

# Smoking Cessation



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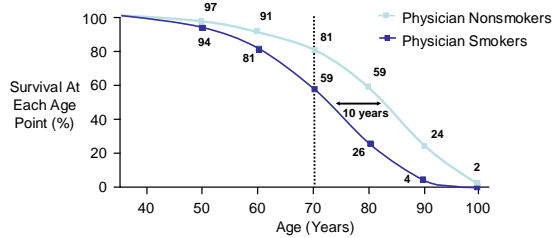
# Smoking Statistics

- About 1/3 of the male adult global population smokes.
- Smoking related-diseases kill one in 10 adults globally, or cause four million deaths. By 2030, if current trends continue, smoking will kill one in six people.
- About 12 times more British people have died from smoking than from World War II.
- Cigarettes cause more than one in five American deaths.
- About one in three cigarettes are consumed in the Western Pacific Region which covers East Asia and the Pacific
- Smoking is the single largest preventable cause of disease and premature death

WHO 2002

# Smoking Reduces Survival an Average of 10 Years

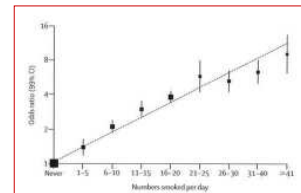
Results From a Study of Male Physician Smokers in the United Kingdom



1. Doll R, et al. *BMJ*. 2004;328:1519-1527.

# Tobacco use is a disease

Odds of MI according to number of cigarettes smoked



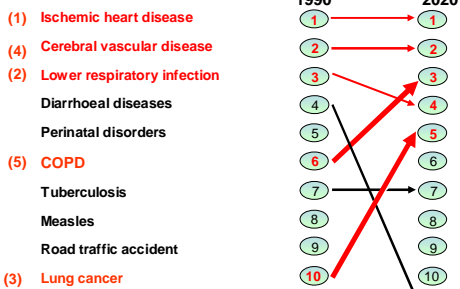
*Lancet*. 2004;364:937-52

ICD 9

Current smoker V15.73

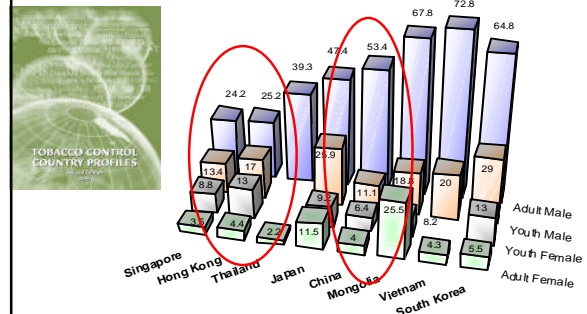
Tobacco use disorder 305.1

Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study



Murray and Lopez *Lancet* 1997;349:1498-1504

# Smoking: Gender- and Age-Specific Prevalence in Asia



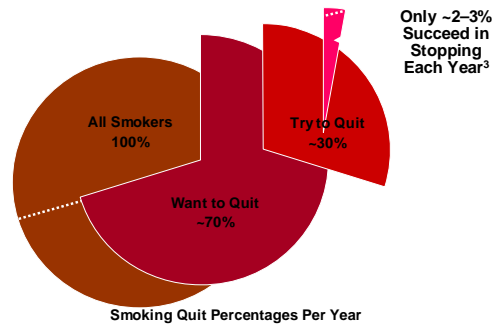
Shafey et al. *Tobacco Control Country Profiles*. 2nd Ed 2003.

## Is quitting difficult?

- “Giving up smoking is the easiest thing in the world. I know because I’ve done it thousands of times.”

– Mark Twain

## Smokers want to quit



1. Bridgwood et al. *Living in Britain: Results for the 1998 General Household Survey 1998*.  
 2. West. *Getting serious about stopping smoking – a review of products, services, and techniques. No Smoking Day 1997*.  
 3. Arnsen JH. *Prim Psychiatry*, 1996;3:27-30.

Why don't smokers quit smoking?  
 Why so difficult?

