

# **The essentials of smoking cessation**

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GP and GPSI in Smoking Cessation  
Wandsworth, London

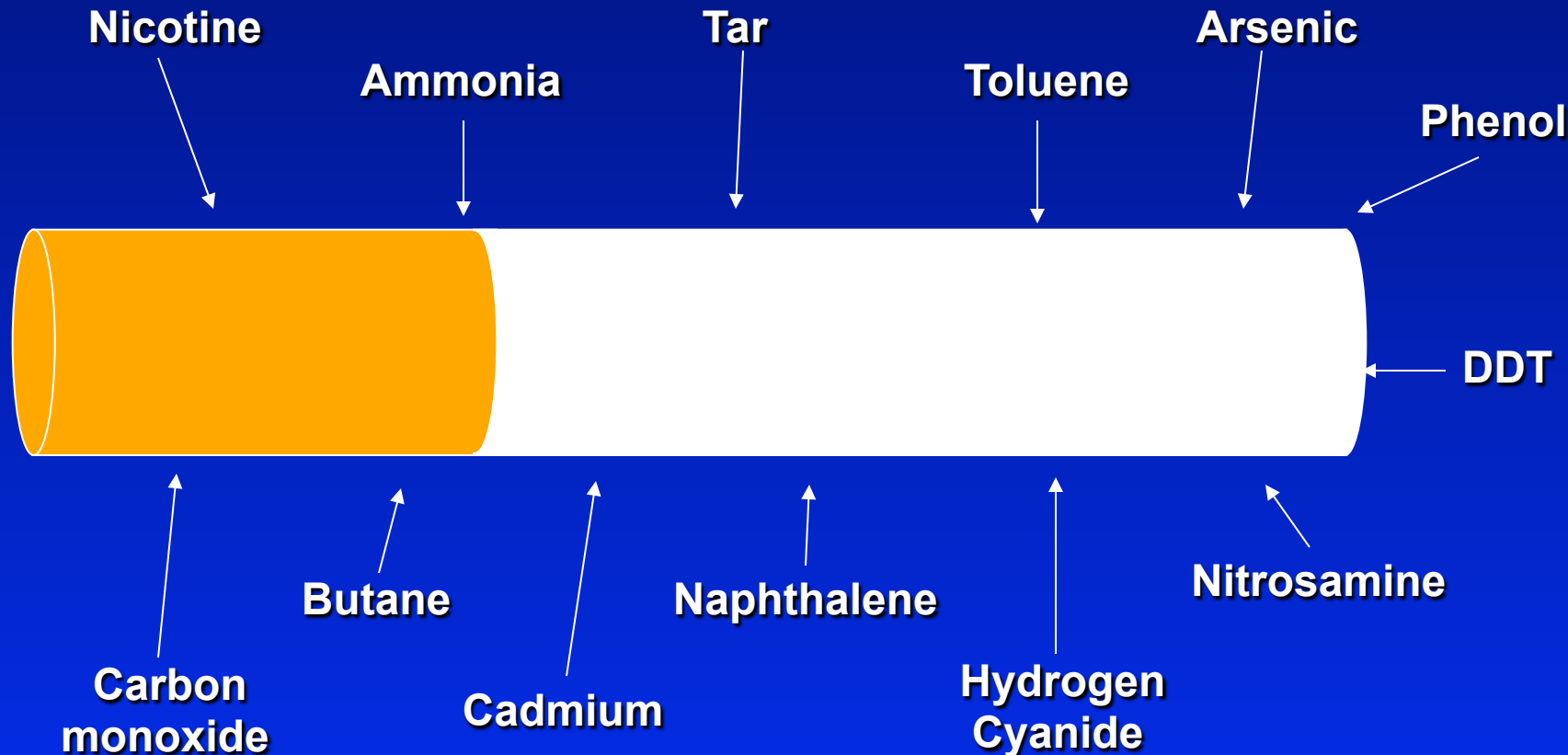
# Smoking: the size of the problem

- Smoking is the largest preventable cause of disease and premature death in the world<sup>1</sup>
- More than 50% of long-term smokers die prematurely due to smoking-related diseases<sup>2</sup>

1. WHO Report on the Global Tobacco Epidemic: the MPOWER package. Geneva, World Health Organization, 2008

2. Doll R, et al. Br Med J 2004;328:1519–27

# What's in a cigarette?



*Cigarette smoke contains more than 4,000 chemicals, including over 60 known carcinogens and metabolic poisons*

# Mortality and Smoking: English doctors in 50-years

## Age-standardised Mortality Rate per 1000 men/year

Cause of death	Never Smoked	Former Smoker	Current Smoker	No of deaths 1951-2001
Ischaemic heart disease	<b>6.19</b>	<b>7.61</b>	<b>10.01</b>	7628
Cerebrovascular disease	<b>2.75</b>	<b>3.18</b>	<b>4.32</b>	3307
Other vascular disease	<b>2.28</b>	<b>2.83</b>	<b>4.15</b>	3052
Other medical conditions	<b>2.26</b>	<b>2.47</b>	<b>3.49</b>	2565
COPD	<b>0.11</b>	<b>0.64</b>	<b>1.56</b>	640
Other respiratory disease	<b>1.27</b>	<b>1.70</b>	<b>2.39</b>	1701
Lung cancer	<b>0.17</b>	<b>0.68</b>	<b>2.49</b>	1052
Cancers of mouth, pharynx, larynx, oesoph.	<b>0.09</b>	<b>0.26</b>	<b>0.60</b>	340
All other neoplasms	<b>3.34</b>	<b>3.72</b>	<b>4.69</b>	3893
External cause	<b>0.71</b>	<b>0.75</b>	<b>1.13</b>	891
All diseases	<b>19.38</b>	<b>24.15</b>	<b>35.40</b>	25 346



# Top 5 causes of death: how many due to smoking (England 2011)

	Total number of deaths	% caused by smoking	Number caused by smoking
Ischaemic heart disease	65,128	14%	9,400
Stroke	40,374	8%	3,400
Cancer of Lung, Bronchus +Trachea	28,044	82%	23,100
Pneumonia	23,565	19%	4,500
COPD	22,346	80%	17,800
<b>TOTAL</b>	<b>179,457</b>	<b>32%</b>	<b>58,200</b>

# **Smoking cessation: primary prevention of CHD**

Positive short- and long-term clinical outcomes<sup>1</sup>

**1 year**

**Excess risk of CHD falls by half  
compared with continuing  
smokers**

**15 years**

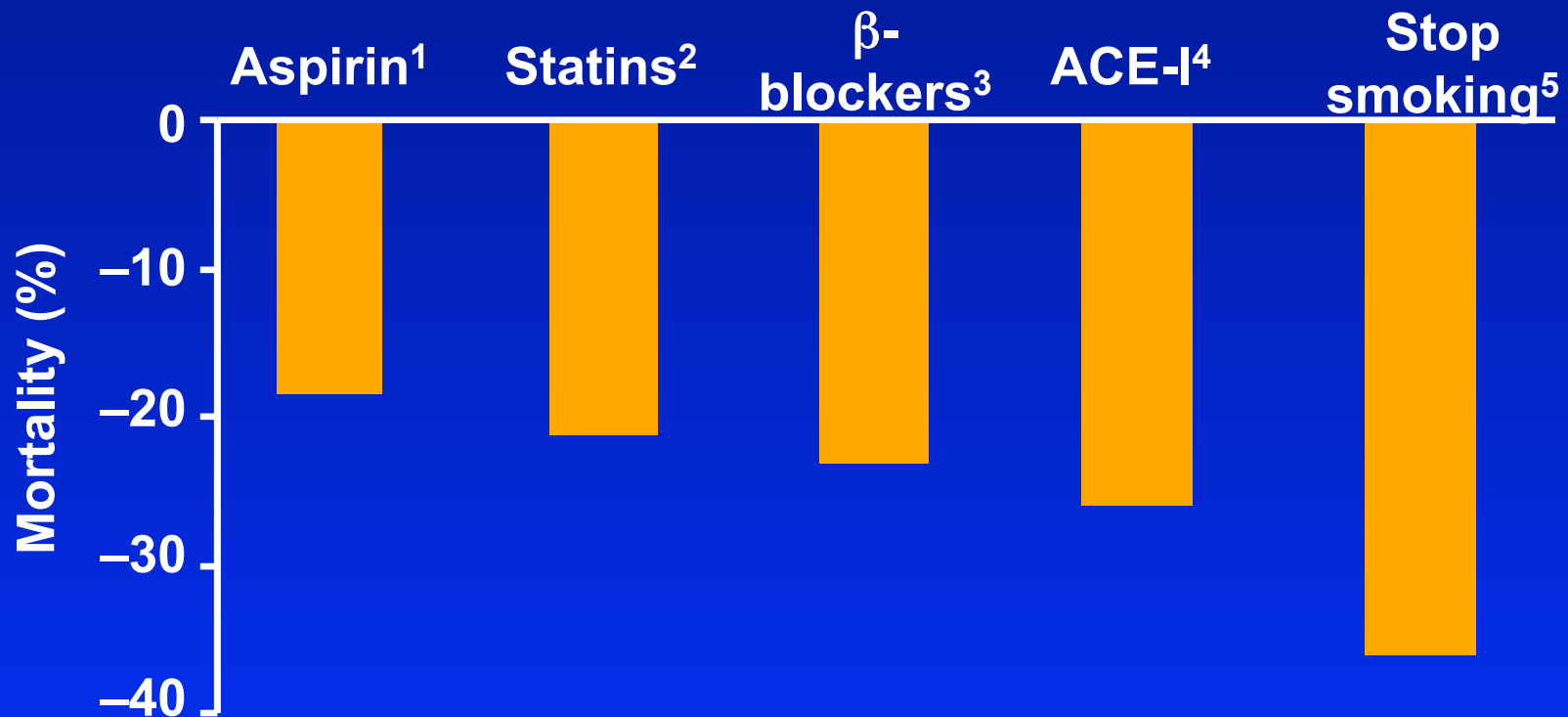
**Risk of CHD is the same as  
someone who never smoked**

