puffs and then an hour of ad-lib vaping

New vapers improve somewhat with practice

- PK data on first use (G1 product) and after 4 weeks of use (N=6)
- 24% increase in peak nicotine (4.6 to 5.7 ng/ml; NS), overall AUC intake increase p < .05

Vansickle & Eissenberg Nicotine & Tobacco Research 2012
Hajek et al. Nicotine and Tobacco Research 2015
Second generation e-cigs provide higher nicotine levels


How quick is the absorption?

**EC used by successful quitters**

- N=923 current US vapers, incl. dual users
- Quitters more likely to use tank systems (54% vs 35%)
- Tank users reported less taste similarity with cigarettes and better effects on craving

Vapers compensate for weaker e-liquids

- 11 vapers abstaining for 12 h
- 6mg or 24mg liquids ad lib
- Used twice as much of the weaker liquid
- Still got much less nicotine: 22ng/ml vs 44ng/ml after an hour of vaping
- However, no difference in ratings of craving and satisfaction
- EU regulation may increase e-liquid use

Dawkins et al. Psychopharmacology 2016

Not yet known

- What determines EC acceptability for individual smokers (some do not need EC to mimic nicotine intake from cigs, others do; some find the switch to EC easy and others don’t)
- How best to encourage more smokers to switch to EC
EC as treatment

‘Effectiveness’ shoehorns EC into medicines mold

- EC are a consumer product, used by smokers and competing with cigarettes
- We do not ask whether Macs are effective in helping people to stop using PCs
- Q1: Are EC replacing cigarettes?
- Q2: Are EC helpful when offered proactively to smokers seeking help?
Is vaping replacing, promoting, or not affecting smoking?

- By far the more important of the two questions
- Possible sources of information
  - Correlations between EC and cigarette sales
  - Correlations between trajectories of vaping and smoking rates
  - Changes in smoking rates in jurisdictions that ban and those that allow vaping

Relationships between sales of cigarettes and sales of EC

- Aware of no such studies
- Should top the list of EC research priorities
- NEEDED !!!
Trajectories of smoking and vaping rates

• Newest data from Welsh Health Survey 2015
  ■ 140,000 smokers vape
  ■ For past 3 years, smoking rate ↓ 1% per year
  ■ Previous decline: 1% over 6 years (2007-2012)

• Rise in vaping is definitely not promoting smoking and may be reducing it

Some other surveys

• US 2013 vs 2014 (N=37,000)
  ■ Tripling of EC use; 6% reduction in smoking prevalence
    2014 US National Health Interview Survey

• Parisian teenagers 2013 vs 2014
  ■ Doubling of EC use; 4% reduction in smoking
    Dautzenberg et al. Rev Mal Respir 2015
Eurobarometer 429

- 48.5 million Europeans tried EC
- 6.1 million quit smoking (13% of those who tried EC; tallies with previous smaller surveys)
- Even assuming that half of these quitters would quit anyway, millions of smokers quit with EC who would not have quit otherwise

*Farsalinos et al, Addiction 2016

US states that ban EC sales to minors and those that do not: Study 1

- 13 states have the ban
- Over 2-year period, states with the bans 0.9% more smoking among 12-17 year olds compared to other states (p<0.01)
- Vaping seems more likely to reduce than to promote smoking

Friedman, J Health Economics, 2016
US states that ban EC sales to minors and those that do not: Study 2

- Youth Risk Behaviour Surveillance System data
- 2007-2013 tobacco and marijuana use
- Purchasing restrictions linked to increased adolescent regular cigarette use by 0.8%


What about the claim that vaping prevents quitting smoking?

- Finding driven by studies that recruited smokers, asked them if they ever used EC, and checked quitting in those that did/did not
- Successful quitters left the sample!
- Those still ill after antibiotics have worse outcomes than those untreated. Not a proof that antibiotics prevent recovery from infection – the method provides no useful information on efficacy

Kalkhoran and Glantz, Lancet Resp 2016
Efficacy in treatment context

- Less important from population health perspective; but relevant for hard-to-reach groups and for stop-smoking services
- For highly dependent smokers with limited resources, behavioural support is likely to facilitate the switch to vaping

Cochrane review 2014

- Effect of EC on smoking reduction and cessation
  - Compared to placebo (conservative)
  - Compared to other treatments
EC vs placebo EC

- **Reduction**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Events</th>
<th>Total</th>
<th>Control Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bullen 2013</td>
<td>186</td>
<td>295</td>
<td>36</td>
<td>73</td>
<td>73.0%</td>
<td>1.28 (1.00, 1.64)</td>
</tr>
<tr>
<td>Capomnietro 2012</td>
<td>51</td>
<td>200</td>
<td>16</td>
<td>100</td>
<td>27.0%</td>
<td>1.59 (0.98, 2.65)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td>495</td>
<td></td>
<td>173</td>
<td>100.0%</td>
<td>1.36 (1.08, 1.72)</td>
</tr>
</tbody>
</table>

Total events: 237, df: 1 (P = 0.43; I² = 0%
Test for overall effect: Z = 2.65 (P = 0.008)