**Addiction!**

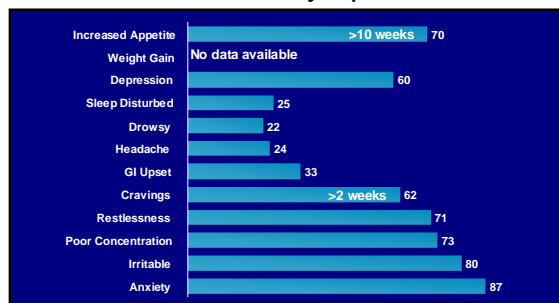


## Addiction

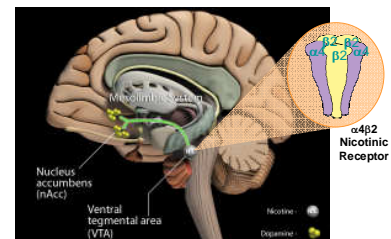
- 1988 Surgeon General's Report<sup>1</sup>
  - Addiction: **compulsive use despite damage to the individual or society** and drug-seeking behavior can take precedence over important priorities
  - Addiction **persists despite a desire to quit** or even repeated attempts to quit
- Most people smoke primarily because they are addicted to nicotine<sup>2</sup>

1. Centers for Disease Control and Prevention. *The Health Consequences of Smoking: Nicotine Addiction; A Report of the Surgeon General*. Washington DC: US Department of Health and Human Services, 1988. 2. Jarvis MJ. *BMJ*, 2004;328:277-279.

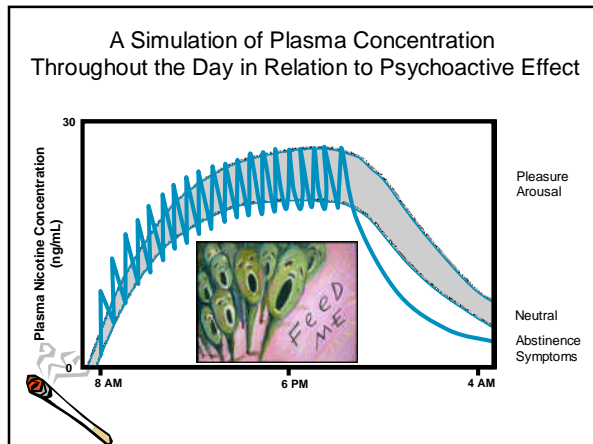
## Most Commonly Reported Withdrawal Symptoms



## Mechanism of Action of Nicotine in the Central Nervous System



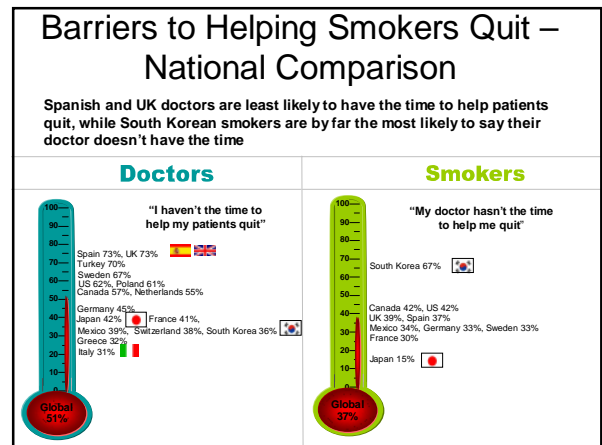
- Nicotine binds preferentially to nicotinic acetylcholinergic (nACh) receptors in the central nervous system; the primary is the  $\alpha 4 \beta 2$  nicotinic receptor in the Ventral Tegmental Area (VTA)
- After nicotine binds to the  $\alpha 4 \beta 2$  nicotinic receptor in the VTA, it results in a **release of dopamine** in the Nucleus Accumbens (nAcc) which is believed to be linked to reward



### Addictive Nature of Nicotine

- Tobacco users are more likely to become dependent (28%) than users of alcohol (5.2%), cannabis (8.2%), or cocaine (11.6%)

