

The most addictive drug
The most dangerous substance

Rob Crane, MD

Clinical Associate Professor
Department of Family Medicine
The Ohio State University
Preventing Tobacco Addiction Foundation
SmokeFree Columbus



**The worst
failure of
American
Public
Health of
the last 100
years**



The worst failure of American Public Health of the last 100 years

An addiction issue for nearly half of your hospitalized patients

How many adult smokers are there in the United States?

**How many adult
smokers are there in
the United States?**

**46 million
(20.6 % of adults)**

2008 National Health Interview Survey – CDC.gov/tobacco

**What Percent of Smokers
Would Like to Quit
and How Many Have
Actually Tried Last Year?**

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Actually Tried Last Year?**

70%

2008 National Health Interview Survey – MMWR 11/13/09

**What Percent of Smokers
Would Like to Quit
and How Many Have
Actually Tried Last Year?**

70% **45% ~ 21 million
people made >24^o
attempt**

2008 National Health Interview Survey – MMWR 11/13/09

**What percent
remained abstinent?**

**What percent
remained abstinent?**

3-5%

National Health Interview Survey, 1999-2001 and 2008 -- CDC

**What percent
remained abstinent?**

3-5%

**_Nearly a million
quit each year**

National Health Interview Survey, 1999-2001 and 2008 -- CDC

**What percent
remained abstinent?**

3-5%

**48 million
ex-smokers**

**_Nearly a million
quit each year**

National Health Interview Survey, 1999-2001 and 2008 -- CDC

"Today we bought a War Stamp for Bobby—and Camels for you!"

Next to those precious letters you write that tell them how you are and what you're doing... the thing men in the service want most from home is cigarettes. When you send cigarettes, remember—the favorite brand in all the services—with men in the Army, the Navy, the Marines, the Coast Guard—is Camel. Men in the service appreciate Camel's rich, full flavor... and Camel's extra mildness.

WHEN "MAIL CALL" brings a carton of Camels—it's always good news from home! For Camels, with their matchless flavor and extra mildness, are first choice with men in all Uncle Sam's armed forces. So, send your man in the service a carton of Camels today. (There are 200 cigarettes in a carton of Camels... and with every one he lights, he'll be thinking of you—glad you thought of him.)

First IN THE SERVICE
With men in the Army, Navy, Marine Corps, and the Coast Guard, the favorite cigarette is Camel. (Based on actual sales records.)

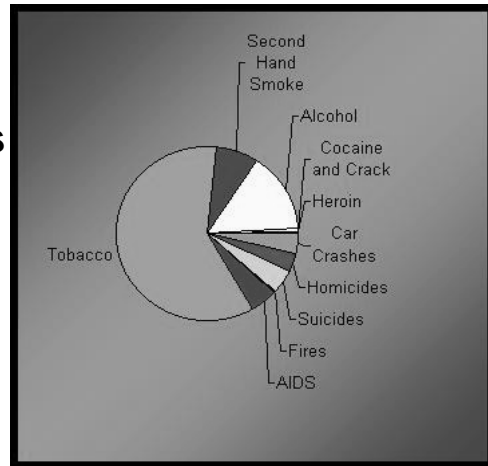
Send him his favorite...
Camels



**How many people
die from tobacco
related disease in
the US every year?**

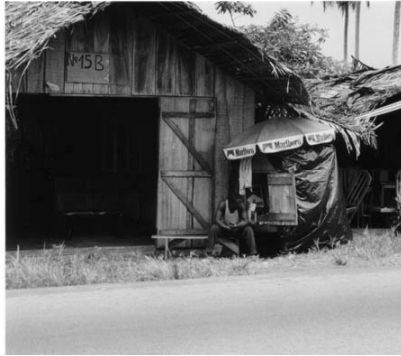
Premature Deaths (10-13 years lost)

- 450,000 annual deaths
- More deaths than all other preventable causes combined
- Tobacco use causes or exacerbates more than 40 distinct serious human illnesses



How many die worldwide

How many die worldwide
5 million



How many die annually worldwide

from malaria?

from AIDS?

H1N1 as of 2/14/2011?

How many die annually worldwide

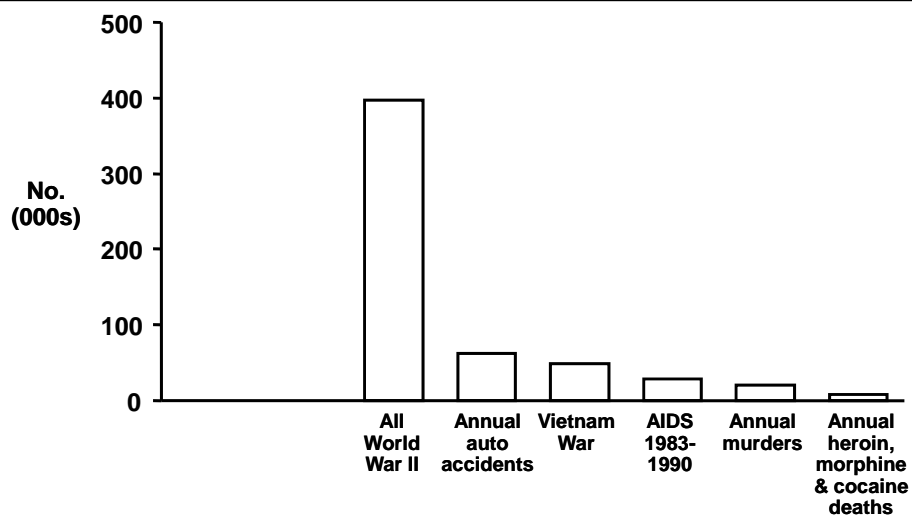
from malaria? 1 million

from AIDS? 2.9 million

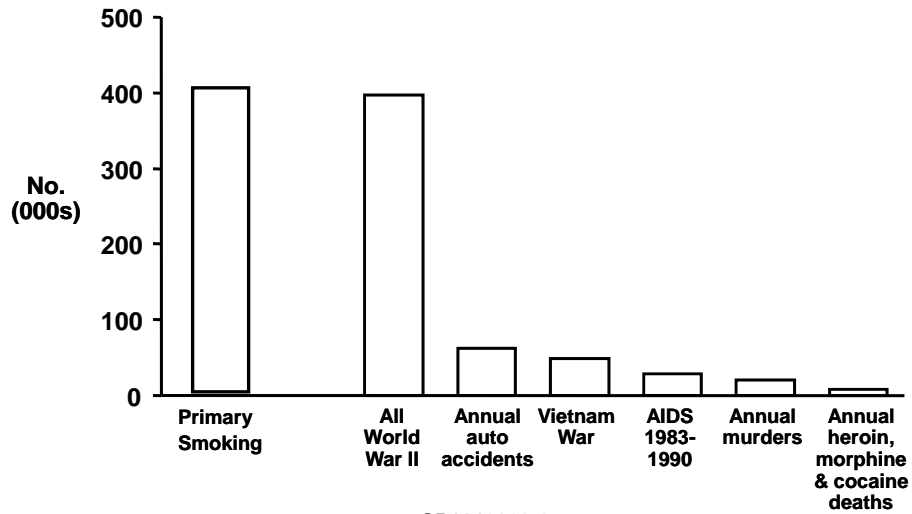
H1N1 as of 2/14/2011? 25,000

The Cigarette Death Epidemic in Perspective

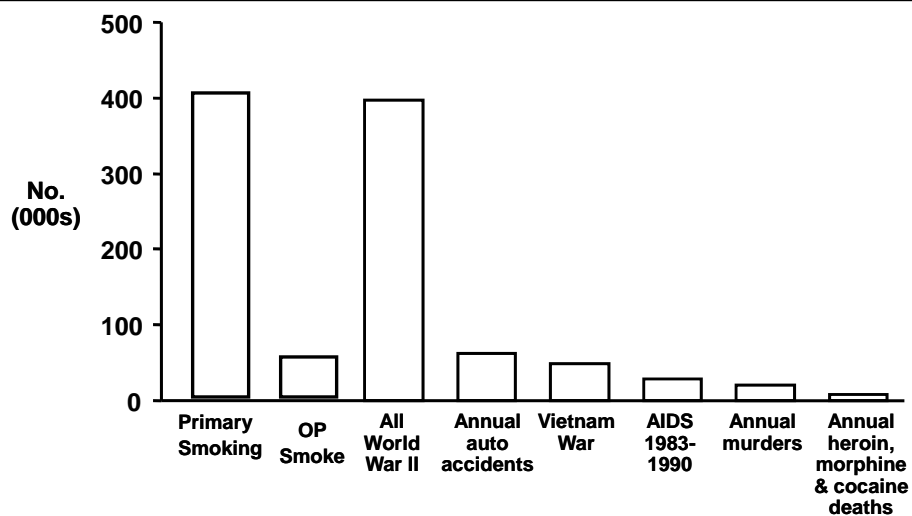
The Cigarette Death Epidemic in Perspective



