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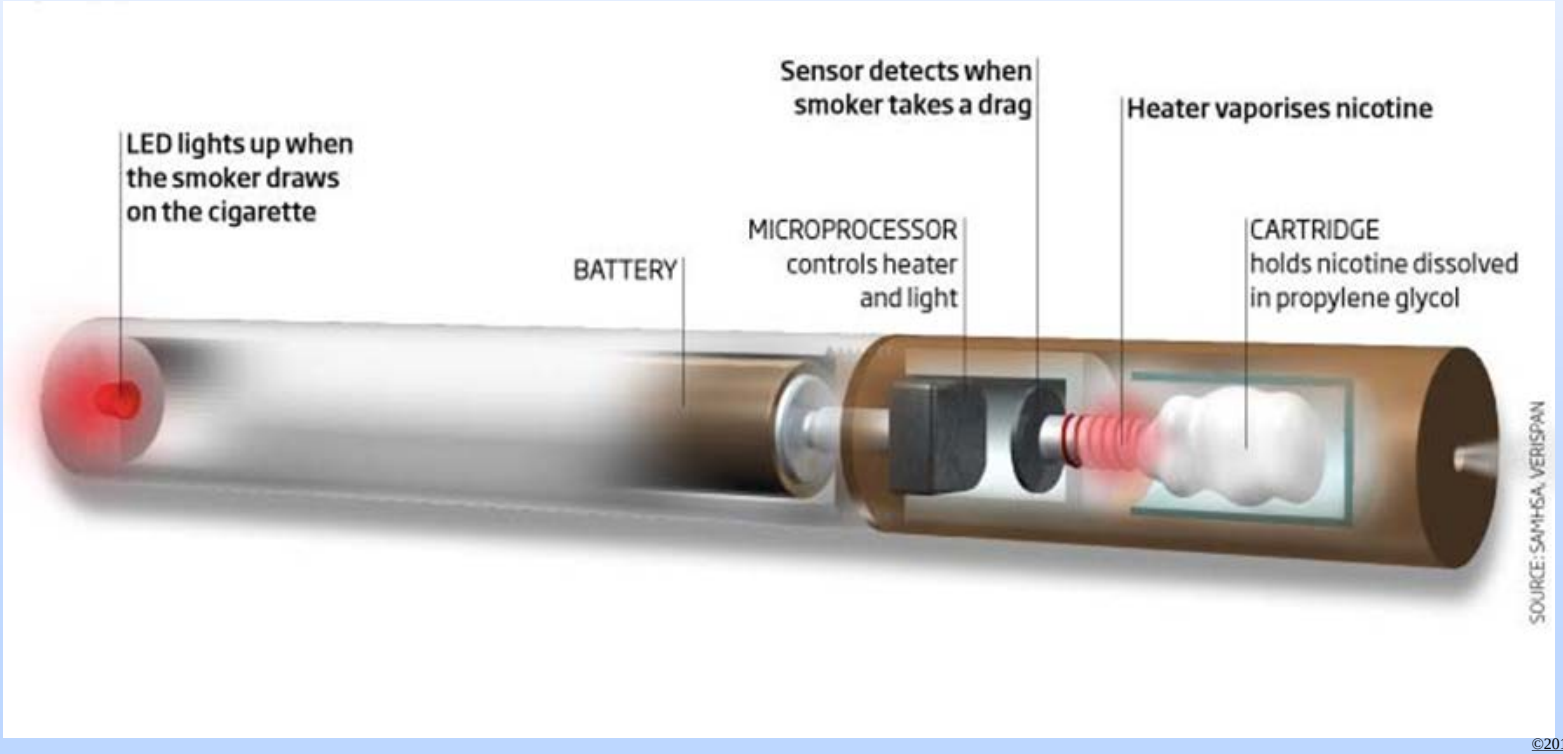
Electronic Nicotine Delivery Systems

Jeff Poterucha, MA

Electronic Nicotine Delivery System (ENDS)

A battery-powered device that provides inhaled doses of vaporized nicotine solution. It is used as an alternative to smoked tobacco products, such as cigarettes, cigars, or pipes.