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CHD = coronary heart disease

# Smoking cessation: secondary prevention of CHD

Impact of treatment on mortality of patients with coronary artery disease

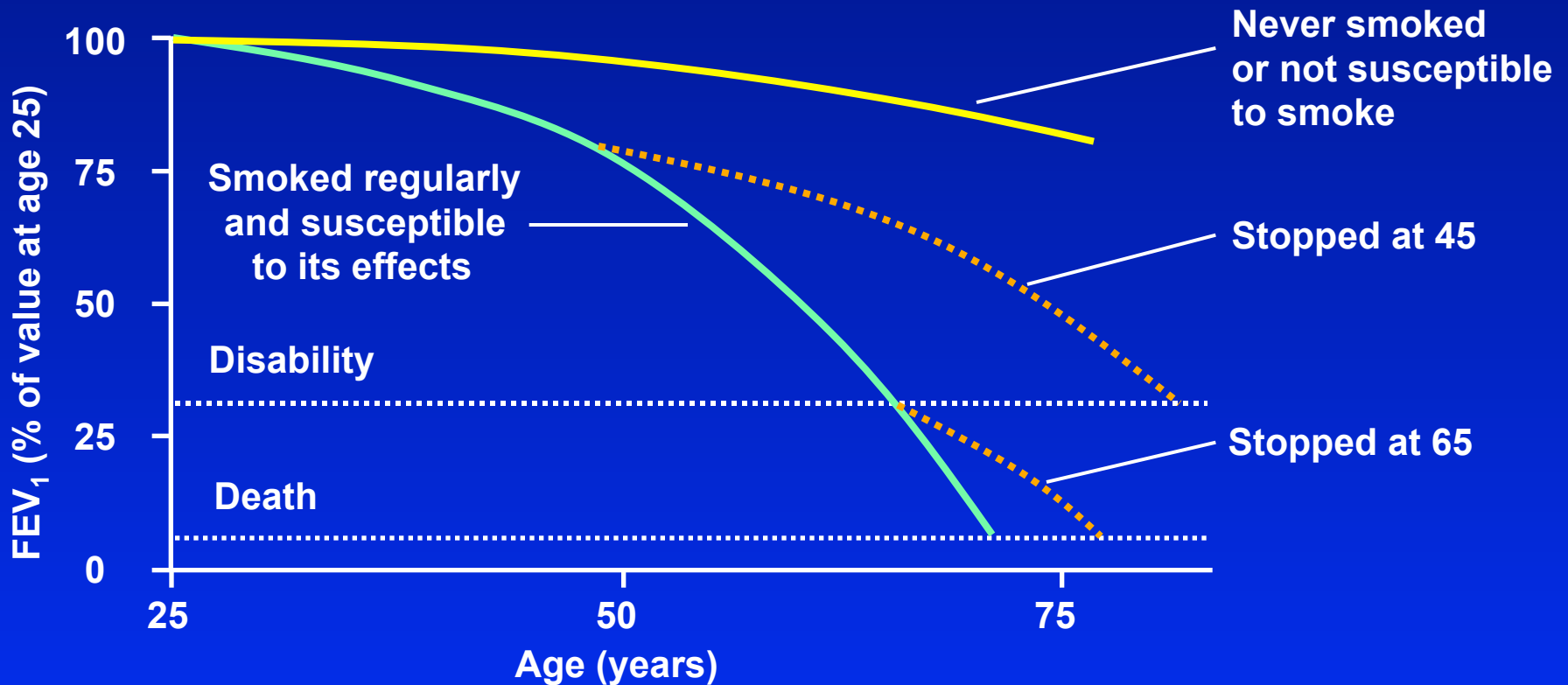


1. Weisman SM, et al. Arch Intern Med 2002;162:2197–202; 2. LaRosa JC, et al. JAMA 1999;282:2340–6

3. Freemantle N, et al. BMJ 1999;318:1730–7; 4. Flather MD, et al. Lancet 2000;355:1575–81

5. Critchley JA and Capewell S. JAMA 2003;290:86–7

# Effect of smoking cessation in COPD



# Stopping smoking and risk for lung cancer death



**Why do people keep smoking?**

# **NICOTINE ADDICTION**

**HABIT**

**BOREDOM**

**STRESS**

**SOCIAL**

**WEIGHT CONTROL**

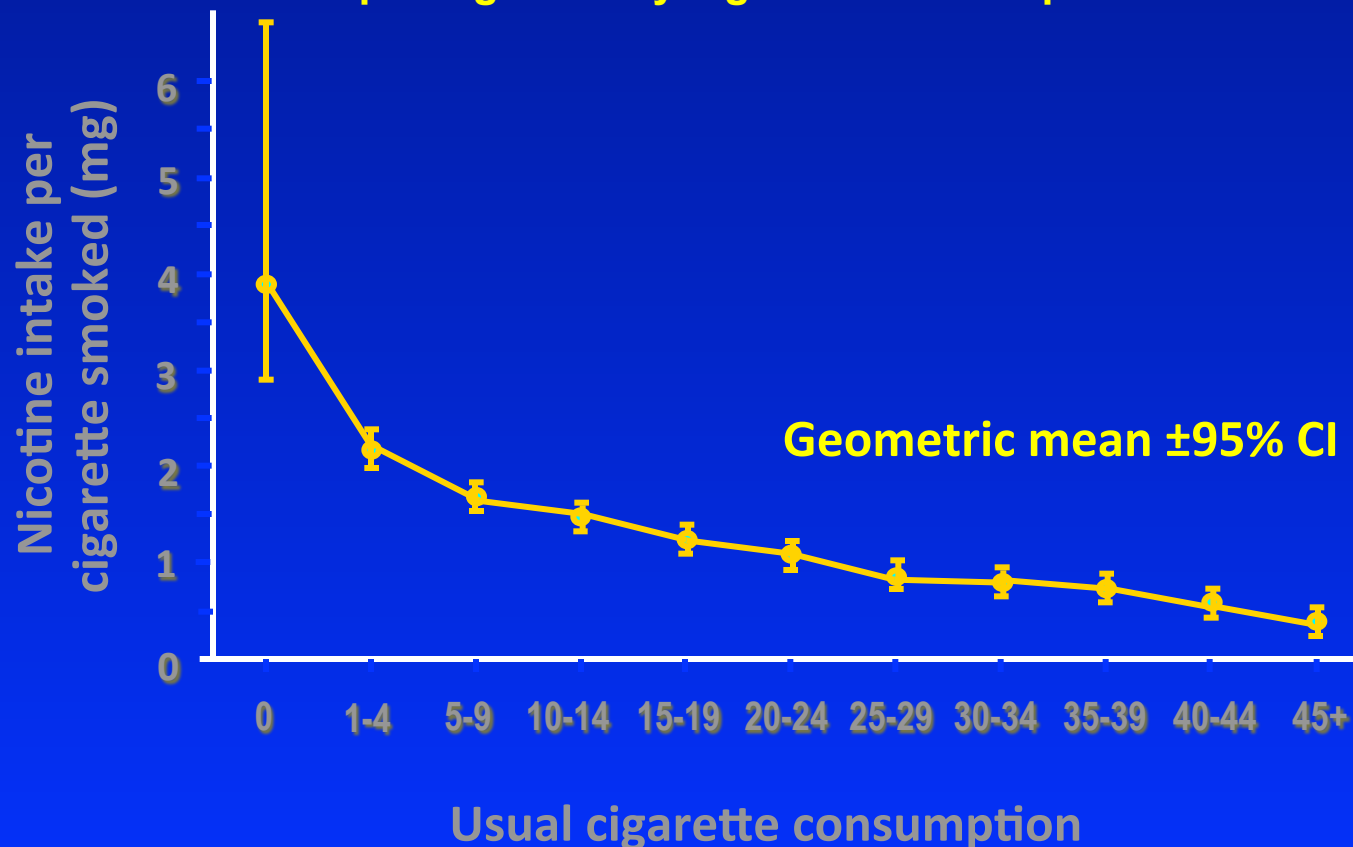
**TASTE**

# **The power of nicotine addiction**

- **60% smoke again post MI (40% within 2 days)**
- **50% smoke again post laryngectomy**
- **50% smoke again post pneumonectomy**
- **80% of women do not stop smoking during pregnancy**