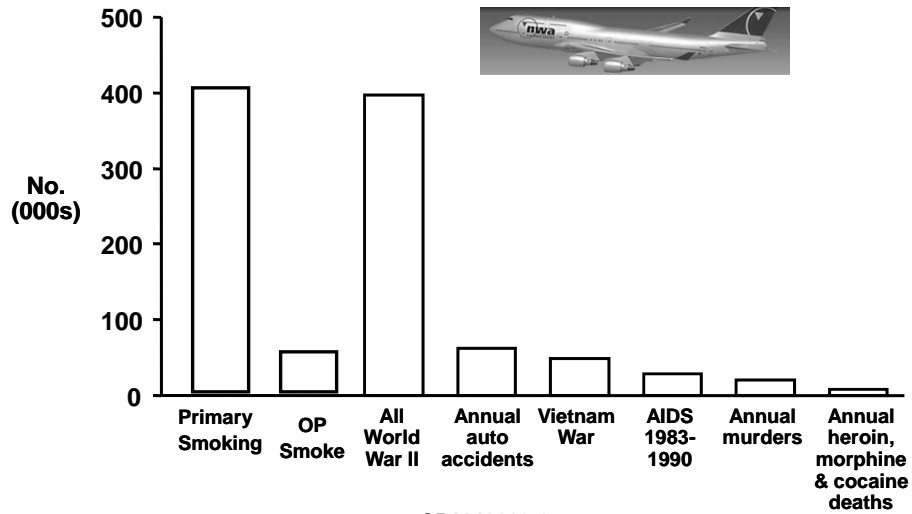
The Cigarette Death Epidemic in Perspective



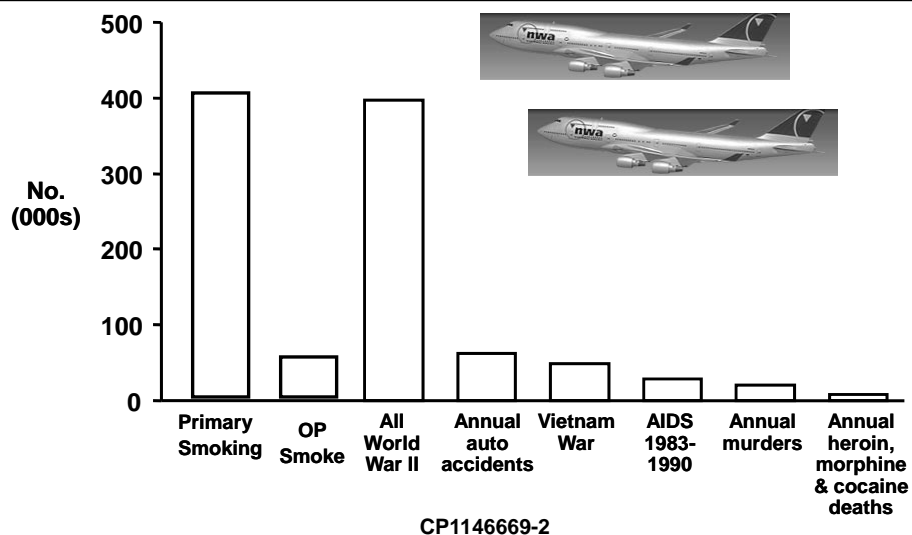
The Cigarette Death Epidemic in Perspective



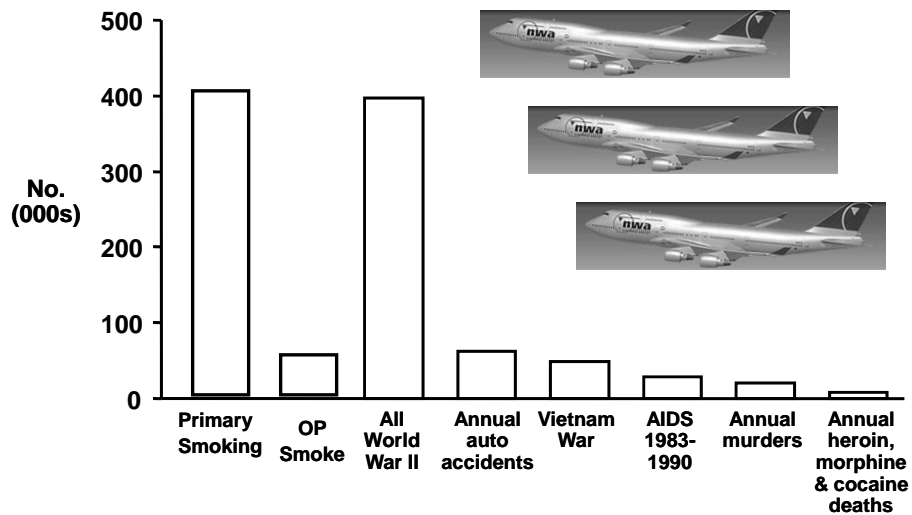
The Cigarette Death Epidemic in Perspective



The Cigarette Death Epidemic in Perspective



The Cigarette Death Epidemic in Perspective



Ohio Youth Tobacco Survey 2008



**What percent of Ohio
high school kids
smoke (as of 2000)?**

Ohio Youth Tobacco Survey 2008



**What percent of Ohio
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33%

Ohio Youth Tobacco Survey 2008



**What percent of Ohio
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**What percent of Ohio
high school kids
smoke (as of 2008)?**

Ohio Youth Tobacco Survey 2008



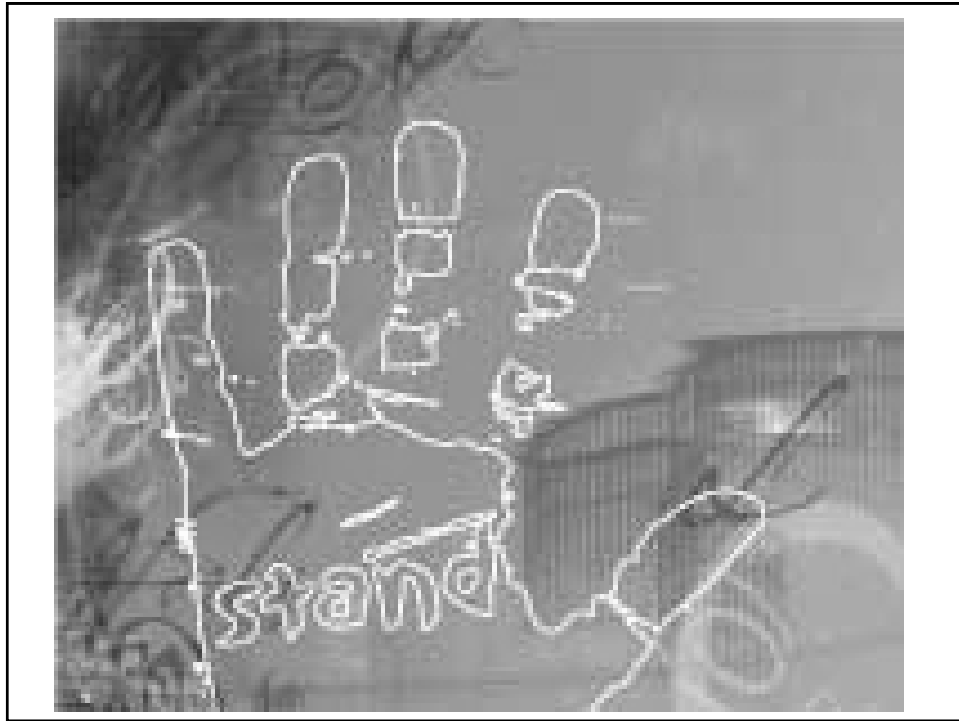
**What percent of Ohio
high school kids
smoke (as of 2000)?**

