

Your Patients and Smokeless Tobacco Products



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Disclosure

- I have no real or perceived vested interests that relate to this presentation nor do I have any relationships with pharmaceutical companies, and/or other corporations whose products or services are related to pertinent therapeutic areas.

Outline

- Tobacco Disease Harm Reduction
- Smokeless Tobacco, Risks and Snus
- Electronic Cigarettes
- Smokeless Tobacco Quitting Guidelines

FSPTC, 2009

- Section 910: Applications for new products
 - Any new product marketed after 2/15/07 will be considered new and needs an application
 - Studies on health risk
 - Full disclosure of ingredients and additives, with description of manufacturing methods
 - Packaging and labeling
 - Within 180 days, the FDA must decide to allow the marketing of the product or reject it
 - If rejected, what can be fixed for approval

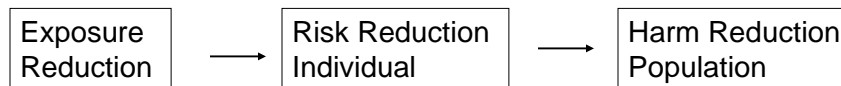
FSPTC, 2009

- Section 911: Modified Risk Tobacco Products
 - Any product marketed to reduce harm
 - Within 2 years define what is a modified risk product and standards for testing (laboratory and human studies, including consumer perception) and post-marketing surveillance
 - Applications include product design, labeling and advertising; and evidence to support the claim includes human testing
 - Decisions within 180 days considers if the product's harm reduction is substantial, whether it increases some exposures, and that the consumer understands the health risk

FSPTC, 2009

- Section 915: Within 36 months, establish rules for testing of tobacco product constituents by brand and sub-brand
- Section 918: Consider fast-tracking cessation products and consider extended-use NRT
- Section 201: 50% of the package and include graphic images
- Section 919: User Fees
 - Year 1: \$85 million
 - Year 10: \$712 million

Methods to Reduce Tobacco Mortality Harm Reduction Paradigm



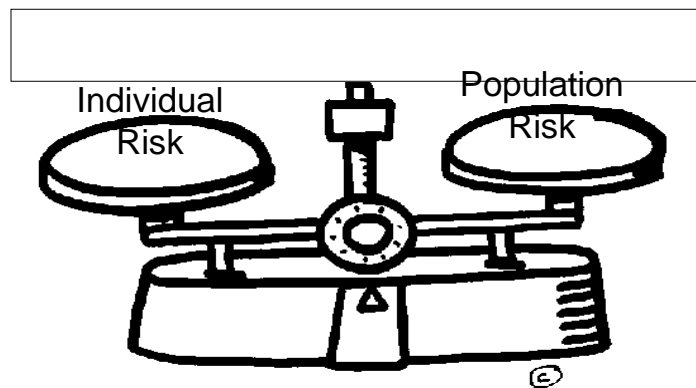
The only known method for harm reduction is complete cessation and long-term abstinence

Potential Reduced Exposure Products

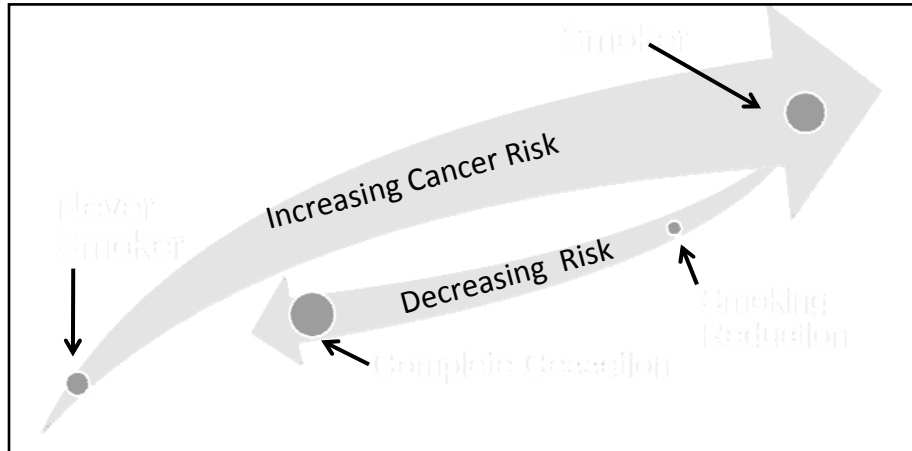
- New tobacco company smoking devices and cigarettes
- Smokeless tobacco
- Nicotine replacement therapy

Is “Less Ought to Be Better”?

