

# **The Evolving Cigarette: Implications for Public Health**

K. Michael Cummings, PhD, MPH  
Medical University of South Carolina  
22nd Century Group's Annual Shareholders Meeting  
April 29, 2017

# *Outline for my talk*

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- Why people smoke?
- Nicotine and the modern cigarette
- The consequences of nicotine addiction
- Why not remove the nicotine?
- Nicotine removal as a basis for tobacco regulation
- Prospects for very low nicotine (VLN) tobacco in the US and elsewhere





WHY DO  
PEOPLE  
SMOKE?



Doc Doctors Ought to Care

# 1988, the reason for continued smoking is redefined



## **The Health Consequences Of Smoking**

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### **NICOTINE ADDICTION**

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*a report of the  
Surgeon General*

**1988**

After carefully examining the available evidence, this Report concludes that:

- Cigarettes and other forms of tobacco are addicting.
- Nicotine is the drug in tobacco that causes addiction.
- The pharmacologic and behavioral processes that determine tobacco addiction are similar to those that determine addiction to drugs such as heroin and cocaine.



# The New York Times

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NEW YORK, FRIDAY, APRIL 15, 1994

75 cents beyond the greater New

## *Tobacco Chiefs Say Cigarettes Aren't Addictive*



Stephen Crowley/The New York Times

Top executives from seven tobacco companies, at a hearing on smoking. They are identified on page A20.

# Why they lied...

TI memo, 1980

September 9, 1980

MEMORANDUM

TO : Mr. Kloepper  
FROM: Mr. <sup>PK</sup>Knopick

Attached please find the technical review of the conference which led to Victor Cohn's "surprise" story of 8/30 that the National Insti-

I'm told, that the entire matter of addiction is the most potent weapon a prosecuting attorney can have in a lung cancer/cigarette case. We can't defend continued smoking as "free choice" if the person was "addicted."

the rise in marijuana use.

In NL 188, we quoted Pollin's predecessor, Dr. Robert DuPont:  
"Cigarette smoking is more addictive than using heroin, hooking two-thirds of the people who ever smoke."

Isn't the question twofold?

0000135335

Did TI miss a chance to attend and present information at NIDA's 1979 meeting which developed the "addictive" language?

Did TI see ADAMHA's newsletter and was it therefore better prepared to respond when this matter became public?

# Nicotine and the modern cigarette



# The American Blend

- Virginia tobacco is flue cured. Flue curing involves the use of heat which turns the green leaves to a bright (hence the name) golden brown color.
- Burley tobacco has a higher amount of nicotine, but can be hard to inhale unless mixed with other tobaccos. Burley tobacco is typically air cured.
- Oriental tobacco also referred to as Turkish tobacco is low in nicotine content and is added to the American blend because of its flavor characteristics. Oriental tobacco is sun cured.





# Total Cigarette Consumption – USA



# Total Cigarette Consumption – USA



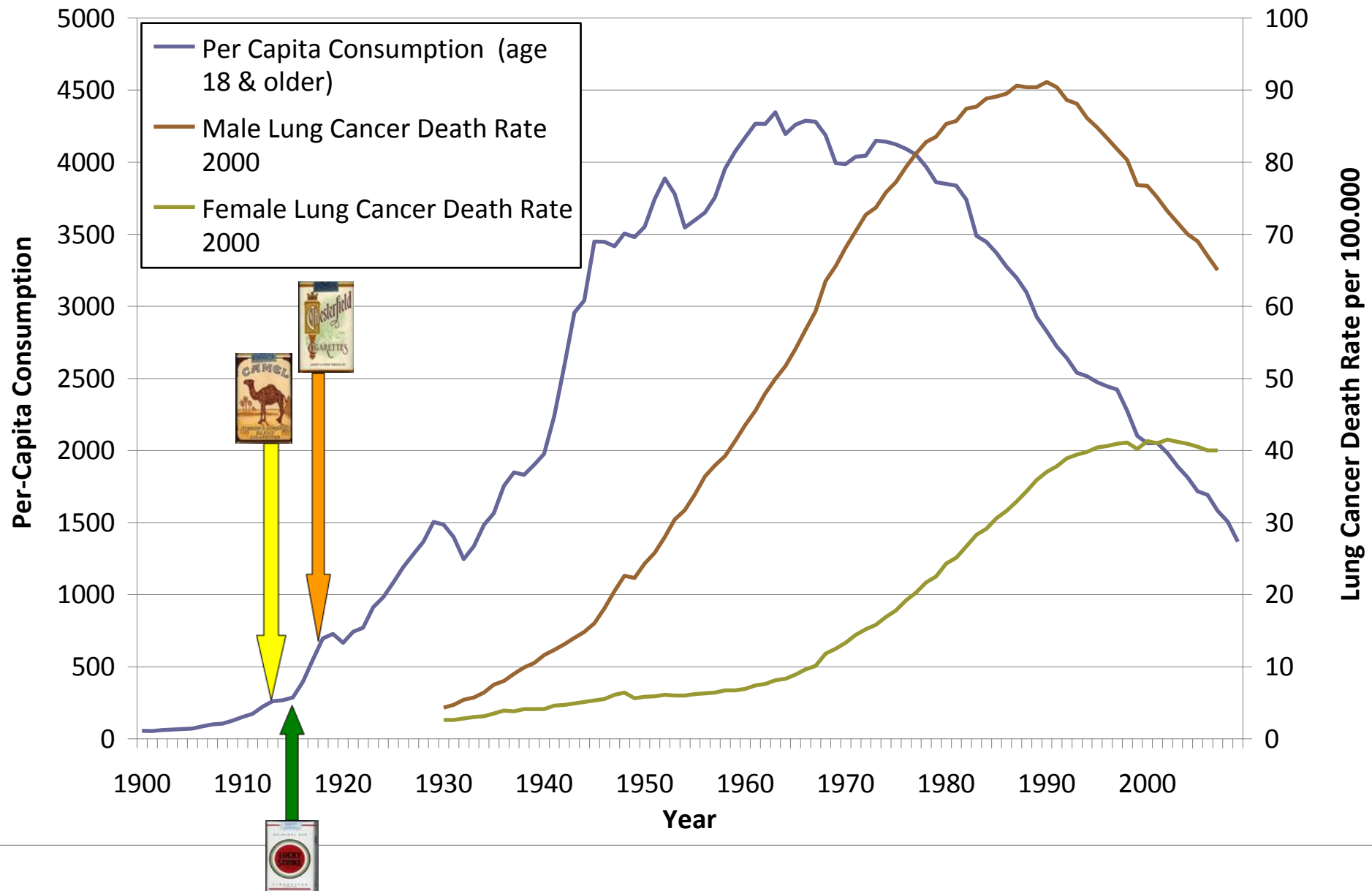
# **The consequences of nicotine addiction**



# MAN-MADE EPIDEMIC

Section IX. Appendix 16 - Physical Documents  
22nd Century Group, Inc.  
MRTPA for VLN™ Cigarette Brand