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History

- First patent in US 1965
- Chinese pharmacist invented current iteration
  - marketed by ‘Ruyan’ in May 2004
- Estimated sales projected to double this year from $500 million last year to $1 billion this year
- Estimated sales to top $17 billion/year by 2017
- 1 in 5 cigarette smokers tried E-cigarette in 2011

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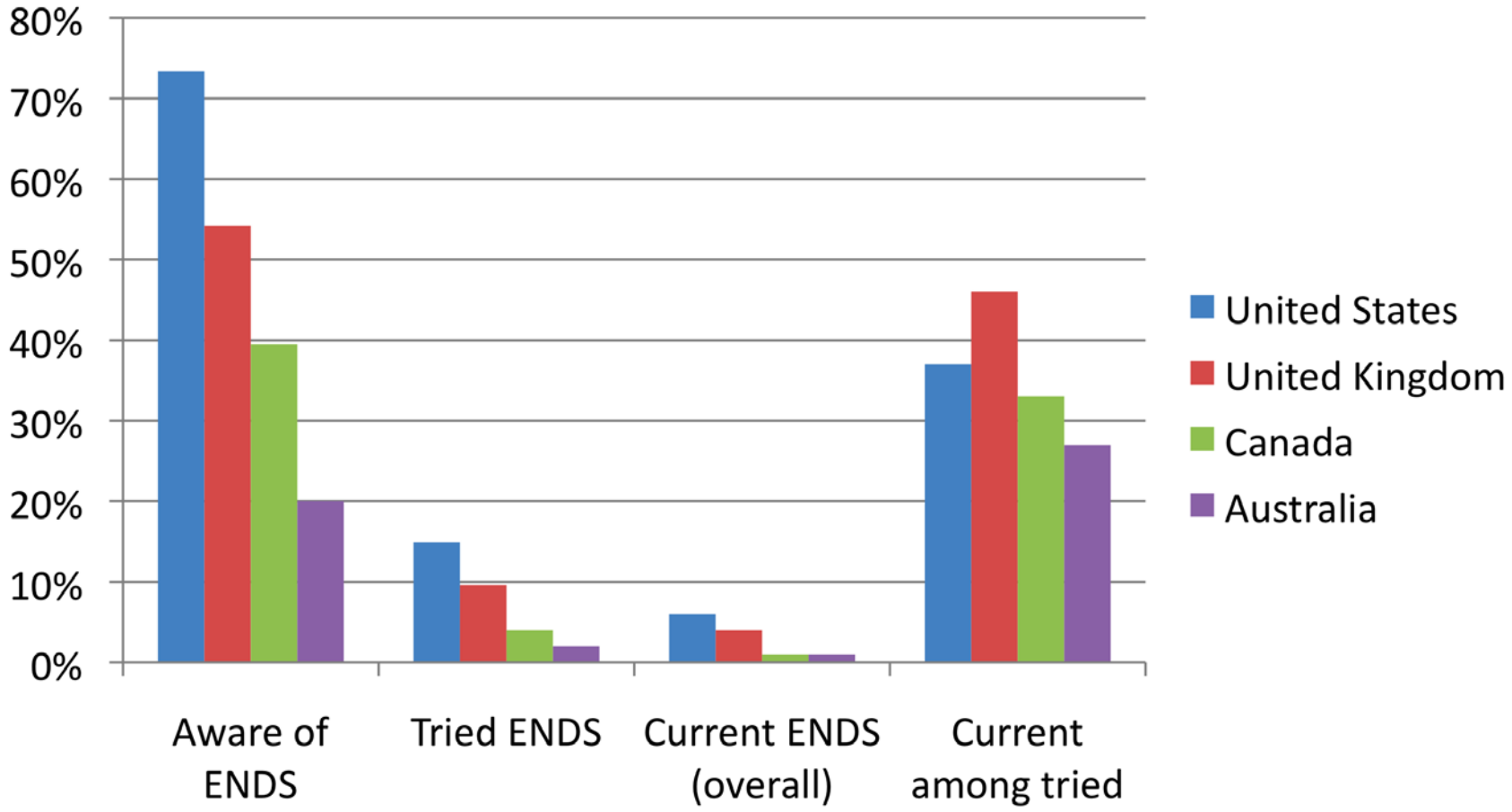
Current and former smokers – 2010



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Big Business

- Njoy raised $75 million from silicon Valley investors – June, 2013

- Vapor CEO say “a generation from now, people may forget what a machine-rolled cigarette looks like.