33%

**What percent of Ohio
high school kids
smoke (as of 2008)?**

19%

Ohio Youth Tobacco Survey 2008



Nicotine changes brains

- **Kid smokers – 1st illicit drug – a gateway**
 - **3X more alcohol use**
 - **8X more marijuana use**
 - **22X more cocaine use**
 - **higher dropout rates**
 - **more likely to experience teen pregnancy**
 - **much more likely to become depressed**
 - **the earlier a kid starts, the heavier a smoker as an adult**

Aside from the fact that nicotine is legal to purchase and use, what is the main difference between the addiction to nicotine and the addiction to cocaine and heroin?



US Congress: Heath Sub Committee - April 1994



**Name 5 different
cancers caused by
tobacco use?**

**15 Distinct Cancers Are
Associated with
Tobacco Use**

- Lung Cancer – 5 types (squamous, large cell, adenocarcinoma, small cell and mesothelioma*)
- Stomach, esophagus
- Kidney, bladder
- Uterus, cervix
- Mouth, naso-pharynx and larynx
- Myelocytic Leukemia

**Cigarette Smoke Contains 4000
distinct chemicals – a selected
few:**

• PARTICULATES	• GAS PHASE
Phenol	Carbon Monoxide
Creosol	Acetaldehyde
Indole	Ammonia
Trace metals: nickel, arsenic	Formaldehyde
Carbazole	Nitrosamines
Benzopyrene	Hydrazine
	Vinyl Chloride

**Smoking and Non-Cancer
Respiratory Disease**

- **Chronic Obstructive Pulmonary Disease (COPD) 25X risk in smoker**
- **Rhinitis, Sinusitis and Laryngitis**
- **Causes and Exacerbates Asthma**
- **Smokers Cough / Chronic Bronchitis**
- **Halitosis**



What are the known effects of smoking during pregnancy?

Reproductive effects

(100,000 smoking attributable fetal and perinatal deaths annually in the US)

PREGNANCY

- Spontaneous Abortion
- Intrauterine Growth Retardation
- Placental Abruption
- Placenta Previa
- Prematurity
- Stillbirth

CHILDREN

- Leading cause of SIDS
- Increase in Attention Deficit Disorder
- Greater tendency toward violence in male offspring



**What percent
of women
smoke
throughout
pregnancy?**



**What percent
of women
smoke
throughout
pregnancy?**

13%

CDC "PRAMS" Study 2004

Secondhand smoke: effects on children

- **Rhinorrhea**
- **Otitis Media (hearing loss)**
- **Pneumonia**
- **Initiation & Exacerbation of Asthma**
- **Decreased lung capacity**
- **Increased time lost from school**

Secondhand smoke: effects on children

- **Rhinorrhea**
- **Otitis Media (hearing loss)**
- **Pneumonia**
- **Initiation & Exacerbation of Asthma**
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**Smoking around a child
is de-facto child abuse**

What is the best measure of nicotine exposure in a closet tobacco user or an secondhand smoke exposed non-smoker?

What is the best measure of nicotine exposure in a closet tobacco user or an secondhand smoke exposed non-smoker?

Cotinine

(48-72 hour metabolite)

**By major category, name
the top four leading
causes of death in the
United States?**

**By major category, name
the top four leading
causes of death in the
United States?**

- 1) Heart Disease**
- 2) Cancer**
- 3) Stroke**
- 4) COPD**

Smoking induced vascular disease

- **Myocardial infarction**
 - Sudden Death
 - Heart Failure
 - Angina
 - Arrhythmia
- **Aortic aneurysm**
- **Stroke**
- **Peripheral vascular disease**

**Do snuff and “spit”
tobacco users suffer
increased
cardiovascular
disease?**

**Note: they show
higher venous levels
of nicotine**

REVERSE DiGIORNO ANALOGY

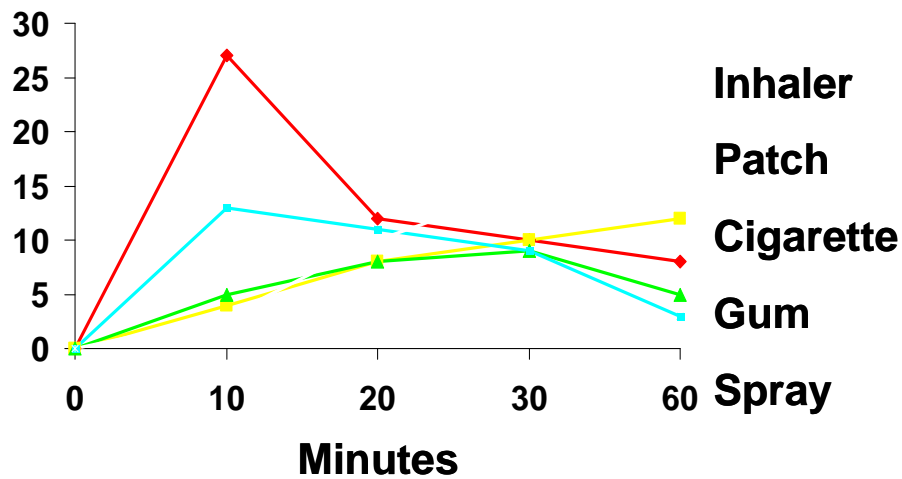


**It's not delivery,
it's**

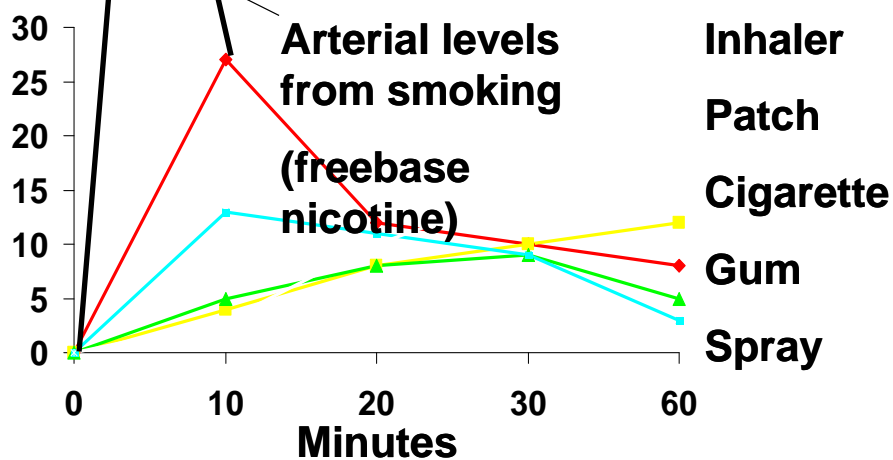
**Nicotine: It's not the drug,
it's the delivery**

- Smoking delivers huge rapid arterial spikes to the brain and spinal cord
- A one pack/day smoker gets 70,000 “freebase” hits per year
- Spiking levels overcome tolerance and troughs allow for receptor resensitization
- Rapid delivery allows for dose titration
- Carbon monoxide and carboxyhemoglobin play a significant role in CV disease