- Less is better if the reduction in risk is measurable, and does not adversely affect known ways to reduce smoking and tobacco control measures



The Risk Continuum and Risk Reduction



- The only known way to reduce risk is to stop smoking
 - Risk reduction depends on smoking history and time since quitting
- Risk reduction estimates for smoking reduction are hypothetical, and may not be measurable in smokers

ST Usage

- About 7.6 million Americans use ST
 - 3.3% of adults (aged 18 years and older)
 - 6.5% of men
 - 0.4% of women
 - 7.0% of American Indian/Alaska Natives
 - 4.3% of whites
 - 1.3% of Hispanics
 - 0.7% of African Americans
 - 0.6% of Asian Americans
- Men use ST more than women by 10-fold
- Most commonly used by young adults up to the age of 25
 - Young white males
 - 13.4% of high school males
 - 2.3% of high school females

http://www.cdc.gov/tobacco/basic_information/smokeless/

Different Types of ST

- Different types available
 - Spit tobacco is ST, so-called because it makes the user salivate and both the tobacco and the saliva is spit.
- Snuff – finely ground or shredded
 - A pinch is either snuffed through the nose or placed between the cheek and gum
 - Dry (fire cured and comes as powder; 1.5% of market) or moist (cured and fermented and comes as fine particles in cans; 73% of market)
 - Newer versions come in sachets
- Chewing tobacco – A wad of tobacco is placed inside the cheek
 - Loose leaf (strips sold in foil pouches; 24% of market), plug (firm or moist as cake or plug; <1% of market) or twist (cured and resembles a rope; <1% of market)
- Skoal and Copenhagen have the largest market share (25%/24%)



*IARC Monographs on the Evaluation of
Carcinogenic Risks to Humans*

VOLUME 89

**Smokeless Tobacco and Some
Tobacco-specific N-Nitrosamines**

LYON, FRANCE
2007

5.5 Evaluation

There is *sufficient evidence* in humans for the carcinogenicity of smokeless tobacco. Smokeless tobacco causes cancers of the oral cavity and pancreas.

There is *sufficient evidence* in experimental animals for the carcinogenicity of moist snuff.

Overall evaluation

Smokeless tobacco is *carcinogenic to humans (Group 1)*.

Smokeless Tobacco Ingredients

- Contains over 28 known, probable or possible carcinogens
 - N-nitrosamines, volatile aldehydes, formaldehyde, acetaldehyde, crotonaldehyde, hydrazine, arsenic, nickel, cadmium, benzo(a)pyrene, and polonium-210
 - Using ST does not involve burning or pyrolysis, and so no incomplete combustion
 - The number of carcinogens is substantially less than for cigarette smoke
- The amount of nicotine delivery varies by product, but is typically 3-4-fold higher than a cigarette when it remains in the mouth for about 30 minutes
 - 2 cans per week equivalent to 1.5 packs per cigarettes per day
 - Starter products have less nicotine, e.g., Skoal Bandits



Snus in Sweden

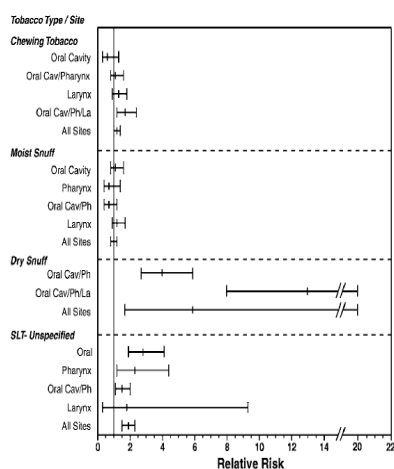
- Sweden has among the lowest rates of smoking and lung cancer among industrialized countries for men
- Sweden is the only country in the EU that allows the use of smokeless products, namely low TSNA snus
- Some tobacco statistics in Sweden:
 - 17.5% of male Swedes in Stockholm are exclusive regular or occasional smokers, but 24.5% of females
 - 12% of male Swedes in Stockholm are exclusive regular or occasional snus users, but 2.2% of females

Official ST Recommendations in U.S.

