

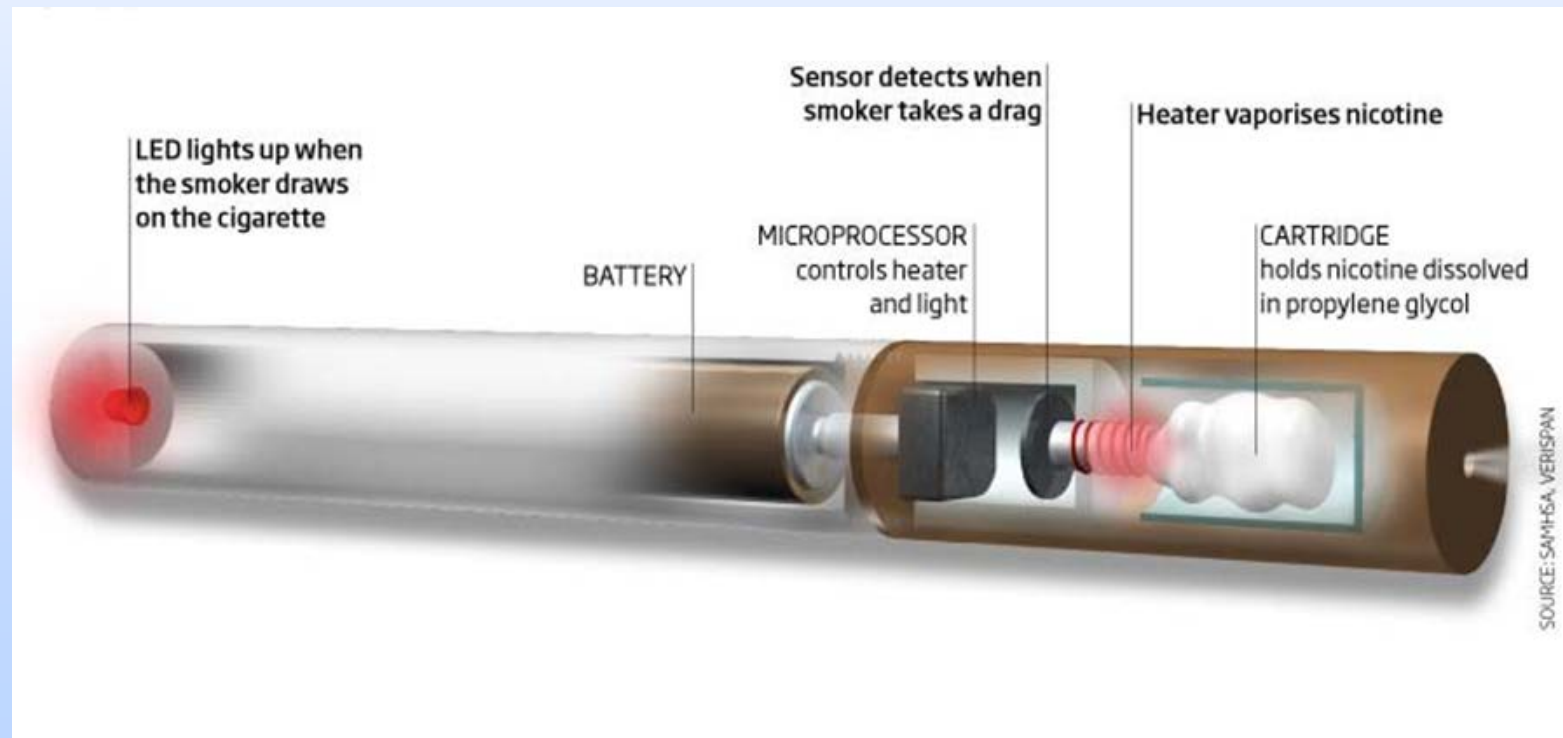


# Electronic Nicotine Delivery Systems

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# Electronic Nicotine Delivery System (ENDS)