Venous Nicotine Levels: Various Delivery Systems



Venous Nicotine Levels: Various Delivery Systems



**Cigarette Smoke Contains 4000
distinct chemicals – a selected
few:**

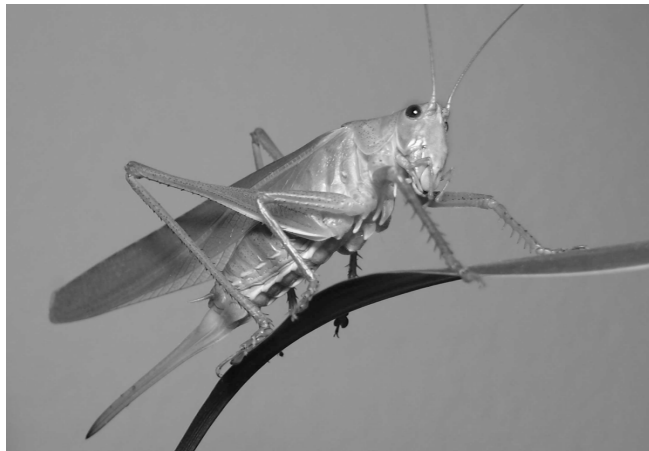
• PARTICULATES	• GAS PHASE
Phenol	Carbon Monoxide
Creosol	Acetaldehyde
Indole	Ammonia
Trace metals: nickel, arsenic	Formaldehyde
Carbazole	Nitrosamines
Benzopyrene	Hydrazine
	Vinyl Chloride

**Other tobacco related
illnesses:**

- **#1 Cause of Erectile Dysfunction**
- **A leading cause of Sensory-Neural hearing loss in adults**
- **#2 Cause of Blindness (Macular Degeneration)**
- **Important factor in premature skin aging**
- **Plays a role in male pattern baldness**
- **Major cause of tooth loss**

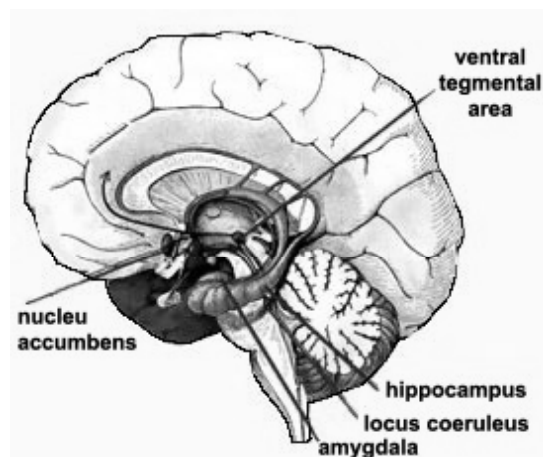
**Why does the tobacco plant
make nicotine?**

**Why does the tobacco plant
make nicotine?**



Where and how does nicotine work?

Where and how does nicotine work?



**What percent of Ohio adults
smoke (as of 2001)**

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• 27.6%

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**What percent of Ohio adults
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smoke (as of 2001)**

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**What percent of Ohio adults
smoke (as of 2009)** BRFSS 2009

• 20.3%

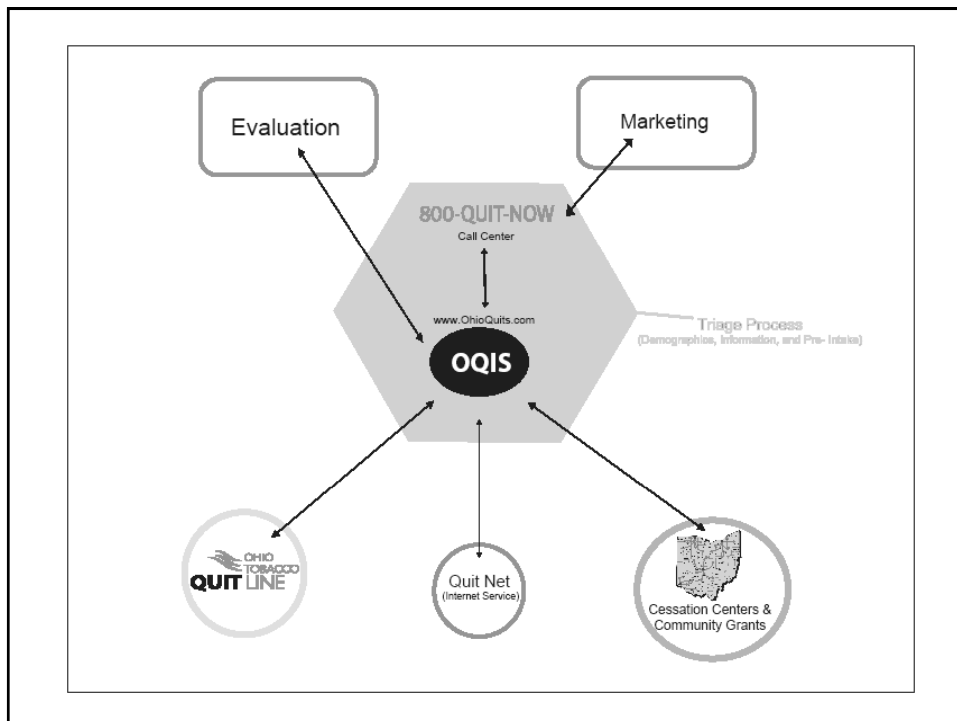
**What percent of Ohio adults
smoke (as of 2001)**

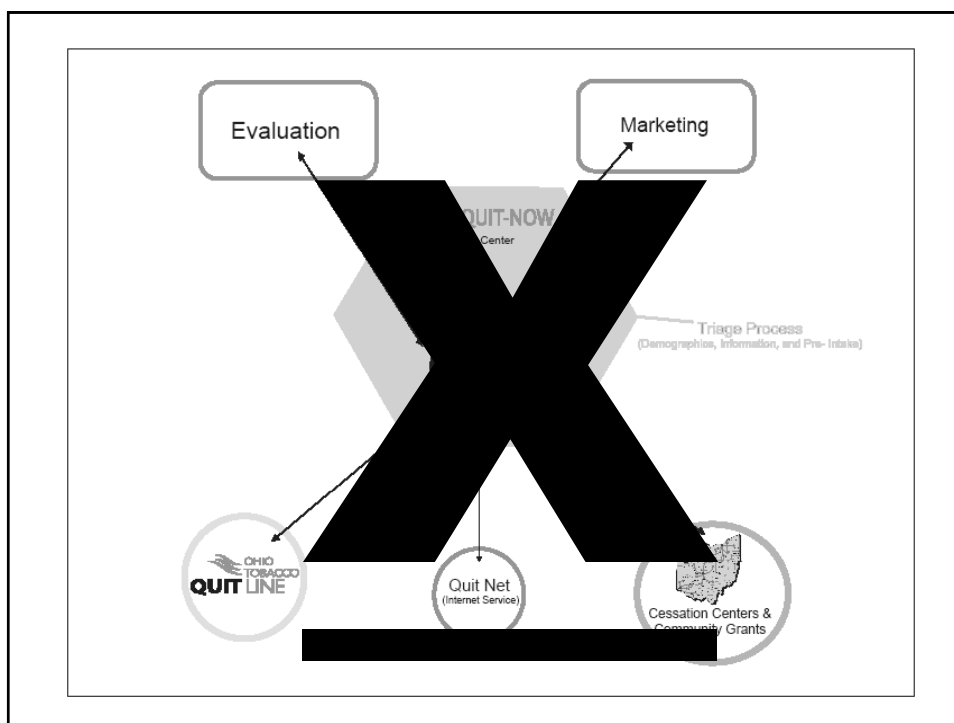
• 27.6%

**What percent of Ohio adults
smoke (as of 2009)** BRFSS 2009

• 20.3%

Why?





What is the major reason people actually quit smoking?

What is the major reason people actually quit smoking?

- **Their doctor or dentist told them to quit**

What is the major reason people actually quit smoking?