## Per-Capita Consumption and Lung Cancer Death Rates

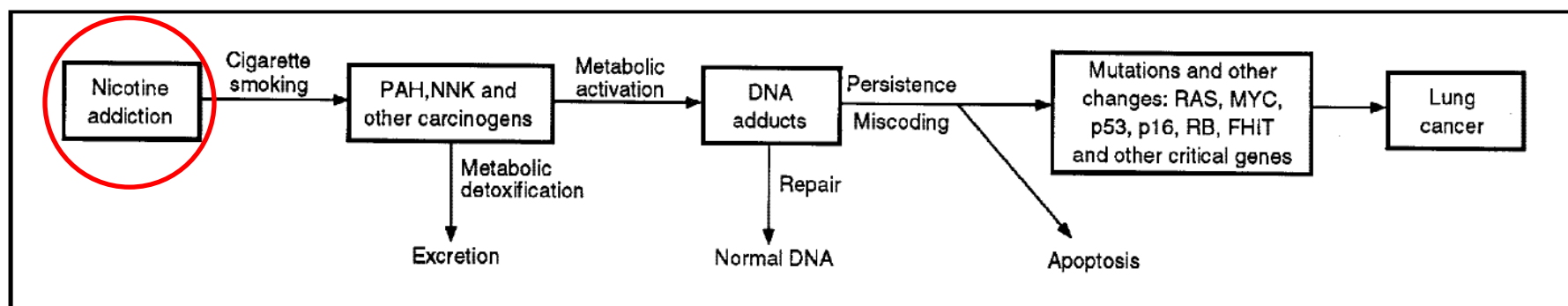


# Annual number of reported lung cancer deaths 1890-2017 (USA) <sup>(1)</sup>

<b>1890's</b>	<b>145</b>
<b>1930</b>	<b>&lt;3,000</b>
<b>1950</b>	<b>18,000</b>
<b>1955</b>	<b>27,000</b>
<b>1962</b>	<b>41,000</b>
<b>2017</b>	<b>~160,000</b>

(1) 1964 Surgeon General's Advisory Committee (Page 25) and the American Cancer Society. Cancer Facts & Figures

# How does cigarette smoking cause cancer?

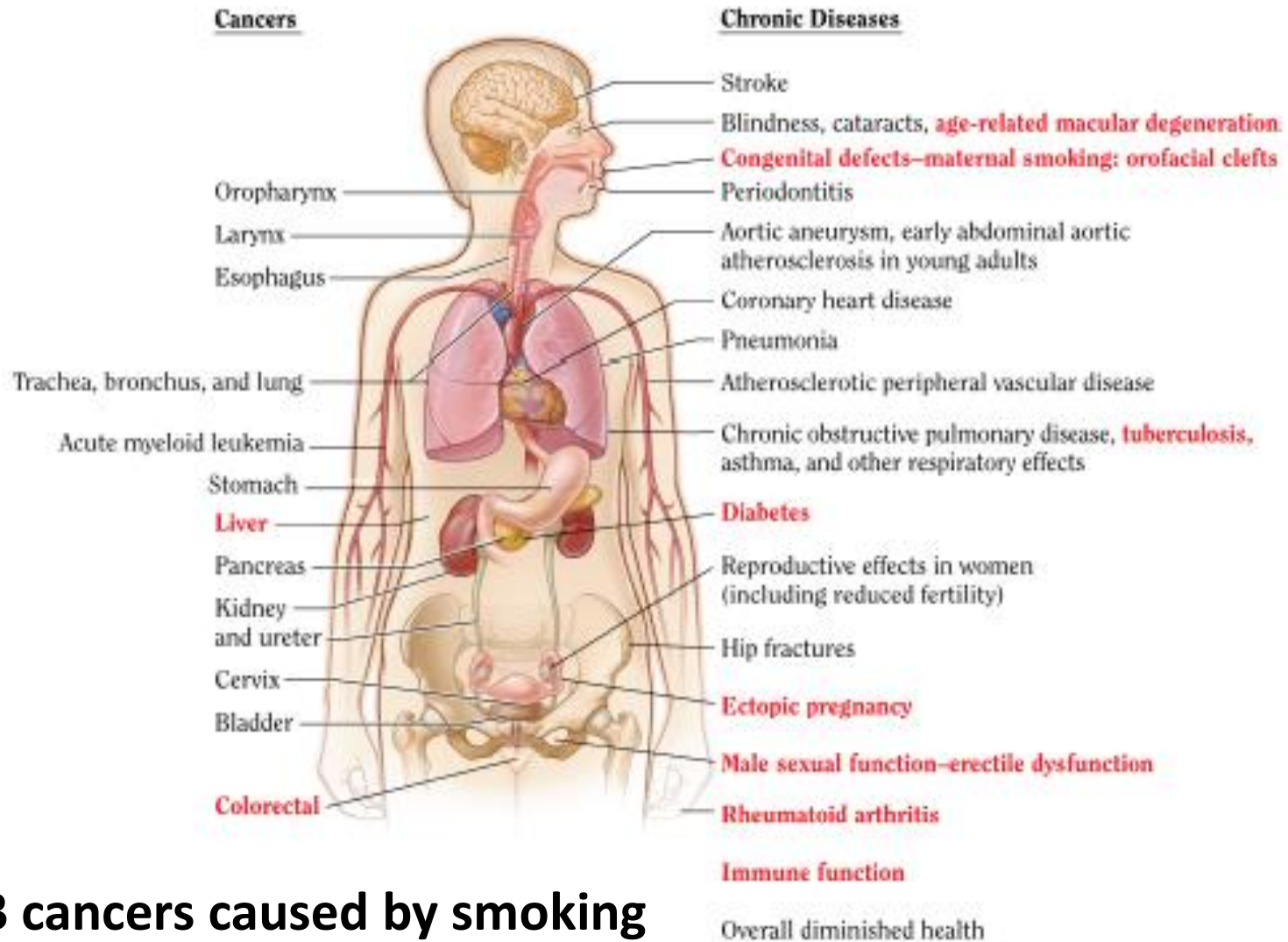


**Fig. 1.** Scheme linking nicotine addiction and lung cancer via tobacco smoke carcinogens and their induction of multiple mutations in critical genes. PAH = polycyclic aromatic hydrocarbons; NNK = 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone.



**1 out of 3  
cancer deaths  
due to smoking**

**Figure 1A The health consequences causally linked to smoking**



**13 cancers caused by smoking**

Source: USDHHS 2004, 2006, 2012.

Note: The condition in **red** is a new disease that has been causally linked to smoking in this report.

# Global Impact in the 21<sup>st</sup> Century

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Nicotine



Addictive Cigarette Use



1 billion premature deaths

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**Why not remove  
the nicotine?**



# Money

## American Tobacco Company

*Light Smoke pamphlet: "it is quite possible to 'denicotinize' a cigarette."*

1936

### Improving the Taste and Character of Cigarette Tobacco

The reduction of these irritant compounds obviously constitutes one of the most important advances made in the processing of cigarette tobaccos during the past quarter century. In the opinion of leading independent research groups, chemists, and physicians who have examined the work in detail, this reduction is one of the most helpful safeguards to the smoker.

#### **CONTROLLING NICOTINE CONTENT**

It is quite possible to "denicotinize" a cigarette by chemical and thermal methods. The makers of Lucky Strike Cigarettes deliberately refrain from this because:

- (1) Such removal of nicotine cannot be secured without affecting adversely certain other desirable taste-constituents.
- (2) Such removal of nicotine produces an emasculated cigarette, shorn of those very qualities which give a cigarette character and appeal.

# RJR 1982 – Nordine Study

However, we cannot ever be comfortable selling a product which most of our customers would stop using if they could. That is to say, if the exit gate from our market should suddenly open, we could be out of business almost overnight.

- Some slow but steady "progress" is being made in developing techniques for stopping smoking; but no universal, easy method is yet in sight.
- The probability of such a method appearing in the near term is small.
- The probability of such a method appearing over the long term approaches 100%.
- If/when that occurs, our options include:

- (1) Go out of business.
- (2) Find a way to eliminate the desire of smokers to stop smoking.
- (3) Provide other products, away from conventional cigarettes, which meet the same needs cigarettes now meet, but without the associated negatives.



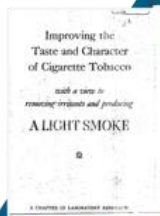
**Cigarettes are  
designed to be  
hard to quit**



## Blending to Optimize Nicotine

Tobacco companies have developed sophisticated R&D programs to maximize nicotine delivery focusing on tobacco blending, the use of additives, and engineering.

