

Breaking the Chains of Nicotine Dependence - A Breakthrough Approach

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Smoking Cessation in 2001

- Smoking contributes to all 4 leading causes of death in industrialised countries.
- The benefits of smoking cessation are undisputed and start from day 1 of quitting
- Nicotine is a highly addictive substance and this addiction remains the greatest stumbling block to smoking cessation
- There are a wide range of therapies now available with one year efficacy at 30% or more

The bad news

Smoking in China

- Overall prevalence rates
 - 61% men and 7% women
 - highest in government staff, peasants and workers
- Predicted mortality
 - 50 million young persons alive today will be eventually killed by tobacco use

Smoking in China

- Mortality from smoking similar to Western countries
 - 50% of smokers die of a smoking related death
 - 25% of smokers die between 35 yo - 69 yo
- Smoking related deaths in China
 - 45% die from COPD, 15% from lung cancer, 8% CHD

Smoking = nicotine addiction

- Medically recognised addiction (DSM-IV, ICD-10)
- Nicotine addiction = heroin or cocaine addiction
- Neurobiological condition where nicotine effects both reward and withdrawal pathways in the brain

Nicotine is highly addictive

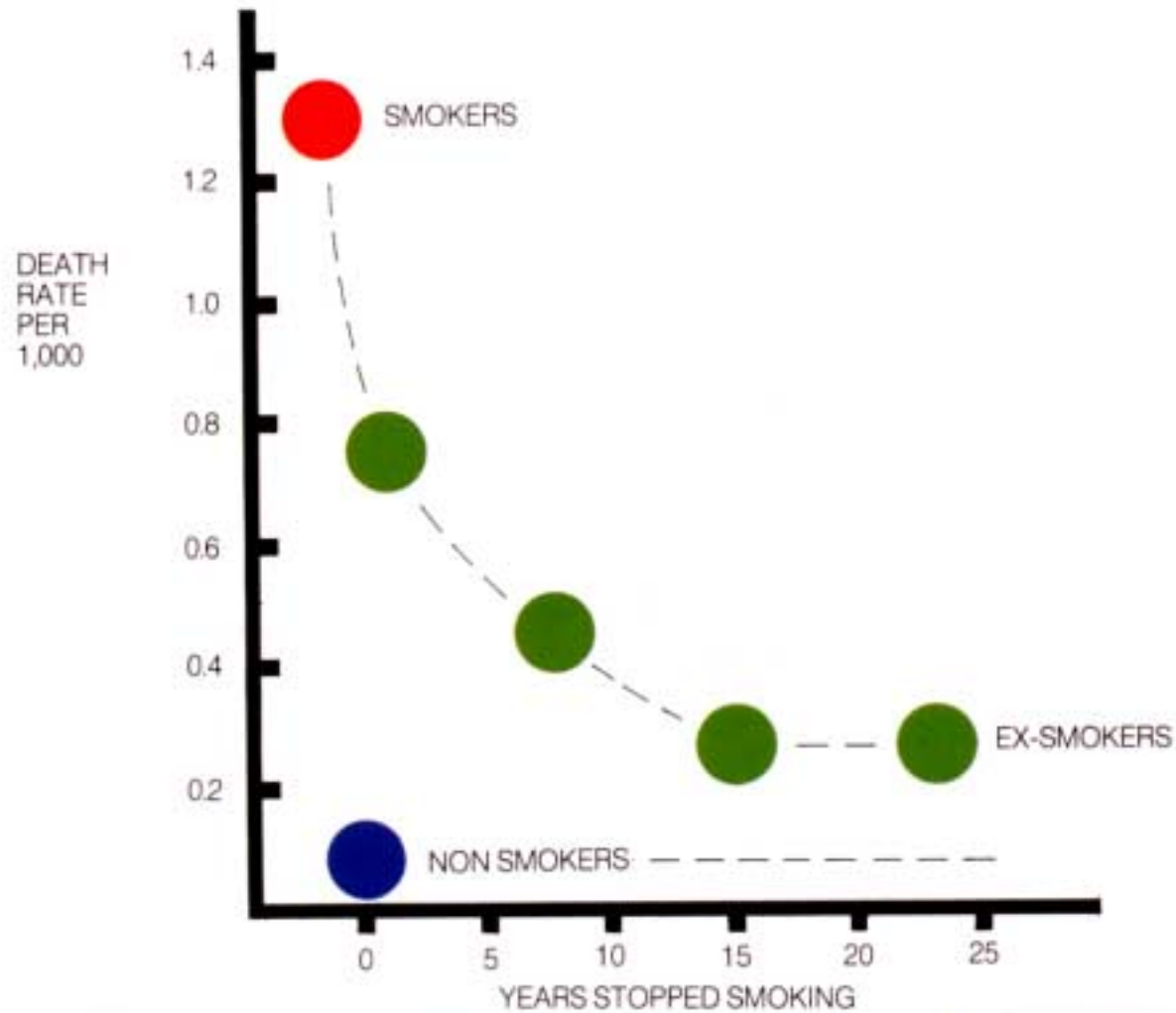
- Mildly pleasant stimulation initially, but it follows the behaviour very quickly (fast positive reinforcement)
- Leads to tolerance, so that higher doses are needed for the same effect
- Leads to brain changes so that smokers feel discomfort when nicotine level is low (negative reinforcement)
- Smoking relieves this discomfort and creates an illusion of positive effects.