- **Their doctor or dentist told them to quit**
- **Their employer made their workplace smokefree**



**True or False:
Well designed and
well funded tobacco
cessation programs
can yield durable
abstinence in most
motivated users.**

What works, what doesn't

<i>Method</i>	<i>1 year abstinence rate</i>
"Cold Turkey" no program	• 3-5%
Structured social change and behavior modification	• 7-16%
Nicotine replacement (NRT)	• 8-16%
NRT plus structured program	• 12-23%
Bupropion (Zyban/Wellbutrin)	• 16-40%
Combination: NRT/Bupropion	• 25-55%
Varenicline (Chantix)	• 22-44%
<p>*Upper range rates almost always reflect highly motivated subjects (ie post MI or hospital inpatients)</p> <p>Low end rate is realistic</p>	

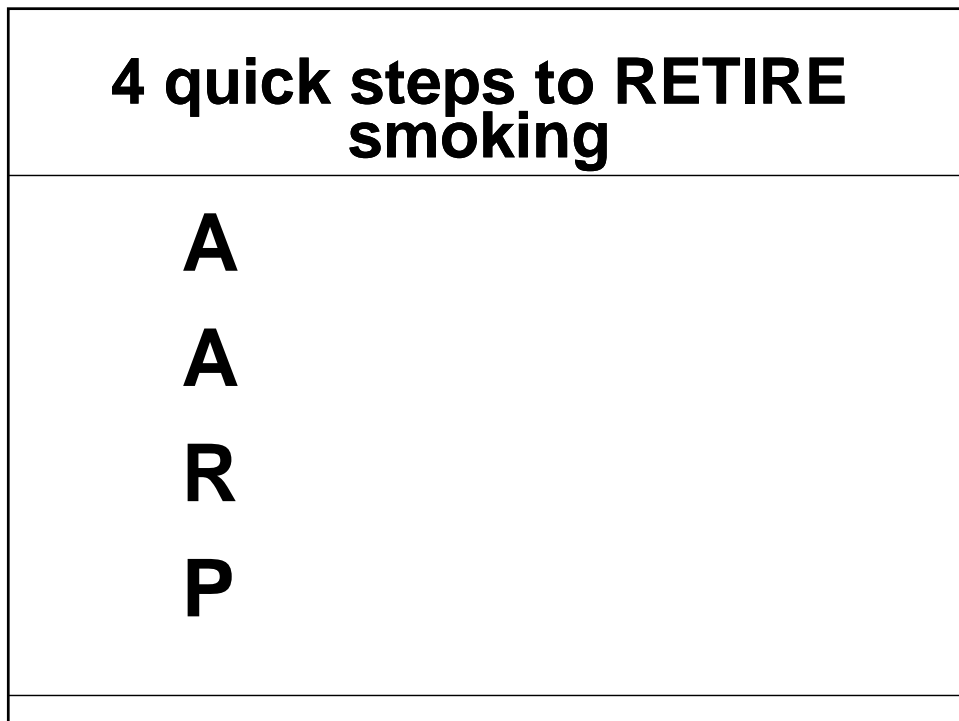
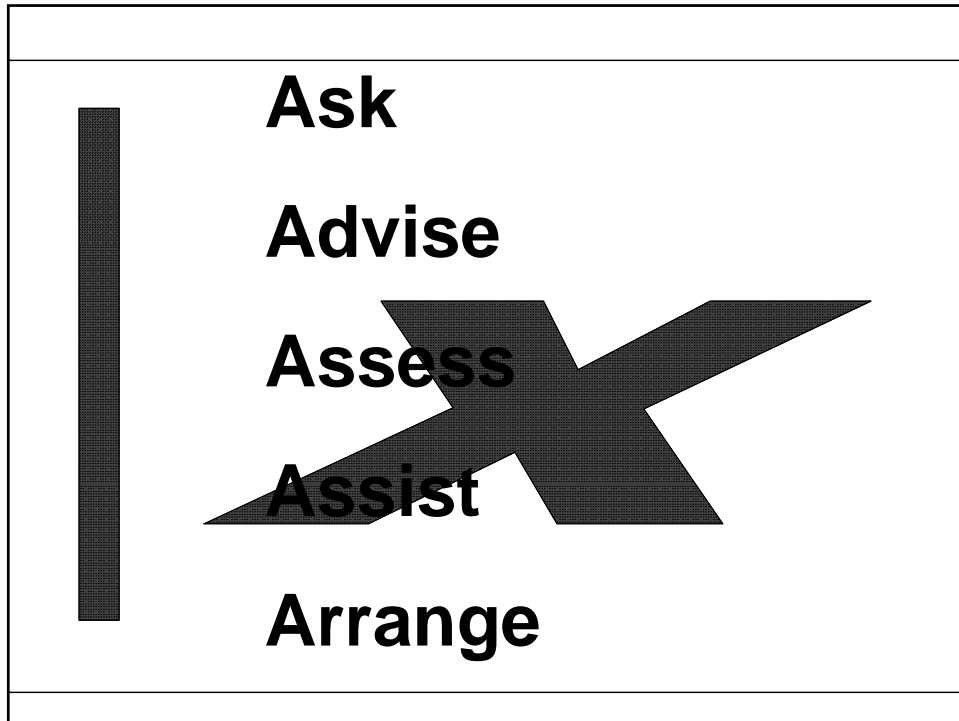
Ask

Advise

Assess

Assist

Arrange



4 quick steps to RETIRE smoking

Ask

Advise

Refer

Prescribe

4 quick steps to RETIRE smoking

Ask every patient about smoking

- A** • This is their #1 risk factor
- R** • Use a sticker or a red pen
- P** • Put it on the problem list
- P** • You aren't nagging. Much more likely to quit smoking than lose weight, exercise or stop drinking

4 quick steps to RETIRE smoking

A

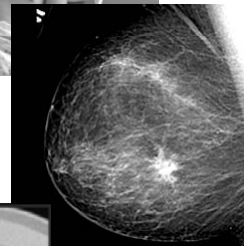
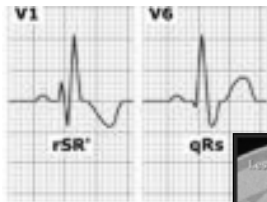
Motivational Interviewing at Teachable Moments

**Advise
to
Quit
P**

During a chest or oral exam

With an abnormal chest xray,
EKG, CT, PFT, doppler, EGD

After a diagnosis of cancer, CV
or lung disease, ED, hearing or
hair loss, diabetes, depression,
or their kid's otitis or asthma



4 quick steps to RETIRE smoking

A

Send to a Cessation Expert

A

- Hospital or Other Tobacco Treatment Center Specialist

Refer

- 800-QUIT-NOW

P

- You probably don't treat heroin or meth addiction

- Tobacco treatment requires time and expertise.

800 QUIT NOW

Counseling: positive dose response

- **Set a quit date.** Ideally, the quit date should be within 2 weeks. Just “cutting down” worthless.
- **Tell family, friends, and coworkers** and request support. Please don’t “bum me one.”
- **Anticipate challenges** to the upcoming quit attempt, particularly during the critical first week. These include nicotine withdrawal symptoms. Alcohol induces cravings, reduces resolve.
- **Remove** tobacco products from your environment. Prior to quitting, avoid smoking in places where you spend a lot of time (e.g., work, home, car). Make your home smoke-free.

Counseling: positive dose response

- **“One puff is enough!”**
- **Statistically the first week is absolutely critical**

4 quick steps to RETIRE smoking

A

Triple the Chance of Success

NRT (patch + short acting)

A

and/or

R

Bupropion SR 150 mg
daily x 3 then 150 mg BID

Prescribe

or

Varenicline 0.5 mg daily x 3,
BID x 4, then 1 mg BID

What's the economic cost?

