

# ***SMOKING CESSATION & VASCULAR MEDICINE***

## **The Preventive Priority!**

**Andrew Pipe, CM, MD**

***Division of Prevention & Rehabilitation***

***University of Ottawa Heart Institute***



# Declaration of Interest

*In the past I have received research and educational support from, and/or served as a consultant to:*

**PFIZER**

**JOHNSON & JOHNSON**



# Further Declaration

***I will discuss the 'off-label' use of medications.***



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OTTAWA MODEL  
FOR SMOKING CESSATION  
MODÈLE D'OTTAWA  
POUR L'ABANDON DU TABAC



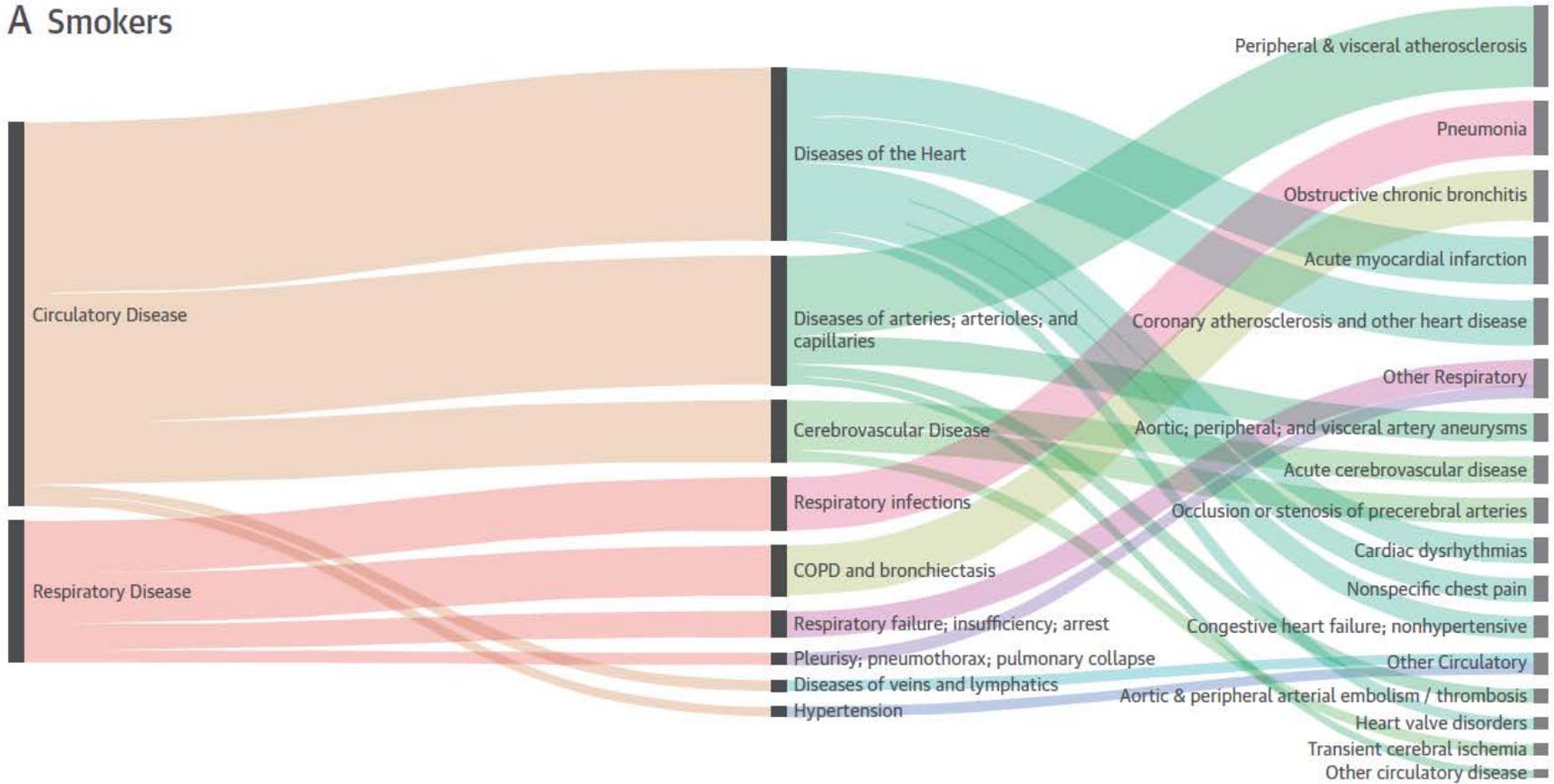
# ***Smoking Cessation***

***“The single, most powerful,  
preventive intervention in  
clinical practice.”***

Woolf SH. *JAMA* 1999;282(24):2358-65.

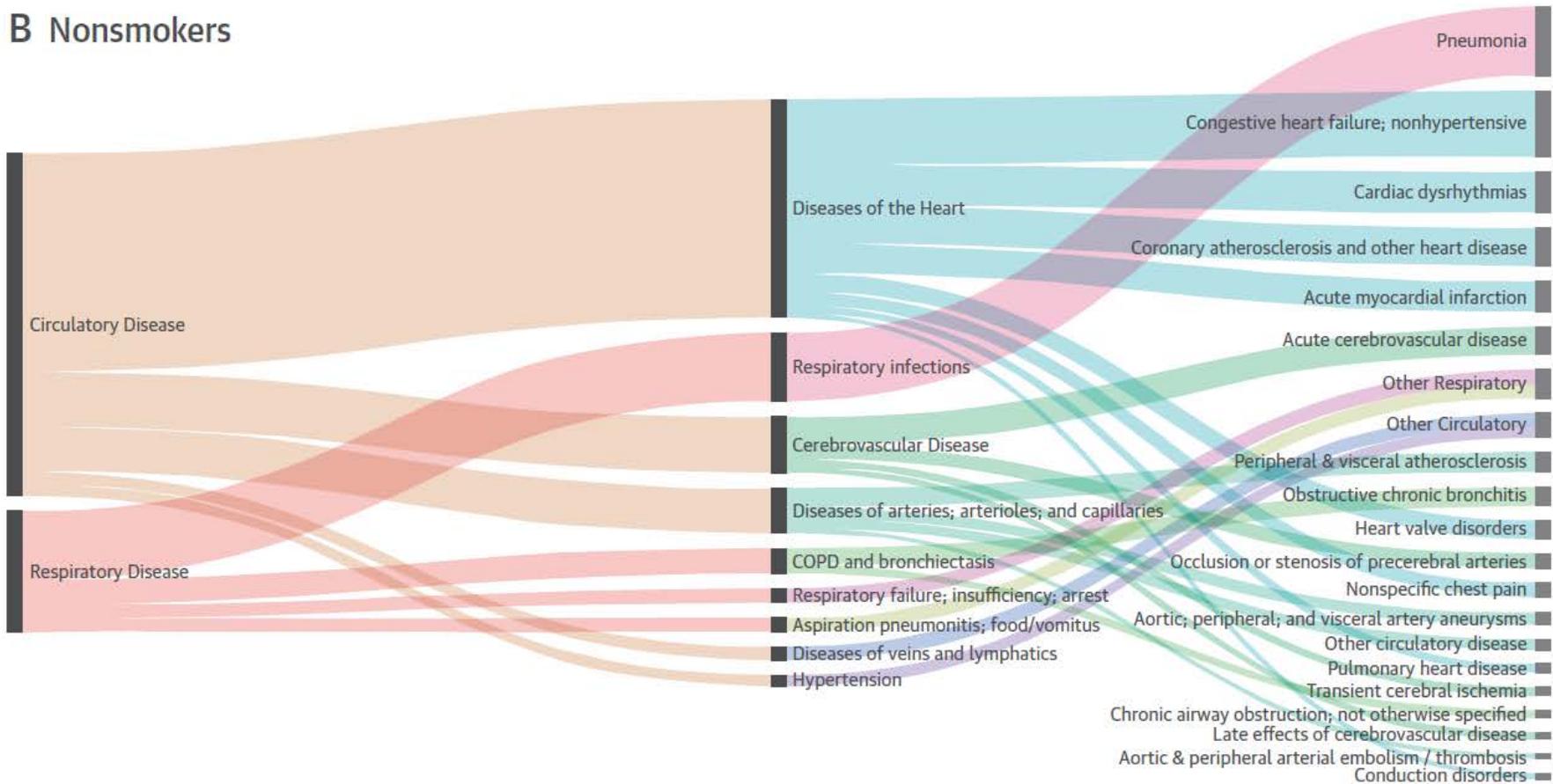
# Reasons for Hospitalization

## A Smokers

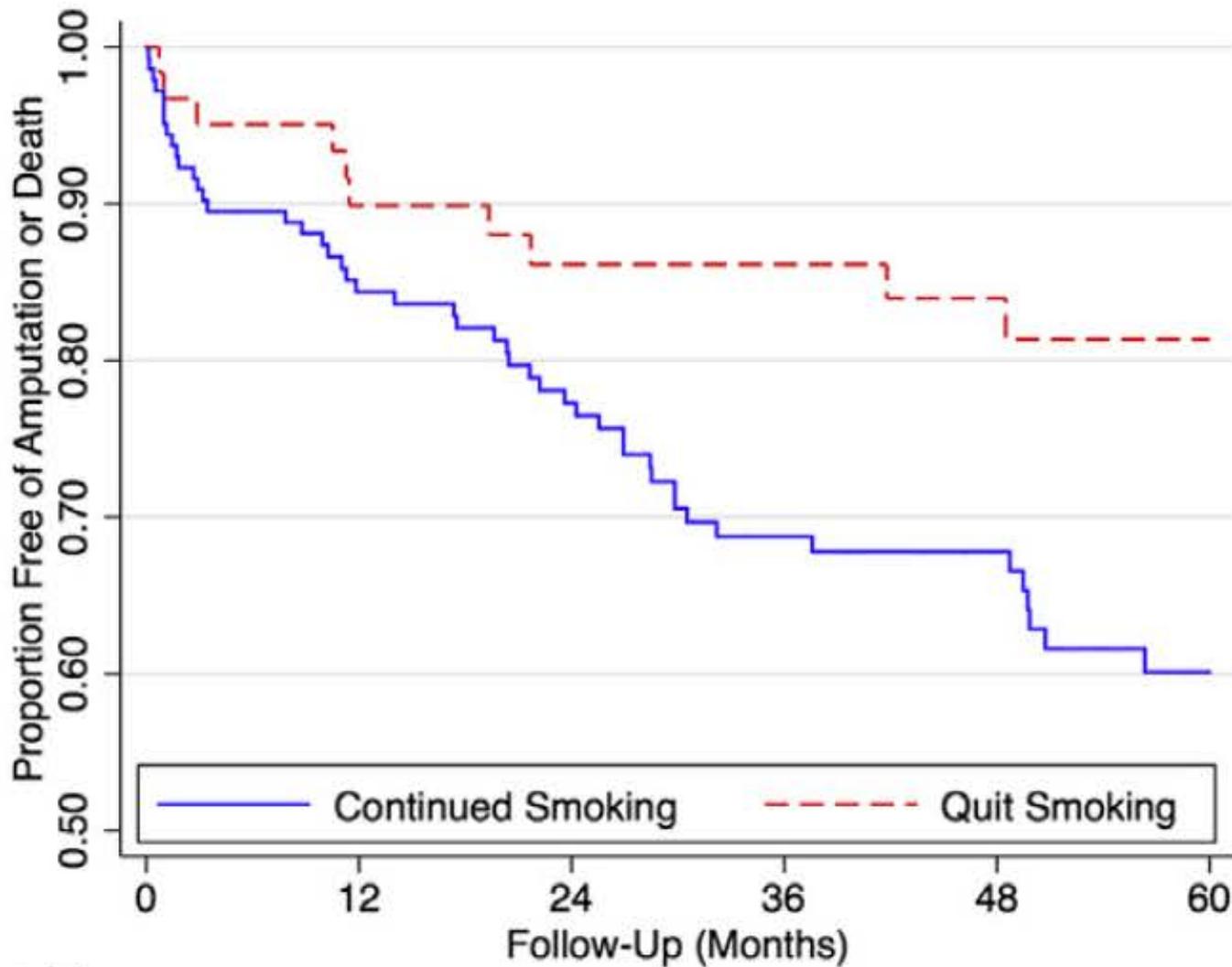


# Reasons for Hospitalization

## B Nonsmokers

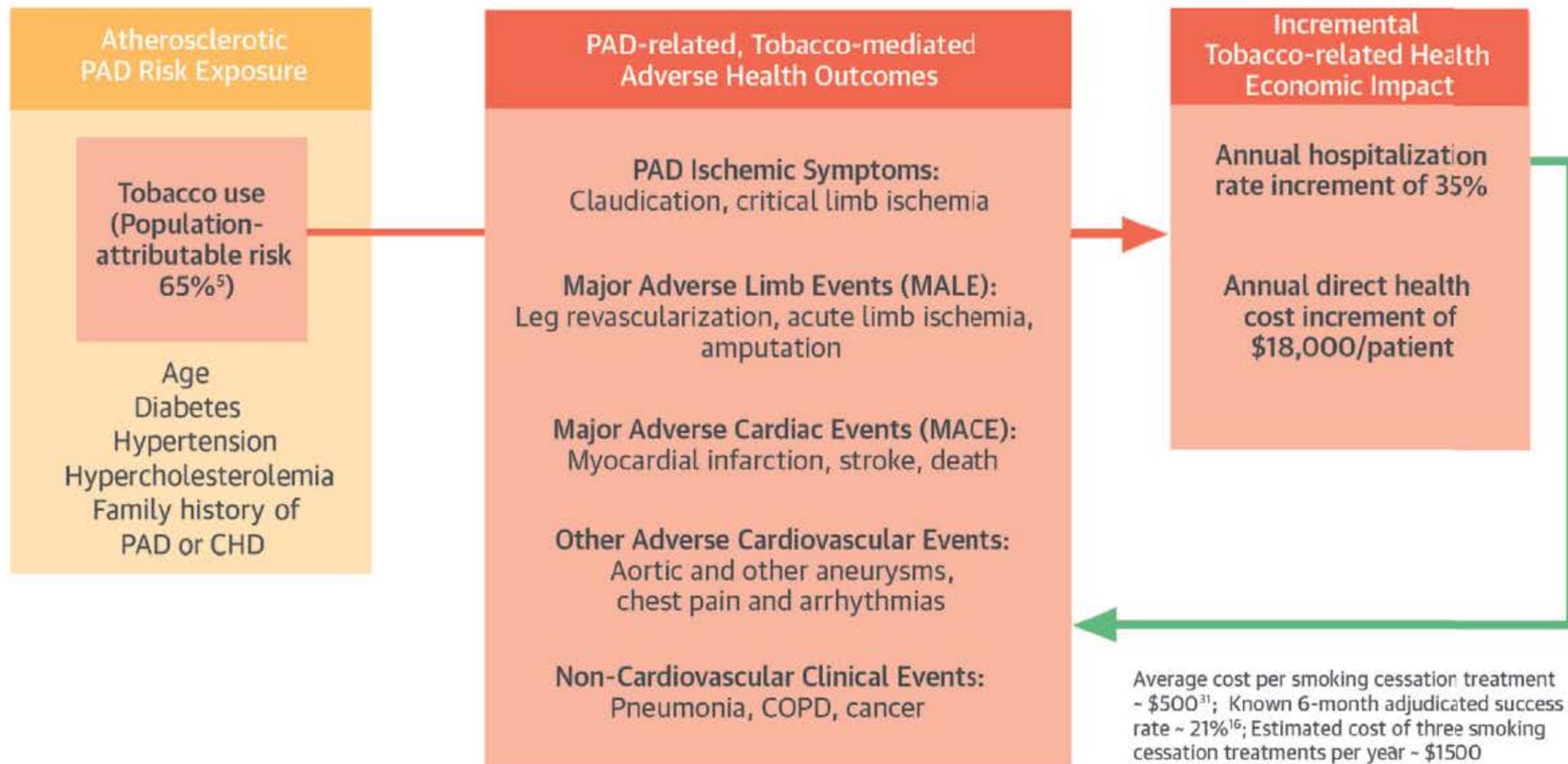


## ***Amputation-free survival among patients who continued vs quit smoking***



***Armstrong EJ et al. J Vasc Surg 2014;60:1565-71***

## Impact of Tobacco on PAD Clinical Events and Cost



Tobacco is the single most powerful modifiable cause of atherosclerotic PAD, markedly increasing the risk of CVD (MACE and MALE) and non-CVD clinical events and hospitalizations. This is associated with an immense increase in annual health care costs. Smoking cessation is effective and costs very little.

**Duval S et al. *J Am Coll Cardiol* 2015;66:1566-74**



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# Tobacco Addiction

***"...it is difficult to identify any other condition that presents such a mix of lethality, prevalence ... and neglect***

***...despite effective and readily available interventions."***

*Treating Tobacco Use and Dependence. Clinical Practice Guideline. US DHHS. 2000.*



***Smoking Cessation***  
**The Most Important  
CVD Intervention !**



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# Smoking diminishes benefit of blood pressure control

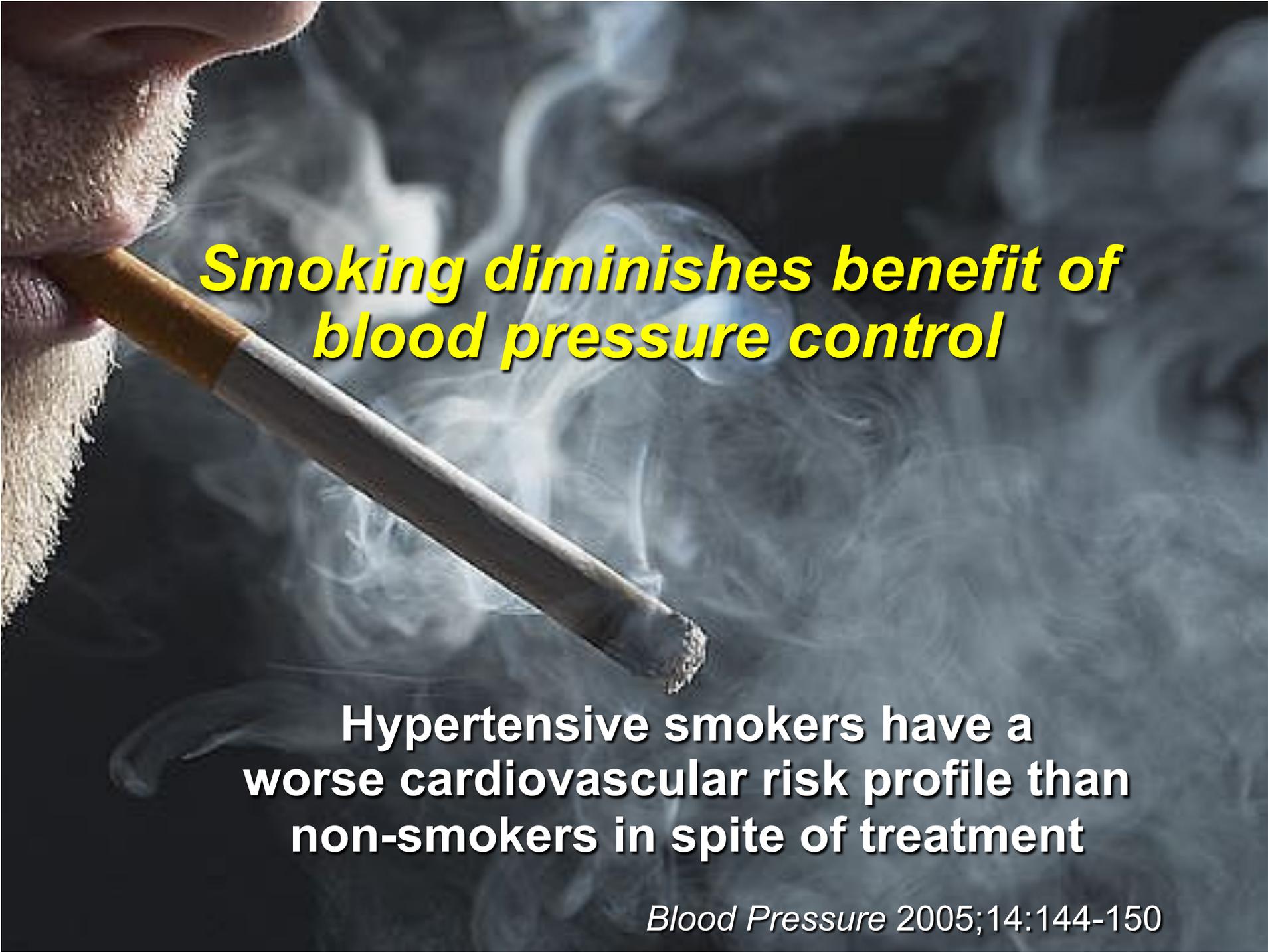
Journath G, et al. Blood Press. 2005; 14(3):144-150.

## Smoking cessation is superior to other proven cardiovascular interventions

Critchley JA, Capewell S. JAMA. 2003;290(1):86-97.