Quitting smoking is the **ONLY**
way to reduce tobacco-related
deaths in the medium term and is
the best thing that smokers can
do to improve their own
individual health risks

The good news

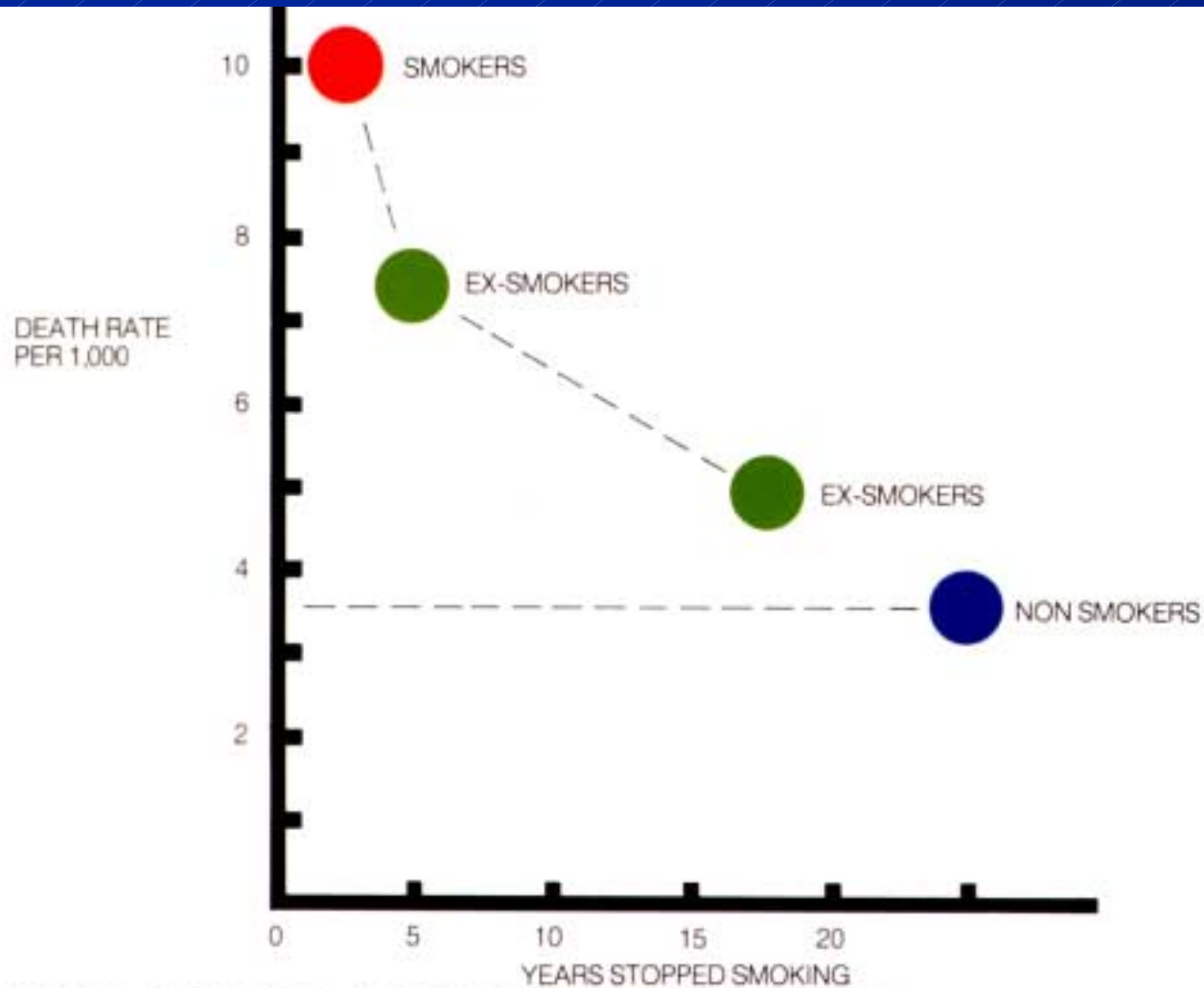
Smoking- benefits of quitting

- Smoking cessation at 50 yo reduces the risk of dying within 15 years by 50%
- Effects on health after last cigarette
 - 20 mins = BP and HR drop to normal
 - 48hrs = no nicotine left in body
 - 5 years = risk of heart attack falls by half
 - 10 years = risk of heart attack same as never smoked
 - 10 years = risk of lung cancer falls by half
 - 20 years = risk of lung cancer similar to never smoked



FALL IN DEATH RATE FROM LUNG CANCER AFTER STOPPING SMOKING

DOLL, R. and PETO, R, BRITISH MEDICAL JOURNAL, 1979. Photograph 8



FALL IN DEATH RISK FROM CORONARY HEART DISEASE AFTER STOPPING SMOKING

U.S. PUBLIC HEALTH SERVICE
THE HEALTH CONSEQUENCES OF SMOKING, 1979. Photograph 4

Nicotine withdrawal syndrome

- *Main relevant subjective symptoms:*
 - Mood changes: Irritable/aggressive, depressed, restless. Lasts on average under 4 weeks. Can be severe.
 - Urges to smoke: Frequency usually declines within weeks, but bouts of strong urges can occur long-term. Similar to or greater than cravings for other addictive drugs.
 - Increased hunger: Usually until the new body weight stabilises, over several months. The average weight gain is about 5kg over the first year.

Most smokers quit by themselves

But there are now a range of effective aids which can make the task of quitting easier