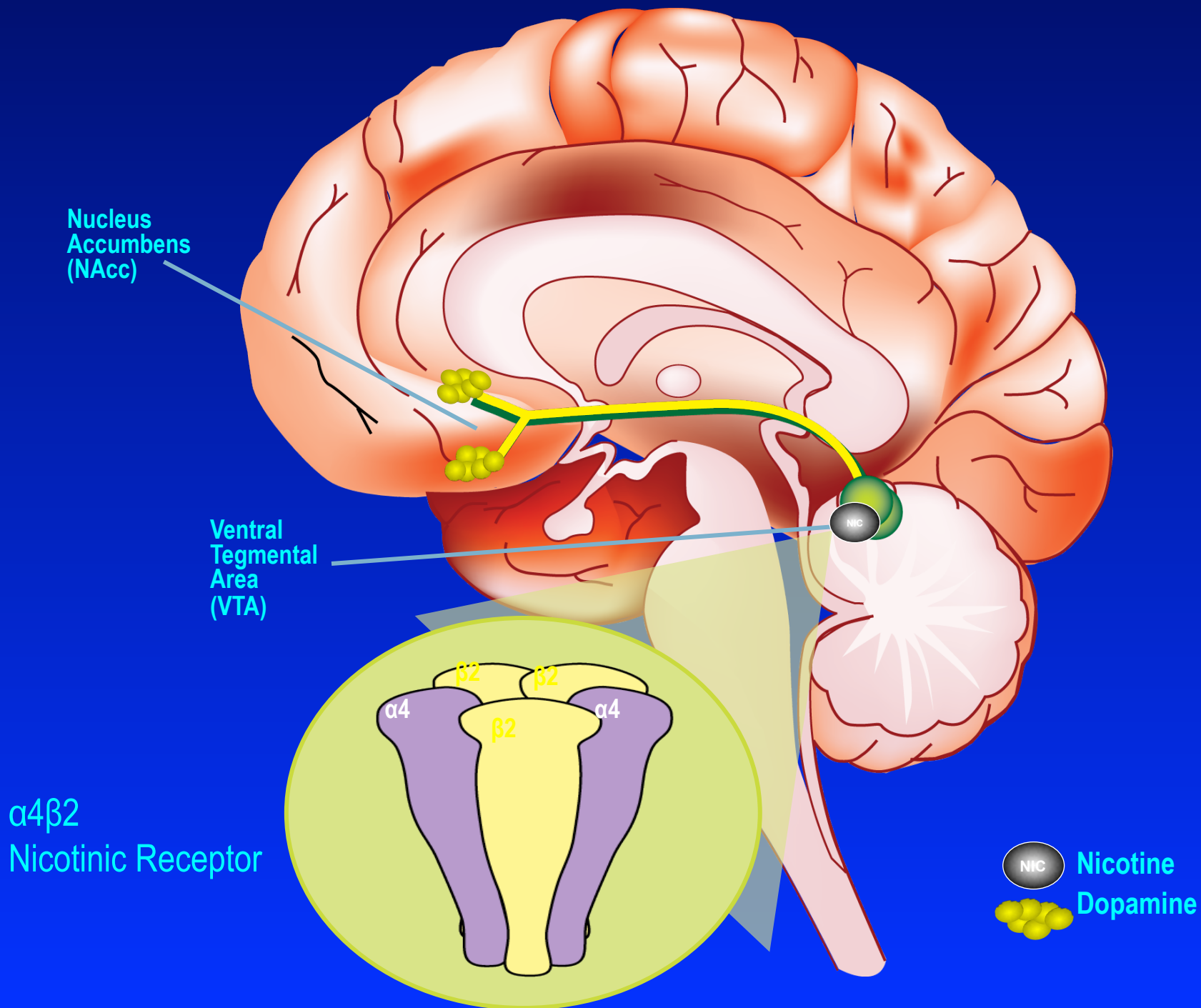
# Cigarette Consumption and Nicotine Intake: Do Light or Occasional Smokers Take in Less Per Cigarette?

Nicotine intake per cigarette by cigarette consumption: HSE 1998-2004





# **Mechanics of nicotine addiction**



**The dopamine triggered by  
inhaled nicotine rapidly gets  
reabsorbed which leads to.....**

**low mood and craving  
which leads to.....**

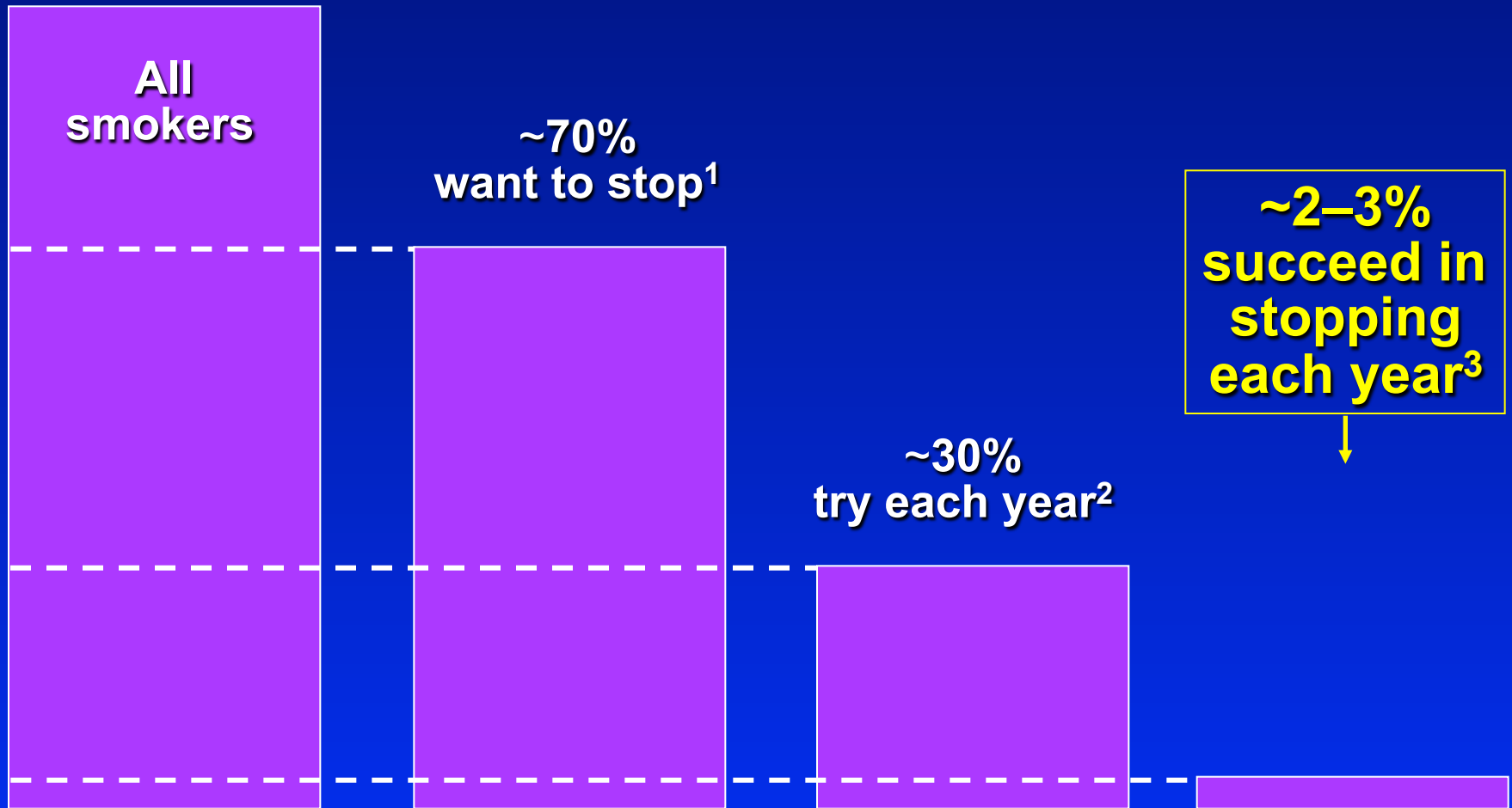
**Regular smoking leads to a  
300%+ increase in brain  
nicotine receptors**

“For most smokers, smoking is a chronic relapsing organic brain disease and not a lifestyle choice.”

# On stopping smoking:

- It takes 24-48 hours for nicotine to leave the body
- It takes 8-12 weeks for the nicotine receptors to down-regulate

# Smokers want to stop



# **Stopping smoking: What works, what doesn't**



# 3 Keys to stopping successfully:

- Wanting to stop smoking

But for 97% of smokers wanting to stop is not enough, they need:

- Good quality support
- Evidence based treatments

# Long term cessation rates

	No Pharmacotherapy	Pharmacotherapy (eg NRT)
Willpower alone	2-3%	4-6%
Support (trained adviser)	10-15%	20-30%

# Proven smoking cessation interventions

- Brief advice from a healthcare professional
- Behavioural support
- Pharmacotherapy
  - Nicotine Replacement Therapy
  - Bupropion (Zyban)
  - Varenicline (Champix)

# Giving advice to smokers

Smoking advice from a healthcare professional (HCP), especially a GP, can be one of the most important triggers for a quit attempt

# How advice is given currently?

- Either badly or not at all
- Why:
  - Lack of time
  - HCP feels it is ineffective
  - Lack of knowledge or training

**What is the most common advice  
which GPs make to smokers?**

**Advice to stop smoking**

# Advice to stop v No Advice

- When seeing their GP a similar % try to quit with:
  - advice to stop
  - mention of smoking (with no advice to stop)
  - no mention of smoking!

# Problems with “advice to stop”

- Negative message
- Nagging
- Nothing new
- Encourages conflict and denial
- Frustrating for both doctor and smoker
- Takes longer
- Puts you off doing it again