### Impact of Smoking on Cardiovascular Events in Patients With Coronary Disease Receiving Contemporary Medical Therapy (from the Treating to New Targets [TNT] and the Incremental Decrease in End Points Through Aggressive Lipid Lowering [IDEAL] Trials)

Paul Frey, MD<sup>a</sup>, David D. Waters, MD<sup>a,\*</sup>, David A. DeMicco, PharmD<sup>c</sup>, Andrei Breazna, PhD<sup>c</sup>,  
Larry Samuels, PhD<sup>c</sup>, Andrew Pipe, CM, MD<sup>d</sup>, Chuan-Chuan Wun, PhD<sup>c</sup>, and  
Neal L. Benowitz, MD<sup>b</sup>



***Smoking diminishes benefit of  
blood pressure control***

**Hypertensive smokers have a  
worse cardiovascular risk profile than  
non-smokers in spite of treatment**

*Blood Pressure 2005;14:144-150*

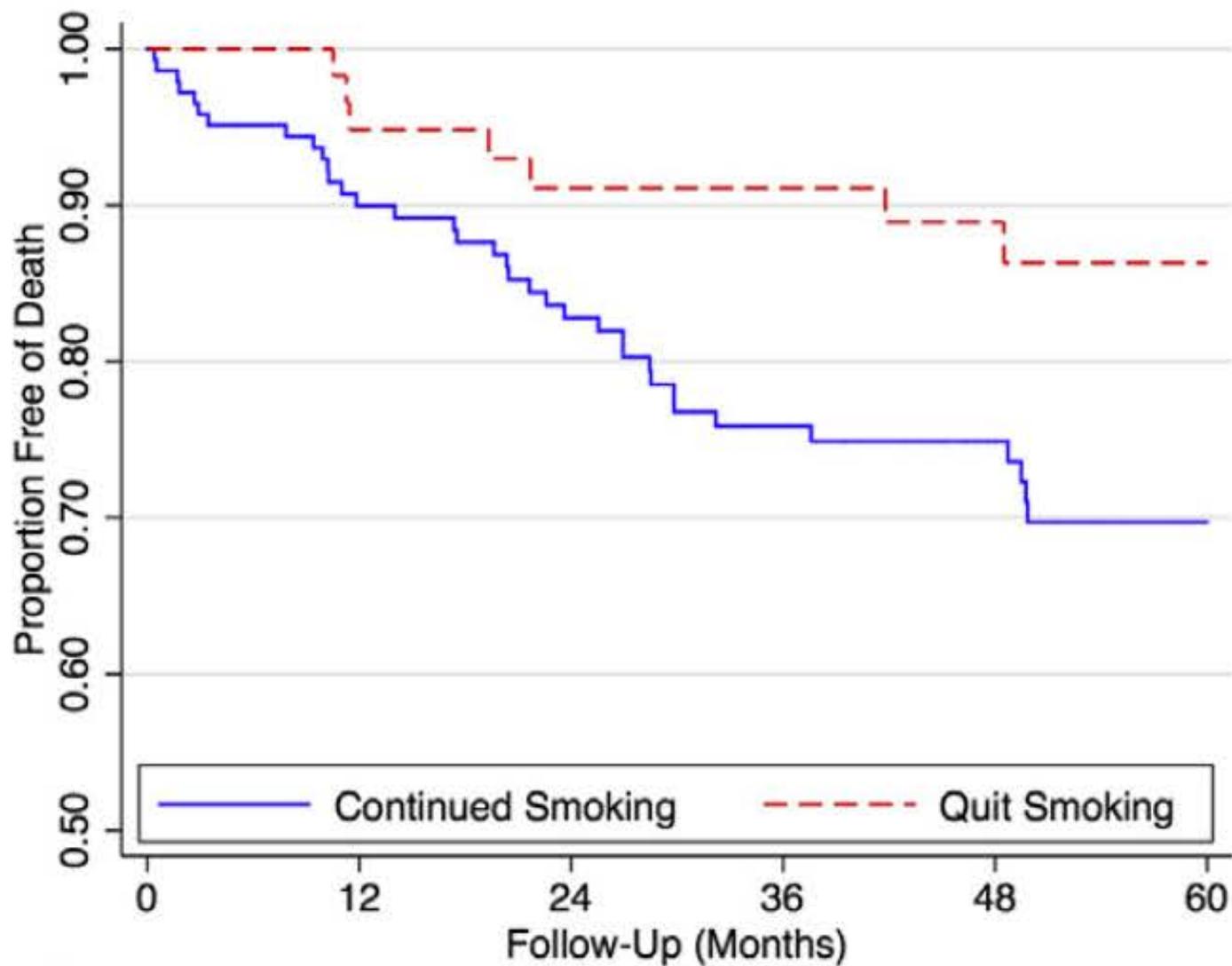
# ***Smoking diminishes benefits of statins***

***61% higher risk***  
***of events for***  
***smokers compared***  
***with nonsmokers***  
***treated with statins for***  
***secondary prevention***



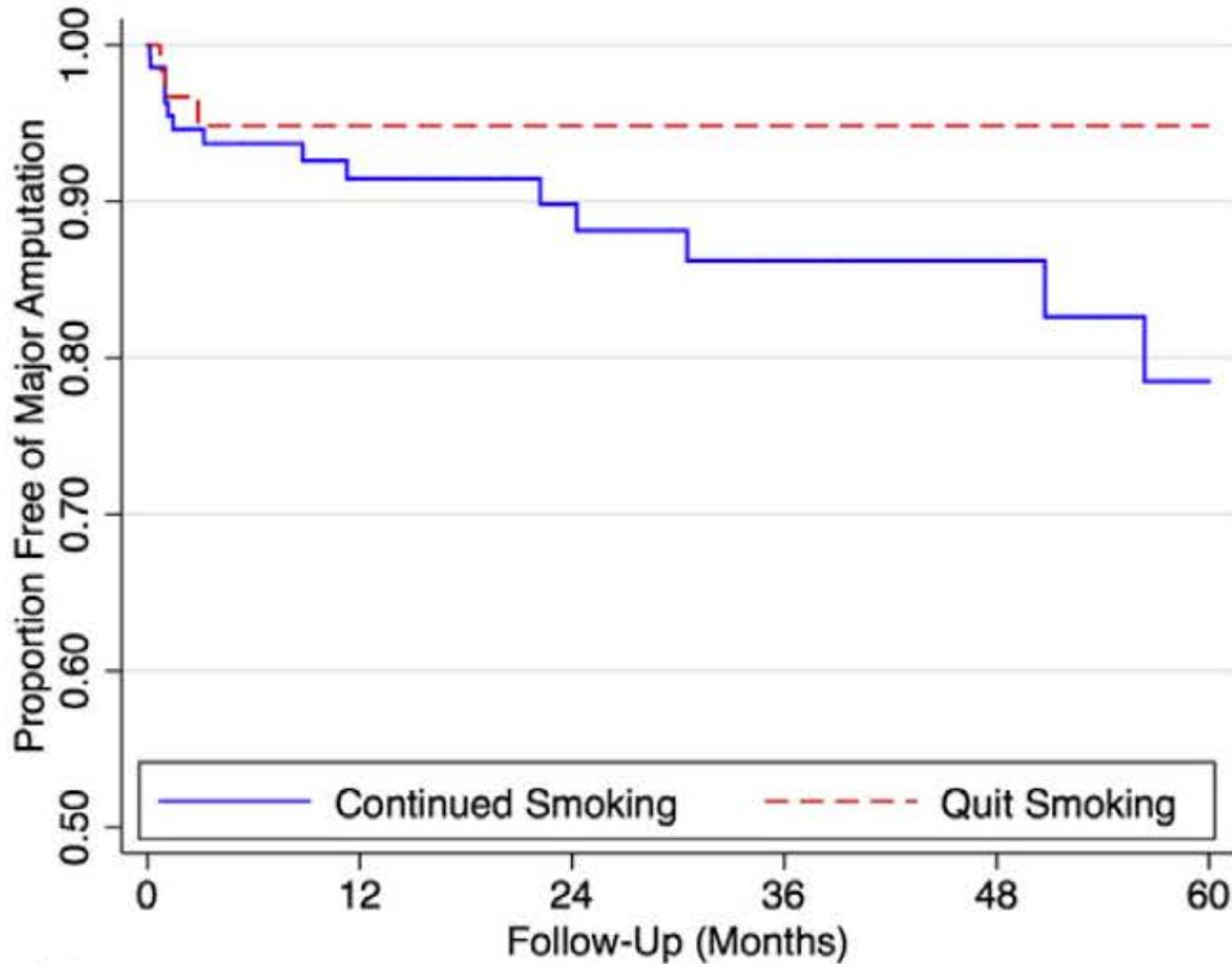
Milionis HJ et al. *Angiology* 2001;52:575-587

## Mortality among patients who continued vs quit smoking



Armstrong EJ et al. *J Vasc Surg* 2014;60:1565-71

## ***Rates of major amputation among patients who continued vs quit smoking***



***Armstrong EJ et al. J Vasc Surg 2014;60:1565-71***



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## Cost Effectiveness



*per life-year saved:*

<b><i>Smoking Cessation</i></b>	<b><i>\$ 2,000 – 6,000</i></b>
<b><i>R<sub>x</sub> of Hypertension</i></b>	<b><i>\$ 9,000 – 26,000</i></b>
<b><i>R<sub>x</sub> of Hyperlipidemia</i></b>	<b><i>\$ 50,000 – 196,000</i></b>

Benowitz NL *Prog Cardiovasc Dis* 2003;46:91-111



The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

## 21st-Century Hazards of Smoking and Benefits of Cessation in the United States

Prabhat Jha, M.D., Chinthanie Ramasundarahettige, M.Sc.,  
Victoria Landsman, Ph.D., Brian Rostron, Ph.D., Michael Thun, M.D.,  
Robert N. Anderson, Ph.D., Tim McAfee, M.D., and Richard Peto, F.R.S.

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### CONCLUSIONS

Smokers lose at least one decade of life expectancy, as compared with those who have never smoked. Cessation before the age of 40 years reduces the risk of death associated with continued smoking by about 90%.

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N ENGL J MED 368;4 NEJM.ORG JANUARY 24, 2013

***Smoking cessation at age 60, 50, 40, & 30  
increases life expectancy by 3, 6, 9, 10  
years, respectively***



***Chen D, Wu LT. Drug Alcohol Depend 2015;154:14-24***

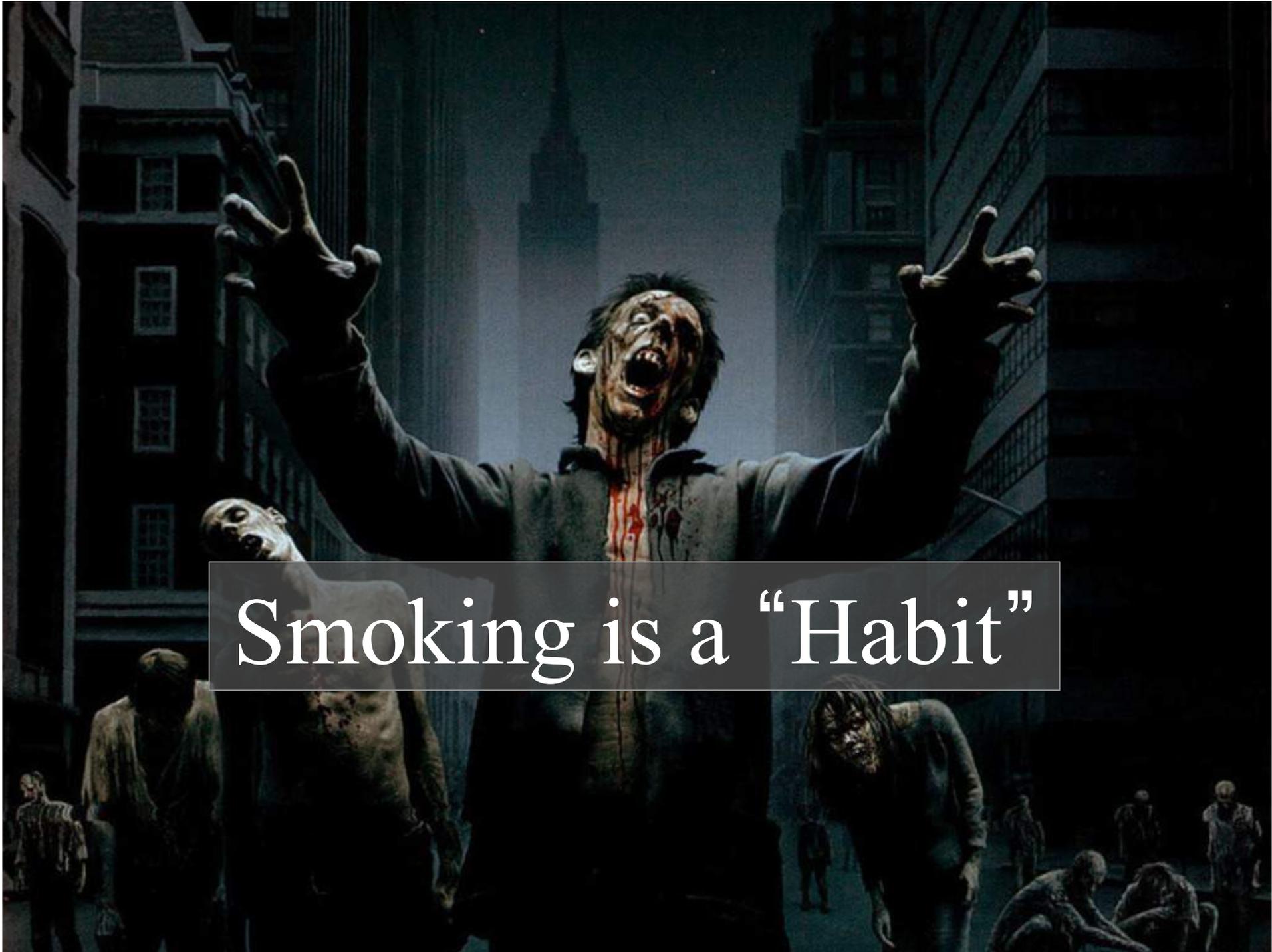


***Slaying Zombies!***

**“Zombie Concepts”**

Zombies are everywhere!





Smoking is a “Habit”

## **Probability of dependence after trying a substance at least once**

<b>Tobacco</b>	<b>32%</b>
<b>Heroin</b>	<b>23%</b>
<b>Cocaine</b>	<b>17%</b>
<b>Alcohol</b>	<b>15%</b>
<b>Stimulants</b>	<b>11%</b>
<b>Anxiolytics</b>	<b>9%</b>
<b>Cannabis</b>	<b>9%</b>
<b>Analgesics</b>	<b>8%</b>
<b>Inhalants</b>	<b>4%</b>



*Stahl's Essential Psychopharmacology, 3<sup>rd</sup> ed. 2008*

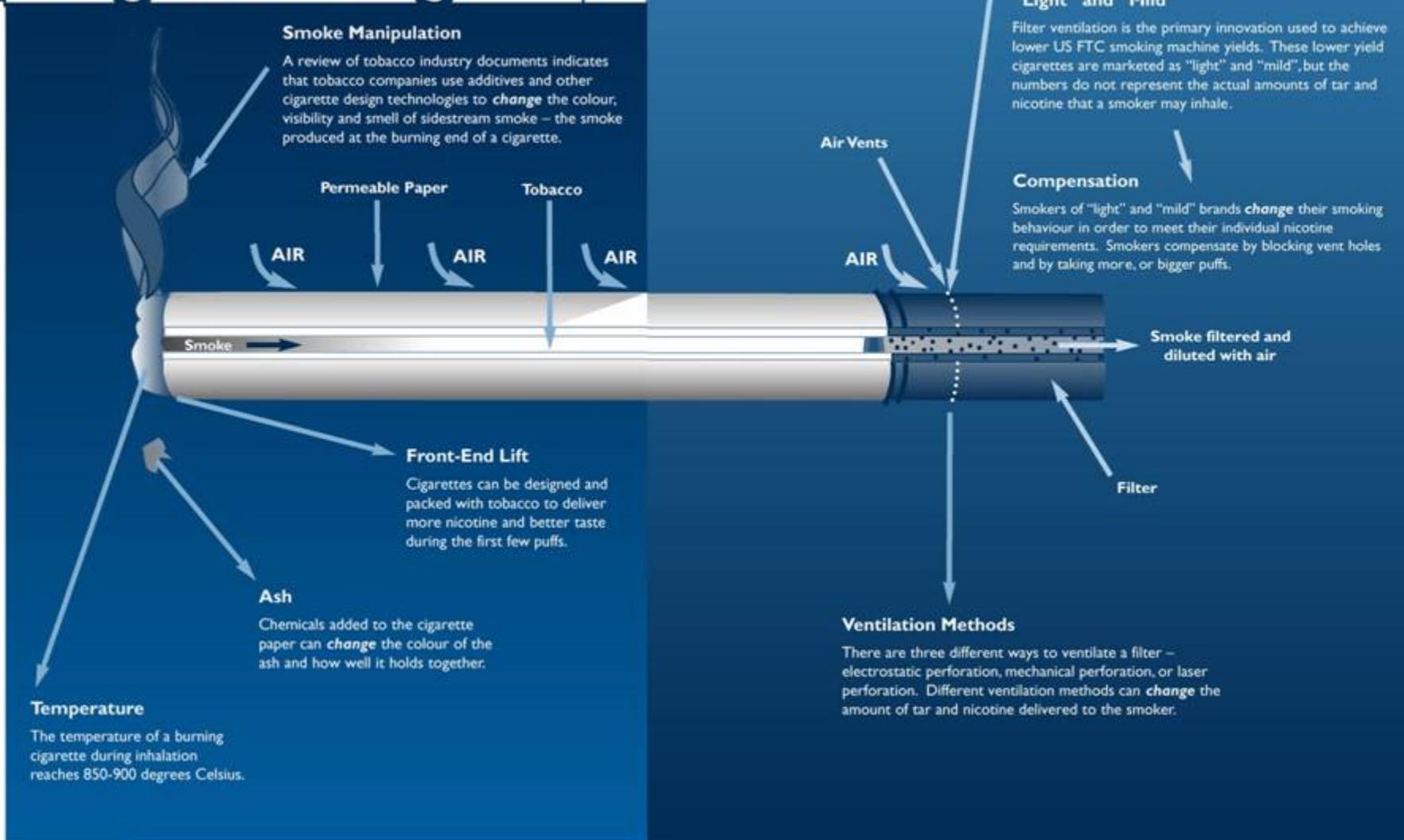


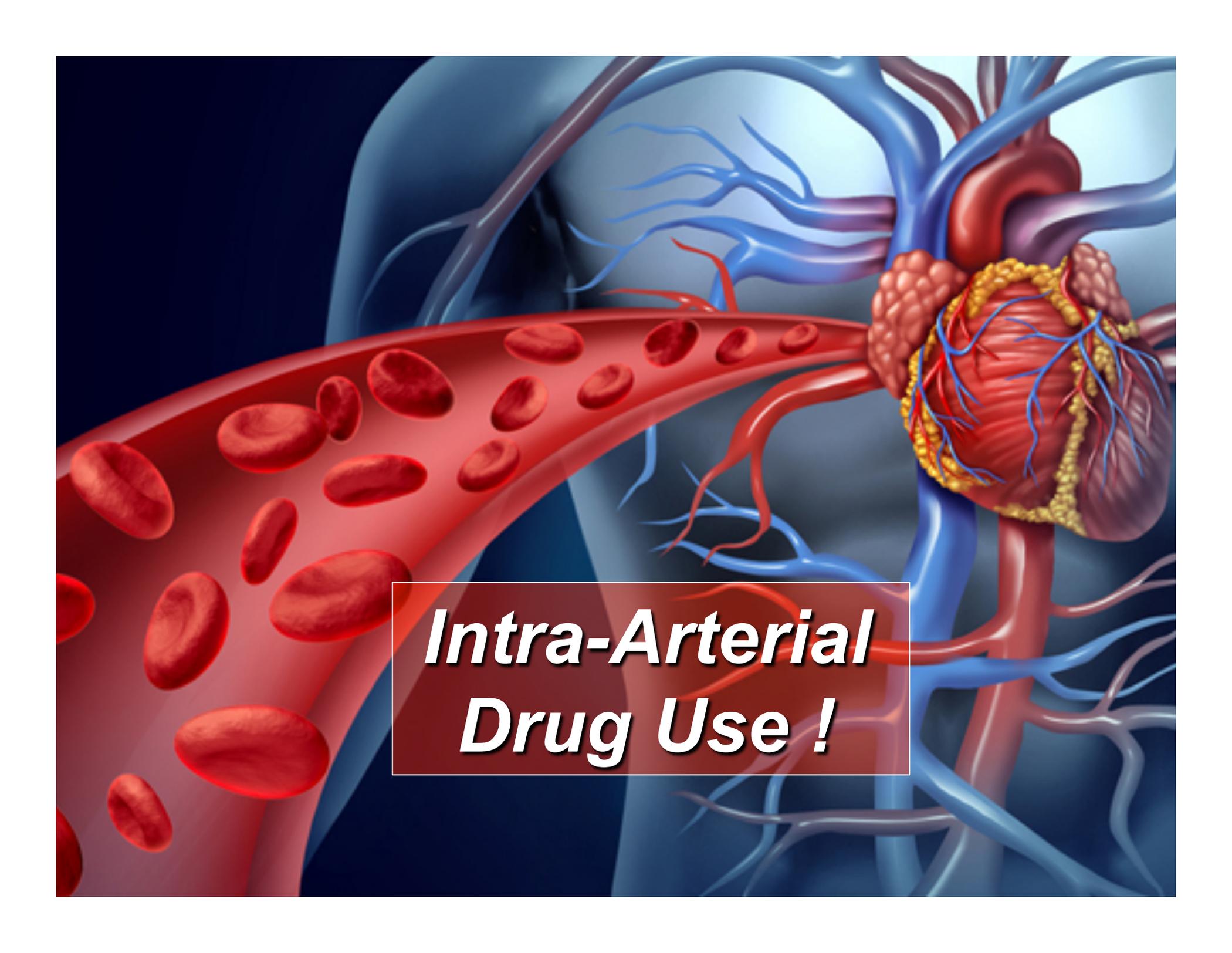
“A Cigarette is just a Cigarette”



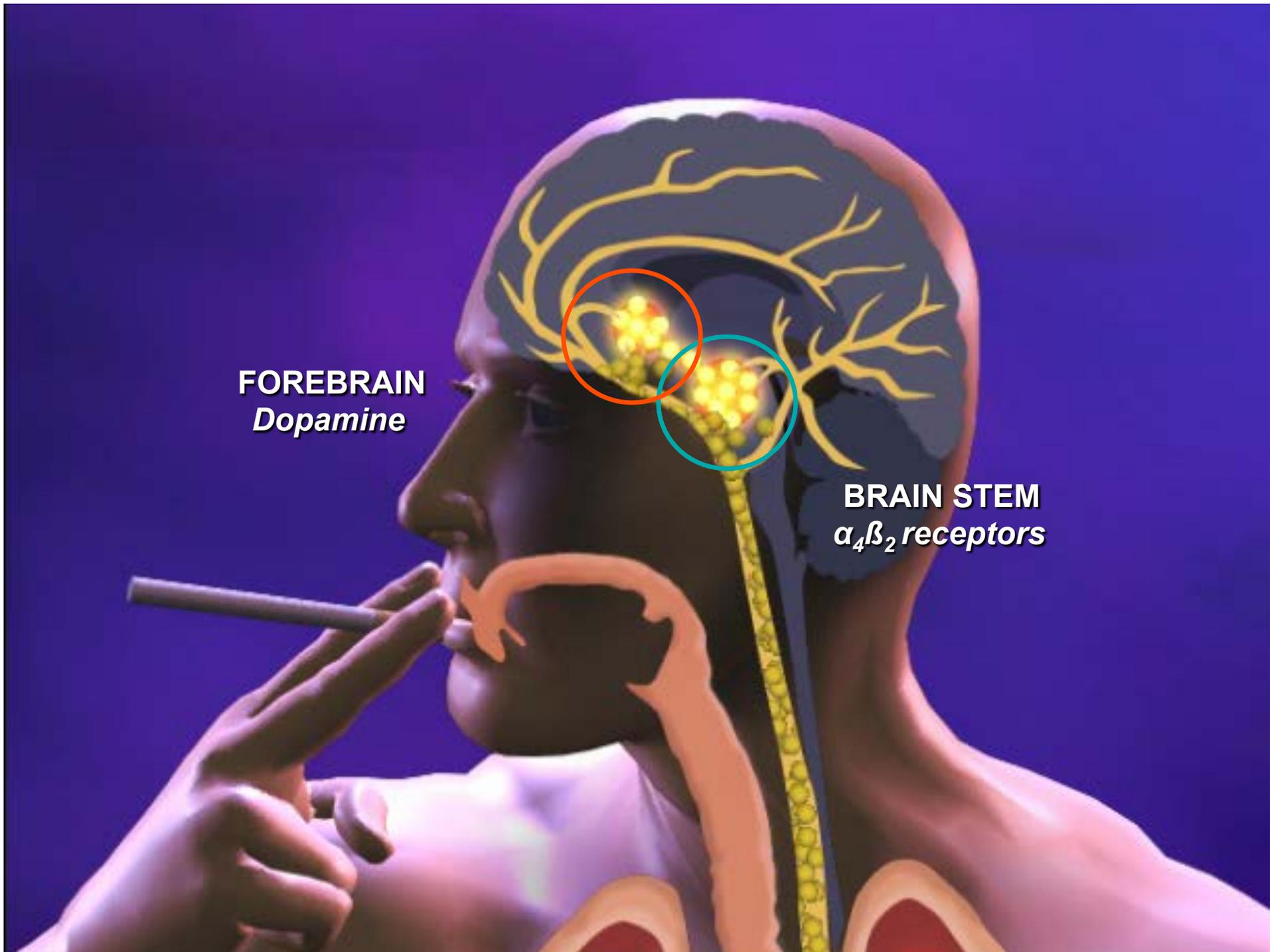
A Drug Delivery Device

# Cigarette engineering



An anatomical illustration of the human circulatory system. The heart is shown in the center, with blue veins and red arteries branching out. A large red artery is shown in a cross-section in the foreground, filled with red blood cells. The background shows a stylized human torso with the circulatory system highlighted in blue and red.