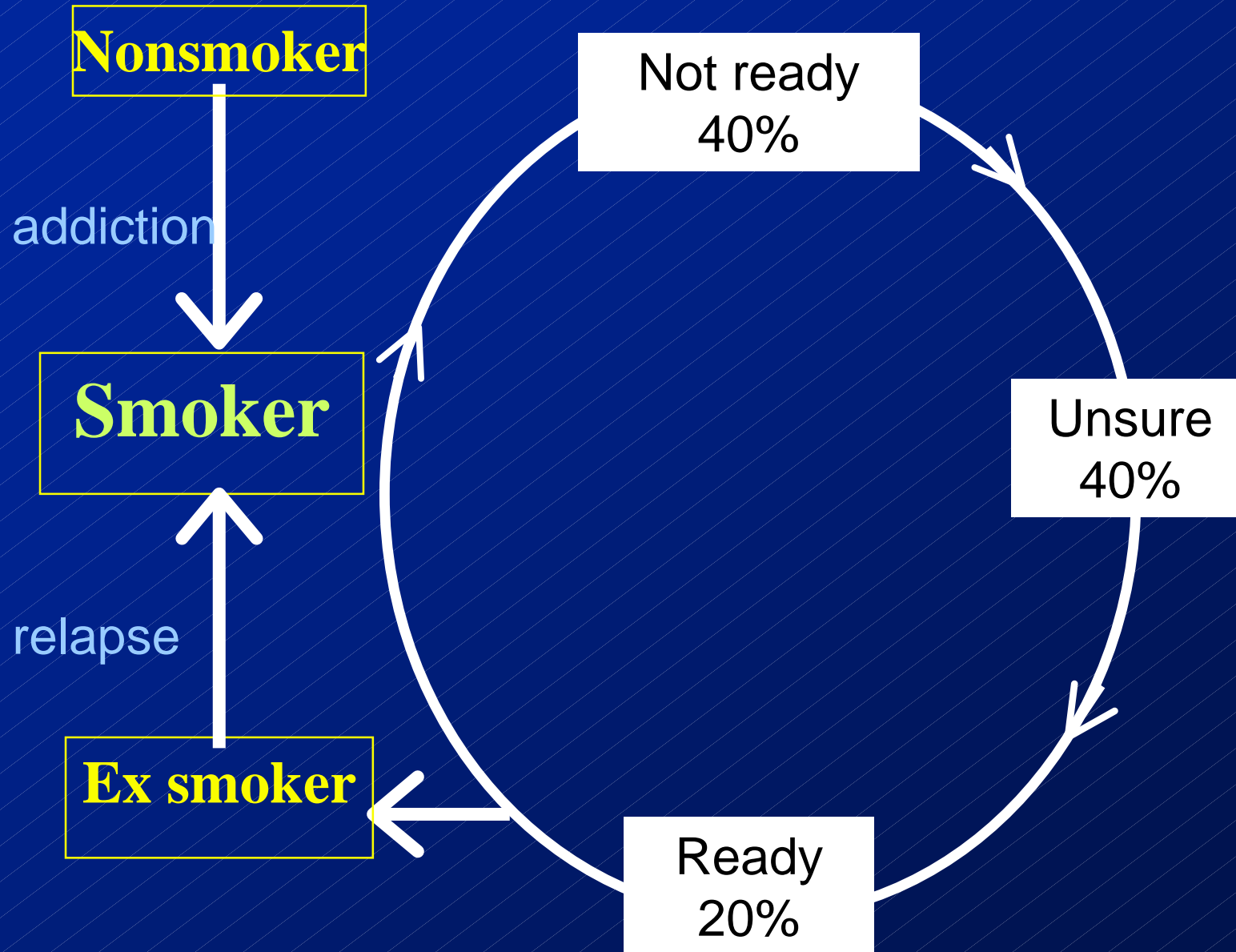
The 5 A's of smoking cessation

- **Ask** - about current and past tobacco use
- **Assess** - motivation to quit, lung function
- **Advise** - rewards of smoking cessation (hazards of smoking) - personalise
- **Assist** - prepare to quit, set date, discuss treatment options and behavioural aspects
- **Arrange** - referral to smoking cessation therapist, pharmacotherapy

Ask

- Identify the smokers and those they expose (spouses, children, work-mates)
- Obtain a smoking history (pack years, quit attempts, reasons for failing)
- Update smoking status with each visit/admission

Stages of Readiness to Quit



Assess

- Determine the smokers readiness to quit
(not ready, unsure, ready)
- Establish the presence of any end organ damage (CHD, PVD, cerebrovascular disease)
- Check lung function by spirometry

Advise

- Provide clear supportive messages
- Emphasise both the benefits and pitfalls of continued smoking
- Personalise the message for each smoker