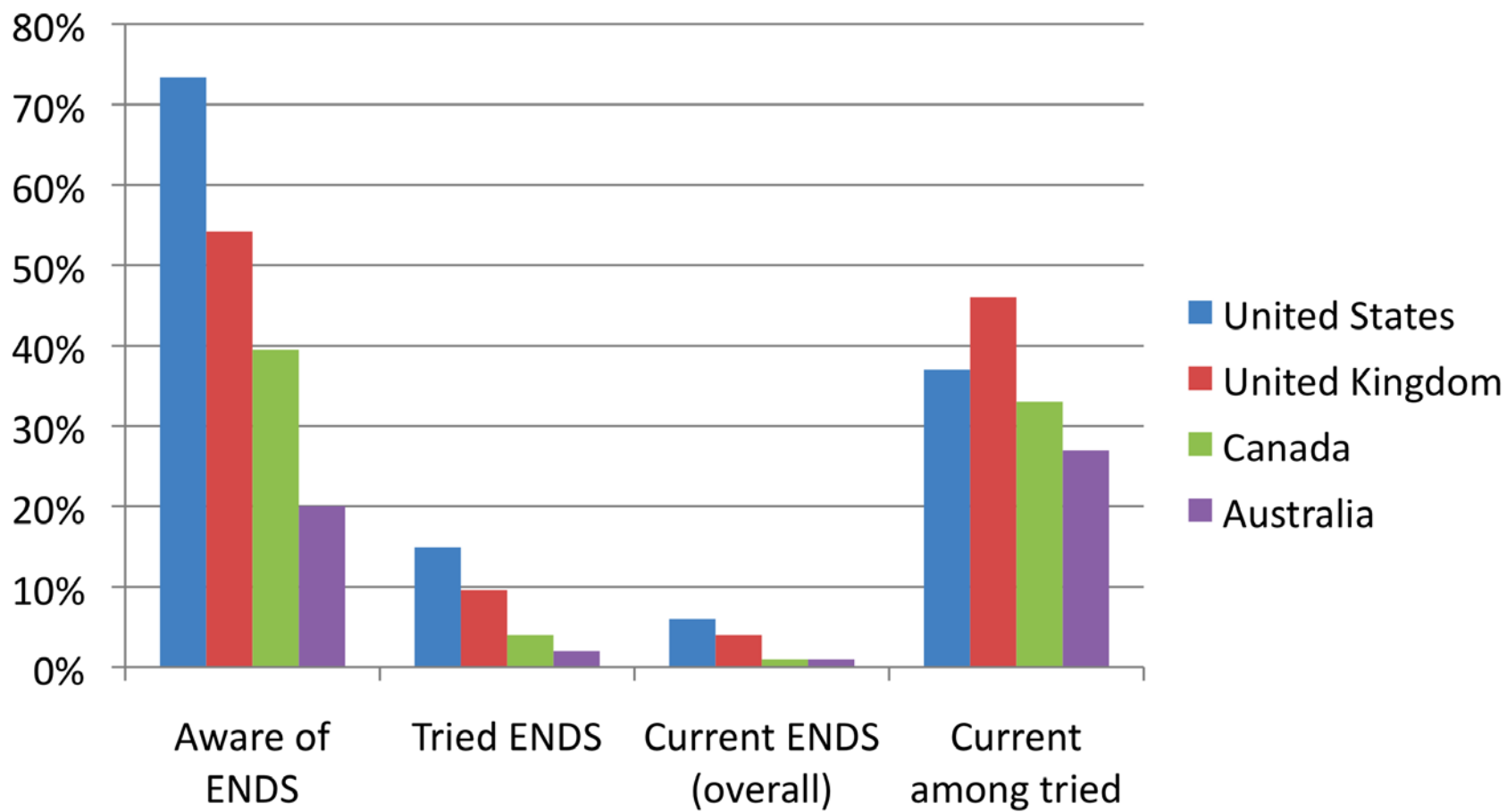
A battery-powered device that provides inhaled doses of vaporized nicotine solution. It is used as an alternative to smoked tobacco products, such as cigarettes, cigars, or pipes.