### Barriers to helping smokers quit

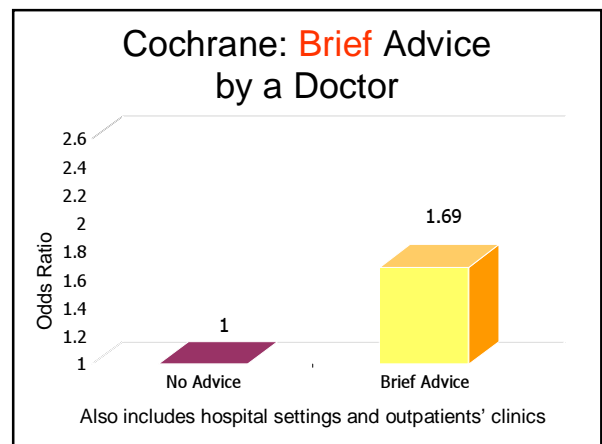



### A Physician's Time is Valuable

Primary care in European countries with publicly owned and staffed systems, 1997

N=6495	Spain	Finland	Portugal	Sweden	Average
Days waiting for a consultation					
0-1 day	92	39	50	37	57
2-4 days	8	22	10	9	13
5-8 days	0	33	15	27	18
>8 days	0	6	25	27	13
Patients/week by doctor (average)	154	94	89	90	103
Duration of consultation (%)					
<5 min	52	29	30	36	37
5-9 min	35	27	25	27	29
10-14 min	10	29	29	17	22
>15 min	3	15	16	20	13

Adapted from: 1. Ortún V, Casasnovas L. El Sistema Nacional de Salud en España. Informe de una década. Fundación BBV, Bilbao, 1999. 2. World Health Organization. Health Care Systems in Transition. Spain, 2000. Available at: <http://www.euro.who.int/document/e70504.pdf>. Accessed April 2007.





**Brief** Clinician Intervention  
( < 3 minutes)

U.S. Preventive Services Task Force. Counseling to prevent tobacco use and tobacco-caused disease: recommendation statement 2003

**Messages to convey**

Smoking is dangerous

Smoking is addictive

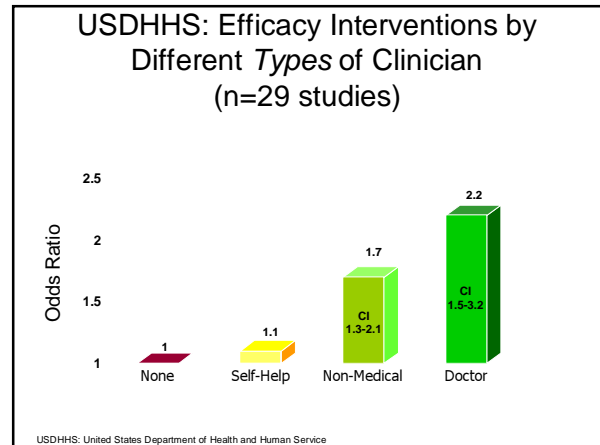
There are **effective** treatments

**Motivation**

Give advise regarding *personal health risks*




**Beauty !!  
Impotency !!**



**Tool for motivation**

- REMEMBER
- SPIROMETRY
- CXR
- Sputum cytology

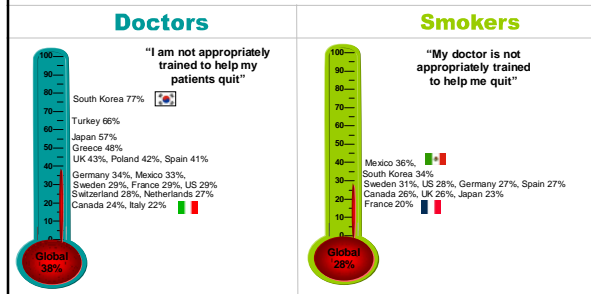


**Motivation**

- Smokers who are not interested in stopping or reducing should be advised that the physician will **return to the question at a later visit**

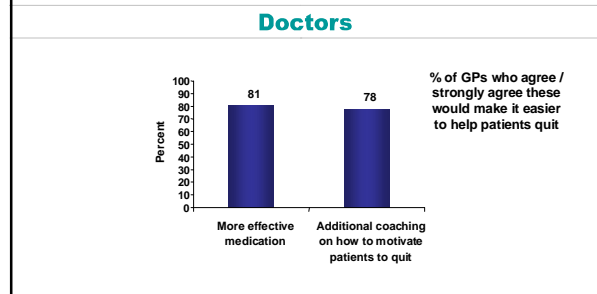
## Barriers to Helping Smokers Quit – National Comparison (2)

South Korean doctors are most likely and Italian doctors the least likely to say they are not appropriately trained to help patients quit



## Doctors' "Wish List"

General practitioners would like more effective medication and additional coaching