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Tobacco companies

- Looking to e-cigarettes for growth
- Giant tobacco companies join the business
  - Altria
  - Reynolds American
  - Lorillard

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Marlboro maker Altria to jump into e-cigarettes

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RICHMOND, VA. | The Marlboro Man may soon be hitching his wagon to a new kind of cigarette.

Altria Group Inc., owner of the nation's biggest cigarette maker, Philip Morris USA, announced Thursday that its NuMark subsidiary plans to introduce an electronic cigarette during the second half of the year, making it the last of the major domestic tobacco companies to enter the growing category.

While it's a small market compared with traditional tobacco products, "there's no denying that adult tobacco consumers have shown some interest in it," Altria CEO Marty Barrington said in a conference call with investors. Details on the product, the market it will enter and whether it will be under the top-selling Marlboro brand name were not revealed.

The move is the latest in an industrywide push to diversify beyond the traditional cigarette business, which has become tougher in the face of tax hikes, smoking bans, health concerns and social stigma.

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Altria

BRITISH AMERICAN TOBACCO

“Vaping”

To inhale vapor from an e-cigarette

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E-Liquid Solution Composition

- Propylene glycol
  - 95% of volume of e-liquids
  - Vapor that carries nicotine into body
  - Added to some foods, cosmetics, & medicines
- Nicotine
  - Varying amounts
- Flavoring & coloring agents
- Impurities & Additives

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People are using E-cigarettes:

1. To try something new
2. Reduce cigarette consumption
3. Quit smoking
4. Cheaper than cigarettes

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How are People Using ENDDs?

	Number of comments
To quit smoking	53
For health, as e-cigarettes were perceived to be less toxic than tobacco	49
Less expensive than regular cigarettes	26
Can be smoked everywhere, including smoke-free places	21
To avoid disturbing other people, or producing environmental tobacco smoke or the smell of stale smoke	20
For the pleasure of smoking, including the pleasure of inhaling and smoking-related actions	19
To reduce cigarette consumption	14
Curious to test a new product	10
Ecigarettes taste and smell good	8
Previously failed to quit with either nicotine patch or bupropion	3
To get nicotine	2
Total (from three open-ended fields)	*225*

Etter JF. BMC Public Health. 2010 May 4;10:231.

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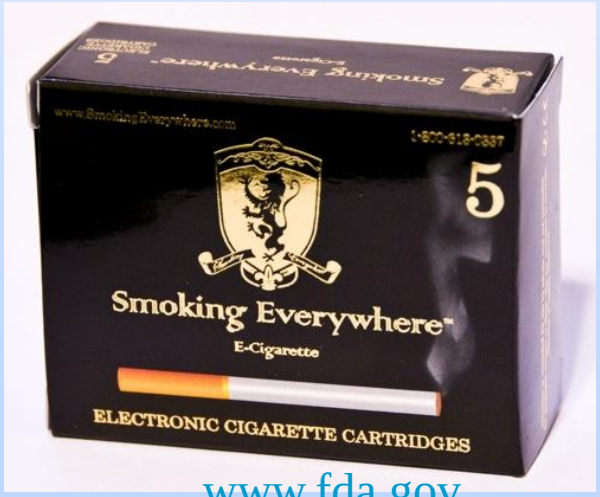
Safety Considerations

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

- In 2009, FDA's Center for Drug Evaluation, Division of Pharmaceutical Analysis (DPA) analyzed:
  - 2 samples of electronic cigarettes & components from two leading brands
    - 18 of the flavored, nicotine, and no-nicotine cartridges
  - Nicotine inhaler (control)



www.fda.gov

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U.S. Food and Drug Administration
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- DPA's analysis:
  - Diethylene glycol in one cartridge @ 1%
    - Ingredient used in antifreeze & toxic to humans
  - Tobacco-specific nitrosamines (TSNA's) in 1/2 of samples
    - Human carcinogen
  - Tobacco-specific impurities detected in a majority of the samples tested
    - May be harmful to humans
      - Anabasine
      - Myosmine
      - β-nicotyrine

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Safety – Short-Term Effects

- Nicotine Poisoning
- Pulmonary Issues
- Cardiovascular Effects

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Pulmonary Effects

- 30 healthy smokers (Athens, Greece)
  - Minimum of 5 pack-years
  - Aged 19-56 years
  - 14 male
- E-cigarette use for 5 minutes
- ENDDs associated with a significant increase in airway resistance