- 1986 – Surgeon General says that that ST is “is not a safe substitute for smoking cigarettes. It can cause cancer and a number of noncancerous conditions and can lead to nicotine addiction and dependence.”
- 1991 – National Cancer Institute recommends stopping use of all ST
- Developing consensus that ST is an alternative to smoking for smokers who cannot or will not quit???
 - Personal observations
 - Still, ST is not safe

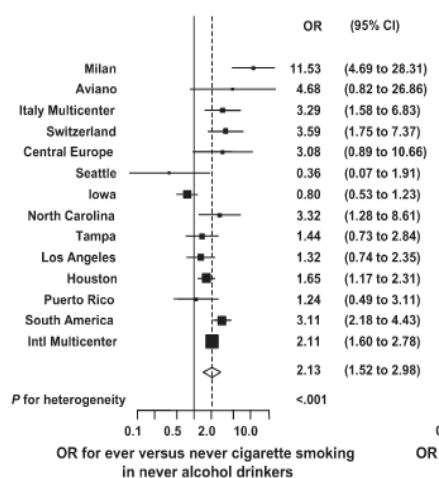
Oropharyngeal Cancer Risk

Smokeless Tobacco



Rodu and Jansson, 2004

Cigarettes



Hashbibe, et al., 2007

Snus and Cancer Risk Swedish Construction Workers

	Number	Person-years	Oral cancer			Lung cancer			Pancreatic cancer		
			Cases	IR	RR (95% CI)†	Cases	IR	RR (95% CI)	Cases	IR	RR (95% CI)
Tobacco use											
Never-users of any tobacco	87821	1751072	50	3.1	1 (ref)	136	8.6	1 (ref)	63	3.9	1 (ref)
Ever-users of snus	37755	698542	10	2.6	0.8 (0.4-1.7)	18	6.4	0.8 (0.5-1.3)	20	8.5	2.0 (1.2-3.3)
Ex-users	2937	50469	1	1.9	0.7 (0.1-5.0)	3	8.5	0.9 (0.3-3.0)	2	6.6	1.4 (0.4-5.9)
Current users	34818	648074	9	2.7	0.9 (0.4-1.8)	15	6.0	0.8 (0.4-1.3)	18	8.8	2.1 (1.2-3.6)
Snus consumed*											
1-9 g/day	6704	134390	2	1.9	0.7 (0.2-2.8)	7	8.6	1.0 (0.5-2.1)	6	7.6	1.9 (0.8-4.3)
≥10 g/day	30683	564152	8	3.1	0.9 (0.4-2.0)	10	4.8	0.7 (0.4-1.3)	13	8.5	2.1 (1.1-3.8)
p for trend					0.8			0.2			0.01

Exposure status was that noted at entry. RR estimates obtained in models adjusted for attained age as time scale and BMI. IR=incidence rate per 100 000 person-years, standardised to age distribution of person-years experienced by all workers using 5-year age categories. *Analysis excluded 368 snus users without dose information, therefore totals for number of cases in dose-specific categories do not match exactly with corresponding totals of cases in ever-users.

Table 3: Relative risks of oral, lung, and pancreatic cancer in relation to snus use in 125 576 never-smokers

Luo, et al, 2007

Smoking and Cancer Risk Swedish Construction Workers

	Number	Person-years	Oral cancer			Lung cancer			Pancreatic cancer		
			Cases	IR	RR (95% CI)	Cases	IR	RR (95% CI)	Cases	IR	RR (95% CI)
Never-users of any tobacco	87821	1751072	50	3.1	1.0 (ref)	136	8.6	1.0 (ref)	63	3.9	1.0 (ref)
Ever-smokers	154321	3153168	198	5.3	2.0 (1.4-2.7)	2062	54.7	7.2 (6.0-8.5)	385	10.2	2.8 (2.1-3.7)
Ex-smokers	51012	1069923	48	3.1	1.1 (0.8-1.7)	329	19.8	2.6 (2.2-3.2)	105	6.3	1.8 (1.3-2.4)
Current smokers	103309	2083245	150	6.9	2.5 (1.7-3.5)	1733	82.3	10.2 (8.6-12.2)	280	13.0	3.5 (2.6-4.6)

Combined use of snus and smoking tobacco was allowed in these analyses, but 37 755 men who used snus only were excluded. IR=incidence rate per 100 000 person-years, standardised to age distribution of person-years experienced by all workers using 5-year age categories. *RR estimates obtained in models adjusted for attained age as time scale, BMI, and snus use.