**What's the economic
cost?**

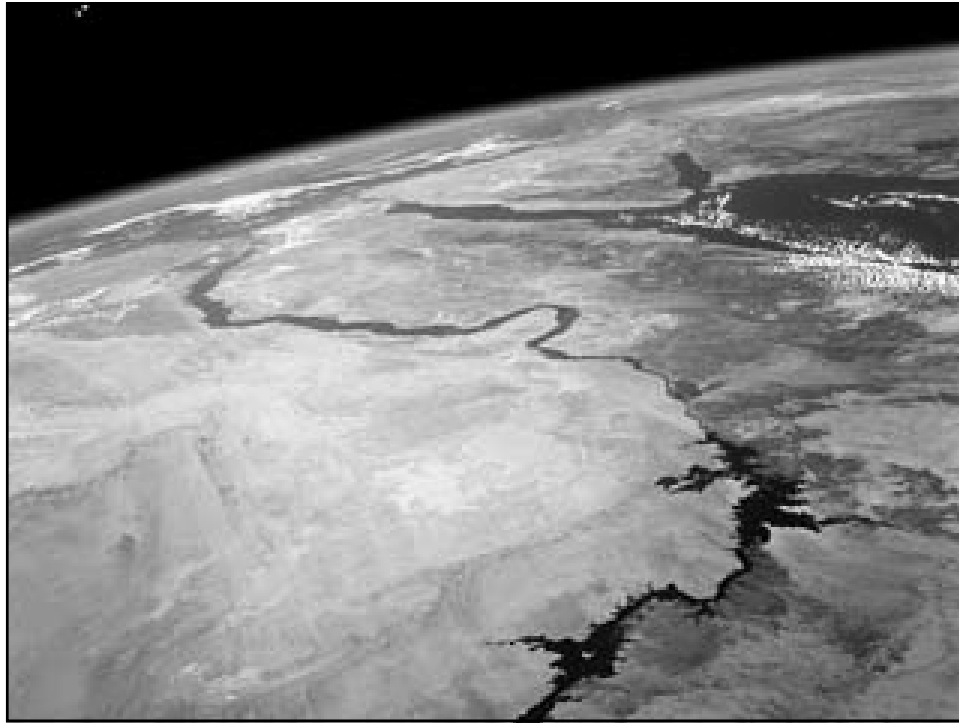
\$196 Billion

**What's the economic
cost?**

\$196 Billion

Cost to employers

\$4200/employee/year



What I'd like you to remember

Your:

- **Patient's deadly disease**
- **Public health duty**
- **Political responsibility**

Pharmacotherapy of Smoking Cessation



Cari Brackett, Pharm.D.

Associate Clinical Professor

The Ohio State University College of Pharmacy

Department of Family Medicine



Comparative Odds of Cessation Success:

Available Options

Odds of Abstinence Consequent to Smoking Cessation Therapies

Table 1 Odds ratios of abstinence with first- and second-line smoking cessation therapy^{21,31,60}

Treatment	Odds Ratio (95% CI)*
First-line therapies	
NRT: All forms, pooled (meta-analysis of 123 studies with ≥6 mo follow-up)	1.77 (1.66–1.88)
Gum	1.66 (1.52–1.81)
Patch	1.81 (1.63–2.02)
Inhaler	2.14 (1.44–3.18)
Lozenge	2.05 (1.62–2.59)
Nasal spray	2.35 (1.63–3.38)
Bupropion (meta-analysis of 19 trials with ≥6 mo follow-up)	2.06 (1.77–2.40)
Varenicline [†]	Gonzales et al (2006) ⁴⁵ (phase 3 trial of 1,027 smokers) 12 wk: 3.85 (2.70–5.50) 52 wk: 3.09 (1.95–4.91) Jorenby et al (2006) ⁴⁶ (phase 3 trial of 1,025 smokers) 12 wk: 3.85 (2.69–5.50) 52 wk: 2.66 (1.72–4.11)
Second-line therapies	
Nortriptyline (meta-analysis of 6 trials with ≥6 mo follow-up)	2.14 (1.49–3.06)
Clonidine (meta-analysis of 6 trials with ≥12 wk follow-up)	1.89 (1.30–2.74)

CI = confidence interval; NRT = nicotine replacement therapy.

*Odds ratios are derived from *Cochrane Review* articles unless otherwise noted.

[†]Due to the relatively recent availability of clinical trial data for varenicline, there is currently no *Cochrane Review* or other meta-analysis of this agent.

With Permission:

Nides M. Update on Pharmacologic Options for Smoking Cessation Treatment. *Am J Med* (2008) Vol 121 (4A), S20–S31.

Odds of Abstinence Consequent to Smoking Cessation Therapies

	Abstinence Rates
NRT _{In aggregate}	1.77 _{at > 6 months}
Bupropion	2.06 _{at > 6 months}
Varenicline	2.6 _{at 12 months}
Nortriptyline	2.14 _{at > 6 months}
Clonidine	1.89 _{at > 12 weeks}

Pharmacologic Options for Smoking Cessation

	Comments	Precautions	Dosage
Nicotine Patch	16 removal hours if insomnia.	Pregnancy category D	< 10 cigarettes/d, 14 mg patch. ≥ 10/d, 21 mg patch.
Nicotine Gum	Heavy smokers respond better to 4 mg than 2 mg formulation. <u>NRT Overall:</u> Women may respond less well than men.	Pregnancy category C	> 9 and < 20-30 pieces per day X 6 weeks.

Nides M. Update on Pharmacologic Options for Smoking Cessation Treatment. Am J Med (2008) Vol 121 (4A), S20–S31.

Pharmacologic Options for Smoking Cessation

	Comments	Precautions	Dosage
Varenicline	Partial agonism prevents craving as well as blocking physiologic effect (reinforcement). Withdrawal is attenuated.	Pregnancy category C. Nausea is prominent Emotional destabilization!	0.5 mg daily, escalating to 1 mg bid. (Is this dose indeed optimal?)
Bupropion SR	Suppresses weight gain. Safe in CVD.	Pregnancy category C. Insomnia. Caution with seizure disorder.	Escalate to 150 mg bid X 12 weeks.

Nides M. Update on Pharmacologic Options for Smoking Cessation Treatment. Am J Med (2008) Vol 121 (4A), S20–S31.

Pharmacologic Options for Smoking Cessation

	Comments	Precautions	Dosage
Nortriptyline	Efficacy similar to bupropion or varenicline. Use limited by adverse effects.	Pregnancy category D. Avoid in CVD. Lethal in overdose. Dysrhythmia!	Begin 25 mg qd 10 – 28 days prior to quit date. Escalate to 75-100 mg daily X 12 weeks. Taper to d/c.
Clonidine	Oral or transdermal delivery.	Pregnancy category C. Rebound hypertension with d/c.	Begin 3 days prior to quit date. 0.15 – 0.75 mg po qd or 0.1-0.3 mg patch. Taper with d/c.

Nides M. Update on Pharmacologic Options for Smoking Cessation Treatment. Am J Med (2008) Vol 121 (4A), S20–S31.

- **A Cochrane Review determined that all forms of NRT approximately double (O.R. 1.5-2) the chance of long-term abstinence from smoking.**

- **All forms of NRT tested (gum, patch, nasal spray, and inhaler) produce roughly similar quit rates and are equally effective at reducing the frequency, duration, and severity of urges to smoke.**

- **There is some controversy as to whether NRT is less effective for women than men, particularly at 1-year follow-up.**

Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.:
CD000146. DOI: 10.1002/14651858.CD000146.pub2.

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Vol. 168 No. 18, October 13, 2008

Review Article

Smoking Cessation Interventions for Hospitalized Smokers
A Systematic Review
Nancy A. Rigotti, MD; Marcus R. Munafo, PhD; Lindsay F. Stead, MSc
Arch Intern Med. 2008;168(18):1950-1960.

Background A hospital admission provides an opportunity to help people stop smoking. Providing smoking cessation advice, counseling, or medication is now a quality-of-care measure for US hospitals. We assessed the effectiveness of smoking cessation interventions initiated during a hospital stay.

Methods We searched the Cochrane Tobacco Addiction Review Group's register for randomized and quasirandomized controlled trials of smoking cessation interventions (behavioral counseling and/or pharmacotherapy) that began during hospitalization and had a minimum of 6 months of follow-up. Two authors independently extracted data from each article, with disagreements resolved by consensus.

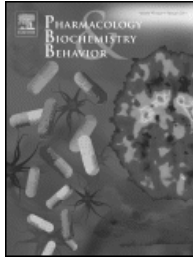
Results Thirty-three trials met inclusion criteria. Smoking counseling that began during hospitalization and included supportive contacts for more than 1 month after discharge increased smoking cessation rates at 6 to 12 months (pooled odds ratio [OR], 1.65; 95% confidence interval [CI], 1.44-1.90). No benefit was found for interventions with less postdischarge contact. Counseling was effective when offered to all hospitalized smokers and to the subset admitted for cardiovascular disease. Adding nicotine replacement therapy to counseling produced a trend toward efficacy over counseling alone (OR, 1.47; 95% CI, 0.92-2.35). One study added bupropion hydrochloride to counseling, which had a nonsignificant result (OR, 1.56; 95% CI, 0.79-3.06).