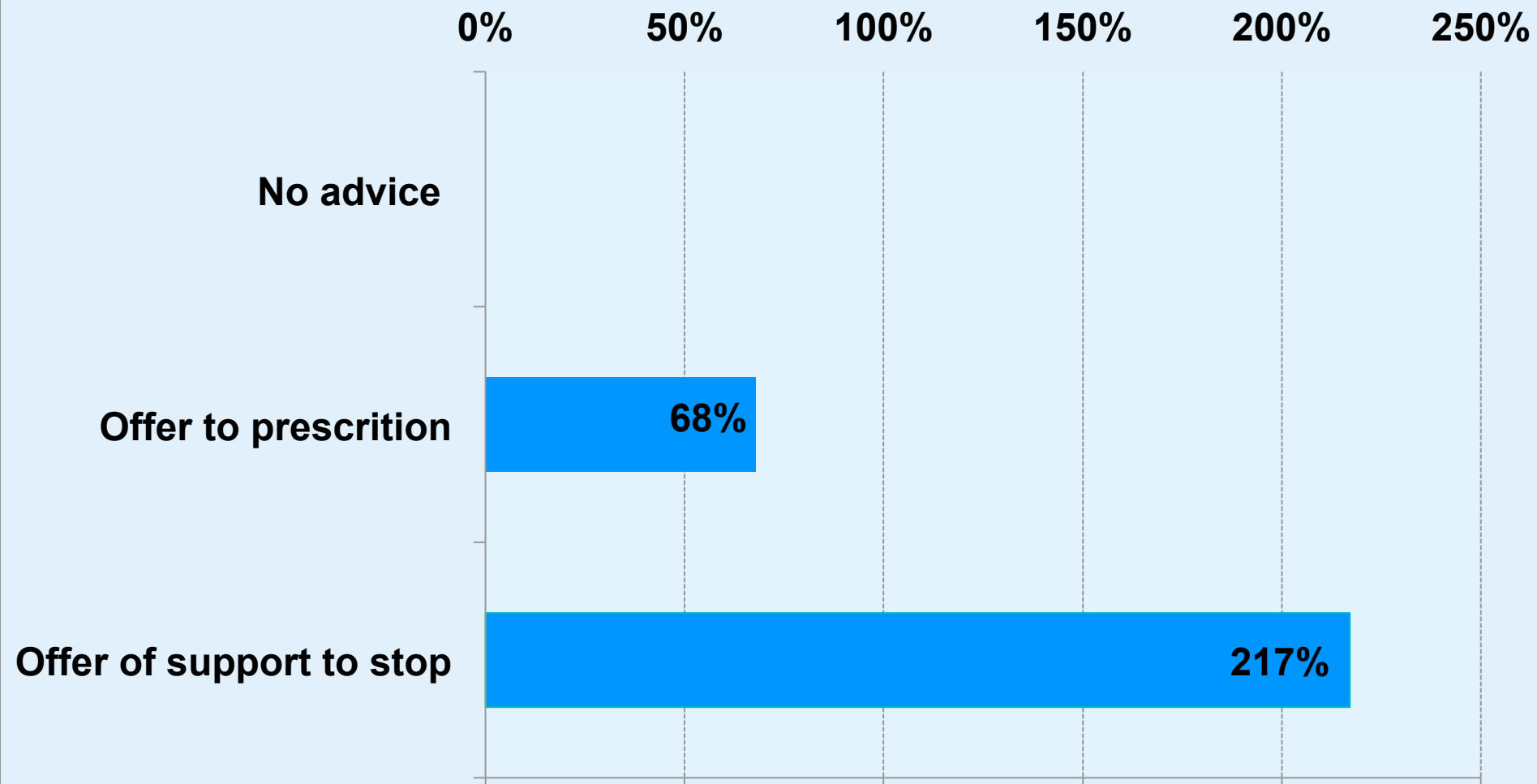
**Ideas for a better form of advice?**

**Advice HOW to stop smoking**

# Long-term cessation rates

	No Pharmacotherapy	Pharmacotherapy
Willpower alone	2-3% (46% of attempts <sup>1</sup> )	4-6% (49% of attempts <sup>1</sup> )
Support (trained adviser)	10-15%	20-30% (4% of attempts <sup>1</sup> )

## Increase in chances of stopping compared with no advice



# Concept of Very Brief Advice (VBA) for smokers

- 1 Establish and record smoking status (QOF)
- 2 Advise how to stop “the best way is with support and treatment”
- 3 Offer support and treatment (QOF 2012/13)

# VBA DELIBERATELY DOES NOT:

- advise smokers to stop
- ask how much or what they smoke
- even ask if they want to stop

# Benefits of very brief advice (VBA):

- Brief! (<30 seconds or it won't be used)
- Records smoking status (future VBA as 70%+ relapse)
- Opportunistic (suitable for almost any consultation)
- Positive (or you put them off trying)
- Not confrontational or nagging (not telling them to stop)
- Informative (saying how to stop)
- Engaging (new information)
- Evidence based
- Satisfies QOF
- NOT a smoking cessation consult (that's for next time)
- Very simple: **MINIMUM EFFORT, MAXIMUM REWARD**

# **Module on VBA:**

BMJ Learning website  
search “VBA”

or [www.ncsct.co.uk/VBA](http://www.ncsct.co.uk/VBA)

# **Keys to good quality stop smoking service in a General Practice :**

- The advisor
- The consultations



# Keys to a successful advisor

- Willing
  - Available
  - Flexible
  - Empathetic
  - Skilled listener and communicator
  - Positive
  - Motivational
  - Realistic
  - Knowledge of smoking cessation
  - Cost effective
- 
- ie. should be carefully selected, not just delegated

# Keys to successful consultations

- Smoker owns the attempt
- Choice of support and treatment options
- Systems to make treatments easy to obtain
- Same advisor throughout
- Not telling smoker to stop but how to stop
- Routine use of CO monitoring
- Expect and normalise failure
- Enough time
- Good record keeping (Targets!)

# E-Cigarettes Summary

- Not tested or licensed for smoking cessation
- Safety and efficacy in delivering nicotine not known
- Unregulated so great variability
- Likely to be much safer than cigarettes
- Unlikely to cause risk from passive smoking
- May be as addictive
- MHRA – 2016 some will be licensed as medicines
- Until then none can be recommended

# Pharmacotherapy for nicotine dependence

- Nicotine Replacement Therapy (NRT)
- Bupropion (Zyban)
- Varenicline (Champix)

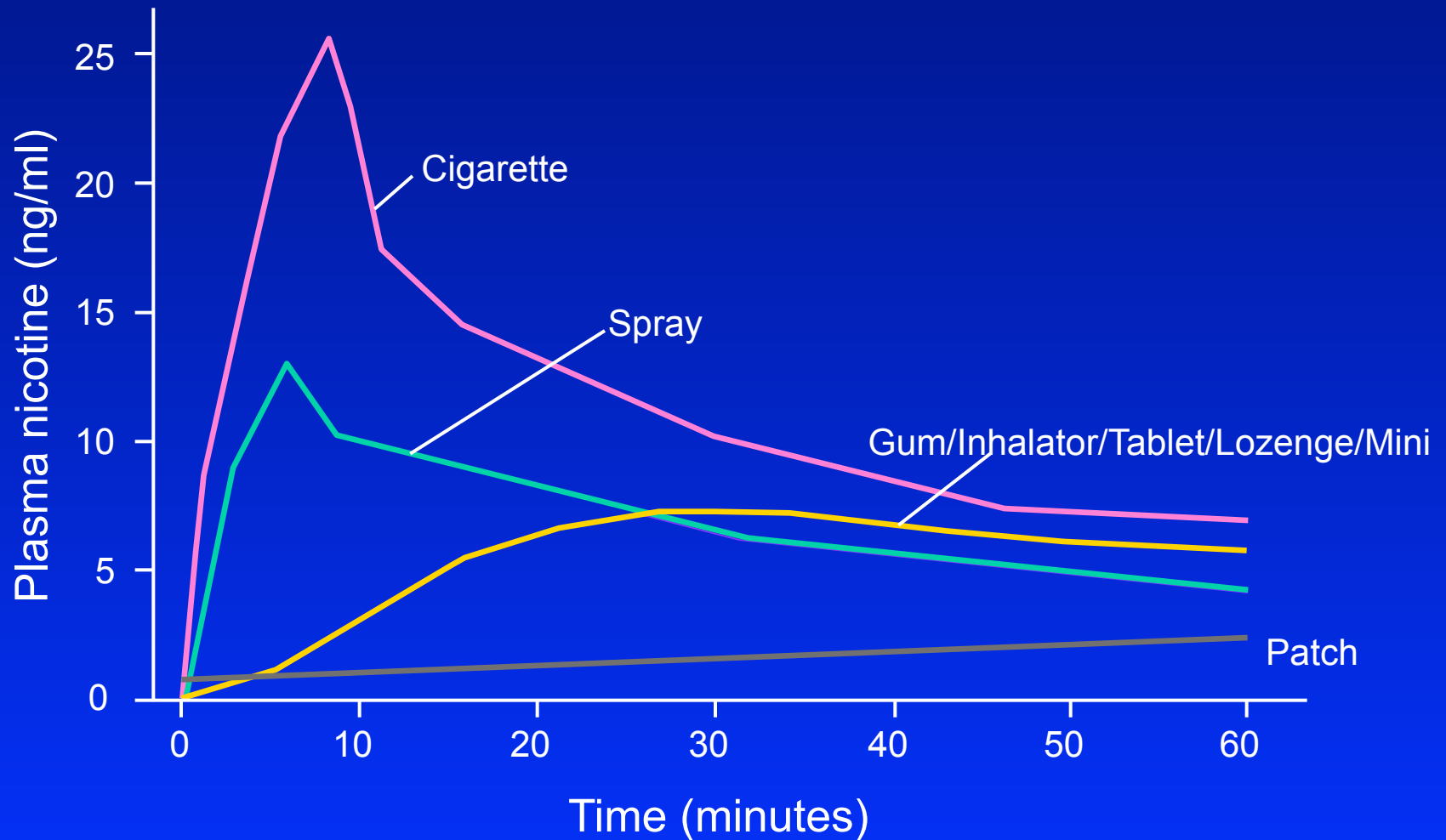
# Nicotine replacement therapy

- Available in nine different forms
- Based on nicotine weaning<sup>1</sup>
- Significantly reduces withdrawal symptoms and cravings vs placebo<sup>2</sup>
- Significantly increases smoking cessation rate vs placebo (odds ratio = 1.77)<sup>3</sup>
- Treatment lasts 8–12 weeks with gradual withdrawal

# NRT- Use and dosage

● Patch	16 or 24 hours	Variety, all of 3 strengths
● S/L tabs	upto 40/day	2mg
● Mini lozs	upto 15/day	4mg
● Lozenges	min 9 max 15/day	2mg or 4mg
● Gum	upto 15 or 25/day	2mg or 4mg
● Inhalator	6-12 cartridges/day	10mg
● Oral Spray	upto 64 sprays/day	1mg
● Nasal Spray	upto 64 sprays/day	1mg

# Plasma nicotine levels – contrast between cigarettes and NRT



# Newer uses of NRT

- Combining patch and an acute NRT product (e.g. inhalator) improves efficacy <sup>1</sup>
- Starting NRT 2-4 weeks pre-quit date doubles the odds of quitting <sup>1</sup>
- NRT to aid reduction increases the rate of attempts to stop and long-term abstinence rates <sup>2</sup>

<sup>1</sup> Stead, L.F., et al., *Nicotine replacement therapy for smoking cessation*. Cochrane Database Syst Rev, 2008(1): p. CD000146.