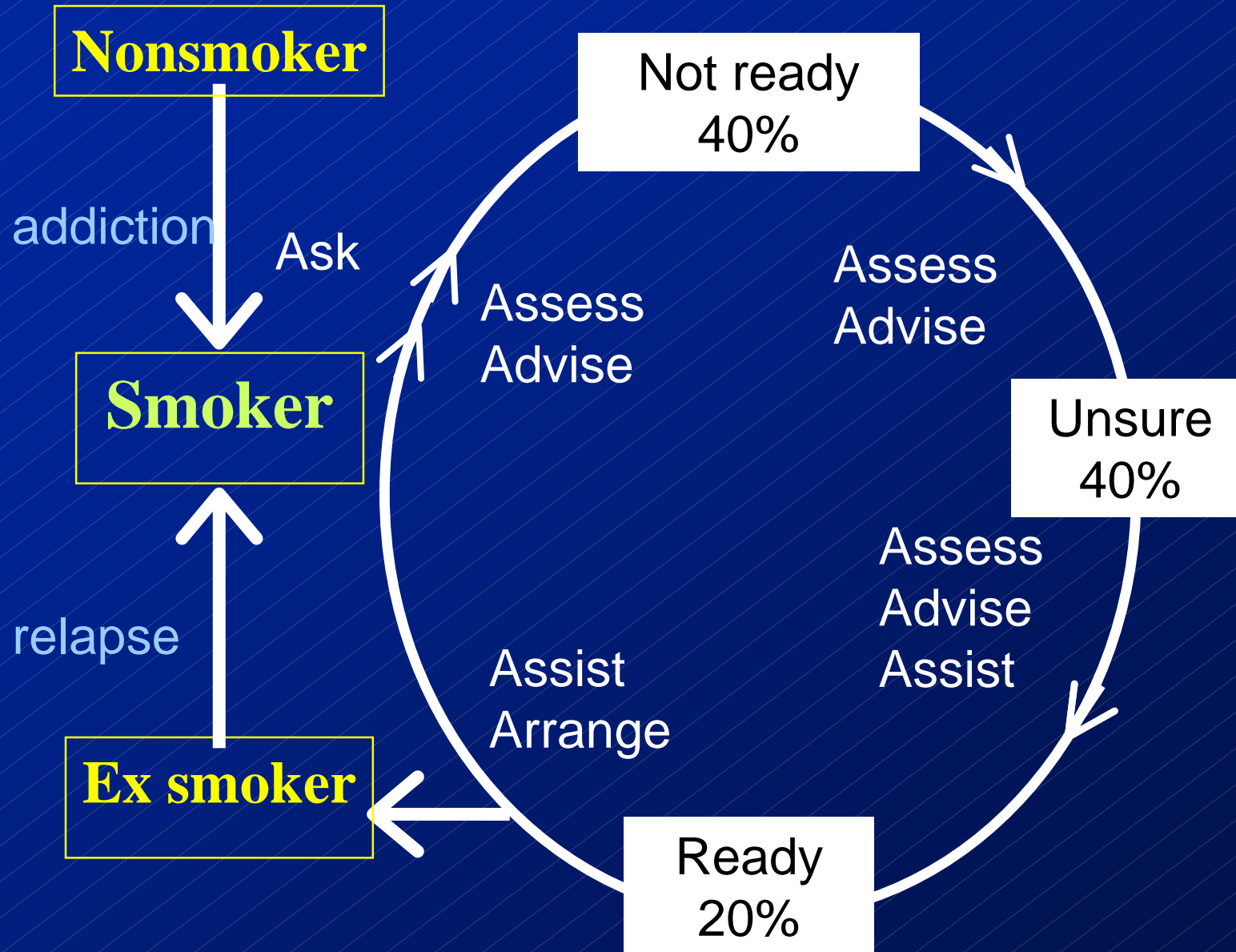
Assist

- Encourage cutting down
- Explore barriers to quitting
- Discuss treatment options
- Plan a quit date

Arrange

- Referral to smoking cessation therapist or group
- Prescribe nicotine replacement therapy and/or bupropion (Zyban)
- Regular follow up to advise on pharmacotherapy (doses, side-effects)

Stages of Readiness to Quit



Aids to Smoking Cessation

- NON PHARMACOLOGICAL
 - Self-help materials
 - Simple Advice from a Health Professional
 - Behavioral counseling
 - Hypnosis
 - Acupuncture

Aids to Smoking Cessation

- PHARMACOLOGICAL
 - Nicotine Replacement Therapy
 - Bupropion
 - Clonidine
 - Other antidepressants
 - Mecamylamine
 - Lobeline
 - Herbal Preparations

Advice from Doctors and Nurses

- 31 trials (more than 26,000 smokers)
- Primary care, hospital wards, outpatient clinics, industrial clinics
- SIMPLE ADVICE INCREASES THE QUIT RATE
- Odds Ratio 1.69 (95% CI: 1.45 to 1.98)
- More intensive advice slightly more effective
- Main effect is to motivate a quit attempt

Behavioral Counseling

- Specialised smoking cessation clinics or counselors
- BOTH ONE-TO-ONE TREATMENT OR GROUP THERAPY WORK
- Counseling more effective than brief advice
- No difference between different psychological approaches (except aversion therapy which is ineffective)
- No difference between effectiveness of group therapy or individual counseling
- Groups are probably more cost effective

Other Non-pharmacological Therapies

- Hypnosis
 - no more effective than other behavioral interventions
- Acupuncture
 - any short-term effects are likely to be placebo related