Conclusions Offering smoking cessation counseling to all hospitalized smokers is effective as long as supportive contacts continue for more than 1 month after discharge. Adding nicotine replacement therapy to counseling may further increase smoking cessation rates and should be offered when clinically indicated, especially to hospitalized smokers with nicotine withdrawal symptoms.

“Offering smoking cessation counseling to hospitalized is effective SO LONG AS it continues for MORE THAN ONE MONTH after discharge.

Adding NRT to counseling may further increase cessation rates, and should be offered to patients with withdrawal symptoms.”

Arch Int Med; 2008; 168 (16) 1950 – 60 s



Nicotine metabolic rate predicts successful smoking cessation with transdermal nicotine: A validation study

Smokers who are faster metabolizers were less likely to be abstinent vs. slow metabolizers; 28% vs. 42%.

Among abstainers, plasma nicotine levels decreased linearly across the 3-HC/cotinine ratio. These data support the value of the 3-HC/cotinine ratio as a biomarker to predict success with transdermal nicotine for smoking cessation.

Pharmacology Biochemistry and Behavior. 2009; 92: 6-11

Nicotine & Tobacco Research

Sex Differences in Long-Term Smoking Cessation Rates Due to Nicotine Patch

Absolute quit rates at 6 months for nicotine and placebo patch were 20.1% and 10.8% in men, and 14.7% and 10.1% in women.

The odds ratio for quitting due to nicotine vs. placebo patch was lower in women (OR=1.61) than in men.

Nicotine & Tobacco Research 2007; 10 (7) :1245-1251.

Varenicline: Mechanisms of Action

- ☐ Binds with high affinity to BOTH $\alpha_4\beta_2$, α_7 *and* $5HT_3$ neuronal nicotinic acetylcholine receptors
- ☐ 2 effects:
 - stereospecific blockade of nicotine binding AND...
 - *either* full or partial agonism of receptors
- ☐ $\alpha_4\beta_2$ partial agonist → ameliorates pleasure of nicotine
- ☐ α_7 & $5HT_3$ full agonist → decreases mesolimbic DA abstinence

**Labeled Treatment
Duration is 12 Weeks
With Option to Repeat
Once.**



**Patients Choose a “Quit” Date and
Must Begin Taking Varenicline One
Week Prior to That Date.**



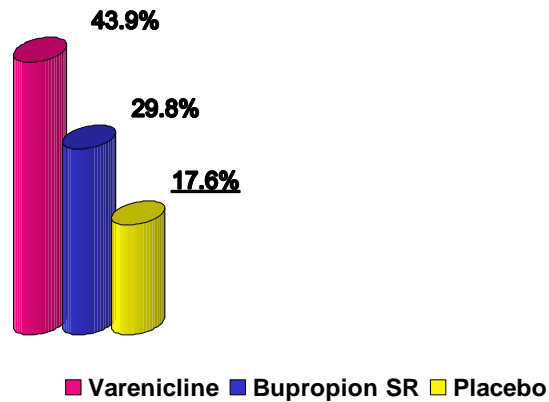
FDA-Approved Treatment Regimen:

Days 1 - 3: 0.5 mg once daily

Days 4 - 7: 0.5 mg twice daily

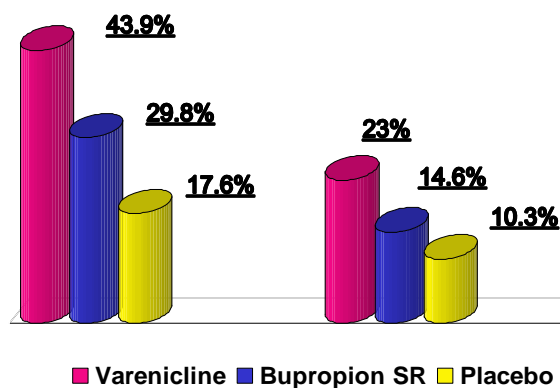
**Day 8 - End of treatment: 1 mg
twice daily**

Continuous Abstinence at 12 Weeks:



Jorenby et al. JAMA 2006;296:56-63

Continuous Abstinence at 12 and 52 Weeks:



Jorenby et al. JAMA 2006;296:56-63

Twelve vs. Twenty Four Weeks of Treatment

1: JAMA. 2006 Jul 5;296(1):64-71.

Comment in:
JAMA. 2006 Jul 5;296(1):94-5.

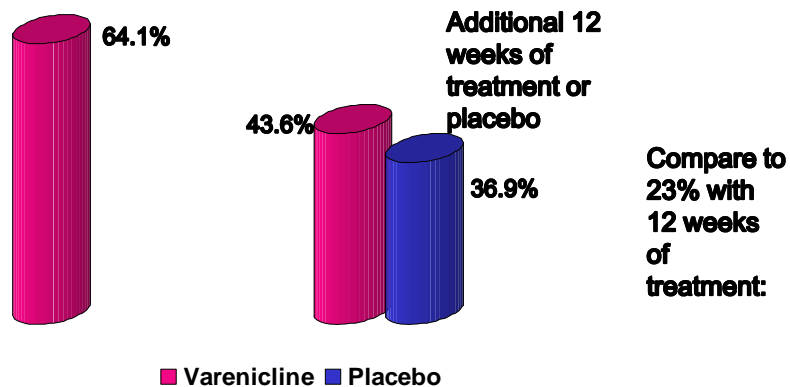
Effect of maintenance therapy with varenicline on smoking cessation: a randomized controlled trial.

Tonstad S, Tonnesen P, Hajek P, Williams KE, Billing CB, Reeves KR; Varenicline Phase 3 Study Group.

Department of Preventive Cardiology, Ulleval University Hospital, and University of Oslo, Oslo, Norway.
serena.tonstad@uus.no

Tonstad et al. JAMA 2006; 296 : 64-71

Continuous Abstinence at 52 Weeks:



Tonstad et al. JAMA 2006; 296 : 64-71

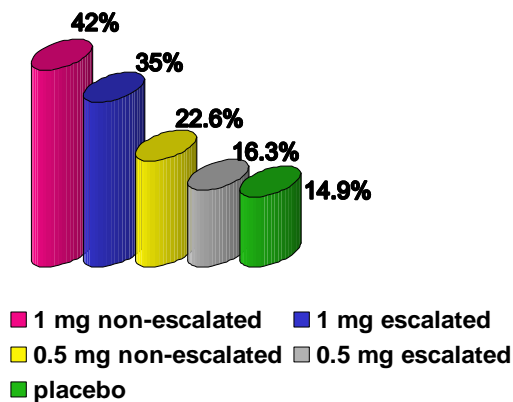
Adverse Effects

- * Nausea 16 - 30%
- * Vomiting 1 - 5%
- * Headache 19 - 15%
- * Abnormal dreams 9 - 13%
- * Insomnia 19 - 18%
- * Flatulence 9 - 6%
- * Constipation 5 - 8%