***Intra-Arterial  
Drug Use !***

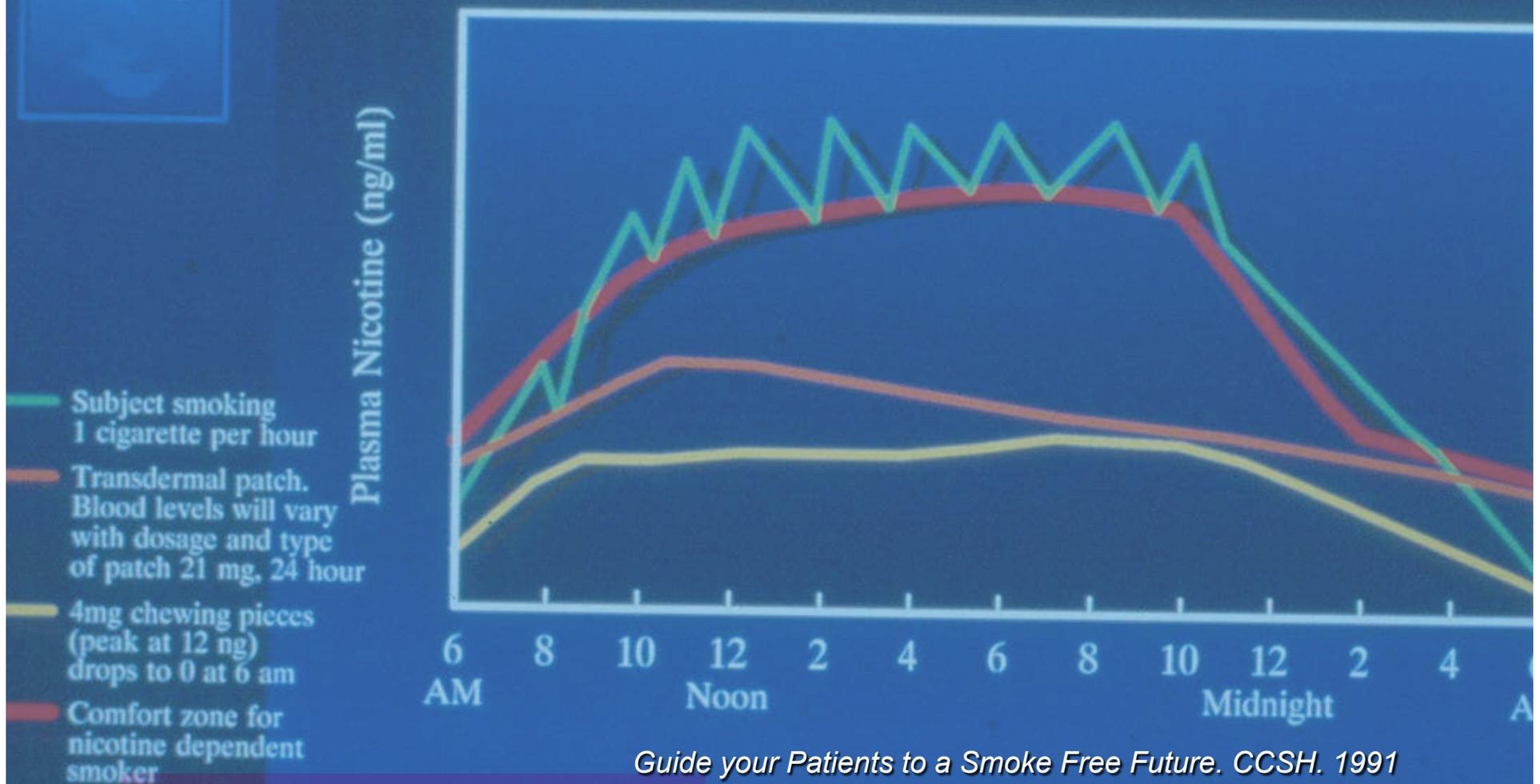


**FOREBRAIN**  
*Dopamine*

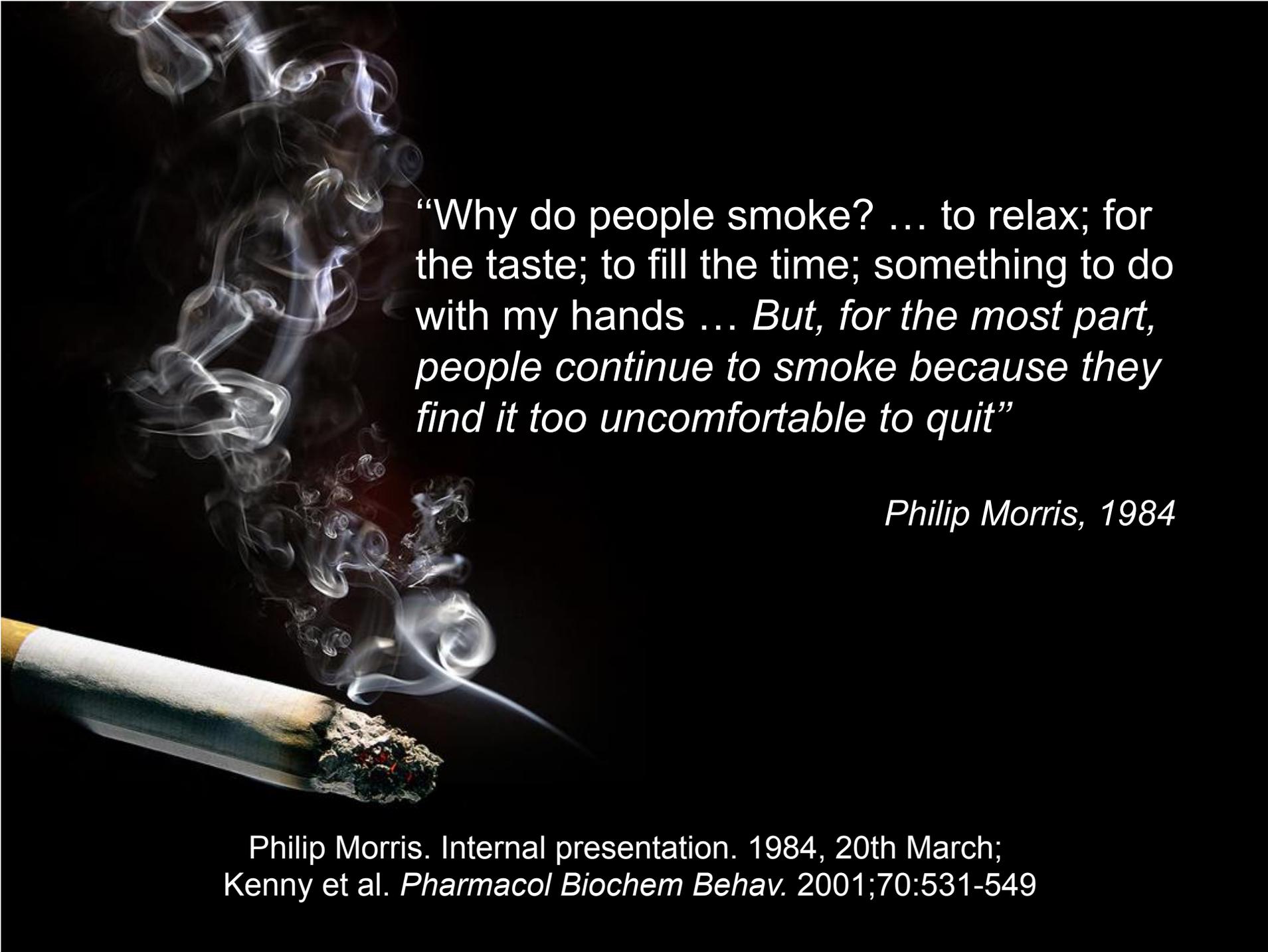
**BRAIN STEM**  
 *$\alpha_4\beta_2$  receptors*

A  
SMOKE  
FREE  
FUTURE

# A Day in the Life of Blood Nicotine



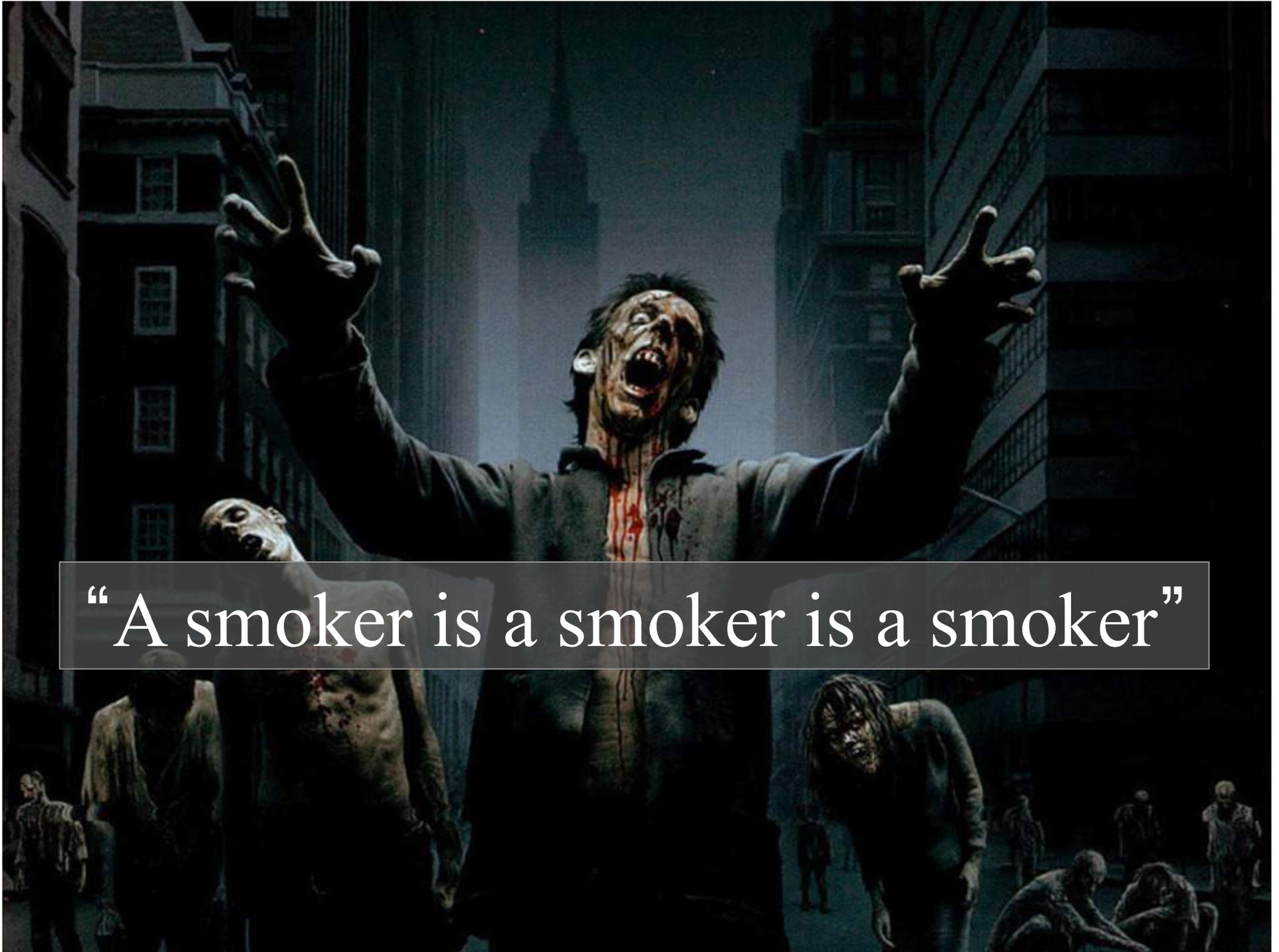
Guide your Patients to a Smoke Free Future. CCSH. 1991

A lit cigarette is shown in the lower-left corner, with a thick plume of white smoke rising and curling upwards against a solid black background. The smoke is illuminated from the side, creating a soft glow and highlighting its intricate, swirling patterns. The cigarette itself is partially lit, with a dark, charred tip and a small amount of ash visible.

“Why do people smoke? ... to relax; for the taste; to fill the time; something to do with my hands ... *But, for the most part, people continue to smoke because they find it too uncomfortable to quit*”

*Philip Morris, 1984*

Philip Morris. Internal presentation. 1984, 20th March;  
Kenny et al. *Pharmacol Biochem Behav.* 2001;70:531-549



“A smoker is a smoker is a smoker”

# CANNABIS USE IN CANADA

Canada has one of the highest rates  
of cannabis use in the world.



40%

OF CANADIANS HAVE  
USED CANNABIS



10%

OF CANADIANS HAVE  
USED CANNABIS IN  
THE PAST YEAR



20%

OF CANADIANS  
AGED 15-24 YEARS  
USED CANNABIS IN  
THE PAST YEAR



70%

OF CANADIAN  
CANNABIS USERS ARE  
AGE 25 OR OLDER



**Centre for Addiction and Mental Health (CAMH)**

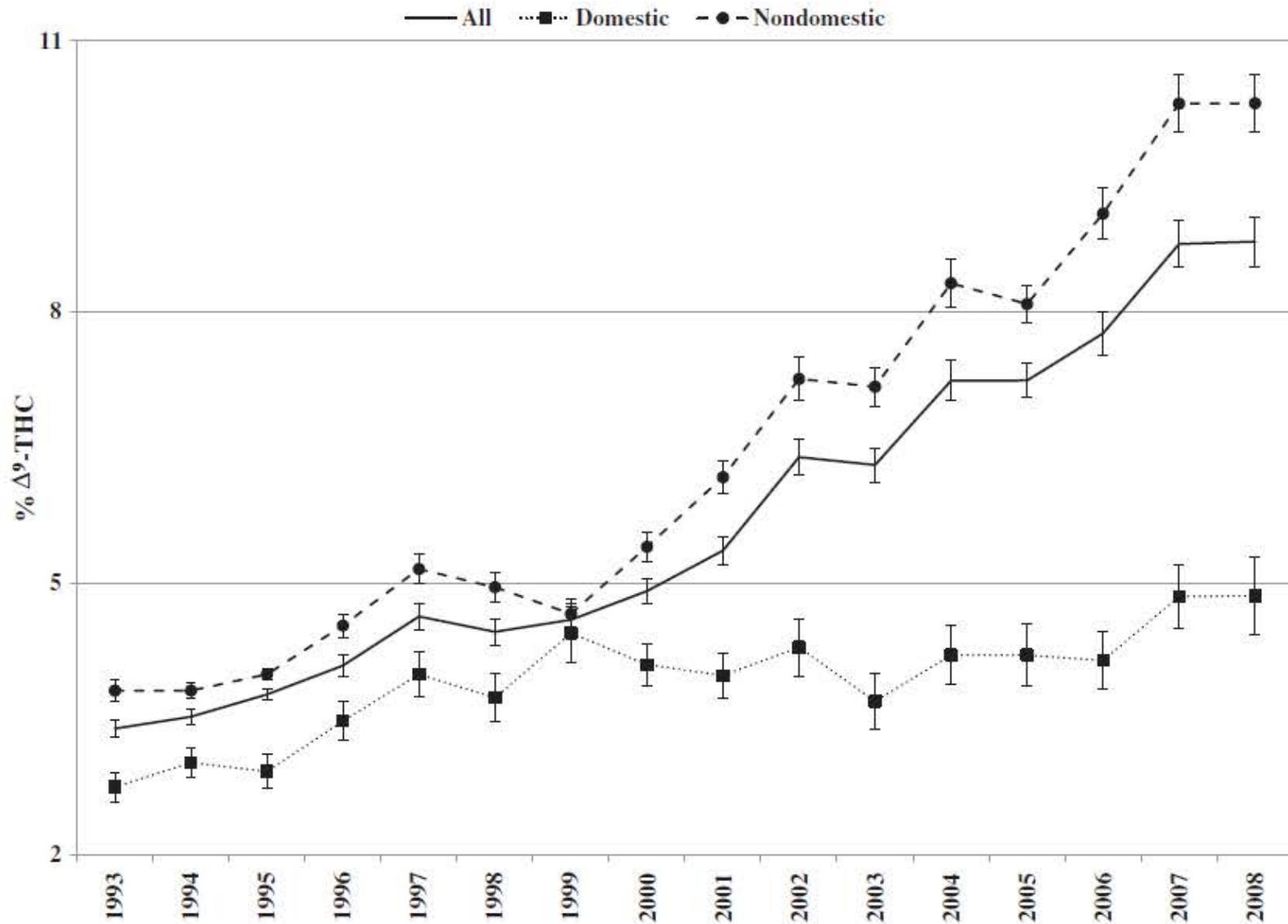


## *Cannabis Sativa*

Principal Cannabinoids:  $\Delta^9$  THC, Cannabinol, Cannabidiol

“Marijuana can be considered a very crude drug containing a very large number of chemical and pharmacological constituents, the properties of which are only slowly being understood.”

*$\Delta^9$ -THC concentration of domestic and nondomestic samples with 95% confidence intervals.*



A close-up photograph of a person's hand holding a lit cigarette. The cigarette is held between the fingers, and a plume of white smoke rises from the tip. The background is a soft, out-of-focus green. A semi-transparent white text box is overlaid on the center of the image.

*Many studies focusing on the duration of impairment were conducted when marijuana typically had a much lower concentration.*

*The applicability of these studies to today's more potent varieties is questionable as the duration of effect may be longer.*

## ***Adverse Effects of Short-Term Use of Marijuana***

Impaired short-term memory, making it difficult to learn and to retain information

Impaired motor coordination, interfering with driving skills and increasing the risk of injuries

Altered judgment, increasing the risk of sexual behaviors that facilitate the transmission of sexually transmitted diseases

In high doses, paranoia and psychosis

***N Engl J Med 2014;370:2219-2227***



## ***Adverse Effects of Long-Term or Heavy Use of Marijuana***

Addiction (in about 9% of users overall, 17% of those who begin use in adolescence, and 25 to 50% of those who are daily users)\*

Altered brain development\*

Poor educational outcome, with increased likelihood of dropping out of school\*

Cognitive impairment, with lower IQ among those who were frequent users during adolescence\*

Diminished life satisfaction and achievement (determined on the basis of subjective and objective measures as compared with such ratings in the general population)\*

Symptoms of chronic bronchitis

Increased risk of chronic psychosis disorders (including schizophrenia) in persons with a predisposition to such disorders

\* The effect is strongly associated with initial marijuana use early in adolescence.

***N Engl J Med 2014;370:2219-2227***

## ***Level of Confidence in the Evidence for Adverse Effects of Marijuana on Health and Well-Being***

<b>Effect</b>	<b>Overall Level of Confidence*</b>
Addiction to marijuana and other substances	High
Abnormal brain development	Medium
Progression to use of other drugs	Medium
Schizophrenia	Medium
Depression or anxiety	Medium
Diminished lifetime achievement	High
Motor vehicle accidents	High
Symptoms of chronic bronchitis	High
Lung cancer	Low

\* The indicated overall level of confidence in the association between marijuana use and the listed effects represents an attempt to rank the strength of the current evidence, especially with regard to heavy or long-term use and use that starts in adolescence.