Relative effectiveness of therapies

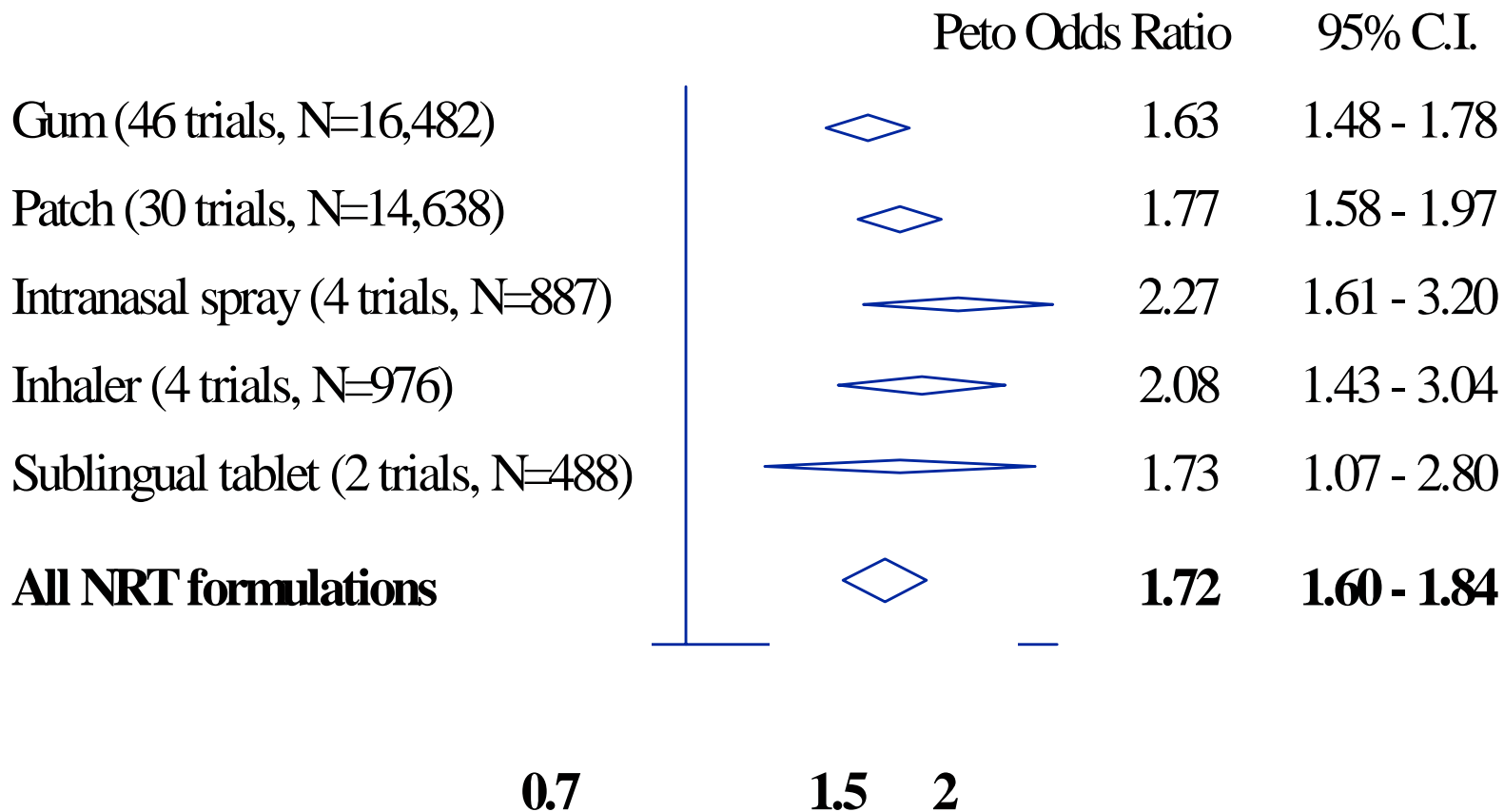
“Therapy”	Odds ratio
Self help materials	1.0 - 1.5
Simple advise by health workers	1.4 - 1.9
Behavioural counselling/groups	1.6 - 2.7
NRT	1.6 – 2.8
Bupropion	1.9 – 3.9

Acupuncture in 16 RCT showed no benefit over “sham” acupuncture

Nicotine replacement therapy (NRT)

- NRT is recommended for up to 3 months
- NRT has a great safety record
- Doubles success rates of behavioural therapies
- Gum/patch/inhalar/nasal spray/lozenges
- Similar efficacy for all types
- Customised to smokers preference

Meta-analysis of nicotine replacement therapy trials



Efficacy of NRT

- All of the trials of NRT have included some form of (at least) brief advice to smokers
- Most effective if targeted to smokers motivated to quit and with high levels of nicotine dependency
- Little evidence about role of NRT amongst smokers with low dependency (<10-15/day)

Nicotine replacement therapy:caution

- Should not be given for unstable cardiac disease
 - poorly controlled hypertension
 - unstable angina
- Close monitoring when given with bupropion

Nicotine replacement therapy: summary

- Clinical trials show NRT is effective, safe and very well tolerated.
- Greatest efficacy when doses are optimised to maintain serum nicotine levels
- Administered using one or a combination of preparations tailored to suit the smoker