Table 2: Relative risks of oral, lung, and pancreatic cancer in relation to tobacco smoking status at entry

Luo, et al, 2007

Similar Exposure to a Tobacco-Specific Carcinogen in Smokeless Tobacco Users and Cigarette Smokers

Stephen S. Hecht,¹ Steven G. Carmella,¹ Sharon E. Murphy,¹ William T. Riley,² Chap Le,¹ Xianghua Luo,¹ Marc Mooney,¹ and Dorothy K. Hatsukami¹
 Cancer Epidemiol Biomarkers Prev 2007;16(8). August 2007

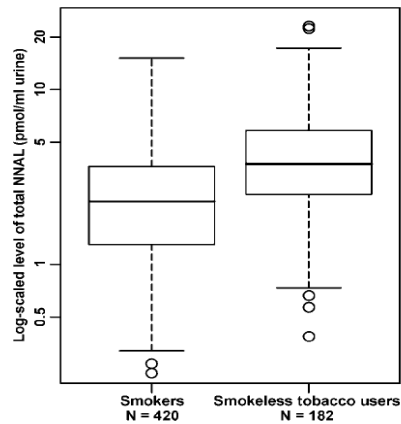
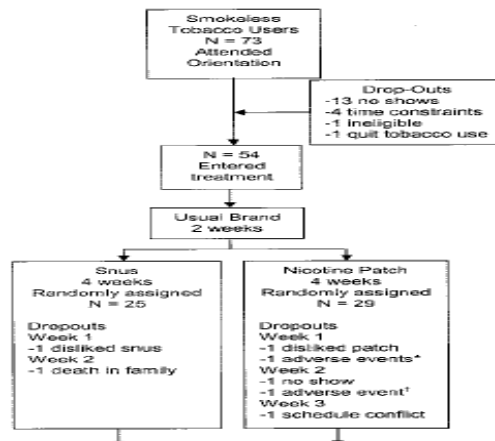


Figure 1. Log-scaled level of total NNAL (pmol/ml urine) in the urine of

Evaluation of Carcinogen Exposure in People Who Used “Reduced Exposure” Tobacco Products

Dorothy K. Hatsukami, Charlotte Lemmonds, Yan Zhang, Sharon E. Murphy, Chap Le, Steven G. Carmella, Stephen S. Hecht

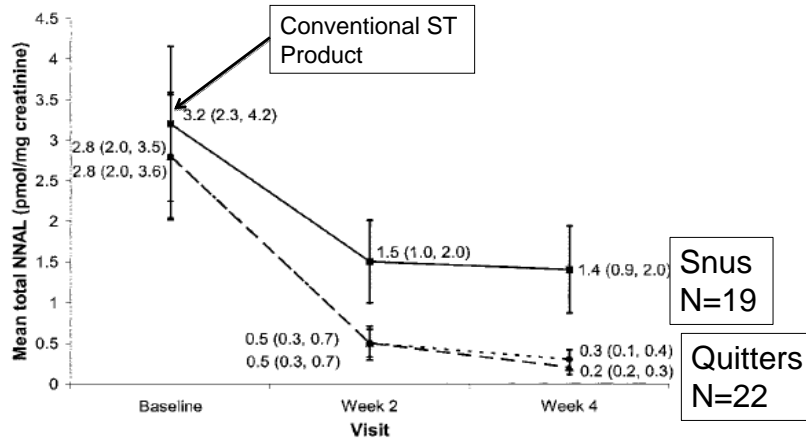
Journal of the National Cancer Institute, Vol. 96, No. 11, June 2, 2004



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Journal of the National Cancer Institute, Vol. 96, No. 11, June 2, 2004



All the fuss about smoking got me thinking I'd either quit or smoke True.

I smoke True.

Ca. 1970

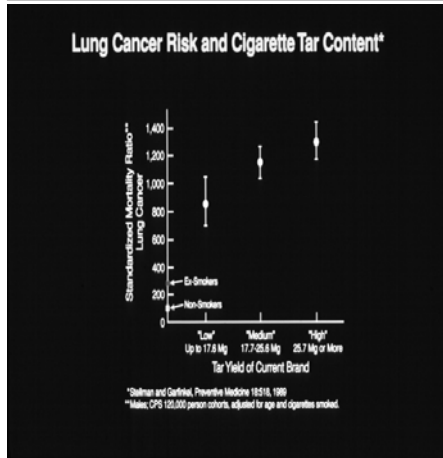
Regular 11 mg. "tar", 0.9 mg. nicotine, 100's. Menthol 13 mg. "tar", 0.8 mg. nicotine, av. per cigarette. FTC Report April 75.