### Blending for Nicotine Delivery



#### 1935 Early Nicotine Manipulation

A 1935 American Tobacco Company document noted that the "removal of nicotine produces an emasculated cigarette, some of those very qualities which give a cigarette character and appeal."

1935, American Tobacco Company



"Cigarette smoke should contain as little as possible (preferably at the zero level) of the polycyclic hydrocarbons, should possess satisfactory flavor to please the consumer, and should contain sufficient nicotine to supply the necessary requirements of the smoker with respect to this compound (nicotine)."

1959, Dr. Alan Rodgman, Analytics Chemist,  
R.J. Reynolds Tobacco Company

The nicotine delivery of a cigarette is carefully engineered into the product "we can regulate fairly precisely the nicotine and sugar levels (in tobacco) to almost any desired level management might require."

1963, R.B. Griffith, Brown & Williamson Director of Research

"In a sense, the tobacco industry may be thought of as being a specialized, highly ritualized, and stylized segment of the pharmaceutical industry. Tobacco products contain and deliver nicotine, a potent drug with a variety of physiological effects."

1972, Claude Teague, Assistant Director,  
R.J. Reynolds Tobacco Company



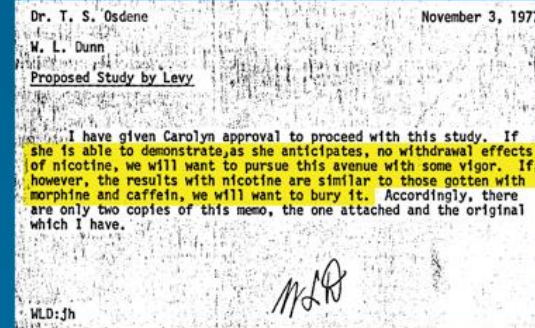
"...without the chemical compound (nicotine) the cigarette market would collapse, Phillip Morris would collapse, and we'd all lose our jobs and our consulting fees."

1977, William Dunn,  
Director Smoker Psychology Program, Philip Morris

### Industry Denials



While publicly downplaying the role of nicotine in cigarette design, inside the companies the role of nicotine in cigarette design was front and center.



# Precise Control

Manufacturers control the level of nicotine in cigarette through tobacco growing, blending, the use of additives, and filtration design.



A likeness of Jean Nicot, French diplomat, after whom "nicotine" and "Nicotiana Tabacum" were named.

## MORE OR LESS NICOTINE

Nicotine levels are becoming a growing concern to the designers of modern cigarettes, particularly those with lower "tar" deliveries. The Kimberly-Clark tobacco reconstitution process used by LTR INDUSTRIES permits adjustments of nicotine to your exact requirements. These adjustments will not affect the other important properties of customized reconstituted tobacco produced at LTR INDUSTRIES: low tar delivery, high filling power, high yield and the flexibility to convey organoleptic modifications. We can help you control your tobacco.



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# 1961 - Low Tar Smokers Smoke More

*"As we know, all too often the smoker who switches to a hi-fi cigarette winds up smoking more units in order to provide himself with the same delivery [of nicotine] which he had before."*



Memo from Philip Morris VP  
Helmut Wakeham

1963, B&W

*“we can regulate fairly precisely the nicotine and sugar levels (in tobacco) to almost any desired level management might require.”*

1963, R.B. Griffith, Brown & Williamson Director of Research



The fraud  
of lights  
and low tar

Filter ventilation



# **Nicotine removal as a basis for tobacco regulation**



# The NEW ENGLAND JOURNAL of MEDICINE

## SOUNDING BOARD

Volume 331:123-125

July 14, 1994

Number 2

## **Establishing a Nicotine Threshold for Addiction -- The Implications for Tobacco Regulation**

On February 25, 1994, the Food and Drug Administration (FDA) released a letter to the Coalition on Smoking or Health announcing its intention to consider regulating cigarettes. The agency's premises were that the vast majority of tobacco users self-administer the product for the drug effects of nicotine and to sustain addiction and that cigarette manufacturers control the levels of nicotine in cigarettes to maintain this addiction. The FDA further raised the possibility of regulating cigarettes on the basis of their nicotine content to prevent addiction.

# Assumptions

- There is a threshold nicotine exposure level that is necessary to sustain nicotine addiction.
- Reducing the nicotine content of cigarettes to below this threshold would reduce the addictiveness of cigarettes, preventing children from becoming addicted smokers and giving smokers greater freedom to stop smoking when they decide to quit.
- Nicotine levels would be sufficiently low that compensation to maintain nicotine levels in the body would not be possible.
- Such a policy appears to be technologically feasible.

1988

BENSON & HEDGES BREAKTHROUGH

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THE SMOOTH TASTE OF A LIGHT

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SURGEON GENERAL'S WARNING:  
Quitting Now Greatly  
Reduces Serious Risks to  
Your Health.  
By Pregnant Women May  
Cause Injury, Premature Birth, Ab  
ortion.





# Genetically Modified and Bio-Engineered Tobacco



In the 1980s  
cigarette  
manufacturers  
began investigating  
genetic  
bio-engineering of  
tobacco plants as a  
way to control  
nicotine delivery.

# The government weighs in...



Nicotine in cigarettes and smokeless tobacco is a drug and these products are nicotine delivery devices under the Federal Food, Drug, and Cosmetic Act.

*U.S. Food and Drug Administration*  
Fed. Reg. Vol. 60, No. 155, Aug. 11, 1995

## **Simulation of the Population Health Impact of a Proposal to Mandate Nicotine Reduction in Cigarettes**

(Tsengs et al, *Prev Med* 2005, 40:170)

“Policy makers would be hard-pressed to identify another domestic public health intervention, short of historical sanitation efforts, that has offered this magnitude of benefit to the population.”

# June 22, 2009



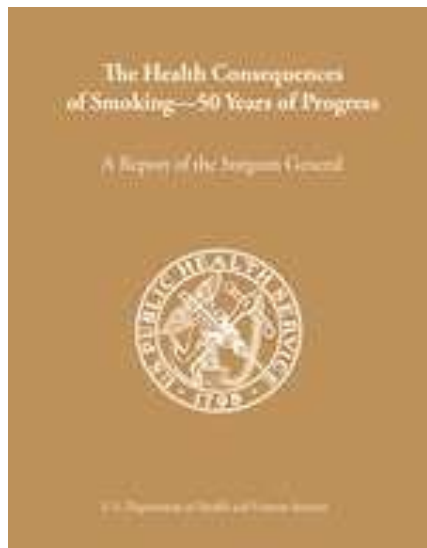
*The law gives the FDA the authority to regulate the advertising and packaging of cigarettes, along with ingredients such as nicotine and flavorings that affect how easily the public is drawn into smoking and how addictive the habit is once started.*

## Section 907 of Act: Tobacco Product Standards

### Limitation on Power Granted to the Food and Drug Administration

Because of the importance of a decision of the Secretary to issue a regulation

- A. **banning** all cigarettes, all smokeless tobacco products, all little cigars, all cigars other than little cigars, all pipe tobacco, or all roll-your-own tobacco products; or
  - B. requiring the **reduction of nicotine** yields of a tobacco product **to zero**,
- the **Secretary is prohibited** from taking such actions under this Act



# The Tobacco Endgame

Strategy to eradicate or reduce to minimal levels the use of (and disease caused by) combustible tobacco products.



# BUSINESS TODAY

Grove Potter, Executive Business Editor  
849-3492 • gpotter@buffnews.com

THE BUFFALO NEWS

Sunday, March 6, 2011

## Cultivating a novel way to quit smoking

*Clarence company  
growing tobacco with  
95% less nicotine*

BY DAVID ROBINSON

NEWS BUSINESS REPORTER

Joseph Pandolfino wants to help smokers quit — by letting them smoke as much as they want.