<sup>2</sup> Moore, D., et al., *Effectiveness and safety of nicotine replacement therapy assisted reduction to stop smoking: systematic review and meta-analysis*. Bmj, 2009. 338: p. b1024.



# Considerations for patients using NRT

- **USE ENOUGH!**  
Avoid under-dosing and irregular use.
- **LONG ENOUGH!**  
Don't stop early, continue 8-12 weeks.
- **NOT A PUFF!**  
Slower and less efficient source of nicotine than cigarettes so can not compete.

# Bupropion SR

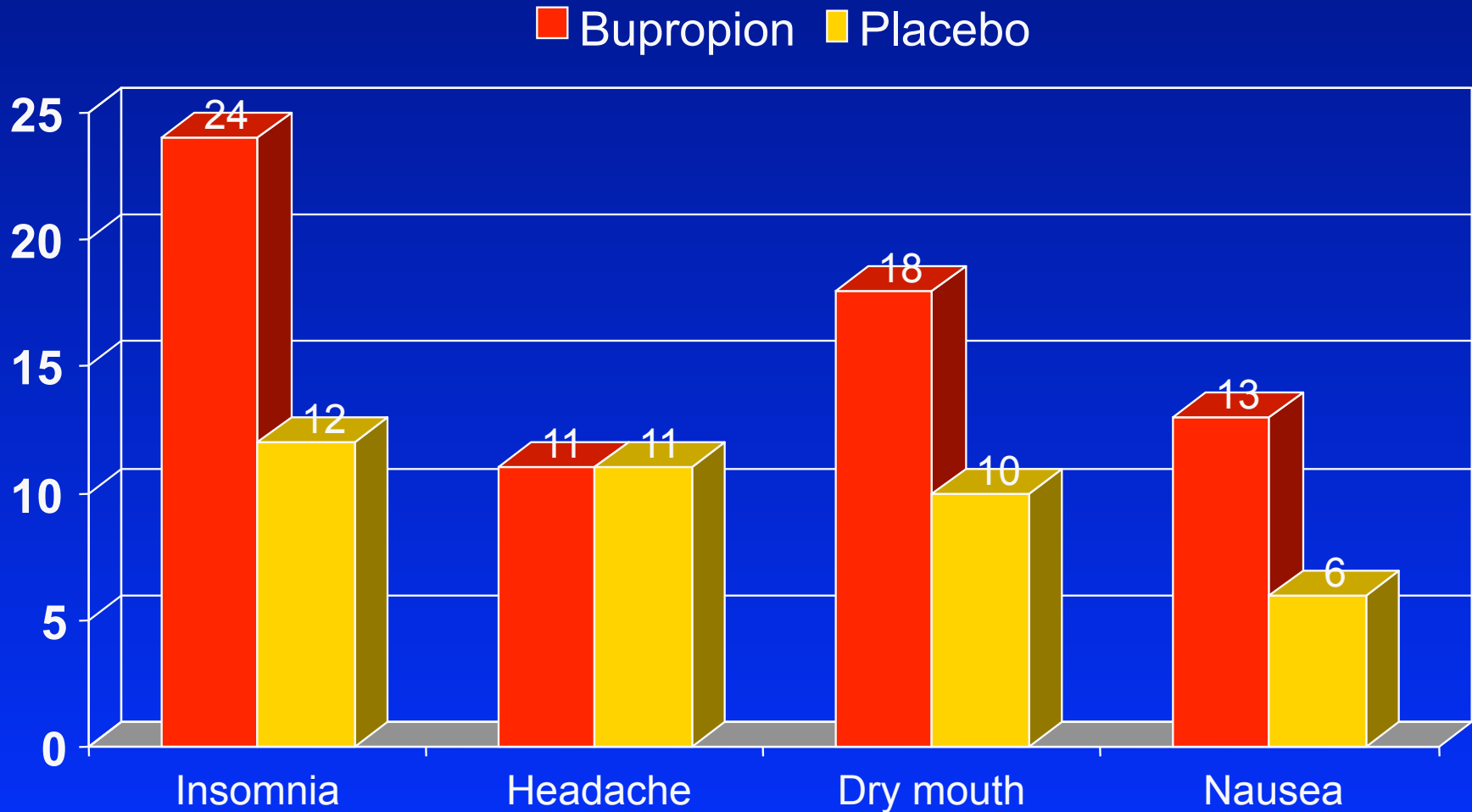
- Non-nicotine prescription tablet originally developed to treat depression<sup>1</sup>
- Modifies dopamine levels and noradrenergic activity<sup>1</sup>
- Significantly increases smoking cessation rate vs placebo (odds ratio = 1.94)<sup>2</sup>

1.Bupropion (Zyban) prescribing information. Available at [http://us.gsk.com/products/assets/us\\_zyban.pdf](http://us.gsk.com/products/assets/us_zyban.pdf)

2.Hughes et al. Cochrane Database Syst Rev 1996. CD000031

# Adverse events on bupropion

Bupropion in smokers with CVD. McRobbie 2001



Guidance on the use of nicotine replacement therapy (NRT) and bupropion for smoking cessation

This section provides the following information: the lead firm's guidance on the use of a worker replacement survey (WRS) and its applicability to working conditions. The remainder of the document is structured as follows:

- 24. Cite last word used prior to
- 25. The book ending is
- 26. Evidence
- 27. Populations For the 80%
- 28. See first research
- 29. Population of
- 30. Evidence of an increase

Approved At: Approved Committee:

It appeared in the *New York Times* and *Washington*

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More arguments at [good.gri.org.uk](http://good.gri.org.uk)  
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## 1. Guidance

- 1.1 Nicotine replacement therapy (NRT) and bupropion are recommended for smokers who have expressed a desire to quit smoking.
- 1.2 NRT or bupropion should normally only be prescribed as part of a stimulus-contingent treatment (SCT), in which the smoker makes a commitment to stop smoking on or before a particular date (target stop date). Smokers should be offered advice and encouragement to aid their attempt to quit. Ideally, initial prescription of NRT or bupropion should be sufficient to last only until 2 weeks after the target stop date. Normally, this will be after 2 weeks of NRT therapy, and 3-4 weeks for bupropion, to allow for the different methods of administration and mode of action. Second prescriptions should be given only to people who have demonstrated that their quit attempt is continuing on assessment.
- 1.3 It is recommended that smokers who are under the age of 18 years, who are pregnant or breastfeeding, or who have a stable cardiovascular disorder, should discuss the use of NRT with a relevant health-care professional before it is prescribed.
- 1.4 Bupropion is not recommended for smokers under the age of 18 years, as toxicity and efficacy have not been evaluated for this group. Women who are pregnant or breastfeeding should not use bupropion.
- 1.5 If a smoker's attempt to quit is unsuccessful with treatment using either NRT or bupropion, the NHS should normally fund no further attempts within 6 months. However, if external factors interfere with an individual's initial attempt to stop smoking, it may be reasonable to try again sooner.
- 1.6 There is currently insufficient evidence to recommend the use of an NRT and bupropion in combination.
- 1.7 In deciding which of the available therapies to use and in which order they should be prescribed, practitioners should take into account:
  - Intention and motivation to quit, and likelihood of compliance
  - The availability of counselling or support
  - Previous usage of smoking cessation aids
  - Contraindications and potential for adverse effects
  - Personal preference of the smoker