Warning: The Surgeon General Has Determined That Cigarette Smoking is Dangerous to Your Health.

The low tar, low nicotine cigarette. Think about it.

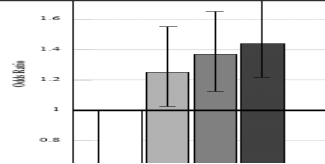
Incorrect Interpretations from Epidemiology – CPS1 *“If you cant quit, switch to lights, just don’t compensate”*

1989 Publication – Lung Cancer Mortality

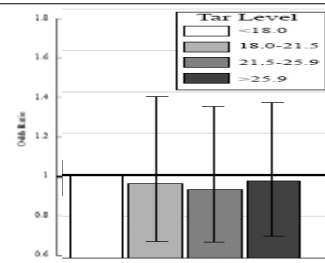


Baseline Analysis

Monograph 13, 2002 – Odds Ratios



Baseline Analysis



Flat CPD and no Quitters

“Are E-Cigarettes a Bridge Product to Smoking or Abstinence? Or Neither?”



Gift Wrap Gift Certificates Saving Calculator

E-CIGARETTES CHOICE

HOME HOW IT WORKS BENEFITS TESTIMONIALS

BROWSE

OUR CATEGORIES

- Starter Kits
- Starter Kit Bundles
- Disposable E-Cigs
- Refill Cartridges
- E-Liquid
- Batteries & Chargers
- E-Cigarette Skinz
- Accessories
- Vaporizers

E-CIGARETTE ORDERS/EMAILS

CHEAPER THAN TOBACCO CIGARETTES
NO SECOND-HAND SMOKE

It doesn't take a degree in rocket science to know that tar and a few thousand other ingredients — including the 70 or so known carcinogens and poisons found in cigarette tobacco make these seem like a blessing. E cigarettes have no tobacco, smoke, or combustion involved in their operation. E-Cigarettes contain about 20 ingredients which are used in our food, health and beauty products. E cigarettes have about the same amount of TSNA's (tobacco specific nitrosamines) as in FDA approved Nicotine Replacement Therapy products.


Toxic Tobacco Smoke contains many additional chemicals, including tar and Carbon Monoxide. Tar is a sticky substance that forms in the lungs, causing lung cancer and respiratory distress. Tobacco is the leading cause of preventable death in the world and is responsible for more than 5 million deaths each year.

Carbon monoxide limits the amount of oxygen that the red blood cells spread throughout your body causing the smoker to become easily winded when exercising or performing strenuous life functions including sex.

Buying tobacco cigarettes is expensive. In most areas of the US the cost is more than two times the amount you will spend on our No7 rechargeable/refillable kits per year because of taxation. We deliver to your door. That means you also save the time and expense of traveling to the store.

There has never been a forest fire or house fire blamed on the electronic cigarette. No hot ash to burn clothing and furniture.

- “Lacks known carcinogens and poisons in cigarette smoke
- No combustion
- Contains ingredients found in food and beauty products
- Same amount of TSNA as NRT
- Lacks tar, which causes lung cancer
- Lacks CO that causes windedness during sex
- Cheaper than cigarettes
- No hot ash to cause fires”



RECEIVE COUPON CODES
Receive new Coupon Codes, Submit your email & enjoy Offers.

SUBMIT

Lots of Competition

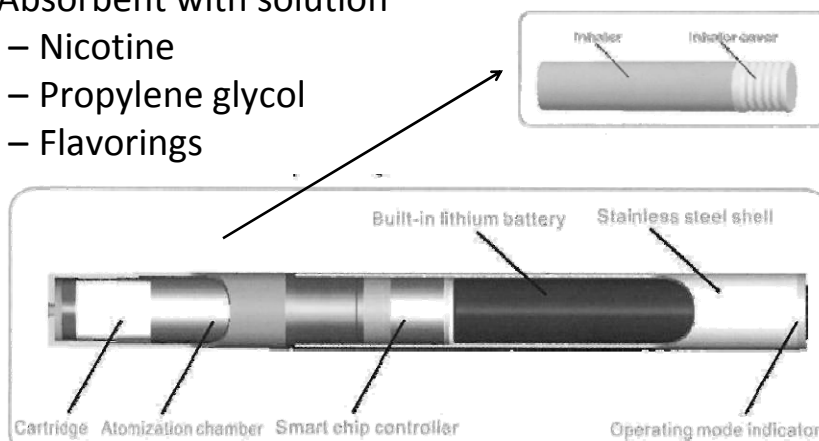


“Electronic cigarette uses advanced microelectronic technology and supercritical physical atomization technology to atomize the high-purity and exciting nicotine dilution extracted from tobacco into smoke for smoker’s sucking and accordingly meet the needs of those smokers.”