Pandolfino's company, 22nd Century Group in Clarence, is developing a genetically modified type of tobacco that has 95 percent less nicotine than so-called "light" cigarettes.

The idea is that, by drastically reducing nicotine levels in the cigarettes, smokers who want to quit will be able to continue smoking as much as they want during a six-week, prescription-only treatment program, while reducing their exposure to addictive nicotine.

"These look and taste just like conventional cigarettes," said Pandolfino, 22nd Century's founder and chief executive officer. "The only difference



22nd Century's Henry Sicignano III, left, and Joseph Pandolfino work with genetically modified tobacco.

under development and need various government approvals before hitting the market, could offer smokers a new way to try to kick their unhealthy habit.

"It's a completely different approach to smoking cessation," said

ioral aspects of smoking."

The company's very low nicotine cigarette, called the X-22, is in the midst of clinical trials required by the U.S. Food and Drug Administration, which has to approve the smoking cessation aid before it could be sold commercially. To win approval the

ting smokers to quit.

So far, company executives said the results have been encouraging. A Phase II clinical trial conducted at the University of Minnesota using 22nd Century's tobacco found that 43 percent of the participants managed to go four weeks without smoking, better than others who used nicotine lozenges or cigarettes with higher, but still reduced, nicotine levels. Those results still held six weeks after the trial ended, which is significant because most smokers who try to quit end up returning to their old habit.

About two of every five U.S. smokers try to quit each year, but only about 2 percent to 5 percent actually succeed in quitting in the long run. It typically takes eight to 11 tries before a smoker actually is finally able to give up cigarettes for good.

Pandolfino said the X-22 tries to strike a middle ground between quitting cold turkey and using products, such as pills, patches and lozenges, that give smokers reduced, but intermediate-level, exposure to nicotine.

Several studies have shown that

# Health risks are still present in X-22 cigarette

TOBACCO • from D1

so-called "light" cigarettes, with lower tar and nicotine levels, accomplished little, because smokers compensated for the lower tar and nicotine levels by smoking more cigarettes and by taking longer and deeper puffs.

"It's less of a shock than quitting cold turkey," he said. "When you have intermediate nicotine levels, what happens is you compensate for it and you smoke more cigarettes."

Sicignano said the X-22 still has all the health and cancer risks associated with conventional cigarettes.

"They're certainly not safe," he said. "You're still inhaling smoke and all the toxins."

Dr. Michael Cummings, the chairman of the department of health behavior at Roswell Park Cancer Institute and the director of the New York State Smokers' Quitline, said the nicotine in cigarettes is what makes it



*"We certainly need to be  
looking for better  
cessation aids.  
Anything's worth a try  
when the consequences  
are dire."*

*Dr. Michael Cummings,  
Roswell Park Cancer  
Institute*



Leader in research and development on the tobacco plant, mainly on the nicotine biosynthetic pathway, uniquely positioned to contribute to tobacco harm reduction.

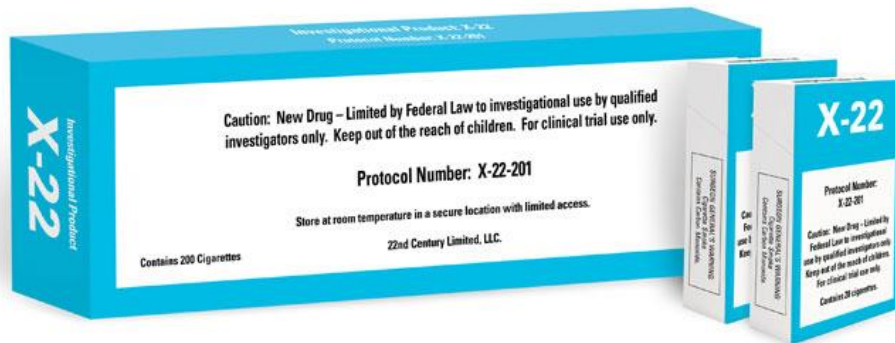


Variable Nicotine-Level Research Cigarettes



SPECTRUM® features 24 styles, 11 regular and 13 menthol versions, with 8 different levels of nicotine content. SPECTRUM® is strictly for research purposes and is not sold as a commercial cigarette.





## X-22: Smoking Cessation Aid In Development



Very low tar to nicotine ratio cigarettes



The tobacco in MAGIC 0 contains approximately 95% less nicotine than tobacco in leading cigarette brands formerly referred to in the United States as “light” cigarettes.



# In development, possible MRTPT

# CLINICAL TRIALS

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## Nicotine intake and dose response when smoking reduced–nicotine content cigarettes

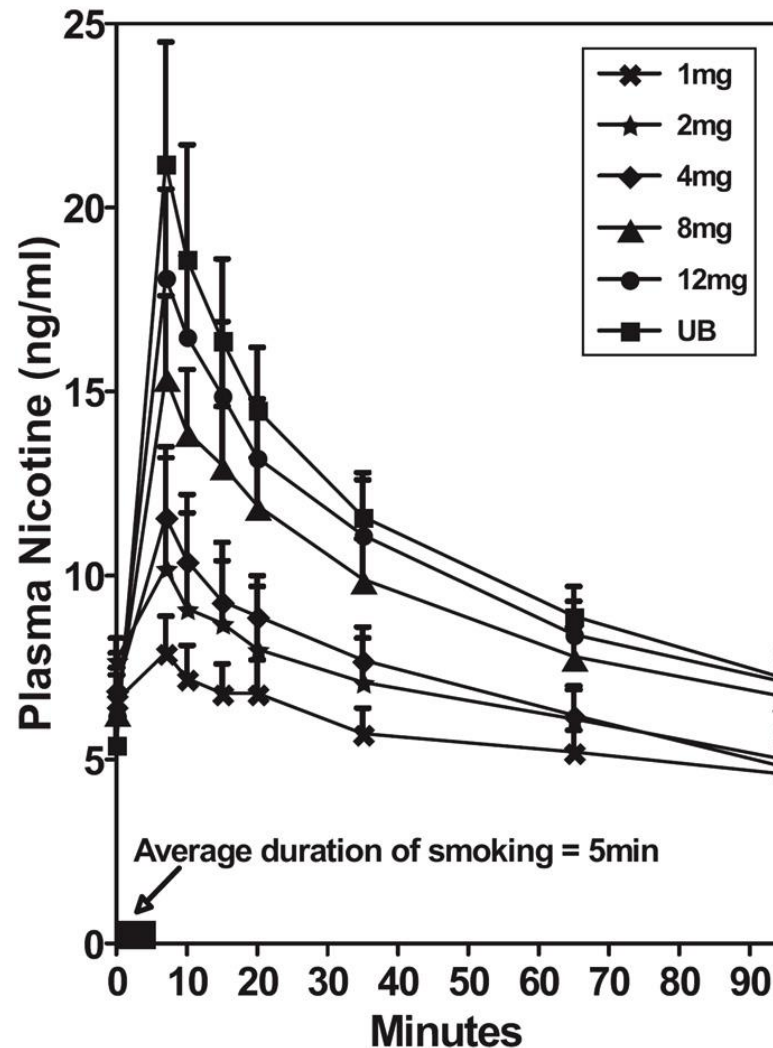
*Conclusions:* Our study suggests that reduced–nicotine content cigarettes are reasonable candidates for trying to reduce the level of nicotine addiction in smokers. The flat nicotine dose–cardiovascular response curve is consistent with other studies demonstrating tolerance to the cardiovascular effects of nicotine.