# 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

# Current and former smokers – 2010







# 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.

# Tobacco companies

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

# Marlboro maker Altria to jump into e-cigarettes

1 Comment /  58 Shares /  12 Tweets /  Stumble /  Email

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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.





# “Vaping”

To inhale vapor from an e-cigarette



# 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



# People are using E-cigarettes:

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

# 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
E-cigarettes taste and smell good	8
Previously failed to quit with either nicotine patch or bupropion	3
To get nicotine	2
<i>Total (from three open-ended fields)</i>	225



Etter JF. BMC Public Health. 2010 May 4;10:20...

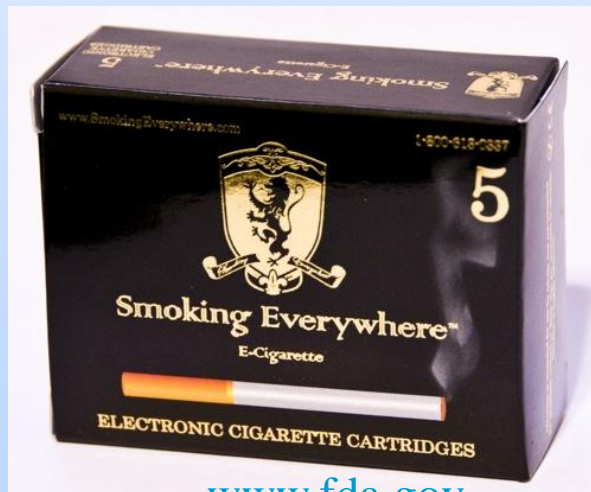
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# Safety Considerations



- 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](http://www.fda.gov)





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



- 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
      - $\beta$ -nicotyrine



# Safety – Short-Term Effects

- Nicotine Poisoning
- Pulmonary Issues
- Cardiovascular Effects



# Health related effects reported by E cigarette Users in Online Forums

## Top Health/Safety Posts

N = 543 Posts

409 symptoms identified

- 78 Positive
- 326 Negative



## E cig in Online forums (cont.)

- Most adverse events occurred in the mouth/throat and respiratory, neurologic and digestive systems.
- Negative symptom reporters often >one symptom
- Positive symptoms usually single event and most frequent in respiratory system

## E cig online forums (cont.)

- Some negative symptoms may be due to nicotine overdose
  - Nausea, vomiting, change in heart rhythm, confusion, dizziness, and fatigue.
- Positive symptoms
  - Improved breathing, less cough, asthma relief, cleared bronchitis.

# Study limitations

- Online forums biased toward negative reporting
- Does not consider past smoking history and pre-existing medical conditions

# Safety – Long-Term Effects

- Research is extremely limited
- Concerns
  - Prolonged inhalation of chemicals
  - Net public health effect