- Smoking Anywhere Manual

E-Cigs Common Components

- Battery
- Heating element
- Absorbent with solution
 - Nicotine
 - Propylene glycol
 - Flavorings



Refill Process



Scientific Evaluation of ENDS and Associated Health Claims

- Safety Assessment
 - Chemical and toxicological studies of filler and aerosol
 - Human use conditions (limited human testing)
 - Comparator is other nicotine delivery devices
- Health claims assessment
 - Randomized switching studies and cross-sectional studies, accounting for compensation
 - Consumer use, perception and abuse liability measures
 - Biomarkers and Topography
 - Adverse Events
- Surveillance – use, impact on smoking, and health effects

FDA Testing Of ENDS - Methods



- Small pilot study
- Compared “Njoy” and Smoking “Everywhere” to Nicotrol Inhaler
- Analyzed cartridge content and the vapor specifically for nicotine, tobacco smoke alkaloids, TSNAs, and DEG
- 100 cc puffs every 60s

FDA Testing Of ENDS - Findings

- Lower nicotine content and delivery than claimed, although FDA concluded that “high” yields exceeded Nicotrol levels
 - QC issues and the 0 nicotine cartridges still had some nicotine
- TSNAs found at trace levels
- Diethylene glycol found in one cartridge
 - DEG is not in cigarettes
- Anabasine detected in some cartridges

FDA Nicotine Testing

Product	Nicotine/Cartridge (mg)		Nicotine/puff (ug)		
	Manufacturer Claim	FDA Report	Manufacturer claim	FDA per 100ml puff	Applies to Apples
Smoking Everywhere – High	16 (20 cigs)	5.98	NA	31.5	<ul style="list-style-type: none"> • 1 cartridge = 20 cigarettes • See note*
Njoy - Menthol High	18 (20 cigs)	6.76	NA	26.8-43.2	1 cartridge = 20 cigarettes
Nicotrol Inhaler	10 (1 cig)	Not tested	50**	15.2	80 puffs over 20min = 1 cigarette

*"Security system which stops automatically if too many inhalations occur within a short time space ..."
 **Nicotrol inhaler puff yield calculated by prescribing info claim of 4 mg yield based on 80 deep inhalations over 20 minutes (50% absorption follows, mostly through buccal mucosa)

FDA Testing Limitations

- Pilot study with sound methodology
- Unknown optimal puffing profile
 - Initial use and compensatory use for smokers, former smokers and initiators
 - Puff volume, duration, frequency and number of puffs
- Unknown changes in vapor with later puffs or battery charge
- Limited chemical assessment
- Not a market survey
- Not a human study with biomarkers

Laugesen Report - 2008

- Ruyan e-cigarette
- Private company – Health New Zealand
 - Assays done by commercial laboratories funded by company
- Methods
 - Variety of methods to detect multiple chemical constituents
 - Puffing methods poorly described
- Also found trace levels of TSNA in the cartridge
- Other compounds detected
 - Acetaldehyde
 - Acetone
 - Formaldehyde
 - PAHs
- Lower levels than cigarettes, but higher than FDA-approved NRT
- Limitations of FDA testing apply here

Laugesen Report - 2008

- “Propylene glycol is virtually non-toxic”
 - Effects of electronic heating not tested on long term toxicity including cancer for humans or animals
 - “Fog machine analogy” and cosmetics does not apply
 - Metabolism is different for persons with kidney and liver disease, some racial groups
 - Higher levels than in tobacco

Unintended Consequences of ENDS – What needs to be studied?