## Non-pharmacological treatment

## Non-Pharmacologic Treatment for Smoking Cessation

Comparison	N Trials	N Participants	Pooled OR* (95% CI)
<b>Physician advice<sup>1</sup></b>			
Brief vs no advice (usual care)	17	>13,000	1.74 (1.48–2.05)
Intensive vs minimal advice	15	>9,000	1.44 (1.24–1.67)
<b>Individual counseling<sup>2</sup></b>			
Vs minimal behavior intervention	17	>6,000	1.56 (1.32–1.84)
<b>Group counseling<sup>3</sup></b>			
Vs self-help	16	>4,000	2.04 (1.60–2.60)
Vs no intervention	7	815	2.17 (1.37–3.45)
<b>Proactive Telephone counseling<sup>4</sup></b>			
Vs less intensive interventions	13	>16,000	1.56 (1.38–1.77)
<b>Self-help<sup>5</sup></b>			
Vs no intervention	11	>13,000	1.24 (1.07–1.45)

\*Abstinence assessed at least 6-months following intervention.  
 1. Lancaster T, Stead LF. Cochrane Database Syst Rev. 2004;(4):CD001652. 2. Lancaster T, Stead LF. Cochrane Database Syst Rev. 2005;(2):CD001292. 3. Stead LF, Lancaster T. Cochrane Database Syst Rev. 2005;(4):CD001007. 4. Stead LF et al. Cochrane Database Syst Rev. 2005;(4):CD002850. 5. Lancaster T, Stead LF. Cochrane Database Syst Rev. 2005;(3):CD001118.

## Weekly versus basic smoking cessation support in primary care: a randomised controlled trial

Paula Reynolds, Karen Brown, Gail Saunders, David Altabelli, Elaine Johnson, Alison R Martin, Nikita Dhillon

Behavioural support for smoking cessation

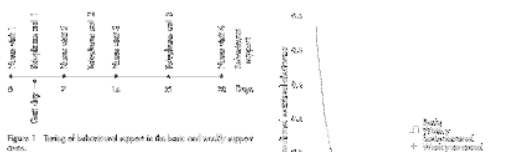


Figure 1. Timing of behavioral support in the basic and weekly support arms.

Consider the checklist of behavioral support interventions from various guidelines, applying them to the basic and weekly support arms. Primary care smoking cessation treatment should provide behavioral support with sufficient opportunity to ensure it is used appropriately, and those in need of support should be referred to specialists.

## A Randomized Controlled Clinical Trial of Auricular Acupuncture in Smoking Cessation

Table 1. Effectiveness of auricular acupuncture in smoking cessation compared with usual care

Intervention	Number of participants (n)	Number of smokers (n)	OR (95% CI)
Physician advice	100	50	1.00
Auricular acupuncture	100	45	0.90 (0.60-1.35)
Physician advice + auricular acupuncture	100	55	1.10 (0.75-1.60)
Physician advice + group counseling	100	60	1.20 (0.80-1.80)
Physician advice + self-help	100	58	1.15 (0.75-1.75)
Physician advice + telephone counseling	100	52	1.05 (0.70-1.55)
Physician advice + group counseling + self-help	100	65	1.30 (0.85-1.95)
Physician advice + group counseling + telephone counseling	100	62	1.25 (0.80-1.90)
Physician advice + group counseling + self-help + telephone counseling	100	70	1.40 (0.90-2.15)



J Chin Med Assoc 2007

Intervention	Relative risk (95% CI)	Number of people who quit (95% CI)
Acupuncture (n=100)	1.00	10 (10)
Acupuncture + Nicotine Replacement Therapy (n=100)	1.25 (0.85, 1.85)	12 (10, 14)
Acupuncture + Nicotine Replacement Therapy + Behavioral Support (n=100)	1.50 (1.00, 2.25)	15 (12, 18)

*J Chin Med Assoc 2007*

**Cochrane Review 2006:**

- There is no consistent evidence that acupuncture is effective for smoking cessation
- Further research is justified

## Pharmacological Treatment



### Pharmacotherapy for Tobacco Dependence

- Nicotine replacement therapy (NRT)
- Antidepressants
  - Bupropion SR
- Varenicline