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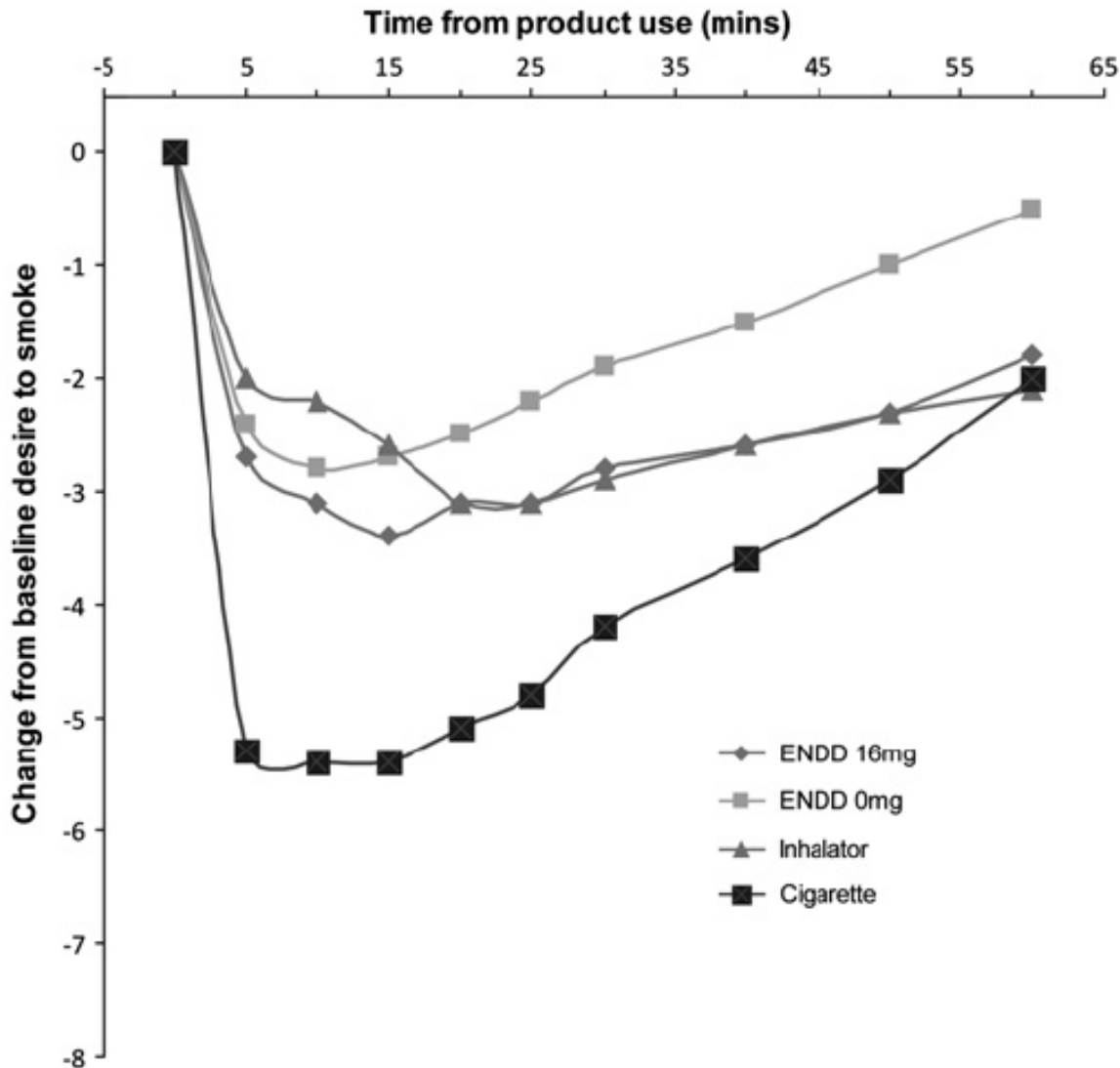


# Efficacy Considerations

# Efficacy of e-cig

- Little data to demonstrate either efficacy or safety
- More research is needed
- A few surveys and small RCTs

## 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  $\geq 10$  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



# Efficacy

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

Three groups of 100 smokers each

## Group A

7.2 mg. nicotine  
cartridges for 12  
weeks

## Group B

7.2 mg. nicotine  
cartridges for 6 weeks  
then 5.4 mg. cartridges  
6 weeks

## Group C

No-nicotine  
cartridges for 12  
weeks.

# Results

- Declines in cpd and CO levels noted in all groups ( $p < 0.001$  vs. baseline)
- No consistent differences among groups
- Smoking reduction noted in 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

# Viability of Stop Smoking Aid?

## FDA approved NRT

- Delivers consistent dose
- Reduces cravings & symptoms of withdrawal
- Effective as smoking cessation treatment
- Highly regulated