- Exposure to harmful chemicals leading to health effects such as lung and other cancers through laboratory and human studies
- Nicotine toxicity
- Delaying or subverting smoking cessation
- Enticing former smokers to resume smoking
- Serving as a gateway for new smokers

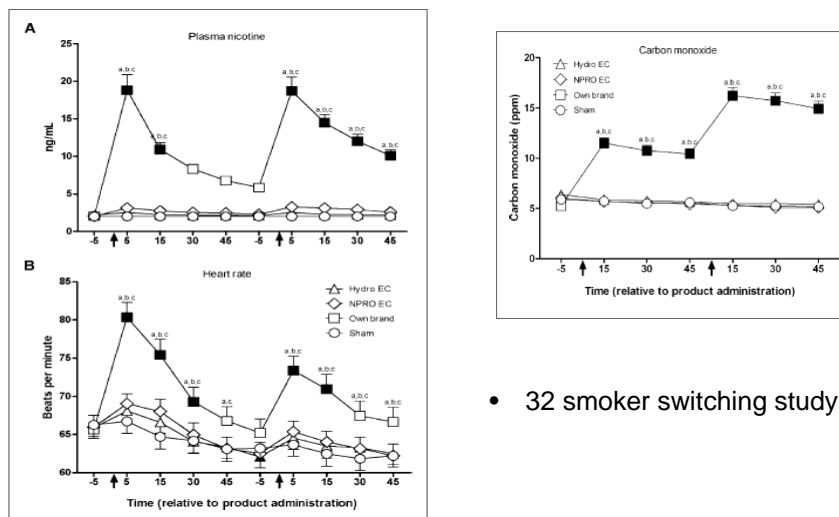
Cancer Epidemiol Biomarkers Prev; 19(8) August 2010

Research Article

Cancer
Epidemiology,
Biomarkers
& Prevention

A Clinical Laboratory Model for Evaluating the Acute Effects of Electronic “Cigarettes”: Nicotine Delivery Profile and Cardiovascular and Subjective Effects

Andrea R. Vansickel, Caroline O. Cobb, Michael F. Weaver, and Thomas E. Eisenberg

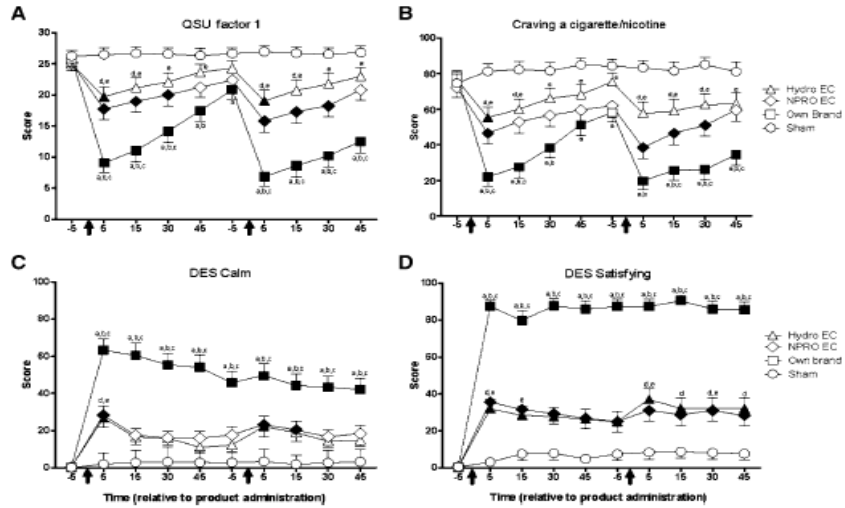


- 32 smoker switching study

Research Article

A Clinical Laboratory Model for Evaluating the Acute Effects of Electronic “Cigarettes”: Nicotine Delivery Profile and Cardiovascular and Subjective Effects

Andrea R. Vansickel, Caroline O. Cobb, Michael F. Weaver, and Thomas E. Eisenberg



Research paper

Effect of an electronic nicotine delivery device (e cigarette) on desire to smoke and withdrawal, user preferences and nicotine delivery: randomised cross-over trial

C Bullen,¹ H McRobbie,² S Thornley,³ M Glover,⁴ R Lin,⁵ M Laugesen⁶

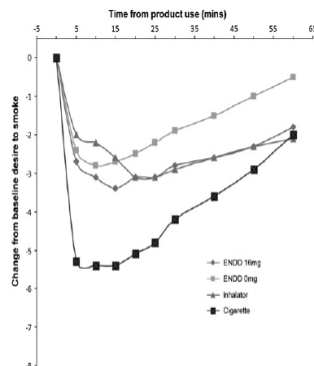


Figure 2 Change in desire to smoke from baseline over the first hour after each product use.

Table 3 Pharmacokinetic properties of usual cigarette, 16 mg ENDD and Nicorette inhalator

Product	Mean tmax (min) (95% CI)	Mean Cmax (ng/mL) (95% CI)*
Usual cigarette (n 9)	14.3 (8.8 to 19.9)	13.4 (6.5 to 20.3)
16 mg ENDD (n 8)	19.6 (4.9 to 34.2)	1.3 (0.0 to 2.6)
Nicorette inhalator (n 10)	32.0 (18.7 to 45.3)	2.1 (1.0 to 3.1)

ENDD, electronic nicotine delivery device.