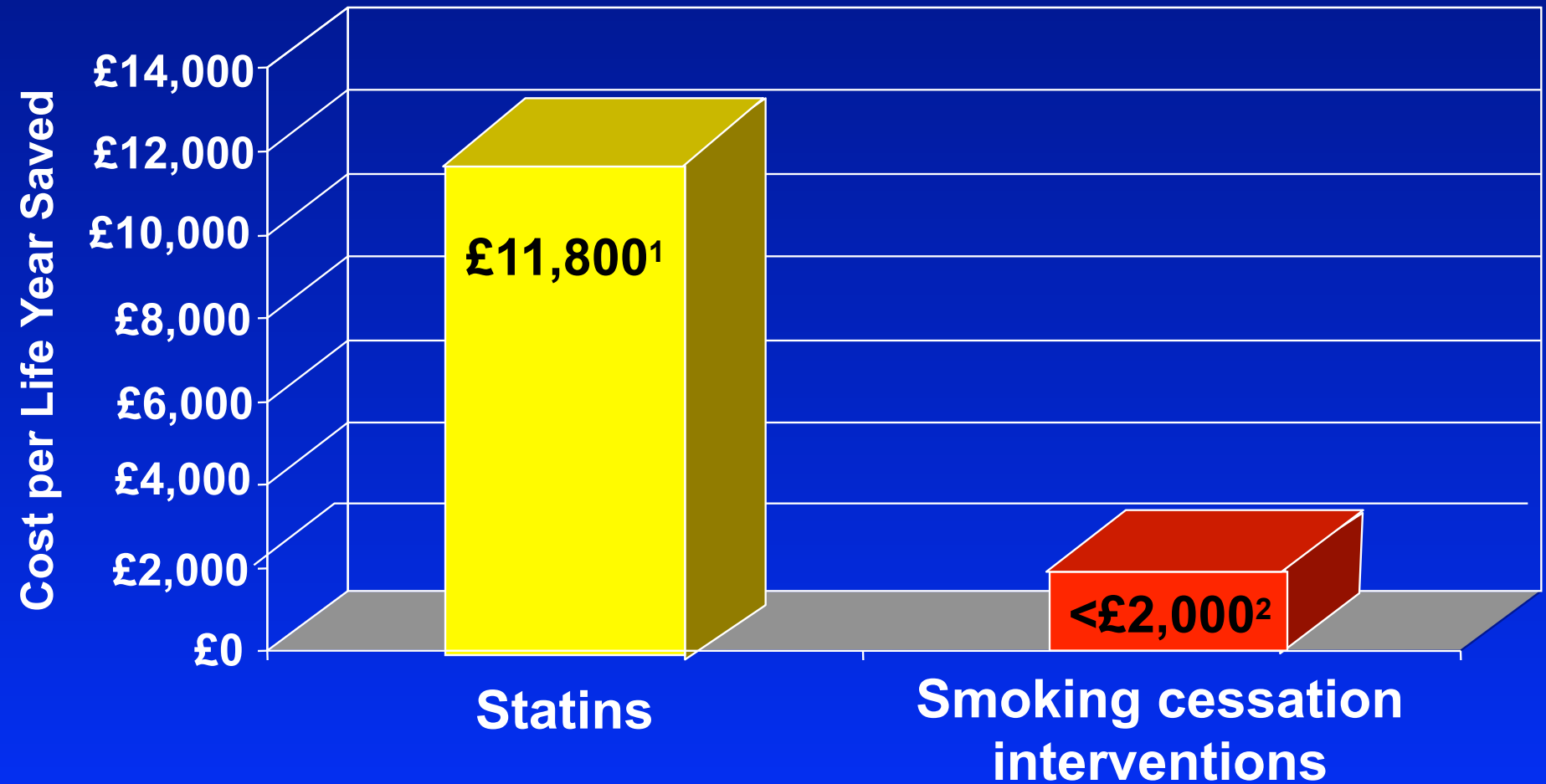
# NICE Guidance on NRT & Bupropion

# April 2002

- “Both bupropion and NRT are considered to be among the most cost effective **of all** healthcare interventions.”
- “Estimates of cost-effectiveness..... are below £2000 per Life Year Gained”

NICE April 2002

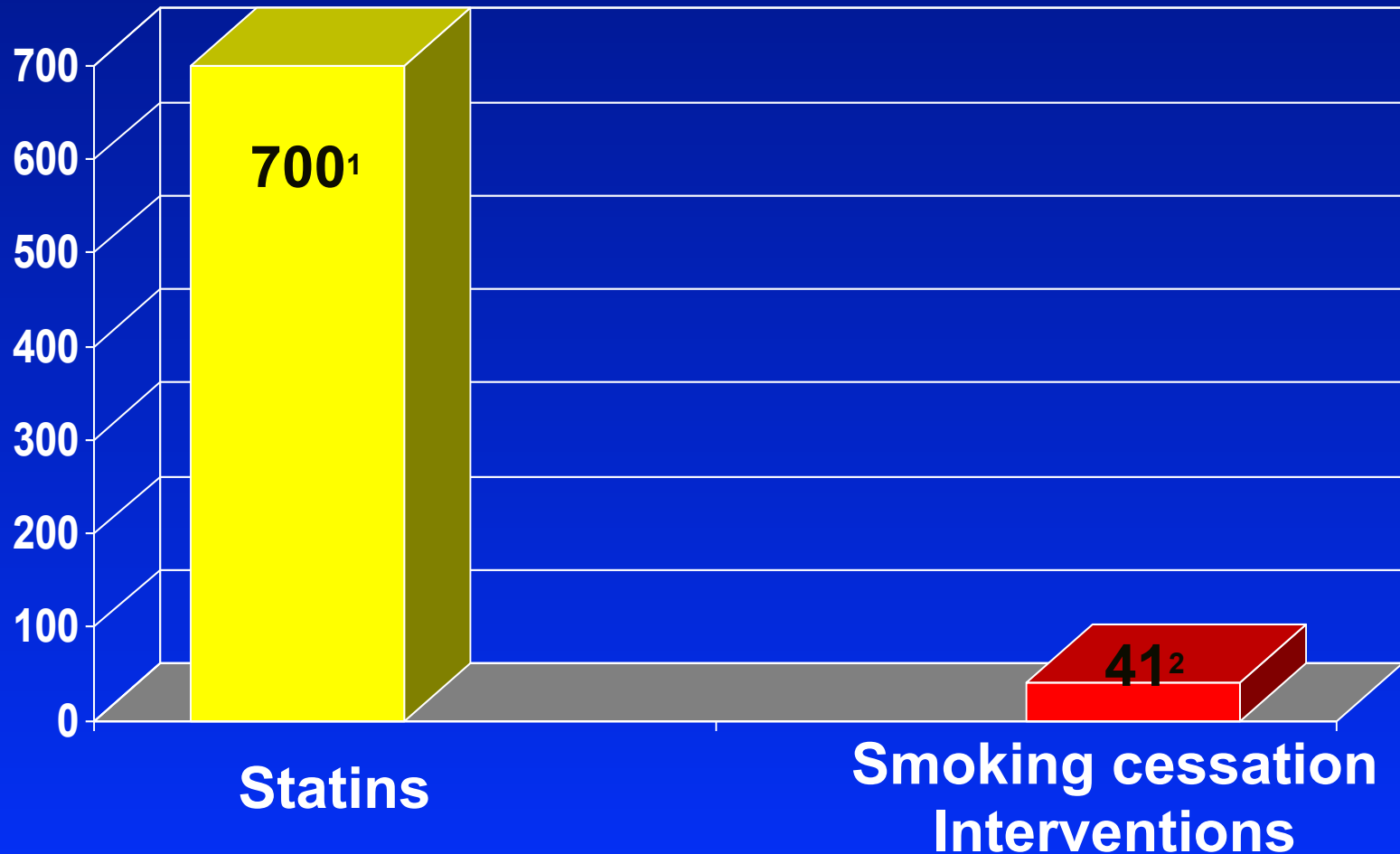
# Cost Per Life Year Gained



1. Raithatha N, Smith RD. BMJ 2004; 328: 400-2.
2. NICE Smoking Cessation Guidance 2002.

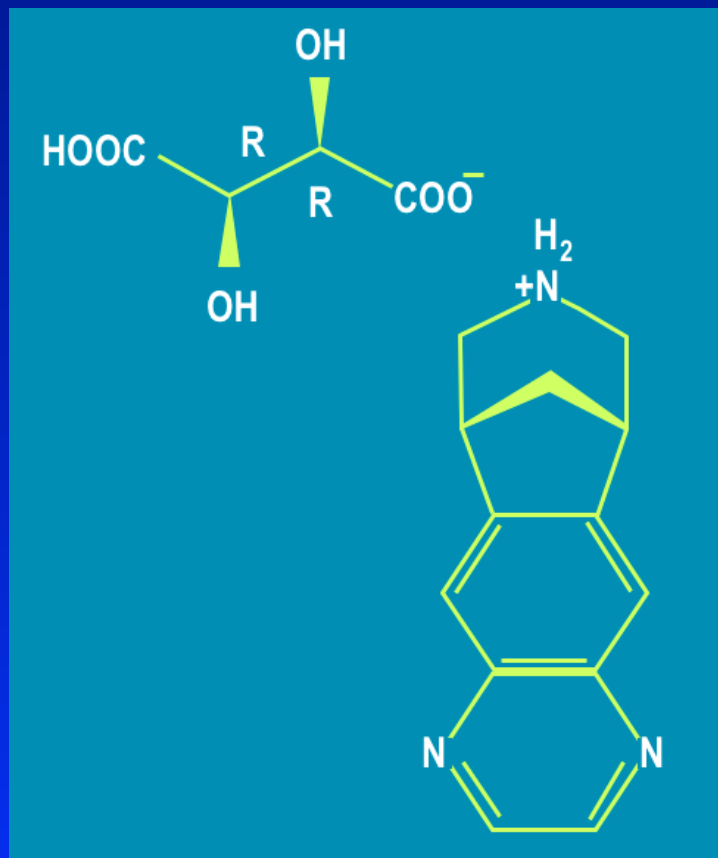
# NHS Annual Expenditure (£millions)

(approx. £ millions expenditure annually)



1. Gibson L. BMJ 2004; 328: 1221.
2. NHS smoking statistics (England), April-Sept 2004.

# Varenicline (Champix)

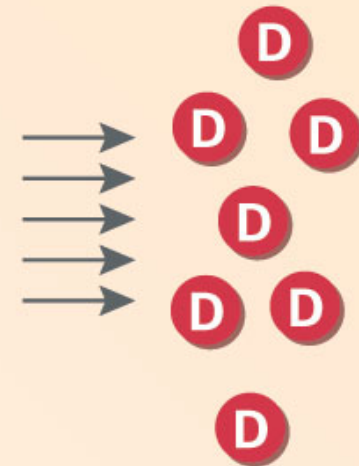
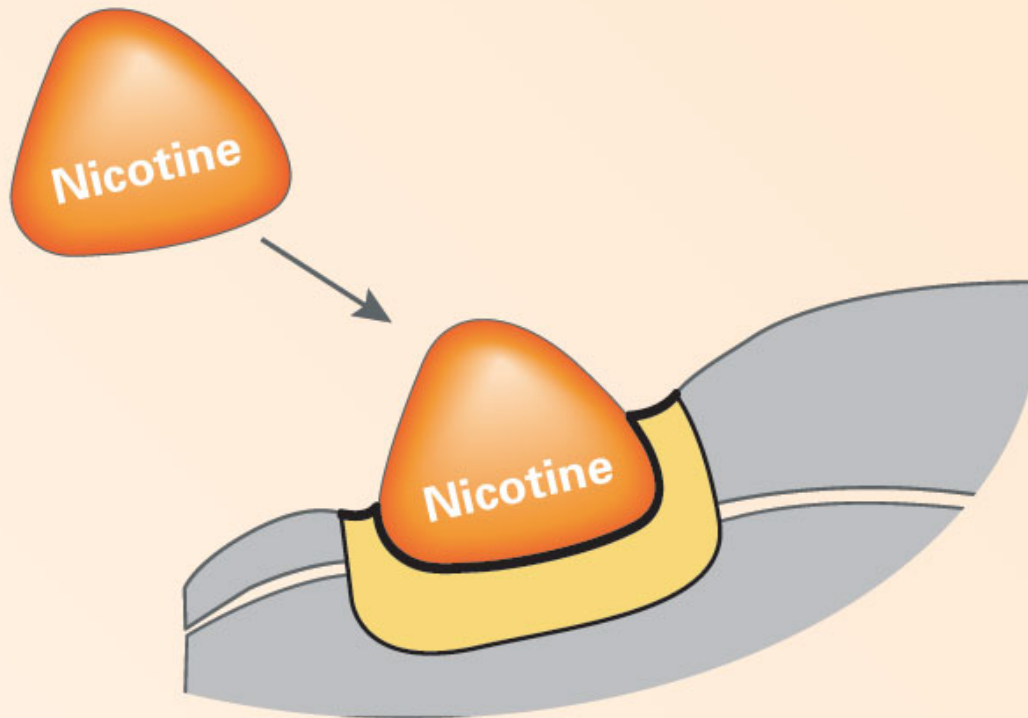