***N Engl J Med 2014;370:2219-2227***

*“Impaired short-term memory, making it difficult to learn and retain information.”*





4 Hours after smoking  
6 hours after eating.  
8 hours after 'getting high'



## ***University of Ottawa Heart Institute Quit Smoking Programme***

### ***Characteristics of Marijuana Users (18% of QSP patients)***

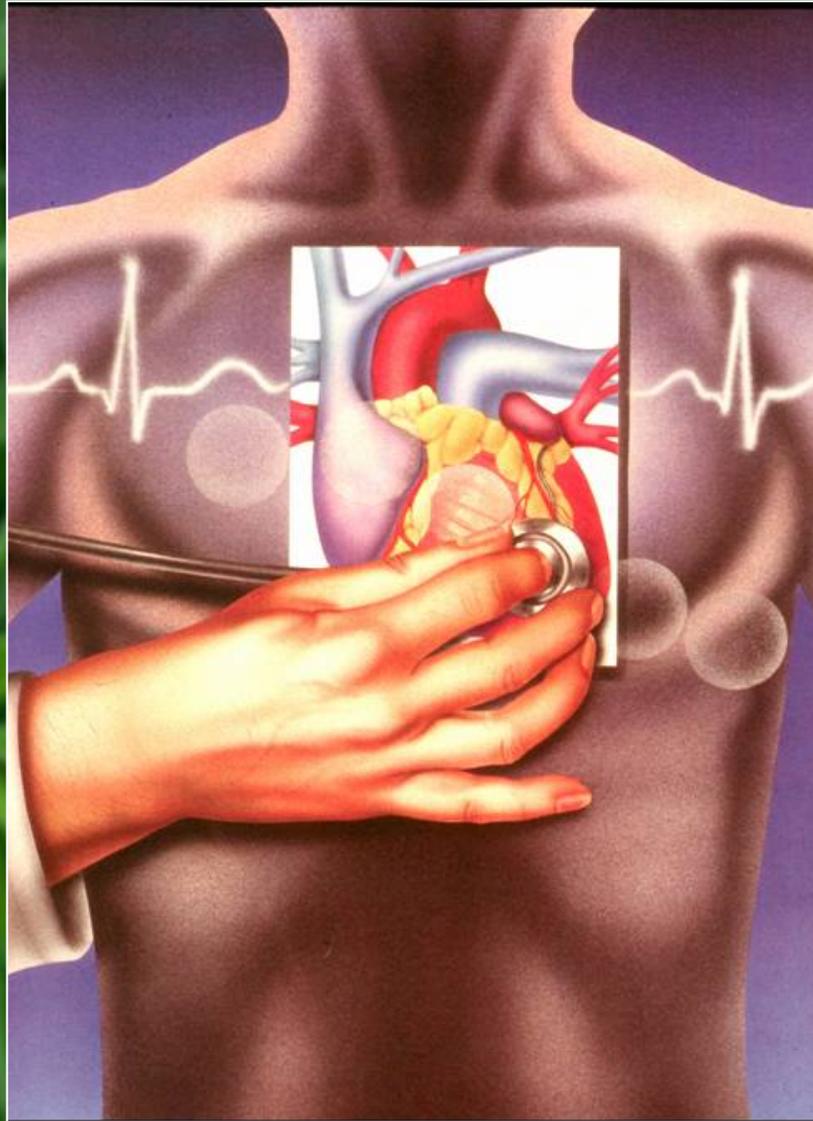
**56% Male**

**Average Age 49**

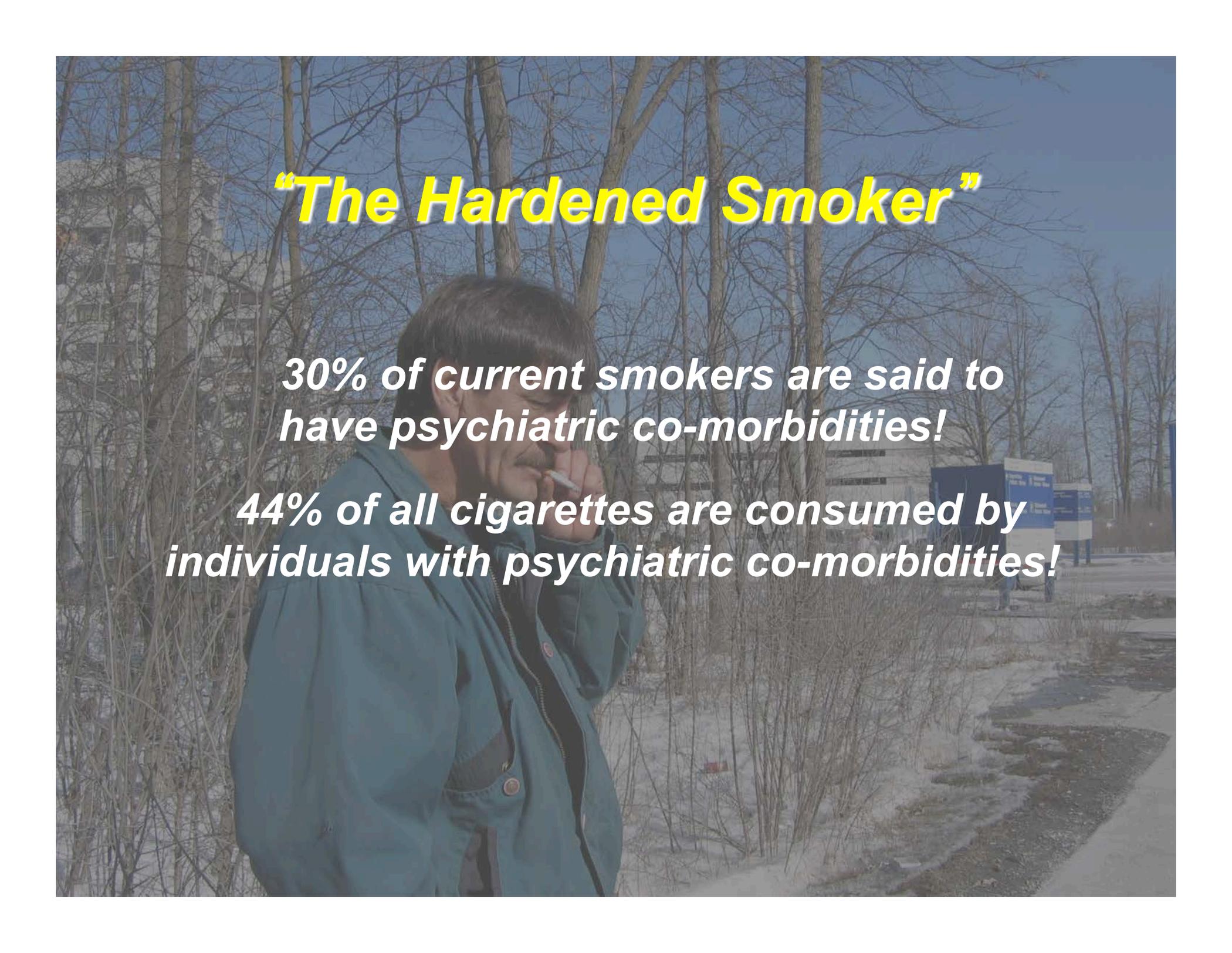
Grade 9-11	16%	Working	49%
Grade 12	19%	Unemployed	12%
Some post-secondary	42%	Disability	31%
No response	23%	Retired	7%



*“Addiction (in about 9% overall, 17% of those who began use in adolescence and 25-50% of daily users).”*



????????

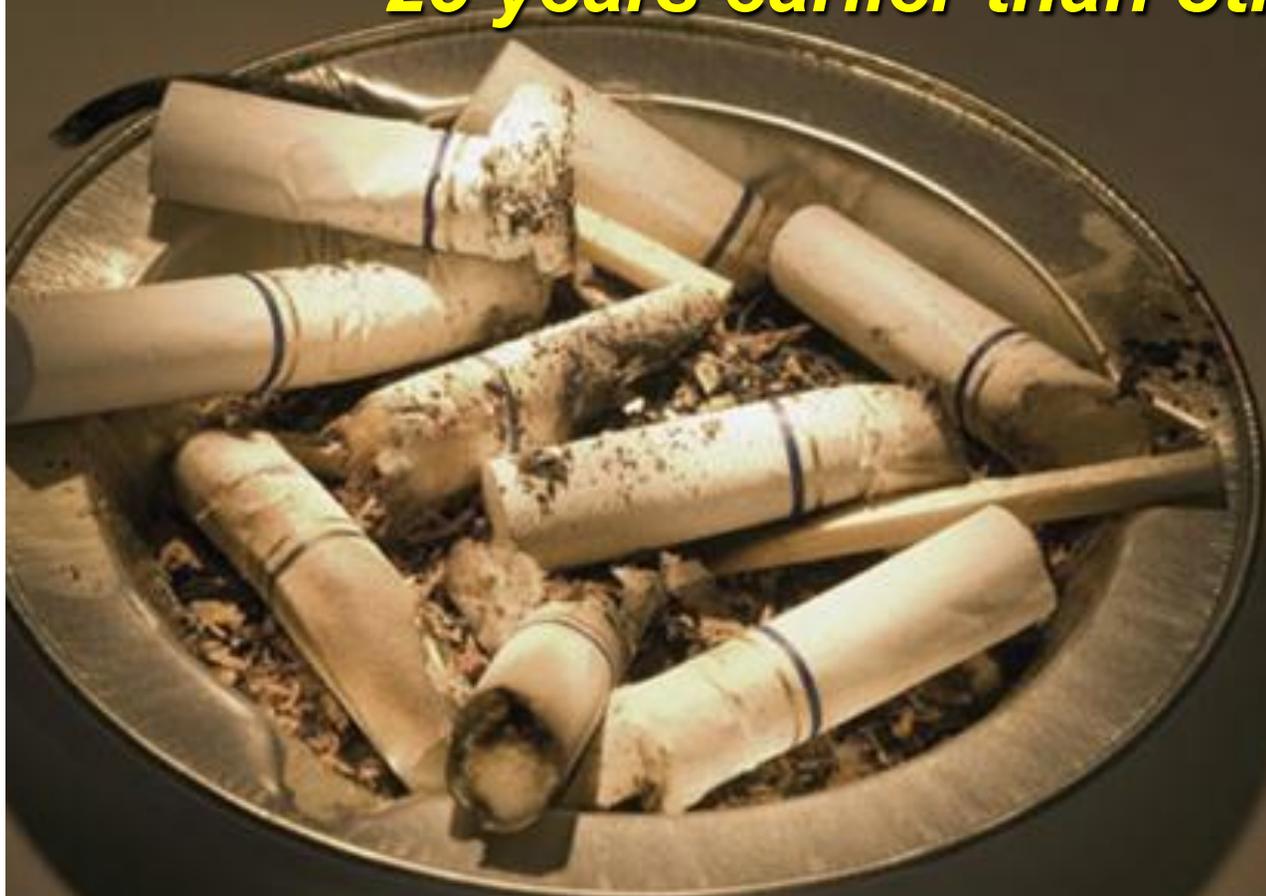
A photograph of a man with dark hair and a mustache, wearing a teal jacket, smoking a cigarette. He is standing outdoors in a winter setting with bare trees and a building in the background. The image is overlaid with text.

## ***“The Hardened Smoker”***

***30% of current smokers are said to have psychiatric co-morbidities!***

***44% of all cigarettes are consumed by individuals with psychiatric co-morbidities!***

***Persons with chronic mental illness die  
25 years earlier than others ...***

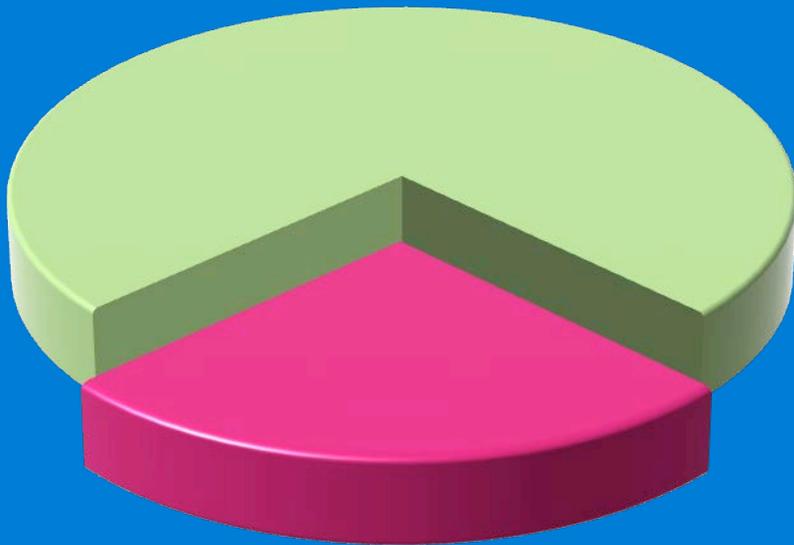


***... Tobacco addiction is the major  
contributor to that premature mortality.***

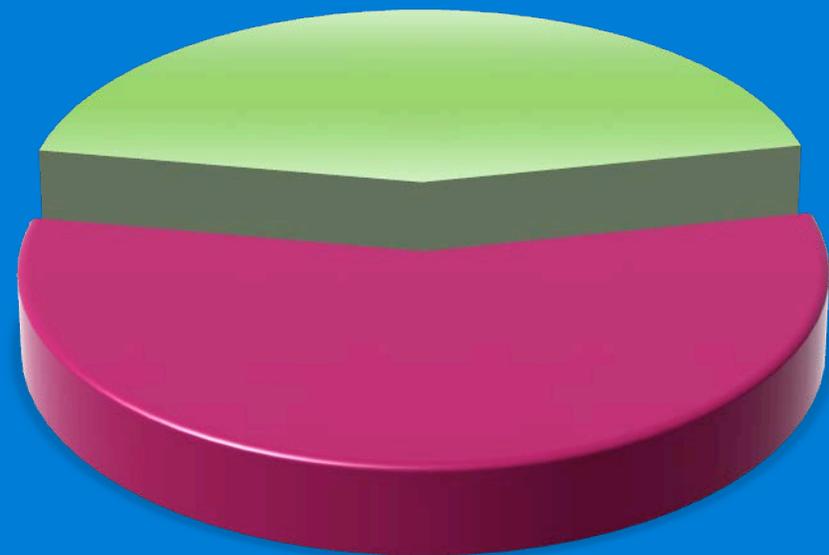
*Annu Rev Public Health 2010;31:297-314*

# Depression and Smoking

General Population

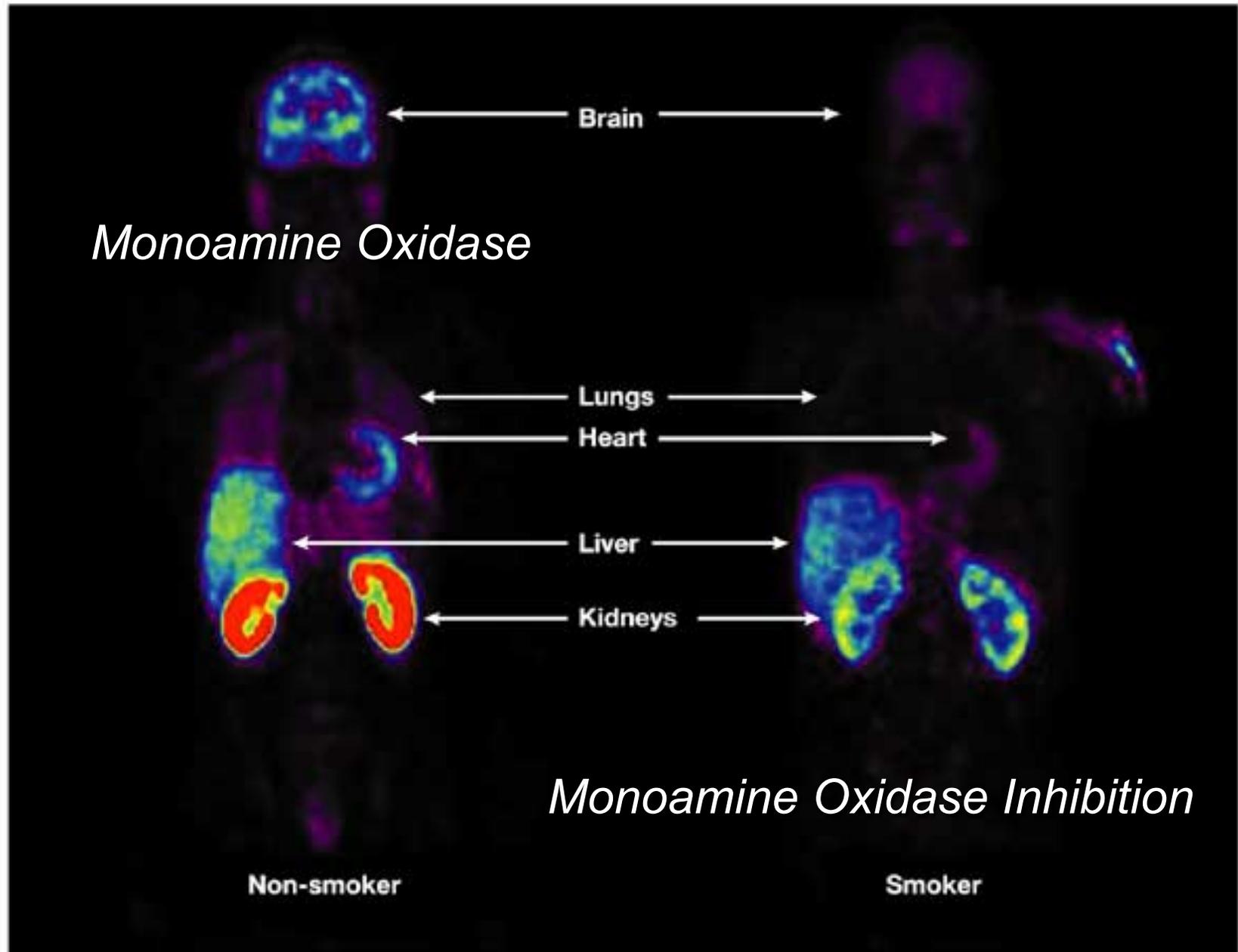


Depressed Population



■ Non-Smokers ■ Smokers

Farrell et al. *Int Rev Psychiatry*. 2003;15:43-49; Mackay et al. *The Tobacco Atlas*. 2nd ed. 2006.



# ***Smoking & Symptomatology***



In patients with schizophrenia, smoking may be associated with improvements in specific symptoms and cognitive measures ...

Compton et al. *Harv Rev Psychiatry*. 2006;14(4):212-222

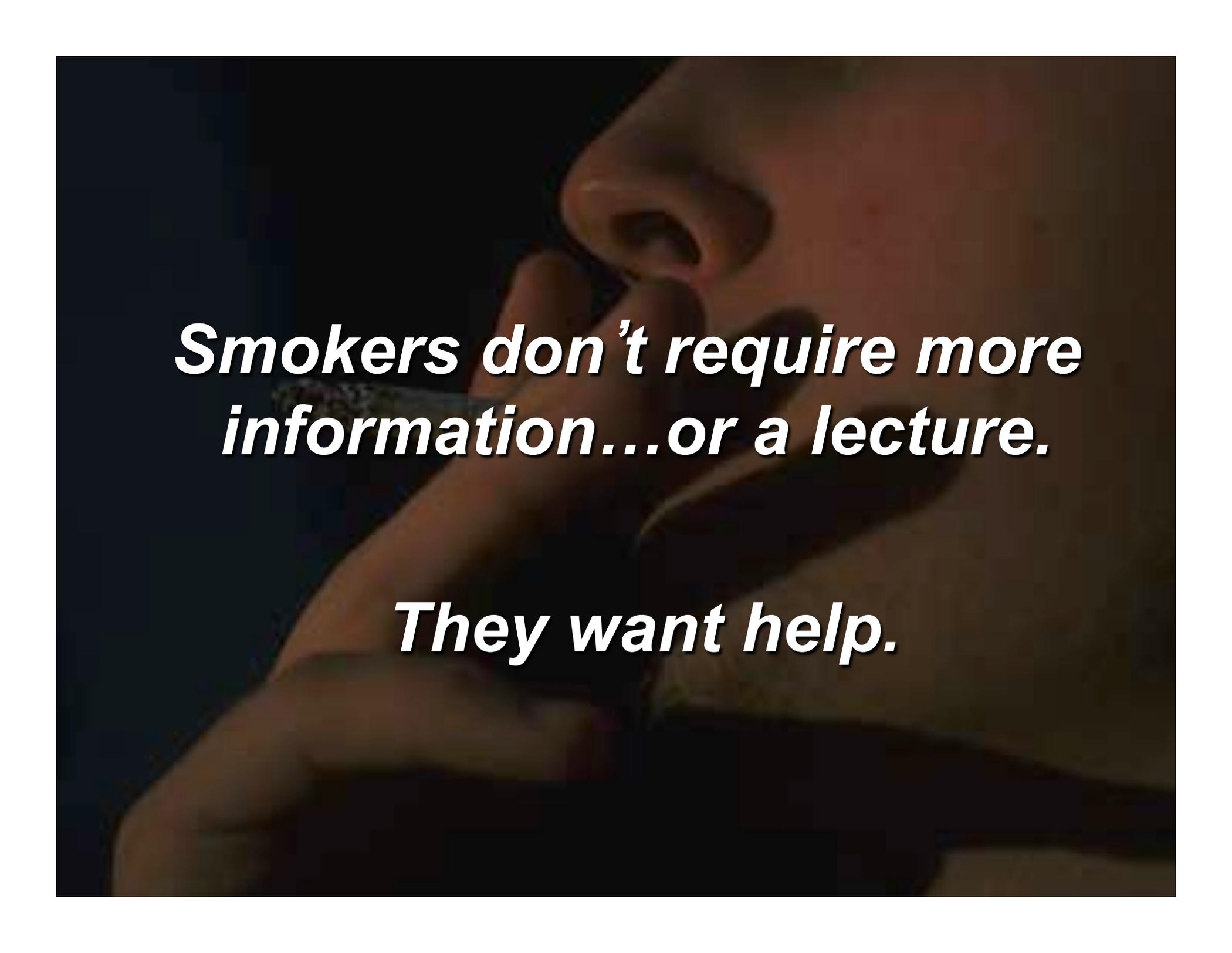
A dark, horror-themed image showing a zombie in a city street. The zombie is in the center, with its arms raised and a pained or screaming expression. It has blood on its face and chest. In the background, there are other zombies and tall buildings. A semi-transparent grey box with white text is overlaid on the image.

Psychiatric patients can't quit smoking.