- **Cessation**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Events</th>
<th>Total</th>
<th>Control Events</th>
<th>Total</th>
<th>Weight</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Bullen 2013</td>
<td>21</td>
<td>289</td>
<td>2</td>
<td>73</td>
<td>47.3%</td>
<td>1.77 (0.54, 5.77)</td>
</tr>
<tr>
<td>Capomnietro 2012</td>
<td>22</td>
<td>200</td>
<td>4</td>
<td>100</td>
<td>52.7%</td>
<td>2.75 (0.97, 7.76)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td>489</td>
<td></td>
<td>173</td>
<td>100.0%</td>
<td>2.29 (1.05, 4.96)</td>
</tr>
</tbody>
</table>

Total events: 43, df: 1 (P = 0.58; I² = 0%
Test for overall effect: Z = 2.09 (P = 0.04)

EC vs nicotine patch

- **Reduction**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Events</th>
<th>Total</th>
<th>Control Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bullen 2013</td>
<td>106</td>
<td>269</td>
<td>138</td>
<td>295</td>
<td>100.0%</td>
<td>1.38 [1.19, 1.60]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td>289</td>
<td>295</td>
<td>100.0%</td>
<td>1.38 [1.19, 1.60]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 186, df: 1 (P < 0.0001)

- **Cessation**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Events</th>
<th>Total</th>
<th>Control Events</th>
<th>Total</th>
<th>Weight</th>
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<td>21</td>
<td>289</td>
<td>17</td>
<td>295</td>
<td>100.0%</td>
<td>1.28 [0.68, 2.34]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td>289</td>
<td>295</td>
<td>100.0%</td>
<td>1.26 [0.68, 2.34]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 21, df: 1 (P = 0.46)
Test for overall effect: Z = 0.72 (P = 0.46)
Small effects, but promising

- Achieved with inferior EC models
  - Poor nicotine delivery; Poor batteries; Problems with leakage and functioning
- NZ trial: Little beh. support; support is likely to increase effect as with NRT
- Italian trial: Smokers not planning to quit
- Low certainty and confidence in the size of the effect, but not the direction (100+ trials of NRT vs placebo show NRT helps)

Cochrane Update

- Currently in preparation, but only one new small RCT with short outcome (Adriaens et al. 2014)
- Smokers not intending to quit
- N=32 given refillable EC (18mg/mL)
- N=16 control group – no EC provided
- 2 months CO-validated quit rates
  - 34% vs 0%
Some other softer data

<table>
<thead>
<tr>
<th>Help at last quit attempt</th>
<th>N</th>
<th>% quit</th>
<th>OR</th>
<th>LCI</th>
<th>UCI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>E-cigarette</td>
<td>46</td>
<td>54.35</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>ref</td>
</tr>
<tr>
<td>No meds/e-cigarette</td>
<td>227</td>
<td>29.96</td>
<td>0.14</td>
<td>0.05</td>
<td>0.37</td>
<td>0.0001</td>
</tr>
<tr>
<td>NRT</td>
<td>113</td>
<td>37.17</td>
<td>0.23</td>
<td>0.08</td>
<td>0.66</td>
<td>0.0062</td>
</tr>
<tr>
<td>Varenicline/bupropion</td>
<td>76</td>
<td>40.79</td>
<td>0.40</td>
<td>0.13</td>
<td>1.23</td>
<td>0.1096</td>
</tr>
</tbody>
</table>

Adjusting for: demographics, survey mode, quit intention, HSI, time since QA, total # of Qas, interwave interval.
Other significant predictors of being quit: HSI, p=0.06 and time since last quit attempt.
No significant country interaction, p=0.86.

*unweighted frequencies and percentages

ITC longitudinal and US+UK data Preliminary findings (N=462) (Hitchman, SRNT 2015)
UK stop-smoking service data
(HSCIC monitoring data, 2015)

5,863 smokers who made a serious quit attempt in the past year

'How long did your attempt last before you went back to smoking?'
- 'I am still not smoking'
- Quitting with EC (N=454): 20%
- No aid (N=3,477): 15.4%
- Quitting with OTC NRT (N=1,922): 10.1%

Brown et al. Addiction 2014
Are EC ‘effective’?

- EC are a revolutionary development, early in their trajectory
- Vaping has started to replace smoking
  - Media scares and hostile regulations may be slowing down the process
- EC can help smokers seeking help to quit smoking

EC as treatment

- EC help smokers quit smoking and help those who do not quit to reduce smoking
- The effects of 1G ECs with low nicotine delivery were modest
- Further studies are needed with better EC products
Also

- Smokers who quit successfully with EC have significantly lower weight gain
- Quitting with EC may improve overall cardiovascular and metabolic risk profile


Stopped smoking in past 12M: Higher when EC available

Prevalence estimate and 95% confidence intervals. Smoking Toolkit Study
Success rate in those who tried to quit: Higher when EC available

Prevalence estimate and 95% confidence intervals. Smoking Toolkit Study

EC and UK stop-smoking services
Interest in services is declining

Population data: Smoking Toolkit Study

- Monthly household surveys
- Each month involves a new representative sample of ~1800; smokers ~450
- Data collected on electronic cigarettes since second quarter 2011
- For more info see [www.smokinginengland.info](http://www.smokinginengland.info) (Prof. West)
Smokers are quitting with EC

- Source: Smoking Toolkit Study
- N=10756 adults who smoke and tried to stop or who stopped in the past year
- Method is coded as any (not exclusive) use

Use of nicotine products in recent quitters

N=1159 adults who stopped in the past year; increase p<0.001 for e-cigs and all nicotine; decrease p<0.001 for NRT
Smoking prevalence is declining

Cigarette smoking prevalence continues to decline

The success rate in those who have tried to stop smoking increased from 2011

Graph shows prevalence estimate and upper and lower 95% confidence intervals.