Bupropion (Zyban)

Atypical antidepressant that inhibits neuronal uptake of noradrenaline and dopamine

DA

Mesolimbic Dopamine System

Nucleus Accumbens

Prefrontal Cortex

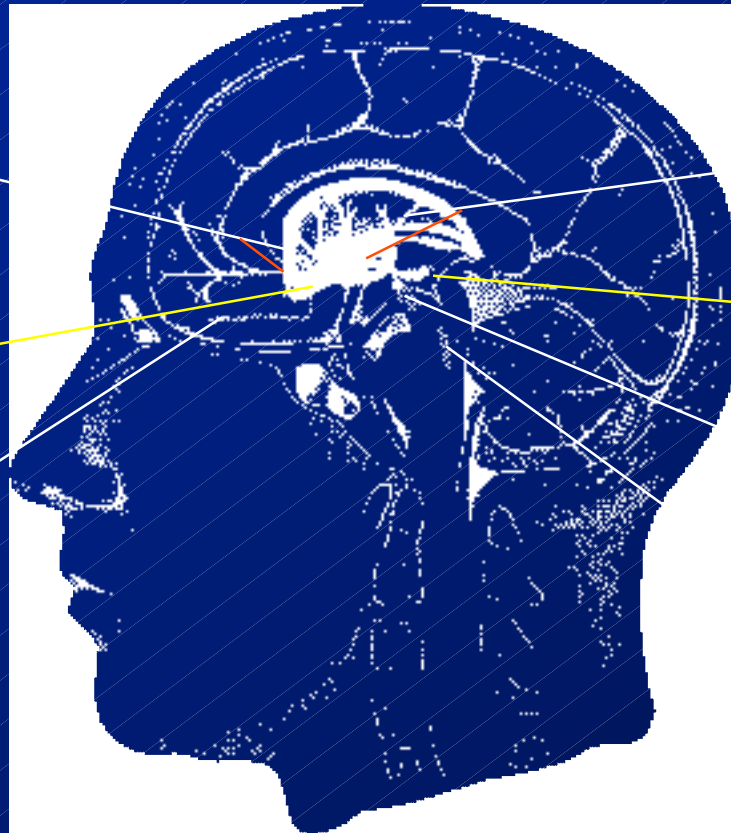
Nigrostriatal Projection

Ventral Tegmental Area

Substantia Nigra

Locus Ceruleus

NE

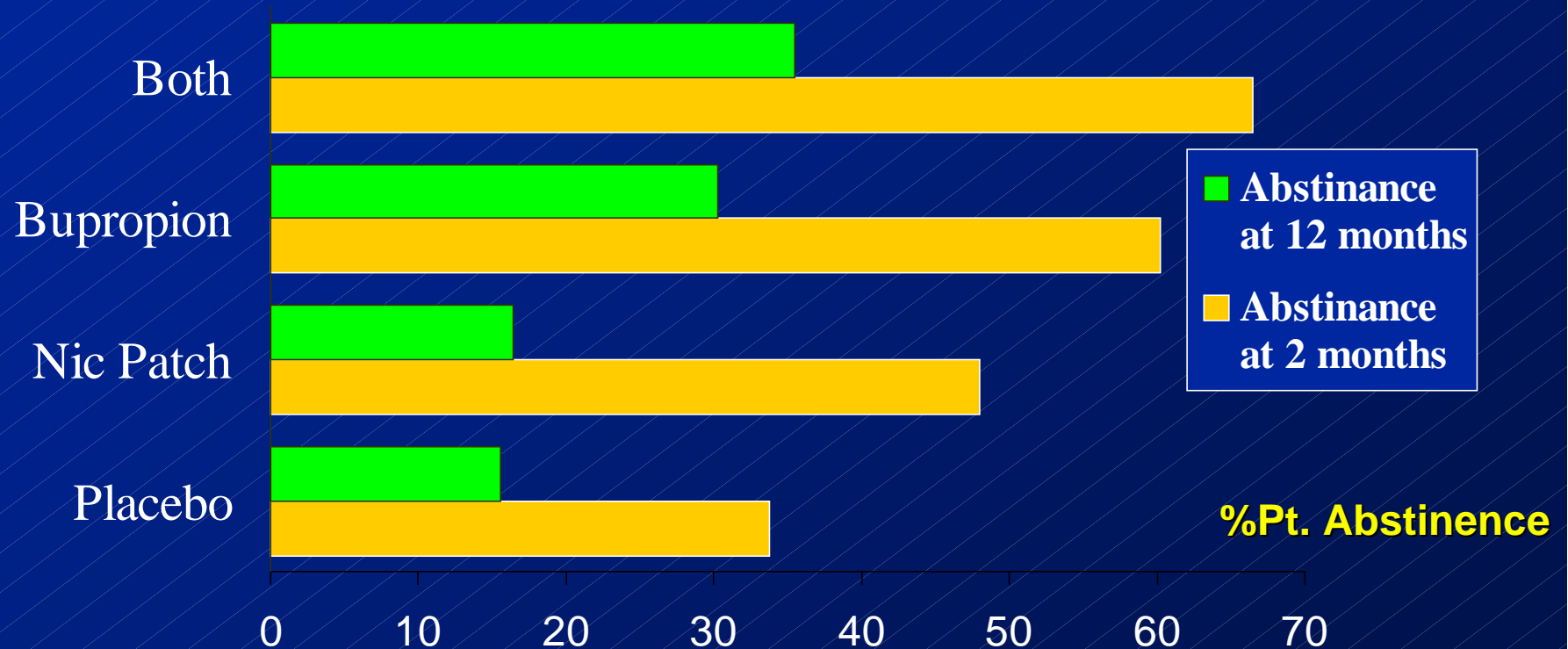


Bupropion

- Slow release form licensed in USA, parts of Europe, New Zealand
- EFFECTIVE WHEN OFFERED WITH BEHAVIOURAL SUPPORT (OR 2.73, CI: 1.90-3.94)
- More effective than nicotine patch alone
- Its effectiveness can be further increased by addition of Nicotine Replacement Therapy

Bupropion & Nicotine Patch Study

- End of Treatment and One Year Abstinence n = 893



Jorenby et al New Eng J Med 1999 340; 685-91

Dosage and Administration

- Patients should set a **quit date** within the first 2 weeks of treatment with Zyban, generally in the second week
- Start Zyban ≥ 7 days before target quit date
 - 150 mg every morning for first 3 days
 - For most patients, titrate to recommended and maximum dose of 300 mg/day (150 mg b.i.d., ≥ 8 hours between doses)
- Doses above 300 mg/day should not be used
- Continue Zyban 150 mg b.i.d. for **at least 7 weeks**
- Continue treatment for certain individuals (eg. **relapse**)

Side effects of Bupropion

- Dry mouth (10% vs. 5% placebo)
- Insomnia (35% vs. 20% placebo)
 - delay p.m. dose > 4 hours before going to bed
- Seizures (1/1000 anticipated... however)
 - NONE in any of the smoking cessation trials

Bupropion and seizures

- Bupropion does not cause seizures
- Bupropion lowers the seizure threshold comparable to other antidepressants