### Nicotine Replacement Therapy (NRT)

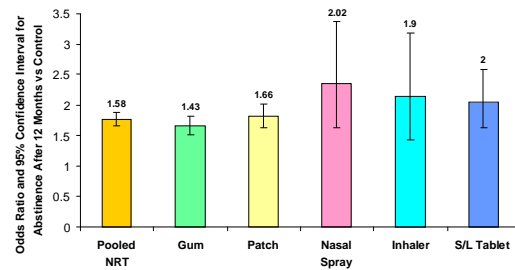
- How NRT works
  - First, replace the nicotine from cigarettes to control withdrawal symptoms, while the patient is abstaining from smoking
  - Second, gradually phase out all nicotine when the addiction becomes manageable without NRT

### Different forms of NRT

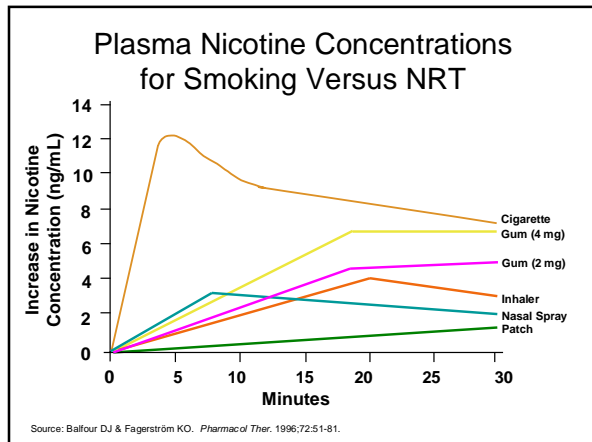
- **Nicotine transdermal patches**
  - 16 h patch 5mg, 10mg, 15mg
  - 24 h patch 7mg, 14mg, 21mg
- **Nicotine chewing gum**
  - 2mg, 4mg
- Nicotine sublingual tablet 2mg, 4mg
- Nicotine **inhalator cartridge** plus mouthpiece 10mg
- Nicotine **nasal spray** 10 mg/ml, 0.5 mg per puff
- Nicotine **lozenge** 1, 2mg and 4mg



### NRT – Efficacy of Different Preparations After 12 Months' Use



Stead et al. *The Cochrane Library*, 2008.



### Strengths and Limitations of NRT

<p><b>Strengths</b></p> <ul style="list-style-type: none"> <li>• Availability</li> <li>• Safety</li> <li>• Variety of choices</li> </ul>	<p><b>Limitations</b></p> <ul style="list-style-type: none"> <li>• Slow delivery</li> </ul>
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There are **no contraindications** for NRT, if the alternative is smoking!

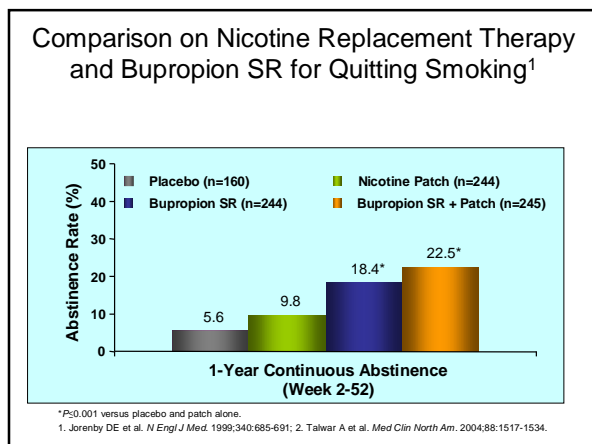
### Bupropion SR (Zyban®)

- Developed as an antidepressant, later found to be effective for smoking cessation<sup>1</sup>
- There are 2 potential MOAs:
  - Blocks reuptake of dopamine and norepinephrine<sup>2,3</sup>
  - Non-competitive inhibition of  $\alpha 3\beta 2$  and  $\alpha 4\beta 2$  nicotine receptors<sup>4,5</sup>

1. Package Insert, bupropion SR hydrochloride [Zyban®], GlaxoSmithKline; 2. Henningfield JE et al. *CA Cancer J Clin.* 2005;55:281-299; 3. Foulds J et al. *Expert Opin Emerg Drugs.* 2004;9:39-53; 4. Slemmer JE et al. *J Pharmacol Exp Ther.* 2000;295:321-327; 5. Roddy E. *Br Med J.* 2004;328:509-511.