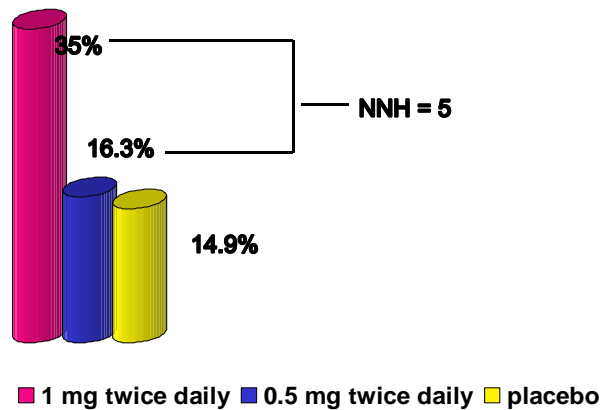
Gonzales et al. JAMA 2006;296:47-55

Incidence of Nausea



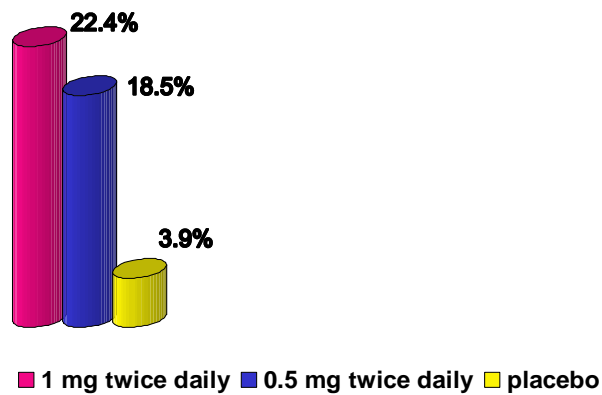
Oncken C. et al. Arch Intern Med 2006; 166 : 1571-7

Incidence of Nausea



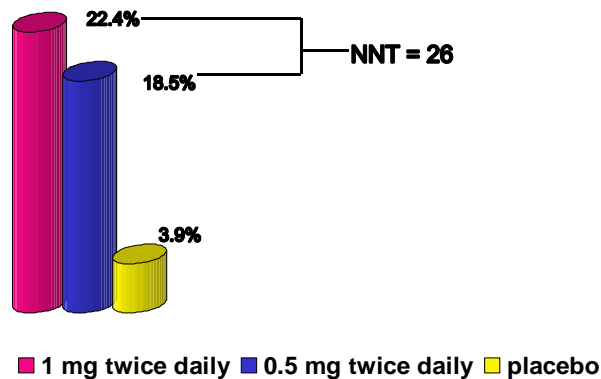
Oncken C. et al. Arch Intern Med 2006; 166 : 1571-7

Continuous Abstinence at 52 Weeks: (24 weeks of treatment)



Oncken C. et al. Arch Intern Med 2006; 166 : 1571-7

Continuous Abstinence at 52 Weeks:



Oncken C. et al. Arch Intern Med 2006; 166 : 1571-7

Question:

Might 0.5 mg twice daily be useful for a patient who experiences side effects?



Additional Thoughts and Questions:

Varenicline does elicit some degree of drug-seeking behavior in rats. Should we taper doses at the end of treatment rather than discontinue abruptly?

Additional Thoughts and Questions:

Recovery is life-long. Should we entertain a “Plan C” approach to smoking cessation and endorse varenicline at home for “as needed” use in conditions of high or sustained stress?



Varenicline versus transdermal nicotine patch for smoking cessation: results from a randomized open-label trial

The week 52 abstinence rate was 26.1% for varenicline and 20.3% for NRT (OR 1.40, $p=0.056$). Varenicline significantly reduced craving, withdrawal symptoms and smoking satisfaction compared with NRT

Thorax 2008;63:717-724 doi:10.1136/thx.2007.090647

Concurrent Nicotine Replacement and Varenicline:

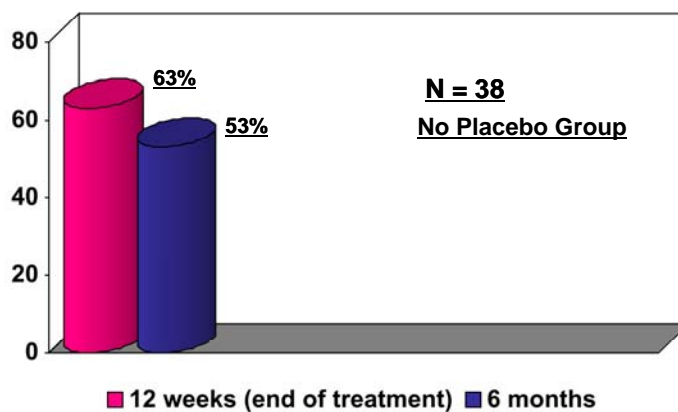
Co-administration of varenicline and nicotine patch:

36% discontinuation due to adverse effects with concurrent treatment vs 6% with varenicline plus placebo



Data on file: Pfizer, Inc.

Biochemical Abstinence at 12 Weeks: Varenicline 1 mg bid and Bupropion SR 150 mg bid



Nicotine Tob Res. 2009;11(3): 234-9

EUROPEAN JOURNAL OF CANCER PREVENTION

European Journal of Cancer Prevention:
November 2008 - Volume 17 - Issue 6 - pp 535-544
doi: 10.1097/CEJ.0b013e3282f75e48
Reviews: Lung Cancer

Effectiveness of smoking cessation interventions among adults: a systematic review of reviews

“Group behavioral therapy OR 2.17, bupropion OR 2.06, intensive physician advice OR 2.04, nicotine replacement therapy OR 1.77, individual counseling OR 1.56, telephone counseling OR 1.56, and tailored self-help interventions OR 1.42.

A 10% increase in price increased cessation rates by 3-5%.

Comprehensive clean indoor laws increased quit rates by 12-38%.”

Question:

Does nicotine metabolism rate predict successful (10-week) smoking cessation with bupropion?

Slow metabolizers had equivalent quit rates with placebo or bupropion (32%).

Rapid metabolizers had low quit rates with placebo (10%), and much higher rates with bupropion (34%).

Clin Pharmacol Ther. 2008; 84: 320-25.

Human Molecular Genetics

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Oxford Journals > Life Sciences & Medicine > Human Molecular Genetics > Volume 18, Issue 1

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A common genetic variant in the 15q24 nicotinic acetylcholine receptor gene cluster (*CHRNA5-CHRNA3-CHRNA4*) is associated with a reduced ability of women to quit smoking in pregnancy

Rachel M. Freathy¹, Susan M. Ring², Beverley Shields³, Bruna Galobardes², Beatrice Knight³, Michael N. Weedon¹, George Davey Smith^{2,4}, Timothy M. Frayling¹ and Andrew T. Hattersley^{3,*}

Hum Mol Genet. 2009; 18(15): 2922-7

“A recent genome-wide association study demonstrated an association between a common polymorphism (rs1051730) in the nicotinic acetylcholine receptor gene cluster and both smoking quantity and nicotine dependence.

Each additional copy of the risk allele was associated with a 1.27-fold higher odds of continued smoking during pregnancy.

The same risk allele was also associated with heavier smoking before pregnancy and in the first trimester.

Our data support the role of genetic factors in influencing smoking cessation during pregnancy.”

Hum Mol Genet. 2009; 18(15): 2922-7

Pharmacogenetics & Genomics:
February 2008 - Volume 18 - Issue 2 - pp 121-128
doi: 10.1097/FPC.0b013e3282f44daa
Original Articles

Association of COMT Val108/158Met genotype with smoking cessation

Munafò, Marcus R.^a; Johnstone, Elaine C.^b; Guo, Boliang^d; Murphy, Michael F.G.^c; Aveyard, Paul^e

Conclusions: The COMT genotype influences smoking cessation in smokers treated with the NRT transdermal patch. Further study must investigate the role of multiple genetic variants in treatment responses.

Effect of abstinence challenge on brain function and cognition in smokers differs by COMT genotype
COMT, nicotine abstinence, and brain function

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“The val allele of the catechol-O-methyltransferase (COMT) polymorphism has been linked with nicotine dependence and with cognitive performance. These data suggest a novel brain-behavior mechanism that may underlie the increased susceptibility to nicotine dependence and smoking relapse associated with the COMT val allele.”



A Vaccine against Nicotine for Smoking Cessation: A Randomized Controlled Trial

Subjects with highest antibody levels showed higher continuous abstinence from month 2 until month 6 (56.6%) than placebo-treated participants (31.3%) while medium and low antibody levels did not increase abstinence rates.

After 12 months, the difference in continuous abstinence rate between placebo and high antibody response was maintained (difference 20.2%, $P = 0.012$).

PLoS ONE. 2008; 3(6): e2547. doi:10.1371/journal.pone.0002547