***Most smokers with mental health problems would like to quit, and the quit rates are only slightly lower than for the general population.***

*Annu Rev Public Health 2010;31:297-314*



***Smokers don't require more  
information...or a lecture.***

***They want help.***

# *Clinician's Advice*



***Clear***  
***Strong***  
***Personalized***

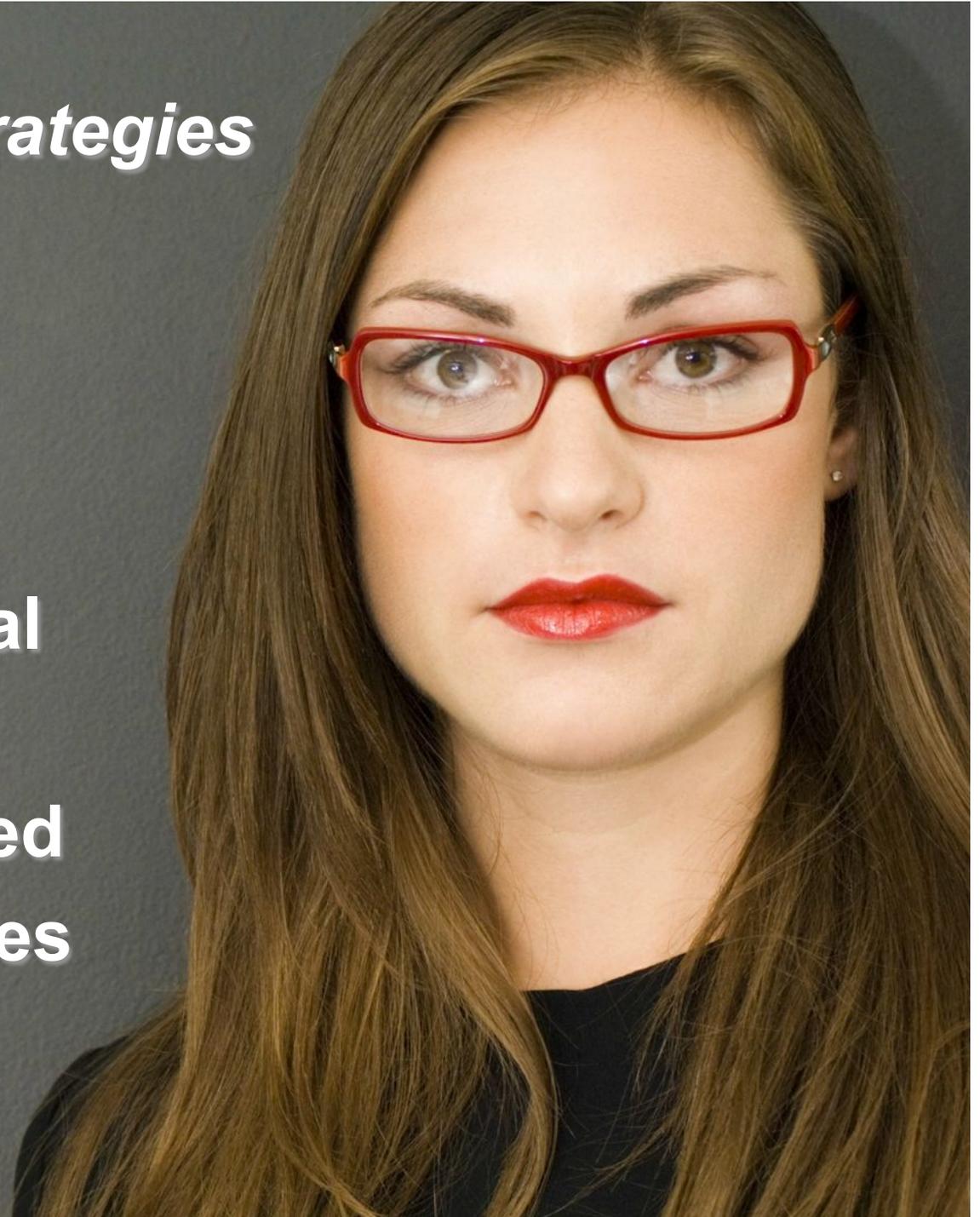
*“unambiguous and non-judgmental”*

**Matched by an institutional  
commitment to “best practice” !**

# *Behavioural Strategies*

**Tactical  
Strategic  
Situational**

**Patient Centred  
M-I Approaches**





## ***Caffeine Ingestion***

- *Caffeine metabolism altered by cessation*
- *Caffeine levels may rise: 2-3 x higher !*
- *Consider reducing caffeine intake*
- *Consider substituting de-caffeinated drinks*
- *Be aware of similarities between 'caffeinism' and withdrawal symptoms*



***Pharmacotherapy***

**3 “First Line Therapies”**

**NRT**

**bupropion**

**varenicline**



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***Sometimes the doorway has to be  
opened wider, or held open longer...***

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***Titrate Therapy:***  
***Dose***  
***Duration***  
***Combination***

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# ***Nicotine Replacement Therapy***

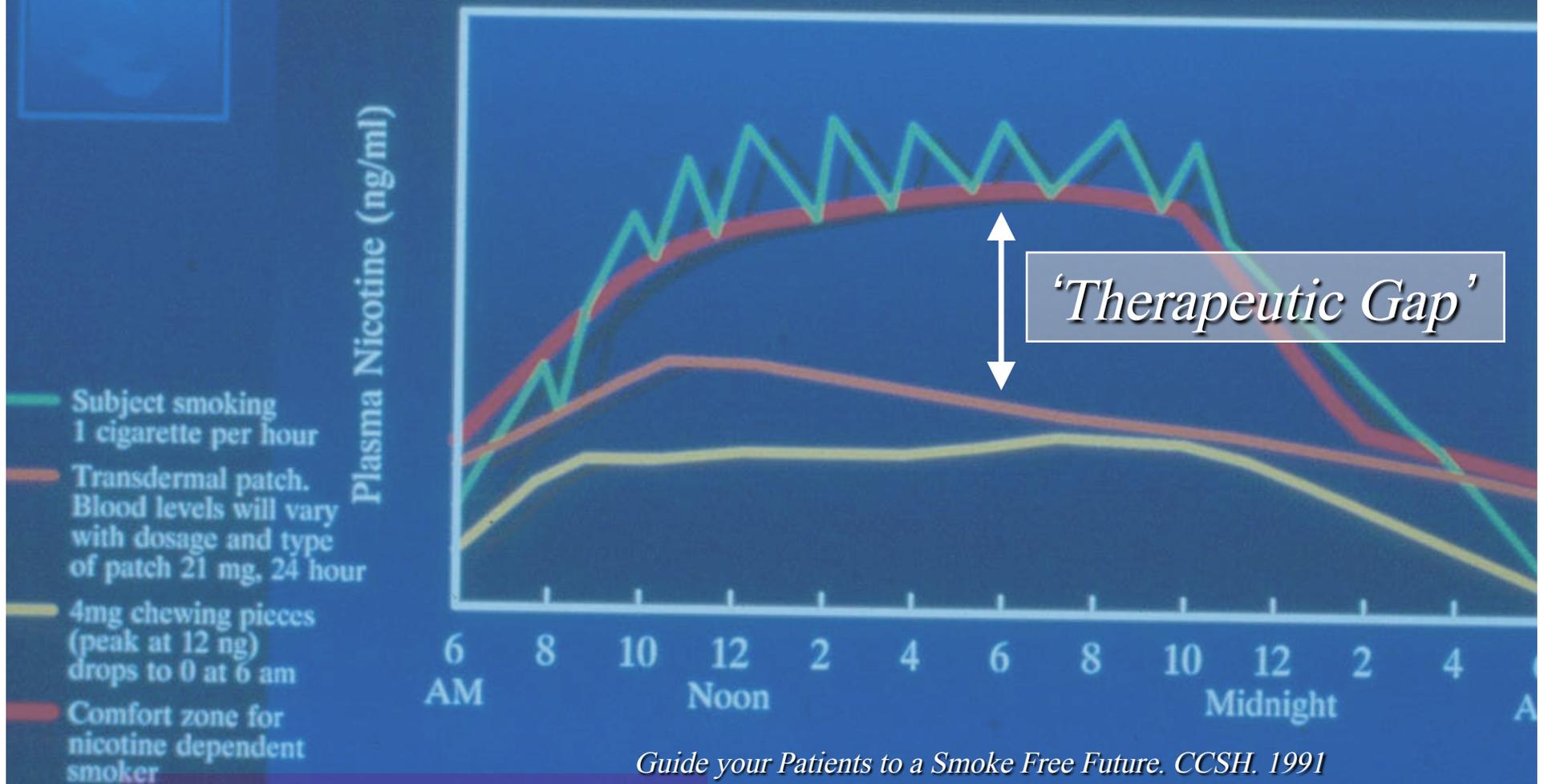
***Rationale***  
***Products***

- The 'Patch'***
- Chewing Pieces***
- Lozenges***
- Nicotine 'Inhaler'***
- Nicotine Spray***

***Advantages***  
***Shortcomings***

A  
SMOKE  
FREE  
FUTURE

# A Day in the Life of Blood Nicotine



Guide your Patients to a Smoke Free Future. CCSH. 1991



# *Standard Orders*

*1 pack a day*                      **21 mg +    and Inhaler**

*2 packs a day*                      **42 mg +    and Inhaler**

*3 packs a day*                      **further titration *prn***

***In every case recognize the need for titration***

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A dark, atmospheric scene from a zombie movie. In the center, a zombie with a bloody, screaming face and outstretched arms stands prominently. He is wearing a dark jacket with blood splatters. To his left, another zombie is partially visible, and to his right, a third zombie is hunched over. The background shows a city street at night with tall buildings and a hazy, foggy atmosphere. A semi-transparent grey box with white text is overlaid across the middle of the image.

You can't use NRT in cardiac patients!



## ***“Zombie Concepts”***

***“The safety of nicotine-replacement therapy in cardiovascular disease patients is supported by data from randomized trials, efficacy studies, observational data and physiologic studies.”***

Joseph AM, Fu, *Progress in Cardiovascular Diseases* 2003;45:429-441



## ***NRT and CV Risk***

***“Clinical trials of NRT in patients with underlying, stable cardiovascular disease suggest that nicotine does not increase cardiovascular risk.”***

Benowitz NL, Gourlay SG. *J Am Coll Cardiol* 1997;29:1422-31.



## ***NRT and CV Risk***

***“High-dose nicotine treatment, even with concomitant smoking, caused no short-term adverse effects on the cardiovascular system.”***

Zevin S, Peyton J, Benowitz NL. *Clin Pharmacol Ther* 1998;64:87-95.



## ***NRT and CV Risk***

***“The use of nicotine patches did not cause aggravation of myocardial ischemia or arrhythmia in coronary patients and therefore can be used as a method to promote smoking cessation in this high-risk group.”***

Tzivoni D, Keren A, Meyler et al. *Cardiovasc Drugs Ther* 1998;12:239-244.



## ***NRT and CV Risk***

***“The use of NRT is not associated with any increase in the risk of myocardial infarction, stroke, or death.”***

**N = 33,247**

Hubbard R, Lewis S, et al. *Tobacco Control* 2005;14:416-421



## ***NRT and CV Risk***

***“Patients with pre-existing cardiovascular disease represent one of the groups most likely to benefit from smoking cessation and our results should encourage the use of NRT in these individuals.”***

Hubbard R, Lewis S, et al. *Tobacco Control* 2005;14:416-421

# UOHI Smoking Cessation Programme

## Use of NRT in the Cardiac Setting

	<i>Smoking Patients</i>	<i>NRT</i>	<i>Male NRT</i>	<i>Female NRT</i>	<i>ACS</i>	<i>% ACS NRT</i>
2004-2005	<b>1,016</b> (23%)	<b>194</b> (19%)	<b>149</b> (20%)	<b>45</b> (17%)	<b>176</b>	<b>68</b> (39%)
2005-2006	<b>1,489</b>	<b>657</b> (44%)	<b>477</b> (46%)	<b>180</b> (41%)	<b>501</b>	<b>318</b> (63%)
2006-2007	<b>1,065</b>	<b>638</b> (60%)	<b>453</b> (60%)	<b>185</b> (60%)	<b>342</b>	<b>240</b> (70%)



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# ***Smoking Cessation***

***“The single, most powerful,  
preventive intervention in  
clinical practice.”***

Woolf SH. *JAMA* 1999;282(24):2358-65.



# 3 Generations of E-Cigarettes

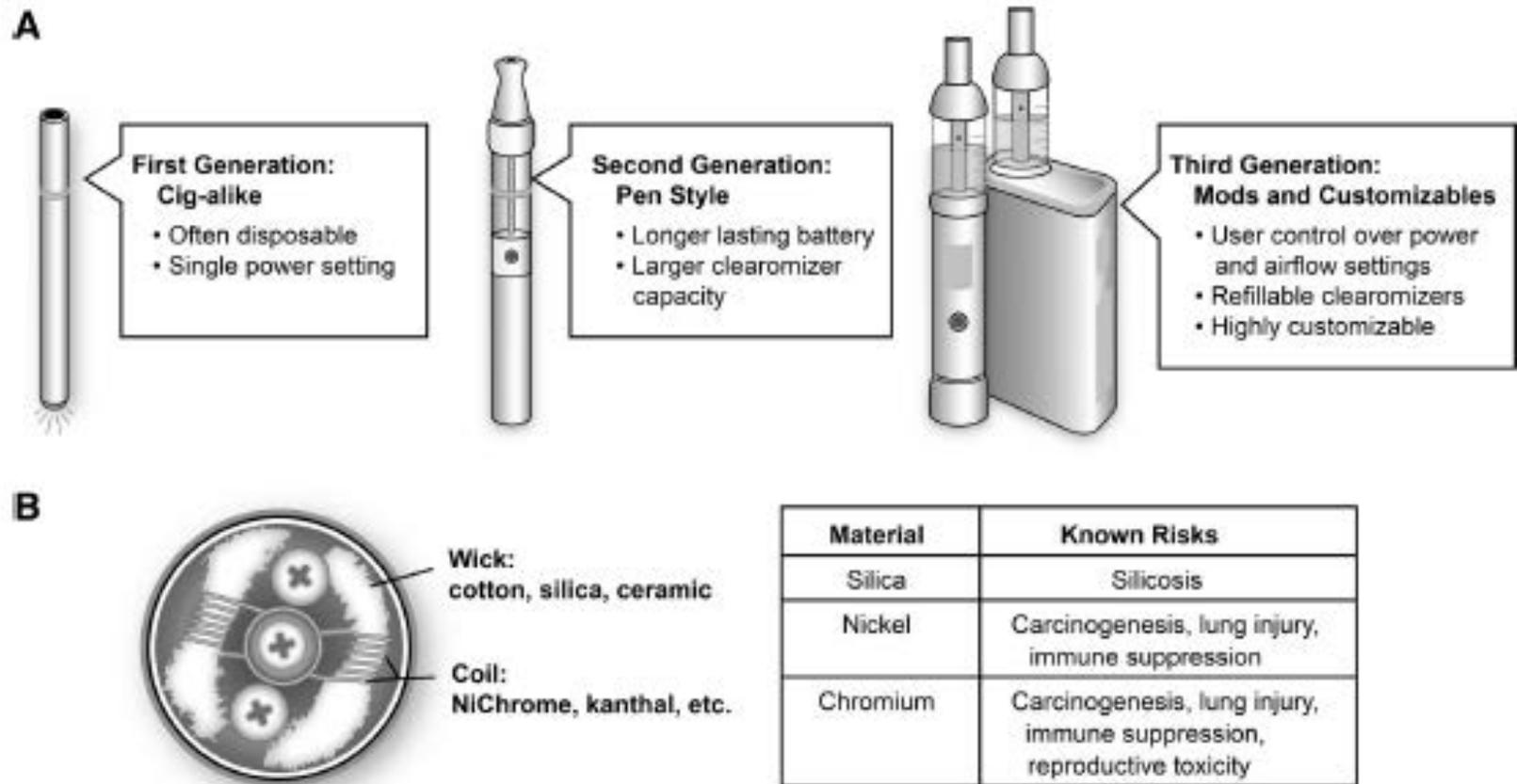
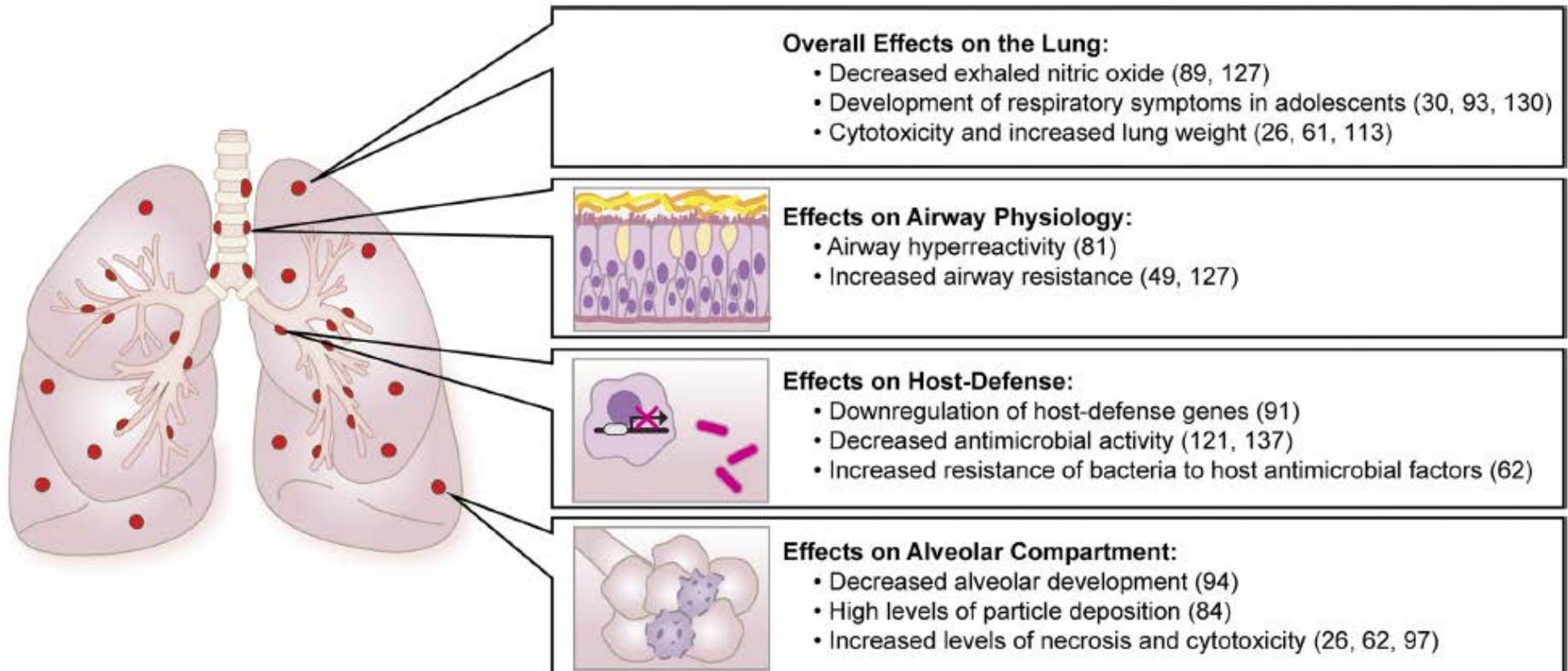
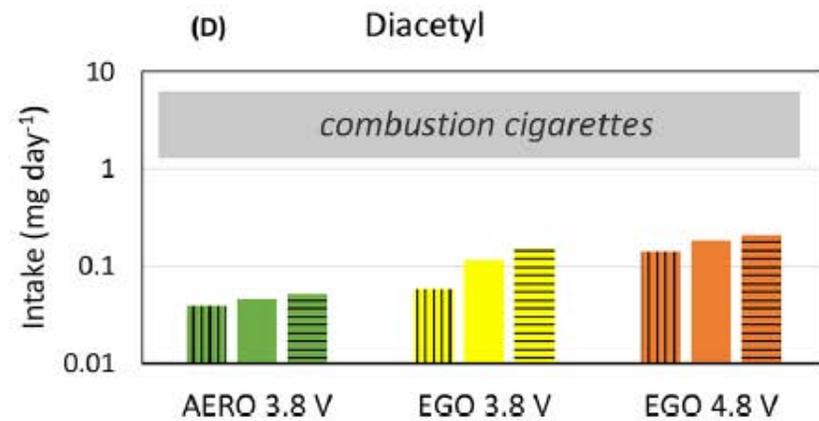
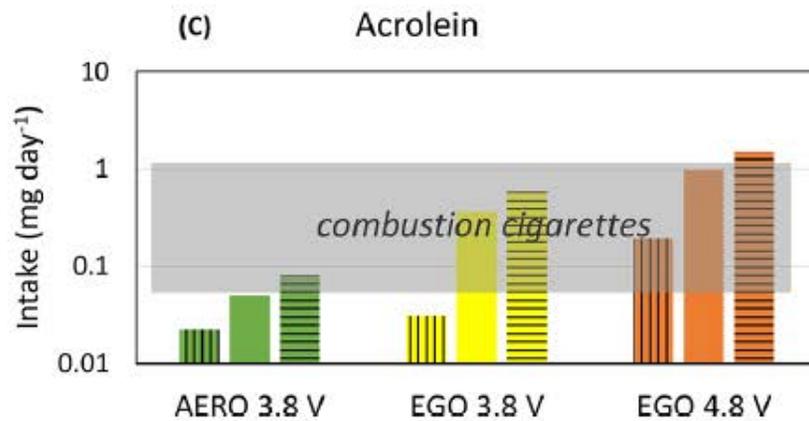
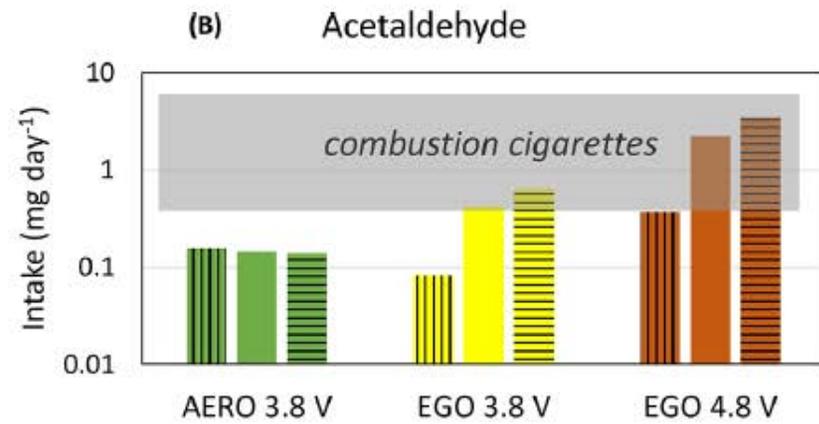
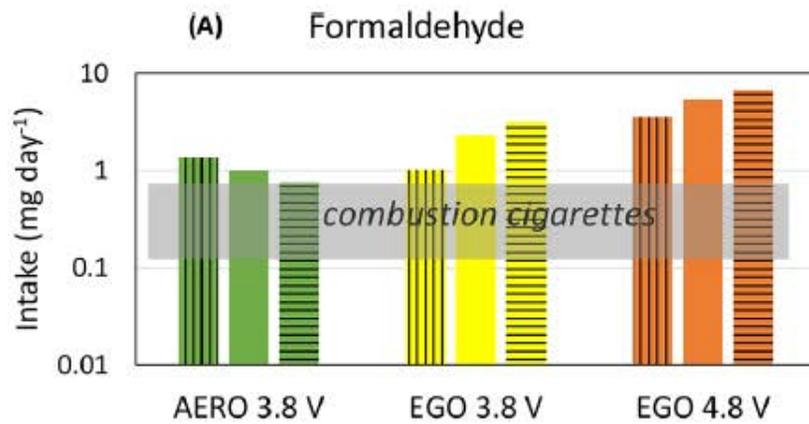


Fig. 1. *A*: the three generations of e-cigarettes. Beginning with the early cig-a-like devices, e-cigs introduced to the market more recently incorporate increased user control over the physics of aerosolization and e-liquid composition. *B*: e-cigarette atomizers contain wicking materials to transfer e-liquids from a storage tank in close proximity to a heating filament made from one of several types of metal alloys. Many of the commonly employed materials have well-described health risks.