- Although the reported seizure rate on bupropion is 1/1000 clinical trials involving over 3,000 patients reported no seizures.

Bupropion: contraindications

- Seizures or past history of seizures
- During pregnancy or breast feeding
- History of
 - bulimia or anorexia nervosa
 - severe head injury
- Concomitant use with anti-depressants

Bupropion: caution

- Patients with severe liver disease or cirrhosis
- Concomitant use with drugs metabolised by
 - CYP 2B6 eg cyclophosphamide
 - CYP 2D6 eg flecainide, metoprolol, anti-
psychotics

Bupropion: Summary

- Clinical trials show Bupropion is currently the most effective agent for smoking cessation
- Bupropion is well tolerated, non-addictive and has no withdrawal symptoms
- Screening patients for contraindications is necessary for safe prescribing

Zyban - GlaxoSmithKline New Zealand



Smoking Cessation: NZ perspective

- Adopted US guidelines
- NRT is sold direct to consumer
- NRT now subsidized by the government
- Smoking cessation products are advertised on TV
- Various organizations are funding the
 - training of cessation therapist
 - running of cessation clinics
- Government subsidy on zyban under review

My opinion

- Is Bupropion safe?
- NRT vs Bupropion?
- Is direct to consumer (DTC) marketing appropriate for smoking cessation drugs?
- Can the GP do this on their own?
- Who should pay?

Smoking Cessation in 2001: Summary

- Smokers are coming under increasing pressure
 - restrictions on where smoking is allowed
 - greater taxes on cigarettes
 - adverse effects of passive smoking
- There is now a range of effective pharmacological preparations and non-pharmacological approaches for smoking cessation.



Thank you