*Corrected for baseline nicotine levels.

- 40 smoker switching study

ST Addiction

- ST habits develop from nicotine addiction
 - Not getting sick when using ST
 - Dip in different settings
 - Switching to stronger products
 - Swallows juice
 - Sleeps with dip or chew in mouth
 - Dips or chews first thing in the morning
 - Strong cravings

ST Cessation - I

- Utilize evidence-based treatment, counseling techniques and referral options
 - Target nicotine addiction
- Recommendations mimic smoking cessation guidelines
 - Develop the intent to quit
 - Identify your reasons
 - Choose a quit date, but not today. Consider why that date
 - Cut back before you quit by tapering down and using ST in less places
 - Identify substitutes, e.g., sugar-free gum, sunflower seeds
 - Identify your triggers, e.g., meals, working out, driving, at work
 - Delay acting on your cravings – about 10 minutes at first
 - Switch to lower nicotine product, but avoid increasing use

ST Cessation - II

- Have a quit plan
 - Have a substitute to satisfy craving
 - Change routines to avoid triggers
 - Remove all ST from home, car, work, etc.
 - Avoid drinking alcohol
 - Get your teeth cleaned
 - Avoid ST-using friends
 - Rally your support team and keep busy with them
 - Utilize quit lines and/or classes
 - NRT and Chantix – not approved by FDA for ST because of insufficient research
 - Some forms of NRT might better mimic ST use (lozenge and gum), but nicotine delivery is much less
 - Other quitting aids not tested: hypnosis, acupuncture, herbs and supplements, tobacco lozenges

ST Cessation - III

- Deal with withdrawal symptoms
- Have a plan for slips – most ST users do not quit the first time
 - Avoidance is first plan
 - Don't rationalize
 - If a slip occurs, slip back to the quit
 - Do not equate slipping with failure
 - Make a new quitting plan if the slip transitions to a relapse that includes addressing why you slipped and what did not work

Reasons People Quit ST

- To avoid health problems
- To prove I can do it
- I have sores or white patches in my mouth
- To please someone I care about
- To set a good example for my kids or other kids
- To save money
- I don't like the taste
- I have gum or tooth problems
- It's disgusting
- Because it's banned at work or school
- I don't want it to control me
- My girlfriend (or a girl I'd like to date) hates it
- My wife hates it
- My physician or dentist told me to quit

(<http://www.nidcr.nih.gov/OralHealth/Topics/SmokelessTobacco/>)

Nicotine Withdrawal Symptoms

- Dizziness (which may last only 1 or 2 days after quitting)
- Depression
- Feelings of frustration, impatience, and anger
- Anxiety
- Irritability
- Trouble sleeping (including trouble falling asleep and staying asleep, and having bad dreams or even nightmares)
- Trouble concentrating
- Restlessness
- Headaches
- Tiredness
- Increased appetite

<http://www.cancer.org/Cancer/CancerCauses/TobaccoCancer/SmokelessTobaccoandHowtoQuit/index>

Withdrawal Symptoms Response

- Urges and cravings -- especially in the places you used to use most
 - Wait it out, deep breathing and exercise
- Feeling irritable, tense, restless, impatient
 - Walk away from the situation. Deep breathing and exercise. Ask others to be patient.
- Constipation/irregularity
 - Add fiber to your diet
- Hunger and weight gain
 - Eat regular meals. Feeling hungry is sometimes mistaken for the desire to dip or chew
 - Drink lots of water
 - Increase physical activity to increase metabolism
- Desire for sweets
 - Reach for low-calorie sweet snacks (like apples, sugar-free gums and candies).

Summary

- Harm reduction strategies are integrated into FDA legislation
 - Still a research question
- ST is still considered not safe
 - As an alternative to smoking remains a research question
 - Impact on use and harm
- Snus does not appear to be worse than U.S. conventional ST, and may be better, but impacts on ST use and smoking needs to be evaluated
- E-cigs draw lots of media attention
 - Actual use unclear
 - Nicotine delivery device that needs evaluation by FDA
- Primary mission for tobacco control is cessation of all tobacco products
 - ST cessation counseling mimics smoking cessation counseling

Thank You