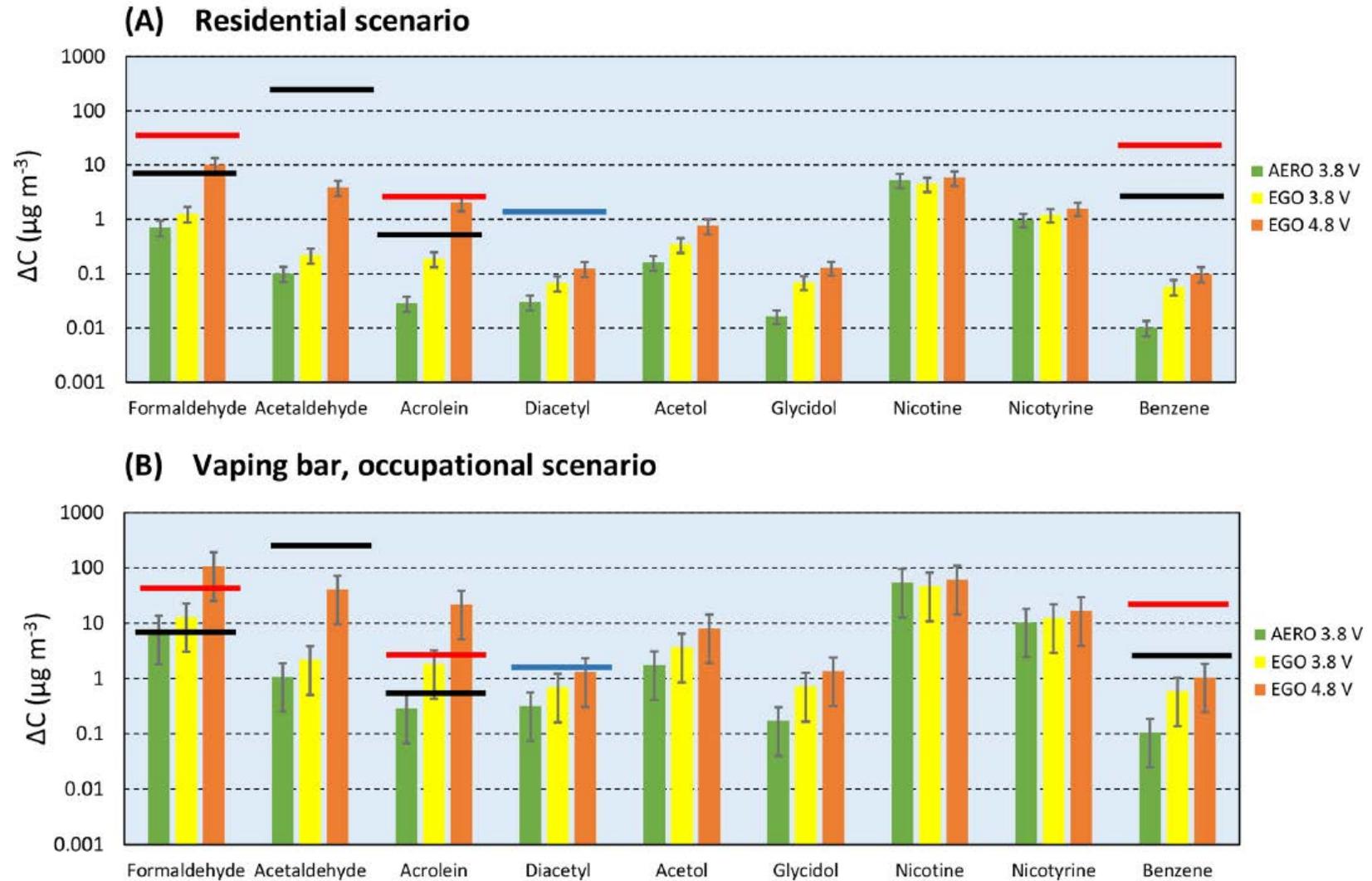
# *Pulmonary Toxicity of E-Cigarettes*



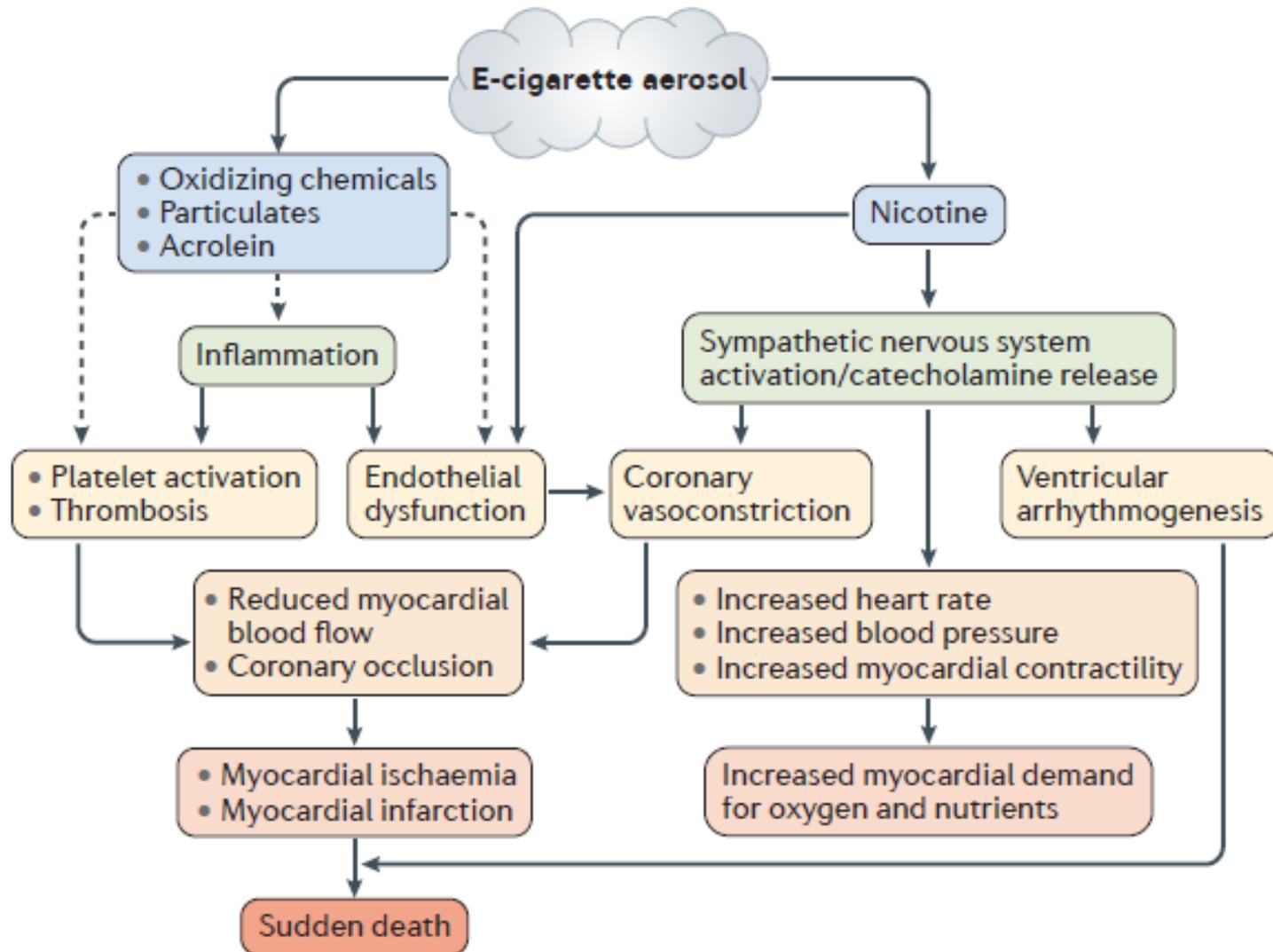
# Cigarettes vs E-Devices



# Change in Indoor VOC Concentrations



# E-Cigarettes & Acute Cardiac Events



*Harm reduction potential – Vapour vs. Smoke  
Cessation of smoking? Dual-Use?  
Tobacco industry – Perpetuation of smoking?  
Initiation of smoking? – Adolescents?*



# The E-cigarette.

Brief report

## **A Descriptive Report of Electronic Cigarette Use After Participation in a Community-Based Tobacco Cessation Trial**

Elana Curry BS<sup>1</sup>, Julianna M. Nemeth PhD<sup>1</sup>, Amy Wermert MPH<sup>1</sup>, Sara Conroy MS<sup>2</sup>, Abigail Shoben PhD<sup>3</sup>, Amy K. Ferketich PhD<sup>2</sup>, Mary Ellen Wewers PhD<sup>1</sup>

*“Among adult Appalachian smokers enrolled in community-based tobacco cessation treatment, use of e-cigarettes post-treatment was associated with lower abstinence rates at 12 months.”*

*“Post treatment e-cigarette use was associated with less success in achieving abstinence at 12 months, as compared to non-use.”*

# Electronic Cigarettes for Smoking Cessation

Christopher Bullen



Evidence for their efficacy as cessation aids, based on several randomised trials of now obsolete e-cigarettes, suggests a modest effect equivalent to nicotine patch. E-cigarettes are almost certainly far less harmful than tobacco smoking, but the health effects of long-term use are as yet unknown. Dual use is common and almost as harmful as usual smoking unless it leads to quitting.

If patients who smoke are unwilling to quit or cannot succeed using evidence-based approaches, e-cigarettes may be an option to be considered after discussing the limitations of current knowledge.



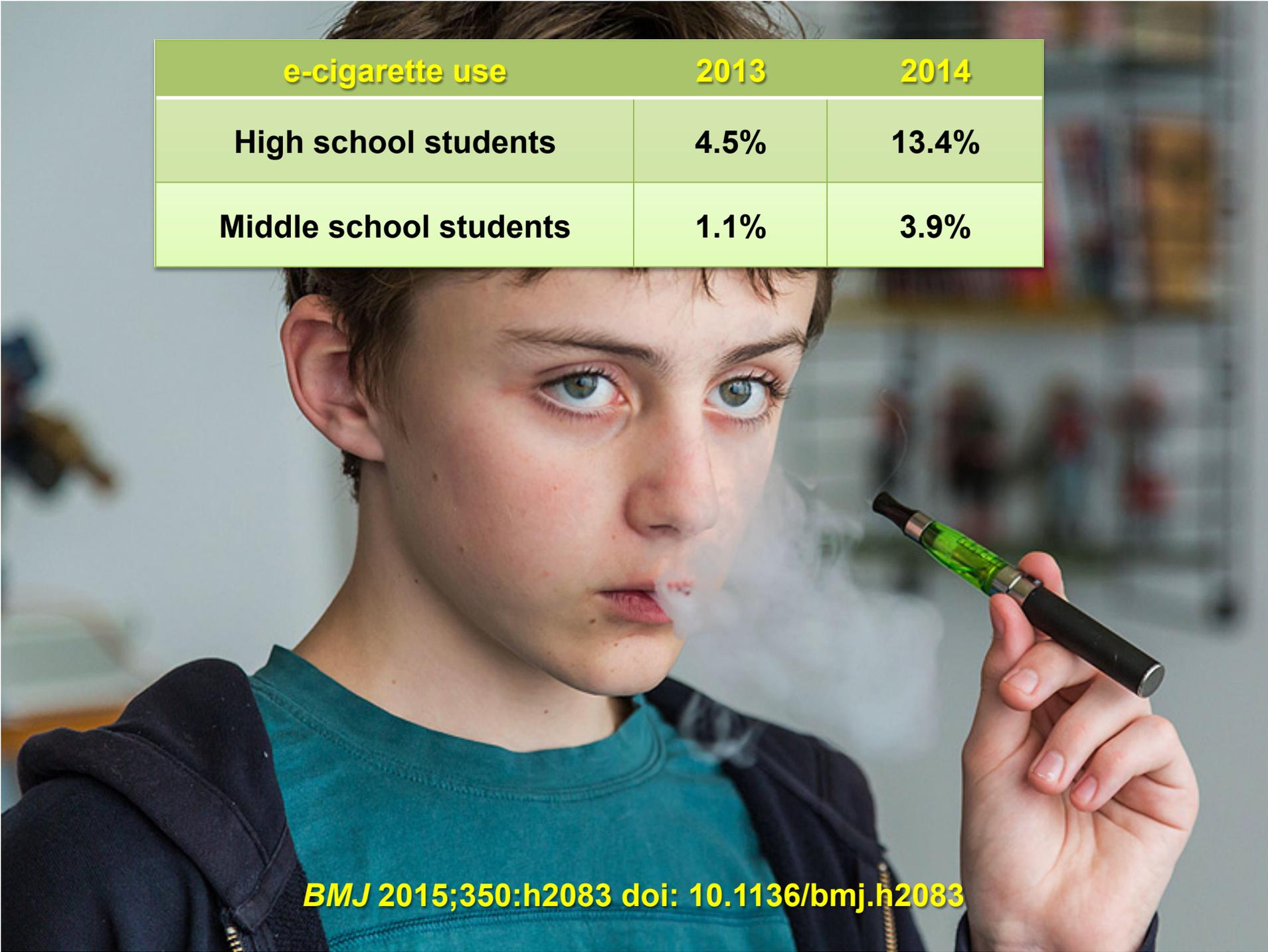
**Cochrane**  
**Library**

Cochrane Database of Systematic Reviews

## Electronic cigarettes for smoking cessation (Review)

**Citation:** Hartmann-Boyce J, McRobbie H, Bullen C, Begh R, Stead LF, Hajek P. Electronic cigarettes for smoking cessation. *Cochrane Database of Systematic Reviews* 2016, Issue 9. Art. No.: CD010216. DOI: 10.1002/14651858.CD010216.pub3.

*“We could not determine if EC was better than a nicotine patch in helping people stop smoking...”*



<b>e-cigarette use</b>	<b>2013</b>	<b>2014</b>
<b>High school students</b>	<b>4.5%</b>	<b>13.4%</b>
<b>Middle school students</b>	<b>1.1%</b>	<b>3.9%</b>

**BMJ 2015;350:h2083 doi: 10.1136/bmj.h2083**

# E-cigarette use as a predictor of cigarette smoking: results from a 1-year follow-up of a national sample of 12th grade students

Richard Miech, Megan E Patrick, Patrick M O'Malley, Lloyd D Johnston

**Results** Among youth who had never smoked a cigarette by 12th grade, baseline, recent vapers were more than 4 times (relative risk (RR)=4.78) more likely to report past-year cigarette smoking at follow-up, even among youth who reported the highest possible level of perceived risk for cigarette smoking at baseline.

**Conclusions** These results contribute to the growing body of evidence supporting vaping as a one-way bridge to cigarette smoking among youth. Vaping as a risk factor for future smoking is a strong, scientifically-based rationale for restricting youth access to e-cigarettes.

Miech R, et al. *Tob Control* 2017;**0**:1–6. doi:10.1136/tobaccocontrol-2016-053291

## RESEARCH

# Electronic cigarette use and smoking initiation among youth: a longitudinal cohort study

David Hammond PhD, Jessica L. Reid MSc, Adam G. Cole MSc, Scott T. Leatherdale PhD

## Conclusion

The current study provides strong evidence that e-cigarettes are associated with initiation of cigarette smoking among youth; however, the controversy as to whether e-cigarette use “causes” cigarette-smoking initiation will undoubtedly persist.

# WHY QUIT? SWITCH TO BLU

blu is the smart choice for smokers wanting a change. Take back your freedom to smoke when and where you want without ash or smell.

blu is everything you enjoy about smoking and nothing else.

Nobody likes a quitter, so make the switch today.

Visit [blucigs.com](http://blucigs.com)



\* New blu Smart Pack





**Cigarette Technology Alert**

Find Out  
How Megan Can...

# Smoke Anywhere

Learn More

New Smoking Technology Featured On:



# Wild Candy Flavors GUMMY BEARS





# Electronic cigarettes for smoking cessation and reduction (Review)

McRobbie H, Bullen C, Hartmann-Boyce J, Hajek P

**Citation:** McRobbie H, Bullen C, Hartmann-Boyce J, Hajek P. Electronic cigarettes for smoking cessation and reduction. *Cochrane Database of Systematic Reviews* 2014, Issue 12. Art. No.: CD010216. DOI: 10.1002/14651858.CD010216.pub2.



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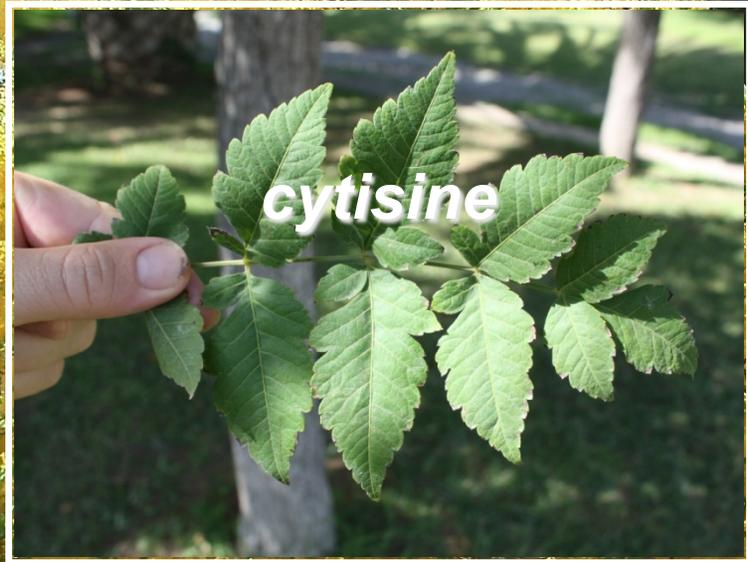
Review

## **Electronic Cigarettes for Smoking Cessation: A Systematic Review**

**Muhannad Malas MPH<sup>1</sup>, Jan van der Tempel MPhil<sup>2</sup>, Robert Schwartz PhD<sup>3</sup>,  
Alexa Minichiello MScPI<sup>4</sup>, Clayton Lightfoot BA<sup>4</sup>, Aliya Noormohamed MSPH<sup>5</sup>,  
Jaklyn Andrews MA<sup>4</sup>, Laurie Zawertailo PhD<sup>5</sup>, Roberta Ferrence PhD<sup>6</sup>**

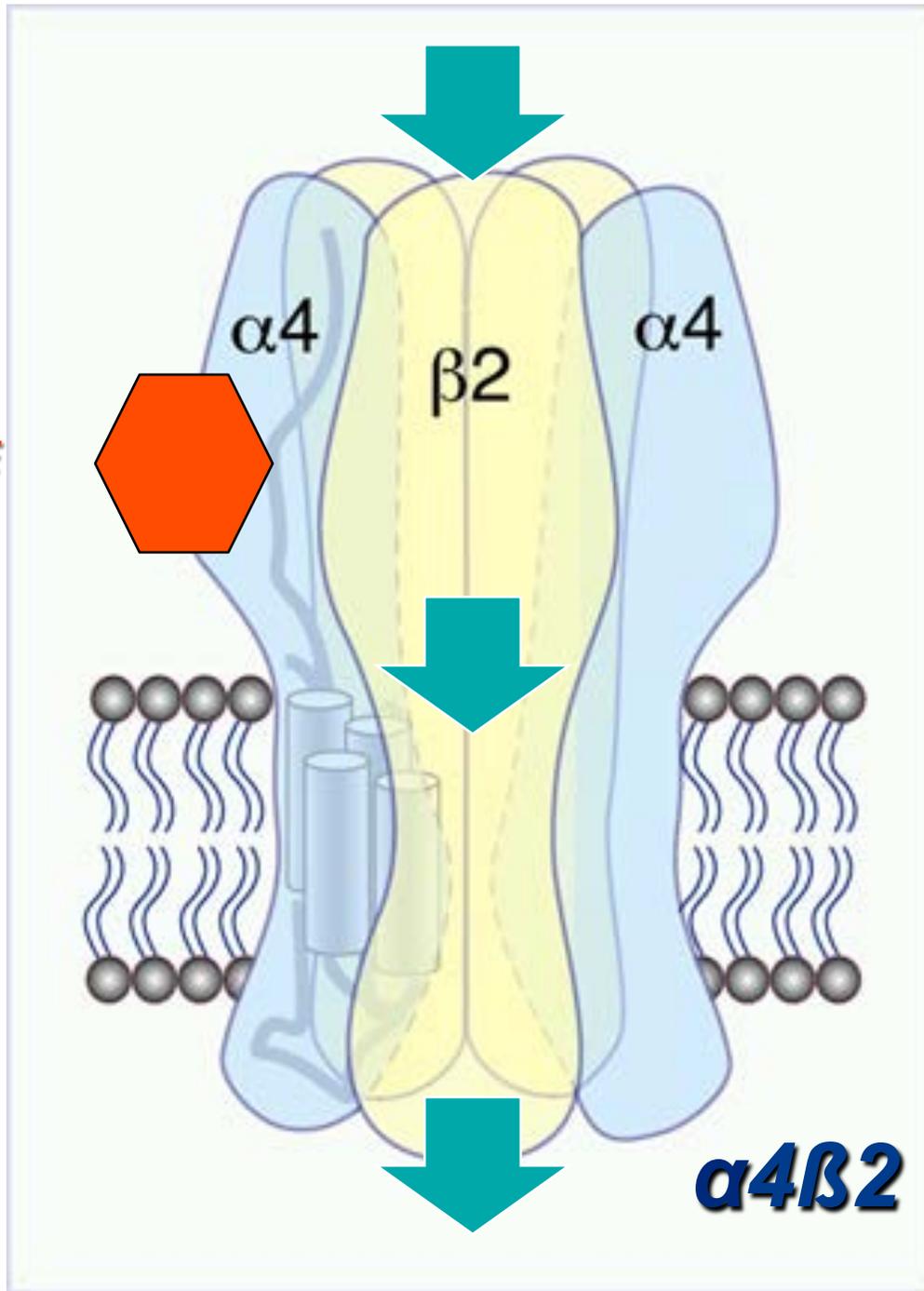
In accordance with the GRADE system, the quality of the evidence in support of e-cigarettes' effectiveness in helping smokers quit was assessed as very low to low, and the evidence on smoking reduction was assessed as very low to moderate.

While inconclusive due to low quality, overall the existing literature suggests e-cigarettes may be helpful for some smokers for quitting or reducing smoking.