- Specifically designed
- Oral prescription medicine
- Targets the  $\alpha 4 \beta 2$  nicotinic acetylcholine receptor



# Nicotine mode of action

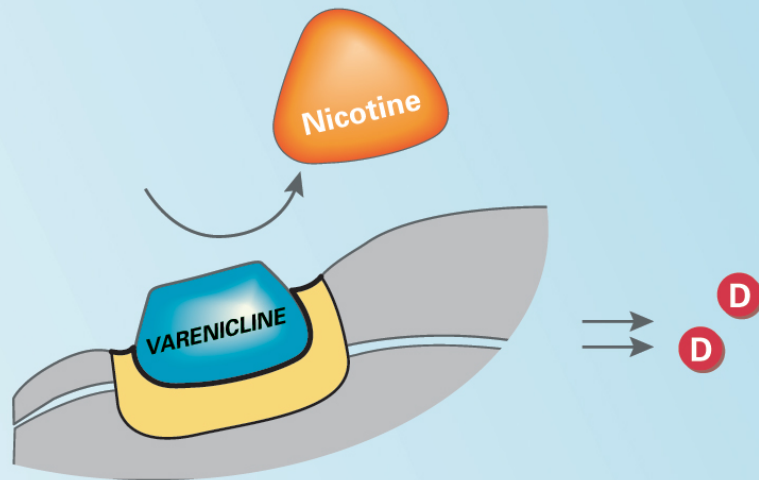
**D** = Dopamine



$\alpha 4 \beta 2$  receptor in the brain

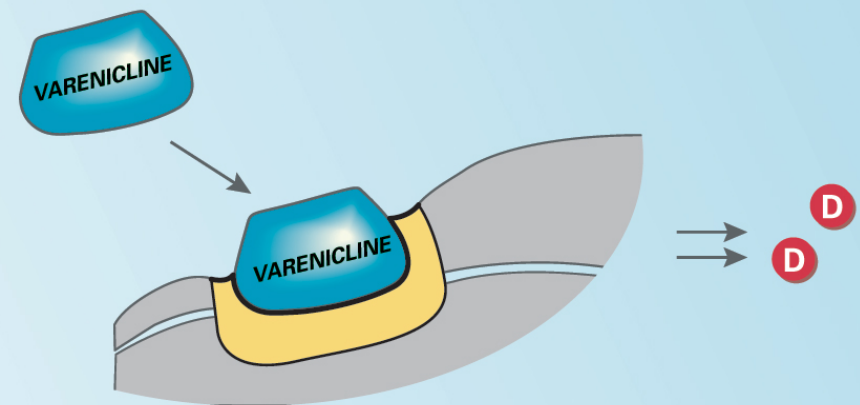
# Varenicline- partial nicotine agonist

## Varenicline with nicotine



$\alpha 4 \beta 2$  receptor in the brain

## Varenicline mode of action



$\alpha 4 \beta 2$  receptor in the brain

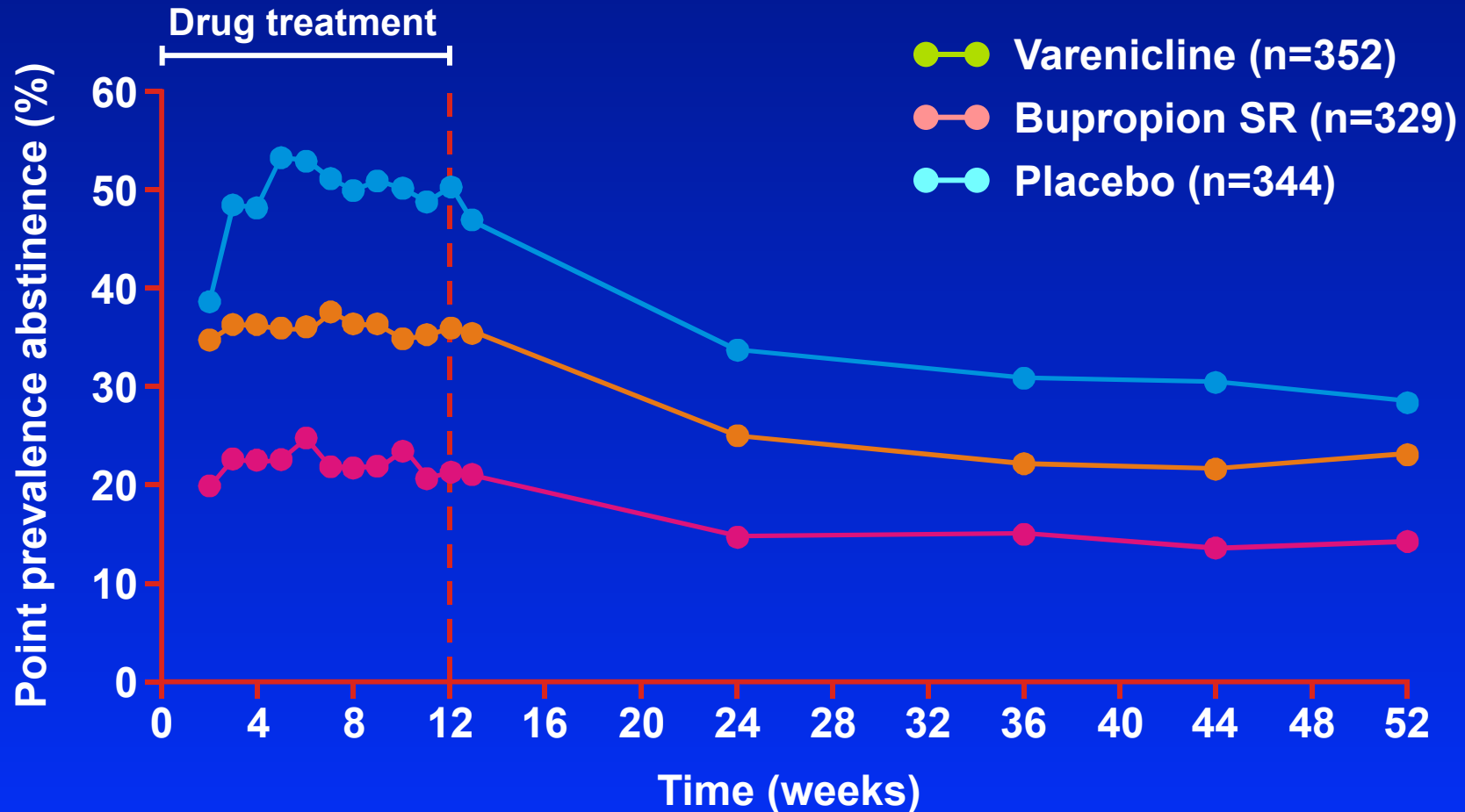
## Part blocking

- Reduces the pleasurable effects of smoking and potentially the risk of full relapse after a temporary lapse<sup>1-4</sup>