## Electronic Cigarettes

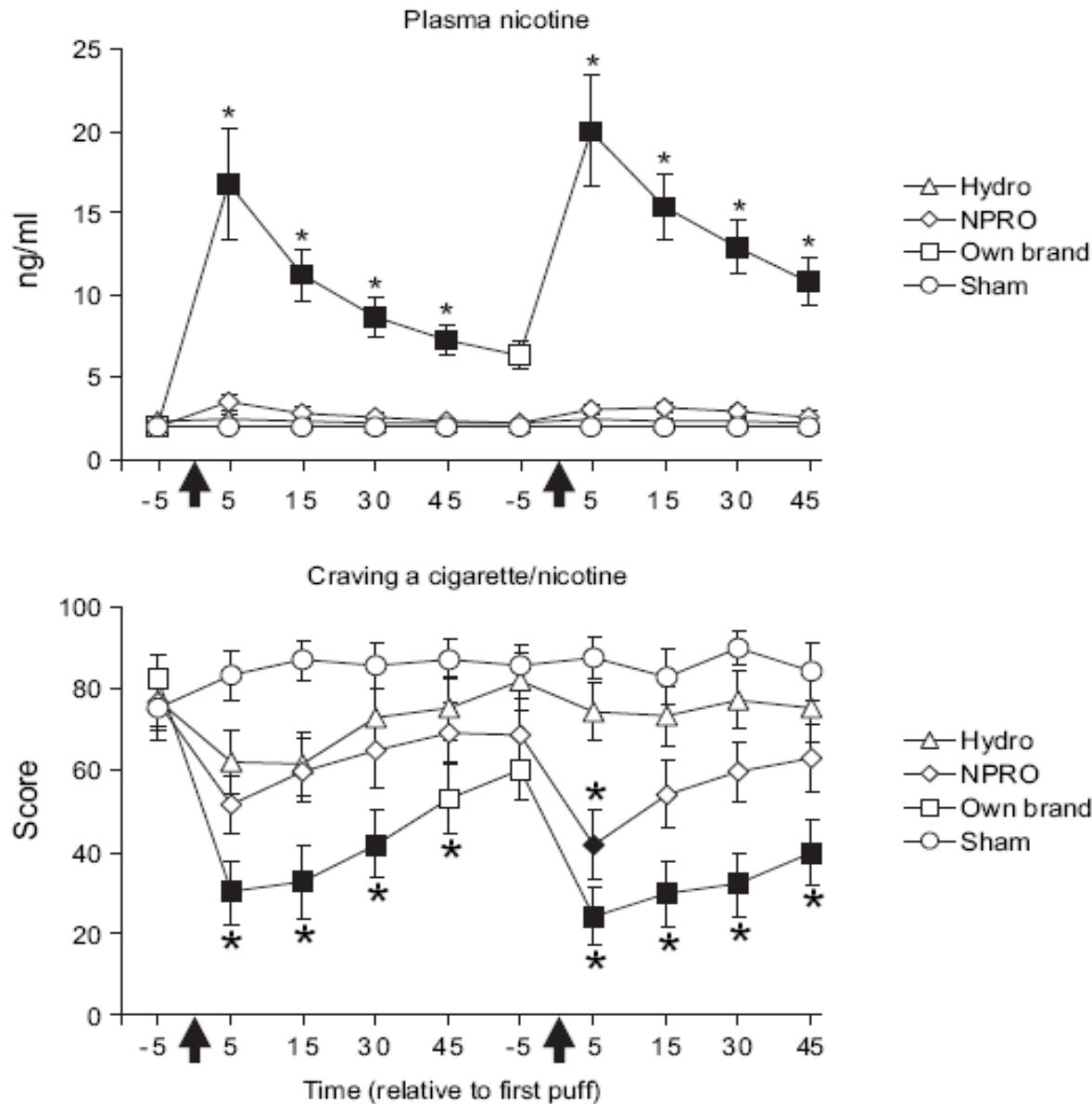
- Research mixed and very limited
- Relying on anecdotal accounts
- Little to no regulation



- 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



# Effects on Desire to Smoke



## Crown 7 Hydro



## Njoy NPRO



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

# Legal status

- 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

# 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
- Establishing rules to regulate as tobacco, not more strictly as a therapeutic aid



# Restrictions on e-cigarettes

- As of July 1 –banned from minors in Indiana  
at least 12 other states –similar ban

--California –e-cigs subject to same restrictions  
as cigarettes

U.S. airlines don't allow them on planes

Some airports do allow

# Addressing the E-Cig with Patients

- Determine your position
  - NDC policy
  - Mayo policy
- Discuss with patients
- Assist with evidence-based tobacco treatment

# 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