**Neal L. Benowitz, MD, Peyton Jacob III, PhD, and Brenda Herrera** *San Francisco, Calif*



# Plasma Nicotine when Smoking Cigarettes of Different Nicotine Content

(Benowitz, CPT 2006)



# Clinical trials of reduced nicotine content cigarettes overview

- Smokers do not like VLN cigarettes
- Smokers do reduce daily nicotine intake, but non-compliance is common (80+ %)
- Smokers of regular cigarettes seek alternative sources of nicotine in particular high reward value situations (such as first cigarette of day)

# Subject quotes regarding research cigarettes

- Subjects report that:
  - the “cigarettes are nasty and their harshness is difficult to get used to.”
  - “is smoking a lot of the research cigarettes, though the cigarettes taste crappy.”
  - “cigarettes are very light – don’t satisfy...”
  - “cutting filter in half and packing the cigarettes” as they are very loose.
  - “hates these cigarettes”
  - “cigarettes taste like smoking air.”
  - “craving to eat – I am eating lots of ice cream.”
  - “cigarettes are ok – but not a real cigarette.”

## Subject quotes from research group quitters

- Subjects report that:
  - “I no longer feel the need to have coffee and cigarettes first thing in the morning.”
  - is smoking less “thinks nicotine doesn’t have the hold on me anymore.”
  - “experiences less craving”
  - “not smoking so much at work anymore”
  - “smoking these cigarettes are like quitting and therefore might as well quit.”
  - “doesn’t have a craving to smoke first thing in the morning anymore – thinking about quitting – thinks it will be easy.”
  - “smoking is losing its pleasure.”
  - “craving is going away”

## RESEARCH REPORT

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# Smoking in the absence of nicotine: behavioral, subjective and physiological effects over 11 days

**Eric C. Donny, Elizabeth Houtsmuller & Maxine L. Stitzer**

Behavioral Pharmacology Research Unit, Department of Psychiatry, Johns Hopkins University School of Medicine, Baltimore, MD, USA

nicotine content. **Conclusions** These effects highlight the importance of non-nicotine sensorimotor stimuli as determinants of the maintenance of smoking behavior and suggests that extinction of conditioned reinforcement in the absence of nicotine progresses slowly.

## EDITORIAL

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doi:10.1111/j.1360-0443.2006.01727.x

# Denicotinized cigarettes: a new tool to combat cigarette addiction?

JED E. ROSE

*Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Center for Nicotine and Smoking*

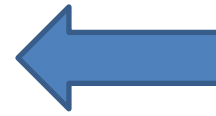
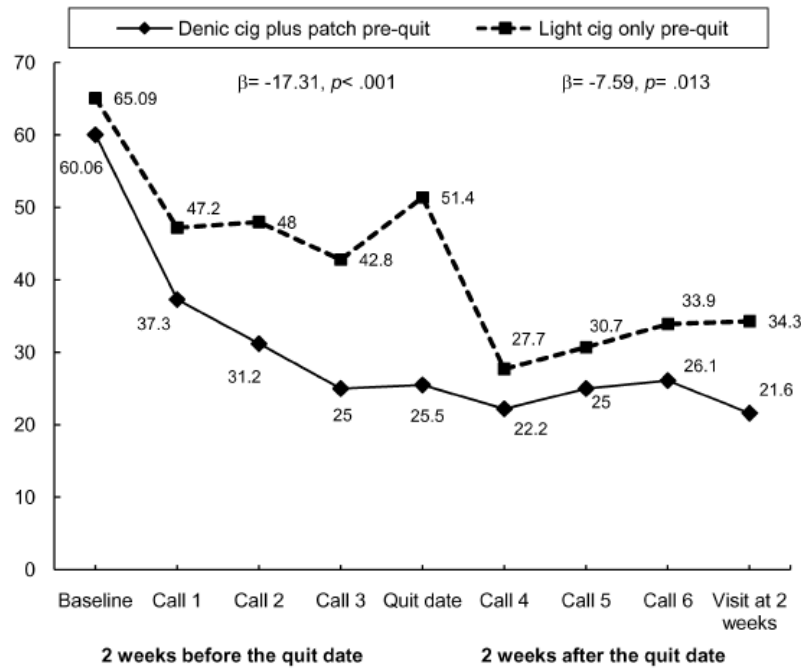


# Treating smokers before the quit date: Can nicotine patches and denicotinized cigarettes reduce cravings?

**Hamed Rezaishiraz, Andrew Hyland, Martin C. Mahoney, Richard J. O'Connor, K. Michael Cummings**

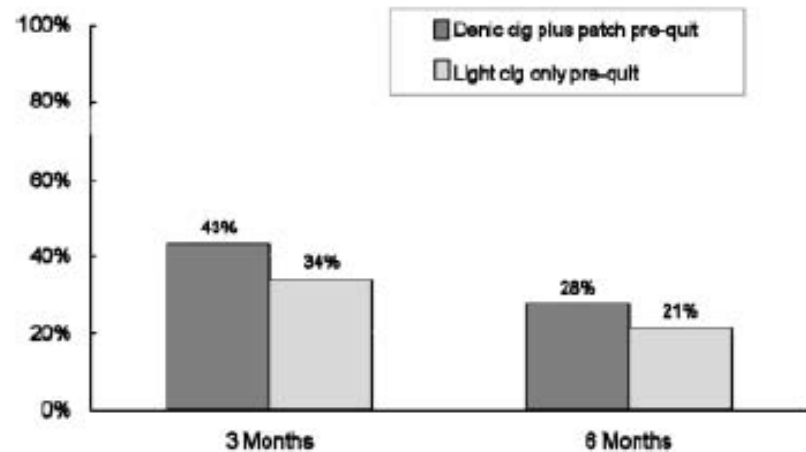
Received 18 August 2006; accepted 15 February 2007

The present study investigated whether treatment with the combination of denicotinized cigarettes and 21-mg nicotine patch for 2 weeks before a designated quit date could lessen cravings for smoking, thereby helping smokers abstain from smoking. The study was a randomized controlled clinical trial conducted at Roswell Park Cancer Institute, Buffalo, New York, in 2004 and 2005. Patients included 98 adult heavy smokers (using 20 or more cigarettes/day). Half of the subjects received 2 weeks of combination of denicotinized cigarettes (Quest 3) and 21-mg nicotine patch for 2 weeks before the quit date. The remaining smokers were switched to light cigarettes (Quest 1) during the 2 weeks before the quit date. After the quit date, all subjects received counseling for smoking cessation and were provided nicotine patches for up to 8 weeks after the quit date. Self-reported cravings for smoking, withdrawal symptoms, and smoking abstinence were measured at predetermined intervals using phone-based surveys and in clinical visits. The group that used denicotinized cigarettes and nicotine patch before quitting reported less frequent and less intense cravings for cigarettes in the 2 weeks before and after the designated quit date. Self-reported withdrawal symptoms and quit rates did not differ significantly between the groups. **The use of a denicotinized cigarette combined with the nicotine patch appears to lessen cravings to smoke in the immediate postcessation period.** A larger, better-powered study is needed to test if this treatment combination has merit for increasing quit rates.