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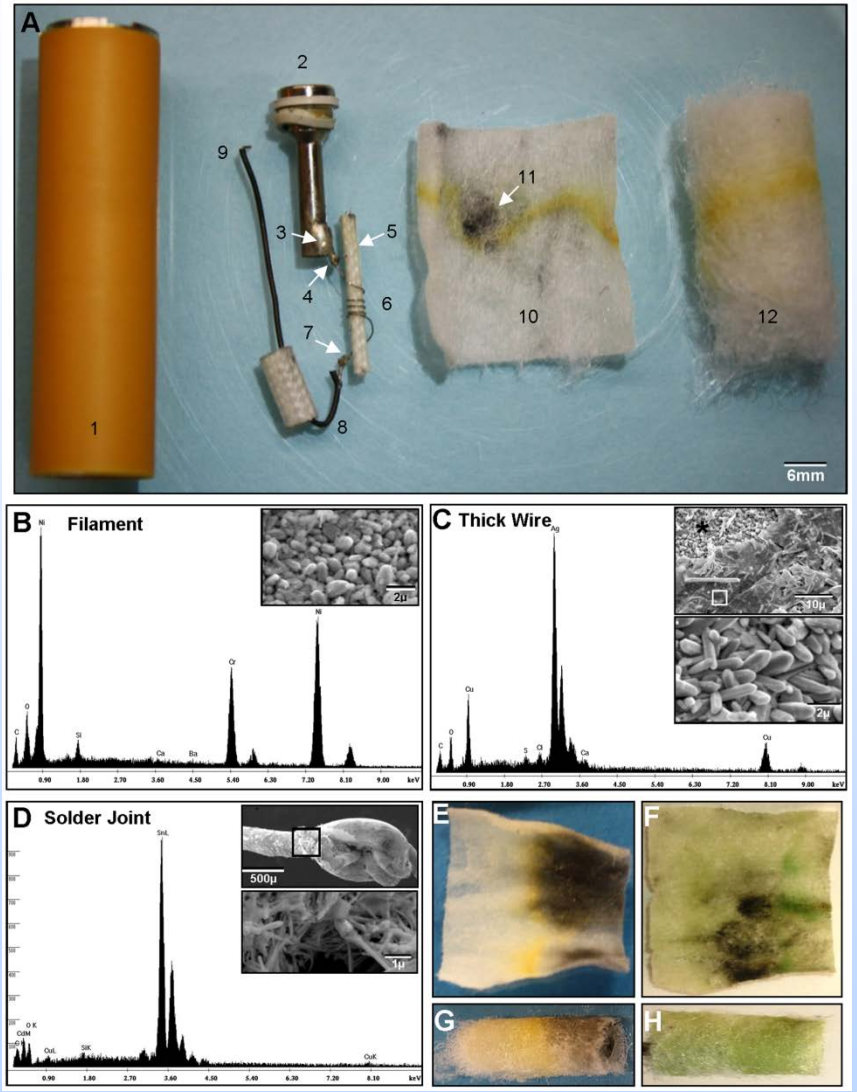
Vardavas CI, et al. Chest. 2011 Dec 22. PubMed PMID: 22194587.

Heavy metals particles & nanoparticles in electronic cigarettes

- E-cigarette cartomizer contents and aerosols analyzed
  - Leading Brand
  - 22 Kits over 2 year period
  - 100 puffs/day
- Results
  - Aerosol contained particles comprised of tin, silver, iron, nickel, aluminum, and silicate
  - Nanoparticles of tin, chromium and nickel.
- Concentrations of 9 of 11 were higher or equal to concentrations in cigarette smoke.