Base: All adults

Base: Smokers who tried to stop in the past year

Graph shows prevalence estimate and upper and lower 95% confidence intervals.
The nicotine/cigarette market

The cigarette and nicotine market are both declining

N=78696 adults  
Nicotine data only from last year smokers  
nondaily nicotine: <1 pw=0.1, 1+ pw=0.5

UK stop-smoking service data
(HSCIC monitoring data, 2015)
**Stop smoking services 2015**

### LSSS Quit rate by therapy (April 2015-Dec 2015)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>N</th>
<th>% quit OR LCI UCI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Licensed medication and an unlicensed NCP consecutively</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unlicensed NCP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varenicline only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combination of a licensed medication and an unlicensed NCP concurrently</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Did not use any licensed medication or unlicensed NCP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupropion only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Licensed NCP and/or Bupropion and/or Varenicline consecutively</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single NCP only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combination NDs concurrently</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Other significant predictors of being quit: HSI, p=0.06 and time since last quit attempt

No significant country interaction, p=0.86

*unweighted frequencies and percentages

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**ITC longitudinal and US+UK data**

**Preliminary findings (N=462) (Hitchman, SRNT 2015)**

<table>
<thead>
<tr>
<th>Help at last quit attempt</th>
<th>N</th>
<th>% quit</th>
<th>OR</th>
<th>LCI</th>
<th>UCI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>E-cigarette</td>
<td>46</td>
<td>54.35</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>ref</td>
</tr>
<tr>
<td>No meds/e-cigarette</td>
<td>227</td>
<td>29.96</td>
<td>0.14</td>
<td>0.05</td>
<td>0.37</td>
<td>0.0001</td>
</tr>
<tr>
<td>NRT</td>
<td>113</td>
<td>37.17</td>
<td>0.23</td>
<td>0.08</td>
<td>0.66</td>
<td>0.0062</td>
</tr>
<tr>
<td>Varenicline/bupropion</td>
<td>76</td>
<td>40.79</td>
<td>0.40</td>
<td>0.13</td>
<td>1.23</td>
<td>0.1096</td>
</tr>
</tbody>
</table>

Adjusting for: demographics, survey mode, quit intention, HSI, time since QA, total # of QAs, interwave interval

Other significant predictors of being quit: HSI, p=0.06 and time since last quit attempt

No significant country interaction, p=0.86
What services do?

- Most now support smokers who want to quit with EC, but do not facilitate use
- Leicester service reported increased service uptake and quit rates after including EC
- City of London service piloted offering EC starter packs

City of London pilot study

- EC starter pack as an optional addition to standard treatment
- 100 offers: 69 accepted
- 65% validated 4W quitters (45% stopped other meds); 45% in no-EC group (p=0.06)
- EC+varenicline = 85% quit rate
- Positive client feedback, no problem with buying own supplies later

Hajek et al. Addiction Research and Treatment, 2015
What should services do?

- Varenicline and NRT remain treatments with the best evidence for safety and efficacy
- Services should consider supplementing them with EC and providing starter packs, especially to low-income smokers
- This may increase the reach and possibly efficacy and help more smokers

NCSCT Briefing

- ncsct.co.uk/usr/pub/Electronic_cigarettes._A_briefing_for_stop_smoking_services.pdf
MHRA licensed product

- E-Voke produced by BAT
- 15mg of nicotine per cartridge
- SPC states
  - on repeated use, peak plasma 6 ng/ml
  - T-max 8 minutes
- Much slower than tank EC; very low dose; looks like cig; produced by tobacco company
- Services may be forced to use this rather than better products

Why is there such an emotional opposition to EC?

- Category error? EC look a bit like cigarettes and provide nicotine
No risk needed, smoking is about to disappear anyway?

But safer nicotine delivery devices are coming !!!

- In 1998, Kodak had 170,000 employees and sold 85% of all photo paper worldwide
- Within a few years it was bankrupt
- The market for stop smoking medications is shrinking already
- Cigarette market will follow
- Big players keen to slow down the process
- Why are some PH activists helping them?
Why are PH activists helping tobacco industry fight rival?

- Anti-EC activists believe that use of nicotine, whether harmful or not, is morally wrong. Nicotine use has been declining, EC may re-introduce it

BUT

- Without health risks, nicotine use differs little from caffeine use, and in the meantime, smokers are dying

- The snus story shows dangers of ideology

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Public health priorities

Ensuring EC regulation does not favour cigarettes

Encouraging smokers to switch from smoking to vaping