Cigarette cravings

Quit rates



# The combined effect of very low nicotine content cigarettes, used as an adjunct to usual Quitline care (nicotine replacement therapy and behavioural support), on smoking cessation: a randomized controlled trial

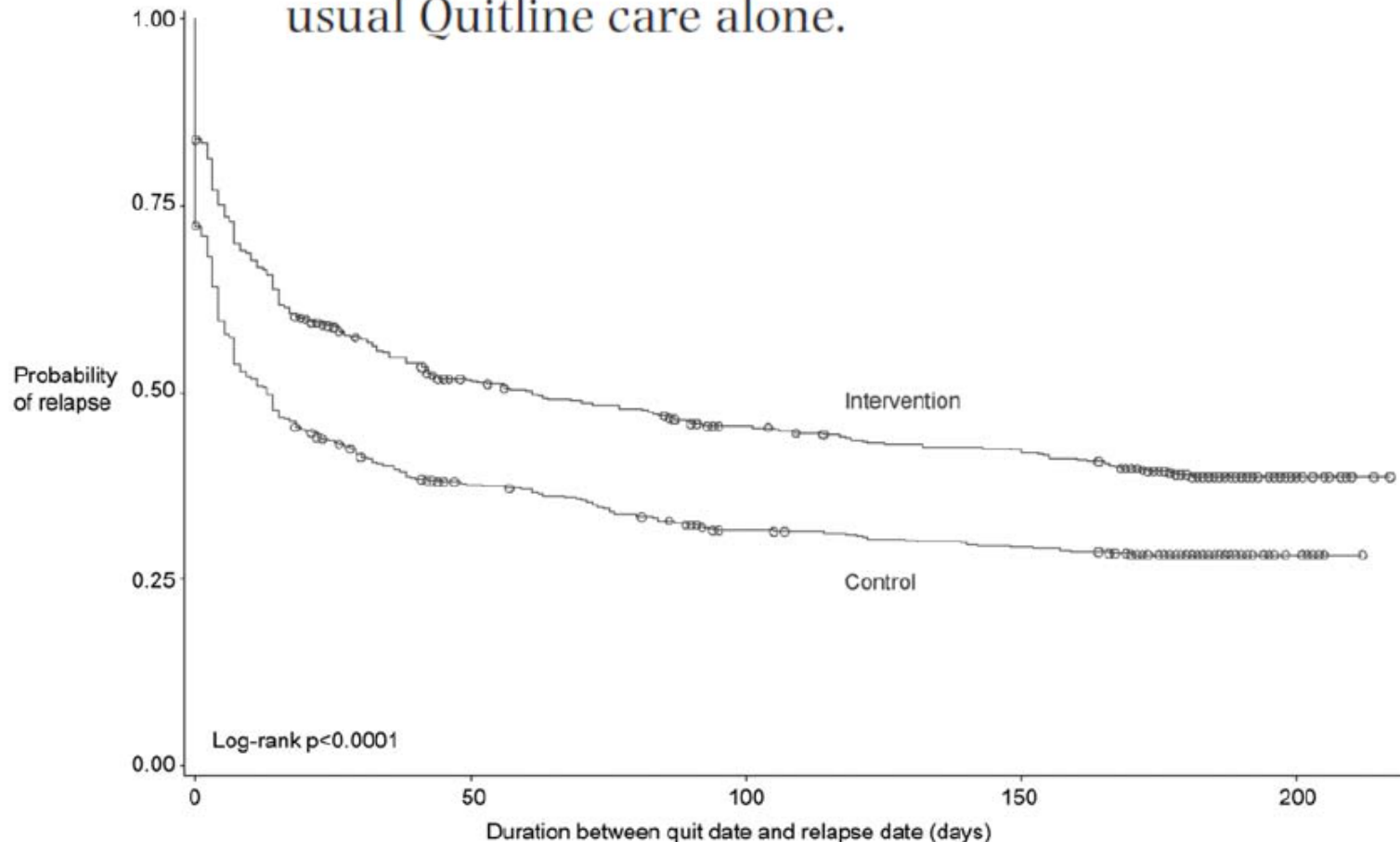
Natalie Walker<sup>1</sup>, Colin Howe<sup>1</sup>, Chris Bullen<sup>1</sup>, Michele Grigg<sup>2,3</sup>, Marewa Glover<sup>4</sup>,  
Hayden McRobbie<sup>5</sup>, Murray Laugesen<sup>6</sup>, Varsha Parag<sup>1</sup> & Robyn Whittaker<sup>1</sup>

Clinical Trials Research Unit, School of Population Health, The University of Auckland, Auckland, New Zealand,<sup>1</sup> The Quit Group, Wellington, New Zealand,<sup>2</sup> Litmus, Wellington, New Zealand,<sup>3</sup> Centre for Tobacco Control Research, Social and Community Health, School of Population Health, The University of Auckland, Auckland, New Zealand,<sup>4</sup> UK Centre for Tobacco Control Studies, Wolfson Institute of Preventive Medicine, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, England<sup>5</sup> and Health NZ Ltd, Christchurch, New Zealand<sup>6</sup>

## ABSTRACT

**Aim** To determine the combined effect of very low nicotine content (VLNC) cigarettes and usual Quitline care [nicotine replacement therapy (NRT) and behavioural support] on smoking abstinence, in smokers motivated to quit. **Design** Single-blind, parallel randomized trial. **Setting** New Zealand. **Participants** Smokers who called the Quitline for quitting support were randomized to either VLNC cigarettes to use whenever they had an urge to smoke for up to 6 weeks after their quit date, in combination with usual Quitline care (8 weeks of NRT patches and/or gum or lozenges, plus behavioural support) or to usual Quitline care alone. **Measurements** The primary outcome was 7-day point-prevalence smoking abstinence 6 months after quit day. Secondary outcomes included continuous abstinence, cigarette consumption, withdrawal, self-efficacy, alcohol use, serious adverse events and views on the use of the VLNC cigarettes at 3 and 6 weeks and 3 and 6 months. **Findings** A total of 1410 participants were randomized (705 in each arm), with a 24% loss to follow-up at 6 months. Participants in the intervention group were more likely to have quit smoking at 6 months compared to the usual care group [7-day point-prevalence abstinence 33 versus 28%, relative risk (RR) = 1.18, 95% confidence interval (CI): 1.01, 1.39,  $P = 0.037$ ; continuous abstinence 23 versus 15%,  $RR = 1.50$ , 95% CI: 1.20, 1.87,  $P = 0.0003$ ]. The median time to relapse in the intervention group was 2 months compared to 2 weeks in the usual care group ( $P < 0.0001$ ). **Conclusions** Addition of very low nicotine content cigarettes to standard Quitline smoking cessation support may help some smokers to become abstinent.

Participants were randomized to VLNC cigarettes plus usual Quitline care (NRT and behavioural support) or usual Quitline care alone.



	No. of subjects	Event	Censored	Median relapse duration (95% CI)
Intervention	705	391 (55.5%)	314 (44.5)	61 (41, 90)
Usual care	705	465 (66.0%)	240 (34.0)	13 (7, 17)