Williams M, Villarreal A, Bozhilov K, Lin S, Talbot P (2013) Metal and Silicate Particles Including Nanoparticles Are Present in Electronic Cigarette Cartomizer Fluid and Aerosol. PLoS ONE 8(3)

Safety – Long-Term Effects

- Research is extremely limited
- Concerns
  - Prolonged inhalation of chemicals
  - Net public health effect
    - Youth
    - Dual use
    - Harm reduction ≠ cessation

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Efficacy Considerations

Efficacy of electronic cigarettes

- Little data to demonstrate efficacy
- Research is growing, but more is needed

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U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

- E-cigarette cartridges labeled as “no nicotine”
  - Low levels of nicotine present in all cartridges tested, except one.
- 3 different E-cigarette cartridges
  - Same label
  - Markedly different amount of nicotine with each puff.
  - Range: from 26.8 to 43.2 mcg nicotine/100 mL puff
- One high-nicotine cartridge delivered 2 x as much nicotine as the nicotine inhaler

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Do ENDDs Alleviate Craving?

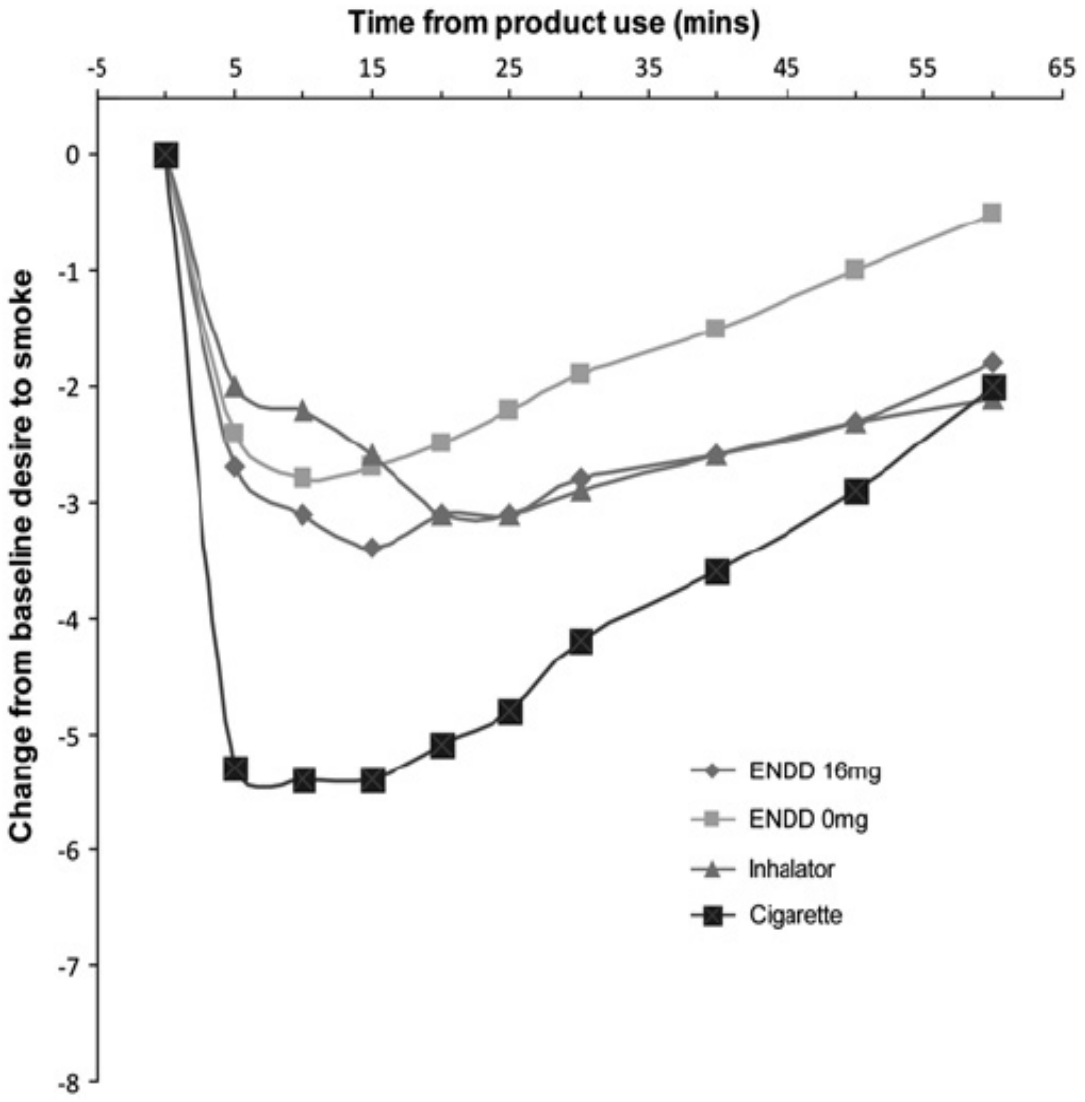


Figure 2 Change in desire to smoke from baseline over the first hour after each product use.