### Bupropion Dosing

- Initiate at 150 mg in the morning
- Increase dose to 150 mg twice daily on Day 7
- Continue treatment for 7-9 weeks



### Contraindications of Bupropion

- Hypersensitivity
- History of **seizure** or low threshold for seizure
- History of eating disorders
- Recent/current use if monoamine oxidase inhibitors (MAOIs)
- Severe hepatic cirrhosis
- Bipolar disorder

**\*Bupropion interacts with a number of commonly used drugs, including some antidepressants, type 1c antiarrhythmics, and antipsychotics**

## Bupropion

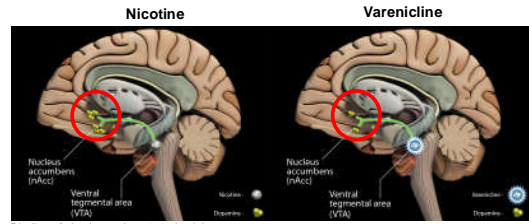
### ADVANTAGES

- It is active via oral
- It is easy to use.
- Odds ratio for success is 2.10 ( 95%CI, 1,62-2,73).
- Delayed weight gain.

### DISADVANTAGES

- It can produce drugs interactions.
- Insomnia and dryness of mouth

## Varenicline: A Highly Selective $\alpha 4\beta 2$ Receptor Partial Agonist

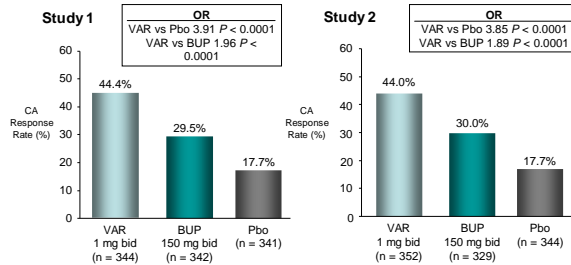


Binding of nicotine at the  $\alpha 4\beta 2$  nicotinic receptor in the VTA is believed to cause release of dopamine at the NAcc

Varenicline is an  $\alpha 4\beta 2$  nicotinic receptor partial agonist, a compound with **dual agonist and antagonist activities**: lesser amount of dopamine release from the VTA at the NAcc as well as the prevention of nicotine binding at the  $\alpha 4\beta 2$  receptors.

1. Coe JW et al. Presented at the 11th Annual Meeting and 7th European Conference of the Society for Research on Nicotine and Tobacco. 2005. Prague, Czech Republic. 2. Piciotto MR et al. *Nicotine Tob Res.* 1999; Suppl 2:S121-S125.

## 4-Week Continuous Abstinence (CA) Response Weeks 9–12<sup>1</sup>

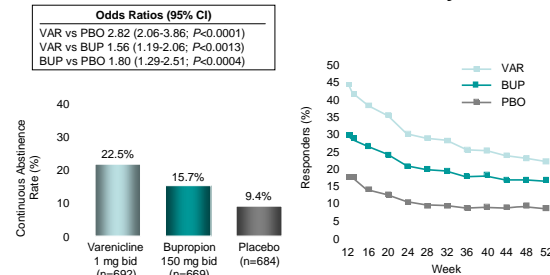


Nausea was reported by 28.8% of patients treated with varenicline 1 mg bid. The discontinuation rate for this adverse event was 2.7%. Nausea was generally described as mild or moderate.

VAR = varenicline, Pbo = placebo, BUP = bupropion; OR = Odds ratio.

1. Champix Summary of Product Characteristics. Pfizer Ltd, Sandwich, UK. 2006.

## Continuous Abstinence Rates: Weeks 9 to 52 Pooled Analyses



VAR=varenicline, BUP=bupropion, PBO=placebo

Gonzales DH et al. Society for Research Nicotine and Tobacco Paper sessions, PA9-2. 2006.