**Figure 2** Kaplan-Meier curve for time to first relapse (days)

*The NEW ENGLAND JOURNAL of MEDICINE*

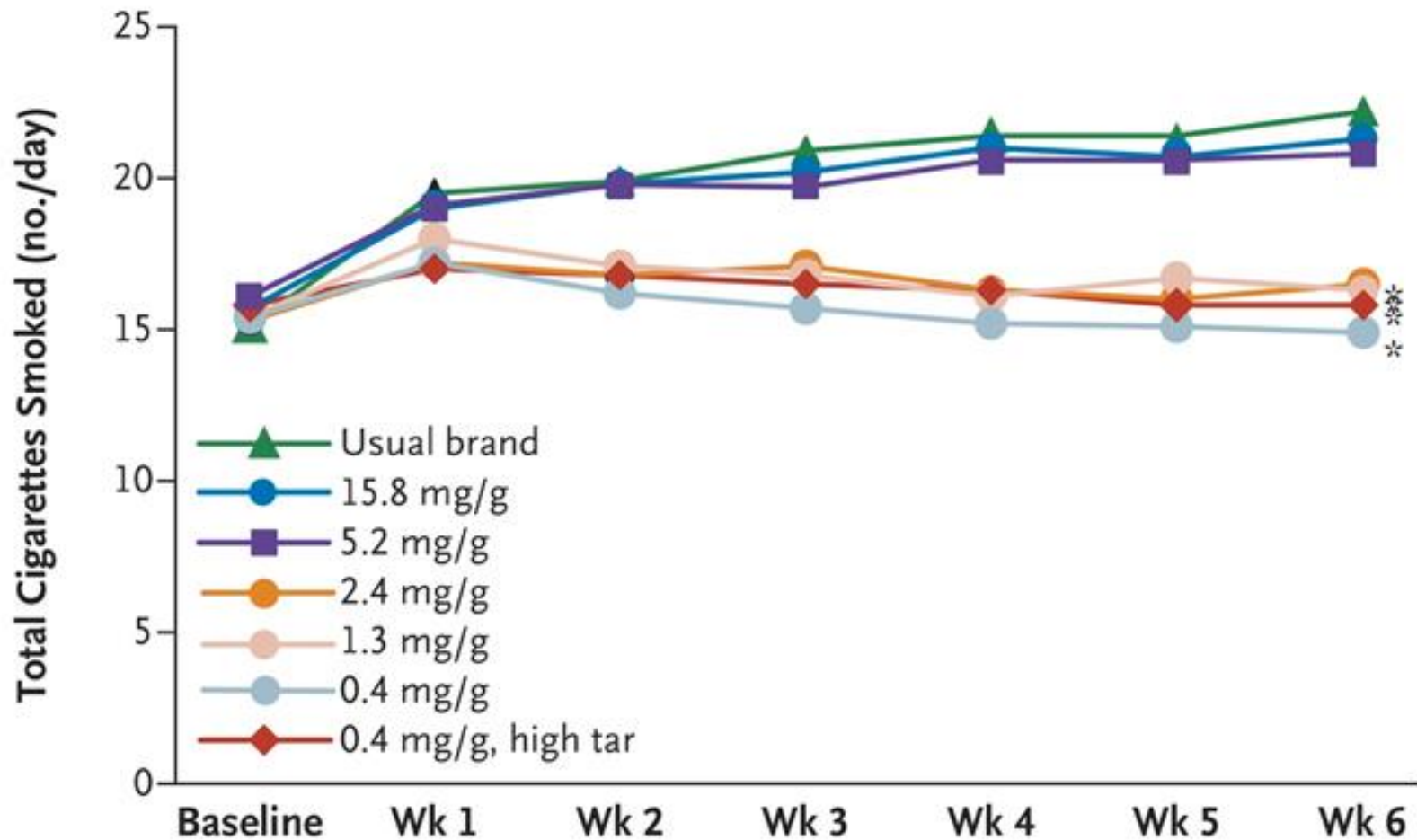
**SPECIAL ARTICLE**

# Randomized Trial of Reduced-Nicotine Standards for Cigarettes

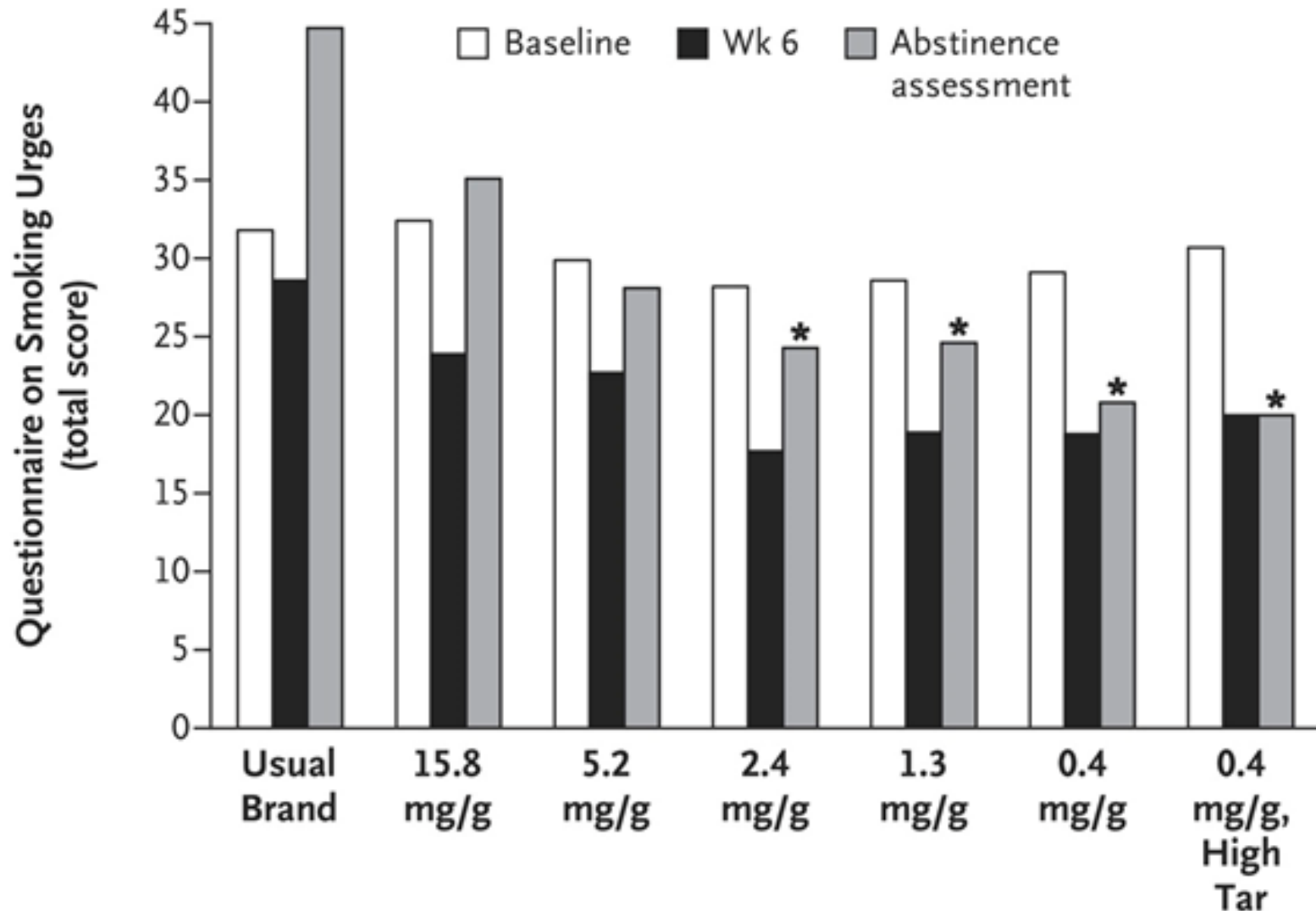
Eric C. Donny, Ph.D., Rachel L. Denlinger, B.S., Jennifer W. Tidey, Ph.D.,  
Joseph S. Koopmeiners, Ph.D., Neal L. Benowitz, M.D., Ryan G. Vandrey, Ph.D.,  
Mustafa al'Absi, Ph.D., Steven G. Carmella, B.A., Paul M. Cinciripini, Ph.D.,  
Sarah S. Dermody, M.S., David J. Drobes, Ph.D., Stephen S. Hecht, Ph.D.,  
Joni Jensen, M.P.H., Tonya Lane, M.Ed., Chap T. Le, Ph.D.,  
F. Joseph McClernon, Ph.D., Ivan D. Montoya, M.D., M.P.H., Sharon E. Murphy, Ph.D.,  
Jason D. Robinson, Ph.D., Maxine L. Stitzer, Ph.D., Andrew A. Strasser, Ph.D.,  
Hilary Tindle, M.D., M.P.H., and Dorothy K. Hatsukami, Ph.D.