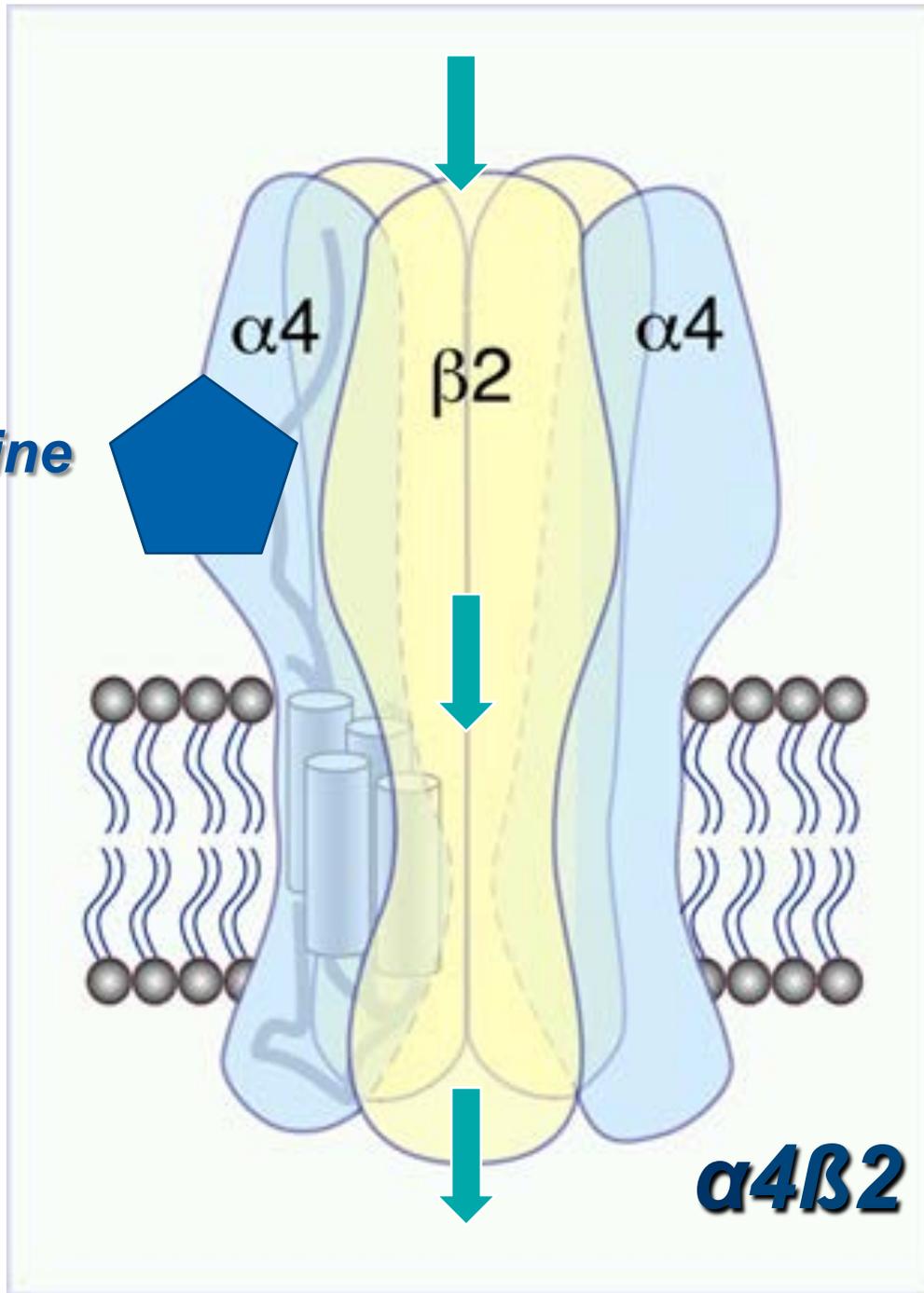
***Golden Rain***

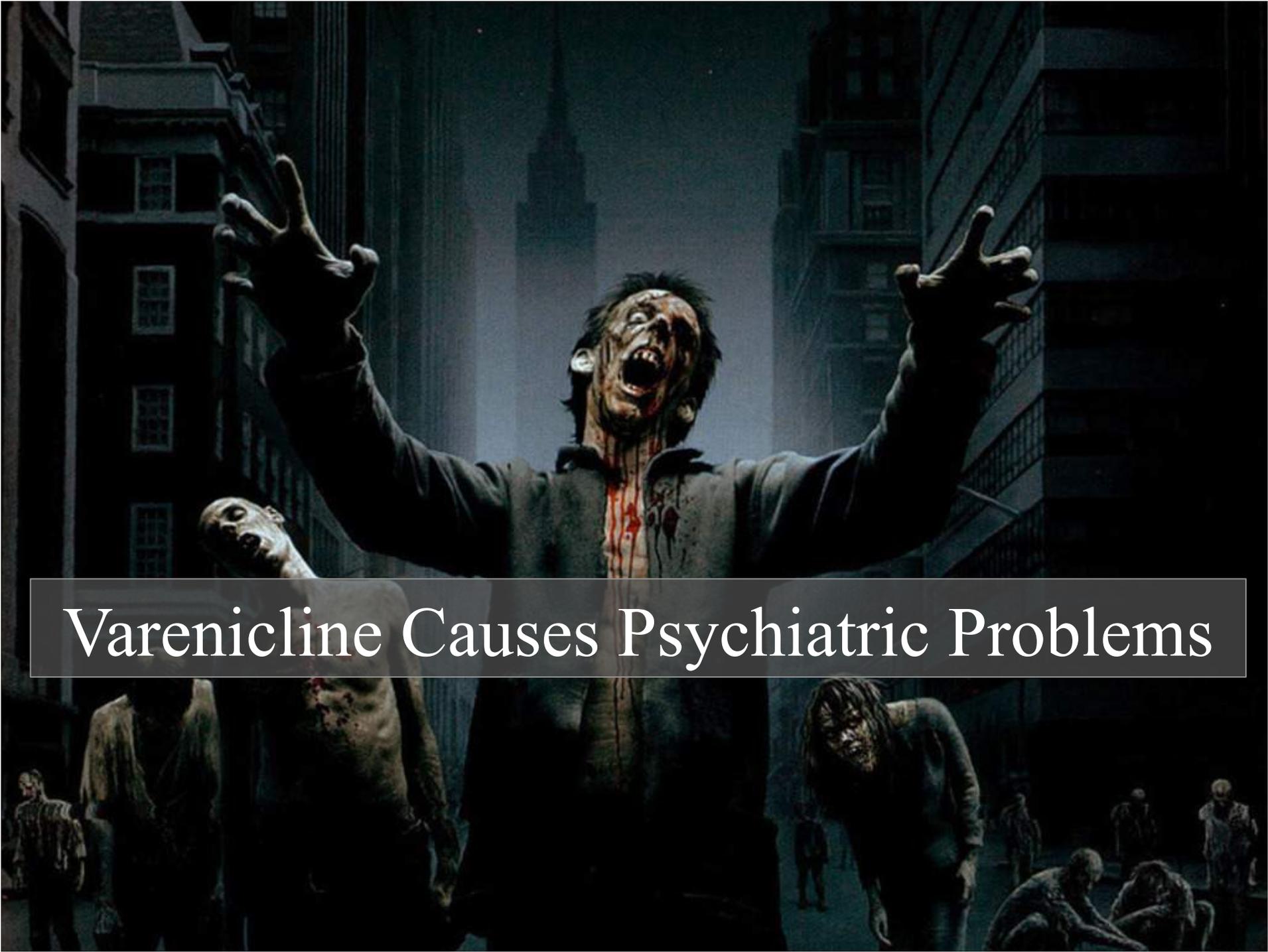
**NICOTINE**



**$\alpha 4 \beta 2$  receptor**

**Varenicline**





Varenicline Causes Psychiatric Problems

A large, bright full moon is the central focus, set against a deep blue, gradient night sky. The moon's surface shows various craters and dark spots. Below the moon, the dark blue surface of a body of water is visible, with some white foam from waves in the foreground. The overall scene is serene and nocturnal.

***Systematic studies do not support the view that varenicline causes neuropsychiatric side effects other than sleep disturbance and vivid dreams.***

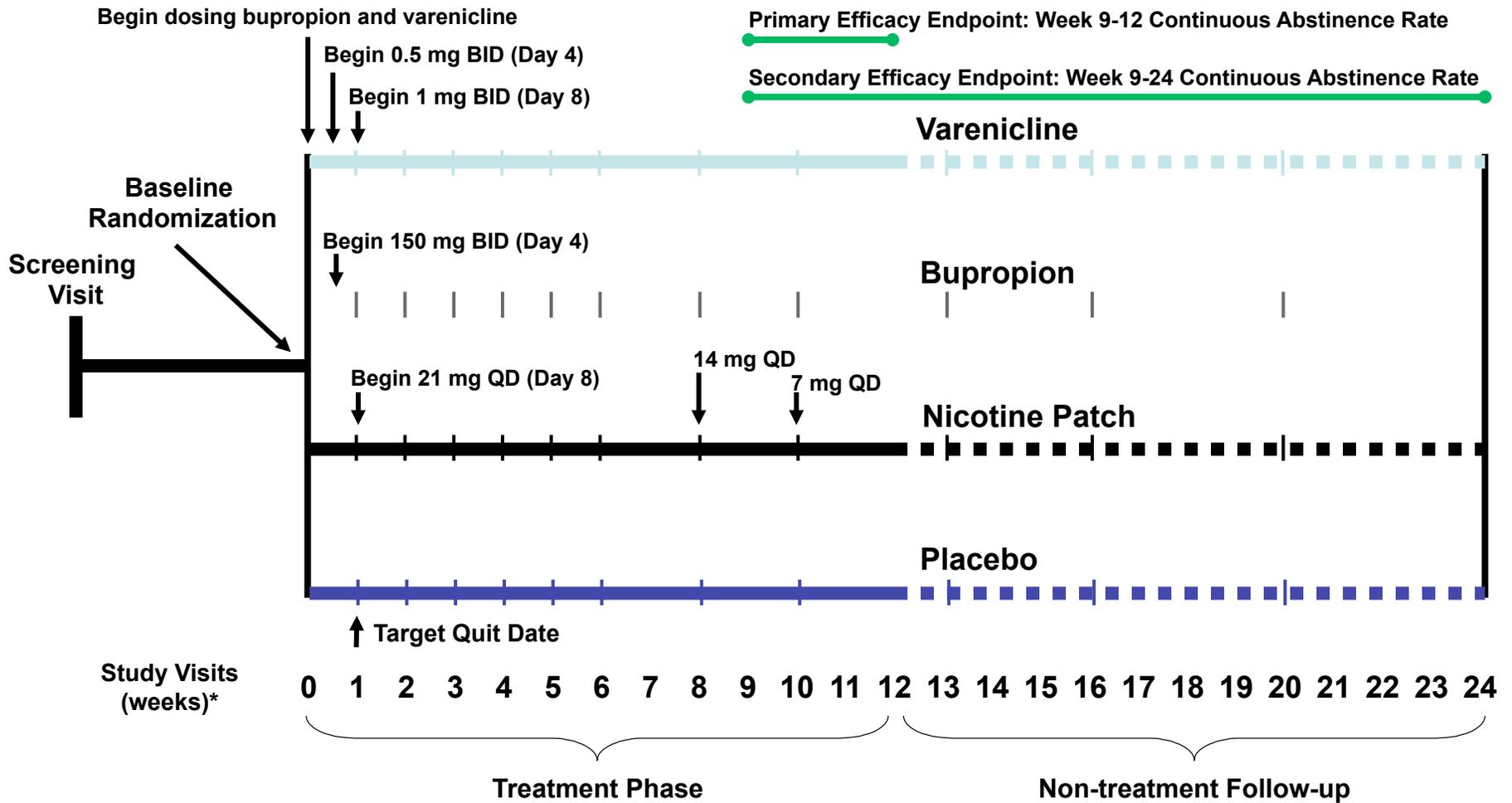
***Expert Opin Pharmacother 2011;12(11):1799-1812***

# **“EAGLES”**



# 'EAGLES' – Study Design

8000 subjects: 4000 Psychiatric. 4000 Non-Psychiatric.



\* Up to 15 face-to-face visits and 11 telephone visits

Antenelli RM, Benowitz NL, West R, et al. Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. *Lancet* 2016 Apr 22. [Epub ahead of print]

## *'EAGLES': Severe-Only NPS AEs*

		Varenicline	Bupropion	NRT	Placebo
<b>Non-Psychiatric</b>	Cohort, N	990	989	1006	999
NPS AE Endpoint, total, n (%)		13 (1.3%)	22 (2.2%)	25 (2.5%)	24 (2.4%)
Severe-only, n (%)		1 (0.1%)	4 (0.4%)	3 (0.3%)	5 (0.5%)
<b>Psychiatric</b>	Cohort, N	1026	1017	1016	1015
NPS AE Endpoint, total, n (%)		67 (6.5%)	68 (6.7%)	53 (5.2%)	50 (4.9%)
Severe-only, n (%)		14 (1.4%)	14 (1.4%)	14 (1.4%)	13 (1.3%)

Anthenelli RM, Benowitz NL, West R, et al. Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. *Lancet* 2016 Apr 22. [Epub ahead of print]

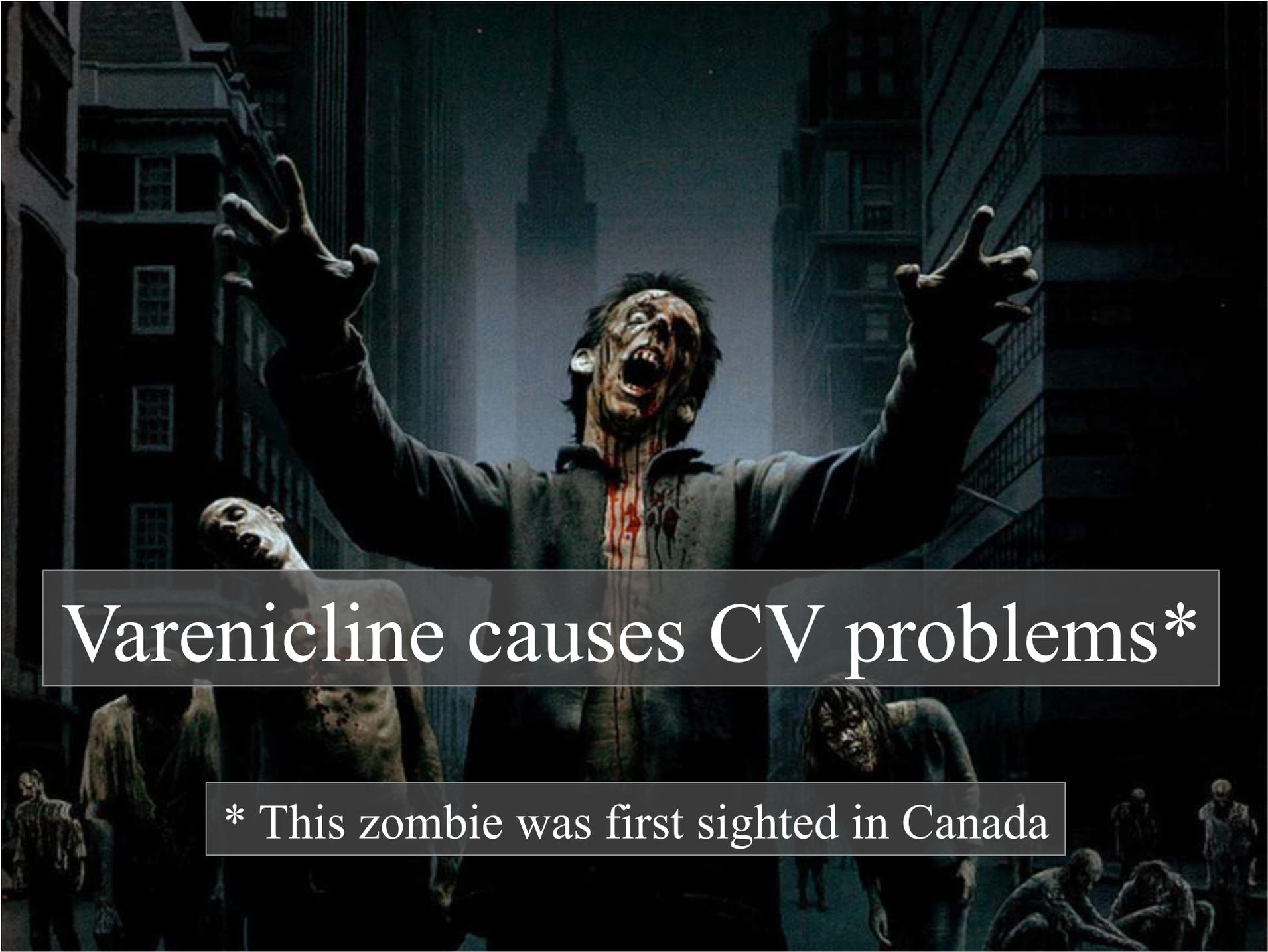
# THE LANCET

www.thelancet.com Published online April 22, 2016 [http://dx.doi.org/10.1016/S0140-6736\(16\)30272-0](http://dx.doi.org/10.1016/S0140-6736(16)30272-0)

## Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial

*Robert M Anthenelli, Neal L Benowitz, Robert West, Lisa St Aubin, Thomas McRae, David Lawrence, John Ascher, Cristina Russ, Alok Krishen, A Eden Evins*

**“The study did not show a significant increase in neuropsychiatric adverse events attributable to varenicline or placebo relative to nicotine patch or placebo. Varenicline was more effective than placebo, nicotine patch, and bupropion in helping smokers achieve abstinence, whereas bupropion and nicotine patch were more effective than placebo.”**

A zombie in a dark, urban setting with its arms raised in a gesture of aggression or pain. The zombie has blood on its face and chest. In the background, other zombies are visible in a dark, foggy city street.

Varenicline causes CV problems\*

\* This zombie was first sighted in Canada

## Risk of serious adverse cardiovascular events associated with varenicline: a systematic review and meta-analysis

Sonal Singh MD MPH, Yoon K. Loke MBBS MD, John G. Spangler MD MPH, Curt D. Furberg MD PhD

*Placebo*

*Varenicline*

Risk of CV Events:                      0.82%                      1.06%

The use of varenicline among tobacco users was associated with a 72% increased risk of serious adverse cardiovascular events.

***Efficacy and Safety of  
Varenicline for Smoking  
Cessation in Patients with  
Cardiovascular Disease:  
A Randomized Controlled Trial***



***Rigotti NA, Pipe AL, Benowitz NL,  
Arteaga C, Garza D, Tonstad S.***

*Circulation* 2010;121(2):221-9

## RESEARCH

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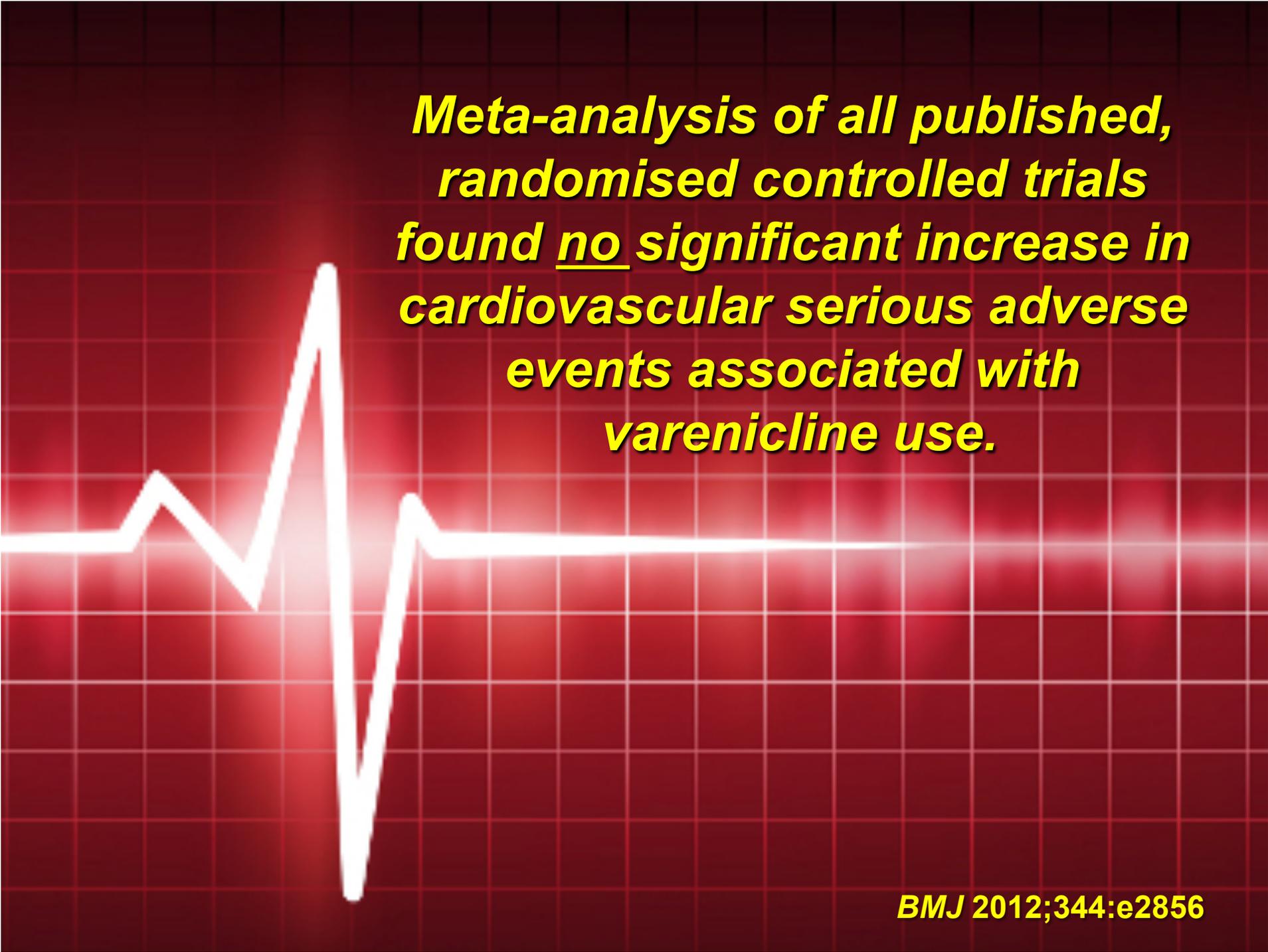
# Risk of cardiovascular serious adverse events associated with varenicline use for tobacco cessation: systematic review and meta-analysis

 OPEN ACCESS

Judith J Prochaska *associate professor*<sup>1</sup>, Joan F Hilton *professor*<sup>2</sup>

<sup>1</sup>Department of Psychiatry and Center for Tobacco Control Research and Education, University of California, San Francisco, CA 94143-0984;

<sup>2</sup>Department of Epidemiology and Biostatistics, University of California

A white ECG line is plotted on a dark red grid background. The line starts on the left, has a small peak, a dip, a large sharp peak, a deep trough, and then continues as a flat line to the right.