## Different doses of varenicline Vs placebo



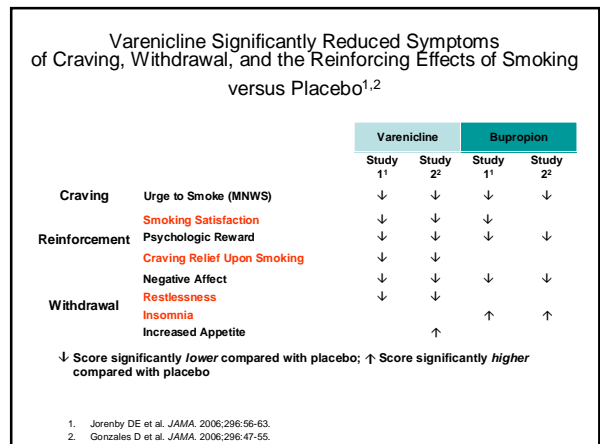
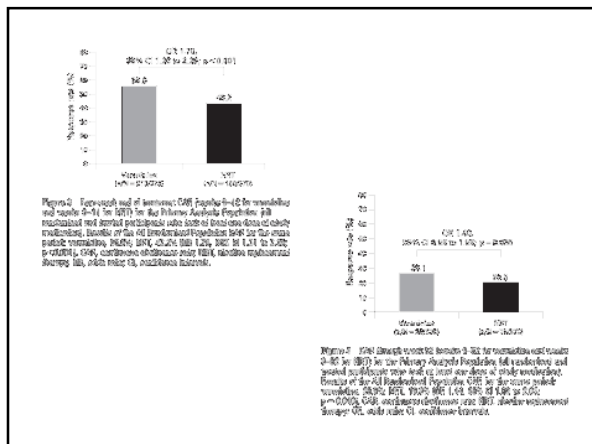
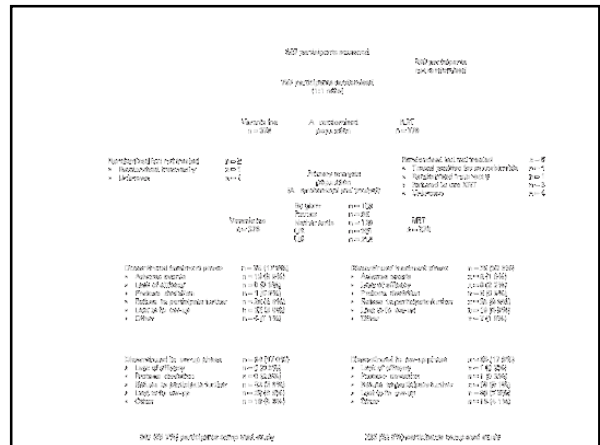
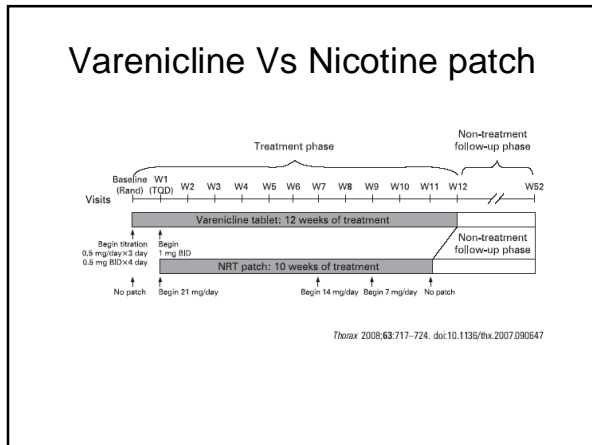
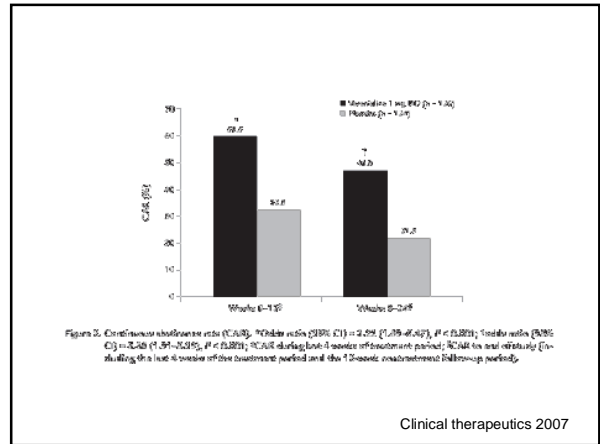
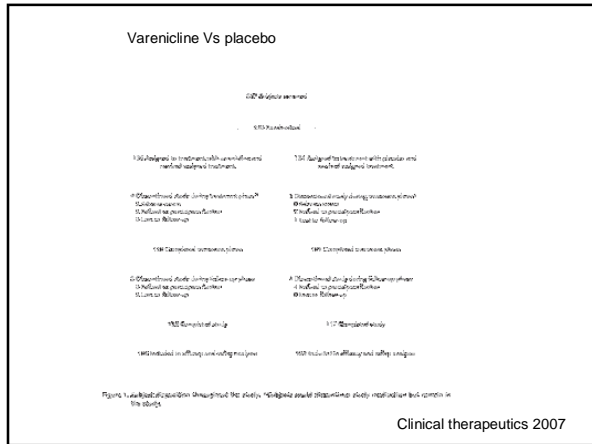
Figure 2. Odds ratio (OR) for continuous abstinence in the nicotine-dependent group. \*P < 0.05 compared with placebo. OR = odds ratio for each treatment group compared with the placebo group.