# Fewer Cigarettes Smoked Per Day



# Less Craving During Cigarette Abstinence



2015

WHO says the  
science supports  
mandated  
reductions of  
nicotine in tobacco  
to render tobacco  
products non-  
addictive

ADVISORY NOTE

# Global Nicotine Reduction Strategy

WHO Study Group on Tobacco Product Regulation (TobReg)



World Health  
Organization

# Cigarette prohibition and the need for more prior testing of the WHO TobReg's global nicotine-reduction strategy

Lynn T Kozlowski

**CAUTION**

We have no direct evidence showing that it works to promote public health in any community anywhere. Such an untested community-level product prohibition is inappropriate for widespread dissemination by evidence-based health organisations.



**8-years after the FDA is given authority to regulate tobacco products we are still waiting for a policy on nicotine reduction**



# Politically difficult because of ...

## Lack of consumer support



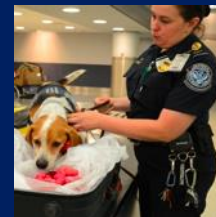
## Affected businesses



## Politics



## Enforcement concerns





# An alternative strategy to help smokers...





## What nicotine is for

*Nicotine induces pleasure and reduces stress and anxiety. Smokers use it to modulate levels of arousal and to control mood. Smoking improves concentration, reaction time, and performance of certain tasks.*

*Relief from withdrawal symptoms is probably the primary reason for this enhanced performance and heightened mood.*

Benowitz NL. Nicotine Addiction. *N Engl J Med.* 2010 Jun 17;362(24):2295–303

## Reduced-risk consumer nicotine market

	Pure nicotine based	Tobacco based
Heated aerosol	<p>Vaping products</p> 	<p>Heated tobacco products "Heat-not-burn"</p> 
Unheated	<p>Ambient nicotine products</p> 	<p>Smokeless tobacco</p> 

Items are not shown to scale

...plus the alternative nicotine product train  
is already heading down the tracks





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Fully Baked | Hunter Vaping Legislation Ready to Replace Deeming Regs

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VAPERS CORNER

(Original Signature of Member)

115TH CONGRESS  
1st SESSION

H. R. \_\_\_\_\_

To protect the public health by providing the Food and Drug Administration with certain authority to regulate e-liquids and personal electronic vaporizers, to reduce the morbidity and mortality resulting from cigarette smoking through the responsible regulation of e-liquids and personal electronic vaporizers as a tobacco harm reduction strategy, and for other purposes.

IN THE HOUSE OF REPRESENTATIVES

Mr. HUNTER introduced the following bill; which was referred to the Committee on \_\_\_\_\_

LEGISLATION (PROPOSED & ENACTED)



# Reduced Nicotine Content Cigarette, E-Cigarettes and the Cigarette End Game

(Benowitz, Donny & Hatsukami, In press in *Addiction*)

*“The reduced nicotine content cigarette and the emergence of non-combusted nicotine products like e-cigarettes should be viewed not as alternatives but as complementary components of regulatory interventions that could virtually end combusted tobacco use.”*

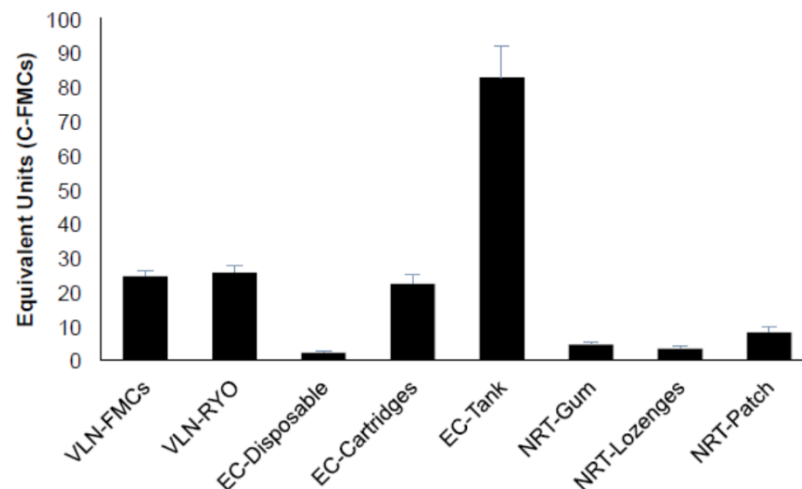


# Nicotine Reduction is Complementary to a Strategy to Encourage Addicted Smokers to Switch to Low Risk Nicotine Products

## A Novel Method for Evaluating the Acceptability of Substitutes for Cigarettes: The Experimental Tobacco Marketplace

Bryan W. Heckman, PhD  
K. Michael Cummings, PhD, 1  
Alexander A. Hirsch, BA  
Amanda J. Quisenberry, PhD  
Ron Borland, PhD, MAPS  
Richard J. O'Connor, PhD  
Geoffrey T. Fong, PhD  
Warren K. Bickel, PhD

Figure 2  
Alternative Product Purchase Data (Means and Standard Errors) for Experiment 4  
(> 10cpd Smokers)



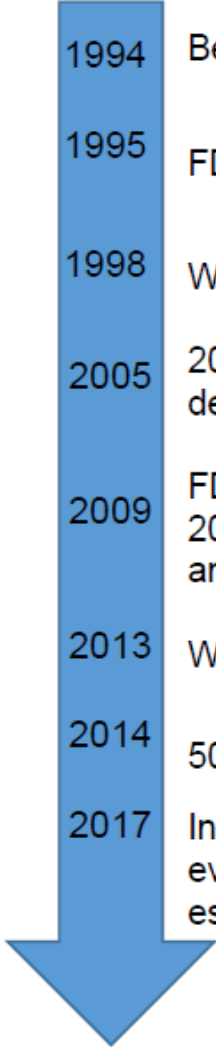


# Prospects for very low nicotine (VLN) tobacco in the US and elsewhere

- Realistically, unlikely that a VLN product standard will happen in the US under the current administration.
- Congress is growing weary of FDA efforts to promote tobacco harm reduction particularly as it relates to vaping products and perhaps other products also.
- The timeline for approving MRTP applications will hopefully accelerate, so 22nd Century's VLN tobacco could be approved for commercialization, with the opportunity to communicate to consumers the benefits of VLN tobacco.
- Ideally, getting VLN tobacco on the market will let consumers start trying, choosing, and using as a way to stop smoking.
- If manufacturers of lower risk nicotine products are serious about moving addicted smokers to non-combusted nicotine products then these businesses should be supportive of a VLN tobacco standard for combustible tobacco to speed up the transition.
- Given the evidence available there is good chance of approval as a stop smoking treatment in the US and elsewhere

# Coal supplied energy: Insights for nicotine reduction strategy

## NICOTINE REDUCTION Event Time Line

- 
- 1994 Benowitz Henningfield NEJM Nicotine Threshold for Addiction – “gradual nicotine reduction proposal”
  - 1995 FDA Advisory Committee considers proposal, raises many research needs: “nation not ready”
  - 1998 WHO SACTob/TobReg uncertain on what to do about nicotine control
  - 2005 2005: Tengs et al. modeling paper evaluates “AMA” proposal and provides optimistic outcome of decreasing smoking prevalence from 25% to 5% outweighing potential black market concerns
  - 2009 FDA Regulatory control over cigarettes and smokeless tobacco law passed and enters into force July 2009 NIH research programs on all aspects of tobacco nicotine research (including reduction) rapidly and greatly expand
  - 2013 WHO TobReg draft report which is released in TobReg WHO monograph in 2015
  - 2014 50<sup>th</sup> Anniversary Surgeon General’s Report (ch. 15 & 16) supports nicotine reduction and ENDS
  - 2017 Increasing research supported by 22<sup>nd</sup> Century combined with efforts towards commercialization will eventually lead to a place where governments will eventually embrace nicotine reduction as an essential element of tobacco harm reduction

ANY  
QUESTIONS  
?