***Meta-analysis of all published,  
randomised controlled trials  
found no significant increase in  
cardiovascular serious adverse  
events associated with  
varenicline use.***

## Cardiovascular Events Associated With Smoking Cessation Pharmacotherapies: A Network Meta-Analysis

Mills EJ et al. *Circulation* 2014;129:28-41

***“Smoking cessation therapies do not appear to raise the risk of serious cardiovascular disease events.”***



## Medication Effectiveness ...

Medication	Number of arms	Estimated odds ratio	% Estimated abstinence rate
Placebo	80	1.0	13.8
Varenicline (2 mg/d)	5	3.1 (2.5-3.8)	33.2 (28.9-37.8)
Nicotine patch	32	1.9 (1.7-2.3)	23.4 (21.3-25.8)
Nicotine gum	15	1.5 (1.2-1.7)	19.0 (16.5-21.9)
Bupropion SR	26	2.0 (1.8-2.2)	24.2 (22.2-26.4)
Patch + Gum (ad lib)	3	3.6 (2.5-5.2)	36.5 (28.6-45.3)
Patch + Bupropion	3	2.5 (1.9-3.4)	28.9 (23.5-35.1)

*Treating Tobacco Use and Dependence. Clinical Practice Guideline. US DHHS. 2008.*

RESEARCH ARTICLE

Open Access



# Combination therapy of varenicline with nicotine replacement therapy is better than varenicline alone: a systematic review and meta-analysis of randomized controlled trials

Ping-Hsun Chang<sup>1,4†</sup>, Chien-Hsieh Chiang<sup>1,2,3†</sup>, Wei-Che Ho<sup>1</sup>, Pei-Zu Wu<sup>1</sup>, Jaw-Shiun Tsai<sup>1,2\*</sup> and Fei-Ran Guo<sup>1,2\*</sup>

## Conclusions

The combination therapy of varenicline with NRT is more effective than varenicline alone in smoking cessation. This effect is more evident if pre-cessation treatment of nicotine patch is administered. The adverse events of combination therapy are comparable to varenicline mono-therapy with the exception of skin reactions. Larger RCTs are needed to make more robust conclusions.



***Smoking is a leading  
cause of hospitalization and  
RE-HOSPITALIZATION***

Public Health Agency of Canada. 2009.

Canadian Institute for Health Information, Health Indicators 2009

# ***Cessation & The Hospital***

***Large numbers of smokers***

***Relevance of smoking to admission***

***Increased motivation to quit***

***Availability of staff***

***Opportunity for systematic approach***

***Availability of Pharmacotherapy***

***Treatment of withdrawal***

***Can arrange follow-up***

***Influence community practice***

# ***“The Ottawa Model”***

**Identification**

**Documentation**

**Counseling**

**Pharmacotherapy**

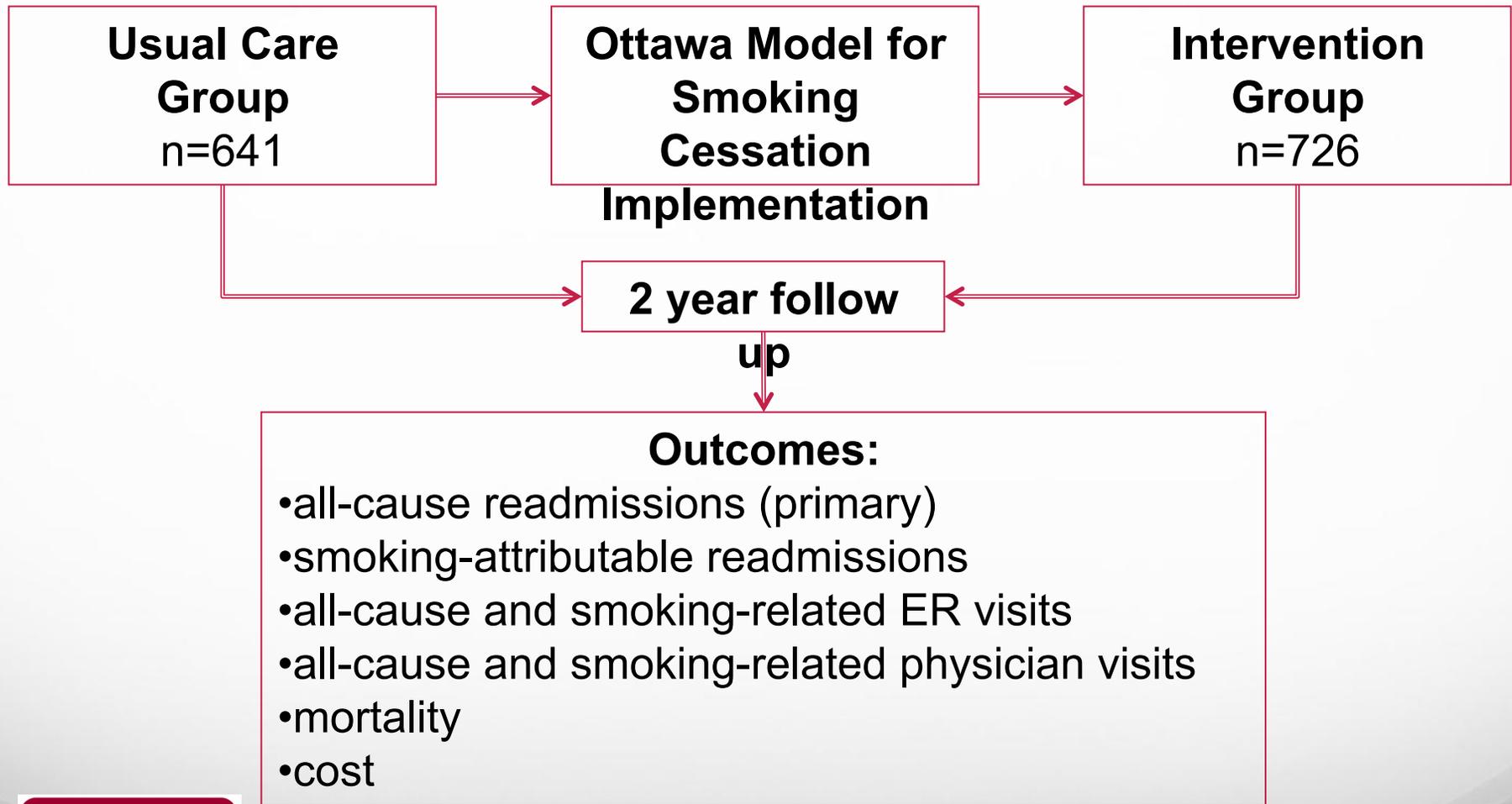
**Long-term follow-up**

Reid RD, Pipe AL, Quinlan B. *Can J Cardiol* 2006;22:775-780



OTTAWA  
MODEL  
FOR SMOKING  
CESSATION

# *An Evaluation of the Ottawa Model*



*n= 14 hospitals*  
*K-A Mullen PhD, Unpublished Data.*  
*2015*

***The Ottawa Model results in significant reductions in 30-day healthcare utilization***



**50%**

**All-cause  
readmissions**  
(p=.0007)

NNT: 16



**45%**

**Smoking-related  
readmissions**  
(p=.0002)

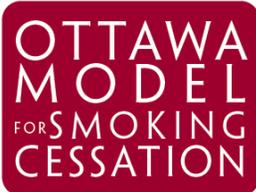
NNT: 38



**30%**

**ER visits**  
(p=.001)

NNT: 23

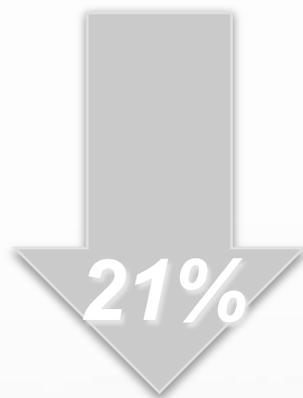


***The Ottawa Model results in significant reductions in 2-year healthcare utilization and risk of death***



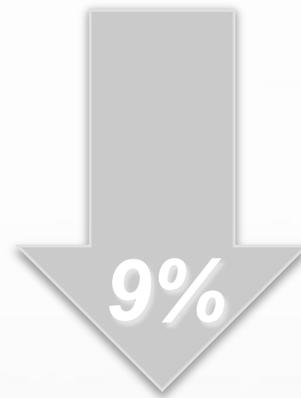
**All-cause readmissions**  
( $p < .0001$ )

NNT: 7



**Smoking-related readmissions**  
( $p < .0001$ )

NNT: 10



**ER visits**  
( $p = .04$ )

NNT: 25



**Death**  
( $p = .0002$ )

NNT: 14



*Primary Care*

OTTAWA MODEL  
FOR SMOKING CESSATION  
IN PRIMARY CARE

MODÈLE D'OTTAWA  
POUR L'ABANDON DU TABAC  
EN SOINS PRIMAIRES

# THE 3As: ASK, ADVISE, ACT

30  
SECONDS

Reception/ Triage  
Nurse

## ASK AND DOCUMENT

Include tobacco use question as one of the patient's vital signs

*Have you used any form of tobacco in the last 7 days?*

2  
MINUTES

Physician/Nurse  
Practitioner

## ADVISE AND REFER

Provide strong, personalized, non-judgmental advice to quit with offer of support

10-20  
MINUTES

Smoking Cessation  
Counsellor (Nurse, NP,  
Pharmacist, RRT)

## ACT

For Patient who is **READY TO QUIT**:  
QUIT PLAN VISIT

- Strategic counselling
- Pharmacotherapy
- Follow-up/OMSC Smoker's Follow-up Program

For Patient who is **NOT READY TO QUIT**:

- Follow-up/OMSC Smoker's
- Follow-up Program



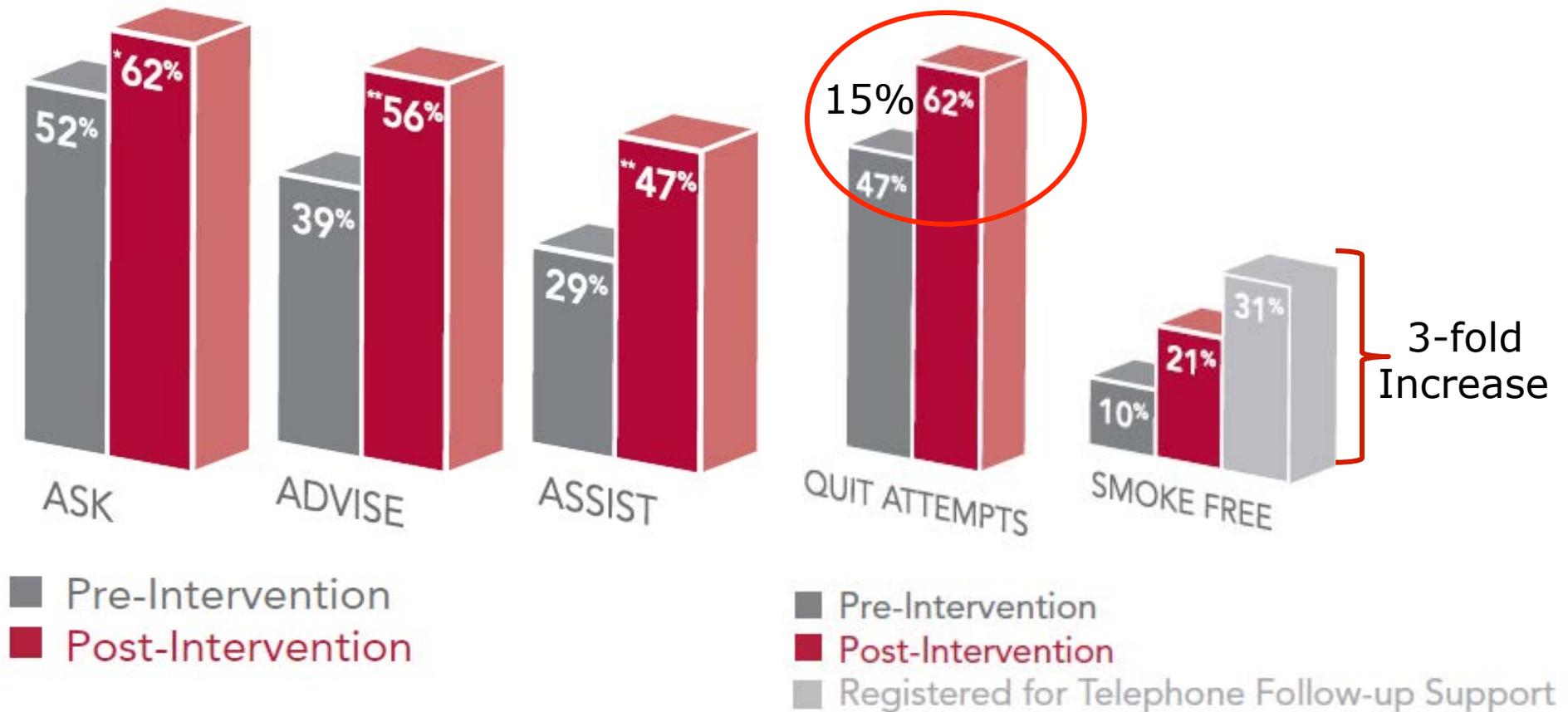
# SMOKING CESSATION IN PRIMARY CARE

## Delivering evidence-based smoking cessation treatment in primary care practice

*Experience of Ontario family health teams*

Sophia Papadakis MHA PhD Marie Gharib Josh Hambleton MHA Robert D. Reid PhD MBA Roxane Assi Andrew L. Pipe CMMB

Canadian Family Physician • Le Médecin de famille canadien | VOL 60: JULY • JUILLET 2014



The OMSC Primary Care Network has reached over  
**128,000** tobacco users in Ontario!

**106 Partner FHTs, FHNs, CHCs, NPLCs**

**200 Clinics in 13 LHINS**

~ 840 MDs

~ 384 RNs

~ 222 NPs

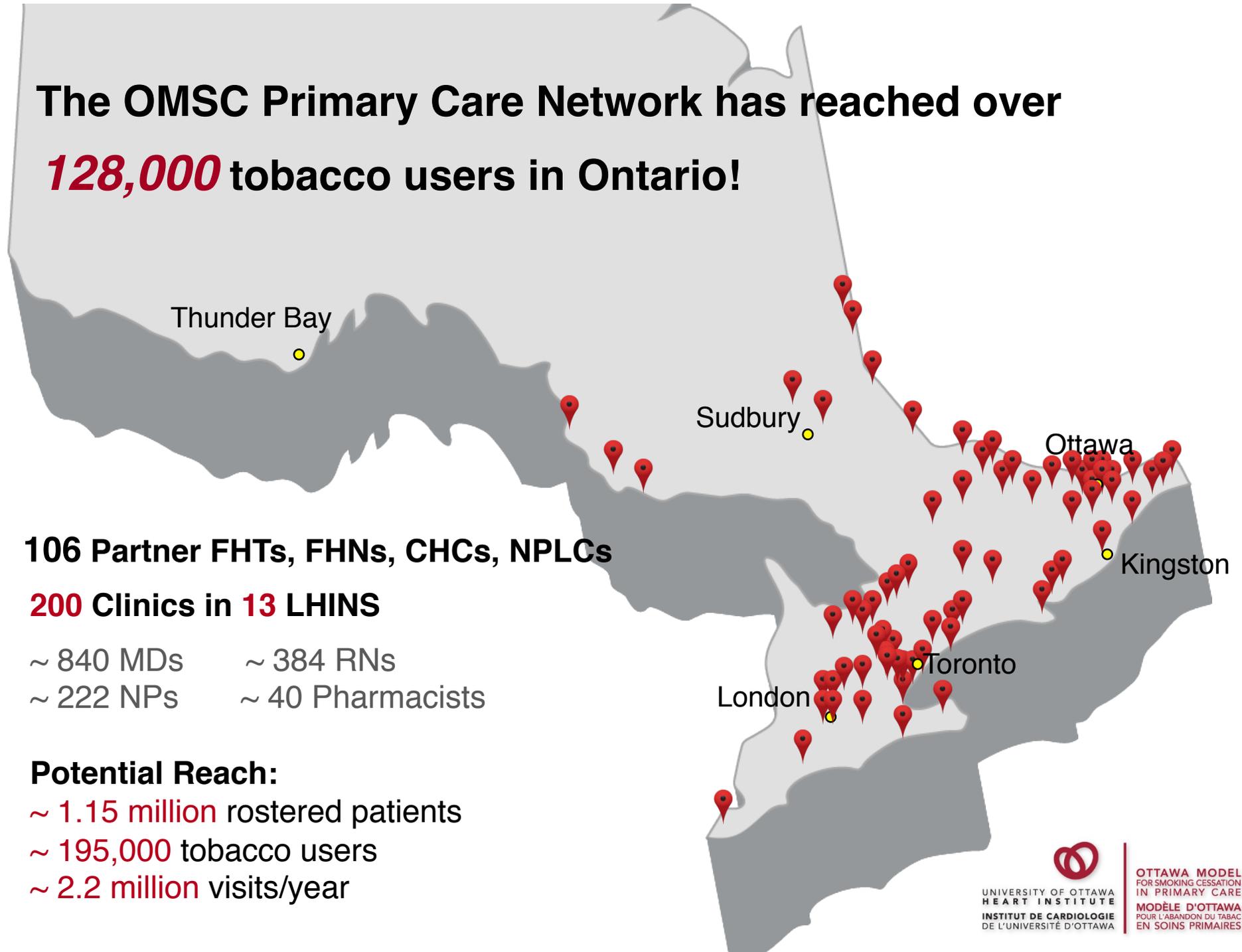
~ 40 Pharmacists

**Potential Reach:**

~ **1.15 million** rostered patients

~ **195,000** tobacco users

~ **2.2 million** visits/year





*“REDUCE TO QUIT”*



*COMBINATION THERAPY*



**KEEP  
CALM  
AND  
BE  
SYSTEMATIC**



UNIVERSITY OF OTTAWA  
HEART INSTITUTE  
INSTITUT DE CARDIOLOGIE  
DE L'UNIVERSITÉ D'OTTAWA

# *Systematic Approaches to Smoking Cessation in EVERY Clinical Setting*



  
UNIVERSITY OF OTTAWA  
HEART INSTITUTE  
INSTITUT DE CARDIOLOGIE  
DE L'UNIVERSITÉ D'OTTAWA

**OTTAWA MODEL**  
FOR SMOKING CESSATION  
**MODÈLE D'OTTAWA**  
POUR L'ABANDON DU TABAC

Contact Information: 613-761-4034  
Email: [scnetwork@ottawaheart.ca](mailto:scnetwork@ottawaheart.ca)

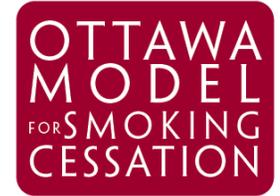


A close-up photograph of a lit cigarette. The cigarette is positioned horizontally, with the lit end on the right. The tip is glowing with a bright orange and red flame, and a small amount of white ash is visible. A thin trail of white smoke is rising from the tip. The background is a plain, light-colored surface.

***Smoking Cessation***  
**The Most Important  
Preventive Intervention !**



UNIVERSITY OF OTTAWA  
HEART INSTITUTE  
INSTITUT DE CARDIOLOGIE  
DE L'UNIVERSITÉ D'OTTAWA



# *Transforming ...*



***Patient Care***



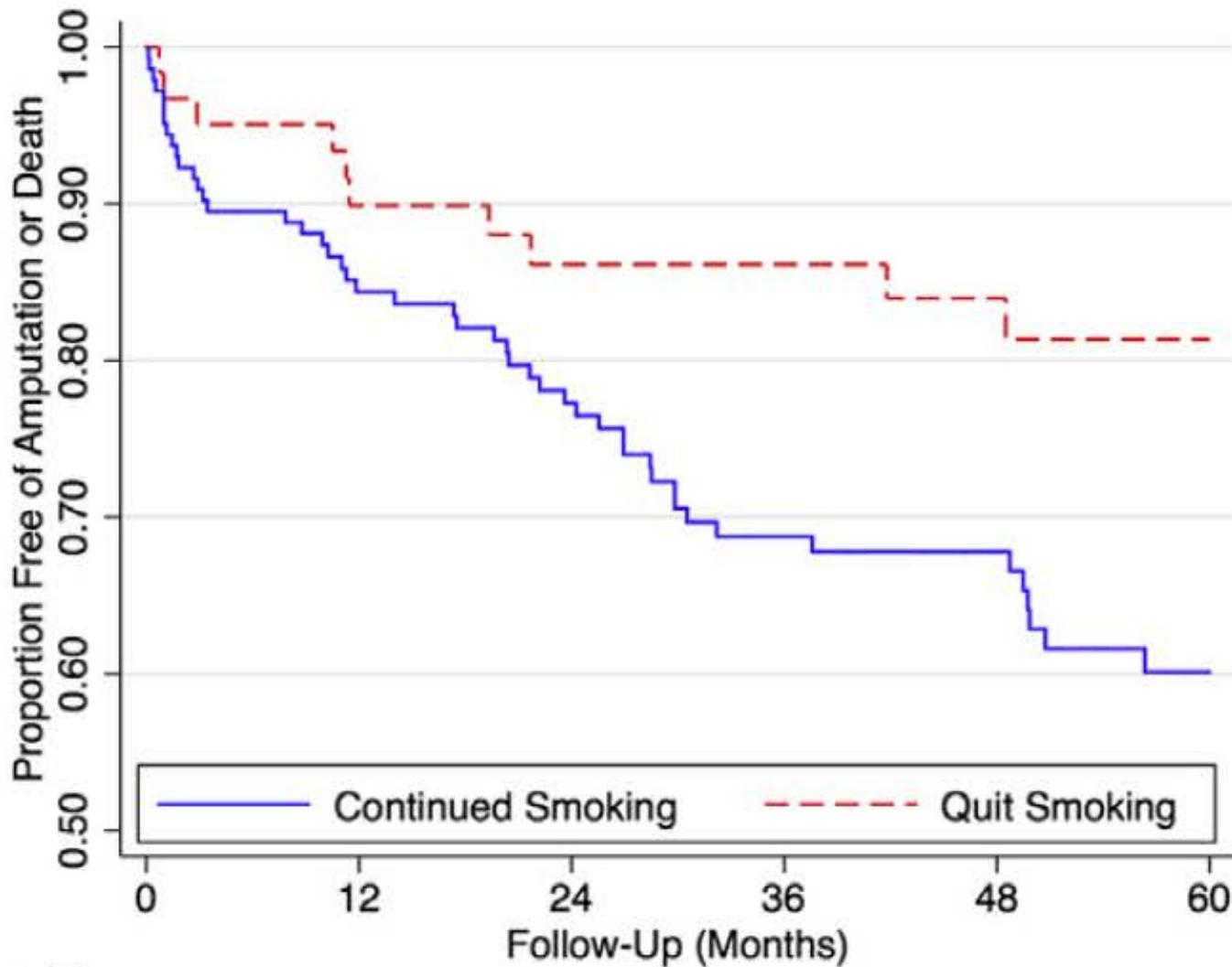
***Professional  
Behaviours***



***Institutional  
Practices***

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## ***Amputation-free survival among patients who continued vs quit smoking***



***Armstrong EJ et al. J Vasc Surg 2014;60:1565-71***