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Treatment	Weeks 9-12		P	Weeks 9-24		P	Weeks 9-52		OR (95% CI)	P
	n/N (%)	OR (95% CI)		n/N (%)	OR (95% CI)		n/N (%)	OR (95% CI)		
Varenicline 0.25 mg BID	70/128 (54.7)	1.88 (1.14-3.10)	0.013	43/128 (33.6)	1.22 (0.71-2.09)	0.464	35/128 (27.3)	1.25 (0.70-2.23)	0.446	
Varenicline 0.5 mg BID	71/128 (55.5)	1.94 (1.17-3.22)	0.01	43/128 (33.6)	1.35 (0.78-2.27)	0.288	37/128 (28.9)	1.38 (0.78-2.46)	0.265	
Varenicline 1.0 mg BID	83/130 (63.8)	2.98 (1.78-4.96)	<0.001	46/130 (35.4)	1.47 (0.87-2.50)	0.149	41/130 (31.5)	1.81 (1.04-3.17)	0.036	
Placebo	51/129 (39.5)	-	-	36/129 (27.9)	-	-	30/129 (23.3)	-	-	-

n = number considered abstinent; N = number of evaluable subjects; OR = odds ratio for each treatment group compared with the placebo group.

Clinical therapeutics 2007



## Adverse Events

Table 1. Varenicline vs. Compared with Placebo.<sup>a</sup>

Variable	Varenicline	Placebo
	% of subjects	
Adverse effect		
Nausea	35.8	11.2
Insomnia	22.0	12.7
Abnormal dreams	14.6	5.0
Headache	16.8	14.3
Other gastrointestinal effects <sup>b</sup>	22.5	11.8
Discontinuation of study drug due to treatment-related adverse event	12.0	8.1

NEJM 2008

## From FDA

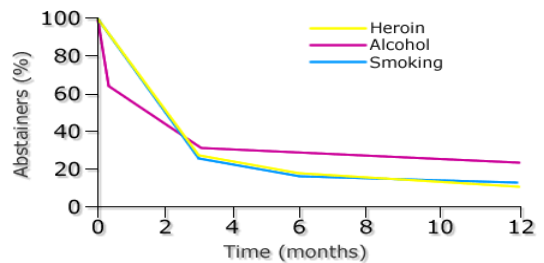
May 16 2008

- Patients should tell their health care provider about any history of psychiatric illness prior to starting Chantix.
- Health care professionals, patients, patients' families, and caregivers should be alert to and monitor for changes in mood and behavior in patients treated with Chantix.
- Patients should immediately report changes in mood and behavior to their doctor.
- Vivid, unusual, or strange dreams may occur while taking Chantix.
- Patients taking Chantix may experience impairment of the ability to drive or operate heavy machinery.

## NICE guidance (National Institute for Health and Clinical Excellence )

- varenicline is superior to NRT and bupropion in achieving continuous abstinence,
- likely to be a cost-effective use of NHS resources

## Nicotine Addiction: A Chronic Relapsing Medical Condition



- More than half of abusers relapsed within 3 months and a majority relapsed within 6 months following treatment

Hunt et al. J Clin Psychol.1971;27:455-456.

Multiple Quit Attempts May Be Necessary!

## Relapse Prevention and Treatment

- **Enhancement of motivation is important for relapse prevention**
- **Training of smokers in copying skills is necessary**
- **Smoking Cessation Programs with regular Follow-up**

## WHO recommendation

- A **public health approach** that seeks to **change the social climate** and promote a supportive environment
- A **health systems approach** that focuses on promoting and integrating clinical best practices (**behavioral and pharmacological**) which help tobacco-dependent consumers increase their chance of quitting successfully;
- A **surveillance, research and information approach** that promotes the **exchange of information and knowledge** so as to increase awareness of the need to change social norms

## Conclusion

Chronic smoking is a disease  
Smokers are patients



There are effective treatment



**You Can Help!**