## Part Stimulating

- Relieves craving and withdrawal symptoms<sup>1-3</sup>

# 'Recruitment' to abstinence

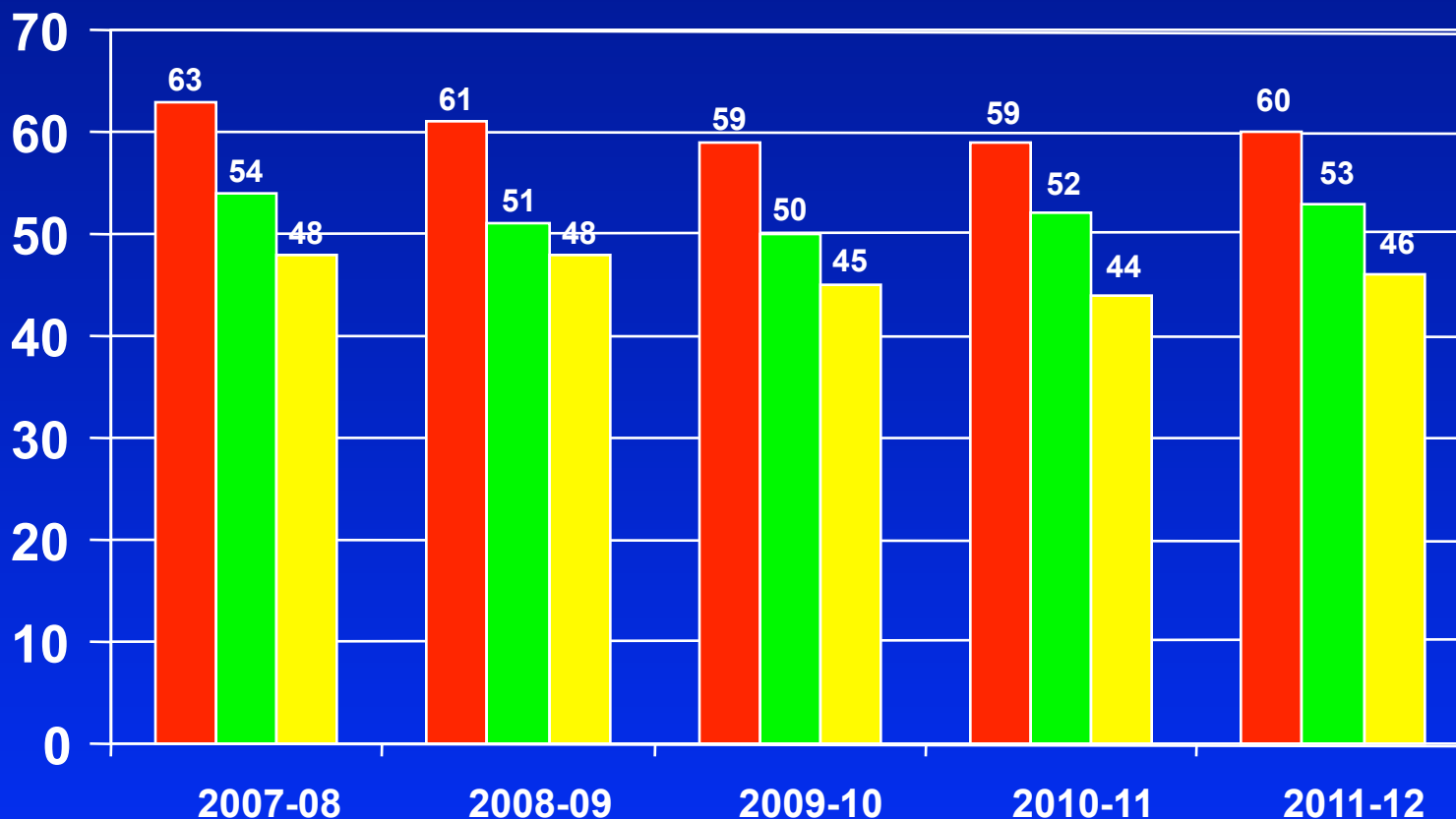


# **The real world!**

2007-2012 English Stop  
Smoking Services Data

# English Stop Smoking Services % 4 week quit rates (DoH)

**Varenicline** **Bupropion** **NRT (Single or Combined)**



Statistics on NHS Stop Smoking Services: England, April to March,  
2008-2009/2009-2010/2010-2011/2011-2012.

# Patient assessment for varenicline:

- INDICATIONS:

- Adults motivated to stop smoking

- CONTRAINDICATIONS:

- End stage renal failure
- Pregnancy
- Under 18
- Allergy

- INTERACTIONS

- No clinically meaningful drug interactions

- CAUTIONS

- Breastfeeding

- History of mental illness


- No specific contraindications
    - Monitor mental state

# Varenicline in patients with diagnosis of major depression

- Greater chance of quitting at end of treatment (35.9%) v placebo (15.6%)
- Difference maintained at a year (20.3%) v (10.4%)
- Improvement in depression and anxiety ratings during treatment was similar to placebo
- Generally well tolerated with common adverse event profile similar to that observed in smokers without psychiatric disorders



# Smoking cessation treatment and risk of depression, suicide, and self harm in the Clinical Practice Research Datalink: prospective cohort study

 OPEN ACCESS

Kyla H Thomas *National Institute for Health Research doctoral fellow*<sup>1</sup>, Richard M Martin *professor of clinical epidemiology*<sup>1</sup>, Neil M Davies *postdoctoral research associate*<sup>2</sup>, Chris Metcalfe *reader in medical statistics*<sup>1</sup>, Frank Windmeijer *professor of econometrics*<sup>3</sup>, David Gunnell *professor of epidemiology*<sup>1</sup>

349 English General Practices  
1<sup>st</sup> Sept 2006 - 31 Oct 2011  
119,546 adult smokers

81,545 NRT  
6,741 bupropion  
31,260 varenicline

45.7% had used antidepressants

# Results and Conclusions

- No evidence that patients prescribed varenicline or bupropion had higher rates of fatal or non-fatal self harm or treated depression compared with those on prescribed nicotine replacement therapy
- “These findings should be reassuring for users and prescribers of smoking cessation medicines”

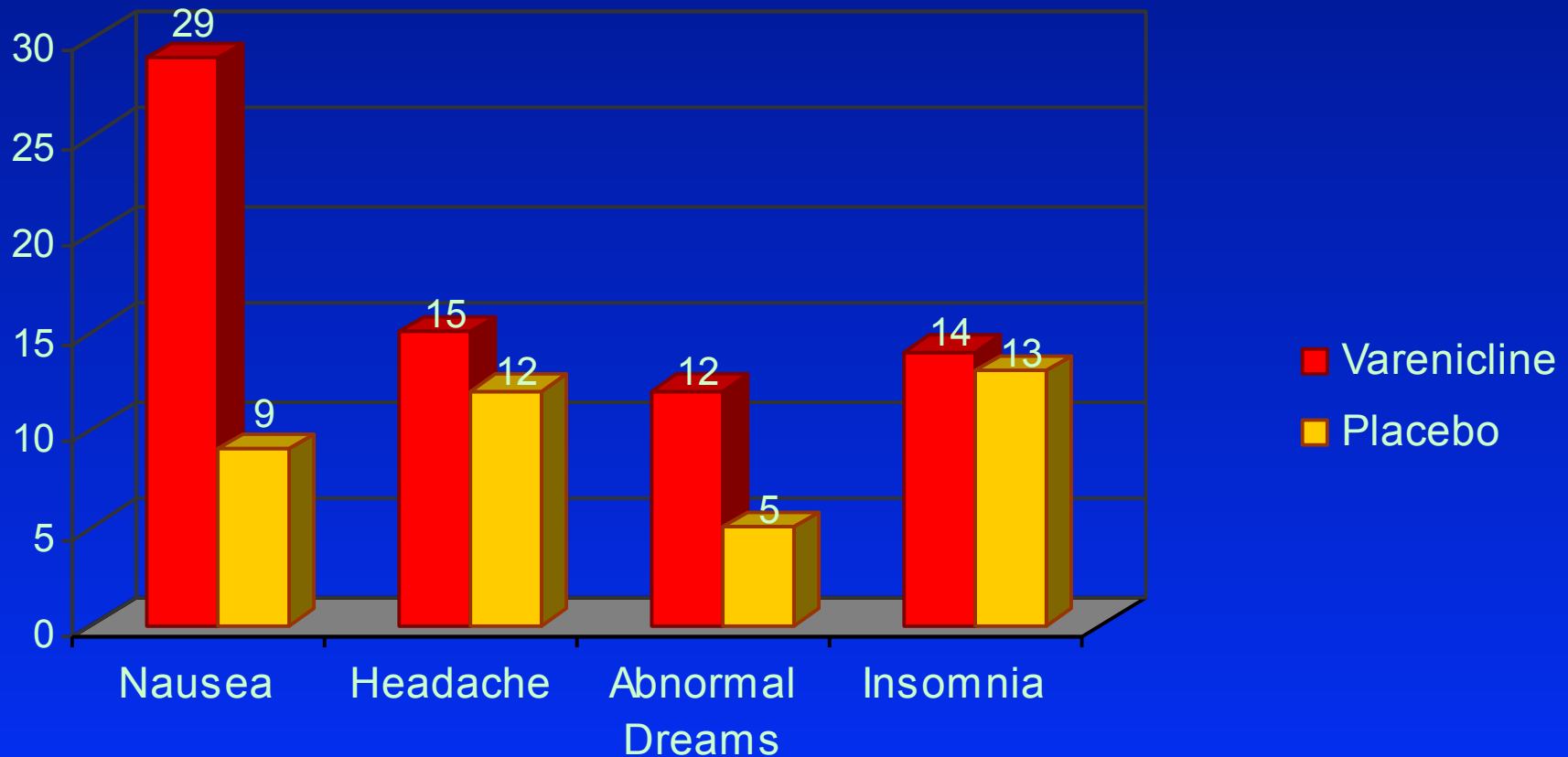
# Varenicline in Mental Health

- 50% of smokers have a history of depression
- Nicotine withdrawal is a powerful psychological syndrome
- Stopping smoking can exacerbate underlying psychiatric illness
- Varenicline has no established link to suicide, suicidality or depression
- No known drug interactions with varenicline so it can be used if stable on an antidepressant

## References:

1. Gunnell D, et al. Varenicline and suicidal behaviour: a cohort study based on data from the GPRD. BMJ 2009;; 339: b3805
2. CHAMPIX Summary of Product Characteristics

# Adverse events on varenicline compared with placebo



# What about nausea?

- Warn before prescribing
- Usually self limiting
- Take with food or water
- Can use anti-emetics ?prochlorperazine (Stemetil)
- Adjust dose

# Dose of varenicline

Quit date	Days 1 – 3:	0.5mg once daily
	Days 4 – 7:	0.5mg twice daily
	Days 8 – 14:	1mg twice daily
	Days 15+	1mg twice daily

- Standard course 12 weeks
- Licensed for up to 24 weeks use

# NHS Stop Smoking Services Guidance 2011/2012

“Since all motivated quitters should be given the optimum chance of success in any given quit attempt, nicotine replacement therapy (NRT), Champix (varenicline) and Zyban (bupropion) should all be made widely available in combination with intensive behavioural support as first-line treatments (where clinically appropriate)”

Reference:

1. LocalStop Smoking Services. Service delivery and monitoring guidance – 2011/12

# Numbers Needed to Treat (NNT) to Obtain 1 Long-Term Quitter?

- Brief advice (<5 mins) = 40<sup>(1)</sup>
- Adding medication to behavioural support.....
- NRT = 23<sup>(2)</sup>
- Bupropion = 20<sup>(2)</sup>
- Varenicline = 10<sup>(2)</sup>



# Numbers Needed to Treat (NNT) to Prevent a Premature Death?

- Brief advice (<5 mins) = 80
- Adding medication to behavioural support.....
- NRT = 46
- Bupropion = 40
- Varenicline = 20