Smokers

- Aged 18 and 70 years
- Smoked ≥ 10 cigarettes
- Overnight abstinence

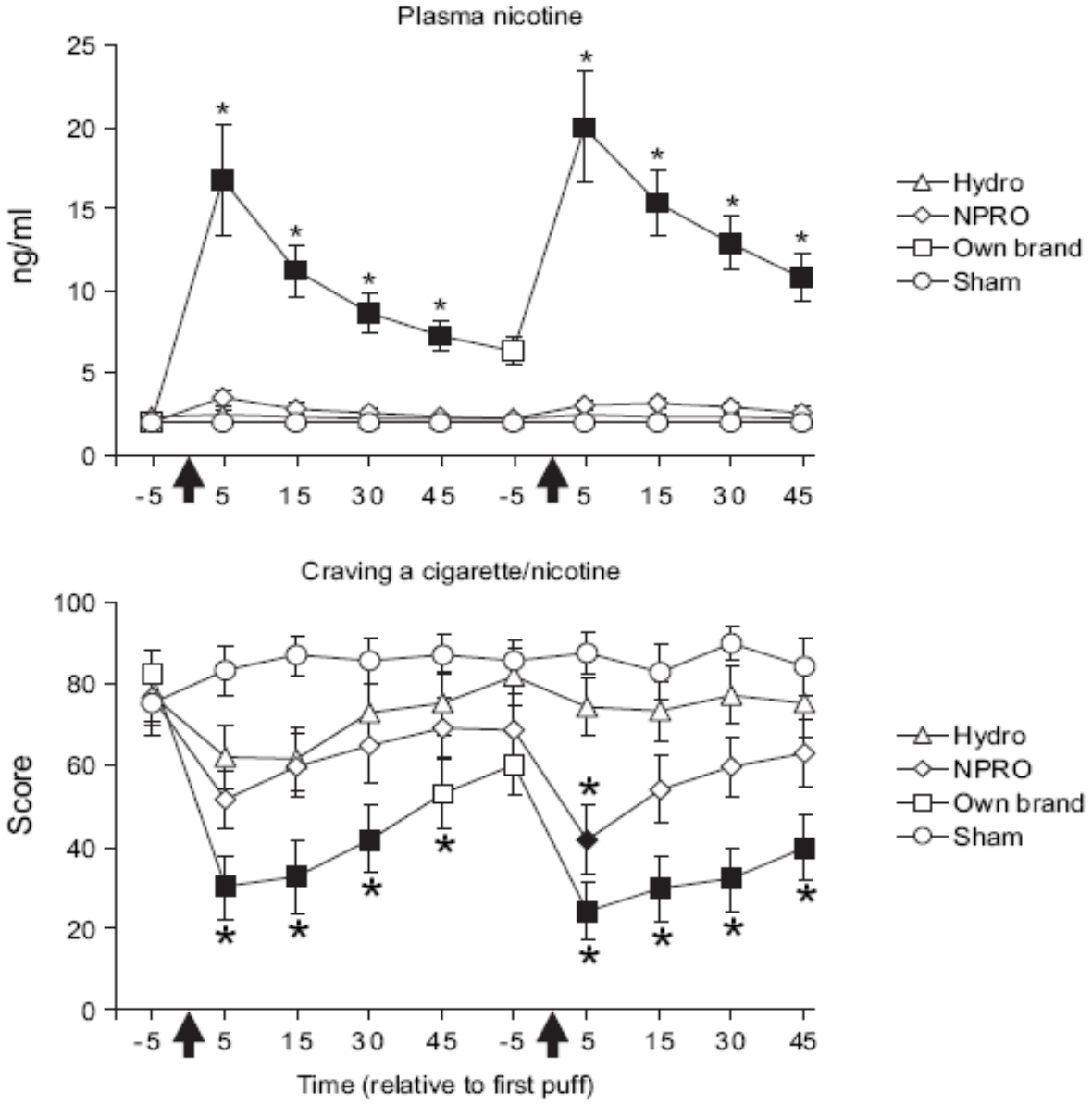
16 mg ENDD less desire to smoke than placebo

No difference in desire to smoke between 16 mg ENDD & inhaler

ENDDs more pleasant than inhaler

Bullen C et al. Tob Control 2010 19: 98-103.

Effects on Desire to Smoke



Crown 7 Hydro

Njoy NPRO

Eissenberg T. Tob Control. 2010 Feb;19(1):87-8..

Efficiency and safety of an electronic cigarette as tobacco cigarettes substitute

- ECLAT study 2013 –Italy (PLOS)
- 12 month RCT in 300 smokers “no” intention to quit

Three groups of 100 smokers each

Group A	Group B	Group C
7.2 mg. nicotine cartridges for 12 weeks	7.2 mg. nicotine cartridges for 6 weeks then 5.4 mg. cartridges 6 weeks	No-nicotine cartridges for 12 weeks.

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Caponnetto P, Campagna D, Cibella F, et al. (2013). Efficiency and safety of an electronic cigarette (ECLAT) as tobacco cigarettes substitute: a prospective 12-month randomized control design study. *PloS One*; **8:** e66317.

Results

- Declines in cpd and CO levels noted in all groups ($p<0.001$ vs. baseline)
- Smoking reduction noted
  - 22.3% at week 12 and 10.3% at 52 weeks.
- Complete abstinence from cigarettes
  - 10.7% at 12 weeks and 8.7% at 52 weeks
- Infrequent withdrawal symptoms reported

Critique per Stanton Glantz UCSF

- This is not a true “randomized control design”—there is not a control group who were NOT using e-cigarettes that would allow assessment of spontaneous quit rates.
- There are issues with the statistical design which when corrected, eliminate the reported statistical significant results

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Electronic cigarettes for smoking cessation

- New Zealand 2013
  - 657 smokers divided into three groups
    - 16 mg. e-cigarette
    - 21 mg. nicotine patch
    - Placebo e-cigarette
- Results
  - 6 months continuous abstinence

  E-Cig – 7.3% 21 mg. patch – 5.8% Placebo – 4.1%
- Conclusion
  - Nicotine e-cigarettes as effective as patches in helping people quit

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Bullen, C, et al. (2013) . *The Lancet* Electronic cigarettes for smoking cessation: a randomised controlled trial. http://dx.doi.org/10.1016/S0140-6736(13)61842-5

Electronic cigarettes for smoking cessation (cont.)

- No statistical difference between three groups
  - Nicotine patch OR typically around 2.0 at 6 months
  - In this study, E-cigarettes nor patch more effective than placebo
- Limitations
  - Not double blind (patches)
  - May be underpowered due to low absolute abstinence rates

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Viable Stop Smoking Aid?

FDA approved NRT

- Delivers consistent dose
- Reduces cravings & symptoms of withdrawal
- Safe for use
- Highly regulated

Electronic Cigarettes

- Inconsistent dosing in some models
- Efficacy research limited
- Short & long-term safety questions remain
- Little to no regulation

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Legal status worldwide

- 2009 Health Canada decided may pose risk and sales/importation illegal
- Australia classifies as unregulated therapeutic goods, and illegal for sale
- As of 2016 UK will regulate as medicine and require safety and efficacy evaluation

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FDA status

- 2009 – FDA attempts to regulate E-Cigs as drug device
- 2010 – Judge Richard J. Leon states E-Cigs should be regulated as tobacco product
- 2011 – FDA appeals decision and loses
- Coming October 2013
  - Establishing rules to regulate as tobacco, not more strictly as a therapeutic aid

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Restrictions around US

- Sales to minors banned in 24 states as of 09/2013
  - California –e-cigs subject to same restrictions as cigarettes
- U.S. airlines don’t allow them on planes
  - Some airports do allow
- Various states with public & work place restrictions

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Addressing the E-Cig with Patients

- Determine your position
  - Mayo policy
- Discuss with patients
  - OARS
  - Respect autonomy
- Assist with evidence-based tobacco treatment

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Key Points

- Battery-powered device that vaporizes nicotine for inhalation
- Gaining in popularity
- Lack of evidence for safety with long-term use
- Lack of evidence to support use as a treatment to help smokers stop smoking
- Legal status in the US – regulated as tobacco

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